

New Treatments for Smoking Cessation

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Abstract

Helping cigarette smokers to permanently stop smoking is one of the most effective ways to prevent cancer. A physician's instruction to a patient to stop smoking and to offer assistance in this endeavor is an important motivator. Current guidelines state that clinicians should encourage all smokers who want to quit to use medications and should offer psychosocial therapies, as well. It has been shown that even brief clinician advice about smoking cessation increases quit rates.

Five medications—bupropion, nicotine gum, nicotine inhaler, nicotine nasal spray, and nicotine patch—and one proven psychosocial therapy (behavior therapy) appear equally effective and safe; i.e., they all double quit rates and are associated with a less than 5% dropout rate due to adverse events.

In 1998, approximately one third of those who attempted to quit smoking used a medication. Attending group behavior therapy to supplement medications increases quit rates but is not essential for medications to work. As there are no proven treatment-matching protocols, patients should choose the treatment(s) they believe will be most effective for them. In the future, people who

continue to smoke will be individuals with severe nicotine dependence or psychiatric symptoms; thus, clinicians will increasingly be called on to provide pharmacotherapy for smoking cessation. (CA Cancer J Clin 2000;50:143-151.)

Motivating Smokers

Most clinician interactions with smokers involve motivating smokers to make a quit attempt. Protocols for such interactions using a brief intervention (two to five minutes) have been well-described in brochures from the National Cancer Institute,¹ the Agency for Health Care Policy Research (AHCPR),² and the American Psychiatric Association³ (Table 1). If a smoker does decide to quit, the clinician is faced with the dilemma of selecting a treatment. How does one decide which, if any, of the proven treatments to recommend? This article reviews the pros and cons of the several treatment options for smoking cessation and illustrates how these can be delivered within a brief intervention.

Motivating Yourself, the Clinician

In this era of increasing financial and legal pressures, it is understandable that clinicians may find it difficult to remember to intervene with their patients who have a disorder that is asymptomatic, is not immediately life-threatening, could be self-cured, is unresponsive to treatment 80% of the time, and is often not considered their responsibility. On the other hand, clinicians' primary interest is promoting the health of their patients, and several studies have shown that **the**

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Table 1
Contact Information for Smoking Cessation Resources
or Referrals to Specialists

National Organizations

American Academy of Addiction Psychiatry

7301 Mission Road, Suite 252
 Prairie Village, KS 66208
 Phone: (913) 262-6161
members.aol.com/addicpsych/private/homepage.htm

American Cancer Society

1599 Clifton Road, NE
 Atlanta, GA 30329-4251
 Phone: (800) ACS-2345
www.cancer.org

American Lung Association

1740 Broadway
 New York, NY 10019
 Phone: (800) LUNG-USA
www.lungusa.org

American Psychiatric Association

1400 K Street NW
 Washington, DC 20005
 Phone: (202) 682-6239
www.apa.org

American Society of Addiction Medicine

4601 North Park Avenue, Arcade
 Suite 101
 Chevy Chase, MD 20815
 Phone: (301) 656-3920
www.asam.org

National Cancer Institute

9000 Rockville Pike
 Building 31 10A16
 Bethesda, MD 20892
 Phone: (800) 4-CANCER
www.nci.nih.gov

Nicotine Anonymous

NAWSO
 PO Box 591777
 San Francisco, CA 94159-1777
 Phone: (415) 750-0328
www.nicotine-anonymous.org

Society for Behavioral Medicine

7611 Elmwood Avenue
 Middleton, WI 53562

Phone: (800) LUNG-USA

Phone: (608) 827-7267

www.sbmweb.org

Society for Research on Nicotine & Tobacco

7611 Elmwood Avenue
 Middleton, WI 53562
 Phone: (608) 836-3787
www.srnt.org

Local Organizations

Your local hospital or worksite
 wellness/Employee Assistance Program
 Your state Department of Health
 Your state alcohol and drug abuse office

Consumer Brochures

Treatment Works: When You Choose to Stop Smoking

American Psychiatric Association

\$19.95/12 (order #2525)
 (202) 682-6268

Quit Smoking Action Plan

American Lung Association

(212) 315-8700
www.lungusa.org

Smart move! A Stop Smoking Guide

American Cancer Society

(800) ACS-2345
www.cancer.org

Pharmaceutical Company Helplines

Glaxo Wellcome (bupropion)

800-822-6784 (UCAN-QUIT)

McNeil Consumer (OTC patch)

800-699-5765

Novartis Consumer (Rx patch)

800-452-0051

SmithKline Beecham (OTC patch)

800-834-5895

SmithKline Beecham (OTC gum)

800-419-4766

Table 2
Important Statistics About Smoking Cessation

- 50% of current smokers will die from smoking if they do not quit.⁵
- Cancers of the colon, lung, stomach, and esophagus have been associated with smoking.
- Stopping smoking decreases the risk of myocardial infarction by 50% in the first year alone. Cancer risk decreases to near normal within 15 years.⁵
- Although 70% of smokers want to stop, only 35% to 45% try to quit in any given year.⁶
- Only 10% to 20% of smokers are ready to stop in the next month.⁷
- Among self-quitters, 50% remain abstinent for two days and 33% for a week.⁹
- For any given quit attempt without therapy, 5% to 10% quit for good.⁹
- Most smokers make five to seven attempts before they stop successfully; thus, 50% of smokers eventually quit smoking.⁶

time spent on smoking cessation advice is the most effective use of a practitioner's time in terms of preventing mortality or morbidity.⁴ In fact, as smoking will cause the deaths of 50% of current smokers⁵ and as most smoking-related illnesses are reversible,⁶ one premature death will have been avoided with every two smokers a clinician persuades and helps to stop smoking. Thus, a clinician who motivates 10 smokers to stop smoking in a year will have prevented five avoidable early deaths. Not a bad return on a total investment of a few hours.

Some Basic Facts About Smoking

About 30% of patients are current smokers. Although 70% of smokers say they

are "interested" in quitting, only 10% to 20% plan to quit in the next month⁷ (Table 2). About 45% of smokers will try to quit in a given year.⁶

In the past, 90% to 95% of smokers quit on their own. However, with the introduction of over-the-counter nicotine gum and patches, and of non-nicotine therapies, about one-third of smokers now use a medication when they try to stop.⁸ In fact, most smokers use a step-wise approach to smoking cessation. They may first try to stop on their own one or more times. Then, they may use booklets or an OTC medication. Next, they may try group therapy or they may see a clinician for a prescription.

When smokers try to stop, relapse occurs quickly.⁹ In those who try to quit on their own, only half succeed for two days and only a third last one week.⁹ Overall, self-quitters have a success rate of 5% to 10%. Although these statistics seem discouraging, most smokers make five to seven quit attempts before they finally succeed. Thus, half of all smokers eventually quit.⁶

One implication of these statistics is that clinicians need to understand that their role is not so much helping with one quit attempt, but rather helping the smoker through several attempts before a final successful one. The other implication is that clinicians need to prompt and re-prompt smokers to make efforts to stop. Offering treatment can not only help smokers stop, but can also motivate smokers to try to stop.¹⁰

Some Basic Facts About Treatment

1. The efficacy of several smoking cessation therapies is well established (Table 3).^{2,3} All proven treatments appear to be equally effective: They all double the chances a quit attempt will be successful (Table 4). None have significant side effects.

Given these facts and the AHCPA guidelines, all smokers interested in quit-

Table 3
Proven Smoking Cessation Therapies

<u>Medications</u>	<u>Availability</u>
Nicotine Gum	OTC
Nicotine Patch	OTC
Nicotine Nasal Spray	Rx
Nicotine Inhaler	Rx
Bupropion	Rx
<u>Psychosocial Therapy</u>	
Behavior Therapy	Group or Individual

OTC = over the counter (without prescription); Rx = available by prescription only

ting smoking should be encouraged to use medications.

Currently, there is anecdotal experience but no proven method for matching particular treatments to particular types of smokers. In fact, early evidence suggests that allowing smokers to choose their own type of treatment produces better outcomes.¹¹ In light of these findings, clinicians are encouraged to provide smokers with information about the proven therapies and treatment resources (Table 1). The American Psychiatric Association,¹² the American Lung Association,¹³ and the American Cancer Society have developed consumer brochures for smokers that outline the pros and cons of the various treatments for smoking and list treatment resources.

2. With other types of drug dependencies, many experts believe psychosocial or self-help therapies are essential and that medication alone is ineffective. This is not the case, however, with nicotine dependence. For example, OTC products such as nicotine gum and patches double quit rates when used without psychosocial therapy¹⁴ (Table 4). Thus, although adding psychosocial therapy certainly increases quit rates, insistence on adjunctive talk therapy as a condition for receiving prescription medication is not based

on scientific evidence.

3. Although most clinicians believe that abrupt cessation is more effective than gradual nicotine reduction, empirical data to support this belief are limited.¹⁵ Patients with a strong preference for gradual reduction should be allowed to use this option. They should be advised, however, not to use a nicotine replacement therapy (NRT) until they have stopped smoking completely. Switching to low tar/low nicotine cigarettes as an approach to reducing nicotine consumption does not appear to produce significant health benefit.¹⁶ Finally, when dealing with smokers who are ambivalent about quitting, it is unclear that aiming for an initial goal of reducing smoking will improve health or will eventually result in smoking cessation.¹⁷

4. Written materials, such as short motivational brochures that can be obtained from several sources (Table 1), should be available as handouts for patients who smoke. A list of local treatment resources is another type of handout that can be helpful.

5. Given that for most smokers, relapse occurs quickly,⁹ the first follow-up contact should be two to three days, not one to two weeks, after the quit date. This follow-up

Table 4
Typical Long-Term Quit Rates

	No Therapy	Brief Advice	Behavior Therapy
No medication or placebo	5%	10%	15%
Medication	10%	20%	30%

can be done via telephone or by a paraprofessional.

6. Recent evidence indicates co-morbid depression and alcohol/drug abuse are important causes for treatment failure. Cessation of smoking may, in a small minority, exacerbate these problems.¹⁸ Thus, smokers with current or past histories of these problems need to be followed closely during cessation attempts.

7. Many smokers, especially women, are concerned about weight gain. Restricting food intake while trying to stop smoking *worsens* smoking outcomes.¹⁹ Most clinicians recommend increasing physical activity or using NRT or bupropion to minimize initial post-cessation weight gain (at least while therapy is used) and not attempting caloric restriction until several months after stopping smoking.¹⁹

8. The cost of medication therapy is about \$3 to \$4 a day, whereas fees for behavioral therapy vary from no cost to \$150 or more per course of therapy. Health plans vary considerably with regard to covered services and medications.

9. Non-nicotine substances in tobacco increase the metabolism of many common drugs, such as theophylline and some antidepressants.²⁰ Thus, the levels of these medications may need to be decreased with cessation. Nicotine replacement itself does not affect levels of these medications.

10. Some of the smokers requesting help from clinicians will have failed all the therapies typically used. Other smokers

may have special problems, such as a sabotaging spouse or co-worker. Clinicians should identify a local psychologist, addiction counselor, other clinician, health educator, etc. with expertise in smoking cessation therapy for referral of smokers who appear to need specialized help (Table 1).

11. Clinicians can learn more about smoking cessation therapies from a variety of sources, such as short articles²¹ and books.²² In addition, they can attend annual educational meetings held by the American Society of Addiction Medicine and the Society for Research on Nicotine and Tobacco (Table 1).

What's New About Old Treatments?

Between 1995 and 1996, nicotine gum and two of the four currently approved nicotine patches became available without prescription. Several studies conducted in OTC settings confirmed that the use of gum or patch doubled cessation rates with no evidence of significant adverse events.²¹ The availability of nicotine gum and transdermal patches without prescription has produced the largest increase in smoking cessation since the 1964 Surgeon General's report on smoking.⁸

Clinicians often recommend or are asked about OTC treatments and this is clearly true for nicotine patches and gum. Since these products were originally marketed, much information has continued to accrue, further enhancing and docu-

menting the efficacy and safety of such therapies. For example, there are no longer any true contraindications to the use of these products in smokers. Almost all researchers agree that nicotine is not a carcinogen,²³ and there is growing consensus that nicotine derived from medications does not promote cardiovascular disease.²⁴ Finally, in addition to the fact that gum and patch formulations are associated with a slower onset and much lower nicotine levels than are cigarettes, they do not produce carbon monoxide and carcinogens.²² Consistent with these findings, the safety and abuse liability records of nicotine gum and patches have been excellent.²⁵

The OTC labeling on nicotine gum and patches instructs smokers to see their clinicians before using the products if they have heart disease, ulcers, or uncontrolled hypertension. This recommendation is made because clinicians may wish to monitor these patients' progress more closely when such individuals stop smoking.

Labeling also directs smokers who are pregnant or breast-feeding to see their health care providers before using nicotine gum or patch. How much of the harm associated with smoking during pregnancy is due to nicotine, carbon monoxide, or other substances is unclear.²⁶ Clearly, the fetus is exposed to much less nicotine with gum or patches than with smoking. Most reviews recommend that nicotine gum or a patch be considered for smoking cessation in those pregnant smokers who want to quit but have failed non-nicotine therapies.²⁶

The OTC labels recommend not using nicotine gum or patches along with other nicotine products. However, three studies have found that the combined use of a nicotine patch plus 2 mg nicotine gum *ad lib* (usually four to eight pieces/day used during craving episodes) increases quit rates by 6% to 7% over either product alone with no increase in side effects.²¹ Thus, many smoking cessa-

tion specialists recommend that patients use a patch plus gum *ad lib* for "high craving situations."

Another labeled warning that has recently been shown not to be a concern is about smoking while using the patch. An initial small case series suggested

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that smoking while wearing a patch could cause myocardial infarctions. Several well controlled studies in patients with active heart disease have shown, however, that this is not true.²³ In fact, a recent study tested smokers wearing a triple-dose nicotine patch (63 mg/day) while smoking 15 cigarettes/day and found no evidence of cardiovascular problems.²⁷

Prescription Nicotine Replacement

NICOTINE NASAL SPRAY

The nicotine nasal spray was designed to rapidly administer higher levels of replacement nicotine. Although it does deliver larger doses more rapidly than nicotine gum and patches, the delivery rate and magnitude are still much lower than those of cigarettes.²⁸ And while the nasal spray also doubles quit rates,²¹ whether it is superior to gum or patches is unknown.

The spray causes nasal and throat irritation, rhinitis, sneezing, coughing, and lacrimation in the large majority of smok-

ers during the first week of use, although tolerance occurs rapidly. Early concerns about the dependence liability of the spray have not been borne out.²¹ Although unconfirmed by trials, nasal spray might be best for smokers who appear to need large doses of nicotine.

NICOTINE INHALER

The nicotine inhaler is a plastic rod containing a plug impregnated with nicotine. It is designed to combine pharmacological and behavioral substitution strategies. When warm air passes over the plug, nicotine vapor is produced. Although described as an inhaler, in actuality, nicotine from the device is absorbed buccally, rather than in the lungs.²⁹ The pharmacokinetics and blood levels of nicotine that result from the "inhaler" are similar, therefore, to those seen with nicotine gum.

This device appears to be helpful for those who desire a behavioral substitute for cigarettes. However, the efficacy of the inhaler is not due solely to behavioral replacement, as active-ingredient inhalers double quit rates compared with placebo inhalers.²¹ Side effects from the inhaler include mild mouth and throat irritation, and coughing. Dependence on the device has not been a significant problem.²¹ The nicotine inhaler loses some bioavailability at temperatures below 10° C.

Non-Nicotine Medications

Many smokers prefer a non-nicotine medication, and many have failed in previous efforts to quit using NRT.

BUPROPION

This medication is an atypical antidepressant that doubles quit rates.²¹ It is prescribed as 300 mg/day of the slow-release preparation, beginning one week prior to the quit date.³⁰ Importantly, bupropion does not appear to work via its antidepressant effects, i.e., it is effective in those with no current or past depressive symptoms.³¹

The most common side effects of bupropion are dry mouth and insomnia.³¹ Seizure risk appears to be minimal with use of the slow-release preparation, doses less than or equal to 300 mg/day, and with appropriate screening for a history of seizures, anorexia, heavy alcohol use, or head trauma.³¹ There are no adequate and well controlled studies in pregnant women. One study found that combining bupropion and a nicotine patch increased short-term quit rates somewhat over bupropion used alone.³¹ Recent trials have suggested that some other antidepressants (e.g., nortriptyline) might be helpful,^{32,33} whereas others (e.g., fluoxetine) do not appear to be beneficial.

CLONIDINE

Clonidine is an alpha-2 antagonist that has also been shown to double quit rates.³⁴ However, the evidence of its efficacy is less robust and it appears to have more side effects (postural hypotension, drowsiness, etc.) than other medications.³⁴ Clonidine is usually used only as a second-line medication.

Psychosocial Therapies

Behavioral therapy is the only proven psychosocial treatment for smoking cessation,^{2,3} doubling quit rates.² Usually administered in a group setting so that smokers also receive social support, it can also be conducted on an individual basis. The major disadvantage of behavior therapy has not been its efficacy but rather its limited availability and acceptability. For example, although several organizations offer behavior therapy (Table 1), in most communities, groups are run only two or three times a year. Thus, if a smoker is ready to stop and wants to try group therapy, he or she often has to wait months for a group to become available. In the meantime, the motivation to stop smoking may diminish. Individual therapy is also often unavailable or, if it is available, is costly due to lack of insurance coverage.

On the other hand, all of the medications discussed here have telephone-based behavior therapy programs that are offered free to interested smokers. At least one study suggests that, although the amount of interpersonal contact in these programs is limited, they still increase quit rates by tailoring therapy to the smoker's specific problems.³⁵

Written materials are often used with both medication and behavioral therapies. Although they do not appear effective when used on their own, they are thought to improve outcomes of other therapies.³⁶

Summary

Many clinicians still approach smoking interventions as unpleasant interactions involving cajoling, berating, or pleading with patients. With the advent of several proven effective therapies, smoking inter-

ventions should instead be viewed as potentially positive interactions in which the clinician can offer support and concrete help to smokers. If even a few patients can be convinced and helped to quit, the practitioner will have made a major contribution to his or her patients' overall health and longevity. **CA**

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