Personality disorders: Overview of pharmacotherapy

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INTRODUCTION

Personality disorders cause significant distress and impairment of social, occupational, and role functioning. They are associated with high rates of psychiatric comorbidity and high risks of morbidity and mortality.

First-line treatment of these disorders is psychotherapy; however, patients with personality disorders may be highly symptomatic and are often prescribed multiple medications in a manner unsupported by evidence. In the absence of trials comparing medications or consensus-based clinical practice guidelines, there is limited information to guide adjunctive pharmacotherapy. Preliminary evidence from meta-analyses of clinical trials provides an early basis to guide treatment and limit the practice of polypharmacy. However, the evidence remains limited by lack of published studies and limitations in study design and sample size. Therefore, clinical practice is largely guided by expert opinion and experience, which support the efficacy of low-dose antipsychotics and mood stabilizers when applied to specified symptom domains.

Pharmacotherapy for personality disorders is reviewed here. The epidemiology, pathogenesis, clinical manifestations, course, assessment, diagnosis and treatment of individual personality disorders are reviewed separately.

- (See "Overview of personality disorders".)
- (See "Antisocial personality disorder: Epidemiology, clinical manifestations, course, and diagnosis".)

- (See "Antisocial personality disorder: Treatment overview".)
- (See "Borderline personality disorder: Epidemiology, pathogenesis, clinical features, course, assessment, and diagnosis".)
- (See "Borderline personality disorder: Psychotherapy".)
- (See "Narcissistic personality disorder: Epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis".)
- (See "Narcissistic personality disorder: Treatment overview".)
- (See "Schizotypal personality disorder: Epidemiology, pathogenesis, clinical manifestations, course, and diagnosis".)
- (See "Schizotypal personality disorder: Psychotherapy".)
- (See "Schizotypal personality disorder: Treatment overview".)

GENERAL PRINCIPLES

- As with other psychiatric disorders and chronic conditions generally, a comprehensive treatment plan that addresses the biological, psychological, and social needs of the patient is useful in promoting mental health, wellness, and overall recovery.

- Prior to treatment, the accuracy of all psychiatric diagnoses should be evaluated, as patients with personality disorders are sometimes misdiagnosed. As an example, a patient with borderline personality disorder may be incorrectly diagnosed with bipolar disorder.

- In general, first-line treatment for personality disorders is psychotherapy. Symptom-focused, medication treatment of personality disorders is generally considered to be an adjunct to psychotherapy. (See "Borderline personality disorder: Treatment overview" and "Borderline personality disorder: Psychotherapy" and "Narcissistic personality disorder: Treatment overview" and "Schizotypal personality disorder: Treatment overview".)

- Psychotherapy and pharmacotherapy may be delivered comprehensively by a single clinician [1] or can be delivered collaboratively by separate clinicians. (See "Collaboration between prescribing physicians and psychotherapists in mental health care".)

- Avoid prescribing medications that can be fatal in overdose, such as tricyclic antidepressants. The risk of death by intentional or accidental suicide should be directly discussed rather than minimized or avoided. (See 'Suicidality' below and "Suicidal ideation and behavior in adults".)

- Avoid prescribing medications that can induce physiological dependence and tolerance, including benzodiazepines, which are especially toxic when combined with alcohol or

opioids. An additional risk of benzodiazepines is behavioral disinhibition associated with this class of medications in patients with personality disorders [2,3].

- Avoid changing medication each time there is a crisis or change in mood symptoms, which may occur frequently and suddenly, and also remit suddenly in some people with personality disorders. Prescribing medication at the time of a crisis often lacks a specific target symptom as well as an endpoint upon which the effects of a medication can be judged.

- Symptom expression in patients with personality disorders often waxes and wanes in relationship to life circumstances. Thus, it may take a number of months to determine whether a particular medication is helpful. Premature additions or changes to medications can lead to unnecessary, ineffective, and/or potentially harmful treatment.

- Education and communication with the patient and key members of their support system (with the patient's consent) may reduce the likelihood of repeated, premature requests to increase or "augment" the medication.

- For patients seeking relief from intense or temporary symptoms such as panic or depersonalization, consider applying stimulation to the parasympathetic nervous system through the following:

  - Applying ice or ice-cold water to the face (mammalian dive reflex) [4].

  - “Paced” breathing techniques – The exhalation phase is at least two to four counts longer than the inhalation phase (eg, inhale while counting to four and exhale while counting to eight) [4].

  Stimulation of the vagal nerve in this manner, in our clinical experience, results in an immediate, direct relief of intense emotions, in contrast to orally administered medications, which do not result in immediate relief due to the necessity for absorption into the body.

- Disclose to patients in the United States that using a medication to treat their symptoms of a personality disorder lies outside of a specific US Food and Drug Administration-approved indications for use of medications. Obtain and document the patient’s informed consent.

INITIAL MANAGEMENT DECISIONS

Deciding to treat with medications — Our decision to treat an individual with a personality disorder with medication is based on the individual patient's risk-benefit profile (including drug efficacy and adverse effects) and their degree of impairment. In general, individuals with personality disorders respond less robustly to medication as compared with individuals with mood, anxiety, or psychotic disorders. However, we have found the addition of medication to be useful for patients with symptoms that are more severe, cause greater impairment, and/or do not respond to nonpharmacologic treatment.

The decision to use medications should be reached through shared decision-making with the patient.

Factors that inform medication selection — Based on clinical experience, we typically select which medication to use based on:

- Which symptom domain includes the most impairing of the patient's symptoms? Which medications are efficacious in treating that domain? (See 'Targeted symptom domains' below.)
- If multiple medication classes are similarly efficacious, which has the fewest adverse effects? (See 'Side effects' below.)
- The patient's history of past drug responsiveness.
- The patient's family history of drug responsiveness.

SYMPTOM-DOMAIN-FOCUSED TREATMENT

In our clinical experience with patients with personality disorders, pharmacotherapy targeting specific symptom domains common across personality disorders can reduce these symptoms more effectively than other medication strategies (eg, medications targeting specific personality disorders).

Trials have tested the efficacy of low-dose antipsychotics, mood stabilizers, antidepressants, and omega-3 fatty acids in reducing symptom severity in these domains. For each symptom domain, meta-analyses compared the efficacy of the three medication classes using effect sizes from placebo-controlled trials of individual medications [5].

Targeted symptom domains — Symptom domains that cause impairment and distress across personality disorders are discussed below.

Cognitive and perceptual disturbances — We typically use a low dose of antipsychotic medications to treat disruptive stress-related, cognitive-perceptual disturbances in individuals with severe personality disorders. Meta-analyses comparing placebo-controlled clinical trials have found that low-dose antipsychotic drugs are more effective than antidepressants or mood stabilizers for treatment of these symptoms [5]. Administration of low-dose antipsychotic medications is discussed elsewhere. (See 'Administration' below.)

A meta-analysis of five clinical trials of antipsychotics compared with placebo in patients with personality disorders found a moderate effect for cognitive-perceptual symptoms (standardized mean difference = 0.56) [5]. No effects of antidepressants or mood stabilizers on cognitive-perceptual symptoms were seen.

Impulsivity or behavioral dyscontrol — We typically use mood stabilizers for the treatment of impulsivity and behavioral dyscontrol in patients with severe personality disorders. For those who also demonstrate recurrent self-harm, we typically add omega-3 fatty acids as an adjunct to a mood stabilizer, given their benign side effect profile and preliminary evidence suggesting efficacy. Administration of these medications is discussed elsewhere. (See 'Administration' below.)

- **Mood stabilizers** – Meta-analyses have found that mood stabilizers are more effective than antidepressants or antipsychotics in the treatment of impulsivity and behavior dyscontrol in individuals with severe personality disorders [5]. Specific trials of mood stabilizers in the treatment of behavior dyscontrol in individuals with personality disorders have been mixed. For example, in a meta-analysis of six clinical trials including 172 individuals, mood stabilizers resulted in a very large effect size for symptoms of impulsivity or behavioral dyscontrol (standardized mean difference 1.51, 95% CI 0.42-2.59) [5]. However, in another trial that included 276 individuals with borderline personality disorder and was not included in the meta-analysis, no clinically relevant differences were seen in outcomes comparing lamotrigine versus placebo [6,7]. However, a limitation of that trial was a failure to target the intervention to participants experiencing primarily affective instability and/or impulsivity as the targeted symptom domain, which may have diluted any effect.

- **Omega-3 fatty acids** – In a meta-analysis with pooled data from four randomized clinical trials studying the use of marine omega-3 fatty acids in participants with borderline personality disorder, moderate quality evidence of clinical benefit to domains of impulsivity and affective symptoms was found [8].

Affective dysregulation — We typically use mood stabilizers or low-dose antipsychotic medications for the treatment of affective dysregulation in this population. Administration of these medications is discussed elsewhere. (See 'Administration' below.)

Meta-analyses have found that mood stabilizers and low-dose antipsychotic drugs are more effective than antidepressants for treatment of affective dysregulation in the population [5]:

- Antidepressants – Antidepressants studied included mianserin, tranylcypromine, amitriptyline, desipramine, phenelzine, fluoxetine, and fluvoxamine. Clinical trials of antidepressants compared with placebo found:
  - No effect for depressed mood (six trials; standardized mean difference = 0.29).
  - Small effect on anxiety (five trials; standardized mean difference = 0.30).
  - Small effect on anger (four trials; standardized mean difference = 0.34).
- Mood stabilizers **–** Mood stabilizers studied included lamotrigine, carbamazepine, topiramate, valproate, and lithium. Clinical trials of mood-stabilizers compared with placebo found:
  - Very large effect for anger (seven trials; standardized mean difference = 1.33).
  - Large effect for anxiety (three trials; standardized mean difference = 0.8).
  - Moderate effect for depressed mood (five trials; standardized mean difference = 0.55).
- Antipsychotics – Antipsychotics studied included flupentixol depot, thiothixene, haloperidol, olanzapine, risperidone, and aripiprazole.
  - Clinical trials of antipsychotics found a moderate to large effect for anger compared with placebo (four trials; standardized mean difference = 0.69).
  - The effect size of antipsychotics on depressed mood, anxiety and mood lability were not clinically significant.

Evidence-based rationale — While we suggest a symptom-domain-focused strategy for treating disabling symptoms in patients with different types of personality disorder, the clinical trials guiding our selection of medications were conducted in patients with either borderline personality disorder or schizotypal personality disorder. It is not clear how well findings from clinical trials of medication in patients with personality disorders generalize to usual clinical

practice. Most drug trials excluded patients with highly prevalent comorbid disorders and patients with suicidality [9-11].

There are no clinical trials directly comparing a symptom-targeted approach with other approaches to pharmacotherapy for personality disorders. Symptom-domain-focused medication treatment is recommended by Dutch and German national practice guidelines [12,13]. In contrast, the United Kingdom's National Institute for Health and Care Excellence clinical practice guidelines recommend not routinely treating patients with personality disorders with medication, due to the weakness of the supporting evidence [14].

Administration — In treating symptoms of a personality disorder, antidepressants and mood stabilizers are dosed as they would be for major depressive disorder and bipolar disorder, respectively, while medication doses of antipsychotics are in general used at a lower dosing range compared with doses used in the treatment of schizophrenia.

- **Mood stabilizers**
  - Lithium 300 to 600 mg, starting at a low dose of 100 to 200 mg daily and titrating over two to three months as tolerated to 600 mg daily. In our clinical experience, targeting a specified blood level in the treatment of severe personality disorders is not necessary, in contrast to the treatment of bipolar disorder.
  - Lamotrigine titrated to 200 mg/day. A standard titration protocol was established by the drug manufacturer to minimize the risk of Stevens-Johnson syndrome (with appropriate dosing adjustments in the setting of other prescribed medications that induce or inhibit UGT1A4):
    - Beginning at 25 mg daily for two weeks
    - Increasing to 50 mg daily for two weeks
    - Increasing to 100 mg daily for one week
    - Then 200 mg daily

    Lamotrigine is not the medication of choice for people with barriers to regular medication adherence. Lamotrigine must be discontinued in the setting of rash or signs of allergic reaction, which may indicate signs and symptoms of serious immune system reaction or Stevens-Johnson syndrome.
- **Antipsychotics**
  - Aripiprazole (2.5 mg) daily dosing as a maintenance medication.

- Risperidone (0.5 to 1.0 mg) beginning at 0.5 mg daily dosing with optional increase to 1 mg daily dosing after one to two months (if tolerated) as a maintenance medication.
- Quetiapine (25 to 150 mg) beginning at 25 mg nightly dosing, with optional increase to 150 mg nightly dosing over several months, as a maintenance medication.

- **Omega-3 fatty acids**
  - Eicosapentaenoic acid – 700 to 1220 mg daily
  - Docosahexaenoic acid – 480 to 908 mg daily

Side effects — Issues regarding the tolerability and adverse effects of antidepressants, antipsychotic, and mood-stabilizing medications are discussed separately.

- (See "Selective serotonin reuptake inhibitors: Pharmacology, administration, and side effects".)
- (See "Atypical antidepressants: Pharmacology, administration, and side effects".)
- (See "Serotonin-norepinephrine reuptake inhibitors: Pharmacology, administration, and side effects".)
- (See "Second-generation antipsychotic medications: Pharmacology, administration, and side effects".)
- (See "Bipolar mania and hypomania in adults: Choosing pharmacotherapy", section on 'Medication doses and side effects'.)

SUBSEQUENT TREATMENT

Individuals with partial response — Patients' expectations should be managed for the role of medications; the benefits are likely to be limited and can take weeks to be fully apparent. Multimodal treatment with nonpharmacologic interventions should be encouraged.

Following a partial response, we typically resist the temptation to augment with another medication. There is no evidence supporting the use of polypharmacy in personality disorders. If the response to a medication is inadequate, we typically taper off the initial medication and gradually start a substitute medication.

Over time patients may note that the medication seems to be "wearing off." This may be an opportunity to discontinue the medication, or with the patient's consent, continue the medication with clarification that the medication is unlikely to resolve symptoms; rather, the

intended effect is to facilitate the patient's overall growth and improved management of their symptoms.

Duration of treatment — The duration of pharmacologic treatment is decided on a case-by-case basis using shared decision making. A subset of patients with severe, chronic symptoms may potentially benefit from continuing with medication treatment for years; however, for most patients engaged in psychotherapy and with psychoeducation about the nature of their disorder, severe symptoms will likely improve over time allowing for gradual tapering after six months to two years of treatment.

There are limited data regarding expected time to onset of medication effect and optimal duration of treatment. Very few randomized trials comparing the drugs with placebo extended beyond 12 weeks in duration. Clinical experience suggests patients may note moderate symptom improvement (some immediately and some over several weeks), especially when combined with psychotherapeutic and psychosocial interventions.

Patients' expectations should be managed for the role of medications; the benefits are likely to be limited and can take weeks to be fully apparent. Multimodal treatment should be encouraged.

SPECIFIC POPULATIONS

Multiple symptom domains — For patients presenting with personality pathology involving multiple domains (eg, affective dysregulation and perceptual disturbance), we work with the patient to assess which symptoms contribute to the overall functional impairment to the greatest degree. The selected domain would suggest a particular class of medication, its use to be weighed based on its risk-benefit profile [15]. (See 'Symptom-domain-focused treatment' above.)

As an example, a patient might identify severe impulsive-behavioral dyscontrol. The clinician may recommend a mood-stabilizing agent and discuss the potential benefits and risks of lamotrigine, lithium, carbamazepine, and valproate. (See "Antiseizure medications: Mechanism of action, pharmacology, and adverse effects".)

Multiple psychiatric disorders — Patients diagnosed with a personality disorder should be assessed for co-occurring psychiatric disorders which, if present, should be treated [16].

For patients with common comorbid conditions in which medication plays a central role, such as bipolar disorder, schizophrenia, or moderate to severe major depressive disorder, it is

reasonable to assess whether the medication prescribed for these disorders will reasonably address the component of the personality pathology.

There are no data to support pharmacotherapy for subthreshold depression or anxiety symptoms. In our clinical experience, psychotherapeutic interventions may be more effective in addressing subthreshold symptoms rather than medications.

Suicidality — Suicidality can be seen in patients with any personality disorder. An increased risk of suicidality is particularly associated with borderline personality disorder. (See "Borderline personality disorder: Epidemiology, pathogenesis, clinical features, course, assessment, and diagnosis", section on 'Suicidality'.)

Suicidal urges or behavior are of potential concern. To the extent the patient is willing to engage in treatment planning, clinical strategies to reduce the risk of suicide should be considered and enacted. Avoid prescribing medications that are toxic in the setting of overdose or are disinhibiting, such as benzodiazepines. In terms of selecting a medication in the setting of suicidality, in our clinical experience, medications that address the most intolerable symptoms domain are of highest yield. (See "Suicidal ideation and behavior in adults", section on 'Management'.)

Individuals treated with polypharmacy — Some patients with a personality disorder will present seeking medication management while already on multiple medications. This would be an opportunity to emphasize one or two medications guided by early evidence, and decrease or discontinue adjunctive medications. Adjuvant medications may be unnecessarily complicating the patient's medication regimen and contributing to side effects and other risks associated with polypharmacy.

SPECIFIC PERSONALITY DISORDERS

The presence of cooccurring conditions, including suicidality, are potential targets of medication treatment in patients with any personality disorder. In addition, some considerations are specific to individual disorders or clusters by type. (See 'Suicidality' above and 'Symptom-domain-focused treatment' above.)

Schizotypal personality disorder — As an adjunct to long-term psychotherapy, targeted pharmacotherapy is supported by small clinical trials and our clinical experience for cognitive-perceptual symptoms, cognitive deficits, and social anxiety in the disorder. Treatment of schizotypal personality disorder is reviewed in detail separately. (See "Schizotypal personality disorder: Psychotherapy".)

Other cluster A disorders — There are no clinical trials of medication for the other cluster A personality disorders. Patients with paranoid personality disorder and schizoid personality disorder both have tendencies toward cognitive-perceptual symptoms. A low-dose antipsychotic can be used, but expectations should be attenuated and risks of medication must outweigh potentially limited benefits of medication treatment. (See 'Cognitive and perceptual disturbances' above.)

Antisocial personality disorder — In general, it is suggested that medication not be used to treat patients with antisocial personality disorder. No medications have been found to be efficacious in the disorder. There may be a role for medication in treating severe aggressive behavior that can be seen in the disorder. (See "Antisocial personality disorder: Treatment overview", section on 'Individuals with aggressive behavior'.)

Borderline personality disorder — Although not adequately tested, pharmacotherapy for personality disorders has been most extensively studied in borderline personality disorder. Results have been variable, with low-dose antipsychotic medication, mood stabilizers, and antidepressants leading to reduction in targeted symptoms in some trials. Suicidality in borderline personality disorder and other personality disorders is discussed above. (See 'Suicidality' above and "Borderline personality disorder: Treatment overview".)

Narcissistic personality disorder — In our and others' clinical experience, medication treatment of patients with narcissistic personality disorder is best kept to a minimum (ie, reserved for severe symptoms that pose a risk to safety and for other co-occurring conditions).

Other cluster B disorders — There are no clinical trials of medication for the other cluster B personality disorder, histrionic personality disorder. Affective dysregulation and impulsivity are commonly seen in patients with this disorder. (See 'Affective dysregulation' above and 'Impulsivity or behavioral dyscontrol' above.)

Avoidant personality disorder — Socially avoidant patterns among patients with avoidant personality disorder have been reconceptualized in terms of social anxiety for the purposes of treatment. (See "Approach to treating social anxiety disorder in adults".)

Other cluster C disorders — Symptoms of affective dysregulation are prominent in dependent personality disorder and obsessive compulsive personality disorder. Suicidal urges or behavior are of potential concern, especially in the setting of loss of control over their environment. (See 'Affective dysregulation' above and 'Cognitive and perceptual disturbances' above.)

FOSTERING TREATMENT ADHERENCE

Adherence with a treatment plan is frequently a challenge for patients with personality disorders. Regular medication management visits will support the development of a therapeutic clinician-patient relationship and provide a framework for ongoing psychoeducation regarding treatment goals and expectations. We use the following methods to foster treatment adherence: (See "Approaches to the therapeutic relationship in patients with personality disorders".)

- **Seeing patients more frequently** – In order to engage patients and foster treatment adherence, seeing patients weekly or twice per month may be helpful. For patients regularly engaged in psychotherapy with another provider, it may be possible to space appointments at monthly intervals or longer. As patients learn to more capably manage their personality disorder symptoms, they may not need to be seen as frequently. In some cases, their care may be transferred to a primary care provider.

- **Increasing the length of visits** – For complex patients, a visit length of 30 to 60 minutes is usually necessary in order to establish the therapeutic frame, convey empathy and compassion, provide psychoeducation, manage expectations, and work together to advance the treatment plan. (See "Approaches to the therapeutic relationship in patients with personality disorders" and "Overview of the therapeutic relationship in psychiatric practice".)

- **Validating symptoms** – Patients with personality disorders benefit from acknowledgement and validation of their symptoms. This is particularly true with respect to the obvious pain and suffering associated with their experience. As with all patients, those with personality disorders, respond to having their symptoms taken seriously and not minimized. The therapeutic goal is to join with patients to reduce emotional pain and improve functioning.

- **Minimizing polypharmacy** – Limiting the number of medications prescribed and the frequency of dosing can be helpful in maximizing adherence. Medications which require regular dosing to reduce the risk of adverse events, such as with lamotrigine and the risk of Stevens-Johnson syndrome, should only be prescribed to patients for whom adherence to regular medication dosing has been successfully managed. It is useful to inquire about adherence in a nonjudgmental manner. (See 'Individuals treated with polypharmacy' above.)

- **Direct and nonjudgmental communication** – This is particularly important in discussing acceptable boundaries regarding medication usage. As an example, one way of addressing the issue of medication usage may be: “Because I’m concerned about your

health and safety, I will not continue to prescribe this medication if you are taking more than prescribed or saving medication to take all at once." Consider this information a much-needed, and usually welcomed, orientation to the "ground rules" of your therapeutic relationship.

This approach does not imply that the patient is a "drug-abuser" or "medication hoarder." It might be helpful to say, "Given the extreme distress you have been experiencing, anyone in your position might experience an urge to take more than the prescribed dose. I want you to know that this possibility concerns me, and I'd like to work with you to do everything possible to reduce the risk of a medication overdose. I'd like to describe some methods I use to work together to ensure you are able to use this medication safely." Depending on the patient, the nature of your therapeutic relationship, their history of impulsive behavior, and engagement with other healthcare professionals, the clinician may consider dispensing a 30-day supply of medications, or less depending on the toxicity of the agent.

Nonjudgmental communication is helpful for patients with a personality disorder who may be contacting the clinic or the provider directly or repeatedly in a manner that is potentially taxing to available resources. Typically, these communications are the patient's best attempts at keeping the clinician informed and seeking guidance. The interpersonal limitations related to their personality disorder prevent them from discerning the impact of their behaviors on the clinician and other members of the interdisciplinary team.

Underline the types of communication that reinforce the strength of your relationship: "I really appreciate how you called me once to leave a message regarding the side effect improvement. That was the correct use of phone contact and allowed me to feel helpful."

As with any patient, egregious or abusive behaviors should be identified as such and managed with the assistance of administrative and/or security personnel. This may include termination of the therapeutic relationship within legal and ethical limits, which vary across care settings. In many cases, effective communication and conveyance of empathy informed by the understanding of the nature of the interpersonal deficits inherent in the personality disorder can foster productive treatment relationships.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Personality disorders".)

INFORMATION FOR PATIENTS

In the context of a therapeutic relationship and a help-seeking patient, psychoeducation regarding diagnosis and treatment goals can lead to improved insight, functioning, and symptom reduction [1]. The National Institute of Mental Health has created an informational brochure for patients and their families on borderline personality disorder, which includes information about the use of medication [17]. UpToDate offers two types of patient education materials, “The Basics” and “Beyond the Basics.” The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on “patient info” and the keyword(s) of interest.)

- Basics topics (see "Patient education: Borderline personality disorder (The Basics)" and "Patient education: Antisocial personality disorder (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **General principles** – The basic principles we use in the treatment of personality disorders include: (See 'General principles' above.)
  - Developing a comprehensive treatment plan addressing biological, psychological, and social needs of the individual.
  - Using pharmacotherapy as an adjunctive treatment to first-line treatment of psychotherapy.
  - Avoiding medications that can be fatal in overdose (eg, tricyclic antidepressants), or induce physiologic dependence and tolerance (eg, benzodiazepines).
  - Avoiding polypharmacy or frequent medication changes. Symptoms in patients with personality disorders often wax and wane in relationship to life circumstances.

- Paced breathing techniques or applying ice-cold water in addressing intense or temporary symptoms such as panic or depersonalization.

- Educating and communicating with key members of the individuals support system in order to reduce the likelihood of requests to augment or increase medications.

- **Initial management decisions** – The decision to treat an individual with personality disorder with medication should be based on the individual's risk-benefit profile (including drug efficacy and adverse effects) and their degree of impairment. The decision to use medications should be reached through shared decision-making with the patient. (See 'Initial management decisions' above.)

- **Symptom domain focused treatment** – Pharmacotherapy targeting specific symptom domains that are common across personality disorders may reduce symptoms more effectively than targeting specific disorders. Symptom domains that cause impairment and distress across personality disorders and the medication most effective for them include:

  - **Cognitive-perceptual symptoms (eg, hallucinations, paranoid ideation)** – For individuals with cognitive-perceptual disturbances associated with personality disorders, we suggest low-dose antipsychotic medication rather than antidepressants or mood stabilizers (**Grade 2C**). These medications may be more effective for disruptive, stress-related cognitive-perceptual experiences than antidepressants or mood stabilizers. (See 'Cognitive and perceptual disturbances' above.)

  - **Impulsive-behavioral dyscontrol (eg, self-injury, theft, interpersonal conflict)** – For individuals with impulsive-behavioral dyscontrol associated with personality disorders, we suggest mood stabilizers rather than antidepressants or antipsychotic medications (**Grade 2C**). Mood stabilizers are more effective for impulsivity and behavioral dyscontrol than antidepressants or antipsychotics. (See 'Impulsivity or behavioral dyscontrol' above.)

  - **Affective dysregulation (eg, depressed mood, mood lability, anxiety, anger)** – For individuals with affective dysregulation associated with personality disorders, we suggest mood stabilizers or low-dose antipsychotic agents rather than antidepressants (**Grade 2C**). Mood stabilizers and low-dose antipsychotic drugs are more effective for affective dysregulation than antidepressants. (See 'Affective dysregulation' above.)

- **Subsequent treatment** – There are limited data regarding expected time to onset of medication effect and optimal duration of treatment. Few trials comparing medication with placebo extended beyond 12 weeks in duration. For most patients engaged in

psychotherapy and with psychoeducation, severe symptoms will likely improve over time allowing for tapering after six months to two years of treatment. However, a subset of patients with severe, chronic symptoms may potentially benefit from continuing with medication treatment for years. (See 'Subsequent treatment' above.)

- **Specific populations** – Treatment of individuals with pathology in multiple domains should be directed at the symptom that contributes to the greatest degree of functional impairment. Treatment of individuals with multiple or comorbid psychiatric disorders should be directed at addressing the comorbid disorder in addition to the personality disorder. (See 'Specific populations' above.)

- **Fostering treatment adherence** – Adherence with a treatment plan is frequently a challenge for patients with personality disorders. We often use the methods such as increased frequency of visits, symptom validation, and nonjudgmental communication to foster treatment adherence. (See 'Fostering treatment adherence' above.)

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