Treatment of Tobacco Use and Dependence

Nancy A. Rigotti, M.D.

A 66-year-old woman with stable angina and a history of depression smokes 25 cigarettes daily. She would like to stop smoking but is concerned about weight gain. She has tried to quit several times on her own without success. What should her physician recommend?

The Clinical Problem

Tobacco use is the leading preventable cause of death in the United States, responsible for more than 400,000 deaths annually, or 1 of every 5 deaths. Half of regular smokers die prematurely of a tobacco-related disease. The potential health benefits of smoking cessation are substantial. Cessation reduces the risk of tobacco-related diseases, slows the progression of established tobacco-related diseases, and increases life expectancy, even when smokers stop smoking after the age of 65 years or after the development of a tobacco-related disease.

An estimated 70 percent of smokers see a physician each year, providing physicians with substantial opportunity to influence smoking behavior. However, that opportunity presents challenges, as the case vignette illustrates. Many patients continue to smoke despite knowing about or experiencing the health consequences of tobacco use. Some who try to quit repeatedly fail. Most mistakenly believe that stopping smoking requires only willpower and are unaware that effective treatments are available. To help smokers, physicians must be familiar with the spectrum of effective therapies. They must also appreciate that tobacco use has complex physiological and psychological determinants and understand that changing any behavior is a gradual process. Smoking is best regarded as a chronic disease that requires a long-term management strategy, rather than a quick fix.

Currently, 23.5 percent of U.S. adults (25.7 percent of men and 21.5 percent of women) smoke cigarettes. Nearly all smokers acknowledge that tobacco use is harmful to health but underestimate the magnitude of their own risk. Few know the full spectrum of health risks. For many smokers, the risk of future disease does not outweigh the current perceived benefits of smoking or barriers to cessation. Yet 70 percent of smokers report that they want to quit. Approximately one third of smokers try to stop smoking each year, but only 20 percent of them seek help. Fewer than 10 percent of smokers who attempt to quit on their own are successful over the long term. Smokers have a higher rate of success when they seek help with quitting. Even then, several attempts are often required before long-term abstinence is achieved.

The chief physiological obstacle to quitting is the addictive nature of nicotine. Nicotine causes tolerance and physical dependence. When tobacco use is stopped, there is a withdrawal syndrome characterized by irritability, anger, impatience, restlessness, difficulty concentrating, insomnia, increased appetite, anxiety, and depressed mood. Symptoms of nicotine withdrawal are nonspecific, vary widely in intensity and duration, and are not correctly identified by smokers. Symptoms begin a few hours after the last cigarette, peak two to three days later, and wane over a period of several weeks or months.

Psychological factors also contribute to the difficulties that smokers have when they try to quit. Tobacco use is a learned behavior. Cigarettes become part of a smoker’s daily routine, associated with events, such as finishing a meal, that become cues that trigger the desire to smoke. Smokers also use cigarettes to handle stress and negative emotions such as anger or anxiety. To stop smoking, a smoker must learn new coping skills and break old patterns, an incremental process in which attempts to quit often end in the resumption of smoking until abstinence is achieved.

Strategies and Evidence

Two approaches have strong evidence of efficacy for smoking cessation: pharmacotherapy and counseling. Each is effective by itself, but the two in combination achieve the highest rates of smoking cessation. The efficacy of a treatment correlates with its intensity, but even brief interventions by physicians during an office visit promote smoking cessation.
Interventions by Physicians

Randomized, controlled trials conducted in primary care practices demonstrate that a physician’s advice to stop smoking increases the rates of smoking cessation among patients by approximately 30 percent. Providing a brief period of counseling (three minutes or less) is more effective than simply advising the patient to quit and doubles the cessation rate, as compared with no intervention. Effective interventions have a common approach (Fig. 1). Optimal implementation requires support from the health care system to bolster the efforts of individual physicians. Office-based systems that document every patient’s smoking status before the patient sees the physician and remind the physician to address the use of tobacco by patients who smoke triple the likelihood that a physician will intervene.

Counseling

Counseling about smoking cessation can be delivered effectively in person or by telephone. Group or individual counseling is effective when it is provided by trained counselors and includes repeated contacts over a period of at least four weeks. The efficacy of this approach increases as the amount of time spent with the patient increases. Cognitive behavioral methods form the core of most counseling programs. Typically, smokers learn to identify smoking cues, then use cognitive and behavioral methods to break the link between the cues and smoking. They also learn strategies for coping with stress, managing symptoms of nicotine withdrawal, and once they quit, preventing relapse, such as anticipating tempting situations and rehearsing coping strategies.

Smoking-counseling strategies are also summarized in pamphlets and booklets, audiotapes, videotapes, and computer programs. Written self-help material has negligible efficacy when used alone but may augment other interventions. Self-help material is more effective when its content is tailored to an individual patient’s specific concerns or readiness to change.

Pharmacotherapy

The Food and Drug Administration (FDA) has approved five products for smoking cessation: sustained-release bupropion and four nicotine-replacement products (gum, a transdermal patch, a nasal spray, and a vapor inhaler) (Table 1). Each has demonstrated efficacy in randomized double-blind trials, approximately doubling the long-term (one-year) rates of abstinence, as compared with placebo. Most clinical trials combine drug therapy with counseling; typical rates of smoking cessation are 40 to 60 percent at the end of drug treatment and 25 to 30 percent at one year. Few randomized, controlled trials have directly compared one drug with another. Nortriptyline and clonidine have also been found to aid smoking cessation, but they have not been approved by the FDA for this indication.

Nicotine-Replacement Therapy

Nicotine-replacement therapy provides an alternative form of nicotine to relieve symptoms of withdrawal in a smoker who is abstaining from tobacco use. The pharmacokinetic properties of available products differ, but none deliver nicotine to the circulation as fast as does inhaling cigarette smoke. The patch provides a relatively stable, fixed dose of nicotine over a period of 16 or 24 hours. The other products have a more rapid onset and a shorter duration of action, allowing the user to adjust the dose of nicotine. Blood nicotine levels peak 5 to 10 minutes after the administration of nicotine nasal spray, 20 minutes after the user begins chewing nicotine gum or uses a vapor inhaler, and 2 to 4 hours after the application of a nicotine patch. The nicotine gum and the inhaler have similar pharmacokinetic properties since in both the nicotine is absorbed through the oral mucosa.

The use of all nicotine-replacement products increases the long-term rates of smoking cessation and relieves cravings for nicotine and the symptoms of nicotine withdrawal. In meta-analyses of placebo-controlled trials, the nicotine patch doubled the long-term smoking-cessation rate. The use of nicotine gum increases cessation rates by 50 to 70 percent. For heavy smokers (those who smoke at least 25 cigarettes per day), the gum that contains 4 mg of nicotine per piece is more effective than that containing 2 mg per piece. Fewer studies have assessed the nasal spray and the vapor inhaler, but in meta-analyses both products doubled the cessation rates, as compared with placebo inhaler.

One randomized, controlled trial directly compared the four nicotine-replacement products. The efficacy of each product was similar at week 12 of follow-up, but the rates of compliance varied, being highest for the patch, intermediate for the gum, and lowest for the vapor inhaler and the nasal spray. Studies consistently report higher rates of smoking cessation when nicotine-replacement therapy is combined with counseling, although the former is effective even when used alone. Different nicotine-replacement products can be combined safely. In some studies, combining the nicotine patch with gum, inhaler, or nasal spray was more efficacious than the use of any of these products alone.

The safety of nicotine-replacement products is underscored by the fact that the patch and gum, initially sold only by prescription, are now available without a prescription. Although nicotine’s hemodynamic effects increase the myocardial workload, nicotine-
Figure 1. Smoking-Cessation Strategy for Physicians.
This strategy uses the five steps (the “five A’s”) recommended in Public Health Service guidelines: ask, advise, assess, assist, and arrange follow-up.
replacement therapy is safe in patients with cardiovascular disease, including stable angina.\textsuperscript{15,16} The safety of nicotine-replacement therapy has not been studied in patients with unstable angina or in those who have had a myocardial infarction within two weeks before treatment, but the risk of cardiac complications should be lower than with smoking. Unlike smoking, nicotine-replacement therapy does not increase the coagulability of blood or expose a patient to carbon monoxide or oxidizing gases that damage endothelium.\textsuperscript{17} The side effects of these products vary according to the manner in which nicotine is administered (Table 1).

### Non-Nicotine Therapy

Bupropion, an antidepressant with dopaminergic and noradrenergic activity, was efficacious for smoking cessation when combined with counseling in

---

**Table 1. Drugs Used for Smoking Cessation.**

<table>
<thead>
<tr>
<th>Product</th>
<th>Daily Dose</th>
<th>Duration of Treatment</th>
<th>Common Side Effects</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine-replacement therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transdermal patch*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 hr (e.g., Nicoderm CQ)</td>
<td>7–14 mg or 21-mg patch worn for 24 hr†</td>
<td>8 wk</td>
<td>Skin irritation, insomnia</td>
<td>Provides steady level of nicotine; easy to use; unobtrusive; available without prescription</td>
<td>User cannot adjust dose if craving occurs; nicotine released more slowly than in other products</td>
</tr>
<tr>
<td>16 hr (e.g., Nicotrol)</td>
<td>15-mg patch worn for 16 hr†</td>
<td>8 wk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicotine polacrilex gum</td>
<td>1 piece/hr (&lt;24 pieces/day)</td>
<td>8–12 wk</td>
<td>Mouth irritation, sore jaw, dry mouth, hiccups</td>
<td>User controls dose; oral substitute for cigarettes; available without prescription</td>
<td>Proper chewing technique needed to avoid side effects and achieve efficacy; user cannot eat or drink while chewing the gum; can damage dental work; difficult for denture wearers to use; frequency of use needed to avoid side effects; device visible when used</td>
</tr>
<tr>
<td>Nicotine polacrilex gum</td>
<td>2 mg (&lt;25 cigarettes/day)</td>
<td>8–12 wk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicotine polacrilex gum</td>
<td>4 mg (&gt;25 cigarettes/day)</td>
<td>8–12 wk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal spray (Nicotrol NS)*</td>
<td>1–2 doses/hr (1 mg total; 0.5 mg in each nostril) (maximum, 40 mg/day)</td>
<td>3–6 mo</td>
<td>Nasal irritation; sneezing, cough, teary eyes</td>
<td>Most irritating nicotine-replacement product to use; device visible when used</td>
<td></td>
</tr>
<tr>
<td>Vapor inhaler (Nicotrol Inhaler)*</td>
<td>6–16 cartridges/day (delivered dose, 4 mg/cartridge)</td>
<td>3–6 mo</td>
<td>Mouth and throat irritation, cough</td>
<td>User controls dose; hand-to-mouth substitute for cigarettes</td>
<td></td>
</tr>
<tr>
<td>Non-nicotine therapy</td>
<td>150 mg/day for 3 days, then 150 mg twice a day†</td>
<td>7–12 wk (up to 6 mo to maintain abstinence)</td>
<td>Insomnia, dry mouth, agitation</td>
<td>Easy to use (pill), no exposure to nicotine</td>
<td>Increases risk of seizure (&lt;0.1 percent)</td>
</tr>
<tr>
<td>(Zyban or Wellbutrin SR)*</td>
<td>75–100 mg/day**</td>
<td>12 wk</td>
<td>Dry mouth, sedation, dizziness</td>
<td>Easy to use (pill), no exposure to nicotine</td>
<td>Side effects common; should be used cautiously in patients with coronary heart disease</td>
</tr>
<tr>
<td>Clonidine]</td>
<td>0.1–0.3 mg twice a day</td>
<td>3–10 wk</td>
<td>Dry mouth, sedation, dizziness</td>
<td>No exposure to nicotine</td>
<td>Side effects limit use</td>
</tr>
</tbody>
</table>

---

*This product has been approved by the Food and Drug Administration as a smoking-cessation aid. The Public Health Service clinical guidelines also recommend it as a first-line drug for smoking cessation.\textsuperscript{8}†The starting dose is 21 mg per day unless the smoker weighs less than 45.5 kg (100 lb) or smokes fewer than 10 cigarettes per day, in which case the starting dose is 14 mg per day. The starting dose should be maintained for four weeks, after which the dose should be decreased every week until it is stopped.‡The user should chew the gum slowly until he or she experiences a distinct taste, indicating that nicotine is being released. The user should then place the gum between cheek and gum until the taste disappears to allow the nicotine to be absorbed through oral mucosa. The sequence should be repeated for 30 minutes before the gum is discarded. Acidic beverages (such as coffee and soft drinks) reduce the absorption of nicotine and should be avoided for 30 minutes before and during chewing.§Tolerance develops to local side effects during the first week of use.¶Treatment should be started one week before the quitting date.\textsuperscript{§}This agent has not been approved by the Food and Drug Administration as a smoking-cessation aid. The Public Health Service clinical guidelines also recommend it as a second-line drug for smoking cessation.\textsuperscript{8}**Treatment should be started 10 to 28 days before the quitting date at a dose of 25 mg per day, and the dose should be increased as tolerated.
randomized, controlled trials. The efficacy of bupropion when accompanied by minimal levels of psychosocial support, as occurs in medical practice, is unknown. Like nicotine-replacement therapy, treatment with bupropion doubles smoking-cessation rates as compared with placebo treatment. Bupropion lowers the threshold for seizure and is contraindicated in patients who are at risk for seizures. The risk of seizure associated with the use of bupropion is 0.1 percent or less. In one randomized, placebo-controlled trial that directly compared bupropion alone or in combination with the nicotine patch, bupropion produced a significantly higher rate of abstinence at one year than either the nicotine patch or placebo. Treatment with both bupropion and the nicotine patch was safe but did not lead to significantly higher cessation rates than did treatment with bupropion alone (36 percent and 30 percent, respectively). Nonetheless, many clinicians use the combination for smokers who are very dependent on nicotine.

Nortriptyline was effective for smoking cessation in two small studies that used 75 to 100 mg daily for three months, starting 10 to 28 days before the quitting date. No other antidepressant has had demonstrated efficacy for use in smoking cessation in a published trial, nor are there data to support the use of anxiolytic agents for smoking cessation. Treatment with clonidine reduces the symptoms of nicotine withdrawal and has been effective for smoking cessation, but the high frequency of adverse effects limits its use.

Other Methods

Hypnosis and acupuncture have also been suggested as therapies for smoking cessation. However, few controlled trials of hypnosis have been conducted, and acupuncture was found to be ineffective in randomized trials.

Weight Gain after Smoking Cessation

Weight gain averages 2.3 to 4.5 kg (5 to 10 lb) after smoking cessation and is thus a concern for many smokers who are contemplating quitting, especially women. Large weight gains (more than 13 kg) are uncommon, but are more likely in women, nonwhites, and heavy smokers than in other groups. A large weight gain does not negate the benefits of smoking cessation, but this point rarely comforts smokers who are concerned about their weight. In one study, a weight-management program did not avert post-cessation weight gain. Vigorous exercise reduced weight gain and increased abstinence rates in one trial. Whether moderate physical activity has similar benefits is unknown, but exercise has sufficient merits on its own to be recommended routinely. Bupropion and, in some studies, nicotine gum (but not the nicotine patch) temporarily reduced weight gain after smoking cessation, but only while the drug was being administered.

AREAS OF UNCERTAINTY

Most treatment studies have been conducted in healthy adults who were motivated to stop smoking.
Effective treatment for adolescent smokers, for smokers who are not interested in quitting smoking, or for those who repeatedly fail to quit is unclear. For smokers who are reluctant to attempt cessation, experts recommend “motivational interviewing,” a counseling technique developed to help people prepare for a change in behavior.26 The counselor builds empathy by acknowledging a smoker’s ambivalence about stopping smoking, supports the smoker’s autonomy with respect to making a responsible decision, and bolsters a smoker’s self-confidence so that he or she can make a change. The technique is promising and reasonable, but it has not yet been proven to increase cessation rates.

Characteristics associated with a low rate of successful treatment include coexisting psychiatric conditions (current or past depression or schizophrenia), alcohol or substance abuse, strong nicotine dependence, lack of social support for quitting (e.g., a spouse who smokes), and a low level of confidence in one’s ability to quit.8,9 The optimal treatment for such persons is also not known. Most experts advise the use of more intensive treatments for longer periods.

Current and past major depression are more common in smokers than nonsmokers.27 Smokers with a history of depression who attempt to quit smoking not only have lower rates of success but also have more depressive symptoms during nicotine withdrawal and a greater risk of recurrent depression after cessation than do smokers with no history of depression.28 The optimal treatment for smokers with current or past depression is uncertain, but they may require longer and more intensive treatment.8 Bupropion and nortriptyline are effective in smokers with a history of depression.8,9 Nicotine-replacement therapy may also be effective in such patients.29,30 Psychological support appears to be important.31

GUIDELINES

Two sets of clinical-practice guidelines based on independent, systematic reviews of the evidence were released in 2000. The Public Health Service’s Treating Tobacco Use and Dependence (available at http://www.surgeongeneral.gov/tobacco)8 updated a 1996 clinical-practice guideline issued by the Agency for Health Care Policy and Research.32 The guidelines issued by Britain’s Health Education Authority draw on systematic reviews by the Cochrane Collaboration’s Tobacco Addiction Review group (available at http://www.cochrane.org/cochrane/revabstr).9,33,34 The 1996 guidelines of the Preventive Services Task Force are consistent with newer guidelines except that they do not address newer types of pharmacotherapy (available at http://www.odphp.osophs.dhhs.gov/pubs/guidecps).35 In 2001, the Task Force on Community Preventive Services of the Centers for Disease Control and Prevention released evidence-based guidelines for interventions at the level of the health care system (available at http://www.thecommunityguide.org).10 The rate at which physicians provide advice on smoking cessation to their patients is now a standard measure for assessing the quality of care delivered by U.S. health plans.36

Guidelines consistently recommend that physicians assess and record patients’ smoking status; advise smokers to quit; assess their readiness to do so; and assist smokers by offering support, pharmacotherapy (a nicotine-replacement product or bupropion), and referrals to cessation resources. Health care delivery systems (including hospitals) are directed to identify patients’ smoking status, offer smoking-cessation services, and document these actions. The Public Health Service guidelines urge health insurers to cover all recommended treatments, including counseling and pharmacotherapy.8

CONCLUSIONS AND RECOMMENDATIONS

There is broad agreement, based on strong evidence, about what constitutes effective treatment of tobacco use and dependence. Physicians should routinely identify patients’ smoking status and readiness to quit, advise and assist smokers to quit, and offer pharmacotherapy to help them quit (Fig. 1).8 There is insufficient evidence to determine whether nicotine-replacement products or bupropion is superior. Current guidelines and most experts regard them as roughly equivalent.8,9,11 The choice of pharmacotherapy (Table 1) should take the patient’s preferences and past experiences into consideration, unless one agent is contraindicated. A general approach is to start with a single agent and add a second if the smoker has severe withdrawal symptoms, cravings, or difficulty maintaining abstinence. Nicotine-replacement products can safely be combined with one another and with bupropion. Drugs are most effective when accompanied by counseling, whether delivered in person or by telephone. The addition of pharmacotherapy to counseling doubles the cessation rate.11 Counseling is also effective by itself and should not be neglected.

The case vignette highlights common challenges facing physicians who treat smokers. The patient has repeatedly failed to quit smoking on her own, she has coexisting medical and psychiatric conditions, and she is concerned about gaining weight if she does quit smoking.37 Often, smokers who repeatedly fail to quit have never received effective treatments (especially counseling) or have used pharmacotherapy incorrectly. Such patients may also have coexisting psychiatric conditions or substance abuse. When a smoker has a history of depression, careful screening for symptoms of depression is warranted before and during treatment.
In the case of the woman described in the clinical vignette, intensive treatment combining counseling with one or more drugs is warranted; bupropion may be a good choice, since it has proved effective in depressed patients. Strong symptoms of nicotine withdrawal should be expected but can be relieved by pharmacotherapy. The use of two or more products may be necessary. Even though she has stable angina, the patient can safely use either nicotine-replacement therapy or bupropion. She may reduce her risk of weight gain after smoking cessation by participating in a program of moderate exercise and by using bupropion, nicotine gum, or both.

Smoking is a chronic problem, like hypertension or hyperlipidemia, that requires long-term management. Assistance with smoking cessation is a cost-effective intervention that is underused by physicians and inadequately covered by many health insurers. For physicians and health care systems alike, the challenge is implementing effective treatment in routine medical practice.

Supported by a Mid-Career Investigator Award in Patient-Oriented Research from the National Heart, Lung, and Blood Institute (HL04440).

REFERENCES


Copyright © 2002 Massachusetts Medical Society.