

STEP One: ASK about Tobacco Use

➔ Suggested Dialogue

- ✓ Do you, or does anyone in your household, ever smoke or use other types of tobacco?
 - We ask all of our patients about tobacco use, because it can negatively impact your [surgery, radiation, chemotherapy] treatment.
 - Smoking slows the healing process after surgery.
 - Patients who smoke during radiation therapy have reduced treatment efficacy and lower survival than non-smokers.
 - Smoking interacts with many of the chemotherapy medications, and can reduce their effects.

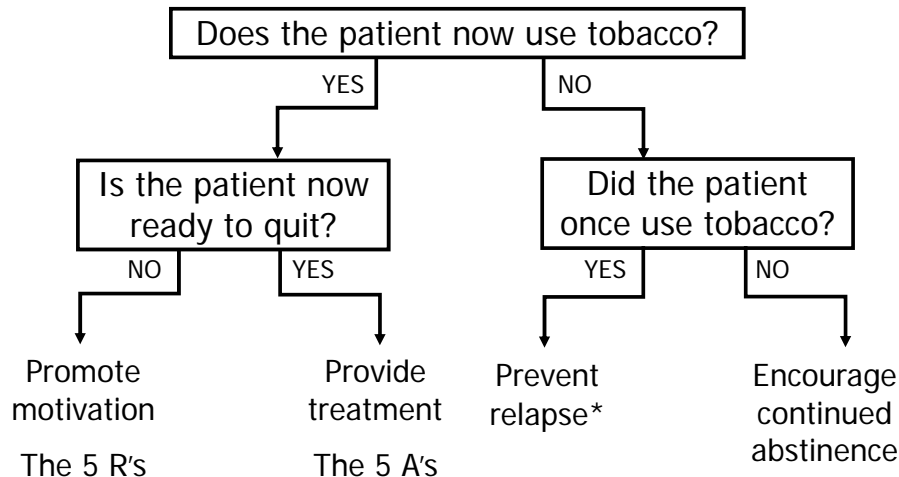
STEP Two: Strongly ADVISE to Quit

Project empathy in your voice; be understanding, not reprimanding.

➔ Suggested Dialogue

- ✓ Quitting is an important component of your treatment for cancer.
 - It's important that you quit as soon as possible, and I can help you.
 - I realize that quitting is difficult. It is the most important thing you can do to protect your health now and in the future. I have training to help my patients quit, and I will work with you to design a specialized treatment plan.

STEP Three: ASSESS Readiness to Quit



* Relapse prevention interventions not necessary if patient has not used tobacco for many years and is not at risk for re-initiation.

STEP Four: ASSIST with Quitting



✓ Assess Tobacco Use History

- Current use: type(s) of tobacco used, brand, amount
- Past use:
 - Duration of tobacco use
 - Changes in levels of use recently
- Past quit attempts:
 - Number of attempts, date of most recent attempt, duration
 - Methods used previously—What did or didn't work? Why or why not?
 - Prior medication administration, dose, adherence, duration of treatment
 - Reasons for relapse

✓ Discuss Key Issues (for the upcoming or current quit attempt)

- Reasons/motivation for wanting to quit (or avoid relapse)
- Confidence in ability to quit (or avoid relapse)
- Triggers for tobacco use
- Routines and situations associated with tobacco use
- Stress-related tobacco use
- Concerns about weight gain
- Concerns about withdrawal symptoms

✓ Facilitate Quitting Process

- Discuss methods for quitting: pros and cons of the different methods
- Set a quit date: more than 2–3 days away but less than 2 weeks away
- Recommend Tobacco Use Log
- Discuss coping strategies (cognitive, behavioral)
- Discuss withdrawal symptoms
- Discuss concept of “slip” versus relapse
- Provide medication counseling: adherence, proper use, with demonstration
- Offer to assist throughout the quit attempt

✓ Evaluate the Quit Attempt (at follow-up)

- Status of attempt
- “Slips” and relapse
- Medication compliance and plans for discontinuation

STEP Five: ARRANGE Follow-up Counseling

- ✓ Monitor patients' progress throughout the quit attempt. Follow-up contact should occur during the first week after quitting. A second follow-up contact is recommended in the first month. Additional contacts should be scheduled as needed. Counseling contacts can occur face-to-face, by telephone, or by e-mail. Keep patient progress notes.
- ✓ Address temptations and triggers; discuss relapse prevention strategies.
- ✓ Congratulate patients for continued success.



WITHDRAWAL SYMPTOMS INFORMATION SHEET

Quitting tobacco use brings about a variety of physical and psychological withdrawal symptoms. For some people, coping with withdrawal symptoms is like riding a roller coaster—there may be sharp turns, slow climbs, and unexpected plunges. **Most symptoms manifest within the first 1 to 2 days, peak within the first week, and subside within 2 to 4 weeks.** Report new symptoms to your health-care provider, especially if severe. Consider the impact of recent medication changes and your caffeine intake.

SYMPTOM	CAUSE	DURATION	RELIEF
Chest tightness	Tightness is likely due to tension created by the body's need for nicotine or may be caused by sore muscles from coughing.	A few days	<ul style="list-style-type: none"> ▪ Use relaxation techniques ▪ Try deep breathing ▪ Use of NRT may help
Constipation, stomach pain, gas	Intestinal movement decreases for a brief period.	1–2 weeks	<ul style="list-style-type: none"> ▪ Drink plenty of fluids ▪ Add fruits, vegetables, and whole-grain cereals to diet
Cough, dry throat, nasal drip	The body is getting rid of mucus, which has blocked airways and restricted breathing.	A few days	<ul style="list-style-type: none"> ▪ Drink plenty of fluids ▪ Avoid additional stress during first few weeks
Craving for a cigarette	Nicotine is a strongly addictive drug, and withdrawal causes cravings.	Frequent for 2–3 days; can happen for months or years	<ul style="list-style-type: none"> ▪ Wait out the urge, which lasts only a few minutes ▪ Distract yourself ▪ Exercise (take walks) ▪ Use of a nicotine medication may help
Depressed mood	It is normal to feel sad for a period of time after you first quit smoking. Many people have a strong urge to smoke when they feel depressed.	1–2 weeks	<ul style="list-style-type: none"> ▪ Increase pleasurable activities ▪ Talk with your clinician about changes in your mood when quitting ▪ Get extra support from friends and family
Difficulty concentrating	The body needs time to adjust to not having constant stimulation from nicotine.	A few weeks	<ul style="list-style-type: none"> ▪ Plan workload accordingly ▪ Avoid additional stress during first few weeks
Dizziness	The body is getting extra oxygen.	1–2 days	<ul style="list-style-type: none"> ▪ Use extra caution ▪ Change positions slowly
Fatigue	Nicotine is a stimulant.	2–4 weeks	<ul style="list-style-type: none"> ▪ Take naps ▪ Do not push yourself ▪ Use of a nicotine medication may help
Hunger	Cravings for a cigarette can be confused with hunger pangs; sensation may result from oral cravings or the desire for something in the mouth.	Up to several weeks	<ul style="list-style-type: none"> ▪ Drink water or low-calorie liquids ▪ Be prepared with low-calorie snacks
Insomnia	Nicotine affects brain wave function and influences sleep patterns; coughing and dreams about smoking are common.	1 week	<ul style="list-style-type: none"> ▪ Limit caffeine intake (and none after 12 noon), because its effects will increase with quitting smoking ▪ Use relaxation techniques
Irritability	The body's craving for nicotine can produce irritability.	2–4 weeks	<ul style="list-style-type: none"> ▪ Take walks ▪ Try hot baths ▪ Use relaxation techniques

Adapted from materials from the National Cancer Institute.



FAGERSTRÖM TEST FOR NICOTINE DEPENDENCE (ADULTS)

- 1. How soon after you wake up do you smoke your first cigarette? Score**
- Within 5 minutes 3
- 6–30 minutes 2
- 31–60 minutes 1
- After 60 minutes..... 0
- 2. Do you find it difficult to refrain from smoking in the places where it is forbidden (e.g., in church, at the library, in cinema)?**
- Yes..... 1
- No 0
- 3. Which cigarette would you hate most to give up?**
- The first one in the morning 1
- Any other 0
- 4. How many cigarettes/day do you smoke?**
- 10 or less 0
- 11–20 1
- 21–30 2
- 31 or more 3
- 5. Do you smoke more frequently during the first hours after waking than during the rest of the day?**
- Yes..... 1
- No 0
- 6. Do you smoke if you are so ill that you are in bed most of the day?**
- Yes..... 1
- No 0

Total Score:

Heatherton TF, Kozlowski LT, Frecker RC, Fagerström K-O. The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. *Br J Addict* 1991;86:1119–1127.



MODIFIED FAGERSTRÖM TOLERANCE QUESTIONNAIRE (ADOLESCENTS)

- 1. How many cigarettes a day do you smoke?** **Score**
- Over 26 cigarettes a day 2
- About 16–25 cigarettes a day 1
- About 1–15 cigarettes a day 0
- Less than 1 a day 0
- 2. Do you inhale?**
- Always 2
- Quite often 1
- Seldom 1
- Never 0
- 3. How soon after you wake up do you smoke your first cigarette?**
- Within the first 30 minutes 1
- More than 30 minutes after waking but before noon 0
- In the afternoon 0
- In the evening 0
- 4. Which cigarette would you hate to give up?**
- First cigarette in the morning 1
- Any other cigarette before noon 0
- Any other cigarette afternoon 0
- Any other cigarette in the evening 0
- 5. Do you find it difficult to refrain from smoking in places where it is forbidden (e.g., church, library, movies)?**
- Yes, very difficult 1
- Yes, somewhat difficult 1
- No, not usually difficult 0
- No, not at all difficult 0
- 6. Do you smoke if you are so ill that you are in bed most of the day?**
- Yes, always 1
- Yes, quite often 1
- No, not usually 0
- No, never 0
- 7. Do you smoke more during the first 2 hours than during the rest of the day?**
- Yes 1
- No 0

Total Score:

Prokhorov AV, Pallonen UE, Fava JL, Ding L, Niaura R. Measuring nicotine dependence among high-risk adolescent smokers. *Addict Behav* 1996;21(1):117–127.

Prokhorov AV, Koehly LM, Pallonen UE, Hudmon KS. Adolescent nicotine dependence measuring by the modified Fagerström Tolerance Questionnaire at two time points. *J Child Adolesc Subst Abuse* 1998;7(4):35–47.



SMOKELESS TOBACCO DEPENDENCE SCALE

- 1. How many tins or pouches of smokeless tobacco do you typically use each week?** Score
- 1 or less each week 0
 - 2–4 each week 1
 - 5 or more each week 2
- 2. How often do you use smokeless tobacco?**
- 1 day each week or less 0
 - 2–5 days each week 1
 - 6–7 days each week 2
- 3. Do you intentionally swallow tobacco juices?**
- No 0
 - Yes 1
- 4. Do you use smokeless tobacco when you are sick or have mouth sores?**
- No 0
 - Yes 1
- 5. How soon after waking from your normal sleeping period do you use chewing tobacco or snuff?**
- After 30 minutes of waking 0
 - Within 30 minutes of waking 1
- 6. Do you smoke cigarettes?**
- No 0
 - Yes 1
- 7. Is it difficult for you not to use smokeless tobacco where its use is restricted or not allowed?**
- No 0
 - Yes 1

Total Score:



DRUG INTERACTIONS WITH TOBACCO SMOKE

Many interactions between tobacco smoke and medications have been identified. Note that in most cases it is the tobacco smoke—not the nicotine—that causes these drug interactions. Tobacco smoke interacts with medications through pharmacokinetic (PK) and pharmacodynamic (PD) mechanisms. PK interactions affect the absorption, distribution, metabolism, or elimination of other drugs, potentially causing an altered pharmacologic response. The majority of PK interactions with smoking are the result of induction of hepatic cytochrome P450 enzymes (primarily CYP1A2). Smokers may require higher doses of medications that are CYP1A2 substrates. Upon cessation, dose reductions might be needed. PD interactions alter the expected response or actions of other drugs. The amount of tobacco smoking needed to have an effect has not been established, and the assumption is that any smoker is susceptible to the same degree of interaction.

The most clinically significant interactions are depicted in the shaded rows.

DRUG/CLASS	MECHANISM OF INTERACTION AND EFFECTS
Pharmacokinetic Interactions	
Alprazolam (Xanax®)	<ul style="list-style-type: none"> ▪ Conflicting data on significance, but possible ↓ plasma concentrations (up to 50%); ↓ half-life (35%).
Bendamustine (Treanda®)	<ul style="list-style-type: none"> ▪ Metabolized by CYP1A2. Manufacturer recommends using with caution in smokers due to likely ↓ bendamustine concentrations, with ↑ concentrations of its two active metabolites.
Caffeine	<ul style="list-style-type: none"> ▪ ↑ Metabolism (induction of CYP1A2); ↑ clearance (56%). Caffeine levels likely ↑ after cessation.
Chlorpromazine (Thorazine®)	<ul style="list-style-type: none"> ▪ ↓ Area under the curve (AUC) (by 36%) and serum concentrations (by 24%). ▪ ↓ Sedation and hypotension possible in smokers; smokers may require ↑ dosages.
Clopidogrel (Plavix®)	<ul style="list-style-type: none"> ▪ ↑ Metabolism (induction of CYP1A2) of clopidogrel to its active metabolite. ▪ Clopidogrel's effects are enhanced in smokers (≥10 cigarettes/day): significant ↑ platelet inhibition, ↓ platelet aggregation; while improved clinical outcomes have been shown, may also ↑ risk of bleeding.
Clozapine (Clozaril®)	<ul style="list-style-type: none"> ▪ ↑ Metabolism (induction of CYP1A2); ↓ plasma concentrations (by 18%). ▪ ↑ Levels upon cessation may occur; closely monitor drug levels and reduce dose as required to avoid toxicity.
Erlotinib (Tarceva®)	<ul style="list-style-type: none"> ▪ ↑ Clearance (24%); ↓ trough serum concentrations (2-fold).
Flecainide (Tambocor®)	<ul style="list-style-type: none"> ▪ ↑ Clearance (61%); ↓ trough serum concentrations (by 25%). Smokers may need ↑ dosages.
Fluvoxamine (Luvox®)	<ul style="list-style-type: none"> ▪ ↑ Metabolism (induction of CYP1A2); ↑ clearance (24%); ↓ AUC (31%); ↓ Cmax (by 32%) and C_{ss} (by 39%). ▪ Dosage modifications not routinely recommended but smokers may need ↑ dosages.
Haloperidol (Haldol®)	<ul style="list-style-type: none"> ▪ ↑ Clearance (44%); ↓ serum concentrations (70%); data are inconsistent therefore clinical significance is unclear.
Heparin	<ul style="list-style-type: none"> ▪ Mechanism unknown but ↑ clearance and ↓ half-life are observed. Smoking has prothrombotic effects. ▪ Smokers may need ↑ dosages due to PK and PD interactions.
Insulin, subcutaneous	<ul style="list-style-type: none"> ▪ Possible ↓ insulin absorption secondary to peripheral vasoconstriction. ▪ Smoking may cause release of endogenous substances that cause insulin resistance. ▪ PK & PD interactions likely not clinically significant, but smokers may need ↑ dosages.
Irinotecan (Camptosar®)	<ul style="list-style-type: none"> ▪ ↑ Clearance (18%); ↓ serum concentrations of active metabolite, SN-38 (~40%; via induction of glucuronidation); ↓ systemic exposure resulting in lower hematologic toxicity and may reduce efficacy. ▪ Smokers may need ↑ dosages.
Methadone	<ul style="list-style-type: none"> ▪ Possible ↑ metabolism (induction of CYP1A2, a minor pathway for methadone). ▪ Carefully monitor response upon cessation.
Mexiletine (Mexitol®)	<ul style="list-style-type: none"> ▪ ↑ Clearance (25%; via oxidation and glucuronidation); ↓ half-life (36%).
Olanzapine (Zyprexa®)	<ul style="list-style-type: none"> ▪ ↑ Metabolism (induction of CYP1A2); ↑ clearance (98%); ↓ serum concentrations (by 12%). ▪ Dosage modifications not routinely recommended but smokers may need ↑ dosages.

Pharmacokinetic Interactions (continued)	
DRUG/CLASS	MECHANISM OF INTERACTION AND EFFECTS
Propranolol (Inderal®)	<ul style="list-style-type: none"> ▪ ↑ Clearance (77%; via side-chain oxidation and glucuronidation).
Riociguat (Adempas®)	<ul style="list-style-type: none"> ▪ ↓ Plasma concentrations (by 50–60%). ▪ Smokers may require dosages higher than 2.5 mg three times a day; consider dose reduction upon cessation.
Ropinirole (Requip®)	<ul style="list-style-type: none"> ▪ ↓ C_{max} (by 30%) and AUC (by 38%) in study with patients with restless legs syndrome. ▪ Smokers may need ↑ dosages.
Tacrine (Cognex®)	<ul style="list-style-type: none"> ▪ ↑ Metabolism (induction of CYP1A2); ↓ half-life (50%); serum concentrations 3-fold lower. ▪ Smokers may need ↑ dosages.
Tasimelteon (Hetlioz®)	<ul style="list-style-type: none"> ▪ ↑ Metabolism (induction of CYP1A2); drug exposure ↓ by 40%. ▪ Smokers may need ↑ dosages.
Theophylline (Theo-Dur®, etc.)	<ul style="list-style-type: none"> ▪ ↑ Metabolism (induction of CYP1A2); ↑ clearance (58–100%); ↓ half-life (63%). ▪ Levels should be monitored if smoking is initiated, discontinued, or changed. Maintenance doses are considerably higher in smokers; ↑ clearance also with second-hand smoke exposure.
Tizanidine (Zanaflex®)	<ul style="list-style-type: none"> ▪ ↓ AUC (30–40%) and ↓ half-life (10%) observed in male smokers.
Tricyclic antidepressants (e.g., imipramine, nortriptyline)	<ul style="list-style-type: none"> ▪ Possible interaction with tricyclic antidepressants in the direction of ↓ blood levels, but the clinical significance is not established.
Warfarin	<ul style="list-style-type: none"> ▪ ↑ Metabolism (induction of CYP1A2) of R-enantiomer; however, S-enantiomer is more potent and effect on INR is inconclusive. Consider monitoring INR upon smoking cessation.
Pharmacodynamic Interactions	
Benzodiazepines (diazepam, chlordiazepoxide)	<ul style="list-style-type: none"> ▪ ↓ Sedation and drowsiness, possibly caused by nicotine stimulation of central nervous system.
Beta-blockers	<ul style="list-style-type: none"> ▪ Less effective BP and heart rate control effects; possibly caused by nicotine-mediated sympathetic activation. ▪ Smokers may need ↑ dosages.
Corticosteroids, inhaled	<ul style="list-style-type: none"> ▪ Smokers with asthma may have less of a response to inhaled corticosteroids.
Hormonal contraceptives (combined)	<ul style="list-style-type: none"> ▪ ↑ Risk of cardiovascular adverse effects (e.g., stroke, myocardial infarction, thromboembolism) in women who smoke and use combined hormonal contraceptives. Ortho Evra patch users shown to have 2-fold ↑ risk of venous thromboembolism compared with oral contraceptive users, likely due to ↑ estrogen exposure (60% higher levels). ▪ ↑ Risk with age and with heavy smoking (≥15 cigarettes per day) and is quite marked in women ≥35 years old.
Serotonin 5-HT ₁ receptor agonists (triptans)	<ul style="list-style-type: none"> ▪ This class of drugs may cause coronary vasospasm; caution for use in smokers due to possible unrecognized CAD.
Adapted and updated, from Zevin S, Benowitz NL. Drug interactions with tobacco smoking. An update. <i>Clin Pharmacokinet</i> 1999;36:425–38 and Kroon LA. Drug interactions with smoking. <i>Am J Health-Syst Pharm</i> 2007;64:1917-21.	



TOBACCO USE LOG

The Tobacco Use Log can help patients to identify activities or situations that trigger the desire to smoke or use other forms of tobacco. It is important for patients to understand these environmental cues so that they can develop coping strategies to overcome the temptation to use tobacco. Clinicians can use this information to suggest alternative behaviors to increase the likelihood of a successful quit attempt. The log is most appropriate for patients who are preparing for a quit attempt, but it can be used with any patient who wants to learn more about his or her smoking behavior.

Instructions for use:

The Tobacco Use Log is a piece of paper that is kept with the patient's tobacco. It can be folded and wrapped around the cigarette pack or can of snuff with a rubber band. Alternatively, patients may keep the log in their wallet or day planner. It is important that the log be readily available at the times when the patient uses the tobacco. Through careful documentation of tobacco use over a period of several days, patient-specific tobacco usage patterns become evident.

1. Instruct the patient to continue his or her regular tobacco use for a period of *at least three days* (including one non-work day). It is preferable to complete the *Tobacco Use Log* for *seven consecutive days*, because usage patterns might fluctuate as a function of the day of the week (e.g. weekends vs. work days). The patient should not attempt to reduce his or her tobacco use during this time. The intent is to document current tobacco use habits and patterns, so that the patient can understand the triggers and situations associated with his or her tobacco use.
2. The following information should be noted in the Tobacco Use Log **each time** tobacco is used:
 - **Time** of day (indicate AM or PM)
 - Description of the **activity/situation at the time of** tobacco use (e.g., were others present?)
 - **Need rating** of the patient's perceived importance of using tobacco, at that time, using the following scale:

Not very important (would <i>not</i> have missed it) 1	Moderately important 2	Very important (would have missed it a great deal) 3
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3. The patient should use a separate log sheet each day. *Note: Heavy tobacco users will require more than one log sheet per day.*
4. Just prior to the quit date, review the Tobacco Use Log with the patient to identify specific situations that trigger tobacco use. Additionally, discuss specific cognitive and behavioral strategies to prevent relapse.

Adapted from The Wrap Sheet and The Daily Cigarette Count (Wrap Sheet). In: The Washington State Pharmacists Association, *Smoking Cessation Training: Pharmacists Becoming Smoking Cessation Counselors*, 1997, pp. 3, 25.



Tobacco Use Log for (date): ___/___/___

	Time	Describe the situation/activity at the time of this tobacco use.	Need Rating Circle one number*		
1.			1	2	3
2.			1	2	3
3.			1	2	3
4.			1	2	3
5.			1	2	3
6.			1	2	3
7.			1	2	3
8.			1	2	3
9.			1	2	3
10.			1	2	3
11.			1	2	3
12.			1	2	3
13.			1	2	3
14.			1	2	3
15.			1	2	3
16.			1	2	3
17.			1	2	3
18.			1	2	3
19.			1	2	3
20.			1	2	3

*Need RATING: Rate the importance of your *need* to use tobacco *for each instance* of use—based on the following scale:

<p align="center">Not very important (would <i>not</i> have missed it)</p> <p align="center">1</p>	<p align="center">Moderately important</p> <p align="center">2</p>	<p align="center">Very important (would have missed it a great deal)</p> <p align="center">3</p>
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COPING WITH QUITTING: COGNITIVE AND BEHAVIORAL STRATEGIES

<p>COGNITIVE STRATEGIES focus on retraining the way a patient thinks. Often, patients will deliberate on the fact that they are thinking about a cigarette, and this leads to relapse. Patients must recognize that thinking about a cigarette doesn't mean they need to have one.</p>	
REVIEW COMMITMENT TO QUIT	Each morning, say, "I am proud that I made it through another day without tobacco!" Remind oneself that cravings and temptations are temporary and will pass. Announce, either silently or aloud, "I am a nonsmoker, and the temptation will pass."
DISTRACTIVE THINKING	Use deliberate, immediate refocusing of thinking toward other thoughts when cued by thoughts about tobacco use.
POSITIVE SELF-TALKS, PEP TALKS	Say, "I can do this," and remind oneself of previous difficult situations in which tobacco use was avoided.
RELAXATION THROUGH IMAGERY	Center mind toward positive, relaxing thoughts.
MENTAL REHEARSAL, VISUALIZATION	Prepare for situations that might arise by envisioning how best to handle them. For example, envision what would happen if offered a cigarette by a friend—mentally craft and rehearse a response, and perhaps even practice it by saying it aloud.
<p>BEHAVIORAL STRATEGIES involve specific actions to reduce risk for relapse. These strategies should be considered prior to quitting, after determining patient-specific triggers and routines or situations associated with tobacco use. Below are strategies for several of the more common cues or causes for relapse.</p>	
STRESS	Anticipate upcoming challenges at work, at school, or in personal life. Develop a substitute plan for tobacco use during times of stress (e.g., use deep breathing, take a break or leave the situation, call a supportive friend or family member, use nicotine replacement therapy).
ALCOHOL	<i>Drinking alcohol can lead to relapse.</i> Consider limiting or abstaining from alcohol during the early stages of quitting.
OTHER TOBACCO USERS	<i>Quitting is more difficult if the patient is around other tobacco users. This is especially difficult if another tobacco user is in the household.</i> During the early stages of quitting, limit prolonged contact with individuals who are using tobacco. Ask co-workers, friends, and housemates not to smoke or use tobacco in your presence.
ORAL GRATIFICATION NEEDS	Have nontobacco oral substitutes (e.g., gum, sugarless candy, straws, toothpicks, lip balm, toothbrush, nicotine replacement therapy, bottled water) readily available.
AUTOMATIC SMOKING ROUTINES	Anticipate routines associated with tobacco use and develop an alternative plan. Examples: MORNING COFFEE: change morning routine, take shower before drinking coffee, drink tea instead of coffee, take a brisk walk shortly after awakening. WHILE DRIVING: remove all tobacco from car, have car interior detailed, listen to an audio book or talk radio, use oral substitutes. WHILE ON THE PHONE: stand while talking, limit call duration, change phone location, keep hands occupied by doodling or sketching. AFTER MEALS: get up and immediately do dishes or take a brisk walk after eating, brush teeth, call supportive friend.
POSTCESSATION WEIGHT GAIN	Do not attempt to modify multiple behaviors at one time. If weight gain is a barrier to quitting, engage in regular physical activity and adhere to a healthful diet (as opposed to strict dieting). Carefully plan and prepare meals, increase fruit and water intake to create a feeling of fullness, and chew sugarless gum or eat sugarless candies. Consider use of pharmacotherapy shown to delay weight gain.
CRAVINGS FOR TOBACCO	Cravings for tobacco are temporary and usually pass within 5–10 minutes. Handle cravings through distractive thinking, take a break, do something else, take deep breaths.



PLANNING FOR CHANGE: THINKING ABOUT QUITTING

(PAGE 1 OF 2)

Understanding the reasons why you smoke, in addition to considering your smoking patterns and routines, are important to the design of a successful quitting plan.

Consider the following before you quit:

WHY DO I STILL SMOKE?

My top 3 reasons for continuing to smoke are:

(1)

(2)

(3)

WHY IS QUITTING IMPORTANT?

My top 3 reasons for wanting to quit smoking are:

(1)

(2)

(3)

WHAT WERE YOUR MAIN DIFFICULTIES WITH QUITTING IN THE PAST?

My top 3 difficulties with quitting in the past were:

(1)

(2)

(3)

WHAT ARE YOUR BARRIERS TO QUITTING NOW?

My top 3 barriers to quitting now are:

(1)

(2)

(3)

WHAT IS THE WORST THING THAT COULD HAPPEN TO YOU IF YOU QUIT SMOKING FOR GOOD?

ARE YOU READY TO QUIT NOW? (WITHIN THE NEXT MONTH)

If YES, what will be your official quit date? ____ / ____ / ____ (ENTER DATE)

If NO, how might it benefit you to quit sooner (instead of later)?



PLANNING FOR CHANGE: GETTING READY TO QUIT

(PAGE 2 OF 2)

Smokers don't plan to fail. Most *fail* to plan. To plan for quitting, you should:

(1) identify triggers for smoking and how to cope with them, (2) identify persons to help you throughout your quit attempt, and (3) choose the best methods—for you—for quitting.

WHAT ARE YOUR THREE MAIN TRIGGERS OR SITUATIONS FOR SMOKING?

To deal with situations when you feel the urge to smoke, you should (1) identify the trigger situation, (2) change what you do or how you do it, and (3) change the thoughts that trigger the desire to smoke.

Trigger #1:

- I will change *what I do* in this situation by:

- I will change *how I think* in this situation by:

Trigger #2:

- I will change *what I do* in this situation by:

- I will change *how I think* in this situation by:

Trigger #3:

- I will change *what I do* in this situation by:

- I will change *how I think* in this situation by:

WHO WILL HELP YOU WITH QUITTING?

My top 3 persons who will have a positive influence on my ability to quit for good:

(1)

(2)

(3)

WHAT FORM OF COUNSELING ASSISTANCE WILL YOU RECEIVE WHILE QUITTING?

WHAT MEDICATION(S) WILL YOU USE FOR QUITTING, AND HOW WILL YOU USE THEM?



RELAPSED SMOKERS WHO ARE READY TO TRY AGAIN: WHAT TO DO?

A 3-STEP PROTOCOL FOR CLINICIANS (PAGE 1 OF 2)

Many smokers who relapse do so because they fail to plan. Often, patients think that they can simply “make” themselves quit and do not avail themselves of the many proven behavior change programs provided by various sources. Furthermore, most smokers do not use a cessation medication or, if they do, they use it incorrectly. Generally speaking, patients significantly under-dose or stop pharmacologic therapy too soon.

You can help relapsed smokers regain abstinence by encouraging them to learn from their prior experiences rather than use those experiences as proof that they cannot quit. To underscore this perspective, inform patients that the best way to quit smoking is to combine a behavior change program with a cessation medication. The following **3-step protocol** will help you provide this information in an efficient, effective manner for patients who are ready to try again:

STEP 1: ASK

- “TELL ME ABOUT YOUR LAST QUIT ATTEMPT(S).”
- “DID YOU USE A SMOKING CESSATION MEDICATION?”
 - If yes: “EXPLAIN HOW YOU USED YOUR MEDICATION.”
 - Reinforce proper usage/ rectify incorrect usage or dosage
 - If no: “WHAT WAS YOUR REASONING FOR NOT USING A MEDICATION?”
- “DID YOU RECEIVE ANY PROFESSIONAL ADVICE OR ENROLL IN A BEHAVIOR CHANGE PROGRAM?”
 - If yes: “TELL ME WHAT YOU LIKED, OR DIDN’T LIKE ABOUT THE ASSISTANCE YOU RECEIVED.”
 - If no: “WHAT WAS YOUR REASONING FOR NOT SEEKING ADVICE OR ENROLLING IN A PROGRAM?”

STEP 2: ADVISE

- “ACCORDING TO THE MOST CURRENT RESEARCH, THE BEST WAY TO QUIT IS TO COMBINE A SMOKING CESSATION MEDICATION WITH A BEHAVIORAL PROGRAM.”

NOTE: Examples of behavior change programs are listed on the reverse side, under the “Refer” section of the protocol.
- “LET’S DISCUSS WHICH MEDICATION(S) WOULD BE BEST FOR YOU.”
- Review current level of tobacco use, past usage of medications, personal preference, precautions/contraindications, etc. to determine best product for current quit attempt.

NOTE: Refer to the Rx for Change *Pharmacologic Product Guide* for dosing instructions, etc. for FDA-approved smoking cessation medications.
- Consider the following options:
 - If prior medication was used correctly, was well tolerated, and appeared to have been effective, consider repeating the same medication regimen in conjunction with an enhanced behavioral program.
 - If prior medication was used incorrectly, carefully review usage instructions.
 - If prior medication was used correctly but did not control urges/withdrawal, or if patient prefers something new, review other medication options, including both single and combination therapy:

CONTINUED ON BACK

RELAPSED SMOKERS WHO ARE READY TO TRY AGAIN: WHAT TO DO?

A 3-STEP PROTOCOL FOR CLINICIANS (PAGE 2 OF 2)

Combination therapy is off-label for some combinations of medications, but it is supported by multiple clinical trials and the *Clinical Practice Guideline for Treating Tobacco Use and Dependence* (p. 118):

- *Safe*: Most smokers are highly tolerant to nicotine from years of smoking. Side effects are rare and easily mitigated by reducing or stopping use.
- *Effective*: Especially in those who failed with one medication. Also useful in patients who are heavily dependent (2 or more packs/day).

Suggested combinations:

- Nicotine patch + *ad libitum* gum, lozenge, inhaler, or nasal spray as needed for breakthrough urges.
- Sustained-release bupropion (Zyban) + nicotine patch

Currently, varenicline (Chantix) is not recommended for combination therapy.

STEP 3: REFER

The amount of counseling that patients receive is linearly related to their success in quitting. More counseling contacts yield higher quit rates. If you do not have the time or expertise to assist patients with quitting and to provide follow-up counseling, refer patients to other resources:

- To a behavior change program:
 - “HERE ARE SOME SUGGESTIONS. WHICH DO YOU THINK WOULD WORK BEST FOR YOU?”
 - 1 800 QUIT NOW, the national toll-free telephone quit line
 - All products are accompanied by a free behavior change program: Refer to usage instructions for enrollment procedures
 - Hospital-based or other local resources (e.g., a group program)
 - www.quitnet.com, an on-line tobacco cessation support program
 - smokefree.gov, an on-line guide for quitting
 - American Lung Association, American Cancer Society, or American Heart Association web-sites or cessation programs (e.g., American Lung Association’s *Freedom From Smoking* group cessation program)
 - Local pharmacist, physician, or other health-care provider specializing in cessation
- To a community pharmacist:
 - “WHEN YOU PURCHASE YOUR SMOKING CESSATION MEDICATION, PLEASE TAKE A FEW MINUTES TO DISCUSS PROPER USAGE WITH THE PHARMACIST, EVEN IF IT IS A PRODUCT YOU HAVE USED IN THE PAST. PROPER USAGE WILL GIVE YOU THE BEST CHANCE OF SUCCESS.”
- To other staff:
 - If you have dedicated cessation staff within your clinic or health-care organization, refer patient to these resources for follow-up counseling.

For more information, see Fiore MC, Jaén CR, Baker TB, et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. Available at: www.surgeongeneral.gov/tobacco.

For complete prescribing information, please refer to the manufacturers’ package inserts.



PHARMACOLOGIC PRODUCT GUIDE: FDA-APPROVED MEDICATIONS FOR SMOKING CESSATION

		NICOTINE REPLACEMENT THERAPY (NRT) FORMULATIONS				BUPROPION SR	VARENICLINE
		GUM	LOZENGE	TRANSDERMAL PATCH	NASAL SPRAY	ORAL INHALER	
PRODUCT	<p>Nicorette¹, Generic OTC 2 mg, 4 mg original, cinnamon, fruit, mint</p>	<p>Nicorette Lozenge,¹ Nicorette Mini Lozenge,¹ Generic OTC 2 mg, 4 mg; cherry, mint</p>	<p>NicoDerm CQ¹, Generic OTC (NicoDerm CQ, generic) Rx (generic) 7 mg, 14 mg, 21 mg (24-hour release)</p>	<p>Nicotrol NS² Rx Metered spray 10 mg/mL aqueous nicotine solution</p>	<p>Nicotrol Inhaler² Rx 10 mg cartridge delivers 4 mg inhaled nicotine vapor</p>	<p>Zyban¹, Generic Rx 150 mg sustained-release tablet</p>	<p>Chantix² Rx 0.5 mg, 1 mg tablet</p>
PRECAUTIONS	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Temporomandibular joint disease Pregnancy³ and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Pregnancy³ and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Pregnancy³ (Rx formulations, category D) and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Underlying chronic nasal disorders (rhinitis, nasal polyps, sinusitis) Severe reactive airway disease Pregnancy³ (category D) and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Recent (≤ 2 weeks) myocardial infarction Serious underlying arrhythmias Serious or worsening angina pectoris Bronchospastic disease Pregnancy³ (category D) and breastfeeding Adolescents (<18 years) 	<ul style="list-style-type: none"> Concomitant therapy with medications/conditions known to lower the seizure threshold Hepatic impairment Pregnancy³ (category C) and breastfeeding Adolescents (<18 years) <p>Warning:</p> <ul style="list-style-type: none"> BLACK-BOXED WARNING for neuropsychiatric symptoms⁴ <p>Contraindications:</p> <ul style="list-style-type: none"> Seizure disorder Concomitant bupropion (e.g., Wellbutrin) therapy Current or prior diagnosis of bulimia or anorexia nervosa Simultaneous abrupt discontinuation of alcohol or sedatives/benzodiazepines MAO inhibitors in preceding 14 days; concurrent use of reversible MAO inhibitors (e.g., linezolid, methylene blue) 	<ul style="list-style-type: none"> Severe renal impairment (dosage adjustment is necessary) Pregnancy³ (category C) and breastfeeding Adolescents (<18 years) <p>Warning:</p> <ul style="list-style-type: none"> BLACK-BOXED WARNING for neuropsychiatric symptoms⁴
DOSING	<p><i>1st cigarette ≤ 30 minutes after waking:</i> 4 mg</p> <p><i>1st cigarette >30 minutes after waking:</i> 2 mg</p> <p>Weeks 1–6: 1 piece q 1–2 hours</p> <p>Weeks 7–9: 1 piece q 2–4 hours</p> <p>Weeks 10–12: 1 piece q 4–8 hours</p> <ul style="list-style-type: none"> Maximum, 24 pieces/day Chew each piece slowly Park between cheek and gum when peppery or tingling sensation appears (~15–30 chews) Resume chewing when tingle fades Repeat chew/park steps until most of the nicotine is gone (tingle does not return; generally 30 min) Park in different areas of mouth No food or beverages 15 minutes before or during use Duration: up to 12 weeks 	<p><i>1st cigarette ≤ 30 minutes after waking:</i> 4 mg</p> <p><i>1st cigarette >30 minutes after waking:</i> 2 mg</p> <p>Weeks 1–6: 1 lozenge q 1–2 hours</p> <p>Weeks 7–9: 1 lozenge q 2–4 hours</p> <p>Weeks 10–12: 1 lozenge q 4–8 hours</p> <ul style="list-style-type: none"> Maximum, 20 lozenges/day Allow to dissolve slowly (20–30 minutes for standard; 10 minutes for mini) Nicotine release may cause a warm, tingling sensation Do not chew or swallow Occasionally rotate to different areas of the mouth No food or beverages 15 minutes before or during use Duration: up to 12 weeks 	<p><i>>10 cigarettes/day:</i> 21 mg/day x 4–6 weeks 14 mg/day x 2 weeks 7 mg/day x 2 weeks</p> <p><i>≤ 10 cigarettes/day:</i> 14 mg/day x 6 weeks 7 mg/day x 2 weeks</p> <ul style="list-style-type: none"> May wear patch for 16 hours if patient experiences sleep disturbances (remove at bedtime) Duration: 8–10 weeks 	<p>1–2 doses/hour (8–40 doses/day) One dose = 2 sprays (one in each nostril); each spray delivers 0.5 mg of nicotine to the nasal mucosa</p> <ul style="list-style-type: none"> Maximum <ul style="list-style-type: none"> – 5 doses/hour or – 40 doses/day For best results, initially use at least 8 doses/day Do not sniff, swallow, or inhale through the nose as the spray is being administered Duration: 3–6 months 	<p>6–16 cartridges/day Individualize dosing; initially use 1 cartridge q 1–2 hours</p> <ul style="list-style-type: none"> Best effects with continuous puffing for 20 minutes Initially use at least 6 cartridges/day Nicotine in cartridge is depleted after 20 minutes of active puffing Inhale into back of throat or puff in short breaths Do NOT inhale into the lungs (like a cigarette) but “puff” as if lighting a pipe Open cartridge retains potency for 24 hours No food or beverages 15 minutes before or during use Duration: 3–6 months 	<p>150 mg po q AM x 3 days, then 150 mg po bid</p> <ul style="list-style-type: none"> Do not exceed 300 mg/day Begin therapy 1–2 weeks prior to quit date Allow at least 8 hours between doses Avoid bedtime dosing to minimize insomnia Dose tapering is not necessary Duration: 7–12 weeks, with maintenance up to 6 months in selected patients 	<p>Days 1–3: 0.5 mg po q AM</p> <p>Days 4–7: 0.5 mg po bid</p> <p>Weeks 2–12: 1 mg po bid</p> <ul style="list-style-type: none"> Begin therapy 1 week prior to quit date Take dose after eating and with a full glass of water Dose tapering is not necessary Dosing adjustment is necessary for patients with severe renal impairment Duration: 12 weeks; an additional 12-week course may be used in selected patients

		NICOTINE REPLACEMENT THERAPY (NRT) FORMULATIONS					BUPROPION SR	VARENICLINE	
		GUM	LOZENGE	TRANSDERMAL PATCH	NASAL SPRAY	ORAL INHALER			
ADVERSE EFFECTS	<ul style="list-style-type: none"> ▪ Mouth/jaw soreness ▪ Hiccups ▪ Dyspepsia ▪ Hypersalivation ▪ Effects associated with incorrect chewing technique: <ul style="list-style-type: none"> – Lightheadedness – Nausea/vomiting – Throat and mouth irritation 	<ul style="list-style-type: none"> ▪ Nausea ▪ Hiccups ▪ Cough ▪ Heartburn ▪ Headache ▪ Flatulence ▪ Insomnia 	<ul style="list-style-type: none"> ▪ Local skin reactions (erythema, pruritus, burning) ▪ Headache ▪ Sleep disturbances (insomnia, abnormal/vivid dreams); associated with nocturnal nicotine absorption 	<ul style="list-style-type: none"> ▪ Nasal and/or throat irritation (hot, peppery, or burning sensation) ▪ Rhinitis ▪ Tearing ▪ Sneezing ▪ Cough ▪ Headache 	<ul style="list-style-type: none"> ▪ Mouth and/or throat irritation ▪ Cough ▪ Headache ▪ Rhinitis ▪ Dyspepsia ▪ Hiccups 	<ul style="list-style-type: none"> ▪ Insomnia ▪ Dry mouth ▪ Nervousness/difficulty concentrating ▪ Nausea ▪ Dizziness ▪ Constipation ▪ Rash ▪ Seizures (risk is 0.1%) ▪ Neuropsychiatric symptoms (rare; see PRECAUTIONS) 	<ul style="list-style-type: none"> ▪ Nausea ▪ Sleep disturbances (insomnia, abnormal/vivid dreams) ▪ Constipation ▪ Flatulence ▪ Vomiting ▪ Neuropsychiatric symptoms (rare; see PRECAUTIONS) 		
	ADVANTAGES	<ul style="list-style-type: none"> ▪ Might serve as an oral substitute for tobacco ▪ Might delay weight gain ▪ Can be titrated to manage withdrawal symptoms ▪ Can be used in combination with other agents to manage situational urges 	<ul style="list-style-type: none"> ▪ Might serve as an oral substitute for tobacco ▪ Might delay weight gain ▪ Can be titrated to manage withdrawal symptoms ▪ Can be used in combination with other agents to manage situational urges 	<ul style="list-style-type: none"> ▪ Once daily dosing associated with fewer adherence problems ▪ Of all NRT products, its use is least obvious to others ▪ Can be used in combination with other agents; delivers consistent nicotine levels over 24 hours 	<ul style="list-style-type: none"> ▪ Can be titrated to rapidly manage withdrawal symptoms ▪ Can be used in combination with other agents to manage situational urges 	<ul style="list-style-type: none"> ▪ Might serve as an oral substitute for tobacco ▪ Can be titrated to manage withdrawal symptoms ▪ Mimics hand-to-mouth ritual of smoking ▪ Can be used in combination with other agents to manage situational urges 	<ul style="list-style-type: none"> ▪ Twice daily oral dosing is simple and associated with fewer adherence problems ▪ Might delay weight gain ▪ Might be beneficial in patients with depression ▪ Can be used in combination with NRT agents 	<ul style="list-style-type: none"> ▪ Twice daily oral dosing is simple and associated with fewer adherence problems ▪ Offers a different mechanism of action for patients who have failed other agents 	
		DISADVANTAGES	<ul style="list-style-type: none"> ▪ Need for frequent dosing can compromise adherence ▪ Might be problematic for patients with significant dental work ▪ Proper chewing technique is necessary for effectiveness and to minimize adverse effects ▪ Gum chewing might not be acceptable or desirable for some patients 	<ul style="list-style-type: none"> ▪ Need for frequent dosing can compromise adherence ▪ Gastrointestinal side effects (nausea, hiccups, heartburn) might be bothersome 	<ul style="list-style-type: none"> ▪ When used as monotherapy, cannot be titrated to acutely manage withdrawal symptoms ▪ Not recommended for use by patients with dermatologic conditions (e.g., psoriasis, eczema, atopic dermatitis) 	<ul style="list-style-type: none"> ▪ Need for frequent dosing can compromise adherence ▪ Nasal administration might not be acceptable or desirable for some patients; nasal irritation often problematic ▪ Not recommended for use by patients with chronic nasal disorders or severe reactive airway disease 	<ul style="list-style-type: none"> ▪ Need for frequent dosing can compromise adherence ▪ Cartridges might be less effective in cold environments ($\leq 60^{\circ}\text{F}$) 	<ul style="list-style-type: none"> ▪ Seizure risk is increased ▪ Several contraindications and precautions preclude use in some patients (see PRECAUTIONS) ▪ Patients should be monitored for potential neuropsychiatric symptoms⁴ (see PRECAUTIONS) 	<ul style="list-style-type: none"> ▪ Should be taken with food or a full glass of water to reduce the incidence of nausea ▪ Patients should be monitored for potential neuropsychiatric symptoms⁴ (see PRECAUTIONS)
			COST/DAY ⁵	2 mg or 4 mg: \$1.90–\$3.70 (9 pieces)	2 mg or 4 mg: \$2.66–\$4.10 (9 pieces)	\$1.52–\$3.48 (1 patch)	\$5.00 (8 doses)	\$8.51 (6 cartridges)	\$2.72–\$6.22 (2 tablets)

¹ Marketed by GlaxoSmithKline.

² Marketed by Pfizer.

³ The U.S. Clinical Practice Guideline states that pregnant smokers should be encouraged to quit without medication based on insufficient evidence of effectiveness and theoretical concerns with safety. Pregnant smokers should be offered behavioral counseling interventions that exceed minimal advice to quit.

⁴ In July 2009, the FDA mandated that the prescribing information for all bupropion- and varenicline-containing products include a black-boxed warning highlighting the risk of serious neuropsychiatric symptoms, including changes in behavior, hostility, agitation, depressed mood, suicidal thoughts and behavior, and attempted suicide. Clinicians should advise patients to stop taking varenicline or bupropion SR and contact a healthcare provider immediately if they experience agitation, depressed mood, and any changes in behavior that are not typical of nicotine withdrawal, or if they experience suicidal thoughts or behavior. If treatment is stopped due to neuropsychiatric symptoms, patients should be monitored until the symptoms resolve.

⁵ Wholesale acquisition cost from Red Book Online. Thomson Reuters, December 2014.

Abbreviations: MAO, monoamine oxidase; NRT, nicotine replacement therapy; OTC, over-the-counter (non-prescription product); Rx, prescription product.

For complete prescribing information and a comprehensive listing of warnings and precautions, please refer to the manufacturers' package inserts.

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ESTIMATED EFFICACY OF METHODS FOR TREATING TOBACCO USE AND DEPENDENCE

TREATMENT METHOD	Estimated Odds Ratio ^a (95% CI)	Estimated Abstinence Rate ^b (95% CI)
Behavioral interventions		
<i>Advice to quit</i>		
No advice to quit	1.0	7.9
Physician advice to quit	1.3 (1.1–1.6)	10.2 (8.5–12.0)
<i>Clinician intervention</i>		
No counseling by a clinician	1.0	10.2
Counseling by a non-physician	1.7 (1.3–2.1)	15.8 (12.8–18.8)
Counseling by a physician	2.2 (1.5–3.2)	19.9 (13.7–26.2)
<i>Format of smoking cessation counseling</i>		
No format	1.0	10.8
Self-help	1.2 (1.0–1.3)	12.3 (10.9–13.6)
Proactive telephone counseling ^c	1.2 (1.1–1.4)	13.1 (11.4–14.8)
Group counseling	1.3 (1.1–1.6)	13.9 (11.6–16.1)
Individual counseling	1.7 (1.4–2.0)	16.8 (14.7–19.1)
Pharmacotherapy		
Placebo	1.0	13.8
<i>First-line agents</i>		
Bupropion SR	2.0 (1.8–2.2)	24.2 (22.2–26.4)
Nicotine gum (6–14 weeks)	1.5 (1.2–1.7)	19.0 (16.5–21.9)
Nicotine inhaler	2.1 (1.5–2.9)	24.8 (19.1–31.6)
Nicotine lozenge (2 mg)	2.0 (1.4–2.8)	24.2 ^d
Nicotine patch (6–14 weeks)	1.9 (1.7–2.2)	23.4 (21.3–25.8)
Nicotine nasal spray	2.3 (1.7–3.0)	26.7 (21.5–32.7)
Varenicline (2 mg/day)	3.1 (2.5–3.8)	33.2 (28.9–37.8)
<i>Second-line agents^e</i>		
Clonidine	2.1 (1.2–3.7)	25.0 (15.7–37.3)
Nortriptyline	1.8 (1.3–2.6)	22.5 (16.8–29.4)
<i>Combination therapy</i>		
Patch (>14 weeks) + <i>ad lib</i> nicotine (gum or nasal spray)	3.6 (2.5–5.2)	36.5 (28.6–45.3)
Nicotine patch + bupropion SR	2.5 (1.9–3.4)	28.9 (23.5–35.1)
Nicotine patch + nortriptyline	2.3 (1.3–4.2)	27.3 (17.2–40.4)
Nicotine patch + nicotine inhaler	2.2 (1.2–3.6)	25.8 (17.4–36.5)

^a Estimated relative to referent group

^b Abstinence percentages for specified treatment method

^c A quitline that responds to incoming calls and makes outbound followup calls. Following an initial request by the smoker or via a fax-to-quit program, the clinician initiates telephone contact to counsel the patient.

^d One qualifying randomized trial; 95% CI not reported in 2008 Clinical Practice Guideline

^e Not approved by the U.S. Food and Drug Administration as a smoking cessation aid; recommended by the USPHS Guideline as a second-line agent for treating tobacco use and dependence

Data from: Fiore MC, Jaén CR, Baker TB, et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service.