Treatment of Tobacco Dependence

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After reviewing the article, the reader should be able to (1) engage patients in a dialogue with the goal of assessing motivation to stop smoking and developing a treatment plan; (2) incorporate tobacco dependence treatment into a chronic disease model that includes systematic screening, behavior change motivation, pharmacotherapy targeted to patients’ needs and preferences, strategies to provide ongoing support, and the effective addressing of relapse; and (3) identify medication treatment options for patients and be able to discuss their proper use, potential adverse effects, and cost.

Cigarette smoking continues to cause substantial death and disability, but more than 1 in 5 adults smoke despite the desire among most smokers to stop and the availability of effective treatments. A systematic process to identify all smokers is crucial. Because tobacco dependence is characterized by relapses and remissions, clinicians should be ready to engage smokers and reengage relapsed smokers with options for new medication strategies and additional counseling resources.


FDA = Food and Drug Administration; NRT = nicotine replacement therapy; SR = sustained release

In the United States, cigarette smoking remains the most important cause of preventable death and disability, causing 30% of cancer deaths and 18% of all deaths. Most patients who smoke would like to stop smoking or have unsuccessfully tried to quit. Addressing tobacco use has become a quality metric of the National Committee for Quality Assurance (Healthcare Effectiveness Data and Information Set [HEDIS]) and the Joint Commission. This article reviews pharmacotherapy and counseling techniques for the treatment of tobacco dependence, providing practical tips to the busy clinician on how to energize treatment efforts and to encourage patients to be persistent in their attempts to stop smoking.

GENERAL APPROACH

A systematic process for identifying the tobacco use status of every patient in all clinical settings should be the first step. Collecting the tobacco use status as a “vital sign” is one approach. To increase the likelihood of addressing tobacco use, clinicians should have this information available before they meet with the patient.

CHRONIC DISEASE MODEL

Permanent tobacco abstinence, the goal of intervention, is rarely achieved with a single treatment. Instead, the quitting process is characterized by relapses and remissions and is best conceptualized using a chronic illness model. Just as we would not consider discontinuing antidiabetic agents for a patient whose hemoglobin A1c was not at goal, we should not discontinue treating patients who relapse to smoking.

Some smokers can achieve long-term tobacco abstinence (>6 months) after a few attempts or even after only one. However, many others try to quit multiple times and relapse. Indeed, relapse is the most likely outcome from any single quit attempt. Most patients will not reach 6 months of abstinence without relapsing, and half of those abstinent at 6 months will relapse during the subsequent 8 years. Like patients with poorly controlled hypertension or diabetes, patients who relapse to smoking should be reengaged in treatment. Medication adjustments and behavioral support should be provided until acceptable therapeutic targets, eg, long-term smoking abstinence, are met. Clinicians can foster confidence in these patients and make them more willing to reengage in treatment by providing consistent screening at follow-up visits and offering new and combined medication options.

STARTING THE CONVERSATION: SCALING QUESTIONS

Patients who are advised to quit smoking by clinicians are more likely to do so and report higher satisfaction with clinical encounters. In busy clinical practices, most patients are asked about smoking and advised to quit, but many fewer receive assistance in quitting or referral to a tobacco treatment specialist. Clinicians may not engage patients in these more in-depth discussions because they do not know how to begin the conversation. To start a dialogue, we ask: “Can we talk about your tobacco use?” If patients wish to engage in this discussion, we use scaling questions, ie, questions that allow the patients to respond using a scale of 0 to 10, to determine their motivation to

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TREATMENT OF TOBACCO DEPENDENCE

make a quit attempt by assessing the importance they place on quitting (“On a scale of 0 to 10, with 0 being not important at all, how important is it for you to stop smoking?”) and their confidence in their ability to do so (“On a scale of 0 to 10, with 0 being not confident at all, how confident are you in your ability to stop smoking?”). The answers to these questions allow the more relevant domain (ie, lower score) to be addressed.

Clinicians can obtain even more precise information by following up on the patients’ answers to the initial questions. For example, if patients assign a value of 3 to the importance they place on quitting, the clinician might ask: “I notice that you are a 3 on the importance scale; why are you not a 0?” Asking patients why they are not lower on the scale can give insight into their own reasons for wanting change, reasons that will likely motivate them more than any the clinician could provide. If patients determine their confidence level to be a 5, the clinician might ask why it is not a 2. Patients can then provide details about what makes them confident that they could make a quit attempt (eg, previously successful quit attempts). Past achievements can be the foundation of future success. The clinician can then elicit from patients what might help to build confidence and skills for quitting smoking by asking: “What would it take to move you to a 7 on the confidence scale?”

With this information, the clinician can personalize a message about becoming tobacco free, educate patients about new treatment options, and identify tools and coping skills to help patients adhere to treatment. This type of patient-centered approach can enhance the working alliance, establish rapport, and facilitate the development of a targeted treatment plan. It can also help the patient reengage in treatment if relapse occurs.15

If patients are willing to make a quit attempt, treatment should be sufficiently intense to maximize the likelihood of success. Medications can be used to address withdrawal symptoms and reduce the intensity of conditioned responses so that patients can more effectively implement behavior changes.

NICOTINE FOR TREATING TOBACCO DEPENDENCE

All available pharmacotherapies indicated for the treatment of tobacco dependence can be used effectively as monotherapies, and such an approach is appropriate for lighter smokers (≤10 cigarettes per day). Our general approach to treating nicotine withdrawal symptoms in moderate and heavy smokers (>10 cigarettes per day) is to offer combination treatment, eg, the nicotine patch to provide continuous dosing and 1 of the short-acting nicotine replacement products (ie, nicotine gum, nicotine nasal spray, nicotine inhaler, nicotine lozenge) to cover urges and cravings. We often combine sustained-release (SR) bupropion with nicotine replacement (eg, nicotine patches or short-acting nicotine replacement therapy [NRT]) if there are no contraindications. Busy clinicians can facilitate decisions on treatment plans by asking patients: “What have you tried before and what would you be interested in trying this time?”

Although combination therapy with multiple NRTs or with a combination of an NRT and bupropion SR is not approved by the Food and Drug Administration (FDA), available evidence suggests that better smoking abstinence rates are achieved with combination therapy than with monotherapy.16-19

NICOTINE PATCH

We recommend a graded approach to initial nicotine patch dosing. As a rough guide, the patch dose should be the same or slightly more than the number of cigarettes smoked per day. For example, an initial nicotine patch dose of 35 mg/d (21 mg + 14 mg patches) would be appropriate for patients who smoke 30 cigarettes per day.

Therapy can be altered as needed depending on patients’ abstinence and withdrawal symptoms. If patients continue to smoke during the first 2 weeks of patch therapy, the treatment plan must be altered. Patch doses should be increased for patients who experience substantial withdrawal symptoms, such as irritability, anxiety, frustration, loss of concentration, craving, or frequent use of short-acting nicotine-replacement products. Many patients who have not had success with nicotine patches may have been underdosed and may attribute nicotine withdrawal symptoms to the nicotine patch rather than to inadequate NRT. Patients can be reassured that the patches are not causing adverse effects if symptoms are alleviated with the use of short-acting nicotine-replacement products. The primary adverse effect of too much nicotine is nausea.

Patients should receive 4 weeks of treatment with the initial patch dose; after that, the dose can be “stepped down” by 7 to 14 mg every 2 weeks. Patients are asked to contact us if they feel uncomfortable about stepping down the dose; in such cases, the current dose is maintained and no further stepping down occurs for 1 or 2 weeks. Although nicotine patches are available over the counter, prescriptions are provided to all patients because we do not always know if patients’ insurance will cover pharmacologic treatment of tobacco dependence. To save time, we write 1 prescription for both the initial patch dose (enough for 4 weeks of treatment) and for the step-down doses needed every 2 weeks thereafter. The pharmacist can work with patients to determine how much to dispense at any one time to avoid “sticker shock” (ie, unaffordable medication cost) that may discourage medication use and a quit attempt.
The most common adverse effect of nicotine patch therapy is skin irritation at the patch site, which is usually characterized by erythema and pruritus but may be more severe with edema and vesicles. To avoid such irritation, we advise patients to rotate application sites on relatively hairless parts of the body between the neck and waist. If the patches come off because of perspiration, we tell patients to use skin tape to keep them in place. Mild skin reactions can be treated with topical corticosteroids; more severe reactions may require patch discontinuation. On rare occasions, a generalized rash occurs and patches must be discontinued; however, if necessary for adequate symptom relief, use of other nicotine-replacement products can continue, and the dose can be increased. The 21-mg dose can be purchased for about $3.50 per patch for brand names.

**Nicotine Gum**

Nicotine gum is available in both 2-mg and 4-mg doses. We rarely use the gum as monotherapy, usually recommending either the 2-mg or 4-mg gum in combination with nicotine patch therapy. We instruct our patients to use the gum to treat cravings and withdrawal symptoms.

Patients should be instructed in the proper use of nicotine gum. They should chew the gum a few times until they feel a mild tingling or peppery taste indicating nicotine release and then “park” the gum between the cheek and gum for several minutes before resuming chewing. Repeated cycles of “chew and park” will allow gradual nicotine absorption and should be continued for approximately 30 minutes per piece of gum. Patients who are “gum chewers” may find it difficult to avoid continuous gum chewing. Patients should avoid carbonated or acidic beverages before and during use because an acidic oral environment binds the nicotine and decreases its absorption across the buccal mucosa.

Although patients are instructed to use as many as 20 pieces of gum per day as needed, most patients use too few pieces. The most common adverse effects are nausea and indigestion, which can be minimized with proper technique. Other reported adverse effects include sore gums. A 4-mg dose of nicotine gum costs approximately $0.40.

**Nicotine Lozenge**

Like nicotine gum, the nicotine lozenge delivers nicotine through the oral mucosa and provides active self-dosing in response to cravings. Compared with nicotine gum, the nicotine lozenge is easier to use and has fewer limitations due to oral health issues such as dental work or temporomandibular joint syndrome.

The nicotine lozenge is available in 2-mg and 4-mg doses. As monotherapy, the recommended dose for cigarette smokers is based on the time to first cigarette in the morning, which is an indicator for severity of dependence. For patients whose first cigarette is within 30 minutes of waking, the 4-mg strength is indicated, and for smokers whose first cigarette is more than 30 minutes after waking, the 2-mg strength is suggested. The lozenge should be placed between the cheek and gum and not chewed or swallowed whole. Patients should not eat or drink during use or during the 15 minutes before because an acidic oral environment reduces nicotine absorption. In combination with nicotine patch therapy, we usually recommend the 2-mg dose. The most common adverse effects with the nicotine lozenge are headache, diarrhea, heartburn, hiccups, and nausea. Each 4-mg lozenge costs approximately $0.50.

**Nicotine Nasal Spray**

The nicotine nasal spray delivers nicotine and reduces withdrawal symptoms more quickly than any of the other nicotine replacement delivery systems. However, it delivers nicotine less quickly than cigarette smoking, and it does not achieve the high arterial concentrations seen with inhalation of tobacco smoke. We typically recommend the nasal spray to patients who say they smoke to obtain a “quick hit.”

Each spray contains 0.5 mg of nicotine, and 1 dose is 1 spray in each nostril (total of 1 mg). To guide their use of the product, clinicians can advise patients that 1 spray in each nostril can deliver as much nicotine as 1 cigarette. Patients should be instructed to spray it against the lower nasal mucosa and not to sniff it up into the upper nasal passages. We suggest that patients use the nasal spray to manage urges and cravings. Most patients will use 12 to 16 doses per day initially if the spray is being used as monotherapy. We often recommend that patients use the nasal spray in combination with nicotine patch therapy.

The most common adverse effects are nasal and eye irritation and a cough that usually subsides in the first week. The nicotine nasal spray costs approximately $5.00 per day for 12 doses.

**Nicotine Inhaler**

The nicotine inhaler, available by prescription, delivers vaporized nicotine to the oral mucosa where it is absorbed. Approximately 80 puffs during a 20-minute period are needed to obtain 2 mg of nicotine. Because the inhaler resembles a cigarette rod, we use it with patients for whom the behavioral and tactile aspects of smoking (ie, cigarette handling, cigarette with coffee) are an important trigger. The most frequent adverse effects are mouth or throat irritation and occasional coughing. Each nicotine inhaler cartridge costs approximately $1.00.
NONNICOTINE PHARMACOTHERAPY

BUPROPION SR

Bupropion SR is a monocyclic antidepressant that inhibits the reuptake of dopamine and norepinephrine but that also has a direct competitive inhibitory effect on the nicotine acetylcholine receptor. Bupropion SR approximately doubles the smoking abstinence rates compared with placebo.21 Patients begin taking bupropion SR 1 week before their quit-smoking date, at an initial dose of 150 mg/d for 3 days followed by 150 mg twice daily for approximately 6 to 12 weeks, although it can be safely used longer. Long-term treatment with bupropion SR may reduce or delay relapse to smoking. Bupropion SR can be stopped abruptly and does not require tapering.

We consider bupropion SR to be an “anticraving” medication. It can be used in combination with NRT and with varenicline. Because it may attenuate weight gain among continuously abstinence smokers, it may be particularly useful for smokers concerned about weight gain after cessation of tobacco use.

In studies using the immediate-release form of bupropion, seizures were observed in patients with eating disorders. Although the risk may be lower with the SR form of bupropion, contraindications include a history of seizures, serious head trauma with loss of consciousness, use of medications that lower seizure threshold, or an eating disorder (anorexia nervosa or bulimia). The main adverse effects are insomnia and dry mouth. Cardiovascular and sexual adverse effects are uncommon. Bupropion SR is available in a generic form at a cost of approximately $2.40 per day.

VARENICLINE

Varenicline, approved by the FDA in May 2006 for smoking cessation, is a partial nicotine agonist of the α4β2 subtype of the nicotinic acetylcholine receptor. The partial agonist activity relieves nicotine withdrawal symptoms and cravings, while the antagonist activity blocks the reinforcing effects of continued cigarette smoking.

The findings of 2 large, randomized, multicenter clinical trials assessing the efficacy of varenicline compared with placebo and bupropion SR for tobacco abstinence have been published.22,23 At 3 months, the odds that patients would quit smoking with varenicline were 2-fold higher than with bupropion SR and 4-fold higher than with placebo. Varenicline was also observed to decrease craving, withdrawal symptoms, and smoking satisfaction. Patients who are treated with varenicline for 6 months are more likely to be abstinent at 1 year than those who receive only 3 months of therapy.24 Although no head-to-head comparisons of varenicline and NRT have been conducted, indirect evidence suggests that varenicline is superior to NRT.25

The recommended dosing for the first week of treatment with varenicline is 0.5 mg once daily for 3 days and then twice daily for 4 days; the dosage is then “ramped up” to 1 mg twice daily for 11 weeks. In some locations, starter packs are available that provide the appropriate doses for the first month of therapy. Patients should plan to quit on day 8 (target quit day) of therapy, the point at which the target dose of varenicline is reached. We continue varenicline for an additional 3 months beyond the initial 3-month treatment if patients are at a self-identified increased risk of relapse. Varenicline need not be tapered when discontinued. The efficacy and safety of the use of NRT with varenicline have not been established.

The most common adverse effect of varenicline is nausea, which is usually mild to moderate. Vivid dreams have also been reported. Nausea can be minimized by taking the pills with food, which does not decrease bioavailability. The FDA has informed health care professionals that suicidal thoughts, aggressive and erratic behavior, and drowsiness can be associated with the use of varenicline.26 Investigations into these associations are ongoing, and clinicians should monitor patients for behavior and mood changes. Varenicline is available at approximately $4.00 per day.

ADDITIONAL RESOURCES

A dose-response relationship exists between counseling time and successful tobacco dependence treatment outcomes.7 Even brief counseling (2-3 minutes) by a clinician has a measurable effect. Effective counseling enhances motivation and supports commitment to quit smoking and can be provided face to face, via the telephone, or through the Internet.7,27 For busy clinicians, lengthy counseling is frequently impractical, so knowledge of additional resources is helpful.

Individual and group counseling programs are becoming more widely available. Many hospitals, health departments, and health care facilities have tobacco treatment specialists, and more allied health professionals are becoming certified.28,29 Certification as a tobacco treatment specialist can provide assurance to the referring clinician that evidence-based treatment is provided.

Tobacco treatment counseling via the telephone is available in every state in the United States and every province in Canada, as well as in many other countries. Currently, the simplest way for clinicians to encourage patients to use a tobacco quitline is to tell them to call 1-800-QUITNOW after leaving the office. Through the National Network of Tobacco Cessation Quitlines, callers will be routed to the tobacco quitline in their state. States provide differing levels of support; patients can find what is available to
them when they call. Clinicians can also learn about the state-specific service offerings through the National Quitline Consortium Web site (http://www.naquitline.org).20

The Internet may also be effective in providing support to patients who are trying to quit smoking. A number of Web sites have been developed to support quit attempts, such as the American Legacy website “Become an Ex” (http://www.becomeanex.org) and Quitnet (http://www.quitnet.com).

CONCLUSION

Smoking can be effectively addressed within a busy clinical practice using strategies similar to those used to manage other chronic medical conditions. By opening up a relatively brief dialogue, clinicians can engage and reengage patients in tobacco dependence treatment. Nicotine replacement therapies, bupropion SR, varenicline, and combinations of these therapies may motivate smokers to make a quit attempt and relapsed smokers to try again. Busy clinicians can also direct patients to an increasing number of resources, including tobacco treatment specialists, the tobacco quitline, local support groups, and the Internet, to assist them in achieving their goal of smoking cessation.

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REFERENCES


CME Questions About Cessation of Smoking

1. A patient informs you that his orthopedic surgeon told him to quit smoking before having a lumbar discectomy scheduled in 8 weeks. The patient wants to quit, does not think that he can quit all at once, and wishes that he did not like smoking so much. Which one of the following should be the next step in the treatment of this patient?

a. Begin varenicline and encourage the patient to quit smoking on the first day of treatment

b. Begin nicotine replacement therapy (NRT) and set a quit date

c. Begin sustained-release (SR) bupropion and encourage the patient to quit smoking on the first day of treatment

d. Begin varenicline and allow the patient to continue smoking for the first 7 days of medication with a quit date on the eighth day.

e. Begin varenicline without setting a quit date and see if the patient is able to quit on his own
2. A patient who has smoked 40 cigarettes per day for 25 years has been using two 21-mg nicotine patches per day for 2 weeks to help her quit smoking. She reports that she is doing better than she had expected but continues to smoke 3 or 4 cigarettes a day. Which one of the following reflects the best treatment for this patient?
   a. Stop the nicotine patches
   b. Discuss coping skills that can help the patient manage situations that trigger her to smoke
   c. Begin varenicline because it has been shown to be most effective in managing cravings
   d. Offer the patient a choice from among the short-acting NRTs and elicit coping skills that can help the patient manage situations in which she currently smokes
   e. Encourage the patient, refer the patient to specialist counseling for tobacco dependence, but do not add any new NRT

3. A patient informs you that he smokes and would be willing to discuss it with you. Which one of the following communication strategies would be most effective in this scenario?
   a. Review the diseases caused by smoking
   b. Assess motivation to quit with scaling questions
   c. Refer to the telephone quitline
   d. Review the pharmacotherapeutic treatment options
   e. Set up another appointment at which treatment options can be discussed

4. Your patient relapses to smoking after 6 months of continuous abstinence. Which one of the following management strategies is most likely to be effective?
   a. Wait until the patient is ready to stop again and be wary of providing advice that might be offensive or shaming
   b. Assess the patient’s motivation for making another quit attempt, help build confidence by eliciting discussion about past success, and encourage the patient to reengage in the treatment that led to 6 months of abstinence
   c. Prescribe varenicline
   d. Advise the patient to stop again as soon as possible so as not to jeopardize any health gains that have accrued through being abstinent from tobacco
   e. Assess the causes of relapse and recommend therapy to address the underlying factors that caused relapse

5. A 45-year-old woman who smokes 2 packs of cigarettes per day and has a history of seizures wishes to stop smoking. She tells you that her aunt had success with the nicotine inhaler and that she wishes to try it as well. Which one of the following would be the best initial medication regimen for this patient?
   a. Bupropion SR with the nicotine patch
   b. Nicotine inhaler alone
   c. Varenicline
   d. Varenicline and two 21–mg nicotine patches
   e. Nicotine inhaler and two 21-mg nicotine patches

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