Determining better ways to identify and treat individuals with co-occurring substance use disorders (SUDs) and other psychiatric disorders has become increasingly important from clinical, research, and policy perspectives. Several observations have driven this imperative: (1) Co-occurring SUDs with other psychiatric disorders are prevalent (Conway, Compton, Stinson, & Grant, 2006; Kessler et al., 1996; Regier et al., 1990; Swendsen et al., 2010) and associated with worse clinical and functional outcomes than either SUDs or other psychiatric disorders alone (Hser et al., 2006; Mueller et al., 1994; Ritsher et al., 2002); (2) many people with these co-occurring disorders do not receive adequate treatment (Substance Abuse and Mental Health Services Administration [SAMHSA], 2002); and (3) compared to psychiatric patients without co-occurring SUDs, patients with co-occurring disorders tend to use more costly treatments such as emergency and hospital care (Dickey & Azeni, 1996; Mark, 2003). Together, these observations have led to the development of specific new treatments designed or adapted for this population.

Within SUD populations, multiple SUDs are common (Conway et al., 2006; Kessler et al., 1997; Regier et al., 1990; Swendsen et al., 2010). While these individuals also may be considered “dually diagnosed,” this chapter focuses exclusively on patients who have an SUD plus a non-SUD co-occurring psychiatric disorder. We refer to non-SUD psychiatric disorders simply as “psychiatric disorders” to distinguish them from SUDs. Additionally, this chapter excludes co-occurring nicotine dependence and psychiatric disorders, a topic that is important and broad enough to require independent attention (Ziedonis et al., 2008; see Chapter 6, this volume).
In this chapter, we review psychosocial and psychopharmacological treatments for patients with co-occurring SUDs and other psychiatric disorders.

EPIDEMIOLOGY

Studies in SUD and psychiatric treatment-seeking populations (McLellan & Druley, 1977; Ross et al., 1988) have suggested high prevalence rates of co-occurring SUDs and psychiatric disorders. However, treatment-seeking samples may not be representative of community populations, since they tend to have higher rates of comorbidity and may have more severe manifestations of the disorder for which they are seeking treatment. Thus, epidemiological studies of prevalence rates in community populations are important in assessing the true comorbidity prevalence rate.

The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) is the largest and most recent study to date that examines the epidemiology of SUDs and co-occurring psychiatric disorders in a community sample. Conducted in 2001–2002, with a follow-up reinterview wave carried out in 2004–2005, NESARC specifically sought out data on co-occurring conditions, asking questions about alcohol, tobacco, and other substance use, along with inquiries on psychiatric/psychological disorders, family history and medical conditions, and gambling, among others. Data were collected from randomly selected individuals based on household data from the 2000 Census, with an 81% response rate. NESARC results demonstrate that SUDs and psychiatric disorders are commonly co-occurring in community populations (Compton et al., 2007; Hasin et al., 2007; Hasin & Kilcoyne, 2012). When adjusted for other sociodemographic factors, lifetime alcohol use disorder was significantly associated with mood disorders (odds ratio [OR] = 2.4), anxiety disorders (OR = 2.3), and personality disorders (OR = 2.8). Likewise, 12-month and lifetime drug use disorders were significantly associated with alcohol use disorders, nicotine dependence, and mood, anxiety, and personality disorders (ORs = 2.2–9.0).

The two previous major psychiatric epidemiological studies, the Epidemiologic Catchment Area (ECA) study (Regier et al., 1990) and the National Comorbidity Study (NCS), carried out from 1990 to 1992 (Kessler et al., 1996), similarly demonstrate that co-occurring SUDs and psychiatric disorders are prevalent in community populations. Methodological advancements of the NCS included an expanded scope of the community sample (e.g., the ECA sampled from within five U.S. communities; the NCS sampled nationally representative households) and an advanced version of the Diagnostic and Statistical Manual of Mental Disorders (i.e., DSM-III-R; American Psychiatric Association, 1987). Also, while both studies surveyed most of the more common psychiatric disorders, the ECA did not include posttraumatic stress disorder (PTSD), whereas the NCS did. Neither epidemiological survey included Axis II disorders other than antisocial personality disorder. Despite these limitations and differences between the two studies, their results were often qualitatively similar, although the magnitude of their estimates differed somewhat at times. Among persons with psychiatric disorders, the ECA estimated that 30% had a co-occurring SUD. The prevalence varied by diagnosis, however; co-occurring SUDs were most common in individuals with antisocial personality disorder, followed by those with...
bipolar I disorder. In SUD populations, the ECA and NCS estimated that over half would experience psychiatric disorders in their lifetime. These lifetime estimates do not merely reflect rare or historical periods in an individual's history; the 12-month comorbidity prevalence rate of these disorders was also quite high. For example, the NCS estimated that over 33% of those with bipolar disorder experienced an SUD within 12 months, followed by nearly 20% of those with major depression and 15% of those with an anxiety disorder. From 2001 to 2003, a substantial portion (87.6%) of the NCS study population was reinterviewed in the National Comorbidity Survey-2 (NCS-2; Swendsen et al., 2010), allowing for updated diagnostic assessments (i.e., based on DSM-IV-TR; American Psychiatric Association, 2000) and demonstrating significant prospective risks posed by baseline mental disorders for the onset of SUDs in the follow-up time frame.

In Australia, the 2007 National Survey of Mental Health and Wellbeing (NSMHWB) revealed similarly high rates of comorbidity compared to the U.S. surveys, with 25.4% of individuals with an anxiety, affective, or SUDs having at least one other class of disorder (Teesson, Slade, & Mills, 2009). In particular, the NSMHWB estimated that individuals with an alcohol use disorder were more than twice as likely to have an anxiety disorder and were 4.5 times more likely to have any mental disorder compared to the rest of the sample (Teesson et al., 2010).

THE RELATIONSHIP BETWEEN SUBSTANCE ABUSE AND PSYCHOPATHOLOGY

While determining which disorder is primary in patients with co-occurring SUDs and psychiatric disorders can be useful in clinical research, it may provide little benefit in the clinical management of these patients. Patients with two disorders typically require treatment for both. In patients with co-occurring cannabis dependence and psychosis, for example, it is interesting scientifically to consider whether cannabis use led to the development of psychopathology or vice versa (Moore et al., 2007), but clinically, patients require both SUD and psychiatric treatment to be helped most effectively. On the other hand, the exception is patients who present with temporary psychiatric symptoms caused by the substance use or its withdrawal, which resolve with treatment; an example of this would be psychosis induced by methamphetamine use (Grelotti, Kanayama, & Pope, 2010).

Meyer (1986) offered a now-classic framework to consider six possible ways in which SUD and other psychopathology may be related:

1. Psychopathology may be a risk factor for SUDs. As described previously, studies of patient and community samples indicate that the risk of having a co-occurring SUD is elevated in persons with psychiatric disorders. For example, dopaminergic dysfunction in patients with schizophrenia has been hypothesized to increase their risk of SUDs—particularly cocaine use disorders (Green et al., 1999; Smelson et al., 2002b). Another theory, widely known as the “self-medication hypothesis” (Krantzian, 1989, 1997; Krantzian & Albanese, 2008), suggests that psychopathology leads patients to use substances in an attempt to decrease unwanted psychiatric symptoms.
SPECIAL POPULATIONS

...state that over half the lifetime estimates do not fit the 12-month criterion; the 12-month criterion is used in the text. For example, the
...of SUDs, depression and 15% of SUDs and MDD. The remaining portion (87.6%)
...Hospital (2000) and demonstrate links between depression and SUDs for the onset
...health and wellbeing, compared to the U.S. general population. In particular, the
...frequency of mental health disorders were more than twice as likely to have any
...SUDs (Bowers et al., 2010).

Co-occurring SUDs and psychiatric disorders typically lead to a negative cycle of dependence and psychiatric symptoms. Whether cannabis use causes depression or vice versa (Moore et al., 2011) has been debated. Treatment of psychiatric disorders may help patients who present with SUDs, or its withdrawal, may exacerbate psychiatric symptoms induced by substance use disorder.

One possible way in which SUDs may contribute to psychiatric disorders is through dopaminergic mechanisms. Studies have shown that drugs of abuse, such as amphetamines, can increase dopamine levels, which may lead to increased reward-seeking behaviors and decreased sensitivity to negative consequences. This can contribute to the development of psychiatric disorders such as addiction and depression.

For example, a patient with insomnia due to PTSD nightmares may use alcohol or marijuana to induce sleep. Although research has not found direct connections between particular psychopathological symptoms and specific substances (rather, patients tend to misuse a wide variety of substances to "treat" a range of symptoms), the general principle is an important one. It is discussed in more detail in the next item.

2. Psychiatric disorders and co-occurring SUDs may serve to modify the course of each other in terms of symptomatology, rapidity of onset, and response to treatment. Also, as we described more below, there is considerable evidence that comorbidity is associated with worse outcomes. For example, there is evidence that patients with schizophrenia and co-occurring SUDs do not respond as well to similar doses of first-generation antipsychotic medications as those without SUDs (Bowers et al., 1990).

3. Psychiatric symptoms may result from chronic intoxication. Drug and alcohol use can result in a variety of psychiatric symptoms, such as depression, anxiety, euphoria, psychosis, and dissociative states. Most such symptoms disappear, however, within hours (e.g., cocaine-induced paranoia; Satel et al., 1991) to weeks (e.g., alcohol-induced anxiety or depression; Brown et al., 1991; Brown & Schuckit, 1988).

4. Long-term substance use can lead to psychiatric disorders that may not remit. Alcohol-induced, long-term cognitive changes, such as those seen in alcohol-induced persisting dementia, exemplify one way in which chronic use of a substance can create enduring change.

5. Substance abuse and psychopathological symptoms may be meaningfully linked. Some individuals may use alcohol or drugs in ways that enhance their psychiatric symptoms. For example, patients with antisocial personality disorder who seek disinhibition and aggression may use alcohol or cocaine, and patients with bipolar disorder may use cocaine or other stimulants to augment a euphoric mood (Weiss et al., 1986, 1988).

6. The SUD and psychiatric disorder may be unrelated. The presence of two disorders within an individual does not imply a causal link. For example, both alcohol dependence and depressive disorders are common in the general population; many people with both disorders are not depressed because they drink, nor do they drink because they are depressed. As another example, Brunette et al. (1997) studied the relationship between severity of substance abuse and severity of schizophrenic symptoms in patients diagnosed with both disorders, and found weak relationships and no consistent patterns of relationships between the two sets of symptoms.

The "Self-Medication Hypothesis"

One potential explanation for the increased prevalence rate of co-occurring SUDs among patients with psychiatric disorders has been the "self-medication hypothesis" (Krantzian, 1985, 1997; Krantzian & Albanese, 2008), which postulates that certain drugs may be particularly reinforcing for particular patients because of their specific psychopathology.
Two fundamental assumptions underlie this hypothesis: first, that substances are abused to relieve psychological pain, not just to create euphoria; and second, that there is specificity between patients' 'drug of choice' and the particular intolerable emotions or symptoms that they are attempting to alleviate. For example, patients with social anxiety may be drawn to alcohol to decrease their symptoms, while patients who are prone to violence and anger outbursts may prefer the calming effects of opioids to the potentially disinhibiting effects of alcohol. Another recently discussed example might be the high prevalence of nicotine use in patients with schizophrenia, who might be drawn to smoking cigarettes (due to biological predispositions based on alterations in nicotinic acetylcholine receptors) as a way to modulate antipsychotic medication side effects or to self-medicate negative symptoms and cognitive deficits (Dalack et al., 1998; Winterer, 2010).

A major criticism of the self-medication hypothesis has been its heavy reliance on anecdotal data from patients in psychotherapy and the relative paucity of empirical studies testing it (Aharonovich et al., 2001). Additionally, intoxicants may produce very different effects acutely compared to the effects of chronic administration. Studies of individuals with heroin (Meyer & Mirin, 1979), cocaine (Post et al., 1974), and alcohol (Mendelson & Mello, 1966) use disorders have indicated a dichotomy between the acute effects of these drugs in producing euphoria or tension relief and the chronic or high-dose effects in producing dysphoria. Several researchers have sought to test empirically the self-medication hypothesis in larger samples. The results have tended not to support the specificity of using a particular addictive substance to alleviate specific psychopathology or mood states (Aharonovich et al., 2001; Weiss, Griffin, et al., 1992). However, while not necessarily a validation of the theory that patients use addictive substances to alleviate certain mood states, there is evidence that treating a co-occurring psychiatric disorder (Cornelius et al., 1997; Greenfield et al., 1998) and remission of its symptoms (Hasin et al., 1996) can improve SUD outcomes.

Other Theories

Weiss (1992) suggests three additional mechanisms by which psychopathology can make an individual more vulnerable to SUDs.

1. Psychopathology may interfere with an individual's judgment or ability to appreciate consequences. Individuals with psychiatric disorders may be more vulnerable to SUDs, because the impaired judgment that is often present in many psychiatric syndromes can interfere with one's ability or willingness to understand or change one's behavior. For example, severely depressed patients may have insight regarding the destructive effect of their drinking but continue to drink due to the pessimism about the possibility and value of change that is part of their depressive disorder. Similarly, the recklessness, irritability, and grandiosity of patients with mania or hypomania may interfere with their capacity to appreciate the harmful nature of their substance use.

2. Psychopathology may accelerate the process of substance dependence by leading to more dysphoria either during chronic use or early abstinence. It is possible

3. Psychopathology may facilitate the use of substance use to avoid some severe mood symptoms. It may be that patients with chronic substance use disorders or alcohol use disorders manifest some evidence of increased mood symptoms. For example, some patients with SUDs may experience more severe mood symptoms when they are not using substances, and when they resume using substances they feel it facilitates some symptoms of schizophrenia and paranoia (Aharonovich et al., 2001). Thus, multiple theories may be at play in the maintenance of problem behaviors.

DIAGNOSING patients WITH SUDs

The task of determining whether a patient has a co-occurring psychiatric disorder or an independent mood disorder is a well-studied (Mood and Anxiety Disorders Task Force, 2000) and complex one. It is necessary to determine whether the use of substances is due to intoxication or withdrawal, or whether the substance use is the manifestation of a mood disorder or a comorbid psychiatric disorder that occurs independently. Moreover, it is important to determine whether the diagnosis of alcohol or drug dependence, the major axis diagnosis, results in the manifestation of a mood disorder or whether it is the reverse. In this section, we will discuss the criteria for making a diagnosis of a mood disorder in a patient with a SUD.

Given these considerations, it is important to determine whether the patient is truly suffering from a separate and independent mood disorder or whether the patient is suffering from a mood disorder due to the use of substances. It is also important to determine whether the patient is suffering from a mood disorder due to the use of substances or whether the patient is suffering from a mood disorder due to the presence of a psychiatric disorder. It is also important to determine whether the patient is suffering from a mood disorder due to the presence of a psychiatric disorder or whether the patient is suffering from a mood disorder due to the presence of a psychiatric disorder and the use of substances.

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that substances are associated with intolerable emotions, for example, patients with chronic pain, while patients with mood disorders may experience the calming effects of drugs. Furthermore, substances recently discussed in the context of schizophrenia, their interactions, and dispositions based on their ability to modulate antipsychotic medications and cognitive deficits.

The heavy reliance on substances and the paucity of empirically validated antipsychotic treatment options for schizophrenia (Post et al., 2005) have indicated a need for interventions that address affect or tension regulation in schizophrenia. Several research findings have been based on larger samples. Notably, a recent study (Marinovich et al., 2012) suggests that in particular addictive diseases, such as nicotine or alcohol, a validation of the role of substance use in maintaining mood states, particularly in schizophrenia (Cornelius et al., 2011; Schuman et al., 1996) can

Psychopathology can

be a crucial factor in determining or ability to engage in treatment. However, substance use can be a barrier to understanding or engaging in treatment. In many psychiatric disorders, the ability to understand or manage one's own behavior may be impaired due to the persistent effects of their depressive symptoms. In some cases, patients with mania may experience the harmful nature of substance use.

Dependence by Substance. It is possible

to recognize that patients with underlying psychopathology may experience more dysphoria from chronic substance use or more severe withdrawal symptoms when discontinuing drugs or alcohol. Although this potential mechanism has received little study, there is some evidence that cocaine abusers with major depressive disorder may report more severe mood symptoms during abstinence compared to cocaine abusers without depression (Gawin & Kleber, 1986).

3. Psychopathology may reinforce the social context of drug use. Some patients with severe psychiatric illness may be drawn to a drug-using subculture because they feel it facilitates socialization or a new peer group. For example, some patients with schizophrenia have described using substances to socialize or be accepted by peers, even though substances increased the risk of psychosis (Drake et al., 1989; Spencer et al., 2002).

Thus, multiple possible motivations and causes contribute to the initiation and maintenance of problematic alcohol and drug use in patients with psychiatric disorders.

DIAGNOSING PSYCHIATRIC DISORDERS IN PATIENTS WITH SUDs

The task of determining whether a patient is suffering from a substance-induced disorder or an independent psychiatric disorder can be complicated and has not been well-studied (Mora et al., 2012; Torrens et al., 2011). Substances of abuse can cause a wide range of psychiatric symptoms. Clinicians evaluating such patients need to determine whether the disturbance is independent of substance use or related to intoxication or withdrawal. For example, when examining a patient who has a long history of alcohol dependence and depressive symptoms, it can be difficult to determine whether the depressive symptoms result from the direct pharmacological effects of alcohol, the many losses experienced as a result of the alcohol use, feelings of discouragement about the inability to stop drinking, or an independent mood disorder. Other etiologies, such as metabolic disturbances, head trauma, and personality disorders, must also be considered in the differential diagnosis of depressive symptoms in alcohol-dependent patients (Jaffe & Ciraulo, 1986). In a recent study, Torrens et al. (2011) compared risk factors for substance-induced versus independent psychiatric disorders in a population with co-occurring SUDs and psychiatric disorders. They found that mood and anxiety disorders were more likely to be independent. Subjects recruited from nontreatment setting were more likely to have substance-induced disorders than were subjects recruited from a treatment setting (OR = 3.5).

Given these considerations, one could ideally establish diagnostic rules to assist in determining whether a psychiatric syndrome is due to substance use or represents a separate and independent disorder. For example, some clinicians may establish a rule that a patient must be abstinent from alcohol and drugs for at least 4 weeks before one can make a diagnosis. Unfortunately, one does not always have the luxury of observing such lengthy abstinent periods (either by historical report or in the present) in which to assess this. In such circumstances, guidelines, as opposed to strict
rules, can be helpful. For example, several studies have observed that for alcohol-dependent patients with major depressive disorder, treating the depression can have a positive impact on drinking (Cornelius et al., 1997; Greenfield et al., 1998). Thus, while DSM-5 (American Psychiatric Association, 2013) criteria for substance-induced depressive disorder suggest at least 4 weeks of symptom persistence during abstinence before a clinician can diagnose an independent depressive disorder, it also notes that clinicians can diagnose an independent disorder if other convincing factors are in place (e.g., a history of recurrent non-substance/medication-related episodes or symptoms that preexisted before onset of substance use). Certain disorders, such as eating disorders and PTSD, can be diagnosed readily, even in the context of substance use or withdrawal, since their symptoms do not closely resemble substance-related syndromes. Indeed, for a diagnosis such as PTSD, which tends to be underdiagnosed in patients with SUDs, the greater danger is to delay diagnosis; waiting for a period of abstinence may prevent needed treatment for the co-occurring disorder (Najavits, 2004).

Finally, clinicians should consider whether the patient’s symptoms are what would be expected upon discontinuation of the abused substance. If there is considerable overlap between the observed symptoms and what one would expect from the drug discontinuation syndrome, then the clinician should wait until (1) the symptoms resolve, or (2) no longer are consistent with what would be expected with drug cessation (i.e., the syndrome one would expect to see after 1 week versus 1 month of alcohol abstinence). Alternatively, if there is little overlap between the symptoms observed and the expected abstinence syndrome (e.g., bulimia nervosa in an opioid-dependent patient), then the diagnosis can be made without waiting for an extended abstinence period.

**DIAGNOSING SUDs IN PATIENTS SEEKING TREATMENT FOR PSYCHIATRIC DISORDERS**

Co-occurring SUDs are often overlooked in patients seeking treatment for psychiatric disorders. The first step in the accurate diagnosis of SUDs is systematically to ask the patient about the presence of substance use. Structured clinical assessments have been demonstrated to improve detection of SUDs compared to routine assessment in outpatient severe and persistently mentally ill (SPMI; Breakey et al., 1998) and inpatient (Albanese et al., 1994) populations; they have also outperformed urine toxicology testing (Albanese et al., 1994). Unfortunately, the increasing acuity of patients on inpatient units and the demanding time constraints of outpatient psychiatric practice (Woodward et al., 1991) may pose challenges to the systematic assessment of SUDs. In one outpatient study, combining multiple standardized clinical instruments improved rates of detection but raised similar concerns about time constraints of routine clinical work and resultant underdetection (Wusthoff et al., 2011). In another outpatient study, adding the four-item CAGE (Cut down, Annoyed, Guilty, Eye-opener) Questionnaire (Ewing, 1984) improved the sensitivity of detecting SUDs from 62 to 97% in an SPMI population (Breakey et al., 1998). However,

self-report alone, alongside other methods of assessment is necessary (Landsman et al., 1989; Cornish et al., 1997).

Finally, continued monitoring of the patient’s response to treatment, especially if the patient reports no negative consequences of substance use in the treatment setting, will be negative consequences for the patient’s future treatment setting, and will probably lead to lesser adherence to the treatment and benefitting from that treatment.

**TREATMENT OF SUDs AND OTHER PSYCHIATRIC DISORDERS**

Association between SUDs and Psychotic Disorders

In both SUD and non-SUD populations, co-occurring SUDs and psychotic disorders co-occur in their “singly diagnostic” forms (Najavits et al., 2002). Evidence is mixed, such as in the case of depression and substance use (Rounsaville et al., 1996). The effects of SUD type on the prevalence of a co-occurring psychiatric disorder is worse for alcohol outpatients (Albanese et al., 1994) and evidence for its prevalence is lacking (Najavits et al., 2002).

There is also evidence that co-occurring SUDs and depression in men (Compton et al., 1996; Rounsaville et al., 2003; Rounsaville and Fischman, 1996; Pöpper et al., 2015) has been associated with an increased risk of suicide and co-occurring psychotic disorders. For women, except for phobia and avoidant disorder (Compton et al., 1996), the evidence is mixed (Najavits et al., 1987).
self-report alone, without urine toxicology, can also lead to underdetection of substance use (Claassen et al., 1997).

Finally, contingencies play an important role in patients' willingness to self-report substance use. If patients are repeatedly encouraged to be honest in their self-reports, and if they are told (and more importantly, if they believe) that there will be no negative consequences of reporting use (e.g., being discharged from a treatment program or reported to a probation officer or employer), then they are more likely to be forthcoming in reporting their use. If, however, they are concerned that there will be negative consequences, then they are less likely to do so. Thus, self-reports of use in an emergency department, where a patient is unlikely to know the clinician and will probably not believe (whether it is true or not) that there will be no negative consequences for disclosing use, are likely to be suspect. However, in an outpatient treatment setting, in which a patient has an opportunity to build a relationship with a clinician or treatment team, and perhaps sees other patients self-disclosing and benefiting from that disclosure, self-reports are likely to be more valid (Weiss et al., 1998).

TREATMENT OF PATIENTS WITH CO-OCurring SUDs AND OTHER PSYCHIATRIC DISORDERS

Association between Co-Occurring Disorders and Treatment Outcome

In both SUD and psychiatric treatment-seeking populations, patients with co-occurring SUDs and psychiatric disorders typically experience worse outcomes than their “singly diagnosed” peers (Ritsher et al., 2002; Schaar & Ojeheggen, 2001; Najavits et al., 2007). However, there are specific populations in which the evidence is mixed, such as populations with SPMI (Farris et al., 2003; Gonzalez & Rosembeck, 2002) and antisocial personality disorder (Cacciola et al., 1995; Kranzler et al., 1996). The effect of other psychiatric disorders on SUD outcomes may vary by SUD type. For example, whereas co-occurring major depression appears to predict worse alcohol outcomes (Brown et al., 1998; Greenfield et al., 1998), there is less evidence for its predicting worse cocaine outcomes (McKay et al., 2002; Rohsenow et al., 2002).

There is also evidence (albeit somewhat inconsistent) that gender may play a role in mediating the effect of co-occurring psychiatric disorders on SUD outcome. Major depression in men has been associated with worse SUD outcome (Compton et al., 2003; Rounsaville et al., 1987), although this is not a consistent finding (Kranzler et al., 1996; Powell et al., 1992). In contrast, some studies suggest that female gender has been associated with similar or better SUD outcomes among patients with co-occurring psychiatric disorders (Compton et al., 2003; Rounsaville et al., 1987), except for phobia, which was associated in one study with worse SUD outcome in women (Compton et al., 2003). Finally, whereas antisocial personality disorder in men has been associated with worse outcomes (Compton et al., 2003; Kranzler et al., 1996), the evidence in women has been mixed (Compton et al., 2003; Rounsaville et al., 1987).
A Heterogeneous Population

Since patients with co-occurring disorders comprise a heterogeneous population, it follows that their treatment should perhaps reflect that heterogeneity (Weiss, Mirin, et al., 1992); a “one size fits all” approach therefore will likely not be optimal. However, providing group treatments tailored to patients with some degree of diagnostic homogeneity (e.g., patients with bipolar disorder and SUDs) can be a difficult strategy to implement if one is unable to recruit a large enough clinical population for these groups. Similarly, even within diagnostically homogeneous groups, considerable heterogeneity in illness severity and functioning may still exist. Ries et al. (1997) have suggested a conceptual approach that divides patients with co-occurring SUDs and psychiatric disorders into four major subgroups, according to the severity (i.e., major or minor) of each disorder. Although this is a somewhat crude way to classify patients, it may be helpful in developing an outpatient group treatment program for patients with co-occurring disorders.

An additional consideration is that not all patients are similar in terms of insight regarding their SUD, nor are they similarly ready to address it. Thus, patients who cannot decide whether to address their substance use may do better in a group focused on resolving that issue, as opposed to a group in which all participants are actively engaged in treatment and making lifestyle changes to support sobriety. We know of no studies, however, that have tested this idea empirically. It is possible, for example, that having a mix of patient severity levels in one group gives patients the opportunity to learn from those further along in their recovery. This is a central principle of Alcoholics Anonymous, and it appears to have strong anecdotal support. Treatments that focus on particular co-occurring diagnoses (e.g., bipolar patients with SUDs) also have not been directly compared to more general thematic groups (e.g., co-occurring disorder groups that are more general, encompassing a wide variety of diagnoses). Thus, it remains an empirical question how the heterogeneity of patients with co-occurring SUDs and psychiatric disorders should best be addressed within the realistic constraints of specific clinical settings.

Sequential, Parallel, and Integrated Treatment Models

There are three major models in which patients with co-occurring SUDs and psychiatric disorders are treated: sequential, parallel, and integrated treatment. We discuss each below.

In sequential treatment, the more acute condition is treated first, followed by the less acute co-occurring disorder. Often, this sequential approach is attempted when one condition is perceived to be more acute than another. Sometimes, however, it may occur because of the perception that one condition is secondary to another, that staff may not be trained to treat it, or because the condition is perceived as iatrogenic and must be addressed at the start of treatment. Historically, PTSD was perceived in these ways until quite recently, for example (Najavits et al., 2008). When sequential treatment does occur, the same staff may treat both disorders or the second disorder may be treated after transfer to a different program or facility. For example, a patient with mania and a cocaine use disorder needs mood stabilization before initiating substance abuse treatment and withdrawal delirium, then antidepressant medication. In other cases (i.e., when the delirium is acute), treatment has the patient with the acute disorder, a term referred to different treatment programs or facilities.

In parallel treatment, the same treatment team provides the addiction treatment. Typically, staff members have different levels of expertise, but new co-occurring disorder treatment programs may be confusing to the patient. In SUD treatment, both addiction depression and anxiety, the clinician may choose to treat in psychiatric programs, but not stress its potential.

Unfortunately, different experiences of programs may provide insight into substance use and attempt to integrate circumstances, patients present the information.

In integrated treatment setting, and integrated treatment programs, fostered by the described earlier.

Integrated Behavioral with Co-Occurring Disorders

Integrated psychological interventions with co-occurring severe and persistent disorders (Brown et al., 1997; Weiss, Mirin, et al., 1992; Ball, 1998; Linhares, et al., 2001; Najavits et al., 2009). With suicidal patients (Ejek et al., 1999).
substance abuse treatment. Conversely, a patient with major depression and alcohol withdrawal delirium is not in a position to discuss treatment adherence to antidepressant medication. Instead, this issue is best addressed when the patient is more stable (i.e., when the delirium has been fully treated and has subsided). Although sequential treatment has the advantage of providing an increased level of attention to the more acute disorder, a typical disadvantage of this model is that patients are often transferred to different clinicians to address the less acute disorder, and the interrelationship between the two disorders may never be adequately addressed.

In parallel treatment, both disorders are treated simultaneously, but not by the same treatment team. For example, a patient may receive treatment for an SUD in an addiction treatment program and for a psychiatric disorder in a mental health clinic. Typically, staff members of each program are very well-versed in their own areas of expertise, but not in the other. However, major cross-training efforts relative to co-occurring disorders have improved this situation in the past decade. The different treatment programs may also have different treatment philosophies, which may be confusing to the patient (Mueser et al., 1992; Ridgely et al., 1990). For example, in SUD treatment programs, clinicians may attribute psychiatric symptoms (e.g., depression and anxiety) to substance use; when a patient attempts to obtain relief, the clinician may view this as “drug-seeking” behavior. Alternatively, staff members in psychiatric programs may tend to minimize the importance of substance use and not stress its potential negative consequences.

Unfortunately, patients treated in parallel or sequential programs often have different experiences based on the treatment settings they enter. The two different programs may provide patients with different feedback on the relationship between their substance use and psychological symptoms. Patients in these situations are then left to attempt to integrate these sometimes disparate approaches themselves. In these circumstances, patients may be accused of “manipulating” and “splitting staff” when they present information obtained in one program that is contradictory to another.

In integrated treatment, the management of both disorders occurs in one treatment setting, and the same clinician or team of clinicians manages both illnesses. Integrated treatment has become increasingly interesting to researchers and clinicians, fostered by the belief that it is more effective than the other treatment models described earlier.

**Integrated Behavioral Therapies for Patients with Co-Occurring Disorders**

Integrated psychosocial treatments have been developed for diverse patient populations with co-occurring SUDs and psychiatric disorders, including patients with severe and persistent mental illness (Drake et al., 2001; McHugo et al., 1999), depression (Brown et al., 2006; Lydecker et al., 2010; Cornelius et al., 2011); bipolar disorder (Weiss et al., 2000, 2007, 2009; Weiss & Connery, 2011), personality disorders (Ball, 1998; Linehan et al., 2002), and anxiety disorders such as PTSD (Brady et al., 2001; Najavits et al., 1998; Najavits, 2002; Mills et al., 2012), obsessive–compulsive disorder (Fals-Stewart & Schafer, 1992), social phobia (Randall et al., 2001), and suicidal patients (Esposito-Smythers et al., 2011). We describe here some examples...
of the many interventions developed, limiting our discussion to treatments with an
evidence base of at least one randomized controlled clinical trial, in an effort to be
illustrative rather than comprehensive.

**Integrated Group Therapy**

Integrated group therapy (IGT) for bipolar disorder and substance abuse, developed
by Weiss and Conner (2011) and colleagues (Weiss et al., 2000, 2007, 2009), is
a manual-based group psychotherapy based on cognitive-behavioral therapy (CBT)
principles, intended for patients with co-occurring bipolar disorder and SUDs, and
focused on the relationship between mood symptoms and substance use or abstinence.
Arranged around a “central recovery rule” of maintaining abstinence and adherence
to prescribed medications, IGT takes into account the essential link between these
two behaviors in this traditionally difficult-to-treat population. IGT has had three
positive trials, including two randomized controlled trials (RCTs) in which it out-
performed standard group drug counseling (Weiss et al., 2000, 2007, 2009); in the
most recent study, IGT led to decreased substance use, increased likelihood and rate
of achieving abstinence, and increased rates of “good clinical outcome,” a composite
measure of substance use and mood simultaneously (Weiss et al., 2009).

**Seeking Safety**

Seeking Safety (SS; Najavits, 2002; Najavits et al., 1998) involves a phase-based
framework for PTSD and SUD recovery in which safety is defined the first stage
of treatment. In SS, safety is the overarching goal: helping clients attain safety in
their relationships, thinking, behavior, and emotions. It is a present-focused, CBT
approach focused on psychoeducation and coping skills, and designed for flexible
use: group or individual format; both genders; all settings (e.g., outpatient, inpatient,
residential); all types of trauma and substances; and any clinician. It offers up to 25
topics, each representing a safe coping skill, such as Asking for Help, Compassion,
Setting Boundaries in Relationships, Taking Good Care of Yourself, Creating Mean-
ing, Coping with Triggers, Healing from Anger, and Detaching from Emotional Pain
(Grounding). The topics can be conducted in any order, using as few or as many as
are possible within the available time frame. It strives to be emotionally engaging,
with simple, humanistic language, a quotation to start each session, and interactive
exercises (for additional details, see the website www.seekingsafety.org). SS has
had positive outcomes in RCTs including male veterans (Boden et al., 2012) and
adolescent girls (Najavits et al., 2006), and is the only model thus far to outperform
a control on both PTSD and SUDs (see Najavits & Hien, 2013, for a review of the
points covered here). Studies of full-dose SS have shown more positive outcomes than
partial-dose SS. The largest study of SS to date was conducted as part of the National
Institute on Drug Abuse Clinical Trials Network. That study, despite being a partial-
dose of SS (less than half the model) found that at end of treatment SS outperformed
the comparison of Women’s Health Education (WHE) on therapeutic alliance, HIV
risk, and eating disorder symptoms, as well as eight out of nine secondary analyses
focused on subsamples of the study (including heavy stimulant users and alcohol
misusers) (Ruglass et al., 2011). Patients improved; SUDs were less likely to see a
treatment at baseline, and a smaller group of PTSD severity. In light of recent consensus
studies, it has not outperformed led to greater PTSD—SUD sample size (Hien, Lam, Uhr et
Dam, Ehring, Vedel et al., 2013).

**Integrated Dual Diagnosis Treatment**

Integrated dual diagnosis treatment mental health and substance use disorders involves
cross-trained clinicians providing comprehensive care in a collaborative 
community outpatient or day treatment setting. There is currently no stage of recovery
(entry, early, late) to the provision of a wide range of interventional interventions
for schizophrenia and SUDs (Morrens et al., 2011).
treatments with an effect size, in an effort to improve outcomes for patients with substance use or abstinence.

Integrated Dual Disorders Treatment

Integrated dual disorders treatment (IDDT; Drake et al., 2001) focuses on providing mental health and SUD treatment concurrently by a team of interdisciplinary, cross-trained clinicians within the same setting. Additional features include assertive community outreach; stage-wise interventions that are determined by the client’s stage of recovery (engagement, persuasion, active treatment, and relapse prevention); provision of a wide range of ancillary services; time-unlimited services; and motivational interventions. The model has had various positive outcomes for patients with schizophrenia and SUD, when compared to treatment as usual (TAU), for example (Morrens et al., 2011).

Dialectical Behavior Therapy

Dialectical behavior therapy (DBT) is a CBT approach designed for patients with borderline personality disorder. It has four key modules: mindfulness, distress tolerance, emotion regulation, and interpersonal effectiveness. It uses a conceptual approach from applied behavior analysis, “chain analysis,” to identify sequential events that form the behavior sequence. It relies on a combination of group therapy, individual therapy, and, for the clinician, peer supervision and support. DBT organizes treatment into stages and targets that are strongly adhered to so as to promote effective outcomes, first addressing behaviors that could lead to the patient’s death (e.g., suicide), then behaviors that could lead to premature termination from therapy, then behaviors that destroy the quality of life, and then addressing the need for alternative skills. DBT for substance abusers (Dimelf & Linehan, 2008) is a modified version of DBT for patients with SUDs to promote abstinence and reduce relapse. There have been numerous research studies of DBT, including a meta-analysis that found moderately positive effects for the model; it has been studied in some SUD samples as well, with modest positive results (Linehan et al., 1999, 2002; Harned et al., 2008; Dimelf & Linehan, 2008; see also www.behavioraltech.org).

Motivational Interviewing/Motivational Enhancement

Motivational interviewing (MI), developed by Miller and Rollnick (1991, 2002), utilizes theory derived from several psychotherapeutic models: systems, client-centered, CBT, and social psychology. MI is also called “motivational enhancement therapy” (MET), because it is often a brief treatment, conducted in as few as two sessions,
sometimes aimed at helping the patient accept other psychotherapy (e.g., CBT). Guidelines for modifying MI in patients diagnosed with SUDs and psychotic disorders have been published (Carey et al., 2001; Martino et al., 2002). Recent randomized controlled trials of MI in diverse populations with co-occurring disorders suggest that MI may improve the likelihood of making the transition to outpatient treatment (Swanson et al., 1999), improve SUD outcomes (Graeber et al., 2003), and decrease psychiatric hospitalization (Daly & Zuckoff, 1998). A recent review on the application of MI to various mental health disorders co-occurring with SUDs, including anxiety, depression, and eating disorders, suggest promise but also needs further study, with more rigorous scientific testing (Westra et al., 2011). In recent years, too, MET has often been combined with CBT to improve outcomes, including studies addressing comorbidity (e.g., Easton et al., 2012; Cornelius et al., 2011).

**Overall Issues in Comorbidity Behavioral Therapies**

The past several decades have seen remarkable progress in attending to co-occurring disorders. Various novel and creative approaches have been developed and tested in outcome trials. However, conclusions at this point are mixed and further research is warranted.

First, more research is needed to compare integrated versus single, sequential, or parallel treatment approaches. In general, research on manualized behavioral therapies for SUDs consistently find that they do not outperform each other (Carroll & Rounsaville, 2007; Imel et al., 2008; Sellman, 2010), and certain integrated approaches may not necessarily outperform single-diagnosis approaches (Torchalla et al., 2012; Donald et al., 2005). Yet integrated treatments may have other virtues beyond just outcomes: They may increase engagement, may be perceived as highly relevant, may be easier to implement or teach, or be of lower cost than single, sequential, or parallel approaches.

Second, it is important to note that results have sometimes been surprising. Some studies indicate either no difference in SUD outcomes between co-occurring versus non-co-occurring treatment (e.g., Mills et al., 2012; Schadé et al., 2008; Ball, 2007) or worse outcomes (e.g., Randall et al., 2001). Many factors may play into the heterogeneity of findings, including methodology issues (Horsfall et al., 2009), who conducts the study (e.g., the treatment developer or independent scientists), and the nature of the treatments themselves. More research with high-quality treatments and study designs are needed. Also, there are encouraging new treatment developments, including the burgeoning technology-based approaches, such as computer-delivered care (e.g., Kelly et al., 2012).

**SELF-HELP GROUPS AND INDIVIDUALS WITH CO-OCCLUDING SUDs AND PSYCHIATRIC DISORDERS**

As in other substance-using populations (Miller et al., 1997; Ritsher et al., 2002), self-help group attendance has been associated with improved substance use outcomes.
15. Co-Occurring SUDs and Other Psychiatric Disorders

in populations with co-occurring SUDs and psychiatric disorders (Brooks & Penn, 2003; Ritsher et al., 2002). Whether this is a reflection of self-help groups’ improving outcomes directly or a self-selection bias (i.e., patients attending self-help groups may be more likely to remain abstinent because they are more motivated) is unclear.

Despite the fact that self-help groups are both free of charge and geographically accessible (Kurtz, 1997), many patients with co-occurring disorders do not attend these meetings (Noordsy et al., 1996). Some clinicians may be reluctant to recommend self-help groups to patients with co-occurring disorders because of concerns that self-help group members might express negative attitudes towards psychotropic medication (Humphreys, 1997). However, recent research indicates that while this sometimes occurs (Noordsy et al., 1996), it is not prevalent (Meissen et al., 1999). Moreover, official Alcoholic Anonymous (AA; 1984) literature states that psychiatric medication, when legitimately prescribed, is appropriate. When educating patients about the interaction between psychiatric symptoms, drug and alcohol use, and medications, clinicians should inform patients that while some self-help group members may criticize the use of medications, this contradicts official AA policy.

Clinicians may also be concerned that these groups only focus on SUDs (Humphreys, 1997) and may therefore not be as helpful to patients who are struggling with other psychiatric disorders. Recent research suggests that some patients and AA contacts (i.e., persons listed in the AA directories as experienced members) agree (Meissen et al., 1999; Noordsy et al., 1996). However, by encouraging patients to focus on obtaining what AA and similar groups offer, and not expecting AA to provide services outside of its stated mission, clinicians can help patients with co-occurring disorders to take advantage of these groups.

To address some of the concerns described earlier, several dual focus self-help groups have emerged for participants with co-occurring SUDs and psychiatric disorders (e.g., Double Trouble in Recovery, Dual Recovery Anonymous, and Dual Disorders Anonymous; Bogenschutz et al., 2006; Magura et al., 2003). Similar to the literature on self-help groups in the SUD population, positive associations have been found between attendance at dual focus self-help groups and abstinence (Magura et al., 2003), as well as psychiatric/quality of life (Magura et al., 2002) outcomes. Again, whether this is a result of self-selection bias regarding the characteristics of patients who attend these meetings is unclear.

General Treatment Themes for Patients with Co-Ocurring SUDs and Psychiatric Disorders

Because of the limitations of the empirical literature described earlier regarding psychosocial treatments, it may be helpful to draw on general recommendations provided by various writers on this subject (Bellack & DiClemente, 1999; Carey, 1995; Drake et al., 2001; Drake & Mueser, 2000; Najavits et al., 1996; Rounsaville & Carroll, 1997; Ziedonis et al., 2000; Najavits, 2002; Najavits & Capezza, 2014). Although treatment modalities differ, some common themes can help guide clinicians who must decide how to intervene with their patients. The suggestions are as follows:
IV. SPECIAL POPULATIONS

- Be empathic and provide support for the difficulty of living with two disorders, but also emphasize accountability (e.g., the presence of a psychiatric disorder is not an excuse to use substances).
- Assist patients in setting a goal to stop substance use. Explore patients’ perceptions of the relationship between their substance use and their psychiatric disorders. As part of this process, also explore the longer-term relationship between the two (e.g., an individual may report drinking to reduce social anxiety and initially feel better, then feel worse the following day) and discuss the advantages of a substance-free life.
- Educate patients and their family members about the symptoms of both disorders, and the causal connections between them.
- Monitor symptoms of both disorders and how they interact over time (including the use of biological measures such as urine screens for substance use when indicated).
- Monitor adherence to medications, since nonadherence is a significant risk for relapse.
- To improve functioning and foster the rewards of abstinence, assist patients in developing social, relationship, or vocational skills.
- Attend to patient safety, including attention to the human immunodeficiency virus (HIV) and suicidality, both of which have been found to be increased in patients with co-occurring disorders (Mahler, 1995; Weiss & Hufford, 1999).
- Have available resources to refer patients to self-help groups for each disorder.
- Discuss with patients what to do and whom to call in case of emergency.
- Provide positive reinforcement for improvements, however small, in each disorder.
- For patients who have had significant periods of recovery, acknowledge these successes and, in a positive way, ask them how they accomplished it. Doing so reminds patients of prior successes and can mitigate the feelings of hopelessness and discouragement that often accompany relapse.
- Take a relapse history to help identify triggers to relapse (e.g., discontinuing medications or treatment, engaging in high-risk behaviors such as socializing where alcohol is present).
- Expect occasional breaks in treatment attendance, and engage in active outreach.
- Recognize that patients may be more motivated to work on one disorder than the other, and may need encouragement to attend to both.
- Understand that the clinician too may feel more connection or engagement with one disorder over the other. For example, depression may evoke more sympathy than an SUD.
- Be aware of subtypes and subpopulations even within a particular comorbidity. For example, treatment of depression–SUD comorbidity may differ based on whether psychotic symptoms are present; based on age (e.g., adolescent vs. geriatric), and so forth.
- Provide referral to additional treatments and conduct a thorough assessment of case management needs, including treatment of physical health problems.

PHARMACOTHERAPY FOR CO-OCCURRING SUDs AND OTHER PSYCHIATRIC DISORDERS

The literature regarding co-occurring disorders in the field reflects the importance of examining, in part based on the use of validated methods to assess the efficacy of antidepressants, antipsychotics, and mood stabilizers (Ciraulo & Jaffe, 2008). These treatments have been incorporated as standard care. This is true not only for pharmacological but also for psychological and more recent neurobiological and psychological components.

Major Depressive Disorder

Multiple meta-analyses have shown that co-occurring depression affects outcomes (Tremblay et al., 2011; Yudofsky et al., 2011). The mixed efficacy of pharmacological measures (e.g., antidepressants) for substance use disorders is well known. Studies that have specifically examined the efficacy of antidepressants have yielded larger effects after 1 week of abstinence than among those with transient depression. One such study comparing depression and dysthymia with clomipramine, the same drug used to treat OCD, showed no significant improvement in depression scores for patients with a history of alcohol use disorder, compared to a placebo control group (Breslau et al., 2010). A recent meta-analysis found that antidepressant use is associated with better outcomes and greater treatment adherence compared to placebo. For the treatment of co-occurring depression and substance use disorders, evidence suggests that antidepressant use is preferred for treatment.
PHARMACOTHERAPY FOR PATIENTS WITH CO-OCCURRING SUDs AND OTHER PSYCHIATRIC DISORDERS

The literature regarding when to prescribe pharmacotherapy for patients with co-occurring disorders has evolved considerably in the past 20 years. Previous consensus in the field reflected reluctance to prescribe psychotropic medications in this population, in part based on methodologically flawed studies. For example, older studies examining the use of antidepressants in alcoholics often did not use standardized methods to assess the depressed population, had inadequate dosing or duration of antidepressants, and sometimes measured mood or drinking outcomes, but not both (Ciraulo & Jaffe, 1981). More recently, integrated pharmacological and psychosocial treatments have been increasingly accepted and are now often provided to patients as standard care. However, few trials have integrated novel psychosocial treatments with novel pharmacotherapies, and most treatments instead either focus on new pharmacological or new psychosocial interventions. In spite of this, clinical practice and more recent research have emphasized the importance of integrating pharmacological and psychotherapeutic treatment options.

Major Depression

Multiple meta-analyses of antidepressant medication efficacy in patients with co-occurring depression and SUDs have examined both mood and SUD outcomes (Loevinger et al., 2011; Nunes & Levin, 2004; Torrens et al., 2005). Results have shown mixed efficacy of antidepressants in this population, with better outcomes on depressive measures (comparable to results seen in patients with depression alone) than substance use outcomes, and without clear evidence to suggest use of one particular agent. Studies that required at least 1 week of abstinence before treating the depression yielded larger effect sizes and lower placebo response, suggesting that requiring even 1 week of abstinence before initiating medication treatment can successfully screen out transient depressive symptoms. Studies that exhibited better depression outcomes as a result of antidepressants also showed decreased quantity of substance use, and best outcomes occurred in studies combining antidepressants with psychotherapy. One such study used fluoxetine and CBT in depressed alcoholics, with improved depression and drinking outcomes (Cornelius et al., 1997). In another study, combining sertraline and CBT led to less drinking and improved depression compared to placebo (Moak et al., 2003). One study showed efficacy for desipramine in improving depression scores and length of abstinence from alcohol in a 6-month, double-blind, placebo-controlled trial (Mason et al., 1996). In a single-site trial, Pettinati et al. (2010) found that a combination of sertraline and naltrexone led to improved drinking outcomes and reduced depression compared to either sertraline or naltrexone alone, indicating that this combination may have value for the depressed and actively drinking patient. Most studies examining use of antidepressants in patients with co-occurring depression and cocaine use disorders have shown some effectiveness in antidepressant outcomes but little impact on cocaine use (Torrens et al., 2005). Some evidence suggests that stimulating antidepressants (e.g., tricyclics and bupropion) are preferred for treating depression in the context of cocaine use disorders (Rounsaville,
Although antidepressants have been studied in patients with co-occurring depression and opioid use disorders, mostly in patients receiving methadone maintenance treatment, most studies have shown no improvement in outcomes of either illness (Nunes & Levin, 2004). An exception might be the tricyclic antidepressants imipramine and doxepin, which in this population have shown some benefit in reducing substance use, likely indirectly via positive effects on depression (Nunes et al., 1998; Nunes & Levin, 2004; Titievsky et al., 1982).

**Bipolar Disorder**

Although face validity would suggest that stabilizing mania or hypomania in patients with bipolar disorder would improve impulse control and judgment, and would therefore lead to decreased substance use, the literature is thin regarding the efficacy of mood-stabilizing medications on bipolar and SUD outcomes. A number of open-label prospective trials using medications for patients with an SUD and a bipolar or bipolar spectrum disorder have been conducted (i.e., with lithium, anticonvulsants, and antipsychotics), with results generally showing improvements in mood symptoms but inconclusive or unclear results regarding SUD outcomes (Brady et al., 1995; Brown et al., 2002, 2003a, 2003b; Calabrese et al., 2001; Gawin & Kleber, 1984; Geller et al., 1998; Nunes et al., 1990). An open-label pilot trial by Gawin and Kleber (1984) indicated that lithium may be effective in reducing cocaine use in patients with cyclothymia and cocaine abuse. However, an open-label trial of lithium in patients with bipolar spectrum disorders and cocaine abuse (Nunes et al., 1990) demonstrated little efficacy in mood or cocaine outcome measures. An open-label trial with valproate in patients with bipolar disorder and an SUD (Brady et al., 1995) resulted in improvement in mood and substance use measures. An open trial of lithium plus valproate in patients with rapid-cycling bipolar I or II disorder and alcohol, cannabis, and/or cocaine dependence (Calabrese et al., 2001) showed improvement in mood symptoms and a 25% remission rate in SUDs after 6 months. Open-label trials of lamotrigine (Brown et al., 2003a) and quetiapine (Brown et al., 2002) in patients with bipolar disorder and cocaine dependence suggest that these medications may be associated with improved mood symptoms and cocaine craving, although not with significant reductions in cocaine use. An add-on RCT of citicoline (Brown et al., 2007) in this same population resulted in decreased cocaine use and no changes in mood. Several double-blind, placebo-controlled studies assessing the efficacy of mood stabilizers or antipsychotic medications in patients with bipolar disorder and SUDs have been conducted (Brady et al., 2002; Brown et al., 2008, 2012; Geller et al., 1998; Salloum et al., 2005). Geller et al. (1998) conducted a double-blind, placebo-controlled, 6-week trial of lithium in adolescents with bipolar disorder and substance dependence, and found lithium to be efficacious for outcomes in both disorders (Geller et al., 1998). Brady et al. (2002) compared carbamazepine in cocaine-dependent individuals with and without a co-occurring affective disorder (note that less than half of the sample with affective disorders had bipolar I disorder, bipolar II disorder, or cyclothymia) in a 12-week, double-blind, placebo-controlled trial. The affective disorder group treated with carbamazepine showed a nonstatistically significant trend toward less cocaine use, while treatment with carbamazepine did not have any impact on cocaine use in the bipolar disorder or placebo group. Social interventions in both groups, however, had fewer heavy drinkers (Brown et al., 2002a). Bipolar disorder, depression, and mood symptoms of SUDs have a decrease in the difference in urine volume in administering quetiapine, and improved treatment of alcohol use (Brown et al., 2007). Results of all of these studies underscore the fact that improving psychosocial functioning is the most important tool for treating patients with SUDs, in addition to medications. However, this needs to be further investigated. Data objectively suggest that there is a treatment effect, as can be seen as primary prevention strategies.

**Schizophrenia**

Most of the literature regarding schizophrenia and SUDs has small sample size, with small sample sizes on relapse prevention studies of the first-generation antipsychotics. Most data regarding psychiatric systems in schizophrenia and SUDs show that the first-generation antipsychotics (Levin et al., 1984; Sayers et al., 2006; Sowden et al., 2006; Moritz et al., 2006) quetiapine has been shown to reduce relapse and improving substance use outcomes in patients with schizophrenia, though no clear differences in antipsychotic agents have been identified (Sayers et al., 2006). Overall, first-generation antipsychotic agents have been shown to be effective in improving relapse outcomes (Buckley et al., 2006; LeDuc & Mittlenzer, 2009; & Caroff, 2009); however, treatment of co-occurring schizophrenia and SUDs is associated with decreased efficacy, though without documented unique pharmacologic or neurosystem deficits of these conditions (LeDuc & Mittlenzer, 2009).
have any impact on individuals without affective disorders. In a 24-week, double-blind, placebo-controlled trial, Salloum et al. (2005) randomized 59 patients with bipolar disorder and alcohol dependence receiving lithium carbonate and psychosocial interventions to also receive valproate or placebo. Mood symptoms improved in both groups, while patients in the lithium plus valproate group had significantly fewer heavy drinking days. In a 10-week, double-blind, placebo-controlled trial, Brown et al. (2012) compared lamotrigine to placebo in 120 outpatients with bipolar disorder, depressed or mixed mood state, and cocaine dependence. No difference in mood symptoms occurred between the groups, and lamotrigine was associated with a decrease in the amount of money spent on cocaine (though without a significant difference in urine drug screen results). Two double-blind, placebo-controlled trials administering quetiapine to patients with alcohol dependence and bipolar I disorder (treated with mood stabilizers) resulted in no improvement over placebo in measures of alcohol use (Brown et al., 2008; Stedman et al., 2010). Generally speaking, the results of all of these trials confirm the safety and effectiveness of mood stabilizers in improving psychiatric symptoms in patients with co-occurring disorders, but fewer data objectively demonstrate a decrease in substance use, and results of most trials can be seen as preliminary.

**Schizophrenia**

Most of the literature on the pharmacological treatment of patients with schizophrenia and SUDs is limited to retrospective or open-label prospective studies, often with small sample sizes and/or lacking comparison groups. For example, an open trial of desipramine added to antipsychotic treatment in an integrated dual diagnosis relapse prevention program showed promise in reducing cocaine use and improving psychiatric symptoms (Ziedonis et al., 1992). Two open-label trials have found the first-generation depot antipsychotic flupenthixol decanoate to decrease cocaine (Levin et al., 1998b) and alcohol (Soyska et al., 2003) use in patients diagnosed with schizophrenia and SUDs. Multiple preliminary reports suggest the potential benefit of second-generation antipsychotic medications such as clozapine, olanzapine (Littrell et al., 2001; Smelser et al., 2006), risperidone (Smelser et al., 2002a; Rubio et al., 2006), quetiapine (Brown et al., 2003b), and aripiprazole (Beresford et al., 2005) in improving substance use outcomes in populations with co-occurring schizophrenia, though no conclusive data support the efficacy of first- or second-generation antipsychotic agents over the other (Petris, Leslie, et al., 2006; San et al., 2007; Sayers et al., 2005). Generally speaking, the atypical antipsychotic clozapine has shown the most promise in the treatment of patients with schizophrenia and SUDs (Buckley et al., 1994; Drake et al., 2000; Green et al., 2003; San et al., 2007; Lybrand & Caroff, 2009; Zimmet et al., 2000). In one RCT (enrolling 31 patients with co-occurring schizophrenia and cannabis use disorder), clozapine treatment was associated with decreased cannabis use compared to other antipsychotic medications, though without differences in symptoms or functioning (Brunette et al., 2011). The unique pharmacological receptor activity of clozapine may correct underlying reward system deficits of patients with schizophrenia and SUDs (Green et al., 1999, 2008; LeDuc & Mittleman, 1995). Additionally, when administered in low doses (50 mg or
Another pharmacological intervention that may not have abuse potential was the use of buspirone, a noncontrolled studies of the use of buspirone in patients with either generalized anxiety disorder (GAD) or panic disorder with or without panic attacks (Fava et al., 1994). It was found that patients with panic disorder with or without panic attacks had a decrease in anxiety and alcohol use symptoms after 12 weeks of treatment with buspirone. Although there have been no randomized controlled trials of the use of buspirone in patients with social anxiety disorder, several open-label studies have shown that patients who received buspirone had a decrease in anxiety symptoms. A recent study found that buspirone was effective in improving a patient's quality of life and social functioning. The findings from these reports add further to concerns that the long-term use of benzodiazepines in these populations may offer the risk of abuse or dependence without great potential for clinical benefit.
SPECIAL POPULATIONS

Another pharmacological alternative in this population is buspirone, which does not have abuse potential. Thus far, there have been three double-blind, placebo-controlled studies of buspirone in patients with alcohol dependence and anxiety—either generalized anxiety disorder (GAD; Tollefson et al., 1992), GAD and “other nonpanic anxiety” (Malcolm et al., 1992), or “anxious alcoholism” (Kranzler et al., 1994). Two of the studies found that buspirone was associated with improvements in anxiety and alcohol use outcomes (Kranzler et al., 1994; Tollefson et al., 1992). Although there have been concerns that buspirone’s anti-anxiety effect is more limited in patients with a prior history of benzodiazepine use (Schweizer et al., 1986), a pooled analysis of eight placebo-controlled, randomized trials of patients with GAD (DeMartinis et al., 2000) indicated that patients with either remote (defined as at least 1 month duration) or no prior benzodiazepine treatment experienced improved anxiolysis, fewer adverse events, and clinical improvement similar to that on benzodiazepines compared to patients with recent benzodiazepine treatment. Thus, patients who have not received benzodiazepines for at least 1 month may benefit from buspirone. An RCT of buspirone for patients with co-occurring opioid dependence (on methadone maintenance treatment) and anxiety found that buspirone did not significantly reduce anxiety symptoms, though was associated with trends toward decreased depressive symptoms and slowed relapse rates (McRae et al., 2004).

In patients with co-occurring PTSD and SUDs, one RCT indicated that certain subtypes of patients might benefit from selective serotonin reuptake inhibitor (SSRI) treatment (Brady et al., 2005). In 94 patients with current alcohol dependence and PTSD randomly assigned to receive sertraline or placebo for 12 weeks, those participants with less severe alcohol dependence and earlier-onset PTSD had significantly fewer drinks per drinking day. The SSRI paroxetine has similarly been found to be effective in one randomized, placebo-controlled trial in patients with co-occurring social anxiety disorder and alcohol dependence (Randall, Johnson, et al., 2001). Participants receiving paroxetine showed improvements in anxiety and alcohol dependence symptoms. A follow-up randomized, placebo-controlled trial in patients with co-occurring social anxiety disorder and alcohol dependence (Thomas et al., 2008) found paroxetine to be effective in decreasing social anxiety and self-reported use of alcohol for self-medication purposes (i.e., to cope in order to engage with others in social settings), though it did not correlate with decreases in overall alcohol use.

Attention-Deficit/Hyperactivity Disorder

Attention-Deficit/Hyperactivity Disorder (ADHD; Levin et al., 1999) is often seen in populations with co-occurring SUDs and psychiatric disorders, they may worsen the course of the SUDs or be subject to abuse themselves (Gawin et al., 1985). At the same time, it has also been observed that a childhood history of ADHD worsens outcomes for cocaine dependence (Carroll & Rounsaville, 1993). Therefore, improving a patient’s difficulties with inattention and hyperactivity may have beneficial effects on substance abuse as well (Levin et al., 1999). Consistent with this, prospective studies of children who received stimulant treatment for ADHD indicate...
that stimulants have a protective effect against future development of SUDs as an adult (Wilens, 2003; Mannuzza et al., 2003).

Although not as well-studied as stimulants, nonstimulant medications that lack abuse potential are possible alternatives in the treatment of ADHD. In adult populations, bupropion (Wilens et al., 2002) desipramine (Wilens et al., 1996), and atomoxetine (Michelson et al., 2003) have undergone double-blind, placebo-controlled studies and have demonstrated effectiveness in the treatment of hyperactivity and inattention. Little research on these medications, however, has included patients with active SUDs. In one RCT of atomoxetine, adults with ADHD and alcohol abuse or dependence (Wilens et al., 2008) showed clinically significant improvement in ADHD symptoms with atomoxetine compared to placebo, but no difference in time to relapse of heavy drinking. In a single-blind trial of bupropion for patients with ADHD and cocaine abuse (Levin et al., 2002) and an open-label study of venlafaxine, patients with ADHD and alcohol use disorder (Upadhyaya et al., 2001) showed improvements in hyperactivity and inattention, as well as substance use outcomes. In a single-blind trial of sustained-release bupropion, adults with ADHD and SUDs (of all types) showed clinically significant reductions in ADHD symptoms but not SUD markers (Wilens et al., 2010). These results need to be replicated in larger, more rigorous studies.

Clinical trials of methylphenidate in adults with ADHD and a history of cocaine use disorders have also shown promising results. Both open-label trials of long-acting methylphenidate (Castaneda et al., 2000; Levin et al., 1998) and a double-blind, placebo-controlled study of regular methylphenidate (Schubiner et al., 2002) in adults with ADHD and cocaine dependence have all been consistent in that ADHD symptoms improved and no escalation of the stimulant dose was observed. However, while the open trial by Levin et al. (1998a) observed reductions in cocaine craving and use, Schubiner et al. (2002) found no evidence of improved cocaine outcomes in their double-blind, placebo-controlled trial. In a follow-up double-blind, placebo-controlled trial of sustained-release methylphenidate in adults with ADHD and cocaine dependence (all of whom also received weekly individual CBT), Levin et al. (2007) found no difference between methylphenidate and placebo relative to ADHD symptoms (though the majority of both groups showed > 30% improvements in symptoms). Cocaine-positive urine samples, however, decreased significantly in the methylphenidate group, especially among those who also had improvements in ADHD symptoms. In another RCT, Levin et al. (2006) compared sustained-release methylphenidate or sustained-release bupropion to placebo in adults with ADHD and opioid dependence on methadone maintenance; they found no significant differences in ADHD symptoms (with improvement noted in all treatment groups), along with no increase in cocaine use among any groups. In one double-blind, placebo-controlled pilot study of sustained-release methylphenidate, 24 adults with ADHD and amphetamine dependence (abstinent at time of enrollment) showed improvement in self-rated ADHD symptoms in both groups (not statistically different), as well as no differences in drug use, craving for amphetamine, or retention in treatment (Konst eius et al., 2010). In a small crossover trial of sustained release methylphenidate (Szobot et al., 2008), adolescents with ADHD and co-occurring SUDs had more improvement in symptoms of ADHD among those with co-occurring SUDs who were receiving placebo compared, however. Despite limitations, it is suggested to treat ADHD with stimulants in these patients.

What to Do When ADHD and SUDs Coincide

As evidenced in the previous section, treatment of ADHD can result in people with SUDs achieving abstinence in the specific population. The medical dilemma is often presented by patients with ADHD disorders or ADHS and SUDs (cocaine/benzodiazepines).

Pharmacotherapies and medication treatments (Ciraulo & Naccarato, 2009) have to receive adequate attention in these patients before being abandoned. Physicians should be well-versed in the treatment options. (Naccarato, 2010) with the dose and side effects of the treatment options (Ciraulo & Naccarato, 2009) before prescribing any medication. It is important to explore the benefit and potential for improvement from different treatments before initiating any medication treatment. The most effective medications for ADHD are typically selected when prescribed. (Ciraulo & Naccarato, 2009)

- Select pre-school age stimulants with a shorter half-life and other medication types are therefore recommended.

- For benzodiazepine use, a tapering schedule is particularly effective when combined with the behavioral and medication treatments to control symptoms. These medications should be used sparingly and with caution due to the potential for patient compliance, and the potential for addiction as well.

- Use objective and evidence-based standardized treatment guidelines (Barkley, 1988) can be particularly effective.

- Monitor side effects, and adjust treatment accordingly.
improvement in ADHD symptoms than patients receiving placebo. A multisite trial of adolescents with ADHD and SUDs, however, found no more reduction of ADHD or SUD symptoms in those receiving osmotic-release methylphenidate than in those receiving placebo (Riggs et al., 2011). There was no worsening in substance use, however. Despite limited evidence that stimulants may be safely used in this population to treat ADHD without worsening SUD outcomes (and perhaps improving them), their use in these patients remains controversial.

**What to Do When the Pharmacological Treatment for the Co-Occurring Psychiatric Disorder Has Abuse Potential**

As evidenced in numerous studies, treating a co-occurring psychiatric disorder can often result in positive outcomes in reducing substance use, as well as improvements in the specific psychiatric disorder for which it is prescribed. However, what if the pharmacological treatment has the potential to worsen or create a new SUD? This dilemma is often considered in treating patients with SUDs and co-occurring anxiety disorders or ADHD, when clinicians ask themselves, “Is it safe to prescribe stimulants/benzodiazepines for this patient?”

Pharmacotherapies that do not have abuse potential should be considered first-line treatments before prescribing stimulants or benzodiazepines in these populations (Ciraulo & Nace, 2000; Levin et al., 1999), and it is important that patients receive adequate trials (i.e., dose and duration) of these medications before they are abandoned. Psychosocial treatments with demonstrated efficacy should also be tried before prescribing an abusable medication. For example, CBT has demonstrated efficacy for anxiety disorders (Beck, Wright, Newman, & Liese, 1993) and should be explored before prescribing a benzodiazepine. If these first-line treatments fail to improve the anxiety or ADHD symptoms, then the following guidelines are suggested when prescribing stimulants or benzodiazepines in these patient populations (Ciraulo & Nace, 2000; Levin et al., 1999):

- **Select preparations that limit the potential for abuse.** Medications with longer half-lives or sustained-release preparations have lower abuse potential and are therefore preferable in these populations. Select as low a dose as possible. For benzodiazepines, avoid as-needed-basis prescribing in lieu of a fixed dosing schedule. Limit the number of pills given with each prescription, keep a log of the pills prescribed, and check state-based prescription monitoring programs to minimize potential for doctor shopping (i.e., obtaining prescriptions for controlled substances from multiple providers at the same time). Frequent patient contact can help the clinician assess whether the medication is helpful, as well as whether it is being overused.

- **Use objective measures to document improvements.** For example, using a standardized assessment such as the Adult Behavior Checklist (Murphy & Barkley, 1996) or the Beck Anxiety Inventory (Beck, Epstein, Brown, & Steer, 1988) can help document improvements (or the lack thereof).

- **Monitor substance use.** Patients should be asked about alcohol and drug use,
and other sources of information (urine screens, collateral information from family members) should be strongly considered.

- Enlist family members’ help in supporting and monitoring the patient. Verify the efficacy and appropriate use of the medication with family members.
- Patients should safeguard medications. While the patient may not abuse the medication, family members, roommates, or friends may.
- Monitor prescriptions. Keep careful track of the number of pills prescribed, check prescription monitoring programs, and beware of warning signs of abuse such as premature requests for refills, “lost prescriptions,” or prescriptions obtained from multiple providers in a short period of time. These usually indicate overuse of the medication.

Pharmacotherapy Targeting Substance Dependence in Populations with Co-Occurring SUDs and Other Psychiatric Disorders

Although pharmacotherapies aimed specifically at decreasing alcohol or drug use (e.g., naltrexone, disulfiram, acamprosate) have been proven and accepted to be efficacious in improving SUD outcomes in non-dually diagnosed populations, their application in populations with co-occurring disorders has lagged behind. Recent data on their safety and potential efficacy in co-occurring populations may be helpful in increasing their use (Petrakis et al., 2005). For example, concerns that disulfiram may cause or exacerbate psychosis (Mueser et al., 2003) has contributed to a reluctance to prescribe it in patients with SPMI (Kingsbury & Salzman, 1990). Published case reports (Brenner et al., 1994), case series (Kofod et al., 1986; Mueser et al., 2003), and RCTs (Petrakis, Nich, et al., 2006), however, have described its tolerability and potential benefit for improving alcohol outcomes. Additionally, evidence suggests that naltrexone may similarly improve drinking outcomes in patients with alcohol dependence and schizophrenia (Bakshi et al., 2002; Petrakis et al., 2004), bipolar disorder (Sonne & Brady, 2000; Brown et al., 2009), and major depression (Salloum et al., 1998; Petrakis et al., 2007). In one randomized, placebo-controlled trial, Petrakis et al. (2004) successfully treated 31 patients with schizophrenia and comorbid alcohol abuse or dependence for 12 weeks in an outpatient setting using naltrexone or placebo, in addition to patients’ neuroleptic medication. Patients receiving naltrexone had significantly fewer drinking days, less heavy drinking days, and decreased craving, with no changes in schizophrenia symptoms or status. Additionally, among male military veterans with alcohol dependence and PTSD, naltrexone and disulfiram were found to be more effective than placebo in reducing alcohol consumption (Petrakis, Poling, et al., 2006). Both naltrexone and disulfiram alone were associated with reduced alcohol consumption, though the combination did confer extra benefit and was associated with more side effects in the PTSD group. Additionally, disulfiram showed more benefit than naltrexone in reducing PTSD symptoms in this study. In a randomized, controlled, 8-week trial of acamprosate in patients with co-occurring alcohol dependence and bipolar disorder (types I and II), acamprosate was well tolerated, without any worsening in depressive or manic symptoms and with some benefit on alcohol outcomes among completers in the last 2 weeks of the trial (Tolliver, Desantis, Brown, Prisciandaro, & Brady, 2012).

FUTURE DIRECTIONS

In the approximately 40% of SUD and addictions fields, outcomes in populations of these disorders, as well as populations. Significantly increasing them with intervention methods for these disorders are hopeful that this field requires the need for practice. Morbidity based on different and increased attention to the need, comorbidities over disorder diagnosis). Efforts will contribute to these efforts that will transform

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FUTURE DIRECTIONS

In the approximately 30 years since researchers and clinicians in the mental health and addictions fields first noted the high prevalence rate of comorbidity and worse outcomes in populations with co-occurring SUDs and psychiatric disorders, important strides have been made in further understanding the epidemiology and sequelae of these disorders, as well as the critical need to develop specific treatments for these populations. Significant progress has been made in developing new treatments, testing them with increasing methodological rigor, and developing optimal treatment methods for these often poorly served patient populations. In the next decade, we are hopeful that this continued research effort will translate into improved treatment methods and outcomes in these patients. Some important future directions include the need for practice guidelines relevant to SUD comorbidity; how to address comorbidity based on different treatment settings (e.g., primary care vs. specialty care); and increased attention to diagnostic decision making when symptom profiles of particular comorbidities overlap (e.g., substance misuse is part of the borderline personality disorder diagnosis). We are hopeful that the next decade will see continued research efforts that will translate into improved clinical care of these patients.

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IV. SPECIAL POPULATIONS


15. Co-Occurring SUDs and Other Psychiatric Disorders


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15. Co-Occurring SUDs and Other Psychiatric Disorders


15. Co-Occurring SUD


V. SPECIAL POPULATIONS

- Behavioral therapy for depression.
- Psychotropic or affective disorder.
- Diagnostic issues in dual diagnosis.
- Integrated residential programs.
- Alcoholics anonymous.
- Substance abuse.
- Alcoholism in severe mental illness.
- Symptoms of ADHD in adults.
- Sexuality and substance abuse.
- Use disorder: A practical guide to trauma and PTSD.
- Dependence.
- Addiction.
- Adolescents with PTSD.
- Barriers to care of persons with dual diagnoses.
- Care of substance use disorders.
- Cognitive-behavioral therapy for women.
- Brief coping skills training for cocaine abuse.
- The prevalence of psychiatric disorders in patients with alcohol use disorders.
- Treatment of cocaine dependence and depression.

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15. Co-Occurring SUDs among mental disorders


V. SPECIAL POPULATIONS

Co-Occurring SUDs and Other Psychiatric Disorders


**CORE FEATURES**

Behavioral and drug addictions are chronic diseases that involve short-term reward and long-term negative outcomes. Adherence to treatment is a core definitional feature of substance use disorders (Potenza, 2006). Therefore, the utility of the term "addiction" has become a heuristic value but remains problematic.

Although various behavioral addictions (e.g., gambling, shopping) are considered, this chapter focuses on the core problem of substance use disorders. The literature review in this chapter is based on recent meta-analyses and the potential for comorbidity with SUDs and the potential for future research. It seems likely that such efforts for addictions...