Published in final edited form as:

J Psychiatr Pract. 2005 September ; 11(5): 315–339.

Improving the Care of Individuals with Schizophrenia and Substance Use Disorders: Consensus Recommendations

DOUGLAS M. ZIEDONIS, MD, MPH, DAVID SMELSON, PsyD, RICHARD N. ROSENTHAL, MD, STEVEN L. BATKI, MD, ALAN I. GREEN, MD, RENATA J. HENRY, MEd, IVAN MONTOYA, MD, JOE PARKS, MD, and ROGER D. WEISS, MD

ZIEDONIS and SMELSON: University of Medicine and Dentistry of New Jersey—Robert Wood Johnson Medical School; ROSENTHAL: Columbia University College of Physicians & Surgeons and St. Luke's Roosevelt Hospital Center, New York; BATKI: SUNY Upstate Medical University; GREEN: Dartmouth Medical School; HENRY: Delaware Department of Health & Social Services; MONTOYA: National Institute of Drug Abuse; PARKS: Missouri Department of Mental Health; WEISS: McLean Hospital, Harvard Medical School.

Abstract

National attention continues to focus on the need to improve care for individuals with co-occurring mental illnesses and substance use disorders, as emphasized in the 2003 President's New Freedom Commission Report on Mental Health and recent publications from the Substance Abuse and Mental Health Services Administration (SAMHSA). These reports document the need for best practice recommendations that can be translated into routine clinical care. Although efforts are underway to synthesize literature in this area, few focused recommendations are available that include expert opinion and evidence-based findings on the management of specific co-occurring disorders, such as schizophrenia and addiction. In response to the need for user-friendly recommendations on the treatment of schizophrenia and addiction, a consensus conference of experts from academic institutions and state mental health systems was organized to 1) frame the problem from clinical and systems-level perspectives; 2) identify effective and problematic psychosocial, pharmacological, and systems practices; and 3) develop a summary publication with recommendations for improving current practice. The results of the consensus meeting served as the foundation for this publication, which presents a broad set of recommendations for clinicians who treat individuals with schizophrenia. "Integrated treatment" is the new standard for evidence-based treatment for this population and recommendations are given to help clinicians implement such integrated treatment. Specific recommendations are provided concerning screening for substance use disorders in patients with schizophrenia, assessing motivation for change, managing medical conditions that commonly occur in patients with dual diagnoses (e.g., cardiovascular disease, liver complications, lung cancer, HIV, and hepatitis B or C infections) and selecting the most appropriate medications for such patients to maximize safety and minimize drug interactions, use of evidence-based psychosocial interventions for patients with dual diagnoses (e.g., Dual Recovery Therapy, modified cognitive-behavioral therapy, modified motivational enhancement therapy, and the Substance Abuse Management Module), and key pharmacotherapy principles for treating schizophrenia, substance use disorders, and comorbid anxiety, depression, and sleep problems in this population. Finally the article reviews programmatic and systemic changes needed to overcome treatment barriers and promote the best outcomes for this patient population. An algorithm summarizing the consensus recommendations is provided in an appendix to the article.

Keywords

dual diagnosis; schizophrenia; substance use disorders; comorbidity; integrated treatment; consensus recommendations; psychosocial interventions; Dual Recovery Therapy; cognitive-behavioral therapy; motivational enhancement therapy; Substance Abuse Management Module; pharmacotherapy; antipsychotics

RATIONALE FOR THE CONSENSUS MEETING

Many individuals with schizophrenia have a co-occurring substance use disorder,¹⁻³ often involving the use of alcohol, tobacco, or other drugs. Substance use disorders cause many negative consequences for patients with schizophrenia even when the individual uses only minimal quantities infrequently. Patients with schizophrenia and comorbid substance use disorders are best treated in mental health settings, since many addiction settings lack the resources and staff capacity to treat psychiatric disorders. Co-occurring schizophrenia and addiction present unique challenges that are best addressed through integrated treatment programs and systems-level interventions.⁴

Recently, a flurry of national attention has focused on improving care for individuals with co-occurring mental illnesses and substance use disorders. Prominent parts of this initiative include the 2003 President's New Freedom Commission Report on Mental Health,⁵ the Substance Abuse and Mental Health Services Administration (SAMHSA) 2002 Report to Congress on the Prevention and Treatment of Co-Occurring Substance Abuse Disorders and Mental Disorders,⁴ and the 2005 SAMHSA Treatment Improvement Protocol Series 42 on Substance Abuse Treatment for Persons with Co-Occurring Disorders.⁶ All three documents acknowledge the seriousness of co-occurring addiction and mental illness and highlight the need to develop best practice recommendations that can be translated into routine clinical care. Several major published documents summarize the existing literature in this area, and a number of efforts are underway to synthesize these documents so that clinicians can begin implementing these recommendations. In spite of these readily available reports, few focused recommendations have appeared that include expert opinion and evidence-based findings concerning the management of specific types of co-occurring disorders, such as schizophrenia and addiction.

In response to the need for a set of user-friendly consensus recommendations, Comprehensive Neuroscience, Inc. partnered with the NASMHPD Research Institute, Inc., the research arm of the National Association of State Mental Health Program Directors, to fill this void. These organizations identified a lead expert (DZ) in the area of co-occurring disorders who helped to select other experts from academic institutions and state mental health systems. The group held a consensus meeting with a mandate to:

1. frame the problem of co-occurring schizophrenia and addiction from both clinical and systems-level perspectives;
2. identify both effective and problematic psychosocial, pharmacological, and systems practices with this population;
3. develop a publication that summarizes the information on the first two points and also includes specific recommendations and clinical tips that can be used to improve current practice.

The results of the consensus meeting, which served as the foundation for this publication, have helped define a broad set of recommendations that can be used to guide the development and

dissemination of future reports on the treatment of co-occurring schizophrenia and addiction. A summary of the consensus recommendations is provided in an Appendix to this article.

DEFINING THE POPULATION

“Co-occurring disorders” and “dual diagnosis” are broad terms used to refer to the simultaneous presentation of one or more mental health disorders with one or more substance use disorders. Although these terms can be used to describe many different combinations of clinical disorders, this article focuses on the co-occurrence of *schizophrenia spectrum disorders* with substance use disorders, including abuse of, or dependence on, alcohol, tobacco, or other drugs. Co-occurring substance use disorders occur in 50%–70% of individuals with schizophrenia.^{1,3,7} Because, as noted above, even infrequent use of relatively minimal quantities of substances can cause clinically relevant problems in individuals with schizophrenia, the consensus of the panel was to include individuals with relatively mild substance use problems in our definition of the target population. The decision to include individuals who use any substance, including tobacco, in our definition is consistent with the current definition of co-occurring disorders used by SAMHSA^{4,6} as well as definitions used by other organizations such as the American Psychiatry Association in its new Practice Guideline for the Treatment of Patients with Substance Use Disorders.⁸

OVERVIEW OF CLINICAL TREATMENT

Effective clinical management of patients with co-occurring schizophrenia-spectrum and substance use disorders involves a comprehensive baseline assessment, careful screening for substance use problems and medical consequences of substance use, continuous monitoring of clinical status and adherence to treatment, and coordination of care. All patients are likely to require acute and chronic stabilization of psychosis through medication management, psychosocial interventions, and case management. In some cases, individuals will also require medications to manage intoxication and withdrawal symptoms. Psychosocial interventions, such as social skills training, motivational enhancement therapy, psychoeducation, and relapse prevention, can help reduce the likelihood of relapse to addiction or psychosis and thus reduce the morbidity and sequelae associated with substance use and medical disorders. To treat this population, one must understand the multidimensional aspects of schizophrenia and the ways in which substance abuse affects these symptoms and can create new behavioral and emotional problems. Substance use has a dramatic impact on the course of schizophrenia, with effects varying by type of substance, route of administration, severity of the problem, and stage and duration of use. Depending on the type of substance used and the stage of drug use, patients may exhibit symptoms of mania, psychosis, depression, suicidality, anxiety, cognitive impairment, and personality disorder.⁹⁻¹⁴

INTEGRATED TREATMENT AS THE STANDARD OF CARE

“Integrated treatment” is the new standard for evidence-based treatment for this population, and there is strong evidence supporting its effectiveness.¹⁵ However, there are many different perspectives on how integrated treatment should be defined and what types of programs constitute examples of integrated treatment.³ In the most general sense, integrated treatment describes a flexible combination of treatments from the mental health and addiction fields that are blended together in the treatment of an individual with co-occurring mental illness and addiction. The term is used by some practitioners to refer to a simple combination of medications and psychosocial treatments for both mental illness and addiction, but it can also describe a more complex, philosophically and structurally seamless integration of mental health and addiction treatment approaches and levels of care. It is highly preferable that integrated treatment be implemented in a single treatment program or by a single treatment

provider. Thus, integrated treatment practitioners need an understanding of both mental illness and addiction, as well as access to the resources needed to integrate and modify these treatment approaches which have historically been taught and provided separately.

The most extensive literature on “integrated treatment programs” involves programs that include multiple interventions as well as “integrated clinical intervention studies” that focus on adding either a new medication or psychosocial treatment to an existing treatment regimen. Integrated treatment is implemented on many levels—by individual clinicians, treatment programs, and clinical systems that include mental health and addiction treatment organizations as well as related systems such as the criminal justice system, health care providers, HIV services, and vocational services. Although integrated treatment is desirable from all perspectives,⁴ this paper focuses on integrated psychosocial treatment, case management, medication, and systems approaches that can be implemented by individual clinicians.¹⁶⁻²¹ We therefore do not review the many model programs developed for this population, but instead refer interested readers to the SAMHSA 2002 *Report to Congress*⁴ and 2005 *Treatment Improvement Protocol Series 42*⁶ for examples of integrated programs and systems.

The authors do acknowledge, however, that an understanding of integrated treatment does require consideration of the systems-level perspective. Policy and organizational change are essential in removing systemic barriers to integrated treatment. These barriers include inflexible and mutually exclusive funding streams for mental health and substance abuse, separate systems of care, disparate health insurance coverage, differences in workforce competencies, and limited research resulting in limited evidence-based practices. Although no studies have yet compared differential costs and service outcomes in states in which substance abuse and mental health are managed under a single agency versus those in which they are not, the single-agency model appears likely to be cost-effective and facilitate the delivery of integrated care.

SCREENING AND ASSESSMENT

Screening for Substance Use and Substance Use Disorders

Screening and assessment, although complicated in this patient population, are critical components in developing a comprehensive treatment plan and serve as the foundation for the entire course of treatment. For instance, clinicians often need to uncover a substance use disorder in a patient with a clear diagnosis of schizophrenia or need to tease apart a complicated presentation of psychosis and active substance use when the diagnosis is unclear. All patients with psychiatric symptoms should be assessed for substance use and a possible substance use disorder, because substance use alone can cause psychosis, mania, anxiety, depression, or cognitive impairment. For example, psychosis can be caused by use or abuse of or withdrawal from numerous substances and even prescription medications, including amphetamines, phencyclidine (PCP), marijuana, tobacco or marijuana dipped in formaldehyde, hallucinogens, cocaine, alcohol, steroids, anticonvulsants, and anti-parkinsonian medications. Thus, in assessing a patient with a known or suspected schizophrenia spectrum disorder, clinicians also need to screen for the presence of substance use and a possible substance use disorder.

The assessment should include screening questions that ask directly about patterns of use (quantity, frequency, route of administration, age of onset, and last use) of all substances. Some clinicians have found the Timeline Follow-Back interview, in which a calendar is used to cue memories of recent use, to be helpful in assessing substance use among patients with serious, persistent mental illness.¹⁷ Don't neglect to ask about and track use of caffeine and tobacco, use of both of which is very common in this population and may exacerbate health or mental health symptoms. For example, caffeine may exacerbate symptoms of anxiety. Tobacco use is also a clue to probe more closely for use of other substances. For example, smoking more than

25 cigarettes in a day (heavy smoking) is associated with a four-fold increased risk for alcohol and other drug use disorders.²²

When a patient admits to using one substance, it is useful to ask about what other substances are used with that substance. Although polysubstance use is common in this population, many patterns of polysubstance use are not spontaneously reported; instead, only one substance is often mentioned. For example a patient may admit to using the club drug “ecstasy,” the street-name for MDMA (3–4 methylenedioxymethamphetamine) which is chemically similar to the stimulant methamphetamine and the hallucinogen mescaline. By asking “what else are you using with ecstasy?” the clinician may discover that the patient is using this substance in combination with other substances, including other club drugs such as ketamine, or is even adding sildenafil (Viagra) and/or fluoxetine (Prozac) with the goal of reducing the side effects of the ecstasy. A more common scenario in which multiple substances are used involves patients with schizophrenia who report smoking marijuana. They should be asked about other substance use, especially whether they “dip” their marijuana into formaldehyde alone or formaldehyde with phencyclidine (PCP). Even the combination of marijuana and formaldehyde alone can cause a toxic delirium and long-lasting psychotic symptoms that may persist up to 6 months if untreated.

Further complicating assessment, the misuse of prescription drugs can produce symptoms of intoxication, medication side effects can be mistaken for negative symptoms, and negative symptoms can be mistaken for depression. Prescription medications that are commonly misused and abused by this population include anti-anxiety drugs, sedative-hypnotic agents, and anticholinergic medications.²³

After obtaining self-reports concerning substance use from the patient and perhaps from significant others, objective screening tests can uncover active unreported use. These objective screening tests include a urine or blood toxicology test for most specific substances, alcohol breathalyzer for alcohol, and carbon monoxide (CO) breathalyzer for tobacco smoking. Of these measures, urine toxicology tests are the most frequently used. However, the validity, reliability, and ability to detect the presence of substances with these objective screening tests depends on several factors, including the frequency and intensity of substance use, the type of test performed, the sensitivity level of the test, the type of drug, and the formulation (e.g., short- vs. long-acting). Table 1 summarizes maximum detection times for different substances of abuse.

After assessing for the presence and use of substances, the next phase of assessment is to evaluate the severity of the substance use and gather clues that might suggest the need for a more extensive evaluation. This task is often done using available screening instruments that are either 1) self-report questionnaires and structured interviews or 2) clinical laboratory tests that can detect biochemical changes associated with substance use. These screening tests have different sensitivities and specificities.

Clinicians find the following self-report instruments helpful in identifying the need to probe further for substance use in this population: the Alcohol Use Disorders Identification Test (AUDIT),²⁵ the Michigan Alcohol Screening Test (MAST),²⁶ the shortened version of the Drug Abuse Screening Test (DAST-10),²⁷ and the Dartmouth Assessment of Lifestyle Instrument (DALI).²⁸ Some of these and other screening/assessment tools are available free of charge by obtaining the new SAMHSA Treatment Improvement Protocol 42⁶ that focuses on co-occurring disorders (information on how to download or order copies is provided in reference 6 of the article). Standard self-report screening tools for substance abuse focus on possible negative consequences and problems in social functioning (e.g., losing employment, alienating a spouse).²⁴ However, these consequences will be less sensitive in detecting many

cases of substance use in persons with schizophrenia since this population is likely to have such problems already because of the psychiatric illness. In assessing for problems related to substance use, clinicians should keep in mind that the negative consequences of substance abuse that are most common in this population include episodes of homelessness, legal problems, verbal threats, violence, nonadherence to treatment, need for high doses of antipsychotics, medical problems, frequent emergency room visits or hospitalizations, and suicidal ideation/attempts.^{6,9-11,14,29-31}

In addition to self-report questionnaires, objective clinical laboratory procedures can not only help detect the presence of a substance but can also provide objective evidence suggestive of problematic use of alcohol or other substances. These measures can be helpful in corroborating findings from the clinical interview and self-report questionnaires in the general population but have not been studied adequately among individuals with schizophrenia and substance abuse.³² These objective markers, which are most commonly used to assess problem alcohol use, can be affected by other medical conditions (e.g., nonalcoholic liver damage, metabolic disorders) or the use of other medications or substances. The three most widely used tests are the gamma-glutamyl transferase (GGT), carbohydrate-deficient transferrin (CDT), and the mean corpuscular volume (MCV). The GGT and CDT tests are similar in their ability to identify problem drinking; however, there are a few conditions other than heavy drinking that will elevate CDT levels.³³ Unfortunately there has been only limited study of these markers in patients with co-occurring schizophrenia and problem alcohol use.

To summarize, to screen for substance use in a patient with schizophrenia, we recommend the following minimum measures:

1. Screening questions to assess quantity, frequency, and intensity of substance use
2. Urine test
3. Self-report screening instruments to uncover possible need to probe further
4. Probe for negative consequences of substance use. It is vital to assess for negative consequences that are relevant to this population, rather than relying on standard substance abuse instruments or focusing solely on quantity of use.

Additional screening measures may, of course, be added as the clinician sees fit.

Establishing a Substance Use Disorder Diagnosis

Establishing a substance use disorder diagnosis can sometimes be complicated, especially if the patient minimizes his or her substance-related problems or attributes them to other causes. Since patients with psychiatric illnesses tend to suffer more severe consequences from lower levels of substance use, clinicians may be lulled into a false sense of security by focusing only on the amount or frequency of substance use reported. Instead, clinicians should consider any amount of reported substance use as a confirmation of use. However, establishing a diagnosis of a substance use disorder requires focusing on the possible consequences of usage; the amount of time focused on obtaining and using substances or being affected by using substances; and the presence of withdrawal symptoms.

Creating a timeline of pertinent issues (e.g., onset of psychiatric symptoms, substances used, periods of abstinence, and treatment episodes) is useful in organizing the clinical history in general and also beginning to help patients make the connection between their substance use and the consequences in their lives. In addition, the timeline technique can be helpful in beginning to differentiate schizophrenia from a substance-induced psychotic disorder and a concurrent depressive disorder from a substance-induced depressive disorder. When obtaining a complete substance use and psychiatric history, it is important to ask about history of

psychosocial and pharmacological treatment, severity of symptoms, and family history of mental illness and substance use disorders. When patients are poor informants, clinicians can review hospital records and seek collateral information from family members or other treatment providers.

Assessing Motivation for Change

When a substance use disorder has been uncovered, it is critical to assess the patient's motivation to address the substance abuse. Motivation and other clinical characteristics are fluctuating states rather than stable traits and require ongoing monitoring. Most patients with schizophrenia have relatively low motivation to address their substance use disorder.³⁴ Motivation is often seen as an internal state that is affected by one's desire to change, one's sense of one's ability to change, the number of reasons the person has to change, his or her insight into the relationship between substance use and his or her problems, and the person's commitment to change. A commonly used model of motivation, developed by Prochaska and DiClemente, includes five stages of readiness to change: precontemplation, contemplation, preparation, action, and maintenance.³⁵ Most individuals with schizophrenia who use/abuse substances are in the lower motivational levels (precontemplation and contemplation) and are not prepared to address their substance use without clinical intervention and motivational enhancement efforts.³⁴ External motivators (e.g., family, mental health staff, the legal system) can often be used to enhance low internal motivation.

There are several practical clinical tools clinicians can use to structure an evaluation of motivation to stop using substances. One method is the Importance, Confidence, and Readiness to Quit Ruler which uses a 0 to 10 scale assessment and asks about the importance of quitting to the patient, the patient's confidence in his or her ability to quit, and the patient's readiness to quit. Other assessment tools include the "Decisional Balance" in which the patient is asked to talk about the pros and cons of use (more motivated patients have more concern about negative consequences and have few positive reasons for using substances). Asking specifically when a patient thinks he or she would be ready to quit can also be very helpful in assessing motivation. In tobacco dependence treatment, patients have historically been asked when they would like to set their "quit date". We find this can be a useful strategy for any substance. Simple measures may also have predictive validity. For example, one study found that a 5-point Likert scale of current motivation for treatment was able to predict eventual abstinence.³⁶ The patient's motivation may vary across different substances, so readiness to stop using each substance should be assessed separately and motivation to stop each specific substance should be routinely monitored. One useful tool for assessing motivation is the Dual Recovery Status Exam,³ which includes ongoing routine assessment of both psychiatric and addiction symptoms including motivation, cravings, last substance use, involvement in 12-step programs and activity related to treatment plans, current mental status, and medication adherence.

Evaluating for Medical Consequences of Substance Use and Comorbid Medical Conditions

Care of all individuals with schizophrenia should include routine medical evaluation by appropriate medical staff. During the assessment, clinicians should check for medical consequences of substance use in order to facilitate diagnostic assessment, encourage patients to seek needed medical attention, and ensure an appropriate choice of psychiatric medications. The medical consequences that are discovered will vary according to the type of substance being used and the route of administration. Medical illnesses can mimic psychiatric disorders such as psychosis, depression, mania, and anxiety. Substance abuse can also mimic psychiatric disorders and can cause or exacerbate medical illness.

Too often, individuals with co-occurring mental and substance use disorders have not undergone recent, comprehensive medical assessments that included history, physical examination, and laboratory tests. This may be due to insufficient access to health care and/or the chaotic and disorganized lifestyles associated with substance abuse. Since the consequences of substance abuse in persons with schizophrenia may include infection with human immunodeficiency virus (HIV), hepatitis B and C, and other sexually transmitted diseases,³⁷ it is especially important to correct such inadequate medical screening. Unfortunately, this patient population is not only poorly adherent with medication but also with following through on medical care. Clinicians should anticipate difficulties with patient engagement in and adherence to medical screening and care and work closely with primary care providers to try to ensure treatment adherence.

There are numerous specific medical consequences that can occur as a result of using different substances. Many substances, by increasing sedation, intoxication, or seizure risk, increase the risk of trauma, especially head trauma. In addition, cardiovascular and infectious diseases are common among individuals who abuse any substance. In the following sections, we first review the common health consequences associated with alcohol and tobacco use/abuse and then discuss cardiovascular and infectious diseases in more detail.

Health consequences of alcohol abuse—Alcohol-related problems can affect almost all organ systems, most prominently the gastrointestinal and central nervous systems causing seizures, dementia, gastritis, ulcers, blackouts, pancreatitis, and liver disease. Alcohol's impact on the liver can lead to altered metabolism of psychiatric medications that are metabolized in the liver. Chronic alcohol use has a direct effect on neuronal tissue and is a neurotoxin. Some of the more severe forms of alcohol-related injury to the central nervous system clearly have lasting effects on cognition, behavior, and the ability to consistently follow treatment recommendations. Heavy alcohol consumption results in atrophy of gray and white matter, particularly in the frontal lobes, cerebellum, and limbic structures and also raises the risk of ischemic and hemorrhagic stroke.³⁸ Clinicians must be aware of clients' cognitive status so that they do not misinterpret poor comprehension or cognitive limitation as treatment resistance.

Health consequences of tobacco use—Tobacco use not only increases pulmonary and cardiac disease, but is the major single cause of cancer mortality in the United States, accounting for about 90% of cases of lung cancer.³⁹ Early studies suggesting a reduced risk for lung and other cancers in smokers with schizophrenia have been refuted by more recent findings using larger samples, which indicate cancer rates similar to or greater than those of controls; there is also no support for genetic protection against cancer in families with schizophrenia.⁴⁰ In one study, half of all the excess cases of cancer risk in schizophrenia were attributable to lung cancer.⁴¹

Cardiovascular disease—Schizophrenia and substance use disorders can both increase the risk of cardiovascular disease. Persons with schizophrenia appear to be at greater risk than the general population for cardiovascular morbidity and mortality, with elevated levels of all of the modifiable risk factors, such as obesity, smoking, diabetes, hypertension, hyperlipidemia, poor diet, excessive intake of alcohol and salt, lack of exercise, and lack of access to routine medical screening (e.g., measurement of cholesterol and other serum lipid levels).⁴²⁻⁴⁵ Many antipsychotic medications can contribute further to these problems by causing weight gain, although medication-induced weight gain is not unique to patients with psychotic disorders, since mood disorders have also been linked to increased rates of obesity⁴⁶ and certain antidepressants and mood stabilizers are also associated with weight gain. Rates of Type II (non-insulin-dependent) diabetes are also higher in patients with schizophrenia than in the general population, likely due to a combination of factors including side effects of antipsychotic

medication, poorer overall physical health, less healthy lifestyles, and poorer health care. Consensus recommendations from a recent conference on physical health monitoring of patients with schizophrenia included regular monitoring of body mass index, blood glucose level, and lipid profiles as well as cardiac monitoring/electrocardiograms.⁴⁷ Nutritional interventions, including a cholesterol-lowering diet, use of lipid lowering medication, and exercise, should also be considered.

Individuals with substance use disorders, particularly those who use stimulants, nicotine, and alcohol, are also at increased risk for cardiovascular disease. For example, use of cocaine and other stimulants is associated with myocardial ischemia due to vasospasm and increased cardiac workload. The combination of cocaine and alcohol in the body can create a new metabolite (cocaethylene) that is particularly cardiotoxic and can prolong the cocaine high.^{48,49} Alcohol also causes a reversible and dose-dependent increase in the cardiovascular risk factors of high-density lipoprotein (HDL)-cholesterol and blood pressure.⁵⁰ Although there have been reports that alcohol may have some protective qualities in some individuals, there are no reports of this in individuals with schizophrenia. This issue may not have been studied in this population given the potentially negative impact of even low doses of alcohol on the psychological/psychiatric functioning of individuals with schizophrenia.

Infectious diseases—All substance users are at increased risk for infectious diseases including hepatitis B and C, HIV, other sexually transmitted diseases, and tuberculosis. Infection can occur through blood exchange from intranasal use and risky sexual behavior. Increased sexual promiscuity associated with drug use, as well as exchanging sex for drugs, increases the probability of having unprotected sex and multiple partners. Rates of hepatitis testing and vaccination remain low among drug abusers in general as well as among those with co-occurring disorders.^{51,52} Among persons with severe mental illness, men with hepatitis C have increased lifetime rates of drug-related risk behaviors (needle use, needle sharing, and crack cocaine use), whereas women have higher lifetime rates of sexually risky behaviors (i.e., having unprotected sex in exchange for drugs, money, or gifts, or unprotected vaginal or anal sex).^{53,54} In patients with HIV or hepatitis C infections, central nervous system effects can result from the medications used to treat the infections as well as from direct viral invasion of the brain, thus increasing the risk for many other psychiatric problems including anxiety disorders, sleep disorders, mood disorders, depression, mania, psychosis, dementia, delirium (confusion), and personality disorders.⁵⁵ The central nervous system effects of substance use can also exacerbate the neuropsychiatric effects of these viral infections (e.g., HIV). For a review of the challenges involved in treating patients with such a triple diagnosis (HIV infection, substance abuse, and a psychiatric disorder), readers are referred to a review by Batki.⁵⁶ A recent study suggested that use of atypical antipsychotics may be associated with better adherence to treatment in patients with co-occurring schizophrenia and HIV infection.⁵⁷

TREATMENT PLANNING

It is important that individuals who have serious mental illness and co-occurring substance use disorders be included as active participants in treatment planning. However, because this population is often less motivated for treatment, the initial treatment plan should focus on small but meaningful goals that are readily attainable, and interventions should be tailored to the patient's readiness to change (Table 2). The initial plan may be as basic as using the first few sessions to develop an ongoing dialogue about the necessary level of care, rather than pushing for an immediate commitment to a more intensive level of care. The complete treatment plan should also include a comprehensive medical workup, choice of medication and therapy options, ongoing assessment, monitoring of medication adherence, and strategies for managing ongoing psychiatric problems, interactions between substance use and the psychiatric condition, and associated medical problems. Abstinence may not be an immediate goal but,

whenever possible, treatment plans should include reconnection with family and friends, who can often serve as important support systems for long-term sobriety and psychiatric stability. Thus, the treatment plan should reflect the individual's level of motivation and can be viewed as a working document that needs to be renegotiated and revised on a regular basis as the individual progresses towards recovery and sobriety.

PSYCHOSOCIAL INTERVENTIONS

Psychosocial interventions are an integral component of treatment for individuals with co-occurring schizophrenia and addiction. Psychosocial treatment approaches emphasize improving daily functioning, creating environmental supports, and managing problems in a goal-oriented manner. Initial treatment should focus on engagement and developing a continuous therapeutic alliance marked by optimism, respect, and empathy. Ongoing treatment works to increase motivation through enhancing desire to change, develop self-efficacy that change is possible, manage cognitive limitations, and enhance interpersonal skills.

Successful evidence-based psychosocial practices for this population have either been adapted from evidence-based treatments for schizophrenia, such as assertive community treatment (ACT) outreach, case management, illness education, family interventions, and social skills training, or they have fully integrated these traditional mental health treatments with core psychosocial treatment approaches to addiction, such as motivational enhancement therapy (MET),^{58,59} cognitive-behavioral strategies for relapse prevention, 12-step facilitation, and addiction recovery concepts.^{6,60}

Key Principles of Psychosocial Treatment for Patients with Dual Diagnoses

Five principles should guide psychosocial treatment for co-occurring disorders:

1. Develop a supportive therapeutic alliance and focus on motivational enhancement approaches during the engagement phase.
2. Integrate evidence-based psychosocial treatments for addictions (MET, relapse prevention, and 12-step facilitation) with evidence-based mental health psychosocial treatments.
3. Help the patient acquire abstinence and recovery skills.
4. Encourage positive healthy support from others, including attendance at 12-step meetings.
5. Utilize short-term case management approaches during vulnerable periods to promote treatment adherence and maximize retention.

Evidence-Based Psychosocial Approaches for Integrated Treatment of Co-Occurring Disorders

Several clinical therapy manuals have been developed and tested for efficacy in the treatment of co-occurring schizophrenia and addiction. The four that are widely available are the Dual Recovery Therapy (DRT) approach,⁶⁰ modified cognitive-behavioral therapy (CBT),¹⁶ modified MET,^{60,61} and the Substance Abuse Management Module (SAMM).²⁰ These four approaches, which are described below, are perhaps more similar than different, since they all include elements of motivation, relapse prevention, and social skills training. These approaches are supportive of patients being involved in 12-step recovery meetings (e.g., Alcoholics Anonymous) that are great resources for positive healthy support and models for a program of recovery. Case management approaches for this population are also described below. While the existing literature does not lend itself to recommending a specific psychosocial treatment

or case management approach, the superiority of an integrated treatment approach has been well established.^{4,6}

Dual Recovery Therapy (DRT)⁶⁰ integrates substance abuse relapse prevention, psychiatric social skills training, MET, and the “recovery language” of 12-step programs in linked group and individual treatment sessions. Role-playing techniques are used to develop problem-solving and communication skills. The therapist monitors the interactions between substance use and psychiatric problems and adjusts the treatment emphasis accordingly. MET and 12-step recovery language address low motivation and take advantage of the common lexicon of 12-step programs that are already familiar to many patients. DRT begins with twice-weekly individual sessions, and then shifts to one individual and one group session weekly. These sessions are linked, with individual sessions used to reinforce the material discussed during the group sessions. Later in the recovery process, the focus shifts towards reducing dysfunctional relationships and increasing healthy relationships.^{3,60}

Modified Cognitive-Behavioral Therapy (CBT)¹⁶ is another integrated approach for patients with schizophrenia and drug dependence. Treatment includes relapse prevention and motivational interviewing strategies. Patients are initially helped to improve their social skills and problem-solving strategies. They are provided with information about cravings and triggers of drug use and the unique difficulties associated with substance abuse for people with schizophrenia. Skill-building is practiced in small group sessions twice a week for approximately 6 months. Groups are highly structured, and early successes are strongly reinforced to enhance self-efficacy. The therapy accommodates the cognitive limitations of schizophrenia by focusing on a small number of specific skills. Abstinence is reinforced by providing positive reinforcement (i.e., small amounts of money) for drug-free urine test results.

Modified Motivational Enhancement Therapy^{60,61} is a strategy that particularly targets patients with lower motivation. In this approach, traditional MET is modified for the patient with schizophrenia. The MET approach was originally developed as a brief intervention for use in a large National Institute on Alcohol Abuse and Alcoholism (NIAAA) psychosocial treatment study of alcohol dependence. MET was an expansion of traditional motivational interviewing (MI) and added “personalized feedback” from the baseline assessment as a way to further enhance motivation to change. The MI component is an approach to the patient that is empathic, client-centered, respects readiness to change, embraces ambivalence, and is directive. The personalized feedback component includes providing normative data to the patient based on assessment findings (objective and subjective) and includes other motivational strategies such as doing decisional balances (Pros & Cons) and developing Change Plans with the patient's direct input.

One way to adapt MET for patients with schizophrenia spectrum disorders and other serious mental illnesses has been described as a five-step “collaborative, motivational, harm reduction” approach.⁶¹ It includes 1) developing a working alliance, 2) helping the patient evaluate the pros and cons of substance use (decisional balance), 3) formulating individualized goals, 4) encouraging an environment and lifestyle that are supportive of abstinence, and 5) teaching skills for managing crises.

In other modified MET approaches, specific strategies are matched to different motivational levels, there is an acknowledgement that there are many problems to address (e.g., use of multiple substances, medication compliance), and that there is a need for a much longer engagement period and length of treatment. In addition, this population has lower self-efficacy, has cognitive impairment, and needs mental health treatment, so that the modified MET approach includes higher levels of therapist activity and uses behavioral strategies that involve briefer, more concrete language, more repetitions, and the need to pay particular attention to

the patient's alertness and adapt the interventions according to the level of alertness. Modified MET is also integrated with other mental health treatments, rather being a stand-alone approach.⁶⁰

The Substance Abuse Management Module (SAMM)²⁰ is based on relapse prevention, harm reduction, and social skills training. For ease of implementation, it incorporates a limited subset of skills (e.g., dealing with craving, talking to one's doctor) that are believed to be crucial to drug avoidance and disease management, and it relies heavily on repeated skills practice. This model is grounded in social skills training and includes a focus on enhancing problem solving and communication skills to promote healthier recovery and abstinence from substances. The use of role playing in group treatment sessions is common in this model. In such role plays, the therapist may help the group identify a problem to focus on related to promoting recovery or abstinence and then have the group consider ways to address the problem and have peers model how to manage the problem. The therapist may assume an active role as a coach in the role play and help the group provide positive feedback and helpful constructive criticism for those involved in the role play.

Case Management—Case management is used to help patients bridge gaps in the mental health system and navigate social service systems, with the aim of improving treatment engagement and establishing successful community reintegration. Treatment attrition is common among individuals with schizophrenia and substance use disorders and significantly worsens outcomes, even with the most sophisticated psychosocial approaches.⁶²⁻⁶⁵ Studies have reported treatment completion rates ranging from 15% to 33%,⁶⁶⁻⁶⁸ with one study reporting that only 8% of patients made the transition to outpatient treatment.⁶⁸ Augmenting psychosocial treatment with case management can improve adherence and reduce fragmentation of care. Case managers can also play a role in facilitating links with medical treatments. Research suggests that case management, including short-term approaches, can be helpful for this population, and is particularly important for non-adherent and poorly motivated individuals.

A variety of case management approaches have been developed, including the Broker Model,⁶⁹ ACT,⁷⁰ and intensive case management,⁷¹ all of which have similar components: 1) a needs assessment; 2) development of a comprehensive service plan; 3) outreach and ongoing coordination of services; 4) monitoring and assessment of service delivery; and 5) evaluation and follow-up.

Recent research has focused on short-term approaches that target vulnerable periods in recovery (e.g., after an interpersonal loss). This allows limited case management resources to be used more efficiently and provides care to larger numbers of individuals. Rosenheck and Dennis⁷² conducted a naturalistic study examining a 1-year ACT intervention aimed at engaging patients with severe mental illness in other mainstream mental health services. Results suggested that successful linkage to community-based treatment services was a more important predictor of symptom change than length of case management services. Other studies have found that time-limited case management services delivered through emergency room settings can reduce hospital utilization and other healthcare expenditures.^{73,74} A study by Smelson et al.⁷⁵ investigated preliminary outcomes from a new 8-week linkage intervention called "time-limited case management (TLC)" that integrates intensive outreach, DRT,⁶⁰ and peer support to assist in the transition from acute psychiatric treatment to outpatient care and promote outpatient treatment engagement. This approach was unique in that it combined specialized dual diagnosis treatment with intensive case management delivered by the same clinician. The individuals who received the TLC intervention had a higher show rate at the day treatment center intake appointment, attended more days of treatment at the day center, had greater pharmacy refill compliance, and were less likely to be lost to follow-up at 8 weeks than

the comparison group. A 6-month post-intervention evaluation of outcomes found that this approach significantly reduced re-hospitalization, increased outpatient treatment adherence, and improved substance use and mental health treatment outcomes.⁷⁶

Involvement in Twelve-Step Meetings

Twelve-step meetings such as Alcoholics Anonymous are an important resource and source of support for patients with co-occurring schizophrenia and addiction. Because of difficulties with stigma and acceptance in the general population, these individuals often do best at 12-step meetings that are offered at mental health centers. Sometimes these 12-step meetings have different names than those used for meetings in the general population (e.g., Alcoholics Anonymous); for example, they may have names such as Dual Recovery Anonymous or Double Trouble or Double Trudgers. These modified 12-step meetings address both addiction and mental illness. The 12-step oriented meetings provide support and education about addiction recovery concepts and help promote a sense of hope and connection to others. Participants learn to see recovery not as a cure, but rather as a way of living a meaningful life within the limitations of their dual diagnoses and as a process of restoring self-esteem and establishing a personal commitment to growth, discovery, and transformation.

PHARMACOTHERAPY

Medication plays a vital role in the management of schizophrenia in all patients, including those who also abuse substances. Dual diagnoses, however, require that clinicians consider new treatment options and strategies. For example, memory problems in schizophrenia may preclude prescribing disulfiram, and the seizure risk, sedation, and liver disease caused by substance addiction may influence choice of antipsychotic medications. In addition, this population often has symptoms of depression, anxiety, and sleep disturbance for which it may be risky to use medications with abuse potential.

Key Principles of Pharmacotherapy for Patients with Dual Diagnoses

The following principles should guide pharmacotherapy for co-occurring disorders:

1. Treat clear symptom clusters, rather than non-specific complaints.
2. Consider relative safety and side-effect profiles in selecting and dispensing medications and avoid medications with abuse liability and addiction potential.
3. Choose strategies that enhance medication adherence (e.g., motivational discussions that focus on long-term goals and pros and cons of taking medication, use of longer-acting pills, depot injections, and pill monitoring).
4. Be aware of potential interactions between psychotropic medications and substances of abuse.

Treat clear symptom clusters—Because this area of pharmacotherapy is complex and often involves multiple medications, it is generally recommended that medications be limited to those that treat clear symptom clusters related to an Axis I diagnosis. Treating non-specific complaints in patients with co-occurring disorders may not be helpful and can reinforce self-medication behavior. However, clinicians must always treat psychosis in every symptomatic individual even if the patient continues to use substances. Also, it is common for patients to stop taking medications when they lapse back into substance use. These patients may discontinue medication in part as a reaction to their doctor's concerns about the risks of combined use. However, they should be encouraged to continue taking antipsychotic medications even if they are using substances, since stopping the antipsychotic medication may be more dangerous than concurrent medication and substance use.

Consider safety and side-effect profiles of medications and avoid medications with abuse liability and addiction potential—

Many medications and illicit substances have synergistic effects on the brain, resulting in increased sedation, risk of seizures, and confusion. Clinicians should avoid medications that have these types of side effects, including those with strong anticholinergic or orthostatic properties. Similarly, the risk of a suicide attempt is increased dramatically in states of acute intoxication; therefore, medications with a low risk of overdose are preferable. It is also extremely important to avoid medications with addiction potential in persons with co-occurring disorders (e.g., use of benzodiazepines to treat agitation and anxiety in patients with schizophrenia and substance use disorders). In addition to using care in medication selection, certain strategies of dispensing drugs can reduce risk and improve safety of use; these include dispensing only the exact amount of medication needed for a brief period of time (2–4 weeks), limiting refills, and making refills contingent on returning for follow-up appointments.

Choose strategies that enhance medication adherence—

People with co-occurring substance use disorders are more likely to be nonadherent with medication regimens than those with schizophrenia alone. Given the risk of medication abuse and misuse, providers should use every appointment as an opportunity to ask patients about how they take their medication, to review proper use of medications, to promote medication adherence, and to provide medication education. When possible, medication regimens should be simplified (e.g., using once-a-day regimens, long-acting pills, or depot injections). A good principle is to “start low and go slow” in dosing medications. Medications that are not helpful should be discontinued and medications with side effects that contribute to poor adherence should be avoided. Patients may tend to take more medication than prescribed because they grow impatient waiting for the medication to work, not necessarily to get “high.”⁷⁷ Providers should be aware that patients may encounter pressure to stop taking medications in some 12-step group meetings.⁷⁸ Clinicians should also encourage adherence by promoting hope as well as realistic expectations about the efficacy of medication, educating about and monitoring for side effects, and enlisting family help with monitoring and contracting.

Be aware of potential interactions between psychotropic medications and substances of abuse—

It is also important to keep in mind that most substances of abuse can interact in significant ways with psychiatric medications and may reduce their effectiveness. Some substances alter blood levels of medications and can increase side effects. For instance, coffee and tea, like cigarettes, are known to alter the metabolism of some psychiatric medications as a function of their effects on liver enzyme activity. Opioids can increase sedation, constipation, and other adverse effects of psychiatric medications.

Such interactions can also affect either the central or peripheral nervous systems and may cause increased seizure risk, liver toxicity, and cardiac effects. Therefore, certain medications should be avoided entirely in persons with known liver disease, cardiac disease, or seizure disorders. Alcohol and cocaine can cause transient arrhythmias and EKG abnormalities including prolongation of the QT interval. Alcohol and cocaine used together can be metabolized into a new metabolite called cocaethylene that may be cardiotoxic.^{48,49} Thus, medications that prolong the QT interval (such as ziprasidone) should not be used in patients with prolonged baseline QTc intervals. While some studies suggest a possible therapeutic role for clozapine in the treatment of cocaine addiction (see discussion of “Medications to Treat Substance Use Disorders” later in the article), a study by Farren et al.⁷⁹ found that, while clozapine reduces subjective responses to cocaine, it also increases serum cocaine levels in a dose-dependent manner and was associated with a near syncopal episode in one subject, so that more study is needed on this interaction.

Cigarette smoking has a profound influence on the cytochrome P450 system in the liver, which is responsible for the metabolism of many commonly used antipsychotic and antidepressant medications. The major effect is not due to nicotine but to the inhaled polycyclic aromatic hydrocarbons in smoke, which induce the cytochrome (CYP 1A2) isoenzymes to clear medications from the bloodstream more efficiently.^{80,81} Tobacco smoking can substantially lower blood levels of newer “atypical” antipsychotics, such as clozapine and olanzapine, and tobacco smoking has a moderate effect on older, conventional antipsychotics, such as haloperidol, fluphenazine, chlorpromazine, and thioridazine. Clinicians should consider that tobacco smoking's modulation of antipsychotic metabolism may be a factor that increases treatment resistance and any change in smoking status (reducing/ceasing use) necessitates close monitoring for increased medication side effects due to increased medication blood levels.⁸² Caffeine is also metabolized by the CYP 1A2 cytochrome system; thus, the high levels of caffeine consumption found in this heavy-smoking population may be at least partly understood as the result of the reduction of serum caffeine levels as a result of smoking's effect on the CYP 1A2 system.⁸²

Medications to Treat Schizophrenia

Most treatment algorithms and expert consensus panels support the use of atypical antipsychotics as first-line agents for schizophrenia.⁸³⁻⁸⁷ The existing studies that have evaluated the use of antipsychotics in patients with co-existing schizophrenia and substance use disorders include case reports, open-label trials, and randomized clinical trials (Table 3). Consistent with schizophrenia treatment guidelines, the clinical evidence supports the use of atypical antipsychotics (e.g., aripiprazole, olanzapine, quetiapine, risperidone, or ziprasidone, and in some cases clozapine) over the older conventional antipsychotics as first-line agents for individuals with co-occurring schizophrenia and addiction (see Table 3). Overall, atypical antipsychotics are perceived to be associated with fewer side effects and they have a lower incidence of extrapyramidal symptoms (EPS); they may also improve cognition.¹⁰⁴ Atypical antipsychotics as a class of medications do have side effects that must be monitored, including weight gain, hyperlipidemia, elevated glucose, increased cerebrovascular events, and other side effects common also to traditional antipsychotics. There is currently little evidence to suggest that one atypical antipsychotic is better than another for this population. Most clinical experts suggest selecting the medication that seems best for the individual patient, taking safety, toxicity, and side effects into consideration.

Some studies^{95,96,104} in this population support the use of clozapine in spite of the possibility of side effects that have limited its use in this population (e.g., increased risk of seizures, sedation, liver enzyme elevation, myocarditis, orthostatic hypotension, and the need for regular blood tests to monitor for agranulocytosis). Other published schizophrenia guidelines cited above recommend clozapine as a second-line agent. Our consensus group was mixed on whether clozapine should remain as a second-line agent or potentially be a first-line agent in this population. Most had concerns about clozapine as a first-line agent because of its side effects; however, based on the research literature, some thought clozapine might be appropriate, especially for more motivated patients in well integrated, specialized co-occurring disorder treatment programs.

In general, because most atypical antipsychotics have fewer cardiac and motor side effects, they provide a greater safety margin than the older antipsychotics. With the exception of clozapine, the risk of seizures with these medications is low. Even with clozapine, the risk can be managed by keeping the dose below the seizure threshold (if known for a particular patient), by avoiding rapid dose escalations, or by combining clozapine with divalproex, an anti-seizure drug. Excessive sedation can result when quetiapine, olanzapine, or clozapine are combined

with some substances of abuse, but this should not preclude the use of these atypical antipsychotics.

The use of atypical antipsychotic medications may have important implications for managing drug craving in people with schizophrenia and cocaine dependence. Research has suggested that, in response to cocaine cues, individuals with cocaine dependence and schizophrenia in the early stage of acute withdrawal display a heightened desire to use cocaine at a rate twice that of those without schizophrenia.^{106,107} Given this state of increased craving, research has focused on the use of atypical antipsychotics as anti-craving agents in individuals with schizophrenia who primarily abuse cocaine, with promising preliminary findings from studies concerning risperidone,⁹⁹ olanzapine,¹⁰⁵ and quetiapine.¹⁰⁸ There is also some evidence that atypical antipsychotics may be of benefit in treating nicotine dependence in people with psychotic disorders.¹⁰⁹

Medications to Treat Anxiety, Depression, and Sleep Difficulties

Careful consideration must be given when deciding whether to use medications to manage co-occurring anxiety, depression, and sleep disturbance in patients with schizophrenia and addiction. In addition to medications, education and cognitive-behavioral treatment should also be considered to address these problems. Anxiety, depression, and sleep difficulties are common in individuals in early abstinence, who may experience “protracted withdrawal.” Symptoms include irritability, depressed mood, frustration, insomnia, tremor, and increased autonomic activity. Although these problems will eventually resolve, they can be distressing and may contribute to relapse to substance use. The use of medications without abuse potential, such as selective serotonin reuptake inhibitors (SSRIs) and buspirone, is preferred, although there are few studies evaluating the use of SSRIs with people with schizophrenia and a substance use disorder. Benzodiazepines should be avoided with this population as they have abuse potential, can be sedating, and may produce memory problems. These sedating/amnestic effects can be synergistic with alcohol and other drugs.

The non-SSRI antidepressants venlafaxine, mirtazapine, and bupropion are also generally considered safe for individuals who are substance abusers and are better options than the older tricyclic antidepressants. The safety of nefazodone in substance abusers is still debated due to concerns about liver toxicity and central nervous system depression. Tricyclic antidepressants should be used with great caution because they have the potential to produce cardiac, orthostatic hypotensive, and anticholinergic side effects.

Medications to Treat Substance Use Disorders

Many medications targeting specific stages of substance use treatment (i.e., detoxification, protracted abstinence, and maintenance) can be safely prescribed for patients with schizophrenia (Table 4). Unfortunately, these medications are underutilized, both in the general population and in populations with dual diagnoses. All patients with schizophrenia first require stabilization of their psychiatric medications before medications to treat substance use are added to their treatment regimen. The choice of medications to treat substance use disorders varies according to the specific substance(s) involved.

Alcohol—Medications approved by the U. S. Food and Drug Administration (FDA) to treat alcohol dependence include disulfiram, naltrexone, and the newly approved acamprosate.

Clinical experience with the use of disulfiram in individuals with schizophrenia is mixed, and randomized controlled trials are lacking. Because of the potential alcohol-disulfiram reaction, a patient being treated with disulfiram must be able to fully understand the risks of the medication and refrain from drinking. The clinician must therefore determine that the

individual with schizophrenia has adequate judgment, memory, and control over impulsivity before prescribing disulfiram. At high doses of disulfiram (1,000 mg/day), there is a risk of increased psychotic symptoms or agitation due to the dopamine-beta-hydroxylase blocking effect of the drug. However, at lower doses (125–250 mg/day), the medication seems to be well tolerated.

Clinical experience suggests that naltrexone may help patients with schizophrenia and alcohol dependence, especially patients for whom the use of disulfiram is a concern.^{110,111} Studies to date have not found any serious negative interactions between naltrexone and other psychiatric medications including antipsychotics, lithium, and antidepressants.¹¹²

Cocaine—No medications have been approved by the FDA to treat cocaine dependence. Several studies of co-occurring cocaine addiction and schizophrenia have used tricyclic medications (desipramine, imipramine) with limited benefit. Atypical antipsychotic medications may have some ability not only to treat psychosis and mania, but also to directly reduce cocaine craving (see discussion in the earlier section on “Medications to Treat Schizophrenia”). The use of atypical antipsychotics is associated with improved outcomes in patients with schizophrenia and cocaine use disorders compared with patients receiving traditional antipsychotics (see Table 3).^{99,105,113}

Tobacco—Six treatments for tobacco dependence are currently approved by the FDA. Five are different types of nicotine replacement therapies (NRT): gum, transdermal patch, inhaler, nasal spray, and the recently approved lozenge. The only FDA-approved non-nicotine treatment is bupropion SR, a well-known antidepressant. Collectively, these six are considered first-line medication treatments with established safety and efficacy. Nortriptyline and clonidine may be helpful as second-line medication treatments for tobacco dependence, although they have more side effects.

The probability that persons with schizophrenia will quit smoking is about half that in the general population. Bupropion has been helpful in more than one trial in reducing smoking in patients with schizophrenia.^{114–116} In addition, despite its dopaminergic properties, bupropion has been well tolerated in individuals with schizophrenia, with no evidence that it worsens psychotic symptoms. Preliminary work suggests that treatments such as nicotine replacement, although safe and generally well tolerated, have lower than expected success rates in patients with schizophrenia and schizoaffective disorder.^{117,118} The nicotine nasal spray is well tolerated by patients with schizophrenia, and a recent case series provided promising early results for this treatment.¹¹⁹ The nasal spray has unique features, such as a rapid onset of action, intermittent dosing, and more immediate craving relief.

Opioids—Opioid dependence is uncommon in individuals with schizophrenia, and there have been no reported studies with this population. Clinical experience suggests that both methadone and buprenorphine are safe treatment options. Clinicians, however, should be careful of medications that are metabolized by the CYP 3A4 isoenzyme, which could potentially interact with methadone. These include tricyclic antidepressants and SSRIs, which raise methadone levels, and carbamazepine, which reduces methadone levels.

Marijuana—No medications have been approved by the FDA to treat marijuana dependence. Marijuana/ cannabis is one of the most commonly used illicit drugs by individuals with schizophrenia¹²⁰ and increases the risk for other drug abuse and may be a vehicle for consuming substances such as PCP, amphetamines/ cocaine, and heroin. Marijuana use among individuals with schizophrenia can lead to increased frequency of delusions and hallucinations, increased symptoms of anxiety and depression, and impaired short-term memory and lower

motivation.^{121,122} More studies are needed in this population on treatments for marijuana dependence.

PROGRAM AND SYSTEM CHANGE

Systems-level issues have a direct impact on the effective delivery of treatment for co-occurring schizophrenia and substance abuse disorders. The following section first provides a brief overview of the systems perspective and the most common systems problems that can interfere with effectively addressing co-occurring disorders and then outlines actions that organizations can take to overcome these problems.

Obstacles To Treatment

The service needs of this population cut across multiple systems of care, including primary health care, long-term care, criminal justice, child and family protective services, entitlement systems, victim/trauma services, and mental health and substance abuse treatment.

Poor system integration is the largest obstacle to treating this population. Services are often fragmented, redundant, excessively focused on specific disorders, and unaccountable to the consumer. There is often little or no communication or collaboration among various departments or levels of government, which have separate administrative structures, constituencies, mandates, and target groups.¹²³⁻¹²⁵ Further inefficiency is caused by disparate health insurance benefits and the differing criteria used by a myriad of payors, including Medicaid, state payors, and managed care; inconsistent definitions of medical necessity; and a lack of parity for substance abuse and co-occurring disorders. Program funding is typically driven by diagnosis and is awarded contingent upon significant restrictions and rules that force programs to focus exclusively on mental health or substance abuse problems. When services rely on disparate funding streams, they are frequently required to collect and maintain inconsistent and even incompatible sets of information. This can make comparative program evaluation and description difficult or impossible.

Work force issues—Issues related to the work force form the second obstacle that can interfere with providing integrated care. Mental health and substance abuse clinicians each receive little training in the other's field, and tend to be uncomfortable working outside of their knowledge base. Despite the existence of evidence-based practices for treating the population with co-occurring disorders, only a small minority of clinicians receives such training. Also, relatively few valid and reliable assessment screening tools exist to guide treatment decisions. Different philosophies guide the mental health and substance abuse treatment communities, each of which embraces different beliefs with regard to mandated vs. voluntary treatment, the role of confrontation as a therapeutic tool, the use of medications, causal factors related to each set of disorders, the concept of recovery, and staging of treatment interventions. It is no surprise, therefore, that mental health and substance abuse professionals each tend to view treating problems from the other domain as foreign and burdensome.⁴

Critical Ingredients for Change

Overcoming these barriers is not an insurmountable task. There are four critical ingredients in making system-level change: leadership, development of a common language and set of terms, organizational assessment, and internal change process.

Leadership is a necessary ingredient of the change process; it defines the vision and establishes a set of expectations that staff are encouraged, supported, and expected to follow. Its importance cannot be overestimated in setting standards of care, initiating and convening a dialogue, building relationships, and continuing to motivate staff during the change process.

The development of a common language and set of terms to describe the full range of people with co-occurring disorders is helpful. The NASADAD/NASMHPD Conceptual Framework,¹²⁵ based upon the work of Rosenthal et al.¹⁹ and Ries,¹²⁶ helps frame the systems of care for serving people with co-occurring disorders and does so in terms of symptom severity, locus of care, and the level of service system coordination needed to manage these populations.

Organizational assessment—Before undertaking program change, it is necessary for each agency to first assess its unique situation and to share the results with staff. Program managers should assess the prevalence of current and past substance abuse disorders in those currently in treatment and in the larger population served. Most organizations will discover they already are treating many persons with co-existing disorders, and staff should be helped to understand the extent of co-occurring disorders in their existing caseloads. A chart review of current clients can help to determine the extent of adequate documentation, treatment interventions, referrals, and collaboration with outside treatment providers. To increase awareness and documentation of co-occurring disorders, it is important to begin by identifying minimal assessment and screening questions for both types of disorders.

Assessing motivation is part of the patient evaluation and helps to organize a motivation-based approach to care in which a mental health treatment program and system has both abstinence-oriented treatment and also non-abstinence-oriented management approaches. Programs and systems must support other critical clinical issues such as having physical and substance abuse consultation available in addition to developing integrated programs that address both mental health and addiction disorders. Other services within programs include case management and assertive community services, medications for both schizophrenia and substance use disorders, and Dual Recovery 12-step meetings on site and in the community.

Internal change process—When undertaking organizational change, initially focus more on improving your organization's internal capabilities than on collaborating with external organizations. All organizations tend to be more internally directed than externally directed, and they are usually more successful at internal initiatives, especially over longer time frames. Focus on developing services that are integrated and comprehensive, where treatment is flexibly organized around a cross-trained team that is able to offer clinical intervention for both mental health and substance use disorders. Use an incremental approach in developing services, one that focuses on building on strengths and pursuing a series of small steps rather than undertaking a large, high-profile initiative. If the goal is to merge existing substance abuse and mental health services, focus on the commonalities between the two approaches, especially in early phases of the project. Enlist the commitment of key administrative figures, and identify energetic and effective leaders within your organization and empower them to begin to identify needed changes in programming.

Staff resistance may also have to be addressed; such resistance is likely be rooted in a fear that caseloads will rise, or that personnel are incapable of treating an unfamiliar population. Staff can be engaged in the process by being asked to identify training needs, current obstacles to providing optimal treatment, and current program goals, and linking each of these to improving co-occurring disorders services and training. This should be done in a non-punitive manner, with an emphasis on incremental but meaningful improvement at both the individual and program levels. Gaining expertise in treating both disorders should be framed not as an added burden, but as an opportunity to provide better and more efficient treatment for clients.

Managers should appoint a work group to review the credentials and areas of expertise of medical and psychosocial treatment staff, to identify strengths and weaknesses, and to define minimal competencies. Training should include case presentations and conferences jointly attended by professionals from each field. Social events or joint staff meetings aimed at

bringing together mental health and substance abuse treatment staff can promote professional bonding and an exchange of ideas. Finally, a harder but equally vital task is to develop methods to overcome funding and regulatory barriers, such as organizing substance abuse and mental health services under the same administrative entities, and having a single commissioner or local manager responsible for overseeing both systems of care.

Resources—There are several important resources available to help administrators and policy makers make system-level changes. For an excellent general guide to organizational change, see “The Change Book,” published by the Addiction Technology Transfer Centers, and available online at <http://www.nattc.org/resPubs/changeBook.html>.

An excellent guide to developing co-occurring disorder programming is “Strategies for Developing Treatment Programs for People with Co-Occurring Substance Abuse and Mental Health Disorders,” published by SAMHSA and available online at <http://www.nccbh.org/cooccurringreport.pdf>.

SAMHSA has also developed a National Resource Training Center for Co-Occurring Disorders, the Co-Occurring Center of Excellence (COCE), available online at <http://coce.samhsa.gov>.

CONCLUSION

Co-occurring substance abuse disorders are common in patients with schizophrenia and cause a myriad of serious consequences, including deterioration of psychiatric symptoms, medical problems, homelessness, legal problems, social isolation, and discord. Fortunately, effective programs and integrated psychosocial treatment approaches exist for this population. There is also empirical literature and case-based knowledge available to guide the selection and management of pharmacological interventions for both psychosis and substance use disorders. However, there are significant organizational barriers to systematically disseminating and implementing evidence-based interventions; these include disparate funding streams and requirements, fragmented services, and a lack of cross-training among the front-line treatment providers. Coordinated efforts at the national, state, and program levels will be required to remove these barriers and to provide optimal care for this vulnerable population.

This article summarizes conclusions from a consensus meeting on how to better manage co-occurring addiction and schizophrenia. There is a clear need to implement changes in training and systems, as well as a need for new research initiatives to address gaps in the literature and increase our understanding of the clinical issues in this area. It is hoped that incorporation of the suggestions in this article, which are based on a summary of current evidence-based literature and the consensus of experienced clinicians, may enhance training and clinical outcomes.

Acknowledgements

This article is based upon the proceedings of a consensus meeting “Improving the Management of Care for Individuals with Severe Mental Illness and Co-occurring Substance Use Disorders,” held March 4–5, 2004, in Philadelphia, PA. The meeting and subsequent manuscript development were supported by unrestricted educational grants from Eli Lilly and Co. and AstraZeneca.

APPENDIX: Summary of consensus recommendations

I. Screening and assessment

- Screen for use of all substances and types of substance use disorders.

- Screen for alcohol, tobacco, caffeine, and all other substances.
- Employ direct screening questions about patterns of use.
- Employ objective tests of use (e.g., urine tests, alcohol breathalyzer, CO meter for tobacco).
- Employ screening instruments for problem substance use.
- Assess for negative consequences of substance use.
- Establish a substance use disorder diagnosis.
 - Do a timeline to assess mental illness, addiction, and life events.
 - Consider differential diagnosis for psychotic and substance use disorders.
- Assess and reassess patient's motivation to address each specific disorder or substance use problem.

II. Most common medical consequences of substance use in individuals with schizophrenia

- Individuals with schizophrenia are at increased risk for cardiovascular and metabolic disorders.
- Most substance use creates or further increases medical risks:
 - Cocaine increases the risk of cardiac disease, stroke, and seizures.
 - Tobacco increases the risk for many health problems, including cancers and cardiovascular disease; it also alters medication metabolism.
 - Alcohol increases cardiac problems, seizure risk, sedation, and intoxication.
 - Opioids increase adverse effects of psychiatric medications.
- Needle use, sexual promiscuity, and unsafe sexual behavior associated with substance abuse increase the risk of infections, such as sexually transmitted diseases, HIV, and hepatitis B and C.

III. Assessing and managing medical consequences of substance use

- Assess for medical consequences of substance use, especially as they may affect the response to, and the adverse effects of, psychiatric medications.
- Take a medical history and perform a physical examination and laboratory tests.
- Refer for appropriate medical treatment.
- Anticipate difficulties with engagement in and adherence to medical care and work closely with primary care providers to try to ensure adherence.

IV. Treatment plan development

- Tailor interventions to the patient's individual needs, preferences, level of care, and readiness to change.

- Include medication and therapy options and ongoing assessment/monitoring.
- Be prepared for interactions among mental illness, substance use, and associated medical problems.
- Encourage reconnection with and involvement of family and friends as a step towards long-term recovery.
- Periodically renegotiate and revise the treatment plan.

V. Psychosocial approaches

- Integrate evidence based psychosocial treatments for addiction, including motivational enhancement therapy, relapse prevention, and 12-step facilitation.
- Integrated treatment leads to improved outcomes.
- The initial treatment focus should be on developing a therapeutic alliance.
- Successful treatment approaches also enhance motivation and address psychiatric stabilization, skills acquisition, and relapse prevention.
- Promote positive healthy support from others, including 12-step meetings.
- Short-term case management approaches have been successful, showing that case management is most important during vulnerable periods, and as a tool to navigate services and maximize treatment retention.

VI. Medication management

- Treat schizophrenia with medications recommended in the Texas Medication Algorithm Project (TMAP), the American Psychiatric Association (APA) Practice Guidelines, and other consensus-driven guidelines.
- Atypical antipsychotics are first-line choices because of their better side-effect profile and initial evidence-based studies in this population.
- Start low and go slow in dosing.
- Continue antipsychotic medications even in the presence of continued substance use.
- Whenever possible, avoid sedating medications, medications that cause physical dependence with abuse liability, and medications that potentiate the effects of substances of abuse.
- Simplify dosing strategies for improved treatment adherence.
- Minimize refill quantities for enhanced safety from overdose.
- Consider adding addiction treatment medications when appropriate.

VII. Key agency or systems-level issues and recommendations for implementing services for patients with co-occurring schizophrenia and substance use disorders

- Develop leaders, an overall vision, and a comprehensive plan.
- Confront funding and regulatory barriers to optimal treatment of co-occurring disorders.

- Obtain necessary mental health and addiction treatment skills by training existing staff and hiring new staff.
- Address staff resistance to change by providing orientation concerning co-occurring disorders, training, and reassurance that the changes will improve patient care.
- Make screening and assessment for substance use disorders routine.
- Develop integrated programs that address both disorders.
- Make staff familiar with medications for both schizophrenia and substance use disorders.
- Introduce a motivation-based approach to care, with both abstinence-oriented treatment and non-abstinence-oriented management approaches.
- Make physical and substance abuse consultation available.
- Offer Dual Recovery 12-step meetings on site.
- Provide case management and assertive community treatment services.

References

1. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse. *JAMA* 1990;264:2511–8. [PubMed: 2232018]
2. de Leon J. Smoking and vulnerability for schizophrenia. *Schizophr Bull* 1996;22:405–9. [PubMed: 8873291]
3. Ziedonis DM. Integrated treatment of co-occurring mental illness and addiction: Clinical intervention, program, and system perspectives. *CNS Spectrums* 2004;9:892–904. [PubMed: 15618940]
4. Substance Abuse and Mental Health Services Administration (SAMHSA). Report to Congress on the prevention and treatment of co-occurring substance abuse disorders and mental disorders. Washington, DC: 2002 [April 18, 2005]. at <http://alt.samhsa.gov/reports/congress2002/index.html>
5. President's New Freedom Commission on Mental Health. Apr 32003 [April 26, 2005]. at <http://www.mental-healthcommission.gov/reports/reports.htm>
6. SAMHSA. Substance Abuse Treatment for Persons With Co-Occurring Disorders. Treatment Improvement Protocol (TIP) Series 42. SAMHSA; Rockville, MD: 2005 [March 7, 2005]. DHHS Publication No. (SMA) 05–3922 Available at www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat5.chapter.74073. Copies can also be ordered at <http://store.health.org/catalog/results.aspx?h=publications&topic=103>
7. Sacks S, Sacks J, De Leon G, et al. Modified therapeutic community for mentally ill chemical “abusers”: Background; influences; program descriptions; preliminary findings. *Subst Use Misuse* 1997;32:1217–59. [PubMed: 9261918]
8. American Psychiatric Association. Practice guideline for the treatment of patients with substance use disorders: Alcohol, tobacco, and other drugs. (in press)
9. Caton CLM, Shrout PE, Eagle PF, et al. Risk factors for homelessness among schizophrenic men: A case-control study. *Am J Pub Health* 1994;84:265–70. [PubMed: 8296951]
10. Cuffel B, Shumway M, Chouljian T. A longitudinal study of substance use and community violence in schizophrenia. *J Nerv Ment Disease* 1994;182:704–8. [PubMed: 7989915]
11. Haywood TW, Kravitz HM, Grossman LS, et al. Predicting the “revolving door” phenomenon among patients with schizophrenic, schizoaffective, and affective disorders. *Am J Psychiatry* 1995;152:856–61. [PubMed: 7755114]
12. Serper MR, Alpert M, Richardson NA, et al. Clinical effects of recent cocaine use on patients with acute schizophrenia. *Am J Psychiatry* 1995;152:1464–9. [PubMed: 7573585]

13. Smelson DA, Davis CW, Di Pano R, et al. Executive and motor skill functioning among cocaine-dependent schizophrenics and non-drug-abusing schizophrenics. *J Nerv Ment Dis* 2002;190:200–2. [PubMed: 11923656]
14. Soyka M, Albus M, Immler B, et al. Psychopathology in dual diagnosis and non-addicted schizophrenics: Are there differences? *Eur Arch Psychiatry Clin Neurosci* 2001;251:232–8. [PubMed: 11829210]
15. Drake RE, Essock SM, Shaner A, et al. Implementing dual diagnosis services for clients with severe mental illness. *Psychiatr Serv* 2001;52:469–76. [PubMed: 11274491]
16. Bellack AS, DiClemente CC. Treating substance abuse among patients with schizophrenia. *Psychiatr Serv* 1999;50:75–80. [PubMed: 9890583]
17. Carey KB. Reliability and validity of the time-line follow-back interview among psychiatric outpatients: A preliminary report. *Psychol Addict Behav* 1997;11:26–33.
18. Rosenthal RN, Hellerstein DJ, Miner CR. A model of integrated services for outpatient treatment of patients with comorbid schizophrenia and addictive disorders. *Am J Addict* 1992;1:339–48.
19. Rosenthal RN. Mental illness/chemical addiction: A guide to emergency services assessment and treatment manual. NY State Office of Mental Health, Division of Clinical Support Systems, Albany. 1992
20. Shaner A, Eckman T, Roberts LJ, et al. Feasibility of a skills training approach to reduce substance dependence among individuals with schizophrenia. *Psychiatr Serv* 2003;54:1287–9. [PubMed: 12954948]
21. Ziedonis, D.; Steinberg, ML.; Smelson, D., et al. Co-occurring addictive and psychotic disorders.. In: Graham, AW.; Schultz, TK.; Mayo-Smith, MF., et al., editors. *Principles of addiction medicine*. Vol. 3rd edition. American Society of Addiction Medicine; Chevy Chase, MD: 2003. p. 1297-1320.
22. Ziedonis DM, Kosten TR, Glazer WM, et al. Nicotine dependence and schizophrenia. *Hosp Community Psychiatry* 1994;45:204–6. [PubMed: 7910577]
23. Teitelbaum LM, Carey KB. Tips on using the Addiction Severity Index in psychiatric settings. *The Behavior Therapist* 1997;20:19–21.
24. Carey KB, Correia CJ. Severe mental illness and addictions: Assessment considerations. *Addict Behav* 1998;23:735–48. [PubMed: 9801713]
25. Saunders JB, Aasland OG, Babor TF, et al. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project Early Detection of Persons with Harmful Alcohol Consumption II. *Addiction* 1993;88:791–804. [PubMed: 8329970]
26. Skinner HA, Sheu WJ. Reliability of alcohol use indices. The Lifetime Drinking History and the MAST. *J Stud Alcohol* 1982;43:1157–70. [PubMed: 7182675]
27. Skinner HA. The Drug Abuse Screening Test. *Addict Behav* 1982;7:363–71. [PubMed: 7183189]
28. Rosenberg SD, Drake RE, Wolford GL, et al. Dartmouth Assessment of Lifestyle Instrument (DALI): A substance use disorder screen for people with severe mental illness. *Am J Psychiatry* 1998;155:232–8. [PubMed: 9464203]
29. Bartels SJ, Teague GB, Drake RE, et al. Substance abuse in schizophrenia: Service utilization and costs. *J Nerv Ment Dis* 1993;181:227–332. [PubMed: 8473874]
30. Mueser KT, Bellack AS, Blanchard JJ. Comorbidity of schizophrenia and substance abuse: Implications for treatment. *J Consult Clin Psychol* 1992;60:845–56. [PubMed: 1460148]
31. Ziedonis DM, Fisher W. Motivation-based assessment and treatment of substance abuse in patients with schizophrenia. *Dir Psychiatry* 1996;16:1–8.
32. Allen JP, Litten RZ. The role of laboratory tests in alcoholism treatment. *J Subst Abuse Treat* 2001;20:81–5. [PubMed: 11239731]
33. Helander, A. Biological markers of alcohol use and abuse in theory and practice.. In: Agarwal, DP.; Seitz, HK., editors. *Alcohol in health and disease*. Marcel Dekker; New York: 2001. p. 177-205.
34. Ziedonis DM, Trudeau K. Motivation to quit using substances among individuals with schizophrenia: Implications for a motivation-based treatment model. *Schizophr Bull* 1997;23:229–38. [PubMed: 9165633]
35. Prochaska JO, DiClemente CC, Norcross JC. In search of how people change: Applications to addictive behaviors. *Am Psychol* 1992;47:1102–14. [PubMed: 1329589]

36. Ries RK, Ellingson T. A pilot assessment at one month of 17 dual diagnosis patients. *Hosp Community Psychiatry* 1990;41:1230–3. [PubMed: 2249802]
37. Rosenberg SD, Goodman LA, Osher FC, et al. Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness. *Am J Public Health* 2001;91:31–7. [PubMed: 11189820]
38. Mukamal KJ. Alcohol consumption and abnormalities of brain structure and vasculature. *Am J Geriatr Cardiol* 2004;13:22–8. [PubMed: 14724398]
39. Centers for Disease Control and Prevention. The health consequences of smoking: A report of the Surgeon General. 2004. Available at http://www.cdc.gov/tobacco/sgr/sgr_2004/
40. Dalton SO, Laursen TM, Mellekjaer L, et al. Risk for cancer in parents of patients with schizophrenia. *Am J Psychiatry* 2004;161:903–8. [PubMed: 15121657]
41. Lichtermann D, Ekelund J, Pukkala E, et al. Incidence of cancer among persons with schizophrenia and their relatives. *Arch Gen Psychiatry* 2001;58:573–8. [PubMed: 11386986]
42. Davidson S, Judd F, Jolley D, et al. Cardiovascular risk factors for people with mental illness. *Aust N Z J Psychiatry* 2001;35:196–202. [PubMed: 11284901]
43. Allison DB, Fontaine KR, Heo M, et al. The distribution of body mass index among individuals with and without schizophrenia. *J Clin Psychiatry* 1999;60:215–20. [PubMed: 10221280]
44. Dixon L, Postrado L, Delahanty J, et al. The association of medical comorbidity in schizophrenia with poor physical and mental health. *J Nerv Ment Dis* 1999;187:496–502. [PubMed: 10463067]
45. Herran A, de Santiago A, Sandoya M, et al. Determinants of smoking behaviour in outpatients with schizophrenia. *Schizophr Res* 2000;41:373–81. [PubMed: 10708347]
46. McElroy SL, Kotwal R, Malhotra S, et al. Are mood disorders and obesity related? A review for the mental health professional. *J Clin Psychiatry* 2004;65:634–51. [PubMed: 15163249]
47. Marder SR, Essock SM, Miller AL, et al. Physical health monitoring of patients with schizophrenia. *Am J Psychiatry* 2004;161:1334–49. [PubMed: 15285957]
48. McCance EF, Price LH, Kosten TR, et al. Cocaethylene: Pharmacology, physiology, and behavioral effects in humans. *J Pharmacol Exp Ther* 1995;274:215–23. [PubMed: 7616402]
49. McCance-Katz EF, Kosten TR, Jatlow P. Concurrent use of cocaine and alcohol is more potent and potentially more toxic than use of either alone: A multiple-dose study. *Biol Psychiatry* 1998;44:250–9. [PubMed: 9715356]
50. Flegal KM, Cauley JA. Alcohol consumption and cardiovascular risk factors. *Recent Dev Alcohol* 1985;3:165–80. [PubMed: 3883442]
51. Kuo I, Sherman SG, Thomas DL, et al. Hepatitis B virus infection and vaccination among young injection and non-injection drug users: Missed opportunities to prevent infection. *Drug Alcohol Depend* 2004;73:69–78. [PubMed: 14687961]
52. Kellerman SE, Hanson DL, McNaghten AD, et al. Prevalence of chronic hepatitis B and incidence of acute hepatitis B infection in human immunodeficiency virus-infected subjects. *J Infect Dis* 2003;188:571–7. [PubMed: 12898445]
53. Butterfield MI, Bosworth HB, Meador KG, et al. Gender differences in hepatitis C infection and risks among persons with severe mental illness. *Psychiatr Serv* 2003;54:848–53. [PubMed: 12773599]
54. Stoskopf CH, Kim YK, Glover SH. Dual diagnosis: HIV and mental illness: A population-based study. *Community Ment Health J* 2001;37:469–79. [PubMed: 11504140]
55. Fernandez F, Levy JK. Psychopharmacotherapy of psychiatric syndromes in asymptomatic and symptomatic HIV infection. *Psychiatr Med* 1991;9:377–94. [PubMed: 1924828]
56. Batki SL. Drug abuse, psychiatric disorders, and AIDS. Dual and triple diagnosis. *West J Med* 1990;152:547–52. [PubMed: 2190423]
57. Bagchi A, Sambamoorthi U, McSpiritt E, et al. Use of antipsychotic medications among HIV-infected individuals with schizophrenia. *Schizophr Res* 2004;71:435–44. [PubMed: 15474915]
58. Miller, WR.; Rollnick, S. Motivational interviewing: Preparing people to change addictive behavior. Guilford; New York: 1991.
59. Miller, WR.; Zweben, A.; DiClemente, CC., et al. Motivational enhancement therapy manual. US Department of Health and Human Services; Rockville, MD: 1995. NIH Publication No. 94–3723
60. Ziedonis DM, Stern R. Dual recovery therapy for schizophrenia and substance abuse. *Psychiatr Ann* 2001;31:255–64.

61. Carey KB. Substance use reduction in the context of outpatient psychiatric treatment: A collaborative, motivational, harm reduction approach. *Community Ment Health J* 1996;32:291–306. [PubMed: 8790970]
62. Bartels SJ, Drake RE. A pilot study of residential treatment for dual diagnoses. *J Nerv Ment Dis* 1996;184:379–81. [PubMed: 8642391]
63. Blankertz LE, Cnaan RA. Serving the dually diagnosed homeless: Program development and interventions. *J Ment Health Adm* 1993;20:100–12. [PubMed: 10171526]
64. Hanson M, Kramer TH, Gross W. Outpatient treatment of adults with coexisting substance use and mental disorders. *J Subst Abuse Treat* 1990;7:109–16. [PubMed: 2388311]
65. Hellerstein DJ, Rosenthal RN, Miner CR. A prospective study of integrated outpatient treatment for substance-abusing schizophrenic patients. *Am J Addict* 1995;4:33–42.
66. Rahav M, Rivera JJ, Nuttbrock L, et al. Characteristics and treatment of homeless, mentally ill, chemical-abusing men. *J Psychoactive Drugs* 1995;27:93–1. [PubMed: 7602445]
67. Burnam MA, Morton SC, McGlynn EA, et al. An experimental evaluation of residential and nonresidential treatment for dually diagnosed homeless adults. *J Addict Dis* 1995;14:111–34. [PubMed: 8929936]
68. Bennett ME, Bellack AS, Gearon JS. Treating substance abuse in schizophrenia: An initial report. *J Subst Abuse Treat* 2001;20:163–75. [PubMed: 11306219]
69. Mueser KT, Bond GR, Drake RE, et al. Models of community care for severe mental illness: A review of research on case management. *Schizophr Bull* 1998;24:37–47. [PubMed: 9502546]
70. Johnson B, Montgomery P. Chronic mentally ill individuals reentering the community after hospitalization. Phase II: The urban experience. *J Psychiatr Ment Health Nurs* 1999;6:445–51. [PubMed: 10818867]
71. Schaedle R, McGrew JH, Bond GR, et al. A comparison of experts' perspectives on assertive community treatment and intensive case management. *Psychiatr Serv* 2002;53:207–10. [PubMed: 11821553]
72. Rosenheck RA, Dennis D. Time-limited assertive community treatment for homeless persons with severe mental illness. *Arch Gen Psychiatry* 2001;58:1073–80. [PubMed: 11695955]
73. Okin RL, Boccia A, Azocar F, et al. The effects of clinical case management on hospital service use among ER frequent users. *Am J Emerg Med* 2000;18:603–8. [PubMed: 10999578]
74. Witbeck G, Hornfield S, Dalack GW. Emergency room out-reach to chronically addicted individuals: A pilot study. *J Subst Abuse Treat* 2000;9:39–43. [PubMed: 10867299]
75. Smelson DA, Losonczy MF, Castles-Fonseca K, et al. Preliminary outcomes from a community linkage intervention for individuals with co-occurring substance abuse and serious mental illness. *Journal of Dual Diagnosis* 2005;1:47–59.
76. Smelson DA, Losonczy MF, Ziedonis D, et al. A brief community linkage intervention for veterans with a persistent mental illness and a co-occurring substance abuse disorder. 2005Submitted for publication[Can you update?]
77. Weiss RD, Greenfield SF, Najavits LM, et al. Medication compliance among patients with bipolar disorder and substance use disorder. *J Clin Psychiatry* 1998;59:172–4. [PubMed: 9590667]
78. Rychtarik RG, Connors GJ, Dermen KH, et al. Alcoholics Anonymous and the use of medications to prevent relapse: An anonymous survey of member attitudes. *J Stud Alcohol* 2000;61:134–8. [PubMed: 10627107]
79. Farren CK, Hameedi FA, Rosen MA, et al. Significant interaction between clozapine and cocaine in cocaine addicts. *Drug Alcohol Depend* 2000;59:153–63. [PubMed: 10891628]
80. Zevin S, Benowitz NL. Drug interactions with tobacco smoking. An update. *Clin Pharmacokinet* 1999;36:425–38. [PubMed: 10427467]
81. Desai HD, Seabolt J, Jann MW. Smoking in patients receiving psychotropic medications: A pharmacokinetic perspective. *CNS Drugs* 2001;15:469–94. [PubMed: 11524025]
82. Bozikas VP, Papakosta M, Niopas I, et al. Smoking impact on CYP1A2 activity in a group of patients with schizophrenia. *Eur Neuropsychopharmacol* 2004;14:39–44. [PubMed: 14659985]
83. McEvoy JP, Scheifler PL, Frances A. The expert consensus guideline series: Treatment of schizophrenia 1999. *J Clin Psychiatry* 1999;60(suppl 11):1–80.

84. Kane JM, Leucht S, Carpenter D, et al. The expert consensus guideline series: Optimizing pharmacologic treatment of psychotic disorders. *J Clin Psychiatry* 2003;64(suppl 12):1–100.
85. Miller AL, Hall CS, Buchanan RW, et al. The Texas Medication Algorithm Project antipsychotic algorithm for schizophrenia: 2003 update. *J Clin Psychiatry* 2004;65:500–8. [PubMed: 15119912]
86. Lehman AF, Lieberman JA, Dixon LB, et al. Practice guideline for the treatment of patients with schizophrenia. *Am J Psychiatry* (2nd edition) 2004;161(suppl 2):1–56. [PubMed: 15000267]
87. Department of Veterans Affairs and Department of Defense. Management of Psychoses, MODULE J: Psychoses and Schizophrenia Treatment. VA/DoD Evidence-Based Clinical Practice Guideline Working Group, Veterans Health Administration, Department of Veterans Affairs, and Health Affairs, Department of Defense; Washington, DC: May. 2004 Office of Quality and Performance publication 10Q-CPG/PSY-04 (Can be accessed at www.oqp.med.va.gov/cpg/PSY/psy_cpg/content/ModJ/modA_fr.htm)
88. Albanese MJ, Khantzian EJ, Murphy SL, et al. Decreased substance use in chronically psychotic patients treated with clozapine. *Am J Psychiatry* 1994;151:780–1. [PubMed: 8166327]
89. Marcus P, Snyder R. Reduction of comorbid substance abuse with clozapine. *Am J Psychiatry* 1995;152:959. [PubMed: 7755141]
90. Buckley PF. Novel antipsychotic medications and the treatment of comorbid substance abuse in schizophrenia. *J Subst Abuse Treat* 1998;15:113–6. [PubMed: 9561949]
91. Tsuang JW, Eckman TE, Shaner A, et al. Clozapine for substance-abusing schizophrenic patients. *Am J Psychiatry* 1999;156:1119–20. [PubMed: 10401473]
92. Tsuang JW, Eckman T, Marder S, et al. Can risperidone reduce cocaine use in substance abusing schizophrenic patients? *J Clin Psychopharmacol* 2002;22:629–30. [PubMed: 12454567]
93. Buckley P, Thompson P, Way L, et al. Substance abuse among patients with treatment-resistant schizophrenia: Characteristics and implications for clozapine therapy. *Am J Psychiatry* 1994;151:385–9. [PubMed: 8109646]
94. Conley RR, Kelly DL, Gale EA. Olanzapine response in treatment-refractory schizophrenic patients with a history of substance abuse. *Schizophr Res* 1998;33:95–101. [PubMed: 9783349]
95. Lee ML, Dickson RA, Campbell M, et al. Clozapine and substance abuse in patients with schizophrenia. *Can J Psychiatry* 1998;43:855–6. [PubMed: 9806095]
96. Drake RE, Xie H, McHugo GJ, et al. The effects of clozapine on alcohol and drug use disorders among patients with schizophrenia. *Schizophr Bull* 2000;26:441–9. [PubMed: 10885642]
97. Zimmet SV, Strous RD, Burgess ES, et al. Effects of clozapine on substance use in patients with schizophrenia and schizoaffective disorder: A retrospective survey. *J Clin Psychopharmacol* 2000;20:94–8. [PubMed: 10653215]
98. Littrell KH, Petty RG, Hilligoss NM, et al. Olanzapine treatment for patients with schizophrenia and substance abuse. *J Subst Abuse Treat* 2001;21:217–21. [PubMed: 11777671]
99. Smelson DA, Losonczy MF, Davis CW, et al. Risperidone decreases craving and relapses in individuals with schizophrenia and cocaine dependence. *Can J Psychiatry* 2002;47:671–5. [PubMed: 12355680]
100. Rosenheck, R.; Kosten, TR. Risperdal for substance-dependent psychotic patients.. Presented at the College on Problems of Drug Dependence Meeting; Bal Harbour, Florida. June 6, 2003;
101. Poling J, Kosten TR. Risperidone for substance dependent psychotic patients. *Addictive Disorders & Their Treatment* 2005;4:1–3.
102. Levin FR, Evans SM, Coomaraswamy S, et al. Flupenthixol treatment for cocaine abusers with schizophrenia: A pilot study. *Am J Drug Alcohol Abuse* 1998;24:343–60. [PubMed: 9741939]
103. Rosenthal, RN.; Ozden, A.; Miner, CR., et al. Effects of atypical neuroleptics in the dually diagnosed.. Presented at Tenth Winter Workshop on Schizophrenia; Davos, Switzerland. February 5–11, 2000;
104. Green AI, Burgess ES, Dawson R, et al. Alcohol and cannabis use in schizophrenia: Effects of clozapine vs. risperidone. *Schizophr Res* 2003;60:81–5. [PubMed: 12505141]
105. Smelson DA, Ziedonis DM, Losonczy MF, et al. A double-blind study comparing olanzapine to haloperidol for reducing cue-elicited craving in individuals with schizophrenia and cocaine dependence. *Schizophr Res* 2003;60:303.

106. Carol G, Smelson DA, Losonczy MF, et al. Alcohol and drug abuse: A preliminary investigation of cocaine craving among persons with and without schizophrenia. *Psychiatr Serv* 2001;52:1029–31. [PubMed: 11474045]
107. Smelson DA, Losonczy MF, Kilker C, et al. An analysis of cue reactivity among persons with and without schizophrenia who are addicted to cocaine. *Psychiatr Serv* 2002;53:1612–6. [PubMed: 12461224]
108. Brown ES, Nejtek VA, Perantie DC, et al. Quetiapine in bipolar disorder and cocaine dependence. *Bipolar Disord* 2002;4:406–11. [PubMed: 12519101]
109. George TP, Ziedonis DM, Feingold A, et al. Nicotine transdermal patch and atypical antipsychotic medications for smoking cessation in schizophrenia. *Am J Psychiatry* 2000;157:1835–42. [PubMed: 11058482]
110. Batki SL, Dimmock J, Cornell M, et al. Directly observed naltrexone treatment of alcohol dependence in schizophrenia: Preliminary analysis. *Alcohol Clin Exp Res* 2002;26(suppl 5):470. (abstract)
111. Petrakis IL, O'Malley S, Rounsaville B, et al. Naltrexone augmentation of neuroleptic treatment in alcohol abusing patients with schizophrenia. *Psychopharmacology (Berl)* 2004;172:291–7. [PubMed: 14634716]
112. Farren CK, O'Malley S. A pilot double blind placebo controlled trial of sertraline with naltrexone in the treatment of opiate dependence. *Am J Addict* 2002;11:228–34. [PubMed: 12202015]
113. Zimmet SV, Strous RD, Burgess ES, et al. Effects of clozapine on substance use in patients with schizophrenia and schizoaffective disorder: A retrospective survey. *J Clin Psychopharmacol* 2000;20:94–8. [PubMed: 10653215]
114. Evins AE, Mays VK, Rigotti NA, et al. A pilot trial of bupropion added to cognitive behavioral therapy for smoking cessation in schizophrenia. *Nicotine Tob Res* 2001;3:397–403. [PubMed: 11694208]
115. George TP, Vessicchio JC, Termine A, et al. A placebo controlled trial of bupropion for smoking cessation in schizophrenia. *Biol Psychiatry* 2002;52:53–61. [PubMed: 12079730]
116. Weiner E, Ball MP, Summerfelt A, et al. Effects of sustained-release bupropion and supportive group therapy on cigarette consumption in patients with schizophrenia. *Am J Psychiatry* 2001;158:635–7. [PubMed: 11282701]
117. Ziedonis DM, George TP. Schizophrenia and nicotine use: Report of a pilot smoking cessation program and review of neurobiological and clinical issues. *Schizophr Bull* 1997;23:247–54. [PubMed: 9165635]
118. Williams JM, Ziedonis DM. Addressing tobacco among individuals with a mental illness or an addiction. *Addict Behav* 2004;29:1067–83. [PubMed: 15236808]
119. Williams JM, Ziedonis DM, Foulds J. A case series of nicotine nasal spray in the treatment of tobacco dependence among patients with schizophrenia. *Psychiatr Serv* 2004;55:1064–6. [PubMed: 15345771]
120. DeQuardo JR, Carpenter CF, Tandon R. Patterns of substance abuse in schizophrenia: Nature and significance. *Psychiatr Res* 1994;28:267–75.
121. Negrete JC, Knapp WP, Douglas DE, et al. Cannabis affects the severity of schizophrenic symptoms: Results of a clinical survey. *Psychol Med* 1986;16:515–20. [PubMed: 3489951]
122. Raphael B, Wooding S, Stevens G. Comorbidity: Cannabis and complexity. *J Psychiatr Pract* 2005;11:161–76. [PubMed: 15920390]
123. National Association of State Mental Health Program Directors (NASMHPD) and National Association of State Alcohol and Drug Abuse Directors (NASADAD). Exemplary methods of financing integrated service programs for persons with co-occurring mental health and substance use disorders. NASMHPD-NASADAD Task Force on Co-Occurring Disorders; Alexandria, VA and Washington, DC: 2002.
124. National Association of State Mental Health Program Directors (NASMHPD) and National Association of State Alcohol and Drug Abuse Directors (NASADAD). Financing and marketing the new conceptual framework for co-occurring mental health and substance use disorders: A blueprint for systems change. Second National Dialogue of the Joint NASMHPD-NASADAD Task Force on Co-Occurring Disorders; Alexandria, VA and Washington, DC: 2002.

125. National Association of State Mental Health Program Directors (NASMHPD) and National Association of State Alcohol and Drug Abuse Directors (NASADAD) Joint Task Force on Co-Occurring Mental Health and Substance Use Disorders. The evolving conceptual framework for co-occurring mental health and substance use disorders: Developing strategies for systems change. Final Report, April, 2004 (Can be accessed at <http://www.nasmhpd.org>)
126. Ries RK. The dually diagnosed patient with psychotic symptoms. *J Addict Dis* 1993;12:103–22. [PubMed: 8251538]

Table 1

Maximum detection times for substances of abuse in urine toxicology screening

<i>Substance</i>	<i>Maximum detection time</i>
Alcohol	24 hours
Amphetamines	4 days
Barbiturates	21 days
Benzodiazepines	6 weeks
Cocaine	7 days
Hallucinogens	7 days
Heroin	2 days
Marijuana	3 days (casual use) 12 weeks (chronic, heavy use)
Methadone	7 days

Table 2

Motivational tasks for clinicians during progressing stages of change

<i>Stage</i> [*]	<i>Defining characteristic</i>	<i>Motivational tasks for clinician</i>
Stage I Precontemplation	No awareness of problem or intention to make a change.	Raise doubt and provide information to increase client's perception of risks and problems with current behavior.
Stage II. Contemplation	Ambivalence about change.	Tip the balance—evoke questions about making a change and discuss risks of not changing; strengthen the client's self-efficacy to change current behavior, but no action.
Stage III. Preparation	Window of opportunity when a client considers change and develops a commitment to action.	Help client determine the best course of action to take in seeking change. Focus on small but meaningful steps.
Stage IV. Action	Begins to implement the solution or plan.	Help client take steps towards change. Support initial steps towards change; provide corrective feedback.
Stage V. Maintenance	Develops new behaviors to maintain changes and solution.	Help client identify and use strategies to prevent relapse; support success; and reinforce motivation and self-efficacy.
Stage VI. Relapse	Resumption of problem: normal and expected. Likely to abandon change if demoralized.	Help client renew process of contemplation, determination, and action, without becoming stuck or demoralized because of relapse.

* Based on Prochaska and DiClemente's five-stage model of readiness to change³⁵

Table 3

Medication studies of patients with co-occurring schizophrenia and substance use disorders

NIH-PA Author Manuscript	3a: Case reports				
	Author	Type	Meds	Subjects	N
	Albanese et al. 1994 ⁸⁸	Case, state hospital	Clozapine 500 mg	Schizophrenia, AUD	2
	Marcus and Snyder 1995 ⁸⁹	Case series, CMHC	Clozapine	Schizophrenia	13 nicotine (8 history of SUD) [8 a subset??]
	Buckley 1998 ⁹⁰	Case, state hospital	Clozapine 650 mg	Treatment-resistant schizophrenia, alcohol, cocaine	1
	Tsuang et al. 1999 ⁹¹	Case, DD-OPD	Clozapine 550 mg	Treatment-resistant schizophrenia, alcohol, cocaine	1
NIH-PA Author Manuscript	Tsuang et al. 2002 ⁹²	Case, DD-OPD	Switch to risperidone 8 mg	Schizophrenia, cocaine dependence	2
	3b: Outcomes with atypical antipsychotics in patients with and without substance use disorders				
	Author	Type	Meds	Subjects	N
	Buckley et al. 1994 ⁹³	Prospective, OPD group therapy	Clozapine	Treatment-resistant schizophrenia/schizoaffective, alcohol, cocaine	118 (29 with history of SUD, 7 of whom had current SUD)
	Conley et al. 1998 ⁹⁴	Prospective open label	Olanzapine (maximum 25 mg/day)	Treatment-resistant schizophrenia, BPRS > 45	60 (23 with history of SUD > 6 mo ago; 74% AUD)
	3c: Atypical antipsychotics compared with other agents in patients with substance use disorders				
NIH-PA Author Manuscript	Author	Type	Meds	Subjects	N
	Lee et al. 1998 ⁹⁵	Observational cross-sectional, day treatment	Clozapine vs. other	Schizophrenia/schizoaffective	204 (35 clozapine); past SUD: 57% clozapine, 50% other
	Drake et al. 2000 ⁹⁶	Retrospective	Clozapine vs. other	Schizophrenia/schizoaffective and SUD (69.5% AUD)	151 (36 clozapine)
	Zimmet et al. 2000 ⁹⁷	Retrospective chart review, clozapine clinic	Clozapine	Schizophrenia/schizoaffective + current SUD	28
	Littrell et al. 2001 ⁹⁸	Prospective open label	Olanzapine (mean dose = 16.6 mg/day)	Schizophrenia/schizoaffective + AUD/SUD (cocaine)	30 (23 abuse, 7 dependence)
	Smelson et al. 2002 ⁹⁹	Prospective open label, VAMC	Switch from conv to risperidone up to 6 mg	Schizophrenia + cocaine dependence	18 (8 risperidone)
NIH-PA Author Manuscript	Rosenheck and Kosten 2003 ¹⁰⁰	Retrospective VA database review	Maintained vs changed meds, target risperidone	Schizophrenia: N = 9,066	1,909 changed meds (515 SUD); 510 to risperidone (123 SUD)
	Poling and Kosten 2005 ¹⁰¹	Retrospective VA database review	Risperidone [vs. what??]	Schizophrenia + SUD	150 risperidone
	Levin et al. 1998 ¹⁰²	Prospective, open label, 4 week inpatient, 6 week OPD	Switch to flupenthixol 40 mg q2 weeks	Schizophrenia/schizoaffective + SUD (cocaine)	8
	Rosenthal et al. 2000 ¹⁰³	Post hoc, naturalistic, DD-OPD	Ad lib atypicals vs. conventionals	Schizophrenia/schizoaffective + AUD/SUD (cocaine)	78
	Green et al. 2003 ¹⁰⁴	Retrospective chart review, CMHC	Clozapine vs. risperidone	Schizophrenia/schizoaffective + AUD/SUD (cannabis)	41 (33 clozapine, 8 risperidone)
NIH-PA Author Manuscript	Smelson et al. 2003 ¹⁰⁵	Double-blind randomized	Olanzapine vs. haloperidol	Schizophrenia + SUD (cocaine)	34

3a: Case reports				
	Author	Type	Meds	Subjects
	Follow-up	Measures	Outcomes	N
NIH-PA Author Manuscript	6 months	Alcohol abstinence	Decreased paranoid symptoms; increased socialization; alcohol abstinence	
	Unspecified		Self-reported increased organization, 11/13 reduced or abstinent Tnico-tine???	
	Unspecified	Clinical assessment	Improved positive and negative symptoms, subjective decrease in craving	
	Unspecified	Weekly UTOX	Patient achieved cocaine and alcohol abstinence	
	8-week trial	Weekly UTOX	Reductions in cocaine use, mild reductions in craving	
	Follow-up	Measures	Outcomes	
	6 months	BPRS, HAM-D, GAS, QOL, Simpson-Angus, SADS-C factors	No difference in outcomes between patients with history of SUD vs nonSUD in clozapine dose; BPRS; GAS; positive, negative, or disorganized symptoms; Simpson-Angus; or treatment response	
	7 weeks	BPRS, CGI, SANS, Barnes, AIMS, Simpson-Angus, no SUD outcomes	No differences between patients with history of SUD vs nonSUD on BPRS, CGI, SANS, Barnes, Simpson-Angus, or treatment response (20% decrease in BPRS)	
	Follow-up	Measures	Outcomes	
	Unspecified	Current SUD diagnosis	Current SUD: 0% clozapine, 13% other; reduction across groups $\chi^2 p < 0.01$; between groups $p = 0.01$	
NIH-PA Author Manuscript	Every 6 months for 3 years	UTOX, BPRS, AUS, DUS, SATS	Clozapine: significant decrease in alcohol severity and days of use, 79% AUD remission > 6 months versus 33.7% on other drugs, $p = 0.001$	
	Not specified	Clinician rating 5-point substance use and global symptoms scale	85% decreased substance use; 75% alcohol abstinent; decreased cannabis 90%, cocaine 86.7%; correlation decreased SUD and global sx	
	Every month for a year	PANSS, Service Use, UTOX, BAC, AIMS, Simpson-Angus	62% decrease in positive and 45% in negative sx; 21/30 (70%) early full remission SUD, 9/30 (30%) early partial remission SUD	
	Weekly for 6 weeks	PANSS, Cue-elicited craving VAS, relapse	Intensity of cue reaction: risperidone 7.88 vs conventional 25.6; Depression: risperidone 39 vs. 26; Relapse: risperidone 12.5% vs. 70%	
	Baseline, 6 or 12 months	Global Assessment of Functioning (GAF)	GAF in total sample, +1.3% nonswitched vs. -0.9% switched ($p < 0.0001$); GAF in those switched to risperidone: +3.6% SUD ($n = 123$) vs. +0.5% nonSUD ($n = 387$)	
	3 months before and after baseline	UTOX	Risperidone: significant decrease in +UTOX rates (38% vs. 29%), cocaine (19% vs. 15%), cannabis (13% vs. 10%) [vs. what???	
	10 weeks	PANSS, BDI, UTOX, SATS, AIMS, cocaine craving VAS	UTOX Pre-post nonsignificant; positive and negative sx scores decreased by 31% and 29%; 5 pts had > 75% reduction on UTOX	
	Baseline and 4, 8, and 12 months	Hosp days, SUS, SAPS, SANS, W-QLI; GEE with wO/R/C covariate	More time on O/R/C, lower SAPS score ($Z = -4.28$, $p < 0.001$) independent of treatment/ time? ; no effect on substance use, hospital, W-QLI	
NIH-PA Author Manuscript	1 year	Clinician-rated change in alcohol/cannabis use; abstinence 1st year	1 year abstinence rates ($N = 32$): risperidone 13%, clozapine 54%; $\chi^2 p = 0.05$	
	6 weeks	PANSS, Addiction Severity Index, VCCQ	Olanzapine significantly reduced craving, substance use, symptom severity	

AIMS: Abnormal Involuntary Movement Scale

AUD: alcohol use disorder

AUS:Alcohol Use Scale

BAC: ?????????

Barnes: Barnes Akathisia Rating Scale

BDI: Beck Depression Inventory

BPRS: Brief Psychiatric Rating Scale

CGI: Clinical Global Impressions Scale

CMHC: community mental health center

DD-OPD: dual diagnosis outpatient department

DUS: Drug Use Scale **[SUS the same?]**

GAS: Global Assessment Scale

GEE with wO/R/C covariate **[?????????]**

HAM-D: Hamilton Rating Scale for Depression

PANSS: Positive and Negative Syndrome Scale

QOL: Quality of Life assessment

SADS: Seasonal Affective Disorder Scale

SANS: Scale for the Assessment of Negative Symptoms

SAPS: Scale for the Assessment of Positive Symptoms

SATS =??

Simpson-Angus: Simpson-Angus Rating Scale for Extrapyramidal Side Effects

SUD: substance use disorder

UTOX: urine toxicology screen

VAS: Visual Analog Scale

VCCQ: **[??????????]**

W-QLI: Wisconsin Quality of Life Index

Table 4

Medications for treatment of substance use disorders*

<i>Substance use disorder</i>	<i>Indication for medication</i>	<i>Medication options</i>
Alcohol	Detoxification	Benzodiazepines Barbiturates
	Protracted withdrawal	Acamprosate (Campral)
	Protracted abstinence	Disulfiram (Antabuse) Naltrexone (Revia)
Cocaine	Protracted abstinence	None FDA approved
Tobacco	Detoxification and protracted abstinence	Nicotine replacements (gum, patch, lozenge, spray, inhaler)
Opioid	Detoxification	Bupropion
		Methadone
		Clonidine
		Clonidine/naltrexone
		Buprenorphine
	Maintenance	Methadone Buprenorphine
	Protracted abstinence	Naltrexone
Amphetamine	Withdrawal and craving	None FDA approved
Marijuana	Withdrawal and craving	None FDA approved

* Source of information: Ziedonis 2004³