Rx for Change

Clinician-Assisted Tobacco Cessation

1

TRAINING OVERVIEW

- Epidemiology of Tobacco Use
- Nicotine Pharmacology & Principles of Addiction
- Drug Interactions with Smoking
- Assisting Patients with Quitting
- Medications for Cessation
- Patient Encounters

2

EPIDEMIOLOGY of TOBACCO USE

3

"CIGARETTE SMOKING…

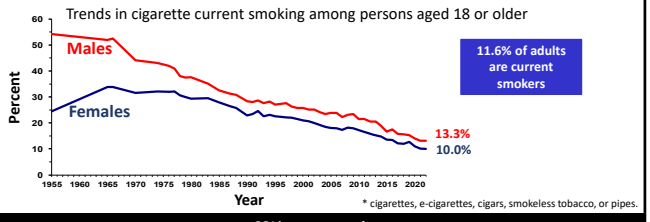
is the chief, single, avoidable cause of death in our society and the most important public health issue of our time."

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

All forms of tobacco are harmful.

4

TRENDS in ADULT SMOKING, by SEX—United States, since 1955

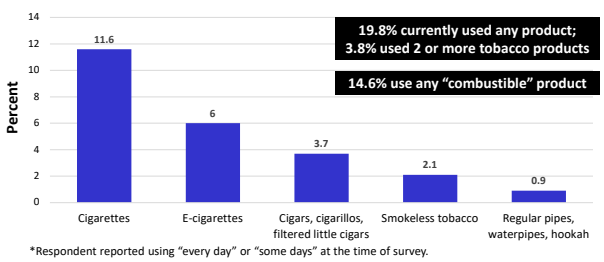


68% want to quit
53% tried to quit in the past year

Graph provided by the Centers for Disease Control and Prevention. Estimates since 1992 include some-day smoking.

5

CURRENT* ADULT USE of ANY FORM of TOBACCO or E-CIGARETTES, U.S., 2022

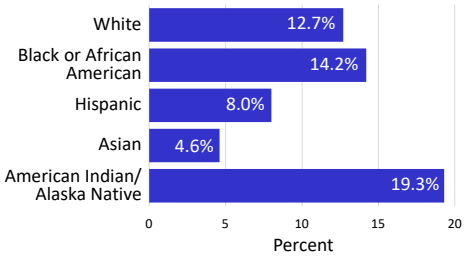


*Respondent reported using "every day" or "some days" at the time of survey.

CDC, 2022 National Health Interview Survey Highlights.

6

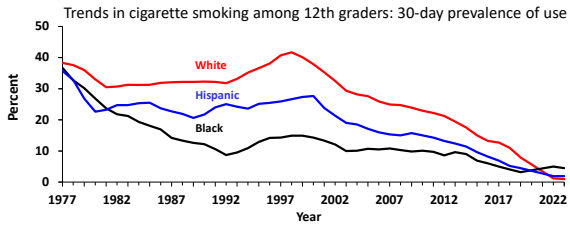
PREVALENCE of ADULT CIGARETTE SMOKING, by RACE/ETHNICITY—U.S., 2022



CDC, 2022 National Health Interview Survey Highlights.

7

TRENDS in TEEN SMOKING, by ETHNICITY—U.S., 1977–2023



Institute for Social Research, University of Michigan, Monitoring the Future Project
www.monitoringthefuture.org

8

PUBLIC HEALTH versus "BIG TOBACCO"

The biggest opponent to tobacco control efforts is the tobacco industry itself.

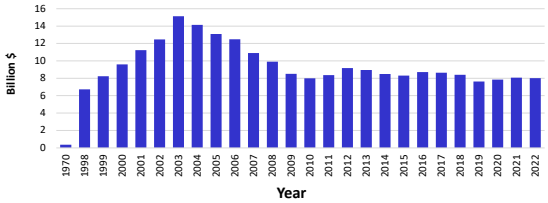
Nationally, the tobacco industry is outspending our state tobacco control funding.

For every $1 spent by the states, the tobacco industry spends $12.50 to market its products.

9

TOBACCO INDUSTRY ADVERTISING

- $8.01 billion spent in the U.S. in 2022 – $21.9 million a day



Federal Trade Commission (FTC). (2024). *Cigarette Report for 2022.*

10

The TOBACCO INDUSTRY

- For decades, the tobacco industry publicly denied the addictive nature of nicotine and the negative health effects of tobacco.
- **April 14, 1994:** Seven top executives of major tobacco companies state, under oath, that they believe nicotine is not addictive: http://www.jeffreywigand.com/7ceos.php
  - Tobacco industry documents indicate otherwise
  - Documents available at http://legacy.library.ucsf.edu
- The cigarette is a heavily engineered product, designed to maximize bioavailability of nicotine and addictive potential
- Reinventing themselves to promote non-combustible addictive products.

Profits over people.

11

An EFFECTIVE MARKETING STRATEGY: "LIGHT" CIGARETTES

The difference between Marlboro and Marlboro Lights…

an extra row of ventilation holes

Image courtesy of Mayo Clinic Nicotine Dependence Center - Research Program / Dr. Richard D. Hurt
The Marlboro and Marlboro Lights logos are registered trademarks of Philip Morris USA.

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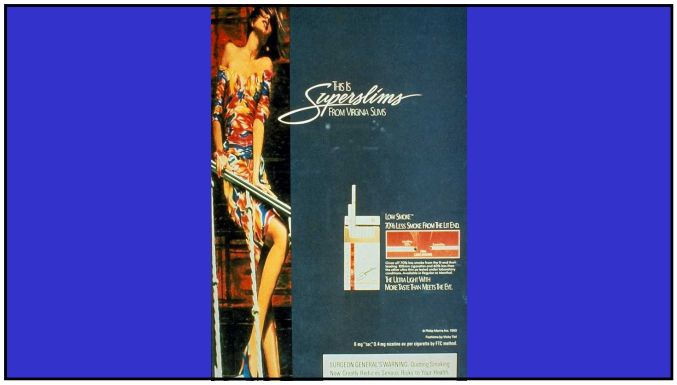

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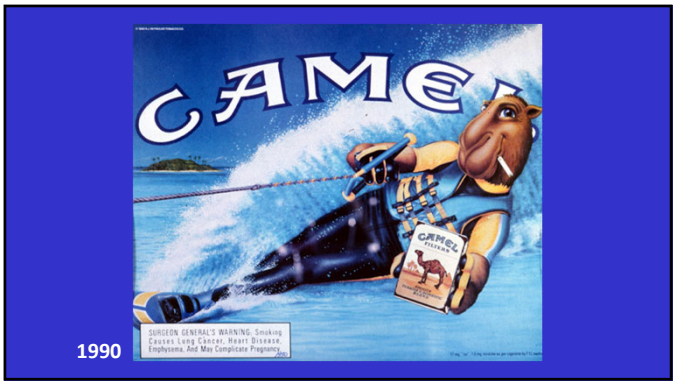

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COMPOUNDS in TOBACCO SMOKE

An estimated 8,700 compounds in tobacco smoke, including 72 proven or suspected human carcinogens

Gases

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

Particles

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

Nicotine is the addictive component of tobacco products, but it does NOT cause the ill health effects of tobacco use.

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ANNUAL U.S. DEATHS ATTRIBUTABLE to SMOKING, 2005–2009

		Percent of all smoking-attributable deaths
Cardiovascular & metabolic diseases	160,600	33%
Lung cancer	130,659	27%
Pulmonary diseases	113,100	23%
Second-hand smoke	41,280	9%
Cancers other than lung	36,000	7%
Other	1,633	<1%

TOTAL: >480,000 deaths annually

U.S. Department of Health and Human Services (USDHHS). (2014). *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General.*

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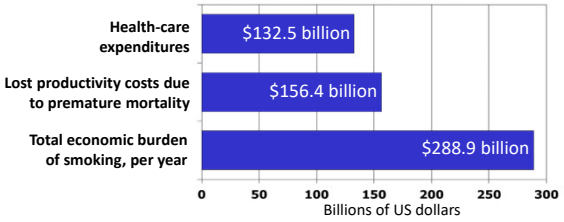
ANNUAL SMOKING-ATTRIBUTABLE ECONOMIC COSTS



Societal costs: $20.52 per pack of cigarettes smoked

U.S. Department of Health and Human Services (USDHHS). (2014). *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General.*

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2014 REPORT of the SURGEON GENERAL: HEALTH CONSEQUENCES OF SMOKING

MAJOR DISEASE-RELATED CONCLUSIONS:

- Cigarette smoking is causally linked to diseases of nearly all organs of the body, diminished health status, and harm to the fetus.
  - Additionally, many adverse effects on the body such as inflammation and impaired immune function.
- Exposure to secondhand smoke is causally linked to cancer, respiratory, and cardiovascular diseases, and to adverse effects on the health of infants and children.
- Disease risks from smoking by women have risen over the last 50 years and for many tobacco-related diseases are now equal to those for men.

U.S. Department of Health and Human Services (USDHHS). (2014). *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General.*

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HEALTH CONSEQUENCES of SMOKING

- Cancers
  - Bladder/kidney/ureter
  - Blood (acute myeloid leukemia)
  - Cervix
  - Colon/rectum
  - Esophagus/stomach
  - Liver
  - Lung
  - Oropharynx/larynx
  - Pancreatic
- Pulmonary diseases
  - Asthma
  - COPD
  - Pneumonia/tuberculosis
  - Chronic respiratory symptoms
- Cardiovascular diseases
  - Aortic aneurysm
  - Coronary heart disease
  - Cerebrovascular disease
  - Peripheral vascular disease
- Reproductive effects
  - Reduced fertility in women
  - Poor pregnancy outcomes (e.g., congenital defects, low birth weight, preterm delivery)
  - Infant mortality
- Other: cataract, diabetes (type 2), erectile dysfunction, impaired immune function, osteoporosis, periodontitis, postoperative complications, rheumatoid arthritis

U.S. Department of Health and Human Services (USDHHS). (2014). *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General.*

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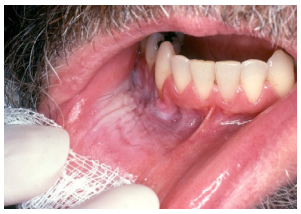
HEALTH CONSEQUENCES of SMOKELESS TOBACCO USE

Periodontal effects
- Gingival recession
- Bone attachment loss
- Dental caries

Oral leukoplakia

Cancer
- Oral cancer
- Pharyngeal cancer



Oral Leukoplakia
Image courtesy of Dr. Sol Silverman - University of California San Francisco

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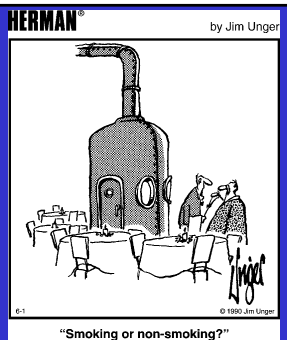

"Smoking or non-smoking?"

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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.

U.S. Department of Health and Human Services (USDHHS). (2006). *The Health Consequences of Involuntary Exposure to Tobacco Smoke: Report of the Surgeon General.*

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QUITTING: HEALTH BENEFITS

Time Since Quit Date

Circulation improves, walking becomes easier Lung function increases	2 weeks to 3 months	Lung cilia regain normal function Ability to clear lungs of mucus increases
	1 to 9 months	Coughing, fatigue, shortness of breath decrease
Excess risk of CHD decreases to half that of those who continue to smoke	1 year	
	5 years	Risk of stroke is reduced to that of people who have never smoked
Lung cancer death rate is similar to half that of those who continue to smoke 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

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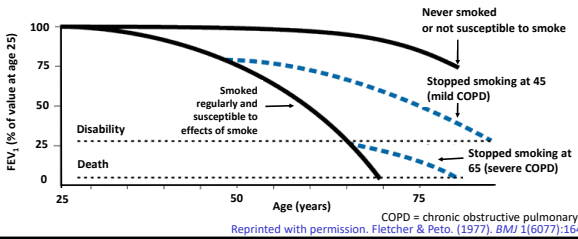
BENEFICIAL EFFECTS of QUITTING: PULMONARY EFFECTS

AT ANY AGE, there are benefits of quitting.

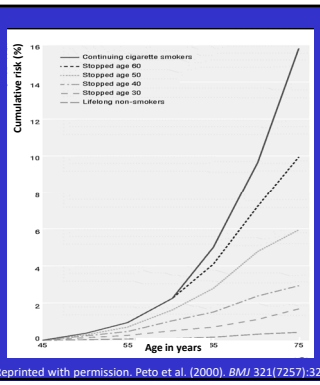


COPD = chronic obstructive pulmonary disease

Reprinted with permission. Fletcher & Peto. (1977). *BMJ* 1(6077):1645–1648.

26

Reduction in cumulative risk of death from lung cancer in men



Reprinted with permission. Peto et al. (2000). *BMJ* 321(7257):323–329.

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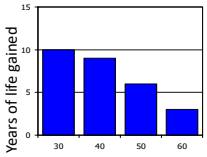
SMOKING CESSATION: REDUCED RISK of DEATH

- 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.

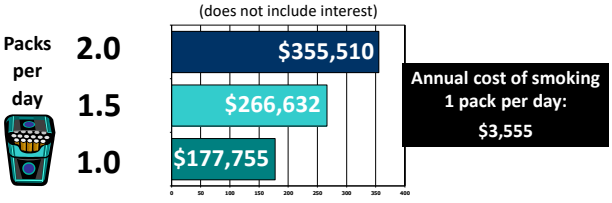
Doll et al. (2004). *BMJ* 328(7455):1519–1527.

28

FINANCIAL IMPACT of SMOKING

Buying cigarettes every day for 50 years at $9.74 per pack*

(does not include interest)



Annual cost of smoking 1 pack per day: $3,555

* Average national cost, as of January 5, 2025. Campaign for Tobacco-Free Kids. (2024). https://www.tobaccofreekids.org/assets/factsheets/0202.pdf

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EPIDEMIOLOGY of TOBACCO USE: SUMMARY

- Fewer than one in five adults are current smokers; smoking prevalence varies by sociodemographic characteristics
- Nearly half a million U.S. deaths are attributable to smoking annually
- Smoking costs the U.S. an estimated $288.9 billion annually
- For the individual, a smoking a pack-a-day costs $3555, annually, plus associated health-care costs
- At any age, there are benefits to quitting smoking
- The biggest opponent to tobacco control efforts is the tobacco industry

30

NICOTINE PHARMACOLOGY and PRINCIPLES of ADDICTION

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NICOTINE ADDICTION
U.S. Surgeon General's Report

- Cigarettes and other forms of tobacco are addicting.
- Nicotine is the drug in tobacco that causes addiction.
- The pharmacologic and behavioral processes that determine tobacco addiction are similar to those that determine addiction to drugs such as heroin and cocaine.

U.S. Department of Health and Human Services. (1988). *The Health Consequences of Smoking: Nicotine Addiction. A Report of the Surgeon General.*

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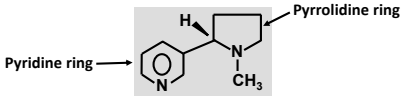
CHEMISTRY of NICOTINE



Nicotiana tabacum

Natural liquid alkaloid

Colorless, volatile base $pK_a = 8.0$

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PHARMACOLOGY

Pharmacokinetics

Effects of the body on the drug
- Absorption
- Distribution
- Metabolism
- Excretion

Pharmacodynamics

Effects of the drug on the body

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NICOTINE ABSORPTION

Absorption is pH-dependent
- In acidic media
  - Ionized ➲ poorly absorbed across membranes
- In alkaline media
  - Nonionized ➲ well absorbed across membranes
  - At physiologic pH (7.4), ~31% of nicotine is nonionized

At physiologic pH, nicotine is readily absorbed.

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NICOTINE ABSORPTION:
BUCCAL (ORAL) MUCOSA

The pH inside the mouth is 7.0.

Acidic media (limited absorption)	**Alkaline media** (significant absorption)
Cigarettes	Pipes, cigars, spit tobacco, oral nicotine products

Beverages can alter pH, affect absorption.

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NICOTINE ABSORPTION: SKIN and GASTROINTESTINAL TRACT

- Nicotine is readily absorbed through intact skin.
- Nicotine is well absorbed in the small intestine
  - Low bioavailability (20-45%) due to first-pass hepatic metabolism.

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NICOTINE ABSORPTION: LUNG

- Nicotine is "distilled" from burning tobacco
- Carried in tar droplets to the lungs
- Nicotine is rapidly absorbed across respiratory epithelium
  - Lung pH = 7.4
  - Large alveolar surface area
  - Extensive capillary system
- Approximately 1-2 mg of nicotine is absorbed from each cigarette

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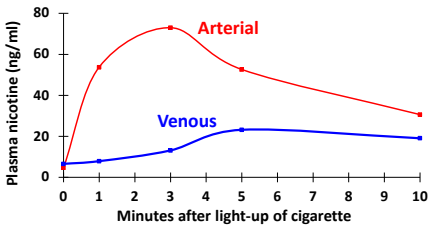
NICOTINE DISTRIBUTION



Nicotine reaches the brain within 10–20 seconds.

Henningfield et al. (1993). *Drug Alcohol Depend* 33:23–29.

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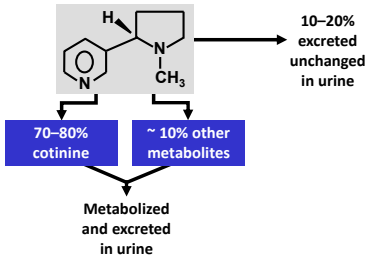
NICOTINE METABOLISM



Adapted and reprinted with permission. Benowitz et al. (1994). *J Pharmacol Exp Ther* 268:296–303.

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NICOTINE EXCRETION

- Half-life
  - Nicotine $t_{½}$ = 2 hr
  - Cotinine $t_{½}$ = 16 hr
- Excretion
  - Occurs through kidneys (pH dependent; ↑ with acidic pH)
  - Through breast milk

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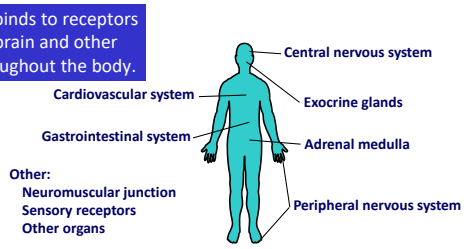
NICOTINE PHARMACODYNAMICS

Nicotine binds to receptors in the brain and other sites throughout the body.



Nicotine has predominantly stimulatory effects.

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NICOTINE PHARMACODYNAMICS (cont'd)

Central nervous system
- Pleasure
- Arousal, enhanced vigilance
- Improved task performance
- Anxiety relief

Cardiovascular system
- ↑ Heart rate
- ↑ Cardiac output
- ↑ Blood pressure
- Coronary vasoconstriction
- Cutaneous vasoconstriction

Other
- Appetite suppression
- Increased metabolic rate
- Skeletal muscle relaxation

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NEUROCHEMICAL and RELATED EFFECTS of NICOTINE

NICOTINE		
	→ Dopamine	→ Pleasure, appetite suppression
	→ Norepinephrine	→ Arousal, appetite suppression
	→ Acetylcholine	→ Arousal, cognitive enhancement
	→ Glutamate	→ Learning, memory enhancement
	→ Serotonin	→ Mood modulation, appetite suppression
	→ β-Endorphin	→ Reduction of anxiety and tension
	→ GABA	→ Reduction of anxiety and tension

Benowitz. (2008). *Clin Pharmacol Ther* 83:531–541.

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WHAT IS ADDICTION?

"Compulsive drug use, without medical purpose, in the face of negative consequences"

Alan I. Leshner, Ph.D.
Former Director, National Institute on Drug Abuse
National Institutes of Health

Nicotine addiction is a chronic condition with a biological basis.

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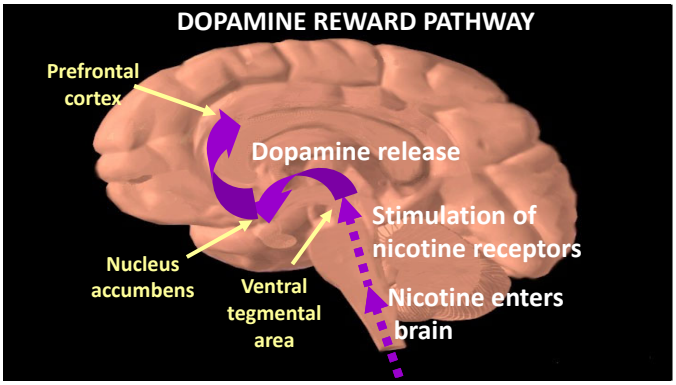

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CHRONIC ADMINISTRATION of NICOTINE: EFFECTS on the BRAIN

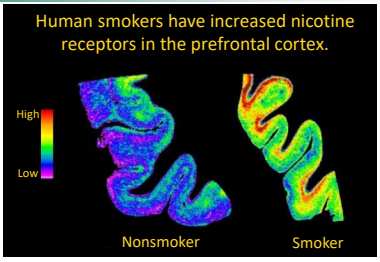
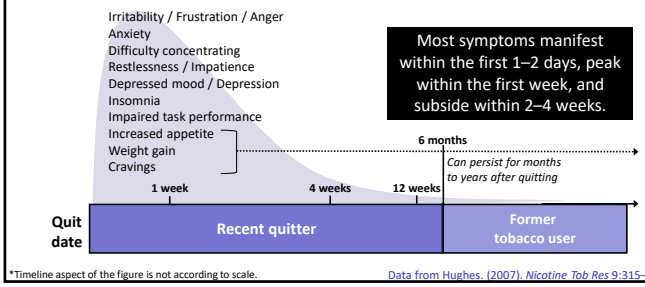


Image courtesy of George Washington University / Dr. David C. Perry
Perry et al. (1999) *J Pharmacol Exp Ther* 289:1545–1552.

47

NICOTINE WITHDRAWAL SYMPTOMS: Time Course*



*Timeline aspect of the figure is not according to scale.

Data from Hughes. (2007). *Nicotine Tob Res* 9:315–327.

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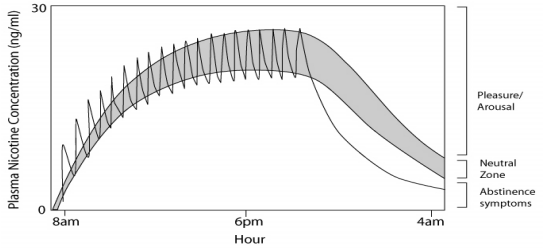
NICOTINE ADDICTION CYCLE



Reprinted with permission. Benowitz. (1992). *Med Clin N Am* 2:415–437.

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NICOTINE ADDICTION

- Tobacco users maintain a minimum serum nicotine concentration in order to:
  - Prevent withdrawal symptoms
  - Maintain pleasure/arousal
  - Modulate mood
- Users self-titrate nicotine intake by:
  - Smoking/dipping/vaping more frequently
  - Smoking/vaping more intensely

Benowitz. (2008). *Clin Pharmacol Ther* 83:531–541.

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ASSESSING NICOTINE DEPENDENCE

Fagerström Test for Nicotine Dependence (FTND)

- Developed in 1978 (8 items); revised in 1991 (6 items)
- Most common research measure of nicotine dependence; sometimes used in clinical practice
- Responses coded such that higher scores suggest higher levels of dependence
- Scores range from 0 to 10; score of greater than 5 suggest substantial dependence

Heatherton et al. (1991). *British Journal of Addiction* 86:1119–1127.

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FACTORS CONTRIBUTING to TOBACCO USE

Individual
- Sociodemographics
- Genetic predisposition
- Coexisting medical conditions

Tobacco Use

Pharmacology
- Alleviation of withdrawal symptoms
- Weight control
- Pleasure, mood modulation

Environment
- Tobacco advertising
- Conditioned stimuli
- Social interactions

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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.

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NICOTINE PHARMACOLOGY and ADDICTION: SUMMARY

- Tobacco products are effective delivery systems for the drug nicotine.
- Nicotine is a highly addictive drug that induces a constellation of pharmacologic effects, including activation of the dopamine reward pathway in the brain.
- Tobacco use is complex, involving the interplay of a wide range of factors.
- Treatment of tobacco use and dependence requires a multifaceted treatment approach.

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DRUG INTERACTIONS with TOBACCO SMOKE

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PHARMACOKINETIC DRUG INTERACTIONS with TOBACCO SMOKE

Drugs that may have a *decreased effect* due to induction of CYP1A2:

- Caffeine
- Clozapine
- Erlotinib
- Fluvoxamine
- Irinotecan*
- Haloperidol
- Olanzapine
- Pirfenidone
- Pomalidomide
- Riociguat
- Ropinirole
- Tasimelteon
- Theophylline

*induction of glucuronidation

Smoking cessation will reverse these effects.

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DRUG INTERACTION: TOBACCO SMOKE and CAFFEINE

- Constituents in tobacco smoke induce CYP1A2 enzymes, which metabolize caffeine
  - Caffeine levels increase ~56% upon quitting
- Challenges:
  - Nicotine withdrawal effects might be enhanced by increased caffeine levels
  - Insomnia can be due to ↑ caffeine levels or a side effect of a smoking cessation drug (e.g., varenicline or bupropion)
- Decrease caffeine intake (e.g., roughly half) when quitting
- For individuals with a typical bedtime, suggest eliminating caffeine by early afternoon

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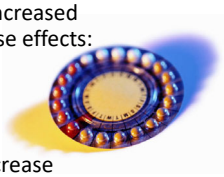
PHARMACODYNAMIC DRUG INTERACTIONS with TOBACCO SMOKE

Individuals who smoke and 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.

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DRUG INTERACTIONS WITH TOBACCO SMOKE

Many interactions between tobacco smoke and medications have been identified. 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 response to those drugs. Most PK interactions with smoking result from induction of hepatic cytochrome P450 enzymes (primarily CYP1A2). People who smoke may require higher doses of medications that are CYP1A2 substrates. Upon cessation, dose reductions might be required. 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 a person with any level of smoking is susceptible to the same degree of interaction. **The most clinically significant interactions appear in the shaded rows. Commonly available brand names are shown in parentheses.**

Drug/Class	Mechanism of Interaction and Effects
Pharmacokinetic Interactions	
Alprazolam (Xanax®)	• Conflicting data on significance, but possible ↓ plasma concentrations (up to 50%); ↓ half-life (35%).
Caffeine	• ↑ Metabolism (induction of CYP1A2); ↑ clearance (56%). • Caffeine levels likely ↑ after cessation; recommend reduction in caffeine upon cessation.
Cilostazol	• ↓ Plasma concentrations (by 20%).
Chlorpromazine (Thorazine®)	• ↓ AUC (36%)↓ plasma concentrations (by 24%). • ↑ Levels upon cessation have been reported causing sedation and hypotension.
Clopidogrel (Plavix®)	• ↑ Metabolism (induction of CYP1A2) of clopidogrel to its active metabolite. • Clopidogrel's effects may be enhanced in smokers (≥10 cigarettes/day); may be dependent on CYP1A2 genotype; might also ↑ risk of bleeding. • Smoking cessation should still be recommended in the at-risk populations needing clopidogrel.
Clozapine (Clozaril®)	• ↑ 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.
Duloxetine (Cymbalta®)	• ↓ AUC (33%) • Dosage modifications not routinely recommended.
Erlotinib (Tarceva®)	• ↑ Clearance (24%); ↓ trough plasma concentrations (2-fold).
Flecainide	• ↑ Clearance (61%); ↓ trough plasma concentrations (by 25%). • Smokers may need ↑ dosages.

The shaded rows indicate clinically significant drug interactions.

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DRUG INTERACTIONS with TOBACCO SMOKE: SUMMARY

Clinicians should be aware of their patients' smoking status:

- Clinically significant interactions result the combustion products of tobacco smoke, not from nicotine.
- Constituents in tobacco smoke (e.g., polycyclic aromatic hydrocarbons; PAHs) may enhance the metabolism of other drugs, resulting in an altered pharmacologic response.
- Changes in smoking status might alter the clinical response to the treatment of a wide variety of conditions.
- Drug interactions with smoking should be considered when patients start smoking, quit smoking, or markedly alter their levels of smoking.

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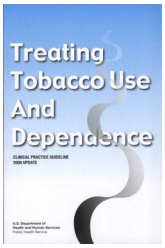
ASSISTING PATIENTS with QUITTING

62

CLINICAL PRACTICE GUIDELINE for TREATING TOBACCO USE and DEPENDENCE

- Update released May 2008
- Sponsored by the U.S. Department of Health and Human Services, Public Heath Service with:
  - Agency for Healthcare Research and Quality
  - National Heart, Lung, & Blood Institute
  - National Institute on Drug Abuse
  - Centers for Disease Control and Prevention
  - National Cancer Institute



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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.

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METHODS for QUITTING

- Pharmacologic
  - FDA-approved medications
- Nonpharmacologic
  - Counseling and other non-drug approaches

Counseling and medications are both effective, but the combination of counseling and medication is more effective than either alone.

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

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NONPHARMACOLOGIC METHODS

Recommended:

- Formal cessation programs
  - Self-help programs
  - Individual counseling
  - Group programs
  - Telephone counseling
    - 1-800-QUITNOW
  - Web-based counseling
    - www.smokefree.gov
    - www.becomeanex.org

Not recommended:

- "Cold turkey"
- Unassisted tapering (reduced frequency of use)
- Acupuncture therapy
- Hypnotherapy

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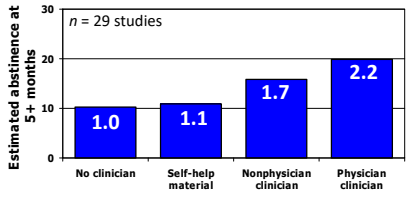
EFFECTS of CLINICIAN INTERVENTIONS

With help from a clinician, the odds of quitting approximately doubles.



Compared to patients who receive no assistance from a clinician, patients who receive assistance are 1.7–2.2 times as likely to quit successfully for 5 or more months.

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

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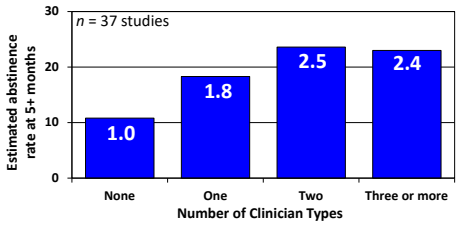
The NUMBER of CLINICIAN TYPES CAN MAKE a DIFFERENCE, too



Compared to individuals who do not receive assistance from clinicians, those who receive assistance from two or more clinician types are 2.4–2.5 times as likely to quit successfully for 5 or more months.

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

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IMPACT OF NOT ADDRESSING TOBACCO?

- 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; Conroy et al., 2005; Winpenny et al., 2017).

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

Barzilai et al. (2001). *Prev Med* 33:595–599
Conroy et al. (2005). *Nicotine Tob Res* 7 Suppl 1:S29–S34
Winpenny et al. (2017). *Health Serv Res* 52:207-219.

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The 5 A's

- ASK
- ADVISE
- ASSESS
- ASSIST
- ARRANGE

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

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The 5 A's (cont'd)

ASK about tobacco use; with a tone that conveys sensitivity, concern and is non-judgmental

- Consider tobacco use assessment to be as important as other vital signs
  - "Do you smoke or use other types of tobacco or nicotine, such as e-cigarettes?"
  - "We ask all of our patients, because tobacco smoke can affect how some medicines work."
  - "We care about your health, and we have resources to help our patients quit smoking."
- "Has there been any change in your smoking/tobacco use/vaping status?"

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The 5 A's (cont'd)

ADVISE tobacco users to quit (clear, strong, personalized)

- "Quitting smoking is the most important thing you can do for your health."
- "Quitting is the most important thing you can do to...[control your asthma, reduce your chance for another heart attack, better manage your diabetes, etc.]"
- "The best way to quit is to combine a tobacco cessation medication with a support program—we are trained to help our patients quit."
- "I can help you select medications to increase your chances of quitting for good."

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The 5 A's (cont'd)

ASSESS readiness to make a quit attempt

ASSIST with the quit attempt

- Not ready to quit: enhance motivation
- Ready to quit: design a treatment plan
- Recently quit: relapse prevention

73

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) post-cessation

Provide assistance throughout the quit attempt.

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

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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

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The (DIFFICULT) DECISION to QUIT

- Faced with change, most people are not ready to act.
- Change is a process, not a single step.
- Typically, it takes multiple attempts.

HOW CAN I LIVE WITHOUT TOBACCO?

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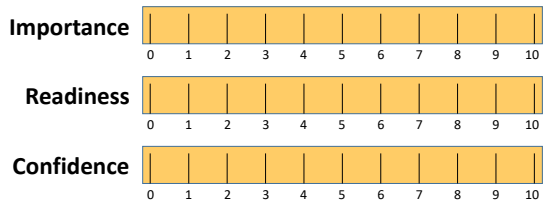
USE of RULERS



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ASSESSING READINESS to QUIT

Patients differ in their readiness to quit.

- STAGE 1: Not ready to quit in the next month
- STAGE 2: Ready to quit in the next month
- STAGE 3: Recent quitter, quit within past 6 months
- STAGE 4: Former tobacco user, quit > 6 months ago

Assessing a patient's readiness to quit enables clinicians to deliver relevant, appropriate counseling messages.

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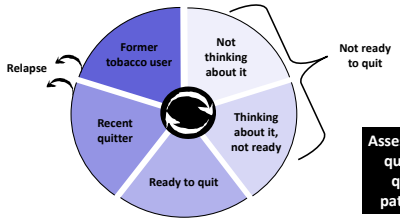
ASSESSING READINESS to QUIT (cont'd)

For most patients, quitting is a cyclical process, and their readiness to quit (or stay quit) will change over time.



Assess readiness to quit (or to stay quit) at each patient contact.

79

ASSESSING READINESS to QUIT (cont'd)

STAGE 1: Not ready to quit

Not thinking about quitting in the next month

- Some patients are aware of the need to quit.
- Patients struggle with ambivalence about change.
- Patients are not ready to change, yet.
- Pros of continued tobacco use outweigh the cons.
- Patients have inadequate motivation to quit.

GOAL: Start thinking about quitting.

80

STAGE 1: NOT READY to QUIT Counseling Strategies

DO

- Strongly advise to quit
- Guide patient to find a strong personal motivation to quit by:
  - Providing information
  - Asking noninvasive questions; identify reasons for tobacco use
  - Raising awareness of health consequences/concerns
- Demonstrate empathy, foster communication

DON'T

- Persuade
  - Leave decision up to patient
- "Cheerlead"
- Tell patient how bad tobacco is, in a judgmental manner
- Provide a treatment plan

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STAGE 1: NOT READY to QUIT Counseling Strategies (cont'd)

Consider asking:

"Do you plan to quit, someday?" → **If NO**: Advise patients to quit, and offer to assist (if or when they change their mind).

If YES

"What might be some of the benefits of quitting now, instead of later?"

Most patients will agree: there is no "good" time to quit, and there are benefits to quitting sooner as opposed to later.

"What would have to change for you to decide to quit sooner?"

Responses will reveal some of the barriers to quitting.

82

STAGE 1: NOT READY to QUIT Counseling Strategies (cont'd)

The 5 R's—Methods for enhancing motivation:

- Relevance
- Risks
- Rewards
- Roadblocks
- Repetition

Tailored, motivational messages

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

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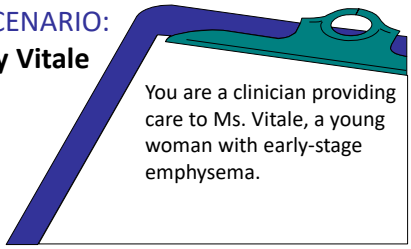
STAGE 1: NOT READY to QUIT A Demonstration

CASE SCENARIO:
Ms. Lilly Vitale



You are a clinician providing care to Ms. Vitale, a young woman with early-stage emphysema.

84

ASSESSING READINESS to QUIT (cont'd)

STAGE 2: Ready to quit

Ready to quit in the next month

- Patients are aware of the need to, and the benefits of, making the behavioral change.
- Patients are getting ready to take action.

GOAL: Achieve cessation.

85

STAGE 2: READY to QUIT Three Key Elements of Counseling

- Assess tobacco use history
- Discuss key issues
- Facilitate quitting process
  - Practical counseling (problem solving/skills training)
  - Social support delivered as part of treatment

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STAGE 2: READY to QUIT Assess Tobacco Use History

- Praise the patient's readiness
- Assess tobacco use history
  - Current use: type(s) of tobacco, amount
  - Past use: duration, recent changes
  - Past quit attempts:
    - Number, date, length
    - Methods/medications used, adherence, duration
    - Reasons for relapse

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STAGE 2: READY to QUIT Discuss Key Issues

- Reasons/motivation to quit
- Confidence in ability to quit
- Triggers for tobacco use
  - What situations lead to temptations to use tobacco?
  - What led to relapse in the past?
- Routines/situations associated with tobacco use
  - When drinking coffee
  - While driving in the car
  - When bored or stressed
  - While watching television
  - While at a bar with friends
  - After meals or after sex
  - During breaks at work
  - While on the telephone
  - While with specific friends or family members who use tobacco

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STAGE 2: READY to QUIT Discuss Key Issues (cont'd)

Stress-Related Tobacco Use

THE MYTHS	THE FACTS
"Smoking gets rid of all my stress."	There will always be stress in one's life.
"I can't relax without a cigarette."	There are many ways to relax without a cigarette.

People who smoke confuse the relief of withdrawal with the feeling of relaxation.

STRESS MANAGEMENT SUGGESTIONS:
Deep breathing, shifting focus, taking a break.

89

On average, quitters gain 9 to 11 pounds, but there is a wide range.

90

STAGE 2: READY to QUIT
Discuss Key Issues (cont'd)

Weight Gain

- Discourage strict dieting while quitting
  - Encourage healthful diet and meal planning
  - Suggest increasing water intake or chewing sugarless gum
  - Recommend selection of nonfood rewards
- When fear of weight gain is a barrier to quitting
  - Consider pharmacotherapy with evidence of delaying weight gain (bupropion SR or 4-mg nicotine gum or lozenge)
  - Assist patient with weight maintenance or refer patient to specialist or program

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STAGE 2: READY to QUIT
Discuss Key Issues (cont'd)

Withdrawal Symptoms

- Most pass within 2–4 weeks after quitting
- Cravings can last longer, up to several months or years
  - Often can be ameliorated with cognitive or behavioral coping strategies
- Refer to Withdrawal Symptoms Information Sheet
  - Symptom, cause, duration, relief

Most symptoms manifest within the first 1–2 days, peak within the first week, and subside within 2–4 weeks.

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STAGE 2: READY to QUIT
Discuss Key Issues (cont'd)

Living with Another Person who Smokes

- Discuss importance and negotiate where and when he/she will smoke, but **do not make demands**
- "Please keep your cigarettes where I won't find them."
  - Give the individual one ashtray: "Please keep this clean and hidden from me."
- Surprise them with a gift at the end of your first month of quitting as a thank you

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STAGE 2: READY to QUIT
Discuss Key Issues (cont'd)

Alcohol and Socializing

- Explore alternative ways to socialize
- Avoid going to a bar
- If they do go, advise patients:
  - Don't drink alcohol, or limit drinks to one or two
  - Have a plan and practice it
  - Visualize yourself saying "No thank you, I don't smoke" several times before going out

94

STAGE 2: READY to QUIT
Discuss Key Issues (cont'd)

Smoking After Meals

- Immediately get up from the table
- Brush teeth
  - While doing so, look in the mirror and confirm commitment to quitting—"I can do this!"
- Take a short walk
- Call a supportive friend

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STAGE 2: READY to QUIT
Discuss Key Issues (cont'd)

Boredom

- Advise patients to:
  - Always carry a book/newspaper/crossword puzzle
  - Plan ahead, avoiding long periods of inactivity
  - Learn to enjoy doing nothing from time to time; rethink the belief that it's necessary to always be doing something
  - Restart an old hobby or start to exercise

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STAGE 2: READY to QUIT
Facilitate Quitting Process

- Discuss methods for quitting
  - Discuss pros and cons of available methods
  - Pharmacotherapy: a treatment, not a crutch!
  - Importance of behavioral counseling
- Set a quit date
- Recommend Tobacco Use Log
  - Helps patients to understand when and why they use tobacco
  - Identifies activities or situations that trigger tobacco use
  - Can be used to develop coping strategies to overcome the temptation to use tobacco

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STAGE 2: READY to QUIT
Facilitate Quitting Process (cont'd)

Tobacco Use Log: Instructions for use

- Continue regular tobacco use for 3 or more days
- Each time any form of tobacco is used, log the following information:
  - Time of day
  - Activity or situation during use
  - "Importance" rating (scale of 1–3)
- Review log to identify situational triggers for tobacco use; develop patient-specific coping strategies


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

	Time	Describe the situation/activity at the time of this tobacco use.	Need Rating (1=low, 3=high)
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:

Not very important (would not have missed it)	Moderately important	Very important (would have helped if in great deal)
1	2	3

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STAGE 2: READY to QUIT
Facilitate Quitting Process (cont'd)

- Discuss coping strategies
  - Cognitive coping strategies
    - Focus on retraining the way a patient thinks
    - Occur prior to the situation or "in the moment"
  - Behavioral coping strategies
    - Involve specific actions to reduce risk for relapse
    - Occur prior to the situation or "in the moment"

HANDOUT

99

TEACH and
ENCOURAGE COPING

- Think in terms of "alternatives"
- There is **always** some other way to think or something else to do in every situation (to avoid smoking)
- Use a variety of techniques
- Foster creativity

100

TEACH and
ENCOURAGE COPING: STEP #1

- Ask:
  - "What could you do differently in this situation so you won't be prompted to want a cigarette?"
  - "How could you think differently in this situation, so that you aren't triggered to want to smoke?"

101

TEACH and
ENCOURAGE COPING: STEP #2

- If they provide a reasonable alternative, be supportive
- If they say "I don't know" or "I can't think of anything"
  - Suggest a coping technique (or two)
  - Make suggestions appropriate to their lifestyle

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STAGE 2: READY to QUIT
Facilitate Quitting Process (cont'd)

Cognitive Coping Strategies

- Review commitment to quit
- Distractive thinking
- Positive self-talk
- Relaxation through imagery
- Mental rehearsal and visualization

Remind yourself that urges are brief.

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STAGE 2: READY to QUIT
Facilitate Quitting Process (cont'd)

Cognitive Coping Strategies: Examples

- Thinking about cigarettes doesn't mean you have to smoke one:
  - "Just because you think about something doesn't mean you have to do it!"
  - Tell yourself, "It's just a thought," or "I am in control."
- As soon as you get up in the morning, look in the mirror and say to yourself:
  - "I am proud that I made it through another day without tobacco."
- Reframe how you think about yourself:
  - Begin thinking of yourself as a non-smoker, instead of as a struggling quitter

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STAGE 2: READY to QUIT
Facilitate Quitting Process (cont'd)

Behavioral Coping Strategies

- Control your environment
  - Tobacco-free home and workplace
  - Remove cues to tobacco use; actively avoid trigger situations
  - Modify behaviors that you associate with tobacco: when, what, where, how, with whom
- Substitutes for smoking
  - Water, sugar-free chewing gum or hard candies (oral substitutes)
- Minimize stress where possible, obtain social support, take a break, and alleviate withdrawal symptoms

105

STAGE 2: READY to QUIT
Facilitate Quitting Process (cont'd)

- Provide medication counseling
  - Promote adherence
  - Discuss proper use, with demonstration
- Discuss concept of "slip" versus relapse
  - "Let a slip slide."
- Offer to assist throughout quit attempt
  - Follow-up contact #1: first week after quitting
  - Follow-up contact #2: in the first month
  - Additional follow-up contacts as needed
- Congratulate the patient!

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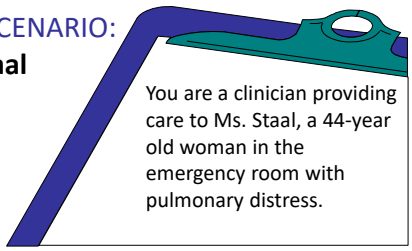
STAGE 2: READY to QUIT
A Demonstration

CASE SCENARIO:
Ms. Staal



You are a clinician providing care to Ms. Staal, a 44-year old woman in the emergency room with pulmonary distress.

107

ASSESSING
READINESS to QUIT (cont'd)

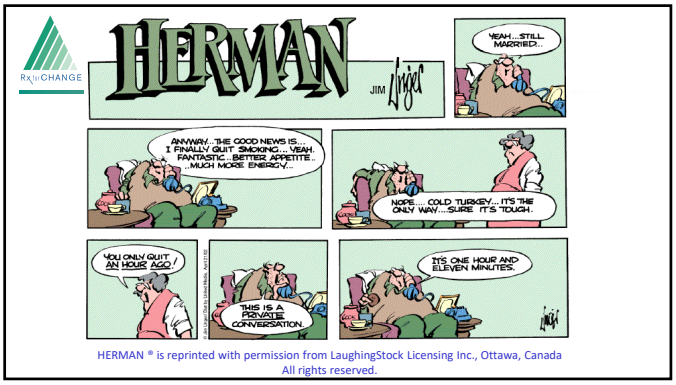
STAGE 3: Recent quitter

Actively trying to quit for good

- Patients have quit using tobacco sometime in the past 6 months and are taking steps to increase their success.
- Withdrawal symptoms occur.
- Patients are at risk for relapse.

GOAL: Remain tobacco-free for at least 6 months.

108



109

STAGE 3: RECENT QUITTERS
Evaluate the Quit Attempt

- Tailor interventions to match each patient's needs
- Status of attempt
  - Ask about social support
  - Identify ongoing temptations and triggers for relapse (negative affect, others who smoke, eating, alcohol, cravings, stress)
  - Encourage healthy behaviors to replace tobacco use
- Slips and relapse
  - Has the patient used tobacco/inhaled nicotine at all—even a puff?
- Medication adherence, plans for termination
  - Is the regimen being followed?
  - Are withdrawal symptoms being alleviated?
  - How and when should pharmacotherapy be terminated?

110

STAGE 3: RECENT QUITTERS
Facilitate Quitting Process

Relapse Prevention

- Congratulate success!
- Encourage continued abstinence
  - Discuss benefits of quitting, problems encountered, successes achieved, and potential barriers to continued abstinence
  - Ask about strong or prolonged withdrawal symptoms (change dose, combine or extend use of medications)
  - Promote smoke-free environments
- Schedule additional follow-up as needed

111

STAGE 3: RECENT QUITTER
A Demonstration

CASE SCENARIO:
Mr. Angelo Fleury

You are a clinician providing follow-up care to Mr. Angelo Fleury, who recently quit and is experiencing difficulty sleeping and coping with job-related stress.

112

ASSESSING
READINESS to QUIT (cont'd)

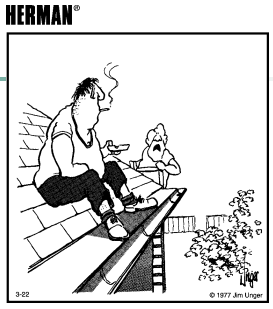
STAGE 4: Former tobacco user

Tobacco-free for 6 months

- Patients remain vulnerable to relapse.
- Ongoing relapse prevention is needed.

GOAL: Remain tobacco-free for life.

113



"I knew you hadn't quit smoking!"

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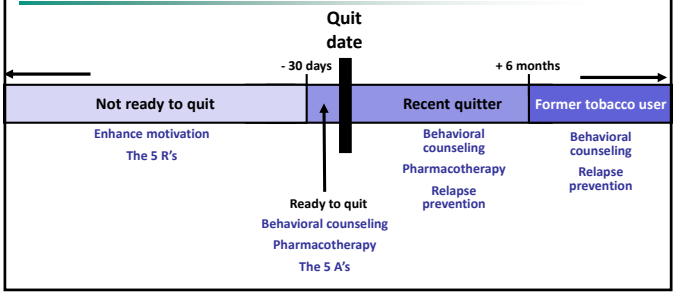
STAGE 4: FORMER TOBACCO USERS

- Assess status of quit attempt
- Congratulate continued success
- Inquire about and address slips and relapse
- Plans for termination of pharmacotherapy
- Review tips for relapse prevention

Continue to assist throughout the quit attempt.

115

READINESS to QUIT: A REVIEW



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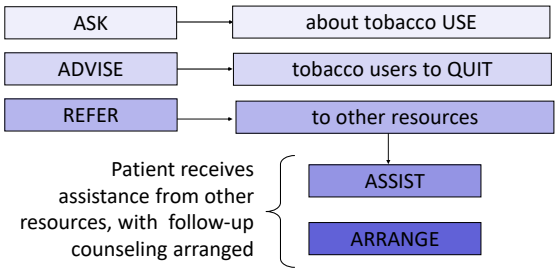
COMPREHENSIVE COUNSELING: SUMMARY

- Routinely identify tobacco users (ASK)
- Strongly ADVISE patients to quit
- ASSESS readiness to quit at each contact
- Tailor intervention messages (ASSIST)
  - Be a good listener
  - Minimal intervention in absence of time for more intensive intervention
- ARRANGE follow-up
  - Use the referral process, if needed

117

BRIEF COUNSELING: ASK, ADVISE, REFER



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BRIEF COUNSELING: ASK, ADVISE, REFER (cont'd)

- 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 group programs or the toll-free quitline
    1-800-QUIT-NOW

This brief intervention can be achieved in less than 1 minute.

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WHAT ARE "TOBACCO QUITLINES"?

- Tobacco cessation counseling, provided at no cost via telephone to all Americans
- Staffed by highly trained specialists
- Up to 4–6 personalized sessions (varies by state)
- Some state quitlines offer pharmacotherapy at no cost (or reduced cost)
- Nearly 30% success rate for patients who use the quitline and a medication for cessation (versus 13% for quitline use alone)

Quitlines have broad reach and are recommended as an effective strategy in the Clinical Practice Guideline.

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

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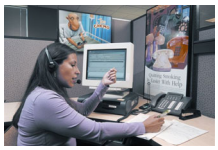
WHEN a PATIENT CALLS the QUITLINE

- Caller is routed to language-appropriate staff
- Brief Questionnaire
  - Contact and demographic information
  - Smoking behavior
- Choice of services
  - Individualized telephone counseling
  - Quitting literature mailed within 24 hrs
  - Referral to local programs, as appropriate



The Tobacco Quitline is a formal cessation program, with multiple sessions. It is NOT a crisis hotline.

121

MAKE a COMMITMENT…

Address tobacco use
with all patients.

At a minimum,
make a commitment to incorporate brief tobacco interventions as part of routine patient care.

Ask, Advise, and Refer.

122

WHAT IF…

a patient asks if *you* smoke or vape?

123

HELPING PATIENTS QUIT IS a CLINICIAN'S RESPONSIBILITY

TOBACCO USERS DON'T PLAN TO FAIL.
MOST FAIL TO PLAN.

Clinicians have a professional obligation to address tobacco use and can have an important role in helping patients plan for their quit attempts.

THE DECISION TO QUIT LIES IN THE HANDS OF EACH PATIENT.

124

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.

125

MEDICATIONS for CESSATION

126

TOBACCO DEPENDENCE: A 2-PART PROBLEM

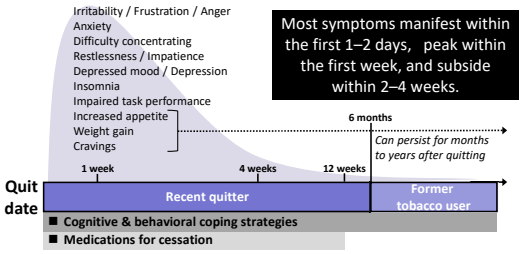
Tobacco Dependence

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

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

127

NICOTINE WITHDRAWAL SYMPTOMS: Time Course* and Management



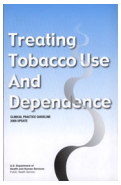
*Timeline aspect of the figure is not according to scale.

Data from Hughes. (2007). *Nicotine Tob Res* 9:315–327.

128

PHARMACOTHERAPY

"Clinicians should encourage all patients attempting to quit to use effective medications for tobacco dependence treatment, except where contraindicated or for specific populations* for which there is insufficient evidence of effectiveness."



** Includes pregnant women, smokeless tobacco users, light smokers, and adolescents.*

Medications significantly improve success rates.

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

129

PHARMACOTHERAPY: Use in SPECIAL POPULATIONS

Pharmacotherapy is **not** recommended for:

- Pregnant women who smoke
  - Insufficient evidence of effectiveness
- Smokeless tobacco users
  - No FDA indication for smokeless tobacco cessation
- Individuals smoking fewer than 10 cigarettes per day
- Adolescents
  - Insufficient evidence of effectiveness
  - Nonprescription sales of nicotine replacement therapy (NRT) products (i.e., patch, gum, lozenge) are restricted to adults ≥18 years of age
  - NRT use in minors requires a prescription

Recommended treatment is behavioral counseling.

130

FDA-APPROVED MEDICATIONS for CESSATION

Nicotine gum*
- Nicorette (OTC)
- Generics (OTC)

Nicotine lozenge*
- Nicorette (OTC)
- Generics (OTC)

Nicotine patch*
- Habitrol (OTC)
- NicoDerm CQ (OTC)
- Generics (OTC)

Nicotine nasal spray *
- Nicotrol NS (Rx)

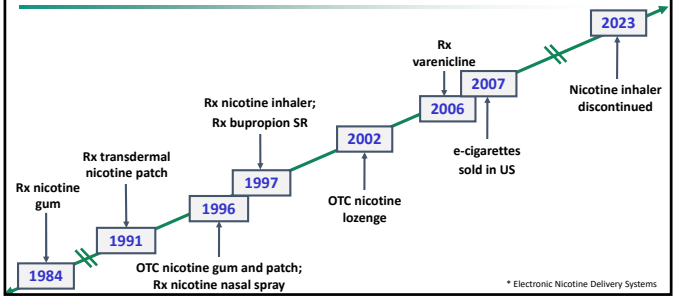
Bupropion SR
- Generic (Rx)

Varenicline
- Generic (Rx)

* Nicotine replacement therapy (NRT) products.

131

TIMELINE for MEDICATIONS and ENDS*



* Electronic Nicotine Delivery Systems

132

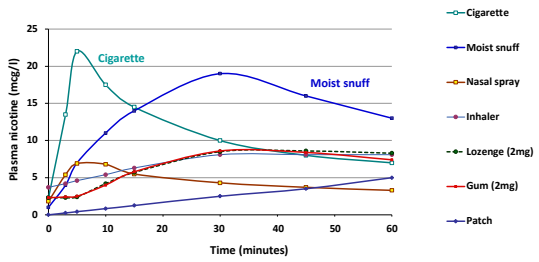
NICOTINE REPLACEMENT THERAPY (NRT) RATIONALE for USE

- Reduces physical withdrawal from nicotine
- Eliminates the immediate, reinforcing effects of nicotine that is rapidly absorbed via tobacco smoke
- Allows patient to focus on behavioral and psychological aspects of tobacco cessation

Use of NRT products approximately doubles quit rates.

133

PLASMA NICOTINE CONCENTRATIONS for NICOTINE-CONTAINING PRODUCTS



134

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.

135

NICOTINE GUM
Nicorette; generics

- Resin complex
  - Nicotine
  - Polacrilin
- Sugar-free chewing gum base
- Contains buffering agents to enhance buccal absorption of nicotine
- Available: 2 mg, 4 mg; original, mint (various), fruit, and cinnamon flavors

136

NICOTINE LOZENGE
Nicorette Lozenge, Nicorette Mini Lozenge; generics

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

137

NICOTINE GUM & LOZENGE: DOSING

Dose based on the "time to first cigarette" (TTFC) as an indicator of nicotine dependence

Use the 2 mg gum/lozenge:

If first cigarette of the day is smoked **more than 30 minutes** after waking

Use the 4 mg gum/lozenge:

If first cigarette of the day is smoked **within 30 minutes** of waking

138

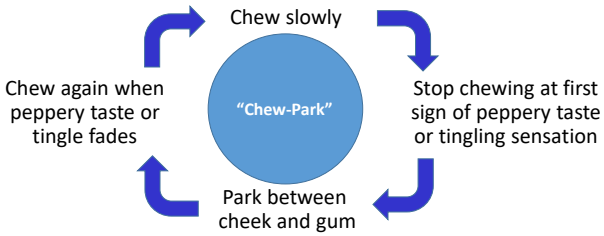
NICOTINE GUM & LOZENGE: DOSING (cont'd)

Recommended Usage Schedule		
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**

Begin with a minimum of 9 pieces daily when used as monotherapy

139

NICOTINE GUM: DIRECTIONS FOR USE



140

NICOTINE LOZENGE: DIRECTIONS for USE

- Place in mouth and allow to dissolve slowly (nicotine release may cause warm, tingling sensation)
- Do not chew or swallow
- Occasionally rotate to different areas of the mouth
- Lozenges will dissolve completely in about 20–30 minutes

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NICOTINE GUM/LOZENGE: ADDITIONAL PATIENT EDUCATION

- To improve chances of quitting, when used a monotherapy, use at least nine pieces daily during the first 6 weeks
- The gum/lozenge will *not* provide the same rapid satisfaction that smoking provides
- The effectiveness of the nicotine gum/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 gum or lozenge.

142

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

- Chewing the lozenge or using incorrect gum chewing technique can cause excessive and rapid release of nicotine, resulting in:
  - Lightheadedness/dizziness
  - Nausea and vomiting
  - Hiccups
  - Irritation of throat and mouth

143

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

- Adverse effects of nicotine gum and lozenge:
  - Mouth and throat irritation
  - Hiccups
  - Gastrointestinal complaints (dyspepsia, nausea)
- Adverse effects associated with nicotine gum:
  - Jaw muscle ache
  - May stick to dental work

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NICOTINE GUM/LOZENGE: SUMMARY

ADVANTAGES

- 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
- Relatively inexpensive

DISADVANTAGES

- Need for frequent dosing can compromise adherence
- Gastrointestinal adverse effects (nausea, hiccups, and dyspepsia) may be bothersome
- Specific to nicotine gum:
  - Problematic with significant dental work
  - Proper chewing technique is necessary for effectiveness and to minimize adverse effects
  - Might not be acceptable or desirable for some patients

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NICOTINE PATCH

Habitrol; NicoDerm CQ; generic

- Continuous (24-hour) nicotine delivery system
- Nicotine is well absorbed across the skin
- Transdermal delivery to systemic circulation avoids hepatic first-pass metabolism
- Plasma nicotine levels are lower and fluctuate less than with smoking

146

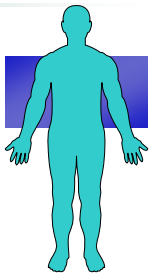
NICOTINE PATCH: DOSING

Product	Light Smoking	Heavy Smoking
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)
Habitrol Generic	≤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)

147

NICOTINE PATCH: DIRECTIONS for USE

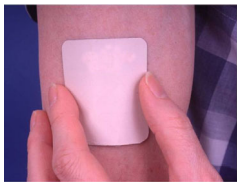
- Choose an area of skin on the upper body or upper outer part of the arm
- Make sure skin is clean, dry, hairless, and not irritated
- Apply patch to different area each day
- Do not use same area again for at least one week



148

NICOTINE PATCH: DIRECTIONS for USE (cont'd)

- Remove protective liner and 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



149

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—leaving it on longer may lead to skin irritation
- Adhesive remaining on skin may be removed with rubbing alcohol or acetone
- Dispose of used patch by folding it in half so the adhesive sides stick together

150

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
  - Can unpredictably effect nicotine delivery
  - Patch may be less effective
- Keep new and used patches out of the reach of children and pets
- Remove patch before MRI procedures

151

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

Common adverse effects include:

- Irritation at patch application site (generally within the first hour)
  - Mild itching
  - Burning
  - Tingling
- Sleep disturbances
  - Abnormal or vivid dreams
  - Insomnia

152

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
  - Confirm patient is rotating patch application sites
  - Avoid use in patients with dermatologic conditions (e.g., psoriasis, eczema, atopic dermatitis)

153

NICOTINE PATCH: SUMMARY

ADVANTAGES

- 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 hrs
- Relatively inexpensive

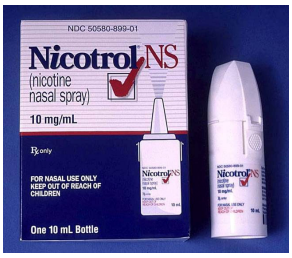
DISADVANTAGES

- 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)

154

NICOTINE NASAL SPRAY
Nicotrol NS

- Aqueous solution of nicotine in a 10-ml spray bottle
- Each metered dose actuation delivers
  - 50 mcL spray
  - 0.5 mg nicotine
- ~100 doses/bottle
- Rapid absorption across nasal mucosa



155

NICOTINE NASAL SPRAY: DOSING & ADMINISTRATION

- One dose = 1 mg nicotine (2 sprays, one 0.5 mg spray in **each** nostril)
- Start with 1–2 doses per hour
- Increase as needed to maximum dosage of 5 doses per hour or 40 mg (80 sprays; ~½ bottle) daily
- At least 8 doses daily for the first 6–8 weeks
- Termination:
  - Gradual tapering over an additional 4–6 weeks
  - Recommended maximum duration of therapy is 3 months

156

NICOTINE NASAL SPRAY: DIRECTIONS for USE

- Press in circles on sides of bottle and pull to remove cap

157

NICOTINE NASAL SPRAY: DIRECTIONS for USE (cont'd)

- Prime the pump (spray into a tissue before first use)
  - Re-prime (1–2 sprays) if spray not used for 24 hours
- Blow nose (if not clear)
- Tilt head back slightly and insert tip of bottle into nostril as far as comfortable
- Breathe through mouth, and spray once in each nostril
- Do not sniff or inhale while spraying

158

NICOTINE NASAL SPRAY: DIRECTIONS for USE (cont'd)

- If nose runs, gently sniff to keep nasal spray in nose
- Wait 2–3 minutes before blowing nose
- Avoid contact with skin, eyes, and mouth
  - If contact occurs, rinse with water immediately because nicotine is absorbed through skin and mucous membranes

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NICOTINE NASAL SPRAY: ADDITIONAL PATIENT EDUCATION

- What to expect (first week):
  - Hot peppery feeling in back of throat or nose
  - Sneezing
  - Coughing
  - Watery eyes
  - Runny nose
- Adverse effects should lessen over a few days
  - Regular use during the first week will help in development of tolerance to the irritant effects of the spray
- If adverse effects persist after a week, contact health care provider and consider alternative treatment

160

NICOTINE NASAL SPRAY: SUMMARY

ADVANTAGES

- Can be titrated to rapidly manage withdrawal symptoms
- Can be used in combination with other agents to manage situational urges

DISADVANTAGES

- Need for frequent dosing can compromise adherence
- Nasal administration might not be acceptable/desirable for some patients; nasal irritation often problematic
- Not recommended for use by patients with chronic nasal disorders or severe reactive airway disease
- Cost of treatment

161

BUPROPION SR Generics

- Non-nicotine cessation aid
- Mechanism of action: atypical antidepressant thought to affect levels of various brain neurotransmitters
  - Dopamine
  - Norepinephrine
- Clinical effects
  - ↓ craving for cigarettes
  - ↓ symptoms of nicotine withdrawal

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BUPROPION: PHARMACOKINETICS

Absorption
- Bioavailability: 5–20%

Metabolism
- Undergoes extensive hepatic metabolism (CYP2B6)

Elimination
- Urine (87%) and feces (10%)

Half-life
- Bupropion (21 hours); metabolites (20–37 hours)

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BUPROPION: CONTRAINDICATIONS

- Seizure disorder
- Current or prior diagnosis of bulimia or anorexia nervosa
- Abrupt discontinuation of alcohol, benzodiazepines, barbiturates and antiepileptic drugs
- Use of MAO inhibitors (within 14 days of initiating or discontinuing therapy)

164

BUPROPION: WARNINGS and PRECAUTIONS

Use with caution in the following populations:

- Patients with an elevated risk for seizures, including:
  - Severe head injury
  - Concomitant use of medications that lower the seizure threshold (e.g., other bupropion products, antipsychotics, tricyclic antidepressants, theophylline)
  - Severe hepatic impairment
- Patients with underlying neuropsychiatric conditions

For a comprehensive listing of warnings and precautions, refer to the manufacturer's prescribing information.

165

BUPROPION: WARNINGS and PRECAUTIONS (cont'd)

- Neuropsychiatric symptoms and suicide risk
  - Changes in mood (including depression and mania)
  - Psychosis/hallucinations/paranoia/delusions
  - Homicidal ideation
  - Aggression/hostility/anxiety/panic
  - Suicidal ideation, suicide attempt, completed suicide

FDA boxed warning removed Dec 2016

Advise patients to stop taking bupropion SR and contact a health care provider immediately if symptoms such as agitation, depressed mood, or changes in behavior or thinking that are not typical are observed or if the patient develops suicidal ideation or suicidal behavior.

166

BUPROPION SR: DOSING

To ensure therapeutic plasma levels of the drug are achieved, begin therapy 1 to 2 weeks PRIOR to the quit date.

Initial treatment
- 150 mg orally in the morning for 3 days

Then…
- 150 mg orally twice daily for 7–12 weeks
- Doses must be administered at least 8 hours apart
- Tapering not necessary when discontinuing therapy

167

BUPROPION: ADVERSE EFFECTS

Common adverse effects include the following:
- Insomnia (avoid bedtime dosing)
- Dry mouth
- Nausea

Less common but reported effects:
- Anxiety/difficulty concentrating
- Constipation
- Tremor
- Skin rash

168

BUPROPION SR: SUMMARY

ADVANTAGES

- Twice daily oral dosing is associated with better adherence
- Might delay weight gain
- Might be beneficial in patients with depression
- Can be used in combination with NRT agents
- Relatively inexpensive

DISADVANTAGES

- Seizure risk is increased
- Several contraindications and precautions preclude use in some patients
- Patients should be monitored for neuropsychiatric symptoms

169

VARENICLINE
Generics

- Non-nicotine cessation aid
- Mechanism of action: partial nicotinic receptor agonist that binds with high affinity and selectivity at $\alpha_4\beta_2$ neuronal nicotinic acetylcholine receptors
  - Stimulates low-level agonist activity
  - Competitively inhibits the binding of nicotine
- Clinical effects
  - ↓ symptoms of nicotine withdrawal
  - Blocks dopaminergic stimulation responsible for reinforcement & reward associated with smoking

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VARENICLINE:
PHARMACOKINETICS

Absorption

- Virtually complete (~90%) after oral administration; not affected by food

Metabolism

- Undergoes minimal metabolism

Elimination

- Primarily renal through glomerular filtration and active tubular secretion; 92% excreted unchanged in urine

Half-life

- 24 hours

171

VARENICLINE:
WARNINGS and PRECAUTIONS

- Neuropsychiatric symptoms and suicide risk
  - Changes in mood (including depression and mania)
  - Psychosis/hallucinations/paranoia/delusions
  - Homicidal ideation
  - Aggression/hostility/anxiety/panic
  - Suicidal ideation, suicide attempt, completed suicide

FDA boxed warning removed Dec 2016

Advise patients to stop taking varenicline and contact a health care provider immediately if symptoms such as agitation, depressed mood, or changes in behavior or thinking that are not typical are observed or if the patient develops suicidal ideation or suicidal behavior.

172

VARENICLINE:
WARNINGS and PRECAUTIONS (cont'd)

In some patients, use of varenicline has been associated with:

- Seizures
- Enhanced effects of alcohol
- Accidental injury
- Cardiovascular events
- Somnambulism
- Angioedema and hypersensitivity reactions
- Serious skin reactions

These are rare events; most have NOT been causally linked to varenicline use.

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VARENICLINE:
STANDARD DOSING

Patients should begin therapy 1 week PRIOR to their quit date. The dose is gradually increased to minimize treatment-related nausea and insomnia.

	Treatment Day	Dose
Initial dose titration	Day 1 to day 3	0.5 mg qd
	Day 4 to day 7	0.5 mg bid
	Day 8 to end of treatment*	1 mg bid

* Up to 12 weeks

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VARENICLINE TREATMENT REGIMENS

FIXED QUIT
- Set quit date for 1 week after starting varenicline
- Continue treatment for 12 weeks

FLEXIBLE QUIT
- Start taking varenicline and pick a quit date between 8 to 35 days from treatment initiation
- Continue treatment for 12 weeks

GRADUAL QUIT
- Start taking varenicline and reduce smoking by 50% within the first 4 weeks, an additional 50% in the next 4 weeks, and continue until complete abstinence by 12 weeks

175

VARENICLINE: ADVERSE EFFECTS

Common adverse effects include the following:
- Nausea
- Abnormal dreams
- Insomnia
- Headache

Less common adverse effects:
- Gastrointestinal (flatulence, constipation)
- Taste alteration

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VARENICLINE: ADDITIONAL PATIENT EDUCATION

- Doses should be taken after eating, with a full glass of water
- Nausea and insomnia are usually temporary side effects
  - If symptoms persist, notify your health care provider
- May experience vivid, unusual or strange dreams during treatment
- Use caution driving, drinking alcohol, and operating machinery until effects of quitting smoking with varenicline are known

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VARENICLINE: SUMMARY

ADVANTAGES
- Twice daily oral dosing is associated with better adherence
- Offers an alternative mechanism of action for individuals who have not tolerated or have not responded to other agents
- Most effective agent for smoking cessation

DISADVANTAGES
- Cost of treatment
- Patients should be monitored for potential neuropsychiatric symptoms

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Articles

Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial

Anthenelli RM et al. Lancet 2016;387:2508-2520.

179

VARENICLINE and BUPROPION SR: Safety

The "EAGLES study": FDA-mandated clinical trial
- 8,144 participants (4,116 with a psychiatric disorder)
- 140 multinational centers
- 24-week, double-blind; active and placebo-controlled:
  - **Varenicline:** standard dosing, 12 wks
  - **Bupropion SR:** standard dosing, 12 wks
  - **Nicotine patch:** 21 mg/day with standard taper, 12 wks
  - **Placebo:** 12 wks
- All arms: 13 counseling visits, 11 telephone calls
- Follow-up through 24 wks; outcome = continuous abstinence

Anthenelli RM et al. Lancet 2016;387:2508-2520.

180

The "EAGLES" STUDY: SAFETY DATA

Incidence of Moderate or Severe Neuropsychiatric Adverse Events

Patient cohort	Varenicline	Bupropion SR	Nicotine patch	Placebo
Non-psychiatric	1.3%	2.2%	2.5%	2.4%
Psychiatric	6.5%	6.7%	5.2%	4.9%

No significant differences in neuropsychiatric events by treatment arm

Anthenelli RM et al. Lancet 2016;387:2508-2520.

181

THE "EAGLES" STUDY: EFFICACY DATA (Weeks 9-24)

Continuous abstinence

Patient cohort	Varenicline	Bupropion SR	Nicotine patch	Placebo
Non-psychiatric	25.5%	18.8%	18.5%	10.5%
Psychiatric	18.3%	13.7%	13.0%	8.3%

Highest efficacy with varenicline

Anthenelli RM et al. Lancet 2016;387:2508-2520.

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COMBINATION PHARMACOTHERAPY

Combination NRT [first-line, recommended treatment approach]

- Long-acting formulation (patch)
  - Produces relatively constant levels of nicotine

PLUS

- Short-acting formulation (gum, lozenge, nasal spray)
  - Allows for acute dose titration as needed for nicotine withdrawal symptoms

Other combinations [evidence less compelling]

- Bupropion + NRT
- Varenicline + NRT
- Varenicline + bupropion SR

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TREATMENT OPTIONS

Multiple Treatment Comparison Meta-Analysis

Comparison (# randomized controlled trials)	Odds ratio^ (95% CI)
Nicotine patch vs Placebo (n=105)	**1.4** (1.2–1.6)
Bupropion SR vs Placebo (n=71)	**1.4** (1.3–1.6)
Short-acting NRT* vs Placebo (n=120)	**1.4** (1.3–1.6)
Combination NRT vs Placebo (n=86)	**1.9** (1.6–2.3)
Varenicline vs Placebo (n=67)	**2.3** (2.0–2.7)

^ Smoking cessation at 6 months to 5 years (predominantly 6 to 12 months)
* Includes nicotine gum, inhaler, lozenge/microtab, mouth spray, nasal spray

Strong evidence that combination NRT and varenicline are more effective than bupropion SR or NRT monotherapy.

Lindson et al. *Cochrane Database Syst Rev* 2023;9:CD015226.

185

COMBINATION NRT: TREATMENT REGIMENS

Nicotine patch

Dose: 21 mg/day x 4–6 weeks → 14 mg/day x 2-3 weeks → 7 mg/day x 2-3 weeks

PLUS

Short-acting agent options

- **Nicotine gum or lozenge** (2 mg/4 mg)
  Dose: Use 1 piece q 1–2 hours *as needed*

and/or

- **Nicotine nasal spray** (0.5 mg/spray)
  Dose: Use 1 spray in each nostril q 1–2 hours *as needed*

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ESSENTIAL QUESTION for SELECTION of NRT PRODUCT(s)*

"Would it be a challenge for you to take a medication frequently throughout the day (e.g., a minimum of 8 or 9 times)?"

- With the exception of the nicotine patch, all NRT formulations require frequent dosing throughout the day.
- If patient is unable to adhere to the recommended dosing, these products should be ruled out as monotherapy because they aer less likely to be effective.

* Product-specific screening—e.g., for warnings, precautions, and personal preferences—is also essential.

187

"Drugs don't work…

…in patients who don't take them."

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

Medication adherence should be addressed at each encounter.

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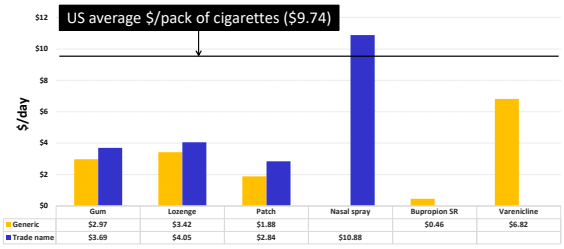
MEDICATIONS for TOBACCO CESSATION COMPARATIVE DAILY COSTS



	Gum	Lozenge	Patch	Nasal spray	Bupropion SR	Varenicline
Generic	$2.97	$3.42	$1.88		$0.46	$6.82
Trade name	$3.69	$4.05	$2.84	$10.88		

*Wholesale acquisition cost from Red Book Online. Thomson Reuters, 2024.

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SUMMARY

- To maximize success, interventions should include behavioral counseling and one or more medications
- Encourage the use of effective medications by all patients attempting to quit smoking
  - Exceptions include medical contraindications or specific populations for which there is insufficient evidence of effectiveness
- First-line medications that reliably increase long-term smoking cessation rates:
  - Bupropion SR
  - Nicotine replacement therapy (as monotherapy or combination therapy)
  - Varenicline
- Varenicline and combination NRT demonstrate the highest efficacy

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PUTTING IT ALL TOGETHER: PATIENT ENCOUNTERS

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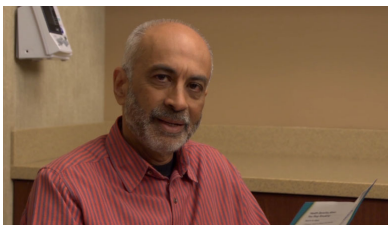
PATIENT ENCOUNTER #1



"But I've tried everything. None of these quit smoking medicines *ever* work for me!"

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PATIENTS WHO HAVE RELAPSED AFTER USING MEDICATIONS

- **Step 1: Ask**

"What medications have you tried in the past?"

- "Tell me how you used them."

"Did you receive any professional advice or enroll in a quitting support program?"

- IF YES: "Tell me what you liked, or didn't like, about it."
- IF NO: "What are your thoughts about enrolling in a formal quitting program this time?

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PATIENTS WHO HAVE RELAPSED AFTER USING MEDICATIONS

- **Step 2: Advise**

"The best way to quit is to combine a smoking cessation medication with a support program."

For patients who are willing to use medication(s):

- Conduct a tobacco use history; determine viable treatment options
- Consider patient preferences, insurance coverage, and cost

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PATIENTS WHO HAVE RELAPSED AFTER USING MEDICATIONS

- **Step 2: Advise (cont'd) and Assist**
  - Patients with previous failed quit attempts using medication(s) for cessation
    - **IF the prior medication was used incorrectly:**
      - Carefully review usage instructions / emphasize adherence (daily / duration)
    - **IF the prior medication was used correctly,** was well-tolerated, and appeared to have been effective:
      - Consider repeating same medication in **combination with an enhanced behavioral support program**

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PATIENTS WHO HAVE RELAPSED AFTER USING MEDICATIONS

- **Step 2: Advise and assist (cont'd)**
  - **IF the prior medication was used correctly but did not control withdrawal symptoms, or patient prefers a different medication:**
    - Review alternative options
    - Emphasize importance of the behavioral aspects of quitting
    - Promote adherence (daily use and full duration of therapy)

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"Drugs don't work…

…in patients who don't take them."

C. Everett Koop, MD
U.S. Surgeon General, 1982-1989

Medication adherence should be addressed at each encounter.

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The 5 A's

- ASK
- ADVISE
- ASSESS
- ASSIST
- ARRANGE

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

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PATIENT ENCOUNTER #2

- **Your health screening intake form for Greg** reveals that he is a 54 yo male with controlled HTN, hyperlipidemia, depression, chronic rhinitis

- Current medications:
  - Valsartan 80mg QAM for HTN
  - Atorvastatin 40mg QAM for hyperlipidemia
  - Bupropion XL 300mg QAM for depression
  - Fluticasone (50mcg/spray), 1 spray in each nostril QAM for rhinitis

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KEY CONSIDERATIONS FOR GREG

- **Tobacco use history:**
  - Current use: 25 cigarettes/day x 25 years
  - No other forms of tobacco or vaping
  - Smokes within 20 min of waking
  - Previous quit attempts: "many" (cold turkey, gum, patch)
  - Longest duration tobacco-free: 2 weeks (patch)
  - Last quit attempt, 10 months ago (patch only)
  - Reasons for relapse: withdrawal, other smokers

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KEY CONSIDERATIONS FOR GREG (cont'd)

- **Key issues for upcoming quit attempt:**
  - Reasons, motivation for wanting to quit: worsening CVD
  - Father died young, of an acute MI
  - Caffeine: 2 cups of coffee in the morning; 1 cola with lunch and dinner
- **Importance, Readiness, and Confidence ratings:**
  - Importance of quitting: 10
  - Readiness to quit: 10
  - Confidence for quitting: 9

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SCREENING CONSIDERATIONS: HIGH-RISK PATIENTS

- Cardiovascular disease with:
  - Myocardial infarction in past 2 weeks
  - History of arrhythmias or irregular heartbeat
  - Unstable angina or chest pain with strenuous activity
- History of mental health disorder(s) AND is perceived to not be stable
- Pregnant or planning to become pregnant (N/A)

If YES – Consult with or refer Greg to a primary care provider, psychiatrist, or other provider, as appropriate.

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MEDICATION SELECTION FOR GREG

- **Key considerations for medication selection:**
  - Previous failed quit attempts with monotherapy (patch, gum)
  - Did not like chewing the gum
  - Challenges adhering with complex regimens
  - Taking bupropion XL 300mg daily for depression x 18 mo
  - Concerned about side effects of varenicline
  - Chronic rhinitis

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DRUG INTERACTION: TOBACCO SMOKE and CAFFEINE

- Assess caffeine intake from all sources
- Caffeine levels increase ~56% upon quitting
- Challenges:
  - Nicotine withdrawal effects may be enhanced by increased caffeine levels
  - Insomnia can be due to ↑ caffeine levels or a side effect of a smoking cessation drug (e.g., 24-hr nicotine patch, bupropion SR, varenicline)
- Recommendations:
  - Decrease caffeine intake when quitting
  - Stop consumption by early afternoon for individuals with a typical bedtime

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COMBINATION NRT: TREATMENT REGIMENS

Nicotine patch

Dose: 21 mg/day x 4–6 weeks → 14 mg/day x 2-3 weeks → 7 mg/day x 2-3 weeks

PLUS

Short-acting agent options

- **Nicotine gum or lozenge** (2 mg/4 mg)
  Dose: Use 1 piece q 1–2 hours *as needed*

  and/or
- **Nicotine nasal spray** (0.5 mg/spray)
  Dose: Use 1 spray in each nostril q 1–2 hours *as needed*

Combination therapy increases dosing flexibility and overall plasma nicotine concentration.

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GREG'S QUESTION

"Chantix…isn't that the drug with all the horrible side effects?"

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Articles

Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial

Robert M Anthenelli, Neal L Benowitz, Robert West, Lisa St Aubin, Thomas McRae, David Lawrence, John Ascher, Cristina Russ, Alok Krishen, A Eden Evins

Summary

Background Substantial concerns have been raised about the neuropsychiatric safety of the smoking cessation medications varenicline and bupropion. Their efficacy relative to nicotine patch largely relies on indirect comparisons, and there is limited information on safety and efficacy in smokers with psychiatric disorders. We compared the relative neuropsychiatric safety risk and efficacy of varenicline and bupropion with nicotine patch and placebo in smokers with and without psychiatric disorders.

Methods We did a randomised, double-blind, triple-dummy, placebo-controlled and active-controlled (nicotine patch: 21 mg per day with taper) trial of varenicline (1 mg twice a day) and bupropion (150 mg twice a day) for 12 weeks with 12-week non-treatment follow-up dose at 140 centres (clinical trial centres, academic centres, and outpatient clinics) in 16 countries between Nov 30, 2011, and Jan 13, 2015. Participants were motivated-to-quit smokers with and without psychiatric disorders who received brief cessation counselling at each visit. Randomisation

Anthenelli RM et al. Lancet 2016;387:2508-2520.

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GREG at 14-DAY FOLLOW-UP

"I've been having a hard time sleeping – do you think that's the Chantix?"

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Which of the following might be contributing to Greg's insomnia?

A. Bupropion XL – unlikely, he has been on this medication for 18 months
B. Varenicline – possible, insomnia occurs in 13% of patients
C. Drug interaction between tobacco smoke and caffeine – likely, if he is still consuming caffeine
D. Nicotine withdrawal symptoms – can cause insomnia (see graph)

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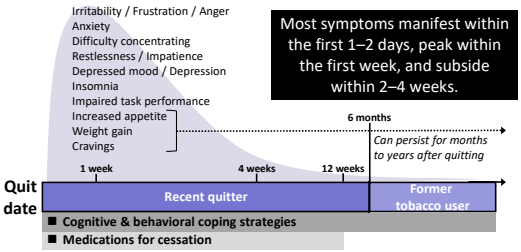
NICOTINE WITHDRAWAL SYMPTOMS: Time Course* and Management



*Timeline aspect of the figure is not according to scale.

Data from Hughes. (2007). *Nicotine Tob Res* 9:315–327.

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PATIENT ENCOUNTER #3

Marisol is a 28 year-old female who would like to speak with the pharmacist about use of medications to quit vaping.

What questions do you want to ask?

212

KEY CONSIDERATIONS for MARISOL

- **Tobacco use history**
  - Current: disposable nicotine salt (5%) device (~8 mL/week) x 1 year
  - Vapes within 5 min of waking
  - Past: 20 cigarettes/day x 10 years; 1st cigarette within 10 min of waking
  - Past quit attempts: 1 year ago ("cold-turkey"), switched to vaping
- **Medical history**
  - No chronic medical problems

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KEY CONSIDERATIONS for MARISOL

- **Issues to address for upcoming quit attempt:**
  - Motivation for quitting: cost and increased vaping over past year
    - Importance of quitting: 10/10
    - Confidence in ability to quit: 5/10; *"I think it will be much harder to stop vaping than it was to quit smoking."*
    - Readiness to quit: 10/10
  - Primary concern: strong addiction to vaping *"I have a vape pen in my hands at ALL times. It's starting to become an issue at work."*
  - Interest in cessation medications: Yes; cost is a concern
  - Triggers: immediately upon waking; friends who smoke/vape
  - Interest in behavioral support: Not sure

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CESSATION APPROACHES for ENDS: LIMITED EVIDENCE to GUIDE TREATMENT

- Behavioral counseling throughout quit attempt
- Pharmacotherapy
  - Nicotine replacement therapy
    - If patient has switched from smoking to vaping: start with pre-vaping # cigarettes/day and TTFC to guide initial dosing
    - If user has only vaped nicotine: estimate nicotine intake
      - ≥20 mg/day, start with 21 mg patch
      - <20 mg/day, start with 14 mg patch
      - Add short-acting NRT for break-through
    - Early follow-up to assess response and adjust dosing as needed
  - Varenicline or Bupropion SR

Therapeutic Research Center. (2019). Help patients break the e-cigarette habit. *Pharmacists Letter* (December).

215

MEDICATION SELECTION for MARISOL

- **Key considerations for medication selection:**
  - If NRT selected:
    - Previous smoking history: ~20 cigarettes/day
    - Estimate nicotine use from current vaping
      - 5% nicotine solution = 50 mg/mL * 8 mL/week * 1 week/7 days = ~57 mg/day
      - Actual nicotine yield is highly variable
    - Start with combination NRT
      - Initial regimen: 21 mg patch + 4 mg gum or lozenge every 1-2 hour as needed
  - If bupropion SR or varenicline selected:
    - Use standard dosing
- **Schedule follow-up within 24-48 hours**

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MARISOL: FOLLOW-UP

- Marisol calls the pharmacy the next afternoon (8 hours after initiating the following regimen):
  - Nicotine patch (21 mg)
  - Nicotine gum (4 mg every 1-2 hours; total 7 pieces)
- Reports:

"I'm comfortable…not experiencing strong urges to vape and no withdrawal symptoms like when I quit 'cold turkey' last time. That said, my jaw is getting sore."

What is your assessment and plan for Marisol?

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MARISOL: FOLLOW-UP (cont'd)

- Congratulate early success
- Current regimen controlling withdrawal symptoms, but usage of short-acting nicotine is on pace for >35 mg/day
  - Reassess use of gum (chewing technique, drug interaction with food/beverages)
  - Consider adding a 2nd patch:
    7 or 14 mg; providing total of 28-35 mg nicotine from patch daily
  - Consider switching to the lozenge or alternating nicotine lozenge with gum
- Discuss behavioral coping strategies
- Recommend follow-up within 48 hours

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MARISOL: FOLLOW-UP (cont'd)

- Telephone follow-up, 2 days later:
  - Vape-free since quit date
  - Withdrawal symptoms "much better"
  - Nicotine patch (28 mg daily; 21 mg + 7 mg patch)
  - Nicotine gum or lozenge (4 mg every 1-2 hours; 6 pieces daily)
  - Tolerating NRT (no rash, sleep disturbances, nausea, or jaw ache)
  - Concerns about socializing with friends who smoke or vape

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MARISOL: FOLLOW-UP (cont'd)

- Congratulate success
- Suggest additional behavioral support
  - Tobacco quitline, web-based program or application, group counseling
  - Further develop coping strategies for key triggers
- Schedule 14-day follow-up
- Discuss plans for tapering NRT; might need longer duration of therapy
  - Nicotine patch:
    28 mg x 6 weeks → 21 mg x 3 weeks → 14 mg x 3 weeks → 7 mg x 3 weeks
  - Nicotine gum/lozenge: continue as needed
  - Reassess with each nicotine patch dose reduction; adjust as needed
- Encourage contact as needed; schedule end of treatment follow-up

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SUMMARY

- Treatment should be individualized to meet the needs of each patient.
- Tobacco/vaping history and prior quit attempts provide useful information to guide future attempts.
- Work with the patient to create the treatment plan.
  - There are two parts to smoking, thus there are two parts to quitting: both need to be addressed.
- Arrange follow-up, and tweak regimens as needed.

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