

## Treating Tobacco Use and Dependence: The OB/GYN Patient

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## "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*

Smoking has profound negative health consequences on both the fetus and the mother and is the main cause of obstetric morbidity and mortality.

## HEALTH CONSEQUENCES of SMOKING


- Cancers
  - Acute myeloid leukemia
  - Bladder and kidney
  - Cervical
  - Esophageal
  - Gastric
  - Laryngeal
  - Lung
  - Oral cavity and pharyngeal
  - Pancreatic
- Pulmonary diseases
  - Acute (e.g., pneumonia)
  - Chronic (e.g., COPD)

- Cardiovascular diseases
  - Abdominal aortic aneurysm
  - Coronary heart disease
  - Cerebrovascular disease
  - Peripheral arterial disease
- Other effects: cataract, osteoporosis, periodontitis, poor surgical outcomes

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

## HEALTH CONSEQUENCES of SMOKING: REPRODUCTIVE HEALTH

- Reduced fertility in women
- Pregnancy and pregnancy outcomes
  - Placenta previa
  - Placental abruption
  - Preterm premature rupture of membranes
  - Preterm delivery
  - Low infant birth weight
- Infant mortality
  - Sudden infant death syndrome (SIDS)



INDIANA -- Smoking during pregnancy, 18.1% (U.S. median, 10.2%)

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

## QUITTING: HEALTH BENEFITS

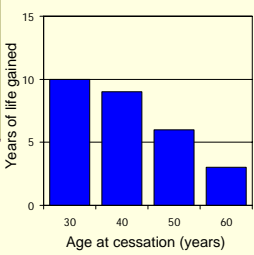
**Time Since Quit Date**

- 2 weeks to 3 months: Circulation improves, walking becomes easier; Lung function increases up to 30%
- 1 year: Excess risk of CHD decreases to half that of a continuing smoker
- 10 years: Lung cancer death rate drops to half that of a continuing smoker; Risk of cancer of mouth, throat, esophagus, bladder, kidney, pancreas decrease

- 1 to 9 months: Lung cilia regain normal function; Ability to clear lungs of mucus increases
- 1 year: Coughing, fatigue, shortness of breath decrease
- 5 years: Risk of stroke is reduced to that of people who have never smoked
- after 15 years: Risk of CHD is similar to that of people who have never smoked

## SMOKING CESSATION: REDUCED RISK of DEATH

- Prospective study of 34,439 male British doctors
- Mortality was monitored for 50 years (1951–2001)



On average, cigarette smokers die approximately 10 years younger than do nonsmokers.

Among those who continue smoking, at least half will die due to a tobacco-related disease.

Doll et al. (2004). *BMJ* 328(7455):1519–1527.

## COMPOUNDS in TOBACCO SMOKE

An estimated 4,800 compounds in tobacco smoke, including 11 proven human carcinogens

### Gases

- Carbon monoxide
- Hydrogen cyanide
- Ammonia
- Benzene
- Formaldehyde



### Particles

- Nicotine
- Nitrosamines
- Lead
- Cadmium
- Polonium-210

Nicotine is **NOT** the primary culprit for the negative health effects of tobacco use in adults.

## NICOTINE in Pregnancy

- May contribute to:
  - Uteroplacental insufficiency via vasoconstriction
  - Fetal neurotoxicity resulting in delayed or impaired brain development
  - Slowed maturation of pulmonary cells
  - Increased risk for SIDS
- These risks are based primarily on animal studies
- Note: Nicotine replacement therapy (NRT) provides considerably lower levels of nicotine than does tobacco use.

## DRUG INTERACTIONS with SMOKING

Clinicians should be aware of their patients' smoking status:

- Clinically significant interactions result not from nicotine but from the combustion products of tobacco smoke.
- These tobacco smoke constituents (e.g., polycyclic aromatic hydrocarbons; PAHs) may enhance the metabolism of other drugs, resulting in a reduced pharmacologic response.
- Smoking might adversely affect the clinical response to the treatment of a wide variety of conditions.

HANDOUT

## PHARMACOKINETIC DRUG INTERACTIONS with SMOKING

- Drugs that may have a *decreased effect* due to induction of CYP1A2:
  - Caffeine
  - Fluvoxamine
  - Olanzapine
  - Tacrine
  - Theophylline

Smoking cessation will reverse these effects.

## PHARMACODYNAMIC DRUG INTERACTIONS with SMOKING

Smokers who use combined hormonal contraceptives have an increased risk of serious cardiovascular adverse effects:

- Stroke
- Myocardial infarction
- Thromboembolism



This interaction **does not** decrease the efficacy of hormonal contraceptives.

Women who are 35 years of age or older AND smoke at least 15 cigarettes per day are at significantly elevated risk.

## Helping Patients Quit

What works?

## The CLINICIAN's ROLE in PROMOTING CESSATION

- Tobacco users expect to be encouraged to quit by health professionals.
- Screening for tobacco use and providing tobacco cessation counseling are positively associated with patient satisfaction (Barzilai et al., 2001).

**Failure to address tobacco use tacitly implies that quitting is not important.**

Barzilai et al. (2001). *Prev Med* 33:595-599.

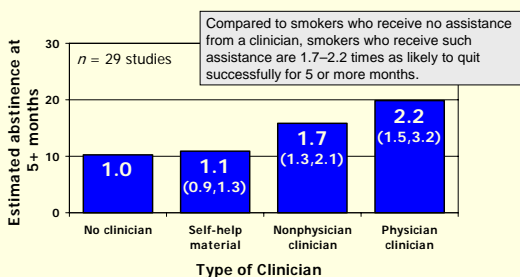
## CLINICAL PRACTICE GUIDELINE for TREATING TOBACCO USE and DEPENDENCE

- Released May 7, 2008
- Sponsored by the Agency for Healthcare Research and Quality of the U.S. Public Health Service with
  - American Legacy Foundation
  - Centers for Disease Control and Prevention
  - National Cancer Institute
  - National Institute for Drug Addiction
  - National Heart, Lung, & Blood Institute
  - Robert Wood Johnson Foundation
  - University of Wisconsin

The 2008 Guideline is a distillation of more than 8,700 research articles.

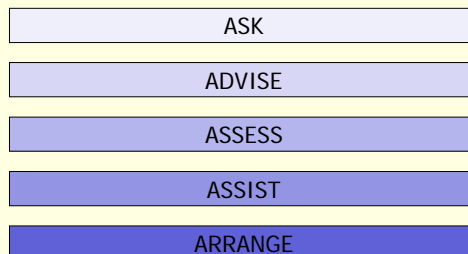
[www.surgeongeneral.gov/tobacco/](http://www.surgeongeneral.gov/tobacco/)

## EFFECTS of CLINICIAN INTERVENTIONS



Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline.* Rockville, MD: USDHHS, PHS.

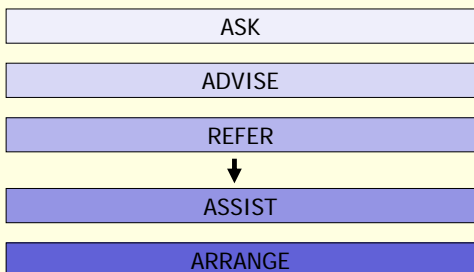
## Comprehensive Intervention: The 5 A's



HANDOUT

Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline.* Rockville, MD: USDHHS, PHS.

## Brief Intervention: Ask-Advise-Refer



Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline.* Rockville, MD: USDHHS, PHS.

## The 5 A's: ASK

- **ASK** all patients about tobacco use
  - Record on medical chart, flag chart for future reference, and follow-up at future visits
  - "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."
  - "[Condition X] often is caused or worsened by smoking. Do you, or does someone in your household smoke?"
  - Ask in a way that promotes disclosure

## The 5 A's: Ask (cont'd)

Create a questionnaire:

- A. I have never smoked, or I have smoked less than 100 cig/life
- B. I stopped smoking **before** I became pregnant and am not smoking now
- C. I stopped smoking **after** I became pregnant and am not smoking now
- D. I smoke some now but have cut back since I found out I was pregnant
- E. I smoke regularly now, the same as I have

## How To Respond

- If A, congratulate
- If B or C, congratulate and reinforce quit
- If D or E:
  - Classify as "smoker"
  - Document status in chart
  - Proceed with intervention
    - Advise and Refer (brief intervention)
    - Advise, Assess, Assist, Arrange (5 A's)

## 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 the health of you and your baby, 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."
  - "Quitting early in pregnancy will provide the greatest benefit to you and your baby."

## How to Advise: Pregnant Women

- Review potential negative effects to mother, fetus and birth process
- Review benefits for mother and child
- Help the patient to identify a powerful, internal reason to quit
  - What other reasons may there be for quitting?
- Do not:
  - Scare
  - Shame
  - Intimidate

## 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

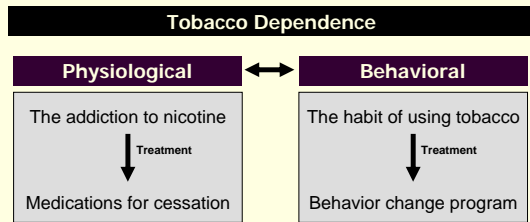
Number of sessions	Estimated quit rate*
0 to 1	12.4%
2 to 3	16.3%
4 to 8	20.9%
More than 8	24.7%

\* 5 months (or more) postcessation

**PROVIDE ASSISTANCE THROUGHOUT THE QUIT ATTEMPT**

Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: USDHHS, PHS (p. 86).

## TOBACCO DEPENDENCE: A 2-PART PROBLEM



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

## CPG Recommendations: Medications

“Numerous effective medications are available for tobacco dependence, and clinicians should encourage their use by all patients attempting to quit smoking—except when medically contraindicated or with specific populations for which there is insufficient evidence of effectiveness (i.e., pregnant women, smokeless tobacco users, light smokers, and adolescents).”

Strength of evidence = A

Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: USDHHS, PHS (p. vii).

## CPG Recommendations: Effectiveness of Medications in Pregnant Women

- Lack of sufficiently-powered, conclusive studies
- Panel did not make a recommendation regarding medication use during pregnancy

Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: USDHHS, PHS (p. 170).

## CPG Recommendations: Safety of Medications in Pregnant Women

“Nicotine most likely does have adverse effects on the fetus during pregnancy. Although the use of NRT exposes pregnant women to nicotine, smoking exposes them to nicotine plus numerous other chemicals that are injurious to the woman and fetus. These concerns must be considered in the context of inconclusive evidence that cessation medications boost abstinence rates in pregnant smokers.”

Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: USDHHS, PHS (p. 172).

## CPG Recommendations: Psychosocial Interventions for Pregnant Women

“Because of the serious risks of smoking to the pregnant smoker and the fetus, whenever possible pregnant smokers should be offered person-to-person psychosocial interventions that exceed minimal advice to quit.”

Strength of evidence = A

Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: USDHHS, PHS (p. 165).

## CPG Recommendations: Psychosocial Interventions for Pregnant Women (cont'd)

“Although abstinence early in pregnancy will produce the greatest benefits to the fetus and expectant mother, quitting at any point in pregnancy can yield benefits. Therefore clinicians should offer effective tobacco dependence interventions to pregnant smokers at the first prenatal visit as well as throughout the course of pregnancy.”

Strength of evidence = B

Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: USDHHS, PHS (p. 165).

## CPG Recommendations: Psychosocial Interventions for Pregnant Women (cont'd)

Pregnant smokers	Number of arms	Estimated odds ratio (95% CI)	Estimated abstinence rate (95% CI)
Usual care	2	1.0	8.6
Self-help materials	2	1.9 (1.2-2.9)	15.0 (10.1-21.6)

Pregnant smokers	Number of arms	Estimated odds ratio (95% CI)	Estimated abstinence rate (95% CI)
Usual care	8	1.0	7.6
Psycho-social intervention	9	1.8 (1.4-2.3)	13.3 (9.0-19.4)

Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: USDHHS, PHS (pp. 166, 169).

## Examples of Effective Psychosocial Interventions with Pregnant Smokers

- Physician advice regarding smoking-related risks (2-3 min), videotape with information on risks, barriers, and tips for quitting, midwife counseling in one 10-min session, self-help manual, and follow-up letters
- Pregnancy-specific self-help manuals and one 10-min counseling session with a health educator
- One 90-min counseling session with bimonthly telephone follow-up calls during pregnancy and after delivery

Fiore et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: USDHHS, PHS (p. 167).

## Ask-Advise-Refer (brief intervention): Your Role

- Can be done in fewer than 3 minutes
- Do not feel obligated to conduct the entire cessation program, just start it!
- Begin the process by:
  - **Asking** patients to about tobacco use
  - **Advising** patients to quit
    - Recommend a medication, if appropriate
  - **Referring** patients to other resources



## “Can’t I Just Cut Back?”

- No clinical evidence of efficacy
- Most individuals who cut back compensate by smoking differently
- Many quickly return to baseline
- No way to know effect of even one cigarette on fetus – there is no safe level of tobacco use

“Quitting smoking is like learning any new behavior. It is important to create a plan and stick to it.”

## Where to Refer: Behavior Change Programs

- **1 800 QUIT NOW**
- All products have free behavior change programs that accompany product
- Hospital/Community
  - Workplace group programs
  - Hospital-based group programs
- Healthcare professional specialist
- Websites:
  - [www.quitnet.com](http://www.quitnet.com)
  - [www.acog.org](http://www.acog.org)



## Where to Refer: Social Support

- Encourage creation of support network:
  - Formal program for quitting
  - On line support: [www.quitnet.com](http://www.quitnet.com)
    - Chat rooms for pregnant smokers
  - Family
  - Friends
  - Co-workers
  - Church group

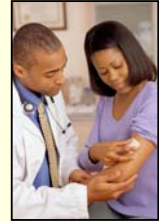
## An Important Consideration: Influence of Family Members

- Does husband/significant other smoke?
- Does mother or grandmother smoke?
  - What was her experience while pregnant?
- Are there other smokers in household?



## Where to Refer: Cessation Medications

- Non prescription:
  - Nicotine transdermal patch
  - Nicotine gum
  - Nicotine lozenge
- Prescription:
  - Nicotine transdermal patch
  - Nicotine oral Inhaler
  - Nicotine nasal spray
  - Bupropion SR
  - Varenicline

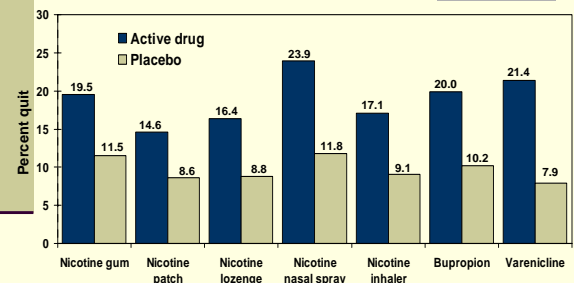


HANDOUT

## Why Use a Cessation Medication?

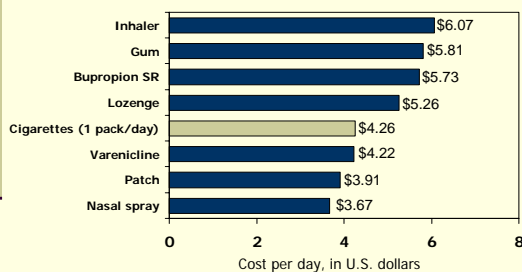
- Withdrawal is substantial in most smokers
  - Irritability
  - Anxiousness
  - Impatience
  - Restlessness
- If "Cold Turkey":
  - Most return to smoking to relieve withdrawal
- Medications:
  - Substantially reduce or eliminate withdrawal so quitter can focus on behavior change
  - Approximately double chances of quitting

## LONG-TERM ( $\geq 6$ 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*; Cahill et al. (2007). *Cochrane Database Syst Rev*.

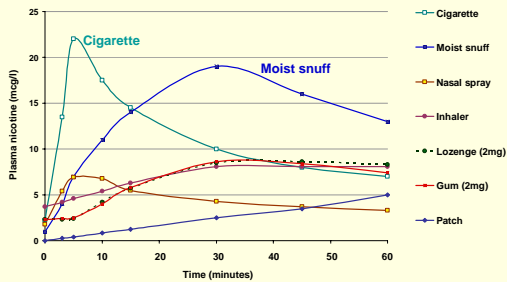
## COMPARATIVE DAILY COSTS of PHARMACOTHERAPY



## Nicotine from Smoking vs. NRT

- Smoking:
  - Rapid administration via lungs
    - Peak: 11 seconds
  - Frequent consumption of cigarette
  - High dose of nicotine
- NRT Use:
  - Slow to very slow administration (oral/skin)
    - Peak 15 min to 6 hours
  - Less frequent administration
  - Much lower dose

## PLASMA NICOTINE CONCENTRATIONS for NICOTINE-CONTAINING PRODUCTS



With permission, from *Rx for Change: Clinician-Assisted Tobacco Cessation*. <http://rxforchange.ucsf.edu>

## Medication Recommendations

- Behavioral interventions: first line of treatment
- Pregnancy classifications for medications:
  - Zyban: Category C
  - Chantix: Category C
  - Rx NRT: Category D
- If NRT is chosen:
  - Clearly discuss pros/cons
    - Document
  - Monitor blood levels throughout
  - Have frequent follow up

## If NRT is Chosen:

- Generally use with woman smoking > 20/day
- Ad libitum forms (gum, lozenge, inhaler)
- Use only PRN to deal with cravings
- If using patch:
  - Use only while awake (16 hours)
  - Use for shortest period possible
  - Downside: continuous exposure
- Strongly encourage continued participation in behavior change programs

## A Call To Action!

- Integrate tobacco cessation interventions into routine patient care for ALL patients of ALL ages
  - Pregnancy opens a window of opportunity to intervene with a smoker
- You can have a profound effect on reducing the negative effects of tobacco:
  - Make **ASK** a vital sign
  - Make **ADVISE** a priority for all users
  - Make **REFER** a common practice

## Questions?

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## 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?

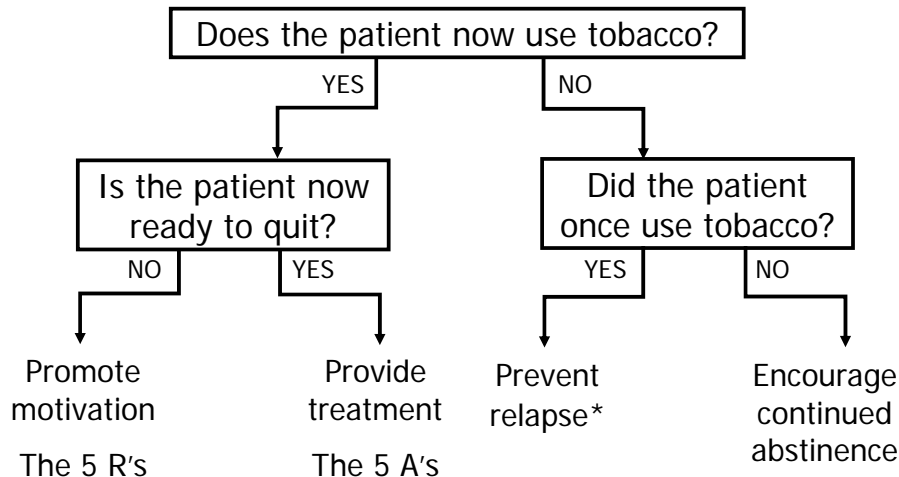
## STEP Two: Strongly ADVISE to Quit

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



### ✓ 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.



## 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
<b>Pharmacokinetic Interactions</b>	
Alprazolam (Xanax)	<ul style="list-style-type: none"> <li>Conflicting data on significance of a PK interaction. Possible ↓ plasma concentrations (up to 50%); ↓ half-life (35%).</li> </ul>
Bendamustine (Treanda)	<ul style="list-style-type: none"> <li>Metabolized by CYP1A2. Manufacturer recommends caution in using in smokers due to likely ↓ bendamustine concentrations, with ↑ concentrations of its two active metabolites.</li> </ul>
Caffeine	<ul style="list-style-type: none"> <li>↑ Metabolism (induction of CYP1A2); ↑ clearance (56%).</li> <li>Likely ↑ caffeine levels after cessation.</li> </ul>
Chlorpromazine (Thorazine)	<ul style="list-style-type: none"> <li>↓ Area under the curve (AUC) (36%) and serum concentrations (24%).</li> <li>↓ Sedation and hypotension possible in smokers; smokers may need ↑ dosages.</li> </ul>
Clozapine (Clozaril)	<ul style="list-style-type: none"> <li>↑ Metabolism (induction of CYP1A2); ↓ plasma concentrations (18%).</li> <li>↑ levels upon cessation may occur; closely monitor drug levels and reduce dose as required to avoid toxicity.</li> </ul>
Erlotinib (Tarceva)	<ul style="list-style-type: none"> <li>↑ Clearance (24%); ↓ trough serum concentrations (2-fold).</li> </ul>
Flecainide (Tambocor)	<ul style="list-style-type: none"> <li>↑ Clearance (61%); ↓ trough serum concentrations (25%).</li> <li>Smokers may need ↑ dosages.</li> </ul>
Fluvoxamine (Luvox)	<ul style="list-style-type: none"> <li>↑ Metabolism (induction of CYP1A2); ↑ clearance (24%); ↓ AUC (31%); ↓ plasma concentrations (32%).</li> <li>Dosage modifications not routinely recommended but smokers may need ↑ dosages.</li> </ul>
Haloperidol (Haldol)	<ul style="list-style-type: none"> <li>↑ Clearance (44%); ↓ serum concentrations (70%).</li> </ul>
Heparin	<ul style="list-style-type: none"> <li>Mechanism unknown but ↑ clearance and ↓ half-life are observed. Smoking has prothrombotic effects.</li> <li>Smokers may need ↑ dosages due to PK and PD interactions.</li> </ul>
Insulin, subcutaneous	<ul style="list-style-type: none"> <li>Possible ↓ insulin absorption secondary to peripheral vasoconstriction; smoking may cause release of endogenous substances that cause insulin resistance.</li> <li>PK &amp; PD interactions likely not clinically significant; smokers may need ↑ dosages.</li> </ul>
Irinotecan (Camptosar)	<ul style="list-style-type: none"> <li>↑ 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.</li> <li>Smokers may need ↑ dosages.</li> </ul>
Mexiletine (Mexitol)	<ul style="list-style-type: none"> <li>↑ Clearance (25%; via oxidation and glucuronidation); ↓ half-life (36%).</li> </ul>
Olanzapine (Zyprexa)	<ul style="list-style-type: none"> <li>↑ Metabolism (induction of CYP1A2); ↑ clearance (98%); ↓ serum concentrations (12%).</li> <li>Dosage modifications not routinely recommended but smokers may require ↑ dosages.</li> </ul>
Propranolol (Inderal)	<ul style="list-style-type: none"> <li>↑ Clearance (77%; via side chain oxidation and glucuronidation)</li> </ul>
Ropinirole (Requip)	<ul style="list-style-type: none"> <li>↓ C<sub>max</sub> (38%) and AUC (30%) in study with patients with restless legs syndrome.</li> <li>Smokers may need ↑ dosages.</li> </ul>
Tacrine (Cognex)	<ul style="list-style-type: none"> <li>↑ Metabolism (induction of CYP1A2); ↓ half-life (50%); serum concentrations three-fold lower.</li> <li>Smokers may need ↑ dosages.</li> </ul>
Theophylline (Theo Dur, etc.)	<ul style="list-style-type: none"> <li>↑ Metabolism (induction of CYP1A2); ↑ clearance (58–100%); ↓ half-life (63%).</li> <li>Levels should be monitored if smoking is initiated, discontinued, or changed.</li> <li>↑ Clearance with second-hand smoke exposure.</li> <li>Maintenance doses are considerably higher in smokers.</li> </ul>
Tricyclic antidepressants (e.g., imipramine, nortriptyline)	<ul style="list-style-type: none"> <li>Possible interaction with tricyclic antidepressants in the direction of ↓ blood levels, but the clinical importance is not established.</li> </ul>
Tizanidine (Zanaflex)	<ul style="list-style-type: none"> <li>↓ AUC (30–40%) and ↓ half-life (10%) observed in male smokers.</li> </ul>
<b>Pharmacodynamic Interactions</b>	
Benzodiazepines (diazepam, chlordiazepoxide)	<ul style="list-style-type: none"> <li>↓ Sedation and drowsiness, possibly caused by nicotine stimulation of central nervous system.</li> </ul>
Beta-blockers	<ul style="list-style-type: none"> <li>Less effective antihypertensive and heart rate control effects; might be caused by nicotine-mediated sympathetic activation.</li> <li>Smokers may need ↑ dosages.</li> </ul>
Corticosteroids, inhaled	<ul style="list-style-type: none"> <li>Asthmatic smokers may have less of a response to inhaled corticosteroids.</li> </ul>
Hormonal contraceptives	<ul style="list-style-type: none"> <li>↑ Risk of cardiovascular adverse effects (e.g., stroke, myocardial infarction, thromboembolism) in women who smoke and use oral contraceptives. Ortho Evra patch users shown to have 2-fold ↑ risk of venous thromboembolism compared to oral contraceptive users, likely due to ↑ estrogen exposure (60% higher levels).</li> <li>↑ Risk with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women age 35 and older.</li> </ul>
Opioids (propoxyphene, pentazocine)	<ul style="list-style-type: none"> <li>↓ Analgesic effect; smoking may ↑ the metabolism of propoxyphene (15–20%) and pentazocine (40%). Mechanism unknown.</li> <li>Smokers may need ↑ opioid dosages for pain relief.</li> </ul>

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



# PHARMACOLOGIC PRODUCT GUIDE: FDA-APPROVED MEDICATIONS

		NICOTINE REPLACEMENT THERAPY (NRT) FORMULATIONS				BUPROPION SR	VARENICLINE
		GUM	LOZENGE	TRANSDERMAL PATCH	NASAL SPRAY		
PRODUCT	Nicorette <sup>1</sup> , Generic OTC 2 mg, 4 mg; original, cinnamon, fruit, mint, orange	Commit <sup>1</sup> , Generic OTC 2 mg, 4 mg cherry, mint	Nicoderm CQ <sup>1</sup> , Generic <sup>2</sup> OTC (Nicoderm CQ, generic) Rx (generic) 7 mg, 14 mg, 21 mg (24-hour release)	Nicotrol NS <sup>3</sup> Rx Metered spray 0.5 mg nicotine in 50 µL aqueous nicotine solution	Nicotrol Inhaler <sup>3</sup> Rx 10 mg cartridge delivers 4 mg inhaled nicotine vapor	Zyban <sup>1</sup> , Generic Rx 150 mg sustained-release tablet	Chantix <sup>3</sup> Rx 0.5 mg, 1 mg tablet
PRECAUTIONS	<ul style="list-style-type: none"> <li>▪ Pregnancy category: not applicable for OTC formulations</li> <li>▪ Recent (≤ 2 weeks) myocardial infarction</li> <li>▪ Serious underlying arrhythmias</li> <li>▪ Serious or worsening angina pectoris</li> <li>▪ Temporomandibular joint disease</li> </ul>	<ul style="list-style-type: none"> <li>▪ Pregnancy category: not applicable for OTC formulations</li> <li>▪ Recent (≤ 2 weeks) myocardial infarction</li> <li>▪ Serious underlying arrhythmias</li> <li>▪ Serious or worsening angina pectoris</li> </ul>	<ul style="list-style-type: none"> <li>▪ Pregnancy category: D for prescription patch, not applicable for OTC formulations</li> <li>▪ Recent (≤ 2 weeks) myocardial infarction</li> <li>▪ Serious underlying arrhythmias</li> <li>▪ Serious or worsening angina pectoris</li> </ul>	<ul style="list-style-type: none"> <li>▪ Pregnancy category: D</li> <li>▪ Recent (≤ 2 weeks) myocardial infarction</li> <li>▪ Serious underlying arrhythmias</li> <li>▪ Serious or worsening angina pectoris</li> <li>▪ Underlying chronic nasal disorders (rhinitis, nasal polyps, sinusitis)</li> <li>▪ Severe reactive airway disease</li> </ul>	<ul style="list-style-type: none"> <li>▪ Pregnancy category: D</li> <li>▪ Recent (≤ 2 weeks) myocardial infarction</li> <li>▪ Serious underlying arrhythmias</li> <li>▪ Serious or worsening angina pectoris</li> <li>▪ Bronchospastic disease</li> </ul>	<ul style="list-style-type: none"> <li>▪ Pregnancy category: C</li> <li>▪ Concomitant therapy with medications or medical conditions known to lower the seizure threshold</li> <li>▪ Severe hepatic cirrhosis</li> </ul> <p><b>Contraindications:</b></p> <ul style="list-style-type: none"> <li>▪ Seizure disorder</li> <li>▪ Concomitant bupropion (e.g., Wellbutrin) therapy</li> <li>▪ Current or prior diagnosis of bulimia or anorexia nervosa</li> <li>▪ Simultaneous abrupt discontinuation of alcohol or sedatives (including benzodiazepines)</li> <li>▪ MAO inhibitor therapy in previous 14 days</li> </ul>	<ul style="list-style-type: none"> <li>▪ Pregnancy category: C</li> <li>▪ Severe renal impairment (dosage adjustment is necessary)</li> </ul> <p><b>Warnings:</b></p> <ul style="list-style-type: none"> <li>▪ Neuropsychiatric symptoms (behavior changes, agitation, depressed mood, suicidal ideation or behavior)</li> <li>▪ Safety and efficacy have not been established in patients with serious psychiatric illness</li> </ul>
DOSING	<p>≥25 cigarettes/day: 4 mg &lt;25 cigarettes/day: 2 mg</p> <p>Week 1–6: 1 piece q 1–2 hours</p> <p>Week 7–9: 1 piece q 2–4 hours</p> <p>Week 10–12: 1 piece q 4–8 hours</p> <ul style="list-style-type: none"> <li>▪ Maximum, 24 pieces/day</li> <li>▪ Chew each piece slowly</li> <li>▪ Park between cheek and gum when peppery or tingling sensation appears (~15–30 chews)</li> <li>▪ Resume chewing when taste or tingle fades</li> <li>▪ Repeat chew/park steps until most of the nicotine is gone (taste or tingle does not return; generally 30 min)</li> <li>▪ Park in different areas of mouth</li> <li>▪ No food or beverages 15 min before or during use</li> <li>▪ Duration: up to 12 weeks</li> </ul>	<p>1<sup>st</sup> cigarette ≤30 minutes after waking: 4 mg 1<sup>st</sup> cigarette &gt;30 minutes after waking: 2 mg</p> <p>Week 1–6: 1 lozenge q 1–2 hours</p> <p>Week 7–9: 1 lozenge q 2–4 hours</p> <p>Week 10–12: 1 lozenge q 4–8 hours</p> <ul style="list-style-type: none"> <li>▪ Maximum, 20 lozenges/day</li> <li>▪ Allow to dissolve slowly (20–30 minutes)</li> <li>▪ Nicotine release may cause a warm, tingling sensation</li> <li>▪ Do not chew or swallow</li> <li>▪ Occasionally rotate to different areas of the mouth</li> <li>▪ No food or beverages 15 minutes before or during use</li> <li>▪ Duration: up to 12 weeks</li> </ul>	<p>&gt;10 cigarettes/day: 21 mg/day x 4 weeks (generic) 6 weeks (Nicoderm CQ)</p> <p>14 mg/day x 2 weeks 7 mg/day x 2 weeks</p> <p>≤10 cigarettes/day: 14 mg/day x 6 weeks 7 mg/day x 2 weeks</p> <ul style="list-style-type: none"> <li>▪ May wear patch for 16 hours if patient experiences sleep disturbances (remove at bedtime)</li> <li>▪ Duration: 8–10 weeks</li> </ul>	<p>1–2 doses/hour (8–40 doses/day)</p> <p>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"> <li>▪ Maximum – 5 doses/hour – 40 doses/day</li> <li>▪ For best results, initially use at least 8 doses/day</li> <li>▪ Patients should not sniff, swallow, or inhale through the nose as the spray is being administered</li> <li>▪ Duration: 3–6 months</li> </ul>	<p>6–16 cartridges/day Individualize dosing; initially use 1 cartridge q 1–2 hours</p> <ul style="list-style-type: none"> <li>▪ Best effects with continuous puffing for 20 minutes</li> <li>▪ Nicotine in cartridge is depleted after 20 minutes of active puffing</li> <li>▪ Patient should inhale into back of throat or puff in short breaths</li> <li>▪ Do NOT inhale into the lungs (like a cigarette) but “puff” as if lighting a pipe</li> <li>▪ Open cartridge retains potency for 24 hours</li> <li>▪ Duration: up to 6 months</li> </ul>	<p>150 mg po q AM x 3 days, then increase to 150 mg po bid</p> <ul style="list-style-type: none"> <li>▪ Do not exceed 300 mg/day</li> <li>▪ Treatment should be initiated while patient is still smoking</li> <li>▪ Set quit date 1–2 weeks after initiation of therapy</li> <li>▪ Allow at least 8 hours between doses</li> <li>▪ Avoid bedtime dosing to minimize insomnia</li> <li>▪ Dose tapering is not necessary</li> <li>▪ Can be used safely with NRT</li> <li>▪ Duration: 7–12 weeks, with maintenance up to 6 months in selected patients</li> </ul>	<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"> <li>▪ Patients should begin therapy 1 week prior to quit date</li> <li>▪ Take dose after eating with a full glass of water</li> <li>▪ Dose tapering is not necessary</li> <li>▪ Nausea and insomnia are side effects that are usually temporary</li> <li>▪ Duration: 12 weeks; an additional 12 week course may be used in selected patients</li> </ul>

NICOTINE REPLACEMENT THERAPY (NRT) FORMULATIONS							BUPROPION SR	VARENICLINE
GUM	LOZENGE	TRANSDERMAL PATCH	NASAL SPRAY	ORAL INHALER				
ADVERSE EFFECTS	<ul style="list-style-type: none"> <li>▪ Mouth/jaw soreness</li> <li>▪ Hiccups</li> <li>▪ Dyspepsia</li> <li>▪ Hypersalivation</li> <li>▪ Effects associated with incorrect chewing technique:               <ul style="list-style-type: none"> <li>– Lightheadedness</li> <li>– Nausea/vomiting</li> <li>– Throat and mouth irritation</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>▪ Nausea</li> <li>▪ Hiccups</li> <li>▪ Cough</li> <li>▪ Heartburn</li> <li>▪ Headache</li> <li>▪ Flatulence</li> <li>▪ Insomnia</li> </ul>	<ul style="list-style-type: none"> <li>▪ Local skin reactions (erythema, pruritus, burning)</li> <li>▪ Headache</li> <li>▪ Sleep disturbances (insomnia, abnormal/vivid dreams); associated with nocturnal nicotine absorption</li> </ul>	<ul style="list-style-type: none"> <li>▪ Nasal and/or throat irritation (hot, peppery, or burning sensation)</li> <li>▪ Rhinitis</li> <li>▪ Tearing</li> <li>▪ Sneezing</li> <li>▪ Cough</li> <li>▪ Headache</li> </ul>	<ul style="list-style-type: none"> <li>▪ Mouth and/or throat irritation</li> <li>▪ Unpleasant taste</li> <li>▪ Cough</li> <li>▪ Rhinitis</li> <li>▪ Dyspepsia</li> <li>▪ Hiccups</li> <li>▪ Headache</li> </ul>	<ul style="list-style-type: none"> <li>▪ Insomnia</li> <li>▪ Dry mouth</li> <li>▪ Nervousness/difficulty concentrating</li> <li>▪ Rash</li> <li>▪ Constipation</li> <li>▪ Seizures (risk is 1/1,000 [0.1%])</li> </ul>	<ul style="list-style-type: none"> <li>▪ Nausea</li> <li>▪ Sleep disturbances (insomnia, abnormal/vivid dreams)</li> <li>▪ Constipation</li> <li>▪ Flatulence</li> <li>▪ Vomiting</li> <li>▪ Neuropsychiatric symptoms (rare; see PRECAUTIONS, above)</li> </ul>	
ADVANTAGES	<ul style="list-style-type: none"> <li>▪ Gum use might satisfy oral cravings</li> <li>▪ Gum use might delay weight gain</li> <li>▪ Patients can titrate therapy to manage withdrawal symptoms</li> </ul>	<ul style="list-style-type: none"> <li>▪ Lozenge use might satisfy oral cravings</li> <li>▪ Lozenge use might delay weight gain</li> <li>▪ Patients can titrate therapy to manage withdrawal symptoms</li> </ul>	<ul style="list-style-type: none"> <li>▪ Provides consistent nicotine levels over 24 hours</li> <li>▪ Easy to use and conceal</li> <li>▪ Once-a-day dosing associated with fewer compliance problems</li> </ul>	<ul style="list-style-type: none"> <li>▪ Patients can titrate therapy to rapidly manage withdrawal symptoms</li> </ul>	<ul style="list-style-type: none"> <li>▪ Patients can titrate therapy to manage withdrawal symptoms</li> <li>▪ Mimics hand-to-mouth ritual of smoking (could also be perceived as a disadvantage)</li> </ul>	<ul style="list-style-type: none"> <li>▪ Easy to use; oral formulation might be associated with fewer compliance problems</li> <li>▪ Can be used with NRT</li> <li>▪ Might be beneficial in patients with depression</li> </ul>	<ul style="list-style-type: none"> <li>▪ Easy to use; oral formulation might be associated with fewer compliance problems</li> <li>▪ Offers a new mechanism of action for patients who have failed other agents</li> </ul>	
DISADVANTAGES	<ul style="list-style-type: none"> <li>▪ Gum chewing may not be socially acceptable</li> <li>▪ Gum is difficult to use with dentures</li> <li>▪ Patients must use proper chewing technique to minimize adverse effects</li> </ul>	<ul style="list-style-type: none"> <li>▪ Gastrointestinal side effects (nausea, hiccups, heartburn) might be bothersome</li> </ul>	<ul style="list-style-type: none"> <li>▪ Patients cannot titrate the dose</li> <li>▪ Allergic reactions to adhesive might occur</li> <li>▪ Patients with dermatologic conditions should not use the patch</li> </ul>	<ul style="list-style-type: none"> <li>▪ Nasal/throat irritation may be bothersome</li> <li>▪ Patients must wait 5 minutes before driving or operating heavy machinery</li> <li>▪ Patients with chronic nasal disorders or severe reactive airway disease should not use the spray</li> </ul>	<ul style="list-style-type: none"> <li>▪ Initial throat or mouth irritation can be bothersome</li> <li>▪ Cartridges should not be stored in very warm conditions or used in very cold conditions</li> <li>▪ Patients with underlying bronchospastic disease must use the inhaler with caution</li> </ul>	<ul style="list-style-type: none"> <li>▪ Seizure risk is increased</li> <li>▪ Several contraindications and precautions preclude use (see PRECAUTIONS, above)</li> </ul>	<ul style="list-style-type: none"> <li>▪ May induce nausea in up to one third of patients</li> <li>▪ Post-marketing surveillance data indicate potential for neuropsychiatric symptoms (see PRECAUTIONS, above)</li> </ul>	
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 <sup>4</sup>	2 mg: \$3.28–\$6.58 (9 pieces) 4 mg: \$4.31–\$6.58 (9 pieces)	2 mg: \$3.66–\$5.26 (9 pieces) 4 mg: \$3.66–\$5.26 (9 pieces)	\$1.90–\$3.89 (1 patch)	\$3.72 (8 doses)	\$5.29 (6 cartridges)	\$3.62–\$6.04 (2 tablets)	\$4.49–\$4.75 (2 tablets)	

<sup>1</sup> Marketed by GlaxoSmithKline.

<sup>2</sup> Transdermal patch formulation previously marketed as Habitrol.

<sup>3</sup> Marketed by Pfizer.

<sup>4</sup> Average wholesale price from Medi-Span Electronic Drug File. Indianapolis, IN: Wolters Kluwer Health, June 2008.

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.**

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