



Smoking Cessation

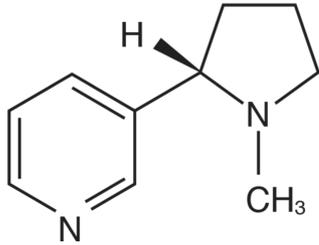
Michelle Okoreeh, MD
Addiction Medicine Fellow

UCLA

Learning Goals

- Review vehicles of nicotine products and their effects on the body
- Review office based assessments to determine nicotine dependency
- Review treatment options of smoking cessation
- Address common patient questions and concerns

Epidemiology



Tobacco is not a drug. **Nicotine is psychoactive**

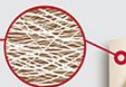
- 20.7% (or about 57.3 million people) report using tobacco products or vaping nicotine in the past 30 days
 - a. 15.0% (or about 41.4 million people) reported smoking cigarettes in the past 30 days
 - b. 3.8% (or about 10.4 million people) reported vaping nicotine in the past 30 days
- Leading cause of preventable disease and death in US
- \$300 billion spent on smoking related illness in US a year

Cigarettes

The design and content of cigarettes continue to make them attractive, addictive, and deadly.¹ Every day, more than 1,300 people in the United States die because of cigarette use.²

Filter^{3,4,5}

- Typically made from bundles of thin, hair-like fibers.
- Designed to trap smoke, but only stops a small portion of the smoke from being inhaled.
- The filter (and ventilation holes) in most cigarettes may lead smokers to inhale more deeply, pulling dangerous chemicals farther into their lungs.



Tipping paper⁶

- Wraps around the filter, connecting it to the rest of the cigarette.
- **Ventilation holes**, if unblocked, dilute inhaled smoke with air.
- Manufacturers have chosen to place the ventilation holes where they are. The holes are largely ineffective. Because of their location, most smokers unknowingly block them with their fingers or lips.



Cigarette paper³

- Holds the tobacco filler.
- Manufacturers add chemicals to the paper to control how fast the cigarette burns.
- Smokers inhale everything that is burned—the tobacco filler, the paper... everything.

Tobacco filler^{7,8,9}

- Made up of chopped tobacco leaves, stems, reprocessed pieces, and scraps.
- Dangerous chemicals can form in and be deposited on tobacco during the processing of the tobacco leaves.
- Other dangerous chemicals are created when the tobacco filler is burned.



Additives^{10,11,12}

Manufacturers can add **hundreds of ingredients** to a cigarette to make smoking more appealing and to mask the harshness of smoke.



Certain **additives**, like sugars, can form cancer-causing chemicals when they are burned.

Sugar and flavor* additives can change the taste of smoke and make it easier to inhale, but no less harmful.



Ammonia and other **chemicals** added to tobacco may increase the absorption of nicotine, which is addictive.

Some additives are **bronchodilators** that could increase the amount of dangerous chemicals absorbed by the lungs.

¹In 2009, The Family Smoking Prevention and Tobacco Control Act banned characterizing flavors in cigarettes, except for tobacco and menthol flavors.

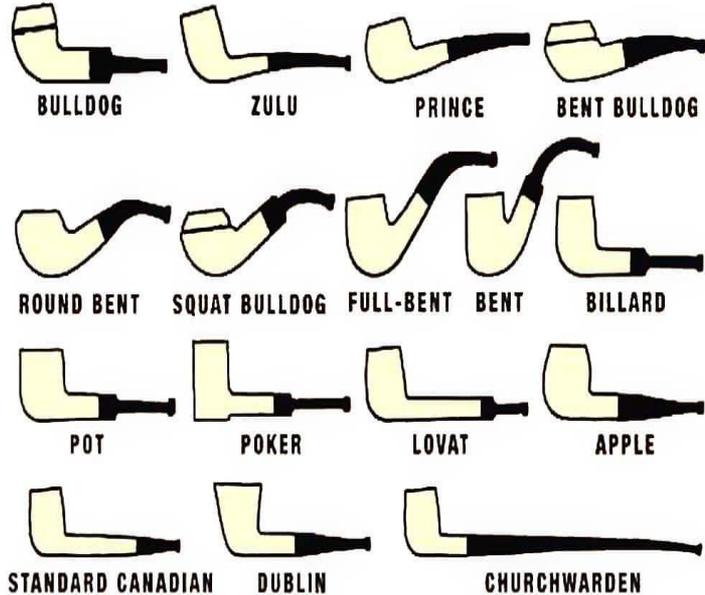
- Filter (designed to “trap” smoke), tipping paper, cigarette paper, tobacco filler, additives (to make more appealing, mask hoarseness of smoke)
- False sense of safety with filters
- 20 cigarettes = 1 pack
- **Hand-rolled cigarettes:** perceived as safer but it's not, varied tobacco amount, cheaper cost

Electronic Nicotine Delivery System (ENDS)



- Uses liquid which contains nicotine derived from tobacco (sometimes synthetic), flavorings, propylene glycol, vegetable glycerin, and others.
- **The liquid is heated to create an aerosol that the user inhales**

Pipes



- Loose leaf tobacco burned in a traditional smoking pipe with a bowl
- 1.4% (an estimated 190,000) of high school students currently smoke pipes
- Dosage often depends on the bowl size of pipe

Cigars and Cigarillos



- Roll of tobacco wrapped in leaf tobacco or in a substance that contains tobacco. Most cigars are **combustible** tobacco products.
- Large cigars can deliver as much as 10 times the nicotine, two times the tar, and more than five times the carbon monoxide of a filtered cigarette
- People try to avoid inhaling smoke but the smoke is absorbed in the mucosa
- Many sizes and flavors

Hookah “Waterpipe Tobacco”

- Maassel, shisha, narghile, or argileh in other countries
- Vapor exposes people to the addictive chemical nicotine and contains many of the same toxic chemicals that are in cigarette smoke
- Misconception: only smoking water vapor and not nicotine
- A typical one-hour hookah session involves inhaling **100–200 times the volume of smoke from a single cigarette**

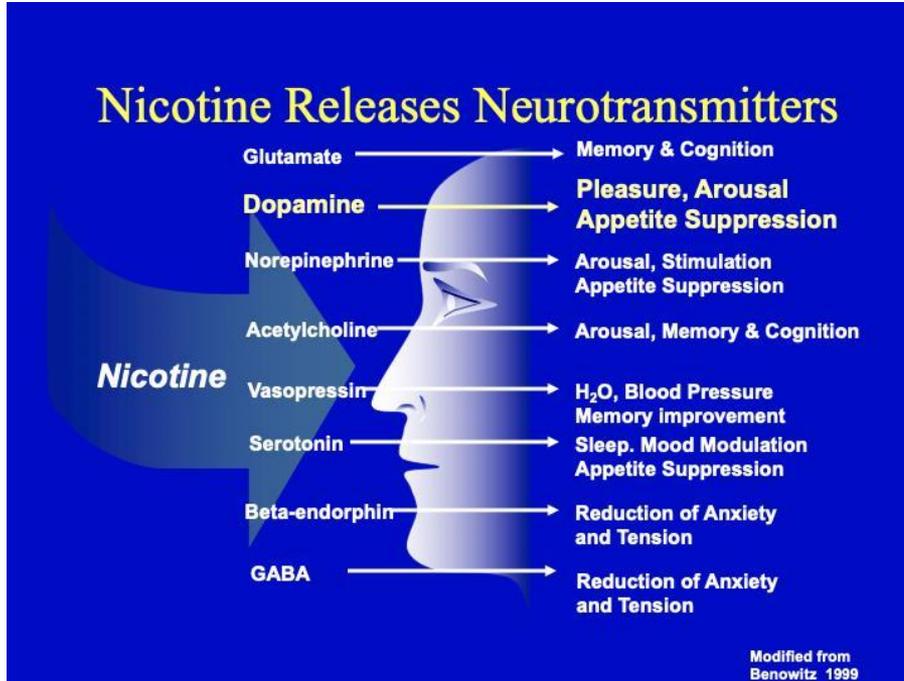


Smokeless Tobacco (noncombustible)

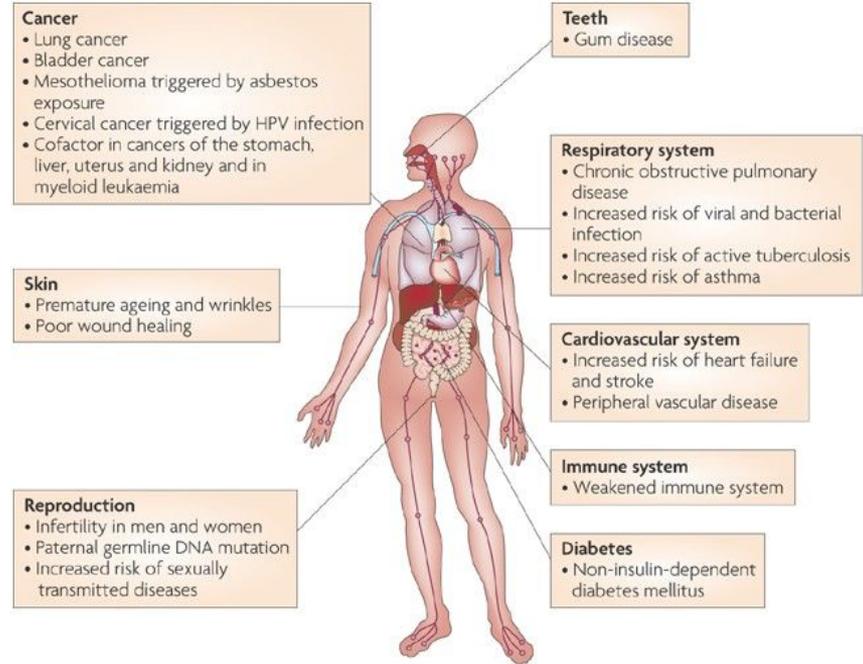


- Product is placed between the gum and the cheek or lip
- **Chewing tobacco** is cured tobacco in the form of loose leaf, plug, or twist
- **Dry snuff** is loose finely cut or powdered dry tobacco that is typically sniffed through the nostrils
- **Moist snuff and snus** are cut tobacco that can be loose or pouched and placed in the mouth. More than 30 chemicals in smokeless tobacco are linked to cancer

Nicotine effects on the body

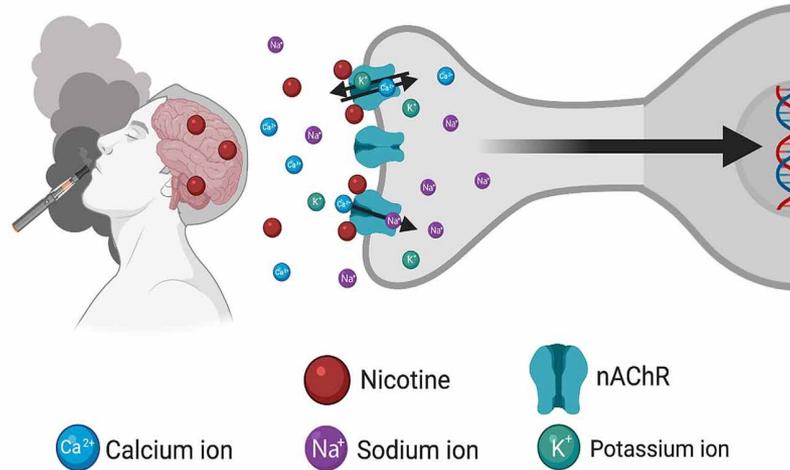


ACAAM



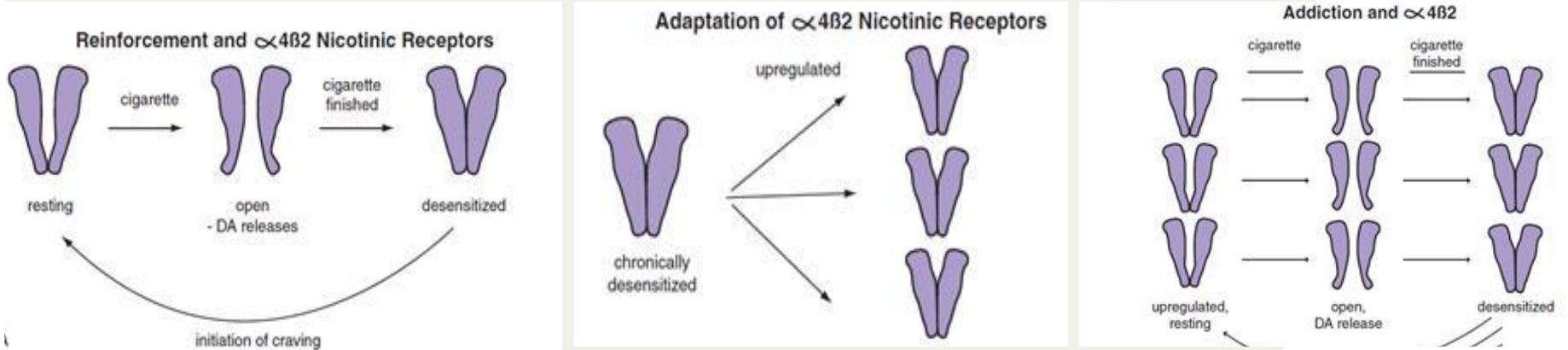
Nature Reviews | Immunology

How does nicotine affect the brain?



- 1** Nicotine delivered by smoking
- 2** Nicotine travels to the brain
- 3** Nicotine activates nicotinic receptors which stimulates the release of Dopamine
- 4** Dopamine released, leading to pleasant feelings of calmness and reward
- 5** Dopamine levels reduce, leading to withdrawal symptoms of stress and anxiety
- 6** Withdrawal triggers desire for another cigarette

How does nicotine affect the brain?



How is nicotine metabolized?

- 70-90% metabolized in the liver to cotinine
- Faster metabolizer may increase risk of addiction.
Check metabolite ratio
- Pregnant Women > Women > Men
 - **18 to 22 weeks of pregnancy** and appears to fall by 4 weeks after childbirth (Bowker, 2015)
- Caucasians > African Americans /Asians
- Smoke contains aromatic hydrocarbons that induce CYP1A2, which lowers levels of many medications (Zevin 1999).



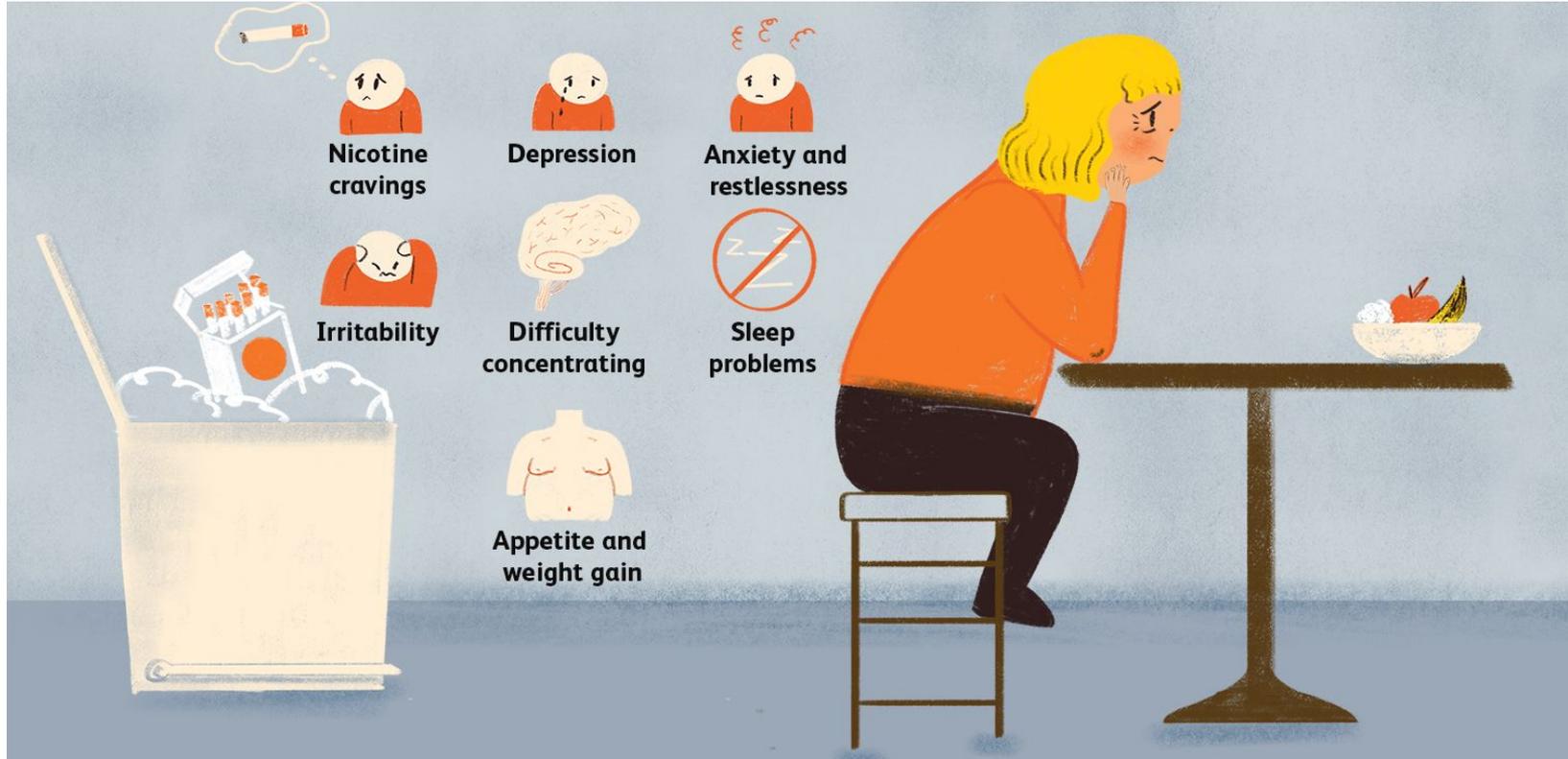
DRUG INTERACTIONS WITH TOBACCO SMOKE

Many interactions between tobacco smoke and medications have been identified. Note that in most cases it is the tobacco smoke—not the nicotine—that causes these drug interactions. Tobacco smoke interacts with medications by influencing the absorption, distribution, metabolism, or elimination of other drugs, potentially causing an altered pharmacologic response. Because of these interactions, smokers may require higher doses of medications. Upon cessation, dose reductions might be needed.

The most clinically significant interactions are depicted in the shaded rows.

Drug/Class	Mechanism of Interaction and Effects
Pharmacokinetic Interactions	
Alprazolam (Xanax)	<ul style="list-style-type: none"> • Conflicting data on significance, but possible ↓ plasma concentrations (up to 50%); ↓ half-life (35%).
Bendamustine (Treanda)	<ul style="list-style-type: none"> • Metabolized by CYP1A2. Manufacturer recommends using with caution in smokers due to likely ↓ bendamustine concentrations, with ↑ concentrations of its two active metabolites.
Caffeine	<ul style="list-style-type: none"> • Metabolism (induction of CYP1A2); ↑ clearance (56%). Caffeine levels likely ↑ after cessation.
Chlorpromazine (Thorazine)	<ul style="list-style-type: none"> • ↓ Area under the curve (AUC) (36%) and serum concentrations (24%). • ↓ Sedation and hypotension possible in smokers; smokers may require ↑ dosages.
Clopidogrel (Plavix)	<ul style="list-style-type: none"> • ↑ Metabolism (induction of CYP1A2) of clopidogrel to its active metabolite. • Clopidogrel's effects are enhanced in smokers (≥10 cigarettes/day): significant ↑ platelet inhibition, ↓ platelet aggregation; improved clinical outcomes have been shown (smokers' paradox; may be dependent on CYP1A2 genotype); tobacco cessation should still be recommended in at-risk populations needing clopidogrel.
Clozapine (Clozaril)	<ul style="list-style-type: none"> • ↑ Metabolism (induction of CYP1A2); ↓ plasma concentrations (18%). • ↑ Levels upon cessation may occur; closely monitor drug levels and reduce dose as required to avoid toxicity.
Erlotinib (Tarceva)	<ul style="list-style-type: none"> • ↑ Clearance (24%); ↓ trough serum concentrations (2-fold).
Flecainide (Tambocor)	<ul style="list-style-type: none"> • ↑ Clearance (61%); ↓ trough serum concentrations (25%). Smokers may need ↑ dosages.
Fluvoxamine (Luvox)	<ul style="list-style-type: none"> • ↑ Metabolism (induction of CYP1A2); ↑ clearance (24%); ↓ AUC (31%); ↓ plasma concentrations (32%). • Dosage modifications not routinely recommended but smokers may need ↑ dosages.
Haloperidol (Haldol)	<ul style="list-style-type: none"> • ↑ Clearance (44%); ↓ serum concentrations (70%).
Heparin	<ul style="list-style-type: none"> • Mechanism unknown but ↑ clearance and ↓ half-life are observed. • Smokers may need ↑ dosages due to PK and PD changes.

Nicotine Withdrawal Symptoms



Quick Office-Based Assessment

- Have you **EVER** smoked cigarettes or used tobacco products?
- When is the last time you used tobacco products?
- What quantity of tobacco or nicotine product do you use?

Population	Recommendation	Grade
Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years	The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.	B

Heaviness Smoking Index (HSI)

1. At present, how long after waking do you wait before having your first cigarette?

Within 5 minutes [3 points]

6-30 minutes [2 points]

31-60 minutes [1 point]

over 60 minutes [0 points]

2. How many cigarettes per day do/did you smoke?

10 or less [0 points]

11-20 [1 point]

21-30 [2 points]

30 or more [3 points]

Evaluation tool for patient with daily smoking use

Nicotine dependence is categorized into a three-category variable:

- low (0-1)
- medium (2-4)
- high (5-6).

Treatment: Non-pharmacotherapy

- The 3 A's and 5 R's
 - Ask, Advise, Assist
 - Relevance, Risk, Reward, Roadblock, Repetition
- Clinician Advice to Quit
- Repetitive Transcranial Magnetic Stimulation (rTMS): FDA approved for cessation
- Incentive based programs
- Technology based treatment
- <https://kickitca.org> is the new 1-800-NO- BUTTS

Treatment: Nicotine Replacement



Lozenge



Gum

- Chewing gum releases nicotine, which is absorbed in oral mucosa
- Both come in 2mg and 4 mg doses
 - 4mg dose if smoke <30 mins after waking
 - 2mg dose if smoke >30 mins after waking
 - Chew and Park method
- Adverse effects: GI irritation may occur if nicotine is swallowed and not absorbed
 - **Gum:** caution if TMJ issue, poor dentition, or dental appliances
 - **Lozenge:** Mouth irritation/ulcers, sore throat, hiccups possible side effect
 - **Avoid Acidic Beverages, absorption requires basic pH**

Treatment: Nicotine Replacement



Inhaler (10mg cartridge)

- Patient may use up to 6-16 cartridges per day
- Puff in short breaths, or inhale into the back of the throat
- Nicotine delivered more rapidly than other forms of NRT: 20 minutes may yield best results
- Adverse Effects: Localized irritation of mouth or throat. May cause bronchospasm



Nasal Spray

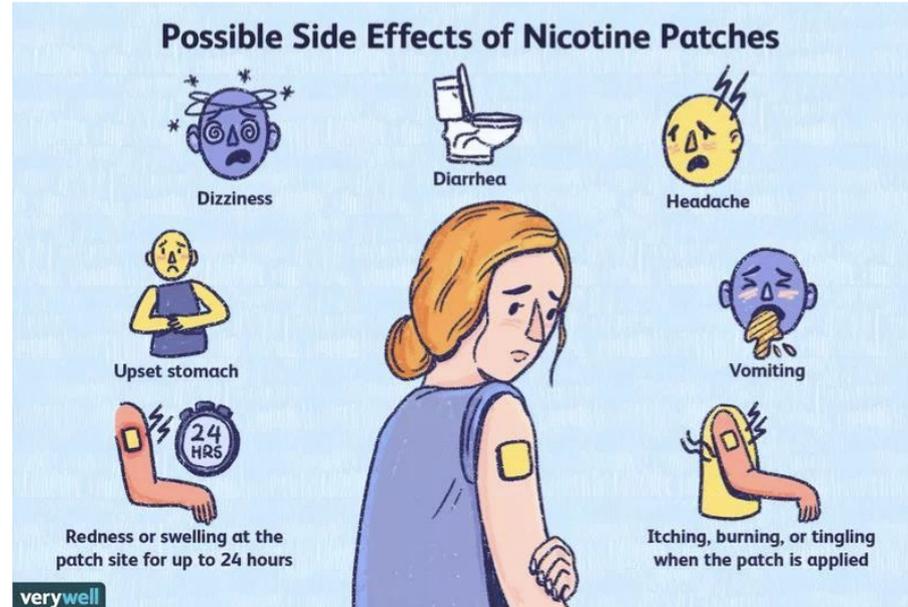
- Nicotine through nasal mucosa
 - One dose is 1mg (2 sprays, one in each nostril)
 - One-two sprays per hour, max 10 sprays per hour
- Max dose: 40mg (80 sprays)/day
- Adverse effects: nasal irritation (common), can trigger cravings in patients with his history of using drugs intranasally

Treatment: Nicotine Replacement

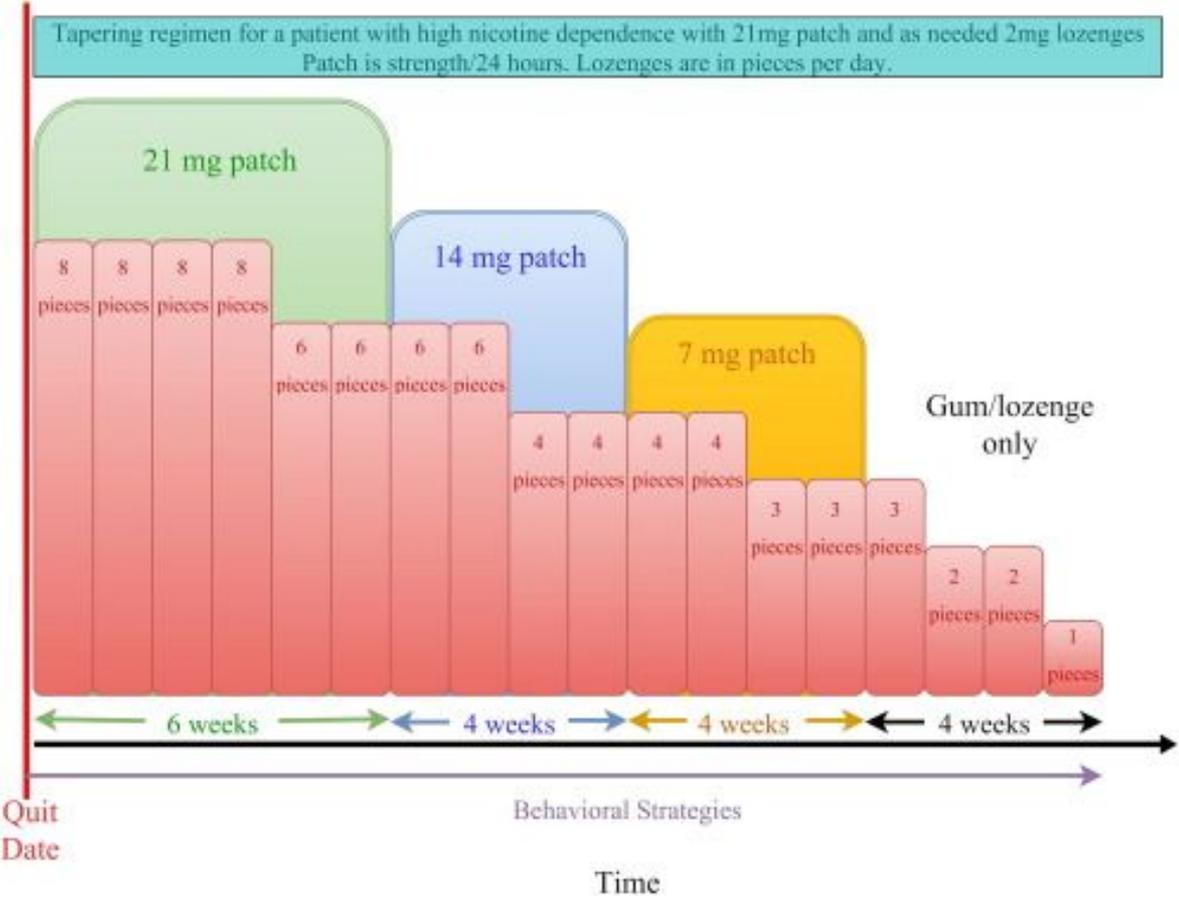


Patch

- Long lasting
- Comes in 7mg, 14mg or 21mg patches
- Dose based on # of cigarettes during the day
- Adverse effects: vivid dreams or insomnia



Example NRT Taper Plan



Sometimes patients need two 21mg patches

Treatment: Varenicline (Chantix)

- Selectively bind to the alpha-4 Beta-2 nicotinic receptor
 - Blocks nicotine from binding and stimulates receptor-mediated activity at much lower levels than nicotine
- Dosing
 - Begin one to five weeks prior to planned quit date
 - **Starter pack:** 0.5mg daily for three days, 0.5mg BID for four days
 - **Continuing pack:** 1mg BID thereafter
- Adverse Effects
 - Nausea, disordered sleep, vivid dreams
 - No longer a black box warning for neuropsychiatric symptoms (2016)
 - Pfizer: voluntary recall 2021 due to unacceptable nitroamine derivative levels. Shortages persist
 - Due to shortages, FDA allowing interim acceptable intake limit of 185ng/day (usually ~37 ng/day).. Benefits outweigh risks of continued tobacco exposure



Treatment: Bupropion HCL sustained release (Zyban)

- Inhibits NE and Dopamine reuptake, antagonist effect on nAChRs
 - May effect dopaminergic activity on the pleasure and reward pathways
- **Contraindications**
 - **Seizure disorders, bulimia/anorexia nervosa**
- Dose
 - Begin one week prior to target quit date
 - Abrupt quitting seems to be more effective
 - 150mg/day for 3 days, then 150mg BID thereafter
 - At least 12 weeks of treatment recommended
- Adverse Effects
 - Dry mouth, insomnia, anxiety

What's the best treatment option?

Long acting + Short Acting NRT

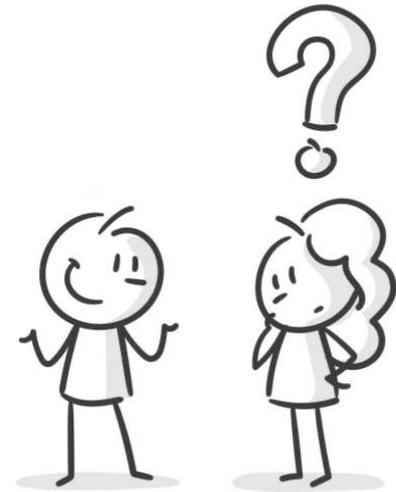
Bupropion + NRT

Varenicline + Bupropion

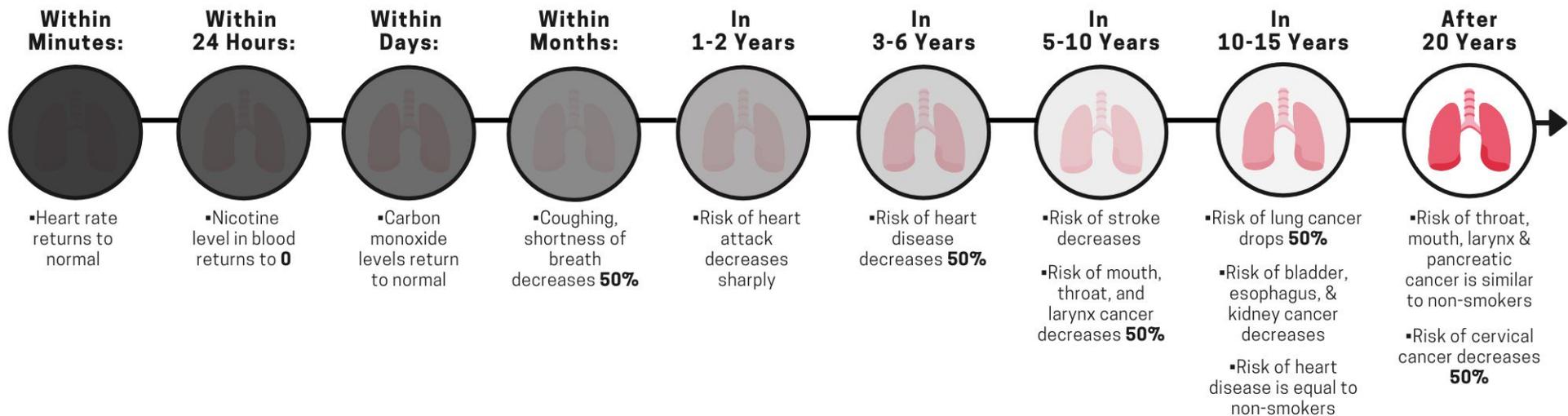
Varenicline + NRT

Varenicline + NRT + Bupropion

Common patient questions and concerns



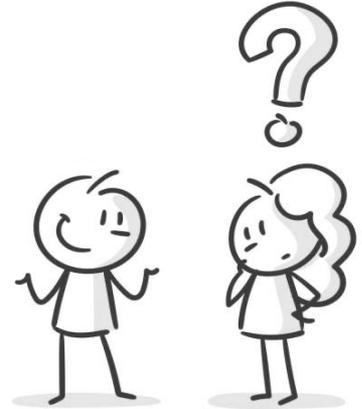
“I’ve been smoking for so long, what’s done is done. Can’t reverse time now!”



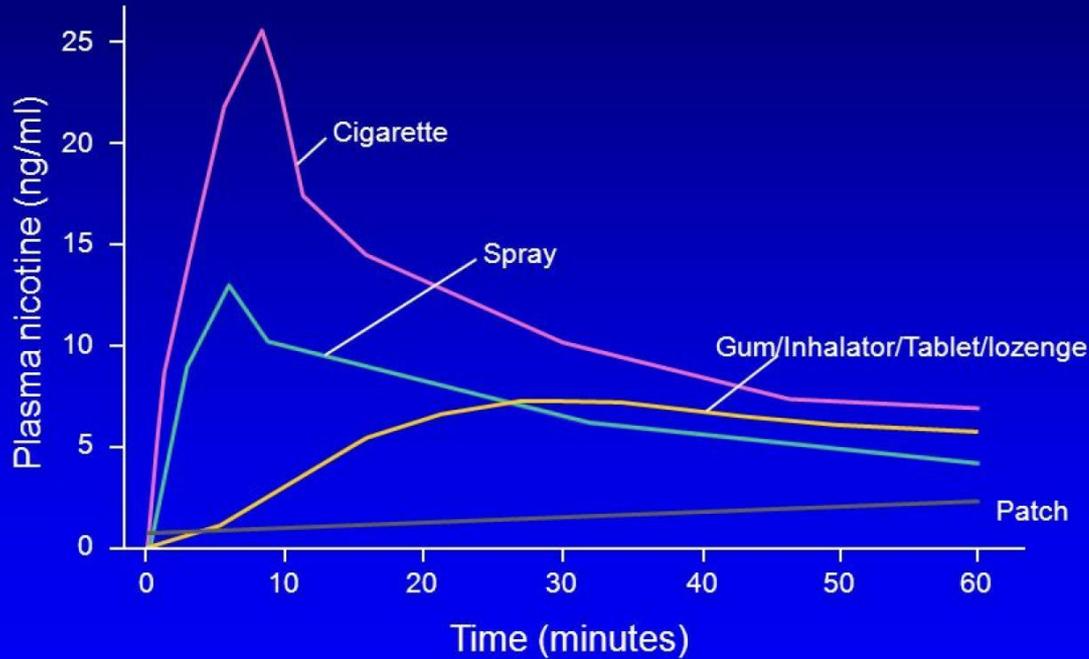
Quitting smoking results in immediate health benefits, and some or all of the reduced life expectancy can be recovered depending on the age a person quits

“You’re just replacing nicotine with nicotine when you use the lozenges, patches, gums and stuff. ”

The amount of nicotine in NRT is lower compared to a cigarette. It also takes longer for nicotine to get to the brain and to give you a nicotine hit. This means it's much easier to stop using NRT than it is to stop smoking.



Plasma nicotine levels – contrast between cigarettes and NRT

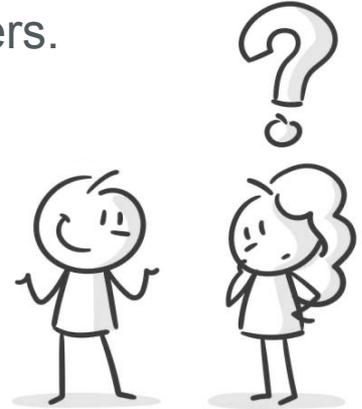


Adapted from: Tobacco Advisory Group of the Royal College of Physicians 2000.

“ What about e-cigarettes? I heard they are better than cigarettes and can they help me stop smoking?”

E-cigarettes have been proposed as a method to reduce the harms of tobacco use and as a nicotine replacement product.

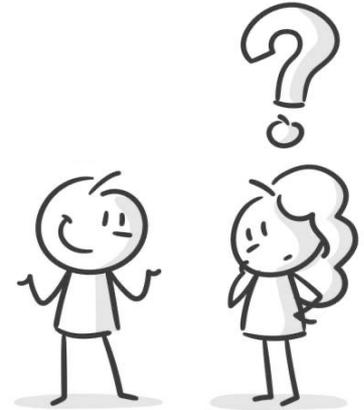
However, e-cigarettes can also cause nicotine dependence, so users may need treatment for nicotine dependence similar to that for tobacco users.



“ It’s all a mind thing. I can do this cold turkey and it won’t cost me a thing!”

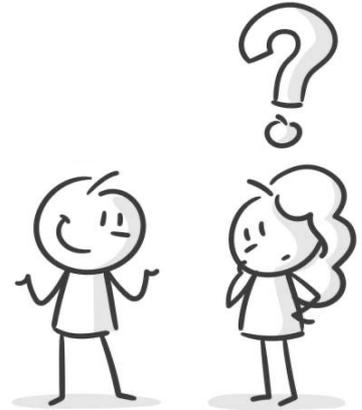
How much money do you spend on purchasing tobacco/cigarettes?

What will you do with all that money you’ll be saving?



“I don’t want to gain weight”

- Start or increase physical activity.
- Reassure smokers that some weight gain after quitting is common and usually is self-limiting with lifestyle changes.
- Suggest low-calorie substitutes to smoking such as sugarless chewing gum, vegetables, or mints.
- Maintain patients on medication known to delay weight gain (e.g., bupropion SR, NRTs—particularly 4-mg nicotine gum and lozenge).
- Refer smokers to a qualified weight loss professional or evidence-based program for personalized dietary and exercise programs.



Welcome to Kick It California

We're a free program that helps Californians kick smoking, vaping, and smokeless tobacco with the help of proven, science-based strategies. Take the first step toward quitting.

Start Now



Thank you!

© Randy Glasbergen
glasbergen.com



"I never actually quit smoking, I just ran out of places where I'm allowed to do it!"

References

Le Foll, B., Piper, M.E., Fowler, C.D. *et al.* Tobacco and nicotine use. *Nat Rev Dis Primers*8, 19 (2022). <https://doi.org/10.1038/s41572-022-00346-w>

Kim JE, Tsoh JY. Cigarette Smoking Among Socioeconomically Disadvantaged Young Adults in Association With Food Insecurity and Other Factors. *Prev Chronic Dis.* 2016;13:E08. Published 2016 Jan 14. doi:10.5888/pcd13.150458

NIDA. 2022, February 8. What is the scope of tobacco, nicotine, and e-cigarette use in the United States?. Retrieved from <https://nida.nih.gov/publications/research-reports/tobacco-nicotine-e-cigarettes/what-scope-tobacco-use-its-cost-to-society> on 2022, May 12

ACAAM: Nicotine Use Disorder: Hot Topics for carrying the torch” 2021 Lecture Series

Hajek P, Phillips-Waller A, Przulj D, et al. A randomized trial of e-cigarettes versus nicotine-replacement therapy. *N Engl J Med* 2019; 380(7):629–637. doi:10.1056/NEJMoa1808779

Oh AY, Kacker A. Do electronic cigarettes impart a lower potential disease burden than conventional tobacco cigarettes? Review on e-cigarette vapor versus tobacco smoke. *Laryngoscope* 2014; 124(12):2702–2706. doi:10.1002/lary.24750

Tsoh JY, Chi FY, Mertens JR, and Weisner CM. *Drug Alcohol Depend.* 2011 Apr 1; 114 (2-3): 110-118.

- Cochrane review:“incentives improve smoking cessation rates at long-term follow-up” (Notely, 2019)
- GE employees had higher rates of smoking cessation at 9 or 12 months & at 15 or 18 months when offered financial incentives compared to employees who were not (Volpp, 2009)
- Reward based programs provided higher rates of abstinence over deposit-based programs for smoking cessation (Halpern, 2015)