New Developments in Smoking Cessation*

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Research on smoking has increased in the past several years, and many new therapeutic modalities have been developed. Primary intervention for smoking cessation begins with systematic identification of smokers and a formal diagnosis of nicotine dependence. Providing self-help brochures without clinical advice has marginal efficacy, but these can be useful as an adjunct to clinician intervention. Several large studies have shown that physician advice alone can lead to quit rates of up to 10%, and follow-up for patients trying to quit can double cessation rates. Behavioral therapy alone has demonstrated cessation rates of approximately 20% for those willing to participate. Drug therapy remains the most attractive method of smoking cessation for many patients. The standard approach has been nicotine substitution using one of the four forms of nicotine replacement (gum, patches, nasal spray, inhaler) currently available. The efficacy of nicotine replacement products is similar, with each agent providing a doubling of the cessation rate. Thus, the choice of agent depends on patient factors and preference. Bupropion is the first nonnicotine-containing agent approved for smoking cessation, with cessation rates ranging from 10.5 to 24.4%, depending on dose. One-year follow-up suggests a continued benefit with this agent. The combination of bupropion and transdermal nicotine has also been shown to be effective for smoking cessation in clinical trials. Effective approaches to smoking cessation should combine identification of smokers, provision of advice at each visit, and widespread availability of treatment.

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Key words: bupropion; drug therapy; nicotine; smoking cessation; therapy; tobacco

Abbreviations: AHCPR = Agency for Health Care Policy and Research; FDA = Food and Drug Administration; NCI = National Cancer Institute; NNS = nasal nicotine spray

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moking remains a very common habit in the United States, with recent estimates showing that 23.5% of adults are still smoking.1 In the last few years, there has been a great increase in research on smoking, and several new therapeutic modalities have been developed. This article reviews a general approach to smoking cessation, with an emphasis on developments in drug therapy that are based on Agency for Health Care Policy and Research (AHCPR) guidelines.2 The guidelines emphasize systematic identification of smokers, provision of physician advice on cessation, and use of drug therapy to assist smokers in cessation.

Identification of Smokers and Diagnosis of Nicotine Dependence

One of the primary interventions for smoking cessation is systematic identification of smokers. AHCPR guidelines advocate adding smoking to the vital sign list. Research by Fiore et al3 has shown that this simple maneuver triggers the clinician to initiate discussions about quitting. Providers also should make a formal diagnosis of nicotine dependence. Sharing a medical record diagnosis of tobacco dependence with the smoker actually triggers a number of patients to quit smoking.4 In addition, nicotine dependence on the problem list can be a reminder for smoking-cessation counseling. Finally, those patients who are heavily nicotine dependent are most likely to require drug therapy for cessation.

The “gold standard” for diagnosis of nicotine dependence comes from the Diagnostic and Statistical Manual of Mental Disorders IV criteria, which include two tobacco-related diagnoses: nicotine dependence (305.10) and nicotine withdrawal (292.00; Table 1).5 The key features required for the diagnosis of nicotine dependence are continued use despite wanting to quit, prior quit attempts, persistent use in the face of physical illness, tolerance, and presence of withdrawal symptoms. Based on these criteria, the vast majority (nearly 90%) of medical patients who smoke have nicotine dependence.6 The Fagerstrom Score is a quicker approach that is more adaptable to busy clinic settings.7 This questionnaire includes nine items, but for clinical purposes, the two key questions are as follows: (1) Does the patient smoke within 5 min of awakening? (2) Does the patient smoke > 25 cigarettes/day? Those patients who answer affirmatively to both questions are highly dependent on nicotine.8

Provision of Self-Help Brochures

When given to unselected smokers, self-help brochures such as the National Cancer Institute (NCI) booklets or the American Lung Association program9 have marginal efficacy in helping smokers to quit. Those smokers who are actively trying to quit may be helped by these brochures, but the cessation rates are not high. The best role of these materials is as an adjunct to clinician advice. The NCI booklets are free of charge or at low cost, and should be placed prominently in the doctor’s office and in hospitals. These materials can be ordered from the NCI (telephone, 1–800-4-CANCER), and although the quit rate is relatively low, the cost is minimal.

Doctor Advice

Physician advice to encourage smoking cessation has been studied extensively over the last 15 years. An early meta-analysis showed an overall cessation rate of 8.4% at
Table 1—Criteria for Tobacco-Related Diagnoses*

<table>
<thead>
<tr>
<th>No.</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tolerance as defined by either of the following:</td>
</tr>
<tr>
<td></td>
<td>A need for markedly increased amounts of nicotine to achieve desired effect.</td>
</tr>
<tr>
<td></td>
<td>Markedly diminished effect with continued use of the same amount of the nicotine (ie, absence of nausea, dizziness, and other symptoms of initial nicotine use).</td>
</tr>
<tr>
<td>2</td>
<td>Withdrawal as manifested by either of the following:</td>
</tr>
<tr>
<td></td>
<td>The characteristic withdrawal syndrome for nicotine. The same or a closely related substance is taken to relieve of avoid withdrawal symptoms.</td>
</tr>
<tr>
<td>3</td>
<td>Nicotine is often taken in larger amounts or over a longer period than was intended.</td>
</tr>
<tr>
<td>4</td>
<td>There is a persistent desire or unsuccessful effort to cut down or control substance use.</td>
</tr>
<tr>
<td>5</td>
<td>A great deal of time is spent in activities necessary to obtain nicotine or recover from its effects.</td>
</tr>
<tr>
<td>6</td>
<td>Important social, occupational, or recreational activities are given up or reduced because of substance use.</td>
</tr>
<tr>
<td>7</td>
<td>The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.</td>
</tr>
<tr>
<td>8</td>
<td>Characteristic withdrawal symptoms.</td>
</tr>
<tr>
<td>9</td>
<td>Substance often taken to relieve or avoid withdrawal symptoms.</td>
</tr>
</tbody>
</table>

292.0 nicotine withdrawal.

1 Daily use for at least several weeks.
2 Abrupt cessation or reduction of nicotine, followed in 24 h by four or more of the following: Dysphoric or depressed mood, Insomnia, Irritability, frustration, or anger, Anxiety, Difficulty concentrating, Restlessness, Decreased heart rate, and/or Increased appetite or weight gain.
3 The symptoms in No. 2 cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
4 The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

*Adapted from the Diagnostic and Statistical Manual of Mental Disorders IV.5

6 months with brief (<5 min) physician advice.10 Since then, there have been several large studies of physician advice that have shown quit rates of up to 10%.11,12 Cromwell et al13 estimated cost-effectiveness for all the interventions recommended by the AHCPR guidelines. The average estimated cost per quitter was $3,779, and the cost per quality-adjusted life year saved was only $1,915. These values are comparable to those for cervical cancer screening and pneumonia vaccination, and are much lower than other commonly recommended preventive interventions, such as hypertension screening for men aged 40 years, which costs $23,335/yr of life saved.

Follow-up for patients trying to quit can increase the effectiveness of physician advice and double the cessation rates. The physician can personalize the quitting message by highlighting the patient’s risk factors for tobacco-associated illness and emphasizing the direct benefits of cessation. Several studies14-16 have shown that smoking-specific risk factor feedback (pulmonary function testing and carbon monoxide testing) can double the quit rates attained in primary care settings.

The stage-of-change model developed by Fava et al17 is very helpful in understanding the quitting process. They found that smokers can be grouped into stages using a few simple questions, and that these stages predict the chance of quitting. These stages also help the busy clinician tailor counseling and therapy. With a few simple questions, one can place patients into a stage of change and then provide stage-appropriate advice and therapy (Table 2).18,19

**BEHAVIORAL THERAPY**

Behavioral therapy has been studied extensively, and cessation rates average 20% for those willing to participate. For example, Lande et al20 found that the quit rates with the American Lung Association and American Cancer Society programs were 16% and 22%, respectively, at 1 year. The main disadvantage of this approach is that relatively few smokers (about 5%) are interested in attending classes at any given time.21 The cost-effectiveness data developed by Cromwell et al13 showed, however, that group sessions were the most cost-effective approach to delivering smoking-cessation interventions. Although relatively few patients want to go to classes, physicians should nevertheless have a list of referral smoking cessation clinics in their area for the recalcitrant smokers who express an interest in attending them, and for those who have failed to respond to simpler approaches.

The key components to an effective behavioral program are assessment of stages of change, identification of barriers to quitting, and development of cessation and relapse-prevention plans. Most programs now combine this with pharmacotherapy. Simple computer-tailored cessation messages may be an effective alternative for behavioral support. Strecher et al22 showed that the quit rate more than doubled with such an approach, and this concept has been incorporated into patient-support programs provided by several manufacturers of smoking cessation products.

**DRUG THERAPY**

Drug therapy is the most attractive means of smoking cessation for many patients and physicians. It fits within the medical model and offers the hope of a “magic bullet.” However, lack of knowledge of the pharmacology of these agents, use of drugs without concomitant behavioral interventions, and unrealistic expectations on the part of patients and physicians tend to compromise the results of drug therapy. The standard approach to drug therapy for smoking cessation has been nicotine substitution. Recently, antidepressants23 have been shown to be effective as single agents and in combination with nicotine replacement. Other drug therapies, such as clonidine,24 antianx-
Table 2—Stages of Change in Smoking Cessation*  

<table>
<thead>
<tr>
<th>Stage</th>
<th>Key Identifier</th>
<th>Appropriate Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precontemplation</td>
<td>Does not want to quit smoking</td>
<td>Feedback to raise awareness of smoking-related problems</td>
</tr>
<tr>
<td>Contemplation</td>
<td>Wants to quit, but not in next month</td>
<td>Identify barriers to awareness of smoking, review prior quit attempts</td>
</tr>
<tr>
<td>Action</td>
<td>Wants to quit within next month or has quit for &lt; 1 mo</td>
<td>Find successes, pros and cons of continued smoking</td>
</tr>
<tr>
<td>Maintenance</td>
<td>Has quit for at least 1 mo</td>
<td>Plan for relapse, avoid trigger situations, consider nicotine</td>
</tr>
<tr>
<td>Relapse</td>
<td>Quit and now smoking on a daily basis</td>
<td>Replacement or bupropion</td>
</tr>
</tbody>
</table>

*Adapted from Prochaska.19

...and nicotine antagonists,26 show some promise, but have not yet been shown to be effective in large trials.

Nicotine Replacement

Today, there are four forms of nicotine replacement available: nicotine gum, nicotine patch, nicotine nasal spray, and nicotine inhaler. The efficacy of nicotine replacement products is similar, with each agent leading to a doubling of the cessation rate, so the choice of agent will depend on patient factors and preference. In some heavily dependent smokers, it may be beneficial to combine nicotine replacement products (eg, gum and patch).27 This review focuses on transdermal nicotine, since it is the most commonly used product, and highlights differences among the agents.

Transdermal Nicotine: Nicotine can be absorbed through the skin, and sustained levels approaching those seen with smoking are easily attained with transdermal nicotine. The steady-state nicotine levels are similar to those obtained with other nicotine replacement products. Meta-analyses have combined these data with unpublished trials, and concluded that nicotine replacement doubled the baseline cessation rate, and that this effect was not altered by other factors, such as intensity of behavioral counseling.28,29 However, there continued to be marked relapse after therapy was discontinued. Generally, the adverse effects of transdermal nicotine are mild and rarely cause discontinuation of drug therapy (6%). Most commonly seen is short-lived skin irritation (erythema, irritation, mild edema) that is seen in 30 to 50% of patients. A small percent of patients (<5%) manifest contact dermatitis, which may recur on rechallenge with the patch. A few patients with contact dermatitis have had skin reactions when rechallenged with cigarettes. Rotation of patch sites may help limit skin irritation. Nightmares and sleep disturbance are sometimes seen, in which case, removal of the patch before bed can resolve the problem.

...and is ischemia may be less than seen with continued smoking. There have been several widely publicized cases of myocardial ischemia in patients who continued to smoke while using transdermal nicotine, although the actual rates of ischemia may be less than seen with continued smoking. Two trials that focused on smokers with cardiovascular disease showed no increased rates of angina or myocardial infarction.30,31

The randomized trials have all used relatively short-term therapy with the patch. One begins with the highest-dose patch for a given system for 4 to 6 weeks, then tapers to the next dose for 4 to 6 weeks, with a final taper of 2 weeks if there is a third dose level for the particular patch used. Most studies of the patch and the package inserts recommend 8 to 12 weeks of therapy including a tapering period. To ensure active follow-up of patients, it is best to prescribe nicotine replacement in small quantities (ie, not >2-week supply at a time). In this way, patients can call in for follow-up and renewal of medication. This allows the provider to check on the success of the quit attempt, to deal with slips or relapse immediately, and also to monitor for any side effects. Since many patients will suffer a relapse with nicotine replacement therapy, physicians often ask whether retreatment is warranted. Considering the stage-of-change model, it is predictable that many patients will need to recycle through treatment. A study by Gourlay et al32 found that an additional 4 to 5% of smokers who failed to respond to initial patch therapy will succeed when offered it a second time. So, the success rate with retreatment using the same drug therapy is relatively low, and this would suggest that one should try another form of nicotine replacement or bupropion in those who have not succeeded.

If the patient is very small (<110 lb), does not smoke very much (<10 cigarettes/d), or has active cardiovascular disease, one should start with a lower-dose patch. If the patient is heavy (>350 lb), starts smoking very much (>50 cigarettes/d), or has active cardiovascular disease, one should try another form (eg, gum and patch).27
It currently costs $639 annually. Without any behavioral help, one should expect very low quit rates with nicotine patch (on the order of 5%). As mentioned above, the nicotine levels obtained with patch therapy are about 50% of those seen with smoking. A provocative study by Sachs et al\(^36\) found that short-term patch therapy are about 50% of those seen with smoking. Multimodality Approach to Lung Cancer

Without any physician advice or behavioral support,\(^35\) one should expect very low quit rates with nicotine patch (on the order of 5%).

There has been no reduction in the cost of transdermal nicotine since it became available without a prescription. A provocatively high dose of nicotine gum actually resulted in a lower quit rate with active gum than with placebo treatment (8% nicotine gum, 13% placebo gum). The product inserts for all transdermal nicotine products indicate that it should be used as part of a cessation program. Yet, many patients receive the patch without any physician advice or behavioral support,\(^35\) Without any behavioral help, one should expect very low quit rates with nicotine patch (on the order of 5%).

Nicotine Polacrilex: Nicotine gum is the oldest form of nicotine replacement. It is available in two strengths (2 mg and 4 mg) and is a nonprescription product. The key point about nicotine gum pharmacology is that the absorption takes place buccally. Nicotine that is swallowed tends to lead to GI side effects, and, in any case, undergoes extensive first-pass metabolism by the liver, resulting in minimal blood levels. Thus, to use nicotine gum effectively, the patient must chew it a few times to soften the gum until a tingling sensation is felt. Then the gum should be left alone (“chew and park”), and given a couple of more bites when the tingling goes away. Rapid chewing of the gum leads to excessive saliva production and GI side effects. The 4-mg gum is much more effective, and should be the primary form of gum used for most smokers (those who smoke > 15 cigarettes/d). Typical doses begin with 10 to 15 pieces/d, and most smokers settle at about 5 to 8 pieces/d after the first week or two of therapy. Nicotine gum has been used long term (5 years) in the Lung Health Study, and there were no long-term side effects noted.\(^39\)

Antidepressants and Smoking Cessation

Bupropion is the first nonnicotine-containing agent to be approved by the FDA for smoking cessation. Bupropion is a noncyclic antidepressant that has most of its neurochemical effect on the dopamine and norepinephrine transmitter systems. It has been used as a second-line antidepressant, and is also effective for patients with mania, adult attention deficit disorder, and other psychiatric conditions. Bupropion is available in two sustained-release forms (Wellbutrin and Zyban; Glaxo-Wellcome; Research Triangle Park, NC). The Zyban form was developed specifically for smoking cessation, and comes with a smoker support program that includes tailored messages on quitting and relapse prevention. Zyban is used in a somewhat lower maximal dose than Wellbutrin for depression. The initial study on bupropion has just been published and enrolled \(> 600\) patients.\(^48\) Importantly, the investigators excluded patients with current depression. Patients were randomized to placebo or bupropion, \(50\) mg bid, \(150\) mg qd, and \(150\) mg bid, and treated for 6 weeks.

Nasal Nicotine Spray: Nasal nicotine spray (NNS) was approved by the US Food and Drug Administration (FDA) in 1997. Each spray contains 0.5 mg of nicotine, and a dose is defined as one spray in each nostril. In the clinical trials, subjects were allowed to take up to 5 doses/h, with a maximum of 40 doses/d (40 mg of nicotine). As would be predicted, the most common adverse reactions related to nasal and throat irritation, coughing, runny eyes and nose, sinusitis, palpitations, and nausea. The cessation rates in trials with NNS at 1 year range from 15 to 25%.\(^40–42\) A meta-analysis of nicotine replacement suggested that NNS and the inhaler might have higher quit rates than the patch or gum.\(^43\) However, experienced tobacco researchers who have tested all the products find little difference in the overall quit rates.

Inhaled Nicotine: The nicotine inhaler has been approved by the FDA, but is not yet available in pharmacies.\(^45\) It consists of a mouthpiece and a nicotine-impregnated cartridge. Each inhaler contains 10 mg of nicotine, and 1 mg of menthol to decrease the irritation from the nicotine. A single puff contains 13 \(\mu\)g of nicotine. Thus, a smoker needs to get about 80 puffs to obtain the nicotine in a typical cigarette. The dose that has been successful in recent trials is to use four inhalers per day, with each inhaler being used for 500 puffs. This high-frequency dosing is necessary, since early trials had poor quit rates when less frequent use of the inhaler was allowed.\(^45\) One practical consideration is that the absorption of nicotine from the inhaler may be diminished in cold weather (<10°C [<50°F]). Outdoor workers may find other forms of nicotine replacement more acceptable. In research settings, the inhaler is well tolerated, with transient mouth and throat irritation being the most common adverse events. The cessation rates with the inhaler have been from 11 to 18% at 1 year.\(^46,47\) The nicotine inhaler may be the best choice for the person who needs something to do with his or her hands, since it requires very frequent handling of the inhalers and cartridges.
The cessation rates at the end of therapy were 10.5%, 13.7%, 18.3%, and 24.4%, respectively. Follow-up to 1 year suggested a continued benefit to bupropion therapy. Data from a study of bupropion combined with transdermal nicotine show high long-term quit rates with the combination therapy.49 The retail cost of bupropion is relatively high, at about $90 for 60 tablets of 150-mg strength. A typical duration of therapy is 7 to 12 weeks. Thus, a 3-month course of full-dose therapy would be about $270. Unfortunately, many insurers are not paying for bupropion therapy for smoking cessation, and are restricting the use of the drug to psychiatrists only.

There are several contraindications for the use of bupropion: seizure disorders, history of anorexia or bulimia, and uncontrolled hypertension. In the single-agent trial, the drug was well tolerated, with most common serious adverse events with bupropion being insomnia and dry mouth. In the combined trial with transdermal nicotine, several subjects developed worsening hypertension, so monitoring of BP during combined therapy is prudent.

Given the current data, it makes sense to use bupropion in those patients who are unable to tolerate, who have failed, or who do not want to use nicotine replacement. As a single agent combined with some behavioral counseling, one should not expect long-term cessation rates > 15 to 20%. Since the success of cessation with single-drug therapy (nicotine or bupropion) is not very high, the most rational approach for the recalcitrant smoker is to use combination therapy. This would include patients who have high levels of nicotine dependence, who have a history of psychiatric problems, or for those who have failed to respond to prior therapy. The cost of a combined treatment program will be about $600 for 12 weeks, and one should expect 1-year quit rates on the order of 25 to 30%.

Two studies have shown that a tricyclic antidepressant, nortriptyline, can be effective for smoking cessation. These results suggest that there may be other antidepressants that can help smokers quit.50,51 All of the antidepressants are being tested in patients without current depression, and the effect of the agents does not seem to depend on a history of prior depression or on the presence of depressive symptoms during cessation. At present, the mechanism of action of the antidepressants for smoking cessation is speculative, but clearly involves more than just treating an underlying tendency to depression.

**Summary of Drug Therapy for Smoking Cessation**

The only proven agents are the various forms of nicotine replacement and bupropion, both of which are effective when combined with instruction on its use, counseling, and follow-up (Table 3). Drug therapy is not a panacea and requires some behavioral support in order to have

<table>
<thead>
<tr>
<th>Type</th>
<th>Route of Absorption</th>
<th>Dosage</th>
<th>Doses Per Day</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine replacement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gum</td>
<td>Buccal</td>
<td>2 mg, 4 mg</td>
<td>20</td>
<td>Avoid rapid chewing, do not use immediately after acid beverages (eg, coffee, sodas)</td>
</tr>
<tr>
<td>Patch</td>
<td>Skin</td>
<td>21 mg, 14 mg, 7 mg, 22 mg, 11 mg</td>
<td>One</td>
<td>Change patch site daily, remove at bedtime if sleep disorder, multiple patches in very heavy smokers</td>
</tr>
<tr>
<td>NNS</td>
<td>Nasal</td>
<td>0.5 mg/spray Two sprays/dose</td>
<td>40 sprays, 40 doses</td>
<td>Nasal/throat irritation common, resolves with continued treatment</td>
</tr>
<tr>
<td>Inhaler</td>
<td>Lung</td>
<td>13 μg/puff</td>
<td>400 puffs</td>
<td>Need to use very frequently to achieve adequate levels</td>
</tr>
<tr>
<td>Bupropion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single agent</td>
<td>GI</td>
<td>150 mg daily, ↑ to 150 mg bid after 3 to 4 days; start 1 wk before quit day; treat for 7 to 12 wk</td>
<td>NA</td>
<td>Adverse effects: headache, insomnia, dry mouth</td>
</tr>
<tr>
<td>Combined with patch</td>
<td>GI/skin</td>
<td>150 mg daily, ↑ to 150 mg bid after 3 to 4 days; start 1 wk before quit day; start patch on quit day; treat for 7 to 12 wk, taper patch after completing bupropion</td>
<td>NA</td>
<td>Adverse effects: headache, insomnia, dry mouth, worsening hypertension</td>
</tr>
</tbody>
</table>

*NA = not applicable.
optimal effectiveness. As mentioned earlier, the cost analyses deriving from the AHCPR guidelines show that pharmacotherapy for smoking cessation is very cost-effective compared with other preventive therapies.52

**Integration of Smoking Cessation: Strategy into Practice**

In general, research studies on smoking cessation are based on one-time interventions. These data form the basis for the AHCPR guidelines; however, one-time interventions do not mimic the realities of clinical practice. As health-care providers, we may see smokers regularly over a period of years and have multiple opportunities for addressing smoking cessation. Long-term studies have shown that an organized practice that systematizes the components of this strategy can result in major reductions in smoking prevalence. Russell et al.30 trained general practitioners in brief counseling and use of nicotine gum, and provided chart reminder stickers along with easy referral to smoking cessation clinics. They found that the rate of decline in overall smoking prevalence was double that of brief advice-only practices (5.5% vs 2.1%).50 Sollberg et al.30 organized their family practice to identify smokers, systematize brief advice following a stage-of-change model, and simplify follow-up. They found that the overall quit rate was 20% over a 2-year period.51 As the AHCPR guidelines become integrated into Health Plan Employer Data and Information Set report cards,52 managed care organizations will increasingly be taking a system-wide approach to smoking cessation. This will include the key elements of identification of smokers, provision of advice at each visit, and widespread availability of treatment for smoking cessation.

**Conclusion**

Although the cessation rates with therapy for nicotine dependence are relatively low, systematic application of these principles in doctors’ offices is feasible, and over time will result in clinically important quit rates. Integration of smoking cessation into physician practice is a cornerstone of lung cancer prevention. As health-care providers, we can help our patients quit smoking by using the following multifaceted approach: (1) identify all smokers and diagnose nicotine dependence; (2) provide self-help smoking cessation brochures; (3) provide brief, tailored advice to all smokers; (4) refer recalcitrant smokers to specialized clinics; and (5) use nicotine replacement and/or bupropion in combination with brief counseling and active follow-up.

**References**


7 Fagerstrom KO. Measuring degree of physical dependence to tobacco smoking with reference to individualization of treatment. Addict Behav 1978; 3:235–241


16 Risser NL, Belcher DW. Adding spirometry, carbon monoxide and pulmonary symptom results to smoking cessation counseling: a randomized trial. J Gen Intern Med 1990; 5:16–22

17 Fava JL, Velicer WF, Prochaska JO. Applying the transtheoretical model to a representative sample of smokers. Addict Behav 1995; 20:189–200


19 Prochazka AV. Medical approach to smoking cessation. Semin Respir Crit Care Med 1996; 17:290–297


49 Fiscella K, Franks P. Cost-effectiveness of the transdermal nicotine patch as an adjunct to physicians’ smoking cessation counseling. JAMA 1996; 275:1247–1251
52 Davis BM. Healthcare report cards and tobacco measures. Tob Control 1997; 6:S70–S77