**TRAINING OVERVIEW**

- Epidemiology of Tobacco Use
- Forms of Tobacco
- Nicotine Pharmacology & Principles of Addiction
- Drug Interactions with Smoking
- Assisting Patients with Quitting
- Medications for Cessation
- Tobacco Trigger Tapes
- Role Playing with Case Scenarios and Video Counseling Sessions

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**EPIDEMIOLOGY of TOBACCO USE**

"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.

---

**WORLDWIDE PREVALENCE of ADULT TOBACCO USE (Men/Women)**

<table>
<thead>
<tr>
<th>Country</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>17%</td>
<td>13%</td>
</tr>
<tr>
<td>USA</td>
<td>16%</td>
<td>12%</td>
</tr>
<tr>
<td>Brazil</td>
<td>17%</td>
<td>11%</td>
</tr>
<tr>
<td>Greece</td>
<td>41%</td>
<td>35%</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>51%</td>
<td>17%</td>
</tr>
<tr>
<td>China</td>
<td>45%</td>
<td>2%</td>
</tr>
<tr>
<td>UK</td>
<td>23%</td>
<td>20%</td>
</tr>
<tr>
<td>France</td>
<td>34%</td>
<td>28%</td>
</tr>
<tr>
<td>South Africa</td>
<td>22%</td>
<td>9%</td>
</tr>
<tr>
<td>Japan</td>
<td>36%</td>
<td>11%</td>
</tr>
<tr>
<td>India</td>
<td>23%</td>
<td>3%</td>
</tr>
<tr>
<td>Iran</td>
<td>23%</td>
<td>2%</td>
</tr>
<tr>
<td>Australia</td>
<td>15%</td>
<td>12%</td>
</tr>
<tr>
<td>Mexico</td>
<td>16%</td>
<td>5%</td>
</tr>
</tbody>
</table>

---

**TRENDS in ADULT SMOKING, by SEX—U.S., 1955–2017**

<table>
<thead>
<tr>
<th>Year</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>1955</td>
<td>15.8%</td>
<td>12.2%</td>
</tr>
<tr>
<td>1960</td>
<td>14.0%</td>
<td></td>
</tr>
<tr>
<td>1965</td>
<td>12.2%</td>
<td>11.2%</td>
</tr>
<tr>
<td>1970</td>
<td>10.5%</td>
<td>10.0%</td>
</tr>
<tr>
<td>1975</td>
<td>9.0%</td>
<td>8.0%</td>
</tr>
<tr>
<td>1980</td>
<td>7.0%</td>
<td>6.0%</td>
</tr>
<tr>
<td>1985</td>
<td>5.0%</td>
<td>4.0%</td>
</tr>
<tr>
<td>1990</td>
<td>3.5%</td>
<td>3.0%</td>
</tr>
<tr>
<td>1995</td>
<td>2.0%</td>
<td>2.0%</td>
</tr>
<tr>
<td>2000</td>
<td>2.0%</td>
<td>2.0%</td>
</tr>
<tr>
<td>2005</td>
<td>1.0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>2010</td>
<td>1.0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>2015</td>
<td>1.0%</td>
<td>1.0%</td>
</tr>
</tbody>
</table>

---

68% want to quit
55% tried to quit in the past year
STATE-SPECIFIC PREVALENCE of SMOKING among ADULTS, 2014–2015

PREVALENCE of ADULT SMOKING, by RACE/ETHNICITY—U.S., 2017

PREVALENCE of ADULT SMOKING, by EDUCATION—U.S., 2017


PUBLIC HEALTH versus “BIG TOBACCO”

TOBACCO INDUSTRY MARKETING

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 $12.4 to market its products.

Copyright © 1999-2019 The Regents of the University of California. All rights reserved. Updated January 2019.
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/ceos.php
- Tobacco industry documents indicate otherwise
- Documents available at http://legacy.library.ucsf.edu
- The cigarette is a heavily engineered product.
- Designed and marketed to maximize bioavailability of nicotine and addictive potential
- Profits over people

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.
SMOKING in MOVIES

- Cigarette smoking is pervasive in movies
  - Evident in at least ¾ of box-office hits
  - Average, 10.9 smoking incidents per hour

- There is a dose-response, causal relationship between exposure to smoking in movies and youth smoking initiation

70% of adults support assigning an "R" rating to movies with smoking.

For more information on smoking in movies, go to http://smokefreemovies.ucsf.edu

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Cigarette smoking is causally linked to diseases of nearly all organs of the body, diminished health status, and harm to the fetus. Additionally, smoking has many adverse effects on the body, such as causing inflammation and impairing 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.

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
- 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

HEALTH CONSEQUENCES of SMOKELESS TOBACCO USE

- Periodontal effects
  - Gingival recession
  - Bone attachment loss
  - Dental caries
- Oral leukoplakia
- Cancer
  - Oral cancer
  - Pharyngeal cancer

QUITTING: HEALTH BENEFITS

<table>
<thead>
<tr>
<th>Time Since Quit Date</th>
<th>Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 weeks to 3 months</td>
<td>Lung cilia regain normal function</td>
</tr>
<tr>
<td></td>
<td>Ability to clear lungs of mucus increases</td>
</tr>
<tr>
<td></td>
<td>Excess risk of CHD decreases to half that of a continuing smoker</td>
</tr>
<tr>
<td></td>
<td>Coughing, fatigue, shortness of breath decrease</td>
</tr>
<tr>
<td>1 year</td>
<td>Lung cancer death rate drops to half that of a continuing smoker</td>
</tr>
<tr>
<td>5 years</td>
<td>Risk of stroke is reduced to that of people who have never smoked</td>
</tr>
<tr>
<td>10 years</td>
<td>Risk of cancer of mouth, throat, esophagus, bladder, kidney, pancreas decreases</td>
</tr>
<tr>
<td>15 years</td>
<td>Risk of CHD is similar to that of people who have never smoked</td>
</tr>
<tr>
<td></td>
<td>Circulation improves, walking becomes easier</td>
</tr>
<tr>
<td></td>
<td>Lung function increases</td>
</tr>
</tbody>
</table>

There is no safe level of second-hand smoke.
**BENEFICIAL EFFECTS of QUITTING: PULMONARY EFFECTS**

*AT ANY AGE, there are benefits of quitting.*

[Graph showing reduction in cumulative risk of death from lung cancer in men]

**SMOKING CESSION: 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.

[Graph showing years of life gained after smoking cessation]

**FINANCIAL IMPACT of SMOKING**

- Buying cigarettes every day for 50 years at $6.26 per pack
  (does not include interest)

<table>
<thead>
<tr>
<th>Packs per day</th>
<th>Dollars lost, in thousands</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>$114,245</td>
</tr>
<tr>
<td>100</td>
<td>$228,490</td>
</tr>
<tr>
<td>200</td>
<td>$342,735</td>
</tr>
</tbody>
</table>

Annual cost of smoking 1 pack per day: $2,285


**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 $2,285 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

**FORMS of TOBACCO**

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FORMS of TOBACCO

- Cigarettes
- Smokeless tobacco (chewing tobacco, oral snuff)
- Pipes
- Cigars
- Clove cigarettes
- Bidis
- Hookah (waterpipe smoking)
- Electronic cigarettes ("e-cigarettes")*

*E-cigarettes are devices that deliver nicotine and are not a form of tobacco.

Image courtesy of the Centers for Disease Control and Prevention / Rick Ward

AMERICAN CIGARETTES

- Most common form of tobacco used in U.S.
- Sold in packs (20 cigarettes/pack)
- Total nicotine content, per cigarette:
  - Average 13.5 mg (range, 11.9 to 14.5 mg)
- Machine-measured nicotine yield:

<table>
<thead>
<tr>
<th>Type of Cigarette</th>
<th>Yield per cigarette</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full-flavor (regular)</td>
<td>1.1 mg</td>
</tr>
<tr>
<td>Light</td>
<td>0.8 mg</td>
</tr>
<tr>
<td>Ultra-light</td>
<td>0.4 mg</td>
</tr>
<tr>
<td>Average (all brands)</td>
<td>0.9 mg</td>
</tr>
</tbody>
</table>

Marlboro and Marlboro Light are registered trademarks of Philip Morris, Inc.

SMOKELESS TOBACCO

- Chewing tobacco
  - Looseleaf
  - Plug
  - Twist
- Snuff
  - Moist
  - Dry

The Copenhagen and Skoal logos are registered trademarks of U.S. Smokeless Tobacco Company, and Red Man is a registered trademark of Swedish Match.

SMOKELESS FORMS of TOBACCO

Estimated 8.8 million users in the U.S. in 2013 (3.4%)

- Adult males (6.5%) more likely than adult females (0.4%) to be current users
- Prevalence highest among
  - Young adults aged 18-25 years
  - Residents of the Midwest and Southern U.S.
  - Residents of nonmetropolitan areas

Significant health risks

- Numerous carcinogens
- Nicotine exposure comparable to that of smokers, leading to
  - Physical dependence
  - Withdrawal symptoms after abstinence

NICOTINE CONTENT in SMOKELESS TOBACCO PRODUCTS

<table>
<thead>
<tr>
<th>Dose</th>
<th>Product</th>
<th>pH</th>
<th>Total free nicotine (mg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Hawken Wintergreen</td>
<td>5.2–5.7</td>
<td>0.01–0.02</td>
</tr>
<tr>
<td></td>
<td>Skoal Bandits Wintergreen</td>
<td>6.9–7.1</td>
<td>0.5–1.0</td>
</tr>
<tr>
<td>Medium</td>
<td>Skoal Long Cut Straight</td>
<td>7.5–7.6</td>
<td>2.4–3.7</td>
</tr>
<tr>
<td>High</td>
<td>Kodiak Wintergreen</td>
<td>8.2–8.4</td>
<td>5.8–6.5</td>
</tr>
<tr>
<td></td>
<td>Copenhagen</td>
<td>7.6–8.6</td>
<td>3.1–9.4</td>
</tr>
</tbody>
</table>


HEALTH CONSEQUENCES of SMOKELESS TOBACCO USE

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

Oral leukoplakia

Cancer
- Oral cancer
- Pharyngeal cancer

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

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PIPE TOBACCO

- Prevalence of pipe smoking in the U.S. is less than 1%
- Pipe smokers have an increased risk of death due to:
  - Cancer (lung, oral cavity, esophagus, larynx)
  - Chronic obstructive pulmonary disease
- Risk of smoking tobacco-related death: cigarettes > pipes ≈ cigars

CIGARS

- Estimated 12.4 million cigar smokers in the U.S. in 2013
- Tobacco content of cigars varies greatly
- One cigar can deliver enough nicotine to establish and maintain dependence
- Cigar smoking is not a safe alternative to cigarette smoking

CLOVE CIGARETTES (also known as KRETEKS)

- Mixture of tobacco and cloves
- Imported from Indonesia
- In 2012, an estimated 3.0% of 12th graders in the U.S. reported smoking kreteks in the past year
- Two times the tar and nicotine content of standard cigarettes

BIDIS

- Imported from India
- Resemble marijuana joints
- Available in candy flavors
- In 2010, an estimated 1.4% of 12th graders in the U.S. reported smoking bidis in the past year
- Deliver 3-fold higher levels of carbon monoxide and nicotine and 5-fold higher levels of tar when compared to standard cigarettes

HOOKAH (WATERPIPE SMOKING)

- Also known as Sheisha, Narghile, Goza, Hubble bubble
- Tobacco flavored with fruit pulp, honey, and molasses
- Increasingly popular among young adults in coffee houses, bars, and lounges
  - In 2012, 18.3% of 12th graders and 25.7% of U.S. college students had smoked hookah in the past year
- Nicotine, tar and carbon monoxide levels comparable to or higher than those in cigarette smoke

ELECTRONIC CIGARETTES

- Generally similar in appearance to cigarettes, cigars, pipes, or pens
- Battery-operated devices that create a vapor for inhalation
  - Simulates smoking but does not involve combustion of tobacco
- Also known as E-cigarette, E-hookah, Hookah pen, Vapes, Vape pen, Vape pipe, Electronic nicotine delivery system (ENDS)
**ELECTRONIC CIGARETTES: Components**

- Power source
  - Rechargeable or disposable battery
- Cartridge containing liquid solution
  - Propylene glycol
  - Glycerin
  - Flavorings (tobacco, fruit, chocolate, mint, cola, candy, etc.)
  - Nicotine (0-36 mg/mL)
- Electronic atomizer/vaporizer
  - Heating element vaporizes liquid at temperatures 65-120 °C

---

**ELECTRONIC CIGARETTES: Potential health risks**

- Propylene glycol may cause respiratory irritation and increase the risk for asthma
- Glycerin may cause lipid pneumonia on inhalation
- Nicotine is highly addictive and can be harmful
  - Refill cartridges with high concentrations of nicotine are a poisoning risk, especially in children
- Carcinogenic substances are found in some aerosols
- Use of e-cigarettes leads to emission of propylene glycol, particles, nicotine, and carcinogens into indoor air
  - Long-term safety of second-hand exposure to e-cigarette aerosols is unknown

**ELECTRONIC CIGARETTES: Indoor Air Pollution**

- E-cigarettes are not emission-free
- During vaping sessions, compounds and particles emitted into the indoor air include
  - Propylene glycol
  - Glycerin
  - Heavy metals
  - Nicotine
  - Flavoring agents
  - Polycyclic aromatic hydrocarbons
- Levels of most substances lower than conventional cigarettes
- Long-term safety of second-hand exposure to e-cigarette aerosols is unknown


**ELECTRONIC CIGARETTES: Current Trends and Evidence**

- Predominantly used by smokers and smokers who are considering quitting
- Used as an alternative to cigarette smoking and as an aid for cessation
  - Perceived as less harmful than conventional cigarettes
- Use is increasing among adolescents and young adults

**ELECTRONIC CIGARETTES: Current Trends and Evidence, cont’d**

- Can reduce the desire (craving) to smoke cigarettes and alleviate nicotine withdrawal symptoms
- Some smokers reduce the number of cigarettes smoked or quit smoking as a result of using e-cigarettes
- Have not been proven effective as an aid for sustained smoking cessation

Long-term safety and efficacy data are lacking.

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FORMS of TOBACCO: SUMMARY

- Cigarettes are, by far, the most common form of tobacco used in the U.S.
- Other forms of tobacco and nicotine delivery devices exist, and some are increasing in popularity.
- All forms of tobacco are harmful.
- The safety/efficacy of e-cigarettes is not established.
- Attention to all forms of tobacco is needed.

NICOTINE PHARMACOLOGY and PRINCIPLES of ADDICTION

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.

CHEMISTRY of NICOTINE

Nicotiana tabacum

Natural liquid alkaloid
Colorless, volatile base $pK_a = 8.0$


PHARMACOLOGY

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

Pharmacodynamics
Effects of the drug on the body

NICOTINE ABSORPTION

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

At physiologic pH, nicotine is readily absorbed.
NICOTINE ABSORPTION: Buccal (Oral) Mucosa

The pH inside the mouth is 7.0.

<table>
<thead>
<tr>
<th>Acidic media (limited absorption)</th>
<th>Alkaline media (significant absorption)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarettes</td>
<td>Pipes, cigars, spit tobacco, oral nicotine products</td>
</tr>
</tbody>
</table>

Beverages can alter pH, affect absorption.

NICOTINE ABSORPTION: Skin and Gastrointestinal Tract

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

NICOTINE ABSORPTION: Lung

- Nicotine is "distilled" from burning tobacco and carried in tar droplets.
- Nicotine is rapidly absorbed across respiratory epithelium.
  - Lung pH = 7.4
  - Large alveolar surface area
  - Extensive capillary system in lung
- Approximately 1 mg of nicotine is absorbed from each cigarette.

NICOTINE DISTRIBUTION

- Nicotine reaches the brain within 10–20 seconds.

NICOTINE METABOLISM

10–20% excreted unchanged in urine

70–80% cotinine

10% other metabolites

Metabolized and excreted in urine


NICOTINE EXCRETION

- Half-life
  - Nicotine t½ = 2 hr
  - Cotinine t½ = 16 hr
- Excretion
  - Occurs through kidneys (pH dependent; ↑ with acidic pH)
  - Through breast milk
Nicotine binds to receptors in the brain and other sites in the body.

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

Nicotine has predominantly stimulatory effects.

NEUROCHEMICAL and RELATED EFFECTS of 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

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.

DOPAMINE REWARD PATHWAY
- Prefrontal cortex
- Dopamine release
- Nucleus accumbens
- Ventral tegmental area
- Stimulation of nicotine receptors
- Nicotine enters brain

CHRONIC ADMINISTRATION of NICOTINE: EFFECTS on the BRAIN
- Human smokers have increased nicotine receptors in the prefrontal cortex.

Image courtesy of George Washington University / Dr. David C. Perry

Perry et al. (1999). J Pharmacol Exp Ther 289:1545–1552
NICOTINE WITHDRAWAL SYMPTOMS:
Time Course*

<table>
<thead>
<tr>
<th>Quit date</th>
<th>Recent quitter</th>
<th>Former tobacco user</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 week</td>
<td>Irritability / Frustration / Anger</td>
<td>6 months</td>
</tr>
<tr>
<td>4 weeks</td>
<td>Anxiety</td>
<td>Can persist for months to years after quitting</td>
</tr>
<tr>
<td>12 weeks</td>
<td>Difficulty concentrating</td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>4 weeks</td>
<td>Insomnia</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>Restlessness / Impatience</td>
<td></td>
</tr>
<tr>
<td>12 weeks</td>
<td>Depressed mood / Depression</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>Increased appetite</td>
<td></td>
</tr>
<tr>
<td>12 weeks</td>
<td>Weight gain</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>Cravings</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>Most symptoms manifest within the first 1–2 days, peak within the first week, and subside within 2–4 weeks.</td>
<td></td>
</tr>
</tbody>
</table>


NICOTINE ADDICTION CYCLE


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 more frequently
  - Smoking more intensely
  - Obstructing vents on low-nicotine brand cigarettes


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 indicate higher levels of dependence
- Scores range from 0 to 10; score of greater than 5 indicates substantial dependence


FACTORS CONTRIBUTING to TOBACCO USE

- Individual
  - Sociodemographics
  - Genetic predisposition
  - Coexisting medical conditions
- 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

<table>
<thead>
<tr>
<th>Physiological</th>
<th>Behavioral</th>
</tr>
</thead>
<tbody>
<tr>
<td>The addiction to nicotine</td>
<td>The habit of using tobacco</td>
</tr>
<tr>
<td>Medications for cessation</td>
<td>Behavior change program</td>
</tr>
</tbody>
</table>

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

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.

PHARMACOKINETIC DRUG INTERACTIONS with SMOKING

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

- Bendamustine
- Haloperidol
- Tasimelteon
- Caffeine
- Olanzapine
- Theophylline
- Clozapine
- Riociguat
- Erlotinib
- Ropinirole
- Fluvoxamine
- Tacrine
- Irinotecan (clearance increased and systemic exposure decreased, due to increased glucuronidation of its active metabolite)

Smoking cessation will reverse these effects.

PHARMACODYNAMIC DRUG INTERACTIONS with SMOKING

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

- Stroke
- Myocardial infarction
- Thromboembolism

This interaction does not decrease the efficacy of hormonal contraceptives.

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

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Drug Interactions with Tobacco Smoke

Many interactions between tobacco smoke and medications have been identified. Note that in most cases to the tobacco smoke—not the nicotine—causes these drug interactions. Tobacco smoke interacts with medications through pharmacokinetic (PK) and pharmacodynamic (PD) mechanisms. PK interactions affect the absorption, distribution, metabolism, or elimination of other drugs, potentially causing an altered pharmacologic response. The majority of PK interactions are mediated by the cytochrome P450 (CYP450) system. Tobacco products, through smoke inhalation, can increase the activity of CYP450 enzymes. PD interactions are the receptor or cellular response to a drug. Inhalation of smoke products may affect PD interactions and the expected response or actions of other drugs. The amount of tobacco smoking needed to have an effect has not been established, and the assumption is that any smoker is susceptible to the same degree of interaction. The most clinically significant interactions are depicted in the shaded rows.

<table>
<thead>
<tr>
<th>Drug</th>
<th>PK Interaction</th>
<th>PD Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen (Tylenol)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Decreased clearance</td>
<td>N/A</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Decreased intestinal absorption</td>
<td>N/A</td>
</tr>
<tr>
<td>Chloramphenicol (Tabloid)</td>
<td>Decreased clearance</td>
<td>N/A</td>
</tr>
<tr>
<td>Disopyramide (Norpace)</td>
<td>Decreased clearance</td>
<td>N/A</td>
</tr>
<tr>
<td>Diazepam (valium)</td>
<td>Decreased clearance</td>
<td>N/A</td>
</tr>
<tr>
<td>Ethanol (Tang)</td>
<td>Decreased clearance</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Clinicians should be aware of their patients’ smoking status:
- Clinically significant interactions result from 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.

Assisting Patients with Quitting

- Update released May 2008
- Sponsored by the U.S. Department of Health and Human Services, Public Health 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

Tobacco Dependence: A 2-Part Problem

- Tobacco Dependence
  - Physiological: The addiction to nicotine
  - Behavioral: The habit of using tobacco

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.

NONPHARMACOLOGIC METHODS

- Cold turkey: Just do it!
- Unassisted tapering (fading)
  - Reduced frequency of use
  - Lower nicotine cigarettes
  - Special filters or holders
- Assisted tapering
  - QuitKey (PICS, Inc.)
    - Computer developed taper based on patient's smoking level
    - Includes telephone counseling support

NONPHARMACOLOGIC METHODS (cont'd)

- Formal cessation programs
  - Self-help programs
  - Individual counseling
  - Group programs
  - Telephone counseling
    - 1-800-QUITNOW
    - www.smokefree.gov
    - www.quitnet.com
    - www.becomeanex.org
- Acupuncture therapy
- Hypnotherapy
- Massage therapy

EFFECTS of CLINICIAN INTERVENTIONS

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

<table>
<thead>
<tr>
<th>Type of Clinician</th>
<th>Estimated abstinence at 5+ months</th>
</tr>
</thead>
<tbody>
<tr>
<td>No clinician</td>
<td>1.0</td>
</tr>
<tr>
<td>Self-help material</td>
<td>1.1</td>
</tr>
<tr>
<td>Nonphysician clinician</td>
<td>1.7</td>
</tr>
<tr>
<td>Physician clinician</td>
<td>2.2</td>
</tr>
</tbody>
</table>

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.

\( n = 29 \) studies


The NUMBER of CLINICIAN TYPES CAN MAKE a DIFFERENCE, too

Compared to smokers who receive assistance from no clinicians, smokers 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.

<table>
<thead>
<tr>
<th>Number of Clinician Types</th>
<th>Estimated abstinence at 5+ months</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>1.0</td>
</tr>
<tr>
<td>One</td>
<td>1.8</td>
</tr>
<tr>
<td>Two</td>
<td>2.5</td>
</tr>
<tr>
<td>Three or more</td>
<td>2.4</td>
</tr>
</tbody>
</table>

\( n = 37 \) studies


WHY SHOULD CLINICIANS ADDRESS 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).
- Failure to address tobacco use tacitly implies that quitting is not important.

The 5 A’s

- ASK
- ADVISE
- ASSESS
- ASSIST
- ARRANGE


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The 5 A’s (cont’d)

**ASK** about tobacco use

- "Do you ever smoke or use other types of tobacco or nicotine, such as e-cigarettes?"
- "I take time to ask all of my patients about tobacco use—because it’s important."
- "Condition X often is caused or worsened by smoking. Do you, or does someone in your household smoke?"
- "Medication X often is used for conditions linked with or caused by smoking. Do you, or does someone in your household smoke?"

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

- "It’s important that you quit as soon as possible, and I can help you."
- "Cutting down while you are ill is not enough."
- "Occasional or light smoking is still harmful."
- "I realize that quitting is difficult. It is the most important thing you can do to protect your health now and in the future. I have training to help my patients quit, and when you are ready, I will work with you to design a specialized treatment plan."

**ASSESS** readiness to make a quit attempt

**ASSIST** with the quit attempt

- Not ready to quit: enhance motivation (the 5 R’s)
- Ready to quit: design a treatment plan
- Recently quit: relapse prevention

**ARRANGE** follow-up care

<table>
<thead>
<tr>
<th>Number of sessions</th>
<th>Estimated quit rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 1</td>
<td>12.4%</td>
</tr>
<tr>
<td>2 to 3</td>
<td>16.3%</td>
</tr>
<tr>
<td>4 to 8</td>
<td>20.9%</td>
</tr>
<tr>
<td>More than 8</td>
<td>24.7%</td>
</tr>
</tbody>
</table>

* 5 months (or more) postcessation

Provide assistance throughout the quit attempt.


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

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?
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.

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.

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.

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.

GOAL: Start thinking about quitting.

ASSESSING READINESS to QUIT (cont’d)

Counseling Strategies

DO
- Strongly advise to quit
- Provide information
- Ask noninvasive questions; identify reasons for tobacco use
- Raise awareness of health consequences/concerns
- Demonstrate empathy, foster communication
- Leave decision up to patient

DON’T
- Persuade
- “Cheerlead”
- Tell patient how bad tobacco is, in a judgmental manner
- Provide a treatment plan

Consider asking:

“Do you ever plan to quit?”

IF YES
Advise patients to quit, and offer to assist (if or when they change their mind).

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

“What might be some of the benefits of quitting now, instead of later?”
Responses will reveal some of the barriers to quitting.

“What would have to change for you to decide to quit sooner?”
STAGE 1: NOT READY to QUIT
counseling strategies (cont’d)

The 5 R’s—Methods for enhancing motivation:
- Relevance
- Risks
- Rewards
- Roadblocks
- Repetition

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.

STAGE 2: READY to QUIT
three key elements of counseling

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

GOAL: Achieve cessation.

Discuss Key Issues

- 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

STAGE 2: READY to QUIT
clinical practice guideline

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

<table>
<thead>
<tr>
<th>THE MYTHS</th>
<th>THE FACTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Smoking gets rid of all my stress.&quot;</td>
<td>There will always be stress in one’s life.</td>
</tr>
<tr>
<td>“I can’t relax without a cigarette.”</td>
<td>There are many ways to relax without a cigarette.</td>
</tr>
</tbody>
</table>

Smokers confuse the relief of withdrawal with the feeling of relaxation.

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

---

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

**Concerns about 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

**Concerns about 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

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

**Living with Another Smoker**
- 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 smoker one ashtray: "Please keep this clean and hidden from me."
- Surprise the smoker with a gift at the end of your first month of quitting as a thank you

---

**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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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.

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"

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

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)

TEACH and ENCOURAGE COPING

TEACH and ENCOURAGE COPING: STEP #1

TEACH and ENCOURAGE COPING: STEP #2

Remind yourself that urges are brief.
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.

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

Cognitive Coping Strategies: Examples

- 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

Behavioral Coping Strategies

- 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!

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

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.

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.
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, smokers, 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?

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

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.

STAGE 4: Former tobacco user

GOAL: Remain tobacco-free for life.

Tobacco-free for 6 months

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

ASSESSING READINESS to QUIT (cont’d)

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.
READINESS to QUIT: A REVIEW

- Not ready to quit
- Ready to quit

Recent quitter
- Tobacco use

Former tobacco user
- Tobacco use

- Behavioral counseling
- Pharmacotherapy
- Relapse prevention

Ready to quit
- Behavioral counseling
- Pharmacotherapy
- Relapse prevention

Quit date
- 30 days
- + 6 months

Enhance motivation
- The 5 R’s

The 5 A’s
- Behavioral counseling
- Relapse prevention

- 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

BRIEF COUNSELING: ASK, ADVISE, REFER

- ASK about tobacco USE
- ADVISE tobacco users to QUIT
- REFER to other resources

Patient receives assistance from other resources, with follow-up counseling arranged

ASSIST

ARRANGE

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)
- 28.1% success rate for patients who use the quitline and a medication for cessation

Most health-care providers, and most patients, are not familiar with tobacco quitlines.

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

Quitlines have broad reach and are recommended as an effective strategy in the 2008 Clinical Practice Guideline.
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.

WHAT IF...

a patient asks you about your use of tobacco?

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.

DR. GRO HARLEM BRUNTLAND, FORMER DIRECTOR-GENERAL of the WHO:

“If we do not act decisively, a hundred years from now our grandchildren and their children will look back and seriously question how people claiming to be committed to public health and social justice allowed the tobacco epidemic to unfold unchecked.”

MEDICATIONS for CESSATION

Courtesy of Mell Lazarus and Creators Syndicate. Copyright 2000, Mell Lazarus.

There is no place for tobacco in any health-care setting.

TOBACCO DEPENDENCE: A 2-PART PROBLEM

**Tobacco Dependence**

- **Physiological**
  - The addiction to nicotine
  - Treatment
  - Medications for cessation

- **Behavioral**
  - The habit of using tobacco
  - Treatment
  - Behavior change program

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

NICOTINE WITHDRAWAL SYMPTOMS: Time Course* and Management

**Quit state**

- Recent quitter
- Former tobacco user

**Symptoms**

- Irritability / Frustration / Anger
- Anxiety
- Difficulty concentrating
- Palpitations / Irritability
- Depressed mood / Depression
- Insomnia
- Impaired task performance
- Increased appetite
- Cravings
- Weight gain
- Covings
- Difficulty concentrating
- Restlessness / Impatience
- Depressed mood / Depression
- Insomnia
- Impaired task performance
- Increased appetite
- Cravings
- Weight gain
- Covings

**Timeline**

- 1 week
- 4 weeks
- 12 weeks
- 6 months

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


**Recent quitter**

- Most symptoms manifest within the first 1–2 days,
- Peak within the first week,
- And subside within 2–4 weeks.

**Former tobacco user**

- Can persist for months to years after quitting.

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.

"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.

Recommended treatment is behavioral counseling.

FDA-APPROVED MEDICATIONS for CESSATION

**Nicotine polacrilex gum* **
- Nicorette (OTC)
- Generic nicotine gum (OTC)

**Nicotine lozenge***
- Nicorette (OTC)
- Generic nicotine lozenge (OTC)

**Nicotine transdermal patch***
- NicoDerm CQ (OTC)
- Generic nicotine patches (OTC)

**Nicotine inhaler***
- Nicotrol (Rx)

**Nicotine nasal spray***
- Nicotrol NS (Rx)

**Bupropion SR***
- Zyban (Rx)
- Generic bupropion SR (Rx)

**Varenicline***
- Chantix (Rx)

* Includes nicotine replacement therapy (NRT) products.

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

NRT products approximately doubles quit rates.
**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.

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**NICOTINE GUM**

Nicorette; generics

- Resin complex
  - Nicotine
  - Polacrilex

- Sugar-free chewing gum base

- Contains buffering agents to enhance buccal absorption of nicotine

- Available: 2 mg, 4 mg; original, cinnamon, fruit, and mint (various) flavors

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**NICOTINE LOZENGE**

Nicorette Lozenge and Nicorette Mini Lozenge; generics

- Nicotine polacrilex formulation
  - Delivers \( \sim 25\% \) 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

---

**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

**Recommended Usage Schedule**

<table>
<thead>
<tr>
<th>Weeks 1–6</th>
<th>Weeks 7–9</th>
<th>Weeks 10–12</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 piece q 1–2 h</td>
<td>1 piece q 2–4 h</td>
<td>1 piece q 4–8 h</td>
</tr>
</tbody>
</table>

Do not use more than 24 pieces of GUM or 20 LOZENGES per day.
NICOTINE GUM: DIRECTIONS FOR USE

- Park between cheek & gum
- Chew slowly
- Chew again when peppery taste or tingle fades
- Stop chewing at first sign of peppery taste or tingling sensation

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

NICOTINE GUM/LOZENGE: DIRECTIONS for USE (cont’d)

- Chew 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

NICOTINE GUM/LOZENGE: ADDITIONAL PATIENT EDUCATION

- To improve chances of quitting, 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.

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

NICOTINE GUM/LOZENGE: SUMMARY

ADVANTAGES

- Might serve as an oral substitute for tobacco
- Might delay weight gain
- Can be titrated to manage withdrawal symptoms
- Can be used in combination with other agents to manage situational urges
- Relatively inexpensive

DISADVANTAGES

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

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TRANSDERMAL NICOTINE PATCH
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

TRANSDERMAL NICOTINE PATCH: DOSING

<table>
<thead>
<tr>
<th>Product</th>
<th>Light Smoker</th>
<th>Heavy Smoker</th>
</tr>
</thead>
<tbody>
<tr>
<td>NicoDerm CQ</td>
<td>&lt;10 cigarettes/day</td>
<td>&gt;10 cigarettes/day</td>
</tr>
<tr>
<td></td>
<td>Step 2 (14 mg x 6 weeks)</td>
<td>Step 1 (21 mg x 4 weeks)</td>
</tr>
<tr>
<td></td>
<td>Step 3 (7 mg x 2 weeks)</td>
<td>Step 2 (14 mg x 2 weeks)</td>
</tr>
<tr>
<td></td>
<td>Step 3 (7 mg x 2 weeks)</td>
<td>Step 3 (7 mg x 2 weeks)</td>
</tr>
<tr>
<td>Generic</td>
<td>&lt;10 cigarettes/day</td>
<td>&gt;10 cigarettes/day</td>
</tr>
<tr>
<td></td>
<td>Step 2 (14 mg x 6 weeks)</td>
<td>Step 1 (21 mg x 4 weeks)</td>
</tr>
<tr>
<td></td>
<td>Step 3 (7 mg x 2 weeks)</td>
<td>Step 2 (14 mg x 2 weeks)</td>
</tr>
<tr>
<td></td>
<td>Step 3 (7 mg x 2 weeks)</td>
<td>Step 3 (7 mg x 2 weeks)</td>
</tr>
</tbody>
</table>

TRANSDERMAL NICOTINE PATCH: DIRECTIONS for USE

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

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

- Remove 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

TRANSDERMAL NICOTINE PATCH: ADDITIONAL PATIENT EDUCATION

- Water will not harm the nicotine patch if it is applied correctly; patients may bathe, swim, shower, or exercise while wearing the patch
- Do not cut patches to adjust dose
  - 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

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

Common adverse effects include:
- Irritation at the patch application site (generally within the first hour)
  - Mild itching
  - Burning
  - Tingling
- Sleep disturbances
  - Abnormal or vivid dreams
  - Insomnia
- After patch removal, skin may appear red for 24 hours
- If skin stays red more than 4 days or if it swells or a rash appears, contact health care provider—do not apply new patch
- Local skin reactions (redness, burning, itching)
  - Usually caused by adhesive
  - Up to 50% of patients experience this reaction
  - Fewer than 5% of patients discontinue therapy
- Avoid use in patients with dermatologic conditions (e.g., psoriasis, eczema, atopic dermatitis)

**TRANSDERMAL NICOTINE PATCH: SUMMARY**

**ADVANTAGES**
- 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)

**NICOTINE INHALER**

Nicotrol Inhaler

- Nicotine inhalation system consists of:
  - Mouthpiece
  - Cartridge with porous plug containing 10 mg nicotine and 1 mg menthol
  - Delivers 4 mg nicotine vapor, absorbed across buccal mucosa

**NICOTINE INHALER: SCHEMATIC DIAGRAM**


**NICOTINE INHALER: DOSING**

- Initial treatment (up to 12 weeks)
  - Start with at least 6 cartridges/day during the first 3–6 weeks of treatment
  - Increase prn to maximum of 16 cartridges/day
  - In general, use 1 cartridge every 1–2 hours
- Gradually reduce daily dosage over the following 6–12 weeks
- Recommended maximum duration of therapy is 6 months
NICOTINE INHALER: DIRECTIONS for USE

- Align marks on the mouthpiece

NICOTINE INHALER: DIRECTIONS for USE (cont’d)

- Pull and separate mouthpiece into two parts

NICOTINE INHALER: DIRECTIONS for USE (cont’d)

- Press nicotine cartridge firmly into bottom of mouthpiece until it pops down into place
- Line up the markings on the mouthpiece again and push the two pieces back together so they fit tightly
- Twist top to misalign marks and secure unit

NICOTINE INHALER: ADDITIONAL PATIENT EDUCATION

- Adverse effects associated with the nicotine inhaler include:
  - Mild irritation of the mouth or throat
  - Cough
  - Hiccups
  - Gastrointestinal complaints (dyspepsia, nausea)
- Severity generally rated as mild, and frequency of symptoms declined with continued use

NICOTINE INHALER: ADD’L PATIENT EDUCATION (cont’d)

- During inhalation, nicotine is vaporized and absorbed across oropharyngeal mucosa
- Inhale into back of throat or puff in short breaths
- Nicotine in cartridges is depleted after about 20 minutes of active puffing
  - Cartridge does not have to be used all at once—try different schedules (e.g., 5 minutes at a time) to find what works best
  - Open cartridge retains potency for 24 hours
- Mouthpiece is reusable; clean regularly with mild detergent

NICOTINE INHALER: ADD’L PATIENT EDUCATION (cont’d)

- Use inhaler at room temperature (>60°F); in cold environments, the delivery of nicotine vapor may be compromised
- Use the inhaler longer and more often at first to help control cravings (best results are achieved with frequent continuous puffing over 20 minutes)
- Effectiveness of the nicotine inhaler may be reduced by some foods and beverages

Do NOT eat or drink for 15 minutes BEFORE or while using the nicotine inhaler.
NICOTINE INHALER: SUMMARY

**ADVANTAGES**
- Might serve as an oral substitute for tobacco
- Can be titrated to manage withdrawal symptoms
- Mimics the hand-to-mouth ritual of smoking
- Can be used in combination with other agents to manage situational urges

**DISADVANTAGES**
- Need for frequent dosing can compromise adherence
- Cartridges might be less effective in cold environments (≤60°F)
- Cost of treatment

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

NICOTINE NASAL SPRAY: DIRECTIONS for USE

- Press in circles on sides of bottle and pull to remove cap
- Prime the pump (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
- 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
  - Nicotine is absorbed through skin and mucous membranes

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

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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

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

BUPROPION SR: Zyban; 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
- 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)

BUPROPION: PHARMACOKINETICS

CONTRAINDICATIONS

- Patients with a seizure disorder
- Patients with a current or prior diagnosis of bulimia or anorexia nervosa
- Patients undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates and antiepileptic drugs
- Patients taking MAO inhibitors (within 14 days of initiating or discontinuing therapy)

WARNINGS and PRECAUTIONS

Bupropion should be used 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.
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

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.

BUPROPION SR: DOSING

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

**Initial treatment**
- 150 mg po q AM for 3 days

**Then...**
- 150 mg po bid for 7–12 weeks
- Doses must be administered at least 8 hours apart
- Tapering not necessary when discontinuing therapy

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

BUPROPION SR: SUMMARY

**ADVANTAGES**
- Oral dosing is simple and associated with fewer adherence problems
- Might delay weight gain
- Bupropion might be beneficial in patients with depression
- Can be used in combination with NRT agents
- Relatively inexpensive (generic formulations)

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

VARENICLINE

- Nonnicotine cessation aid
- Partial nicotinic receptor agonist
- Oral formulation

VARENICLINE: MECHANISM of ACTION

- Binds with high affinity and selectivity at α₄β₂ neuronal nicotinic acetylcholine receptors
- Stimulates low-level agonist activity
- Competitively inhibits 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

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.

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 and most have not been causally linked to varenicline use.

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.

<table>
<thead>
<tr>
<th>Treatment Day</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial dose titration</td>
<td></td>
</tr>
<tr>
<td>Day 1 to day 3</td>
<td>0.5 mg qd</td>
</tr>
<tr>
<td>Day 4 to day 7</td>
<td>0.5 mg bid</td>
</tr>
<tr>
<td>Day 8 to end of treatment*</td>
<td>1 mg bid</td>
</tr>
</tbody>
</table>

* Up to 12 weeks

Varenicline Quit Approaches

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

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

- GRADUAL QUIT approach
  - 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

Images from: https://www.pfizerpro.com/product/chantix/quit-approaches

Varenicline: ADVERSE EFFECTS

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

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

VARENICLINE: SUMMARY

ADVANTAGES
- Oral dosing is simple and associated with fewer adherence problems
- Offers a different mechanism of action for persons who have failed other agents
- Most effective agent for cessation when used as monotherapy

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

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

- Active drug
- Placebo

<table>
<thead>
<tr>
<th>Medication</th>
<th>Percent Quit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine gum</td>
<td>16.3</td>
</tr>
<tr>
<td>Nicotine patch</td>
<td>15.7</td>
</tr>
<tr>
<td>Nicotine lozenge</td>
<td>21.0</td>
</tr>
<tr>
<td>Nicotine nasal spray</td>
<td>23.9</td>
</tr>
<tr>
<td>Nicotine inhaler</td>
<td>17.1</td>
</tr>
<tr>
<td>Bupropion</td>
<td>19.7</td>
</tr>
<tr>
<td>Varenicline</td>
<td>26.5</td>
</tr>
</tbody>
</table>

COMBINATION PHARMACOTHERAPY

Regimens with enough evidence to be “recommended” first-line

- Combination NRT
  - Long-acting formulation (patch)
    - Produces relatively constant levels of nicotine
  - Short-acting formulation (gum, inhaler, lozenge, nasal spray)
    - Allows for acute dose titration as needed for nicotine withdrawal symptoms
- Bupropion SR + Nicotine Patch

TREATMENT OPTIONS

Multiple Treatment Comparison Meta-Analysis

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine gum vs Placebo</td>
<td>1.7 (1.5–1.9)</td>
</tr>
<tr>
<td>Bupropion SR vs Placebo</td>
<td>1.9 (1.6–2.1)</td>
</tr>
<tr>
<td>Nicotine patch vs Placebo</td>
<td>1.9 (1.7–2.1)</td>
</tr>
<tr>
<td>Other NRT* vs Placebo</td>
<td>2.0 (1.8–2.4)</td>
</tr>
<tr>
<td>Combination NRT vs Placebo</td>
<td>2.7 (2.1–3.7)</td>
</tr>
<tr>
<td>Varenicline vs Placebo</td>
<td>2.9 (2.4–3.5)</td>
</tr>
</tbody>
</table>

*Includes nicotine nasal spray, lozenge, and inhaler

COMBINATION NRT: TREATMENT REGIMENS

- Nicotine patch
  - Dose: 21 mg/day x 4–6 wks → 14 mg/day x 2 wks → 7 mg/day x 2 wks
  - PLUS
- Nicotine gum or lozenge
  - (2 mg/4 mg; based on TTFC)
    - Dose: Use 1 piece q 1–2 hours as needed (use at least 4-5/day)
  - OR
- Nicotine inhaler
  - (10 mg cartridge; delivers 4 mg nicotine vapor)
    - Dose: Use 1 cartridge q 1–2 hours as needed
  - OR
- Nicotine nasal spray
  - (0.5 mg/spray)
    - Dose: Use 1 spray in each nostril q 1–2 hours as needed

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

Data adapted from Hartmann-Boyce et al. (2018). Cochrane Database Syst Rev
Cahill et al. (2019). Cochrane Database Syst Rev
Hughes et al. (2014). Cochrane Database Syst Rev

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IDENTIFY KEY ISSUES to STREAMLINE PRODUCT SELECTION*

- Do you prefer a prescription or nonprescription medication?
- Would it be a challenge for you to take a medication frequently throughout the day (e.g., a minimum of 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 will be ineffective.

Asking these two questions will significantly reduce the time required for product selection.

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

ADHERENCE IS KEY to QUITTING

- Promote adherence with prescribed regimens
  - Daily use (use according to dosing schedule, NOT as needed)
  - Full duration of treatment regimen

- Consider telling the patient:
  - "If used properly, the medicines can make you more comfortable while you are quitting."
  - "Medicines for quitting work best if you take them on a regular schedule, to prevent withdrawal symptoms before they occur. If you wait until you're already craving a cigarette, it will be too late. The medicines don't work as quickly as inhaled nicotine from a cigarette."

ADHERENCE IS KEY to QUITTING (cont’d)

When providing medication counseling, it is important to emphasize three key facets of adherence:

- Correct strength of medication
- Taken daily, according to a fixed schedule
- Taken for the full duration of therapy

At each encounter, assess withdrawal and adjust treatment as needed.

COMPARATIVE DAILY COSTS of PHARMACOTHERAPY

<table>
<thead>
<tr>
<th></th>
<th>Gum</th>
<th>Lozenge</th>
<th>Patch</th>
<th>Nasal spray</th>
<th>Inhaler</th>
<th>Nicotine Patch</th>
<th>Varenicline</th>
<th>Bupropion SR</th>
<th>Varenicline and NRT</th>
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<tbody>
<tr>
<td><strong>Trade</strong></td>
<td>$1.49</td>
<td>$4.97</td>
<td>$2.26</td>
<td>$2.95</td>
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<td>$8.25</td>
<td>$15.90</td>
<td>$15.90</td>
<td>$8.25</td>
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<tr>
<td><strong>Generic</strong></td>
<td>$1.90</td>
<td>$3.33</td>
<td>$1.52</td>
<td>$2.58</td>
<td>$0.10</td>
<td>$0.00</td>
<td>$0.00</td>
<td>$0.00</td>
<td>$0.00</td>
</tr>
</tbody>
</table>

Average pack of cigarettes in the US, $6.26

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 include:
  - Bupropion SR
  - Nicotine replacement therapy (as monotherapy or combination therapy)
  - Varenicline
- Varenicline and combination NRT approaches demonstrate the highest level of efficacy