CHAPTER 4.
EARLY INTERVENTION, TREATMENT, AND MANAGEMENT OF SUBSTANCE USE DISORDERS

Chapter 4 Preview

A substance use disorder is a medical illness characterized by clinically significant impairments in health, social function, and voluntary control over substance use. Substance use disorders range in severity, duration, and complexity from mild to severe. In 2015, 20.8 million people aged 12 or older met criteria for a substance use disorder. While historically the great majority of treatment has occurred in specialty substance use disorder treatment programs with little involvement by primary or general health care, a shift is occurring toward the delivery of treatment services in general health care practice. For those with mild to moderate substance use disorders, treatment through the general health care system may be sufficient, while those with severe substance use disorders (addiction) may require specialty treatment.

The good news is that a spectrum of effective strategies and services are available to identify, treat, and manage substance use problems and substance use disorders. Research shows that the most effective way to help someone with a substance use problem who may be at risk for developing a substance use disorder is to intervene early, before the condition can progress. With this recognition, screening for substance misuse is increasingly being provided in general health care settings, so that emerging problems can be detected and early intervention provided if necessary. The addition of services to address substance use problems and disorders in mainstream health care has extended the continuum of care, and includes a range of effective, evidence-based medications, behavioral therapies, and supportive services. However, a number of barriers have limited the widespread adoption of these services, including lack of resources, insufficient training, and workforce shortages. This is particularly true for the treatment of those with co-occurring substance use and physical or mental disorders.
This chapter provides an overview of the scientific evidence supporting the effectiveness of treatment interventions, therapies, services, and medications available to identify, treat, and manage substance use problems and disorders.

**KEY FINDINGS***

- Well-supported scientific evidence shows that substance use disorders can be effectively treated, with recurrence rates no higher than those for other chronic illnesses such as diabetes, asthma, and hypertension. With comprehensive continuing care, recovery is now an achievable outcome.

- Only about 1 in 10 people with a substance use disorder receive any type of specialty treatment. The great majority of treatment has occurred in specialty substance use disorder treatment programs with little involvement by primary or general health care. However, a shift is occurring to mainstream the delivery of early intervention and treatment services into general health care practice.

- Well-supported scientific evidence shows that medications can be effective in treating serious substance use disorders, but they are under-used. The U.S. Food and Drug Administration (FDA) has approved three medications to treat alcohol use disorders and three others to treat opioid use disorders. However, an insufficient number of existing treatment programs or practicing physicians offer these medications. To date, no FDA-approved medications are available to treat marijuana, cocaine, methamphetamine, or other substance use disorders, with the exception of the medications previously noted for alcohol and opioid use disorders.

- Supported scientific evidence indicates that substance misuse and substance use disorders can be reliably and easily identified through screening and that less severe forms of these conditions often respond to brief physician advice and other types of brief interventions. Well-supported scientific evidence shows that these brief interventions work with mild severity alcohol use disorders, but only promising evidence suggests that they are effective with drug use disorders.

- Well-supported scientific evidence shows that treatment for substance use disorders—including inpatient, residential, and outpatient—are cost-effective compared with no treatment.

- The primary goals and general management methods of treatment for substance use disorders are the same as those for the treatment of other chronic illnesses. The goals of treatment are to reduce key symptoms to non-problematic levels and improve health and functional status; this is equally true for those with co-occurring substance use disorders and other psychiatric disorders. Key components of care are medications, behavioral therapies, and recovery support services (RSS).

- Well-supported scientific evidence shows that behavioral therapies can be effective in treating substance use disorders, but most evidence-based behavioral therapies are often implemented with limited fidelity and are under-used. Treatments using these evidence-based practices have shown better results than non-evidence-based treatments and services.

- Promising scientific evidence suggests that several electronic technologies, like the adoption of electronic health records (EHRs) and the use of telehealth, could improve access, engagement, monitoring, and continuing supportive care of those with substance use disorders.

*The Centers for Disease Control and Prevention (CDC) summarizes strength of evidence as: “Well-supported”: when evidence is derived from multiple controlled trials or large-scale population studies; “Supported”: when evidence is derived from rigorous but fewer or smaller trials; and “Promising”: when evidence is derived from a practical or clinical sense and is widely practiced.8
Continuum of Treatment Services

Substance use disorders typically emerge during adolescence and often (but not always) progress in severity and complexity with continued substance misuse.\textsuperscript{9,10} Currently, substance use disorders are classified diagnostically into three severity categories: mild, moderate, and severe.\textsuperscript{2}

Substance use disorder treatment is designed to help individuals stop or reduce harmful substance misuse, improve their health and social function, and manage their risk for relapse. In this regard, substance use disorder treatment is effective and has a positive economic impact. Research shows that treatment also improves individuals’ productivity,\textsuperscript{11} health,\textsuperscript{11,12} and overall quality of life.\textsuperscript{13-15} In addition, studies show that every dollar spent on substance use disorder treatment saves $4 in health care costs and $7 in criminal justice costs.\textsuperscript{11}

Mild substance use disorders can be identified quickly and reliably in many medical and social settings. These common but less severe disorders often respond to brief motivational interventions and/or supportive monitoring, referred to as guided self-change.\textsuperscript{16} In contrast, severe, complex, and chronic substance use disorders often require specialty substance use disorder treatment and continued post-treatment support to achieve full remission and recovery. To address the spectrum of substance use problems and disorders, a continuum of care provides individuals an array of service options based on need, including prevention, early intervention, treatment, and recovery support (Figure 4.1). Traditionally, the vast majority of treatment for substance use disorders has been provided in specialty substance use disorder treatment programs, and these programs vary substantially in their clinical objectives and in the frequency, intensity, and setting of care delivery.

Key Terms

- **Substance Use Disorder Treatment.** A service or set of services that may include medication, counseling, and other supportive services designed to enable an individual to reduce or eliminate alcohol and/or other drug use, address associated physical or mental health problems, and restore the patient to maximum functional ability.\textsuperscript{3}

- **Continuum of Care.** An integrated system of care that guides and tracks a person over time through a comprehensive array of health services appropriate to the individual’s need. A continuum of care may include prevention, early intervention, treatment, continuing care, and recovery support.\textsuperscript{4}
Figure 4.1: Substance Use Status and Substance Use Care Continuum

<table>
<thead>
<tr>
<th>Positive Physical, Social, and Mental Health</th>
<th>Substance Misuse</th>
<th>Substance Use Disorder</th>
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<td>A state of physical, mental, and social well-being, free from substance misuse, in which an individual is able to realize his or her abilities, cope with the normal stresses of life, work productively and fruitfully, and make a contribution to his or her community.</td>
<td>The use of any substance in a manner, situation, amount, or frequency that can cause harm to the user and/or to those around them.</td>
<td>Clinically and functionally significant impairment caused by substance use, including health problems, disability, and failure to meet major responsibilities at work, school, or home; substance use disorders are measured on a continuum from mild, moderate, to severe based on a person’s number of symptoms.</td>
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Substance Use Status Continuum

Substance Use Care Continuum

<table>
<thead>
<tr>
<th>Enhancing Health</th>
<th>Primary Prevention</th>
<th>Early Intervention</th>
<th>Treatment</th>
<th>Recovery Support</th>
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<tbody>
<tr>
<td>Promoting optimum physical and mental health and well-being, free from substance misuse, through health communications and access to health care services, income and economic security, and workplace certainty.</td>
<td>Addressing individual and environmental risk factors for substance use through evidence-based programs, policies, and strategies.</td>
<td>Screening and detecting substance use problems at an early stage and providing brief intervention, as needed.</td>
<td>Intervening through medication, counseling, and other supportive services to eliminate symptoms and achieve and maintain sobriety, physical, spiritual, and mental health and maximum functional ability. Levels of care include:  • Outpatient services;  • Intensive Outpatient/ Partial Hospitalization Services;  • Residential/ Inpatient Services; and  • Medically Managed Intensive Inpatient Services.</td>
<td>Removing barriers and providing supports to aid the long-term recovery process. Includes a range of social, educational, legal, and other services that facilitate recovery, wellness, and improved quality of life.</td>
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This chapter describes the early intervention and treatment components of the continuum of care, the major behavioral, pharmacological, and service components of care, services available, and emerging treatment technologies:

- **Early Intervention**, for addressing substance misuse problems or mild disorders and helping to prevent more severe substance use disorders.
- **Treatment engagement and harm reduction interventions**, for individuals who have a substance use disorder but who may not be ready to enter treatment, help engage individuals in treatment and reduce the risks and harms associated with substance misuse.
- **Substance use disorder treatment**, an individualized set of evidence-based clinical services designed to improve health and function, including medications and behavioral therapies.
- **Emerging treatment technologies** are increasingly being used to support the assessment, treatment, and maintenance of continuing contact with individuals with substance use disorders.
Early Intervention: Identifying and Engaging Individuals At Risk for Substance Misuse and Substance Use Disorders

Early intervention services can be provided in a variety of settings (e.g., school clinics, primary care offices, mental health clinics) to people who have problematic use or mild substance use disorders. These services are usually provided when an individual presents for another medical condition or social service need and is not seeking treatment for a substance use disorder. The goals of early intervention are to reduce the harms associated with substance misuse, to reduce risk behaviors before they lead to injury, to improve health and social function, and to prevent progression to a disorder and subsequent need for specialty substances use disorder services. Early intervention consists of providing information about substance use risks, normal or safe levels of use, and strategies to quit or cut down on use and use-related risk behaviors, and facilitating patient initiation and engagement in treatment when needed. Early intervention services may be considered the bridge between prevention and treatment services. For individuals with more serious substance misuse, intervention in these settings can serve as a mechanism to engage them into treatment.

Populations Who Should Receive Early Intervention

Early intervention should be provided to both adolescents and adults who are at risk of or show signs of substance misuse or a mild substance use disorder. One group typically in need of early intervention is people who binge drink: people who have consumed at least 5 (for men) or 4 (for women) drinks on a single occasion at least once in the past 30 days. Recent national survey data suggest that over 66 million individuals aged 12 or older can be classified as binge drinkers. Of particular concern are the 1.4 million binge drinkers aged 12 to 17, who may be at higher risk for future substance use disorders because of their young age.

Other groups who are likely to benefit from early intervention are people who use substances while driving and women who use substances while pregnant. In 2015, an estimated 214,000 women consumed alcohol while pregnant, and an estimated 109,000 pregnant women used illicit drugs.

Available research shows that brief, early interventions, given by a respected care provider, such as a nurse, nurse educator, or physician, in the context of usual medical care (for example, a routine medical exam or care for an injury or illness) can educate and motivate many individuals who are misusing substances to understand and acknowledge their risky behavior and to reduce their substance use.

Regardless of the substance, the first step to early intervention is screening to identify behaviors that put the individual at risk for harm or for developing a substance use disorder. Positive screening results should then be followed by brief advice or counseling tailored to the specific problems and interests of the individual and delivered in a non-judgmental manner, emphasizing both the importance of reducing substance use and the individual’s ability to accomplish this goal. Later follow-up monitoring should assess whether the screening and brief intervention were effective in reducing the substance use below risky levels or whether the person needs formal treatment.
Components of Early Intervention

One structured approach to delivering early intervention to people showing signs of substance misuse and/or early signs of a substance use disorder is through screening and brief intervention (SBI).\textsuperscript{22}

Research has shown that several methods of SBI are effective in decreasing "at-risk" substance use and that they work for a variety of populations and in a variety of health care settings.\textsuperscript{22,23} As mentioned earlier, this research has demonstrated positive effects for reducing alcohol use;\textsuperscript{24,25} the research with SBI among those with other substance use disorders has shown mixed results.\textsuperscript{26–29}

In addition, research shows that SBI can be cost-effective. For example, a randomized study compared SBI to screening alone for alcohol and drug use disorders among patients covered by Medicaid in eight emergency medicine clinics in the State of Washington. A year later, investigators compared total Medicaid expenditures between the two groups and found that the costs per member, per month for the SBI group were $185 to $192 lower than the costs for the screening-only group. This added up to a savings of more than $2,200 per patient in one year.\textsuperscript{30}

**SBI: Screening**

Ideally, substance misuse screening should occur for all individuals who present in health care settings, including primary, urgent, psychiatric, and emergency care. Professional organizations, including the American College of Obstetricians and Gynecologists, the American Medical Association, the American Academy of Family Physicians, and the American Academy of Pediatrics recommend universal and ongoing screening for substance use and mental health issues for adults and adolescents.\textsuperscript{31–36} Such screening practices can help identify the severity of the individual’s substance use and whether substance use disorder treatment may be necessary.

Within these contexts, substance misuse can be reliably identified through dialogue, observation, medical tests, and screening instruments.\textsuperscript{37} Several validated screening instruments have been developed to help non-specialty providers identify individuals who may have, or be at risk for, a substance use disorder.

Table 4.1 provides examples of available substance use screening tools, how they are used, and for which age groups. In addition to these tools, single-item screens for presence of drug use (“How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?”) and for alcohol use (“How many times in the past year have you had X or more drinks in a day?”, where X is 5 for men and 4 for women) have been validated and shown in primary care to accurately identify individuals at risk for or experiencing a substance use disorder.\textsuperscript{38–42}
Table 4.1: Evidence-Based Screening Tools for Substance Use

<table>
<thead>
<tr>
<th>Screening Tool</th>
<th>Substance Type</th>
<th>Age Group</th>
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<tbody>
<tr>
<td>Alcohol Screening and Brief Intervention for Adolescents and Youth: A Practitioner’s Guide</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Alcohol Use Disorders Identification Test (AUDIT)</td>
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<tr>
<td>Alcohol Use Disorders Identification Test-C (AUDIT-C)</td>
<td>✓</td>
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<tr>
<td>Brief Screener for Tobacco, Alcohol, and Other Drugs (BSTAD)</td>
<td>✓</td>
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<tr>
<td>CRAFFT</td>
<td>✓</td>
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<tr>
<td>CRAFFT (Part A)</td>
<td>✓</td>
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<tr>
<td>Drug Abuse Screen Test (DAST-10)</td>
<td>✓</td>
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<tr>
<td>DAST-20: Adolescent version</td>
<td>✓</td>
<td></td>
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<tr>
<td>Helping Patients Who Drink Too Much: A Clinicians’ Guide</td>
<td>✓</td>
<td></td>
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<tr>
<td>NIDA Drug Use Screening Tool</td>
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<tr>
<td>NIDA Drug Use Screening Tool: Quick Screen</td>
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<tr>
<td>Opioid Risk Tool</td>
<td>✓</td>
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<tr>
<td>S2BI</td>
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**SBI: Brief Interventions**

Brief interventions (or brief advice) range from informal counseling to structured therapies. They often include feedback to the individual about their level of use relative to safe limits, as well as advice to aid the individual in decision-making.

Motivational interviewing (MI) is a client-centered counseling style that addresses a person’s ambivalence to change. A counselor uses a conversational approach to help their client discover their interest in changing their substance using behavior. The counselor asks the client to express their desire for change and any ambivalence they might have and then begins to work with the client on a plan to change their behavior and to make a commitment to the change process. The main purpose of MI is to examine and resolve ambivalence, and the counselor is intentionally directive in pursuing this goal. It is effective in reducing the substance misuse of patients who come to medical settings for other health-related conditions. In these settings, individuals who receive MI are more likely to adhere to a treatment plan and, subsequently, to have better outcomes.
**Adding Referral to Treatment When Necessary**

When an individual’s substance use problem meets criteria for a substance use disorder, and/or when brief interventions do not produce change, it may be necessary to motivate the patient to engage in specialized treatment. This is called Screening, Brief Intervention, and Referral to Treatment (SBIRT). In such cases, the care provider makes a referral for a clinical assessment followed by a clinical treatment plan developed with the individual that is tailored to meet the person’s needs. Effective referral processes should incorporate strategies to motivate patients to accept the referral. Although the screening and brief intervention components of SBIRT are the same as SBI, referral to treatment helps the individual access, select, and navigate barriers to substance use disorder treatment.

The literature on the effectiveness of drug-focused brief intervention in primary care and emergency departments is less clear, with some studies finding no improvements among those receiving brief interventions. However, at least one study found significant reductions in subsequent drug use. Even if brief interventions are not found to be sufficient to address patients’ drug use disorders, general health care settings still have an important role to play in addressing drug use disorders, by providing medication-assisted treatment (MAT), providing more robust monitoring and care coordination, and actively promoting engagement in specialty substance use disorder treatment.

Trials evaluating different types of screening and brief interventions for drug use in a range of settings and on a range of patient characteristics are lacking. Recently, efforts have been made to adapt SBIRT for adolescents and for all groups with substance use disorders. The results of preliminary studies are promising, but gaps in knowledge about SBIRT for adolescents still need to be filled.

**Treatment Engagement: Reaching and Reducing Harm Among Those Who Need Treatment**

**Populations Who Need Treatment but Are Not Receiving It**

Despite the fact that substance use disorders are widespread, only a small percentage of people receive treatment. Results from the 2015 National Survey of Drug Use and Health (NSDUH) reveal that only about 2.2 million people with a substance use disorder, or about 1 in 10 affected individuals, received any type of treatment in the year before the survey was administered. This “treatment gap” is a large and costly concern for individuals, families, and communities. Of those who needed treatment but did not receive treatment, over 7 million were women and more than 1 million were adolescents aged 12 to 17. Some racial and ethnic groups experience disparities in entering and receiving substance use disorder treatment services. For example, approximately 13 million of those who did not receive treatment were non-Hispanic or non-Latino Whites, about 3 million were Hispanics or Latinos, and about 3 million were non-Hispanic Blacks or African Americans. Among all individuals who met criteria for a substance use disorder, alcohol was by far the most prevalent substance reported, followed by marijuana, misuse of prescription pain relievers, cocaine, and methamphetamines, and about 1 in
10 reported use of multiple substances. Additionally, over 8 million individuals, or about 40 percent of those with a substance use disorder, also had a mental disorder diagnosed in the year before the survey. Nonetheless, only 6.8 percent of these individuals received treatment for both conditions, and 52.0 percent received no treatment at all. Many individuals with substance use disorders also have related physical health problems. Substance use can contribute to medical issues, such as an increased risk of liver, lung, or cardiovascular disease, as well as infectious diseases such as Hepatitis B or C, and HIV/AIDS, and can worsen these health outcomes.

Reasons for Not Seeking Treatment

There are many reasons people do not seek treatment. The most common reason is that they are unaware that they need treatment; they have never been told they have a substance use disorder or they do not consider themselves to have a problem. This is one reason why screening for substance use disorders in general health care settings is so important. In addition, among those who do perceive that they need substance use disorder treatment, many still do not seek it. For these individuals, the most common reasons given are:

- Not ready to stop using (40.7 percent). A common clinical feature associated with substance use disorders is an individual’s tendency to underestimate the severity of their problem and to over-estimate their ability to control it. This is likely due to substance-induced changes in the brain circuits that control impulses, motivation, and decision making.
- Do not have health care coverage/could not afford (30.6 percent).
- Might have a negative effect on job (16.4 percent) or cause neighbors/community to have a negative opinion (8.3 percent).
- Do not know where to go for treatment (12.6 percent) or no program has the type of treatment desired (11.0 percent).
- Do not have transportation, programs are too far away, or hours are inconvenient (11.8 percent).

The costs of care and lack of insurance coverage are particularly important issues for people with substance use disorders. The 2015 NSDUH found that among individuals who needed and made an effort to get treatment but did not receive specialty substance use treatment, 30.0 percent reported that they did not have insurance coverage and could not afford to pay for treatment. Thus, a way to reduce health disparities is to increase the number of people who have health insurance. However, even if an individual is insured, the payor may not cover some types or components of substance use disorder treatments, particularly medications. These challenges are magnified further for those who live in rural areas, where substance use disorder treatment services can be distant and thus difficult to reach, as well as expensive because of travel time and cost.
Strategies to Reduce Harm

Strategies to reduce the harms associated with substance use have been developed as a way to engage people in treatment and to address the needs of those who are not yet ready to participate in treatment. Harm reduction programs provide public health-oriented, evidence-based, and cost-effective services to prevent and reduce substance use-related risks among those actively using substances, and substantial evidence supports their effectiveness. These programs work with populations who may not be ready to stop substance use — offering individuals strategies to reduce risks while still using substances. Strategies include outreach and education programs, needle/syringe exchange programs, overdose prevention education, and access to naloxone to reverse potentially lethal opioid overdose. These strategies are designed to reduce substance misuse and its negative consequences for the users and those around them, such as transmission of HIV and other infectious diseases. They also seek to help individuals engage in treatment to reduce, manage, and stop their substance use when appropriate.

Outreach and Education

Outreach activities seek to identify those with active substance use disorders who are not in treatment and help them realize that treatment is available, accessible, and necessary. Outreach and engagement methods may include telephone contacts, face-to-face street outreach, community engagement, or assertive outreach after a referral is made by a clinician or caseworker. These efforts often occur within or in collaboration with programs for intimate partner violence, homelessness, or HIV/AIDS. One study showed that 41 percent of referrals to treatment among substance-using individuals enrolled in a homelessness outreach project successfully resulted in treatment enrollment. This is notable and promising, but additional research is needed to validate that outreach efforts geared at identifying individuals who need treatment are successful at increasing substance use treatment enrollment and subsequent outcomes.

Educational campaigns are also a common strategy for reducing harms associated with substance use. Such campaigns have historically been targeted toward substance-using individuals, giving them information and guidance on risks associated with sharing medications or needles, how to access low or no-cost treatment services, and how to prevent a drug overdose death. Other education campaigns target the overall public to improve general understanding about addiction, community health and safety risks, and how to access available treatment services. Two examples are SAMHSA’s National Recovery Month, which seeks to increase awareness and understanding of mental and substance use issues, and the Anyone.Anytime. campaign in New Hampshire, which was implemented statewide to educate the public and professionals about addiction, emergency overdose medication, and accessibility to support services for those with opioid use disorders. The National Highway Traffic Safety Administration’s (NHTSA’s) annual Drive Sober or Get Pulled Over campaign is another example, aimed at reducing drunk driving and preventing alcohol-impaired fatalities.

Needle/Syringe Exchange Programs

Drugs such as heroin and other opioids, cocaine, and methamphetamine are commonly used by injection, and this route of administration has been a major source of infectious disease transmission including HIV, Hepatitis B, Hepatitis C, and other blood-borne diseases. Data from the CDC reveal
that even though HIV among people who inject drugs is declining, it is still a significant problem: 7 percent (3,096) of the 47,352 newly diagnosed cases of HIV infection in the United States in 2013 were attributable to injection drug use, and another 3 percent (1,270) involved male-to-male sexual contact combined with injection drug use. Nearly 20,000 people died from Hepatitis C in 2014, and 3.5 million are living with Hepatitis C. New cases of Hepatitis C infection increased 250 percent between 2010 and 2014, and occur primarily among young White people who inject drugs.

Because of these data, providing sterile needles and syringes to people who inject drugs has become an important strategy for reducing disease transmission. The goal of needle/syringe exchange programs is to minimize infection transmission risks by giving individuals who inject drugs sterile equipment and other support services at little or no cost. Additional services from these programs often include HIV/AIDS counseling and testing; strategies and education for preventing sexually transmitted infections, including condom use and use of medications before or after exposure to HIV to reduce the risk of becoming infected (pre-exposure prophylaxis [PrEP] or post-exposure prophylaxis [PEP]); and other health care services. Needle/syringe exchange programs also attempt to encourage individuals to engage in substance use disorder treatment.

Evaluation studies have clearly shown that needle/syringe exchange programs are effective in reducing HIV transmission and do not increase rates of community drug use. However, most of the research has not examined the impact of these programs on Hepatitis C transmission, therefore currently available data are insufficient to address this question.

Naloxone

Opioid overdose incidents and deaths, either from prescription pain relievers or heroin, are a serious threat to public health in the United States. Overdose deaths from opioid pain relievers and heroin have risen dramatically in the past 14 years, from 5,990 in 1999 to 29,467 in 2014, and most were preventable. Rates of opioid overdose deaths are particularly high among individuals with an opioid use disorder who have recently stopped their use as a result of detoxification or incarceration. As a result, their tolerance for the drug is reduced, making them more vulnerable to an overdose. Those who mix opioids with alcohol, benzodiazepines, or other drugs also have a high risk of overdose.

Opioid overdose does not occur immediately after a person has taken the drug. Rather, the effects develop gradually as the drug depresses a person’s breathing and heart rate. This eventually leads to coma and death if the overdose is not treated. This gradual progress means that there is typically a 1- to 3-hour window of opportunity after a user has taken the drug in which bystanders can take action to prevent the user’s death.

Naloxone is an opioid antagonist medication approved by the FDA to reverse opioid overdose in injectable and nasal spray forms. It works by displacing opioids from receptors in the brain, thereby blocking their effects on breathing and heart rate.

The rising number of deaths from opioid overdose has led to increasing public health efforts to make naloxone available to at-risk individuals and their families, as well as to emergency medical technicians, police officers, and other first responders, or through community-based opioid overdose prevention programs. Although regulations vary by state, some states have passed laws expanding access to
naloxone without a patient-specific prescription in some localities. Additionally, some schools across the country are stocking naloxone for use by trained nurses.

Interventions that distribute take-home doses of naloxone along with education and training for those actively using opioids and their peers and family members, have the potential to help decrease overdose-related deaths. Current evidence from nonrandomized studies also suggests that family, friends, and other community members who are properly trained can and will administer naloxone appropriately during an overdose incident. And, despite concern that access to naloxone might increase the prevalence or frequency of opioid use, research demonstrates that neither of these problems has occurred.

**FDA Approval of Naloxone Nasal Spray**

Naloxone, a safe medication that can quickly restore normal breathing to a person in danger of dying from an opioid overdose, is already carried by emergency medical personnel and other first responders. But by the time an overdosing person is reached and treated, it is often too late to save them. To solve this problem, several experimental Overdose Education and Naloxone Distribution (OEND) programs have given naloxone directly to opioid users, their friends or loved ones, and other potential bystanders, along with brief training on how to use this medication. These programs have been shown to be an effective, as well as cost-effective, way of saving lives.

Until recently, only injectable forms of naloxone were approved by the FDA. However, in November 2015, the FDA approved a user-friendly intranasal formulation of naloxone that matches the injectable version in terms of how much of the medication gets into the body and how rapidly. According to the CDC, more than 74 Americans die each day from an overdose involving prescription pain relievers or heroin. To reverse these trends, it is important to do everything possible to ensure that emergency personnel, as well as at-risk opioid users and their loved ones, have access to lifesaving medications like naloxone.

**Acute Stabilization and Withdrawal Management**

Withdrawal management, often called “detoxification,” includes interventions aimed at managing the physical and emotional symptoms that occur after a person stops using a substance. Withdrawal symptoms vary in intensity and duration based on the substance(s) used, the duration and amount of use, and the overall health of the individual. Some substances, such as alcohol, opioids, sedatives, and tranquilizers, produce significant physical withdrawal effects, while other substances, such as marijuana, stimulants, and caffeine, produce primarily emotional and cognitive withdrawal symptoms. Most periods of withdrawal are relatively short (3 to 5 days) and are managed with medications combined with vitamins, exercise, and sleep. One important exception is withdrawal from alcohol and sedatives/tranquilizers, especially if the latter are combined with heavy alcohol use. Rapid or unmanaged withdrawal from these substances can be protracted and can produce seizures and other health complications.

Withdrawal management is highly effective in preventing immediate and serious medical consequences associated with discontinuing substance use, but by itself it is not an effective treatment for any substance use disorder. It is best considered stabilization: The patient is assisted through a period of acute detoxification and withdrawal to being medically stable and substance-free. Stabilization includes
preparing the individual for treatment and involving the individual’s family and other significant people in the person’s life, as appropriate, to support the person’s treatment process. Stabilization is considered a first step toward recovery, much like acute management of a diabetic coma or a hypertensive stroke is simply the first step toward managing the underlying illness of diabetes or high blood pressure. Similarly, acute stabilization and withdrawal management are most effective when following evidence-based standards of care.87

Unfortunately, many individuals who receive withdrawal management do not become engaged in treatment. Studies have found that half to three quarters of individuals with substance use disorders who receive withdrawal management services do not enter treatment.88 One common result of not engaging in continuing care is rapid readmission to a detoxification center, an emergency department, or a hospital. For example, 27 percent of people who received detoxification services not followed by continuing care were readmitted within 1 year to public detoxification services in Delaware, Oklahoma, and Washington.89 Beginning substance use disorder treatment within 14 days of discharge from withdrawal management, however, has been shown to reduce readmission rates.90

One of the most serious consequences when individuals do not begin continuing care after withdrawal management is overdose. Because withdrawal management reduces much of an individual’s acquired tolerance, those who attempt to re-use their former substance in the same amount or frequency can experience physical problems. Individuals with opioid use disorders may be left particularly vulnerable to overdose and even death. It is critically important for health care providers to be prepared to properly assess the nature and severity of their patients’ clinical problems following withdrawal so that they can facilitate engagement into the appropriate intensity of treatment.56

Principles of Effective Treatment and Treatment Planning

Principles and Goals of Treatment

Treatment can occur in a variety of settings but most treatment for substance use disorders has traditionally been provided in specialty substance use disorder treatment programs. For this reason, the majority of research has been performed within these specialty settings.91 The following sections describe what is known from this research about the processes, stages of, and outcomes from traditional substance use disorder treatment programs.

The National Institute on Drug Abuse (NIDA) has detailed the evidence-based principles of effective treatment for adults and adolescents with substance use disorders that apply regardless of the particular setting of care or type of substance use disorder treatment program (Table 4.2).85,92
Table 4.2: Principles of Effective Treatment for Substance Use Disorders

<table>
<thead>
<tr>
<th>Principles of Effective Treatment for Adults</th>
<th>Principles of Effective Treatment for Adolescents</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Addiction is a complex but treatable disease that affects brain function and behavior.</td>
<td>1. Adolescent substance use needs to be identified and addressed as soon as possible.</td>
</tr>
<tr>
<td>2. No single treatment is appropriate for everyone.</td>
<td>2. Adolescents can benefit from a drug abuse intervention even if they are not addicted to a drug.</td>
</tr>
<tr>
<td>3. Treatment needs to be readily available.</td>
<td>3. Routine annual medical visits are an opportunity to ask adolescents about drug use.</td>
</tr>
<tr>
<td>4. Effective treatment attends to multiple needs of the individual, not just his or her drug abuse.</td>
<td>4. Legal interventions and sanctions or family pressure may play an important role in getting adolescents to enter, stay in, and complete treatment.</td>
</tr>
<tr>
<td>5. Remaining in treatment for an adequate period of time is critical.</td>
<td>5. Substance use disorder treatment should be tailored to the unique needs of the adolescent.</td>
</tr>
<tr>
<td>6. Behavioral therapies—including individual, family, or group counseling— are the most commonly used forms of drug abuse treatment.</td>
<td>6. Treatment should address the needs of the whole person, rather than just focusing on his or her drug use.</td>
</tr>
<tr>
<td>7. Medications are an important element of treatment for many patients, especially when combined with counseling and other behavioral therapies.</td>
<td>7. Behavioral therapies are effective in addressing adolescent drug use.</td>
</tr>
<tr>
<td>8. An individual’s treatment and services plan must be assessed continually and modified as necessary to ensure that it meets his or her changing needs.</td>
<td>8. Families and the community are important aspects of treatment.</td>
</tr>
<tr>
<td>9. Many drug-addicted individuals also have other mental disorders.</td>
<td>9. Effectively treating substance use disorders in adolescents requires also identifying and treating any other mental health conditions they may have.</td>
</tr>
<tr>
<td>10. Medically assisted detoxification is only the first stage of addiction treatment and by itself does little to change long-term drug abuse.</td>
<td>10. Sensitive issues such as violence and child abuse or risk of suicide should be identified and addressed.</td>
</tr>
<tr>
<td>11. Treatment does not need to be voluntary to be effective.</td>
<td>11. It is important to monitor drug use during treatment.</td>
</tr>
<tr>
<td>12. Drug use during treatment must be monitored continuously, as lapses during treatment do occur.</td>
<td>12. Staying in treatment for an adequate period of time and continuity of care afterward are important.</td>
</tr>
<tr>
<td>13. Treatment programs should test patients for the presence of HIV/AIDS, Hepatitis B and C, tuberculosis, and other infectious diseases, provide risk-reduction counseling, and link patients to treatment if necessary.</td>
<td>13. Testing adolescents for sexually transmitted diseases like HIV, as well as Hepatitis B and C, is an important part of drug treatment.</td>
</tr>
</tbody>
</table>

Source: National Institute on Drug Abuse, (2012)\(^{31}\) and (2014).\(^{32}\)

The goals of substance use disorder treatment are similar to those of treatments for other serious, often chronic, illnesses: reduce the major symptoms of the illness, improve health and social function, and teach and motivate patients to monitor their condition and manage threats of relapse. Substance use disorder treatment can be provided in inpatient or outpatient settings, depending on the needs of the patient, and typically incorporates a combination of behavioral therapies, medications, and RSS. However, unlike treatments for most other medical illnesses, substance use disorder treatment has traditionally been provided in programs (both residential and outpatient) outside of the mainstream health care system. The intensity of the treatment regimens offered can vary substantially across program types. The American Society of Addiction Medicine (ASAM) has categorized these programs into “levels” of care to guide referral based on an individual patient’s needs.\(^{93-95}\)
Despite differences in care delivery and differences in reimbursement, substance use disorder treatments have approximately the same rates of positive outcomes as treatment for other chronic illnesses. Relapse rates for substance use disorders (40 to 60 percent) are comparable to those for chronic diseases, such as diabetes (20 to 50 percent), hypertension (50 to 70 percent), and asthma (50 to 70 percent).12

The general process of treatment planning and delivery for individuals with severe substance use disorders is described below, along with an explanation of the evidence-based therapies, medications, and RSS shown to be effective in treatment.

**Treatment Planning**

*Assessment and Diagnosis*

Among the first steps involved in substance use disorder treatment are assessment and diagnosis. The diagnosis of substance use disorders is based primarily on the results of a clinical interview. Several assessment instruments are available to help structure and elicit the information required to diagnose substance use disorders. The diagnosis of a substance use disorder is made by a trained professional based on 11 symptoms defined in the Fifth Edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5). These symptoms, which are generally related to loss of control over substance use,96 are presented in Table 1.52 in Chapter 1. The number of diagnostic symptoms present defines the severity of the disorder, ranging from mild to severe (i.e., fewer than 2 symptoms = no disorder; 2 to 3 symptoms = mild disorder; 4 to 5 symptoms = moderate disorder; 6 or more symptoms = severe disorder).97

Conducting a clinical assessment is essential to understanding the nature and severity of the patient’s health and social problems that may have led to or resulted from the substance use. This assessment is important in determining the intensity of care that will be recommended and the composition of the treatment plan.91 Several validated assessment tools can provide information about an individual’s substance use disorder. Table 4.3 gives a brief overview of some of the tools that are available.
Table 4.3: Detailed Information on Substance Use Disorder Assessment Tools

<table>
<thead>
<tr>
<th>Addiction Severity Index (ASI)</th>
<th>Substance Abuse Module (SAM)</th>
<th>Global Appraisal of Individual Needs (GAIN)</th>
<th>Psychiatric Research Interview for Substance and Mental Disorders (PRISM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Semi-structured interview.</td>
<td>• Expanded and more detailed version of the substance use section of the Composite International Diagnostic Interview (CIDI).</td>
<td>• Series of measures (screener, standardized biopsychosocial intake assessment battery, follow-up assessment battery) which integrate research and clinical assessment.</td>
<td>• Semi-structured, clinician-administered interview.</td>
</tr>
<tr>
<td>• Addresses seven potential problem areas in substance using individuals: medical status, employment and support, drug use, alcohol use, legal status, family/social status, and psychiatric status.</td>
<td>• Designed to assess mental disorders as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV).</td>
<td>• Contains 99 scales and subscales, that are designed to measure the recency, breadth, and frequency of problems and service utilization related to substance use (including diagnosis and course, treatment motivation, and relapse potential), physical health, risk/protective involvement, mental health, environment and vocational situation.</td>
<td>• Measures the major DSM-IV diagnoses of alcohol, drug, and psychiatric disorders.</td>
</tr>
<tr>
<td>• Provides an overview of problems related to substance, rather than focusing on any single area.</td>
<td>• Contains four diagnostic sections on tobacco, alcohol, drugs, and caffeine.</td>
<td>• Can assess change over time.</td>
<td>• Provides clear guidelines for differentiating between the effects of intoxication and withdrawal, substance-induced disorders, and primary disorders.</td>
</tr>
<tr>
<td>• Used extensively for treatment planning and outcome evaluation.</td>
<td>• Includes questions about when symptoms began and how recent they are, withdrawal symptoms, and the physical, social and psychological consequences of each substance assessed.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• A shorter, self-report version of the ASI called the ASI-Lite is also available.</td>
<td>• Assesses the respondent’s impairment and treatment seeking.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Can assess substance use disorders quickly and accurately in the clinical setting.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Individualized Treatment Planning**

After a formal assessment, the information is discussed with the patient to jointly develop a personalized treatment plan designed to address the patient’s needs. The treatment plan and goals should be person-centered and include strength-based approaches, or ones that draw upon an individual’s strengths, resources, potential, and ability to recover, to keep the patient engaged in care. Individualized treatment plans should consider age, gender identity, race and ethnicity, language, health literacy, religion/spirituality, sexual orientation, culture, trauma history, and co-occurring physical and mental health problems. Such considerations are critical for understanding the individual and for tailoring the treatment to his or her specific needs. This increases the likelihood of successful treatment engagement and retention, and research shows that those who participate more fully in treatment typically have better outcomes. Throughout treatment, individuals should be periodically reassessed to determine response to treatment and to make any needed adjustments to the treatment plan.
Maintaining Treatment Engagement and Retention

Treatment plans should be personalized and include engagement and retention strategies to promote participation, motivation, and adherence to the plan. Research has found that individuals who received proactive engagement services such as direct outreach and a specific follow-up plan are more likely to remain engaged in services throughout the treatment process.

Treatment providers can improve engagement and retention in programs by building a strong therapeutic alliance with the patient, effectively using evidence-based motivational strategies, acknowledging the patient’s individual barriers, making reminder phone calls, and creating a positive environment. Further, providers who can recommend and/or provide a broad range of RSS, such as child care, housing, and transportation, can improve retention in treatment.

Engaging, effective treatment also involves culturally competent care. For example, treatment programs that provide gender-specific and gender-responsive care are more likely to enhance women’s treatment outcomes. Tailoring treatment to involve family and community is particularly effective for certain groups. For example, American Indians or Alaska Natives may require specific elements in their treatment plan that respond to their unique cultural experiences and to intergenerational and historical trauma and trauma from violent encounters. Language and literacy (including health literacy) may also affect how a person responds to the treatment environment. Race and ethnicity, sexual orientation, gender identity, and economic status can play significant roles in treatment initiation, engagement, and completion.

Substance use disorder treatment programs also have an obligation to prepare for disasters within their communities that can affect the availability of services. A disaster can disrupt a program’s ability to provide treatment services or an individual’s ability to maintain treatment. Individuals in recovery, for example, may relapse due to sudden discontinuation of services or stress when having to cope with effects of a disaster. Individuals receiving MAT could be at risk of serious withdrawal symptoms if medications are stopped abruptly. Others may face challenges without their treatment program’s support. Therefore, planning for disasters and other large scale emergencies is critical to prevent or reduce the impact of interruptions in treatment services.

Treatment Setting and the Continuum of Care

As indicated above, the treatment of addiction is delivered in predominantly freestanding programs that differ in their setting (hospital, residential, or outpatient); in the frequency of care delivery (daily sessions to monthly visits); in the range of treatment components offered; and in the planned duration of care. In general, as patients progress in treatment and begin to meet the goals of their individualized treatment plan, they transfer from clinical management in residential or intensive outpatient programs to less clinically intensive outpatient programs that promote patient self-management.
A typical progression for someone who has a severe substance use disorder might start with 3 to 7 days in a medically managed withdrawal program, followed by a 1- to 3-month period of intensive rehabilitative care in a residential treatment program, followed by continuing care, first in an intensive outpatient program (2 to 5 days per week for a few months) and later in a traditional outpatient program that meets 1 to 2 times per month. For many patients whose current living situations are not conducive to recovery, outpatient services should be provided in conjunction with recovery-supportive housing.

In general, patients with serious substance use disorders are recommended to stay engaged for at least 1 year in the treatment process, which may involve participation in three to four different programs or services at reduced levels of intensity, all of which are ideally designed to help the patient prepare for continued self-management after treatment ends. This expected trajectory of care explains why efforts to maintain patient motivation and engagement are important. Brief summaries of the major levels of the treatment continuum are discussed below.

Medically monitored and managed inpatient care is an intensive service delivered in an acute, inpatient hospital setting. These programs are typically necessary for individuals who require withdrawal management, primary medical and nursing care, and for those with co-occurring mental and physical health conditions. Treatment is usually provided by an interdisciplinary team of health care professionals, available 24 hours a day, who can address serious mental and physical health needs.

Residential services offer organized services, also in a 24-hour setting but outside of a hospital. These programs typically provide support, structure, and an array of evidence-based clinical services. Such programs are appropriate for physically and emotionally stabilized individuals who may not have a living situation that supports recovery, may have a history of relapse, or have co-occurring physical and/or mental illnesses.

Partial hospitalization and intensive outpatient services range from counseling and education to clinically intensive programming. Partial hospitalization programs are used as a step-down treatment option after completing residential treatment and are usually available 6 to 8 hours a day during the work week. These services are considered to be approximately as intensive but less restrictive than residential programs and are appropriate for patients living in an environment that supports recovery but who need structure to avoid relapse.

Outpatient services provide both group and individual behavioral interventions and medications when appropriate. These components of care can be offered during the day, before or after work or school, or in the evenings and weekends. Typically, outpatient programs are appropriate as the initial level of care for individuals with a mild to moderate substance use disorder or as continuing care after completing more intensive treatment. Outpatient programs are also suitable for individuals with co-occurring mental health conditions.
Evidence-based Treatment: Components of Care

Regardless of the substance for which the individual seeks treatment or the setting or level of care, all substance use disorder treatment programs are expected to offer an individualized set of evidence-based clinical components. These components are clinical practices that research has shown to be effective in reducing substance use and improving health and functioning. These include behavioral therapies, medications, and RSS. Treatment programs that offer more of these evidence-based components have the greatest likelihood of producing better outcomes.

Medications and Medication-Assisted Treatment

Five medications, approved by the FDA, have been developed to treat alcohol and opioid use disorders. Currently, no approved medications are available to treat marijuana, amphetamine, or cocaine use disorders. Table 4.4 lists these medications and they are discussed individually in the text that follows.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Use</th>
<th>Dosage Form</th>
<th>DEA Schedule*</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine-</td>
<td>Opioid use</td>
<td>Sublingual film**,118</td>
<td>CIII</td>
<td>Used for detoxification or maintenance of abstinence for individuals aged 16 or older. Physicians who wish to prescribe buprenorphine, must obtain a waiver from SAMHSA and be issued an additional registration number by the U.S. Drug Enforcement Administration (DEA).</td>
</tr>
<tr>
<td>Naloxone</td>
<td>disorder</td>
<td>2mg/0.5mg, 4mg/1mg, 8mg/2mg, and 12mg/3mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sublingual tablet:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.4mg/0.36mg, 2mg/0.5mg, 2.9/0.71mg, 5.7mg/1.4mg, 8mg/2mg, 8.6mg/2.1mg, 11.4mg/2.9mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Buccal film:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.1mg/0.3mg, 4.2mg/0.7mg, 6.3mg/1mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Opioid use</td>
<td>Sublingual tablet:</td>
<td>CIII</td>
<td>This formulation is indicated for treatment of opioid dependence and is preferred for induction. However, it is considered the preferred formulation for pregnant patients, patients with hepatic impairment, and patients with sensitivity to naloxone. It is also used for initiating treatment in patients transferring from methadone, in preference to products containing naloxone, because of the risk of precipitating withdrawal in these patients.</td>
</tr>
<tr>
<td>Hydrochloride</td>
<td>disorder</td>
<td>2mg, 4mg, 8mg, and 12mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>Use</td>
<td>Dosage Form</td>
<td>DEA Schedule*</td>
<td>Application</td>
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<tr>
<td>Probuphine® implants:</td>
<td>Opioid use disorder</td>
<td>80mgx4 implants for a total of 320mg</td>
<td>For those already stable on low to moderate dose buprenorphine. The administration of the implant dosage form requires specific training and must be surgically inserted and removed.</td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td>Opioid use disorder</td>
<td>Tablet: 5mg, 10mg</td>
<td>CII</td>
<td>Methadone used for the treatment of opioid addiction in detoxification or maintenance programs shall be dispensed only by Opioid Treatment Programs (OTPs) certified by SAMHSA and approved by the designated state authority. Under federal regulations it can be used in persons under age 18 at the discretion of an OTP physician.</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>Opioid use disorder; alcohol use disorder</td>
<td>Tablets: 25mg, 50mg, and 100mg</td>
<td>Not Scheduled under the Controlled Substances Act</td>
<td>Provided by prescription; naltrexone blocks opioid receptors, reduces cravings, and diminishes the rewarding effects of alcohol and opioids. Extended-release injectable naltrexone is recommended to prevent relapse to opioids or alcohol. The prescriber need not be a physician, but must be licensed and authorized to prescribe by the state.</td>
</tr>
<tr>
<td>Acamprosate</td>
<td>Alcohol use disorder</td>
<td>Delayed-release tablet: 333mg</td>
<td>Not Scheduled under the Controlled Substances Act</td>
<td>Provided by prescription; acamprosate is used in the maintenance of alcohol abstinence. The prescriber need not be a physician, but must be licensed and authorized to prescribe by the state.</td>
</tr>
<tr>
<td>Disulfiram</td>
<td>Alcohol use disorder</td>
<td>Tablet: 250mg, 500mg</td>
<td>Not Scheduled under the Controlled Substances Act</td>
<td>When taken in combination with alcohol, disulfiram causes severe physical reactions, including nausea, flushing, and heart palpitations. The knowledge that such a reaction is likely if alcohol is consumed acts as a deterrent to drinking.</td>
</tr>
</tbody>
</table>

Notes: *For more information about the DEA Schedule and classification of specific drugs, see Appendix D - Important Facts about Alcohol and Drugs.

**This dosage form may be used via sublingual or buccal routes of administration; sublingual means placed under the tongue, buccal means applied to the buccal area (in the cheek).**

Source: Adapted from Lee et al., (2015).
Like all other FDA-approved medications, those listed in Table 4.4 demonstrate “well-supported” experimental evidence of safety and effectiveness for improving outcomes for individuals with alcohol and opioid use disorders. At the same time, all of these medications have side effects; two (methadone and buprenorphine) have the potential to be misused, and methadone (and to a lesser extent buprenorphine) has the potential for overdose. For these reasons, only appropriately trained health care professionals should decide whether medication is needed as part of treatment, how the medication is provided in the context of other clinical services, and under what conditions the medication should be withdrawn or terminated.

The combination of behavioral interventions and medications to treat substance use disorders is commonly referred to as MAT. MAT is a highly effective treatment option for individuals with alcohol and opioid use disorders. Studies have repeatedly demonstrated the efficacy of MAT at reducing illicit drug use and overdose deaths, improving retention in treatment, and reducing HIV transmission.

Some medications used to treat opioid use disorders can be used to manage withdrawal and as maintenance treatment to reduce craving, lessen withdrawal symptoms, and maintain recovery. These medications are used to help a patient function comfortably without illicit opioids or alcohol while balance is gradually restored to the brain circuits that have been altered by prolonged substance use.

Prescribed in this fashion, medications for substance use disorders are in some ways like insulin for patients with diabetes. Insulin reduces symptoms by normalizing glucose metabolism, but it is part of a broader disease control strategy that also employs diet change, education on healthy living, and self-monitoring. Whether treating diabetes or a substance use disorder, medications are best employed as part of a broader treatment plan involving behavioral health therapies and RSS, as well as regular monitoring.

State agencies that oversee substance use disorder treatment programs use a variety of strategies to promote implementation of MAT, including education and training, financial incentives (e.g., linking funding to the provision of MAT), policy mandates, and support for infrastructure development. Nevertheless, multiple factors create barriers to widespread use of MAT. These include provider, public, and client attitudes and beliefs about MAT; lack of an appropriate infrastructure for providing medications; need for staff training and development; and legislation, policies, and regulations that limit MAT implementation.

**Medication-Assisted Treatment for Opioid Use Disorders**

MAT for patients with a chronic opioid use disorder must be delivered for an adequate duration in order to be effective. Patients who receive MAT for fewer than 90 days have not shown improved outcomes. One study suggested that individuals who receive MAT for fewer than 3 years are more likely to relapse than those who are in treatment for 3 or more years. Three medications are commonly used to treat opioid use disorders: methadone, buprenorphine, and naltrexone.
Methadone is a synthetic opioid agonist that has been used to treat the symptoms of withdrawal from heroin and other opioids. More than 40 years of research support the use of methadone as an effective treatment for opioid use disorder. It is also used in the treatment of patients with chronic, severe pain as a therapeutic alternative to morphine sulfate and other opioid analgesics. Any licensed physician can prescribe methadone for the treatment of pain, but methadone may only be dispensed for treatment of an opioid use disorder within licensed methadone treatment programs.

Long-term methadone maintenance treatment for opioid use disorders has been shown to be more effective than short-term withdrawal management, and it has demonstrated improved outcomes for individuals (including pregnant women and their infants) with opioid use disorders. Studies have also indicated that methadone reduces deaths, HIV risk behaviors, and criminal behavior associated with opioid drug seeking.

The use of methadone to treat opioid use disorders has much in common with treatments for other substance use disorders and other chronic illnesses. However, it has one significant structural and cultural difference. Under regulations dating back to the early 1970s, the federal government created special methadone programs for adults with opioid use disorders. Originally referred to as “methadone treatment programs,” these treatment facilities were created to provide special management of the medical and legal issues associated with the use of this potent, long-acting opioid.

The use of opioid agonist medications to treat opioid use disorders has always had its critics. Many people, including some policymakers, authorities in the criminal justice system, and treatment providers, have viewed maintenance treatments as “substituting one substance for another” and have adhered instead to an abstinence-only philosophy that avoids the use of medications, especially those that activate opioid receptors. Such views are not scientifically supported; the research clearly demonstrates that MAT leads to better treatment outcomes compared to behavioral treatments alone. Moreover, withholding medications greatly increases the risk of relapse to illicit opioid use and overdose death. Decades of research have shown that the benefits of MAT greatly outweigh the risks associated with diversion.

Today, methadone treatment programs, now called Opioid Treatment Programs (OTPs), must be certified by SAMHSA and registered by the U.S. Drug Enforcement Administration (DEA). OTPs are predominantly outpatient programs (approximately 95 percent) that provide pharmacotherapy in combination with behavioral therapies and other RSS. OTPs incorporate principles of harm reduction and benefit both program participants and the community by reducing opioid use, mortality, crime associated with opioid use disorders, and infectious disease transmission. Buprenorphine and naltrexone may also be provided in OTPs.
Individuals receiving medication for opioid use disorders in an OTP must initially take their doses daily under observation. After a period of orientation, patients are typically started at a dose of 20 to 30 mg and gradually increased to 80 mg or more per day, until craving and opioid misuse are significantly reduced. During this period, all dosing occurs at the OTP, but following stabilization and initially positive results, the stabilized patient may be given a “take-home” supply of his or her dose to self-administer per the federal opioid treatment standard regulations 42 CFR 8.12(i).

**Buprenorphine** is available as a sublingual tablet and a sublingual or buccal film. In addition, in May 2016, an implantable formulation of buprenorphine was approved by the FDA. For individuals who are already on a stable low to moderate dose of buprenorphine, the implant delivers a constant low dose of buprenorphine for 6 months. Buprenorphine is associated with improved outcomes compared to placebo for individuals (including pregnant women and their infants) with opioid use disorders, and it is effective in reducing illegal opioid use.

Buprenorphine is a partial opioid agonist, meaning that it binds to and activates opioid receptors but with less intensity than full agonists. As a result, there is an upper limit to how much euphoria, pain relief, or respiratory depression buprenorphine can produce. However, buprenorphine still may result in overdose if used with tranquilizers and/or alcohol, and some diversion has been reported, although studies suggest most diverted buprenorphine is used therapeutically (e.g., to control cravings), not to get high.

Clinical experience and research protocols indicate that buprenorphine initiation and stabilization during the induction period is an important part of successful treatment for individuals with opioid use disorder. Buprenorphine can be prescribed alone or as a combination medication that includes naloxone, an opioid antagonist medication. If this combined medication is taken as prescribed, the naloxone has no appreciable effects. However, if the combined medication is injected, the naloxone component can precipitate an opioid withdrawal syndrome, and in this way serves as a deterrent to misuse by injection.

Buprenorphine may be prescribed by physicians who have met the statutory requirements for a waiver in accordance with the Controlled Substances Act (21 U.S.C. 823(g)(2)(D)(iii)). However, physicians using the waiver are limited in the number of patients they can treat with this medication. This patient limit does not apply to OTPs that dispense buprenorphine on site because the OTP operating in this capacity is doing so under 21 U.S.C. 823(g)(1) and 42 CFR Part 8, and not under 21 U.S.C. 823(g)(2)(B).

When they first receive their waiver, physicians can provide buprenorphine treatment for only up to 30 individuals. After the first year they can request to treat up to 100. However, lack of physician availability to prescribe buprenorphine has been a significant limitation on access to this effective medication. Although approximately 435,000 primary care physicians practice medicine in the United States, only slightly more than 30,000 have a buprenorphine waiver, and only about half of those are actually treating opioid use disorders. To address this limitation and narrow the treatment gap, a final rule was published on July 8, 2016, expanding access to MAT by allowing eligible practitioners to request approval to treat up to 275 patients.
Additionally, on July 22, 2016, the Comprehensive Addiction and Recovery Act (CARA) was signed into law. CARA temporarily expands eligibility to prescribe buprenorphine-based drugs for MAT for substance use disorders to qualifying nurse practitioners and physician assistants through October 1, 2021.

Naltrexone is an opioid antagonist that binds to opioid receptors and blocks their activation; it produces no opioid-like effects and is not abusable. It prevents other opioids from binding to opioid receptors so that they have little to no effect. It also interrupts the effects of any opioids in a person’s system, precipitating an opioid withdrawal syndrome in opioid-dependent patients, so it can be administered only after a complete detoxification from opioids. There is also no withdrawal from naltrexone when the patient stops taking it. Naltrexone may be appropriate for people who have been successfully treated with buprenorphine or methadone who wish to discontinue use but still be protected from relapse; people who prefer not to take an opioid agonist; people who have completed detoxifications and/or rehabilitation or are being released from incarceration and expect to return to an environment where drugs may be used and wish to avoid relapse; and adolescents or young adults with opioid dependence.\textsuperscript{151}

Because naltrexone is not a controlled substance, it can be prescribed or administered by any physician, nurse practitioner, or physician assistant with prescribing authority. Naltrexone comes in two formulations: oral and extended-release injectable. Oral naltrexone can be effective for those individuals who are highly motivated and/or supported with observed daily dosing. Extended-release injectable naltrexone, which is administered on a monthly basis, addresses the poor compliance associated with oral naltrexone since it provides extended protection from relapse and reduces cravings for 30 days.\textsuperscript{152,153}

Medication-Assisted Treatment for Alcohol Use Disorders

A number of factors should be weighed in determining the need for medication when treating an individual for an alcohol use disorder, such as the patient’s motivation for treatment, potential for relapse, and severity of co-existing conditions.\textsuperscript{120} Three FDA-approved medications are currently available to treat alcohol use disorder: disulfiram, naltrexone, and acamprosate.\textsuperscript{117} None of these medications carries a risk of misuse or addiction, and thus none is a DEA-scheduled substance. Each has a distinct effectiveness and side effect profile. Prescribing health care professionals should be familiar with these side effects and take them into consideration before prescribing.\textsuperscript{154} Providers can obtain additional information from materials produced by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and SAMHSA.\textsuperscript{155,156}

Research studies on the efficacy of medications to treat alcohol use disorders have demonstrated that most patients show benefit, although individual response can be difficult to predict.\textsuperscript{154,157} MAT interventions for alcohol use disorders can be provided in both non-specialty and specialty care settings and are most beneficial when combined with behavioral interventions and brief support.\textsuperscript{154}
Disulfiram is a medication that inhibits normal breakdown of acetaldehyde which is produced by the metabolism of alcohol, thus rapidly increasing acetaldehyde in the blood which produces an aversive response. Thus, once disulfiram is taken by mouth, any alcohol consumed results in rapid buildup of acetaldehyde and a negative reaction or sickness results. The intensity of this reaction is dependent on the dose of disulfiram and the amount of alcohol consumed. Effects from a disulfiram-alcohol reaction include warmth and flushing of the skin, increased heart rate, palpitations, a drop in blood pressure, nausea and/or vomiting, sweating, dizziness, and headache. In this way, disulfiram essentially punishes alcohol consumption and indirectly rewards abstinence.

Disulfiram was the first medication approved by the FDA to treat alcohol use disorder and its efficacy has been widely studied. Most studies have demonstrated that disulfiram, when given under supervision, is more effective than placebo in treating alcohol use disorders. A major limitation of disulfiram is adherence, which is typically poor, thereby reducing the medication’s effectiveness. Disulfiram is most effective when its use is supervised or observed, which has been found to increase compliance. Negotiating with the patient to have a spouse or significant other provide supervision offers both the incentive to take the medication and the documentation that the medication is being taken. The best candidates for disulfiram are patients with motivation for treatment and a desire to be abstinent. Thus, an individual who wants to reduce, but not stop, drinking is not a candidate for disulfiram. Disulfiram should also be avoided in individuals with advanced liver disease.

Naltrexone is the opioid antagonist described above that is used to treat opioid use disorder. Because it blocks some opioid receptors, naltrexone counteracts some of the pleasurable aspects of drinking. Unlike disulfiram, naltrexone does not interact with alcohol to produce a severe reaction. As noted before, naltrexone comes in two formulations: oral and extended-release injectable. Many studies have examined the effectiveness of naltrexone in treating alcohol use disorders. Several research reviews have found that it reduces the risk of heavy drinking in patients who are abstinent for at least several days at the time treatment begins. However, as with disulfiram, medication compliance can be a problem with the oral formulation. Adherence to taking the medication increases under conditions where it is administered and observed by a trusted family member or when the extended-release injectable, which requires only a single monthly injection, is used. Naltrexone should not be prescribed to patients with acute hepatitis, renal failure, or liver failure.

Acamprosate is a medication that normalizes the alcohol-related neurochemical changes in the brain glutamate systems and thereby reduces the symptoms of craving that can prompt a relapse to pathological drinking. Acamprosate has been found to be an effective medication when used concurrently with behavioral interventions and, as with other medications for alcohol use disorders, works best in motivated patients. Reviews show that acamprosate is effective in reducing relapse and effective when used to maintain abstinence from alcohol.
Behavioral Therapies

Behavioral therapies can be provided in individual, group, and/or family sessions in virtually all treatment settings. These structured therapies help patients recognize the impact of their behaviors – such as those dealing with stress or interacting in interpersonal relationships – on their substance use and ability to function in a healthy, safe, and productive manner. These therapies also teach and motivate patients in how to change their behaviors as a way to control their substance use disorders.

For evidence-based behavioral therapies to be delivered appropriately, they must be provided by qualified, trained providers. Despite this, many counselors and therapists working in substance use disorder treatment programs have not been trained to provide evidence-based behavioral therapies, and general group counseling remains the major form of behavioral intervention available in most treatment programs. Unfortunately, despite decades of research, it cannot be concluded that general group counseling is reliably effective in reducing substance use or related problems.

The following sections describe behavioral therapies that have been shown to be effective in treating substance use disorders. These therapies have been studied extensively, have a well-supported evidence base indicating their effectiveness, and have been broadly applied across many types of substance use disorders and across ages, sexes, and racial and ethnic groups.

Individual counseling is delivered in structured sessions to help patients reduce substance use and improve function by developing effective coping strategies and life skills. Individual counseling has been extensively studied in many specialty care settings but rarely within non-specialty settings. Most studies support the use of individual counseling as an effective intervention for individuals with substance use disorders. As indicated above, group counseling is a standard part of most substance use disorder treatments, but should primarily be used only in conjunction with individual counseling or other forms of individual therapy.

Cognitive-Behavioral Therapy

The theoretical foundation for Cognitive-Behavioral Therapy (CBT) is that substance use disorders develop, in part, as a result of maladaptive behavior patterns and dysfunctional thoughts. CBT treatments thus involve techniques to modify such behaviors and improve coping skills by emphasizing the identification and modification of dysfunctional thinking. CBT is a short-term approach, usually involving 12 to 24 weekly individual sessions. These sessions typically explore the positive and negative consequences of substance use, and they use self-monitoring as a mechanism to recognize cravings and other situations that may lead the individual to relapse. They also help the individual develop coping strategies.

CBT may be the most researched and evaluated of all the therapies for substance use disorders. Research suggests that self-monitoring and craving-recognition skills can be learned during CBT and that these skills continue to be employed by the individual after treatment has concluded. CBT interventions have been found to be quite effective, and outcomes are enhanced when CBT is combined with other behavioral and/or pharmacologic components of care.
Research has shown that CBT is also an effective treatment for individuals with co-occurring mental disorders. Individuals with a substance use disorder and co-occurring mental disorder who received CBT had significantly improved outcomes on various measures of substance use and mental health symptoms as compared to those who did not receive CBT.103,173,176

**Contingency Management**

Behavior change involves learning new behaviors and changing old behaviors. Positive rewards or incentives for these changes can aid this process. Contingency management, which involves giving tangible rewards to individuals to support positive behavior change,65 has been found to be effective in treating substance use disorders.177 In this therapy, patients receive a voucher with monetary value that can be exchanged for food items, healthy recreational options (e.g., movies), or other sought-after goods or services when they exhibit desired behavior such as drug-free urine tests or participation in treatment activities.65 Clinical studies comparing voucher-based reinforcement to traditional treatment regimens have found that voucher-based reinforcement is associated with longer treatment engagement, longer periods of abstinence, and greater improvements in personal function.177 These positive findings, initially demonstrated with individuals with cocaine use disorders, have been reproduced in individuals with alcohol, opioid, and methamphetamine use disorders.177

Contingency management may be combined with other therapies or treatment components. For example, contingency management has been shown to improve outcomes for adults with cocaine dependence when added to CBT.178 Similarly, contingency management improves outcomes for young adults with marijuana dependence when included withMotivational Enhancement Therapy (described below) and CBT.179

**Community Reinforcement Approach**

Community Reinforcement Approach (CRA) Plus Vouchers is an intensive 24-week outpatient program that uses incentives and reinforcers to reward individuals who reduce their substance use.85 Individuals are required to attend one to two counseling sessions each week that emphasize improving relations, acquiring skills to minimize substance use, and reconstructing social activities and networks to support recovery.85 Individuals receiving this treatment are eligible to receive vouchers with monetary value if they provide drug-free urine tests several times per week.85 Research has demonstrated that CRA Plus Vouchers promotes treatment engagement and facilitates abstinence.85 Recent studies have also shown improvements in psychosocial functioning and abstinence among individuals who received CRA Plus Vouchers compared to those who received an intervention of standard care only.180

CRA without vouchers has been successfully adapted for adolescents. The Adolescent Community Reinforcement Approach (A-CRA) is a similar program targeting 12 to 22 year olds with substance use disorders. A-CRA, which has been implemented in outpatient and residential treatment settings, seeks to increase family, social, and educational and vocational supports to reinforce abstinence and recovery from substance use. The effectiveness of A-CRA has been supported in multiple randomized clinical trials with adolescents from different settings, sexes, and racial groups.181,182 Studies have found that A-CRA increased long-term abstinence from marijuana and alcohol and decreased frequency of other substance use.182
**Motivational Enhancement Therapy**

Motivational Enhancement Therapy (MET) is a counseling approach that uses motivational interviewing techniques to help individuals resolve any uncertainties they have about stopping their substance use. MET works by promoting empathy, developing patient awareness of the discrepancy between their goals and their unhealthy behavior, avoiding argument and confrontation, addressing resistance, and supporting self-efficacy⁴⁶ to encourage motivation and change.⁸⁵,¹⁸³ The therapist supports the patient in executing the behaviors necessary for change and monitors progress toward patient-expressed goals.

MET has been shown to be an effective treatment in a range of populations and has demonstrated favorable outcomes such as reducing substance use and improving treatment engagement.¹⁶⁹ As with other therapies reviewed, MET is often used concurrently with other behavioral interventions.¹⁸⁴ However, the results of MET are mixed for people who use drugs such as heroin, cocaine, and nicotine, and for adolescents.¹⁸⁵,¹⁸⁶ The combination of MET and CBT has shown favorable results for adolescents for multiple substances.¹⁸¹

**The Matrix Model**

The Matrix Model is a structured, multi-component behavioral treatment that consists of evidence-based practices, including relapse prevention, family therapy, group therapy, drug education, and self-help, delivered in a sequential and clinically coordinated manner.⁸⁵ The model consists of 16 weeks of group sessions held three times per week, which combine CBT, family education, social support, individual counseling, and urine drug testing.¹⁸⁷

Several randomized controlled trials over the past 20 years have demonstrated that the Matrix Model is effective at reducing substance misuse and associated risky behaviors.⁸⁵ For example, one study demonstrated the model’s effectiveness in producing sustained reductions in sexual risk behaviors among individuals who use methamphetamines, thus decreasing their risk of getting or transmitting HIV.¹⁸⁷ The Matrix Model has also been adapted to focus more on relationships, parenting, body image, and sexuality in order to improve women’s retention in treatment and facilitate recovery.¹⁸⁹

**Twelve-Step Facilitation Therapy**

Twelve-Step Facilitation (TSF), an individual therapy typically delivered in 12 weekly sessions, is designed to prepare individuals to understand, accept, and become engaged in Alcoholics Anonymous (AA), Narcotics Anonymous (NA), or similar 12-step programs.¹⁹⁰,¹⁹¹ As discussed in the next chapter, 12-step programs and other mutual-aid groups are not themselves medical treatments but fall under the category of RSS. Well-supported evidence shows that TSF interventions are effective in a variety of ways:

- As a stand-alone intervention;¹⁹²-¹⁹⁴
- When integrated with other treatments, such as CBT;¹⁹⁰
- As a distinct component of a multi-treatment package;¹⁹¹ and
- As a modular appendage to treatment.¹⁹⁵
Some substance use disorder treatment programs that employ TSF also typically encourage AA or NA participation through group counseling. However, TSF is quite different from generic group counseling, not only because it is an individual therapy, but also because it involves a systematic set of sequential sessions focused on three key ideas:

- **Acceptance** - realizing that their substance use is part of a disorder, that life has become unmanageable because of alcohol or drugs, that willpower alone will not overcome the problem, and that abstinence is the best alternative;

- **Surrender** - giving oneself to a higher power, accepting the fellowship and support structure of other recovering individuals, and following the recovery activities laid out by a 12-step program; and

- **Active involvement in a 12-step program.**

TSF has been effective in reducing alcohol use during the first month of treatment for individuals with alcohol use disorders, but these effects disappeared rapidly following treatment completion. In one study, alcohol-dependent women were randomly assigned to TSF, CBT, or a standard counseling group. The women who received TSF and CBT over 12 weeks both had better outcomes on perceived social support from friends and on social functioning than those in the counseling group, and the differences between those receiving TSF and CBT were minimal.

In another study, a randomized controlled trial compared a CBT treatment program alone to the same treatment combined with TSF. TSF in addition to CBT increased AA involvement and days of abstinence over a 12-month follow-up period as compared to CBT alone. Statistical analysis showed the benefits of the TSF stemmed from its ability to increase AA participation in the period after treatment ended. Further, another randomized controlled trial of outpatients with severe alcohol use disorder evaluated a treatment that aimed to change people’s social networks away from heavy drinkers and toward non-drinking individuals, including AA members. Those receiving the social network enhancement treatment had 20 percent more abstinent days and greater AA participation at 2-year follow-up than did patients assigned to receive standard case management. Again, AA participation and the number of abstinent friends in the social network were found to account for the treatment’s effectiveness.

Project MATCH, the largest study of alcohol use disorder treatment ever conducted, found that TSF increased rates of continuous abstinence and sustained remission at the same rates as two other evidenced-based treatments—CBT and MET. All three treatments reduced the quantity and frequency of alcohol use immediately after treatment. Further, relative to the CBT and MET treatment conditions, significantly more of the patients receiving TSF treatment maintained continuous abstinence in the year following treatment. The same pattern of results was also evident at follow-up 3 years later. Like the other studies discussed, data analysis showed that the effectiveness of the TSF treatment was based on its differential ability to increase post-treatment participation in AA.
The first clinical trial of TSF for patients in treatment for stimulant use disorder was recently completed. Individuals randomized to TSF had higher rates of attending groups such as Crystal Meth Anonymous and higher rates of abstinence at follow-up as well.199

Given the common group and social orientation and the similar therapeutic factors operating across different mutual aid groups,200-202 participation in mutual aid groups other than AA might confer similar benefits at analogous levels of attendance.203,204 Yet systematic efforts to facilitate entry into non-12-step mutual aid groups have rarely been studied.204 One exception is a clinical trial evaluating SMART Recovery, a cognitive-behavioral, evidence-based mutual aid group. Patients in treatment for “heavy drinking” were randomly assigned to receive face-to-face SMART Recovery meetings or to an online Web meeting. Both groups showed approximately equal rates of post-treatment participation in SMART Recovery and in abstinence.205

Family Therapies
Mainstream health care has long acknowledged the benefits of engaging family and social supports to improve treatment adherence and to promote behavioral changes needed to effectively treat many chronic illnesses.206 This is also true for patients with substance use disorders. Studies of various family therapies have demonstrated positive findings for both adults and adolescents.85 Family therapies engage partners and/or parents and children to help the individual achieve positive outcomes based on behavior change. Several evidence-based family therapies have been evaluated.

Family behavior therapy (FBT) is a therapeutic approach used for both adolescents and adults that addresses not only substance use but other issues the family may also be experiencing, such as mental disorders and family conflict.85 FBT includes up to 20 treatment sessions that focus on developing skills and setting behavioral goals. Basic necessities are reviewed and inventoried with the client, and the family pursues resolution strategies and addresses activities of daily living, including violence prevention and HIV/AIDS prevention.207

Family therapies used specifically for treating substance use disorders in adolescents include Multi-Systemic Therapy (MST), Multi-Dimensional Family Therapy (MDFT), Brief Strategic Family Therapy (BSFT), and Functional Family Therapy (FFT).85 Most of these therapies consist of sessions that include the adolescent and at least one other family member, although MDFT uses a combination of both individual and family sessions.85 These interventions use different approaches, ranging from addressing antisocial behaviors (MST) and unfavorable influences (MDFT) on adolescents to identifying patterns of negative behaviors and interactions within the family (BSFT and FFT).85

Perhaps the most widely studied and applied family therapy has been Behavioral Couples Therapy (BCT). A cardinal feature of BCT is the “daily sobriety contract” between the affected patient and his/her spouse in which the patient states his or her intent not to drink or use drugs, and the spouse expresses support for the patient’s efforts to stay abstinent. BCT also teaches communication and non-substance-associated positive activities for couples. Findings show that BCT produces more abstinence and better functioning relationships than typical individual-based treatment and that it also reduces social costs and intimate partner violence.208
Well-supported evidence demonstrates the effectiveness of substance use disorder therapies that engage the spouse or partner and the family in reducing substance use and/or misuse problems and addressing other issues, such as poor communication, neglect, conflict, and intimate partner violence. In a recent review of controlled studies with alcohol-dependent patients, marital and family therapy, and particularly behavioral couples therapy, was significantly more effective than individual treatments at inducing and sustaining abstinence; improving relationship functioning and reducing intimate partner violence; and reducing emotional problems of children. Similar findings have been shown with patients having opioid and cocaine use disorders and with gay and lesbian families.

**Tobacco Use Cessation Efforts in Substance Use Disorder Treatment Programs**

People with mental and/or substance use disorders account for 40 percent of all cigarettes smoked in the United States. Many substance use disorder treatment facilities and programs have adopted tobacco-free policies and tobacco cessation programs. Research has shown that incorporating tobacco cessation programs into substance use disorder treatment does not jeopardize treatment outcomes and is associated with a 25 percent increase in the likelihood of maintaining long-term abstinence from alcohol and drug misuse.

**Recovery Support Services**

Recovery support services (RSS), provided by both substance use disorder treatment programs and community organizations, help to engage and support individuals in treatment, and provide ongoing support after treatment. These supportive services are typically delivered by trained case managers, recovery coaches, and/or peers. Specific supports include help with navigating systems of care, removing barriers to recovery, staying engaged in the recovery process, and providing a social context for individuals to engage in community living without substance use. RSS can be effective in promoting healthy lifestyle techniques to increase resilience skills, reduce the risk of relapse, and help those affected by substance use disorders achieve and maintain recovery.

Individuals who participate in substance use disorder treatment and RSS typically have better long-term recovery outcomes than individuals who receive either alone. Further, active recovery and social supports, both during and following treatment, are important in maintaining recovery. This has also been demonstrated for adolescents; the combination of behavioral treatments with assertive continuing care has yielded positive results for this age group, beyond treatment alone.
Emerging Treatment Technologies

Technological advancements are changing not only the face of health care generally, but also the treatment of substance use disorders. In this regard, approximately 20 percent of substance use disorder treatment programs have adopted electronic health record (EHR) systems. With the growing adoption of EHRs, individuals and their providers can more easily access and share treatment records to improve coordination of care. In turn, information sharing through EHRs can lead to improved quality and efficiency of service delivery, reduced treatment gaps, and increased cost savings to health systems.

The use of telehealth to deliver health care, provide health information or education, and monitor the effects of care, has also rapidly increased. Telehealth can be facilitated through a variety of media, including smartphones, the Internet, videoconferencing, wireless communication, and streaming media. It offers alternative, cost-effective care options for individuals living in rural or remote areas or when physically travelling to a health care facility poses significant challenges.

Technology-based interventions offer many potential advantages. They can increase access to care in underserved areas and settings; free up time so that service providers can care for more clients; provide alternative care options for individuals hesitant to seek in-person treatment; increase the chances that interventions will be delivered as they were designed and intended to be delivered; and decrease costs. Further, studies show that most individuals already have access to the necessary tools to engage in technology-based care; about 92 percent of United States adults own a cell phone and 85 percent use the Internet.

Research on the effectiveness of technology-assisted care within substance use disorder treatment focuses on three main applications: (1) technology as an add-on to enhance standard care; (2) technology as a substitute for a portion of standard care; and (3) technology as a replacement for standard care. The current evidence base of technology-based interventions for substance use disorder treatment is limited, though it is growing. For this reason, these technologies can only be considered “promising” at this time. Table 4.5 shows the state of evidence supporting innovative technology-assisted interventions, several of which are discussed in the Electronic Treatment Interventions and Electronic Clinical and Recovery Support Tools sections.
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Intervention Overview</th>
<th>Sample (at pretest) /Ethnicity/ Setting Design</th>
<th>Summary/Results</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addiction–Comprehensive Health Enhancement Support System (A-CHESS)</td>
<td>Smartphone-based application offering monitoring, information, communication, and support services.</td>
<td>N = 349 individuals with alcohol dependence entering treatment at residential programs</td>
<td>At 4-, 8- and 12-month follow-up, intervention group reported significantly fewer risky drinking days (1.39 vs. 2.75 days on average) and a higher likelihood of consistent abstinence (51.9% vs. 39.6%) as compared to the control group.</td>
<td>Gustafson et al., (2014)228</td>
</tr>
<tr>
<td>CBT4CBT</td>
<td>Six-module computer-based cognitive behavioral therapy training.</td>
<td>N = 101 cocaine-dependent individuals maintained on methadone</td>
<td>After completing an 8-week program, participants who received the intervention were significantly more likely to attain 3 or more consecutive weeks of abstinence from cocaine than were participants who did not receive the program (36% vs.17%). 6-month follow-up data indicated continued improvement for intervention group.</td>
<td>Carroll et al., (2014)229</td>
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<tr>
<td>HealthCall</td>
<td>60 days of patient automated telephone interactive voice response (IVR) calls to self-monitor alcohol and other health-related behaviors as adjunct to motivational interviewing.</td>
<td>N = 258 HIV-positive individuals reporting alcohol misuse</td>
<td>After 60 days, members of intervention group with alcohol dependence reported significantly fewer drinks per drinking day as compared to control group (3.55 vs. 6.07). Lower rates of drinks per drinking day among intervention group maintained at 12-month follow-up.</td>
<td>Hasin et al., (2013)230</td>
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<tr>
<td>Reduce Your Use</td>
<td>Self-guided web-based treatment program for cannabis use disorder based on cognitive, motivational, and behavioral principles.</td>
<td>N = 225 individuals looking to reduce or cease cannabis use</td>
<td>After 6 weeks, the intervention group reported significantly fewer days of cannabis use in the past month, significantly lower past-month quantity of cannabis use, and significantly fewer symptoms of cannabis abuse compared to the control group. Similar results at 3-month follow-up.</td>
<td>Rooke et al., (2013)231</td>
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### Electronic Assessments and Early Intervention

Several studies have been conducted on technology-assisted screening, assessment, and brief intervention for substance use disorders. Many of these studies focus on Internet-based assessments and brief interventions for at-risk, college-age populations. Examples of evaluated tools include the Check Your Drinking screener,234 electronic alcohol screening and brief intervention (e-SBI),235 Drinker’s Check-up,236 Alcohol electronic Check-Up to Go (e-CHUG),237 and Marijuana eCHECKUP TO GO.238 Other studies assessed interventions that can be implemented in general health care settings, including Project QUIT, a brief intervention in a primary care setting that also includes follow-up coaching calls for individuals who have been identified through screening as engaging in risky drug use,50 and use of kiosks in emergency departments to screen for alcohol and drug use.239 In the latter study, patients in the emergency department were found to be significantly more likely to disclose their substance use at a kiosk compared to a health care professional or other interviewer. Other studies focus on telephone-based assessments and brief interventions related to alcohol and drug use, including DIAL,240 and a telephone-based monitoring and brief counseling intervention.241 Preliminary evidence shows that Web- and telephone-based assessments and brief interventions are superior to no treatment in reducing substance use, and often result in similar or improved outcomes when compared to alternative brief intervention options.236,241-247

<table>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Self-Help for Alcohol and other Drug Use and Depression (SHADE)</strong></td>
<td>Nine sessions of computer-delivered motivational interviewing and cognitive behavior therapy with brief therapist assistance.</td>
<td>N = 274 individuals with comorbid depression and alcohol/cannabis misuse</td>
<td>At 3-month follow-up, the intervention group that received computer-delivered care achieved 4 times the reduction in alcohol consumption compared to the control group, and 2.5 times the reduction of the group who received therapist-delivered care.</td>
<td>Kay-Lambkin et al., (2011)222</td>
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<tr>
<td><strong>Therapeutic Education System (TES)</strong></td>
<td>62 computer-interactive modules teaching skills for achieving and maintaining abstinence, as well as prize-based motivational incentives based on abstinence and treatment adherence.</td>
<td>N = 507 adult men and women</td>
<td>Compared to the control group, those receiving TES reduced dropout from treatment (Hazard Ratio=0.72) and increased abstinence (Odds Ratio=1.62).</td>
<td>Cambell et al., (2015)233</td>
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Note: RCT = randomized controlled trial.
Electronic Treatment Interventions

A larger pool of research studies has assessed the effectiveness of substance use disorder treatment approaches (largely outpatient) that incorporate Web- and telephone-based technology. These interventions focus on a wider range of substances, including alcohol (e.g., *Drinking Less*, *HealthCall*), opioids (e.g., *Therapeutic Education System*, *CBT4CBT*), and marijuana (e.g., *Reduce Your Use*, *SHADE*), and target various subpopulations, including veterans and individuals with co-occurring disorders and other chronic illnesses.

Many of these technology-enhanced treatment interventions are Web-based versions of evidence-based, in-person treatment components such as CBT and MET. Early research suggests the value of applying Web-based treatment approaches for moderate levels of substance misuse and for individuals who may not otherwise seek face-to-face treatment. Among studies evaluating Web-based intervention support as an add-on to standard in-person treatment, preliminary evidence shows reduced substance use, better retention, and higher motivation to change among the intervention group. One study explored replacing traditional in-person CBT with a Web-based version and found at least equivalent outcomes among the intervention group, indicating great potential for these Web-based interventions to broaden the dissemination of evidence-based treatments.

Recent studies of telephone-based interventions as adjuncts to or replacements for standard care interventions showed similarly promising results. For example, one study explored the effect of adding daily self-monitoring calls to an interactive voice response technology system with personalized feedback and compared it to standard motivational enhancement practice. Study results showed that those who received the intervention reduced the number of drinks they had on the days they did drink.

Electronic Clinical and Recovery Support Tools

Several studies have examined the application of technology-assisted tools to RSS. In general, Web- and telephone-based recovery support tools focus on providing remote support to individuals following substance use disorder treatment. Examples of e-recovery support tools include: *A-CHESS*, a smartphone application that provides monitoring, information, communication, and support services to patients, including ways for individuals and counselors to stay in contact; and *MORE*, a Web-based recovery support program that delivers assessments, clinical content, and access to recovery coaching support online. Preliminary evidence shows that technology-assisted recovery support approaches may be effective in helping individuals to maintain their recovery. In 2014, a study found that OTP participants receiving ongoing counseling services through Web-based videoconferencing technology experienced comparable rates of decreased drug use and program attendance as did individuals receiving in-person care.
Considerations for Specific Populations

Culturally Competent Care

A variety of treatment approaches have been developed to address the needs of individuals with substance use disorders. However, disparities exist in the outcomes and effectiveness of substance use treatment for different populations.\textsuperscript{109,254} Research has shown that treatment needs can differ across various populations,\textsuperscript{255,256} suggesting that treatment interventions should be individually tailored and incorporate culturally competent and linguistically appropriate practices relevant to specific populations and subpopulation groups.\textsuperscript{257}

Racial and Ethnic Groups

A study examining a culturally sensitive substance use disorder intervention program targeted at Hispanic or Latino and Black or African American adolescents called Alcohol Treatment Targeting Adolescents in Need (ATTAIN) found significant reductions in alcohol and marijuana use for all racial and ethnic groups.\textsuperscript{258} Cultural factors, including discrimination, acculturation, ethnic pride, and cultural mistrust, were associated with the pre-intervention levels of alcohol and drug use. The study concluded that accounting for these factors when tailoring a substance use disorder intervention is critical to meeting the needs of the community it is aiming to serve.

Many of the interventions developed for substance use disorder treatment services in general have been evaluated in populations that included Black or African American patients, and many of these interventions are as effective for Black or African American patients as they are for White patients.\textsuperscript{259,260} Some motivational interventions that are aligned with the cultural values of the population have been found to reduce substance use among Blacks or African Americans.\textsuperscript{27,257}

*Dialectical Behavior Therapy (DBT)* is an evidence-based therapy that teaches a skill called mindfulness. Multiple research studies have noted that mindfulness, an attentional exercise originally developed in Buddhist cultures, is potentially useful in helping people gain mastery over substance cravings.\textsuperscript{261} A study examining patients in a substance use disorder residential treatment center that incorporated DBT with specific cultural, traditional, and spiritual practices for American Indian or Alaska Native adolescents found that 96 percent of the adolescents in their sample either “recovered” or “improved.”\textsuperscript{262} Treatment included all aspects of comprehensive DBT and included consultation with tribal leaders from the governing body and a medicine man/spiritual counselor from a local tribe.

Asian patients tend to enter treatment with less severe substance misuse problems than do members of other racial or ethnic groups,\textsuperscript{263} place less value on substance use disorder treatment, and are less likely to use such services.\textsuperscript{264} Studies on Asians and Native Hawaiians and Pacific Islanders have identified culturally specific barriers and facilitators to entering and completing substance use treatment (e.g., family, peers, shame, and involvement in the criminal justice system).\textsuperscript{265} Assessing patient experience of shame is an important step when providing substance use disorder treatment to Asian patients because shame and humiliation can be significant barriers to treatment engagement for this population.\textsuperscript{266}
Combining Evidence-based Care with Traditional, Spiritual, and Cultural Beliefs

Agency or Organization:
Desert Visions Youth Wellness Center (Desert Visions), Indian Health Service, Sacaton, Arizona

Purpose:
Desert Visions is a federally-operated adolescent residential center whose purpose is to provide substance use and behavioral health treatment to American Indians and Alaska Natives. Desert Visions offers a multi-disciplinary treatment that includes bio-psychosocial, health, education, and cultural activities. Desert Visions uses Dialectical Behavior Therapy (DBT) as the treatment modality, and clients are taught to use the DBT skills to improve their quality of life.

Goals:

- Provide holistic care and treatment for the physical, spiritual, and emotional needs of American Indian and Alaska Native adolescents.
- Provide superior outcomes in treating substance use/co-occurring disorders.
- Utilize the DBT skill of mindfulness to allow for the introduction of cultural, spiritual, and traditional practices into treatment while still maintaining fidelity to this evidence-based approach. In essence, the goal of using DBT is to combine the best of “Western-Based” interventions with traditional American Indian/Alaska Native interventions.

Outcomes:
A 3-year program/statistical review of outcome data found that of 229 patients who were enrolled in the treatment program:

- 201 met the criteria for clinically significant change, (i.e., “recovered” or “reliable change” or “improved”) and 10 showed no change.
- None of the youth in treatment deteriorated during the treatment period.
- The findings represent a first investigation of the use of DBT within American Indian and Alaska Native populations.

Lesbian, Gay, Bisexual, and Transgender Populations

Lesbian, gay, bisexual, and transgender (LGBT) populations often enter treatment with more severe substance misuse problems, have a greater likelihood of experiencing a substance use disorder in their lifetime, and initiate alcohol consumption earlier than heterosexual clients; thus, developing effective treatment programs that address the specific needs of these populations is critical. For example, the 2013 National Health Interview Survey, conducted by the U.S. Census Bureau, found that a higher percentage of LGBT adults, aged 18 to 64, had five or more drinks on one day in the past year compared to heterosexual adults. Research has also shown that LGB adolescents report higher rates of substance use compared to heterosexual youth; on average substance use among LGB youth was 190 percent higher.
than for heterosexual youth, 340 percent higher for bisexual youth, and 400 percent higher for lesbians and bisexual females. Treatment programs with specialized groups for gay and bisexual clients have shown better outcomes for men compared to gay and bisexual men in non-specialized programs. According to one analysis, a significant minority of the nation’s substance use disorder treatment agencies indicated that they offer treatment services tailored to LGBT populations, although only a small portion (7.4 percent) offered a service that they could identify as an LGBT-specialized service.

Research has shown that treatment providers should be knowledgeable about sexuality, sexual orientation, and unique aspects of LGBT developmental and social experiences. For example, factors such as transphobia or homophobia (both internal and societal), violence, family issues, and social isolation, among other problems, may need to be addressed within the substance use disorder treatment environment for transgender people. It is also important to consider the types of treatment that have been shown effective with the LGBT population. Motivational interviewing, social support therapy, contingency management, and CBT have all demonstrated effectiveness specifically for gay or bisexual men with a substance use disorder.

Veterans

Being a veteran or an active member of the military is a unique way of life that involves experiences and sacrifices by the service member and the member’s family. Military service members, veterans, and their families have needs unlike other individuals that require culturally competent approaches to treatment and services. Veterans report high rates of substance misuse; between 2004 and 2006, 7.1 percent of all veterans met the criteria for a substance use disorder. Studies of female veterans have shown that between 4 and 37 percent of veterans reported alcohol misuse, 7 to 25 percent reported binge drinking, and between 3 and 16 percent reported substance use disorders. Much of the literature on substance use in the military examines the relationship between post-traumatic stress disorder (PTSD) and alcohol and drug use. For example, a large study examined improvement in substance use outcomes among 12,270 veterans who were diagnosed with PTSD and a substance use disorder and treated in specialized intensive veterans’ treatment programs. The study found that treatment in longer-term programs, with prescribed psychiatric medication and planned participation in program reunions for post-discharge support, were all associated with improved outcomes. Reductions in substance use were also associated with improvements in PTSD symptoms and violent behavior. The findings suggested that intensive treatment combined with proper discharge planning for veterans with severe PTSD and a substance use disorder may result in better outcomes than traditional substance use disorder treatment. A study among homeless veterans with a diagnosis of a substance use disorder as well as a mental disorder found that those who took part in a low-intensity wrap-around intervention showed improvements in a number of substance use, mental health, and behavioral health outcomes from the beginning of the study to follow-up 12 months later.

Criminal Justice Populations

It has been estimated that half of the United States prison population has an active substance use disorder. Many incarcerated individuals will experience a lower tolerance for substances due to abstinence while in prison; upon release, many will return to dangerous use levels, not realizing their
tolerance is diminished. This is particularly important as it raises the risk of opioid overdose deaths after release from incarceration; one study found that 14.8 percent of all former prisoner deaths from 1999 to 2009 were related to opioids. There is typically insufficient pre-release counseling and post-release follow-up provided to this population to reduce these risks.

In a randomized controlled trial of methadone maintenance for prisoners, participants were randomly assigned to counseling with passive referral to methadone maintenance treatment (MMT) after release, counseling with transfer to MMT, or counseling with pre-release MMT. Prisoners who received counseling and MMT in prison prior to release and continued with community-based MMT after release were significantly less likely to use opioids and engage in criminal activity post-release. Increased access to opioid agonist maintenance may positively impact the needs of substance use disorders among incarcerated individuals.

Another randomized trial assigned some participants to extended-release naltrexone treatment and others to usual treatment, consisting of brief counseling and referrals to community treatment programs. Those who received extended-release naltrexone had a lower rate of relapse (43 percent vs. 64 percent), and a higher rate of opioid-negative urine samples (74 percent vs. 56 percent), and the average time between treatment and relapse was found to be longer—10.5 weeks, compared with 5.0 weeks for those who received usual treatment. Importantly, positive effects diminished after treatment with extended-release naltrexone was discontinued.

Drug Courts

Drug courts are a diverse group of specialized programs that focus on adult or juvenile offenders, as well as parents under child protective supervision who have substance use-related disorders. Drug courts provide treatment and other services, overseen by a judge, in lieu of being processed through the traditional justice system. By 2015, more than 3,400 drug courts were in operation across the United States. An estimated 55,000 defendants per year participate in adult drug courts, with each court serving a caseload of approximately 50 individuals each year. These interventions seek to harness the coercive power of the criminal justice system to persuade drug-involved offenders to cease their problematic drug use.

Existing research, including randomized controlled trials, have found positive effects of drug courts, including high rates of treatment completion and reduced rates of recidivism, incarceration, and subsequent drug use. Reviews of these evaluations have concluded that the average effect of adult drug court participation is analogous to a drop in recidivism from 50 percent to 38 percent, and that this effect lasts up to 3 years. Drug courts generally find similar reductions as adult drug courts and substantially smaller effects than are found in juvenile drug courts. Larger reductions in recidivism were found in adult drug courts that had high graduation rates and that accepted only nonviolent offenders, suggesting that this intervention may be more effective among that segment of the substance-using population.

Despite the rapid expansion of drug courts, the number of defendants who pass through such programs remains a small proportion of the more than 1 million offenders with substance use disorders who pass through the United States criminal justice system each year. Capacity constraints provide the most important limitation.
Drug court programs require random drug tests and other monitoring measures. Required abstinence involves making sanctions certain and immediate. Hawaii’s Opportunity Probation with Enforcement (HOPE) program has implemented coerced abstinence for the entire probation population. Promising results of a randomized trial have sparked interest in broader replication.\textsuperscript{293} Observed recidivism rates were dramatically lower than for the prior probation population, and the treatment group was incarcerated for roughly half as many days as the control group. Interventions such as HOPE do not necessarily involve substance use disorder treatment; this reflects the reality that many drug-involved offenders do not meet the criteria for substance use disorders. For many individuals, regular monitoring, alongside the adverse consequences of a failed urine test, provide powerful motivation to abstain.\textsuperscript{294}

A further example is the 24/7 Sobriety Project (24/7), a South Dakota innovative program to supervise individuals who were arrested in connection with alcohol-related offenses. It addresses problem drinking by imposing close monitoring, followed by swift, certain, yet modest sanctions when there is evidence of renewed alcohol use. Under 24/7, problem drinkers rearrested for DUI and selected other alcohol-related violations were subject to intensive monitoring and sanctions. As a condition of bail, participants were required to take morning and evening breathalyzer tests or wear continuous alcohol-monitoring bracelets. Between 2005 and 2010, 24/7 participants were ordered to take approximately 3.7 million breathalyzer tests, and achieved a pass rate of approximately 99.3 percent.\textsuperscript{295} A RAND Corporation program evaluation found that 24/7 tangibly improved public safety in counties where the program was implemented at scale.\textsuperscript{295} In counties where the number of 24/7 participants reached one-quarter of DUI arrests, the intervention was associated with a significant reduction in repeat DUI and intimate partner violence arrests. Similar results have been replicated in Montana.\textsuperscript{296}

**Recommendations for Research**

Although the field of treatment for substance use disorders has made substantial progress, additional types of research are needed. Research involving early interventions and various components of treatment must move from rigorously controlled trials to natural delivery settings and a broader mix of patient types. Because rigorously controlled trials must focus on specific diagnoses and carefully characterized patient types, it is often the case that the samples used in these trials are not representative of the real-world populations who need treatment. For example, many opioid medication trials involve “opioid-only” populations, whereas in practice most patients with opioid use disorders also have alcohol, marijuana, and/or cocaine use disorders. Rigorously controlled trials are necessary to establish efficacy, but interventions that seem to be effective in these studies too often cannot be implemented in real-world settings because of a lack of workforce training, inadequate insurance coverage, and an inability to adequately engage the intended patient population.

As has been documented in several chapters within this *Report*, the great majority of patients with substance use disorders do not receive any form of treatment. Nonetheless, many of these individuals do access primary or general medical care in community clinics or school settings and research is needed to determine the availability and efficacy of treatment in these settings and to identify ways in which access to treatment in these settings could be improved. The current failure to acknowledge and address substance use disorders in these settings has reduced the quality and increased the costs
of health care. Moreover, access and referral to specialty substance use disorder care from primary care settings is neither easy nor quick. Better integration between primary care and specialty care and additional treatment options within primary care are needed. Primary care physicians need to be better prepared to identify, assist, and refer patients, when appropriate. If treatment is delivered in primary care, it should be practical for delivery within these settings and attractive, engaging, accessible and affordable for affected patients.

Buprenorphine or naloxone treatment for opioid misuse should also be available in emergency departments. Here, the goals of treatment would be the reduction of substance use combined with better engagement in and adherence to treatment for any associated medical illness. Therefore, treatment research outside of traditional substance use disorder treatment programs is needed.

As of June 2016, four states, plus the District of Columbia, have legalized recreational marijuana, and many more have permitted medical marijuana use. The impact of the changes on levels of marijuana and other drug and alcohol use, simultaneous use, and related problems such as motor vehicle crashes and deaths, overdoses, hospitalizations, and poor school and work performance, must be evaluated closely. Accurate and practical marijuana screening and early intervention procedures for use in general and primary care settings are needed. Not only must it be determined which assessment tools are appropriate for the various populations that use marijuana, but also which treatments are generalizable from research to practice, especially in primary care and general mental health care settings.

Current research suggests that it is useful to educate and train first responders, peers, and family members of those who use opioids to use naloxone to prevent and reverse potential overdose-related deaths. However, more research is needed to identify strategies to encourage the subsequent engagement of those who have recovered from overdose into appropriate treatment. In this work, it will be important to consider contextual factors such as age, gender identity, race and ethnicity, sexual orientation, economic status, community resources, faith beliefs, co-occurring mental or physical illness, and many other personal issues that can work against the appropriateness and ultimately the usefulness of a treatment strategy.

Opioid agonist therapies are effective in stabilizing the lives of individuals with severe opioid use disorders. However, many important clinical and social questions remain about whether, when, and how to discontinue medications and related services. This is an important question for many other areas of medicine where maintenance medications are continued without significant change and often without attention to other areas of clinical progress.

At the same time, it is clear from many studies over the decades that detoxification following an arbitrary maintenance time period (e.g., 90 days, 180 days), or performed without continuing supports, is rarely effective in disengaging patients from opioid use disorders and may lead to relapse and overdose. Thus, more research is needed to explore if, when, and how patients can be transitioned from MAT to non-medication status within the context of “personalized medicine,” to provide both patients and clinical staff appropriate therapeutic guidance.
Regarding personalized medicine, research is needed on how to implement multidisciplinary, collaborative, and patient-centered care for persons with opioid use disorders and chronic pain, in a manner effectively treating both diseases together with any psychiatric comorbidities that may undermine recovery. Precision medicine research is also needed on how to individually tailor such interventions to optimize care management for patient groups in which there is overlap between pain-related psychological distress and stress-related opioid misuse.298
References


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