



## Evidence-Based Best Practices for Promoting Smoking Cessation in South Carolina

The SCORxE smoking cessation best practices offers providers with balanced, evidence-based clinical information to assist in making optimal treatment decisions about medication and psychosocial and behavioral therapy.

### Key Messages for Promoting Smoking Cessation

1. Question and document tobacco use at every visit.
2. Understand the challenge to quit and expect relapse.
3. Identify readiness to quit to best tailor approach to patient.
4. Treatment is effective and multiple options allow for individualized interventions.

### BACKGROUND

A group of primary care physicians, pharmacists, and other health care professionals was created to develop an evidence-based best practices report to focus on promoting smoking cessation in primary care. ***The May 2008 Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline. U.S. Department of Health and Human Services Public Health Service (hereby referred to as PHS Guideline) was the group's primary source of information. Most of the evidence is based on studies of cigarette smoking. In many cases, the PHS Guideline panel believes the results can be generalized to all tobacco users.*** Supplemental information includes additional recommendations from a review of primary literature published since the PHS Guideline was issued. Modifications were made to the PHS Guideline as necessary for the SCORxE project. This document highlights the major elements of the SCORxE best practices report.

Treatment options recommended throughout this document are based on available data derived from various sources. The following symbols, found in parentheses at the end of sentences, indicate the level of evidence for the statements as shown below:

- (Level A) - Multiple well-designed randomized clinical trials, directly relevant to the statement, yielded a consistent pattern of findings.
- (Level B) - Some evidence from randomized clinical trials supported the statement, but the scientific support was not optimal. For instance, few randomized trials existed, the trials that did exist were somewhat inconsistent, or the trials were not directly relevant to the statement.
- (Level C) - Reserved for important clinical situations in which the PHS Guideline panel achieved consensus on the statement in the absence of relevant randomized controlled trials.

The information contained in this summary is intended to supplement the knowledge of clinicians regarding best practices and drug therapy to promote smoking cessation in primary care patients. This information is advisory only and is not intended to replace sound clinical judgment, nor should it be regarded as a substitute for individualized diagnosis and treatment. Special considerations are needed when treating some populations such as adolescents, the elderly, pregnant or breast-feeding women, and patients with certain medical conditions (e.g., cardiac disease, liver and renal impairment).

## SMOKING CESSATION AT-A-GLANCE

- Tobacco use is the number one cause of preventable morbidity and mortality in the U.S.
- Tobacco dependence is an addiction that is hard to kick; it is a chronic disease that often requires repeated intervention and multiple attempts to quit.
- Smoking cessation is one of the most cost-effective preventive care services. Clinically effective treatments exist that can significantly increase long-term abstinence rates.
- Consistent identification and documentation of smoking status and treatment of all tobacco users seen in healthcare are essential.
- Two key questions: “Do you smoke?” and “Do you want to quit?” are important starting points for counseling patients about smoking cessation during the clinical encounter.
- A physician’s advice to patients to quit smoking increases overall abstinence rates; even brief counseling lasting less than three minutes is effective.
- Pediatric visits offer important opportunities to ask and advise parents and caregivers about tobacco use to effectively increase abstinence among adults who smoke.
- Individual, group, and telephone counseling are effective and their effectiveness increases with treatment intensity. Three types of counseling are particularly effective:
  - Practical counseling (problem-solving/skills training);
  - Social support delivered as part of treatment; and
  - Motivational interviewing or motivational enhancement based approaches, primarily effective at increasing future quit attempts in smokers currently unwilling to quit.
- Advising smokers to provide a smoke free home and car for family and others in their care is important to minimize health risks associated with secondhand smoke.
- Proactive telephone quitlines (e.g., S.C. Tobacco Quitline 1-800-QUIT-NOW) provide patients easy access to support and can effectively augment office-based treatment and counseling.
- Counseling and medications are each effective as monotherapy; however, the combination is more effective than either treatment alone.
- Several medications are effective for tobacco dependence and should be considered unless contraindicated or in populations for which evidence of safety and/or efficacy is insufficient (i.e., pregnancy, smokeless tobacco users, light smokers, adolescents).
  - First-line medications that increase long-term abstinence rates are:
    - ✓ Nicotine gum
    - ✓ Nicotine inhaler
    - ✓ Nicotine lozenge
    - ✓ Nicotine nasal spray
    - ✓ Nicotine patch
    - ✓ Bupropion SR
    - ✓ Varenicline
  - Certain combinations of medications may also be considered.

## TOBACCO USE TRENDS AND RELATED HEALTH ISSUES

### Tobacco Use Prevalence

In 2008, one out of five adults in the United States were current smokers<sup>1</sup>. Older smokers age 45 or older comprise 41% of these adults.<sup>2,3</sup> Men (23.1%) were more likely to be smokers than women (18.3%).<sup>1</sup> South Carolina reported similar smoking rates of about 20%, with slightly more male (21.6%) than female (18.7%) smokers. Smoking was reported in 20.1% of Hispanics, 19.2% of Caucasians, and 18.5% of African Americans.<sup>4</sup> Eleven percent of women in the U.S. reported smoking during pregnancy in 2004.<sup>5</sup> Smoking rates in patients with psychiatric disorders are almost double that of the general population.<sup>6</sup>

Smoking is also prevalent among children and adolescents. In 2006, an estimated 3.3 million U.S. adolescents (12 – 17 years old) reported tobacco use within the past month and 2.6 million were current cigarette smokers.<sup>2</sup> South Carolina recorded a high school youth smoking prevalence of 21.8% in 2009, a 3% increase from 2007 that did not reach statistical significance.<sup>7,8</sup> Among current adult smokers, 90% reported trying their first cigarette before age 21.<sup>2</sup> Evidence shows that people who do not smoke before the age of 20 are significantly less likely to take up the habit as an adult.<sup>9</sup>

Light smoking (defined here as anyone who smokes less than 10 cigarettes per day, including individuals who may not smoke daily and those who smoke low-tar/low nicotine cigarettes) is on the rise, possibly due to smoking restrictions and higher costs. Approximately 25.4% of U.S. adult smokers reported smoking 10 or fewer cigarettes per day and 11.6% reported smoking 5 or fewer cigarettes per day.<sup>10</sup> In 2005, 4% of adult men reported smokeless tobacco use (e.g., chewing tobacco, snuff, moist snuff, betel quid), whereas less than 1% of women reported use of smokeless tobacco. Use of smokeless tobacco has been rising among children and adolescents.<sup>2</sup>

### Tobacco-Related Risks and Health Consequences

Tobacco use is the number one cause of preventable morbidity and mortality in the U.S.<sup>1</sup> and has a broad range of effects as detailed below:

**Cardiovascular:** The risk for acute myocardial infarction is nearly three fold greater in current smokers versus never smokers.<sup>11</sup> Smokers with cardiac disease are more likely to have a second heart attack if they continue to smoke.<sup>2</sup> Even at the lowest levels of exposure (one cigarette per day), cigarette smoking is associated with an increased risk for cardiovascular disease.<sup>11</sup>

**Pulmonary:** Chronic obstructive pulmonary disease (COPD) is an inflammatory disease that is predominantly found in patients with a history of cigarette smoking. According to the World Health Organization (WHO), 80 million people worldwide have moderate-to-severe COPD. In 2005, the disease was associated with three million deaths worldwide.<sup>12</sup>

**Cancer:** Smoking and secondhand smoke are two of the risk factors for developing various cancers, including lung cancer, one of the leading causes of death in both men and women. There are approximately 129,000 deaths from lung cancer and 35,000 other cancer deaths attributed to smoking each year.<sup>13</sup>

**Diabetes Mellitus:** Smoking is associated with reduced insulin sensitivity and lower glucose utilization. The risk of developing type 2 diabetes increases with heavy smokeless tobacco use and doubles with heavy smoking (one pack per day).<sup>14</sup>

**Chronic Kidney Disease:** Cigarette smoking increases the risk and progression of chronic kidney disease, estimated to affect more than 11% of the U.S. population.<sup>15</sup>

**HIV-Positive Smokers:** Compared with HIV-positive nonsmokers, HIV-positive smokers are at increased risk of several opportunistic infections and spontaneous pneumothorax and have higher mortality rates.<sup>2</sup>

**Pregnancy and Breastfeeding:** Smoking has been linked to infertility. Smoking also carries serious risks and health consequences for pregnant women and their fetuses: stillbirths; spontaneous abortions; ectopic pregnancy; fetal growth restriction; premature labor and delivery; low birth-weight (an estimated 20% of low birth-weights could be prevented by eliminating smoking during pregnancy); placental abruption; placenta insufficiency; and thrombotic complications. In addition to secondhand smoke exposure, children of women who smoke during breastfeeding are exposed to nicotine secreted in breast milk. Smoking also reduces breast milk production.<sup>2,16,17</sup>

**Children exposed in utero:** In utero exposure to smoking increases the risk of: sudden infant death syndrome (SIDS); respiratory infections; asthma; middle ear disease; orofacial cleft; craniosynostosis; clubfoot; attention deficit disorder; other cognitive, emotional and behavioral problems; and some childhood cancers.<sup>2,16,17</sup>

**Secondhand Smoke:** Secondhand smoke causes immediate and long-term adverse health effects in children and adults. Exposure to secondhand smoke is associated with low birth weight, sudden infant death syndrome, asthma and other respiratory problems in children.<sup>18</sup> Children are exposed to higher levels of secondhand smoke than adults. More than 30% of children in the U.S. are currently exposed to secondhand smoke at home.<sup>19,20</sup>

**Other Tobacco Product Forms:** Smokeless tobacco is not a safe alternative to smoking and carries serious health risks, including: identifiable oral lesions, teeth abrasion, gingival recession, periodontal bone loss, leukoplakia, and oral and pancreatic cancer. In addition, there is no evidence that smokeless tobacco products are an effective aid to quit smoking. Noncigarette smoking tobacco products (cigars, pipes, cigarillos, bidis, loose tobacco, and water pipes [hookahs, narghile]) have been associated with the following conditions: coronary heart disease; COPD; periodontitis; and cancers of the oral cavity, esophagus, larynx, lungs, and stomach.<sup>2</sup>

### **Benefits of Smoking Cessation**

The best proven method for reducing harm in patients who smoke is complete cessation.

**Short-term:** The short-term benefits of smoking cessation include a decrease in the frequency of respiratory problems, fewer sick days, improvement in children's asthma and a general feeling of well-being.<sup>21</sup> Compared to COPD patients who continue to smoke, those who quit have a decreased risk for hospitalizations due to COPD exacerbation and decreased mortality.<sup>12</sup>

**Long-term:** Smoking cessation will lower the risk for coronary heart disease, stroke, COPD, lung cancer, oral cancers and bladder cancer. It also decreases the risk of developing cancer of the cervix, pancreas and kidneys.<sup>21</sup> Cardiovascular mortality risk decreases substantially within two years following smoking cessation.<sup>11</sup> Cardiac patients can reduce their risk of death by at least one-third if they quit smoking after a heart attack or cardiac surgery.<sup>11,22</sup> Smoking cessation at age 35 can add up to 8.5 years of life for men compared to those who continue to smoke. Even smokers who quit at age 65 can add an additional two years to their life expectancy.<sup>23</sup>

### **Smoking Cessation-Related Weight Gain**

Most smokers gain weight when they quit smoking. Weight gain is usually less than 10 pounds, but may be as much as 30 pounds in up to 10% of ex-smokers.<sup>2,24</sup> This weight gain appears to be caused by both increased calorie intake and decreased metabolism. Individuals who resume smoking at pre-cessation levels will usually lose some or all of the weight gained during the quit attempt. For smokers with weight concerns, bupropion SR or nicotine replacement treatment (in particular, nicotine gum and nicotine lozenge) may be the best selections since they have been shown to delay weight gain after quitting (Level B).<sup>2</sup>

### **Smoking Cessation Rate/Relapse Rates**

Most smokers who try to quit smoking still make unaided quit attempts; only 4 to 7% are successful.<sup>2</sup> The evidence is compelling that a physician's advice to patients to quit smoking, even with an intervention lasting less than three minutes, increases overall abstinence rates by 1-3% (Level A).<sup>2,25</sup> Smokers cite a physician's advice to quit as an important motivator for attempting to stop smoking.<sup>2</sup>

Smoking is an addiction that is hard to kick. The addiction is due to a combination of pharmacologic, behavioral, psychological, social and environmental factors.<sup>26</sup> Most smokers make several attempts before they are successful at quitting, with surveyed smokers reporting an average of 4 to 7 attempts.<sup>27,28,29</sup> The relapsing nature of the condition requires ongoing rather than just acute care.<sup>2</sup>

### **Other Considerations**

Few smokers get specific help with quitting, with only 39% of smokers reporting that their clinician discussed either medications or counseling strategies to quit.<sup>2</sup> Although the rate of tobacco dependence interventions has increased in insured patients, there is a need for additional improvement in various populations, including: Medicaid patients, pregnant women, adolescents, older smokers, light smokers, and racial and ethnic minorities. For example, only a quarter to a third of Medicaid patients, pregnant women, and adolescents are offered counseling. Some racial and ethnic minorities are also less likely to receive advice to stop smoking or use tobacco dependence treatment.<sup>2</sup>

## **TREATMENT OPTIONS FOR SMOKING CESSATION**

Treatment with either counseling or medication for smoking cessation is effective at improving abstinence rates (Level A). However, the combination of counseling and medication is more effective for achieving abstinence than either medication or counseling alone (Level A). Medication is not recommended when contraindicated or in special populations or conditions where evidence of safety and/or efficacy is insufficient (i.e., pregnancy, adolescence, smokeless tobacco users, or light smokers).<sup>2</sup>

## **BEHAVIORAL AND PSYCHOSOCIAL INTERVENTIONS**

There are several behavioral and psychosocial interventions for smoking cessation. The effective interventions are usually based on established theories of human behavior. The most commonly used interventions are detailed below. A summary of these interventions and how to use them during the clinical encounter is provided in Table 1.

### **The Transtheoretical Model (TTM) of Behavior Change**

The Transtheoretical Model (TTM) of behavior change developed by Prochaska and DiClemente identifies five stages an individual passes through in order to change an established behavior.<sup>30</sup> Smoking cessation, based on TTM, progresses through five stages (Table 1):

- Precontemplation: Does not want to quit
- Contemplation: Might quit 1-6 months from now
- Preparation: Actively planning to quit
- Action: Actively quitting
- Maintenance: Maintaining abstinence after 6 months

Tobacco dependence is a chronic disorder in which patients have periods of relapse and remission. Two additional stages in the TTM provide a complete picture of the smoking cessation process:

- Relapse: Smoking after quit date (leads to recycling through two or more stages)
- Termination: Quitting considered permanent

Motivation is important throughout the TTM progression and impacts readiness to change, which is a combination of perceived importance of the problem and confidence in the ability to change.<sup>31</sup>

### **Practical Strategies To Increase Smoking Cessation: The 5 A's Approach**

The 5 A's is an approach for treating tobacco use and dependence in the clinical setting recommended by the National Cancer Institute and the American Medical Association (Table 1). Components of the 5 A's include:

- **Ask** about tobacco use;
- **Advise** to quit;
- **Assess** willingness to make a quit attempt;
- **Assist** in quit attempt; and
- **Arrange** follow-up.

It is important to implement all five components, with assistance and follow-up actions chosen based on the patient's smoking status (current, former, never); readiness to change (willing/unwilling to quit); and length of abstinence (recent quitter/long term abstinence) (Tables 1 – 4).

Modifications of the 5 A's have been adopted by various professional organizations to fit their practice needs. For example, the South Carolina Department of Health and Environmental Control (SC DHEC) and the American Academy of Pediatrics promote the 2 A's + R (Ask, Advise, Refer); the American Academy of Family Physicians uses the 2 A's Cessation Model: Ask (about tobacco use) and Act (on that information); and the American Dental Hygienists' Association suggests the 3 A's (Ask, Advise, Assist).

### **Brief Motivational Interviewing Treatment**

Most patients want to quit smoking, but feel they cannot achieve and sustain abstinence. Motivational interviewing is a technique whereby clinicians focus on the patient's desire to quit smoking by developing an awareness of the discordance between knowledge and behavior, and then supporting the patient's self-efficacy in achieving that desire.<sup>32</sup> There are four principles of motivational interviewing (Table 5):

- express empathy,
- develop discrepancy,
- roll with resistance, and
- support self-efficacy.

When the patient is ready to quit smoking, practical counseling that focuses on problem solving/skills training (e.g., build on past success, avoid triggers, limit/abstain from alcohol, stress management) and offering support and encouragement during patient-provider interactions are especially effective.<sup>2</sup>

### **Intensity of Behavioral Interventions**

One intervention lasting less than three minutes increases overall tobacco abstinence rates. All tobacco users should be offered this minimal intervention, even in the absence of more intensive interventions (Level A). Longer person-to-person interactions and multiple sessions that can be provided by more than one provider type (i.e., physician and non-physician) have greater impact (Level A). Two or more sessions significantly increase abstinence rates; four or more interventions are especially effective (Level A). For more intensive interventions, proactive telephone quitlines (e.g., 1-800-QUIT-NOW that offers specialist-delivered counseling), group counseling and individual counseling are all effective tobacco use treatment approaches (Level A).<sup>2</sup>

### **Gradual Reduction Prior to Quitting vs. 'Cold Turkey'**

Abrupt abstinence (i.e., cold turkey with or without medication) may result in better quit rates than gradual reduction of smoking prior to quitting (e.g., 'cut down' or cigarette fading) in patients who quit on their own – they are almost twice as likely to succeed and less likely to relapse. In structured cessation programs, 'cut down' has been shown to be at least as effective as abrupt abstinence. It seems likely that the increased success rate on the part of smokers who choose to quit cold turkey is due to increased motivation.<sup>33</sup>

## MEDICATIONS FOR SMOKING CESSATION

### First-Line Medications

Nicotine replacement therapies (NRTs), bupropion SR, and varenicline are first-line medications that are effective for smoking cessation and are approved by the FDA for this use (Level A).<sup>2,34</sup> Table 6 summarizes standard recommendations on dosing, administration instructions, and duration of treatment.

### Second-Line Medications

Nortriptyline and clonidine are reserved as second-line medications. Both medications approximately double the odds of long-term abstinence compared to placebo treatment (Level A), but they have side effect profiles which limit their widespread use. Neither one is FDA-indicated for smoking cessation.<sup>2,35,36</sup> Table 7 summarizes standard recommendations on dosing, administration instructions, and duration of treatment.

### Medication Combinations

Certain medications can be effectively combined for smoking cessation treatment. Some combinations may yield higher abstinence rates; evidence also suggests that medication combinations may result in greater suppression of tobacco withdrawal symptoms than monotherapy (Tables 6 and 7). Factors to consider in selecting the optimal regimen include: patient preferences; previous smoking cessation attempts (e.g., number of attempts, withdrawal symptoms); current medical conditions; side effect profile; cost; and pharmacology. A combination currently not recommended is varenicline with NRT because of the nicotine antagonist properties of varenicline.

Compared to placebo, the following combinations significantly increase abstinence rates: nicotine patch + lozenge (Level B);<sup>37</sup> nicotine patch + inhaler; long-term nicotine patch + *ad libitum* NRT; nicotine patch + bupropion SR; and nicotine patch + nortriptyline (Level A).<sup>2</sup> Increasing evidence suggests that combining NRT formulations improves efficacy over nicotine patch alone.

### Initiation of Treatment

Smoking cessation medications such as varenicline, bupropion SR, clonidine and nortriptyline are initiated prior to the established quit date (Tables 6 and 7).<sup>2</sup> NRTs are FDA-approved for post-quit use only, although recent research has investigated their use while smoking, either for smoking cessation in patients wanting to quit or smoking reduction in patients not willing to quit but willing to reduce smoking.<sup>2,38,39,40</sup>

In smokers willing to make a quit attempt, the use of the nicotine patch prior to quitting may increase long-term abstinence rates by 80% (Level B).<sup>2,38,40</sup> Current smoking cessation guidelines await more research on this strategy before a recommendation is made.<sup>2</sup> If precessation smoking NRT is used clinically, patients should be advised to cease NRT use if they develop symptoms of nicotine toxicity (e.g., nausea, vomiting, dizziness).

In patients unwilling to quit but willing to reduce smoking, the use of NRT has been shown to approximately double the odds of long-term abstinence. Nicotine gum (for 6–12 months), nicotine inhaler (for 6–24 months), nicotine patch (for up to 6 months), or a combination of these NRTs are helpful for smoking reduction.<sup>2,39</sup> Current smoking cessation guidelines do not recommend any medication use as a standard intervention for smokers unwilling to quit due to insufficient evidence and concerns that this strategy may undermine interest in quitting.<sup>2</sup>

### Duration of Treatment

The usual duration of therapy for smoking cessation medications is 8 to 12 weeks. For some patients, it may be helpful to continue medication treatment for periods longer than is usually recommended (e.g., smokers with persistent withdrawal symptoms during medication treatment; smokers with a history of relapsing after medication discontinuation; smokers interested in long-term therapy).<sup>2</sup> The FDA has approved the use of the nicotine inhaler, the nicotine nasal spray, bupropion SR, and varenicline for up to 6 months of use. Extended treatment with varenicline for an additional 12 weeks has been shown to significantly reduce relapse (risk ratio 1.18, 95% confidence interval 1.03 to 1.36) in patients who had successfully quit smoking following a

short course of treatment.<sup>41</sup> The benefits of extended bupropion SR treatment in patients who had successfully quit with a short course of treatment are unclear.<sup>2,41</sup>

### **Relapse**

Benefits of offering further pharmacotherapy to relapsed smokers are unclear; some evidence suggests it may yield small or no benefit while other evidence suggests that it may be of substantial benefit.<sup>2,36,38</sup> The time interval between quit attempts may be an important factor. A second treatment with smoking cessation medications soon after relapse is associated with a low success rate while a longer gap may improve success rate.<sup>36,38</sup>

### **Treatment Discontinuation**

Of the first-line smoking cessation medications, NRT is usually administered in a step-down dosing fashion (e.g., gum, lozenge, patch), or tapered at the end of treatment (e.g., inhaler, nasal spray). There is no difference in efficacy and tolerability, however, between abrupt discontinuation versus gradual reduction of the nicotine patch.<sup>38</sup> No specific tapering recommendations are made for bupropion SR and varenicline.<sup>2</sup>

Second-line smoking cessation medications, especially clonidine, require gradual tapering before discontinuation. Abrupt discontinuation of clonidine can result in rebound hypertension, particularly in hypertensive patients, as well as in other symptoms such as nervousness, agitation, headache and tremor. Tapering of clonidine dosing over several days to one week is recommended.<sup>35</sup> Abrupt discontinuation of medications with anticholinergic side effects such as nortriptyline can cause cholinergic rebound. A gradual taper of nortriptyline by 25 mg every 3-5 days is recommended.<sup>42</sup>

### **Side Effects**

Side effect profiles of smoking cessation medications vary. Tables 6 and 7 provide common side effects, cautions, warnings and administration instructions for smoking cessation medications. NRTs have a well-established safety and tolerability profile; combination NRT products are also well tolerated with minimal side effects reported.<sup>2,38,43</sup> Despite delivering nicotine, NRTs are associated with a decreased abuse potential because of the slower rate of nicotine absorption and lower overall nicotine plasma concentrations compared to tobacco products.<sup>44</sup>

Reports of serious neuropsychiatric symptoms (including behavioral changes, depressed mood, hostility, and suicidal thoughts) while taking varenicline and bupropion prompted the FDA to require that a boxed warning be added to their package inserts.<sup>36,45</sup> Numerous reports of serious injury linked to traffic accidents or falls have led three U.S. government departments to limit or ban the use of varenicline.<sup>45</sup> While these reports suggest a possible link to serious events, further research is under way to better evaluate causality and magnitude of risk with varenicline use, particularly in vulnerable populations (e.g., patients with preexisting psychiatric conditions).

### **Interactions**

Several drug interactions exist with tobacco smoke independent of nicotine. The polycyclic aromatic hydrocarbons in tobacco smoke induce the hepatic cytochrome P450 (CYP) 1A2, thereby increasing the dosage requirement of several medications. Important examples include caffeine, clozapine, fluvoxamine, olanzapine and theophylline. Upon smoking cessation, the dose of these medications should be decreased to minimize the risk of adverse effects associated with higher levels.<sup>2,46</sup>

Smoking increases the risk of oral contraceptive-induced adverse cardiovascular events. Consider an alternate form of contraception in women who continue to smoke, particularly in heavy smokers age 35 and older (contraindication in select products).<sup>46</sup>

Insulin requirements may be affected by tobacco smoke or NRT products. Nicotine-induced vasoconstriction may reduce subcutaneous absorption of insulin. Increased glucose concentration and decreased response to insulin may be associated with compounds in tobacco smoke or nicotine. Adjustments in insulin may be necessary when NRT is discontinued or upon smoking cessation if NRT is not used.<sup>2,46</sup>

Bupropion and its metabolites inhibit CYP2D6 and can increase the concentration of medications metabolized by this enzyme (e.g., certain antipsychotics, type 1C antiarrhythmics, beta-blockers, and tricyclic antidepressants). Due to the extensive metabolism of bupropion, enzyme inducers (e.g., carbamazepine, phenobarbital, phenytoin) and inhibitors (e.g., cimetidine) may affect its plasma concentration. Bupropion can lower seizure threshold and should be used cautiously with other medications that lower the seizure threshold.<sup>2</sup>

### **Special Considerations**

**Light Smokers.** It is important to identify light smokers, strongly urge them to quit, and provide counseling cessation interventions (Level B). Findings are mixed in the few studies examining the effectiveness of tobacco use medications to sustain abstinence.<sup>2</sup>

**Non-cigarette Tobacco Users.** It is important to identify smokeless tobacco users, strongly urge them to quit, and provide counseling cessation interventions (Level A). Patients using non-cigarette forms of smoking tobacco should receive the same counseling interventions as cigarette smokers (Level C). To date, bupropion SR and NRTs have not been shown to increase abstinence rates among smokeless tobacco users.<sup>2</sup>

**Children and Adolescents.** It is important for clinicians to ask pediatric and adolescent patients about tobacco use and to strongly encourage abstinence among youth (Level C) as well as their parents.<sup>2</sup> Modest evidence supports the use of counseling interventions to help adolescent smokers quit (Level B). NRT has been shown to be safe in adolescents; however, there is little evidence that NRT or bupropion SR are effective in promoting long-term smoking abstinence in this age group.<sup>2,9</sup>

**Pregnant Women.** A recent meta-analysis reported that about 24% of women were able to quit smoking during pregnancy when their smoking treatment intervention provided incentives.<sup>2</sup> Whenever possible, pregnant women who smoke should be offered person-to-person psychosocial interventions (exceeding the minimal advice to quit) because of the serious risk of smoking to the woman and her fetus (Level A).<sup>2,16</sup> Recommendations on medication use during pregnancy are not available at this time due to safety concerns and limited and conflicting evidence of efficacy. Although NRT (i.e., nicotine) is likely less harmful than cigarette smoking during pregnancy, its potential for harm due to direct effects on the fetus is unresolved.<sup>2,16</sup>

**Post-Partum.** Relapse rates within the first year after delivery ranging from 50% to 90% have been reported. There are several strategies that may help prevent and manage post-partum relapse: focusing on health benefits of quitting for the patient, infant, and family members; continuing counseling and cessation skills building at the end of pregnancy and post-partum; providing congratulatory messages and reinforcing the patient's desire to be a good mother; and providing counseling and reassurance to women who relapse and encouraging them to try again.<sup>47</sup>

**Psychiatric Disorders.** All smokers with psychiatric disorders should be offered tobacco dependence treatment, although some clinicians may wish to offer this treatment when psychiatric symptoms are not severe. Bupropion SR and nortriptyline, both effective in treating depression, have been shown to be effective at increasing long-term abstinence rates in smokers with a past history of depression.<sup>2</sup>

**Cardiovascular Disease.** Smokers with cardiac disease are ideal candidates for smoking cessation since their disease may have been caused or exacerbated by smoking and may improve if they quit. These patients should be offered counseling and first-line medications. The nicotine patch, in particular, has been demonstrated as safe in patients with stable coronary heart disease.<sup>2</sup> For patients recovering from ST-elevation myocardial infarction (STEMI), the American College of Cardiology and the American Heart Association recommend counseling and pharmacotherapy (including NRT and bupropion) as appropriate. NRT is not routinely started during hospitalization for STEMI; however, it may be helpful in select patients with severe nicotine withdrawal. NRT may be started at the time of discharge if blood pressure and heart rate are stable.<sup>48</sup>

**Table 1. SMOKING CESSATION AND PATIENT BEHAVIOR**

5 A's Model for Treating Tobacco Use and Dependence – Physician's Actions	Stages of Change – Understanding Where the Patient Is in the Process of Change	Stage of Change Assessment – Physician action matchup
<p><b>Ask</b> about tobacco use</p> <ul style="list-style-type: none"> <li>Identify and document smoking status of every patient at every visit</li> </ul> <p><b>Advise</b> to quit</p> <ul style="list-style-type: none"> <li>In a clear, strong and personalized manner urge every smoker to quit, <i>"It is important for you to quit and I can help."</i></li> </ul> <p><b>Assess</b></p> <ul style="list-style-type: none"> <li>For the current smoker ask, <i>"Are you willing to give quitting a try at this time?"</i></li> <li>For the ex-smoker, ask how recently he/she quit and are there challenges to remaining abstinent</li> <li>Offer motivation and increase patient's confidence in ability to change</li> </ul> <p><b>Assist</b></p> <ul style="list-style-type: none"> <li>Negotiate a plan to quit and implement it with the patient</li> <li>For the patient willing to make a quit attempt, offer medication and/or provide or refer for counseling to help the patient quit</li> <li>For patients unwilling to quit at this time, provide motivational interventions designed to increase future quit attempts</li> <li>For the recent quitter and any with remaining challenges, provide relapse prevention</li> </ul> <p><b>Arrange</b></p> <ul style="list-style-type: none"> <li>All those receiving the previous A's should receive follow-up to review progress</li> <li>If a relapse occurs, review circumstances that caused relapse; review medication use and problems; provide or refer for counseling</li> </ul>	<p><b>Precontemplation</b></p> <ul style="list-style-type: none"> <li>Not thinking about change</li> <li>May be resigned</li> <li>Denial</li> <li>Feeling of no control</li> </ul> <p><b>Contemplation</b></p> <ul style="list-style-type: none"> <li>Weighs pros/cons of smoking cessation</li> </ul> <p><b>Preparation<sup>1</sup></b></p> <ul style="list-style-type: none"> <li>Commits to change</li> <li>Forms a plan of action</li> <li>Experiments with small changes</li> </ul> <p><sup>1</sup> Highly motivated patients may skip preparation and go straight to action</p> <p><b>Action</b></p> <ul style="list-style-type: none"> <li>Takes definitive action to stop smoking</li> <li>Implements plan to stop smoking</li> </ul> <p><b>Maintenance (post quit)</b></p> <ul style="list-style-type: none"> <li>Determined to maintain smoking cessation</li> <li>Incorporates changes as part of a new lifestyle</li> </ul> <p><b>Relapse</b></p> <ul style="list-style-type: none"> <li>May be discouraged by relapse but should be viewed as normal part of smoking cessation</li> </ul>	<p><b>Motivational intervention</b></p> <ul style="list-style-type: none"> <li><b>Relevance, Risks, Rewards, Roadblocks, Repetition (5Rs)</b></li> <li>Express empathy, develop discrepancy, roll with resistance, support self-efficacy</li> </ul> <p><b>STAR (Formulate a quit plan)</b></p> <ul style="list-style-type: none"> <li><b>Set</b> a quit date</li> <li><b>Tell</b> family/friends and obtain support/understanding</li> <li><b>Anticipate</b> challenges and withdrawal/problem solving</li> <li><b>Remove</b> tobacco from environment</li> </ul> <p><b>START</b></p> <ul style="list-style-type: none"> <li><b>Begin</b> medication<sup>1,2</sup></li> <li><b>Counseling</b> (problem solving/skills training) and encouragement</li> <li><b>Follow up</b> within 1 week of quit date by office visit or phone</li> <li><b>2<sup>nd</sup></b> follow-up within 1 month if possible</li> <li><b>Additional</b> follow-ups as needed</li> <li><b>Offer</b> the S.C. Tobacco Quitline 1-800-QUIT-NOW for telephone counseling</li> </ul> <p><sup>1</sup> Unless contraindicated or insufficient evidence (e.g., pregnancy, adolescence, light smokers, smokeless tobacco users)  <sup>2</sup> Varenicline 1 week prior to and bupropion 1-2 weeks prior to abstinence; all other meds on quit date</p> <p><b>Follow-up</b></p> <ul style="list-style-type: none"> <li>Offer congratulations and encourage recommitment to quit</li> <li>Assist with problems associated with quitting (e.g., weight gain, residual withdrawal symptoms)</li> </ul> <p><b>Relapse</b></p> <ul style="list-style-type: none"> <li>Remind patient relapse is common and part of the learning process</li> <li>Assess readiness for another quit attempt, and offer stage-appropriate assistance</li> </ul>

**Table 2. ASSISTING SMOKERS WILLING TO QUIT WITH A PLAN**

**Assist** the smoker by formulating a quit plan, deciding on the most appropriate medication unless counseling alone is the preferred option, and offering practical counseling and social support

- Identify reasons for quitting and benefits of quitting
- Help formulate a quit plan:
  - ✓ Set a quit date, ideally within 2 weeks
  - ✓ If unable to stop 'cold turkey' on quit date, plan to cut down on number of cigarettes or delay smoking each cigarette by 30 minutes
  - ✓ Tell family and friends and coworkers about quitting
  - ✓ Get rid of all tobacco products and strive for smokefree household by quit date
- Review past quit attempts:
  - ✓ What worked
  - ✓ What did not work
- Learn new skills and behaviors:
  - ✓ Reduce stress
  - ✓ Change routine
  - ✓ Replace smoking with low-calorie foods
- Anticipate challenges and nicotine withdrawal symptoms, especially the first few weeks:
  - ✓ Avoid triggers/alter routine
  - ✓ Avoid alcohol to maximize the chance of success
  - ✓ Be careful around other smokers; if at all possible, stay in nonsmoking areas
- Get support from family, friends, and coworkers
- Abstinence is the goal (i.e., not a puff after the quit date)
- Decide on medication (unless counseling alone is preferred or appropriate option) and encourage use
- Initiate nicotine replacement therapy (NRT), bupropion SR, or varenicline unless contraindicated

**Arrange** follow-up in person or through telephone contact

- Schedule first follow-up contact within first week of quitting; second follow-up within the first month; other follow-ups as indicated
- Recommend toll-free helpline for counseling offered through the S.C. Tobacco Quitline: 1-800-QUIT-NOW (1-800-784-8669)
- Option to provide other resources, including links to websites for free materials (e.g., The Tobacco Control Research Branch of the National Cancer Institute at: [www.smokefree.gov](http://www.smokefree.gov))

**Table 3. ASSISTING SMOKERS WHO RECENTLY QUIT**

**Ask** and document smoking status at every visit

- Recent quitters are at high risk for relapse. While there does not appear to be any particular behavioral strategy of counseling that decreases the likelihood of relapse, encouragement and ongoing support is valuable

**Assess** relapse potential

- Ask how long ago the patient quit. Most relapses occur within the first two weeks of quitting
- Ask about urges to smoke or challenges to remain abstinent

**Assist** with encouragement to stay abstinent

- Offer patient the opportunity to discuss:
  - ✓ Benefits that he/she may derive from smoking cessation
  - ✓ Any successes in quitting (e.g., duration of abstinence, reduction in withdrawal)
  - ✓ Challenges to remaining abstinent (e.g., depression, weight gain, significant stressors)
  - ✓ Medication effectiveness and adherence

**Arrange** follow-up

**Table 4. ASSISTING SMOKERS UNWILLING OR UNDECIDED TO QUIT AT THIS TIME**

<p><b>Assist</b> with motivational interventions designed to enhance motivation to quit</p> <ul style="list-style-type: none"> <li>• Relevance <ul style="list-style-type: none"> <li>✓ Encourage the patient to identify, in his/her own words, why quitting is personally relevant</li> </ul> </li> <li>• Risks <ul style="list-style-type: none"> <li>✓ Ask the patient to identify potential negative consequences of smoking then highlight risks most relevant to the patient</li> <li>✓ Explain that smoking low-tar/low-nicotine cigarettes or use of other forms of tobacco (e.g., cigars, pipes, smokeless tobacco) will not eliminate these risks</li> </ul> </li> <li>• Rewards <ul style="list-style-type: none"> <li>✓ Ask the patient to identify potential benefits (e.g., money saved [\$1,971 per year for 1 pack/day smoker]) then highlight benefits most relevant to the patient</li> </ul> </li> <li>• Roadblocks <ul style="list-style-type: none"> <li>✓ Ask the patient to identify barriers then offer problem-solving counseling and/or medication that could address barriers (e.g., depression)</li> </ul> </li> <li>• Repetition <ul style="list-style-type: none"> <li>✓ Repeat motivational interventions at every visit and tell smokers that most people make repeated quit attempts before they are successful</li> </ul> </li> </ul> <p><b>Arrange</b> to repeat on subsequent visits</p>
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**Table 5. MOTIVATIONAL INTERVIEWING STRATEGIES**

<p><b>Express empathy</b></p>	<ul style="list-style-type: none"> <li>• Use open-ended questions to explore: <ul style="list-style-type: none"> <li>✓ The importance of addressing smoking or other tobacco use (e.g., <i>“How important do you think it is for you to quit smoking?”</i>)</li> <li>✓ Concerns and benefits of quitting (e.g., <i>“What might happen if you quit?”</i>)</li> </ul> </li> <li>• Use reflective listening to seek shared understanding: <ul style="list-style-type: none"> <li>✓ Reflect words or meaning (e.g., <i>“So you think smoking helps you to maintain your weight.”</i>)</li> <li>✓ Summarize (e.g., <i>“What I have heard so far is that smoking is something you enjoy. On the other hand, your boyfriend hates your smoking, and you are worried you might develop a serious disease.”</i>)</li> </ul> </li> <li>• Normalize feelings and concerns (e.g., <i>“Many people worry about managing without cigarettes.”</i>)</li> <li>• Support the patient’s autonomy and right to choose or reject change (e.g., <i>“I hear you saying you are not ready to quit smoking right now. I’m here to help you when you are ready.”</i>)</li> </ul>
<p><b>Develop discrepancy</b></p>	<ul style="list-style-type: none"> <li>• Highlight the discrepancy between the patient’s present behavior and expressed priorities, values, and goals - weigh pros and cons: <ul style="list-style-type: none"> <li>✓ <i>“It sounds like you are very devoted to your family. How do you think your smoking is affecting your children?”</i></li> </ul> </li> <li>• Reinforce and support “change talk” and “commitment” language: <ul style="list-style-type: none"> <li>✓ <i>“So, you realize how smoking is affecting your breathing and making it hard to keep up with your kids.”</i></li> <li>✓ <i>“It’s great that you are going to quit when you get through this busy time at work.”</i></li> </ul> </li> <li>• Build and deepen commitment to change: <ul style="list-style-type: none"> <li>✓ <i>“There are effective treatments that will ease the pain of quitting, including counseling and many medication options.”</i></li> <li>✓ <i>“We would like to help you avoid a stroke like the one your father had.”</i></li> </ul> </li> </ul>
<p><b>Roll with resistance</b></p>	<ul style="list-style-type: none"> <li>• Back off and use reflection when the patient expresses resistance: <ul style="list-style-type: none"> <li>✓ <i>“Sounds like you are feeling pressured about your smoking.”</i></li> </ul> </li> <li>• Express empathy: <ul style="list-style-type: none"> <li>✓ <i>“You are worried about how you would manage withdrawal symptoms.”</i></li> </ul> </li> <li>• Ask permission to provide information: <ul style="list-style-type: none"> <li>✓ <i>“Would you like to hear about some strategies that can help you address that concern when you quit?”</i></li> </ul> </li> </ul>
<p><b>Support self-efficacy</b></p>	<ul style="list-style-type: none"> <li>• Help the patient to identify and build on past successes: <ul style="list-style-type: none"> <li>✓ <i>“So you were fairly successful the last time you tried to quit.”</i></li> </ul> </li> <li>• Offer options for achievable small steps toward change: <ul style="list-style-type: none"> <li>✓ Call the S.C. Tobacco Quitline (1-800-QUIT-NOW) for advice and information</li> <li>✓ Read about quitting benefits and strategies</li> <li>✓ Change smoking patterns (e.g., no smoking in the home)</li> <li>✓ Share his or her ideas about quitting strategies</li> </ul> </li> </ul>

**Table 6. FIRST-LINE MEDICATION GUIDELINES FOR SMOKING CESSATION**

Medications* [Brand Examples]	Dosage	Duration	OR (95% CI) <sup>#</sup>	Daily Cost <sup>†</sup> [~ Pack]
<b>Nicotine Gum (i)</b> [Nicorette <sup>®</sup> ]  2 mg, 4 mg  <b>OTC</b>	<b>2 mg: &lt; 25 cigarettes/day</b> <b>4 mg: ≥ 25 cigarettes/day</b> Weeks 1-6: 1 piece q 1-2 h – Minimum: 9 pieces/day – Maximum: 24 pieces/day Weeks 7-9: 1 piece q 2-4 h Weeks 10-12: 1 piece q 4-8 h	Up to 12 weeks	1.5 (1.2-1.7)	\$3.51 - \$3.69 (9 pieces)  [~ ¾ pack]
<b>Nicotine Lozenge (i)</b> [Nicorette <sup>®</sup> ]  2 mg, 4 mg  <b>OTC</b>	<b>2 mg: 1<sup>st</sup> cigarette &gt; 30 min after waking</b> <b>4 mg: 1<sup>st</sup> cigarette ≤ 30 min after waking</b> Weeks 1-6: 1 lozenge q 1-2 h – Minimum: 9 lozenges/day – Maximum: 20 lozenges/day Weeks 7-9: 1 lozenge q 2-4 h Weeks 10-12: 1 lozenge q 4-8 h	Up to 12 weeks	2 mg: 2.0 (1.4-2.8) (iii) 4 mg: 2.8 (1.9-4.0) (iii)	\$3.78 - \$3.96 (9 pieces)  [~ ¾ pack]
<b>Nicotine Patch, 24-hour (i)</b> [Nicoderm CQ <sup>®</sup> ]  7 mg, 14 mg, 21 mg  <b>OTC</b>	<b>If &gt; 10 cigarettes/day: (ii)</b> 21 mg/day x 4-6 weeks; 14 mg x 2 weeks; 7 mg x 2 weeks  <b>If ≤ 10 cigarettes/day: (ii)</b> 14 mg/day x 6 weeks; 7 mg/day x 2 weeks	8 - 10 weeks	1.9 (1.7-2.2)  <b>PATCH plus:</b> + bupropion HCl SR 2.5 (1.9-3.4) (iii) + ad lib gum or spray 3.6 (2.5-5.2) (iii,iv) + lozenge 2.3 (1.5-3.6) (iii,iv) + inhaler 2.2 (1.3-3.6) (iii,iv)	\$2.70 - \$3.13 (1 patch)  [~ ½ pack]
<b>Nicotine Nasal Spray (i)</b> [Nicotrol NS <sup>®</sup> ] (4 bottles/package)  200 sprays/10 ml bottle 0.5 mg/metered spray  <b>Rx</b>	1 dose = 2 sprays (one spray in each nostril) Start with 1-2 doses/hour (Maximum: 5 doses/hour)  – Minimum: 8 doses/day – Maximum: 40 doses/day  Taper at end suggested	12 weeks; up to 6 months in selected patients	2.3 (1.7-3.0)	\$4.39 (8 doses)  [~ ¾ pack]
<b>Nicotine Inhaler (i)</b> [Nicotrol <sup>®</sup> ] (168 cartridges/package)  10 mg/cartridge  <b>Rx</b>	10 mg cartridge (delivers 4 mg) ~ 20 minutes of active puffing  – Minimum: 6 cartridges/day – Maximum: 16 cartridges/day  Taper at end suggested	12 weeks; up to 6 months in selected patients	2.1 (1.5-2.9)	\$7.72 (6 cartridges)  [~1.5 packs]
<b>Bupropion HCl SR</b> [Zyban <sup>®</sup> ]  150 mg SR tablet  <b>Rx</b>	Start 1-2 weeks before quit date Days 1-3: 150 mg q AM Day 4 until end: 150 mg BID (v)  – Maximum: 300 mg/day	7 - 12 weeks; up to 6 months in selected patients	2.0 (1.8-2.2)	\$2.28 (2 tablets, generic)  [~ ½ pack]
<b>Varenicline</b> [Chantix <sup>®</sup> ]  0.5 mg, 1 mg tablet  <b>Rx</b>	Start 1 week before quit date Days 1-3: 0.5 mg q AM Days 4-7: 0.5 mg BID Day 8 until end: 1 mg BID (vi)	12 weeks; up to 6 months in selected patients	3.1 (2.5-3.8) (vi)	\$5.62 (Two 1 mg tablets)  [~ 1 pack]

\* FDA approved in adults only; <sup>#</sup> OR = Estimated odds ratio for treatment versus placebo (95% Confidence Interval); <sup>†</sup> Daily drug cost and daily approximate cigarette pack equivalent [~ Pack] based on September 2010 average South Carolina retail costs; <sup>‡</sup> Breastfeeding recommendations are not provided due to limited/lack of human data. FDA pregnancy ratings: A, controlled studies show no risk; B, no evidence of risk in humans; C, risk cannot be ruled out; D, positive evidence of risk; X, contraindicated in pregnancy.

(i) FDA approved for post-quit use only; (ii) Preliminary evidence suggests that starting nicotine patch 2 weeks prior to quit date versus starting on quit date increases abstinence rates (OR 1.8 [1.2-2.7]); (iii) Based on 3 or fewer studies; (iv) Combination not FDA approved; (v) A lower dose of 150 mg daily does not appear to differ in efficacy; (vi) A lower dose of 0.5 mg BID (OR = 2.1 [1.5 – 3]) is effective but less so than 1 mg BID.

## FIRST-LINE MEDICATION GUIDELINES FOR SMOKING CESSATION (CONTINUED)

	Administration Instructions	Cautions ( <i>Pregnancy</i> <sup>†</sup> )	Side Effects / Comments
Nicotine Gum	<ul style="list-style-type: none"> <li>Chew gum slowly until tingles (~ 15-30 chews), then park between cheek and gum</li> <li>Resume chewing when tingle fades</li> <li>Repeat “chew-park” process until tingle is gone/does not return (~ 30 minutes)</li> <li>No food or beverages except water 15 minutes before or during use</li> </ul>	<ul style="list-style-type: none"> <li>Caution in patients with recent myocardial infarction (within 2 weeks), serious arrhythmias, unstable angina</li> <li>Caution with dentures, dental caps, partial bridges, temporomandibular joint disease</li> <li><i>FDA: C; Briggs: Compatible - maternal benefit &gt;&gt; embryo/fetal risk</i></li> </ul>	<ul style="list-style-type: none"> <li>Mouth soreness; jaw ache</li> <li>Hiccups</li> <li>Dyspepsia</li> <li>Gastrointestinal disturbances: <ul style="list-style-type: none"> <li>Associated with improper use and swallowing large amounts of nicotine</li> </ul> </li> </ul>
Nicotine Lozenge	<ul style="list-style-type: none"> <li>Dissolve slowly in mouth (~ 20-30 minutes); may notice warm tingling sensation</li> <li>Occasionally move to other side of mouth</li> <li>Do not chew or swallow</li> <li>No food or beverages except water 15 minutes before or during use</li> </ul>	<ul style="list-style-type: none"> <li>Caution in patients with recent myocardial infarction (within 2 weeks), serious arrhythmias, unstable angina</li> <li><i>FDA: C; Briggs: Not available</i></li> </ul>	<ul style="list-style-type: none"> <li>Nausea; hiccups; heartburn; indigestion</li> <li>4 mg: Cough (&lt; 10%) and headaches (&lt; 10%)</li> </ul>
Nicotine Patch, 24-hour	<ul style="list-style-type: none"> <li>Apply patch to clean, hairless, dry skin on trunk or upper limbs</li> <li>Rotate application sites</li> <li>If sleep disturbances, remove patch at bedtime</li> <li>Do not cut patch</li> </ul>	<ul style="list-style-type: none"> <li>Caution in patients with recent myocardial infarction (within 2 weeks), serious arrhythmias, unstable angina</li> <li>Avoid in patients with severe eczema or psoriasis</li> <li>Remove metal containing patches (e.g., tan-colored) prior to MRI</li> <li><i>FDA: D; Briggs: Compatible - maternal benefit &gt;&gt; embryo/fetal risk</i></li> </ul>	<ul style="list-style-type: none"> <li>Insomnia</li> <li>Local skin reaction (50%): <ul style="list-style-type: none"> <li>Usually mild</li> <li>Rarely leads to discontinuation</li> <li>Rotate application site to minimize</li> </ul> </li> </ul>
Nicotine Nasal Spray	<ul style="list-style-type: none"> <li>Prime pump before 1st use or if not used for &gt; 24 hours</li> <li>Shake nasal spray before using</li> <li>Deliver with head tilted slightly back</li> <li>Avoid sniffing, inhaling or swallowing</li> </ul>	<ul style="list-style-type: none"> <li>Caution in patients with recent myocardial infarction (within 2 weeks), serious arrhythmias, unstable angina</li> <li>Avoid in patients with severe reactive airway disease and chronic nasal disorders</li> <li>Wait 5 minutes before driving</li> <li>Highest dependence potential</li> <li><i>FDA: D; Briggs: Compatible - maternal benefit &gt;&gt; embryo/fetal risk</i></li> </ul>	<ul style="list-style-type: none"> <li>Nasal irritation (94%), nasal congestion</li> <li>Smell and taste alterations</li> </ul>
Nicotine Inhaler	<ul style="list-style-type: none"> <li>Inhale into back of throat or puff in short breaths; do not inhale into lungs</li> <li>Open cartridge retains potency for 24 hours</li> <li>Use inhaler at room temperature</li> <li>No food or beverages except water 15 minutes before or during use</li> </ul>	<ul style="list-style-type: none"> <li>Caution in patients with recent myocardial infarction (within 2 weeks), serious arrhythmias, unstable angina</li> <li>Caution in patients with severe bronchospastic disease</li> <li><i>FDA: D; Briggs: Compatible - maternal benefit &gt;&gt; embryo/fetal risk</i></li> </ul>	<ul style="list-style-type: none"> <li>Mouth and throat irritation (40%)</li> <li>Cough (32%)</li> <li>Rhinitis (23%)</li> </ul>
Bupropion HCl SR	<ul style="list-style-type: none"> <li>Take 2nd dose in afternoon to reduce insomnia</li> <li>Allow at least 8 hours between doses</li> </ul>	<ul style="list-style-type: none"> <li>Contraindicated in patients with history of seizure or eating disorders</li> <li>Monitor blood pressure when combined with nicotine replacement therapy</li> <li>Monitor for changes in mood, behavior, psychiatric symptoms, and suicidal ideation</li> <li><i>FDA: C; Briggs: Human data suggest low risk</i></li> </ul>	<ul style="list-style-type: none"> <li>Insomnia (35-40%)</li> <li>Dry mouth (10%)</li> <li>Seizures (rare) reported in smoking cessation trials</li> </ul>
Varenicline	<ul style="list-style-type: none"> <li>Take after eating (with a full glass of water) to reduce nausea</li> <li>Take 2<sup>nd</sup> dose at supper to reduce insomnia</li> </ul>	<ul style="list-style-type: none"> <li>Caution in patients with significant renal impairment, serious psychiatric illness</li> <li>Caution driving/operating machinery</li> <li>Monitor for changes in mood, behavior, psychiatric symptoms, and suicidal ideation</li> <li><i>FDA: C; Briggs: No human data - animal data suggest low risk</i></li> </ul>	<ul style="list-style-type: none"> <li>Nausea (up to 30%) <ul style="list-style-type: none"> <li>Dose related</li> <li>May diminish over time</li> <li>Reduced with initial titration</li> </ul> </li> <li>Insomnia; abnormal, vivid, strange dreams</li> <li>Rare serious skin/allergic reactions</li> </ul>

**References:** Briggs, Gerald G., Roger K. Freeman, and Sumner J. Yaffe. *Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk*. Philadelphia, PA: Lippincott, Williams & Wilkins, 2008. Print; Fiore MC, Jaén CR, Baker TB, et al. *Clinical Practice Guideline. Treating Tobacco Use and Dependence: 2008 Update*. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. May 2008, Accessed October 21, 2009; Stead LF, Perera R, Bullen C, et al. Nicotine replacement therapy for smoking cessation. *Cochrane Database of Systematic Reviews* 2008, Issue 1. Art. No.: CD000146. DOI: 10.1002/14651858.CD000146.pub3; Piper ME, Smith SS, Schlam TR, et al. A randomized, placebo-controlled clinical trial of 5 smoking cessation pharmacotherapies. *Arch Gen Psychiatry* 2009;66:1253-1262; Rx for Change: Clinician – Assisted Tobacco Cessation. *Pharmacologic product guide: FDA-approved medications*. Copyright©1999-2010. The Regents of the University of California. Updated April 12, 2010. **For complete prescribing information, please refer to the manufacturers’ package inserts.**

**Table 7. SECOND-LINE MEDICATION GUIDELINES FOR SMOKING CESSATION**

Medications* [Brand Examples]	Dosage	Duration	OR (95% CI) <sup>#</sup>	Daily Cost <sup>†</sup> [~ Pack]
<b>Clonidine</b> [Catapres <sup>®</sup> , Catapres-TTS <sup>®</sup> ]  PO: 0.1 mg, 0.2 mg, 0.3 mg tablet  Transdermal System - once weekly patch: 0.1 mg/day, for 1 week 0.2 mg/day, for 1 week  <b>Rx</b>	Start ≤ 3 days before quit date <ul style="list-style-type: none"> <li>Initial:                             <ul style="list-style-type: none"> <li>PO: 0.1 mg BID</li> <li>Transdermal: 0.1 mg/day</li> </ul> </li> <li>Titration:                             <ul style="list-style-type: none"> <li>0.1 mg/day per week if needed</li> </ul> </li> <li>Range:                             <ul style="list-style-type: none"> <li>PO: 0.15-0.75 mg/day</li> <li>Transdermal: 0.1-0.2 mg/day</li> </ul> </li> </ul>	3 - 10 weeks; taper at end	2.1 (1.2-3.7) (i)	\$0.56 (0.3 mg tablet, generic)  [~1/10 pack]  \$5.42 (0.2 mg patch, generic)  [~1 pack]
<b>Nortriptyline</b> [Pamelor <sup>®</sup> ]  10 mg, 25 mg, 75 mg capsule  10 mg/ 5 ml  <b>Rx</b>	Start 10-28 days before quit date <ul style="list-style-type: none"> <li>Initial: 25 mg/day</li> <li>Titration: increase gradually</li> <li>Target: 75-100 mg/day</li> </ul>	3 months; up to 6 months; taper at end  PATCH plus: + nortriptyline	1.8 (1.3-2.6)  2.3 (1.3-4.2) (i)*	\$0.85 (75 mg capsule, generic)  [~1/6 pack]

\* Not FDA approved for smoking cessation; <sup>#</sup> OR = Estimated odds ratio for treatment versus placebo (95% Confidence Interval); <sup>†</sup> Daily drug cost and daily approximate cigarette pack equivalent [~ Pack] based on September 2010 average South Carolina retail costs.  
 (i) Based on 3 or fewer studies.

**SECOND-LINE MEDICATION GUIDELINES FOR SMOKING CESSATION (CONTINUED)**

Administration Instructions	Cautions (Pregnancy)*	Side Effects / Comments
<b>Clonidine</b>  <ul style="list-style-type: none"> <li>Apply patch to clean, hairless intact skin on trunk every 7 days</li> <li>Rotate application sites</li> <li>Leave patch in place even when bathing or swimming</li> </ul>	<ul style="list-style-type: none"> <li>Caution in elderly</li> <li>Caution driving or operating machinery</li> <li>Monitor blood pressure</li> <li>Avoid abrupt discontinuation                             <ul style="list-style-type: none"> <li>taper over 2-4 days to avoid rebound hypertension, agitation, confusion, and/or tremor</li> </ul> </li> <li>FDA: C; Briggs: Limited human data - animal data suggest risk</li> </ul>	<ul style="list-style-type: none"> <li>Dry mouth (40%)</li> <li>Drowsiness (33%)</li> <li>Dizziness (16%)</li> <li>Sedation (10%)</li> <li>Constipation (10%)</li> <li>Localized skin reaction to patch</li> <li>Prominent side effects limit its usefulness</li> </ul>
<b>Nortriptyline</b>  <ul style="list-style-type: none"> <li>May take in divided doses or as a single dose at bedtime to minimize sedation</li> </ul>	<ul style="list-style-type: none"> <li>Caution in patients with cardiovascular disease</li> <li>Caution driving or operating machinery</li> <li>Consider risk of overdose carefully before prescribing</li> <li>FDA: C; Briggs: human data suggest low risk</li> </ul>	<ul style="list-style-type: none"> <li>Dry mouth (64-78%)</li> <li>Lightheadedness (49%)</li> <li>Tremor (23%)</li> <li>Blurred vision (16%)</li> <li>Urinary retention</li> <li>Sedation</li> <li>Low smoking cessation doses may be better tolerated than higher doses used in depression</li> </ul>

\* Breastfeeding recommendations: clonidine – limited human data, probably compatible; nortriptyline – limited human data, potential toxicity. FDA pregnancy ratings: A, controlled studies show no risk; B, no evidence of risk in humans; C, risk cannot be ruled out; D, positive evidence of risk; X, contraindicated in pregnancy.

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For a complete list of references and detailed report see: <http://www.sccp.sc.edu/SCORxE>

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