Pharmacological management of personality disorders: from evidence to practice

RESEARCH METHODS

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SUMMARY

Clinical guidelines recommend avoiding the use of medications to manage personality disorder. In clinical practice, however, substantial amounts of medication are used. In this article, we summarise the recommendations of guidelines published in various countries in the past 15 years. We review the evidence from randomised controlled trials and recent reviews, discuss the discordance between guidance and clinical practice and give recommendations on what a clinician should consider if they choose to prescribe in cases of severe disturbances in mood or behaviour despite the lack of evidence.

LEARNING OBJECTIVES

After reading this article you will be able to:

- summarise the current evidence and the guidance in relation to the pharmacological management of personality disorder
- make an evidence-based decision if and when it is appropriate to use medication to manage personality disorder
- identify the pros and cons when making decisions about prescribing medication to manage personality disorder.

KEYWORDS

Personality disorders; randomised controlled trial; antidepressants; antipsychotics; anticonvulsants.

Despite recommendations in guidelines to avoid using medications to manage personality disorders (e.g. National Institute for Health and Care Excellence 2015), we know from clinical practice that substantial amounts of medications are used (Stoffers 2010). This article explores why this is might be, with reference to the evidence base and current prescribing guidelines for personality disorders, and offers principles to guide clinicians if they feel that medication might be appropriate, regardless.

The evidence

Methodological issues

Before presenting the evidence on the effectiveness of prescribing in personality disorders, a few thoughts about methodological issues might be useful.

Masked ('blinded') RCTs are generally considered the gold standard for testing the effectiveness of interventions (Houle 2015). An RCT typically compares two groups – one receiving the intervention, the other one not. The latter (control) group receives a placebo (less often an active comparison treatment), such as a pill that looks the same but does not contain an active ingredient. By randomly allocating patients to these two conditions, the design controls for confounding factors, i.e. factors that might influence the outcome, which is particularly important for factors that might not yet be known. Both patients and prescribers are masked regarding the group a patient is in, thus avoiding bias in evaluating the potential effects of the intervention. When comparing the outcomes in the two groups, as the participants are the same in all other respects, logically any differences can be attributed to the treatment tested.

So far so good. What are the issues with this approach though? Most importantly: the patients included in such trials. As RCTs aim to minimise confounding factors, populations included are usually rather homogeneous and do not include participants with complex presentations, such as those with significant comorbidity. In a large community sample with borderline personality disorder (BPD) (Hoertel 2015), it was shown that seven out of ten patients with this diagnosis would not be included in pharmacological trials owing to exclusion criteria. Relatedly, outcomes are also limited in that typically only a few unambiguous outcomes that are easily measured are included in trials. Other methodological issues include conflicts of interest (e.g. where trials are conducted by or with the support of drug companies), small sample sizes and other issues with study quality (Deaton 2018).

Regarding RCTs of pharmacological approaches for personality disorders specifically, the vast majority have been conducted in people with BPD, which is not surprising, given they are more likely to be treatment-seeking as opposed to those with other personality disorders, who tend to be rather treatment-avoidant. The patients commonly included in RCTs do not necessarily reflect clinical reality. In a Cochrane review on pharmacological interventions

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for BPD (Stoffers-Winterling 2022), for example, of 46 trials included, 15 had enrolled only women, 1 only men, and the remainder participants of both genders, but with a predominance of women. Thirty-eight studies excluded patients with current affective or psychotic disorders and 30 excluded those with current substance use problems. Acute suicidality was also often an exclusion criterion. Of the 46 trials, 32 included only out-patients. Only 4 trials had a sample size of over 100.

When evaluating the relevance of study evidence to your clinical practice, the '5 Rs' approach (Nimavat 2020) might be helpful. This approach suggests critical analysis of the findings of a trial in terms of five domains: right question, right population, right study design, right data, and right interpretation. For example, if you are a clinician working in a secure forensic setting with men with personality disorder who present a risk to others, you will have to be cautious when applying to your clinical practice with this group the collated evidence from BPD studies focusing, for example, on female outpatients. However, there is no reason to believe that this evidence is of no relevance to you whatsoever, as there is thus far very little research comparing the effectiveness of interventions for personality disorders in different clinical settings or for patients with different sociodemographic and clinical characteristics.

Cochrane reviews

Cochrane reviews are based on rigorous methodology, including in the selection of studies included. Although this is the right approach from a scientific point of view, it means that the reviews are not always helpful in guiding clinical practice. This is because Cochrane reviews can end up 'empty' – not including any studies at all – or, if there are studies of sufficient quality for inclusion, findings are often described as inconclusive, not allowing clear recommendations to be made. 'We need more high-quality trials' (Stoffers-Winterling 2022) is a common conclusion. We will nevertheless now describe the relevant Cochrane reviews in the field of personality disorders, but complement these with a small number of other reviews.

There are Cochrane reviews on pharmacotherapy for two personality disorders: as one would expect, one of these disorders is BPD, and the other one is antisocial personality disorder (ASPD). Reviews on other personality disorders were planned but never conducted; there is a strong likelihood that they would have been 'empty reviews'.

Borderline personality disorder

The Cochrane review on BPD was first published in 2006, and has been updated twice since (Stoffers 2010; Stoffers-Winterling 2022). The first update (Stoffers 2010) included 28 trials with a total of 1742 participants, whereas the latest review found 46 studies involving 2769 participants (Stoffers-Winterling 2022). It is encouraging to see this increase in high-quality trials; however, Stoffers-Winterling et al (2020) noted a decline in the number of drug trials for BPD since 2015, attributing it to the consolidation of guidance that psychotherapy should be the first-line choice for the disorder. We might therefore be stuck with the evidence as it stands at the moment for some time longer.

The results from the synthesis of available evidence have unfortunately become less not more promising over time, as can be seen comparing the conclusions of the 2010 with the 2022 Cochrane review. The 2010 review concluded: 'The findings were suggestive in supporting the use of second-generation antipsychotics, mood stabilisers, and omega-3 fatty acids, but require replication, since most effect estimates were based on single studies' (Stoffers 2010), whereas the overall conclusion from the latest review was: 'We found mostly very low-certainty evidence that medication may result in no difference in any primary outcome. The rest of the secondary outcomes were inconclusive. Very limited data were available for serious adverse events. The review supports the continued understanding that no pharmacological therapy seems effective in specifically treating BPD pathology' (Stoffers-Winterling 2022).

The latest review found studies on 29 different types of medication. Primary outcomes were defined as BPD symptom severity, self-harm, suicide-related outcomes and psychosocial functioning. Sadly, for these most important outcomes the drugs tested – a variety of antipsychotics, antidepressants and mood stabilisers – showed minimal or no effects, leading to the conclusion above. The secondary outcomes included specific symptoms of or associated with BPD, and of the long list assessed, only five – anger, interpersonal problems, brief psychotic-like symptoms and dissociative phenomena – showed small to medium size effects for particular medications and dietary supplements:

- anger: mood stabilisers, omega-3 fatty acids, antipsychotics, antidepressants
- interpersonal problems: mood stabilisers, antipsychotics
- brief psychotic-like and dissociative symptoms: antipsychotics, omega-3 fatty acid.

These findings may support a symptoms-based approach to the pharmacotherapy of BPD as described below. Notably, however, only a proportion of BPD symptoms seem to respond to the

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drugs tested, the most significant exceptions being affective instability, impulsivity and depressive symptoms. In addition, it is important to note that each positive outcome found was rated as of low or very low certainty, meaning future research is likely to change these findings. The example of mood stabilisers can illustrate this. In the 2010 Cochrane review lamotrigine, topiramate and valproic acid were found to show some positive effect. However, these findings were rated as uncertain, as they were based on trials with samples of between 15 and 56 participants (Stoffers 2010). A large, very well conducted study on lamotrigine with 276 participants running over an entire year in routine care published since (Crawford 2018) did not find any significant effects of the medication, leading to a very much more cautious conclusion on the use of mood stabilisers in the most recent Cochrane review (Stoffers-Winterling 2022).

When considering using medication in BPD, benefits have to be weighed against potential negative effects. In that respect, it is worrying that all but one study testing olanzapine showed an increase rather than a decrease in suicidality, in addition to the side effects known from the use of the medication in other conditions, such as weight gain. Moreover, one RCT, comparing fluoxetine with dialectic behavioural therapy, found higher rate of suicide attempts in the medication group (Simpson et al 2004, cited in Stoffers 2010).

The Cochrane review discussed thus far considered medication as medium- to long-term intervention strategy. However, sometimes medication is needed in an acute crisis. Another Cochrane review (Borschmann 2012) therefore set out to investigate the effectiveness of interventions, including medication, in acute situations in BPD. Unfortunately, this review turned out to be an empty one. Of the 15 studies identified, 13 had to be excluded owing to various exclusion criteria and 2 were ongoing RCTs (of brief psychological interventions) with no results available.

Antisocial personality disorder

The evidence in favour of pharmacological interventions for ASPD is even less promising. A Cochrane review (Khalifa 2020) summarised it. There were 11 studies included, which is an increase of 3 studies since the previous edition of the review in 2010. Only 416 participants were included in these studies and, as one would expect, they were predominantly male. An interesting observation in that review was that none of the studies had set out to recruit individuals with ASPD. Rather, the majority were studies on people with substance use disorders of whom a proportion also happened to have a diagnosis of ASPD; one study recruited prisoners with impulsive behaviour who could also be diagnosed with ASPD. Only four studies (carried about between 1994 and 1997) reported findings in a way that it was possible to extract data only on those with ASPD; they used the following drug classes: anti-epileptics, antidepressants and dopamine agonists (anti-Parkinsonian drugs). All findings were rated as of very low certainty. Three drugs showed an effect: phenytoin, nortriptyline and bromocriptine. Phenytoin was found to be more effective than placebo in reducing impulsive (as opposed to premeditated) aggression in male prisoners. The findings for the two other drugs are less exciting. They were more effective than placebo in reducing anxiety on one measure; nortriptyline also showed some positive effects on alcohol-related outcomes. In out-patients with substance use disorders and mixed personality disorders (not allowing subgroup analysis specifically for ASPD), phenytoin, carbamazepine and valproate were effective in reducing impulsive aggression. On another positive note, generally those with (any kind) of personality disorder did not fare worse than those without such additional diagnosis (a finding that psychotherapy studies also increasingly report (McGuire 2022)). Overall the authors concluded: 'This review concludes that there is insufficient evidence to support or refute the effectiveness of any pharmacological intervention for AsPD'.

Given the potential efficacy of anti-epileptics, another Cochrane review is relevant to our topic. Huband and colleagues (2010) looked at the use of anti-epileptics for aggression and impulsivity transdiagnostically. The review included 14 RCTs on 5 different antiepileptic drugs (carbamazepine, levetiracetam, oxcarbazepine, phenytoin, sodium valproate/divalproex). With the exception of levetiracetam, all of these drugs were found to be effective on some measure of aggression or impulsivity. The evidence was rated as very uncertain, as it was based on few and small studies. Nevertheless, the findings might again support the idea of a symptoms-based rather than a diagnosis-based approach to the pharmacotherapy of personality disorders.

Other evidence

In this section we will point to some reviews and individual studies of less rigorous quality compared with Cochrane reviews, to complement the evidence described thus far.

In a systematic review of 21 RCTs testing medication compared with placebo or head-to-head, Gartlehner et al (2021) concluded that the overall efficacy of pharmacotherapy in BPD is limited. They found only low-certainty evidence that

anticonvulsants may improve specific symptoms in BPD, such as anger, aggression and affective instability. Second-generation antipsychotics improved general psychiatric symptoms but not symptoms specific to BPD.

Clozapine has long been reported to have specific anti-aggressive and anti-suicidal effects and has been used off-label in severe BPD. A recent review (Han 2023) included 24 studies, all of very poor scientific quality with sample sizes under 30. Twelve studies were case reports and only one study (an RCT) compared clozapine with placebo. This single RCT did not, however, manage to recruit the calculated required number of participants. Most studies reported benefits from the use of the medication. A range of outcomes were used, often related to self-harm or suicide attempts. The largest study, representing more than 40% of all pre–post study participants, found a reduction in hospital admissions, days in hospital, concomitant use of medication, and self-harm following initiation of the treatment.

Felthous & Stanford (2015) developed an algorithm for the pharmacological treatment of impulsive aggression after examining 55 studies on pharmacotherapy for aggression. Of these studies, 23 met their quality standards reporting on a range of medications: anti-epileptics (carbamazepine, levetiracetam, oxcarbazepine, phenytoin, sodium valproate/divalproex), lithium, haloperidol, fluoxetine, D-amphetamine and pindolol. The authors also reported positive effects on impulsive aggression for lithium and fluoxetine.

Van Schalkwyk et al (2018) conducted a meta-analysis of 21 studies on antipsychotics for reactive/impulsive aggression transdiagnostically. The overall finding of the review was that antipsychotics are 'broadly effective', with no differences according to agent or diagnosis. Effect sizes were small and similar to those for non-pharmacological interventions; the authors suggest that these factors as well as potential side-effects should be taken into account when making clinical treatment choices.

Finally, it is worth mentioning that there is almost no evidence on the effectiveness of pharmacotherapy in other personality orders. One exception is schizotypal personality disorder, which can be seen as a schizophrenia spectrum disorder. It is therefore not surprising that trials have found some effects of antipsychotic medication (for a short summary see Stoffers-Winterling 2021).

The guidance

There are various guidelines on the use of pharmacotherapy in personality disorders, mostly focusing on BPD. All major guidelines consider psychotherapy as the first-line treatment for BPD and also for ASPD, and they give very cautious recommendations regarding pharmacotherapy for the latter.

We will describe here the recommendations of some guidelines published or updated in the past 15 years, i.e. from 2008 onwards.

The UK's National Institute for Health and Care Excellence (NICE) guidelines state that 'drug treatment should not be used specifically for BPD or for the individual symptoms or behaviour associated with the disorder (for example, repeated self-harm, marked emotional instability, risk-taking behaviour and transient psychotic symptoms)' (NICE 2009a: para.1.3.5.1). The guidelines thereby reject the idea of a symptoms-oriented approach advocated elsewhere. The recommendations suggest that drug treatment may, however, be used for the treatment of comorbid conditions, following the relevant guidance for these disorders. Interestingly (given the lack of evidence) NICE also states that the short-term use of sedative medication – specifically mentioning sedative antihistamines – may be considered in a crisis, bearing in mind that they are not licensed for this indication. These drugs should be used for a maximum of 1 week only. Finally, NICE recommends reviewing the treatment of people with BPD who are on medication with a view to discontinuing this if it is no longer indicated.

For ASPD, likewise, NICE does not recommend drug treatment (NICE 2009b). The text is almost identical to that in the BPD guidelines, suggesting that medication 'should not be routinely used for the treatment of antisocial personality disorder or associated behaviours of aggression, anger and impulsivity' (para. 1.4.3.1). As with BPD, medication could be used for comorbid conditions following the relevant guidelines. As individuals with ASPD often have drug use disorders, particular attention should be paid to adherence and misuse, particularly when prescribing medication that can be addictive and has street value. Overdose is also a concern, owing to the higher prevalence – compared with the general population – of self-harm in DSM-5 Cluster B personality disorders.

Simonsen et al (2019) reviewed and summarised European guidelines on the treatment of personality disorders. They found nine guidelines (from Denmark, Finland, Germany, The Netherlands, Catalonia in Spain, Sweden, Switzerland and two from the UK), five focusing on BPD, one on ASPD and three on personality disorders generally. Although all the guidelines favour psychotherapy as first-line treatment, the review authors found significant differences in other areas, including pharmacological treatment. Some guidelines do not recommend drug treatment for personality disorders, whereas others contradict this advice. Specifically, the guideline from Sweden (for BPD)

mirrors the NICE approach, guidelines from Catalonia (BPD), Denmark (BPD) and Germany (for all personality disorders) are less strict in advising against pharmacological treatment but emphasise that such treatment should be considered carefully and used only as an adjunct to psychotherapy. At the other end of the spectrum are the guidelines from Finland (BPD), The Netherlands (all personality disorders) and Switzerland (BPD), which advocate a symptoms-based approach suggesting specific drug classes for specific symptoms.

The American Psychiatric Association (APA) and the World Federation of Societies of Biological Psychiatry (WFSBP) also issued guidance on the pharmacological treatment of personality disorders, including disorders other than BPD and ASPD, and advocating to some extent a symptoms-based approach (the WFSBP guidelines include BPD, and schizotypal and anxious/avoidant personality disorder). However, these guidelines, dating back to 2001 and 2007 respectively, are now so dated that they will not be considered further here.

Mind the gap

There is considerable discordance between guidance and clinical practice that warrants consideration. A number of studies have found staggering numbers of people with a personality disorder who are prescribed medication. Paton et al (2015) surveyed (self-selected) services in the UK caring for people with personality disorders. Of those with BPD, 92% were prescribed psychotropic medication, with antidepressant and antipsychotic drugs being most common. Although comorbidity was high and one might suspect that this was the main reason for prescribing, further analysis did not support this hypothesis. In fact, prescribing patterns were very similar in those with BPD only and those with BPD and a comorbid condition. Of those with BPD only, 13% were not prescribed any medication, 21% medication from one class of psychotropics and the remainder drugs from two or more classes. Worryingly, those with BPD only were less likely than those with BPD and comorbid conditions to have had their medication reviewed in the past year. Clinicians were also asked to identify reasons for prescribing by selecting from a list of symptoms. Affective dysregulation, particularly depressive symptoms, was the most common reason given, followed by sleep disturbance, anxiety, distress and impulsivity. The choice of drugs suggested that clinicians used a symptoms-based approach. In forensic services in the UK, prescribing for personality disorder was also found to be high, with 80% of patients receiving at least one psychotropic medication, and almost two-thirds prescribed two or more (Völlm 2012). Clinicians indicated that in 65% of cases prescribing was for the management of symptoms of a personality disorder (rather than a comorbid condition).

Studies in other countries show similar findings. Zanarini et al (2015), for example, reported that in a US service 79.7% of people with BPD took antidepressants, 46.6% anxiolytics, 38.6% antipsychotics and 35.9% mood stabilisers. Research also suggests that people with BPD are even more likely to be prescribed psychotropic medication than those with other mental disorders, including major depression (Bender 2006). A European study of nearly 2200 in-patients with BPD (Bridler 2015) revealed further worrying news: quetiapine was the most frequently prescribed drug, with over 30% of patients prescribed this antipsychotic, for which there is almost no evidence of effectiveness in BPD (but evidence for a significant misuse potential); a similar number received benzodiazepines – their long-term use is discouraged not only in BPD.

Exploring the discordance

What might be the reasons then for this unfortunate state of affairs? Several reasons have been suggested in the literature and are partly supported by research findings.

It would appear that a number of clinicians continue to apply a symptoms-based approach to prescribing in BPD, despite meagre evidence to support it. Given that current guidelines in some countries also support this practice, this is not altogether surprising. An accumulation of drugs over time, prescribed during crises, without subsequent review (as shown in Paton 2015) could result in polypharmacy. Overprescribing does, however, also occur in countries with very clear guidance advising against it. Here a lack of access to psychotherapy might be one reason; there might also be pressure to ‘do something’ with perhaps limited resources. This hypothesis is supported by Kadra-Scalzo et al (2021), who found in a large sample of over 3300 patients with (any) personality disorder that those using psychological services were less likely to receive antipsychotic or antidepressant medication or benzodiazepines even after controlling for illness severity.

A qualitative study of UK clinicians treating individuals with BPD (Javed 2022) confirmed that long waiting lists for psychological therapies were a reason for prescribing for patients with high levels of distress. The study also confirmed that clinicians use medication for symptomatic treatment, for example of impulsivity, pseudo-hallucinations and paranoia. Other themes identified in this study included feeling pressured and patients’ high

expectations. Clinicians also commented on the discordance between guidelines and clinical practice; they were critical regarding the limited scope of RCTs in complex cases and suggested that anecdotal evidence and their own as well as patients' experience played an important role in guiding their practice.

Principles for clinicians to guide prescribing

As described above, despite recommendations to the contrary, when a patient has been diagnosed with a personality disorder and shows severe disturbances in mood or behaviour, medication is often prescribed. Principles to guide prescribing have been formulated for such cases (Felthous 2015; Black 2021; Pascual 2023), and we present here their essential points, together with own thoughts about what a clinician should consider before initiating treatment with medication. Box 1 illustrates these points in a fictitious case vignette.

Confirm the diagnosis

The first step is to confirm whether the person actually suffers from a personality disorder. Is their history and collateral information from other sources suggestive of the diagnosis? A structured diagnostic interview should be employed, such as the Structured Clinical Interview for DSM-5 Personality Disorders (SCID-5-CV) (First 2016). The clinician should also assess how severe and pervasive the disorder is and if it actually warrants the use of medication. The patient must be informed of the diagnosis and the implications of treatment. A similarity of a personality disorder to another condition known to respond to medication can sometimes guide as to which medication to choose. Avoidant personality disorder might respond to medication effective for treating social anxiety, obsessive–compulsive personality disorder could be treated with medication used for obsessive–compulsive disorder, and schizotypal personality disorder might respond to low-dose antipsychotics.

Check for comorbidities

Comorbidities are common in people with personality disorder (Tyrer 2022: pp. 57–68). If another psychiatric condition is diagnosed for which evidence-based guidelines are available, it may be more appropriate to follow these, as also recommended in, for example, Khalifa et al (2020). Treating comorbid disorders, such as depression in BPD, can sometimes reduce the severity of symptoms of the personality disorder as well. Comorbidities can also interfere with treatment: for example, if the individual has a substance use problem, certain medication options may be less suited. The clinician should also take into account somatic comorbidities, as these might be relevant to the choice of medication.

BOX 1 Case vignette: best practice in prescribing for a personality disorder

L. is a 38-year-old man who is treated in a psychiatric outpatient setting after being released from prison, where he served a sentence for drug trafficking. L. describes problems with restlessness and impulsivity, which he feels are personality-related and he requests treatment with medication. His records mention a diagnosis of antisocial personality disorder, amphetamine dependence and attention-deficit hyperactivity disorder (ADHD). L. regularly attends a Narcotics Anonymous group. He has no other medical problems and does not take any regular medication at present. He was previously treated with methylphenidate, but this was stopped after he used it in larger doses than prescribed.

The treating clinician takes a thorough psychiatric and medical history and obtains previous records, with the patient's consent. She carries out a structured diagnostic interview (SCID-5-PD) and confirms the diagnosis of antisocial personality disorder. L. meets the DSM-5 diagnostic criteria for substance use disorder of moderate severity. The ADHD diagnosis is confirmed by SCID-5 diagnosis and through clinical interview, previous records and collateral information from L.'s parents.

Given that impulsivity is one of the characteristic criteria of ADHD, L's treating clinician decides to follow the guidelines for the treatment of ADHD. She refers him to a psychoeducational group for adults with ADHD that is offered by the local hospital and to a psychologist specialised in treating adults with ADHD. As regards medication, she suggests atomoxetine, as there is no significant potential for misuse of this medication. She discusses risks and benefits with L., who provides informed consent to start this medication, and she carries out the necessary investigations prior to starting it. She explains to L. that it may take several weeks before he notices an effect from the new medication. To evaluate his response to treatment, she decides to use a validated rating scale. She regularly monitors the effectiveness of the medication and checks for adverse effects.

Identify target symptoms

Identifying target symptoms is perhaps more in line with dimensional approaches to the classification of personality disorders, as exemplified in DSM-5 and ICD-11. It is important to be concrete when identifying potential target symptoms. Possible target symptoms include mood instability, depression/anxiety, psychotic-like symptoms, dissociation, identity disturbance, anger/hostility, self-harm and impulsivity (Black 2021). For people with BPD, the target will often be mood instability and

impulsivity, for which some evidence can be found for the use of medication.

Employ appropriate non-pharmacological methods

Once the diagnosis of a personality disorder and the comorbidities have been established and the target symptoms have been identified, the clinician should check whether the patient can be helped by non-pharmacological methods. For most personality disorders, there is relatively good evidence for psychotherapeutic interventions, so these should always be considered as a first-line treatment. Sometimes adjustments to the person's social environment can be helpful. Other options are relaxation techniques or behavioural interventions such as a therapeutic token economy. With the target symptoms in mind, the clinician should reconsider all available evidence-based psychotherapeutic interventions. Might it be possible to revisit a psychotherapeutic approach that has helped in the past? Is it perhaps time to try a different therapeutic modality?

Choose medication options

The evidence base for the use of medication in personality disorders is weak, but the clinician should still try to choose a drug with efficacy demonstrated through drug trials of sufficient quality. This article and its references provide some information about what medication to consider. Clinicians will be aware that many patients with a personality disorder are prescribed multiple psychotropic medications, a strategy that is not evidence-based and carries the risk of adverse effects. Affordability and availability may also play a role.

Consider risks and benefits, side-effects and contraindications

If a patient is at risk of suicide or self-harm, the clinician should choose medication that is not dangerous in overdose. Benzodiazepines should generally be avoided because of the increased risk of substance use problems in this patient group. Clinicians should also be cautious with second-generation antipsychotics, which can cause weight gain and increase the risk of metabolic syndrome.

Obtain the patient's informed consent

It is important to remember that no medication is approved for the treatment of personality disorders, so the clinician will be prescribing 'off-label'. Even though many patients with personality disorders are prescribed medication, some may be reluctant to take it, especially when informed about the lack of evidence. Getting informed consent is important as it will also help assure treatment adherence. The patient must be informed that the medication is prescribed off-label and understand the limited evidence base. It is advisable to follow the relevant guidelines when doing this (e.g. General Medical Council 2021). Clinicians should ensure that the off-label use is documented in the patient's file. They should record the reason for prescribing the medication and the intended duration of treatment.

Evaluate the response

Once medication has been prescribed, it is important to evaluate its effectiveness. We recommend using validated scales to monitor the improvement of target symptoms, for example the Brief Psychiatric Rating Scale, Beck Depression Inventory or the State–Trait Anger Expression Inventory. A visual analogue scale may be an easy option to use. The clinician must carry out all the relevant tests for the particular drug they have chosen and check regularly for adverse effects. If no improvement in the target symptoms is seen, the medication should be discontinued. This is crucial as it will avoid polypharmacy in the long term.

Conclusions

In this article, we have outlined methodological issues in the evidence base for prescribing in personality disorders and presented the current evidence and guidelines. Even though the use of medication is not well-supported by the evidence, patients with personality disorders are often prescribed medication. Psychotherapeutic interventions should always be considered as a first-line treatment. In individuals with severe disturbances of mood and behaviour, a clinician may decide to prescribe medication, but should only do this after careful consideration of the diagnosis, comorbidities, target symptoms, risk and benefits and with the patient's informed consent. We hope that the new diagnostic criteria for personality disorders in DSM-5 and ICD-11 will help to better evaluate non-pharmacological and pharmacological treatment options and improve care for people with personality disorders.

Data availability

Data availability is not applicable to this article as no new data were created or analysed in this study.

Author contributions

B.V. and D.C. together conceptualised the article, wrote the manuscript and approved the published version.

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MCQs

Select the single best option for each question stem

1 Which of the following methodological problems has been identified in research on the pharmacological management of personality disorders?
a populations included in RCTs are usually quite homogeneous and do not include complex cases
b there is too little funding by major drug companies
c patients with personality disorder rarely agree to take medication
d studies are usually conducted in patients with narcissistic personality disorder
e sample sizes are often too large.

2 The domains explored in the critical analysis of study evidence using the 5 Rs approach are:
a rethink, reuse, reduce, recycle, repurpose
b right approach, right question, right answer, right data, right interpretation
c right people, right message, right medium, right time, right response
d right question, right population, right study design, right data, right interpretation
e none of the above.

3 As regards the use of medication in borderline personality disorder and antisocial personality disorder:
a most guidelines recommend the use of benzodiazepines as first-line treatment
b most guidelines recommend the use of antipsychotics as first-line treatment
c most guidelines recommend psychotherapy as first-line treatment
d most guidelines recommend the use of mood stabilisers as first-line treatment
e most guidelines recommend the use of antibiotics as first line-treatment.

4 Before prescribing medication to treat personality disorder the clinician should:
a confirm the diagnosis
b check for comorbidities
c identify target symptoms
d employ appropriate non-pharmacological methods
e carry out all of the above.

5 As regards prescribing psychotropic medication for a patient with personality disorder:
a such patients are usually unable to give informed consent
b the medication is usually prescribed off-label
c the medication should be continued long term even if there is no response to its use
d benzodiazepines are the treatment of choice because they do not have any side-effects
e antipsychotics are the treatment of choice because they do not have any side-effects.