Review of Treatment Recommendations for Persons With a Co-occurring Affective or Anxiety and Substance Use Disorder

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Objective: **The authors review and evaluate the literature and guidelines on care for individuals with a co-occurring affective or anxiety disorder and substance use disorder.** ***Methods:*** **MEDLINE and PsycINFO computerized searches of the English language literature were conducted for the period 1990–2002. These articles were supplemented with searches of the Cochrane Database of Systematic Reviews (1990 to 2002) and with articles that were sent to the authors by experts in the field to review. Bibliographies of selected papers were hand searched for additional articles. From these searches a total of 219 articles were found, of which 127 were selected for review.** ***Results and discussion:*** **The literature shows that, over the past several decades, treatment for co-occurring disorders has undergone a broad shift in approach, from treating substance abuse before providing mental health care to providing simultaneous treatment for each disorder, regardless of the status of the comorbid condition. Many treatment recommendations are supported by a broad consensus. However, despite this broad agreement, recommendations are often not specific enough to guide clinical care. Most recommendations with specificity are for acute pharmacotherapy, but even specific recommendations lag behind current clinical practice. Although the use of psychotropic medication for mental illness is encouraged, experts disagree as to whether it is necessary to wait for abstinence before beginning pharmacotherapy. In addition, most diagnosis-specific guidelines are silent as to whether the specific treatment recommendation applies to co-occurring disorders. Finally, empirical evidence is lacking for most recommendations. The authors conclude that the mental health and substance abuse treatment fields need to consider its research priorities and how to address the multitude of potential combinations of disorders. (*Psychiatric Services* 56:913–926, 2005)**

The co-occurrence of mental and substance use disorders is prevalent, costly, and a service priority for state mental health and substance abuse agencies (1–6). States are increasingly being asked to provide evidence-based services to persons with dual diagnoses and their families (7,8). These dual diagnosis clients include those who have serious mental illness and a substance use disorder as well as those who have an affective or anxiety disorder who do not meet formal criteria for a serious mental illness and who typically enter treatment through the substance abuse treatment system rather than the mental health system (9,10). Both clinicians and program administrators look to treatment guidelines and other reviews of the empirical evidence to help them decide what services to implement. Policy makers use treatment guidelines to hold the service system accountable for providing evidence-based care.

There are two types of guidelines that address co-occurring disorders: guidelines that were specifically written for co-occurring disorders, and guidelines written for individual mental health and substance use disorders that address comorbidity as a complicating factor. A substantial body of literature based on empirical research exists regarding the treatment of persons with serious mental illness and a co-occurring substance use disorder (11). This literature has been influential in changing the way providers and program administrators deliver care to individuals with a dual diagnosis and how policy makers fund and organize such care (7,8).

However, the treatment models developed for this population may not be applicable to persons with a co-occurring affective or anxiety and substance use disorder, because the research on which it is based is specific to individuals with serious mental illness—usually psychotic disorders.

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This discrepancy is important, because a majority of persons with a dual diagnosis have a co-occurring affective or anxiety disorder, which is not a severe and persistent mental illness (2,4). Furthermore, the widespread application of these models to broader populations would involve substantial effort and expense.

To our knowledge, no systematic reviews have been conducted of the treatment literature for individuals with a nonserious mental illness that summarize both the mental health and substance abuse treatment recommendations and the evidence behind the recommendations. A recent review of the literature on co-occurring disorders (12) did not summarize the findings into recommendations with accompanying levels of evidence, and the review was directed toward substance abuse treatment providers.

In this article we review and evaluate the literature and guidelines on care for individuals with a co-occurring affective or anxiety and substance use disorder. Our objective is to describe how standard treatment practices should be modified when delivered to persons with co-occurring disorders. We identify specific clinical recommendations and the evidence supporting each recommendation. We also discuss the comprehensiveness of the recommendations, identify gaps, and point out how some of the recommendations conflict. We hope that this paper will serve as a document that will be useful to clinicians and program administrators as well as state mental health and substance abuse agencies who want to achieve better outcomes for persons with co-occurring disorders by increasing access to and improving the delivery of evidence-based care.

Methods

We conducted MEDLINE and PsycINFO computerized searches of the English-language literature for the period 1990–2002, using the search terms "guideline*," "treatment," "algorithm," "protocol," and "parameter" plus each of the following key words: "major depression," "depression," "dysthymia," "generalized anxiety disorder," "panic disorder," "manic depression," "PTSD," "bipolar disorder," "substance*," "drug*," "alcohol," "opiate*," "cocaine," and "marijuana." We searched separately for the key words "dual diagnosis," "coexisting," "co-occurring," and "comorbid," along with the key words "substance*," "mental health," and "psych*." We supplemented these articles with searches of the Cochrane Database of Systematic Reviews (1990 to 2002) and with articles that were sent to us by experts in the field to review. Web sites for the Agency for Healthcare Research and Quality, the National Institute on Alcohol Abuse and Alcoholism, the National Institute on Drug Abuse, and the Substance Abuse and Mental Health Services Administration were queried for each of the search strings: "treatment guidelines," "coexisting," "co-occurring," or "dual diagnosis." Bibliographies of selected papers were hand searched for additional articles. From these searches a total of 219 articles were found, of which 127 were selected for review.

Guidelines developed for persons with co-occurring serious mental illness and a substance use disorder may not be applicable to persons with a co-occurring affective or anxiety disorder.

Article titles and abstracts were reviewed to determine inclusion eligibility. All practice guidelines and treatment algorithms pertaining to specific affective and anxiety disorders and to substance abuse were included, as were review articles and government-sponsored consensus documents on the treatment of co-occurring disorders. Articles were excluded if they reported on results of a single program evaluation, if they did not pertain to persons with affective or anxiety disorders and substance use, or if they did not include adults.

The articles we included were abstracted into recommendation tables, which were checked and rereviewed by the research team for clarity and placement of the recommendation in the table. We abstracted the original text of the recommendation to capture important specifications and noted the populations and settings to which the recommendation applied. The tables also summarized the level of evidence behind each recommendation on the basis of four categories: recommendation supported by the results of randomized outcome studies, results of studies with quasi-experimental designs, case studies, and expert opinion. In cases in which the guideline or review article did not give enough detail on the target population or level of evidence, we went back to the original articles cited in the review.

Results and discussion

We grouped similar recommendations into three categories: program and system-level recommendations (Table 1), general (Table 2) and diagnosis-specific (Table 3) mental health treatment recommendations, and substance abuse treatment recommendations (Tables 4 and 5) (13–64). Recommendations concerning clinical care for a mental health disorder were assigned to the mental health treatment recommendations category, and those concerning care for substance abuse were assigned to the substance abuse treatment category, regardless of the treatment setting or whether it was the disorder for which the patient was in treatment.

Table 1 shows program and system-level recommendations for co-occurring disorders. Almost all of the six recommendations are supported only by expert opinion and include many precepts widely held by the field. The recommendations include integration of treatment and services, treatment

Table 1

Program- and system-level treatment recommendations for persons with a co-occurring affective or anxiety disorder and substance use disorder

Recommendation[a]	Diagnosis and setting[b]	Level of evidence[c]
1. Program integration: provide treatment and services:		
in a unified treatment program	SMI, non-SMI; IS (13–17)	EO (13–17), QE (14), RCT (14)
at the primary treatment site	SMI, non-SMI; SAS (14,18), opioid, MHS, SAS (19)	EO (19), QE (14,18)
at a broader system level	SMI, non-SMI; IS (20,21), MCS (22)	EO (20–22)
2. Substance abuse treatment strategies: provide treatment for addictions that:		
is similar to treatment for nonpsychiatric populations; some modification may be needed	SMI; IS (23), SAS (18)	EO (18,23)
places emphasis on reduction of harm from substance use	SMI, non-SMI; SAS (14)	EO (14)
3. Treatment of each disorder: provide treatment of each disorder through:		
appropriate diagnosis-specific and stage-specific treatment, regardless of the status of the comorbid condition	SMI, non-SMI; SAS, MHS, IS (13–15,21)	EO (13–15,21)
sequencing of specific treatment (beginning with substance abuse), accompanied by ongoing assessment and treatment adjustment if mood and anxiety do not improve following improvement in the substance use disorder	Non-SMI; SAS, MHS, IS (21)	EO (21)
4. Medication management: provide medication within a more comprehensive management plan	SMI, non-SMI; MHS, SAS (24)	EO (24)
5. Components of successful programs: successful treatment programs or systems engage individuals with co-occurring disorders in a welcoming manner:	SMI, non-SMI; SAS, MHS, IS (13,15,21,25)	EO (13,15,21,25)
have an attitude of optimism and recovery	SMI, non-SMI; SAS, MHS, IS (13,14,20)	EO (13,14,20)
provide accessible services and help clients obtain support services	SMI, non-SMI; SAS, MHS, IS (13–15,20,21)	EO (13–15,20,21)
provide access to services through any initial contact point	SMI, non-SMI; SAS, MHS (13,14,21)	EO (13,14,21)
provide a continuum of care	SMI, non-SMI; SAS, MHS, IS (13,20,23)	EO (13,20,23)
provide for continuity of care	SMI, non-SMI; SAS, MHS, IS (13–15)	EO (13–15)
are organized so that consumers and families can obtain peer support and recovery programs and are involved in treatment planning	SMI, non-SMI; SAS, MHS, IS (14,15), MCS (22)	EO (14,15,22)
are responsive to the needs, priorities, and capabilities of the client	SMI, non-SMI; SAS, MHS, IS (13,14,20)	EO (13,14,20)
provide aftercare within an intensive treatment program	SMI, non-SMI; SAS (18)	QE (18)
expect longer treatment duration	SMI, non-SMI; SAS (14,18,21)	EO (14,21); QE (18)
provide continuous treatment relationships even in the face of noncompliance	SMI, non-SMI; SAS, MHS, IS (15,25)	EO (15,25)
6. A national system of care should be designed in accordance with established national standards for serving persons with co-occurring disorders	SMI, non-SMI; SAS, MHS (13)	EO (13)

[a] All recommendations apply to persons with co-occurring disorders. If a mental health disorder is not mentioned, it was unspecified in the article.

[b] SMI, seriously mentally ill; SAS, inpatient or outpatient substance abuse treatment setting; MHS, mental health treatment setting; IS, integrated setting; MCS, managed care setting

[c] EO, expert opinion; QE, quasi-experimental; RCT, randomized controlled trial or randomized outcome study

provision for each disorder, and a list of successful treatment program components. A majority of the 35 recommendations in Table 2 are supported solely by expert opinion (N=25). Only five of the recommendations are supported by the highest level of empirical rigor, a randomized outcome study, of which three involve pharmacologic intervention. The 62 recommendations in Table 3 include some recommendations that are common to people without co-occurring disorders and some that are unique to this population. Thirty-eight of the 62 recommendations in Table 3 are supported only by expert opinion. Thirty-two of the 36 general substance abuse recommendations included in Table 4 are supported by expert opinion. Stronger empirical evidence is offered for some of the recommendations involving psychosocial intervention. As can be seen in Table 5,

Table 2

Treatment recommendations for persons with a co-occurring affective or anxiety disorder and substance use disorder (general mental health)

Recommendation	Diagnosis and setting[a,b]	Level of evidence[c]
I. Screening and referral		
1. Screen for substance abuse	Depression in PCS (26); depression in MHS (27); unspecified mental health disorder in PCS (28); unspecified mental health disorder among alcohol, cocaine, and opioid users in unspecified setting (29); unspecified mental health disorder in MHS and IS (21); unspecified mental health disorder in SAS, MHS, or IS (14)	EO (14,21,26,28,29); QE (27)
2. Refer to mental health specialist for further evaluation	Depression in PCS (30); depression or panic or generalized anxiety disorder in PCS (31); posttraumatic stress disorder in PCS or MHS (32); mood and anxiety disorders among opioid users in SAS (33); unspecified mental health disorder among heroin users in PCS (34); unspecified mental health disorder in SAS, MHS, or IS (14); unspecified mental health and substance use in PCS (35)	EO (14,30–35)
3. Refer to programs with staff experienced with both disorders	Bipolar disorder in MHS or IS (36)	EO (36)
II. Assessment and diagnosis		
1. Assessment includes screening; evaluation of background factors, mental health, substance abuse, and related medical and psychosocial problems; diagnosis and severity; and initial matching of individual to treatment	Unspecified mental health disorder in SAS, MHS, or IS (14)	EO (14)
2. Assessment includes psychiatric evaluation; mental status examination; Addiction Severity Index; and physical examination, laboratory work, and urinalysis	Unspecified mental health disorder in IS (37)	EO (37)
3. A comprehensive assessment should establish diagnosis or diagnoses; assess level of functioning; and develop a treatment plan	Unspecified mental health disorder in SAS, MHS, or IS (21)	EO (21)
4. Initiate assessment at point of contact	Unspecified mental health disorder in IS (25)	EO (25)
5. Assess for all legal and illegal substances that can interfere with treatment	Posttraumatic stress disorder in MHS (38)	EO (38)
6. Evaluate whether substance use is causing or exacerbating psychiatric symptoms	Panic disorder among cocaine, stimulant, marijuana, or inhalant users in MHS (39); depression in PCS (30); depression in MHS, SAS, or IS (40)	EO (30,39,40)
7. Diagnose a co-occurring mental health disorder only when the symptoms are not attributable to substance use or a physical illness; this typically implies observation of symptoms after a period of sustained abstinence	Anxiety disorder in MHS, SAS, or IS (41); mood or anxiety disorder in MHS (42); unspecified mental health disorder in IS (21); unspecified mental health disorder among alcohol users in unspecified setting (36); unspecified mental health disorder in PCS (28); mood or anxiety disorder in MHS or IS (21); depression in PCS (30); unspecified mental health disorder in SAS (43); mood or anxiety disorder among opioid users in SAS (19); unspecified mental health disorder among cocaine and heroin users in MS (44)	EO (19,21,28,30, 41–44); QE (21,36)
8. Obtain collateral information to establish patterns of co-occurring disorders	Mood or anxiety disorder in MHS (42); unspecified mental health disorder in MHS or SAS (24,43)	EO (24,42); QE (43)
9. History may be more important than current symptoms in establishing a diagnosis	Unspecified mental health disorder in SAS, MHS (24), or IS (14); mood or anxiety disorder in MHS (42); unspecified mental health and substance use disorder in IS (25)	EO (14,24,25,42)
10. Achieving abstinence through hospitalization may be necessary to accurately arrive at a diagnosis	Bipolar disorder in MHS or IS (36); anxiety disorder in unspecified setting (33)	EO (33,36)
11. Level of functioning is as important for treatment planning as is a specific diagnosis	Unspecified mental health disorder in SAS or IS (45)	EO (45)
12. Assess for motivational stage regarding each condition	Unspecified mental health disorder in SAS, MHS, or IS (14)	EO (14)
13. Develop an individualized, integrated treatment plan, which is	Unspecified mental health disorder in SAS, MHS, or IS (14)	EO (14)

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Table 2

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Recommendation	Diagnosis and setting[a,b]	Level of evidence[c]
defined as a document that outlines the multiple problems a client experiences and recommends specific interventions and goals matched to each problem		
III. Acute treatment		
General		
1. Treat substance abuse first: may provide concurrent psychotherapy and other nonpharmacologic mental health treatments	Unspecified mental health disorder in SAS, MHS, or IS (14); anxiety disorder in unspecified setting (46); depression, panic disorder, and generalized anxiety disorder in MHS (27); panic disorder in MHS (39); depression in MHS (47); depression in MHS, SAS, or IS (40); unspecified mental health disorder among cocaine and heroin users in MS (44); mood and anxiety in unspecified setting (21)	EO (14,21,27,39,40, 44,46,47)
2. Educate about the effect of legal and illegal substance use on psychiatric symptoms	Bipolar disorder in MHS or PCS (48); unspecified mental health in PCS (28); unspecified mental health in SAS, MHS, or IS (14)	EO (14,28,48)
3. Treatment may be an ongoing process	Mood or anxiety disorder among alcohol users in unspecified setting (21)	EO (21)
4. If treatment is unsuccessful, evaluate for substance abuse and treatment adherence	Depression in MHS (27), SAS, or IS (11); posttraumatic stress disorder in PCS or MHS (32); depression in MHS or PCS (47); depression or panic or generalized anxiety disorder in PCS (31); anxiety disorder in MHS, SAS, or IS (41)	EO (11,31,32,41,47); ROS (27)
Psychosocial		
5. Cognitive behavioral therapy is effective	Mood or anxiety disorder in unspecified setting (21,49); unspecified mental health and substance abuse disorder in CJS (14)	EO (14); ROS (21); QE (49)
6. Begin therapy with nonprovocative topics; monitor and respond to an increase in symptoms	Posttraumatic stress, anxiety, or mood disorder in SAS, MHS, or IS (14)	EO (14)
7. Treat substance abuse to enhance compliance with psychotherapy	Posttraumatic stress disorder in MHS or PCS (32)	EO (32)
8. Psychotherapy should be recovery and abstinence oriented	Anxiety disorder and depression in unspecified setting (49)	EO (49)
Pharmacotherapy		
9. Establish diagnosis through abstinence (and subsequent observation) and history before beginning pharmacotherapy	Depression in PCS (50) or MHS (20); mood or anxiety disorder in MHS (42); anxiety disorder in MHS, SAS, or IS (41); anxiety disorder in unspecified setting (33); affective or anxiety disorder among alcohol, cocaine, or opioid users in unspecified setting (29); unspecified mental health disorder in SAS, MHS, or IS (14)	EO (14,20,29,33,41, 42,50); ROS (41)
10. It is not necessary to wait for abstinence before beginning pharmacotherapy	Depression among alcohol users and anxiety disorder in SAS, MHS, or IS (11); unspecified mental health and substance use (25); depression in MHS (41)	EO (11,25); ROS (41)
11. Educate about medication effects and the onset of relief	Anxiety disorder in unspecified setting (46)	EO (46)
12. The choice of pharmacotherapy should depend on the patient's psychiatric condition and the pharmacokinetics of the medication	Depressed and anxious alcohol users in unspecified setting (51)	EO (51)
13. Benzodiazepine use: not recommended	Depression in MHS (52); unspecified mental health disorder in PCS or MHS (53); anxiety disorder in unspecified setting (46); unspecified disorder in unspecified setting (54); unspecified mental health disorder in PCS (28); depression and anxiety disorder in unspecified setting (49); anxious alcohol users in SAS, MHS, or IS (55)	EO (28,46,49,52–54); QE (55)
14. Benzodiazepines: cautious use	Unspecified mental health disorder in unspecified setting (21); depression in MHS (47); panic disorder among alcohol users in unspecified setting (54); bipolar disorder in MHS, SAS, or IS (11); depression or anxiety or panic disorder in PCS (31); anxiety disorder in MHS, SAS, or IS (11,24,33,41)	EO (11,21,31,41,47, 54); QE (24,33)
15. Benzodiazepines may be required	Anxiety disorder in MHS, SAS, or IS (41); unspecified mental health disorder in PCS (28); anxiety disorder or depression in unspecified setting (49)	EO (28); QE (41); ROS (49)
16. Prescribe medications only after making a diagnosis and treatment plan	Anxiety disorder or depression in unspecified setting (49)	EO (49)

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Table 2

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Recommendation	Diagnosis and setting[a,b]	Level of evidence[c]
17. Adjust strategies for monitoring dosage and compliance with psychoactive drug regimens	Anxiety disorder or depression in unspecified setting (49); unspecified mental health disorder in SAS, MHS, or IS (14)	EO (14,49)
18. Use psychopharmacology cautiously	Unspecified mental health disorder in MHS or SAS (24)	EO (24)
19. Be careful of psychotropic drug interactions with methadone	Unspecified mental health disorder in MS (44)	EO (44)
Maintenance	No recommendations identified	

[a] All recommendations apply to individuals with co-occurring disorders. If the type of disorder is not mentioned, it was unspecified in the article.
[b] PCS, primary care setting; MHS, mental health setting; IS, integrated setting; SAS, substance abuse setting; CJS, criminal justice setting; MS, methadone setting
[c] EO, expert opinion; QE, quasi-experimental; ROS, randomized outcome study

only ten recommendations were found for specific substance use disorders (alcohol, cocaine, and opioid use); however, eight of these recommendations are supported by strong empirical evidence. Many of these recommendations involve pharmacologic intervention.

This article reviews treatment recommendations for co-occurring affective or anxiety and substance use disorders and specifies the level of evidence in support of each recommendation. We include recommendations that are in conflict to highlight where the field has not yet reached consensus or where empirical evidence is lacking. To our knowledge, this is the first review of treatment recommendations that specifically focuses on individuals with a co-occurring affective or anxiety and substance use disorder and that includes the level of evidence behind each recommendation.

Over the past several decades treatment for co-occurring disorders has undergone a broad shift in approach, from treating substance abuse before providing mental health care to providing simultaneous treatment for each disorder, regardless of the status of the comorbid condition (13–17, 21). This shift appears to be driven by at least two factors. Although mental disorders may be the direct result of substance abuse, epidemiologic data indicate that most mental disorders temporally precede substance abuse, which suggests that they are two independent disorders and that the substance abuse is exacerbating rather than causing the mental disorder (2,4). A second factor has been the growing recognition that treatment approaches that focus on treating the substance abuse first have not been successful because substance use disorders tend to be episodic and recurrent. It is simply not feasible to expect acute treatment of substance use disorders to result in sustained recovery and thereby pave the way for a simpler approach to treating the mental disorder. Concurrently, there has been an increasing emphasis on psychopharmacology for the treatment of mental disorders, a shift that parallels changes occurring in the treatment of mental disorders among persons who do not have a substance use disorder.

Many treatment recommendations are supported by broad consensus. All diagnosis-specific guidelines recommend that clinicians screen for the presence of a comorbid condition. Similarly, it is broadly believed to be important to conduct a longitudinal evaluation and obtain corroborating diagnostic information from the client's friends and family. It is also recommended that clients be evaluated as to whether they have a substance-induced mental disorder or a separate axis I disorder that is causing the psychiatric symptoms and that they be educated about the side effects of medications and be given information about when they should expect symptoms to improve. All guidelines and reviews for co-occurring disorders recommend some form of "integrated" treatment.

Key issues identified by the review

Recommendations lack specificity. Despite broad agreement, recommendations for the treatment of co-occurring disorders often are not specific enough to guide clinical care. For example, the intervals at which screening should occur and the instruments that should be used are not clear. Also unspecified is the level of workforce competency needed for various treatment tasks. There is no guidance on which of the competing treatments are optimal, and for which clients. This lack of clinical specificity is important, because it means that it is difficult for clinicians and administrators to implement the recommendations.

The definition of "integrated" treatment is particularly problematic. Some authors consider integrated treatment to be a unified treatment program, in which staff is cross-trained and both mental health and substance abuse treatment providers share the same treatment chart and treatment plan. (13–17). Others consider co-location of mental health and substance abuse services or the provision of both types of service at the primary treatment site to be integrated treatment (14,18,19). Still others consider integrated treatment to be the integration of services at a broader system level through interorganizational linkages and referrals (20–22). The lack of a common definition or operational taxonomy that specifies the different types of integrated treatment makes it difficult for public and private payers to evaluate the appro-

Table 3

Treatment recommendations for persons with a co-occurring affective or anxiety disorder and substance use disorder (specific affective or anxiety disorders)

Recommendation	Diagnosis and setting[a,b]	Level of evidence[c]
I. Depression		
1. Treat resistant depression according to standard depression algorithms	Depression in MHS, SAS, or IS (11)	EO (11)
2. The decision to discontinue active or maintenance treatment should be based on the same factors considered in the decision to initiate treatment	Depression in MHS (47)	EO (47)
3. Discontinue antidepressants after six months if abstinence has been maintained and symptoms resolved	Depression in MHS or SAS (24)	EO (24)
4. There is insufficient evidence to determine the optimal treatment selection for depression and substance use	Depression in MHS (52)	EO (52)
5. Combination psychotherapy and pharmacotherapy is an effective treatment	Depressed cocaine users in MS (44); mood or anxiety disorder among opioid users in SAS (19)	ROS (19,44)
6. Cognitive-behavioral therapy may be effective for concurrent depression and alcoholism	Depressed alcoholics in unspecified setting (21)	QE (21)
7. Antidepressants (unspecified): reduce depressive symptoms and improve substance abuse outcomes	Depression among alcohol users in MHS and SAS (56); depression among alcohol users in SAS, MHS, or IS (11); depression among alcohol users in PCS (28); depression among alcohol users in unspecified setting (33,51)	ROS (11,28,33 51,56)
8. No particular category of antidepressant is specifically recommended or contraindicated	Depression in MHS, SAS, or IS (16)	EO (16)
9. Start with selective serotonin reuptake inhibitors	Depression in MHS or SAS (24); depression in MHS, SAS, or IS (11)	EO (11,24)
10. Selective serotonin reuptake inhibitors are effective	Mood or anxiety disorder in MS (19); depressed alcohol users in MHS (52); unspecified mental disorder among alcohol users in unspecified setting (57); depressed alcohol users in unspecified setting (21); depression among alcohol users in MHS or SAS (24)	EO (19); ROS (21, 24,52,57)
11. Fluoxetine and paroxetine may result in acute opiate withdrawal from codeine	Depression among opioid users in MHS (52)	EO (52)
12. Tricyclics have potential drug-drug interaction and must be monitored (blood levels, electrocardiogram)	Depression in MHS (47); mood or anxiety disorder among opioid users in SAS or MHS (19); depressed alcohol users in unspecified setting (11)	EO (11,47); ROS (19)
13. Tricylics are effective for depressive symptoms but are not clearly effective for substance abuse symptoms	Depression in alcohol users in PCS (50); depression or anxiety disorder among alcohol users in MHS or SAS (56); depression in MS (33,44,56); depression in MHS (53); mood or anxiety disorder among alcohol users in unspecified setting (29); depressed cocaine users in unspecified setting (29); depression among cocaine users in SAS (58)	EO (50,58); RCT (29,52,53,56); QE (29,33,44)
14. Amitriptyline and desipramine are not recommended	Mood or anxiety disorder among opioid users in SAS (19); depression among cocaine users in unspecified setting (33)	EO (19); CS (33)
15. Bupropion, mirtazapine, and venlafaxine may have increased liability in a substance-abusing population	Depression in MHS (52); depression in SAS, MHS, or IS (11)	EO (11,52)
16. Trazodone is helpful for insomnia	Depression or anxiety disorder among alcohol users in PCS (50); mood and anxiety among opioid users in SAS (19)	EO (19,50)
17. May use higher doses of antidepressants among patients with alcohol abuse	Depression among alcohol users in unspecified setting (51)	EO (51)
18. Maintenance treatment recommended	Depression in MHS (27)	ROS (27)
II. Bipolar affective disorder		
1. Hospitalize for active substance abuse and manic, mixed, or hypomanic episode; consider hospitalization with major depressive episode	Bipolar disorder in MHS (48)	EO (48)
2. Provide both psychosocial treatment and pharmacotherapy	Bipolar disorder in MHS or IS (36)	EO (36)

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Table 3

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Recommendation	Diagnosis and setting[a,b]	Level of evidence[c]
3. Mood stabilizers are effective for bipolar disorder and may decrease substance abuse	Mood and anxiety disorder among opioid users in SAS (19); bipolar disorder among alcohol users in unspecified setting (29); bipolar disorder in MHS, SAS, or IS (11,16,24); unspecified mental disorder among alcohol and cocaine users in MHS (48); bipolar disorder in PCS, MHS, or IS (28,36)	EO (11,16,19,29,48); QE (29); ROS (24,28,36)
4. Clozapine and olanzapine are alternative mood stabilizers	Bipolar disorder in unspecified setting (11)	EO (11)
5. Use combination pharmacotherapy monotherapy is unsuccessful	Bipolar disorder in SAS, MHS, or IS (11)	EO (11)
III. Generalized anxiety disorder or anxiety disorder not otherwise specified		
1. Use a stepwise treatment approach	Anxiety disorder in SAS, MHS, or IS (14)	EO (14)
2. Treat alcohol withdrawal to reduce anxiety symptoms	Anxiety disorder among alcohol users in SAS, MHS, or IS (55)	EO (55)
3. For generalized anxiety disorder with a comorbid other anxiety disorder: treat the other disorder first	Anxiety disorder in MHS, SAS, or IS (41)	EO (41)
4. Treatment of anxiety symptoms may aid in avoiding substance abuse relapse	Anxiety disorder among alcohol users in SAS, MHS, or IS (55)	EO (55)
5. Manage anxiety disorders initially with nonpharmacologic therapy	Anxiety disorder in unspecified setting (46); anxiety disorder in MHS, SAS, or IS (11,33,41); anxiety disorder in MHS (42)	EO (11,33,41,42,46)
6. Cognitive-behavioral therapy is effective	Anxiety disorder in MHS, SAS, or IS (14,21,41) ROS (21)	EO (14,41);
7. Use a stepwise approach to get anxious patients to participate	Anxiety disorder in MHS, SAS, or IS (14)	EO (14)
8. Use caution before medicating to treat anxiety symptoms	Anxiety disorder among cocaine and heroin users in MS (44); mood or anxiety disorder in MHS (42)	EO (42,44)
9. If treating with medication, start with antidepressants	Anxiety disorder in unspecified setting (24,33,46,49); anxiety disorder or depression in unspecified setting (49); anxiety disorder inMHS or SAS (24); anxiety disorder in MHS, SAS, or IS (11,41); anxiety disorder among alcohol users in PCS (50); anxiety disorder among alcohol users in MHS, SAS, or IS (55)	EO (11,24,33,46,49, 55); ROS (24,41, 46,49,50)
10. Bupropion may be effective for social anxiety disorder	Social anxiety disorder in MHS, SAS, or IS (41)	CS (41)
11. Avoid use of buproprion, nefazodone	Anxiety disorder in MHS, SAS, or IS (11,41)	EO (11,41)
12. Other antidepressant agents are effective	Anxiety disorder in unspecified setting (46)	ROS (46)
13. Tricyclic or monoamine oxidase inhibitor may be effective for phobic anxiety	Anxiety disorder among alcohol users in SAS, MHS, or IS (55)	QE (55)
14. Monotherapy is recommended to minimize the risks of adverse effects in the event of relapse	Anxiety disorder in MHS, SAS, or IS (41)	EO (41)
15. Monitor symptoms every two to four weeks and increase the dosage as tolerated: refer if insufficient response	Anxiety disorder in unspecified setting (46)	EO (46)
16. For anxiety that has not responded to one antidepressant, consider augmenting or changing the pharmacotherapy; or adding psychotherapy	Anxiety disorder in MHS, SAS, or IS (41)	EO (41); ROS (41)
17. Other pharmacotherapy options include beta blockers, clonidine, and guanfacine	Anxiety disorder in unspecified setting (16,33,46,49); anxiety disorder among alcohol users in unspecified setting (29)	EO (16,29,33,46,49)
18. Treat for two to six months before considering whether to stop the medication	Anxiety disorder in unspecified setting (46)	EO (46)
IV. Panic disorder		
1. Psychotherapy is effective	Panic disorder in MHS, SAS, or IS (41)	ROS (41)
2. Treatment for panic disorder is the same as without comorbid substance abuse, except for the benzodiazepine use warning	Panic disorder in MHS, SAS, or IS (16)	EO (16)
3. First-line treatment is selective serotonin reuptake inhibitor plus psychotherapy	Panic disorder in MHS, SAS, or IS (41)	ROS (41)

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Table 3

Continued from previous page

Recommendation	Diagnosis and setting[a,b]	Level of evidence[c]
4. Selective serotonin reuptake inhibitors are effective for panic disorder	Panic disorder in MHS, SAS, or IS (41); panic disorder in MHS or SAS (24); panic disorder and social phobia among opioid users in SAS (19); social phobia and panic disorder in unspecified setting (21)	EO (19,21,24); ROS (19,41)
5. Nefazodone should be used as a last-line option	Panic disorder in MHS, SAS, or IS (41)	EO (41)
6. Warn of drug interactions with alcohol	Panic disorder among alcohol users in MHS (39)	EO (39)
7. Use augmentation strategies when necessary	Panic disorder in MHS, SAS, or IS (41)	ROS (41)
V. Posttraumatic stress disorder (PTSD)		
1. Inpatient psychiatric treatment is contraaindicated on a specialty posttraumatic stress disorder unit until substance abuse has stabilized	PTSD in MHS (38)	CS (38)
2. Psychosocial rehabilitation recommended	PTSD in MHS (38)	EO (38)
3. Treat substance abuse first	PTSD in MHS (38)	EO (38)
4. Treat substance abuse and posttraumatic stress disorder concurrently	PTSD in PCS or MHS (32); PTSD in unspecified setting (21)	EO (21,32)
5. Psychotherapy is effective. The specific type of psychotherapy used depends on the setting and available supports	PTSD in unspecified setting (59); PTSD in MHS, SAS, or IS (41); PTSD among opioid users in SAS (19)	EO (19,41,59)
6. Exposure therapy, mourning, eye movement desensitization reprocessing, and the counting method are considered high risk for substance abuse clients and should be conducted (or at least supervised) only by providers who have formal training in PTSD and only when the client is ready	PTSD in SAS, MHS, or IS (14)	EO (14)
7. Anticipate that treatment may proceed slowly; provide psychoeducation and coping skills	PTSD in SAS, MHS, or IS (14)	EO (14)
8. For clients with a severe trauma history, treatment is likely to be long term. If possible, refer the client to an individual therapist who can work with the client consistently	PTSD in SAS, MHS, or IS (14)	EO (14)
9. Avoid benzodiazepines or use very cautiously	PTSD in PCS or MHS (32,38)	EO (32,38)
10. Selective serotonin reuptake inhibitors are effective	PTSD among alcohol users in MHS, SAS, or IS (21,41)	QE (21); ROS (41)
11. Other medications may be effective	PTSD in MHS, SAS, or IS (41); PTSD in PCS or MHS (32)	EO (32,41); ROS (41)
12. New-generation antipsychotics may be effective for psychotic symptoms	PTSD in MHS, SAS, or IS (41)	ROS (41)
13. Mood stabilizers may be a useful adjunct	PTSD in MHS, SAS, or IS (41)	ROS (41)
14. Maintenance treatment recommended	PTSD in PCS or MHS (32)	EO (32)

[a] All recommendations apply to individuals with co-occurring disorders. If the type of disorder is not mentioned, it was unspecified in the article.
[b] MHS, mental health setting; SAS, substance abuse setting; IS, integrated setting; MS, methadone setting; PCS, primary care setting
[c] EO, expert opinion; ROS, randomized outcome study; QE, quasi-experimental; CS, case study

priateness of treatments and to compare alternative approaches.

Recommendations lag behind current practices. Most recommendations that have specificity are for acute pharmacotherapy, but even specific recommendations lag behind current clinical practice. Many studies have evaluated the use of tricyclic antidepressants for populations with co-occurring disorders; fewer studies have looked at the use of newer antidepressants (65). Yet tricyclics are rarely prescribed now that newer agents are available, so treatment recommendations concerning them are of little relevance.

Some recommendations reflect disagreement about important details. Although the use of psychotropic medication for mental illness is encouraged, experts disagree as to whether it is necessary to wait for abstinence before pharmacotherapy is started (11,14,20,25,29,33,41,42,50). This disagreement does not vary by the specific substances being abused or by the type of mental illness. Although abstinence is the ultimate goal of substance abuse treatment for co-

Table 4

Treatment recommendations for persons with a co-occurring affective or anxiety and substance use disorder (general substance use disorders)

Recommendation	Diagnosis and setting[a,b]	Level of evidence[c]
I. Screening and referral		
1. Screen for psychiatric disorders	Alcohol use disorder in SAS (60); unspecified substance use disorder in SAS (21); unspecified substance use disorder in unspecified setting (49); unspecified substance use disorder in MHS or IS (14)	EO (14,21,49,60)
2. If the patient is suicidal or requires more treatment resources than can be provided by the SA treatment agency, obtain a mental health consultation or refer the patient to a mental health provider	Unspecified substance use disorder in MHS, SAS, or IS (14)	EO (14)
3. Use care in screening for trauma	Unspecified substance use in MHS, SAS, or IS (14)	EO (14)
II. Assessment and diagnosis		
1. Assessment of substance use disorders includes a comprehensive medical and psychological history, including a status examination. In some cases, psychological or neuropsychological testing may be indicated	Heroin use in PCS (34); unspecified substance use disorder in unspecified setting (29)	EO (29,34)
2. Conduct a longitudinal evaluation ratherthan relying on one interview	Unspecified substance use disorder in unspecified setting (29); unspecified substance use disorder in SAS (43)	EO (29,43)
3. Estimating the risk of severe withdrawal symptoms from patient accounts of consumption is not useful	Unspecified substance use disorder in SAS (61)	EO (61)
4. Obtain corroborating information on long-standing patient behaviors from patients' family members	Unspecified substance use disorder in SAS (43)	EO (43)
5. Identify the client's substance use on the continuum of use, abuse, and dependence	Unspecified substance use disorder in SAS (49)	EO (49)
6. It is important for the substance abuse treatment provider to monitor psychiatric symptoms	Unspecified substance use disorder in SAS, MHS, or IS (14)	EO (14)
7. Comorbid psychological conditions may complicate substance abuse treatment	Unspecified substance use disorder in SAS (29)	EO (29)
8. Assess for motivational stage	Unspecified substance use disorder in SAS, MHS, or IS (14)	EO (14)
III. Acute treatment		
General		
1. Patients with a dual diagnosis require treatment of psychiatric symptoms concurrently with detoxification or addiction treatment	Unspecified substance use disorder in unspecified setting (29); heroin use in PCS (34)	EO (29,34)
2. Initial treatment efforts should be directed toward any substance-induced disorder that may be present; once patients are stable, treatment for substance abuse or dependence, as well as any other disorder present, should proceed concurrently in the context of an integrated treatment program	Unspecified substance use disorder in unspecified setting (29)	EO (29)
3. In early recovery, the emphasis should be on supporting recovery, attending 12-step meetings, and participating in other self-help and group therapies; insight-oriented treatments must be carefully measured and limited early on by their potential to increase anxiety and trigger relapse; when psychotherapy is immediately essential, clients should be referred to recovery-oriented psychotherapists who will integrate psychotherapy with mutual self-help approaches	Unspecified substance use disorder with anxiety or mood disorder in SAS, MHS, or IS (14)	EO (14)
4. The first step in changing substance use is to build a working alliance	Unspecified substance use disorder in outpatient MHS (62)	EO (62)
5. Patients with severe psychiatric comorbidity who do not have an established	Unspecified substance use disorder in unspecified setting (29)	EO (29)

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Table 4

Continued from previous page

Recommendation	Diagnosis and setting[a,b]	Level of evidence[c]
treatment relationship and who are at risk of severe withdrawal may require hospitalization		
6. Addiction treatment for co-occurring disorders is fundamentally similar to addiction treatment for a person with abstinence as a goal and with the need to develop specific relapse prevention skills	Unspecified substance use disorder in IS (25)	EO (25)
7. In early recovery as much structure as possible should be provided	Unspecified substance use disorder in MHS (62)	EO (62)
8. Initial treatment progress is defined by movement through the stages of change	Unspecified substance use disorder in IS (25)	EO (25)
Psychosocial		
1. Address cognitive limitations by being more concrete, using simpler concepts through repetition	Unspecified substance use disorder in MHS, SAS, or IS (14)	EO (14)
2. Educate the patient on the self-limited nature of prolonged withdrawal symptoms. Avoid treating prolonged withdrawal symptoms with prescription medications	Unspecified substance use disorder among depressed or anxious persons in unspecified setting (49)	EO (49)
3. Motivational interviewing is effective	Unspecified substance use disorder with depression in MHS (52); unspecified substance use disorder in MHS (62); unspecified substance use disorder in MHS, SAS, or IS (14); unspecified substance use disorder in PCS (28)	EO (28,62); ROS (14,52)
4. Provide relapse prevention education	Unspecified substance use disorder in MHS, SAS, or IS (14); unspecified substance use disorder in PCS (28)	EO (14,28)
5. Useful psychoeducational classes include providing information on mental and substance use disorders, "double trouble" groups, and dual recovery and mutual self-help groups	Unspecified substance use disorder in MHS, SAS, or IS (14); unspecified substance use disorder in PCS (28); cocaine and heroin use in MS (44)	EO (14,28,44)
6. Use contingency management techniques	Unspecified substance use disorder in MHS, SAS, or IS (14)	EO (14)
7. Use harm reduction techniques; may use individual and group interventions	Unspecified substance use disorder in IS (25); unspecified substance use disorder in MHS (62); unspecified substance use disorder in SAS or IS (45)	
8. Shorten the duration of group sessions	Unspecified substance use disorder in MHS, SAS, or IS (14)	EO (14)
9. The primary goal of therapy is abstinence rather than insight	Cocaine and heroin use in MS (44)	EO (44)
10. Modify therapeutic community strategies	Unspecified substance use disorder in SAS (14)	ROS (14)
11. Modify assertive community treatment strategies	Unspecified substance use disorder in SAS (14)	ROS (14)
12. Modify intensive case management strategies	Unspecified substance use disorder in SAS (14)	ROS (14)
Pharmacotherapy		
1. Medications to treat addictions are an ancillary tool to a full recovery program	Unspecified substance use disorder in IS (25)	EO (25)
2. Refer to a psychiatrist or other prescriber for pharmacotherapy; observe and report symptoms and behavior to the prescribing physician to assist in determination of medication needs and to adjust medications on an ongoing basis	Unspecified substance use disorder in SAS (14)	EO (25)
3. Become familiar with common psychotropic medications and instruct the client about the role of medications in the recovery process	Unspecified substance use disorder in SAS (14)	EO (14)
4. Fixed-dosage regimens are recommended	Unspecified substance use disorder in IS (25)	EO (25)
5. Self-help groups are often beneficial	Unspecified substance use disorder in MHS (62); unspecified substance use disorder in IS (37); unspecified substance use disorder in SAS (14)	EO (14,37,62)

[a] All recommendations apply to individuals with co-occurring disorders. If the type of disorder is not mentioned, it was unspecified in the article.
[b] SAS, substance abuse setting; MHS, mental health setting; IS, integrated setting; PCS, primary care setting
[c] EO, expert opinion; ROS, randomized outcome study

Table 5

Treatment recommendations for persons with a co-occurring affective or anxiety disorder and substance use disorder (alcohol, cocaine, and opioid disorders)

Recommendation	Diagnosis and setting[a,b]	Level of evidence[c]
Alcohol		
1. Cognitive-behavioral therapy may be effective for alcohol use disorders	Alcohol use disorder with mood or anxiety disorder in unspecified setting (21)	ROS (21)
2. Among patients with comorbid mood or anxiety symptoms and alcohol disorders: SSRIs may be effective for alcohol use symptoms Minimal evidence exists for the efficacy of lithium and alcohol abuse symptoms Buspirone may be effective for alcohol abuse symptoms	Unspecified substance use disorder with depression in MHS (52); alcohol use disorder with depression or anxiety disorder in PCS (28); alcohol use disorder with mood or anxiety disorder in unspecified setting (21,29,63)	ROS (21,28,29, 52,63)
3. Mood stabilizers may be effective for alcohol withdrawal symptoms	Alcohol use disorder with bipolar disorder in unspecified setting (64)	ROS (64)
4. Patients with impairment or self-destructive symptoms are poor candidates for disulfiram	Alcohol use disorder with depression in unspecified setting	EO (29)
5. Naltrexone may be effective in the management of alcohol abuse	Alcohol use disorder with mood or anxiety disorder in unspecified setting (21); alcohol use disorder with anxiety disorder in unspecified setting (41)	ROS (21,41)
Cocaine		
1. Carbamazepine may be effective among patients with bipolar disorder and cocaine dependence	Cocaine use with bipolar disorder in PCS (28); cocaine use with bipolar disorder in unspecified setting (64)	CS (28,64)
2. Tricyclics may be effective in cocaine-abusing, methadone-maintained patients with depression	Cocaine use with depression in MS (29,58)	ROS (29,58)
3. Cognitive therapy and integrated psychological therapy may be effective among cocaine-abusing patients maintained on methadone	Cocaine and heroin use with depression in MS (44)	ROS (44)
Opioid		
1. Methadone may be effective for patients with mental illness and opiate dependence	Opioid use in SAS (61)	EO (61)
2. Cocaine-abusing patients maintained on methadone may have more success in methadone maintenance treatment than in a therapeutic community	Cocaine and heroin use in SAS (44)	QE (44)

[a] All recommendations apply to persons with co-occurring disorders. If the type of disorder is not mentioned, it was unspecified in the article.
[b] MHS, mental health setting; PCS, primary care setting; MS methadone setting; SAS, substance abuse setting
[c] ROS, randomized outcome study; EO, expert opinion; CS, case study; QE, quasi-experimental

occurring disorders, the relative importance of harm reduction as an interim goal is unclear. These important questions are yet to be resolved.

Recommendations in diagnosis-specific guidelines do not specifically apply to persons with co-occurring disorders. Although most diagnosis-specific guidelines contain a small section documenting the importance of co-occurring disorders, diagnosis-specific guidelines are often silent as to whether the specific treatment recommendations apply to co-occurring disorders (29–31,39,47). Thus there is no evidence for important treatment questions such as how long psychotropic medication should continue once symptoms have remitted, whether and for how long maintenance treatment for substance use or mental disorders is recommended, and whether methadone is efficacious for individuals with opiate addiction who have co-occurring disorders. In the absence of evidence, the presumption is that clinicians should use the same guidelines to treat persons with co-occurring disorders as they use to treat those with a single disorder.

Empirical evidence is lacking for most recommendations. Perhaps the most important issue revealed by our review is that empirical evidence is lacking for most recommendations. Of particular importance is the lack of evidence for the recommendation to treat patients with co-occurring disorders in integrated treatment settings, the need for specialist assessment, and the sequencing of substance abuse and mental health treatment. Most recommendations are supported by expert opinion, and there are few randomized—or even quasi-experimental—designs. When empirical evidence exists, it is usually diagnosis and setting specific, yet the recommendations we found in conducting this review are framed in more general terms. In addition, many recommendations are not easily evaluated for efficacy, such as the recommendation that successful treatment programs be welcoming and accessible and convey an attitude of optimism and recovery.

Some recommendations are supported by empirical evidence, including the recommendation to screen for substance abuse (27) and the effectiveness of specific treatments for de-

pression and anxiety disorders (11, 19,21,24,27–29,32,33,36,41,44,46,49, 50–52,56,57) and for substance abuse (21,28,29,41,44,52,58,63,64).

Conclusions

The results of this review present several challenges and dilemmas. Patients who are seen in clinical practice commonly have multiple problems, yet the efficacy data we have almost always come from treatments of single illnesses. In the absence of data, good practice suggests that each illness should be treated with the most effective treatments for the single illness. However, it would be useful to have more information about how standard treatment approaches should be modified for co-occurring disorders. Without efficacy data and performance measures, it is difficult for public and private payers to evaluate the appropriateness of treatments and hold agencies accountable for evidence-based care.

The enormous number of potential combinations of disorders means that it is unlikely that there will ever be efficacy data for most combinations of disorders. The mental health field needs to consider its research priorities and how to address the multitude of potential combinations. As a first step, we might consider research on treatments and illness combinations that are highly prevalent, or research on treatments with immediate clinical impact. Second, rather than evaluating single treatments or interventions, it may be most useful to evaluate "packages" of best practices that could be applied to a range of disorders. Finally, research related to treatment effects and the realities of implementation in community settings may have more relevance to clinicians and program administrators who are interested in informing clinical management decisions. ♦

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