Department of
Mental Health &
Substance Abuse Services

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Substance Use Best Practice Tool Guide

EVIDENCE-BASED TREATMENTS

Division of Clinical Leadership in Collaboration with the
Division of Substance Abuse Services

Evidence-Based Treatments

Despite the call for evidence-based treatment (EBP) practices in substance use (SU) treatments, only a fraction are validated by the most rigorous evidence in the current scientific literature. Nonetheless, the National Quality Forum (NQF) identified seven core practices for SU treatment that are supported by scientific evidence and merit widespread implementation.

Practice 1. Screening. All patients/clients in general and behavioral healthcare settings (including primary care, urgent care, and emergency care) should be screened for alcohol and other drug use/misuse whenever a care encounter provides the opportunity. A selection of EB screening and assessment tools and links are found in this tool guide.

Practice 2. Initial Brief Intervention. All patients/clients with a positive screen should receive a brief intervention by a healthcare practitioner trained in this technique. Brief intervention should include assessment and follow-up care, including referral to specialty services and systematic monitoring as needed. Tips on brief intervention can be found in the section on Early Intervention in the *Prevention/Early Intervention* module of this guide.

Practice 3. Prescription for Services. Each patient/client assessed and diagnosed with SUDs should receive and sign a written "dosing recommendation" that clarifies the treatment plan, i.e., explicitly prescribes the specific services, initial duration, and quantity of each service. Reassessments should be conducted as necessary and services should match patient needs.

Practice 4. Psychosocial Intervention. Evidence-based psychosocial treatment interventions should be initiated for all patients referred to specialty care treatment of SUDs. Examples of EB psychosocial treatments are included in this module, among others.

Practice 5. Pharmacotherapy. Pharmacotherapy should be considered for all patients diagnosed with alcohol and/or opioid dependence. EB pharmacological treatments are available for those substance use disorders (SUDs). Such patients/clients should be assessed and, if appropriate and consented to, pharmacotherapy should be initiated.

Practice 6. Patient Engagement and Retention. Specialty providers should systematically promote patient/client engagement and improve retention in SUD treatment. EB strategies are included in this tool guide to assist in facilitation of engagement and retention.

Practice 7. Recovery/Chronic Care Management. Efforts should be undertaken to engage patients/clients long-term in the management of their care. EB strategies are available in this tool guide that can assist with those efforts.

All treatments included in this module meet the required research rigor and are indeed evidence-based (EB).

Medication-Assisted Treatments (MATs)

Drug addiction is challenging. Moreover, most substance users have every intention of discontinuing their misuse and/or abuse. In a large number of cases, however, individuals are not able to stop using substances on their own. They need help. Sometimes an individual is able to be successful for a short time, but then he or she will fall back into those old patterns of using. Relapse can occur even if the individual has a strong support system. The reality is that overcoming drug addiction is not an easy feat. It typically takes time to recover. *Further, recovery is a PROCESS, not something that happens in the first decision to be abstinent*. Hence, individuals that truly want to take control of their addiction may need to strongly consider medication-assisted treatment (MAT) AS PART OF THEIR ADDICTION TREATMENT (Chalk & Williams, 2012). ***Medication-assisted treatment*** (MAT) is a term used to describe the use of pharmacological treatments in individuals with substance use disorders (Chalk & Williams, 2012; CMCS, 2014). It is a direct, individualized service for persons with a substance use disorder (SUD) (Fullerton et al., 2014). In addition to providing pharmacological help, MAT integrates counseling and other supports, especially friends and family, thereby incorporating a whole-person approach to the treatment of substance use disorders (SUDs) (SAMHSA/CSAT, 2011; SAMHSA, 2012b). MAT plus therapy can contribute to lowering an individual's risk of contracting hepatitis C or HIV because the potential for relapse is reduced (CMCS, 2014).Research has shown that these combinations are most effective in the treatment of individuals with SUDs (SAMHSA/CSAT/DPT, n.d.).

Medications can provide several important functions as part of the treatment process. They can help with:

- ✓ **Comforting the individual**. Medications can help make withdrawal symptoms and signs less severe as well as assist the person in being more comfortable during the early days and weeks following quitting substance use. Lessening withdrawal can, in turn, assist in the creation of a context for the person to remain abstinent and continue in treatment rather than return to substance use as a way to relieve withdrawal symptoms.

- ✓ **Reducing cravings**. Appropriate medications serve to alleviate the intrusive thoughts and urges around substance use that may lead the individual with SUDs to return to substances.

- ✓ **Altering effects of the substance(s)**. For some of these medications and in certain individuals, these medications eliminate or lessen the effects of substances being used/misused through their own actions in the brain. This action takes away the individual's reason to use the substance of use/misuse in the first place, thereby preventing further relapse.

- ✓ **Retaining the individual in treatment**. Many of the medications have mild but desirable effects sought by individuals with SUD, hence reducing treatment drop out which would interfere with successful recovery (CPDD, n.d.).

At this writing, a variety of medications have been approved by the U.S. Food and Drug Administration (FDA) in the treatment of SUDs: 1) bupropion, nicotine replacement therapy (gum, lozenges, nasal spray, patch, and inhaler), and varenicline for tobacco use disorders (CPDD, n.d.); 2)

acamprosate, disulfiram, and naltrexone (oral and injectable) for alcohol use disorders; and 3) buprenorphine, methadone, and naltrexone (oral and injectable) for opioid use disorders (Chalk & Williams, 2012; CPDD, n.d.; SAMHSA-HRSA/CIHS, 2014). In all cases, the decision as to which medication is prescribed should be based on an understanding of the known pharmacology of the drugs, individual preferences and characteristics of the substance user, and ultimately on the clinician's judgment (Chalk et al., & McLellan, 2013). MATs expand the range of treatment options for persons with addiction to substances, yet national reports continue to show extremely low usage rates in community treatment settings (Chalk & Williams, 2012, e.g.).

MAT continues to be substantially underutilized despite findings of cost effectiveness, clinical effectiveness, and significant reductions in use of detoxification and inpatient services. A study conducted by Roman, Abraham, & Knudsen in 2011 found that less than 30 percent of contemporary substance use treatment programs offered MAT and, of those "offering" programs, less than half of eligible patients actually received medications. It seems that several factors contribute to the low uptake of the evidence-based MAT option, including:

- Agency regulatory policy that forbids or restricts MAT use
- Criteria that other therapies be tried first or the "Fail first" policy
- Initial authorization and reauthorization requirements
- Lack of available prescribers
- Lack of support for existing prescribers
- Limits on dosages that can be prescribed (i.e., lifetime or annual medication limits for MAT)
- Minimal coverage for counseling
- Workforce misunderstandings and attitudes about the nature and use of medications (Roman et al., 2011).

MATs have been recognized for their substantial cost savings. For example, individuals with untreated alcohol use disorders (AUDs) use two times as much health care and cost twice as much as persons who received treatment for their AUD. Research also shows that pregnant women who use/misuse substances and receive MAT demonstrate significantly shorter stays in the hospital compared to those who did not receive MAT. Over a three-year time span, medical costs for Medicaid clients engaged in treatment decreased by 33 percent (CMCS, 2014).

Tobacco and MAT

Nicotine is metabolized and eliminated from the body very quickly so the physical part of nicotine addiction can be broken after seven days of abstinence. The part that takes much longer to overcome is the psychological addiction (Densky, 2012). Its use in the form of cigarettes has shown a marked increase, especially among the youngest (less than 20 years of age) and oldest (over 35 years of age) pregnant mothers (Keegan, Parva, Finnegan, Gerson, & Belden, 2010).

Pharmacological treatments are considered a mainstay for smoking cessation. First-line therapies, as recommended by the FDA because of their evidence of effectiveness consist of nicotine replacement therapies (NRT), bupropion, and varenicline (Douaihy, Kelly, & Sullivan, 2013).

- ✓ **Nicotine replacement therapies** (NRTs). Approved formulations of NRTs include nicotine gum, nicotine lozenge, nicotine vapor inhaler, nicotine nasal spray, and the transdermal nicotine patch. NRTs replace the nicotine obtained from smoking to enhance smoking cessation outcomes and prevent withdrawal symptoms. Started on the quit date, success in quitting on the quit date is highly predictive of end-of-treatment success. Use of NRTs is typically short term, but longer term treatment can produce additional benefits for smokers who are severely addicted. They have been shown to be effective on measures of abstinence (i.e., not even a puff) at the end of clinical trials, as well as at later time points, e.g., six and 12 months, compared to placebo. Combination NRTs have been demonstrated to further improve efficacy, for example combining one medication that allows for passive nicotine delivery such as the transdermal patch with another medication that permits ad libitum nicotine delivery such as inhalers, nasal sprays, or gum. The combination method allows smokers that need slow delivery to achieve a constant concentration of nicotine to relieve withdrawal symptoms and cravings, along with a faster-acting preparation that can be administered as needed for immediate relief of breakthrough withdrawal symptoms and cravings. Labels of these products continue to warn individuals about combining them despite evidence of combination effectiveness (Douaihy et al., 2013). It should also be noted that meta-analyses of these products have indicated them to be effective interventions in achieving sustained abstinence from smoking (The Addiction Recovery Guide, 2014).

- ✓ **Bupropion Sustained-Release** (SR). This medication, marketed as Zyban for smokers, has been effective in helping some people stop smoking (Monson, 2013; The Addiction Recovery Guide, 2014). An atypical antidepressant, the medication has been shown to be effective in enhancing quit rates compared to placebo in both short- and long-term follow-up. Some studies have demonstrated outcomes similar to NRT, but unlike NRT, bupropion is taken one to two weeks before the quit date and then continued post-quit date (Douaihy et al., 2013). Treatment has been associated with reductions in cue-induced activation of the prefrontal and limbic brain regions as well improved ability to resist cue-induced cravings. A six-month follow-up is also recommended for smoking cessation maintenance (The Addiction Recovery Guide, 2014).

- ✓ **Varenicline** (Chantix). This partial nicotine agonist is used for a one to two week period while continuing smoking before actual smoking cessation (Douaihy et al., 2013). It became an FDA- approved treatment to help cigarette smokers stop smoking in 2006 (FDA, 2006). The approved course of treatment is 12 weeks, with successful quitters able to continue 12 more weeks to enhance the likelihood of long-term smoking cessation (The Addiction Recovery Guide, 2014). Unlike nicotine that has a short duration of action, varenicline has a relatively long period of action, requiring only twice daily use. The partial stimulation of varenicline reduces cravings and has been demonstrated to enhance chances of successful

quit attempt, compared to attempts involving unassisted smoking cessation (Douaihy et al., 2013). Its effectiveness was demonstrated in six clinical trials, five of which were randomized controlled. Varenicline was shown to be superior to a placebo in helping people quit smoking. Further, it was shown that persons treated with varenicline were more successful giving up smoking than clients treated with bupropion (FDA, 2006).

In 2012, the FDA issued a warning regarding serious side effects associated with use of varenicline. Compared to a placebo group, the group treated with varenicline (Chantix) experienced higher occurrences of major adverse cardiovascular events. Persons being treated with varenicline for smoking cessation are encouraged to contact their health care professional if they experience new or worsening symptoms of cardiovascular disease (The Addiction Recovery Guide, 2014). The medication also has a black box warning due to associations to suicidal behaviors (Ericson, 2014).

Treatment Summary.

Research studies are continually underway to investigate the benefits of other medications in the treatment of smoking cessation. Anti-smoking vaccines that are given as a series of shots are also still being tested. Results from many of the studies have been promising and safety has been maintained. However, larger studies are needed to demonstrate the efficacy of these treatments before the FDA will approve them for use (ACS, 2014). Stay tuned.

Smokeless Tobacco.

Smokeless tobacco can be defined as tobacco that is not burned. The nicotine in the tobacco, which is addictive, is absorbed through the lining of the mouth. Research has shown that nicotine stays in the blood longer for users of smokeless tobacco than for cigarette smokers (National Cancer Institute, n.d.).

The two main types of smokeless tobacco are chewing tobacco and snuff. Chewing tobacco is typically placed between the cheek and lower lip toward the back of the mouth and can be chewed or held in place. The saliva is either swallowed or spit. Snuff can be packaged dry or moist and may be sold in a variety of different flavors and scents. A pinch or pouch of the moist form is typically placed between the cheek and gums or behind the upper or lower lip. The dry form is sometimes inhaled into the nose (National Cancer Institute, n.d.).

Addiction to smokeless tobacco is as deadly as addiction to cigarette smoking. In fact, many experts will say it is even more dangerous (Densky, 2012; National Cancer Institute, n.d.). As many as 28 chemicals in smokeless tobacco have been found to cause cancer. Moreover the advisory committee to the Surgeon General concluded way back in 1986 that using smokeless tobacco was not a safe substitute for smoking cigarettes. A 2006 panel of experts convened by the National Institutes of Health (NIH) even acknowledged that the range of risks associated with smokeless tobacco products probably varies extensively due to the differing levels of carcinogens, nicotine, and other toxins in the various products (National Cancer Institute, n.d.).

As with cigarette products, smokeless tobacco products must carry warning labels. Further, radio and television advertising is banned. There are new warning labels for these products, which are to be rotated quarterly, that read:

- **WARNING:** THIS PRODUCT MAY CAUSE MOUTH CANCER.
- **WARNING**: THIS PRODUCT MAY CAUSE GUM DISEASE AND TOOTH LOSS.
- **WARNING**: THIS PRODUCT IS NOT A SAFE ALTERNATIVE TO CIGARETTES (Akoury, 2014).

Smokeless tobacco has been directly linked to laryngeal, oral, and pharyngeal cancer, as well as esophageal cancer, tooth loss, and gum disease. The use of these products has been on the increase, especially among America's young people (Akoury, 2014; National Cancer Institute, n.d.).

As a preventive measure, the National Spit Tobacco Education Program (NSTEP) provides education on smokeless tobacco use. The organization targets the general public but specifically is aimed at baseball players and their families, groups for whom the use of smokeless tobacco is extremely high. NSTEP is endorsed and supported by both Major League and Little League Baseball (Cheng et al., 2014).

Pharmacological Treatments: Smokeless Tobacco.

Meta-analytic studies have been a primary source of research on the effectiveness of pharmacological treatments for users of smokeless tobacco. However, nicotine replacement therapy (NRT) has been shown to enhance short-term tobacco abstinence rates, as well as to alleviate craving and withdrawal symptoms for users trying to quit using smokeless tobacco. Bupropion sustained release has demonstrated decreases in craving and weakened post-cessation weight gain among users of smokeless tobacco trying to quit. Long-term abstinence rates (i.e., at least six months) have only been demonstrated with the use of varenicline (Chantix) (Ebbert & Fagerstrom, 2012).

On the whole, findings from studies investigating pharmacological treatments for users of smokeless tobacco have not been as promising as desired. They may hold some promise for increasing abstinence rates for users not interested in quitting. Additional investigations of higher dose NRT and combination pharmacological therapies have been recommended to advance the treatment of users of smokeless tobacco (Ebbert & Fagerstrom, 2012).

Alcohol and MAT

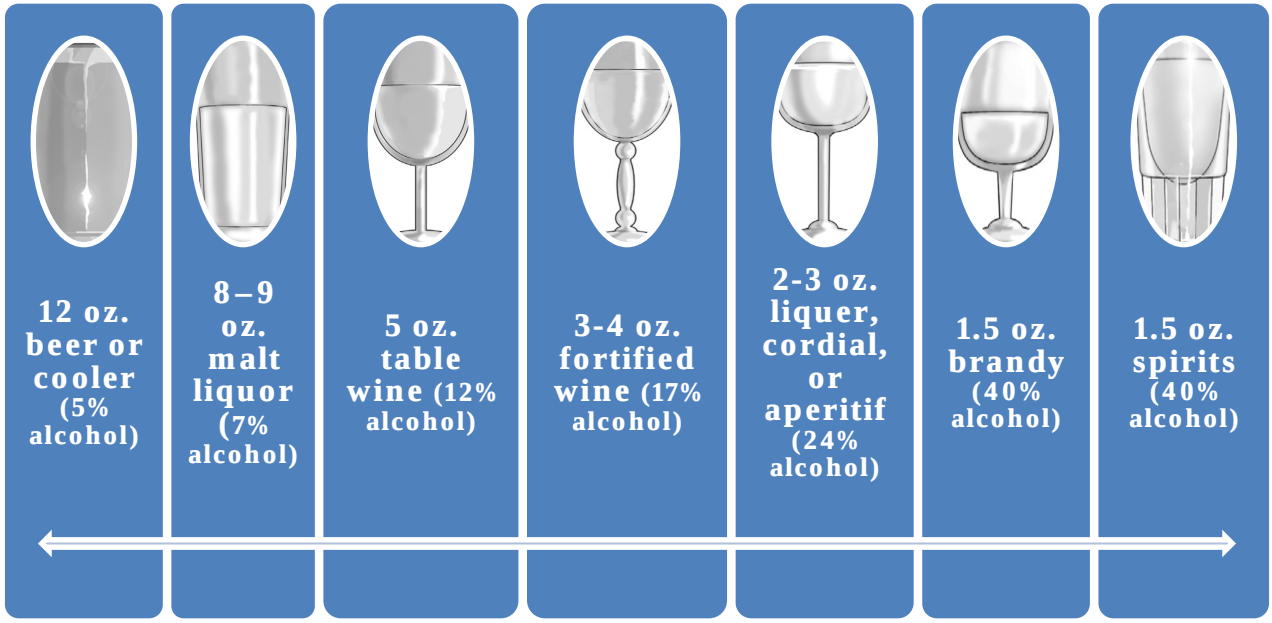
Consumption of alcohol is pervasive in the United States (Pearson, Dube, Nelson, & Caetano, 2009). In excess of 90 percent of adult Americans have consumed alcohol at some point in their lives and nearly 70 percent continue to consume it during adulthood. The majority of adults can drink moderate amounts of alcohol—one drink daily for women and up to two drinks per day for men—and avoid problems related to alcohol consumption. However, 10 to 15 percent of individuals exposed to alcohol come to use/misuse it or become dependent upon it, making alcohol use disorder (AUD) very common (O'Brien, 2012). Recent estimates show as many as 20 percent of patients seen in hospital or primary care setting has a diagnosable AUD (SAMHSA & NIAAA, 2015).

What Is "Too Much" Alcohol?

When drinking causes or elevates the risk of alcohol-related problems or complicates the management of other health problems, drinking has become a problem. Epidemiologic research has shown that women who consume more than three standard drinks in a day (or more than seven per week) and men who consume more than four standard drinks in a day (or more than 14 per week) are at increased risk for alcohol-related problems. Of course, individuals vary in the way they respond to alcohol which means that drinking even at lower levels can be problematic depending on other factors such as coexisting conditions, use of medication, and age. Further, the Surgeon General has urged abstinence for women who are or may become pregnant since 2005 because there is no data on the amount of alcohol that would be safe during pregnancy (NIH/NIAAA, 2007).

What Is a Standard Drink?

In the United States, a standard drink refers to any drink that contains about 14 grams of pure alcohol (1.2 tablespoons or 0.6 fluid ounces). However, many individuals do not know what constitutes a standard drink and thus do not realize how many standard drinks are in the containers in which the drinks are often sold or distributed when purchased. The chart below shows typical standard drink equivalents (NIH/NIAAA, 2007).



Additional examples of standard drinks are provided below. The approximate number of standard drinks in:

✓ **Beer**
- 12 oz. = 1
- 22 oz. = 2
- 16 oz. = 1.3
- 40 oz. = 3.3

✓ **Malt Liquor**
- 12 oz. = 1.5
- 22 oz. = 2.5
- 16 oz. = 2
- 40 oz. = 4.5

✓ **Table Wine**

For **table wine,** the approximate number of standard drinks in
- a standard 750-mL (25-oz.) bottle = 5

✓ **80 Proof Spirits** (hard liquor)
- a mixed drink = 1 or more*
- a fifth (25 oz.) = 17
- a pint (16 oz.) = 11
- 1.75 L (59 oz.) = 39

*It should be noted that estimates of the number of standard drinks in mixed drinks made with hard liquor are difficult and a function of the type of spirits as well as the recipe. A mixed drink, hence, can contain from one to three or more standard drinks (NIH/NIAAA, 2007).

Binge Drinking.

Binge drinking constitutes four or more drinks in a single bout for women and five or more for men (Carroll, 2014; SAMHSAS/CBHSQ, 2014a). Moreover, one in every six adults engages in binge drinking, and that plays a substantial role in most alcohol-related deaths (Shute, 2014). However, alcohol deaths are very preventable, ranking fourth behind smoking, poor nutrition and lack of activity (Shute, 2014). For the combined period of 2010 to 2012, Southern states reported the lowest rates of underage binge alcohol use and Tennessee was among them (SAMHSA/CBHSQ, 2014a).

One in six adults engages in binge drinking, and that plays a substantial role in most alcohol-related deaths (Shute, 2014).

Contrary to popular belief, alcoholics or persons addicted to alcohol, are not the big problem.
Ten percent of all deaths have been linked to excessive drinking. In fact, it is reported that binge drinking, along with heavy regular drinking, shortened the lives of those who died by 30 years (Carroll, 2014; Shute, 2014).

Other Drinking.

Drinking at least five drinks on the same occasion on five or more days in the past 30 days is the definition for ***heavy alcohol use*** (APHA, 2008; SAMHSA/CBHSQ, 2014c). Data from the 2013 National Survey on Drug Use and Health (NSDUH) showed 1.2 percent of adolescents age 12 to 17 as heavy drinkers, based on their alcohol use in the past month. Adults 18 years of age and older represented 6.8 percent of the heavy alcohol users (SAMHSA/CBHSQ, 2014c).

Combined data from the 2011 and 2012 National Survey on Drug Use and Health (NSDUH) showed that of young adults 18 to 25 years of age who used alcohol in the past month, older ages drink alcohol more days than younger ages. The 21-25 year of age group drank 7.5 days per month compared to 5.7 days per month for 18 to 20 year olds. **However**, younger ages drank more drinks per day on they days they drank, with young adults ages 18 to 20 drinking 4.8 drinks and those ages 21 to 25 drinking 3.9 drinks per day (SAMHSA/CBHSQ, 2014b).

Physicians in one study defined ***light drinking*** as 1.2 drinks per day on average, an amount exceeding guidelines established by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) for at-risk drinking for women (ACOG, 2008).

According to the American Public Health Association (2008), ***moderate drinking*** can be defined as:

- Up to two drinks per day – Men
- Up to one drink per day- Women or individuals 65 years and older

Excessive alcohol use leads to a poorer quality of life, hampered productivity in the workplace, decreased academic performance, and other negative consequences and outcomes. Defined, excessive alcohol use includes alcohol impaired driving, drinking while pregnant, underage drinking, and binge drinking (National Prevention Strategy, 2014). The Centers for Disease Control and

Prevention (n.d.) defined excessive alcohol use as follows: alcohol use by pregnant women, alcohol use by underage individuals, heavy drinkers, and binge drinkers.

Medication/Alcohol Interactions.

Alcohol can interact negatively with medications either by enhancing the effects of the medication (particularly in the central nervous system) or by interfering with the metabolism of the medication (generally in the liver). Many classes of prescription medications can interact with alcohol, including antihistamines, antidepressants, antibiotics, benzodiazepines, barbiturates, muscle relaxants, histamine H2 receptor agonists, anti-inflammatory agents, opioids, nonopioid pain medications, and warfarin. Negative side effects are likely when herbal preparations and many over-the-counter medications are taken with alcohol (NIH/NIAAA, 2007).

Pharmacological Treatments.

Treatment involving medications or medication-assisted treatments (MATs) for alcohol dependence should be used adjunctively to psychosocial treatments rather than as replacement. This combination has shown to be more effective than either medication or nondrug therapy alone. To the extent that pharmacological therapy reduces craving and helps maintain abstinence, it likely makes individuals with AUD more agreeable to psychosocial interventions (SAMHSA/CSAT, 2009).

A medical management (MM) strategy has been designed specifically to accompany pharmacological therapy for alcohol use disorders (AUDs). MM not only gives structure, but supplies materials to help clinicians offer their clients strategies for taking medications and staying in treatment; support their clients' efforts in changing their drinking habits; provide recommendations to their clients for changing drinking habits; and stay informed about alcohol dependence and pharmacological therapy research and recommendations (SAMHSA/CSAT, 2009).

Three medications have been approved by the United States Food and Drug Administration (FDA) in the treatment of alcohol use disorders (AUDs). These medicines consist of disulfiram, acamprosate, and naltrexone (oral and extended-release injectable). Counseling and other supports should be part of the MAT package (CPDD, 2013; Douaihy et al., 2013; SAMHSA/CSAT, 2009).

Disulfiram.

Disulfiram, also known as Antabuse®, was the first FDA-approved pharmacological treatment for AUDs. Approval was obtained in 1951. An alcohol-sensitizing or alcohol-aversive agent that initiates an acutely toxic physical reaction when mixed with alcohol, disulfiram causes extremely uncomfortable symptoms such as vomiting, headache, and severe nausea. Research continues to support its establishment as an effective and safe treatment of AUDs in particular client groups (SAMHSA/CSAT, 2009). Individuals having the following profiles are considered good candidates for disulfiram as a pharmacological treatment for AUD:

- Medically appropriate.

- Maintain abstinence from alcohol during treatment.
- Have the capacity to fully understand the consequences associated with alcohol use while taking this medication.
- Can receive supervised dosing.
- Are abstinent from alcohol use (i.e., clients must have abstained from alcohol use at minimum 12 hours and/or breath or blood alcohol levels are zero).
- Treatment motivated and committed to total abstinence.
- Have codependence on or current use/misuse of cocaine (SAMHSA/CSAT, 2009).

Under no circumstances should disulfiram be administered to a client that is in a state of alcohol intoxication or without the client's full knowledge and consent. Neither should disulfiram be used by pregnant women. Not enough is known about the potential risk to the fetus. Clinicians should advise family members and/or other supports about these and other contraindications. The Antabuse® package insert includes a ***black box warning*** (SAMHSA/CSAT, 2009).

Trade name: Antabuse®.

How taken: Tablet by mouth once daily (May be crushed and mixed with water, milk, tea, coffee, soft drink, or fruit juice).

How supplied: 250 or 500 milligram (mg) tablets.

Source: SAMHSA/CSAT, 2009 (TIP 49)

Contraindications

Condition or Circumstance	*Treatment Recommendation*
Clients with histories of cardiac disease, diabetes mellitus, hypothyroidism, epilepsy, cerebral damage, chronic or acute nephritis, hepatic cirrhosis, or hepatic insufficiency	Use with caution. No evidence exists that clients with preexisting liver disease are more likely to suffer severe liver toxicity from disulfiram.
Clients with hepatitis C	If baseline transaminase levels are normal or only moderately elevated (< 5 times the upper limit of normal), carefully monitor liver function.

Condition or Circumstance (continued)	*Treatment Recommendation* (continued)
Clients receiving or who have recently received metronidazole, paraldehyde, alcohol, or alcohol-containing preparations (e.g., cough syrups, tonics). Clients exposed to ethylene dibromide or its vapors (e.g., in paint, paint thinner, varnish, shellac).	Do not use until substances are out of client's system.
Adults ages 61 and older	May need to decrease dosage
Children and adolescents	Prescribe with caution. Medication has not been evaluated for safety or efficacy in these populations.

Source: SAMHSA/CSAT, 2009 (TIP 49)

Taking the medication each day communicates to the individual that he or she will have this unpleasant, uncomfortable reaction if alcohol or alcohol-based products are consumed. Armed with this knowledge, the person can work to refrain from drinking. However, people realize they can avoid the reaction they do not want simply by stopping the medication. Thus, high levels of motivation to abstain are necessary for disulfiram to be effective. In general, older men with worse drinking histories but more socially stable and participating in Alcoholics Anonymous (AA) are more likely to adhere to the regimens of the medication and achieve enhanced outcomes ((Douaihy et al., 2013).

Acamprosate.

Approved in 2004 by the FDA for AUDs, acamprosate (Brand name = Campral®) is a relapse-prevention medication that affects various neurotransmitters, structurally resembles GABA and glutamate (Douaihy et al., 2013), and has a good safety profile (Acamprosate, 2012). Usually initiated after individuals stop drinking, it can be safely used with alcohol or with benzodiazepines. It can also be started during medically supervised withdrawal. It reaches full effectiveness in five to eight days and should be maintained if a client relapses to alcohol use. In general, there is no specific client profile that must be considered if planning to use acamprosate in the treatment of AUDs. Not surprising though, it is most effective for clients that are motivated toward complete abstinence rather than decreased drinking when treatment begins. Acamprosate may also be utilized concurrently by clients undergoing opioid maintenance therapy. The fact that there are no known clinically significant drug interactions associated with acamprosate appears to give it a safety valve for clients that are trying to deal with multiple medical issues and are currently taking many other medications (SAMHSA/CSAT, 2009).

Efficacy for acamprosate has been mixed. In the COMBINE Trial, the largest multisite study of treatment for alcohol dependence to date in this country, the medication showed no greater benefit than placebo for clients dependent on alcohol. It should be noted that the U.S. trials contained limited numbers of individuals and they should have undergone detoxification prior to treatment. Acamprosate has been studied much more extensively in Europe where results have been positive. European studies demonstrated acamprosate's effectiveness over placebo in significantly increasing the proportion of clients who were already abstinent to remain continuously abstinent (Douaihy et al., 2013).

Trade name: Campral®.

How taken: Two tablets by mouth three times daily, with or without food (With some clients, a lower dose may be effective. This lower dose *must* be used with those that have impaired renal function.)

How supplied: 333 mg delayed-release, enteric-coated tablets.

Source: SAMHSA/CSAT, 2009 (TIP 49)

Contraindications

Condition or Circumstance	*Treatment Recommendation*
Clients who are hypersensitive to acamprosate or its components	Do not prescribe acamprosate.
Clients with severe renal impairment (creatinine clearance ≤ 30 mL/min)	Do not prescribe acamprosate.

Source: SAMHSA/CSAT, 2009 (TIP 49)

Benefits associated with treatment of alcohol dependence with acamprosate include limited side effects, no negative liver effects, and no drug interaction profiles. Yet dosing three times a day may negatively impact client adherence. Clinicians might help their clients improve adherence by assisting them in identifying reminders that will work for them, e.g., having them wear "reminder" bracelets, setting alarms on watches/clocks/cell phones, or purchasing three-a-day pill containers (SAMHSA/CSAT, 2009).

Naltrexone.

Naltrexone is an opioid antagonist that was first developed as treatment for opioid addiction. It was not until the mid-1990's that the FDA approved the drug for treatment of AUDs. Naltrexone oral might be referenced as Revia® or Depade® (SAMHSA/CSAT, 2009). Oral naltrexone has demonstrated reductions in intensity and frequency of drinking, reductions in risk of relapse to heavy drinking, and increases in the percentage of days that individuals remain abstinent. Most published controlled studies compared the medication to placebo (Douaihy et al., 2013).

Oral Naltrexone.

Oral naltrexone is an antagonist that blocks the effect of other narcotics and alcohol. First developed in the treatment of opioid addiction, naltrexone was FDA approved for treatment of AUDs in the mid-1990's (SAMHSA/CSAT, 2009). It works to help reduce alcohol cravings and to lessen alcohol's positive effects. Naltrexone showed effectiveness when used in conjunction with other treatments such as counseling, group therapy, Alcoholics Anonymous (AA) meetings, family therapy, and residential or hospital treatment. However, adherence to daily doses is problematic (The Addiction Recovery Guide, 2014).

Oral naltrexone's FDA approval includes a black-box warning for hepatotoxicity, especially when given in excessive doses. It is contraindicated in liver failure or acute hepatitis and use in clients that have active liver disease must be carefully considered. The effects are reversible and have shown to be primarily associated with much higher doses than typically used in routine clinical practice (e.g., at least 300 mg/day). Research further suggests that the negative effects tend to show up only after clients have been on these higher doses for extended periods of time (SAMHSA/CSAT, 2009).

As with other medications used to assist in substance use treatment, it is recommended that signs and symptoms of acute alcohol withdrawal have subsided in advance of treatment initiation. At least three days of abstinence are typically recommended, with seven days preferred. However, it is safe to initiate treatment involving oral naltrexone during medically supervised withdrawal or if the individual is actively drinking. Abstinence lessens withdrawal side effects (SAMHSA/CSAT, 2009).

Clients who are motivated to participate in treatment or those who will allow medication monitoring have been deemed as good candidates for oral naltrexone. It has further been shown that persons with intense alcohol cravings make good candidates for oral naltrexone treatment. Persons being considered for treatment of AUDs with oral naltrexone should be educated about the effects of using opioids and/or other drugs while taking the prescribed medication (SAMHSA, 2015).

The pill form is typically prescribed as a single daily dose. In general, prescriptions run for 12 weeks when individuals who are abstinent to reduce the craving for alcohol early on during treatment, when the risk of relapse is greatest (about.com, 2014). In fact, the label says that oral naltrexone should be taken for a period up to three months for the treatment of AUDs. However, it is recommended that treatment involving oral naltrexone be individualized. Thus, some individuals may be treated for three months while other persons might be treated for as long as 12 months (SAMHSA/CSAT, 2009).

Trade name: ReVia®; Depade®

How taken: Tablet by mouth once daily.

How supplied: 50 mg tablets.

Source: SAMHSA/CSAT, 2009 (TIP 49)

Contraindications

Condition or Circumstance	*Treatment Recommendation*
Clients with moderate to severe renal impairment	Carefully monitor (naltrexone is eliminated through the kidneys)
Clients with active liver disease	Monitor liver function frequently
Clients with serum aminotransferase levels > 5 times the upper limit of normal	Generally avoid, unless potential benefits outweigh risks
Pregnant and nursing women and women of childbearing age	Do not prescribe during pregnancy and nursing unless potential benefits outweigh risks*. Caution that effects on fetus are unknown. Encourage use of effective birth control method

Clients with chronic pain or acute or recurring need for opioid analgesics	Have clients abstain from naltrexone for at least 3 days (conservatively 7 days) before initiating opioid analgesics

*Oral naltrexone is FDA pregnancy category C. Adequate, well-controlled human studies are lacking, and animal studies have shown a risk to the fetus or are lacking as well. There is a chance of fetal harm if the drug is administered during pregnancy; but the potential benefits may outweigh the potential risk. It is unknown whether oral naltrexone is excreted in human milk.

Source: SAMHSA/CSAT, 2009 (TIP 49)

Treatment outcomes are better if naltrexone is not begun until symptoms and signs of acute alcohol withdrawal have subsided. At least three days of abstinence are recommended, with seven days preferable. Clients experience fewer medication side effects if they are abstinent from alcohol when they being treatment with naltrexone. It is safe to begin with naltrexone even if clients do not practice abstinence prior to treatment (SAMHSA/CSAT, 2009).

Research results involving oral naltrexone have not been as positive for clients with more severe alcohol dependence or in long-term treatment in outpatient settings. Not surprising, lack of adherence to the medication regimen played a substantial role in the less-than-favorable findings (Douaihy et al., 2013).

Extended-Release Injectable Form (Vivitrol).

Vivitrol was approved back in 2006 by the FDA for treatment of alcohol addiction (Rubin, 2010). The extended-release form of naltrexone can be taken as a once-a-month depot injection given in a physician's office (CMCS, 2014). It is administered by intramuscular (IM) gluteal injection (SAMHSA/CSAT, 2009). This slow release form of naltrexone has shown efficacy in reducing heavy drinking outcomes because of its increased medication adherence. Studies have further shown its effectiveness in reducing rates of alcohol dependence in the general population. In these studies, the depot form of naltrexone was prescribed and monitored in primary care settings (Douaihy et al., 2013).

Trade name: Vivitrol®

How taken: 380 mg intramuscular injection once every 4 weeks.

How supplied: Single-use cartons, containing the following: one 380 mg vial of Vivitrol microspheres, one vial containing 4 mL (to deliver 3.4 mL) diluent for the suspension of Vivitrol, one 5 mL prepackaged syringe, one 20-gauge ½-inch needle, and two 20-gauge 1.5-inch needles.

Source: SAMHSA/CSAT, 2009 (TIP 49)

Contraindications

Condition or Circumstance	*Treatment Recommendation*
History of sensitivity to polylactide glycolide (PLG) polymer, carboxymethylcellulose, or any components of the diluent	Do not administer injectable naltrexone
Anticipated need for opioid analgesics	Do not administer injectable naltrexone

within the next 30 days	
Patient obesity	Do not administer injectable naltrexone if patient's body mass precludes IM injection with the provided 1.5-inch needle Inadvertent subcutaneous injection may cause a severe injection-site reaction

Source: SAMHSA/CSAT, 2009 (TIP 49)

In clinical trials, individuals receiving the 380 mg IM injection of naltrexone (in addition to psychosocial support) demonstrated a 25 percent decrease in heavy drinking days compared to persons receiving placebo. Significant decreases were also found for individuals receiving a lower dose of injectable naltrexone (190 mg). Their decreases were 17 percent compared to persons receiving placebo (SAMHSA/CSAT, 2009).

Other Promising MATs for AUDs.

Promising results have been shown for ***Gabapentin*** in treating alcohol dependence (Howland, 2013). Currently approved in the treatment of nerve pain and seizures, persons reporting alcohol dependence who participated in a study from 2004-2010 were better able to stay sober. Further, gabapentin did not produce serious side effects (The Addiction Recovery Guide, 2014). Gabapentin (specifically the 1800-mg dosage) was effective in treating alcohol dependence as well as relapse-related symptoms of dysphoria, insomnia, and craving, with a favorable safety profile (Mason, Quello, Goodell, Shadan, Kyle, & Begovic, 2014).

Another anticonvulsant, ***oxcarbazepine*** (Trileptal), may also be useful in the treatment of alcohol dependence by reducing alcohol craving. It treats alcohol withdrawal symptoms through an antikindling effect. However, it was not helpful in preventing DTs or seizures (DeSimone, Tilleman, & Powell, 2014). Several studies have suggested its efficacy in improving abstinence and reducing alcohol consumption. However, additional research is needed to confirm the efficacy of oxcarbazepine in the treatment of alcohol dependence (Wilkins, n.d.).

Ondansetron, marketed as Zofran in the treatment of vomiting and nausea associated with chemotherapy, has been observed to increase abstinence, decrease alcohol consumption, and stop cravings in people who are early-onset alcoholics. Compared to a placebo group, the persons with early-onset alcoholism treated with ondansetron had fewer drinks per day and they experienced an increase in the number of abstinent days per week (The Addiction Recovery Guide, 2014).

The anticonvulsant, mood-stabilizing medication ***Topiramate*** (Topomax) has been tested in the reduction of alcohol cravings. It was found to be more effective than a placebo, significantly decreasing obsessive thoughts and compulsions about alcohol use, increasing wellbeing for those treated, and improving some aspects of quality of life. Thus, Topiramate lessened the risk of relapse (The Addiction Recovery Guide, 2014).

Caution is advised with regard to the use of Topiramate in the treatment of pregnant women that use/misuse alcohol. The FDA says that new data indicates an increased risk of cleft palate and/or cleft lip in the exposed fetus (The Addiction Recovery Guide, 2014).

A study found that the muscle relaxant ***Baclofen***, marketed as Lioresal or Gablofen, reduced alcohol cravings. In addition, there was evidence that the medication has effectiveness in reducing alcohol consumption as well as inducing abstinence. Though the study was small, the evidence supports Baclofen as a potentially useful medication in the treatment of alcohol dependence.

Chantix (varenicline), approved in the treatment of smoking cessation, has been studied as a potential option in the treatment of alcohol dependence. A 2013 study showed individuals treated with Chantix demonstrated significantly lower number of drinks per day, number of drinks per drinking day, weekly percent of heavy drinking days, and alcohol craving compared to a placebo group. It should be noted that Chantix has been linked to a number of serious psychiatric problems including agitation, depression, and suicidal behavior. Other health and safety risks have also been cited, such as seizures, heart attacks, diabetes, falls, and accidents (The Addiction Recovery Guide, 2014).

Opioids and MAT

Opioids are pain-relieving substances. They reduce the intensity of pain signals reaching the brain, affecting those brain areas by controlling emotion to diminish the effects of the painful stimulus (NIDA, 2011). Opioids slow down the actions of the body, such as heartbeat and breathing, and also affect the brain to increase pleasant feelings (SAMHSA, 2014). Medications falling with this class of substances include: oxycodone (e.g., Percocet, OxyContin), hydrocodone (e.g., Vicodin), morphine (e.g., Avinza, Kadian), and codeine. Hydrocodone products tend to be the most frequently prescribed for painful conditions such as injury-related and dental pain. Codeine is most often prescribed for mild pain. Morphine, on the other hand, is used before and after surgical procedures to alleviate more severe pain (NIDA, 2011). Heroin, once believed to be a wonder drug and replacement for morphine, continues to be a drug of choice for individuals who run short on money for the purchase of prescription opiates. Heroin is less expensive as well as illegal (Narconon International, n.d.).

Opioid dependence is a chronic disorder, often relapsing, that also contributes to major medical challenges such as human immunodeficiency virus (HIV)-related illnesses, hepatitis, and other chronic diseases. It is frequently linked to a history of drug-related criminal activity and persons dependent on opioids often have co-occurring mood disorders, especially depression. Antisocial personality disorder is also more prevalent in persons with opioid dependence than in the general population (Krambeer, McKnelly Jr., Gabrielli Jr., & Penick, 2001).

With wider acknowledgement that opioid dependence should be treated as a chronic disease, medications have been approved by the FDA as effective in treatment (Rinaldo & Rinaldo, 2013). Approved medications include buprenorphine (Suboxone®, Bunavail, Subutex®, and Zubsolv®), methadone, and naltrexone (ReVia®, Vivitrol®, Depade®) (SAMHSA-HRSA/CIHS, 2014). Every recipient of medication-assisted treatment for opioid dependence should also receive psychosocial treatment. Supportive medication monitoring, individual and/or group counseling, and attendance at 12-step/mutual help groups should be part of the assisted-treatment package (Sullivan, 2014). Special weight must be given when considering opioid substitution therapy for pregnant women or adolescents (Chalk et al., 2013). Treatment details for these two populations are provided in their respective sections in this document. On the whole, it has been suggested that MAT is more suitable for users of opioids that meet one or more of the following criteria:

- Poor social support
- Unstable housing and/or lifestyle
- Limited financial resources
- No insurance or less than adequate insurance
- Structure of a dispensing situation that must be attended regularly (Chalk et al., 2013; SAMHSA, 2015).

First steps in the medical management of opioid addiction include 1) use of validated screening tools to identify patients who may have a problem with opioid use and 2) further assessment to clearly delineate the scope of the problem when opioid addiction is identified. Consideration must be given to the appropriate treatment approach when treatment is indicated. Assessment should also identify complicating or comorbid emotional or medical conditions. Complete assessment may take several days but it is not recommended that initial treatment be delayed (SAMHSA, 2004).

Thorough assessment will assist in confirmation of the diagnosis. It is designed to determine need for treatment, develop a treatment plan, and establish a baseline measure for evaluating progress. The assessment should encompass all of the following:

- Confirmation of an opioid use disorder diagnosis;
- Establishment of current opioid use;
- Documentation of substance use history;
- Identification of any need to require medically supervised detoxification from opioids as well as benzodiazepines, alcohol, or other sedatives;
- Determination of where and when such detoxification should be accomplished;
- Identification of comorbid psychiatric and medical conditions and disorders and prioritization and coordination of their management;
- Screening for infectious diseases that place opioid users at elevated risk such as Hepatitis C, Hepatitis B, and human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) (SAMHSA, 2015).

The American Society of Addiction Medicine (ASAM) announced the release of its National Practice Guideline for the Use of Medications in the Treatment of Addiction involving Opioid Use in early June 2015. A PDF version containing full text is available for download at http://www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/national-practice-guideline.pdf#search=%22national%20practice%20guideline%20for%20the%20use%20of%20medicat%22. The document can also be found in the *Journal of Addiction Medicine*. The Guideline deals with a number of in MAT topics around opioid use such as the role of drug testing in treatment,

proper duration of buprenorphine treatment, and the growing role of naloxone in reversing opioid overdose. It is intended to help clinicians in managing their clients and clinical decision-making. The Guideline reminds clinicians about informing clients of benefits, risks and alternatives to particular treatments and ensuring their active participation in shared decision making whenever possible (ASAM, 2015).

Pharmacological Treatments.

Pharmacologic medications used to treat opioid addiction consist of three types: agonists, partial agonists, and antagonists. **Agonists** turn on receptors more slowly and hence have a longer lasting action that helps in the prevention of withdrawal. The effects of **partial agonists** are weaker than those of the full agonists. **Antagonists**, on the other hand, block actions of the receptors. Thus, this blocking action serves to slow or diminish relapse if there is a return to formerly used/misused substances (ONDCP, 2012).

Agonist therapies have proven to be the most effective pharmacological treatments for opioid use disorders (OUDs). Methadone and buprenorphine are the most commonly used agonist therapies. They work by occupying the sites stimulated by opioids and turning on the receptors. Thus, these medications have similar actions to those of the used/misused substance but have different pharmacokinetic profiles. Additionally, agonist treatments are usually provided in combination with psychosocial and/or other support services (Douaihy et al., 2013; Thomas et al., 2014). A large number of studies comparing methadone and buprenorphine have shown that 8 mg of sublingual buprenorphine or 16 mg of the tablet form of buprenorphine per day is equivalent to approximately 60 mg of oral methadone per day (SAMHSA/CSAT, 2005).

A large number of studies comparing methadone and buprenorphine have shown that 8 mg of sublingual buprenorphine or 16 mg of the buprenorphine tablet per day is equivalent to approximately 60 mg of oral methadone per day (SAMHSA/CSAT, 2005).

Use/Misuse of opioids, particularly heroin, is further associated with the transmission of sexually transmitted infections (STIs), hepatitis, human immunodeficiency virus (HIV), and other blood-borne diseases that can result from use of unsterile drug paraphernalia and risky behaviors. Treatment involving MAT then not only helps individuals move away from the vicious cycle of addiction, but can assist in the prevention of related adverse health consequences (NIDA, 2012).

The antagonist naltrexone blocks opioids from acting on the brain and takes away the reward of getting high on the problem opioid. This feature makes naltrexone a good choice for preventing relapse. The medication may be helpful when persons using opioids are completely past withdrawal and highly motivated to stay in recovery. Naltrexone may also be recommended for individuals in an early stage of opioid addiction (SAMHSA, 2012b).

Methadone.

MMT is one of the most widely used and effective pharmacological methods for treating addictions, especially addiction to opioids. Research on the treatment began for male addicts in 1964 at the Rockefeller Hospital. Women were not admitted into treatment research until 1967 (Kreek, Borg, Ducat, & Ray, 2010).

Methadone is a long-acting, potent opiate agonist used to treat individuals dependent on opioids. It imitates the action of an opiate like heroin by occupying and activating opioid receptors in the body. Its effects last from 24 to 30 hours. Methadone does not generate the extreme euphoria of short-acting, injectables such as heroin because of its slow, very long period of metabolism. Its potency is greater than most other opioids so it produces a physiological tolerance. As a result, individuals should not abruptly stop taking the drug. Neither does methadone provide protection from the use/misuse of non-opioid drugs such as marijuana, cocaine, benzodiazepines, or alcohol (Chalk et al., 2013).

Methadone for opioid addiction can only be administered by opioid treatment programs (OTPs) that are certified by the Substance Abuse and Mental Health Services Administration (SAMHSA) and licensed by the Drug Enforcement Agency (DEA) (Chalk et al, 2013). Persons on methadone maintenance therapy (MMT) are typically required to visit an OTP daily to obtain their dose of medication under direct clinical observation. A significant history of stabilization should be established for persons on MMT to receive take-home doses (Chalk et al., 2013).

Methadone for opioid addiction can only be administered by appropriately licensed and certified opioid treatment programs (Chalk et al., 2013).

If an individual is deemed eligible for admission to a MMT program, the following should be completed by program staff members:

- Comprehensive physical evaluation prior to admission
- Laboratory workup as indicated
- Psychosocial assessment
- Preliminary treatment plan
- Client orientation during the initial stage of treatment (SAMHSA, 2015).

Usual dispensation of methadone involves daily doses at a methadone treatment facility. It is possible for persons to become eligible for take-home doses based on lack of known criminal activity, absence of behavioral problems at the clinic or recent substance use/misuse, appropriate clinic attendance, and evidence of a stable home life with the ability to safely store the methadone (Fullerton et al., 2014).

Methadone treatment predicts lower risk of infection from the human immunodeficiency virus (HIV), a blood-borne infection that is sometimes linked to intravenous drug use. Research has shown that, while in methadone-maintenance treatment (MMT), individuals use significantly less than they did before they started treatment. Persons in MMT also use less frequently than individuals not in treatment (Chalk, et al., 2013; Lawrinson et al., 2008). Methadone treatment has been recognized as an effective tool in increasing adherence to antiretroviral therapy in people with HIV/ acquired immune deficiency syndrome (AIDS) (World Health Organization [WHO], 2011). The methadone dosage may need to be adjusted when treating persons with HIV because some of the medications developed to treat the infection can accelerate or retard the body's transformation of methadone. In all instances, it is important to develop a full listing of medications being taken by the individual to treat HIV. Another primary concern of methadone treatment is the high relapse rate associated with withdrawal from use, even following long periods of maintenance (Chalk et al., 2013).

In regard to dosing, it is recommended to start low and go slow (i.e., use the safety principle) for early medication dosages in outpatient settings (SAMHSA, 2005). The ASAM Guideline recommends initial dosing of 10 to 30 mg, with reassessment in three to four hours. The second dose should not exceed 10 mg on the first day if withdrawal symptoms are continuing (ASAM, 2015). According to a consensus panel, programs should monitor and adjust patient dosages to ensure they receive therapeutic amounts of medication without regard to arbitrary dose-level ceilings that are not supported by research evidence. (The panel's recommendation applies across all opioid treatment medications.) Decisions regarding dosages should be appropriate and tailored to each patient. Dosages lower than those recommended by the manufacturer may be sufficient for the desired therapeutic effect in many cases, especially when patients have a positive diagnosis for cardiac risk factors (SAMHSA, 2005).

In the first week of treatment, dosage adjustments should be based on how patients feel at the peak period for their medication (e.g., 2-4 hours following a methadone dose has been administered), not on how long the effects of the medication last. About 60 mg has been accepted widely as the low end of effective for most patients. However, other patients may require much more for optimal effect, even higher than 120 mg per day. There is some evidence that patients receiving more than 200 mg of methadone per day can have optimal results with no adverse effects. Nevertheless, treatment providers should be more cautious when providing higher doses, especially as take home, because of possible increased diversion potential. Research has indicated patients with hepatitis C or mental disorders comorbid with their opioid use disorder may need increases of 50 percent or more in methadone dosage to achieve stabilization. Lower doses have been shown to be less effective in facilitating abstinence in patients addicted to heroin (SAMHA/CSAT, 2005).

Recent research on MMT continues to support its effectiveness. For example, the literature continues to show that methadone is more effective than no medication treatment in the reduction of illegal opioid use and retention in treatment. Even when compared with treatments offering no opioid replacement therapy, such as drug-free rehabilitation protocols or detoxification protocols, methadone was significantly more effective in suppression of heroin use (as measurement by urine drug testing) and treatment retention. Similar findings have been demonstrated for individuals receiving interim methadone treatment, which is treatment under daily supervision while the person is awaiting placement in a standard methadone program, compared to just being on a wait list. There has also been some support that MMT reduces substance-related risk factors such as the sharing of injection paraphernalia (Fullerton et al., 2014).

Evidence-Based Treatments

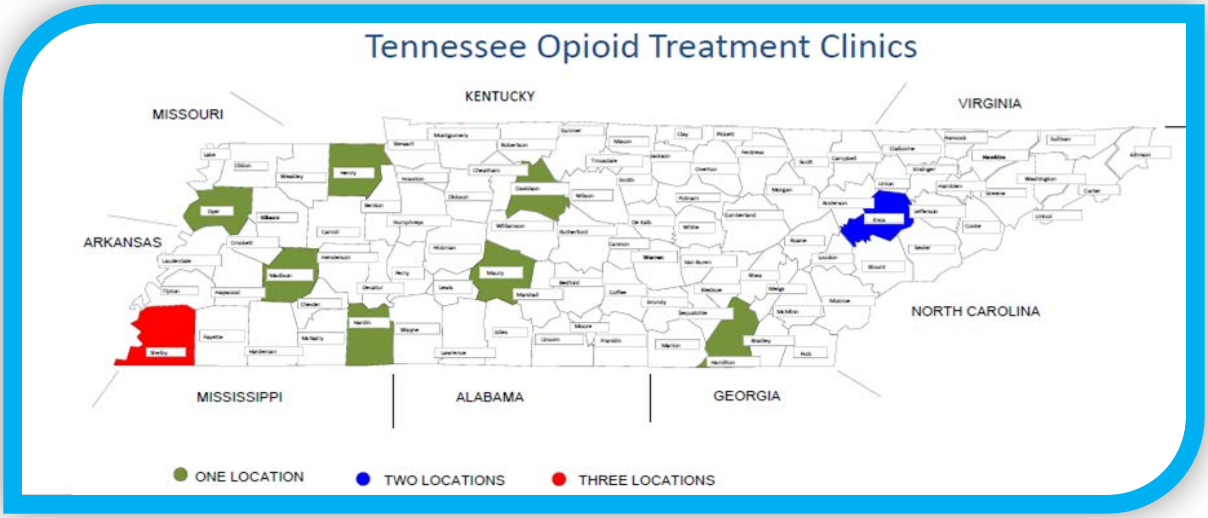
In general, research has shown that higher doses of methadone, i.e., greater than 60 mg, are associated with less heroin use during treatment, fewer withdrawal symptoms, better treatment retention and enhanced abstinence from cocaine (Fullerton et al., 2014; Thomas et al., 2014). MMT has its drawbacks too. The medication can be fatal in overdose and increase risk of severe liver disease if clients continue to use other substances such as alcohol, benzodiazepines, and barbiturates while on MMT. In addition, there is the potential for diversion to illicit trafficking, though there are very strict Federal and state regulatory requirements for OTPs and their clients (Douaihy et al., 2013).

Switching from methadone to another medication in the treatment of opioid use is not recommended unless the client is experiencing intolerable side effects or there is a lack of success in attaining or maintaining treatment goals. It is further recommended that clients switching to buprenorphine from methadone be on low methadone doses at the time of the switch, i.e., 30-40 mg per day or less. Otherwise the client may experience significant discomfort from the medication switch. Switching to oral naltrexone or the extended-release injectable from methadone requires that the client be completely withdrawn from methadone and/or other opioids (ASAM, 2015).

Compared to buprenorphine maintenance, MMT appears to be more effective in retaining people in treatment, particularly if the buprenorphine is prescribed in a flexible dose regimen or at a fixed and low dose (2 - 6 mg per day) (Mattick, Breen, Kimber, & Davoli, 2014). However, some studies have found MMT to be no more effective than nonmedical approaches such as NA over time. Results of one study showed that the MMT group did not differ from the NA group on key outcome variables, i.e., alcohol, barbiturate, and cocaine use or on retention rate. In addition, a substantial proportion in each group failed to return to their illicit substance use during treatment. The prevalence of benzodiazepine misuse and cigarette smoking, however, was lower in the MMT group than for the NA group. Nevertheless, results from this study support abstinence therapies rather than MAT in producing positive outcomes over the long term for persons with opioid use disorders (Khodabandeh et al., 2012).

Tennessee's Methadone Maintenance Treatment (MMT) Programs.

Effective April 1, 2008, TDMHSAS assumed oversight of the state's Opioid Treatment Programs (OTPs). These programs may also be referenced as "medication-assisted treatment" (MAT) programs. More specifically, OTPs were established to provide methadone maintenance therapy (MMT). The department's State Opioid Treatment Authority (SOTA) is responsible for providing medical, pharmaceutical, and administrative oversight to certified OTPs, including, but not limited to, development, education, planning, and implementation of policies and procedures to ensure that opioid addiction treatment is provided at an optimal level (TDMHSAS/SOTA, 2012). There have been only 12 OTPs in the state since April 17, 2014 (TDMHSAS/SOTA, n.d.). (See location map below.)



Source: Tennessee OTP Locations since April 17, 2014.

Persons seeking treatment at an OTP shall be evaluated by the medical director or program physician and clinical staff with appropriate qualifications. The evaluation is designed to determine whether opioid substitution or detoxification would be the most appropriate mode of treatment for the service recipient. Moreover, treatment must be documented as medically necessary. In the event the OTP has a waiting list and health of an expectant mother and/or her unborn baby is more at risk than the health of others waiting for services, pregnant women with substance dependency shall be given priority for admission and services (TDMHSAS, 2012).

Initial assessment must be completed within seven days of admission. It addresses a person's eligibility and need for treatment while also providing indicators for initial dosage level. Included in the initial assessment are:

- Physical examination.
- Relevant health history, specifically acute or chronic medical conditions.
- Personal and family mental health and medical history.
- Identification of currently prescribed medications.
- Personal and family history of substance use/misuse.
- Evaluation of other substances of use/misuse.
- Determination of other opioid dependence.
- Determination of during of addiction.

- Full toxicology screen.
- Tuberculosis screen.
-
- Screening test for syphilis.
- Other tests as appropriate, including HIV testing and EKG, e.g. (TDMHSAS, 2012).

Buprenorphine.

FDA approval of buprenorphine provided another evidence-based MAT option for people with opioid dependence and research findings are primarily favorable (Douaihy et al., 2013). Buprenorphine can be administered at OTPs like methadone but was approved to have administration provided by physicians in office-based settings (Chalk et al., 2013). As required by Federal law, physicians that prescribe buprenorphine must have special certification, meeting designated qualifying requirements, and additionally notify the Secretary of Health and Human Services of their intent to prescribe buprenorphine in the treatment of addiction to opiates. Once certified, the physicians must affix the unique identification number on every buprenorphine prescription they write. The physicians further receive a waiver from the Drug Enforcement Administration (DEA) to provide treatment for opioid dependence in their office for not more than 100 persons at a time (SAMHSA, n.d.). In 2016, the number of patients that can be treated with buprenorphine by certified physicians was increased to 275 in the third year. A waiver to that effect must have been requested and the physicians must have additional credentialing in addiction medicine or addiction psychiatry from a specialty medical board and/or professional society, or practice in a qualified setting as described in the rule (ATForum, 2016). The final rule will be effective as of August 8, 2016 (ASAM staff, 2016).

Buprenorphine is a long-acting (up to 48 hours), high-affinity, partial mu opioid agonist. Thus, it acts as a functional antagonist blocking the effects of pure mu agonists. Because it is a partial agonist, buprenorphine is safer in overdose. Its ceiling effect results in less respiratory depression. (Methadone, on the other hand, is a pure mu agonist.) Moreover, buprenorphine's euphoric effect is considered more diminished than methadone's, thereby making it less likely to be diverted (Douaihy et al., 2013). A partial opioid agonist, buprenorphine is available in both film and tablet formulations (Federation of State Medical Boards, 2013). Two forms were approved by the FDA in the treatment of opiate addiction in 2002, Subutex (buprenorphine hydrochloride) and Suboxone (buprenorphine combined with naloxone) (FDA, 2002; Partnership at Drugfree.org, 2002). These medications became the first medications approved under the Drug Abuse Treatment Act (DATA) of 2000 and for office-based treatment of opioid dependence in this country (Thomas et al., 2014). The "mono" product, buprenorphine alone (Subutex), might also be called "bup" or "buprenorphine mono-formulation (ONDCP, 2012) and has high abuse/diversion potential. As a consequence, the "mono" product should not be prescribed for unsupervised administration unless there are extenuating circumstances. The combination product, buprenorphine/naloxone (Suboxone), has minimal abuse potential. "Mono" and combination buprenorphine products can be administered sublingually (CMCS, 2014; FDA, 2002). Induction should start with a dose of two to four mg, with increases as needed in increments of two to four mg (ASAM, 2015). **The typical**

maintenance dose for Suboxone ranges from 12 mg to 16 mg. Doses higher than 16 mg may be useful on rare occasions but a thorough re-evaluation of the client's treatment needs would be required (Douaihy et al., 2013). Dosing based on reported substance use can be very helpful in targeting eventual final doses of buprenorphine (DVHA/VDH/ADAP, 2012). The table below presents suggested dosing targets;

Table 1. Suggested Guide for Dose Targets

Buprenorphine Doses	Oxycodone	Morphine	Heroin	Methadone
2 mg	30 mg	60 mg	1-2 bags	10 mg
4 mg	60 mg	120 mg	3 bags	20 mg
6 mg	90 mg	180 mg	4 bags	30 mg
8 mg	120 mg	240 mg	6 bags	40 mg
12 mg	180 mg	360 mg	8 bags	60 mg
16 mg	240 mg	480 mg	10 bags	80 mg

Source: DVHA/VDH/ADAP, 2012

As a partial agonist that is less potent than methadone, buprenorphine is further deemed as much safer when taken in the manner prescribed. Moreover, there are fewer side effects with buprenorphine compared to methadone (Chalk et al., 2013; The Partnership for Drugfree.org, 2002).

There are fewer side effects with buprenorphine compared to methadone (Chalk et al., 2013; The Partnership for Drugfree.org, 2002).

Generic forms of buprenorphine were approved by the FDA in 2013 (Chalk et al., 2013). If administered too soon after use of an opioid agonist, buprenorphine can exacerbate withdrawal symptoms. Administration should not occur until at least 12 hours following use of any short-acting opioids and 36 hours following use of methadone (Chalk et al., 2013). Due to the greater vulnerability of the tablet form to diversion and nonmedical use than the sublingual film, the patent-holding company submitted a request to the FDA to eliminate tablet formulations from the market (Federation of State Medical Boards, 2013).

On February 25, 2013, the first two generic versions of Suboxone (Bup/Nx) were approved by the FDA. Initially prices for the brand name and generics were not substantially different. However, prices were expected to drop as more competitors entered the market. The generic version of the sublingual tablets was marketed as Zubsolv. The generic film was marketed as Bunavail (NAABT, 2015). **Probuphine® was recently approved by the FDA on May 26, 2016**. Additional study was required because there were particular concerns about insertion and removal of the implant. As designed, the implant is the "first and only commercialized maintenance treatment for opioid dependence in individuals who have sustained clinical stability on low-to-moderate doses of buprenorphine, i.e., eight mg or less a day. The implants can only be provided by specially trained, certified healthcare providers. Probuphine® **has been available to patients since June 2016**. A six-month course of treatment will cost $4,950. However, the company says a payment assistance program will be put in place to ensure access to Probuphine®for patients (Braeburn Pharmaceuticals, 2016). Buprenorphine, currently available in sublingual tablet and oral formulations, had annual sales in 2012 in the U.S of about $1.5 billion (Poland, 2015). Production ceased for the brand name buprenorphine tablet formulation in March 2013 due to safety concerns related to possible pediatric ingestion of the tablets (Chalk et al., 2013).

Physicians that prescribe buprenorphine must complete special training in order to qualify for the Drug Enforcement Administration (DEA) prescribing waiver (Chalk, 2012; TBME, 2012). As of May 11, 2016, there were 400 physicians listed as certified to prescribe buprenorphine in the State. Physicians decide whether or not they want to be listed in the locator so the number is likely an underestimate. (See the Buprenorphine Physician & Treatment Program Locator at http://buprenorphine.samhsa.gov/bwns_locator/). Buprenorphine treatment programs are authorized under 21 United States Code (U.S.C.) Section 823 (g)(1) to dispense medications. The code gives no authorization to the programs for prescribing. Further, programs registered under 21 U.S.C. Section 823 (g)(1) are not subject to client limits (SAMHSA, n.d.).

A Federal rule change, effective January 7, 2013, modified the dispensing requirements of buprenorphine products for opioid dependence as used in Federally certified and registered opioid treatment programs (OTPs). The rule provides more flexibility in dispensing take-home products by removing restrictions on the time an individual needs to be in treatment in order to receive take-home supplies. OTPs will continue to adhere to all other Federal treatment standards established for methadone (Federal Register, 2012). Nevertheless, OTPs are still required to assess and document each patient's responsibility and stability to handle opioid drug products for unsupervised use. In addition, buprenorphine products may be prescribed to OTP patients by an OTP physician that has a DATA 2000 waiver as long as the physician adheres to his or her patient limits (SAMHSA, 2015).

Buprenorphine doses studied for opioid addiction treatment range from a low of 1–2 mg to as much as 16–32 mg, depending upon the formulation (solution versus tablet), with treatment duration lasting from a few weeks to years (SAMHSA/CSAT, 2004). Research shows that buprenorphine clients in outpatient settings stay in treatment longer (Chalk et al., 2013). When buprenorphine is prescribed at fixed doses (i.e., greater than seven mg per day), treatment retention or suppression of illicit opioid use was not different from methadone prescribed at fixed doses (i.e., 40 mg or more per day) (Mattick, Breen, Kimber, & Davoli, 2014). Moreover, buprenorphine clients experience more rapid resolution of withdrawal symptoms to persons treated through MMT (Chalk et al., 2013). Nevertheless, there is no difference in treatment completion or severity of withdrawal for persons treated with buprenorphine compared to MMT (Chalk et al., 2013). As an additional note, buprenorphine treatment, like methadone, has been recognized as an effective tool in increasing adherence to antiretroviral therapy in people with HIV/AIDS (World Health Organization [WHO], 2011).

Ideally, buprenorphine should be discontinued when an individual has achieved the maximum benefit from treatment and no longer requires continued treatment to maintain a substance-free lifestyle. However, discontinuation should be tapered rather than instituted abruptly. Abrupt discontinuation will result in withdrawal symptoms (SAMHSA/CSAT, 2004). Furthermore, individuals should be well-stabilized before honoring client requests to withdraw from the buprenorphine medication (DVHA/VDH/ADAP, 2012; Ling et al., 2009).

Ling et al. (2009) studied long and short tapers after buprenorphine stabilization on participant outcomes, as measured by opioid free urine tests at the end of each taper period. A long taper comprised 28 days while a short taper consisted of seven days. Data were collected at the end of weekly visits for services, and at one- and three-month follow-ups. Findings provided evidence that clients stabilized on a range of buprenorphine doses can be tapered successfully over seven days. This study indicates a lack of advantage in prolonging the buprenorphine tapering schedule for

weeks (DVHA/VDH/ADAP, 2012; Ling et al., 2009). Table 2 below displays a suggested buprenorphine taper regimen for a seven-day period of time.

Table 2. Suggested Buprenorphine 7-Day Taper Regimen

Stabilization Dose*		8 mg	16 mg	24 mg
Day				
1		8	16	24
2		6	12	20
3		6	10	17
4		4	8	12
5		4	4	8
6		2	2	4
7		2	2	2
8		0	0	0

Source*:* DVHA/VDH/ADAP, 2012

A study by Nielsen, Hillhouse, Thomas, Hasson, & Ling (2013) compared outcomes for users of prescription opioids (PO) versus users of heroin under taper conditions of seven or 28 days, with one- and three-month follow-ups, after buprenorphine stabilization. Results were consistent with the Ling et al. (2009) study. There appears to be no benefit in prolonging the taper period beyond seven days for either group of substance users. The greatest distinction between the groups seemed to be the dosages they were stabilized on. Users of PO tended to be stabilized on buprenorphine dosages not higher than 16 mg, whereas users of heroin tended to require 24 mg for stabilization.

If a patient on methadone wants to switch to buprenorphine, the methadone dose should be tapered to not more than 30 mg per day for a minimum of one week before initiating the buprenorphine induction treatment. The first dose of buprenorphine should be 2 mg of the monotherapy formulation and should not be received until at least 24 hours after the last methadone dose (SAMHSA/CSAT, 2004). No time delay is recommended when switching from buprenorphine to methadone. This switch involves the addition of a full mu opioid agonist to a partial agonist which typically does not result in adverse reactions. When switching to naltrexone from buprenorphine, a period of seven to 14 days should elapse between the last dose of buprenorphine and the start of naltrexone. This delay helps to ensure that the client is not physically dependent on opioids prior to starting naltrexone (ASAM, 2015).

Best practice says office-based treatment of opioid dependence requires prescribing of only FDA-approved medications. This means only buprenorphine/naloxone sublingual (s.l.) film, buprenorphine s.l. tablets, or monoproduct s.l. tablet. No other substances or buprenorphine formulations have been approved for this use. It is further not advisable to administer large prescriptions of buprenorphine/naloxone early in treatment. For example, it is not recommended to give more than a week at a time in the first months until the recipient has stabilized and stopped opioid and/or other substance use. Additionally, the recipient should have demonstrated regular treatment attendance and a check of the controlled substance database should confirm no other prescribers and no evidence of other controlled substance prescriptions (Sullivan, 2014).

Several researchers have further examined buprenorphine treatment outcomes across users of different types of opioids. Moore et al. (2007), e.g., compared outcomes among 200 clients who

reported exclusive use of heroin, use of heroin and prescription opioids, or strictly use of prescription opioids. Demographically, prescription-opioid-only users tended to be younger, have less years of opioid use, and less drug treatment history than heroin-only users. They were also likely to be white, less likely to have Hepatitis C, and have higher incomes. Compared to the heroin-only users, prescription-opioid-only users remained in treatment longer, had a higher percentage of opioid-negative urine samples, and were more likely to complete treatment than heroin-only users. Combination opioid users (heroin and prescription) demonstrated outcomes intermediate between the prescription-opioid-only and heroin-only users (Moore et al., 2007).

Buprenorphine has been shown to work well with pregnant women. Thomas et al. (2014) reviewed 16 adequately designed randomized controlled trials of buprenorphine maintenance treatment (BMT), in addition to seven meta-analyses. These researchers noted improved outcomes for individuals and pregnant women with opioid use disorders compared with placebo (Thomas et al., 2014). Breastfeeding can be considered in pregnant women treated with buprenorphine, depending on individual risk factors (Soyka, 2013).

Research comparing buprenorphine maintenance to tapering for treatment retention is also underway. Results of a randomized clinical trial carried out in primary care settings between February 2009 and February 2013 showed better treatment retention and reduced illegal use of opioids for maintenance versus the taper group. A larger proportion of opioid-positive urine samples were also provided by the taper group also provided (Fiellin et al., 2014). More positive results for buprenorphine tended to occur when there were comparisons to a placebo. Methadone appeared to be better suited over buprenorphine for clients with very severe addiction (Douaihy, 2013).

Effective July 1, 2015, Tennessee physicians were limited to prescribing buprenorphine solely for opioid use. They will no longer be able to prescribe the medication for pain management. The "mono" formulation of the medication, Subutex, was also limited to treatment of opioid dependence for pregnant and nursing women or individuals who have an adverse reaction to naloxone. A Good Samaritan provision establishing protections for individuals seeking emergency medical assistance in the event of a drug overdose from certain criminal drug charges was included in this law, known as the Addiction Treatment Act of 2015 (Kim, 2015).

Naltrexone.

Naltrexone was first developed as treatment for addiction to opioids in 1984. It works by displacing any opioids from a user's opioid receptors and then tightly binding to those receptors for an extended period of time, which makes the receptors unavailable for activation by any self-administered opioid such as heroin (Chalk et al., 2013). To begin naltrexone treatments, however, individuals must have instituted a period of abstinence from opioid use. If a patient has failed to abstain from all opioid use (legal and/or illicit) for a period between seven and 10 days, , administration of naltrexone will produce immediate opioid withdrawal (Chalk et al., 2013; SAMHSA, 2012a). Naltrexone can be taken as a once-a-month injection given in a physician's office or orally in tablets (CMCS, 2014). When taken at a stable dose following detoxification, individuals will no longer experience euphoric effects from use of opioids such as heroin or prescription drugs (Chalk et al., 2013). Naltrexone does not imitate the effects of opioids (ONDCP, 2012). People are less likely to drop out of treatment with naltrexone when there are powerful external motivators, such as the likelihood of losing an important job, upon which adherence is contingent. Having

family members involved in monitoring adherence is also very helpful The medication seems to be particularly useful for highly motivated individuals that have appropriately detoxed and desire a faster detoxification schedule or need additional support to avoid relapse (Chalk et al., 2013).

Any switching to methadone or buprenorphine should be planned, considered, and monitored. The switching process should not be complicated but a time delay is required. It is recommended that clients on oral naltrexone wait a single day prior to switching and those receiving the extended-release formulation not to switch for 30 days (ASAM, 2015).

Drug interactions have been reported when naltrexone is used in conjunction with other medications. For example, the side effects of somnolence and lethargy have been reported when naltrexone is used with some antipsychotic medications such as thioridazine or chlorpromazine. Naltrexone has not been approved by the FDA for treatment of opioid dependency in persons younger than 18 years of age (Chalk et al., 2013).

Caution should further be taken regarding use of naltrexone with pregnant women, breast-feeding women, or women who become pregnant while on naltrexone therapy. Naltrexone is classified as a B3 risk in pregnancy which means that its effects on the fetus are not known. Either animal studies have not shown a clear risk or no adequate, well-controlled studies have been conducted involving pregnant women. Caution is also recommended when the person using opioids is a polydrug user or has depression or other major psychiatric illness (Chalk et al., 2013).

Oral Naltrexone.

Oral naltrexone, approved by the United States Food and Drug Administration (FDA) in the treatment of opioid addiction in 1984, binds to opioid receptors in the body for 24-30 hours (Chalk et al., 2013). A seven to 10-day abstinence period is required prior to beginning naltrexone therapy, to avert withdrawal, relapse, or early dropout. After detoxification (i.e., withdrawal management) has been accomplished or established, stable doses of naltrexone can be administered. Neither withdrawal symptoms nor abuse potential is associated with naltrexone use. The medication has no narcotic effect. Tolerance has been tested and results showed negative even after many months of regular use. Naltrexone is sold under one of the following trade names: Depade®, Trexan®, and Revia® (Chalk et al., 2013; Tetrault & Fiellin, 2012).

While effective, use of this form of naltrexone is plagued by the fact that many clients fail to adhere to the treatment regimen. Research has shown that 50 to 70 percent of persons prescribed oral naltrexone discontinues use (Chalk et al., 2013).

Because Naltrexone blocks the effects of opioids, it is sometimes prescribed for 12 months for those trying to manage drug dependence (about.com, 2014). Its administration is not linked to the development of dependence or tolerance (Drugs.com, 2005). Supplied in 25, 50, and 100 mg tablets (SAMHSA/CSAT, 2005), research indicates that 50 mg of Naltrexone will block the pharmacologic effects of 25 mg of intravenously administered heroin for up to 24 hours. Additional data have suggested that doubling the Naltrexone dose provides blockade for 48 hours and that tripling the dose provides blockade for about 72 hours. A flexible approach to a dosing regimen has been suggested in an effort to enhance adherence. For example, patients may receive 50 mg every weekday and a 100 mg dose on Saturday or they may receive 100 mg every other day, or 150 mg every third day. Several studies have employed the following dosing regimen: 100 mg on Monday,

100 mg on Wednesday, and 150 mg on Friday. This dosing schedule has been shown to be acceptable to many patients striving to maintain their opioid-free state successfully (Drugs.com, 2014). This dosage regimen is recommended in the ASAM Guideline as well (ASAM, 2015).

There have been many trials of oral naltrexone in the treatment of opioid dependence and results show elimination of opioid use among those who adhere to the medication. However, adherence to or outright discontinuation of oral naltrexone is a big problem. Research shows 50-70 percent of persons that have been prescribed oral naltrexone for opioid dependence either discontinue using it or fail to take it as prescribed. Adherence is extremely important because the blocking action of oral naltrexone lasts no longer than 24-36 hours, on average. Thus, a missed dose may result in relapse, which would require new detoxification and naltrexone induction. It is believed that the seven to 10-day abstinence-from-opioid-use requirement prior to beginning naltrexone induction contributes to the poor adherence and early drop out (Chalk et al., 2013). Nevertheless, oral naltrexone has shown to be particularly useful when motivation to abstain is high. It works very well for patients who are closely monitored and have much to lose from being exposed as having relapsed to opiate use (Minozzi et al., 2011). Successful candidates have included medical professionals, other persons with their employment in jeopardy, and people in the criminal justice system, (Kjome & Moeller, 2011). The medication is reported to be of greatest use for persons who take the drug as part of a comprehensive occupational rehabilitative program, behavioral contract, or other compliance-enhancing protocol. While Naltrexone will not reinforce medication adherence, it is expected to have a therapeutic effect when given under external conditions that support continued use of the medication (Drugs.com, 2014).

Successful candidates for oral naltrexone have included medical professionals, other persons with their employment in jeopardy, and people in the criminal justice system (Kjome & Moeller, 2011).

Extended-Release Injectable Form (Vivitrol).

Unlike the oral naltrexone, buprenorphine, and methadone, the extended-release injectable form of naltrexone (Vivitrol) allows people addicted to opioids to take the effective medication once a month versus every day. It was approved in October 2010 by the FDA for treating individuals dependent on opioids. Research supports its effectiveness, producing equally significant reductions in the use of opioids throughout a full month's injection period. In addition, research shows that between 35 to 50 percent of Vivitrol users voluntarily return for their continued monthly injections (Chalk et al., 2013). Vivitrol has shown to be more effective when provided in conjunction with behavioral therapies and social supports (SAMHSA, 2012a).

In addition to having a different frequency of administration, extended-release injectable naltrexone (Vivitrol) has a different route of administration, different restrictions on prescribing/dispensing, different abuse and diversion potential, and no additional requirements, compared to methadone and buprenorphine. This form of naltrexone binds to opioid receptors for up to 30 days (Chalk et al., 2013).

Vivitrol is administered monthly instead of daily like buprenorphine and methadone. Moreover, the drug is injected intramuscularly by an appropriate health care professional, i.e., any person who is licensed to prescribe medicine (SAMHSA, 2012a). It is recommended that injections be

administered in alternating buttocks over the course of treatment. Missed doses should be administered as soon as possible (Krupitsky, 2012). Unlike buprenorphine and methadone, Vivitrol is not an opioid and does not have abuse potential (SAMHSA, 2012a). It is a long-acting form of naltrexone that blocks opioids (Rubin, 2010).

Because Naltrexone displaces the opioids of abuse by binding to those receptors, complete detoxification from opioids is required in advance of initiating or resuming treatment with the extended-release injectable.

Otherwise, the individual will likely go through intense withdrawal. A minimum of seven to 10 days without opioid use is recommended prior to beginning extended-release injectable naltrexone (Vivitrol) (Krupitsky, 2012; SAMHSA, 2012a).

Because Naltrexone displaces the opioids of abuse by binding to those receptors, complete detoxification from opioids is required in advance of initiating or resuming treatment with the extended-release injectable (Krupitsky, 2012, e.g.).

The standard dosage is 380 mg and is not affected by age, weight, or other factors (ASAM, 2015; SAMHSA, 2012a). This means that a 60 year old and a 30 year old would receive the same dosage, e.g. The FDA has not yet approved the use of Vivitrol for persons younger than the age of 18 (SAMHSA, 2012a). It may be possible that clients taking the oral form of naltrexone want to switch to the injection. The writer did not locate any systematically collected data that specifically addressed this issue or whether precautions should be taken (Vivitrol.com, 2013).

A study using claims data from a large health plan in this country examined benefits of extended-release naltrexone in comparison to other medications for opioid dependence. The analysis focused on six-month medication persistence, health care utilization, opioid-related and nonrelated inpatient admissions, detoxification and rehabilitation, outpatient services, and total costs. Total healthcare costs for extended-release naltrexone were not significantly different from buprenorphine or oral naltrexone and were 49 percent lower than for methadone, despite the higher pharmacy costs for this medication. Further, patients treated with extended-release naltrexone further had fewer opioid-related and nonopioid-related hospitalizations, compared to patients receiving any of the FDA-approved oral medications for opioid dependence (Baser, Chalk, Fiellin, & Gastfriend, 2011).

People in the following categories have been deemed good candidates for the extended release injectable form of naltrexone.

- Failed in their methadone or buprenorphine treatment.
- Reported or demonstrated a high level of motivation to achieve and maintain abstinence from opioids.
- Presented with brief and/or less severe history of dependence on opioids.
- Currently facing periods of intense relapse risk into opioid dependence including greatly increased stress.

- Indicated a preference to receive treatment for opioid dependence in an office-based, primary care setting rather than in treatment centers or specialty clinics.

- Expressed desire to reduce the amount of time spent going to daily visits at an OTP (SAMHSA, 2012a).

Precautions.

Physicians should educate clients who are being treated with medications containing naltrexone. In particular, physicians should provide information about mortality risks that exist during and upon discharge from treatment for opioid dependence. Behavioral health professionals and other social supports, such as family and friends, have an important role in reminding individuals in treatment of these risks as well. In general, persons treated with extended-release injectable naltrexone should:

- Wear medical alert jewelry or carry some form of identification so emergency personnel can provide safe and appropriate care involving pain management when the client is unconscious or cannot otherwise communicate (SAMHSA, 2012a).

- *NOT* take naltrexone if they are female and are breast feeding or pregnant (SAMHSA, 2012b).

- Take necessary precautions with naltrexone in the home. Keep it locked in a safe place at all times to prevent its accidental use by others, especially children (SAMHSA, 2012b).

- *NOT* use other opioid medications when taking naltrexone. Naltrexone blocks the effects of opioids, thus preventing those medications from working (SAMHSA, 2012b).

- *NOT* use alcohol, illicit drugs, or drugs that slow breathing while taking naltrexone. The combination of naltrexone and other substances, especially when taken in large amounts, can result in death or overdose (SAMHSA, 2012b).

There are 18 states that require documentation of the use of injectable naltrexone and 20 states plus the District of Columbia that require documentation of behavioral therapy with buprenorphine-naloxone use. It is recommended that care be taken in ensuring that such requirements are not unduly burdensome and consequently limit appropriate access to pharmacotherapy as an effective treatment for opioid use and other substance use disorders (CMCS, 2014).

Barriers to Medication-Assisted Treatment (MAT)

The continued negative health outcomes stemming from alcohol and nicotine use, in addition to the dramatic increase in heroin and other opioid-related overdoses point to the need for greater access to substance use treatment medications. Moreover, MAT for SUDs has proven to be cost effective,

clinically effective, and to significantly reduce use of detoxification and in-client services. Yet medication-assisted treatment (MAT) is underutilized and access remains limited. A 2011 study found fewer than 30 percent of contemporary substance use treatment programs offer medications and less than 50 percent of eligible clients in the programs actually receive medications (SAMHSA-HRSA/CIHS, 2014). Among the factors identified as contributors to the low use of MAT options include:

- Agency regulatory policy that forbids or restricts the use of MAT;
- "Fail first" criteria that requires trial of other therapies first;
- Lack of available prescribers;
- Lack of support for existing prescribers;
- Limits on prescribed dosages;
- Minimal coverage for counseling; and
- Workforce misunderstandings and attitudes about the nature and use of medications in substance use treatment (SAMHSA-HRSA/CIHS, 2014).

Financing and reimbursement barriers at the state level have also been identified. A small three state, six-site pilot project facilitated development of several solutions and policy opportunities (SAMHSA-HRSA/CIHS, 2014).

Research has shown limited adoption of MAT by SUD treatment organizations, particularly in programs that rely heavily on governmental sources of funding. This finding suggests that clients in publicly funded substance-use treatment settings are less likely to have access to evidence-based programs (EBPs) relative to those receiving care from privately financed systems (Knudsen, Abraham, & Oser, 2011).

Conclusion

Abstinence from substance use disorders (SUDs) can be very challenging and MATs can help. MATs are proven evidence-based practices in the treatment of substance use disorders (SUDs) that assist in weaning people off their substances of use/misuse and make the withdrawal process more tolerable. These medications tend to suppress the user's desire to use while, in most cases, still providing a euphoric effect. Similar to most medications, MATs have a long list of potential side effects and present dangers if they are not properly used. Further, they can become a crutch for the user; several of the medications have abuse potential. Equally important, MATs treat only part of the problem. They do not address the traumatic or emotional issues that may have led to the substance use/misuse in the first place. MATs are supposed to be accompanied by counseling and recommendations for attendance at mutual help groups such as NA. Unfortunately, many patients fail to adhere to the counseling/self-help component of MAT (Camp, 2015).

The highest levels of use of medication-assisted treatments have been reported by privately funded treatment programs. As expected, the lowest levels of adoption of MAT protocols were demonstrated in publicly funded programs (Roman et al., 2011).

Psychosocial Treatments

Evidence-based (EB) psychological treatments exist for treating some substance use disorders (SUDs). Treatments are defined as EB based on criteria outlined by Chambless et al. (1998) according to criteria requiring treatments to be efficacious in randomized controlled trials (RCTs) or their logical equivalents. Only studies based on RCTs or their logical equivalents afforded strong causal inferences. Criteria to support the research of identified treatments are shown below:

Status	Criteria
Strong	Support from two well-designed studies conducted by independent investigators
Modest	Support from one well-designed study or several adequately designed studies
Controversial	Conflicting results, or claims regarding mechanisms are unsupported

Source: APA/Div12, 2016.

EB treatments have been found to be effective for dependence on the following substances:

For Use of Mixed Substances

Motivational Interviewing (strong research support) – Motivational Interviewing (MI) is a brief person-centered clinical method for strengthening clients' motivation for and commitment to change. It is particularly indicated for clients who are ambivalent, reluctant, or defensive about change. Strongly rooted in the work of Carl Rogers, the overall spirit of MI is collaborative and empathic. It typically involves one to four sessions. Rather than working from a deficit model in which the therapist provides what the client is missing (e.g., skills, insight, knowledge), MI seeks to evoke the client's own strengths, motivations, and resources. In MI, particular attention is paid to specific aspects of client speech that predict subsequent change. The therapist elicits and explores the client's own reasons for change within an atmosphere of acceptance to minimize resistance and defensiveness.

MI therapists use diverse strategies to evoke and strengthen clients' "change talk." There are specific guidelines for deciding what questions to ask, and what content to reflect and summarize. Studies have demonstrated that therapists adhering to MI-consistent skills are able to significantly increase client change talk, which in turn predicts behavior change outcomes. Therapists learning MI typically begin by developing a strong foundation of client-centered counseling skills (reflective listening, open questions, affirmation, summaries), and then learn to identify, evoke, and strengthen client change talk using these skills strategically (APA/Div12, 2016).

Motivational Enhancement Therapy (MET) (strong research support) – Motivational Enhancement Therapy (MET) employs motivational interviewing along with assessment and personalized feedback. It has been observed to be particularly helpful for less-ready clients, where the initial task is to develop ambivalence about change. It is designed to help the individuals resolve ambivalence regarding his or her use of substances. Identification and alteration of thoughts and behaviors that promote the substance use is the focus of cognitive-behavioral coping skills therapy. The person is educated about the model, collaborating with the therapist to identify and use different thoughts and behaviors and using role-plays and behavioral rehearsals. Homework opportunities are typically provided through this model as well. The community reinforcement approach is a comprehensive cognitive-behavioral approach that focuses on aspects of the person's environment that either supports or hinders his or her substance use. Many techniques are incorporated including teaching new coping skills, involving significant others, and conducting a functional analysis of the substance use. These techniques are designed to assist the individual in creating a reinforcing sober lifestyle (APA/Div12, 2016; Borsari et al., 2011).

MET plus Cognitive Behavior Therapy (strong research support) – Motivational Enhancement Therapy (MET)/Cognitive-Behavioral Therapy (CBT). Initial sessions employ MET in an effort to elicit intrinsic motivation to change substance use/misuse by resolving the person's ambivalence. The CBT component follows, focusing on helping the individual to become abstinent (Chambers et al., 2013). Based on the notion that thoughts cause behaviors and determine the way in which people perceive, interpret, and assign meaning to their environment, the CBT component encourages individuals to examine the pros and cons of their use/use and to create goals that will help them achieve a healthier lifestyle (APA/Div12, 2016; Winters, Botzet, & Fahnhors, 2011).

Prize-Based Contingency Management (strong research support) – The Contingency Management (CM) component is a structured behavioral therapy that involves frequently monitoring the behavior targeted for change, then reinforcing the behavior each time it occurs using tangible, escalating reinforcers. Drug use behavior is typically the behavior targeted for change, but other behaviors such as treatment attendance can also be reinforced. Individuals are reinforced for submitting drug negative urine samples or attending treatment by earning the chance to win prizes ranging from $1 to $100 in value—hence, the prize-based component. Chances to win prizes increase with sustained abstinence or attendance.

Generally CM treatments are in effect for 8-24 weeks and provided as an adjunct to other treatment. It can be integrated with virtually any form of therapy, including CBT, community reinforcement approach therapy, eclectic/standard group treatment, 12-step therapy, motivational enhancement therapy, to name a few. For reinforcement of abstinence, the best outcomes of CM are typically achieved if abstinence from a single drug is reinforced, if onsite urine testing monitoring is conducted at least twice weekly, and if reinforcement magnitude is high. The purpose of the prize CM system is to enhance patient outcomes while minimizing reinforcement and administrative costs (APA/Div12, 2016).

Seeking Safety (strong research support for adults, modest research support for adolescents) – A present-focused, coping skills therapy to help people attain safety from trauma/PTSD and SUD, Seeking Safety (SS) embodies compassionate tone that honors what clients have survived and respects their strengths. It is a first-stage model that can be used at the start of treatment. There are five key principles of SS are: 1) Safety is the overarching goal; 2) Integrated treatment; 3) Focus on ideals (counteracts the loss of ideals in both substance use and trauma); 4) Four content areas: behavioral, cognitive, interpersonal, and case management; and 5) Attention to clinician processes.

There are 25 treatment topics, each with a clinician guide and client handouts. Designed to be flexible in use, the topics can be conducted in any order and number and pacing/length of sessions can be determined by the clinician. Among the topics are Safety, Asking for Help, Healthy Relationships, Red and Green Flags, Setting Boundaries in Relationships, and Taking Good Care of Yourself.

SS can be used with a broad range of vulnerable populations, including those who are severe and chronic, adolescents, military personnel/veterans, criminal justice, homeless, domestic violence, racially/ethnically diverse, mild traumatic brain injury or other cognitive impairment, serious and persistent mental illness, low-reading or illiterate clients, and others. It can further be conducted by a broad range of clinicians. SS was designed for flexible use and can be implemented at low cost (APA/Div12, 2016).

Friends Care (modest research support) – Friends Care (FC) is a six-month aftercare program that should be implemented in stand-alone community facilities. Persons exiting SU treatment programs are contacted up to one month prior to planned discharge to orient them to FC, introduce them to aftercare staff with whom they will be working, and jointly develop preliminary aftercare plans. Services are offered by counselors under the direction of a supervisory case manager, with emphasis placed upon building community supports to drug-free living. At least some of the following services are provided at a frequency specified in the aftercare plan: a) supportive counseling with review and strengthening of risk reduction behaviors/prosocial functioning; b) case management services including skills building for obtaining needed resources; c) work with client's significant other/relevant family; d) obtaining/maintaining employment through skills building in job finding/workplace demeanor; e) affiliation with supportive community organizations/groups; f) review of HIV prevention behaviors; and g) crisis intervention. Guidance is available in the detailed implementation manual.

Guided Self-Change (modest research support) – Guided Self-Change (GSC) Treatment for substance use disorders integrates motivational interviewing, relapse prevention techniques, and cognitive-behavioral to help individuals functionally analyze their alcohol or other drug problems and develop plans of their own for changing. It has been evaluated in English and Spanish, and can be delivered in individual or group formats. GSC is especially applicable for persons whose alcohol or drug problems are not severe. Materials can be downloaded and/or printed from the GSC Web site at http://www.nova.edu/gsc/online_files.html. Among the available materials are therapist and client handouts, clinical tips and tools, client homework assignments, other clinical/motivational handouts and forms, and Timeline Followback (TLFB) forms (APA/Div12, 2016).

For Alcohol Use

Behavioral Couples Therapy for Alcohol Use Disorders (strong research support) – Behavioral Couples Therapy for Alcohol use Disorders, also known as ABCT, is an outpatient treatment for people with AUDs and their intimate partners. It is based on four assumptions—1) intimate partner behaviors/couple interactions can be triggers for drinking; 2) intimate partners can reward abstinence; 3) positive intimate relationships are keys to motivation to change drinking behavior; and 4) reducing distress in relationships lessens risk for relapse. Using CBT, the therapist works with the person who is abusing alcohol and his/her partner to: identify and reduce the partner's behaviors that cue or reinforce the drinking; strengthen the partner's support of efforts of the person's efforts to change through reinforcement of positive change and use of sobriety contracts; increase positive

couple interactions through activities and assignments designed to increase positive feelings and improve constructive communication and problem-solving; and improve person's coping skills and relapse prevention techniques to achieve and maintain abstinence.

The treatment program consists of 2-3 hours of assessment for treatment planning, followed by 12-20 weekly therapy sessions for the person who is drinking along with his/her partner. Treatment follows cognitive-behavioral principles applied to couples therapy and specific therapeutic interventions for AUDs. A typical session follows this sequence:

1) Therapist asks about any drinking since the last session;

2) Couple presents and discusses homework assigned at the last session and use of a sobriety contract, if applicable;

3) Couple discusses any drinking or relational problems since the last session;

4) Therapist presents new material and couple engages in active learning activities in the session related to the new material;

5) Couple discusses upcoming high risk situations; and

6) Therapist assigns new homework.

Optimal implementation of ABCT occurs in the context of an existing clinic or private practice with certified/licensed behavioral health professionals who have a background in treating AUDs and knowledge of CBT (APA/Div12, 2016).

Moderate Drinking (very strong research support) - Moderate Drinking (MD) involves a Web application based on principles of behavioral self-control training. It is an interactive, individualized program that guides people to set goals, self-monitor their behavior, and get detailed feedback on their progress based on their input. However, there is an element of structure. MD modules address motivation, identifying and managing triggers, developing alternatives, problem solving, dealing with lapses and relapses, considering abstinence, and self-monitoring one's mood. The program recommends first choosing a goal (abstinence or moderation), building motivation for change, "doing a 30" (a self-imposed and flexible period of abstinence that can range from 1-30 days), setting drinking goals/limits, and then self-monitoring the drinking. Individuals are asked to enter their self-monitoring data when they log back onto the site, which the program then uses to generate detailed feedback about their progress. It is recommended that people go through the modules in sequence, but its flexibility allows the choosing of which modules might best meet their needs (APA/Div12, 2016).

Prize-Based Contingency Management (modest research support) – See description under "Mixed Substances" above.

For Cocaine Use

Prize-Based Contingency Management (modest research support) – See description under "Mixed Substances" above.

It should be noted that other psychological treatments may also be effective in treating cocaine dependence, but they have not been evaluated with the same scientific rigor as the treatment above.

For Tobacco Use

Smoking Cessation with Weight Gain Prevention (modest research support) – The Smoking Cessation with Weight Gain Prevention program is a cognitive behavioral treatment that fosters tobacco cessation along with weight management. It was designed for smokers who express some reluctance to quit because of concern about gaining weight. Treatment focuses on smoking cessation first, followed by weight control. Using this sequential form of intervention has been found to produce a rate of smoking cessation comparable to treatment for tobacco alone, but with less weight gain. Both the cessation and weight management components incorporate cognitive behavioral elements and are typically provided in a group format. The weight management component also includes meal replacements and physical activity (APA/Div12, 2016).

As for cocaine dependence, other psychological treatments may also be effective in the treatment of tobacco use. Such treatments, however, have not been evaluated with the same scientific rigor as the treatment mentioned above.

For Co-Occurring Disorders

There are six evidence-based practices (EBPs) described in the "Integrated Dual Disorders Treatment Implementation Resource Kit", with *integrated dual disorders treatment* (IDDT) identified as the EBP for co–existing substance use and mental illness (SAMHSA, 2013). An intensive approach, the SAMHSA-endorsed IDDT model features 26 domains. Persons receiving IDDT have a multidisciplinary team comprised of a dual diagnosis clinician and at least two of the following: physician, nurse, case manager, providers of ancillary rehabilitation services such as supportive housing, vocational, etc. A substance use specialist with a minimum of two years of experience should work collaboratively with this team as well. Any interventions (including the ancillary rehabilitation services) must be consistent with and determined by the individual's stage of treatment/recovery. Thus, it must be determined if the individual is in the engagement, persuasion, active treatment, or maintenance/relapse prevention stage of recovery.

Treatment should be provided for as long as necessary, with intensity modified according to need and degree of recovery. Interactions must be based on MI and include expressing empathy, developing discrepancy between goals/continued use, avoiding arguments, rolling with resistance, and supporting hope/self-efficacy. If the person is in the action or relapse prevention stage of recovery, substance use counseling should focus on:

- How to manage cues to use/consequences of use;

- Relapse prevention strategies;
- Alcohol and drug refusal skills;
- Problem-solving skills training;
- Challenging beliefs about substance use; and
- Social skills training and coping skills

Persons in those stages should further be connected to community self-help groups such as AA, NA, etc. While counseling can be provided in different forms and formats, individuals should be offered group treatment specifically designed to address the co-occurring substance use and mental health problems. Significant others should be involved, to the extent possible. Efforts should also be made to enhance the person's health, e.g., encouraging him/her to practice proper diet and exercise or find safe housing (Improving MI Practices.org, n.d.).

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