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Borderline personality disorder

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Correspondence to: Prof Klaus Lieb, Department of Psychiatry and Psychotherapy, University Medical Center Mainz, 55131 Mainz, Germany klaus.lieb@unimedizin-mainz. Borderline personality disorder (BPD) is a mental disorder with a high burden on patients, family members, and health-care systems. The condition was previously regarded as untreatable, but progress in understanding and management has resulted in earlier diagnosis and better treatment outcomes. A coherent syndrome of BPD typically onsets during adolescence (after age 12 years). BPD is often preceded by or co-develops with symptoms of internalising disorders (depression and anxiety), externalising disorders (conduct problems, hyperactivity, and substance use), or both. BPD is associated with various poor outcomes, including low occupational and educational attainment, lack of long-term relationships, increased partner conflict, sexual risk-taking, low levels of social support, low life satisfaction, and increased service use. Psychotherapy is the main treatment for BPD; drug treatment is only indicated for comorbid conditions that require medication, or during a crisis if psychosocial interventions are insufficient. Awareness of BPD by non-specialists, as well as specialists, is key to appropriate early intervention.

Introduction

Borderline personality disorder (BPD) is a severe mental disorder that is characterised by a pervasive pattern of emotion dysregulation, inconsistent identity, and disturbed interpersonal function. The term was coined in 1938 by Adolf Stern, who viewed the disorder as existing at the border between psychosis and neurosis, and BPD was first classified as a mental disorder in the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition in 1980.¹² Since then, much progress has been made in understanding and managing the condition. This Seminar reviews what has been discovered to date, and specifically addresses developments in early diagnosis, epidemiology, aetiology, and treatment options that have arisen since the publication of earlier reviews in this journal.³⁴

Search strategy and selection criteria

We searched PubMed, PsycINFO, and Embase for any entries relating to borderline personality disorder for the period of Jan 1, 2015, to Aug 31, 2020. In each database, we used a combined search strategy of controlled vocabulary (including broader and narrower terms) and text words (including truncation wildcards and synonyms). We used specifiers, optimised for each database, relating to the topics of epidemiology, pathology, genetics, diagnosis, and therapy. In order to select randomised controlled trials, systematic reviews, and meta-analyses, we repeated these searches using appropriate filters of the respective databases but without restriction of the search period. The Cochrane Library (including CDSR, CENTRAL, and Cochrane Clinical Answers) was also searched using controlled vocabulary at this stage. We also considered relevant evidence-based practice guidelines (ie, the British National Institute for Health and Care Excellence [NICE] guidelines and the Australian National Health and Medical Research Council [NHMRC] guidelines). There were no restrictions on language or publication format. We focused on publications of the past 5 years but also included pivotal older publications if appropriate.

Clinical presentation

Case 1

A 17-year-old female patient was admitted to the emergency room after attempting suicide by overdose. Although her act had been impulsive, prompted by a break-up with her boyfriend, she had been hoarding the medication beforehand "in case she could no longer stand it". Her home life was difficult, filled with violence, but she did not want to talk about that experience during admission. She reported having struggled with suicidal thoughts, self-harm, and significant bouts of loneliness since the age of 12 years. The self-harm acts had started as superficial razor blade cuts to her forearms but recently had progressed to inflicting deeper cuts in her genital area; and when this was ineffective in relieving her intermittent unbearable feelings of distress, she would resort to alcohol. She expressed little concern for her physical wellbeing, hatred of her body and person, and recurrent episodes of unreality and out-of-body experiences. She rejected counselling because she felt that she did not deserve to be well. A few days after admission, her boyfriend indicated that he wanted to reconcile, after which she reported that everything was fine again and requested discharge.

Case 2

A 54-year-old female high school teacher presented at a psychiatric outpatient clinic. Although she was coping adequately at the professional level, she had been experiencing extreme strain, mostly due to the retirement of her current therapist. Over many years of therapy, some aspects in her life had improved—she was not self-harming anymore and was managing to live on her own—but she felt infinitely lonely and empty. She was unable to cultivate social relationships and needed all her energy for her job. Life felt like "a quiet sea of desperation". Somatic problems such as joint pain, headaches, and migraines had increased, which she believed was due to the large number of medications she was taking.

Case 3

A 36-year-old male patient came looking for therapeutic support after his wife told him that she wanted to separate and take their daughter with her because she was "fed up with his escapades". He reported feeling intense rage and hatred towards her, and worried that he might seriously harm her. Due to instances of domestic violence, social services had already become involved, and he feared that he might not see his daughter again. When asked, he revealed that the marriage had always been filled with screaming arguments; most physical violence had been directed against objects, but there had been two incidents where he had assaulted his wife when she threatened to leave him. After these outbursts, he felt deeply ashamed and miserable. His last employment was with a security company, which he terminated after believing that his colleagues "were out to get him". He acknowledged that this had been a typical pattern for him in his work life.

The spectrum of BPD

While these three case vignettes may seem to have little in common at first glance, they are prototypical for the wide spectrum of BPD and its variability over the life span. While the first prototype, due to its dangerousness and expressiveness, attracts substantially more professional attention and urgency to intervene, the level of suffering is not necessarily less in the quieter, more hidden second variant, presenting with typical borderline features associated with later life. In the third case, there can be little difficulty in recognising the impact of BPD-driven behaviour on the immediate social environment.

For all its heterogeneity, BPD incorporates three characteristic domains: intense and rapidly changing emotions, including impulsivity; unstable and inconsistent identity; and problems in interpersonal relations. Most, if not all, acute dysfunctional behaviours, such as repetitive self-harm, chronic suicidal thoughts, aggressive outbursts, or sensitivity to rejection, can be understood either as immediate consequences or as a coping strategy of one of these three pathological domains.^{3,5}

Diagnosis and differential diagnosis

In the past decade, there have been substantial changes in the psychiatric nosology of personality disorders. At present, four classification systems are provided for BPD: the traditional criteria for diagnoses in section II of the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5), an alternative model in section III of the DSM-5, and the models presented in the International Classification of Diseases, 10th and 11th revisions (ICD-10 and ICD-11).⁶⁷

Table 1 compares the diagnostic criteria provided in DSM-5 section II against those in ICD-10 and ICD-11 (those in ICD-11 are not yet official). DSM-5 maintains the traditional diagnosis of using nine polythetic criteria, of which at least five must be met to receive a diagnosis of BPD. The ICD-11 mirrors DSM-5 section III, requiring that

the clinician must first determine the severity level of general personality function, and then has the option (but is not required) to further describe personality dysfunction on five dimensional domains (negative affectivity, detachment, dissociality, disinhibition, anankastia). There is also the possiblity to use the borderline pattern descriptor, which closely matches the DSM-5 criteria of section II.

In section III of the DSM-5, the alternative model for personality disorders (AMPD) allows for the diagnosis of BPD in a three-step process. The clinician first determines the presence and severity of the patient's general level of personality function (criterion A: moderate or greater impairment in personality functioning, manifested by difficulties in two or more areas of identity, self-direction, empathy, and intimacy); then determines the severity on five broad pathological trait domains; and can then diagnose BPD if the patient shows high levels in four or more of the seven pathological personality domains: emotional lability, anxiousness, separation insecurity, depressivity, impulsivity, risk-taking, and hostility (at least one of these must be impulsivity, risk-taking, or hostility).

There is currently much research activity in developing and evaluating measures for assessing the new AMPD and ICD-11 formulations of personality pathology, although the usefulness of these measures in clinical settings for diagnosis, treatment planning, and outcomes assessment still has to be established. All three of the newer classification approaches allow for the diagnosis of BPD in adolescents.

Of the three case vignettes presented above, the severity might be estimated as severe in the first and the third cases and moderate in the second; these ratings are also reflected by how many DSM-5 section II criteria were fulfilled (ie, eight criteria in the first, four in the second, and seven in the third). As also described in the three cases, other typical manifestations of the borderline pattern can be seen: view of the self as inadequate, bad, guilty, disgusting, and contemptible; an experience of the self as profoundly different and isolated from other people; a painful sense of alienation and pervasive loneliness; proneness to rejection hypersensitivity, often leading to problems in establishing and maintaining consistent and appropriate levels of trust in interpersonal relationships; and frequent misinterpretation of social signals.

The most frequently used semi-structured interviews and self-report questionnaires are listed and described in the appendix.

Comorbid mental disorders are common in BPD patients and need to be concurrently assessed. Findings of a US-based nationwide epidemiological study suggest that individuals with BPD have lifetime rates of 84.5% for anxiety disorders, 82.7% for mood disorders, and 78.2% for substance use disorders. Decifically, high rates of comorbid post-traumatic stress disorder (PTSD; 30.2%), attention deficit hyperactivity disorder (ADHD, 33.7%), bipolar disorder I (21.6%), and bipolar disorder II (37.7%) have been reported.

See Online for appendix

	DSM-5, section II, 301.83 (borderline personality disorder) ⁶	ICD-10, F60.31 (emotionally unstable personality disorder, borderline type) $^{\rm 8}$	ICD-11, 6D11.5 (prominent personality traits or patterns, borderline pattern) ⁷	
Overview	General criteria for personality disorders plus five or more of the below nine criteria	General criteria for personality disorder plus three or more of the five symptoms for emotionally unstable personality disorder, impulsive type (F60.30)*, plus two or more of the below criteria	General criteria for personality disorders plus borderline pattern (pervasive pattern of instability of interpersonal relationships, self-image, affects, and marked impulsivity) as indicated by many of the below criteria	
Fear of abandonment	Frantic efforts to avoid real or imagined abandonment	Excessive efforts to avoid abandonment	Frantic efforts to avoid real or imagined abandonment	
Unstable relationships	A pattern of unstable and intense interpersonal relationships characterised by alternating between the extremes of idealisation and devaluation	Liability to become involved in intense and unstable relationships, often leading to emotional crisis	A pattern of unstable and intense interpersonal relationships	
Unstable self-image	Markedly and persistently unstable self-image or sense of self (identity disturbance)	Disturbances in and uncertainty about self-image, aims, and internal preferences (including sexual)	Identity disturbance, manifested in markedly and persistently unstable self-image or sense of self	
Impulsivity	Impulsivity in at least two areas that are potentially self-damaging (eg, spending, sex, substance abuse, reckless driving, or binge eating)		A tendency to act rashly in states of high negative affect, leading to potentially self-damaging behaviours	
Self-harm	Recurrent suicidal behaviour, gestures or threats, or self-mutilating behaviour	Recurrent threats or acts of self-harm	Recurrent episodes of self-harm	
Mood instability	Affective instability due to a marked reactivity of mood (eg, intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and only rarely lasting for more than a few days)		Emotional instability due to marked reactivity of mood	
Feelings of emptiness	A chronic feeling of emptiness	Chronic feelings of emptiness	Chronic feelings of emptiness	
Inappropriate anger	Inappropriate, intense anger or difficulty controlling anger (eg, frequent displays of temper, constant anger, or recurrent physical fights)		Inappropriate, intense anger or difficulty controlling anger	
Dissociation/transient paranoid ideation	Transient, stress-related paranoid ideation or severe dissociative symptoms (does not include suicidal or self-mutilating behaviour)		Transient dissociative symptoms or psychotic-like features in situations of high affective arousal	

*For ICD-10 emotionally unstable personality disorder, impulsive type (F60.30), general criteria for a personality disorder must be met plus three or more out of the five following diagnostic criteria, one of which must be (2): (1) marked tendency to act unexpectedly and without consideration of the consequences, (2) marked tendency to quarrelsome behaviour and to conflicts with others, especially when impulsive acts are thwarted or criticised, (3) liability to outbursts of anger or violence, with inability to control the resulting behavioural explosions, (4) difficulty in maintaining any course of action that offers no immediate reward, (5) unstable or capricious mood.

Table 1: DSM-5, ICD-10 and ICD-11 diagnostic criteria for borderline personality disorder

However, overlaps with other disorders often simply reflect shared features (eg, impulsivity is a key marker of BPD and also a key symptom in manic and hypomanic states), although not necessarily shared genetic factors. Depressive symptoms can either be related to the core borderline syndrome or to major depressive disorder (MDD) but offer important clues to differential diagnosis. *Specifically, the depressive symptoms of BPD are volatile, stress-reactive, and mostly remit in parallel with improvements of BPD, whereas MDD-related depressive symptoms are more stable, and may require antidepressant somatic treatment. *IS

The risk of comorbid somatic disorders is also substantially elevated in people with BPD, including increased risks of infectious diseases (eg, HIV, hepatitis), endocrine and metabolic diseases, and cardiovascular and respiratory diseases. The 2 year mortality rate in people with BPD is double that in the general population (odds ratio [OR] 2·30, 95% CI 2·06–2·54), ^{16.17} resulting in a lifetime loss of 6–7 years compared with the general population. ¹⁶ Individuals with BPD should be encouraged and supported to engage in somatic prevention programmes and regular medical check-ups and to seek appropriate treatment for somatic conditions. ¹⁸

Epidemiology and aetiology

Prospective community cohort studies show that although individual differences in maladaptive personality traits such as impulsivity, emotional reactivity, and negative affectivity can be observed in children, they do not crystalise into a coherent syndrome of BPD until the transition to adolescence (after age 12 years), marking adolescence as a sensitive period for the onset of BPD. 19.20 The validity and reliability of BPD diagnosis in adolescents are indicated by evidence supporting a coherent syndrome of BPD in this age group, strong psychometric properties of adolescent BPD assessment tools, marked separation of course and outcome from other disorders, efficacy of disorder-specific treatment, and similarity to adult BPD with respect to prevalence, stability, and risk factors (panel 1).19,24-32 On the basis of the proliferation of research on the developmental aspects of BPD over the past two decades, the prevention of and early intervention in BPD is now recognised as a public health priority.14 Two recent reviews suggest community point prevalences of BPD in adults of 0.7-1.2% and 0.7-2.7%, respectively.^{33,34} Grant and colleagues estimated a lifetime prevalence for BPD of 5.9%.35 However, Trull and colleagues revised the

original scoring algorithms to require that significant distress or impairment be present for each BPD criterion, resulting in a revised prevalence of 2.7%.36 Community prevalence appears to be slightly increased in adolescents (age 12-17 years, 2-3%) and decreased in adults older than 40 years (0.4%). 29,37-39 Prevalence is substantially increased in clinical settings, with studies reporting rates among inpatients and outpatients for adults of 22.4% and 11.8%, respectively, and for adolescents of 11% and up to 35.6%, respectively.34,40 Prevalence studies report higher rates of BPD in women than in men in clinical settings, and mixed results for a gender difference in community settings.33 Most prevalence studies of BPD do not show systematic racial or ethnic differences; however, studies are few, warranting urgent future research attention.34

BPD symptoms first appear in early adolescence, peak in late adolescence and early adulthood, and decline thereafter. In adolescents, the disorder shows relatively low diagnostic stability (14-40%) when diagnosis is categorically defined, but strong rank-order stability (ie, the degree to which the relative ordering of individuals on a given trait is maintained over time; 0.53-0.73), mirroring stability rates in adults. 41,42 BPD is often preceded by or co-develops with symptoms of both internalising disorders (depression and anxiety) and externalising disorders (conduct problems, hyperactivity, and substance use). It is associated with a range of poor outcomes, including low occupational and educational attainment, lack of long-term romantic relationships and friendships, increased partner conflict, sexual risktaking, low levels of social support, low life satisfaction, increased service use, and high levels of internalising, externalising, and psychotic spectrum disorders, even when psychiatric comorbidity is accounted for.¹⁹ Nevertheless, BPD is not as intractable as previously thought. A recent meta-analytic review that synthesised the findings of 11 naturalistic and post-treatment followup studies in adults suggested a mean diagnostic remission rate of 60% (95% CI 49-71).43 Groups with a younger mean age at baseline were more likely to show high remission rates at follow-up, underscoring the importance of early diagnosis and intervention. Studies showed considerable psychosocial functional improvement over time; however, this outcome varied substantially between individuals, suggesting a subgroup of individuals who experienced persistent psychosocial impairment over time. Depending on the specific sample, prospective suicide rates for BPD range from 2% to 6%, which is lower than the rate of 8-10% reported in early studies.44,45 Long-term functional outcomes appeared to be poorer in women than in men, which might be a function of increased severity due to histories of abuse and the impact of gender roles over time.43 Although less studied, predictors of recovery include stable functioning as a spouse or partner and as a parent.46 Together, these findings highlight the

Panel 1: New developments in state-of-the-art assessment and management of borderline personality disorder*

Assessment

- Diagnosis in early adolescence and identification of individuals at risk
- Disclosure and explanation of diagnosis to patient, including psychoeducation about the disorder and treatment options (if patient agrees, also to relevant other people)
- Life-span perspective, including all ages from early adolescence to senior years
- Focus on co-occurring mental disorders

Long-term management

- First-line treatment should be psychosocial interventions
- Clinical staging: adequate, good enough support depending on clinical severity
- Early intervention and indicated prevention for individuals at risk
- Stepped care: reliable, consistent clinical pathways
- · Informed decision making
- Individual crisis plans to prevent and manage crises, and to avoid iatrogenic effects of emergency service use
- Coordination of services across providers
- Involvement of relevant other people
- Focus on psychosocial functioning and life outside therapy
- Educate significant others (ie, relatives, partners, or other people with close relationships, professional caregivers; parents or caregivers of children and young people) about helpful ways of interacting (empathy, non-judgmental attitude, and avoidance of high expressed emotions, blame or overprotection)
- If there are dependent children, provide parenting skills and review children's wellbeing

Common elements of psychotherapies

- Clear setting, transparent treatment framework
- $\bullet \quad \text{Informed focus on borderline personality disorder, individually consented targets} \\$
- Active, supportive, and challenging therapist
- · Validating atmosphere
- Balance of acceptance and change
- Continuous attention to affect
- Teaching skills, providing competence, self-efficacy
- Continuous focus on motivation and collaboration
- Crisis plans

*According to 16,18,21-23

importance of incorporating a strong focus on generalising therapeutic effects to the patient's social and vocational environment, further underscored by recent findings incorporating the perspectives on recovery of those with lived experience.⁴⁷

Theories of the development of BPD delineate how certain factors can interfere with the normal development of emotion regulation, social cognition, or development of adaptive identity function, following a diathesis-stress framework. 48,49 Prospective studies support these theories by showing that environmental risk factors such as harsh or insensitive parenting, emotional neglect, physical or sexual maltreatment, and victimisation by bullying have reciprocal or mediational associations with concurrent or subsequent disruptions in executive functioning, mentalising (ie, the capacity to identify mental states in

oneself and others), emotion regulation, and selfrepresentation.50-56 These studies also show that BPD features seen in children share causal features with adult BPD, and that inherited and environmental risk factors make independent and interactive contributions to BPD aetiology.52 A study of the structure of genetic and environmental risk factors for BPD postulates that most of the genetic effects on individual borderline criteria derive from one highly heritable (55%) general BPD factor, with environmental effects observable in the two specific factors of affective and interpersonal dimensions.57 The first genome-wide association study found a genetic overlap between BPD and bipolar disorder, major depression, and schizophrenia.58 Nonspecificity in causation complicates the picture for delineating a disorder-specific aetiological pathway, and it is more likely that a common aetiology across disorders accounts for the development of BPD. The possibility of epigenetic effects should be evaluated against the background of findings confirming the link between childhood trauma (eg, physical and sexual abuse and emotional neglect) and BPD, keeping in mind possible comorbidity between BPD and other disorders.

Pathophysiology

There is evidence that emotion dysregulation is a central mechanism closely linked to other BPD symptoms. Patients report intense, long-lasting, and strongly fluctuating emotions, which are often experienced as overwhelming and unpredictable.59 Emotional distress and dissociation can hinder executive functioning and goal-directed behaviour,60,61 and when struggling with strong emotions, many patients impulsively turn to maladaptive coping strategies such as self-harm or substance abuse.5 By contrast with ADHD, in which impulsivity is a general factor, impulsive behaviour in BPD is closely linked to high levels of emotional distress. 62,63 A high percentage of patients experience stress-related dissociative experiences such as derealisation, depersonalisation, analgesia, and numbing.64 Reducing aversive tension and terminating dissociation are the main motives for self-harm in BPD.65 Non-suicidal self-injury as a particular form of self-harming dysfunctional behaviour has been associated with stressrelated reduction in pain perception.66

Patients experience instability and disturbances in identity. Empirical research has shown that the subjective lack of coherence along with an objective incoherence in thoughts, feelings, and behaviour distinguishes BPD from other mental disorders. ⁶⁷ Self-esteem is usually extremely negative and highly unstable under daily life conditions. ^{68,69} Experimental research suggests that those affected have a very negative body perception, as well as problems in trusting their own judgment. ^{70,71} The accuracy in self-reflection fluctuates strongly and is affected by current mood, which can contribute to the above-mentioned

problems in long-term self-directed and goal-directed behaviour.

Alterations in social information processing and social cognition might underlie some of the marked interpersonal problems. Patients with BPD not only show hypersensitivity to negative social cues but also have pronounced difficulties in detecting and processing positive social signals and in remembering positive events.61,72-74 This characteristic might contribute to exaggerated rejection sensitivity and difficulties in discriminating between social inclusion and exclusion.74-76 Mistrust and problems in coaxing are central clinical features that have been observed in experimental trust games.77,78 Interestingly, the application of oxytocin, a substance that usually increases trust and cooperation, seems to have opposite effects in people with BPD.79 Other studies point to alterations in processing of socioemotional information, including difficulties in evaluating facial emotions, a negativity bias, and impairments in mentalising.72,80,81 These alterations could interact with adverse attachment experiences, manifesting themselves in interpersonal problems such as a strong ambitendency between an intense need for closeness versus a shamerelated fear of rejection.

Research into the neurobiology of BPD is rapidly growing, following advances in methods and data analytic techniques. Although the precise neurobiological underpinnings remain elusive, disturbances in a corticolimbic circuitry involving the amygdala, hippocampus, insula, anterior cingulate, orbitofrontal cortex, and medial prefrontal cortex seem to contribute to problems in emotion regulation, interpersonal disturbances, and inconsistent identity.82,83 Amygdala hyper-reactivity to threat-related stimuli has been linked to increased emotional responsiveness across several different diagnoses. A recent meta-analysis confirmed that amygdala hyperreactivity is more pronounced in BPD patients than in both healthy and depressed populations.84 Studies found a normalisation of stress levels and amygdala activity through painful stimuli, which may contribute to nonsuicidal self-injury in BPD.85,86 Altered activity of temporolimbic areas (eg, the temporoparietal junction) and default mode network regions has been implicated in alterations in identity and social cognition, such as difficulties in processing social feedback.87,88 Although the idea of diminished prefrontal control of limbic areas makes intuitive sense and might explain the clinically observed impulse control problems in BPD, this model faces several methodological challenges, such as a lack of specificity for disorders or brain regions.89 Deficient dorsolateral and orbitofrontal control might be mainly present in subgroups of patients who show anger-related aggression, but it has not consistently been replicated in relation to impulse control problems. 90,91 Psychotherapy seems to have an effect on emotion regulation by altering neural activation and connectivity.92 After dialectical behaviour therapy (DBT; discussed below), amygdala and prefrontal activity were found to change substantially when patients were instructed to apply different emotion regulation strategies (reappraisal, distraction, and pain).^{93–96}

In terms of neurochemical systems, the hypothalamicpituitary-adrenal axis and serotonergic system have traditionally been a research focus. For the hypothalamicpituitary-adrenal axis, two recent meta-analyses showed conflicting findings, with one indicating significantly lower cortisol level for people with BPD compared with controls, while the other pointed to elevated continuous cortisol output and blunted cortisol following psychosocial challenges. 97,98 Mixed evidence has been found for the serotonergic system (eg, the serotonin transporter gene), and more research is needed to understand its role in BPD.99 Magnetic resonance spectroscopy findings from the anterior cingulate cortex point to a role of increased glutamate neurotransmission in impulsivity, and reduced GABA neurotransmission in aggression.¹⁰⁰ Other studies suggest an involvement of the endogenous opioid system in non-suicidal selfinjury.¹⁰¹ Interpretation of findings is often complicated by methodological aspects such as small sample sizes, absence of control groups, psychotropic medication, trauma history, and comorbidities.

Acute management

Clinical management in acute crisis situations depends to a large extent on whether the patient is already undergoing adequate psychotherapeutic treatment. If no previous treatment has been received, the following steps are recommended (see also panel 2).

The first priority must be addressing crisis behaviours, such as suicide attempts, serious attacks on other people, life-threatening self-injury, frequent unplanned hospital admissions, or dangerous highrisk behaviours. Interventions should be based on a functional behavioural analysis that provides an overview of the exact problem behaviour, the triggering parameters and the most important maintenance parameters, and vulnerability factors such as sleep problems, alcohol or drug misuse, or serious social problems. The therapeutic relationship should be characterised by appreciation of the patient's subjective needs, the need for urgent change in dysfunctional behaviour, and a clear orientation towards problemsolving. Most patients with BPD will benefit from being taught skills to reduce high levels of distress. 102 Under these conditions, inpatient treatment can be rather short, while not creating feelings of rejection and abandonment.

Second, diagnostic procedures, psychoeducation, and education about evidence-based treatment options should be initiated as soon as possible. For most patients with BPD, receiving a diagnosis comes as a relief, as it is reassuring to learn that one's behaviour and experiences can be understood in terms of a coherent syndrome of inter-related symptoms and

Panel 2: Acute management of borderline personality disorder

Acute psychosocial interventions

- Differentiate between suicide attempts, non-suicidal self-injury, and high-risk behaviours
- Offer crisis intervention on an outpatient basis whenever possible
- If inpatient crisis intervention is indicated, keep it as short as possible, and start planning for discharge on the first inpatient day
- Establish if there are dependent children; if yes, ensure they are being properly cared for as long as the patient is not able to do so because of acute crisis
- Crisis intervention should be based on a problem analysis, and it should mainly focus
 on concrete problem-solving
- Create strategies to prevent or handle future crises
- Do not initiate inpatient crisis intervention based on behaviour that is not lifethreatening (eg, self-injury without suicide intent)

Use of medication in acute management

- Use sedative antihistamines or low-potency antipsychotics rather than hypnotics in the acute management of agitation or sleep problems
- Consider concurrent alcohol or illicit drug use in the planning of potential drug treatment
- Inform all involved service providers about medication changes
- Do not use medications that are unsafe in case of overdose (eg, tricyclic antidepressants) or have high addictive potential (eg, benzodiazepines)
- Do not use medication in place of psychosocial interventions
- Do not initiate drug treatment without disclosing potential effects and adverse effects to the patient (informed decision making)

behaviours. Avoiding the diagnosis perpetuates stigma associated with the disorder. Diagnosis is also a prerequisite for providing the patient with psychoeducation.

Third, the patient should be motivated to accept treatment options and helped to find therapeutic support in the short term. Options vary greatly between different countries and mental health systems. Ideally, all individuals with a BPD diagnosis should be provided with a specific psychosocial treatment programme consisting of weekly therapy for at least 6 months by a trained psychiatrist or psychotherapist. If an evidencebased option is not available, psychoeducation, self-help manuals, and outpatient crisis intervention by an experienced mental health professional should be provided. Inpatient stays for crisis intervention should be kept as short as possible. Last, if possible, binding agreements about further treatment should be made between the person affected by BPD and their therapist or therapeutic team, and these agreements should be reviewed after the crisis intervention. If psychotropic drugs have been prescribed, the recommendations made in panel 2 should be followed. 18,21,103 In the case of children and young people, parents should be included in all aspects of decision making, and special attention should be paid to the effects of decisions on young people's education and social lives, which should be maintained as a priority.

Psychosocial interventions

Evidence-based guidelines agree that psychotherapy is the main treatment for BPD. ^{18,21} The latest Cochrane review of psychotherapies for BPD identified as many as 75 relevant randomised controlled trials (RCTs). ¹⁰⁴ Compared with unspecific control conditions, moderate clinically relevant effects have been observed for several parameters: overall BPD severity (standardised mean difference –0.52, 95% CI –0.70 to –0.33), self-harm (–0.32, –0.49 to –0.14), suicidality (–0.34, –0.57 to –0.11), and psychosocial functioning (–0.45,–0.68 to –0.22). For the risk of engaging in suicidal behaviour, a risk ratio of 0.27 (95% CI 0.11–0.67) was reported. ¹⁰⁴

Regarding specific psychological treatments, table 2 describes the most widely used therapies. 104-106 The two most intensively studied treatments have been DBT and mentalisation-based treatment (MBT). Effects on several BPD symptom domains, as well as on depression and psychosocial functioning, have been found for both. 104-106

These two treatments have not yet been compared head-to-head in randomised studies, but data from a naturalistic comparison study suggest that although both show similar outcomes after 12 months, DBT might lead to a steeper decline in self-harm and emotion dysregulation compared with MBT. $^{\tiny 107}$

Transference-focused psychotherapy and schemafocused therapy are also established treatments but have

	Characteristics	Main treatment effects ¹⁰⁴	Evidence level
DBT	BPD core problem: emotional dysregulation stemming from biological vulnerability and invalidating environments; provokes impulsivity and interpersonal turbulences. Modification of behaviour by using strategies of acceptance and change. Techniques: formative and informative exposure to avoided emotions; acquisition of skills to help regulate emotions and find ways to functional behaviour (distress tolerance, emotion regulation, interpersonal effectiveness, mindfulness). Stage-oriented standard outpatient individual therapy, combined with group skills training, telephone coaching, and team consultation, 6 months to 2 years (stage 1: focus on crisis-generating behaviour; stage 2: focus on severe co-occurring mental disorders and severe problems in emotion regulation; stage 3: focus on borderlinetypical long-term patterns such as loneliness, alienation). General strategies: psychoeducation, improvement of functional emotion processing, skills acquisition (stress tolerance, emotion regulation, interpersonal effectiveness, mindfulness), structuring the social environment, telephone support, and team consultation.	DBT vs treatment as usual (N=12, n=720): for BPD severity, SMD -0.60, 95% CI -1.05 to -0.14, N=3, n=149; for self-harm, SMD -0.28, 95% CI -0.48 to -0.07, N=7, n=376; for psychosocial functioning* SMD -0.36, 95% CI -0.69 to -0.03, N=6, n=225; DBT vs waiting list (N=3, n=182): for BPD severity, SMD -0.71, 95% CI -1.08 to -0.33, N=2, n=117; for psychosocial functioning* SMD -0.73, 95% CI -1.11 to -0.36, N=2, n=117	++ for DBT vs treatment as usual; ++ for DBT vs waiting list
МВТ	BPD core problem: developmental trauma in attachment context, resulting in difficulties in mentalisation capacity—ie, capacity to identify mental states in oneself and others (beliefs, wishes, feelings, thoughts). Modification by enhancing mentalising capacity to enhance social learning and epistemic trust. Structured outpatient or day hospital treatment integrating individual and group psychotherapy (12–18 months). Initial phase: psychoeducation; collaborative formulation; formation of treatment alliance; safety planning; identification of mentalising vulnerabilities and contexts that trigger ineffective mentalising. Treatment phase: stabilisation of high-risk behaviours; empathic validation to enhance affect identification and contextualisation; interpersonal focus to explore alternative perspectives; linking learned therapy experience to daily social and personal life; increasing self-reflective and other-reflective capacity when under stress; re-establishing mentalising when ineffective mentalising is triggered; trauma focus, personal narrative work. Final phase: ending treatment; specific focus on BPD processes—eg, fears of abandonment; generalisation of stable mentalising and learned social understanding; mentalising skills to maintain self-care.	MBT vs treatment as usual (N=5, n=552): for self-harm, RR 0-62, 95% CI 0-49-0-80, N=3, n=252; for suicidality, RR 0-10; 95% CI 0-04-0-30, N=3, N=218	++
SFT	BPD core problem: dysfunctional life schemas, thinking patterns control life (eg, detached protector, punitive parent, abandoned child, angry child). Modification by making schemas conscious. Techniques: behavioural, cognitive, imagery, and experiential techniques with a focus on the therapeutic relationship, life outside therapy, and past experiences. 36 months of individual therapy.	SFT vs TFP (N=1, n=86): for BPD severity†, MD‡ -4·95, 95% CI -9·59 to -0·31	+
TFP	BPD core problem: split of positive and negative images of oneself and others following early-experienced aggression results in unintegrated, undifferentiated effects and representations, with difficulty in achieving a realistic, ambivalent view of self and others. Aim: integration of representations of self and others, more balanced and coherent ways of thinking about oneself and others. Modification by systematic exploration and interpretation of transference into an integrated, coherent whole as enacted in the here-and-now by use of techniques such as interpretation, clarification, and confrontation. Individual therapy, twice weekly (12 to 18 months).	TFP vs treatment as usual (N=1, n=104): for BPD severity, MD§ -0·84, 95% CI -1·42 to -0·26	+
STEPPS	BPD core problem: focus on BPD in the context of social and family systems; dysfunctional ways of dealing with emotions lead to distress with and for the social system of families, caregivers, and friends. Aim: enhance problem-solving and emotion regulation skills. Modification by acquisition of behaviour skills and introduction of a shared language to communicate clearly. Techniques: psychoeducation, integration of different stakeholders, skills acquisition. 20-week supplement to ongoing individual therapy of any kind, once weekly in a workshop-like atmosphere, one session of psychoeducation and skills training for peers.	STEPPS vs treatment as usual (N=3, n=393): for BPD severity, SMD -0-39, 95% CI -0-63 to -0-15, N=3, n=273; for psychosocial functioning, MD¶ -7-00, 95% CI -11-43 to -2-57, N=1, n=124	**
estimate based FFP=transferen	behaviour therapy. BPD=borderline personality disorder. SMD=standardised mean difference. N=number of effect est on pooled findings of several RCTs. MBT=mentalisation-based treatment. RR=risk ratio. SFT=schema-focused therapy ce-focused psychotherapy. STEPPS=systems training for emotional predictability and problem solving. RCT=randomis heffect estimates for other outcomes. †Favouring SFT. ‡BPDSI-IV scale. SNumber of BPD criteria. ¶Global Assessment	. MD=mean difference. +=effect estimate based sed controlled trial. *Negative sign indicating be	on a single RCT.

been studied less extensively. Group interventions have been studied as well. Their value has been affirmed by a dismantling study that systematically investigated the effects of the DBT individual and skills training groups and observed better and faster treatment effects when group treatment was involved. ¹⁰⁸ Beneficial effects have also been found for DBT skills training alone. ^{104,109–111} Two group interventions, both intended as add-ons to ongoing individual therapies of either orientation, are supported by evidence from at least two RCTs: systems training of emotional predictability and problem solving (STEPPS), and the less prominent Emotion Regulation Group Treatment, which is based on DBT and acceptance and commitment therapy and showed a reduction of BPD severity and interpersonal problems. ^{104,112,113}

For individuals with comorbid mental disorders, the non-BPD disorder should be managed concurrently with BPD-specific treatment, with the patient's care preferably being coordinated by the BPD therapist.18 Treatment of the comorbid condition should only be prioritised over BPD treatment if the comorbid disorder prevents effective psychotherapy (eg, severe substance use), or if it leads to a life-threatening situation (eg, an eating disorder resulting in a critically low body-mass index).18 Distinct, co-occurring mood episodes must be treated adequately; for example, by prescribing adequate antidepressant medication, following the appropriate clinical guidelines. Adaptations of DBT have been developed for individuals with both BPD and complex PTSD (a severe form of PTSD related to violence interpersonal during childhood adolescence), and these approaches resulted in more pronounced treatment effects relating to both disorders compared with control treatments, standard DBT, or standard cognitive processing therapy. 114-117

DBT has also shown beneficial effects in the treatment of patients with BPD and comorbid substance use disorders. There was an elevated risk of dropping out of treatment, but patients with personality disorders who completed treatment were found to respond similarly to substance use treatment as did those without.¹¹⁸ The evidence for specialist BPD treatments adapted specifically for substance use disorders is still limited.¹¹⁸⁻¹²²

Several BPD-specific treatments have also been evaluated in adolescents, including DBT, STEPPS adapted for adolescents, MBT, and cognitive-analytic therapy. Significant effects of these treatments were observed in a meta-analysis of six RCTs with regard to BPD pathology (Hedge's g –0·89, 95% CI –1·75 to –0·02) and with regard to the frequency of self-injury (odds ratio 0·34, 95% CI 0·16–0·74). 32

Since specialist treatments are resource-intensive and access for most patients is limited, clinical staging models should be used to guide the way to appropriate support depending on clinical severity, rather than aiming for the best-of-all-treatment. 22,123-125 These models suggest that individuals who appear to be in

the early stages of the disorder could benefit from family psychoeducation or training in problem-solving skills provided by generalists, whereas those with persistent BPD pathology and substantial psychosocial impairment are better served by receiving intensive specialist psychosocial treatment. 126 Identifying and treating the disorder in its early stages probably decreases the risk of progressing functional impairment as well as therapeutic nihilism due to discouraging experiences with treatment.14,41 If these recommendations are followed, consistent care pathways are made accessible. This is important, as inconsistent treatment histories in individuals with BPD are associated with suicide attempts and even completed suicides, whereas stepped care models can reduce the need for severe crisis interventions. 127-129 Generalist treatment frameworks have been developed that integrate the common elements of effective specialist treatments (see also panel 1) in order to facilitate access to appropriate treatments for less severely affected individuals; these treatments can be provided by mental health professionals who are not specialists in personality disorders. 22,130 The finding that family members of individuals with BPD have elevated levels of grief and burden in general, compared with relatives of individuals with other severe mental disorders, points to the need for effective interventions and family support.¹³¹ Beneficial effects have been observed for different group interventions for family members. 132-134 Further recommendations for long-term treatment are provided in panel 3.

Pharmacotherapy

Given the weakness of supporting evidence for pharmacotherapy, drugs that used to be routinely prescribed according to individually prevalent BPD symptom domains, such as impulsivity, emotional instability, or cognitive-perceptual symptoms, are no longer recommended (see panel 3).^{18,21,135–137}

In particular, the evidence for selective serotonin reuptake inhibitors (SSRIs) is insufficient to support their use in the treatment of BPD pathology, unless a comorbidity is present that requires antidepressant use. 138-140 With regard to second-generation antipsychotics, the most intensively studied in BPD is olanzapine, for which findings indicate limited benefits and substantial adverse effects, including metabolic changes and an increase in self-harming behaviours. 135,139 There is not enough information to justify the widespread use of quetiapine, which is among the most frequently prescribed drugs in BPD. Only one relevant RCT has been published, which compared the effect of low versus moderate doses on the severity of BPD symptoms; other studies have been initiated but not published. 136,141,142 Finally, a methodologically strong, large-scale pragmatic trial of lamotrigine showed no treatment effects after 1 year of treatment, challenging the use of this substance

Panel 3: Long-term treatment of borderline personality disorder (BPD)

Psychosocial and somatic management

- Start treatment as early as possible to avoid chronic progression of the disorder
- If needed, provide education on BPD and training in adequate interpersonal behaviour to significant others
- Inform individuals with BPD about different specialist treatments
- Define the treatment frame (eg, therapist availability between sessions, contacts during crisis, behaviour that could interfere with therapy); prepare patient from the start for the end of therapy
- · Establish psychosocial care if no specialist treatment is available
- Change treatment or therapist if there is no progress within 6 months
- Focus on psychosocial functioning outside therapy
- Encourage patients to get involved in somatic prevention programmes and yearly check-ups of somatic diseases, or to seek help in case of somatic problems
- Promote problem-solving skills, build on the individual's strengths, and encourage self-efficacy experiences
- Do not withhold group skills training from the patient if no state-of-the-art dialectical behaviour therapy is available
- Do not excessively focus on suicidality, but treat it the same way as you would in any individual without BPD

Pharmacological management

- Use medication only as an add-on to psychosocial interventions
- If drug treatment for comorbid conditions is planned, define target symptoms and a time period, and ensure that treatment effects are assessed and side-effects are monitored
- Review drug prescriptions on a regular basis
- Include patient in discussion when deciding about medication use
- Do not use medication as the sole therapy approach
- Do not continue drug treatment that is not effective
- Do not combine several drugs (ie, avoid polypharmacy)
- Do not use drugs that are unsafe in case of overdose (eg, tricyclic antidepressants) or have high addictive potential (eg, benzodiazepines)

in BPD. ¹⁴³ For other mood stabilisers, the evidence is still weak and inconclusive. ^{136,137,142} In summary, medications currently cannot be recommended for the treatment of BPD. Instead, drug treatment is only indicated if a comorbid condition that requires medication is present (eg, severe depression or severe sleep disturbances), or if in case of crisis psychosocial interventions are not available or sufficiently effective. ^{18,21,144}

Controversies and outstanding research questions

Although much progress has been made in the understanding and management of BPD, several controversies and as-yet unanswered research questions exist.

At present, there is no integrated aetiological model for the development of BPD that is empirically supported. Little is known about the genetic and neurobiological causes of postulated emotional hypersensitivity and the related transactional mechanisms with adverse childhood experience. Likewise, there is a dearth of robust evidence of early warning signals, or of the effects of early intervention programmes that might prevent the development and improve the course of the disorder during adolescence and early adulthood. Although the validity and reliability of BPD diagnoses have been established in adolescence, members of this age group are often not assessed and screened for BPD in routine clinical practice. On the other end of the age spectrum, little is known about the course of BPD and the change of symptoms in later stages of life.

Because specialist treatment is not affordable for most patients, particularly for people from lower socioeconomic status or minority ethnic groups, more research into clinical staging and stage-oriented graded treatment concepts is needed, with short, self-help oriented programmes for mild cases and more complex and lengthier therapies provided by experts for more severe cases. With regard to established treatment programmes, more replication studies are needed that are done with higher methodological rigour and that can explore cultural differences and assessments of longterm outcomes, especially in adolescents and in male patients, as well as studies into the management of patients who do not respond to treatment.145 More treatment studies are also needed that focus on core BPD features, such as existential loneliness, severe alienation, and identity confusion, as well as on male patients with co-occurring antisocial features. In view of the substantially increased stress levels seen in family members of individuals with BPD, and the increased risk of developing BPD among children of mothers with the condition, targeted interventions for these groups need to be developed and evaluated.146

Finally, given the special status of BPD among other personality disorders and the large overlap of BPD symptoms with the new ICD-11 diagnosis of complex PTSD (including emotion dysregulation, negative self-concept, and interpersonal problems), further research is required on differential characteristics and the related consequences on treatment applications. Discussion may be warranted as to whether BPD should be categorised as its own diagnostic entity—eg, as a subcategory of disorders specifically associated with stress. These discussions must also consider alternative approaches generated through lived experience perspectives in finding non-stigmatising ways of talking about BPD, while still leveraging clinical and research advancement in this area.

Contributors

All authors contributed equally to the manuscript and were involved in the literature search, interpretation of studies, and writing. All authors approved the final version of the manuscript.

Declaration of interests

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References

- Stern A. Psychoanalytic investigation of and therapy in the border line group of neuroses. *Psychoanal Q* 1938; 7: 467–89.
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders DSM-III. Washington, DC: American Psychiatric Association, 1980.
- 3 Lieb K, Zanarini MC, Schmahl C, Linehan MM, Bohus M. Borderline personality disorder. *Lancet* 2004; 364: 453–61.
- 4 Leichsenring F, Leibing E, Kruse J, New AS, Leweke F. Borderline personality disorder. *Lancet* 2011; 377: 74–84.
- 5 Gunderson JG, Herpertz SC, Skodol AE, Torgersen S, Zanarini MC. Borderline personality disorder. Nat Rev Dis Primers 2018; 4: 18029.
- 6 American Psychiatric Association, American Psychiatric Association, DSM-5 Task Force. Diagnostic and statistical manual of mental disorders: DSM-5. Washington, DC: American Psychiatric Association. 2013.
- 7 WHO. ICD-11 for mortality and morbidity statistics (version 5/2021). https://icd.who.int/browse11/l-m/en (accessed Sept 3, 2021).
- 8 WHO. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. Geneva: World Health Organization, 2003.
- 9 Zimmermann J, Kerber A, Rek K, Hopwood CJ, Krueger RF. A Brief but Comprehensive Review of Research on the Alternative DSM-5 Model for Personality Disorders. Curr Psychiatry Rep 2019; 21: 02
- 10 Tomko RL, Trull TJ, Wood PK, Sher KJ. Characteristics of borderline personality disorder in a community sample: comorbidity, treatment utilization, and general functioning. I Pers Disord 2014: 28: 734–50.
- 11 Pagura J, Stein MB, Bolton JM, Cox BJ, Grant B, Sareen J. Comorbidity of borderline personality disorder and posttraumatic stress disorder in the U.S. population. J Psychiatr Res 2010; 44: 1190–98.
- 12 Fornaro M, Orsolini L, Marini S, et al. The prevalence and predictors of bipolar and borderline personality disorders comorbidity: Systematic review and meta-analysis. J Affect Disord 2016; 195: 105–18.
- 13 Philipsen A, Feige B, Hesslinger B, et al. Borderline typical symptoms in adult patients with attention deficit/hyperactivity disorder. Atten Defic Hyperact Disord 2009; 1: 11–18.
- 14 Chanen A, Sharp C, Hoffman P. Prevention and early intervention for borderline personality disorder: a novel public health priority. World Psychiatry 2017; 16: 215–16.
- Rao S, Heidari P, Broadbear JH. Developments in diagnosis and treatment of people with borderline personality disorder. Curr Opin Psychiatry 2020; 33: 441–46.
- Schneider F, Erhart M, Hewer W, Loeffler LA, Jacobi F. Mortality and medical comorbidity in the severely mentally ill—a German registry study. *Deutsches Aerzteblatt Online* 2019; published online June 10. https://doi.org/10.3238/arztebl.2019.0405.
- 17 Shah R, Zanarini MC. Comorbidity of borderline personality disorder: current status and future directions. Psychiatr Clin North Am 2018; 41: 583–93.
- 18 NHMRC. Clinical practice guideline for the management of borderline personality disorder. Canberra: National Health and Medical Research Council, 2013 http://www.nhmrc.gov.au/ guidelines/publications/mh25 (accessed Dec 1, 2016).
- 19 Wertz J, Caspi A, Ambler A, et al. Borderline symptoms at age 12 signal risk for poor outcomes during the transition to adulthood: findings from a genetically sensitive longitudinal cohort study. J Am Acad Child Adolesc Psychiatry 2020; 59: 1165–77.e2.
- 20 Sharp C, Vanwoerden S, Wall K. Adolescence as a sensitive period for the development of personality disorder. *Psychiatr Clin North Am* 2018; 41: 669–83.

- 21 NICE. 2018 surveillance of personality disorders (NICE guidelines CG77 and CG78). Surveillance report. 2018. https://www.nice.org. uk/guidance/cg78/evidence (accessed June 22, 2021).
- 22 Hutsebaut J, Willemsen E, Bachrach N, Van R. Improving access to and effectiveness of mental health care for personality disorders: the guideline-informed treatment for personality disorders (GIT-PD) initiative in the Netherlands. Borderline Personal Disord Emot Dysregul 2020; 7: 16.
- 23 Choi-Kain LW, Albert EB, Gunderson JG. Evidence-based treatments for borderline personality disorder: implementation, integration, and stepped care. Harv Rev Psychiatry 2016; 24: 342–56.
- 24 Sharp C, Steinberg L, Temple J, Newlin E. An 11-item measure to assess borderline traits in adolescents: refinement of the BPFSC using IRT. Pers Disord 2014; 5: 70–78.
- 25 Cohen P, Crawford TN, Johnson JG, Kasen S. The children in the community study of developmental course of personality disorder. *J Pers Disord* 2005; 19: 466–86.
- 26 Bornovalova MA, Hicks BM, Iacono WG, McGue M. Stability, change, and heritability of borderline personality disorder traits from adolescence to adulthood: a longitudinal twin study. *Dev Psychopathol* 2009; 21: 1335–53.
- 27 Michonski JD, Sharp C, Steinberg L, Zanarini MC. An item response theory analysis of the DSM-IV borderline personality disorder criteria in a population-based sample of 11- to 12-year-old children. Pers Disord 2013; 4: 15–22.
- 28 Beck E, Bo S, Jørgensen MS, et al. Mentalization-based treatment in groups for adolescents with borderline personality disorder: a randomized controlled trial. J Child Psychol Psychiatry 2020; 61: 594–604.
- 29 Zanarini MC, Horwood J, Wolke D, Waylen A, Fitzmaurice G, Grant BF. Prevalence of DSM-IV borderline personality disorder in two community samples: 6,330 English 11-year-olds and 34,653 American adults. J Pers Disord 2011; 25: 607–19.
- 30 Stepp SD, Lazarus SA, Byrd AL. A systematic review of risk factors prospectively associated with borderline personality disorder: Taking stock and moving forward. Pers Disord 2016; 7: 316–23.
- 31 Winsper C. Borderline personality disorder: course and outcomes across the lifespan. Curr Opin Psychol 2021; 37: 94–97.
- 32 Wong J, Bahji A, Khalid-Khan S. Psychotherapies for adolescents with subclinical and borderline personality disorder: a systematic review and meta-analysis. Can J Psychiatry 2020; 65: 5–15.
- 33 Eaton NR, Greene AL. Personality disorders: community prevalence and socio-demographic correlates. Curr Opin Psychol 2018; 21: 28–32
- 34 Ellison WD, Rosenstein LK, Morgan TA, Zimmerman M. Community and clinical epidemiology of borderline personality disorder. *Psychiatr Clin North Am* 2018; 41: 561–73.
- 35 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 2008; 69: 533-45.
- 36 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 2010; 24: 412–26.
- 37 Bernstein DP, Cohen P, Velez CN, Schwab-Stone M, Siever LJ, Shinsato L. Prevalence and stability of the DSM-III-R personality disorders in a community-based survey of adolescents. Am J Psychiatry 1993; 150: 1237–43.
- 38 Leung S-W, Leung F. Construct validity and prevalence rate of borderline personality disorder among Chinese adolescents. J Pers Disord 2009; 23: 494–513.
- 39 Oltmanns TF, Rodrigues MM, Weinstein Y, Gleason MEJ. Prevalence of personality disorders at midlife in a community sample: disorders and symptoms reflected in interview, self, and informant reports. J Psychopathol Behav Assess 2014; 36: 177–88.
- 40 Ha C, Balderas JC, Zanarini MC, Oldham J, Sharp C. Psychiatric comorbidity in hospitalized adolescents with borderline personality disorder. J Clin Psychiatry 2014; 75: e457–64.
- Winsper C, Marwaha S, Lereya ST, Thompson A, Eyden J, Singh SP. Clinical and psychosocial outcomes of borderline personality disorder in childhood and adolescence: a systematic review. *Psychol Med* 2015; 45: 2237–51.

- 42 Grilo CM, Skodol AE. Longitudinal course and outcomes. In: Skodol AE, Oldham JM, eds. American Psychiatric Association Textbook of Personality Disorders, 3rd edn. Washington, DC: American Psychiatric Association Publishing, 2021; 231–58.
- 43 Álvarez-Tomás I, Ruiz J, Guilera G, Bados A. Long-term clinical and functional course of borderline personality disorder: a meta-analysis of prospective studies. Eur Psychiatry 2019; 56: 75–83.
- 44 Temes CM, Frankenburg FR, Fitzmaurice GM, Zanarini MC. Deaths by suicide and other causes among patients with borderline personality disorder and personality-disordered comparison subjects over 24 years of prospective follow-up. J Clin Psychiatry 2019; 80: 18m12436.
- 45 Black DW, Blum N, Pfohl B, Hale N. Suicidal behavior in borderline personality disorder: prevalence, risk factors, prediction, and prevention. J Pers Disord 2004; 18: 226–39.
- 46 Zanarini MC, Frankenburg FR, Reich DB, Wedig MM, Conkey LC, Fitzmaurice GM. The course of marriage/sustained cohabitation and parenthood among borderline patients followed prospectively for 16 years. J Pers Disord 2015; 29: 62–70.
- 47 Ng FYY, Bourke ME, Grenyer BFS. Recovery from borderline personality disorder: a systematic review of the perspectives of consumers, clinicians, family and carers. *PLoS One* 2016; 11: e0160515.
- 48 Crowell SE, Beauchaine TP, Linehan MM. A biosocial developmental model of borderline personality: Elaborating and extending Linehan's theory. *Psychol Bull* 2009; 135: 495–510.
- 49 Luyten P, Campbell C, Allison E, Fonagy P. The mentalizing approach to psychopathology: state of the art and future directions. Annu Rev Clin Psychol 2020; 16: 297–325.
- 50 Stepp SD, Whalen DJ, Scott LN, Zalewski M, Loeber R, Hipwell AE. Reciprocal effects of parenting and borderline personality disorder symptoms in adolescent girls. *Dev Psychopathol* 2014; 26: 361–78.
- 51 Reinelt E, Stopsack M, Aldinger M, Ulrich I, Grabe HJ, Barnow S. Longitudinal transmission pathways of borderline personality disorder symptoms: from mother to child? *Psychopathology* 2014; 47: 10–16.
- 52 Belsky DW, Caspi A, Arseneault L, et al. Etiological features of borderline personality related characteristics in a birth cohort of 12-year-old children. Dev Psychopathol 2012; 24: 251–65.
- 53 Winsper C, Hall J, Strauss VY, Wolke D. Aetiological pathways to Borderline Personality Disorder symptoms in early adolescence: childhood dysregulated behaviour, maladaptive parenting and bully victimisation. Borderline Personal Disord Emot Dysregul 2017; 4: 10.
- 54 Hallquist MN, Hipwell AE, Stepp SD. Poor self-control and harsh punishment in childhood prospectively predict borderline personality symptoms in adolescent girls. J Abnorm Psychol 2015; 124: 549–64.
- 55 Lereya ST, Winsper C, Tang NKY, Wolke D. Sleep problems in childhood and borderline personality disorder symptoms in early adolescence. J Abnorm Child Psychol 2017; 45: 193–206.
- 56 Carlson EA, Egeland B, Sroufe LA. A prospective investigation of the development of borderline personality symptoms. *Dev Psychopathol* 2009; 21: 1311–34.
- 57 Reichborn-Kjennerud T, Ystrom E, Neale MC, et al. Structure of genetic and environmental risk factors for symptoms of DSM-IV borderline personality disorder. JAMA Psychiatry 2013; 70: 1206–14.
- 58 Witt SH, Streit F, Jungkunz M, et al. Genome-wide association study of borderline personality disorder reveals genetic overlap with bipolar disorder, major depression and schizophrenia. *Transl Psychiatry* 2017; 7: e1155.
- 59 Santangelo P, Reinhard I, Mussgay L, et al. Specificity of affective instability in patients with borderline personality disorder compared to posttraumatic stress disorder, bulimia nervosa, and healthy controls. J Abnorm Psychol 2014; 123: 258–72.
- 60 Krause-Utz A, Walther J-C, Schweizer S, et al. Effectiveness of an emotional working memory training in borderline personality disorder: a proof-of-principle study. *Psychother Psychosom* 2020; 89: 122–24.
- 61 Krause-Utz A, Oei NYL, Niedtfeld I, et al. Influence of emotional distraction on working memory performance in borderline personality disorder. Psychol Med 2012; 42: 2181–92.
- 62 Cackowski S, Reitz A-C, Ende G, et al. Impact of stress on different components of impulsivity in borderline personality disorder. *Psychol Med* 2014; 44: 3329–40.

- 63 Krause-Utz A, Cackowski S, Daffner S, et al. Delay discounting and response disinhibition under acute experimental stress in women with borderline personality disorder and adult attention deficit hyperactivity disorder. *Psychol Med* 2016; 46: 3137-49
- 64 Lyssenko L, Schmahl C, Bockhacker L, Vonderlin R, Bohus M, Kleindienst N. Dissociation in psychiatric disorders: a meta-analysis of studies using the dissociative experiences scale. Am J Psychiatry 2018; 175: 37–46.
- 65 Kleindienst N, Bohus M, Ludäscher P, et al. Motives for nonsuicidal self-injury among women with borderline personality disorder. *J Nerv Ment Dis* 2008; 196: 230–36.
- 66 Koenig J, Rinnewitz L, Warth M, et al. Psychobiological response to pain in female adolescents with nonsuicidal self-injury. J Psychiatry Neurosci 2017; 42: 189–99.
- 67 Wilkinson-Ryan T, Westen D. Identity disturbance in borderline personality disorder: an empirical investigation. Am J Psychiatry 2000; 157: 528–41.
- 68 Winter D, Steeb L, Herbert C, et al. Lower self-positivity and its association with self-esteem in women with borderline personality disorder. *Behav Res Ther* 2018; 109: 84–93.
- 69 Santangelo PS, Reinhard I, Koudela-Hamila S, et al. The temporal interplay of self-esteem instability and affective instability in borderline personality disorder patients' everyday lives. J Abnorm Psychol 2017; 126: 1057–65.
- 70 Winter D, Koplin K, Lis S. Can't stand the look in the mirror? Self-awareness avoidance in borderline personality disorder. Borderline Personal Disord Emot Dysregul 2015; 2: 13.
- 71 Thome J, Liebke L, Bungert M, et al. Confidence in facial emotion recognition in borderline personality disorder. *Pers Disord* 2016; 7: 159–68.
- 72 Kaiser D, Jacob GA, Domes G, Arntz A. Attentional bias for emotional stimuli in borderline personality disorder: a metaanalysis. *Psychopathology* 2016; 49: 383–96.
- 73 Kleindienst N, Hauschild S, Liebke L, et al. A negative bias in decoding positive social cues characterizes emotion processing in patients with symptom-remitted Borderline Personality Disorder. Borderline Personal Disord Emot Dysregul 2019; 6: 17.
- 74 Liebke L, Koppe G, Bungert M, et al. Difficulties with being socially accepted: an experimental study in borderline personality disorder. J Abnorm Psychol 2018; 127: 670–82.
- 75 Domsalla M, Koppe G, Niedtfeld I, et al. Cerebral processing of social rejection in patients with borderline personality disorder. Soc Cogn Affect Neurosci 2014; 9: 1789–97.
- 76 Seidl E, Padberg F, Bauriedl-Schmidt C, et al. Response to ostracism in patients with chronic depression, episodic depression and borderline personality disorder a study using Cyberball. *J Affect Disord* 2020; 260: 254–62.
- 77 King-Casas B, Sharp C, Lomax-Bream L, Lohrenz T, Fonagy P, Montague PR. The rupture and repair of cooperation in borderline personality disorder. *Science* 2008; 321: 806–10.
- 78 Poggi A, Richetin J, Preti E. Trust and rejection sensitivity in personality disorders. Curr Psychiatry Rep 2019; 21: 69.
- 79 Bartz J, Simeon D, Hamilton H, et al. Oxytocin can hinder trust and cooperation in borderline personality disorder. Soc Cogn Affect Neurosci 2011; 6: 556–63.
- 80 Niedtfeld I, Renkewitz F, Mädebach A, et al. Enhanced memory for negative social information in borderline personality disorder. J Abnorm Psychol 2020; 129: 480–91.
- 81 Németh N, Mátrai P, Hegyi P, et al. Theory of mind disturbances in borderline personality disorder: a meta-analysis. *Psychiatry Res* 2018; 270: 143–53.
- 82 Brendel GR, Stern E, Silbersweig DA. Defining the neurocircuitry of borderline personality disorder: functional neuroimaging approaches. Dev Psychopathol 2005; 17: 1197–206.
- 83 Herpertz SC, Schneider I, Schmahl C, Bertsch K. Neurobiological mechanisms mediating emotion dysregulation as targets of change in borderline personality disorder. *Psychopathology* 2018; 51: 96–104.
- 84 Schulze L, Schulze A, Renneberg B, Schmahl C, Niedtfeld I. Neural correlates of affective disturbances: a comparative meta-analysis of negative affect processing in borderline personality disorder, major depressive disorder, and posttraumatic stress disorder. Biol Psychiatry Cogn Neurosci Neuroimaging 2019; 4: 220–32.

- 85 Reitz S, Kluetsch R, Niedtfeld I, et al. Incision and stress regulation in borderline personality disorder: neurobiological mechanisms of self-injurious behaviour. Br J Psychiatry 2015; 207: 165–72.
- 86 Willis F, Kuniss S, Kleindienst N, et al. The role of nociceptive input and tissue injury on stress regulation in borderline personality disorder. *Pain* 2017; 158: 479–87.
- 87 Aguilar-Ortiz S, Salgado-Pineda P, Vega D, et al. Evidence for default mode network dysfunction in borderline personality disorder. *Psychol Med* 2020; 50: 1746–54.
- 88 van Schie CC, Chiu C-D, Rombouts SARB, Heiser WJ, Elzinga BM. Stuck in a negative me: fMRI study on the role of disturbed self-views in social feedback processing in borderline personality disorder. *Psychol Med* 2020; 50: 625–35.
- 89 Sicorello M, Schmahl C. Emotion dysregulation in borderline personality disorder: a fronto-limbic imbalance? *Curr Opin Psychol* 2021; 37: 114–20.
- 90 van Zutphen L, Siep N, Jacob GA, et al. Impulse control under emotion processing: an fMRI investigation in borderline personality disorder compared to non-patients and cluster-C personality disorder patients. *Brain Imaging Behav* 2020; 14: 2107–21.
- 91 Bertsch K, Krauch M, Roelofs K, Cackowski S, Herpertz SC, Volman I. Out of control? Acting out anger is associated with deficient prefrontal emotional action control in male patients with borderline personality disorder. Neuropharmacology 2019; 156: 107463.
- 92 Marceau EM, Meuldijk D, Townsend ML, Solowij N, Grenyer BFS. Biomarker correlates of psychotherapy outcomes in borderline personality disorder: a systematic review. Neurosci Biobehav Rev 2018; 94: 166–78.
- 93 Niedtfeld I, Schmitt R, Winter D, Bohus M, Schmahl C, Herpertz SC. Pain-mediated affect regulation is reduced after dialectical behavior therapy in borderline personality disorder: a longitudinal fMRI study. Soc Cogn Affect Neurosci 2017; 12: 739–47.
- 94 Schmitt R, Winter D, Niedtfeld I, Herpertz SC, Schmahl C. Effects of psychotherapy on neuronal correlates of reappraisal in female patients with borderline personality disorder. Biol Psychiatry Cogn Neurosci Neuroimaging 2016; 1: 548–57.
- 95 Winter D, Niedtfeld I, Schmitt R, Bohus M, Schmahl C, Herpertz SC. Neural correlates of distraction in borderline personality disorder before and after dialectical behavior therapy. Eur Arch Psychiatry Clin Neurosci 2017; 267: 51–62.
- 96 Goodman M, Carpenter D, Tang CY, et al. Dialectical behavior therapy alters emotion regulation and amygdala activity in patients with borderline personality disorder. J Psychiatr Res 2014; 57: 108–16.
- 97 Drews E, Fertuck EA, Koenig J, Kaess M, Arntz A. Hypothalamic-pituitary-adrenal axis functioning in borderline personality disorder: a meta-analysis. Neurosci Biobehav Rev 2019; 96: 316–34.
- 98 Thomas N, Gurvich C, Kulkarni J. Borderline personality disorder, trauma, and the hypothalamus-pituitary-adrenal axis. Neuropsychiatr Dis Treat 2019; 15: 2601–12.
- Calati R, Gressier F, Balestri M, Serretti A. Genetic modulation of borderline personality disorder: systematic review and metaanalysis. J Psychiatr Res 2013; 47: 1275–87.
- 100 Ende G, Cackowski S, Van Eijk J, et al. Impulsivity and aggression in female BPD and ADHD patients: association with ACC glutamate and GABA concentrations. *Neuropsychopharmacology* 2016; 41: 410–18.
- 101 Stanley B, Siever LJ. The interpersonal dimension of borderline personality disorder: toward a neuropeptide model. Am J Psychiatry 2010; 167: 24–39.
- 102 Linehan MM, Comtois KA, Murray AM, et al. Two-year randomized controlled trial and follow-up of dialectical behavior therapy vs therapy by experts for suicidal behaviors and borderline personality disorder. Arch Gen Psychiatry 2006; 63: 757–66.
- 103 Borschmann R, Barrett B, Hellier JM, et al. Joint crisis plans for people with borderline personality disorder: feasibility and outcomes in a randomised controlled trial. Br J Psychiatry. 2013; 202: 357–64.
- 104 Storebø OJ, Stoffers-Winterling JM, Völlm BA, et al. Psychological therapies for people with borderline personality disorder. Cochrane Database Syst Rev 2020; 5: CD012955.
- 105 Cristea IA, Gentili C, Cotet CD, Palomba D, Barbui C, Cuijpers P. Efficacy of psychotherapies for borderline personality disorder: a systematic review and meta-analysis. *JAMA Psychiatry* 2017; 74: 319–28.

- 106 Oud M, Arntz A, Hermens ML, Verhoef R, Kendall T. Specialized psychotherapies for adults with borderline personality disorder: a systematic review and meta-analysis. Aust N Z J Psychiatry 2018; 52: 949–61.
- 107 Barnicot K, Crawford M. Dialectical behaviour therapy vs mentalisation-based therapy for borderline personality disorder. Psychol Med 2019; 49: 2060–68.
- 108 Linehan MM, Korslund KE, Harned MS, et al. Dialectical behavior therapy for high suicide risk in individuals with borderline personality disorder: a randomized clinical trial and component analysis. JAMA Psychiatry 2015; 72: 475–82.
- 109 Soler J, Pascual JC, Tiana T, et al. Dialectical behaviour therapy skills training compared to standard group therapy in borderline personality disorder: a 3-month randomised controlled clinical trial. Behav Res Ther 2009; 47: 353–58.
- 110 McMain SF, Guimond T, Barnhart R, Habinski L, Streiner DL. A randomized trial of brief dialectical behaviour therapy skills training in suicidal patients suffering from borderline disorder. Acta Psychiatr Scand 2017; 135: 138–48.
- 111 Kramer U, Pascual-Leone A, Berthoud L, et al. Assertive anger mediates effects of dialectical behaviour-informed skills training for borderline personality disorder: a randomized controlled trial. Clin Psychol Psychother 2016; 23: 189–202.
- 112 Black DW, Blum N, eds. Systems training for emotional predictability and problem solving for borderline personality disorder: implementing STEPPS around the globe. New York: Oxford University Press, 2017.
- 113 Gratz KL, Bardeen JR, Levy R, Dixon-Gordon KL, Tull MT. Mechanisms of change in an emotion regulation group therapy for deliberate self-harm among women with borderline personality disorder. Behav Res Ther 2015; 65: 29–35.
- 114 Bohus M, Dyer AS, Priebe K, et al. Dialectical behaviour therapy for post-traumatic stress disorder after childhood sexual abuse in patients with and without borderline personality disorder: a randomised controlled trial. Psychother Psychosom 2013; 82: 221–33.
- 115 Harned MS, Korslund KE, Linehan MM. A pilot randomized controlled trial of dialectical behavior therapy with and without the dialectical behavior therapy prolonged exposure protocol for suicidal and self-injuring women with borderline personality disorder and PTSD. Behav Res Ther 2014; 55: 7–17.
- 116 Harned MS, Wilks CR, Schmidt SC, Coyle TN. Improving functional outcomes in women with borderline personality disorder and PTSD by changing PTSD severity and post-traumatic cognitions. Behav Res Ther 2018; 103: 53–61.
- Bohus M, Kleindienst N, Hahn C, et al. Dialectical behavior therapy for posttraumatic stress disorder (DBT-PTSD) compared with cognitive processing therapy (CPT) in complex presentations of PTSD in women survivors of childhood abuse: a randomized clinical trial. JAMA Psych 2020; published online July 22. https://doi.org/10.1001/jamapsychiatry.2020.2148.
- 118 Newton-Howes GM, Foulds JA, Guy NH, Boden JM, Mulder RT. Personality disorder and alcohol treatment outcome: systematic review and meta-analysis. Br J Psychiatry 2017; 211: 22–30.
- 119 Lee NK, Cameron J, Jenner L. A systematic review of interventions for co-occurring substance use and borderline personality disorders. *Drug Alcohol Rev* 2015; 34: 663–72.
- 120 Gregory RJ, Chlebowski S, Kang D, et al. A controlled trial of psychodynamic psychotherapy for co-occurring borderline personality disorder and alcohol use disorder. *Psychotherapy (Chic)* 2008; 45: 28–41.
- 121 Philips B, Wennberg P, Konradsson P, Franck J. Mentalization-based treatment for concurrent borderline personality disorder and substance use disorder: a randomized controlled feasibility study. Eur Addict Res 2018: 24: 1–8.
- 122 Kienast T, Stoffers J, Bermpohl F, Lieb K. Borderline personality disorder and comorbid addiction: epidemiology and treatment. Dtsch Arztebl Int 2014; 111: 280–86.
- 123 Iliakis EA, Sonley AKI, Ilagan GS, Choi-Kain LW. Treatment of borderline personality disorder: is supply adequate to meet public health needs? *Psychiatr Serv* 2019; 70: 772–81.
- 124 Chanen AM, Berk M, Thompson K. Integrating early intervention for borderline personality disorder and mood disorders. Harv Rev Psychiatry 2016; 24: 330–41.

- 125 Hutsebaut J, Debbané M, Sharp C. Designing a range of mentalizing interventions for young people using a clinical staging approach to borderline pathology. Borderline Personal Disord Emot Dysregul 2020; 7: 6.
- 126 Sharp C, Kerr S, Chanen AM. Early identification and prevention of personality pathology: an AMPD-informed model of clinical staging. In: Skodol AE, Oldham JM, eds. The American Psychiatric Association textbook of personality disorders. Washington, DC: American Psychiatric Association, 2021: 259–306.
- 127 Huxley E, Lewis KL, Coates AD, et al. Evaluation of a brief intervention within a stepped care whole of service model for personality disorder. BMC Psychiatry 2019; 19: 341.
- 128 Flynn S, Graney J, Nyathi T, et al. Clinical characteristics and care pathways of patients with personality disorder who died by suicide. B J Psychiatry Open 2020; 6: e29.
- 129 Grenyer BFS, Lewis KL, Fanaian M, Kotze B. Treatment of personality disorder using a whole of service stepped care approach: a cluster randomized controlled trial. PLoS One 2018; 13: e0206472.
- 130 Gunderson JG. The emergence of a generalist model to meet public health needs for patients with borderline personality disorder. Am J Psychiatry 2016; 173: 452–58.
- 131 Bailey RC, Grenyer BFS. Supporting a person with personality disorder: a study of carer burden and well-being. J Pers Disord 2014; 28: 796–809.
- 132 Grenyer BFS, Bailey RC, Lewis KL, Matthias M, Garretty T, Bickerton A. A randomized controlled trial of group psychoeducation for carers of persons with borderline personality disorder. J Pers Disord 2019; 33: 214–28.
- 133 Bateman A, Campbell C, Luyten P, Fonagy P. A mentalizationbased approach to common factors in the treatment of borderline personality disorder. Curr Opin Psychol 2018; 21: 44–49.
- 134 Guillén V, Diaz-Garcia A, Mira A, et al. Interventions for family members and carers of patients with borderline personality disorder: a systematic review. Fam Proc 2021; 60: 134–44.
- 135 Lieb K, Völlm B, Rücker G, Timmer A, Stoffers JM. Pharmacotherapy for borderline personality disorder: Cochrane systematic review of randomised trials. Br J Psychiatry 2010; 196: 4–12.
- 136 Stoffers-Winterling J, Storebø OJ, Lieb K. Pharmacotherapy for borderline personality disorder: an update of published, unpublished and ongoing studies. Curr Psychiatry Rep 2020; 22: 37.

- 137 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.
- 138 Paton C, Crawford MJ, Bhatti SF, Patel MX, Barnes TRE. The use of psychotropic medication in patients with emotionally unstable personality disorder under the care of UK mental health services. J Clin Psychiatry 2015; 76: e512–18.
- 139 Riffer F, Farkas M, Streibl L, Kaiser E, Sprung M. Psychopharmacological treatment of patients with borderline personality disorder: comparing data from routine clinical care with recommended guidelines. *Int J Psychiatry Clin Pract* 2019; 23: 178–88
- 140 Stoffers JM, Lieb K. Pharmacotherapy for borderline personality disorder--current evidence and recent trends. Curr Psychiatry Rep 2015: 17: 534.
- 141 Black DW, Zanarini MC, Romine A, Shaw M, Allen J, Schulz SC. Comparison of low and moderate dosages of extended-release quetiapine in borderline personality disorder: a randomized, double-blind, placebo-controlled trial. Am J Psychiatry 2014; 171: 1174–82.
- 142 Hancock-Johnson E, Griffiths C, Picchioni M. A focused systematic review of pharmacological treatment for borderline personality disorder. CNS Drugs 2017; 31: 345–56.
- 143 Crawford MJ, Sanatinia R, Barrett B, et al. The clinical effectiveness and cost-effectiveness of lamotrigine in borderline personality disorder: a randomized placebo-controlled trial. Am J Psychiatry 2018: 175: 756-64.
- 144 Stoffers-Winterling J, Völlm B, Lieb K. Is pharmacotherapy useful for treating personality disorders? Expert Opin Pharmacother 2021; 22: 393–95.
- 145 Storebø OJ, Ribeiro JP, Kongerslev MT, et al. Individual participant data systematic reviews with meta-analyses of psychotherapies for borderline personality disorder. BMJ Open 2021; 11: e047416.
- 146 Florange JG, Herpertz SC. Parenting in patients with borderline personality disorder, sequelae for the offspring and approaches to treatment and prevention. Curr Psychiatry Rep 2019; 21: 9.
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