Personality disorder 3

Treatment of personality disorder

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The evidence base for the effective treatment of personality disorders is insufficient. Most of the existing evidence on personality disorder is for the treatment of borderline personality disorder, but even this is limited by the small sample sizes and short follow-up in clinical trials, the wide range of core outcome measures used by studies, and poor control of coexisting psychopathology. Psychological or psychosocial intervention is recommended as the primary treatment for borderline personality disorder and pharmacotherapy is only advised as an adjunctive treatment. The amount of research about the underlying, abnormal, psychological or biological processes leading to the manifestation of a disordered personality is increasing, which could lead to more effective interventions. The synergistic or antagonistic interaction of psychotherapies and drugs for treating personality disorder should be studied in conjunction with their mechanisms of change throughout the development of each.

Introduction

Translation of present research into robust clinical recommendations for the treatment of personality disorder is beset with difficulties.1 Study populations are heterogeneous,2 a natural result of the present classification of personality disorder and the different assessment criteria used by different studies. Personality disorder has much comorbidity with other mental disorders.3–5 Symptomatic improvement of a comorbid disorder during treatment is difficult to distinguish from true underlying personality change. Little agreement on core outcomes and measures makes meta-analyses of treatment outcome studies difficult to do, although they have been attempted.6–8 Methodological issues, for example masking of participants and personnel, are frequent, and most studies are done by treatment developers, which is known to affect outcomes in psychological and pharmacological research. Finally, the essential features of personality disorder, substantial impairment of interpersonal function, identity problems, and recognisable social dysfunction, are all difficult to measure. No convincing evidence exists that these core domains of the diagnosis improve significantly or reliably with treatment. Patients might lose a standardised diagnosis of personality disorder during treatment, but even if a formal diagnosis is not present, their vocational and social adaptation remain impaired irrespective of treatment.1–3

Despite all these caveats, reasons for optimism in personality disorder treatment remain. The old notion that these disorders are necessarily long term, stable over time, and associated with poor outcomes can no longer be sustained, particularly for borderline personality disorder, in which the serious epiphenomena, such as suicide attempts, risk taking, misuse of services, and aggressive outbursts improve markedly with treatment. These improvements are substantial in view of the cost of these behaviours for the individual, health services, and society. However, despite these improvements interpersonal dysfunction and social disturbance can continue unabated and identity problems will probably remain. In the long term, patients often continue to feel miserable about their lives, struggle to manage constructive intimate relationships, and under-function in complex social contexts such as employment and education. These difficulties persisting in the long term despite treatment are particularly prominent in patients with severe personality disorder, who also have a high risk of causing harm to themselves or others (particularly those with borderline and antisocial personality disorder), which is of concern. For treatment to be deemed effective it needs to have a robust effect on the core symptoms of a disorder and on the associated social adaptation over the long term. At present, long-term follow-up of treatment is limited.1,11

A further difficulty in the appraisal of treatment for personality disorder is that research is concentrated on a few personality disorders, principally borderline and to a lesser degree antisocial, and as a result any review is necessarily biased towards them. No agreement exists about the discrete nature of the categories of personality disorder, but this Series paper is organised around the

Search strategy and selection criteria

We searched PubMed and Medline for original research or review articles published in English between Jan 1, 2008, and March 31, 2014. We used a combination of the following search terms: “personality”, “personality disorder”, “treatment”, “psychosocial”, “borderline”, “antisocial”, “dissocial”, “pharmacotherapy”, and other named personality disorders (“paranoid”, “schizoid”, “emotionally unstable”, “impulsive”, “histrionic”, “anxious”, “avoidant”, “dependent”, “mixed”, “schizotypal”, “narcissistic”, “obsessive–compulsive”). We selected key articles on the basis of topic covered, the quality of research, and their relevance to the evidence base and clinical treatment. We supplemented these publications with earlier landmark studies and those that were illustrative of key points based on the knowledge of the authors.
three clusters that were used by the American Psychiatric Association to organise the categorical personality disorder classification systems in the Diagnostic and Statistical Manual of Mental Disorders (DSM)-III, DSM-IV, and now DSM-5. Each cluster has observable similarities and was perceived to have a hierarchical order in terms of severity of adaptive failure and treatability: cluster A, the odd, eccentric, socially aversive types, are thought least adaptive and least treatable; cluster B, the emotionally and behaviourally dysregulated types, have major social adaptational difficulties and variable treatability; and cluster C, the anxious, neurotic types, have the least severe adaptive failures (ie, are the best functioning and are thought to have the best outlook and treatability. This Series paper retains clusters because most of the evidence of efficacy or effectiveness derives from them.

**Treatment approaches**
The two main approaches to the treatment of personality disorder are psychosocial treatment and pharmacotherapy. Psychosocial intervention is recommended as the primary treatment for borderline personality disorder and other personality disorders. The rationale for psychosocial intervention, albeit mainly rooted in tradition, lies in the fact that personality and its disorders arise from a complex interaction between genetic determinants and developmental processes, affected by adverse life events, and that the primary manifestations of the disorder are difficulties with personal and social relationships. Treatments range from rigorous behaviour therapy (through problem solving and psychoeducation) to traditional psychoanalytic treatment. Most have been applied in a range of contexts (eg, inpatient, day patient or partial hospital, and outpatient) and offered over variable lengths of time and to different extents, despite the insufficient evidence base other than clinician belief and preference. Different formats such as individual or group treatment, or a mix of both, have been used, again with little evidence favouring one format over another. The UK National Institute for Health and Care Excellence (NICE) guidance suggests that a mixture of group and individual treatments, integrated with other services available to the patient (eg, social care, employment support, and drug and alcohol services), could be optimum for a good outcome. Severity of personality disorder, frequency of sessions, and length of treatment offered, have no obvious relation in the scientific literature with outcomes. These gaps in knowledge, along with the changing organisation of health service provision and high costs, has resulted in therapeutic community inpatient programmes (historically the mainstays of long-term intensive treatment for personality disorder nationally and internationally) being closed or adapted to community contexts, with treatment sessions being offered less frequently over a shorter length of time.

The rationale for pharmacological approaches in the treatment of personality disorders is that the behavioural traits associated with personality disorders might be associated with neurochemical abnormalities of the CNS. The scarce empirical basis for the creation of the axis II disorders in the DSM-III, their heterogeneity, and the absence of evidence to support treatment of individual personality disorders using pharmacotherapy led researchers to largely ignore specific axis II personality disorder categories and to focus instead on dimensions of psychopathology. The most prominent algorithm was proposed by Siever and Davis and developed further by Soloff. They suggested that the four dimensions (affective instability, anxiety-inhibition, cognitive–perceptual disturbances, and impulsivity aggression) that cut across all personality disorder categories should be studied rather than individual symptom clusters or diagnoses. Although heuristically appealing, little evidence exists to lend support to the validity of these proposed dimensions. The dimensions have never been tested in hypothesis driven studies. Nonetheless, the dimensions have been the dominant framework used to understand the evidence of drug effects on personality disorders and to develop treatment recommendations. Additionally, although the algorithm was designed to cut across all personality disorder categories, nearly all clinical trials on the effects of drugs in personality disorders have participants with borderline personality disorder. A systematic review in 2008 noted that more than 70% of all drug trials were on participants with borderline personality disorder and almost all of these were sponsored by the pharmaceutical industry.

In summary, although researchers reasonably suppose that behavioural traits associated with personality disorder could respond to drugs, irrespective of its appeal this psychobiological model remains untested because clinical trials at present focus almost exclusively on borderline personality disorder. Most clinical trials investigating the effect of drugs on personality disorder are poorly designed. Duggan and colleagues point out that most of these trials are underpowered with a mean of 22±4 participants in the treatment group and 19±3 in the control group. The mean duration of treatment was short, averaging 13±2 weeks (median 12 weeks) with restricted follow-up. The number of outcome measures is very large, particularly in relation to the small number of participants.

**Comorbidity**
Comorbidity remains a major concern in the interpretation of even the scarce available data about personality disorders. Most individuals diagnosed with one personality disorder meet criteria for at least one other personality disorder. A substantial proportion of patients have at least one axis I comorbid disorder, particularly depression, anxiety, and alcohol and drug disorders, but in all studies about these disorders the research reports of change in axis I disorders have little detail. Improvement in personality disorder symptoms
might therefore be an improvement in comorbid depressive or anxiety symptoms. Depression and personality disorder interact. Reported depression rates are very high in borderline personality disorder40 and response to antidepressants in depressed individuals with comorbid personality disorder seems lower than in those without comorbid personality disorder.29

**Aims of treatment**
The aims of treatments for personality disorder are more parsimonious than often suggested. Drug treatment only focuses on specific aspects of personality disorder’s pathological effects, such as affective instability and cognitive–perceptual disturbances. Psychosocial treatments, mainly for borderline personality disorder, aim to reduce acute life-threatening symptoms32 and improve distressing mental state symptoms. Some psychosocial treatments target practical issues only,9 leaving other mental health professionals to manage the acute symptoms of risk or violent behaviour. Only a few focus on personal identity,53 some on interpersonal interaction,29 only one on social adjustment,41 and one on the general difficulties of people with mixed personality disorders by use of problem solving and psychoeducation.16 Follow-up of people with personality disorder after treatment (mainly borderline personality disorder) suggests that the initial aims to reduce acute symptoms are largely met but not the more complex aims of improvement of the personality structure itself. The focus (whether it is on behaviour, mental processes, or the interpersonal and social aspects of living), the context, or the form of treatment do not seem to make any discernible difference to these more complex outcomes.

**Cluster A personality disorders**
People with cluster A disorders (schizoid, schizotypal, and paranoid personality disorders) are united by their social aversion, their failures to form close relationships, and their relative (compared with other clusters) indifference to these disabilities. These patients have poor self-awareness and empathic ability. Mental health professionals have made little effort to study or treat people with cluster A disorders; partly because, except perhaps those with schizotypal disorder, they do not experience loneliness or compete with or envy people who enjoy close relationships. Any treatment recommendations are indicative only, being based on clinical evidence alone. No well organised randomised controlled trials of treatment of people with cluster A disorders exist.

Schizotypal personality disorder is not defined as a personality disorder in the International Classification of Diseases-10 and might be more allied to schizophrenia than personality disorders. The disorder differs from other cluster A personality disorders in that social aversion is accompanied by more behavioural eccentricities (ie, bizarre notions such as magical thinking or clairvoyance), and lapses in their sense of reality (dissociation and derealisation). These features increase their presentation to mental health services.

**Psychosocial treatment of cluster A personality disorders**
Beck and Freeman31 suggest that cognitive therapy can effect change in both the cognitive and social disabilities of patients with schizotypal personality disorder but this remains an empirical question.

Although the level of paranoia varies substantially across the general population and even within the different classes of psychiatric disorder, people with paranoid personality disorder pose a quite distinct and not very straightforward clinical entity. People with paranoid personality disorder are keenly vigilant for the aggression and hostility of others, are likely to perceive its presence even when absent, and because their suspicions or unwarranted accusations can be offensive to others, they are apt to invoke the very responses they suspect. This pattern is so self-perpetuating that challenging interventions are rarely welcome let alone acceptable. No treatment trials of people with paranoid symptoms are being done and the disorder is recognised to be a common element in many other personality disorders.36

**Pharmacotherapy of cluster A personality disorders**
Patients with schizotypal personality disorder have been studied in a few small, usually open-label studies using typical and atypical antipsychotics.3 No patients showed some improvement in overall symptom severity but the risk to benefit ratio is unclear. No randomised controlled trials for patients with schizoid or paranoid personality disorder are being done and therefore no robust evidence about the efficacy of drugs in these patients is available at present.

**Cluster B personality disorders**
Cluster B personality disorders (borderline, antisocial, histrionic, and narcissistic) share dramatic, emotional, or erratic characteristics. Research interest is focused on borderline and antisocial personality disorder at present.

**Psychosocial treatment of borderline personality disorder**
Recommendations about the psychosocial treatment of patients with borderline personality disorder have changed greatly during the 40 years that the disorder has been studied. The first psychosocial treatments to be used were psychoanalytic therapies, with the related clinical case reports implicitly suggesting that heroically resolute and skilled psychotherapists could bring about substantial change.3 The obvious issues encountered led to the creative adaption of therapies, making them more specific to the difficulties of people with borderline personality disorder. Psychological treatments were modified and subjected to testing in randomised controlled trials with most delivering improved outcomes on life-threatening behaviours and psychiatric symptoms. Behaviour therapy was radicalised for treatment of borderline personality disorder (dialectical
Panel 1: Five common characteristics of evidence-based treatments for borderline personality disorder

1 Structured (manual directed) approaches to prototypic borderline personality disorder problems
2 Patients are encouraged to assume control of themselves (ie, sense of agency)
3 Therapists help connections of feelings to events and actions
4 Therapists are active, responsive, and validating
5 Therapists discuss cases, including personal reactions, with others

Panel 2: Proposed characteristics for a generalist approach to treating borderline personality disorder

- Treatment providers have previous experience with borderline personality disorder
- Supportive (ie, encouraging, advisory, and educational)
- Focus on managing life situations (not on the in-therapy interactions)
- Non-intensive (ie, once per week, with additional sessions as needed)
- Interruptions are expected; consistent regular appointments are optional
- Psychopharmacological interventions are integrated; group or family interventions are encouraged when necessary

Adapted from Bateman and Gunderson and Links.

behaviour therapy). Cognitive behaviour therapy was schematised (schema focused therapy) or made specific for borderline personality disorder (borderline personality disorder-cognitive behavioural therapy). Psychoanalysis became transference focused (transference focused psychotherapy). Psychodynamic became mentalised (mentalisation based treatment). Psychoeducation became organised (“systems training emotional predictability problem solving”). Integrative therapies coalesced (cognitive analytic therapy). Social-community treatment became nidotheory. Unfortunately, several limitations of public health significance remain in the wake of these specialist treatments. First, borderline personality disorder constitutes about 20% of hospital admissions and outpatient referrals, which means that responsibility for the disorder is difficult for mental health professionals to avoid and that specialist treatments cannot be provided for this number of patients. Second, although these therapies have greatly improved symptomatic outcomes, in itself a major achievement, they have failed to significantly improve social functioning. Third, these therapies need extended training for therapists and extended commitment from patients.

That these specialist treatments seem to have similar effects despite distinct theories and interventions is of great interest. These similarities drew attention to their common features, which are now deemed core requirements for all effective treatments. Panel 1 summarises the characteristics identified in all of the major evidence-based treatments for borderline personality disorder. 33–44

Little reason now exists to expect that a treatment for borderline personality disorder without these characteristics is likely to be successful. Studies in the past decade have called into question how often specialist interventions are actually needed. Early randomised controlled trials of treatment for borderline personality disorder in the 1990s compared specially adapted borderline personality disorder treatments with an erratic and non-formalised treatment as usual. 45–50 These comparator treatments were very inconsistent and used clinicians without training or interest in borderline personality disorder. More recently, four randomised controlled trials mainly designed to show efficacy of treatment for borderline personality disorder, compared specialist treatment with better planned and organised comparison treatment. These control treatments unexpectedly did as well or nearly as well as the empirically validated index treatment, giving further cause for optimism. In two of the trials the manuals for providing an effective generalist approach have been published. These generalist models are designed for use by clinicians who have not done extended training and who are not committed to becoming borderline personality disorder specialists.

This model, summarised in panel 2, can be routinely incorporated into the basic training of all psychiatrists, psychologists, or other clinicians who will be responsible for treating patients with borderline personality disorder, which could have a substantial effect on the delivery and organisation of services.

Patients who fail to respond to a generalist approach might then be referred for the more intensive and borderline personality disorder-specific, evidenced-based treatments. Better still would be evidence-based indicators about mediators and moderators that affect the range of outcomes. Specialist rather than generalist treatment of borderline personality disorder might be needed for patients with comorbidity for two or more personality disorders. But the challenge for the future remains: will the needs of most people with personality disorder be met best by services organised around general psychiatric treatment using clinicians who are personality disorder-informed, or around specialist treatment delivered by highly trained clinicians with access to general psychiatric support? Other major questions remain unanswered. No empirically based knowledge exists about what the relative significance of each of the component processes of borderline personality disorder treatment is in relation to outcome achieved, although some attempts have been made to dismantle aspects of treatment programmes to distinguish how they relate to outcome.
Pharmacotherapy of borderline personality disorder
The present American Psychiatric Association guideline states that symptom targeted pharmacotherapy is an important adjunctive treatment. This therapy is based on Siever and Davis’ dimensions of affective instability (treated with selective serotonin reuptake inhibitor [SSRIs] or monoamine oxidase inhibitors), impulsive aggression (treated with SSRIs or mood stabilisers), and cognitive–perceptual disturbances (treated with low dose antipsychotics). By contrast the UK’s NICE guidelines state that drug treatment should generally be avoided, except in a crisis, and then given for no longer than 1 week. The World Federation of Societies of Biological Psychiatry guidelines stated that moderate evidence exists for antipsychotic drugs being effective for cognitive–perceptual and impulsive–aggressive symptoms, that some evidence exists for SSRIs being effective for emotional dysregulation, and that some evidence exists for mood stabilisers being effective for emotional dysregulation and impulsive–aggressive symptoms. The second Cochrane review saw no evidence for the efficacy of SSRIs, but reported that mood stabilisers could diminish affective dysregulation and impulsive–aggressive symptoms in patients with borderline personality disorder, and that antipsychotic drugs could improve cognitive–perceptual symptoms and affective dysregulation. Some concern exists that several of the trials showing positive outcomes provide unreliable data. The most recent guidelines for treatment of borderline personality disorder from Australia’s National Health and Medical Research Council (NHMRC) again reviewed the scientific literature and included a series of meta-analyses. They concluded that “overall pharmacotherapy did not appear to be effective in altering the nature and course of the disorder. Evidence does not support the use of pharmacotherapy as first line or sole treatment for BPD [borderline personality disorder].” The NICE and NHMRC guideline committees agreed with the Cochrane review and other reviews and meta-analyses that evidence existed that some second generation antipsychotics (notably aripiprazole and olanzapine) and mood stabilisers (notably topiramate, lamotrigine, and valproate) could slightly reduce borderline personality disorder symptoms over the short term. However, as guideline groups they needed to consider the risks and possible benefits of evidence-based treatments. The fact that most of the recommended drugs have substantial long-term risks whereas other treatments such as psychosocial interventions do not have these risks affected their recommendations.

The situation is complicated by the fact that drugs are used very frequently in the treatment of borderline personality disorder despite the scarcity of evidence for their use. Zanarini and colleagues’ reported that 78% of patients with borderline personality disorder were on drugs for more than 75% of the time during a 6 year period. Additionally, 37% of these patients were on three or more drugs. In view of this situation clinicians should be guided towards the drugs with at least some evidence (ie, major tranquillisers and mood stabilisers) and away from those with less evidence (ie, SSRIs, tricyclic antidepressants, and benzodiazepines). NICE have argued that the assumption that drug treatment is justified at all is without evidence and their prescription should not be encouraged. The NICE guidelines explicitly state that if patients have no comorbid illness, efforts should be made to reduce or stop pharmacotherapy (panel 3).

Antisocial personality disorder
So far, few high quality treatment trials have been done in people with antisocial personality disorder. Furthermore, pooling of data has been prevented by the use of different diagnostic criteria and conceptualisations of psychopathy and antisocial personality disorder; differences in the definition and measurement of outcomes; a focus on treatment of incarcerated patients rather than those in the community; and a focus on behavioural and symptomatic rather than personality change in the present scientific literature. More studies have been done on incarcerated individuals with antisocial personality disorder, presumably because this group is especially difficult to engage in treatment in the community, which is perhaps because people with antisocial personality disorder are rejected from clinical services or do not seek care. The primary outcome measure for incarcerated individuals should be re-offending after release rather than psychological and behavioural change during the treatment itself. Some studies on other personality disorders, mainly borderline personality disorder, have included people with comorbid antisocial personality disorder, but were not powered adequately to find out the effectiveness of treatment for this subgroup; reoffence rates are not reported.

Panel 3: Recommendations for the use of drugs in borderline personality disorder

- Drugs should not be used as primary therapy for borderline personality disorder
- The time-limited use of drugs can be considered as an adjunct to psychosocial treatment, to manage specific symptoms
- Cautious prescription of drugs that could be lethal in overdose or associated with substance misuse
- The use of drugs can be considered in acute crisis situations but should be withdrawn once the crisis is resolved
- Drugs might have a role when a patient has active comorbid disorders
- If patients have no comorbid illness, efforts should be made to reduce or stop the drug

Adapted from National Health and Medical Research Council (Australia) and National Institute for Health and Care Excellence (UK) guidelines.
An early review suggested that cognitive behavioural therapy methods combined with training in social skills and problem solving gave the most positive results with both juvenile and adult offenders, in terms of recidivism. However, even this complex intervention did not achieve large reductions in re-offence with mixed groups of offenders. Some restricted evidence exists for the effectiveness of cognitive behavioural therapy in various settings, with the best evidence for the therapy delivered in a group format for people with antisocial personality disorder and substance misuse problems. One trial of cognitive behavioural therapy for antisocial personality disorder targeting antisocial behaviours suggested a reduction in aggressive acts after 1 year of treatment. Effects of enhanced thinking skills on recidivism are variable. Attempts continue to be made to extend therapeutic community principles for at risk offenders in the community. Adolescents with conduct disorder or offending behaviour might benefit from multisystemic therapy or multidimensional foster care. Helgeland and colleagues have linked disruptive behaviour disorders in adolescence with antisocial personality disorder in men and borderline personality disorder in men and women in adulthood, suggesting that early intervention could be important. Some evidence exists that adolescents with borderline traits respond to cognitive analytic therapy, and both mentalisation-based treatment and dialectical behaviour therapy are effective in self-harming adolescents.

**Pharmacotherapy of antisocial personality disorder**

Antisocial personality disorder, in view of its prevalence and importance, is grossly under-represented in evidence from trial data, with only three small studies. The NICE guidelines for antisocial personality disorder conclude that pharmacological interventions should not be routinely used for the treatment of antisocial personality disorder or its associated behaviours. However, NICE do state that pharmacological interventions can be used for comorbid mental disorders. Khalifa and colleagues came to a similar conclusion in a meta-analysis of eight studies of pharmacotherapy for antisocial personality disorder.

**Cluster C personality disorders**

**Psychosocial treatment of cluster C personality disorders**

An early randomised controlled trial of patients with mixed cluster C disorders suggested that psychodynamic therapy improved social function and reduced distress compared with wait-list controls and that changes were maintained throughout follow-up. A subsequent randomised controlled trial comparing short-term psychodynamic therapy with cognitive therapy with a 2 year follow-up showed significant improvements in both groups, with no differences in outcomes between them, although recorded distress fell more in the psychodynamic group. By contrast, Emmelkamp and colleagues reported that cognitive behavioural therapy was more effective than psychodynamic therapy and wait-list control in people with avoidant personality disorder. Other studies of treatment of mixed personality disorders have reported on cluster C disorders. Most recently, in 2014 a multicentre randomised controlled trial of schema focused psychotherapy for cluster C, paranoid, histrionic, or narcissistic personality disorders reported better outcomes compared with regular treatment and compared with clarification-orientated psychotherapy for recovery from personality disorder in terms of interviewer-based outcomes, but not on self-report measures.

Case reports exist on obsessive–compulsive personality disorder, but no randomised trials of treatment exist. One open trial reported beneficial effects of cognitive therapy.

A meta-analysis specifically on the three cluster C disorders concluded that cognitive and psychodynamic treatment resulted in medium to large positive effects, although it was unclear which of the personality disorders benefited most from treatment. Most improvement occurred during treatment, with some additional change occurring during follow-up, which was usually of short duration.

**Pharmacotherapy of cluster C personality disorders**

No randomised controlled trials have been published of drug treatment of patients satisfying the full criteria of any cluster C personality disorder. However the World Federation of Societies of Biological Psychiatry guidelines suggest that studies in patients with social phobia, which consistently report that antidepressants are better than placebo, could be thought of as evidence that these drugs might be effective in patients with avoidant personality disorder.

**Conclusion**

The evidence base for the treatment of personality disorders is limited by the focus on borderline personality disorder, the small sample sizes and short follow-up in clinical trials, the use of a wide range of outcome measures, and poor control of coexisting psychopathology. Nevertheless, some general conclusions are possible. Psychosocial treatment gives grounds for optimism, especially for borderline personality disorder. Treatment should be a structured (usually manual directed) partnership where patients are encouraged to assume control over themselves. Therapists should be active, responsive, validating, focused on managing life situations, and well supervised. Pharmacotherapy should only be used when integrated into psychosocial treatments, should be time limited to manage specific symptoms, and withdrawn when these are resolved. The present array of different psychosocial treatments needs improved synthesis based on understanding of the causes of personality disorder, informed formulation of the underlying mechanisms of change, and delineation of the effective components of treatment. We speculate that
targeted interventions offered for short periods of time, as part of sequenced treatment over a long period of time, rather than delivery of an intensive programme over a fixed time, could improve functional outcomes.

The research community is increasingly interested in developing improved understanding of the underlying, abnormal, psychological and biological processes leading to the manifestation of a disordered personality. Throughout the development of more effective psychotherapies and drugs, information about the interaction of the two, synergistic or antagonistic, should be studied. This joint focus could result in more focused psychotherapies and better drugs. For example, substantial interest exists for the potential effect of targeting N-methyl-D-aspartate signalling because glutamatergic signalling has effects on disinhibition, social cognition, and dissociative symptoms. Research published in 2010 has also suggested that opioid modulation could be a potential mechanism of treatment. Oxytocin is associated with several prosocial behaviours, including parental caregiving and affiliative bonding and has been suggested as a potential treatment for interpersonal symptoms. However, no randomised controlled trials exist for any of these compounds at present. Case studies and small open trials have not been promising. Opioid agonists and antagonists have been ineffective and potentially detrimental in treating patients with borderline personality disorder. Patients with borderline personality disorder given intra-nasal oxytocin were less cooperative and had more attachment anxiety than normal controls. Some people with personality disorder could have paradoxical responses to some drugs such as oxytocin because of pharmacological activation of the attachment processes that underlie some of the manifestations of personality disorder. In the future, drug trials might have to take into account attachment patterns, which will bring greater synthesis to pharmacological and psychological research, and, when combined with neurobiological investigation, might improve the chance of identification of more effective treatments.

Despite the many difficulties outlined, interest and enthusiasm for treatment of patients with personality disorder has increased steadily over the past two decades, along with optimism about their outlook. Hopefully better understanding about the underlying biological and psychosocial developmental processes that lead to the manifestation of a disordered personality will result in more specific psychotherapies and drugs in the future.

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All authors contributed equally.

Declaration of interests
AWB is a codeveloper of mentalisation-based treatment and JG developed good psychiatric management for personality disorder. RM declares no competing interests.

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