Nonprescription Nicotine Replacement Therapy

(a one-hour continuing education program)

This program covers the nicotine patch, lozenge, and gum, including patient education information and a brief overview of the 5 A's framework. Additional behavioral counseling information is provided through handouts.

Goal

To provide clinicians with the knowledge and skills necessary to assist patients in the proper selection and use of nonprescription nicotine replacement therapy.

Learning Objectives

Upon completion of this Rx for Change continuing education program, participants will be able to:

1	List five health risks associated with chronic tobacco use.
2	Identify three nonprescription formulations of nicotine replacement therapy shown to be effective for smoking cessation
3	Be familiar with patient selection characteristics, dosing, and adverse effects for the various nonprescription nicotine replacement therapy formulations.
4	Describe the relative daily costs of nonprescription nicotine replacement therapy compared to cigarette smoking.
5	Identify the five components of successful tobacco cessation counseling.

♪ **NOTE:** This file is formatted for printing double-sided.

NONPRESCRIPTION NICOTINE REPLACEMENT THERAPY

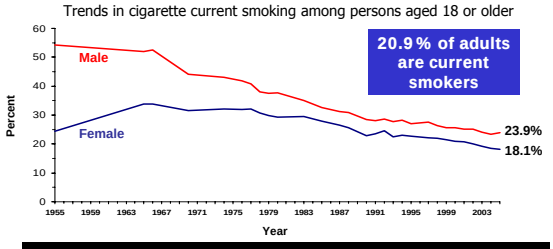
"CIGARETTE SMOKING…

is the chief, single, avoidable cause of death in our society and the most important public health issue of our time."

C. Everett Koop, M.D., former U.S. Surgeon General

TRENDS in ADULT SMOKING, by SEX—U.S., 1955–2005

Trends in cigarette current smoking among persons aged 18 or older



70% want to quit

Graph provided by the Centers for Disease Control and Prevention. 1955 Current Population Survey; 1965–2005 NHIS. Estimates since 1992 include some-day smoking.

ANNUAL U.S. DEATHS ATTRIBUTABLE to SMOKING, 1997–2001

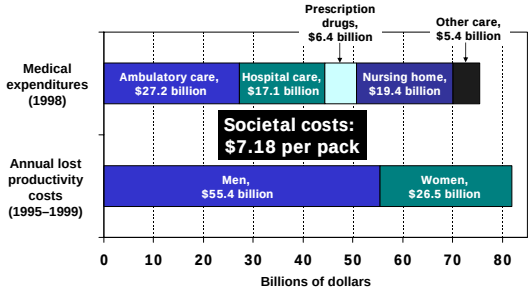
		Percentage of all smoking-attributable deaths*
Cardiovascular diseases	137,979	32%
Lung cancer	123,836	28%
Respiratory diseases	101,454	23%
Second-hand smoke*	38,112	9%
Cancers other than lung	34,693	8%
Other	1,828	<1%

TOTAL: 437,902 deaths annually

* In 2005, it was estimated that nearly 50,000 persons died due to second-hand smoke exposure.

Centers for Disease Control and Prevention. (2005). *MMWR* 54:625–628.

ANNUAL SMOKING-ATTRIBUTABLE ECONOMIC COSTS—U.S., 1995–1999



Centers for Disease Control and Prevention. (2002). *MMWR* 51:300–303.

2004 REPORT of the SURGEON GENERAL: HEALTH CONSEQUENCES OF SMOKING

FOUR MAJOR CONCLUSIONS:

- Smoking harms nearly every organ of the body, causing many diseases and reducing the health of smokers in general.
- Quitting smoking has immediate as well as long-term benefits, reducing risks for diseases caused by smoking and improving health in general.
- Smoking cigarettes with lower machine-measured yields of tar and nicotine provides no clear benefit to health.
- The list of diseases caused by smoking has been expanded.

U.S. Department of Health and Human Services. (2004). *The Health Consequences of Smoking: A Report of the Surgeon General*.

2006 REPORT of the SURGEON GENERAL:
INVOLUNTARY EXPOSURE to TOBACCO SMOKE

- Second-hand smoke causes premature death and disease in nonsmokers (children and adults)
- Children:
  - Increased risk for sudden infant death syndrome (SIDS), acute respiratory infections, ear problems, and more severe asthma
  - Respiratory symptoms and slowed lung growth if parents smoke
- Adults:
  - Immediate adverse effects on cardiovascular system
  - Increased risk for coronary heart disease and lung cancer
- Millions of Americans are exposed to smoke in their homes/workplaces
- Indoor spaces: eliminating smoking fully protects nonsmokers
  - Separating smoking areas, cleaning the air, and ventilation are ineffective

There is no safe level of second-hand smoke.

USDHHS. (2006). *The Health Consequences of Involuntary Exposure to Tobacco Smoke: Report of the Surgeon General.*

QUITTING: HEALTH BENEFITS

Time Since Quit Date

Circulation improves, walking becomes easier Lung function increases up to 30%	2 weeks to 3 months	Lung cilia regain normal function
	1 to 9 months	Ability to clear lungs of mucus increases Coughing, fatigue, shortness of breath decrease
Excess risk of CHD decreases to half that of a continuing smoker	1 year	
Lung cancer death rate drops to half that of a continuing smoker	5 years	Risk of stroke is reduced to that of people who have never smoked
Risk of cancer of mouth, throat, esophagus, bladder, kidney, pancreas decrease	10 years	
	after 15 years	Risk of CHD is similar to that of people who have never smoked

TOBACCO DEPENDENCE: A 2-PART PROBLEM

Tobacco Dependence

Physiological	Behavioral
The addiction to nicotine	The habit of using tobacco
Treatment	Treatment
Medications for cessation	Behavior change program

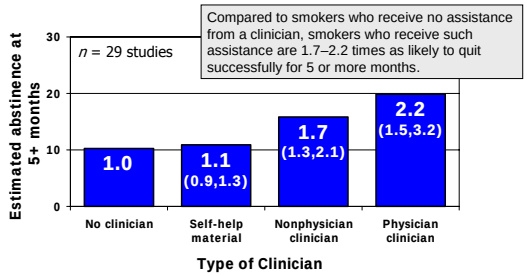
Treatment should address the physiological **and** the behavioral aspects of dependence.

CLINICAL PRACTICE GUIDELINE for TREATING TOBACCO USE and DEPENDENCE

- Released June 2000
- Sponsored by the Agency for Healthcare Research and Quality of the U.S. Public Heath Service with
  - Centers for Disease Control and Prevention
  - National Cancer Institute
  - National Institute for Drug Addiction
  - National Heart, Lung, & Blood Institute
  - Robert Wood Johnson Foundation

www.surgeongeneral.gov/tobacco/

EFFECTS of CLINICIAN INTERVENTIONS



Fiore et al. (2000). *Treating Tobacco Use and Dependence. Clinical Practice Guideline.* Rockville, MD: USDHHS, PHS.

The 5 A's

- ASK
- ADVISE
- ASSESS
- ASSIST
- ARRANGE

HANDOUT

Fiore et al. (2000). *Treating Tobacco Use and Dependence. Clinical Practice Guideline.* Rockville, MD: USDHHS, PHS.

The 5 A's (cont'd)

- ASK about tobacco use
  - "Do you ever smoke or use any type of tobacco?"
    - "I take time to ask all of my patients about tobacco use—because it's important."
  - "Medication X often is used for conditions linked with or caused by smoking. Do you, or does someone in your household smoke?"
  - "Condition X often is caused or worsened by smoking. Do you, or does someone in your household smoke?"

The 5 A's (cont'd)

- ADVISE tobacco users to quit (clear, strong, personalized, sensitive)
  - "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 when you are ready, I will work with you to design a specialized treatment plan."

The 5 A's (cont'd)

- ASSESS readiness to make a quit attempt
- ASSIST with the quit attempt
  - Not ready to quit: provide motivation (the 5 R's)
  - Ready to quit: design a treatment plan
  - Recently quit: relapse prevention

The 5 A's (cont'd)

- ARRANGE follow-up care

Number of sessions	Estimated quit rate*
0 to 1	12.4%
2 to 3	16.3%
4 to 8	20.9%
More than 8	24.7%

* 5 months (or more) postcessation

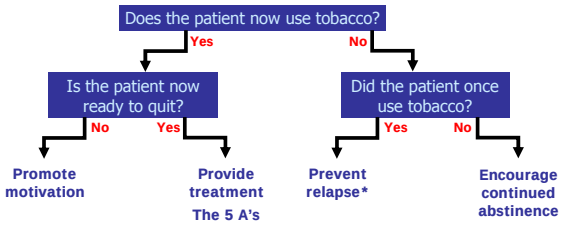
PROVIDE ASSISTANCE THROUGHOUT THE QUIT ATTEMPT

Fiore et al. (2000). *Treating Tobacco Use and Dependence. Clinical Practice Guideline.* Rockville, MD: USDHHS, PHS.

The 5 A's: REVIEW

ASK	about tobacco USE
ADVISE	tobacco users to QUIT
ASSESS	READINESS to make a quit attempt
ASSIST	with the QUIT ATTEMPT
ARRANGE	FOLLOW-UP care

IS a PATIENT READY to QUIT?



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

Fiore et al. (2000). *Treating Tobacco Use and Dependence. Clinical Practice Guideline.* Rockville, MD: USDHHS, PHS.

PHARMACOTHERAPY

"All patients attempting to quit should be encouraged to use effective pharmacotherapies for smoking cessation except in the presence of special circumstances."

Fiore et al. (2000). *Treating Tobacco Use and Dependence. Clinical Practice Guideline.* Rockville, MD: USDHHS, PHS.

PHARMACOLOGIC METHODS: FIRST-LINE THERAPIES

Three general classes of FDA-approved drugs for smoking cessation:

- Nicotine replacement therapy (NRT)
  - Nicotine gum, patch, lozenge, nasal spray, inhaler
- Psychotropics
  - Sustained-release bupropion
- Partial nicotinic receptor agonist
  - Varenicline

Currently, no medications have an FDA indication for use in spit tobacco cessation.

NRT: RATIONALE for USE

- Reduces physical withdrawal from nicotine
- Allows patient to focus on behavioral and psychological aspects of tobacco cessation

NRT APPROXIMATELY DOUBLES QUIT RATES.

NICOTINE PHARMACODYNAMICS: WITHDRAWAL EFFECTS

- Depression
- Insomnia
- Irritability/frustration/anger
- Anxiety
- Difficulty concentrating
- Restlessness
- Increased appetite/weight gain
- Decreased heart rate
- Cravings*

Most symptoms peak 24–48 hr after quitting and subside within 2–4 weeks.

HANDOUT

* Not considered a withdrawal symptom by *DSM*-IV criteria.

American Psychiatric Association. (1994). *DSM*-IV.
Hughes et al. (1991). *Arch Gen Psychiatry* 48:52–59.
Hughes & Hatsukami. (1998). *Tob Control* 7:92–93.

NRT: PRODUCTS

Polacrilex gum
- Nicorette (OTC)
- Generic nicotine gum (OTC)

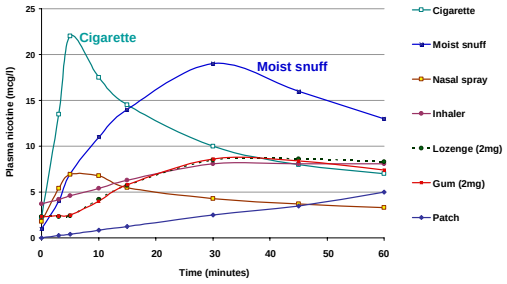
Lozenge
- Commit (OTC)
- Generic nicotine lozenge (OTC)

Transdermal patch
- Nicoderm CQ (OTC)
- Generic nicotine patches (OTC, Rx)

Nasal spray
- Nicotrol NS (Rx)

Inhaler
- Nicotrol (Rx)

PLASMA NICOTINE CONCENTRATIONS for NICOTINE-CONTAINING PRODUCTS



NRT: PRECAUTIONS

- Patients with underlying cardiovascular disease
  - Recent myocardial infarction (within past 2 weeks)
  - Serious arrhythmias
  - Serious or worsening angina

NRT products may be appropriate for these patients if they are under medical supervision.

NRT: PRECAUTIONS (cont'd)

- Patients with other underlying conditions
  - Active temporomandibular joint disease (gum only)
  - Pregnancy
  - Lactation

NRT products may be appropriate for these patients if they are under medical supervision.

NRT: OTHER CONSIDERATIONS

- NRT is not FDA-approved for use in children or adolescents
- Nonprescription sales (patch, gum, lozenge) are restricted to adults ≥18 years of age
  - NRT use in minors requires a prescription
- Patients should stop using all forms of tobacco upon initiation of the NRT regimen

NICOTINE GUM

Nicorette (GlaxoSmithKline); generics

- Resin complex
  - Nicotine
  - Polacrilin
- Sugar-free chewing gum base
- Contains buffering agents to enhance buccal absorption of nicotine
- Available: 2 mg, 4 mg; regular, FreshMint, Fruit Chill, mint, & orange flavor

NICOTINE GUM: DOSING

Dosage based on current smoking patterns:

If patient smokes	Recommended strength
≥25 cigarettes/day	4 mg
<25 cigarettes/day	2 mg

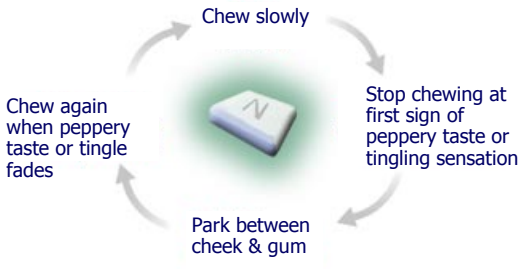
NICOTINE GUM: DOSING (cont'd)

Recommended Usage Schedule for Nicotine Gum		
Weeks 1–6	Weeks 7–9	Weeks 10–12
1 piece q 1–2 h	1 piece q 2–4 h	1 piece q 4–8 h
DO NOT USE MORE THAN 24 PIECES PER DAY.		

NICOTINE GUM: DIRECTIONS for USE

- Chew each piece very *slowly* several times
- Stop chewing at first sign of peppery, minty, or citrus taste or slight tingling in mouth (~15 chews, but varies)
- "Park" gum between cheek and gum (to allow absorption of nicotine across buccal mucosa)
- Resume slow chewing when taste or tingle fades
- When taste or tingle returns, stop and park gum in different place in mouth
- Repeat chew/park steps until most of the nicotine is gone (taste or tingle does not return; generally 30 minutes)

NICOTINE GUM: CHEWING TECHNIQUE SUMMARY



NICOTINE GUM: ADDITIONAL PATIENT EDUCATION

- To improve chances of quitting, use at least nine pieces of gum daily
- The effectiveness of nicotine gum may be reduced by some foods and beverages:
  - Coffee
  - Juices
  - Wine
  - Soft drinks

Do NOT eat or drink for 15 minutes BEFORE or while using nicotine gum.

NICOTINE GUM: ADD'L PATIENT EDUCATION (cont'd)

- Chewing gum will *not* provide same rapid satisfaction that smoking provides
- Chewing gum too rapidly can cause excessive release of nicotine, resulting in
  - Lightheadedness
  - Nausea/vomiting
  - Irritation of throat and mouth
  - Hiccups
  - Indigestion

NICOTINE GUM: ADD'L PATIENT EDUCATION (cont'd)

- Side effects of nicotine gum include
  - Mouth soreness
  - Hiccups
  - Dyspepsia
  - Jaw muscle ache
- Nicotine gum may stick to dental work
  - Discontinue use if excessive sticking or damage to dental work occurs

NICOTINE GUM: SUMMARY

ADVANTAGES

- Gum use may satisfy oral cravings.
- Gum use may delay weight gain.
- Patients can titrate therapy to manage withdrawal symptoms.

DISADVANTAGES

- Gum chewing may not be socially acceptable.
- Gum is difficult to use with dentures.
- Patients must use proper chewing technique to minimize adverse effects.

NICOTINE LOZENGE
Commit (GlaxoSmithKline); generics

- Nicotine polacrilex formulation
  - Delivers ~25% more nicotine than equivalent gum dose
- Sugar-free, mint or cherry flavor (boxed or POP-PAC)
- Contains buffering agents to enhance buccal absorption of nicotine
- Available: 2 mg, 4 mg

NICOTINE LOZENGE: DOSING

Dosage is based on the "time to first cigarette" (TTFC) as an indicator of nicotine addiction

Use Commit Lozenge 2 mg:
If you smoke your first cigarette more than 30 minutes after waking up

Use Commit Lozenge 4 mg:
If you smoke your first cigarette of the day within 30 minutes of waking up

NICOTINE LOZENGE: DOSING (cont'd)

Recommended Usage Schedule for Commit Lozenge		
Weeks 1–6	**Weeks 7–9**	**Weeks 10–12**
1 lozenge q 1–2 h	**1 lozenge q 2–4 h**	**1 lozenge q 4–8 h**
DO NOT USE MORE THAN 20 LOZENGES PER DAY.		

NICOTINE LOZENGE: DIRECTIONS for USE

- Use according to recommended dosing schedule
- Place in mouth and allow to dissolve slowly (nicotine release may cause warm, tingling sensation)
- Do *not* chew or swallow lozenge.
- Occasionally rotate to different areas of the mouth.
- Lozenge will dissolve completely in about 20–30 minutes.

NICOTINE LOZENGE: ADDITIONAL PATIENT EDUCATION

- To improve chances of quitting, use at least nine lozenges daily during the first 6 weeks
- The lozenge will *not* provide the same rapid satisfaction that smoking provides
- The effectiveness of the nicotine lozenge may be reduced by some foods and beverages:
  - Coffee
  - Juices
  - Wine
  - Soft drinks

Do NOT eat or drink for 15 minutes BEFORE or while using the nicotine lozenge.

NICOTINE LOZENGE: ADD'L PATIENT EDUCATION (cont'd)

- Side effects of the nicotine lozenge include
  - Nausea
  - Hiccups
  - Cough
  - Heartburn
  - Headache
  - Flatulence
  - Insomnia

NICOTINE LOZENGE: SUMMARY

ADVANTAGES

- Lozenge use may satisfy oral cravings.
- The lozenge is easy to use and conceal.
- Patients can titrate therapy to manage withdrawal symptoms.

DISADVANTAGES

- Gastrointestinal side effects (nausea, hiccups, and heartburn) may be bothersome.

TRANSDERMAL NICOTINE PATCH
Nicoderm CQ (GlaxoSmithKline); generic

- Nicotine is well absorbed across the skin
- Delivery to systemic circulation avoids hepatic first-pass metabolism
- Plasma nicotine levels are lower and fluctuate less than with smoking

TRANSDERMAL NICOTINE PATCH: PREPARATION COMPARISON

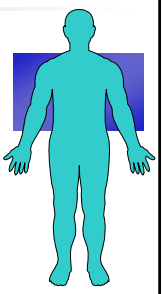
Product	Nicoderm CQ	Generic
Nicotine delivery	24 hours	24 hours
Availability	OTC	Rx/OTC
Strengths	7-mg patch 14-mg patch 21-mg patch	7-mg patch 14-mg patch 21-mg patch

TRANSDERMAL NICOTINE PATCH: DOSING

Product	Light Smoker	Heavy Smoker
Nicoderm CQ	**≤10 cigarettes/day** Step 2 (14 mg x 6 weeks) Step 3 (7 mg x 2 weeks)	**>10 cigarettes/day** Step 1 (21 mg x 6 weeks) Step 2 (14 mg x 2 weeks) Step 3 (7 mg x 2 weeks)
Generic (formerly Habitrol)	**≤10 cigarettes/day** Step 2 (14 mg x 6 weeks) Step 3 (7 mg x 2 weeks)	**>10 cigarettes/day** Step 1 (21 mg x 4 weeks) Step 2 (14 mg x 2 weeks) Step 3 (7 mg x 2 weeks)

TRANSDERMAL NICOTINE PATCH: DIRECTIONS for USE

- Choose an area of skin on the upper body or upper outer part of the arm
- Make sure skin is clean, dry, hairless, and not irritated
- Apply patch to different area each day
- Do not use same area again for at least 1 week



TRANSDERMAL NICOTINE PATCH: DIRECTIONS for USE (cont'd)

- Remove patch from protective pouch

TRANSDERMAL NICOTINE PATCH: DIRECTIONS for USE (cont'd)

- Peel off half of the backing from patch

TRANSDERMAL NICOTINE PATCH: DIRECTIONS for USE (cont'd)

- Apply adhesive side of patch to skin
- Peel off remaining protective covering
- Press firmly with palm of hand for 10 seconds
- Make sure patch sticks well to skin, especially around edges

TRANSDERMAL NICOTINE PATCH: DIRECTIONS for USE (cont'd)

- Wash hands: Nicotine on hands can get into eyes or nose and cause stinging or redness
- Do not leave patch on skin for more than 24 hours—doing so may lead to skin irritation
- Adhesive remaining on skin may be removed with rubbing alcohol or acetone
- Dispose of used patch by folding it onto itself, completely covering adhesive area

TRANSDERMAL NICOTINE PATCH: ADDITIONAL PATIENT EDUCATION

- Water will not harm the nicotine patch if it is applied correctly; patients may bathe, swim, shower, or exercise while wearing the patch
- Do *not* cut patches to adjust dose
  - Nicotine may evaporate from cut edges
  - Patch may be less effective

- Keep new and used patches out of the reach of children and pets
- Remove patch before MRI procedures

TRANSDERMAL NICOTINE PATCH: ADD'L PATIENT EDUCATION (cont'd)

- Side effects to expect in first hour:
  - Mild itching
  - Burning
  - Tingling
- Additional possible side effects:
  - Vivid dreams or sleep disturbances
  - Headache

TRANSDERMAL NICOTINE PATCH: ADD'L PATIENT EDUCATION (cont'd)

- After patch removal, skin may appear red for 24 hours
  - If skin stays red more than 4 days or if it swells or a rash appears, contact health care provider—do not apply new patch
- Local skin reactions (redness, burning, itching)
  - Usually caused by adhesive
  - Up to 50% of patients experience this reaction
  - Fewer than 5% of patients discontinue therapy
  - Avoid use in patients with dermatologic conditions (e.g., psoriasis, eczema, atopic dermatitis)

TRANSDERMAL NICOTINE PATCH: SUMMARY

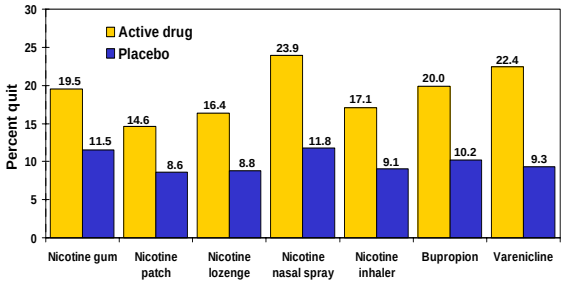
ADVANTAGES

- The patch provides consistent nicotine levels.
- The patch is easy to use and conceal.
- Fewer compliance issues are associated with patch use.

DISADVANTAGES

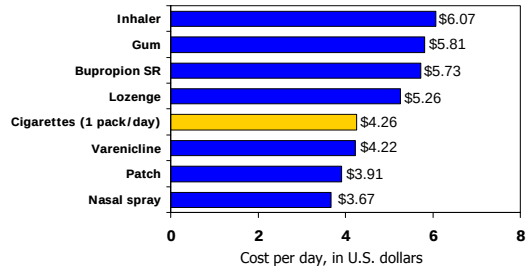
- Patients cannot titrate the dose.
- Allergic reactions to the adhesive may occur.
- Patients with dermatologic conditions should not use the patch.

LONG-TERM (≥6 month) QUIT RATES for AVAILABLE CESSATION MEDICATIONS



Data adapted from Silagy et al. (2004). *Cochrane Database Syst Rev;* Hughes et al., (2004). *Cochrane Database Syst Rev.;* Gonzales et al., (2006). *JAMA* and Jorenby et al., (2006). *JAMA*

COMPARATIVE DAILY COSTS of PHARMACOTHERAPY



COMPLIANCE IS KEY to QUITTING

- Promote compliance with prescribed regimens.
- Use according to dosing schedule, NOT as needed.
- Consider telling the patient:
  - "When you use a cessation product it is important to read all the directions thoroughly before using the product. The products work best in alleviating withdrawal symptoms when used correctly, and according to the recommended dosing schedule."

The RESPONSIBILITY of HEALTH PROFESSIONALS

It is **inconsistent**

to provide health care and

—at the same time—

remain silent (or inactive)

about a major health risk.

TOBACCO CESSATION is an important component of THERAPY.

BRIEF COUNSELING: ASK, ADVISE, REFER

- Brief interventions have been shown to be effective
- In the absence of time or expertise:
  - Ask, advise, and refer to other resources, such as local programs or the toll-free quitline **1-800-QUIT-NOW**

This brief intervention can be achieved in 30 seconds.

STEP One: ASK about Tobacco Use

➲ Suggested Dialogue

✓ Do you ever smoke or use any type of tobacco?

–I take time to talk with all of my patients about tobacco use—because it's important.

✓ Medication X often is used for conditions linked with or caused by smoking. Do you, or does someone in your household smoke?

✓ Condition X often is caused or worsened by exposure to tobacco smoke. Do you, or does someone in your household smoke?

STEP Two: Strongly ADVISE to Quit

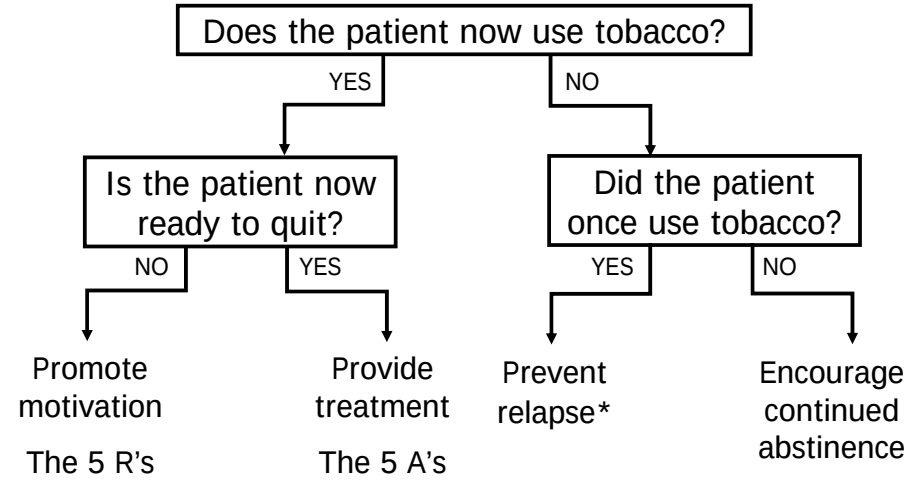
It is important to be sensitive, because patients might be defensive of their smoking. Project empathy in your voice; be understanding, not reprimanding.

➲ Suggested Dialogue

– 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 when you are ready 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.

Fiore MC, Bailey WC, Cohen SJ, et al. *Treating Tobacco Use and Dependence. Clinical Practice Guideline*. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service, 2000.

STEP Four: ASSIST with Quitting

Rx for Change

✓ **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, compliance, 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
- Social support for quitting
- 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: compliance, 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.

TOBACCO CESSATION COUNSELING GUIDESHEET

DRUG INTERACTIONS WITH SMOKING

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 may interact with medications through pharmacokinetic (PK) or 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). 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)	▪ Conflicting data on significance of a PK interaction. Possible ↓ plasma concentrations (up to 50%); ↓ half-life (35%).
Caffeine	▪ ↑ Metabolism (induction of CYP1A2); ↑ clearance (56%). ▪ Likely ↑ caffeine levels after cessation.
Chlorpromazine (Thorazine)	▪ ↓ Area under the curve (AUC) (36%) and serum concentrations (24%). ▪ ↓ Sedation and hypotension possible in smokers; smokers may need ↑ dosages.
Clozapine (Clozaril)	▪ ↑ Metabolism (induction of CYP1A2); ↓ plasma concentrations (18%).
Flecainide (Tambocor)	▪ ↑ Clearance (61%); ↓ trough serum concentrations (25%). ▪ Smokers may need ↑ dosages.
Fluvoxamine (Luvox)	▪ ↑ Metabolism (induction of CYP1A2); ↑ clearance (24%); ↓ AUC (31%); ↓ plasma concentrations (32%). ▪ Dosage modifications not routinely recommended but smokers may need ↑ dosages.
Haloperidol (Haldol)	▪ ↑ Clearance (44%); ↓ serum concentrations (70%).
Heparin	▪ 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	▪ 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; smokers may need ↑ dosages.
Insulin, inhaled (Exubera)	▪ Systemic exposure is greatly increased in smokers; greater maximal insulin concentrations (3–5 fold) and faster (by 20-30 minutes) ; ↑AUC 2–3 fold ▪ Contraindicated in smokers and those who have discontinued smoking for less than 6 months.
Mexiletine (Mexitil)	▪ ↑ Clearance (25%; via oxidation and glucuronidation); ↓ half-life (36%).
Olanzapine (Zyprexa)	▪ ↑ Metabolism (induction of CYP1A2); ↑ clearance (98%); ↓ serum concentrations (12%). ▪ Dosage modifications not routinely recommended but smokers may require ↑ dosages.
Propranolol (Inderal)	▪ ↑ Clearance (77%; via side chain oxidation and glucuronidation)
Tacrine (Cognex)	▪ ↑ Metabolism (induction of CYP1A2); ↓ half-life (50%); serum concentrations three-fold lower. ▪ Smokers may need ↑ dosages.
Theophylline (Theo Dur, etc.)	▪ ↑ Metabolism (induction of CYP1A2); ↑ clearance (58–100%); ↓ half-life (63%). ▪ Levels should be monitored if smoking is initiated, discontinued, or changed. ▪ ↑ Clearance with second-hand smoke exposure. ▪ Maintenance doses are considerably higher in smokers.
Tricyclic antidepressants (e.g., imipramine, nortriptyline)	▪ Possible interaction with tricyclic antidepressants in the direction of ↓ blood levels, but the clinical importance is not established.
Pharmacodynamic Interactions	
Benzodiazepines (diazepam, chlordiazepoxide)	▪ ↓ Sedation and drowsiness, possibly caused by nicotine stimulation of central nervous system.
Beta-blockers	▪ Less effective antihypertensive and heart rate control effects; might be caused by nicotine-mediated sympathetic activation. ▪ Smokers may need ↑ dosages.
Corticosteroids, inhaled	▪ Asthmatic smokers may have less of a response to inhaled corticosteroids.
Hormonal contraceptives	▪ ↑ Risk of cardiovascular adverse effects (e.g., stroke, myocardial infarction, thromboembolism) in women who smoke and use oral contraceptives. ▪ ↑ Risk with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women age 35 and older.
Opioids (propoxyphene, pentazocine)	▪ ↓ Analgesic effect; smoking may ↑ the metabolism of propoxyphene (15–20%) and pentazocine (40%). Mechanism unknown. ▪ Smokers may need ↑ opioid dosages for pain relief.

Adapted from Zevin S, Benowitz NL. Drug interactions with tobacco smoking. *Clin Pharmacokinet* 1999;36:425–438.

COPING WITH QUITTING: COGNITIVE AND BEHAVIORAL STRATEGIES

COGNITIVE STRATEGIES focus on *retraining the way a patient thinks*. Often, patients mentally 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.	
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.
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.	
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, perform self-massage, use nicotine replacement therapy).
ALCOHOL	*Drinking alcohol can lead to relapse.* Consider limiting or abstaining from alcohol during the early stages of quitting.
OTHER TOBACCO USERS	*Quitting is more difficult if the patient is around other tobacco users. This is especially difficult if another tobacco user is in the household.* 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, drink tea instead of coffee, take shower before drinking coffee, take a brisk walk shortly after awakening. WHILE DRIVING: remove all tobacco from car, have car interior detailed, listen to a book on tape or talk radio, use oral substitute. 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, 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 (e.g., nicotine gum, nicotine lozenge, bupropion).
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, perform self-massage.

WITHDRAWAL SYMPTOMS INFORMATION SHEET

Quitting tobacco use brings about a variety of physical and psychological withdrawal symptoms. Most of these symptoms decrease sharply during the first few days after quitting, followed by a continued but slower decline in symptoms during the 2nd and 3rd weeks after quitting. 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 pass within 2 to 4 weeks after quitting.** Report new symptoms to your health-care provider, especially if severe. Consider the impact of recent medication changes.

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	▪ 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	▪ 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	▪ 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	▪ Wait out the urge, which lasts only a few minutes ▪ Distract yourself ▪ Exercise (take walks) ▪ Use of NRT 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	▪ 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	▪ Plan workload accordingly ▪ Avoid additional stress during first few weeks
Dizziness	The body is getting extra oxygen.	1–2 days	▪ Use extra caution ▪ Change positions slowly
Fatigue	Nicotine is a stimulant.	2–4 weeks	▪ Take naps ▪ Do not push yourself ▪ Use of NRT 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	▪ 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	▪ Limit caffeine intake, the effects of which will increase with quitting smoking ▪ Use relaxation techniques
Irritability	The body's craving for nicotine can produce irritability.	2–4 weeks	▪ Take walks ▪ Try hot baths ▪ Use relaxation techniques

Adapted from materials from the National Cancer Institute.

PHARMACOLOGIC PRODUCT GUIDE: FDA-APPROVED MEDICATIONS

	NICOTINE REPLACEMENT THERAPY (NRT) FORMULATIONS						BUPROPION SR	VARENICLINE
	GUM	LOZENGE	TRANSDERMAL PREPARATIONS[1]		NASAL SPRAY	ORAL INHALER		
PRODUCT	Nicorette[2], Generic OTC 2 mg, 4 mg; original, FreshMint[2], Fruit Chill[2], mint, orange[2]	Commit[2], Generic OTC 2 mg, 4 mg mint	Nicoderm CQ[2] OTC 24-hour release 7 mg, 14 mg, 21 mg	Generic Patch OTC/Rx (formerly Habitrol) 24-hour release 7 mg, 14 mg, 21 mg	Nicotrol NS[3] Rx Metered spray 0.5 mg nicotine in 50 μL aqueous nicotine solution	Nicotrol Inhaler[3] Rx 10 mg cartridge delivers 4 mg inhaled nicotine vapor	Zyban[2], Generic Rx 150 mg sustained-release tablet	Chantix[3] Rx 0.5 mg, 1 mg tablet
PRECAUTIONS	▪ Pregnancy (Category D) ▪ Recent (≤ 2 weeks) myocardial infarction ▪ Serious underlying arrhythmias ▪ Serious or worsening angina pectoris ▪ Temporomandibular joint disease	▪ Pregnancy (Category D) ▪ Recent (≤ 2 weeks) myocardial infarction ▪ Serious underlying arrhythmias ▪ Serious or worsening angina pectoris	▪ Pregnancy (Category D) ▪ Recent (≤ 2 weeks) myocardial infarction ▪ Serious underlying arrhythmias ▪ Serious or worsening angina pectoris		▪ Pregnancy (Category D) ▪ 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	▪ Pregnancy (Category D) ▪ Recent (≤ 2 weeks) myocardial infarction ▪ Serious underlying arrhythmias ▪ Serious or worsening angina pectoris ▪ Bronchospastic disease	▪ Pregnancy (Category C) ▪ Concomitant therapy with medications or medical conditions known to lower the seizure threshold ▪ Severe hepatic cirrhosis Contraindications: ▪ Seizure disorder ▪ Concomitant bupropion (e.g., Wellbutrin) therapy ▪ Current or prior diagnosis of bulimia or anorexia nervosa ▪ Simultaneous abrupt discontinuation of alcohol or sedatives (including benzodiazepines) ▪ MAO inhibitor therapy in previous 14 days	▪ Pregnancy (Category C) ▪ Severe renal impairment (dosage adjustment is necessary)
DOSING	*≥25 cigarettes/day:* 4 mg *<25 cigarettes/day:* 2 mg Week 1–6: 1 piece q 1–2 hours Week 7–9: 1 piece q 2–4 hours Week 10–12: 1 piece q 4–8 hours ▪ 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 taste or tingle fades ▪ Repeat chew/park steps until most of the nicotine is gone (taste or tingle does not return; generally 30 min) ▪ Park in different areas of mouth ▪ No food or beverages 15 min before or during use ▪ Duration: up to 12 weeks	*1st cigarette ≤30 minutes after waking:* 4 mg *1st cigarette >30 minutes after waking:* 2 mg Week 1–6: 1 lozenge q 1–2 hours Week 7–9: 1 lozenge q 2–4 hours Week 10–12: 1 lozenge q 4–8 hours ▪ Maximum, 20 lozenges/day ▪ Allow to dissolve slowly (20-30 minutes) ▪ 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	*>10 cigarettes/day:* 21 mg/day x 6 weeks 14 mg/day x 2 weeks 7 mg/day x 2 weeks *≤10 cigarettes/day:* 14 mg/day x 6 weeks 7 mg/day x 2 weeks ▪ May wear patch for 16 hours if patient experiences sleep disturbances (remove at bedtime) ▪ Duration: 8–10 weeks	*>10 cigarettes/day:* 21 mg/day x 4 weeks 14 mg/day x 2 weeks 7 mg/day x 2 weeks *≤10 cigarettes/day:* 14 mg/day x 6 weeks 7 mg/day x 2 weeks ▪ May wear patch for 16 hours if patient experiences sleep disturbances (remove at bedtime) ▪ Duration: 8 weeks	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 ▪ Maximum – 5 doses/hour – 40 doses/day ▪ For best results, initially use at least 8 doses/day ▪ Patients should not sniff, swallow, or inhale through the nose as the spray is being administered ▪ Duration: 3–6 months	6–16 cartridges/day; individualized dosing ▪ Initially, use at least 6 cartridges/day ▪ Best effects with continuous puffing for 20 minutes ▪ Nicotine in cartridge is depleted after 20 minutes of active puffing ▪ Patient should 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 ▪ Duration: up to 6 months	150 mg po q AM x 3 days, then increase to 150 mg po bid ▪ Do not exceed 300 mg/day ▪ Treatment should be initiated while patient is still smoking ▪ Set quit date 1–2 weeks after initiation of therapy ▪ Allow at least 8 hours between doses ▪ Avoid bedtime dosing to minimize insomnia ▪ Dose tapering is not necessary ▪ Can be used safely with NRT ▪ Duration: 7–12 weeks, with maintenance up to 6 months in selected patients	Days 1–3: 0.5 mg po q AM Days 4–7: 0.5 mg po bid Weeks 2–12: 1 mg po bid ▪ Patients should begin therapy 1 week prior to quit date ▪ Take dose after eating with a full glass of water ▪ Dose tapering is not necessary ▪ Nausea and insomnia are side effects that are usually temporary ▪ 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 Preparations		Nasal Spray	Oral Inhaler		
			Nicoderm CQ	Generic Patch				
Adverse Effects	▪ Mouth/jaw soreness ▪ Hiccups ▪ Dyspepsia ▪ Hypersalivation ▪ Effects associated with incorrect chewing technique: – Lightheadedness – Nausea/vomiting – Throat and mouth irritation	▪ Nausea ▪ Hiccups ▪ Cough ▪ Heartburn ▪ Headache ▪ Flatulence ▪ Insomnia	▪ Local skin reactions (erythema, pruritus, burning) ▪ Headache ▪ Sleep disturbances (insomnia) or abnormal/vivid dreams (associated with nocturnal nicotine absorption)		▪ Nasal and/or throat irritation (hot, peppery, or burning sensation) ▪ Rhinitis ▪ Tearing ▪ Sneezing ▪ Cough ▪ Headache	▪ Mouth and/or throat irritation ▪ Unpleasant taste ▪ Cough ▪ Rhinitis ▪ Dyspepsia ▪ Hiccups ▪ Headache	▪ Insomnia ▪ Dry mouth ▪ Nervousness/difficulty concentrating ▪ Rash ▪ Constipation ▪ Seizures (risk is 1/1,000 [0.1%])	▪ Nausea ▪ Sleep disturbances (insomnia, abnormal dreams) ▪ Constipation ▪ Flatulence ▪ Vomiting
Advantages	▪ Gum use might satisfy oral cravings ▪ Gum use may delay weight gain ▪ Patients can titrate therapy to manage withdrawal symptoms	▪ Lozenge use might satisfy oral cravings ▪ Patients can titrate therapy to manage withdrawal symptoms	▪ Provides consistent nicotine levels over 24 hours ▪ Easy to use and conceal ▪ Once-a-day dosing associated with fewer compliance problems		▪ Patients can titrate therapy to manage withdrawal symptoms	▪ Patients can titrate therapy to manage withdrawal symptoms ▪ Mimics hand-to-mouth ritual of smoking	▪ Easy to use; oral formulation might be associated with fewer compliance problems ▪ Can be used with NRT ▪ Might be beneficial in patients with depression	▪ Easy to use; oral formulation might be associated with fewer compliance problems ▪ Offers a new mechanism of action for patients who have failed other agents
Disadvantages	▪ Gum chewing may not be socially acceptable ▪ Gum is difficult to use with dentures ▪ Patients must use proper chewing technique to minimize adverse effects	▪ Gastrointestinal side effects (nausea, hiccups, heartburn) might be bothersome	▪ Patients cannot titrate the dose ▪ Allergic reactions to adhesive might occur ▪ Patients with dermatologic conditions should not use the patch		▪ Nasal/throat irritation may be bothersome ▪ Dependence can result ▪ Patients must wait 5 minutes before driving or operating heavy machinery ▪ Patients with chronic nasal disorders or severe reactive airway disease should not use the spray	▪ Initial throat or mouth irritation can be bothersome ▪ Cartridges should not be stored in very warm conditions or used in very cold conditions ▪ Patients with underlying bronchospastic disease must use the inhaler with caution	▪ Seizure risk is increased ▪ Several contraindications and precautions preclude use (see Precautions, above)	▪ May induce nausea in up to one third of patients ▪ Post-marketing surveillance data not yet available
Web-Site	www.nicorette.com	www.commitlozenge.com	www.nicodermcq.com	www.habitrol.com	www.nicotrol.com	www.nicotrol.com	- - - -	www.chantix.com
Cost/Day[4]	2 mg: $2.65–$5.16 (9 pieces) 4 mg: $3.18–$5.81 (9 pieces)	2 mg: $4.92 (9 pieces) 4 mg: $5.26 (9 pieces)	$3.35–$3.91 (1 patch)	$2.10–$2.94 (1 patch)	$3.67 (8 doses)	$5.25–$6.07 (6 cartridges)	$3.62–$5.73 (2 tablets)	$4.00–$4.22 (2 tablets)

[1] Transdermal patch formulations previously marketed, but no longer available: Nicotrol 5 mg, 10 mg, 15 mg delivered over 16 hours (Pfizer) and generic patch (formerly Prostep) 11 mg and 22 mg delivered over 24 hours.
[2] Marketed by GlaxoSmithKline.
[3] Marketed by Pfizer.
[4] Average wholesale price from 2006 Drug Topics Redbook. Montvale, NJ: Medical Economics Company, Inc., December 2006.

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

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

PLANNING FOR CHANGE: MY QUIT PLAN (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 will it benefit you to quit later?

PLANNING FOR CHANGE: MY QUIT PLAN (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?