Complete Summary

GUIDELINE TITLE

Medication-assisted treatment for opioid addiction in opioid treatment programs: Treatment of co-occurring disorders.

BIBLIOGRAPHIC SOURCE(S)

Treatment of co-occurring disorders. In: Batki SL, Kauffman JF, Marion I, Parrino MW, Woody GE, Center for Substance Abuse Treatment (CSAT). Medication-assisted treatment for opioid addiction in opioid treatment programs. Rockville (MD): Substance Abuse and Mental Health Services Administration (SAMHSA); 2005. p. 189-209. (Treatment improvement protocol (TIP); no. 43).

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- December 12, 2007, Carbamazepine: The U.S. Food and Drug Administration (FDA) has provided recommendations for screening that should be performed on specific patient populations before starting treatment with carbamazepine.
- May 2, 2007, Antidepressant drugs: Update to the existing black box warning on the prescribing information on all antidepressant medications to include warnings about the increased risks of suicidal thinking and behavior in young adults ages 18 to 24 years old during the first one to two months of treatment.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Co-occurring mental disorders associated with opioid addiction including:

- Mood disorders (major depressive disorder, dysthymic disorder, bipolar disorder)
- Anxiety disorders (generalized anxiety disorder, posttraumatic stress disorder, social phobia, obsessive-compulsive disorder, panic disorder)
- Attention-deficit hyperactivity disorder (ADHD)
- Schizophrenia and other psychotic disorders
- Cognitive disorders
- Eating disorders
- Impulse control disorders: pathological gambling
- Sleep disorders
- Personality disorders (antisocial personality disorder, borderline personality disorder, narcissistic personality disorders)

GUIDELINE CATEGORY

Diagnosis
Management
Screening
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Psychiatry
Psychology

INTENDED USERS

Nurses
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers
Substance Use Disorders Treatment Providers

GUIDELINE OBJECTIVE(S)

To provide recommendations on screening, diagnosing, and treating patients in opioid treatment programs (OTPs) who have co-occurring mental disorders

TARGET POPULATION

Patients in medication-assisted treatment for opioid addiction (MAT) with co-occurring mental disorders

INTERVENTIONS AND PRACTICES CONSIDERED

Screening and Assessment

1. Specific screening procedures
2. Screening for cognitive impairment
3. Screening tools
4. Making and confirming a psychiatric diagnosis (using *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* [DSM-IV-TR] criteria)
5. Structured and semistructured interview formats for psychiatric diagnoses
6. Differential diagnosis
7. Timing for confirming a diagnosis

Management

1. Distinguishing non-substance-induced from substance-induced co-occurring disorders
2. General treatment considerations for patients with co-occurring disorders
3. Co-occurring disorders and treatment planning
    - Patients in acute psychiatric danger
    - Patients with established, severe co-occurring disorders
    - Patients with less severe, persisting or emerging symptoms of co-occurring disorders
    - Patients with less severe, presumptively substance-induced co-occurring disorders
4. Models of care
5. Handling emergency situations, including protocol for identifying and handling suicide and homicide risk
6. Counseling, psychotherapy, and mutual-help groups for people with co-occurring disorders in medication-assisted treatment for opioid addiction (MAT)
7. Psychoeducation for patients with co-occurring disorders in MAT
8. Pharmacotherapy for patients with co-occurring disorders in MAT
    - Major depression and bipolar disorder: (selective serotonin reuptake inhibitors [SSRIs], carbamazepine, tricyclic antidepressants, monoamine oxidase [MAO] inhibitors, lithium)
    - Anxiety disorders: (SSRIs, venlafaxine [Effexor®], and tricyclic antidepressants
    - Attention deficit hyperactivity disorder (AD/HD): Stimulants such as methylphenidate (Ritalin®), amphetamine, or atomoxetine (Strattera®)
    - Schizophrenia: antipsychotic medications (clozapine [Clozaril®], olanzapine [Zyprexa®], risperidone [Risperdal®]), quetiapine, ziprasidone [Geodon®], and aripiprazole [Abilify®])

MAJOR OUTCOMES CONSIDERED

- Response to treatment
- Reduction in substance abuse
- Human immunodeficiency virus (HIV) risk behavior and comorbidity
- Side effects of medications
- Drug interactions

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The literature search involved careful consideration of all relevant clinical and health services research findings, practice experience, and implementation requirements.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

After selecting a topic, Center for Substance Abuse Treatment (CSAT) invites staff from pertinent Federal agencies and national organizations to be members of a resource panel that recommends specific areas of focus as well as resources that

should be considered in developing the content for the Treatment Improvement Protocols (TIP). These recommendations are communicated to a consensus panel composed of experts on the topic who have been nominated by their peers. This consensus panel participates in a series of discussions. The information and recommendations on which they reach consensus form the foundation of the TIP. The members of each consensus panel represent substance abuse treatment programs, hospitals, community health centers, counseling programs, criminal justice and child welfare agencies, and private practitioners. A panel chair (or co-chairs) ensures that the contents of the TIP mirror the results of the group's collaboration.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

A large and diverse group of experts closely reviews the draft document. Once the changes recommended by these field reviewers have been incorporated, the Treatment Improvement Protocol (TIP) is prepared for publication, in print and on line.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Unless medication-assisted treatment for opioid addiction (MAT) providers distinguish co-occurring disorders accurately by type and address them appropriately, these disorders likely will complicate patients' recovery and reduce their quality of life. Numerous studies have indicated that rapid, accurate identification of patients' co-occurring disorders and immediate interventions with appropriate combinations of psychiatric and substance addiction therapies improve MAT outcomes. The consensus panel for this Treatment Improvement Protocol (TIP) endorses this view. Many standard treatments for mental disorders can be modified readily for patients with co-occurring disorders in MAT.

Prevalence of Co-Occurring Disorders

The table below lists the most common co-occurring disorders among patients in MAT, based on representative studies.

Common Co-Occurring Disorders in Patients Who Are Opioid Addicted	
Axis I Categories (Clinical Disorders and Other Conditions)	**Axis II Categories (Personality Disorders and Mental Retardation)**
• Mood Disorders Major depressive disorder Dysthymic disorder Bipolar disorder	• Personality Disorders Antisocial personality disorder (APD) Borderline personality disorder Narcissistic personality disorder
• Anxiety Disorders Generalized anxiety disorder Posttraumatic stress disorder (PTSD) Social phobia Obsessive-compulsive disorder Panic disorders • Attention Deficit/Hyperactivity Disorder (AD/HD) • Schizophrenia and Other Psychotic Disorders • Cognitive Disorders • Eating Disorders • Impulse Control Disorders: Pathological Gambling • Sleep Disorders	

Screening for Co-Occurring Disorders

The consensus panel believes that admission and ongoing assessment routinely should incorporate screening for co-occurring disorders. This screening should yield a simple positive or negative result, depending on whether signs or symptoms of co-occurring disorders exist. A negative result generally should rule out immediate action, and a positive result should trigger detailed assessment by a trained professional.

To identify patients in MAT with co-occurring disorders, treatment providers must decide

- When and how to screen patients
- How to integrate psychological screening with standard intake assessment
- Which instruments to use for screening and confirming co-occurring disorders
- What qualifications are needed by staff who conduct screenings
- How to classify symptoms and other evidence
- How to determine the most appropriate treatment methodology and level of care

Specific Screening Procedures

Opioid treatment programs (OTPs) should establish specific screening procedures for co-occurring disorders and train counselors and intake workers to perform these procedures, including how to recognize the presenting symptoms of the most commonly encountered co-occurring disorders. Few significant differences in symptoms of mental disorders exist between patients who are addicted to opioids and other people who are not; therefore, the symptoms described in *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, Text Revision (DSM-IV-TR) are applicable during admission screening. When possible, screening for co-occurring disorders should be linked with other assessments to avoid duplicate efforts by staff and unnecessary burdens on patients' time. An OTP's screening procedures for co-occurring disorders should specify

- Questions or instruments to be used
- When and where to conduct screening segments (e.g., address all safety-related questions during initial intake and defer other questions until applicants are no longer intoxicated or in withdrawal--but wait no longer than a specified period after admission)
- Who conducts screenings
- How to record results
- Cutoff scores or other indicators of positive results for co-occurring disorders
- Exactly how to handle positive results (e.g., whom to inform, how, and when; what constitutes a psychiatric emergency and how to address it)
- How extensively a patient's self-reported information must be corroborated with information from other sources (e.g., family and friends, caseworkers, previous treatment records)
- Which staff members to consult if questions arise about these procedures or the results

Screening for co-occurring disorders usually entails determining

- An applicant's immediate safety and self-control, including any suicide risk, aggression or violence toward others, or domestic or other abuse or victimization and the ability to care for himself or herself (see "Handling Emergency Situations" below)
- Previous diagnosis, treatment, or hospitalization for a mental disorder and, if applicable, why, when, and where, as well as the treatment received and its outcome. Questions about the relationship of mental disorders to substance use--for example, whether a mental disorder was present during abstinence or before the substance use disorder--determine whether a co-occurring disorder is substance induced or independent.
- The applicant's current co-occurring disorder symptomatology based on DSM-IV-TR criteria, including whether any psychotropic medications have been prescribed or are being used (usually included on a screening questionnaire)
- Trauma history (e.g., physical or sexual abuse, living through a natural disaster or war, witnessing death or tragedy). Questions about trauma should be brief and general, without evoking details that might precipitate stress.
- Any history of mental disorder-related symptoms among immediate relatives and their diagnoses, treatments, or hospitalization
- Any unusual aspects of an applicant's appearance, behavior, and cognition. If indications of a cognitive impairment are present, a mental status examination should be conducted.

Screening for Cognitive Impairment

The accuracy of instruments to screen for co-occurring disorders may be compromised if administered to patients with cognitive impairments. A brief preexamination of cognitive functioning during a mental status examination is recommended for individuals who are disoriented with respect to time, place, or person; have memory problems; or have difficulty understanding information in their first language.

Screening Tools

Many States require specific screening or assessment instruments, such as the Addiction Severity Index (ASI), to document baseline patient data. Other important considerations in selecting a screening tool for co-occurring disorders include its psychometric properties and cultural appropriateness and, if the test is self-administered, the literacy level required. The consensus panel believes that no instrument in an OTP can identify co-occurring disorders satisfactorily, and many of the most thoroughly tested are not in the public domain. The ASI records symptoms of mental disorders but does not diagnose.

Making and Confirming a Psychiatric Diagnosis

After a possible co-occurring disorder is identified during screening, an experienced, licensed mental health clinician (e.g., psychiatrist, psychologist, clinical social worker) should perform additional evaluation to make or confirm a diagnosis. Ideally, this expertise is available at the OTP. When it is not, appropriate consultants and referral resources must be substituted, but procedures to use and reimburse these resources should be well established.

DSM-IV-TR Criteria

Although many insurance companies require International Classification of Diseases diagnostic codes for reimbursement purposes, clinicians and researchers in the United States traditionally use the DSM classification system. As this system has evolved over several editions, its authors have made important changes in definitions for substance-related disorders. Specifically, the DSM-IV-TR divides these disorders into two types: substance use disorders and substance-induced co-occurring disorders.

Substance Use Disorders

DSM-IV-TR divides substance use disorders into abuse and dependence with or without physiological features such as tolerance or withdrawal. It also makes distinctions pertaining to early or sustained remission; programs offering agonist, partial agonist, or agonist/antagonist therapy; and treatment while living in a controlled environment (e.g., jail).

Substance-Induced Co-Occurring Disorders

Substance-induced co-occurring disorders are associated with intoxication, withdrawal, and the persistent effects of substances of abuse. Substance-induced

persisting disorders are those in which substance-related symptoms continue long after a person stops using a drug (e.g., prolonged flashbacks from hallucinogen use, substance-induced persistent dementia, substance-induced persistent amnesia). Exhibit 12-2 in the original guideline document shows the association between substance-induced co-occurring disorders and substances of abuse. It is noteworthy that different drugs have been associated with different types of co-occurring disorders and that some (such as opioids) have relatively few or no reported psychotoxic effects, whereas others have many.

Structured and Semistructured Interview Formats for Psychiatric Diagnoses

A number of carefully designed and tested instruments are available to determine DSM-IV or International Classification of Diseases (ICD)-10 diagnoses, although a careful clinical interview usually can serve this purpose. Not all instruments have been updated for DSM-IV-TR diagnoses, but DSM-IV diagnoses are similar. Examples include the

- Structured Clinical Interview for DSM-IV Axis I and II Disorders, Clinical Versions
- Composite International Diagnostic Interview, Core Version 2.1
- Psychiatric Research Interview for Substance Abuse and Mental Health Disorders
- Diagnostic Interview Schedule, Version 4
- Alcohol Use Disorder and Associated Disabilities Interview Schedule.

Differential Diagnosis

Careful assessment including a family history is critical to determine whether presenting symptoms indicate independent co-occurring disorders or disorders induced by substance use or a general medical or neurological condition. In many cases, people who abuse multiple substances have both an independent co-occurring disorder and various substance-induced symptoms precipitated by intoxication or withdrawal. Substance use can magnify symptoms of independent co-occurring disorders.

Timing for Confirming a Diagnosis

Accurate diagnosis of independent co-occurring disorders is difficult during the early phases of MAT because substance-induced symptoms also usually are present. A definitive diagnosis often must wait until a patient is stabilized on treatment medication for a minimum of 5 to 7 days (but preferably 2 to 4 weeks) and any continuing substance use is eliminated. Although several weeks of abstinence may improve the accuracy of diagnoses, symptoms of severe co-occurring disorders (e.g., suicidality, psychotic reaction) need prompt attention and might require more immediate pharmacological treatment or hospitalization. OTPs should be aware that even symptoms of less severe co-occurring disorders can prevent a patient's stabilization and should be addressed quickly.

Guidelines for Distinguishing Non-Substance-Induced From Substance-Induced Co-occurring Disorders

To assist with a differential diagnosis, the following information should be collected and reviewed:

- Previous history of mental disorders and treatment, focusing on temporal relationship of symptoms to substance use and response to previous treatment
- Type, quantity and frequency, and time of last use of illicit substances or prescribed psychotropic drugs (each substance class produces specific physiological and behavioral effects, especially during acute intoxication or withdrawal after prolonged, high-dosage use)
- Family history of mental disorders.

DSM-IV-TR offers the following procedures to ascertain whether a co-occurring disorder is primary or secondary:

- Label the disorder according to predominant symptom pattern and specified criteria (e.g., mood, anxiety, psychotic disorder).
- Consider the co-occurring disorder *primary* (not substance induced) if
    - Symptoms developed before the substance use disorder
    - Symptoms have persisted during 30 days or more of abstinence (depending on the characteristic withdrawal course for each substance)
    - Symptoms are inconsistent with or exceed those produced by the abused substance at the dosage used (e.g., hallucinations after opioid withdrawal, paranoid delusions after low-dose marijuana use)
    - Substance use or another medical disorder cannot account better for the symptoms
- Consider the mental disorder *secondary* (substance induced) if
    - Symptoms developed only during periods of active substance use or within 1 month of intoxication or withdrawal
    - Symptoms are consistent with intoxication or withdrawal from substances used
    - Other features (e.g., age at onset) are atypical for primary co-occurring disorder
    - Another co-occurring or medical disorder does not account better for the symptoms.

Prognosis for Patients With Co-Occurring Disorders

Effects of Co-Occurring Disorders on Treatment Outcomes

The conventional view, which has considerable empirical support, is that unidentified, untreated co-occurring disorders impede progress for patients in MAT and lead to difficulties in engaging patients in treatment, establishing a therapeutic alliance between patients and treatment providers, maintaining adherence to treatment regimens, eliminating substance abuse and other risky behaviors, and preventing premature dropout or early relapse.

Because research on treatment outcomes for patients with opioid addiction and co-occurring disorders usually examines small groups of subjects and because patients in these groups are not homogeneous, the general applicability of current findings is limited. Many confounding factors exist. Despite these limitations,

numerous studies have found that many patients with co-occurring disorders did well when appropriate psychiatric and substance abuse treatments were delivered. The consensus panel recommends more intensive and psychiatrically specific treatment for these patients.

Effects of Symptom Severity

Studies disagree on whether the severity of co-occurring disorder symptoms in patients who are addicted is a useful predictor of treatment outcomes. Early studies found that the severity of co-occurring disorder symptoms, particularly in patients with anxiety or depression, strongly predicted treatment outcomes and that the most severely symptomatic patients had the heaviest substance use and most impaired adjustment, whereas the least symptomatic did best in addiction treatment. However, later studies have found that higher symptom severity, although associated with higher levels of substance use and worse overall adjustment, did not predict treatment response. In one study, drug test results for patients with severe psychopathology improved significantly over time. In another study, patients in MAT for at least 90 days who had co-occurring disorders and high levels of symptom severity had positive treatment responses. Patients with more than one co-occurring disorder engaged in treatment more readily than those who were addicted only, and both groups were similar in average incidence of drug use or criminal activity. Patients with depression, anxiety, suicidal ideation, and other pathologies at intake were twice as likely to attend individual--but not group--counseling sessions and significantly more likely to discuss psychological problems than those reporting none of these symptoms.

Consequently, caution is advised in predicting a simple, stable correlation between symptom severity of co-occurring disorders and treatment outcomes. However, the consensus panel believes that co-occurring disorders can improve substantially but that outcomes depend heavily on additional treatment being provided for these disorders and that patients with severe symptoms may require longer, more intensive treatment.

Prognosis for Specific Co-occurring Disorders

Refer to the original guideline document for a discussion of the following topics:

- Effects of co-occurring APD on progress in MAT
- Effects of co-occurring PTSD on progress in MAT
- Effects of co-occurring AD/HD on progress in MAT

Treatment Issues

General Treatment Considerations for Patients With Co-Occurring Disorders

Clearly, co-occurring disorders should not exclude people with opioid addiction from admission to an OTP. The consensus panel believes that the best strategy is to stabilize these patients' opioid addiction with methadone, buprenorphine, or levo-alpha acetyl methadol (LAAM) while assessing their co-occurring disorder symptoms and choosing the most appropriate treatment course. Although OTP

staff members often focus on the condition that is most severe and threatening, it usually is best to address all of a patient's disorders simultaneously because each can influence the others.

The consensus panel believes that the following principles are essential to manage patients with co-occurring disorders in an OTP:

- Treatment of co-occurring disorders should be integrated or closely coordinated with substance abuse treatment when the former is not available on site.
- Staff members, whether primarily from the substance abuse treatment or mental health fields, should be knowledgeable about treatments for both disorders.
- Psychotropic medications should be prescribed only after patients are stabilized on the treatment medication (which in the panel's experience takes an average of 3 to 7 days for buprenorphine and 3 weeks to a month for methadone), unless an independent co-occurring disorder is evident from past records or clinical examination or significant impairment associated with the symptoms of a co-occurring disorder exists.
- All medications used by patients and patients' adherence to medication regimens should be monitored carefully, for example, via drug testing. Physicians should be careful about prescribing substances with abuse potential, such as benzodiazepines. If such medications are prescribed, the less abusable drugs in a class should be chosen, for example, oxazepam (Serax®) rather than lorazepam, clonazepam, alprazolam, or diazepam.
- Patients resistant to being psychiatrically diagnosed should be assured that it is not shameful but is likely to provide a better understanding of their problems and aid in treatment. Educating patients about co-occurring disorders helps.
- Therapy for patients with co-occurring disorders should be more intensive, on average, than for patients without co-occurring disorders. The primary goal is abstinence from substances. Remission of co-occurring disorder symptoms should be an important secondary goal.

Co-Occurring Disorders and Treatment Planning

Because patients in MAT exhibit a wide range of co-occurring disorders, the consensus panel believes that early treatment planning and resource management should include classifying patients, at least tentatively, into categories based on types and severity of co-occurring disorders, although treatment always should be tailored individually.

Patients in Acute Psychiatric Danger

Patients presenting with suicidal or homicidal ideation or threats--whether resulting from acute intoxication or withdrawal or from an independent co-occurring disorder--or those manifesting psychotic symptoms (e.g., hallucinations, paranoia) that may interfere with their safety and ability to function should be assessed and treated immediately. Although their symptoms may be short lived, admission to a psychiatric unit for brief treatment may be necessary if outpatient care is too risky or problematic. Immediate administration of antipsychotic drugs, benzodiazepines, or other sedatives may be required to establish behavioral

control. A physician, physician's assistant, or nurse practitioner on staff can prescribe medications at the OTP. Otherwise, referral is warranted. In emergencies, OTPs should send patients to affiliated hospital emergency rooms (see "Handling Emergency Situations" below).

Patients with Established, Severe Co-occurring Disorders

Patients in MAT who are not in acute danger but have been diagnosed or treated for severe co-occurring disorders (e.g., schizophrenia, bipolar disorder) should receive medication with the lowest abuse potential for their condition. If an OTP is staffed appropriately and prepared to treat patients with severe co-occurring disorders, these patients can be treated on site. Otherwise, they should be referred to an OTP with these qualifications. If there is no such OTP, patients may need to remain in a less optimal OTP but receive psychiatric treatment at another facility. For referrals, effective communication between OTPs and mental health providers is necessary to coordinate treatment.

Patients with Less Severe, Persisting or Emerging Symptoms of Co-occurring Disorders

Patients in MAT with nondisabling symptoms of less severe co-occurring disorders (e.g., mood, anxiety, and personality disorders), psychiatric treatment histories, or verified diagnoses and current prescriptions for medications to treat such disorders (regardless of whether they are used) should continue or begin medication, psychotherapy, or both for their co-occurring disorders. These patients should continue in MAT if the OTP is staffed to treat them. Although it is desirable for patients to be stabilized on methadone, buprenorphine, or LAAM before other pharmacotherapy is initiated, newer medications with relatively benign side effects can be initiated sooner (e.g., selective serotonin reuptake inhibitors [SSRIs]) if a primary mental disorder is indicated. Such medications may facilitate engagement in MAT and addiction recovery.

Patients with Less Severe, Presumptively Substance-Induced Co-occurring Disorders

The consensus panel recommends that patients in MAT with symptoms of Axis I disorders but no history of primary co-occurring disorders receive no new psychotropic medications until they are stabilized on MAT because their symptoms might remit or significantly diminish after a period of substance abuse treatment. Exceptions include patients who have acute, substance-induced disorders such as extreme anxiety or paranoia that are likely to be transitory but require temporary sedation or antianxiety medication.

Effects of Co-Occurring Disorders on Human Immunodeficiency Virus (HIV) Risk Behaviors and Comorbidity

To decrease the spread of HIV, it is important to treat both substance use and co-occurring disorders and provide education and support for patients who inject drugs.

Models of Care

Although it is not always feasible to provide more specialized services on site, patient adherence to medical treatment was found to drop dramatically when such services were provided through offsite referral. Even when referrals are to services near an OTP, noncompliance may have significant consequences for personal, social, and public health.

If a program cannot provide onsite ancillary services, it is important that staff members identify co-occurring disorders early so that they can refer patients to appropriate resources. It is essential to monitor patient progress and compliance with offsite treatment, which can be done by a counselor, case manager, nurse, or physician's assistant or by assigning one staff member to coordinate and monitor all referrals. Offsite referrals also may be necessary to obtain psychotropic medications and evaluate patients' reactions to them.

Handling Emergency Situations

A high percentage of patients with co-occurring disorders in MAT have reported suicide attempts or difficulty controlling violent behavior during their lifetimes. Patients who present an acute danger to themselves or others or have psychotic symptoms or disordered thinking that could interfere with their safety or that of others should receive immediate, aggressive intervention on admission and throughout treatment. Staff members should be trained to notice indications of suicidal or homicidal risks. These observations should be documented and communicated to designated staff members who can take necessary action, including appropriate medication, notification of family members and involved agencies (e.g., probation office, children's protective services), or transfer of patients to more secure or protective settings. Staff members should understand thoroughly and be prepared to act on an OTP's "duty to warn" about potentially violent behavior by patients.

Risk Factors and Predictors for Suicidal Ideation and Threats

Substance intoxication or withdrawal can cause or exacerbate suicidal ideation or threats, and the presence of co-occurring disorders further increase the risk.

Risk factors do not predict individual behavior, but a high-risk profile merits immediate and ongoing attention.

Protocol for Identifying and Handling Suicide and Homicide Risk

All intake workers, certified addiction counselors, and clinicians should be alert to risk factors for suicide and homicide and should question at-risk patients routinely about suicidal or homicidal thoughts or plans. This is important for patients who appear withdrawn, depressed, angry, or agitated or are known to have experienced a recent significant loss or other source of stress--especially if a co-occurring disorder is suspected or diagnosed or if a patient still is intoxicated or withdrawing from a psychoactive substance. Although the consensus panel believes such screening is helpful, the research evidence supporting its effectiveness is limited.

To aid in screening and referral for suicidality and homicidality, all programs should have protocols in place that specify

- Who asks what questions or uses what specific tool to identify these types of risk
- How identified risks are documented
- Who is informed about risks and is responsible for taking actions and what resources he or she can use (e.g., medications, referral/transfer, family involvement).

Any patient suspected of suicide or homicide risk should be referred immediately to a mental health clinician for further evaluation. If the OTP has no psychologist, clinical social worker, or psychiatrist on staff, it should have arrangements for rapid consultations. Decisions should be made about using antipsychotic medications, benzodiazepines, or other sedatives to establish behavioral control rapidly. Such medications may be needed to alleviate or control symptoms until other mood stabilizers or antidepressants take hold, which can take several weeks. Medication-assisted treatment of acute suicidality should be on an inpatient basis unless family members or friends are willing to be responsible for administering the drugs regularly, keeping the at-risk patient safe, and monitoring his or her reactions.

Patients identified as being at imminent risk of committing suicide or homicide might need hospitalization for short-term observation. Some key factors in this decision are clearly expressed intent, specific and lethal plans, accessible means, limited social or familial resources, severe symptoms of mental illness or psychosis, command hallucinations, hopelessness, and previous suicide or homicide attempts. If a referral is made, the patient should not be left alone until responsibility for monitoring safety is transferred to the referred facility.

Counseling, Psychotherapy, and Mutual-Help Groups for People With Co-Occurring Disorders in MAT

Programs should encourage participation in mutual-help groups that focus on the needs of people with co-occurring disorders. Exhibit 12-3 in the original guideline document lists some of the best known of these groups, along with contact information.

Psychoeducation for Patients With Co-Occurring Disorders in MAT

Group sessions presenting information about topical issues can help patients with co-occurring disorders and their families. Patients can explore relevant themes by emphasizing positive coping strategies and sharing experiences. Possible topics for psychoeductional groups are presented in Exhibit 12-4 of the original guideline document.

Pharmacotherapy for Patients With Co-Occurring Disorders in MAT

Several pharmacological treatments for co-occurring disorders are available and should be used when indicated. Most medications are more effective when used with counseling or psychotherapy in comprehensive MAT.

In many ways, an OTP is an optimal setting to initiate and monitor psychiatric pharmacotherapy for co-occurring disorders because patients attend daily (at least in the early stages of treatment) and onsite physicians and other staff can observe their reactions to psychotropic medications as well as to methadone or other addiction treatment medications.

When psychotropic medications are used in an OTP, they should be prescribed

- In a comprehensive program that integrates medical, psychiatric, and social interventions and supports patient compliance with medication dosing schedules
- In the context of a multidisciplinary-team approach in which regularly scheduled team meetings ensure that all members are aware of the patient's progress in treatment
- With careful selection of medications because some patients may attempt to get high on any medication prescribed. Some medications (e.g., amitriptyline, tramadol, benzodiazepines) have little abuse potential in other populations but pose a significant risk of abuse in this population.

If patients in an OTP are prescribed other medications in addition to addiction treatment medications, the consensus panel recommends the following procedures:

- All prescribed psychotropic medications should be to treat suspected or confirmed co-occurring disorders, not to alleviate normal discomfort.
- Fixed, rather than "prn" or "as needed," doses of psychotropic medications should be prescribed because, especially early in MAT, patients addicted to opioids have difficulty regulating medications of any kind. Whenever possible, given resource availability, potentially abusable medications should be dispensed by OTP staff along with addiction treatment medication.
- Patients receiving psychotropic medications should be educated about each drug's expected benefits, potential disadvantages and limitations, side effects, implications for pregnancy and breast-feeding, length of time before full effects should begin, and potential to cause tolerance and withdrawal. This education can be done individually or in a group, but all information should be communicated both in writing and orally.
- An onsite (full- or part-time) physician or psychiatrist should have regular contact with each patient with a co-occurring disorder to review medication response and compliance. This professional also should supervise counselor interactions with these patients and participate in team meetings to discuss treatment plans.

OTPs should consider a hierarchical approach to treating patients with co-occurring disorders, starting with psychosocial interventions such as increased counseling or psychotherapy (unless the patient has a disorder clearly needing medication). Depending on severity and acuity of symptoms, treatment providers may be able to use nonpharmacological approaches such as psychotherapy, either alone or with psychiatric medications. If these psychosocial approaches are ineffective or of limited benefit, providers should select psychiatric medications with the lowest abuse potential that are likely to be effective. The psychiatric medications should be, in most instances, adjunctive to other ongoing

interventions, not a substitute for them. However, other factors to consider include

- The potential effect of medication side effects on compliance
- Potential negative interactions with addiction treatment medication or other drugs
- Lethality if the drug is used impulsively or intentionally for suicide
- Potential effects on a patient's physical condition--for example, whether the drug might injure an already damaged liver or increase blood pressure in a hypertensive patient

Some studies have found that methadone may, by itself, relieve some symptoms of mood and anxiety disorders but not Axis II personality disorders. From a practical viewpoint and assuming sufficient time to observe patients before further intervention, the consensus panel believes that the best approach is careful observation during the first weeks of MAT to determine whether symptoms of co-occurring disorders diminish before psychiatric medications are considered.

Medications for Major Depression and Bipolar Disorder

The hierarchical approach described in the previous two paragraphs for treating patients in MAT with co-occurring disorders should be used to determine which patients diagnosed with major depression or bipolar disorder may benefit from antidepressant medication. The table below summarizes interactions of some antidepressant medications with methadone and recommended treatment response. Antidepressants have been used successfully to treat depression in patients in MAT.

Interactions of Some Medications for Depression and Bipolar Disorder With Methadone and Recommended Treatment Response in MAT

Medication Type and Examples	Action With Methadone	Recommended Treatment Response
SSRIs • Fluvoxamine (Luvox®) • Fluoxetine (Prozac®) • Sertraline (Zoloft®)	Some SSRIs inhibit metabolism of methadone and increase methadone blood levels. Fluoxetine and sertraline do not increase methadone levels significantly. Fluvoxamine is the most dangerous SSRI and should be avoided for patients in MAT.	Observe patients carefully for signs of methadone overmedication during the first weeks of treatment with SSRIs. Methadone withdrawal symptoms may occur after discontinuation of fluvoxamine.
Carbamazepine (Tegretol®)	Carbamazepine speeds production of liver enzymes that metabolize methadone and can cause severe opioid withdrawal symptoms.	Avoid carbamazepine and use alternatives such as valproate (Depakote®). Increase and/or split the methadone dosage to increase its blood levels.
Tricyclics • Desipramine • Nortriptyline	Methadone impairs the metabolism of tricyclics and can cause increased tricyclic medication blood levels.	Adjust doses of tricyclic medications as needed; monitor blood levels if clinically indicated.

Interactions of Some Medications for Depression and Bipolar Disorder With Methadone and Recommended Treatment Response in MAT		
Medication Type and Examples	**Action With Methadone**	**Recommended Treatment Response**
• Imipramine • Doxepin		
Monoamine oxidase (MAO) inhibitors	MAO inhibitors may have dangerous interactions with certain foods and substances of abuse.	Use extreme caution in prescribing these medications in MAT.
Lithium	None.	Monitor closely because window between therapeutic and toxic dose is narrow.

Bipolar disorder in patients in MAT can be treated with antipsychotic or mood-stabilizing medications. Mood stabilizers shown to be effective include lithium, valproate, and carbamazepine. Lamotrigine (Lamictal®) also has been shown to be effective.

Anxiety Disorders

Anxiety disorders, including panic disorder, PTSD, and others, can be treated with psychotherapy, pharmacotherapy, or both. These disorders can be treated effectively with antidepressant medications such as the SSRIs, venlafaxine (Effexor®), and the tricyclics. Patients sometimes respond better to one drug class or a specific drug in a class. Therefore, another antidepressant should be considered if patients do not respond to their first one after a 4- to 8-week trial. Some antidepressants also have sedative effects (e.g., mirtazapine [Remeron®], trazodone, and some tricyclic antidepressants), which might be beneficial for patients with insomnia when these drugs are taken before bedtime, or for patients with high levels of anxiety. Nonsedating antidepressants might be especially useful for patients with psychomotor inhibition.

The well-documented abuse potential of benzodiazepines has led to a common belief that they are contraindicated in patients receiving methadone. However, evidence suggests major differences in the abuse liability of benzodiazepines. Those with a slower onset of action such as oxazepam rarely are mentioned as substances of abuse, have a wide margin of safety, and are effective in reducing anxiety, even over extended periods. Several case reports have indicated that benzodiazepines, particularly those with low abuse liability, may be used safely for patients with substance use disorders).

The consensus panel believes that patients who have a history of benzodiazepine abuse should not be disallowed from receiving previously prescribed benzodiazepines, provided that they are monitored carefully and have stopped the earlier abuse. They may be attempting to reduce symptoms of co-occurring disorders, and, when they receive a prescribed medication with low abuse liability and are monitored for their co-occurring anxiety and substance use disorders, improvement and cessation of other benzodiazepine use may occur naturally. Some drug-testing laboratories can determine specific types of benzodiazepines

used. If such a resource is available, testing can determine whether patients are using only their prescribed benzodiazepines or supplementing them with others obtained illicitly. The latter would indicate a need to change patients' treatment plans.

AD/HD

Stimulants such as methylphenidate (Ritalin®) are the treatment of choice for childhood AD/HD. Stimulant treatment in adulthood also is potentially effective but carries the obvious risk of abuse by patients in MAT. Use of cocaine could be an attempt to control symptoms of AD/HD. If AD/HD is severe, treatment providers should consider treatment with medications such as methylphenidate, amphetamine, or atomoxetine (Strattera®) because these medications reduce AD/HD symptoms and address cocaine or other stimulant use. However, they should be monitored carefully because some patients have abused them by injection, and medical complications can result from long-term injection use. Tricyclic antidepressants also are effective for some patients in MAT with co-occurring AD/HD and depression, and these drugs carry no addiction liability. Recently, the nonstimulant atomoxetine was approved to treat AD/HD and may prove advantageous for patients in MAT with co-occurring AD/HD. However, because atomoxetine is metabolized by the cytochrome P450 system of liver enzymes, the potential for interaction with methadone exists, and it should be used cautiously until more information is available.

Schizophrenia

Patients in MAT who have schizophrenia often have profound impairment in thinking and behavior and are unlikely to fit in well in many OTPs. Antipsychotic medication, along with psychosocial intervention, is the mainstay of treatment. Newer atypical antipsychotic medications for schizophrenia are preferred over older "typical" agents, which carry a risk of movement disorders such as tardive dyskinesia, a neurological syndrome caused by long-term use of neuroleptic medications.

Newer antipsychotic medications (clozapine [Clozaril®], olanzapine [Zyprexa®], risperidone [Risperdal®]), quetiapine, ziprasidone [Geodon®], and aripiprazole [Abilify®]) have fewer side effects, are more effective in many cases, and should be considered as the initial treatment for some patients or as a second option for those not responding to more traditional medications.

Collaboration Between Counselors and Physicians

Many counselors have little or no psychiatric background and need training in

- Working with patients who may have co-occurring disorders but who resist evaluation or respond only partially to treatment
- Exploring stereotypes and feelings about what it means to have a co-occurring disorder
- Helping patients keep physician appointments, understand information, and follow physician recommendations
- Supporting patients to try medication if recommended

- Supporting patients to tolerate side effects long enough to determine whether medications help
- Providing guidance about when to contact a physician to report side effects or lack of relief from or worsening symptoms
- Supporting patients to continue taking medication, even when they feel better

Physicians need training or guidance in

- Providing education to OTP staff about co-occurring disorders and medications
- Recognizing common misunderstandings about and resistances to medication in addiction treatment
- Creating protocols that make good use of counselor ability to provide detailed observations and ongoing feedback on patients' conditions

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Recommendations are based on a combination of clinical experience and research-based evidence.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate treatment of patients in medication-assisted treatment for opioid addiction (MAT) who have co-occurring mental disorders, resulting in optimal treatment outcomes

POTENTIAL HARMS

Side effects and interactions of pharmacological agents

See Exhibit 12-5 in the original guideline document for a description of interactions between some medications for depression and bipolar disorder and methadone.

CONTRAINDICATIONS

CONTRAINDICATIONS

Fluvoxamine is the most dangerous selective serotonin reuptake inhibitor (SSRI) and should be avoided for patients in medication-assisted treatment for opioid addiction (MAT).

QUALIFYING STATEMENTS

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The opinions expressed herein are the views of the consensus panel members and do not necessarily reflect the official position of Center for Substance Abuse Treatment (CSAT), Substance Abuse and Mental Health Services Administration (SAMHSA), or Department of Health and Human Services (DHHS). No official support of or endorsement by CSAT, SAMHSA, or DHHS for these opinions or for particular instruments, software, or resources described in this document is intended or should be inferred. The guidelines in this document should not be considered substitutes for individualized client care and treatment decisions.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Chapter 14, Administrative Considerations, in the original guideline document, covers the challenging administrative aspects of managing and staffing the complex and dynamic environment of an opioid treatment program (OTP). Successful treatment outcomes depend on the competence, values, and attitudes of staff members. To develop and retain a stable team of treatment personnel, program administrators must recruit and hire qualified, capable, culturally sensitive individuals; offer competitive salaries and benefit packages; and provide good supervision and ongoing training. Implementing community relations and community education efforts is important for opioid treatment programs. Outreach and educational efforts can dispel misconceptions about medication-assisted treatment for opioid addiction and people in recovery. Finally, the chapter provides a framework for gathering and analyzing program performance data. Program evaluation contributes to improved treatment services by enabling administrators to base changes in services on evidence of what works. Evaluation also serves as a way to educate and influence policymakers and public and private payers.

Refer to Chapter 14 in the original guideline document for full details (see "Companion Documents" field in this summary).

IMPLEMENTATION TOOLS

Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Treatment of co-occurring disorders. In: Batki SL, Kauffman JF, Marion I, Parrino MW, Woody GE, Center for Substance Abuse Treatment (CSAT). Medication-assisted treatment for opioid addiction in opioid treatment programs. Rockville (MD): Substance Abuse and Mental Health Services Administration (SAMHSA); 2005. p. 189-209. (Treatment improvement protocol (TIP); no. 43).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE COMMITTEE

Treatment Improvement Protocol (TIP) Series 43 Consensus Panel

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Steven L. Batki, MD (*Chair*), Professor and Director of Research, Department of Psychiatry, SUNY Upstate Medical University, Syracuse, New York; Janice F. Kauffman, RN, MPH, LADC, CAS (*Co-Chair*), Vice President, Addiction Treatment Services, North Charles Foundation, Inc., Cambridge, Massachusetts; Director, Addiction Psychiatry Service, Department of Psychiatry, Brigham and Women's Hospital, Boston, Massachusetts; Assistant Professor of Psychiatry, Harvard Medical School, Boston, Massachusetts; Ira Marion, MA (*Co-Chair*), Executive Director, Division of Substance Abuse, Albert Einstein College of Medicine, Bronx, New York; Mark W. Parrino, MPA (*Co-Chair*), President, American

Association for the Treatment of Opioid Dependence, New York, New York; George E. Woody, MD (*Co-Chair*), Treatment Research Institute, University of Pennsylvania/MIRECC Philadelphia VAMC, Philadelphia, Pennsylvania; Patrick Abbott, MD, Medical Director, Center on Alcoholism, Substance Abuse, and Addictions, University of New Mexico, Albuquerque, New Mexico; Leslie Amass, PhD, Principal Investigator, Friends Research Institute, Inc., Los Angeles, California; Hector D. Barreto, MD, MPH, Medical Director, Center for Drug-Free Living, Orlando, Florida; Michael D. Couty, Director, Division of Alcohol and Drug Abuse, Missouri Department of Mental Health, Jefferson City, Missouri; Vashti Jude Forbes, RN, BC, MSN, LCDC, Associate Director, Substance Abuse and Specialized Services, Austin Travis County Mental Health and Mental Retardation Center, Austin, Texas; Ron Jackson, MSW, Executive Director, Evergreen Treatment Services, Seattle, Washington; Karol A. Kaltenbach, PhD, Director, Maternal Addiction Treatment Education and Research, Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania; Judith Martin, MD, FASAM, Medical Director, 14th Street Clinic & Medical Group, Inc., Oakland, California; Violanda T. Nunez, MSW, Executive Director, Ayudantes, Inc., Santa Fe, New Mexico; J. Thomas Payte, MD, Medical Director, Drug Dependence Associates, San Antonio, Texas; Norma J. Reppucci, RN, Director, Operations for Eastern MA and NH, Community Substance Abuse Centers, Malden, Massachusetts; Yong S. Song, PhD, Assistant Clinical Professor and Program, Director, Opiate Treatment Outpatient Program, University of California, San Francisco, San Francisco, California; Jo L. Sotheran, PhD, Associate Research Scientist, Mailman School of Public Health, Columbia University, New York, New York; Trusandra Taylor, MD, Physician Advisor, Parkside Recovery Methadone Maintenance, Philadelphia, Pennsylvania

Editorial Advisory Board: John D. Crowley, Crowley Associates, Elgin, South Carolina; Herbert D. Kleber, MD, Professor of Psychiatry, Columbia University College of Physicians & Surgeons, New York, New York; Stewart B. Leavitt, PhD, Leavitt Medical Communications, Glenview, Illinois; Jocelyn Sue Woods, MA, President, National Alliance of Methadone Advocates, New York, New York; Joan Zweben, PhD, Executive Director, 14th Street Clinic & Medical Group, Inc., East Bay Community Recovery Project, Berkeley, California

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Not available at this time.

Print copies: Available from the National Clearinghouse for Alcohol and Drug Information (NCADI), P.O. Box 2345, Rockville, MD 20852. Publications may be ordered from NCADI's Web site or by calling (800) 729-6686 (United States only).

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Executive summary. Medication-assisted treatment for opioid addiction in opioid treatment programs. p. xvii-xx. (Treatment improvement protocol (TIP); no. 43).
- Introduction. Medication-assisted treatment for opioid addiction in opioid treatment programs. p. 1-10. (Treatment improvement protocol (TIP); no. 43).
- History of medication-assisted treatment for opioid addiction. Medication-assisted treatment for opioid addiction in opioid treatment programs. p. 11-23. (Treatment improvement protocol (TIP); no. 43).
- Pharmacology of medications used to treat opioid addiction. Medication-assisted treatment for opioid addiction in opioid treatment programs. p. 25-42. (Treatment improvement protocol (TIP); no. 43).
- Administrative considerations. Medication-assisted treatment for opioid addiction in opioid treatment programs. p. 225-240. (Treatment improvement protocol (TIP); no. 43).
- Appendix D: Ethical considerations in MAT. Medication-assisted treatment for opioid addiction in opioid treatment programs. p. 297-304. (Treatment improvement protocol (TIP); no. 43).

Electronic copies: Available from the National Library of Medicine Health Services/Technology Assessment (HSTAT) Web site. Also available in Portable Document Format (PDF) from SAMHSA's National Clearinghouse for Alcohol and Drug Information (NCADI) Web site.

The following are also available:

- Knowledge Application Program. KAP keys for clinicians. Based on TIP 43: Medication-assisted treatment for opioid addiction in opioid treatment programs. Rockville (MD): Substance Abuse and Mental Health Services Administration (SAMHSA); 2005. 20 p. Electronic copies: Available in Portable Document Format (PDF) from the SAMHSA Web site.
- Quick guide for clinicians. Based on TIP 43: Medication-assisted treatment for opioid addiction in opioid treatment programs. Rockville (MD): Substance Abuse and Mental Health Services Administration (SAMHSA); 2005. 39 p. Electronic copies: Available in Portable Document Format (PDF) from the SAMHSA Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on December 28, 2005. The information was verified by the guideline developer on January 23, 2006. This summary was updated by ECRI on November 16, 2006, following the FDA advisory on Lamictal (lamotrigine). This summary was updated by ECRI on

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