Treatment-Resistant Depression
The Importance of Identifying and Treating Co-occurring Personality Disorders

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KEYWORDS
- Depression • Treatment-resistant depression • Personality traits
- Personality disorder • Borderline personality disorder

KEY POINTS
- Treatment-resistant depression (TRD) is common and produces significant burden to individuals and society. Comprehensive and individualized approaches are needed to address this complex clinical situation.
- Diagnostic reevaluation is indicated in cases of TRD to determine the numerous factors that could be playing a role in the treatment resistance.
- Diagnostic reevaluation in the setting of TRD should include assessment for personality disorders, because these are common contributors to treatment resistance and are often not adequately addressed.
- There are validated psychotherapeutic interventions that have proved effective in treating personality disorders to help patients improve both self-functioning and interpersonal functioning.

INTRODUCTION
Treatment-resistant depression (TRD) is a significant burden to individual patients and society because many individuals with depression do not achieve or sustain remission, despite multiple pharmacologic interventions and treatment settings. Review of the literature reveals many approaches to addressing TRD, including augmentation of antidepressants with atypical antipsychotics and other medications, aerobic exercise, manual-based psychotherapies, and a variety of neurostimulation strategies.¹ Despite this variety of treatment approaches, TRD remains a common and burdensome condition, and each case of TRD requires a thoughtful and individualized treatment approach with attention to the biological, psychological, medical, social, cultural, and spiritual factors involved.

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Reevaluating the Diagnosis in Treatment-Resistant Depression

TRD often has multiple contributing factors that need to be identified so that they can be addressed with a comprehensive and individualized treatment plan. Reevaluating the clinical diagnoses to help clarify the contributing causes of treatment resistance is an essential component in the assessment of patients with TRD. Common causes of treatment resistance can include misdiagnosis of bipolar depression as unipolar depression, co-occurring substance use disorders, untreated medical conditions, cognitive impairments, trauma disorders, and co-occurring personality disorders. Considering all of these factors in a methodical and thoughtful way is essential in the diagnostic assessment of patients with TRD (Fig. 1).

Many psychiatrists have observed treatment resistance resulting from cases in which bipolar depression or mixed states of bipolar disorder have not been recognized and the symptoms have been treated as a unipolar depression. In these cases, the medication regimen often has included antidepressants indicated to treat major depressive disorder but not bipolar disorder. Antidepressants in the setting of bipolar disorder are often ineffective and can potentially exacerbate the symptoms of the bipolar illness and lead to agitation, restlessness, and increased anxiety. Considering the possibility of an underlying bipolar disorder in these cases is often the key to achieving a more effective pharmacologic approach.

In other cases of TRD, there is an underlying substance use disorder (eg, alcohol abuse), untreated or undertreated medical condition (eg, hypothyroidism, cardiovascular disease), underlying cognitive impairment (eg, mild cognitive impairment, dementia), or underlying trauma disorder (eg, posttraumatic stress disorder) complicating or confounding the successful treatment of the depressive episode. Careful history taking, physical examination, urine drug screens, basic medical screening laboratory tests, neurocognitive testing, and brain imaging can often be useful in identifying these contributors of treatment resistance so that appropriate interventions for these complicating factors can be recommended.

In addition to the aforementioned contributors to TRD, co-occurring personality disorders, including a poorly integrated or disrupted sense of self, can contribute significantly to treatment resistance and enduring depressive symptoms. For example, in an avoidant personality disorder there can be low self-esteem, feelings of inferiority, excessive feelings of shame or inadequacy, preoccupation with and sensitivity to criticism or rejection, avoidance of social activity, lack of energy for engaging in life, and a deficit in the capacity to feel pleasure. As another example, in borderline personality disorder (BPD) there can be a poorly developed or unstable self-image; excessive self-criticism; chronic feelings of emptiness; mood instability; frequent feelings of being down and hopeless; feelings of low self-worth; and thoughts of suicide, including

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Fig. 1. Diagnostic assessment in TRD. D/O, disorder.
suicidal behavior. It is evident when reviewing the criteria for personality disorders that it can be challenging to distinguish symptoms related to TRD from enduring traits associated with the personality disorder that are fairly stable across time and consistent across different situations. In these cases, the underlying personality structure needs to be addressed specifically as a part of the comprehensive treatment plan if the patient’s symptoms are going to be adequately resolved.

**Differences in the Quality of Depression with and Without Personality Disorders**

Patients with depression and comorbid personality disorders have been shown to differ from patients with depression alone on various measures, including those with personality disorders showing earlier onset, higher severity scores, less social support, more psychosocial stressors, and poorer response to antidepressant medication.

Previous investigators have also examined the relationship of personality traits and disorder to depressive subtype and outcomes in depressed inpatients. It has been reported that personality disorders are more common in unipolar nonmelancholic depressed patients compared with unipolar melancholic or bipolar depressed patients. Furthermore, personality disorder has been related to earlier onset of depressive illness and worse outcome within the unipolar nonmelancholic group of patients. Obsessive traits have been found to be most common in unipolar melancholic patients, whereas histrionic, hostile, and borderline traits have been found to be predominant in nonmelancholic depressed patients. The outcomes described in this study provide additional support for the idea that assessment of personality disorders is an important part of the evaluation in patients with depression, and particularly for patients with a unipolar nonmelancholic subtype of depression.

**Further Exploration of Depression Co-occurring with Personality Disorders**

The frequent phenomenon of co-occurring depression and personality disorders can be understood from a psychological standpoint by assessing factors that contribute to both depression and personality structure. For example, it has been reported that among types of childhood maltreatment, emotional and physical neglect were the strongest predictors of depression. Because neglectful and inconsistent caregivers during childhood can also contribute to a poorly integrated sense of self that is a hallmark of certain personality disorders, it is sensible that depression and personality disorders can often co-occur in cases in which there is a history of childhood neglect. As an example of underlying personality disorder complicating the treatment of depression, it has been reported that patients with BPD have a poorer acute response to electroconvulsive therapy. Therefore, one of the gold standards for treating severe and persistent major depressive episodes can be rendered less effective in patients with BPD. In addition, it has been suggested that a diagnosis of BPD has a significant impact on the course of symptoms in self-harming adolescents. Specifically, adolescents with BPD have been shown to have poorer treatment outcomes, including significantly higher levels of clinician-rated and self-reported depressive symptoms and lower levels of global functioning than those without BPD.

TRD can occur in the setting of a biological depression without an underlying personality disorder, in the setting of a biological depression comorbid with a personality disorder, or in the setting of a personality disorder in which the TRD is primarily a manifestation of the enduring traits of the personality disorder (Fig. 2). In some cases, the biological depression can lead to symptoms that appear to others as a personality disorder. This situation can occur when the biological depression, caused by a unipolar or bipolar affective disorder, leads to symptoms such as...
avoidance, self-criticism, feelings of emptiness, and suicidal behavior, which are common in personality disorders. In these cases, the treatment of the depression and the pseudo–personality disorder is often a biological intervention (eg, medication, neurostimulation) with adjunctive psychotherapeutic intervention (Fig. 3). The ability for biological treatment of depression to seemingly alter personality characteristics, such as self-confidence, has also been well described.8

In contrast, in some cases, the personality disorder can be the primary cause of persistent depressive symptoms and impairment in social and occupational functioning. In these cases, the primary treatment needed is psychotherapy to address the personality disorder, with the possibility of adding an adjunctive biological intervention (Fig. 4). Given the inadequacy of biological interventions alone in treating the persistent depressive symptoms caused by a personality disorder, specific treatment of the personality disorder is indicated. Therefore, it is important for an assessment of personality functioning to take place during the initial assessment and during ongoing follow-up assessments.

Multiple investigators have described the interplay between affective disorders and personality disorders, with a large body of research dealing specifically with connections between affective disorders and BPD. In generally considering the effects of personality disorders on functioning and well-being in the setting of major depressive
disorder (MDD), it has been shown that co-occurring personality disorders contribute to impairments in both social and emotional functioning and also decreased sense of well-being. Furthermore, personality disorders at baseline have been shown to predict accelerated relapse after an episode of major depression.

Gunderson and colleagues have done extensive research on the longitudinal course in personality disorders. It has been reported that the course of BPD is characterized by high rates of remission, low rates of relapse, and also severe and persistent impairments in social functioning. This finding points to the importance of identifying and treating co-occurring personality disorders when they occur, so as to improve the social and occupational functioning for patients recovering from depression. This improvement in social and occupational functioning can also be an important factor leading to the patients' recovery from depression.

Gunderson and colleagues also evaluated the interactions of BPD and mood disorders over a 10-year period showing that BPD and MDD showed strong reciprocal effects, delaying each disorder's time to remission and accelerating time to relapse.

Galione and Zimmerman compared depressed patients with and without personality disorder. Depressed patients with personality disorder had a younger age of onset; more depressive episodes; greater likelihood of atypical symptoms; and a higher prevalence of comorbid anxiety disorders, substance use disorders, and number of previous suicide attempts.

Zimmerman and colleagues set out to distinguish bipolar II depression from MDD with comorbid BPD. It was shown that patients with MDD comorbid with BPD were more often diagnosed with posttraumatic stress disorder, current substance use disorder, somatoform disorder, and other nonborderline personality disorders, whereas clinical ratings of anger, anxiety, paranoid ideation, and somatization were significantly higher. It was also reported that the patients with MDD comorbid with BPD were rated lower on the Global Assessment of Functioning scale, had poorer current social functioning, and made significantly more suicide attempts.

Additional Factors in the Diagnostic Assessment for Personality Disorders

To determine the possible contribution of a personality disorder to TRD, a careful diagnostic interview needs to be conducted, with particular focus on the quality of the patient’s relationships and on the amount of integration present in the patient’s sense of self and others. By including a focus on underlying personality structure and interpersonal functioning during the assessment, clinicians are more likely to identify cases in
which personality disorders are a prominent factor in perpetuating the depression. For example, when the patient’s depressed mood and comorbid symptoms are highly variable depending on the specific circumstances of the moment or in response to an interpersonal conflict, then the clinician should further assess whether the depressive symptoms are primarily related to a personality disorder. This affective instability based on the external circumstances is often seen in patients with a borderline personality structure, who lack a stable and integrated sense of self and others.

It has been shown that patients with BPD show more self-criticism than depressed patients without BPD. It has also been shown that the psychological constructs of emptiness and abandonment fears are highly associated with borderline disorders. Therefore, the occurrence of these psychological constructs should trigger a more in-depth assessment for BPD as a factor complicating the clinical picture.

A history of self-harm is another important area of assessment in patients being assessed for depression, because self-harm is related to lower levels of global functioning, higher severity of depressive symptoms, and higher levels of self-reported emotional dysregulation. Because self-harm is a common symptom in BPD, this history being present indicates a clear need to assess the personality structure of patients who have self-harmed so that an appropriate intervention can be recommended.

Previous investigators have proposed that a comprehensive clinical assessment combines both an assessment of symptoms and also an assessment of identity, level of defense mechanisms, and global reality testing with a focus on internal representations of self, others, and relationship patterns. The diagnosis of a borderline personality organization and moderate to severe symptoms has been reported to indicate the need for a validated treatment of BPD.

**Consideration of Treatment Options for Personality Disorders**

An examination of 3 treatments for BPD (dialectical behavioral therapy [DBT], transference-focused psychotherapy, and dynamic supportive treatment) showed that patients in all 3 treatment groups showed significant positive change in depression, anxiety, global functioning, and social adjustment across 1 year of treatment. DBT has been shown to be useful in addressing high suicide risk in individuals with BPD. General psychiatric management (GPM) for patients with BPD is another paradigm developed as an outpatient intervention that can be delivered by independent community health professionals. GPM can be particularly useful if more resource-intensive services such as DBT programs are not available. Mentalization-based therapy (MBT) provides another empirically supported approach to BPD that could be considered.

**Case Studies**

To show how TRD can be approached by addressing the underlying personality structure of the patient, selected aspects of 2 cases are briefly described here. Characteristics that could identify specific patients have been changed so that confidentiality is maintained.

**Mr G: finding a voice**

Mr G, a 50-year-old, separated manager of a transportation company, presented to the psychiatric clinic reporting a chronically depressed mood throughout his adulthood and a persistent inability to discuss his emotions and needs with other people. Biological intervention in other settings had not been effective at relieving his depression or in providing relief to his constant feelings of guilt, self-criticism, and passivity.
When asked what he would like help with he replied, “I want to be able to tell other people how I feel without becoming emotional.”

Mr G was financially supporting his girlfriend, several of her family members, his adult children, and his ex-wife, despite her having another significant other and a separate life. He was working more than 80 h/wk as a manager of a transportation company to make enough money to support these multiple households financially. He stated that he frequently berates himself for sleeping in on the weekends and feels guilty about not getting more done around the house when he was off from work over the weekend. He described that he has not had the desire to ride his motorcycle like he used to and he becomes guilty when he sees it. He reported that he feels “used” and does not tell people what he wants. He added that he would like to be divorced from his wife and free from paying her mortgage, but he is unable to ask for a divorce, stating, “It’s easier to not deal with it…everybody is in control of everything but me…I don’t think I’ll ever achieve happiness unless I can tell people what I want.” He frequently returned to the theme that he is a “doormat.” It was evident that at both work and home there was a consistent pattern of him seeing himself as a doormat across multiple domains in his life and with many different people. He described feeling “stuck” in his current circumstances.

When asked about this pattern of being a doormat for others and not being able to assert himself, he was able to describe that his passive nature may be an effort to be “the opposite” of his father. It was noted that his desire to not be like his father was serving to keep him emotionally connected with his father nonetheless.

Mr G’s parents divorced when he was 11 years old. His father was harsh, excessively punitive, and frequently told him, “You can do nothing right.” After the divorce of his parents, Mr G and his 2 younger siblings were moved around to various apartments in dangerous neighborhoods because of the financial strain of his father’s absence. Mr G acknowledged that his inability to ask for a divorce after 9 years could be a demonstration of trying to be the opposite of his father.

Mr G arrived to one session upset about a work meeting earlier in the day; however, he was passive during the meeting and did not advocate for himself. He described, “My feelings won’t be perceived well…they’ll say I’m negative…they’ll say I have to go…the person running the meeting doesn’t like me…I get belittled all the time by people who don’t know what they are talking about…I feel dismissed and belittled…I checked out…I can’t debate it, because I’m never going to win.” When asked to imagine how the situation would have played out if he had responded more assertively he replied, “They’d be angry.” It was evident that he was experiencing his boss at work as unfairly dismissive and belittling, similar to the way he experienced his father as a child, when self-advocacy or expression of anger was not an option for him.

The inability for Mr G to express anger, even when appropriate, and his inability to advocate for his own needs were identified as central themes that were keeping Mr G in a constant state of despair and feeling put on by others. It was clear that his anger was defended against by his becoming passive and, in his words, a doormat. By identifying this pattern and consistently commenting on this defense to Mr G during sessions, his ability to express anger in the sessions slowly increased.

There were several instances during his therapy during which Mr G developed a significant amount of anger showing up in the transference. One such example was on display during a discussion around a missed appointment, which he initially explained by his statement, “Sometimes I forget things.” At the suggestion that his missed appointment could be an unconscious response to the challenge of being in therapy, he became visibly angry during the session and then missed the next session. The following session began with Mr G discussing his irritation that his girlfriend was
frequently forgetting things. When asked if this comment could be a masked expres-
sion of his irritation at himself for forgetting his last appointment, he became angry and
stated, “I never forget anything. I didn’t forget my last appointment. I went home and
fell asleep and didn’t wake up.”

Several more months of providing a holding environment for Mr G to become more
comfortable expressing his anger enabled Mr G to see that it is possible to express
anger and other emotions without destroying himself or others in the process. The
shame and guilt associated with his anger lessened, and he came to realize that
appropriate expression of anger was an expected and appropriate human behavior.
This progress was demonstrated in session when he described his “mini-break-
through,” during which he was able to advocate for himself in a situation with a
coworker in which he previously would have remained silent, resented the situation,
and directed his anger inward.

Once free to express his wishes and advocate more readily for himself, Mr G no
longer was bound to be a doormat for others, which had been leading to a negative
view of himself and frequent resentment toward others. He was no longer as burdened
by the weight of the world, and he was freer to pursue happiness in his life.

Ms S: finding the self-compassion within
Ms S, a 55-year-old, twice divorced customer service representative, presented to the
clinic to undergo treatment of her chronic depression, obsessive compulsive behav-
iors, attentional difficulties, and anxiety. Ms S described that her chronic depression
was frequently severe and caused significant impairment in her social and occupa-
tional functioning. Her chronic symptoms included depressed mood, anhedonia,
hypersomnia, decreased interest in the world, excessive guilt, low energy, poor con-
centration, poor appetite, and feeling “disconnected” from her family and friends. On
initial presentation she reported various current stressors, including a job she disliked
and found unfulfilling, significant financial difficulties, and fear of foreclosure on her
home, which was in disrepair and almost uninhabitable because of her hoarding.
She described feeling like, “My very presence is an embarrassment,” and that she
has felt this way for years.

Ms S described enduring many medication trials in the past to help manage her
depression; however, she had been exquisitely sensitive to side effects with most
medications that were tried. She had been treated with an array of selective serotonin
reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, mood stabilizers,
and antipsychotic medications to no avail. She described a particularly bad experi-
ence with lithium when she ended up hospitalized because of adverse effects of the
medication.

Early in the course of therapy, Ms S’s notable masochistic traits became evident.
One example of this was seen in her compliant acceptance of a job that she found
humiliating and painful coupled with an unwillingness to seek another position. She
would frequently describe the horrible work conditions, lack of training opportunities,
and unsupportive management that she contended with. Despite having a college de-
gree in education and a history of competent performance working in the insurance
industry, she resigned herself to a customer service job in which she felt constantly
guilty over not being able to satisfy her customers in addition to receiving poor treat-
ment from her employers. When queried whether changing jobs was a possibility, she
was dismissive, stated that no new jobs are listed in the county, and remained deter-
mined to suffer through the day-to-day painful experience of her current job.

Ms S also demonstrated her masochism in her inability to allow herself
any modicum of joy. During the period surrounding her daughter’s wedding, Ms S
expressed significant depressed feelings, disconnection, and guilt, stating, “I feel like [my daughter] is leaving me and it is not fair to feel that way…she’s entitled to her own life…I feel bad that I’m not happy about her wedding…I can’t shake the feeling of sadness…I feel empty inside…I feel very sad and alone…I feel a huge sense of loss…her getting married is the beginning of me having to face the mess I’ve created for myself.”

Another example of Ms S’s inability to allow herself to experience positive emotion showed up when she received positive feedback at work, noting her development of an effective working relationship with staff at another location, which was improving customer service. After relating this positive feedback she continued, “Nothing is different…I’m tired, discouraged, disappointed at myself…discouraged at life in general…work isn’t any better…I feel like I’m not pulling my weight just like I feel in the rest of my life…it’s another environment where I haven’t lived up to my capabilities…every second the rug can be pulled from under me and it would be my fault…I’m just so disappointed in myself…my life wasn’t supposed to be like this…I expected more of myself…I feel like a major failure.”

Because of the notable and extreme sense of guilt, shame, and self-criticism that Ms S displayed across many different scenarios, this was formulated as an area of central importance. Previous investigators have described that identifying the sources of the masochism, be it parents, culture, religion, or otherwise, is an essential part of treating masochism in that it can help patients gain insight into the motives behind the masochistic thoughts and behaviors.23

In this vein, Ms S was encouraged to explore the invalidating and sometimes hostile home environment she experienced as a child. She described, “Growing up, Dad was always mad, and Mom was always sad.” She stated that she was the middle child in the household and “tried to please everybody.” Although she tried to please her parents, she would frequently feel inadequate in her ability to make things right in her household and this caused her significant distress and guilt. In one session she stated, “With my mom’s mental illness and my dad’s sternness, I always felt like I had done something to make them unhappy…the thought of disappointing my father scared me to death…I spent my life so my dad wouldn’t be mad and my mom wouldn’t be unhappy…I feel like I’ve let everybody down…my mom, my dad, and my daughter.” When she lamented in a subsequent session, “I don’t have a right to expect to feel good or a right to feel happy because my house is in disarray and my finances are a mess,” it was evident that she was continuing to experience the unrelenting guilt over not being able to make things right, similar to what she experienced in childhood.

In another session, Ms S provided another illustrative example of the guilt that she experienced as a young child. She related a story dating to when she was 10 years old when she went for a ride in the car with her father. During the trip her father asked both her and her sister which way he should turn, because both ways led to their destination. She said turn right and her sister said turn left. After her father turned right, the car hit a nail in the road and caused a flat tire that needed to be fixed. Ms S responded at the time with a tremendous amount of guilt and personal responsibility. She described, “I felt responsible…I still feel that sense of responsibility…I feel personally responsible that my life hasn’t turned out well…due to my financial indiscretions I have no right to have fun…I walk around my whole life feeling bad because I feel responsible for everything bad that’s happened…I should have been able to make it better and to do something so that everybody wouldn’t be hurting.” Ms S carried with her a strong sense of responsibility for her family’s dysfunction growing up, which continued to undermine her sense of worthiness throughout her adulthood.
From the point of identifying the origin of Ms S’s harsh and critical inner voice, the therapeutic task included lessening the power that this voice held over her. Over the next several sessions, Ms S was able to explore feelings toward her mother for being unavailable at times because of her mental illness and hospitalizations and at other times becoming angry and yelling at the children. Ms S was able to acknowledge the anger she harbored toward her mother and how her mother’s critical voice contributed to her poor self-esteem. In becoming more comfortable with acknowledging her anger toward her mother, Ms S was able to direct less of her anger toward herself through self-criticism, which had been perpetuating her depression and contributing to treatment resistance.

The goal for the therapeutic holding environment for Ms S was to provide the space for her to develop self-compassion as a replacement to her self-criticism. This goal was addressed in therapy by helping Ms S gain insight into her suffering so that she could treat herself with more patience and understanding. Working through many sessions in therapy, Ms S slowly started replacing her self-critical internal voice with an internal voice more nurturing and accepting of imperfection. After several months of working on a more self-compassionate inner voice, Ms S discussed what her daughter wanted for her, stating, “She wants to see me happy and feel successful...to be in a relationship...because she knows I have a lot to give.” Ms S was starting to give herself the permission to get well.

Further Discussion of Case Studies

In the case of Mr G, participation in psychotherapy enabled him to achieve significant relief from his depressive symptoms and improvement in both social and occupational functioning. Although the biological intervention of medication management had not been effective, the psychotherapeutic intervention ultimately allowed for relief from the feelings of guilt, self-criticism, and passivity that had limited his capacity to advocate for himself and make decisions in support of his well-being and happiness. During the course of treatment, he developed the capacity to advocate for a more manageable work schedule and request more shared responsibility from those he had been financially supporting so he could achieve a better work-life balance. He also developed a greater capacity to advocate for his own needs in his interpersonal relationships, which he could readily notice and appreciate. This psychological growth in Mr G occurred over approximately 2 years of weekly psychodynamically informed supportive psychotherapy. This type of psychotherapy both reinforces the patient’s adaptive coping mechanisms and strengths and provides a safe space to explore the maladaptive defense mechanisms that are present, underlying motivations influencing behavior, and patterns that have developed in interpersonal relationships over time. Focus on the transference, and particularly the anger that presented in the room during sessions, was a very useful technique that allowed Mr G to gain better insight into his own psychological functioning.

Ms S was also able to achieve significant relief from her depressive symptoms and an improvement in functioning as a result of her participation in psychotherapy. Although several medication trials were not adequate to achieve remission of her depression, the psychotherapeutic intervention provided her a framework to allow herself to heal. Similar to the case of Mr G, the personal growth in Ms S occurred over approximately 2 years of weekly psychodynamically informed supportive psychotherapy. Because of a fragile sense of self that often left her feeling dejected and self-critical, a supportive and encouraging therapeutic relationship helped to build a trustworthy foundation for some of the deeper insight-oriented work that occurred later in the course of treatment. Early in the treatment, cognitive behavioral techniques...
were also used to help Ms S achieve more immediate control of her hoarding behavior, which was contributing to a significant amount of daily stress. Ultimately, a psychodynamic psychotherapy approach, with a focus on how her experiences in childhood have significantly affected her thought patterns, emotions, and behavior throughout her adulthood, proved to be a key element of Ms S’s ability to free herself from her compulsive masochism. During the latter part of the treatment, her improvement in social functioning was evident in her positive descriptions of her new role as grandmother and in her reengagement as a positive presence in her daughter’s life.

SUMMARY

Although the dual-diagnosis approach of treating 2 disorders simultaneously is frequently discussed in the setting of substance use disorders co-occurring with affective disorders, this dual-diagnosis terminology is not often applied in the setting of personality disorders co-occurring with depression. However, similar to how depression often cannot be effectively treated in the setting of active substance abuse, depression often cannot be effectively treated in the setting of an active personality disorder, unless the personality disorder is addressed in an effective way. Therefore, it would be sensible to adopt the dual-diagnosis approach when a patient is experiencing TRD and a personality disorder is diagnosed or suspected.

Psychotherapy can be particularly useful in managing symptoms of depression and also comorbid symptoms that contribute to treatment resistance, including personality disorders. Acceptance and commitment treatment, cognitive behavioral analysis system of psychotherapy, DBT, and mindfulness-based cognitive therapy have all shown evidence for treatment of TRD. Current evidence also supports the efficacy of psychodynamic psychotherapy. A review of the effectiveness of psychodynamic psychotherapy has shown a trend toward larger effect sizes at follow-up, indicating continued improvement in symptoms after the course of therapy has ended.

Given that there are now multiple validated methods for treating various personality disorders, psychotherapy to address underlying personality disorders should be considered as a first-line, standard-of-care approach in the setting of TRD when there is a personality disorder diagnosed or suspected.

Reasons that have been given to explain the difficulty in treating comorbid personality disorders include the significant time commitment that treatment requires, a shortage of clinicians trained in treating personality disorders, and the presumed high cost of effective treatment. However, given the exceedingly high costs of TRD to both individuals and society, it is essential for clinicians to recognize the significant role that personality disorders can play in TRD and recommend a treatment plan to address the personality disorders when present. Given the long-recognized observation by clinical psychotherapists and the emerging research evidence that personality disorders can be effectively treated, a strong case can be made that investing resources into treatment of personality disorders must be a priority in modern psychiatry.

In the case examples described earlier, it was the psychotherapeutic intervention of providing a safe and supportive holding environment to foster the development of greater insight and self-compassion that enabled Mr G and Ms S to gain traction in their journeys of recovery.

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