



Smoking Cessation

**Smoking Cessation
Guideline Team**

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These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

Patient population: Adult and adolescent smokers

Objectives: Provide a framework for care providers to assist patients in smoking cessation. Systematic efforts include the following: 1) Assess and document smoking status of every patient. 2) Provide smoking cessation intervention to all smokers. 3) Treat behavioral/psychological aspects of cigarette addiction with advice and counseling. 4) Treat biologic aspects of cigarette addiction with pharmacological therapies.

Key Points

- ASK** all patients about smoking status and assess smoker’s readiness to quit. Smoking status should be documented in the medical record.
- ADVISE** all smokers to seriously consider making a quit attempt using a clear and personalized message. Advice as brief as 3 minutes is effective [A*].
- ASSESS** all smokers willingness to make a quit attempt. If not yet ready to quit, offer motivational intervention using the 5 “R’s” - relevance, risks, rewards, roadblocks, repetition.
- REFER** patients interested in quitting within 30 days to a Tobacco Treatment Specialist or other appropriate tobacco cessation program. Alternatively, health care providers can directly provide the following treatment.

Treatment options

- **ASSIST** those ready to make a quit attempt:
 - Set a quit date. Quit date abstinence is a strong predictor of long term success [C*].
 - Give advice on quitting and provide supplementary materials.
 - Prescribe pharmacologic therapy as appropriate. Nicotine replacement therapies, bupropion hydrochloride, and varenicline have been proven effective [A*].
- **ARRANGE** follow-up either with phone call or office visit.
 - Prevent relapse by congratulating successes and reinforcing reasons for quitting.
 - Assess any difficulties with pharmacologic therapy.

* Levels of evidence reflect the best available literature in support of an intervention or test:
A=randomized controlled trials; B=controlled trials, no randomization; C=observational trials; D=opinion of expert panel.

Clinical Background

Clinical Problem

Smoking-related deaths account for a fourth of all deaths in this country. Estimated annual cost of smoking-related medical care is \$75 billion. Approximately 25% of American men and women continue to smoke. Of these, approximately 70% see a physician each year. A great majority of smokers report a desire to quit smoking and cite physician advice as an important motivator for making a quit attempt [C*].

While rates of smoking among high school students are at their lowest levels in the past decade, each day, nearly 4,400 young people between the ages of 12 and 17 years initiate cigarette smoking, with 2,200 becoming daily smokers. Currently 23% of high school students in the United States are cigarette smokers. Among adults who have ever smoked daily, 82% first tried cigarettes and 53% smoked daily before age 18 years. According to recent estimates,

almost one half of current adolescent smokers who continue to smoke regularly will die from a smoking-related disease. Although cessation is less common among adolescents than adults, interest in quitting is strong: nearly three fourths of adolescent smokers have seriously thought about quitting, 64% report having made a quit attempt, and 40% of daily smokers report having tried to quit at least once and failed. On the other hand, there is limited evidence regarding the efficacy of brief clinician interventions in treating tobacco use in adolescence. Thus in many cases, expert opinion rather than empirical data is used to guide clinical interventions for young smokers.

Exposure of nonsmokers to environmental tobacco smoke (ETS) is another preventable cause of morbidity and mortality associated with tobacco use. Exposure to ETS is recognized as a cause of heart disease, and accounts for around 3000 lung cancer deaths per year in adults.

(Continued on page 5)

Figure 1. Clinician's Actions to Help Patients Quit Smoking

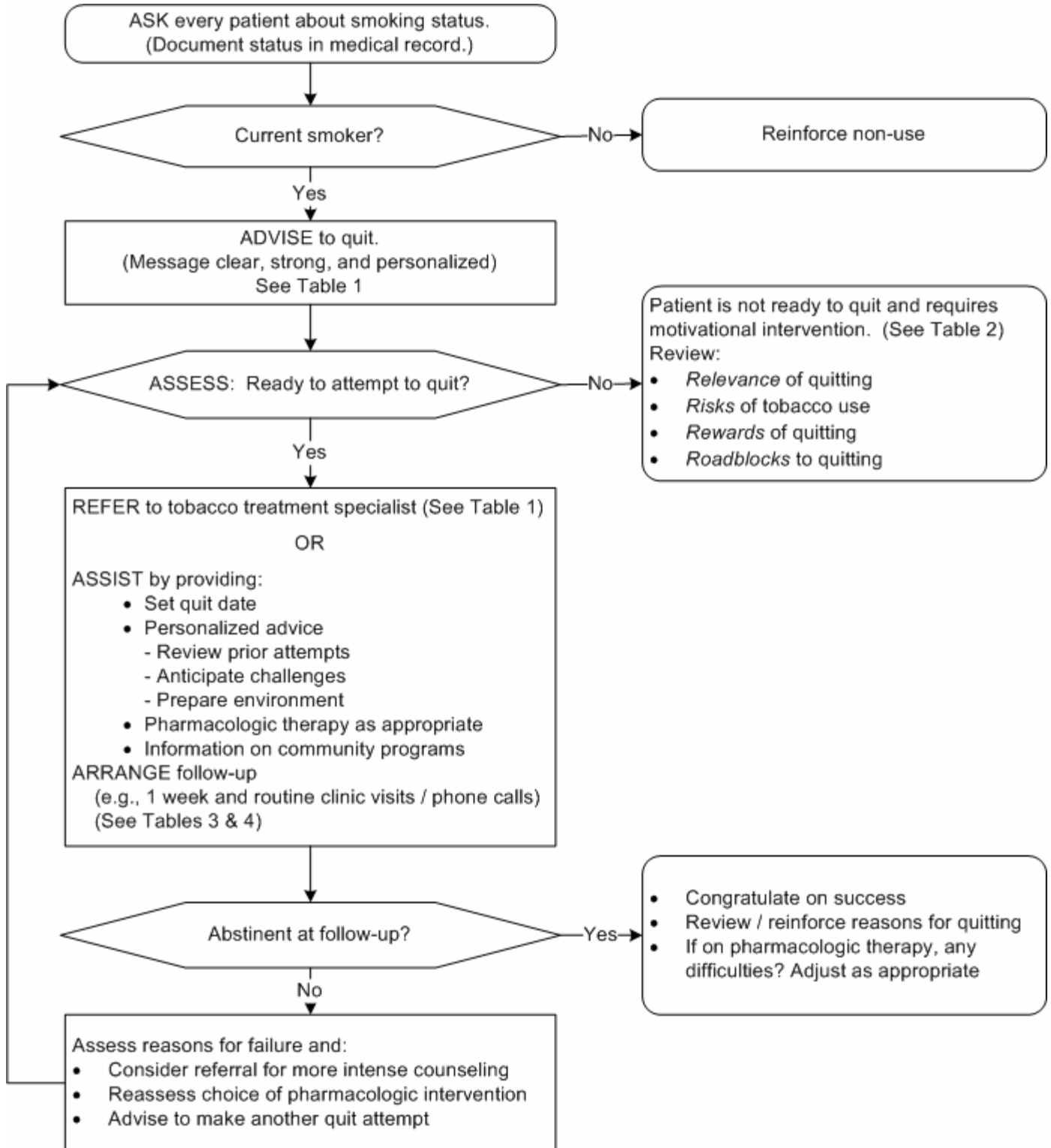


Table 1. Initial Interventions for Smoking Cessation

<p>ADVISE Advise the patient.</p>	<p>ASSESS Determine the patient’s willingness to make a quit attempt.</p>	<p>REFER Refer patients to tobacco treatment specialist.</p>
<p>Brief clinician intervention</p> <p>Advice should be:</p> <ul style="list-style-type: none"> • Clear - “I think it is important for you to quit smoking now, and I will help you.” • Strong - “As your clinician, I need you to know that quitting smoking is the most important thing you can do to protect your current and future health.” • Personalized - Tie smoking to current health/illness, and/or social and economic costs of tobacco, and/or impact on children or others in household. “The frequency of your child’s ear infections is certainly related to your smoking habit.” 	<p>Brief clinician intervention</p> <p>“Are you ready to make a quit attempt with in the next 30 days?”</p> <ul style="list-style-type: none"> • If the patient is willing: “Most patients who are thinking about quitting do much better if they talk with a tobacco treatment specialist. I would like to make that referral for you.” • If the patient is unwilling to make a quit attempt: Provide a motivational intervention (5R’s - Relevance, Risks, Rewards, Roadblocks, Repetition – see table 2). • If the patient is in a special population (e.g., pregnant or breastfeeding smoker), consider providing additional information. 	<p>Referral</p> <ul style="list-style-type: none"> • Refer to tobacco treatment specialist affiliated with your practice or region. (For example, at UMHS, refer to the Tobacco Consultation Service: fax 647-1516 or online at www.med.umich.edu/mfit/tobacco) • Refer to tobacco cessation program in your area (e.g., American Cancer Society or American Lung Association). Listings of programs are often available from state or local public health departments. • Refer to a quit line (e.g., in the State of Michigan, Michigan Quitline: 800-480-7848)

**Table 2. "5 R's" of Motivational Intervention
For Patients Not Yet Ready to Make a Quit Attempt**

Relevance

Tie smoking to current health/illness, and/or social and economic costs of tobacco use, motivation level/readiness to quit, and/or the impact of smoking on children and others in the household. For example, “Your child’s asthma flare is certainly related to your smoking habit. It would be in your child’s best interest for you to set a quit date in the near future.”

Risks

Ask patient to identify potential negative consequences of smoking:

- Acute risks - shortness of breath, exacerbation of asthma, impotence, infertility
- Long term risks - heart attacks, strokes, lung and other cancers, COPD
- Environmental risks - increased risk of lung cancer in spouse and children; higher rates of smoking by children; increased risk for SIDS, asthma, middle ear disease and respiratory infection in children

Rewards

Ask patient to identify 1) any positive benefits they currently derive from smoking. Discuss alternative methods for filling the potential void after cessation. 2) the potential rewards of smoking cessation including improved health, improved taste, money saved, healthier children, freedom from addiction.

Roadblocks

Ask patient to identify barriers to quitting smoking (e.g., partner or co-worker who smokes, fears about quitting smoking, etc.).

Repetition

Repeat above strategies every time an unmotivated patient has a visit.

Table 3. Treatment Interventions for Smoking Cessation

<p style="text-align: center;">ASSIST</p> <p style="text-align: center;">Aid the patient in quitting.</p>	<p style="text-align: center;">ARRANGE</p> <p style="text-align: center;">Arrange follow-up at the same visit patient sets quit date.</p>
<p>1. Help the patient with a quit plan.</p> <ul style="list-style-type: none"> • Set a quit date and record this on patient’s chart. Ask the patient to mark this on his/her calendar. Quit date abstinence is a strong predictor of long-term success [C*]. • Patient should inform family, friends, co-workers of quit plan and request support. • Have patient remove cigarettes from home, car and workplace environments. • Review previous quit attempts. • Anticipate challenges, particularly during the first critical few weeks, i.e., nicotine withdrawal symptoms. <p>2. Consider referral to intensive counseling (multi-session, group or individual). Referral considerations include:</p> <ul style="list-style-type: none"> • Multiple, unsuccessful quit attempts initiated by brief intervention. • Increased need for skill building (coping strategies/problem solving), social support and relapse prevention. • Psychiatric co-factor, such as depression, eating disorder, anxiety disorder, attention deficit disorder, or alcohol abuse. <p>3. Encourage pharmacologic therapies as appropriate. See Pharmacologic Therapies section and Table 4.</p> <p>4. Give key advice on successful quitting.</p> <ul style="list-style-type: none"> • Abstinence. Total abstinence is essential [D*], not even a single puff after quit date. • Alcohol. Drinking alcohol is strongly associated with relapse[C*]. • Other smokers in the household. The presence of other smokers in the household, particularly a spouse, is associated with lower success rates [C*]. Patient should consider quitting with significant other, or develop specific plan to stay quit in a household where others still smoke. <p>5. Provide supplementary educational materials</p> <ul style="list-style-type: none"> • UMHS Patient Education materials: <ul style="list-style-type: none"> - “How to use your nicotine product” - “Tips for quitting smoking” • National Cancer Institute pamphlet - “Clearing the Air” 	<p>1. Schedule follow-up. Contact either in person or by telephone. If the patient is scheduled to return for a clinic appointment, follow-up cessation counseling should be done at that time. Other follow-up may be done over the telephone.</p> <p>2. Timing. Follow-up contact should occur soon after the quit date, preferably during the first week [C*]. Extending treatment contacts over a number of weeks appears to increase cessation rates [D*]. Further follow-up as needed.</p> <p>3. Actions during follow-up:</p> <ul style="list-style-type: none"> • If abstinent: <ul style="list-style-type: none"> – Congratulate success and stress importance of remaining abstinent. – Review benefits to be derived from quitting. – Inquire regarding problems encountered and offer possible solutions to maintaining abstinence. • If smoking: <ul style="list-style-type: none"> – Review circumstances and elicit re-commitment to total abstinence. – Remind patients that a lapse can be used as a learning experience. – Identify problems, suggest alternative behaviors and anticipate challenges in the immediate future. – Re-assess choice of pharmacologic intervention as needed. – Consider referral to a more intense or specialized program.

Table 4. Dosing and Administration of Medications for Tobacco Cessation

Agent	Available Dosages/Cost	Dosing	Duration	Instructions	Side Effects
<p>Nicotine Lozenge Full dose of nicotine is released gradually by placing a lozenge in the mouth and sucking on it until it dissolves completely.</p>	<p>Over-the-Counter Commit Lozenge 2, 4 mg \$40 / 72-count packs</p>	<p>9 lozenges/daily during initial 6 weeks of therapy. 4 mg if first cigarette within 30 min of awakening; 2 mg if more than 30 min after awakening. 1 lozenge q 1-2 hrs for 6 wks, then q 4-8 hrs for last 3 wks.</p>	12 weeks	<p>Place the lozenge in mouth and allow to dissolve slowly over 20-30 mins. Do not chew, bite, or swallow lozenge. Avoid eating or drinking acidic beverages (i.e., orange juice, coffee) 15 min prior to, during, or after using a lozenge.</p>	<p>Headache, diarrhea, flatulence, heartburn, hiccups, nausea, coughing, sore throat, and upper respiratory infection (occurring in > 5% of patients).</p>
<p>Transdermal nicotine patch Continuous delivery of nicotine provides constant blood levels. Requires 2-3 days to achieve maximal serum levels.</p>	<p>Over-the-Counter Nicoderm CQ 21, 14, 7 mg/ 24 hr All: \$97 / 28 patches</p> <p>Nicotrol 15mg/16 hr \$97 / 28 patches</p> <p>Other Generic Nicotine Transdermal Patches 21, 14, 7 mg - \$45 / 28 patches</p>	<p>>10 cigs per day, start with highest dose of given brand.</p> <p>5 - 10 cigs per day, use mid-range dose [D*].</p>	<p>8 weeks. No increase in cessation with longer duration.</p> <p>Suggest:</p> <ul style="list-style-type: none"> • Weeks 1-4: highest dose of given brand • Weeks 4-6: next lowest dose of brand • Weeks 6-8: lowest dose <p>Taper recommended for psychological reasons, but does not increase efficacy.</p>	<p>No smoking while on patch, rotate to new hairless skin site each day, remove before bed if insomnia. May consider supplement with 2 mg gum first 48 hrs while plasma levels building.</p>	<p>Skin reactions including pruritus, edema, rash; sleep disturbance.</p>
<p>Nicotine Gum (polacrilex): Maximum nicotine levels achieved within 20-30 minutes of chewing.</p>	<p>Over-the-Counter Nicorette - 2 and 4 mg sticks</p> <p>2 mg - \$47 / 110 sticks 4 mg - \$53 / 110 sticks</p> <p>Generic nicotine polacrilex (various) 2 mg - \$30 / 110 sticks 4 mg - \$40 / 110 sticks</p>	<p>≥ 20 cigs per day, use 4 mg stick q one hour [A*].</p> <p>< 20 cigs per day, use 2 mg stick q one hour.</p>	2-3 months	<p>Chew until spicy flavor begins, then “park” between cheek and gum for absorption. Remove after 1/2 hour. Acidic beverages decrease absorption.</p>	<p>Jaw fatigue, hiccups, belching, nausea.</p>

(continued on next page)

Table 4. Dosing and Administration of Medications for Tobacco Cessation, continued

Agent	Available Dosages/Cost	Dosing	Duration	Instructions	Side Effects
Nicotine Nasal Spray Maximum levels of nicotine reached within 5 -10 minutes. Levels begin to fall within 30 minutes of dose. Most closely mimics nicotine delivery pattern of cigarette.	Prescription Nicotrol NS 1 mg = 1 spray each nostril = 1 dose 1-10 ml spray - \$37 (no generic)	Spray q 30-60 minutes prn craving. Maximum 40 doses/day.	2-3 months	Careful instruction on spray technique (see patient education handout).	Nasal irritation / rhinorrhea (98% of pts), sneeze, cough. Decreased severity of effects after first week.
Nicotine Inhaler Nicotine absorbed through mouth and throat (not lungs) when smoker “puffs” on cylinder delivering nicotine and menthol. Peak nicotine levels in 20 minutes.	Prescription Each inhaler cartridge with 10 mg nicotine Nicotrol inhaler: 42 cartridge / 1 mouthpiece - \$103 / 168 spray cartridge (no generic)	80 puffs =1mg Requires 3-4 puffs /minute for 20-30 minutes. Use prn or q 1 hour. Each cartridge good for approx. 20 minutes of continuous puffing.	2-3 months	Must puff more frequently than cigarettes.	Cough, mouth and throat irritation.
Bupropion hydrochloride *	Prescription 75, 100 mg \$300 / full 7-week course (brand) \$66 / full 7-week course (generic)	150 mg orally in the morning for 3 days, then increase to 150 mg 2 times a day (max dose 300 mg/day)	7-12 weeks	Start 1 week before quit date	Insomnia, dry mouth, nausea, and seizures (1 in 1000). Contraindications: Seizure disorder, major head trauma, eating disorder, or on Wellbutrin® or MAO inhibitors.
Bupropion hydrochloride SR (Zyban®) **	Prescription 150 mg SR \$238 / full 7-week course (brand) \$150/ full 7-week course (generic)	150 mg/day for 3 days, then 150 mg daily or BID	7-12 weeks	Start 1 week before quit date	Insomnia, dry mouth, nausea, and seizures (1 in 1000). Contraindications: Seizure disorder, major head trauma, eating disorder, or on Wellbutrin® or MAO inhibitors.
Varenicline** (Chantix®)	Prescription 0.5, 1 mg \$336 12-week course	Start with 0.5 mg daily for three days, then 0.5 mg BID for four days, then 1 mg BID	12 weeks, with option to continue for another 12 weeks	Start one week before quit date. Take after eating, with a full glass of water	Nausea, insomnia, and unusual dreams.

* Not FDA-approved for this use

** Black Box Warning: Serious neuropsychiatric symptoms have occurred in pts taking Chantix, including changes in behavior, agitation, depressed mood, suicidal ideation, and attempted and completed suicide.

AWP = Average Wholesale Price. For brand drugs, Average Wholesale Price minus 10%. AWP from Amerisource Bergen Wholesale Catalog, 2/15/06. For generic drugs, Maximum Allowable Cost plus \$3 from BCBS of Michigan MAC List, 12/29/05.

In infants and children, exposure to ETS causes middle ear infections and effusions, exacerbates 400,000 to 1 million cases of asthma annually, and causes 150,000 to 300,000 cases of lower respiratory tract infections each year.

Lack of time, lack of knowledge about counseling, and lack of familiarity with current pharmacologic therapies may all contribute to inadequate intervention being done by clinicians. Therefore, it is imperative that every clinician become comfortable and knowledgeable with an approach to assist patients with smoking cessation.

Rationale for Recommendations

An updated brief clinic intervention is known as the “3-A’s and Refer” model: **Ask, Advise, Assess and Refer**. The key component of the initial assessment is to consistently and accurately identify all smokers. Once it is established that a patient smokes, clinician advice as brief as 3 minutes can be effective in smoking cessation [A*]. The clinician then assesses patient readiness to quit. If the patient is willing to make a quit attempt, it is recommended that he or she be referred to a Tobacco Treatment Specialist.

Ask/Advise/Assess

All patients should be asked about their smoking status and assessed for their willingness to quit (Table 1). If a patient smokes, this should be documented in the medical record so that intervention can be offered. Techniques to remind physician of a patient’s smoking status include smoking status stickers, listing tobacco use on active problem list, or including tobacco status as part of the vital signs. Brief clinician advice should be offered to the patient, including a personalized message as to why it is important to quit smoking now. Patients should then be asked about their willingness to quit smoking in the next month.

Refer

If patients are willing to make a quit attempt, the clinician has two options. The first option is to refer the patient to a Tobacco Treatment Specialist (TTS) or other appropriate tobacco cessation program. A TTS is a trained health professional who specializes in the treatment of tobacco dependence as part of his or her professional role. The TTS demonstrates the knowledge and skills to provide effective and evidence-based treatment for tobacco dependence. The TTS also serves as a resource and consultant to other healthcare professionals. The TTS can also provide the most effective and appropriate treatment to special populations (e.g. patients with a variety of co-morbidities, chemical dependency, or pregnancy). Many health care organizations have a TTS on staff. Local tobacco treatment specialists can be identified by state tobacco control agencies or through the Association for Treatment of Tobacco Use and Dependence (www.attud.org). Many national organizations such as the American Cancer Society and American Lung Association offer tobacco cessation programs. Listings of local programs can often be obtained through state and local health departments.

The second option is to treat the patient (see Treatment, below). Several factors make health care settings ideal for delivery of smoking cessation interventions. As stated above, at least 70% of smokers see a physician each year. As many as 70% of these smokers report a desire to quit and have made at least one serious quit attempt. Smokers also report that advice from a clinician is an important motivator to quit.

Treatment - Counseling

Results of the Public Health Service guideline panel meta-analysis showed that brief intervention increases long-term quit rates. In addition, there is a strong dose response relationship between the intensity of person-to-person contact and successful outcomes [A*]. When providing counseling, health care providers should be aware that barriers to smoking cessation include, but are not limited to, severe withdrawal during previous quit attempts, the presence of other smokers in the home or workplace, stressful life circumstances, psychiatric co-morbidities (i.e. depression, alcoholism), multiple quit attempts, and low motivation. Identifying these barriers during initial assessment will help to provide a tailored approach during counseling. In addition to clinician counseling in the office, intensive counseling (frequently defined as a minimum of weekly meetings for the first 4 - 7 weeks of cessation) significantly enhances cessation rates. However, participation in intensive counseling is based largely on patients’ motivation to quit [C*]. In some locations, if physicians formally refer patients to a tobacco cessation program, a third party may cover the fee with patients paying a reduced or no fee.

The evidence for the effectiveness of counseling in adolescent smokers is less robust. However, some studies do demonstrate that smoking cessation counseling in the primary care setting can improve adolescent smokers’ quit rates [A*].

Typically, only a minority of smokers are willing to quit at any point in time, and many clinicians will spend more time promoting the motivation to quit than assisting in quit attempts. See Table 2 for the 5 R’s of Motivational Intervention.

There is mixed evidence to support counseling to reduce environmental tobacco smoke (ETS) exposure in the home. In a systematic review of 18 studies, 12 of the 18 studies documented reduction of ETS exposure for children in both intervention and comparison groups. However, in only four of the 18 studies was there a statistically significant intervention effect. Three of these successful studies utilized intensive counseling interventions targeted to smoking parents. There is little difference between the well infant, child respiratory illness, and other child illness settings as contexts for parental smoking cessation interventions [B*].

Treatment - Pharmacologic Therapies

Nicotine replacement therapy (NRT), bupropion hydrochloride (Zyban®), and varenicline (Chantix®) have been shown to significantly improve cessation rates [A*]. Therefore, pharmacologic therapy should be recommended to all patients except in the presence of specific contraindications. Bupropion and varenicline are the two non-nicotine products with FDA approval for smoking cessation. Non-FDA approved agents with potential benefit in smoking cessation include nortriptyline and clonidine.

The utility of pharmacologic therapy for adolescents has been examined in a number of small studies. While the evidence indicates that these therapies are safe, they seem to be more effective when coupled with counseling. Additional, larger trials are ongoing to evaluate this issue. In the meantime, nicotine replacement therapy or bupropion may be considered for use in adolescent smokers [D*].

The following sections discuss choosing among the various forms of NRT, bupropion, varenicline, and other agents.

Nicotine replacement therapies (NRT). NRT has been used for many years, but alternative methods of delivery continue to be developed and new combinations are being tried.

Pharmacologic properties of nicotine. A smoker absorbs 1-3 mg of nicotine per cigarette regardless of nicotine-yield ratings on the box. Nicotine results in increased release of catecholamines, vasopressin, endorphins, cortisol, and ACTH. These biochemical changes lead to addiction as smokers experience pleasure, increased arousal, decreased anxiety, and decreased hunger with increased metabolic rate. Within hours of cessation of cigarettes, smokers begin to experience the nicotine withdrawal syndrome that peaks at 48 hours. Symptoms of nicotine withdrawal include: craving, anxiety, restlessness, irritability, depressed mood, increased appetite, and difficulty concentrating.

Demonstration of efficacy. The various nicotine replacement therapies (NRT) significantly decrease symptoms of the withdrawal syndrome as smokers abruptly stop smoking [A*]. The different formulations of NRT provide alternate methods for delivery and have slightly different onset of action and duration. In meta-analyses, cessation rates with transdermal nicotine range from 15-31 per hundred with a trend toward decreased efficacy in the most highly dependent smokers (≥ 32 cigarettes / day or Fagerstrom nicotine dependence score > 6) [A*]. Nicotine gum studies demonstrate a similar range of cessation rates with greatest efficacy seen with the 4mg gum in highly dependent smokers [A*]. Nasal spray cessation rates range from 26-28 per hundred, also with greatest efficacy in the most dependent smokers [A*]. Inhaler studies report cessation rates similar to that of the nasal spray [A*].

The efficacy of all forms of NRT is improved with concomitant counseling, but there is evidence for the effectiveness of NRT, even in the absence of counseling.

Level of dependence and dosing. In very highly dependent smokers, 4 mg gum is superior to 2 mg and most effective with counseling [A*]. High dose patch therapy (i.e., 44 mg/24hr = two patches) is safe and decreases withdrawal symptoms in highly dependent smokers, but does not increase long term cessation rates [A*]. Those smoking 5 or fewer cigarettes per day have been shown to have few symptoms of nicotine withdrawal when they quit [C*] and may not require nicotine replacement therapy [D*].

For those using nicotine gum, spray or inhaler, it is important that they are instructed in technique and dosing frequency so that underdosing does not occur. See Table 4 for dosing and administration recommendations. The patient should also be provided with the educational handout, "How to Use Your Nicotine Product."

Choosing among various nicotine replacement therapies. A single randomized study comparing the 4 nicotine replacement therapies showed similar abstinence rates at 12 weeks, despite the fact that the nasal spray and inhaler groups had lower compliance with prescribed methods of use. Therefore, choice of NRT may be tailored to patients' preferences, side effects, and previous attempts. The transdermal patch offers convenience, minimal instruction, and minimal side effects. The continuous transdermal release of nicotine from the patch does not produce the peaks and troughs that are similar to cigarette smoking. Alternatively, gum, spray, or inhaler therapy may allow for a "quick fix" when cravings occur; this more closely simulates the nicotine peaks of actual cigarette smoking. It is of note that the reinforcing effects of a bolus of nicotine have been suggested to contribute to the habitual use of nicotine. Eight to 25% of gum users, 10-43% of spray users, and 16% of inhaler users who quit smoking were still using the nicotine replacement therapy beyond 6 months [A*].

Combining nicotine replacement therapies. At least 3 randomized, controlled trials have examined the efficacy of combining either patch plus gum, patch plus inhaler, or patch plus nasal spray. While all show significantly improved early (6 week) abstinence rates, only the patch plus spray showed improved effectiveness over the patch alone at one year (27 per 100 versus 11 per 100.) One-third of those abstainers at one year were still using the nasal spray [A*]. Given the additional cost of dual therapies and limited benefit, this approach is best reserved for highly addicted smokers with several previous failed quit attempts [D*].

Patients with cardiovascular disease. The patch and nasal spray have demonstrated safety in patients with stable coronary artery disease [A]. These agents have not been evaluated in patients with unstable angina, recent myocardial infarction, uncontrolled congestive heart failure, or unstable arrhythmia. While patients should be reminded not to smoke while using these products, studies have shown no increase in cardiac event rates when patients smoke while wearing the patch [C*]. Nicotine gum and inhaler have not been specifically studied in this population.

Bupropion hydrochloride (Zyban®, Wellbutrin®). Bupropion was initially developed and marketed as an antidepressant medication (Wellbutrin®). It has both dopaminergic and adrenergic actions, and also appears to be an antagonist at the nicotinic acetylcholinergic receptor. Bupropion appears to aid smoking cessation by blocking nicotine effects and relieving withdrawal. In a meta-analysis of 24 controlled trials, bupropion doubled cessation rates compared to placebo (OR=2.06, 95% CI 1.70-4.09) [A*]. Generic bupropion (SR or regular) is a substantial cost savings over brand.

Dosing and administration. The manufacturer recommends initiation of drug therapy 1 week prior to the quit date. The recommended dosage schedule includes a starting dose of 150 mg per day for three days, then increasing to twice per day. While there was less weight gain with this dose of bupropion, there were no significant differences in smoking cessation rates among patients receiving total daily doses of 150 or 300 mg at 6 or 12 months [A*]. Therefore, patients who cannot afford or tolerate 300 mg/day may achieve successful results on 150 mg/day. The appropriate total duration of bupropion has not been studied.

Contraindications. Bupropion hydrochloride (Zyban®) is contraindicated in patients with seizure disorder, past or present eating disorder, and in patients being treated with Wellbutrin® or MAO inhibitors. To reduce seizure risk, the manufacturer recommends not exceeding maximum daily dose of 300 mg or single dose of 150 mg. Doses should be taken at least 8 hours apart. It should be used with caution in patients with predisposition to seizure (i.e., head trauma, alcohol withdrawal, concomitant use with other medications that lower seizure threshold: antipsychotics, antidepressants, theophylline.)

Choosing between bupropion hydrochloride or nicotine replacement. A single trial sponsored by the manufacturer of Zyban, compared bupropion, bupropion/nicotine patch combination, nicotine patch and placebo. At 1 year, bupropion and combination therapy had higher rates of smoking cessation than either the patch alone or placebo. (30 per hundred smokers with bupropion; 16 per hundred smokers with the nicotine patch.) There was no significant benefit of combination therapy over bupropion alone. The study suffered from an intervention discontinuation rate of 35%.

This single study suggests that bupropion may be superior to nicotine patch therapy [A*]. No conclusions may be drawn about the superiority of bupropion over other nicotine products. Given this single study, it remains reasonable to consider patient preferences, previous quit attempt experiences and cost when choosing among pharmacologic therapies [D*].

For smokers who have previously been unsuccessful, one randomized study showed higher success rates for both bupropion alone or in combination with the nicotine patch, compared to nicotine patch alone [A*].

Varenicline (Chantix®). Varenicline is a partial agonist for $\alpha_4\beta_2$ nicotinic acetylcholine receptor subtypes. As such, it provides a low-to-moderate level of dopamine stimulation to reduce nicotine craving and withdrawal symptoms. In two short term studies, varenicline resulted in substantially higher quit rates compared to placebo at 12 weeks (OR=3.85, 95% CI 2.70-5.50, number needed to treat=4) [A*]. Differences in abstinence remained significant even at 1 year. In both studies, varenicline was also superior to bupropion (OR=1.93, 95% CI, 1.40-2.68, number needed to treat=6) [A*].

Dosing and administration. The manufacturer recommends initiation of drug therapy 1 week prior to the quit date. The recommended dosage schedule includes a starting dose of 0.5 mg per day for three days, then increasing to twice per day for the next four days, followed by 1 mg twice a day, beginning on the quit date. The appropriate total duration of varenicline has not been studied, but ranged from 12-24 weeks in published studies. In addition, since varenicline is a nicotine agonist, it should not be used in conjunction with NRT products. The FDA recently issued a warning for varenicline, stating that serious neuropsychiatric symptoms have occurred in pts taking Chantix, including changes in behavior, agitation, depressed mood, suicidal ideation, and attempted and completed suicide.

Other pharmacologic therapies. A meta-analysis of 6 placebo-controlled trials of clonidine revealed a pooled odds ratio for benefit over placebo of 1.89 (CI 1.30-2.74). In only one of the 6 trials did clonidine show a statistically significant effect. Dry mouth and sedation were common side effects. Placebo-controlled studies of nortriptyline have documented a pooled odds ratio for benefit over placebo of 2.79 (CI 1.70-4.59). Dry mouth was also a common side effect of nortriptyline. Selective serotonin reuptake inhibitors do not increase cessation rates.

To date, neither nortriptyline nor clonidine has FDA approval as an aid in smoking cessation. These drugs may best be used as second-line agents when patients cannot take or do not wish to take either NRT, bupropion, or varenicline [D*].

Effect of smoking cessation on other drugs. Properties of smoke other than nicotine (benzopyrenes) increase metabolism of other drugs. In particular, theophylline half-life will increase within one week after smoking cessation. In addition, plasma caffeine concentrations increase greatly with cessation. Patients should be made aware that baseline caffeine intake may have greater physiologic effect and may be misinterpreted as nicotine withdrawal.

Weight Gain

Most smokers who quit will gain weight, but the majority will gain less than 10 pounds [C*]. The clinician should acknowledge this and encourage patients to adopt a healthy lifestyle that includes moderate exercise and healthy diet. However, very restrictive dieting at the same time may be counterproductive [C*]. A reminder to the patient to work

on one issue at a time and that you will assist the patient with any weight gain issues as needed may be helpful [D*].

Although bupropion at a dose of 300mg/day had a lower percentage weight gain after 7 weeks of therapy as compared to placebo, this effect was not sustained at 6 months and therefore is not likely to be any better than NRT for prevention of post-cessation weight gain [A*]. Nicotine gum may delay post-cessation weight gain, but the weight is usually gained once gum use ceases [C*].

Special Populations

Pregnant patients. Intensive counseling interventions increase quit rates during pregnancy [A*]. If intensive counseling is not possible, brief in-office counseling still has a beneficial effect and should be offered. Few studies have addressed the safety of nicotine replacement therapy or bupropion in pregnancy directly; however, studies show that less nicotine and fewer metabolites cross the placenta with the use of NRT than with smoking itself. FDA pregnancy risk categories are: bupropion - category B, nicotine transdermal, spray and inhaler - category D, nicotine gum - category C, varenicline - category C. Therefore cautious use of bupropion with NRT (especially nicotine gum) may be considered after reviewing risks and benefits with the patient.

Breastfeeding women. Smoking leads to a significant reduction in breast milk volume and increases the likelihood of early discontinuation [A*]. Data support the use of bupropion plus NRT in nursing mothers, with increased cessation rates. The safety profile is favorable, as less nicotine and fewer metabolites are found in breast milk with NRT, compared to smoking more than ½ pack per day. Additionally, eliminating environmental exposure to the infant is a favorable outcome. It is not known whether varenicline is excreted in human milk.

Racial and Ethnic Minorities. Smoking cessation treatment has been shown to be effective across both racial and ethnic minorities [A*]. Little research has examined intervention specifically designed for a particular ethnic or racial group; however, it is recommended that, when possible, smoking cessation treatment should be tailored to the specific ethnic or racial population with which they are used [C*]. It is essential that counseling or self-help materials be conveyed in a language understood by the smoker.

Psychiatric co-factors. If presence of psychiatric co-factors, such as depression, eating disorder, anxiety disorder, attention deficit disorder, or alcohol abuse, strongly consider referral to intensive counseling [B*]. Treatment of co-factors must be undertaken in preparation for smoking cessation.

Non-cigarette tobacco users. Spit tobacco users should be identified and strongly urged to quit tobacco use, using the same counseling interventions recommended for smokers [A*]. The clinicians should provide a clear message that the use of spit tobacco is not a safe alternative to smoking. However, several studies have found that use of nicotine

gum and nicotine patch have not increased the abstinence rates in spit tobacco users.

Users of cigars, pipes, and other non-cigarette combustible forms of tobacco should be identified, strongly urged to quit, and offered the same counseling interventions recommended for smokers [C*].

Gender concerns. Smoking cessation treatments are shown to benefit both women and men [B*]. Two studies suggest that some treatments are less efficacious in women than in men. Women may face different stressors and barriers to quitting (e.g., greater likelihood of depression, greater weight control concerns, and hormonal cycles). This research suggests cessation programs that address these issues would be more effective in treating women [D*]. Few studies have examined programs targeted to one gender.

Older smokers. Smoking cessation treatments have been shown to be effective for older adults and should be provided, as cessation improves pulmonary function and cerebral circulation [A*]. Several studies have found cessation rates among motivated older adults similar to those for younger adults; however, supportive counseling and social support may be of more value to prevent relapse than education or skills training [A*].

Hospitalized smokers. Providing hospitalized patients with high-intensity behavioral counseling and follow-up of at least 30 days has been shown to increase cessation rates [A*]. NRT supplementation can also be useful in this population. Briefer interventions (<20 minutes, delivered only during the hospitalization) have not yet been shown to be helpful. Additional treatment can include self-help brochures or audio/video tapes, chart prompts reminding physicians to advise for cessation, pharmacological therapy, hospital counseling, and post-discharge counseling telephone calls. Hospitalization should be used as a springboard to promote smoking cessation.

Controversial Areas

Other cessation aids. There is good evidence to recommend against the use of additional modalities such as hypnosis, laser, acupuncture, and acupressure as aids to smoking cessation [A]. None of these modalities have been shown to be superior to placebo in a number of meta-analysis.

Information the Patient Needs to Know

Supplementary materials. The UMHS produces two useful patient education handouts:

- "How to use your nicotine product"
- "Tips for quitting smoking"

Additionally, the National Cancer institute produces the pamphlet, "Clearing the Air" (NIH Pub. 03-1647). You may obtain 20 free copies at a time by calling 1 800-4-CANCER (1-800-422-6237). It is also available online at http://www.smokefree.gov/pubs/clearing_the_air.pdf

Preparation and effects. Review with patients the following additional information about preparing for quitting and related factors.

- **Review handout(s).** The handout(s) provide many useful tips to help you with your quit attempt. Read these and make plans before your quit attempt.
- **NRT/bupropion/varenicline.** Nicotine replacement therapies, bupropion, and varenicline are most effective when used correctly. If you have any uncertainties about proper use, this should be clarified.
- **Caffeine.** You are likely to perceive greater effects from your usual caffeine consumption after you quit smoking and may need to decrease your intake.
- **Theophylline.** If you take theophylline, levels should be checked approximately 2 weeks after you quit smoking.

Organizing a Health Care Site to Support Smoking Cessation Efforts

Successful intervention programs require coordinated efforts at a health care site. Several clinic personnel may be involved in the operational steps of “Asking, Advising, Assessing, and Referring”. Clinicians should help their clinics develop a coordinated plan of tasks and who will perform them. Some specific areas for planning include:

- **Record smoking status.** Institute an office system to identify all smokers:
 - Identify where smoking status will be recorded. Options include making smoking status part of vital signs, placing smoking status stickers on charts, or including smoking status on a section of the Problem Summary List.
 - Determine who will routinely ask and record the information.
 - Instruct staff regarding their roles in documentation.
 - Reinforce the value of the documentation.
- **Smoking cessation follow-up.** Develop a system and assigned role(s) at the health care site to:
 - Ensure the availability of patient education materials on smoking cessation.
 - Establish procedures for clinicians to provide a designated follow-up person with information on patients who are setting quit dates. Coordinate follow-up phone calls in conjunction with quit dates.
 - Provide follow-up cessation counseling as needed at subsequent clinic visits.
 - Refer patients to more intensive counseling programs for smoking cessation, as needed.

Strategy for Literature Search

The update of literature beyond the search performed for the initial UMHS Smoking Cessation Guideline began with a literature search performed to produce “Treating Tobacco Use and Dependence. A Clinical Practice Guideline,” US

Public Health service, 2000 June (see complete reference below). The guideline team then updated the PHS literature search through a Medline search of literature Jan., 1999 – April 2005. This search used the major keywords of: smoking [prevention & control], smoking cessation, tobacco use [prevention & control, rehabilitation]. The search was restricted to literature that was also referenced as either guidelines or controlled trials, as studies of humans, and as published in English. Specific searches were performed for the topics: counseling (includes assessment); pharmacologic treatment; other therapies (including complementary/alternative); pregnancy; adolescents; older adults; prevention (includes physician interactions with children and adolescents, counseling about having a smoke free home, and avoiding environmental tobacco smoke); and other smoking cessation guidelines, reviews of trials, or trials not included above.

The literature search for this project was conducted prospectively. The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was a single cycle. Conclusions were based on prospective randomized clinical trials (RCTs) if available, to the exclusion of other data. If RCTs were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

Disclosures

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

None of the members of the Smoking Cessation Guideline Team have relationships with commercial companies whose products are discussed in this guideline. (The members of the team are listed on the front page of this guideline.)

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Annotated Reference

Fiore MC, Bailey WC, Cohen SJ, et al. *Treating Tobacco Use and Dependence*. Clinical Practice Guideline.

Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. June 2000.

This 108 page guideline is an updated version of the 1996 Smoking Cessation Clinical Practice sponsored by the Agency for Health Care Policy and Research (now the Agency for Healthcare Research and Quality [AHRQ]), U.S. Department of Health and Human Services. The original guideline reflected the extant scientific research literature published between 1975 and 1994. The updated guideline adds literature published between 1995 and 1999. Findings include: multiple efficacious treatments exist, these treatments can double or triple the likelihood of long-term cessation, many cessation treatments are appropriate for primary care settings, and the use and impact of cessation treatments can be increased by supportive health system policies. Sections address screening and assessment, treatment structure and intensity, treatment elements, and special populations and special topics. This is the single most comprehensive practical reference currently available on the topic of smoking cessation.