Chapter 16. Tobacco Use Disorder

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SECTION QUICK LINKS

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Tobacco use continues to be a leading cause for increased medical morbidity and mortality in the United States and throughout the world. Use of tobacco commonly begins in adolescence and often rapidly progresses to a nicotine use disorder. Cigarettes are the most common tobacco product; however, many other alternative tobacco products have become popular, including electronic cigarettes and smokeless oral tobacco. In the United States, individuals with mental illness and substance use disorders disproportionately consume 44% of all the cigarettes, likely contributing to significant health disparities in this subgroup (Lasser et al. 2000). To help smokers quit, there are medication options, evidence-based psychosocial treatments, and extensive national and community resources.

Tobacco use disorder is a common comorbidity witnessed by all health care providers in all health care systems. System-based and public health approaches, such as tobacco-free campuses and electronic record prompts, help agencies to implement evidence-based psychosocial and pharmacological treatments (Centers for Disease Control and Prevention 2013).

Prevalence of Tobacco Use

In the United States, nearly one in every five persons (19% or 43.8 million) 18 years or older is a smoker, and rates have not substantially changed since 2005 (20.9%) (Centers for Disease Control and Prevention 2012). The way people smoke, however, has changed, in part because of tobacco control policies, such as workplace smoking bans, excise cigarette taxes, and the denormalization of smoking. Among smokers, the percentage of "heavy" smokers (i.e., those smoking more than 30 cigarettes per day) decreased from 12.6% in 2005 to 9.1% in 2011, while the percentage of daily smokers who smoke between 1 and 9 cigarettes per day increased from 16.4% to 22% (Centers for Disease Control and Prevention 2012). A growing trend is to smoke only on "some days" or "nondaily" versus "daily." Between 21% and 33% of all adult smokers can be considered nondaily, intermittent smokers, and this pattern, along with use of alternative tobacco products (e.g., smokeless tobacco, water pipe or hookah, electronic cigarettes), is expected to continue (Centers for Disease Control and Prevention 2012; Shiffman 2009).

Cigarette smoking rates vary substantially across subpopulations. Smoking, for example, is more common among men than among women (21.6% vs. 16.5%; Centers for Disease Control and Prevention 2012). Compared with the general population, smoking rates tend to be lowest (7.9%) among individuals 65 and older, likely because of premature death (Centers for Disease Control and Prevention 2012). Among racial/ethnic populations, American Indians/Alaska Natives have the highest prevalence (31.5%), followed by non-Hispanic whites (20.6%) and non-Hispanic blacks (19.4%). Hispanics (12.9%) and Asians (9.9%) have the lowest prevalence of cigarette use (Cokkinides et al. 2012).

Among youths, cigarette use in the past 30 days ranges from 5.2% among middle school students to 18.1% among high school students, with more male (19.9%) than female (16.1%) smokers. Among youths, the prevalence rate among non-Hispanic Caucasians is highest (20.3%), followed by Hispanics (17.5%) and then non-Hispanic blacks (10.5%) (Centers for Disease Control and Prevention 2012).

Smokeless tobacco (e.g., snuff and chew) rates in the United States among those 12 years and older remained stable between 2002 and 2007 at about 3%–4%. Use of these smokeless products is more common among high school students (6.7%) and Native Americans (9.8%). Most smokeless tobacco users (about 85%) also smoke cigarettes at some point in their lives, and 40% currently use both (Substance Abuse and Mental Health Services Administration 2009). Alternative tobacco products are also increasingly available. Tobacco sticks, strips, or orbs, as well as hookah bar smoking through flavored water, are designed to appeal to young consumers, and advertising subtly implies that they can be used to help quit smoking. The fastest growing newer tobacco products are the Electronic Nicotine Delivery Devices (ENDS), also known as electronic cigarettes or e-cigarettes, which were being used by 2.7% of adults in 2010 (Regan et al. 2013) and increased to 8.1% of adults in 2012 (Zhu et al. 2013).

Health Consequences of Tobacco Use

About 50% of smokers die of a tobacco-caused disease. Compared with nonsmokers, premature mortality risk is significantly higher even in people who smoke as few as one to four cigarettes

per day (Bjartveit and Tverdal 2009). Cardiovascular, pulmonary, and oncological diseases are the leading causes of death (U.S. Department of Health and Human Services 2010). Other associated conditions include cataracts, premature aging of skin, gum disease, postoperative infections, hip fractures, and possibly spontaneous abortion, sudden infant death syndrome, and childhood asthma (U.S. Department of Health and Human Services 2004). Smokeless tobacco is linked to tooth decay, tooth loss, gum disease, high blood pressure, cardiovascular disease, and cancers of the mouth, larynx, and pharynx (World Health Organization 2007).

Benefits of Cessation

Smokers who quit reduce their risk of premature death and receive cardiac and pulmonary benefits within days or weeks of quitting (U.S. Department of Health and Human Services 1990). They perceive improved quality of life, feeling of vitality, and ability to perform the tasks of daily living. They have financial savings from cigarettes, increased employment options, fewer restrictions at work, fewer missed days and increased productivity at work, more relationship options, fresher breath and enhanced ability to taste foods, and more freedom in public settings (American Psychiatric Association 2006; Fiore et al. 2008; Ziedonis et al. 2006).

Pharmacokinetics of Nicotine

Tobacco smoke enters the lungs and is quickly absorbed into the arterial system, and nicotine enters the brain within 7–15 seconds after inhalation. Nicotine precipitates the release of several neurotransmitters within the midbrain or reward pathway. As nicotine is distributed to other bodily tissues, blood concentrations in the brain rapidly begin to decline. With this decrease in nicotine levels, symptoms of cravings may emerge in dependent smokers in as little as 20–30 minutes after smoking a cigarette. Because smoking provides symptomatic relief, a vicious cycle is created and dependence on nicotine is maintained.

The metabolism of nicotine takes place mainly in the liver, where the primary active by-product, cotinine, is further metabolized to trans-3′-hydroxycotinine. Nicotine is metabolized quickly and has a half-life of about 2 hours. Cotinine can be detected in the urine, saliva, and blood for about 7–14 days. Breath carbon monoxide level is used as a surrogate measure for tobacco use when individuals smoke cigarettes, and exhaled carbon monoxide levels correlate with cotinine levels (American Psychiatric Association 2006). Variability in the rate of nicotine and cotinine metabolism occurs across individuals in part because of gender, racial, and ethnic differences. For instance, the rate of nicotine metabolism is faster among women. Compared with individuals of Asian and African American descent, those of Caucasian and Hispanic descent metabolize nicotine at a slower rate (Pérez-Stable and Benowitz 2011). Metabolism rates correlate positively with the risk for a nicotine use disorder, and fast metabolizers may be more vulnerable to certain cancers (Pérez-Stable and Benowitz 2011).

Neurobiology of Nicotine

Studies of the neurobiology of nicotine have focused on the mesolimbic reward circuitry in the midbrain of the central nervous system (CNS) (Kenny and Markou 2006). Within this pathway, dopaminergic neurons originating in the ventral tegmental area project to the nucleus accumbens and prefrontal cortex, in addition to other regions. Acutely, nicotine, like most drugs of abuse, increases release of dopamine in the nucleus accumbens, and this phenomenon is associated with reward or reinforcement. Negative mood symptoms are associated with low dopamine activity in the reward circuit of the CNS, a condition that arises when nicotine administration is stopped in animals physically dependent on nicotine; the same processes are believed to operate to cause the negative mood symptoms in humans that are associated with the nicotine withdrawal syndrome. Nicotine withdrawal includes symptoms of cravings, difficulty sleeping, irritability, moodiness/anxiety, restlessness, decreased heart rate, and difficulty concentrating. Several other neurotransmitters have been implicated in the rewarding effects of nicotine, including glutamate, acetylcholine, and γ-aminobutyric acid. The ventral tegmental area receives input from many brain regions by all three of these neurotransmitters, suggesting that this area of the brain serves as a final common pathway for nicotine reward and vulnerability to a nicotine use disorder. Although nicotine initially stimulates the reward circuitry of the brain, chronic nicotine exposure may lower stress tolerance by sensitizing brain structures and pathways involved in stress reactivity—most notably, the hypothalamic-pituitary-adrenal (HPA) pathway and amygdala. HPA circuitry may overact during nicotine withdrawal, producing anxiety and drug-seeking behavior (Briand and Blendy 2010).

Assessment and Treatment Interventions

Almost 70% of smokers in the United States express an interest in quitting smoking, and about 50% of smokers do make a quit attempt each year (Centers for Disease Control and Prevention 2011). The long-term abstinence rate for smokers who use a medication and/or psychosocial/behavioral counseling is typically 25%–30%, and when both interventions are used together, the likelihood of a successful quit attempt increases to about 35%–45% (Fiore et al. 2008). These statistics argue strongly in favor of the use of combined evidence-based interventions to achieve long-term cessation. Table 16–1 lists free smoking cessation community resources, and Table 16–2 outlines treatment interventions based on motivational level (Ziedonis et al. 2006).

Assessment and Treatment Interventions

Free smoking cessation community resources for smokers

View Large

Assessment and Treatment Interventions Free smoking cessation community resources for smokers

Internet resources	Quitlines	Mobile apps
Make Smoking History www.makesmokinghistory.org	National Network of Tobacco Cessation Quitlines 1-800-QUIT-NOW	Text2Quit www.text2quit.com
Quit Net www.quitnet.com	American Cancer Society 1-800-227-2345	Smokefree TXT www.smokefree.gov/smokefreetxt
Become An EX www.becomeanex.com	American Lung Association 1-800-586-4872	My Quit Coach www.livestrong.com/quit-smoking-app
Centers for Disease Control and Prevention www.cdc.gov/tobacco	National Cancer Institute 1-877-44-U-QUIT	Become An Ex www.becomeanex.com
American Cancer Society www.cancer.org		
American Lung Association www.lung.org		
Nicotine Anonymous www.nicotine-anonymous.org		

Source. Adapted and updated from Ziedonis et al. 2006.

Assessment and Treatment Interventions

Motivationally tailored treatment interventions for tobacco use disorder

View Large

Assessment and Treatment Interventions Motivationally tailored treatment interventions for tobacco use disorder

Interventions for clients with lower motivation to quit	Interventions for clients with higher motivation to quit
• Personalized feedback tools and motivational interviewing	• Seven FDA-approved medications
• Five R's: relevance, risk, rewards, roadblocks, and repetition	o Five nicotine replacement therapies (patch, gum, lozenge, inhaler, nasal spray)
• Behavioral disconnects	o Bupropion
• Wellness and recovery groups	o Varenicline
• Learning About Healthy Living groups	• Psychosocial treatments
• Nicotine Anonymous and other community resources (Internet / apps, Quitline)	o Cognitive-behavioral therapies
	o Mindfulness-based interventions
	o Social support
	• Community resources (Quitline, Internet/apps, Nicotine Anonymous)

Assessment and Treatment Planning

The U.S. Preventive Services Task Force recommends that all health care providers use the five A's: Ask, Advise, Assess, Assist, and Arrange follow-up. First, the providers should ask all patients about whether they smoke, and advise them to quit if they do. For all tobacco users, the provider should list nicotine use disorder on the problem list and in the treatment plan, and should assess for the patient's level of motivation to quit. Advice to quit should be personalized to the individual and delivered in an encouraging and unequivocal manner. Studies have shown that health care providers who simply advise their patients to quit, compared with providers who do nothing, are able to influence quitting behaviors and cessation (Fiore et al. 2008). After assessing whether a patient is ready to quit, the provider should assist the patient by encouraging the use of medication and either face-to-face counseling or a telephone quitline (see Table 16–1). Finally, health care providers should arrange to discuss again in a follow-up visit or arrange and refer the patient to treatment.

If time permits, tobacco users should be further screened for the severity of physical dependence, tolerance, and withdrawal symptoms, including the amount of tobacco consumed (typically screened by number of cigarettes smoked per day) and the time to first cigarette in the morning (< 30 minutes is a sign of early morning withdrawal). Craving and wanting to use tobacco are the hallmark symptoms of a nicotine use disorder and should be assessed and monitored; the health care provider should also try to understand what triggers the individual's tobacco craving and use. Assessing for social supports that could help or hinder quit attempts is important. Understanding past quit attempt methods and relative success will help in treatment planning; it is informative to determine whether nicotine replacement therapy (NRT) medications were used properly. Assessing current motivation or interest to quit is important for treatment and should be documented in the treatment plan, because different evidence-based treatments are tailored to a smoker's level of motivation.

Brief Psychosocial Interventions for Smokers Not Ready to Quit

Typically, about 30% of smokers are ready to quit within 30 days after reporting that they want to quit. A strategy exists to help the remaining 70% who are less motivated and thus still ambivalent about quitting or unprepared to quit. To enhance motivation to quit smoking, Rollnick et al. (1997) developed an easy-to-use brief intervention that derives from the principles of motivational interviewing (MI). In MI, the clinician asks questions that are designed to elicit the client's own motivation for behavior change (e.g., to quit smoking) rather than directly providing information for this purpose. In the brief intervention Rollnick and colleagues developed for smokers, the clinician begins by asking, "On a scale from 1 to 10, where 1 is not at all important to give up smoking and 10 is extremely important, what number would you give yourself at the moment?" Self-motivational statements are then elicited by a follow-up question. For example, if a client were to say he were a 5 on the scale, the clinician would ask, "Why are you a 5 and not a 1?" This prompts the client to provide a self-motivational statement that identifies personally relevant risks of smoking and rewards of quitting. This conversation may uncover the client's fear of failure, attribution of pleasure or stress management with smoking, fear of gaining weight with quitting, and lack of support for quitting especially if the person lives with an active smoker. These responses and others relevant to the individual create a personalized feedback message and also target a way to present relevant educational information. The clinician can also ask a parallel question that focuses on the smoker's confidence that he could quit: "On a scale from 1 to 10, with 1 meaning that you are not at all confident and 10 meaning that you are 100% confident that you could give up and remain a nonsmoker, what number would you give yourself now?" The clinician then follows the same procedure just described for assessing importance or motivation and eliciting reasons for confidence and roadblocks to greater confidence. Smokers who are engaged in a conversation about their own self-provided reasons for quitting (highlighting their ambivalence), while working with a provider who evokes collaboration and empathy, will likely attempt to quit and/or become successful in quitting (American Psychiatric Association 2006).

In addition to the provision of MI, education is important in helping to motivate smokers to quit. Information on the benefits of quitting and on community resources can be helpful to guide a discussion at the time of literature presentation and at follow-up. Learning About Healthy Living (treatment manual available free online; http://rwjms.umdnj.edu/addiction/documents/2012lahl.pdf) provides educational resources on wellness and the effects of smoking on health, as well as strategies to help tobacco users with lower motivation, in group or individual treatment, to start to consider setting quit goals. Attending Nicotine Anonymous or other support groups can build confidence and hope (Ziedonis et al. 2006).

Psychosocial Interventions for Individuals Ready to Quit

Tobacco users who are trying to quit will benefit from information about the quitting process, available evidence-based pharmacological and psychosocial treatment interventions, community-based resources, and help with developing problem-solving strategies for coping with cravings and triggers. A list of free smoking cessation community resources is provided in Table 16–1. Clinicians should provide information on the quitting process, the consequences of ongoing

tobacco use, the benefits of quitting, the advantages and possible side effects of the different medication options, the importance of both psychosocial treatment and medications, and the symptoms and typical course of nicotine withdrawal. Because smokers often vacillate in their motivation to quit, clinicians need to empathically listen to clients describe these challenges and their ambivalence about quitting, while at the same time helping clients to collaboratively develop problem-solving strategies to overcome these challenges. Cognitive-behavioral therapy focuses on identifying triggers, understanding the triggers and associations, and identifying strategies for coping with or avoiding the triggers. Clients are usually easily able to identify their tobacco use triggers (e.g., activities associated with tobacco use, such as drinking coffee or alcohol, driving, stress, and being around other smokers). These and similar strategies regarding other smoking triggers can help build self-efficacy and should be initiated and practiced prior to quitting.

Studies support the use of mindfulness skills in promoting successful quitting (Brewer et al. 2011). Mindfulness skills can promote increased awareness of bodily sensations, acceptance of the craving symptoms, development of mindfulness approaches (meditation, body scan, etc.), and ultimately an uncoupling of cravings and linked positive reinforcements as a way to lessen the reactivity to urges and associated triggers. Some clients desire to gradually reduce the number of cigarettes used each day before quitting; however, success in quitting is unrelated to whether or not there is an initial reduction in use. Thus, clinicians can simply support client preference. Although there is no evidence base to support the efficacy of the use of relaxation training alone, hypnosis, or acupuncture for treatment of nicotine use disorder, many individuals believe they benefited from these approaches. There is a need for high-quality studies and evaluation of each of these approaches alone and in the context of evidence-based treatments (American Psychiatric Association 2006).

Tobacco Use Disorder Treatment Medications

The U.S. Food and Drug Administration (FDA) has approved seven medications to help with acute and protracted withdrawal symptoms; these medications include five NRT options, bupropion SR (sustained release), and varenicline (see Table 16–2). Medication algorithms suggest either monotherapy using any of the seven medications, or a combination of NRTs, or NRT and bupropion. The choice depends on the patient's preference, the patient's past experiences, assessment of correct use of medications in past attempts, medical and psychiatric comorbidities, and the severity of the nicotine use disorder and past withdrawal symptoms. The literature supports the use of multiple medications together, including choices such as combining the NRT patch (a long-acting, passive NRT medication) with a shorter-acting NRT form that requires active dosing (gum, lozenge, inhaler, spray) or combining bupropion SR with an NRT medication. Of note (American Psychiatric Association 2006; Fiore et al. 2008; Ziedonis et al. 2006), the FDA has recently stated reduced concern about the safety of using multiple NRTs or taking them for longer than 8–12 weeks (U.S. Food and Drug Administration 2013).

Nicotine Replacement Therapies

NRT medications come in five forms: transdermal patch, gum, lozenge, inhaler, and nasal spray. The patch, gum, and lozenge are available over-the-counter. Compared with tobacco products,

NRT medications are relatively safe to use because they contain only nicotine and not the 4,000 additional chemicals, including approximately 70 carcinogens, found in smoking tobacco. In addition, NRT medications have low abuse liability; even the abuse liability of the nicotine nasal spray, which is the highest among the NRTs, is still much lower than that of cigarettes and e-cigarettes. Although NRTs are relatively safe medications, there are serious risks of using an NRT in individuals with a myocardial infarction in the past 2 weeks, serious arrhythmias, or serious or worsening angina. NRT should be used cautiously in pregnant, adolescent, and light or intermittent tobacco users, and patients should be warned about the serious risks for children who ingest NRT (Fiore et al. 2008).

The nicotine patch delivers nicotine through the skin. The patch is available in 7-, 14-, and 21-mg doses. The 21-mg dose is recommended for people who smoke more than 10 cigarettes per day and should be used for at least 6–8 weeks, followed by the 14-mg patch for 2 weeks, and then the 7-mg patch for 2 weeks. More common side effects include skin reactions of erythema, tingling where the patch is applied, and local skin irritation and edema; however, the dropout rate due to skin reactions is low. These skin effects can be minimized by rotating where the patch is applied on the body. Myalgia is a less common side effect. Some smokers report vivid and sometimes unpleasant dreams and/or insomnia with overnight use of the patch. Removing the patch at bedtime will usually alleviate these nighttime problems.

Nicotine gum is available in 2- and 4-mg doses. The 4-mg dose is recommended for more tobacco-dependent individuals (i.e., those who smoke < 25 cigarettes per day). Recommendations are for one piece of gum every 1–2 hours (with a maximum of 24/day) for at least 4–8 weeks, followed by one piece every 2–4 hours for 2 weeks, and then one every 4–8 hours for 2 weeks, for a total of 8–12 weeks. Tobacco users who begin with the 4-mg gum may also have their gum titrated to the 2-mg dose. Additional pieces can also be used as needed to help alleviate a craving. To be effective, the nicotine in the gum must be absorbed by the oral mucosa, which requires that the gum be chewed in a manner different from chewing gum. Individuals should crunch the gum until it tingles and then "park" the nicotine gum between their cheek and gum of their jaw until the tingle goes away, and then repeat the process. Clients should be advised to avoid acidic beverages (e.g., coffee, soft drinks) for 15–30 minutes before and after each NRT use because the acidity of these beverages prevents absorption of the nicotine in the oral mucosa. Side effects from the gum include irritation in the mouth and throat, mouth ulcers, hiccups, and chewing-related jaw ache. Users also may experience gastrointestinal symptoms (flatulence, indigestion, and heartburn), which is usually related to improper use (i.e., swallowing the nicotine released from the gum).

The nicotine lozenge is available in 2- and 4-mg doses. The 4-mg dose is recommended for more tobacco-dependent individuals (i.e., those who use tobacco within 30 minutes of waking). The lozenge is also absorbed in the mouth and should be slowly sucked and not chewed. The daily dosing regimen is similar to that for the gum; however, more nicotine is absorbed at the same dosage with the lozenge versus the gum. Dosing is initially usually one per hour for about 9–15 lozenges per day with a maximum of 20 for a total of 12 weeks. The strategy to support better oral mucosa absorption (avoiding acidic beverages) is also needed for the lozenge. The lozenge is often preferred over the gum because it is easier to use and more nicotine is absorbed, so fewer

pieces are often needed. Side effects, which are typically mild, include mouth and throat irritation, indigestion, hiccups, and gastrointestinal symptoms.

The nicotine inhaler requires a prescription and consists of a two-piece plastic mouthpiece that looks similar to a cigarette and a replaceable plastic nicotine cartridge that is placed into the mouthpiece prior to use. The nicotine is sucked out of the mouthpiece into the oral mucosa (not into the lungs), and the process only partially imitates the sensation of smoking. As with the gum and lozenge, the absorption of the inhaled nicotine is through the oral mucosa, and again acidic beverages should be avoided for 15–30 minutes before and after use. Tobacco users should use 6–16 cartridges per day, and each nicotine cartridge lasts for about 20 minutes of puffing (or could be used partially, such as 4 times for 5 minutes each). Side effects of the inhaler include irritation of the mouth and throat, cough, headache, nausea, runny nose, and gastrointestinal symptoms.

The nasal spray requires a prescription and comes in a 10-mL spray bottle. One dose consists of two sprays, one spray to each nostril. Initial treatment should be one to two doses every hour, and usage should not exceed 40 doses per day. Some evidence suggests that the nicotine nasal spray may be a good choice for highly dependent smokers because it is the fastest of the NRTs to deliver nicotine to the brain and achieves high peak blood levels; however, the spray is still much slower acting than the cigarette or e-cigarette. Common side effects with the spray include nose and throat irritation, coughing, runny nose, and watery eyes, although these side effects usually subside within a couple of days of use.

The efficacy of the four short-acting NRTs (gum, lozenge, inhaler, and nasal spray) depends on the correct administration of these products. Although a user can take, for example, an additional lozenge or piece of gum on an as-needed basis when a craving develops, these medications have little efficacy when used only in this way. An important exception, however, is when these medications are used in combination with the NRT patch or bupropion; under these circumstances, as-needed use by the client is recommended.

Bupropion

Bupropion SR is a non-nicotine-based medication pill that requires a prescription. The recommended initial dose is 150 mg every morning, with the addition of a second dose of 150 mg every evening equating to a recommended total dosage of 300 mg/day. Some patients complain of side effects (e.g., difficulty sleeping) at the 300-mg dosage; for these individuals, the clinician may consider a maintenance dose of 150 mg/day. Starting 7–10 days before cessation, bupropion 150 mg/day should be given for 3–7 days, based on side effects and clinical judgment. Bupropion is recommended for 8–12 weeks; however, it can be taken beyond 6 months based on clinical judgment. Bupropion SR is contraindicated for tobacco users with a history of seizures or head injury, or for those who are taking other medications that may lower the seizure threshold. The most common side effects are dry mouth, nausea, and insomnia. Less commonly occurring side effects are agitation, depressed mood, and suicidal thoughts and behavior. Because of these more severe psychiatric side effects, the FDA issued a black box warning about these effects and recommends close monitoring of patients who are taking bupropion. Finally,

there is some evidence that bupropion may help to reduce the expected postcessation weight gain (typically 5–10 pounds are gained without bupropion) (Farley et al. 2012).

Varenicline

Varenicline is the only other non-nicotine-based medication, other than bupropion SR, FDA-approved for smoking cessation. Varenicline is taken for 7 days before smoking cessation. The patient begins with a 0.5-mg dose once a day for 3 days, followed by 0.5 mg bid for 4 days. The dose should be increased to 1.0 mg bid on a smoker's quit day and the medication continued at that dosage for 11–23 more weeks. Varenicline appears to help prevent relapse once smoking abstinence is achieved, and long-term use (up to 12 months) appears to maintain tobacco abstinence (Tonstad et al. 2006). Nausea is the most common side effect; however, there are also risks for other gastrointestinal symptoms (constipation, flatulence, and vomiting) and sleep disturbances (insomnia, abnormal dreams). The FDA has issued black box warnings for neuropsychiatric symptoms and severe cardiac symptoms. The neuropsychiatric symptoms associated with varenicline have included agitation, depressed mood, and suicidal ideation and behavior. The severe cardiac symptoms may include angina pectoris, nonfatal myocardial infarction, need for coronary revascularization, and new diagnosis of peripheral vascular disease (U.S. Department of Health and Human Services 2008). More research is needed to clarify whether there is a causal relationship between varenicline and these serious symptoms; however, patients must be informed of these potential side effects, and caution must be used for those with positive histories of these symptoms, especially suicidal ideation and serious cardiac disorders. Varenicline should be avoided in smokers who are psychiatrically unstable.

Tobacco Use and Psychiatric Comorbidity

Approximately 40% of people with any type of psychiatric disorder living in the community are current smokers, and this rate is over two times that in the general population. Smoking rates vary by psychiatric diagnosis, including affective disorder (35%), generalized anxiety disorder (45%), alcohol dependence (66%), schizophrenia (70%), drug dependence (75%), and bipolar disorder (85%). Tobacco use disorder rates are much higher in mental health and addiction treatment settings than in community settings (American Psychiatric Association 2006; Hitsman et al. 2009; Ziedonis et al. 2008). Many factors might explain the higher rates, including limited access to treatment, the mental health treatment culture's acceptance of use, targeted tobacco industry marketing, lower employment and educational levels, and genetic predisposition (Lind et al. 2010). Heavy smoking is common, and many smokers with psychiatric disorders are very effective and efficient at inhaling more milligrams of nicotine per cigarette than the average smoker. Individuals with behavioral health disorders live an 8- to 25-year shorter life span depending on their psychiatric disorder and whether they are tobacco users (American Psychiatric Association 2006).

Effect of Tobacco Cessation on Psychiatric Symptoms

Clinicians should carefully monitor their clients with a history of psychiatric disorders for a reemergence or worsening of psychiatric symptoms following a quit attempt. Some smokers with a history of recurrent depression will have a relapse of the depressive disorder; however, many will not, and some will have an overall reduction in their psychiatric symptoms (Hitsman et al. 2009; Ziedonis et al. 2008). Quitting smoking does not appear to jeopardize alcohol and other drug abstinence (Kalman et al. 2010). Of note, severe nicotine withdrawal symptoms can mimic symptoms of psychiatric disorders, caffeine intoxication, or agitation because of elevated psychiatric medication blood levels. Education about symptoms of nicotine withdrawal and potential increase in medication side effects or caffeine intoxication can be helpful. Monitoring mental status may uncover the need for psychiatric treatment if symptoms are severe or persist 6–8 weeks (Ziedonis et al. 2008).

The tars and non-nicotine polycyclic aromatic hydrocarbons from tobacco smoke alter the metabolism of many psychiatric medications by increasing the rate of metabolic clearance of the medication, and can lower blood concentrations of the medication up to 40% (Desai et al. 2001). Medications metabolized in the liver by the cytochrome P450 system's CYP1A2 isoenzyme are affected. Nicotine is metabolized through the CYP2D6 isoenzyme and does not alter the psychiatric medication blood levels; therefore, NRT medications do not change blood levels of psychiatric medications.

Table 16–3 lists psychiatric medications affected by smoking status. Smokers, compared with nonsmokers, are likely to require higher doses of these medications to achieve the same blood level of the medication. Smoking cessation results in a normalization and slowing down of the metabolism of the psychiatric medications, which results in increased medication blood levels. Clinicians must closely monitor for increased side effects from the psychiatric medications, and this increase may require dose adjustments (Ziedonis et al. 2008).

Tobacco Smoke's Effect on Psychiatric Medication Metabolism

Effect of smoking on serum levels of psychiatric medications

View Large

Tobacco Smoke's Effect on Psychiatric Medication Metabolism Effect of smoking on serum levels of psychiatric medications

Drug/class	Effect of tobacco smoke
Antipsychotics	
Chlorpromazine	Serum levels may be lower (by 24%)
Clozapine	Serum levels may be lower (by 28%) Faster medication clearance
Fluphenazine	Serum levels may be lower

Drug/class	Effect of tobacco smoke
Haloperidol	Serum levels may be lower (by 70%) Faster medication clearance (by 44%)
Olanzapine	Faster medication clearance (by 98%)
Amisulpride	No known effect
Quetiapine	No known effect
Risperidone	No known effect
Ziprasidone	No known effect
Hypnotics and anxiolytics	
Benzodiazepines (diazepam, lorazepam, chlordiazepoxide)	No known effect
Alprazolam	Serum levels may be lower (by up to 50%) Conflicting data on significance
Clonazepam	Serum levels may be lower
Loprazolam	Serum levels may be lower
Nitrazepam	Serum levels may be lower
Oxazepam	Serum levels may be lower
Antidepressants	
Fluvoxamine	Serum levels may be lower (by 47%) Faster medication clearance
Mirtazapine	Serum levels may be lower
Tricyclic antidepressants (amitriptyline, nortriptyline)	Interaction unclear/possible decrease in serum levels
Clomipramine	Serum levels may be lower
Imipramine	Serum levels may be lower

Source. Adapted and updated from Zevin and Benowitz 1999.

Key Points

1. Tobacco use disorder is still common (20% of U.S. population) and is the leading cause for increased morbidity and mortality, especially among individuals with psychiatric disorders.
2. There are many health-related and other benefits of quitting, including reduced morbidity and mortality and enhanced financial savings, relationship and employment options, and self-esteem.
3. All health and mental health care clinicians should assess for tobacco use, advise tobacco users to quit, and document this in treatment plans.

4. Evidence-based treatment interventions are available for tobacco users with lower and higher motivation to quit, and the combination of psychosocial interventions and medications provides the best outcomes, especially with use of community resources.

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Suggested Readings

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