Tobacco Use Disorder Update 2023

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Disclosure Statement

- Dr. Julianne Himstreet, faculty for this CE activity, has no relevant financial relationship(s) with ineligible companies to disclose.
- The opinions provided in this presentation are those of Dr. Julianne Himstreet and does not represent the opinions of the Veterans Health Administration.

Learning Objectives

1. List the types of non-cigarette tobacco and nicotine products.
2. Describe the recommendations from the U.S. Preventive Services Task Force (USPSTF) on Tobacco smoking cessation in adults.
3. Review how to the 5As (ask about tobacco, advise to quit, assess willingness to quit, assist in quitting, and arrange follow up) and the “ask, advise, refer” approaches can be used to assess a patient’s tobacco use.
4. Discuss key components of nicotine addiction and the role of pharmacotherapy.
5. Explain how pharmacotherapy is used and how to provide information to patients on proper use and safety concerns.

Pre-Test Questions

1. Which of the following is not one of the 5A's to help tobacco users through the process of quitting?
    a. Ask – Do you currently use tobacco?
    b. Advise – Use clear, strong, personalized messages
    c. Assess – Are you willing to give quitting a try in the next 30 days
    d. Allow – Provide medications if on formulary
    e. Arrange – Set up follow up sessions or attendance in a tobacco use treatment clinic

2. What is the most worrisome health problem regarding e-cigarettes?
    a. FDA has proposed rules regulating the sale of e-cigarettes
    b. Products are often flavored in ways that appeal to adults
    c. The awareness of e-cigarettes is rising among the general public
    d. E cigarette liquid contains unknown ingredients, and little is known of the health consequences
    e. The efficacy of e-cigarettes as an aid for sustained smoking cessation has not been established

3. What is most common adverse effect of varenicline?
    a. Suicidal ideation
    b. Depression
    c. Nausea and vomiting
    d. Constipation
    e. Increased urination

4. Patients prescribed the nicotine patch, should be counseled to:
    a. Apply the patch to the lower legs
    b. Avoid swimming or showering with the patch
    c. Cut the patches in order to adjust the dose
    d. Apply the patch to the same area for a week
    e. If you slip and smoke, continue using patch and try not to smoke

5. The US Preventative Services Task Force recommendations include which of the following statements as interventions for Tobacco Smoking Cessation in Adults:
    a. Recommends electronic cigarettes (ENDs) for tobacco cessation in nonpregnant adults.
    b. Recommends clinicians ask all adults about tobacco use, advise them to stop using tobacco, and provide behavioral interventions and US FDA approved pharmacotherapy for cessation to nonpregnant adults who use tobacco.
    c. Recommends US FDA approved pharmacotherapy for all pregnant adults who use tobacco.
    d. Current evidence is insufficient to assess the balance of benefits and harms of electronic cigarettes (ENDs) for tobacco cessation in adults, including pregnant person. Clinicians should direct patients who use tobacco to other tobacco cessation interventions with proven effectiveness and established safety.
    e. B and D are correct

Tobacco Use: The Problem

- **Tobacco use is the #1 cause of preventable death and disease in the U.S.**
- **Cigarette use causes 480,000 deaths each year in the U.S.**
- **50% of adult smokers will die from smoking-related causes**
- **Nicotine may be as addictive as heroin, cocaine, or alcohol**
- **Tobacco use is a chronic, relapsing condition**
- **Current smoking has decreased significantly since rates peaked in the 1960s**
  - **Men: rates declined from 52% in 1965 to 15.8% in 2017**
  - **Women: rates declined from 34.1% in 1965 to 12.2% in 2017**

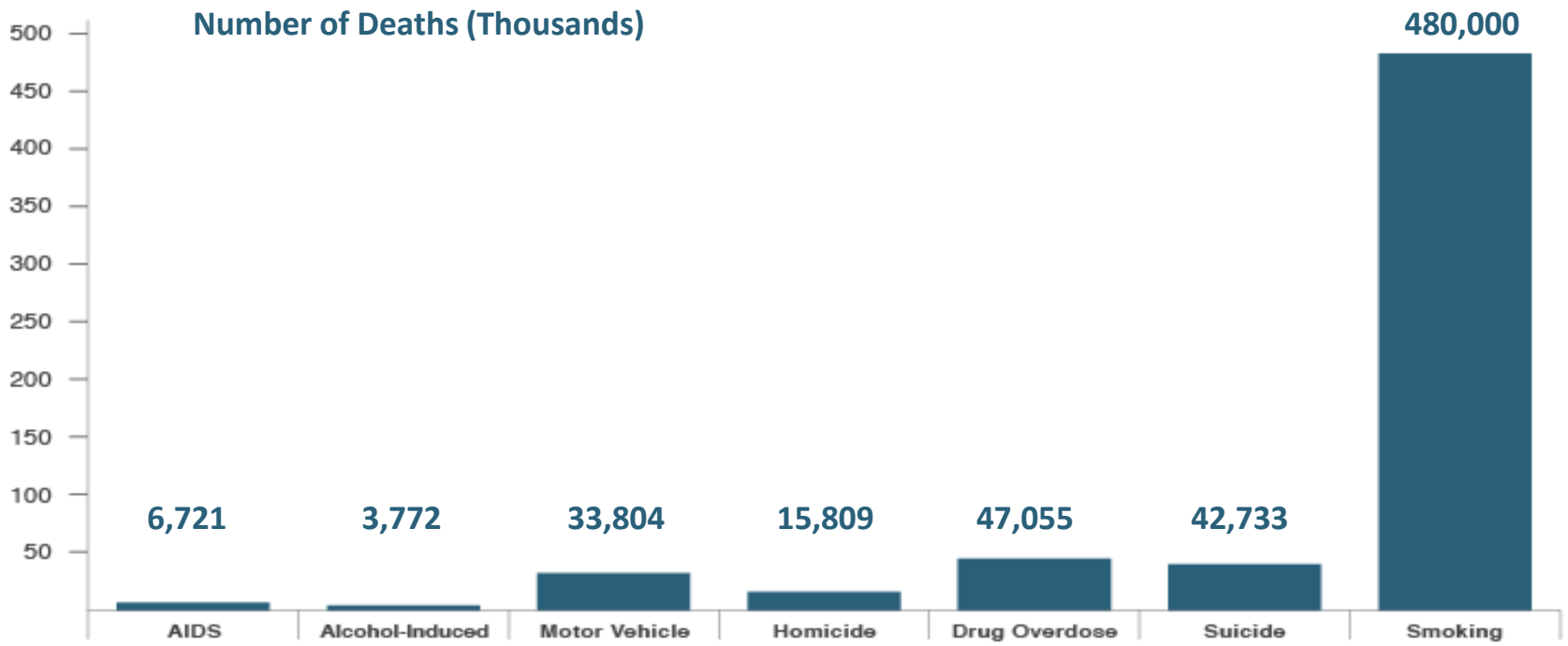
Centers for Disease Control and Prevention. Current Cigarette Smoking Among Adults—United States, 2016. Morbidity and Mortality Weekly Report 2018;67(2):53-9 [accessed 2018 Feb 22].

Centers for Disease Control and Prevention (2016). *Smokeless Tobacco: Health Effects* (Fact Sheets). Retrieved January 6, 2017 from https://www.cdc.gov/tobacco/data_statistics/fact_sheets/smokeless/health_effects/index.htm

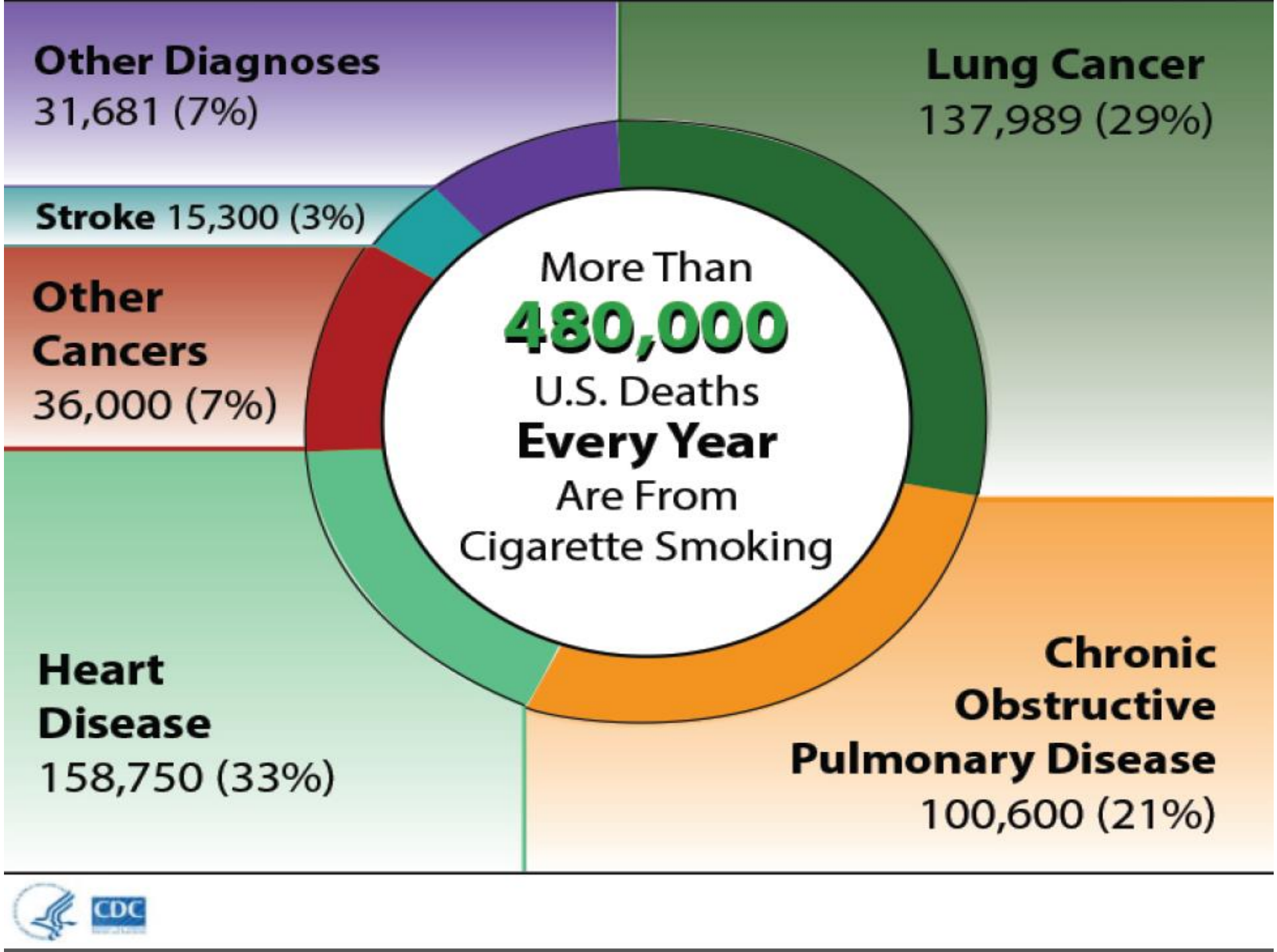
Centers for Disease Control and Prevention (2016). *Smoking & Tobacco Use* (Fact Sheets). Retrieved January 6, 2017 from https://www.cdc.gov/tobacco/data_statistics/fact_sheets/fast_facts/

U.S. Department of Health and Human Services (2014). The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

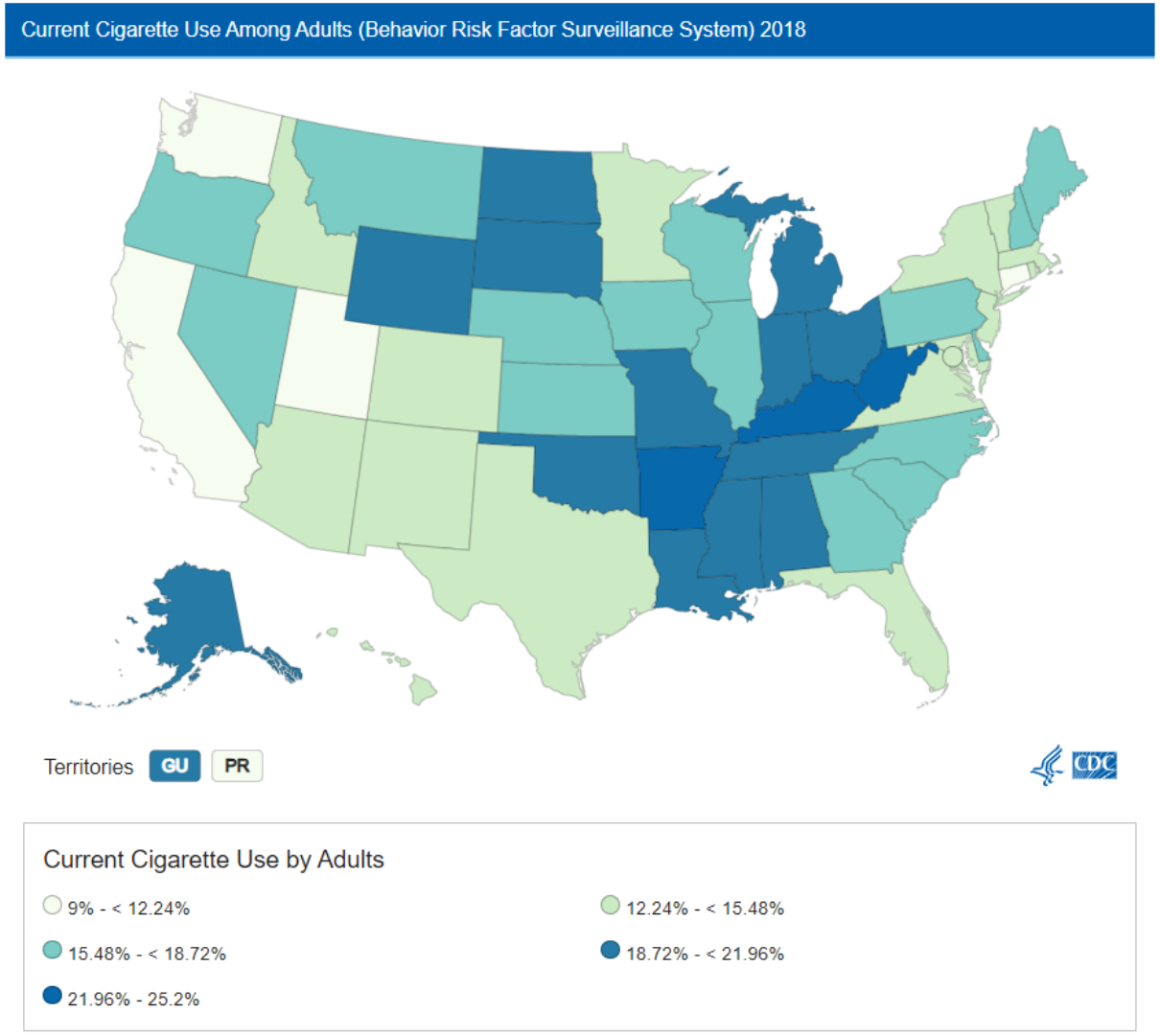
Comparative Causes of Annual Deaths in the U.S., 2014



Centers for Disease Control and Prevention, National Center for Health Statistics. *FastStats - Statistics by Topic* [webpage]. Retrieved December 7, 2016 from http://www.cdc.gov/nchs/fastats/default.htm

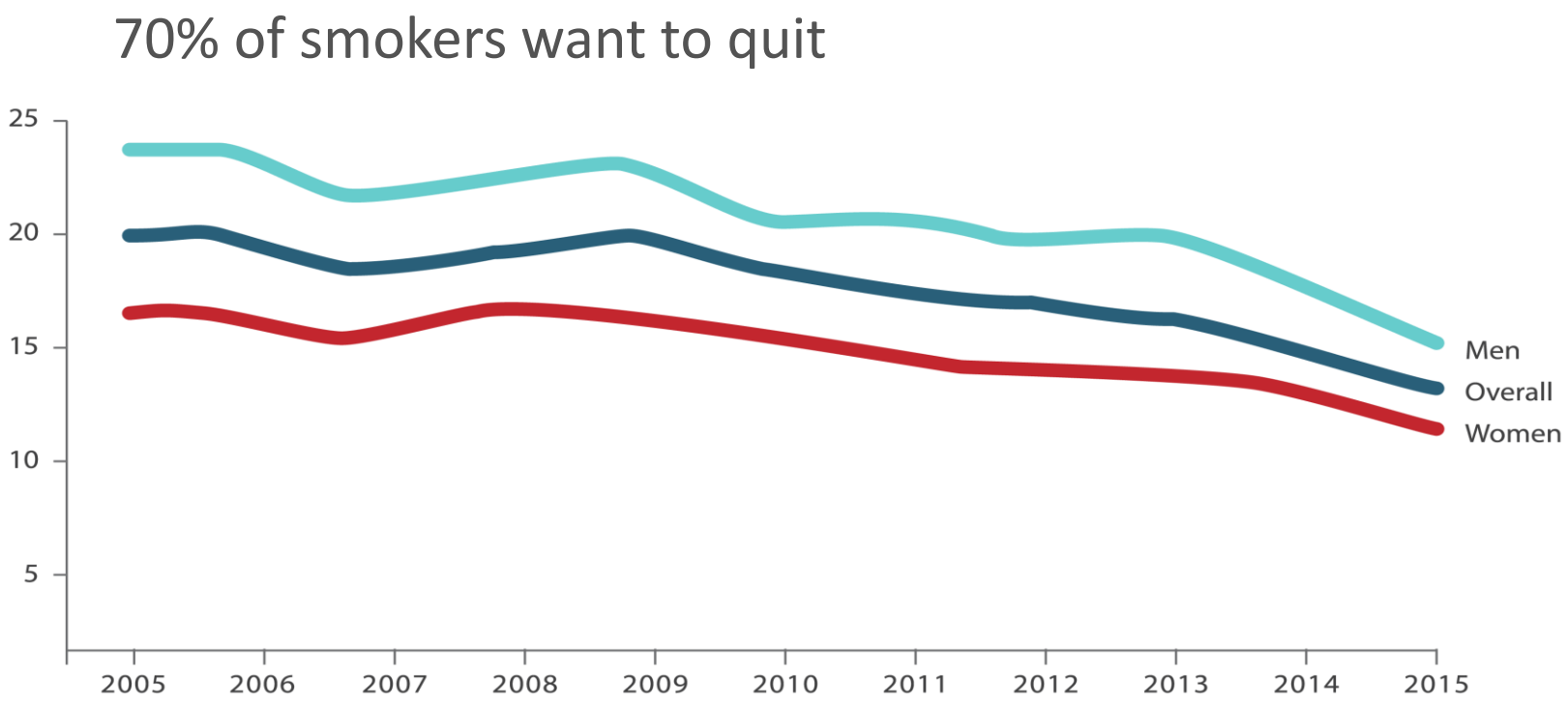

Other Diagnoses
31,681 (7%)
Lung Cancer
137,989 (29%)
Stroke 15,300 (3%)
Other Cancers
36,000 (7%)
More Than
480,000
U.S. Deaths
Every Year
Are From
Cigarette Smoking
Heart Disease
158,750 (33%)
Chronic Obstructive Pulmonary Disease
100,600 (21%)
CDC

Current Cigarette Use Among Adults



[Current Cigarette Smoking Among Adults in the United States | CDC]

Trends in Adult Smoking, By Sex U.S. 2005–2015



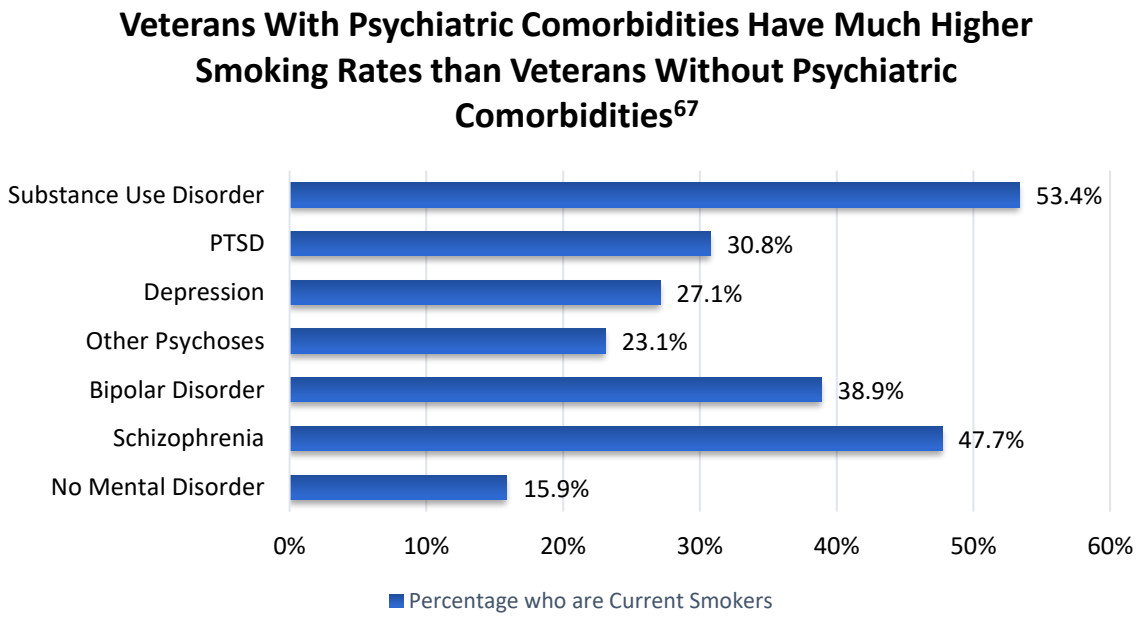
Centers for Disease Control and Prevention. (2007). Tobacco use among adults—United States, 2006. *MMWR* 56:1157–1161. Retrieved from https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5644a2.htm

Centers for Disease Control and Prevention (2016). Current cigarette smoking among adults — United States, 2005-2015. *Morbidity and Mortality Weekly Report, 65*(44), 1205-1211. Retrieved from https://www.cdc.gov/mmwr/volumes/65/wr/mm6544a2.htm?s_cid=mm6544a2_w

U.S. Department of Health and Human Services (2014). The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

Smoking as a Health Disparity Issue

- Smoking is a health disparity issue, with higher rates of smoking among the following groups
  - Lower income and educational levels
  - American Indians, Alaskan native populations
  - Populations with co-morbid psychiatric or substance use disorders.



Benowitz, N. L., Schultz, K. E., Haller, C. A., Wu, A. H., Dains, K. M., & Jacob, P. (2009). Prevalence of smoking assessed biochemically in an urban public hospital: a rationale for routine cotinine screening. *American Journal of Epidemiology, 170*(7), 885-891. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2765360/

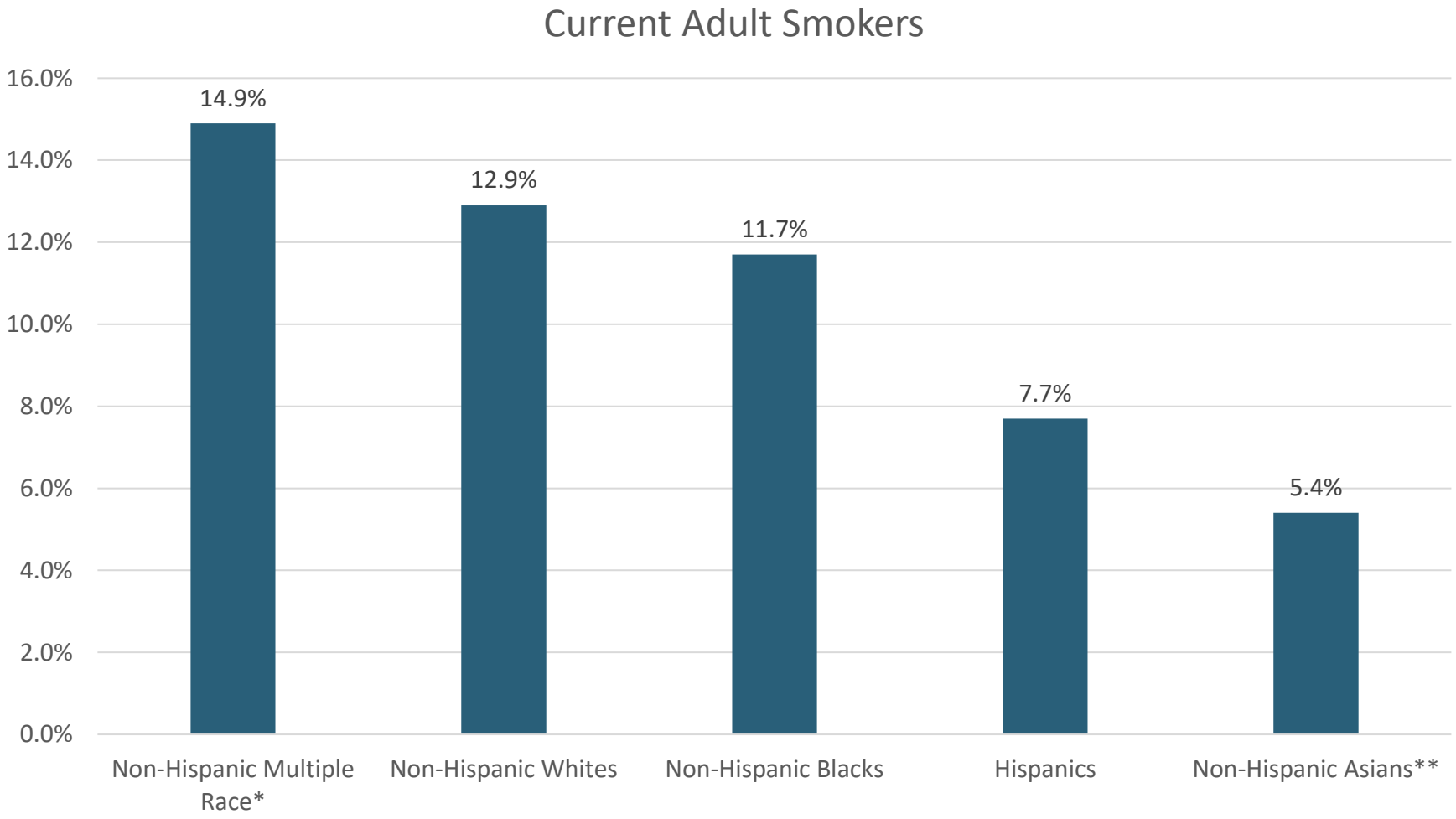
Substance Abuse and Mental Health Services Administration (2013). Adults with Mental Illness or Substance Use Disorder Account for 40 Percent of All Cigarettes Smoked. *The NSDUH Report*. Retrieved from https://www.samhsa.gov/data/sites/default/files/spot104-cigarettes-mental-illness-substance-use-disorder/spot104-cigarettes-mental-illness-substance-use-disorder.pdf

Smoking as a Health Disparity Issue – Mental Health

Tobacco Users with Mental Illness	On average die several years earlier than individuals without mental illness. Most deaths are due to smoking-related disease.
	Have a greater risk of dying from cardivascular disease, respiratory illnesses, and cancer than those without mental illness.
	Half of the mortality for people with schizophrenia, bipolar disorder, and depression is from tobacco-related diseases.
	Tobacco use predicts future suicidal behavior in Veterans, independent of age, gender, psychiatric disorder, service connection and severity of medical comorbidities.

Benowitz, N. L., Schultz, K. E., Haller, C. A., Wu, A. H., Dains, K. M., & Jacob, P. (2009). Prevalence of smoking assessed biochemically in an urban public hospital: a rationale for routine cotinine screening. *American Journal of Epidemiology, 170*(7), 885-891. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2765360/

Smoking Rates Vary by Race, 2021

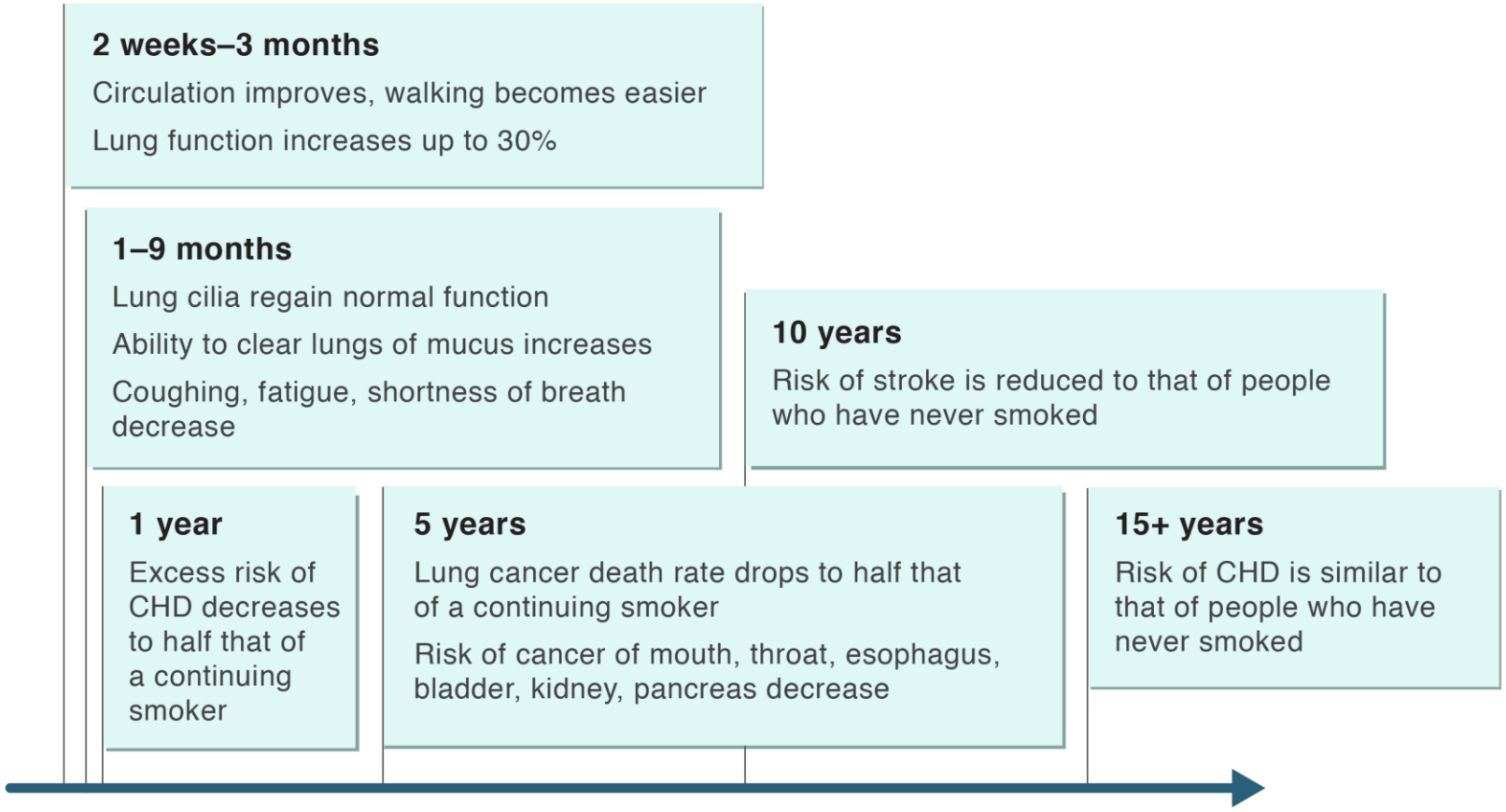


*Non-Hispanic **multiple racial groups** includes adults who were categorized as "non-Hispanic American Indian or Alaska Native and any other group.

****Non-Hispanic Asians does not include Native Hawaiian or Other Pacific Islanders.**

[Current Cigarette Smoking Among Adults in the United States | CDC]

Quitting: Health Benefits



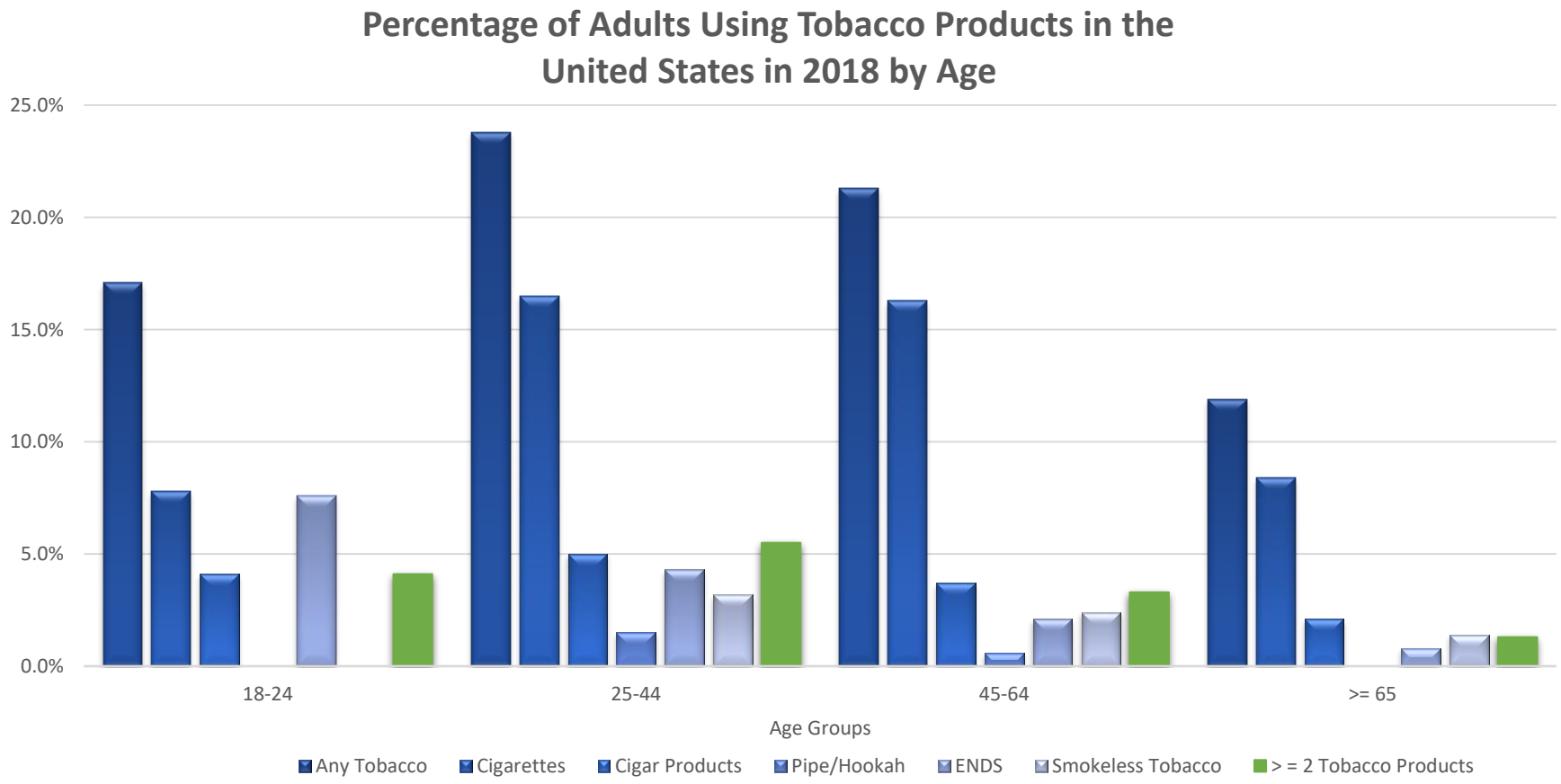
American Cancer Society. http://www.cancer.org/
American Lung Association. *Benefits of Quitting*. Retrieved December 20, 2016 from http://www.lung.org/stop-smoking/i-want-to-quit/benefits-of-quitting.html
U.S. Department of Health and Human Services (1990). *The Health Benefits of Smoking Cessation. A Report of the Surgeon General*. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention and Health Promotion, Office on Smoking and Health. DSSH Publication No. (CDC) 90-8416.

FORMS of TOBACCO

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

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

Tobacco Products Used in the United States by Age



Creamer MR, Wang TW, Babb S, et al. Tobacco Product Use and Cessation Indicators Among Adults — United States, 2018. MMWR Morb Mortal Wkly Rep 2019;68:1013–1019. DOI: http://dx.doi.org/10.15585/mmwr.mm6845a2external icon

American Cigarettes

- 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:

Type of cigarette	Yield per cigarette
Full-flavor (regular)	1.1 mg
Light	0.8 mg
Ultra-light	0.4 mg
Average (all brands)	0.9 mg

- Smoker's nicotine yield, per cigarette:
  - Approximately 1 to 2 mg

What if our food was labeled like tobacco, would we eat it?

If nobody smoked, one of every three cancer deaths in the United States would not happen.

- Cigarette packages are required by FDA to have ONE of the following statements:
  - Cigarettes are addictive
  - Tobacco smoke can harm your children
  - Cigarettes cause fatal lung disease
  - Cigarettes cause cancer
  - Cigarettes cause strokes and heart disease
  - Smoking during pregnancy can harm your baby
  - Smoking can kill you
  - Tobacco smoke causes fatal lung disease in nonsmokers
  - Quitting smoking now greatly reduces serious risks to your health

Smokeless Tobacco

- Types
  - Chewing tobacco
    - Loose leaf, plug, or twist
    - Can come in a variety of flavors
  - Snuff
    - Moist, dry or in packets (also called Snus)
  - Dissolvable
    - Lozenges, sticks, strips, orbs
- Prevalence
  - 2.4% in 2018

Health Concerns from Smokeless Tobacco

- Cancer-causing chemicals
  - Tobacco specific nitrosamines
    - Formed during growing, curing, fermenting, and aging of tobacco
    - Amount varies by product
  - Other harmful chemicals
    - Polonium-210
      - Cancer causing element found in tobacco fertilizer
    - Polynuclear aromatic hydrocarbons (polycyclic aromatic hydrocarbons)
      - Formed when tobacco is cured with heat
    - Harmful metals
      - Arsenic, beryllium, cadmium, chromium, cobalt, lead, nickel, mercury

http://www.cdc.gov/tobacco/data_statistics/fact_sheets/smokeless/use_us/index.htm

At least 28 cancer-causing chemicals have been found in smokeless tobacco.

Cigars

- Cigars sold in U.S.
  - Large cigars
  - Cigarillos
  - Little cigars
- Prevalence
  - 3.9% of all adults in 2018
    - 6.8% of males
    - 1.1% of females

http://www.cdc.gov/tobacco/data_statistics/fact_sheets/tobacco_industry/cigars/index.htm

Cigars

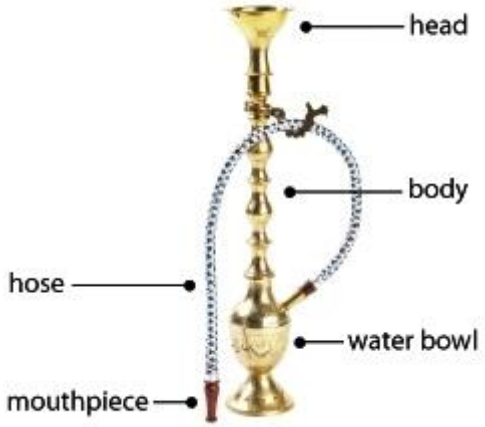
- Risks increase with regular daily use
  - Cancer
    - Lung, esophagus, larynx, oral cavity
  - Gum disease and tooth loss
  - Cardiovascular disease
  - Emphysema and chronic bronchitis

Pipe

- About 1% of adults in U.S. smoke pipes
- Risks
  - Cancer
    - Lung, oropharynx, esophagus, colon and rectum, pancreas, and larynx
    - Rates similar to cigarette and cigar smokers

Hookah Smoke

- Compared to cigarette smoking
  - Smoke from hookah is at least as toxic as cigarette smoke
  - A 1 hour hookah session
    - 200 puffs from the hookah
      - 1 cigarette = 10-20 puffs
    - Smoke inhaled during the session is about 90,000 ml
      - 1 cigarette = 500-600 ml
  - Is the smoke safer since it has passed through water?
    - No! Smoke from hookah has high levels of toxic agents similar to cigarette smoking
      - Associated with lung cancer, stomach cancer, esophageal cancer, bladder cancer, reduced lung function, decreased fertility
    - Tobacco juices from hookah can cause mouth irritation and increase the risk of oral cancers



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Electronic Nicotine Delivery Systems (ENDS)

- Vaporizers
- Vape pens
- Hookah pens
- Electronic cigarettes
- E-pipes

Electronic Nicotine Delivery Systems (ENDS)

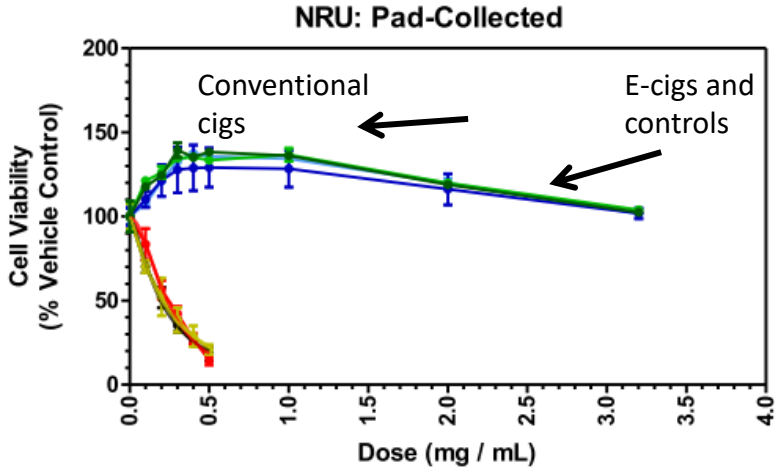
- Dramatically increased use in youth
  - From 2016 use in the past 30 days
    - High school students 4.3% to 11.3%
    - Middle school students 0.6% to 3.9%
- Adults
  - 3.2% of adults in 2018
  - Commonly see dual use with other tobacco products

Electronic Nicotine Delivery Systems (ENDS)

- Marketing on ENDS
  - Many companies making statements that have not been validated by clinical studies
    - ENDS aerosol is harmless “water vapor” and as safe as clean air
  - Lack of standardization of products
  - Lack of knowledge of ingredients
  - Similar issues to nutraceuticals

Nicotine content and toxins in e-cigarettes

- Study compared toxins in the vapors of 12 e-cigarettes to a nicotine inhaler
  - Toxicants were detected in the e-cigarette vapor, were 9-450x lower than in cigarette smoke
  - Trace amounts of toxicants were also detected from the nicotine inhaler
  - Some toxicants were at similar levels in both the e-cigarettes and the inhaler
- Analysis of 10 of the most popular e-liquids found the nicotine content was close to the amount on the label. Some impurities were detected at levels higher than allowed for nicotine-containing medicines, but thought to be below the level that they would cause harm.
- A Lorillard study found that e-cigarette vapor was less cytotoxic than vapor from Marlboro or other conventional cigarettes



Etter et al., *Addiction*, 2013
Goniewicz et al., *Tob Control*, 2013
Misra et al., *Int J Environ Res Pub Health*, 2014

Toxins in e-cigarettes

- **Nitrosamines, tobacco-specific impurities**, other potentially harmful compounds have been identified in e-liquids and aerosols
  - While levels vary between products, these are generally found at lower concentrations than the levels in conventional cigarettes, in some cases at similar concentrations to those found in NRT
- **Metal particles** (tin, nickel, copper, lead, chromium) found in e-liquids and aerosols, in some cases in the vapor at higher concentrations than found in conventional cigarette smoke
  - Thought to be due to engineering of device and internal components, such as solder joints and heating element
- Analyzed urine levels of toxicants and carcinogen metabolites from vaping of 28 e-cig users who had not smoked conventional cigs for 2 months
  - Found significantly lower levels of toxicants and carcinogens in e-cig users compared to conventional cig users
- **No** manufacturing or pharmaceutical standards regulate the levels of impurities
  - New FDA regulations will start providing more regulation

Hajek et al., 2014
Hecht et al., 2014
Williams et al., 2013

e-Liquids, e-Juices

- Base of propylene glycol or glycerin + nicotine + flavorings
- Many flavors
- Different nicotine strengths
- Mix your own

Long term health effects of e-cigarettes

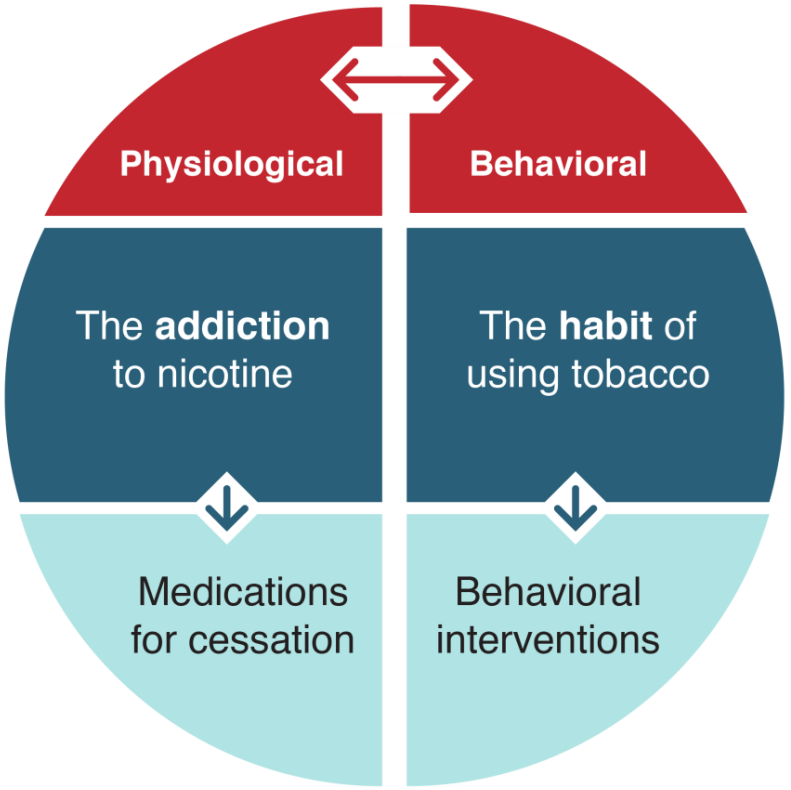
→ **UNKNOWN**

- Some researchers speculate that the long-term effects are likely to be less severe than conventional cigarettes due to the lower levels of toxicants
- E-cigarettes have only been around for ~20 years and in widespread use only within the past 15 years.
- Long term effects of use can take decades to develop

Hajek et al., 2014

Tobacco Dependence is a Chronic Disease

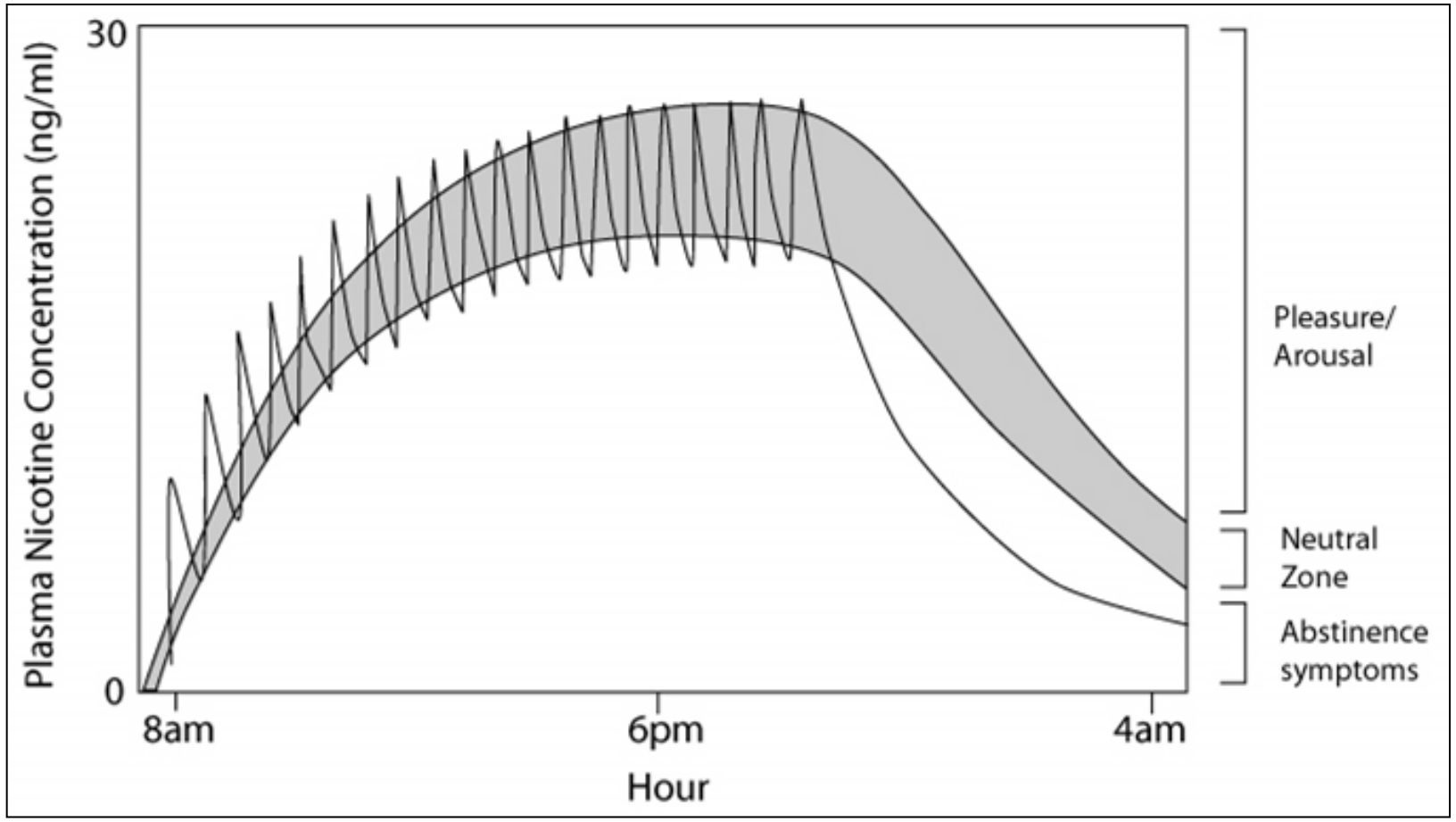
Treatment should address the physiological **and** the behavioral aspects of dependence



Nicotine Addiction

- Characteristics of Nicotine Addiction
  1. Tolerance
     - Larger quantities needed to produce the same effect
  2. Withdrawal
     - Physical symptoms occurring when tobacco stopped
  3. Dependent behaviors
     - Continued use despite knowledge of known harms

Nicotine Addiction Cycle



Med Clin N Am 76(2), Benowitz NL, Cigarette smoking and nicotine addiction, pp. 415–437, Copyright 1992.

Quit Attempts & Treatment Utilization

- 70% of smokers report wanting to quit
- About half of all people who smoke try to quit each year
- Only 3-5% of quit attempts are successful
- Although effective treatments exist, more than two-thirds of quit attempts do not use evidence-based treatment

Smoking Cessation: A report of the Surgeon General. Executive Summary. US Department of Health and Human Services. Center for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion. Office on Smoking and Health. 2020. https://www.hhs.gov/sites/default/files/2020-cessation-sgr-executive-summary.pdf

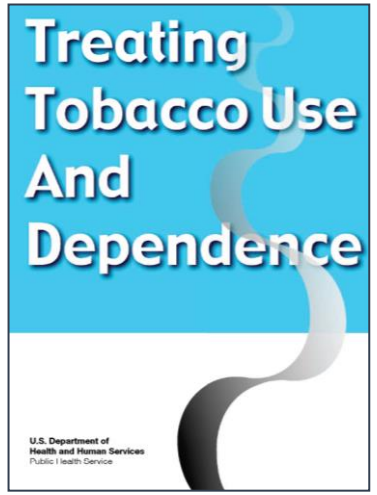
Quit Attempts & Treatment Utilization

- Less than 30% of people who make a quit attempt use medication
- Less than 7% of people who make a quit attempt use behavioral counseling
- Less than 5% of people use both medication and behavioral counseling during their quit attempt

Smoking Cessation: A report of the Surgeon General. Executive Summary. US Department of Health and Human Services. Center for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion. Office on Smoking and Health. 2020. https://www.hhs.gov/sites/default/files/2020-cessation-sgr-executive-summary.pdf

Evidence-based Smoking Cessation Treatments Exist: 2008 Clinical Practice Guideline

- 2008 Update: Treating Tobacco Use and Dependence, U.S. Department of Health and Human Services – Public Health Service (PHS)
- The 2008 update of the PHS guideline has been adopted nationally as the standard to guide evidence-based tobacco use treatment in VHA



Tobacco Use and Dependence Guideline Panel. Treating tobacco use and dependence: 2008 Update: Clinical Practice Guideline. US Department of Health and Human Service; 2008. Treating Tobacco Use and Dependence: 2008 Update - NCBI Bookshelf (nih.gov)

CPG 2008: Main Findings on Treating Tobacco Use

- Every smoker should be screened for tobacco use and willingness to quit at each session
- All smokers should be offered pharmacotherapy to assist in quitting
- Brief advice given by MD and non-MD clinicians effective in increasing quit rates
- Dose-response relationship between counseling intensity and effectiveness

  While more intensive counseling is more efficacious, even brief counseling (2 minutes) can double quit rate

US Preventive Services Task Force Recommendation Statement - 2021

- Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Persons.
  1. Recommends that clinicians ask ALL adults about tobacco use, advise them to stop using tobacco and provide behavioral interventions and US FDA approved pharmacotherapy for cessation to nonpregnant adults who use tobacco.
  2. Recommends clinicians ask ALL pregnant persons about tobacco use, advise them to stop using tobacco and provide behavioral interventions for cessation to all pregnant persons who use tobacco.
     - Current evidence is insufficient to assess the balance of benefits and harms of pharmacotherapy interventions for tobacco cessation in pregnant persons.
  3. Current evidence is insufficient to assess the balance of benefits and harms of electronic cigarettes (ENDs) for tobacco cessation in adults, including pregnant person. Clinicians should direct patients who use tobacco to other tobacco cessation interventions with proven effectiveness and established safety.

Recommendation: Tobacco Smoking Cessation in Adults, Including Pregnant Persons: Interventions | United States Preventive Services Taskforce (uspreventiveservicestaskforce.org)

The “5 A’s” Model
Helping Tobacco Users Through the Process of Quitting

Ask Do you currently use tobacco?

Advise Use clear, strong, personalized messages:

- ***I think it is important that you quit smoking. I can help.***
- ***Quitting smoking is one of the most important things you can do to protect your health.***
- ***Smoking interferes with your psychiatric medications.***
- ***Stopping smoking can improve your mood.***

Assess Are you willing to give quitting a try in the next 30 days?

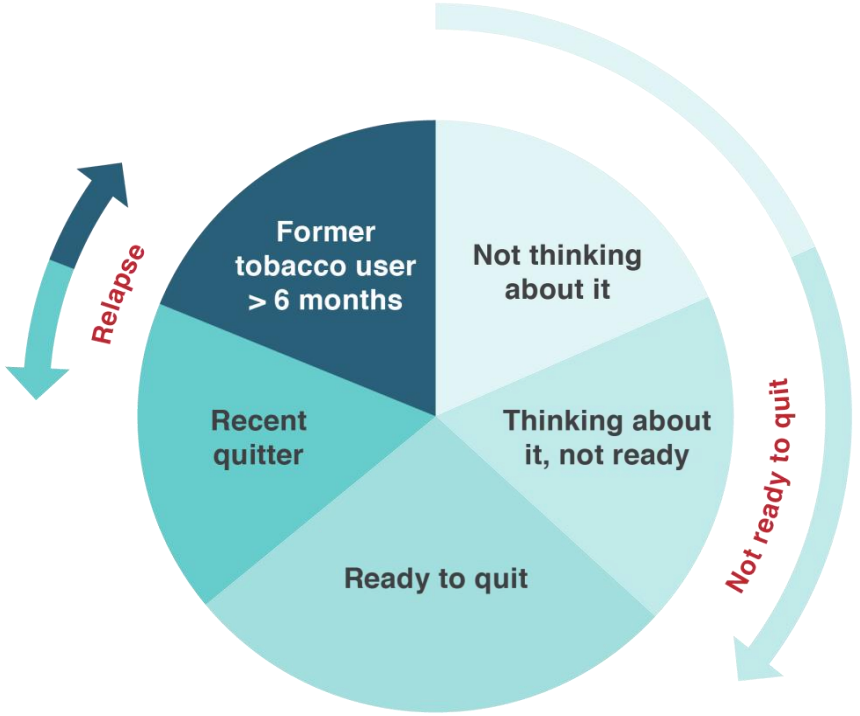
Assist Help patients with quitting – provide behavioral counseling and pharmacotherapy interventions

Arrange Set up follow-up sessions and/or attendance in a tobacco use treatment clinic

Stages of Quitting

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

- Assess readiness to quit (or to stay quit) at each patient contact.
- In patients not ready to quit, work on enhancing motivation to change and encourage in initial change efforts (e.g., reduction)
- In patients ready to quit, encourage use of evidence-based treatment
  - behavior counseling, medications, referring if necessary
- In patients who have quit, support abstinence



Prochaska, J. O., & DiClemente, C. C. (1982). Transtheoretical therapy: Toward a more integrative model of change. *Psychotherapy: Theory, Research & Practice, 19*(3), 276–288. https://doi.org/10.1037/h0088437

Hazelden Foundation. (1998). *Survey on current and former smokers—1998*. Center City, MN: Hazelden Foundation.

Treatment Recommendations – Counseling: For Smokers Not Willing to Make a Quit Attempt at This Time

- Recommendation: Motivational intervention techniques appear to be effective in increasing a patient's likelihood of making a future quit attempt. Therefore, clinicians should use motivational techniques to encourage smokers who are not currently willing to quit to consider making a quit attempt in the future. **Strength of Evidence = B**

  Some evidence suggests that extensive training is needed before competence is achieved in the MI technique (CPG 2008: p.105)

Motivational Interviewing

“

I see you are smoking 2 packs a day. As your provider, I’m concerned about the impact on your health. Is it okay if we talk about that for a few minutes?

Have you thought about quitting smoking?

When you think of the pros and cons of smoking, how do they stack up for you these days?

If you look at this list of things you could work on to improve your heart health/blood pressure, diabetes…, which one(s) seem like something you might be ready to talk about?

”

Motivational Interviewing: Importance and Confidence Rulers

“

On a scale of 0 to 10, with 0 meaning not important and 10 meaning very important, how important do you think it is for you to quit using tobacco?

On a scale of 0 to 10, with 0 meaning not at all confident and 10 meaning completely confident, how confident do you feel about quitting?

Why are you at a __instead of a (lower number here) __? and/or What would need to happen to make your ____increase to (slightly higher number)___?

”

When a Patient is Ready to Quit: FACILITATE the Quitting Process

- Provide medication counseling
  - Promote consistent use as prescribed
  - Discuss proper use, with demonstration
- Discuss concept of “slip” versus relapse
  - Slip: smoking one or a few cigarettes
  - Relapse: going back to regular, daily smoking
  - 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 and preferably 6 months or more (remember, tobacco use disorder is a CHRONIC disease)
- Congratulate the patient!

Medications for Tobacco Cessation

Combination Therapy

Most evidence for:

- Nicotine replacement therapy (NRT) long-acting, patch + short-acting lozenge, nasal spray, or gum*
- Bupropion + NRT (lozenge, nasal spray, gum, or patch)

Other combinations but evidence limited:

- Varenicline and nicotine patch
- Varenicline and bupropion

CPG 2008 Recommendation: Certain combinations of first-line medications have been shown to be effective smoking cessation treatments. Therefore, clinicians should consider using these combinations of medications with their patients who are willing to quit.

*Nicotine inhaler was discontinued by the manufacturer in April 2023, pharmacies can sell inhaler until supply exhausted.

Medications for Tobacco Cessation

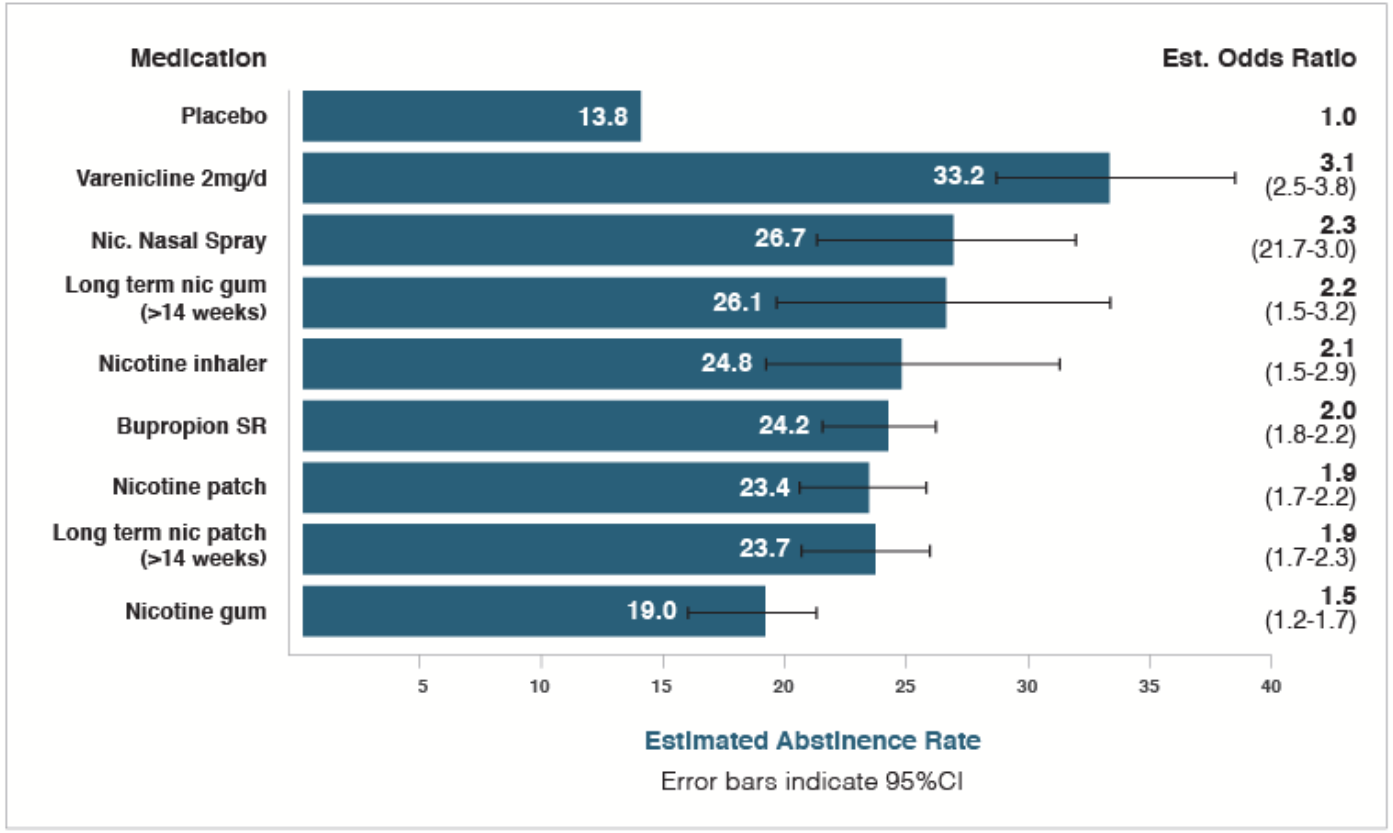
Monotherapy Therapy

- Nicotine replacement therapy (NRT)*
  - Nicotine patch
  - Nicotine gum
  - Nicotine lozenge
  - Nicotine nasal spray
- Non-nicotine pharmacotherapy
  - Bupropion
  - Varenicline

*Nicotine inhaler was discontinued by the manufacturer in April 2023, pharmacies can sell inhaler until supply exhausted.

Effectiveness of Monotherapies

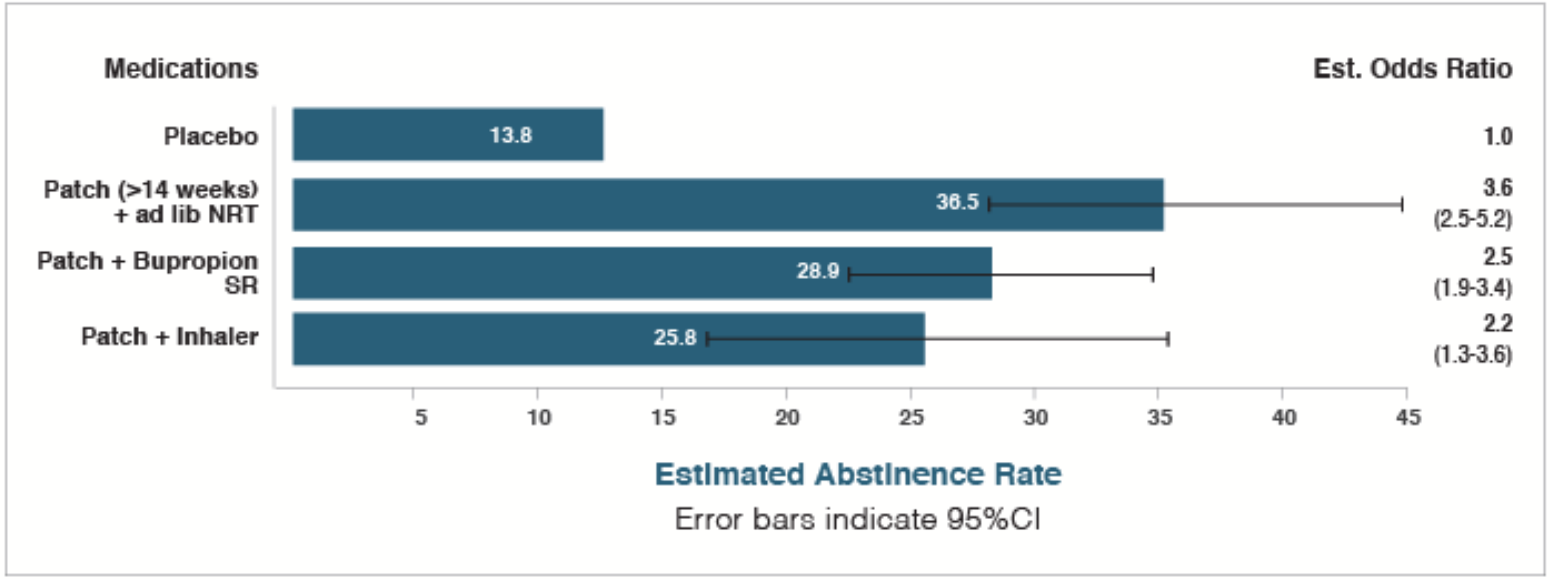
CPG Table 6.26: Effectiveness and abstinence rates for monotherapies vs. placebo at 6 months postquit (n=83 studies)



Fiore, M. C., Jaén, C. R., Baker, T. B., Bailey, W. C., Benowitz, N. L., Curry, S. J., Dorfman, S. F., Froelicher, E. S., Goldstein, M. G., Healton, C. G., Henderson, P. N., Heyman, R. B., Koh, H. K., Kottke, T. E., Lando, H. A., Mecklenburg, R. E., Mermelstein, R. J., Mullen, P. D., Orleans, C. T., Robinson, L., Stitzer, M. L., Tommasello, A. C., Villejo, L., & Wewers, M. E. (2008, May). *Treating tobacco use and dependence: 2008 update. Clinical practice guideline*. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service.

Effectiveness of Combination Therapies

CPG Table 6.26: Effectiveness and abstinence rates for smoking medication combinations vs. placebo at 6 months post-quit (n=83 studies)



- Certain combinations of first-line medications have been shown to be effective
  - **Strength of evidence: A**
- Effective combinations are long term nic patch + ad lib NRT, nic patch + inhaler, nic patch + bupropion
  - Long term patch + ad lib NRT associated with highest quit rates vs. placebo
- Clinicians should consider factors of cost, tolerability, compliance

Fiore, M. C., Jaén, C. R., Baker, T. B., Bailey, W. C., Benowitz, N. L., Curry, S. J., Dorfman, S. F., Froelicher, E. S., Goldstein, M. G., Healton, C. G., Henderson, P. N., Heyman, R. B., Koh, H. K., Kottke, T. E., Lando, H. A., Mecklenburg, R. E., Mermelstein, R. J., Mullen, P. D., Orleans, C. T., Robinson, L., Stitzer, M. L., Tommasello, A. C., Villejo, L., & Wewers, M. E. (2008, May). *Treating tobacco use and dependence: 2008 update. Clinical practice guideline*. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service.

How to Assess Nicotine Dependence

- Time to first cigarette upon waking better correlated with dependence
- Heaviness of Smoking Index

1. How soon after waking do you smoke your first cigarette?
    a. Less than five minutes (3 points)
    b. 5 to 30 minutes (2 points)
    c. 31 to 60 minutes (1 point)
2. How many cigarettes do you smoke each day?
    a. More than 30 cigarettes (3 points)
    b. 21 to 30 cigarettes (2 points)
    c. 11 to 20 cigarettes (1 point)

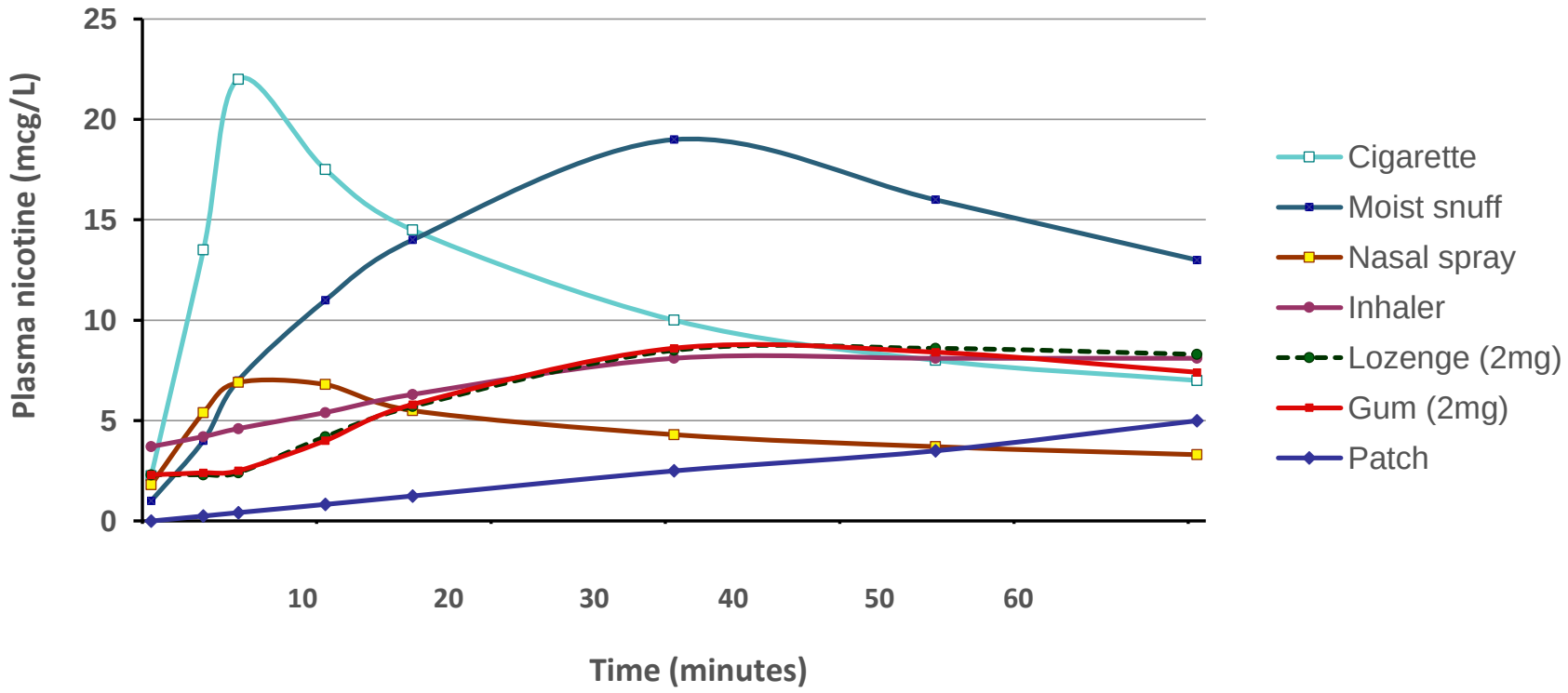
Scoring: 5-6=heavy dependence; 3-4=moderate; 0-2=light

Nicotine Replacement Therapy

- Reduces withdrawal symptoms and cravings by providing nicotine in place of smoking
- Includes:
  - Nicotine patch
  - Nicotine gum
  - Nicotine lozenge
  - Nicotine inhaler and nicotine nasal spray*

  (*non-formulary)
- Best if used in combination
- During counseling, can check to see if patients are using NRT correctly

Plasma Nicotine Concentrations for Nicotine-Containing Products



Choi, J. H., Dresler, C. M., Norton, M. R., & Strahs, K. R. (2003). Pharmacokinetics of a nicotine polacrilex lozenge. *Nicotine & Tobacco Research, 5*(5), 635-644.

Fant, R. V., Henningfield, J. E., Nelson, R. A., & Pickworth, W. B. (1999). Pharmacokinetics and pharmacodynamics of moist snuff in humans. *Tobacco Control, 8*(4), 387-392. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1759743/

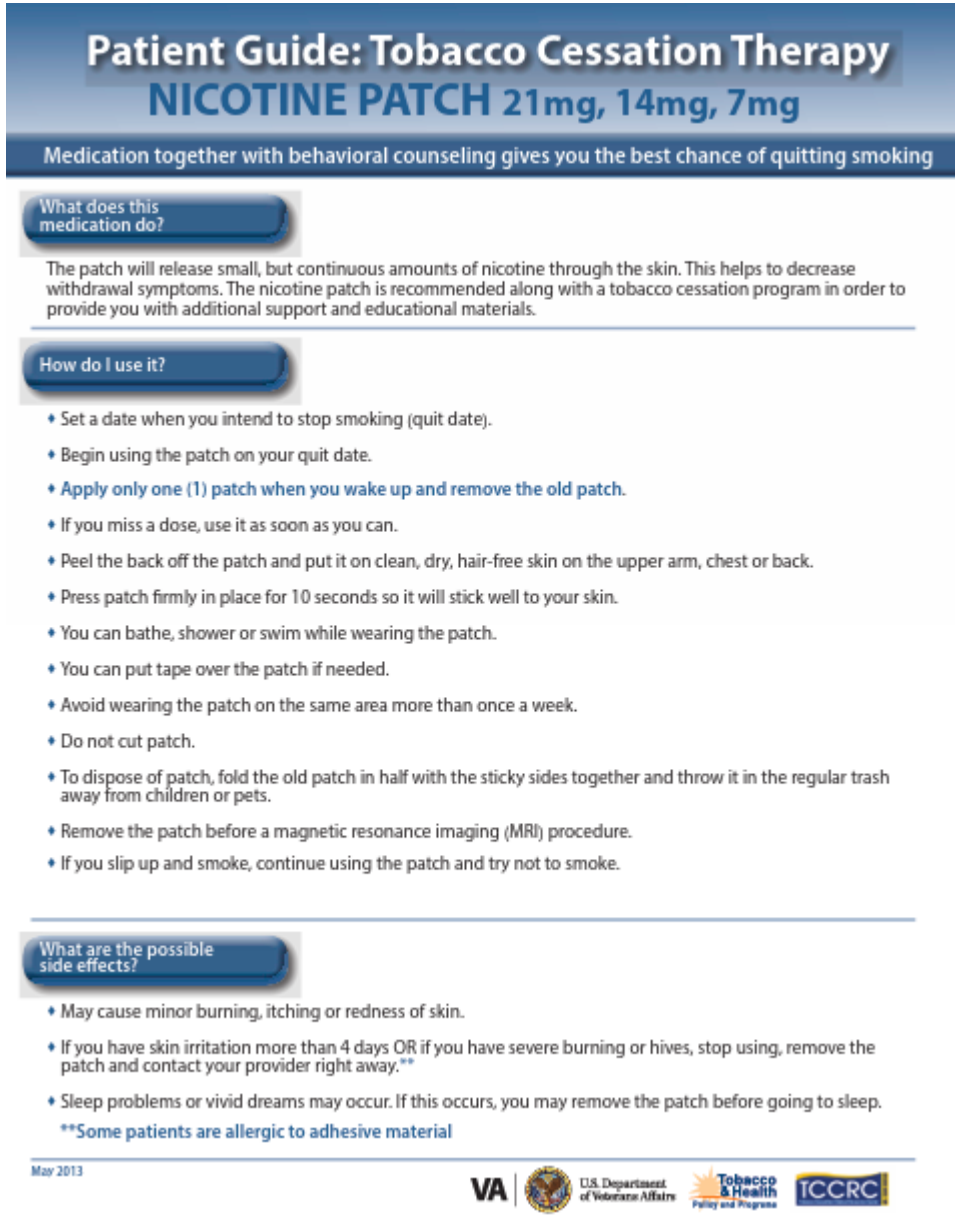
Schneider, N. G., Olmstead, R. E., Franzon, M. A., & Lunell, E. (2001). The nicotine inhaler: clinical pharmacokinetics and comparison with other nicotine treatments. *Clinical Pharmacokinetics, 40*(9), 661–684.

Nicotine Patch

- Provides a continuous source of nicotine through the skin
- Replaced every 16 – 24 hours
- Rotate the site the patch is applied to prevent skin irritation
- More effective if used in combination with nicotine gum or lozenge ad lib for strong cravings
- If trouble sleeping – recommend patients remove before sleeping
- If slip and smoke, recommend patients continue using patch and try not to smoke
- Dosing
  - Smoking more than 10 cigarettes a day use 21mg patch
  - Smoking 10 or less cigarettes a day use 14mg patch
  - After 6-12 weeks, lower the dose to the next level, then after 2-4 weeks, lower to the next level. Then stop.

For more information on nicotine patch dosing see:

www.publichealth.va.gov/docs/smoking/cessationguidelinepart3_508.pdf



Patient Guide: Tobacco Cessation Therapy
NICOTINE PATCH 21mg, 14mg, 7mg

Medication together with behavioral counseling gives you the best chance of quitting smoking

What does this medication do?

The patch will release small, but continuous amounts of nicotine through the skin. This helps to decrease withdrawal symptoms. The nicotine patch is recommended along with a tobacco cessation program in order to provide you with additional support and educational materials.

How do I use it?

- Set a date when you intend to stop smoking (quit date).
- Begin using the patch on your quit date.
- Apply only one (1) patch when you wake up and remove the old patch.
- If you miss a dose, use it as soon as you can.
- Peel the back off the patch and put it on clean, dry, hair-free skin on the upper arm, chest or back.
- Press patch firmly in place for 10 seconds so it will stick well to your skin.
- You can bathe, shower or swim while wearing the patch.
- You can put tape over the patch if needed.
- Avoid wearing the patch on the same area more than once a week.
- Do not cut patch.
- To dispose of patch, fold the old patch in half with the sticky sides together and throw it in the regular trash away from children or pets.
- Remove the patch before a magnetic resonance imaging (MRI) procedure.
- If you slip up and smoke, continue using the patch and try not to smoke.

What are the possible side effects?

- May cause minor burning, itching or redness of skin.
- If you have skin irritation more than 4 days OR if you have severe burning or hives, stop using, remove the patch and contact your provider right away.**
- Sleep problems or vivid dreams may occur. If this occurs, you may remove the patch before going to sleep.

**Some patients are allergic to adhesive material

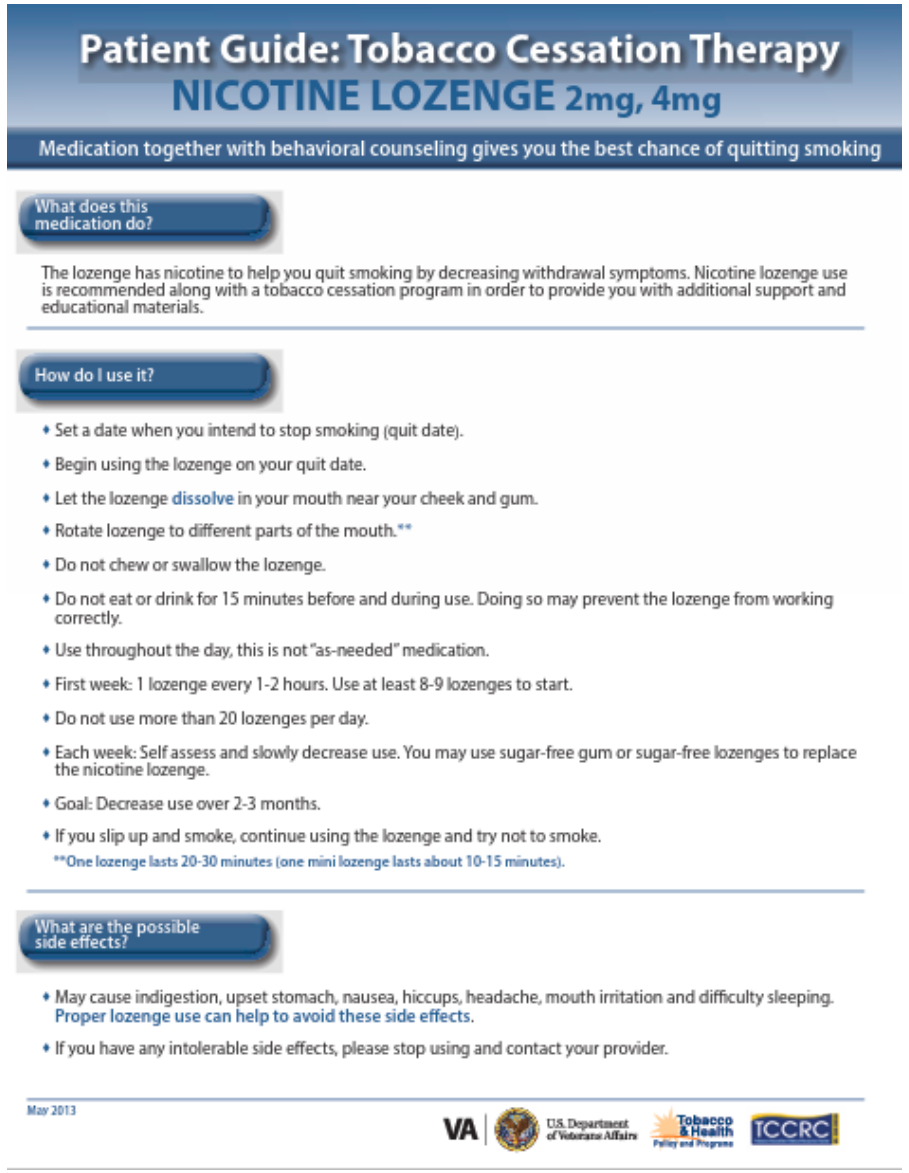
May 2013

VA | U.S. Department of Veterans Affairs | Tobacco & Health Policy and Programs | TCCRC

Nicotine Lozenge

- Place lozenge in mouth and park between the cheek and gum
  - Nicotine absorbed through the lining of the mouth
  - Do not eat or drink for 15 min before or after using the lozenge. Acidic beverages (soda, coffee) can reduce nicotine absorption.
  - Occasionally move from one side of the mouth to the other
  - Do not chew the lozenge, avoid swallowing
- If patient has nausea – check to see if they are using the lozenge correctly
- Can be used ad lib to control strong tobacco cravings
- Dosing is based on when you have your first cigarette of the day
  - If first cigarette is within 30 minutes of waking use 4mg lozenge
  - If first cigarette is more than 30 minutes after waking use 2mg lozenge
  - If combining nicotine patch and nicotine lozenge, consider using 2mg lozenge.

For more information on nicotine lozenge dosing see:
www.publichealth.va.gov/docs/smoking/cessationguidelinepart3_508.pdf



Patient Guide: Tobacco Cessation Therapy
NICOTINE LOZENGE 2mg, 4mg

Medication together with behavioral counseling gives you the best chance of quitting smoking

What does this medication do?

The lozenge has nicotine to help you quit smoking by decreasing withdrawal symptoms. Nicotine lozenge use is recommended along with a tobacco cessation program in order to provide you with additional support and educational materials.

How do I use it?

- Set a date when you intend to stop smoking (quit date).
- Begin using the lozenge on your quit date.
- Let the lozenge dissolve in your mouth near your cheek and gum.
- Rotate lozenge to different parts of the mouth.**
- Do not chew or swallow the lozenge.
- Do not eat or drink for 15 minutes before and during use. Doing so may prevent the lozenge from working correctly.
- Use throughout the day, this is not "as-needed" medication.
- First week: 1 lozenge every 1-2 hours. Use at least 8-9 lozenges to start.
- Do not use more than 20 lozenges per day.
- Each week: Self assess and slowly decrease use. You may use sugar-free gum or sugar-free lozenges to replace the nicotine lozenge.
- Goal: Decrease use over 2-3 months.
- If you slip up and smoke, continue using the lozenge and try not to smoke.

**One lozenge lasts 20-30 minutes (one mini lozenge lasts about 10-15 minutes).

What are the possible side effects?

- May cause indigestion, upset stomach, nausea, hiccups, headache, mouth irritation and difficulty sleeping. Proper lozenge use can help to avoid these side effects.
- If you have any intolerable side effects, please stop using and contact your provider.

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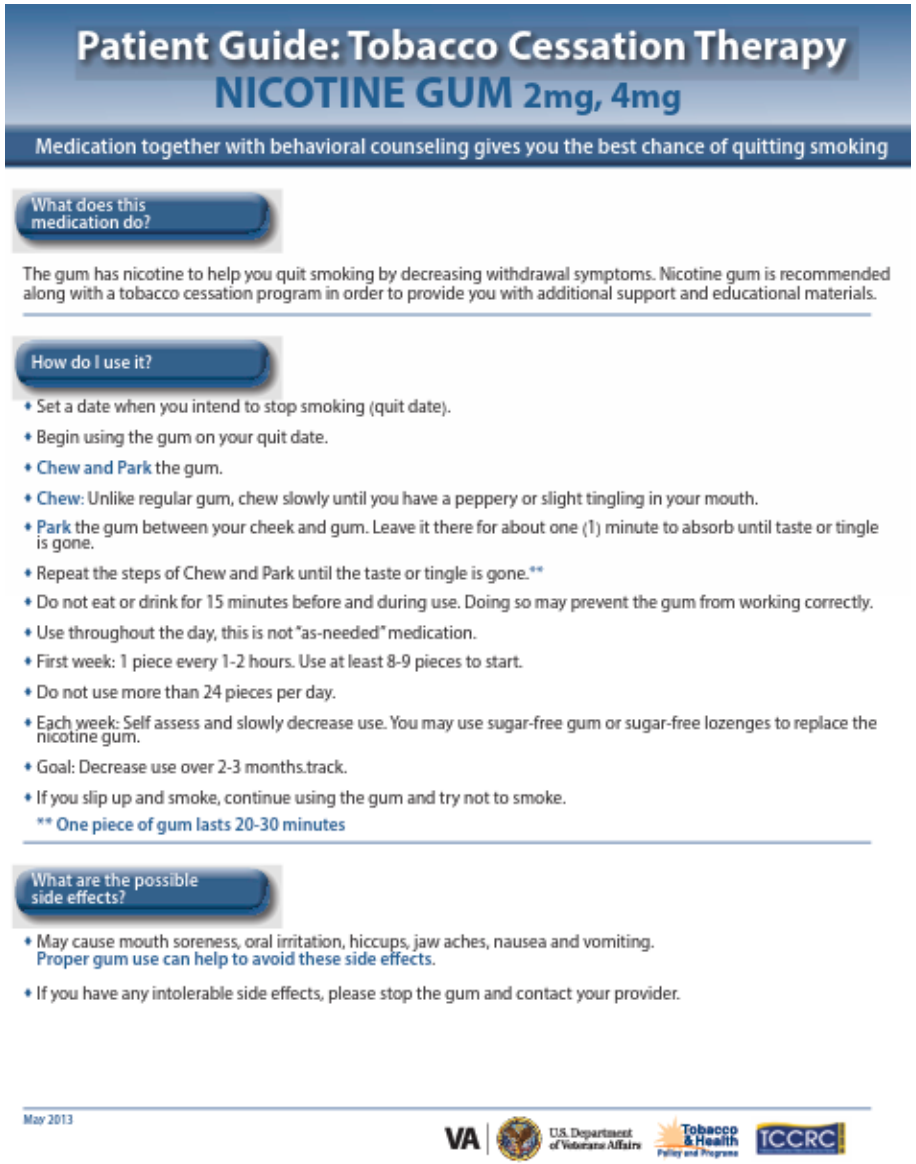
Nicotine Gum

- "Bite and Park" method
  - Patient bites down on gum a few times until tastes nicotine (peppery) or feels tingling sensation
  - Gum is parked between the cheek and gum until taste/sensation goes away
  - Bite and repeat until gum has lost its taste (~30 min)
- Remind patients not to use like chewing gum
- Can be used ad lib to control strong tobacco cravings
- Do not eat or drink for 15 min before or after using gum. Acidic beverages (soda, coffee) can reduce nicotine absorption.
- If patient has nausea – check to see if they are using the gum correctly
- Dosing is based on when you have your first cigarette of the day
  - If first cigarette is within 30 minutes of waking use 4mg gum
  - If first cigarette is more than 30 minutes after waking use 2mg gum
  - If combining nicotine patch and nicotine lozenge, consider using 2mg gum

For more information on nicotine gum dosing see:
www.publichealth.va.gov/docs/smoking/cessationguidelinepart3_508.pdf



Patient Guide: Tobacco Cessation Therapy
NICOTINE GUM 2mg, 4mg

Medication together with behavioral counseling gives you the best chance of quitting smoking

What does this medication do?

The gum has nicotine to help you quit smoking by decreasing withdrawal symptoms. Nicotine gum is recommended along with a tobacco cessation program in order to provide you with additional support and educational materials.

How do I use it?

- Set a date when you intend to stop smoking (quit date).
- Begin using the gum on your quit date.
- Chew and Park the gum.
- Chew: Unlike regular gum, chew slowly until you have a peppery or slight tingling in your mouth.
- Park the gum between your cheek and gum. Leave it there for about one (1) minute to absorb until taste or tingle is gone.
- Repeat the steps of Chew and Park until the taste or tingle is gone.**
- Do not eat or drink for 15 minutes before and during use. Doing so may prevent the gum from working correctly.
- Use throughout the day, this is not "as-needed" medication.
- First week: 1 piece every 1-2 hours. Use at least 8-9 pieces to start.
- Do not use more than 24 pieces per day.
- Each week: Self assess and slowly decrease use. You may use sugar-free gum or sugar-free lozenges to replace the nicotine gum.
- Goal: Decrease use over 2-3 months.track.
- If you slip up and smoke, continue using the gum and try not to smoke.

** One piece of gum lasts 20-30 minutes

What are the possible side effects?

- May cause mouth soreness, oral irritation, hiccups, jaw aches, nausea and vomiting. Proper gum use can help to avoid these side effects.
- If you have any intolerable side effects, please stop the gum and contact your provider.

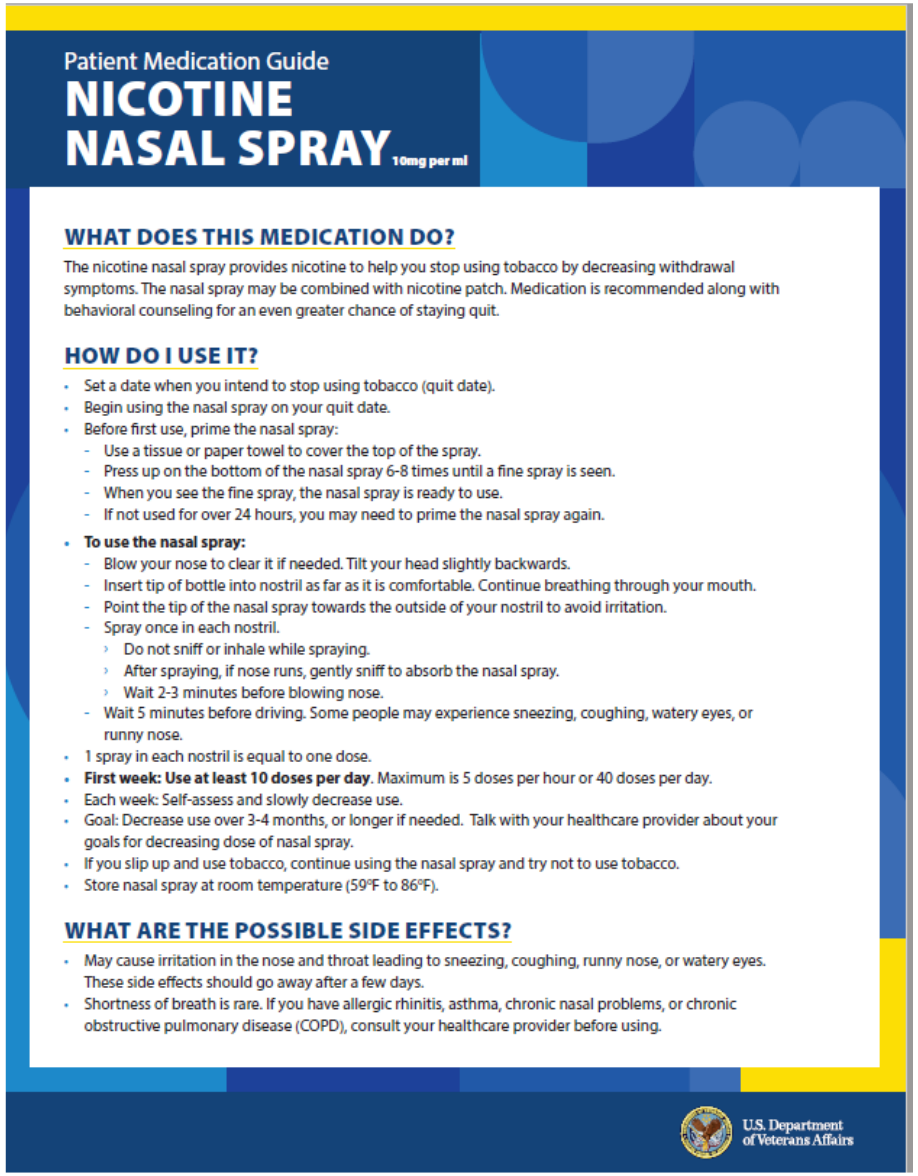
May 2013

VA | U.S. Department of Veterans Affairs | Tobacco & Health Policy and Programs | ICCRC

Nicotine Nasal Spray

- Dose
  - monotherapy max is 40 doses per day or 5 doses per hour
  - one dose = 1 spray in each nostril

- Quickest onset and absorption of all the nicotine replacement therapies
- Can be used combination with patch, but higher nicotine levels
- Can cause tearing for 5-10 minutes
- Nasal irritation is common, can exacerbate reactive airway disease



Patient Medication Guide

NICOTINE NASAL SPRAY 10mg per ml

WHAT DOES THIS MEDICATION DO?

The nicotine nasal spray provides nicotine to help you stop using tobacco by decreasing withdrawal symptoms. The nasal spray may be combined with nicotine patch. Medication is recommended along with behavioral counseling for an even greater chance of staying quit.

HOW DO I USE IT?

- Set a date when you intend to stop using tobacco (quit date).
- Begin using the nasal spray on your quit date.
- Before first use, prime the nasal spray:
  - Use a tissue or paper towel to cover the top of the spray.
  - Press up on the bottom of the nasal spray 6-8 times until a fine spray is seen.
  - When you see the fine spray, the nasal spray is ready to use.
  - If not used for over 24 hours, you may need to prime the nasal spray again.
- **To use the nasal spray:**
  - Blow your nose to clear it if needed. Tilt your head slightly backwards.
  - Insert tip of bottle into nostril as far as it is comfortable. Continue breathing through your mouth.
  - Point the tip of the nasal spray towards the outside of your nostril to avoid irritation.
  - Spray once in each nostril.
    - Do not sniff or inhale while spraying.
    - After spraying, if nose runs, gently sniff to absorb the nasal spray.
    - Wait 2-3 minutes before blowing nose.
  - Wait 5 minutes before driving. Some people may experience sneezing, coughing, watery eyes, or runny nose.
- 1 spray in each nostril is equal to one dose.
- **First week: Use at least 10 doses per day**. Maximum is 5 doses per hour or 40 doses per day.
- Each week: Self-assess and slowly decrease use.
- Goal: Decrease use over 3-4 months, or longer if needed. Talk with your healthcare provider about your goals for decreasing dose of nasal spray.
- If you slip up and use tobacco, continue using the nasal spray and try not to use tobacco.
- Store nasal spray at room temperature (59°F to 86°F).

WHAT ARE THE POSSIBLE SIDE EFFECTS?

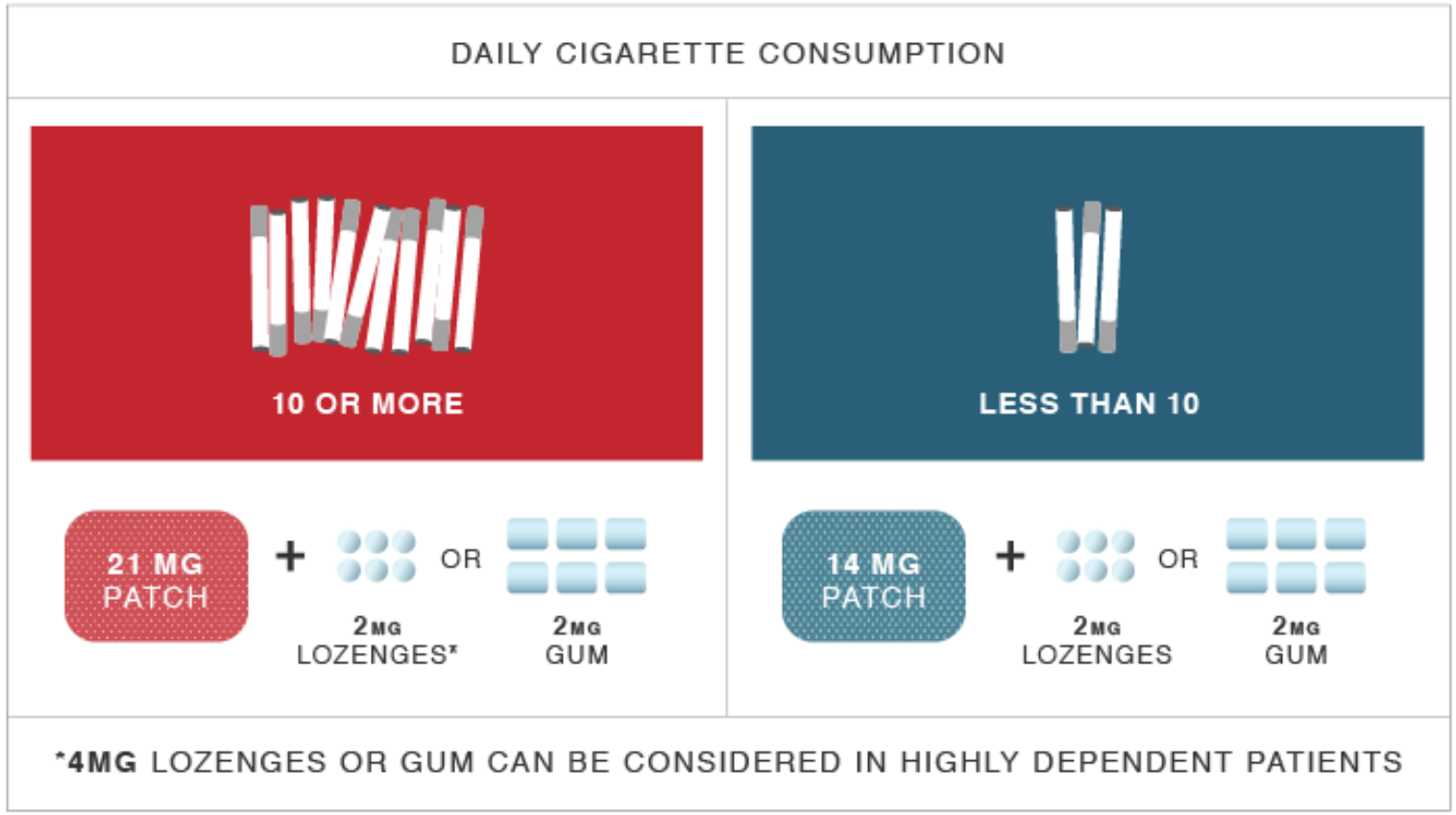
- May cause irritation in the nose and throat leading to sneezing, coughing, runny nose, or watery eyes. These side effects should go away after a few days.
- Shortness of breath is rare. If you have allergic rhinitis, asthma, chronic nasal problems, or chronic obstructive pulmonary disease (COPD), consult your healthcare provider before using.

U.S. Department of Veterans Affairs

For more information on nicotine lozenge: www.publichealth.va.gov/docs/smoking/cessationguidelinepart3_508.pdf

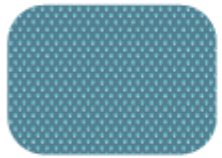
Combination Nicotine Replacement Therapy (NRT)

Recommended Starting Dose



Combination Nicotine Replacement Therapy (NRT)

Start on target quit date



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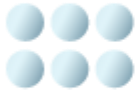


OR

NICOTINE PATCH

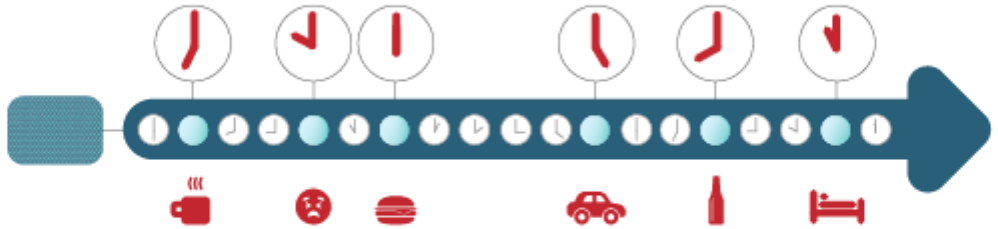
USE 1 PATCH EVERY 24 HOURS TO MAINTAIN BASAL NICOTINE LEVELS

SHORT ACTING NRT

6–10 LOZENGES OR PIECES OF GUM PER DAY

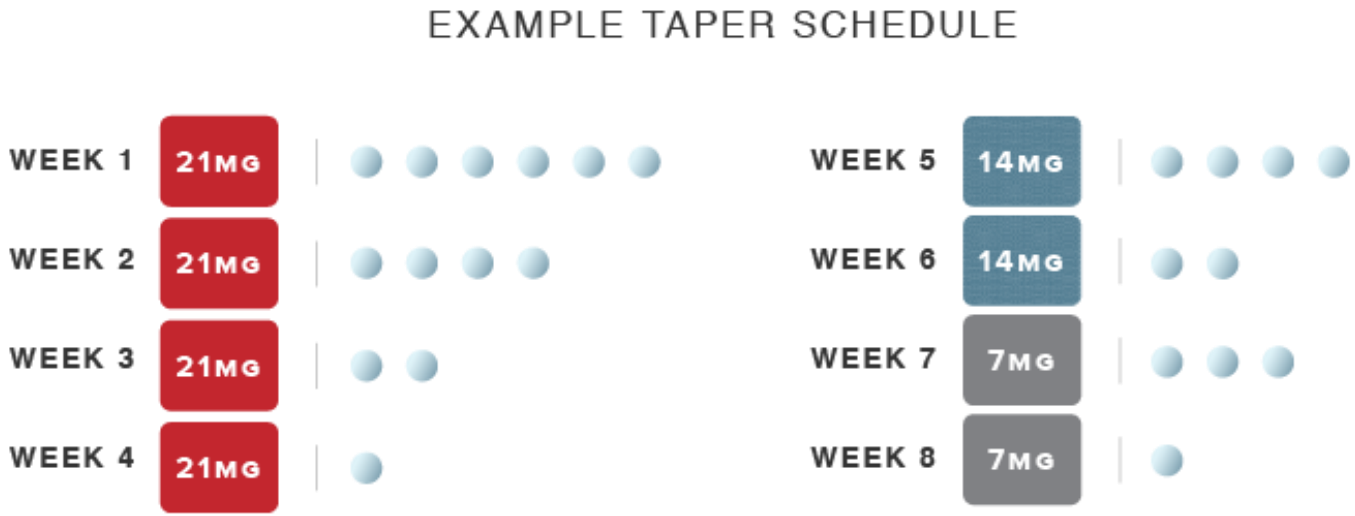
AS NEEDED FOR BREAKTHROUGH CRAVINGS

Example combo NRT use for one day



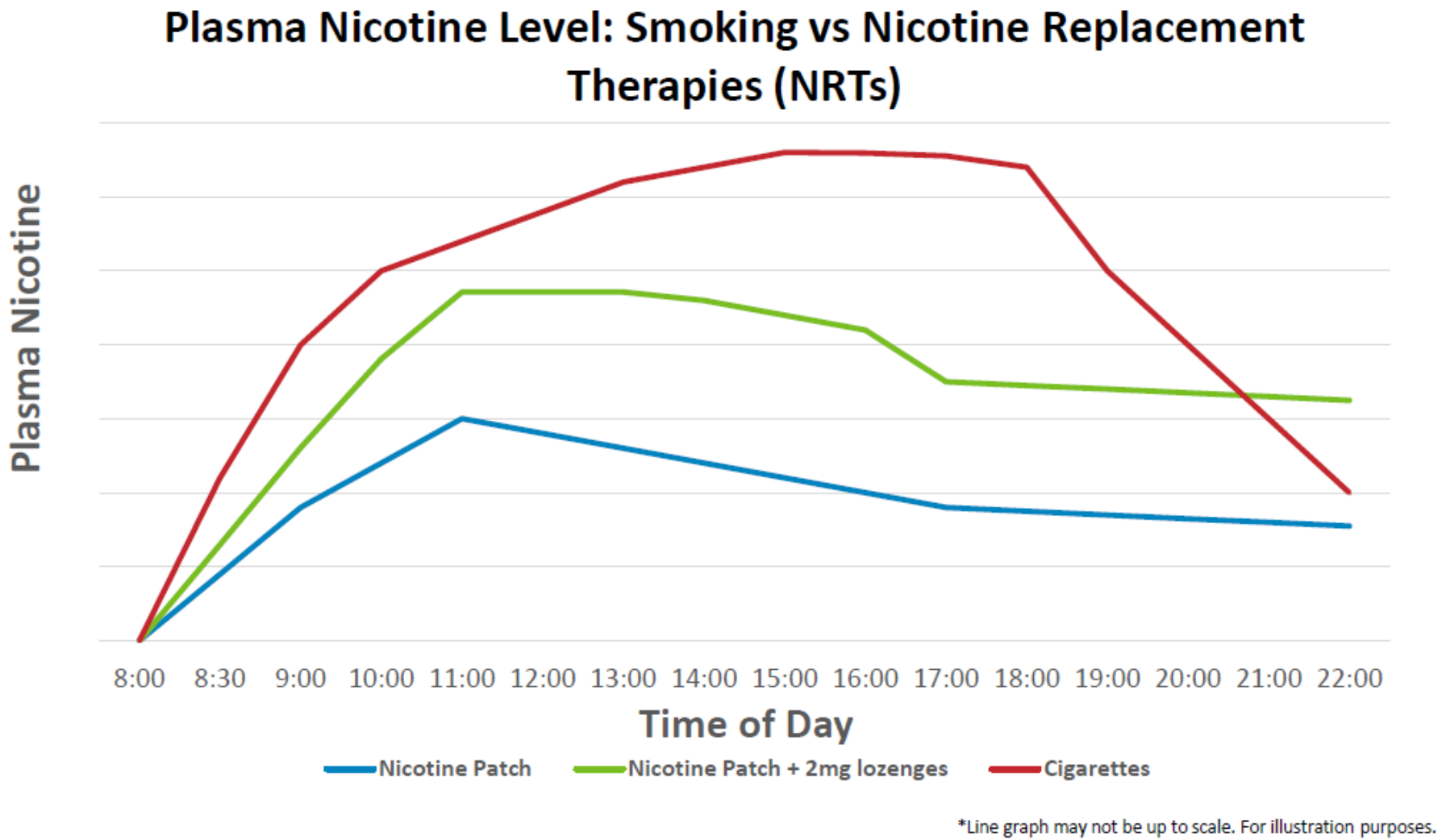
Combination Nicotine Replacement Therapy (NRT)

Reduce dosage over the next 2–6 months



Tapering may be extended past 6 months, particularly for patients with high nicotine dependence or trouble reducing dose of NRT

Combination Nicotine Replacement Therapy (NRT)



*Line graph may not be up to scale. For illustration purposes.

Bupropion

- Mechanism of action
  - Blocks reuptake of dopamine and norepinephrine in reward center, with metabolite hydroxybupropion may also act as nicotine antagonist at alpha-4-beta-2 receptors
  - Can be used in combination with NRT

Adverse effects
- Insomnia/sleep disturbances
- Dry mouth
- Rash
- Seizures (~1 in 1000 patients)

Cautions
- Seizures (relative contraindication)
- Conditions that lower seizure threshold
  - Eating disorders
  - Alcohol withdrawals

Varenicline

- Partial agonist/antagonist at the alpha-4-beta-2 nicotinic acetylcholine receptors
- Reduces tobacco cravings and symptoms of withdrawal and also makes tobacco use less enjoyable

Adverse drug events

- Commonly causes nausea, headaches, and sleep disturbances
- Rarely causes patients to have violent thoughts, intent, or actions towards themselves or others

Cautions

- Seizure risk/history
- May reduce alcohol tolerance

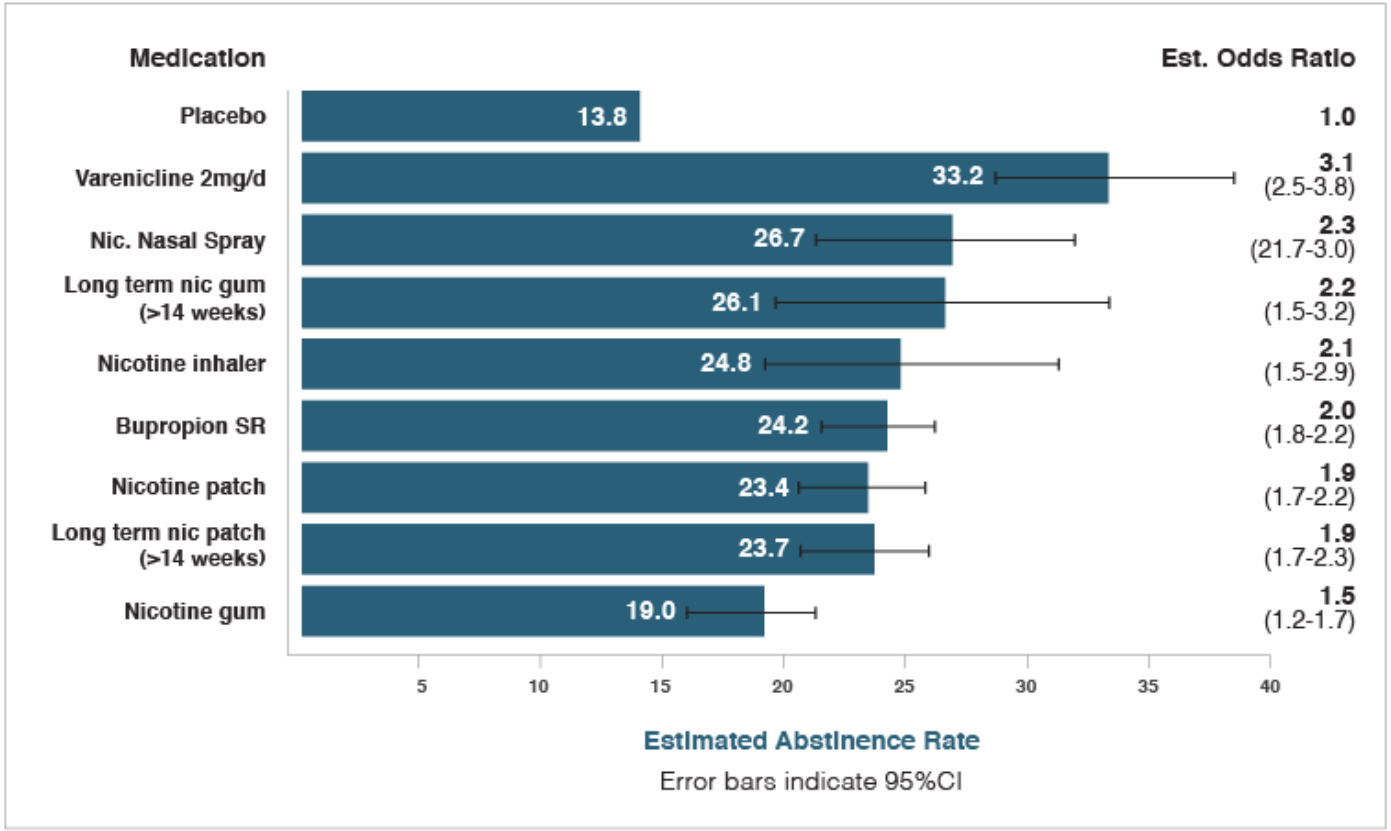
Varenicline

- Patients with stable mental illness had **no increased risk** in neuropsychiatric adverse events[1] (Eagles Trial)
  - Randomized, double-blinded trial (N = 8144) Compared to NRTs and bupropion
  - Primary endpoint was incidence of moderate and severe neuropsychiatric events
- VA study comparing Varenicline to nicotine patch with/without psychiatric diagnosis found no increased risk of hospitalizations due to neuropsychiatric symptoms[2]
  - Propensity Scored matched
  - Limitations: retrospective and database accuracy
- Other smaller studies found that in general patients with stabled mental illness have no issues on varenicline

1. Anthenelli et al. Lancet 2016.; 2. Cunningham et al. Addiction. 2016.

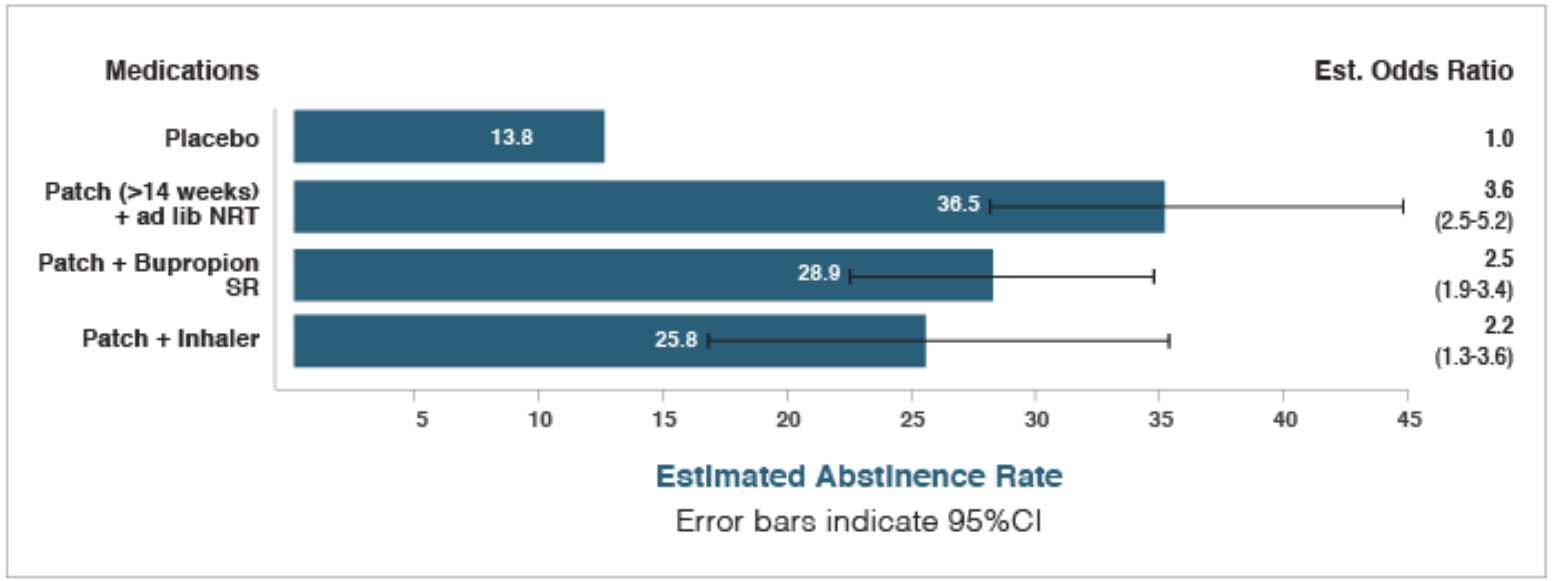
Effectiveness of Monotherapies

CPG Table 6.26: Effectiveness and abstinence rates for monotherapies vs. placebo at 6 months postquit (n=83 studies)



Effectiveness of Combination Therapies

CPG Table 6.26: Effectiveness and abstinence rates for smoking medication combinations vs. placebo at 6 months postquit (n=83 studies)



- Certain combinations of first-line medications have been shown to be effective
  - **Strength of evidence: A**
- Effective combinations are long term nicotine patch + ad lib NRT, nicotine patch + inhaler, nicotine patch + bupropion
  - Long term patch + ad lib NRT associated with highest quit rates vs. placebo
- Clinicians should consider factors of cost, tolerability, compliance

Tobacco Smoke Drug Interactions

- Tobacco smoke (specifically, poly-aromatic hydrocarbons) induces CYP1A2 hepatic enzymes
- CYP1A2 metabolized drugs including those for Alzheimer's disease, some antipsychotics, and warfarin
  - Bottom Line: medications are eliminated quicker from the body
- Smoking cessation REVERSES tobacco smoke-induced CYP1A2 hepatic enzyme levels to normal
  - This will increase plasma concentrations in patients whose dose was established while smoking
  - Watch out for potential side effects but won’t affect EFFICACY
- Nicotine replacement will not alter the effect

Long Term use of Tobacco Cessation Medications

- NRTs have been studied long term up to 52 weeks[1-4]
  - No difference in abstinence rates
  - No reported safety concerns
- Bupropion have been studied up to 52 weeks for smoking cessation[1-3,5-6]
  - No difference in abstinence rate
  - Used long term for depression
- Varenicline mainly studied for 6 months and 1 study did look at 52 weeks vs placebo[1-3,7]
  - Increase abstinence vs placebo but no data vs 6 months of varenicline use
  - Appears safe to use

1. Tobacco Use and Dependence Guideline Panel (2008); 2. 2020 Surgeon General Report (2020); 3. USPSTF (2021). JAMA; 4. Schnoll et al (2015). JAMA Intern Med. 2015.; 5. Hays et al. (2009) Nicotine Tob Res.; 6. Killen et al. (2006) J Consult Clin Psychol.; 7. Williams et al. (2007) Current Med Res Opin.

Long Term use of Tobacco Cessation Medications

- Extended treatment is appropriate to prevent lapse/relapse to tobacco use
- Safe to use in patients
  - Safety data available for up to 1 year for NRTs and varenicline use
    - Lack of long-term safety data greater than 1 year, but safer than relapsing back to tobacco use
  - Bupropion is used chronically for depression
- Efficacy data for medication use longer than 6 months is weak, but appropriate in some cases (Harm reduction)
- Literature is limited for greater than 1 year

Tobacco Cessation Pharmacotherapy during Pregnancy

- Medication use during pregnancy is still controversial
  - Fetal risk cannot be ruled out
  - Limited literature for safety and efficacy
- USPSTF
  - Convincing evidence on the benefit of behavioral interventions to achieve tobacco smoking cessation in pregnant persons and preventing infant low birth weight is substantial.
  - Inadequate evidence on pharmacotherapy due to few available studies on benefits of NRT and no studies reporting on the benefits of bupropion, varenicline, or e-cigarettes to achieve tobacco smoking cessation in pregnant persons or to improve outcomes.
  - Inadequate evidence on the harms of pharmacotherapy interventions due to few available studies on NRT and no studies reporting harms of bupropion SR, varenicline, or e-cigarettes for tobacco smoking cessation in pregnant persons who smoke.

Oregon Pharmacist Tobacco Cessation Program

Fee for service professional billing for retail and community pharmacists

- Eligibility
  - How to become an eligible prescribing pharmacist
    - Oregon Board of Pharmacy requirements
      - Training
      - Enroll as an Oregon Medicaid provider
      - Must abide by all Oregon Board of Pharmacy rules
- Smoke Free Oregon has information about pharmacist prescribing and map with pharmacies participating (Self-reporting)
- Smoke Free Oregon has Information about pharmacist prescribing and a map with pharmacies participating (self-reporting to the list) https://smokefreeoregon.com/oregonians/helping-people-quit-tobacco/health-care-and-service-providers/

Here is the link to add your pharmacy https://smokefreeoregon.com/contact-us/

Pharmacists in Oregon can now counseling patients and prescribe quit smoking medications on the spot.

Oregon Pharmacist Tobacco Cessation Program

- Training
  - Courses developed with guidance from the Oregon Board of Pharmacy. College of Pharmacy - CE (instructure.com)
    - Successful Implementation of Patient Assessment and Proper Billing: Overview of the healthcare payer environment in the United States and how Medicaid is administered, credentialing/enrollment and billing mechanics utilized to build a pharmacy prescribing and reimbursement model, and the fundamentals of medical billing including HCPCS, CPT, and ICD10 codes.
  - Tobacco cessation counseling: Training for the pharmacist to prescribe tobacco cessation products. This course was developed with guidance from the Accreditation Council for Pharmacy Education.
    - **460 Oregon Pharmacists have received training to prescribe tobacco cessation therapies**
    - Tobacco_Protocol_8.2020.pdf (oregon.gov)
      - Pathway for pharmacist to follow when screening a patient for tobacco use and prescribing cessation therapy.

Questions

Post-Test Questions

1. Which of the following is not one of the 5A's to help tobacco users through the process of quitting?
    a. Ask – Do you currently use tobacco?
    b. Advise – Use clear, strong, personalized messages
    c. Assess – Are you willing to give quitting a try in the next 30 days
    d. Allow – Provide medications if on formulary
    e. Arrange – Set up follow up sessions or attendance in a tobacco use treatment clinic

2. What is the most worrisome health problem regarding e-cigarettes?
    a. FDA has proposed rules regulating the sale of e-cigarettes
    b. Products are often flavored in ways that appeal to adults
    c. The awareness of e-cigarettes is rising among the general public
    d. E cigarette liquid contains unknown ingredients, and little is known of the health consequences
    e. The efficacy of e-cigarettes as an aid for sustained smoking cessation has not been established

3. What is most common adverse effect of varenicline?
    a. Suicidal ideation
    b. Depression
    c. Nausea and vomiting
    d. Constipation
    e. Increased urination

4. Patients prescribed the nicotine patch, should be counseled to:
    a. Apply the patch to the lower legs
    b. Avoid swimming or showering with the patch
    c. Cut the patches in order to adjust the dose
    d. Apply the patch to the same area for a week
    e. If you slip and smoke, continue using patch and try not to smoke

5. The US Preventative Services Task Force recommendations include which of the following statements as interventions for Tobacco Smoking Cessation in Adults:
    a. Recommends electronic cigarettes (ENDs) for tobacco cessation in nonpregnant adults.
    b. Recommends clinicians ask all adults about tobacco use, advise them to stop using tobacco, and provide behavioral interventions and US FDA approved pharmacotherapy for cessation to nonpregnant adults who use tobacco.
    c. Recommends US FDA approved pharmacotherapy for all pregnant adults who use tobacco.
    d. Current evidence is insufficient to assess the balance of benefits and harms of electronic cigarettes (ENDs) for tobacco cessation in adults, including pregnant person. Clinicians should direct patients who use tobacco to other tobacco cessation interventions with proven effectiveness and established safety.
    e. B and D are correct