Co-Occurring Disorders and Treatment Complexity Within Personality Disorders

J. Christopher Fowler, Ph.D.
John M. Oldham, M.D.

Abstract: Excessive comorbidity within personality disorders and other psychiatric disorders is a perennial problem in psychiatric diagnosis and treatment. Questions of etiology, disorder hierarchies, and treatment decisions are problems clinicians face on a daily basis. From a pragmatic view, the presence of multiple psychiatric disorders co-occurring within the context of a personality disorder can be viewed as proxy for psychiatric severity particularly as it relates to impairments in interpersonal relating, affective instability, and impulsivity. By extension, impairments in the above facets of functioning can alert clinicians to a range of potential treatment challenges including forming and maintaining a treatment alliance, sustaining treatment adherence, and targeting symptoms for medication treatment. Evidence from high-quality efficacy studies demonstrate significant, and in some cases lasting, symptom and behavioral change, especially for patients diagnosed with borderline personality disorder.

The phenomena of co-occurring personality disorders (PDs) has been a persistent problem because most patients diagnosed with a personality disorder meet criteria for more than one (1–4). Clinicians tend to rely on implicit prototypes (5, 6) for determining diagnoses and are unlikely to include hierarchical rankings of PDs in the diagnostic process. Empirical efforts to ascertain hierarchies have failed (7), thus making it difficult for clinicians to determine which personality disorder to diagnose and treat. Although there are a number of explanations for the high rate of PD co-occurrence, it appears that this is an artifact of a criterion count system that does not reflect daily clinical practice, which is closer to a prototype matching system (8, 9).

While comorbidity among personality disorders may eventually decline if a dimensional or prototype matching approach is adopted (6, 10), there should be no changes in patterns of comorbidity (in this country at least) in the immediate future, since the content of the PD section of DSM−5 will be unchanged from that of DSM-IV-TR. Even if the alternative model for PDs, presented in Section III of DSM−5, were to be utilized, it is unlikely that the substantial prevalence of co-occurring disorders such as mood, anxiety, and substance dependence (4, 11) would be eliminated. This perspective raises perplexing questions regarding development, order of onset, etiology, and sequence of treatment priorities.

In the absence of definite answers to resolving the issues involving potentially inflated co-occurring disorders, a pragmatic approach is to regard the degree of co-occurrence as a marker of psychiatric severity. From this vantage point, co-occurring disorders that include a personality disorder may serve as one of several markers for treatment complexity (12).

As evidence for this approach, consider the following: Co-occurring disorders substantially increase the risk of poor outcome, even when patients

Author Information and CME Disclosure
J. Christopher Fowler, Ph.D., The Menninger Clinic, Houston, TX and Baylor College of Medicine, Houston, TX

John M. Oldham, MD, The Menninger Clinic, Houston, TX and Baylor College of Medicine, Houston, TX

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Address correspondence to J. Christopher Fowler, Ph.D., Menninger Clinic, 12301 Main Street, Houston, TX 77035; e-mail: cfowler@menninger.edu

and clinicians are adherent to evidence-based treatments. Indirect evidence from meta-analyses of depression outcomes implicates co-occurrence of PDs with poor outcome and, by extension, more complex treatment. For example, the presence of a personality disorder in the context of major depression doubles the risk of poor outcome when compared with depressed subjects without a personality disorder (13). In a reanalysis of the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) results (14), researchers found that patients without any co-occurring disorders tolerated medication better, had higher rates of treatment response (51.6% versus 39.1%), and showed better rates of remission from depressive symptoms (34.4% versus 24.7%) than patients with comorbidity.

While co-occurring disorders may serve as a proxy for treatment complexity, there is mounting evidence that severity of symptoms and degree of impairment in social and occupational functioning also have an impact on response to treatment (15–17). Secondary analyses of the NIMH Treatment of Depression Collaborative Research Program (18) found that numerous markers of psychiatric severity predicted negative outcome across all treatments (pretreatment depression severity, social dysfunction, cognitive dysfunction, low expectation of improvement, combined major depressive disorder and dysthymia, and duration of current episode). In a 2-year follow-up of subjects with borderline personality disorder (BPD), the Collaborative Longitudinal Personality Disorders Study (CLPS) found that severity of BPD (as manifested by higher number of borderline personality disorder criteria, greater functional impairment, and greater interpersonal relationship instability) predicted poorer outcome (19). Evidence is also mounting to suggest that severity of psychiatric disturbance has far greater implications for treatment outcome than any single diagnosis. A reanalysis of the CLPS data found that general severity of psychiatric disturbance was most predictive of current and prospective dysfunction, and the personality trait level criteria that loaded most highly on the severity dimension were preoccupation with social rejection, fear of social ineptness, feelings of inadequacy, anger, identity disturbance, and paranoid ideation (20). The cross-cutting nature of these personality traits is suggestive of central disturbances of PDs of all types (21).

The complexity of treating individuals with greater severity of psychiatric disturbance is compounded by underlying features of interpersonal hypersensitivity among patients with PDs. Heightened rejection sensitivity, poor affect regulation, and intense interpersonal conflicts negatively impact consistent delivery of treatment (somatic and psychosocial). This is especially prominent among patients with BPD and has been proposed as a phenotype for the disorder (22). Not surprisingly then, interpersonal hypersensitivity is a contributor to frequent ruptures and is a likely underlying factor influencing high rates of premature termination among individuals with PDs. It is widely understood that individuals with personality disorders have higher rates of global service utilization (23). However, individuals with Cluster B personality disorders tend to have poorer treatment adherence and higher dropout than patients with other psychiatric disorders such as depression (24). A recent meta-analysis (25) of 669 studies including 83,834 patients found that dropout from treatment was greatest for patients with a personality disorder (25.6%). Higher rates of personality disorder criteria are also associated with higher dropout (26).

A literature review by members of the DSM−5 workgroup for personality and personality disorders revealed an overarching pattern of distorted and maladaptive thinking about oneself, and impaired interpersonal relationships as central, defining features of the personality disorders (21, 27). Numerous studies indicate that maladaptive patterns of mental representations form a common substrate of core impairments across personality disorders (28). Thus, internal working models that inform the individual's attachment style constitute an overarching domain of personality function that impacts the quality of relationships, including those with health care professionals (29).

Clinicians are familiar with the challenges of engaging patients with personality disorders due to their preset biases and assumptions about relationships. Psychiatrists and psychologists involved in a practice research network described five distinct enduring relational patterns in the psychotherapies of 181 patients with personality disorders engaged in long-term psychotherapy (30). Four of the five transference patterns described (angry/entitled, anxious/preoccupied, avoidant/counterdependent, and sexualized) are particularly problematic in maintaining a viable therapeutic alliance.

Examination of specific personality disorders reveals unique features that create challenges in providing medical and psychological care. For example, individuals with avoidant PD are burdened with a sense of self as defective and shame ridden, with expectations of being abandoned by others because of personal shortcomings and are thus more prone to limit contact, while those with obsessive–compulsive PD are burdened by a schema of self-imposed, unrelenting standards that tends to

subvert the importance of the other (31). Patients with paranoid PD typically view the self as weak and inadequate in the face of hostile and dangerous others (32). Patients with narcissistic PD have a predominant bias pervaded by distrust toward others and feeling excluded or harmed (33) and are prone to externalize and blame others for interpersonal conflict (34). By contrast, individuals with BPD have repeatedly been found to express and experience overelaborated and complex views of others with a particular bias toward hostile attributions of others' actions and intentions (35–37). This pattern has been observed in laboratory paradigms assessing neurological structure of social cognition and distrust (38). Recent findings from a study of adolescents with BPD traits demonstrate that overactive, inaccurate attributions represent a common pathway to BPD (39). As a result of these distorted representations of self and others, BPD patients have great difficulty creating a helpful mental image of treatment providers and the treatment relationship (40). This mistrust, combined with hypersensitivity to rejection and insecure attachment styles, creates significant challenges for establishing and maintaining a viable treatment alliance and reasonable adherence to a treatment model.

In addition to the complexities of forming and maintaining an alliance, deciding which of the many psychiatric disorders to approach first has proven to be a major conundrum for clinicians. APA practice guidelines emphasize single disorders and give preference to initial treatment of clinical syndromes such as anxiety and mood disorders. The American Psychiatric Association's Practice Guideline Watch for major depressive disorder (41) suggests strategies for treating patients with co-occurring conditions who are unresponsive to first-line agents, yet definitive evidence for "best practices" for co-occurring conditions is still unavailable. Thus there is limited guidance on which disorders to target first in the case of significant comorbidity. This is in part due to competing models of the etiology and relationship among the psychic disorders including the notion of hierarchies. One model poses that personality disorders such as BPD constitute an underlying dominant form of psychopathology that accounts for co-occurring depression, while a second model would suggest that BPD is better understood as an atypical presentation of severe biologically based depressive disorder. A third model emphasizes true independence of the two disorders and a fourth assumes overlapping etiological factors that predispose individuals with either disorder to develop the second.

A longitudinal study of symptom interactions found that between 60 to 70% of patients with depression and BPD demonstrated improvement when BPD symptomatology was the primary focus of treatment, followed by decreases in depression. Conversely, targeting mood and depression as the primary focus of treatment did not significantly impact BPD features subsequently (42). Of great importance was the fact that BPD criteria associated with affect instability, anger, emptiness, self-injurious behaviors, and psychotic experiences were most predictive of remission of depressive symptoms. Similar findings were reported in another longitudinal analysis of patients with dysthymia and BPD: improvement in BPD features was followed by reduction of dysthymic features but not vice versa (43). These studies indicate that BPD may represent an underlying dominant form of psychopathology that drives or is responsible for the expression of other disorders such as depression. The clinical implications are relatively clear in that treating borderline features early in treatment (especially features associated with affect instability) may bring about improvements in depression.

Psychotherapies that focus interventions on personality impairments reinforce the above findings more generally across PDs. A series of meta-analyses on the effectiveness of psychotherapy for treatment of personality disorders demonstrated that psychodynamic and cognitive behavioral psychotherapies of mid- to long duration were effective in reducing depression and the burden of global psychiatric symptoms, even when co-occurring disorders were present (44–46). There is far less evidence on the effectiveness of psychotherapies and medications in the treatment of specific PDs other than BPD; nonetheless, some evidence has emerged in the past decade (47). Effectiveness of dynamic and cognitive psychotherapy for avoidant personality disorder (AVPD) has been demonstrated. In this study, CBT proved to be superior to brief dynamic therapy in improving avoidance, social phobia, and obsessive symptoms (48). A long-term (52-week) form of CBT showed reductions in depression and personality symptoms at the end of treatment of patients with AVPD, and of patients with obsessive-compulsive personality disorder (OCPD) (49). Other studies have demonstrated a poorer response for individuals with AVPD compared with other Cluster C diagnoses (50) and greater relapse following treatment termination (51). Some evidence suggests that psychosocial treatment such as contingency management can be of limited benefit for patients with antisocial personality disorder (ASPD) and comorbid cocaine dependence (52), while a randomized controlled trial carried out in the

United Kingdom found that a combination of multisystemic therapy (MST) and youth offender teams was effective in reducing nonviolent criminal behavior at treatment termination and at 18-month follow-up in a cohort of adolescents (average age of 15) with emerging ASPD (53). What is abundantly clear is the fact that more systematic efficacy and effectiveness studies must be conducted involving patients with PDs, especially those PDs with relatively high prevalence rates such as AVPD, OCPD, and ASPD.

Psychotropic medications are prescribed for patients with PDs with substantial frequency, and some evidence supports symptom-targeted use of antidepressants, antipsychotics, and mood stabilizers to reduce impulsivity and aggression, and to a lesser extent to reduce psychotic-like symptoms and to improve cognitive deficits characteristic of schizotypy (54). Double-blind placebo-controlled trials have demonstrated some benefit of divalproex sodium for patients with Cluster B personality disorders who demonstrate impulsive aggression (55).

The vast majority of effectiveness and efficacy studies target BPD symptomatology, therefore more is known about effective treatment for this disorder. The American Psychiatric Associations guideline for treatment of BPD (56) and the subsequent guideline watch (57) confirm that psychotherapy represents the primary treatment for this disorder with adjunctive, symptom-targeted pharmacotherapy to mitigate severity of core symptoms. A persuasive review of data from approximately 24 randomized controlled trials of BPD (58) demonstrates clear and compelling evidence that several forms of psychotherapy help borderline patients decrease the frequency of self-destructive behaviors (59–65) as well as common secondary symptoms of depression, anxiety, and substance abuse (66–68). Recent evidence indicates that durable gains can be achieved with decreased suicide attempts and service use, improved global psychiatric functioning, and reduced ratings of borderline functioning at 5-years posttreatment with long-term mentalization-based treatment (59).

While no specific "brand" of treatment has clearly demonstrated superiority to date, several common factors have been identified in individual psychotherapies for BPD. Treatments that include a clear treatment framework, attention to affect and the treatment relationship, an active therapist, and exploratory and change-oriented interventions appear to be core features of effective treatments (69).

A number of studies indicate the adjunctive benefit of pharmacotherapy for patients with BPD. Several meta-analyses of pharmacotherapy of BPD indicate that drug treatment, especially with mood stabilizers and antipsychotics, may be effective for treating affective dysregulation and impulsive-behavioral dyscontrol (70, 71). A meta-analysis of randomized controlled trials suggests that drug treatment, especially with mood stabilizers and second-generation antipsychotics, may be effective for treating a number of core symptoms and associated psychopathology, but the evidence does not currently support effectiveness for overall severity of borderline personality disorder (71). A recent meta-analysis indicated that mood stabilizers significantly reduced anger, while antidepressants had a moderate effect on anger reduction but a small effect on depression. Antipsychotics had a moderate effect on anger (70). Antipsychotics have also been shown to be effective in reducing cognitive-perceptual symptoms (72). The clinical implications are relatively clear: pharmacotherapy should target specific symptoms such as affect dysregulation, but clinicians should not expect dramatic improvement in overall BPD symptomatology. While the majority of patients with BPD are prescribed psychotropic medications for sustained periods, caution is warranted because those with BPD are at greater risk of abusing prescription medications in psychiatric and general medical practices (73).

Further research is needed to validate the approach taken by the 2001 guideline to select one of three different medication algorithms on the basis of the predominance of cognitive-perceptual symptoms, affective dysregulation symptoms, or impulse dyscontrol symptoms. One retrospective report from the NIMH Collaborative Longitudinal Personality Disorders Study produced mixed results on this question (74).

Conclusions

Despite considerable confusion regarding the comorbidity puzzle inherent in the diagnosis and treatment of individuals with personality disorders, the last decade of research has yielded high-quality efficacy studies of psychotherapeutic and psychopharmacological approaches that demonstrate reduction in debilitating symptoms common to specific personality disorders as well as cross-cutting symptoms of suicide-related behaviors, hospitalization, and relapse. This evidence from high-quality randomized control trials is particular promising given the fact that most of the studies included patients with comorbid mood, anxiety, and substance use disorders. Unlike many efficacy studies conducted on a single disorder (75), treatment studies of personality disorders include patients with co-occurring disorders and are more realistic and therefore more generalizable to general populations.

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NOTES