

Nicotine Addiction and Pharmacological Aids for Tobacco Treatment

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Webinar Objectives

- Describe nicotine addiction
- Identify PHS identified first-line pharmacological aids available for tobacco treatment including dosing guidelines and the pros and cons of each
- Describe strategies of combination pharmacological therapies

What is Nicotine?

- The most common cause of drug addiction in the world
- Naturally occurring in the tobacco plant
- A colorless alkaloid that turns brown when burned
- Nicotine is absorbed through the mucosa, skin, and lungs

Nicotine



- In pure state - clear, oily toxin
- Binds in brain and muscles
- Nicotine poisoning symptoms:
 - Nausea, salivation, abdominal pain, vomiting, sweating, dizziness, mental confusion, rapid heart beat
 - Convulsions, respiratory failure due to paralysis of respiratory muscles



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 (7.3–7.5),
nicotine is readily absorbed.**



Beverages can alter pH, affect absorption



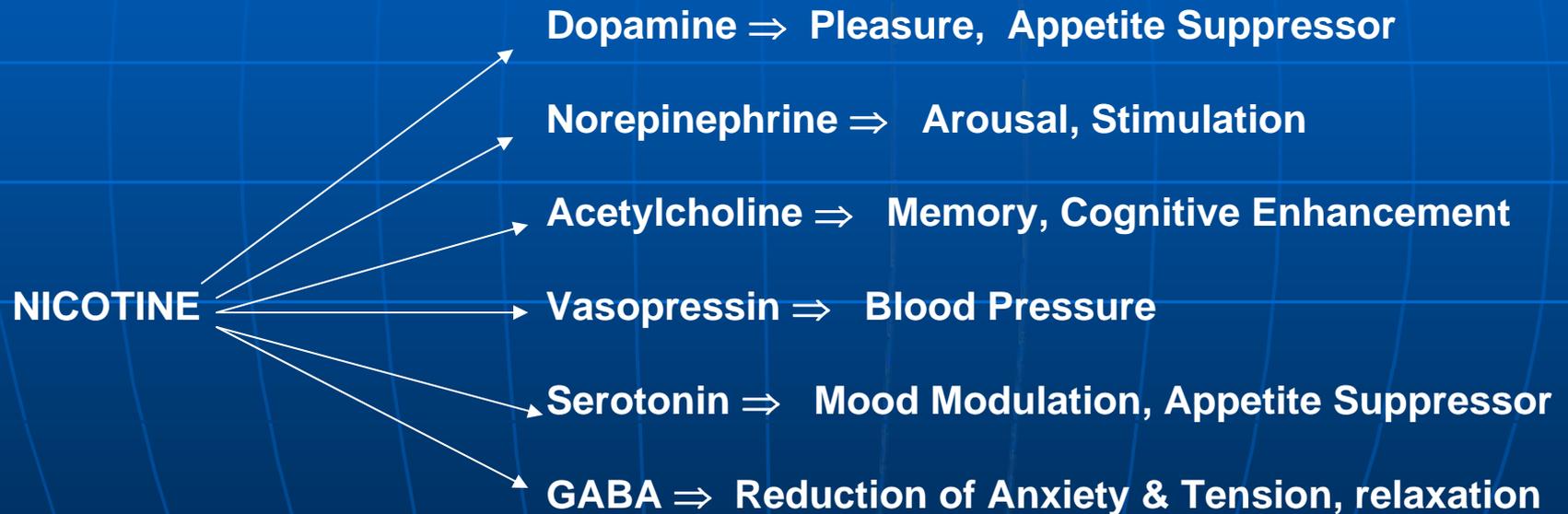
Nicotine Absorption

- Nicotine is “distilled” from burning tobacco and carried in tar droplets
- Nicotine is rapidly absorbed across respiratory epithelium
 - pH of the lung is 7.4
 - Surface area of alveoli is large
 - Capillary system in lung is extensive

Nicotine Metabolism

- Metabolized in liver to cotinine
- Nicotine half-life is 2 hours, cotinine is 20 hours
- Toxic levels 40-60mg
- Some individuals have more rapid metabolisms, leading to more cigarettes smoked per day and potentially earlier addiction as a teenager
- For example: males > females
Caucasian > African American

Effects of Selected Neurotransmitters & Hormones



Benowitz, N. (1999).

BIOLOGY of NICOTINE ADDICTION: ROLE of DOPAMINE

Nicotine
stimulates
dopamine release

Pleasurable feelings

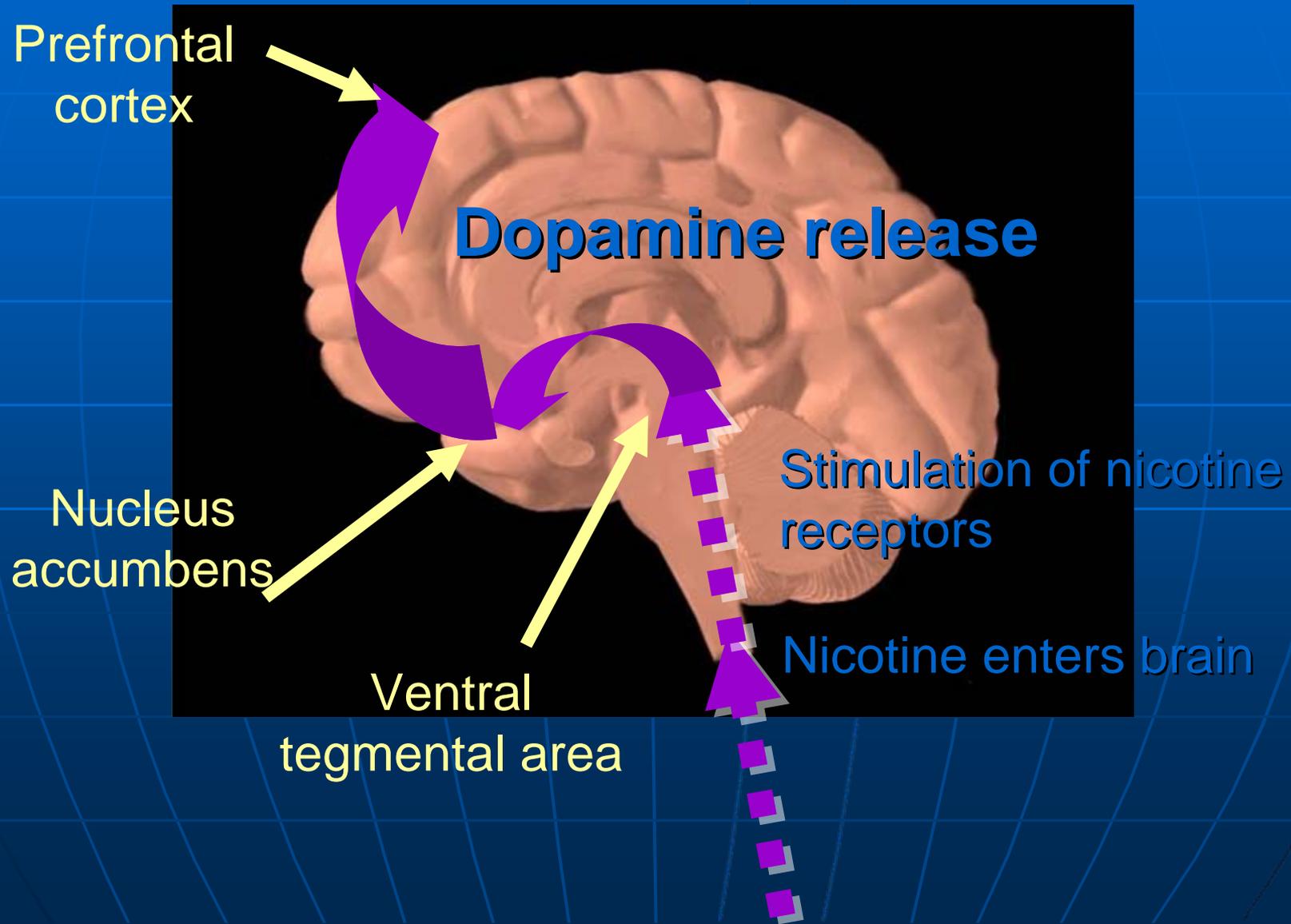
Repeat administration

Tolerance develops

Nicotine addiction
is *not* just a bad habit.

*Discontinuation leads to
withdrawal symptoms.*

Dopamine Reward Pathway



Negative Effects

- Increases both blood level of glucose and insulin production
- Enhances platelet aggregation which can lead to thrombotic events
- Increased risk for cancer of various body organs
- Increases bowel tone and activity, saliva and bronchial secretions, heart rate, blood pressure, and may also increase sweating, nausea, and bouts of diarrhea
- Decreased blood flow especially to extremities and skin

Nicotine Withdraw

- Withdraw begins within 2 hours after the last cigarette peaks at 48-72 hours
- Symptoms of withdraw:
 - Cravings
 - Anxiety
 - Restlessness
 - Irritability
 - Depressed mood
 - Difficulty concentrating
 - Increased appetite
 - Stomach cramps
 - Coughing
 - Constipation
 - Mouth sores



"Smythe put your cubicle together. He just quit smoking, so he's been a little distracted."

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Summary

- Tobacco products are **effective delivery systems** for the drug nicotine
- Nicotine is a **highly addictive drug** that induces a constellation of pharmacologic effects
- Nicotine activates the **dopamine reward pathway** in the brain, which reinforces continued tobacco use
- Tobacco users who are dependent on nicotine **self-regulate tobacco** intake to maintain pleasurable effects and prevent withdrawal

Mini Quiz

1. True or False – Drinking water prior to using a piece of nicotine gum will not effect nicotine absorption?
2. True or False – Exposure to nicotine increase blood sugar level but decreases insulin levels?

Mini Quiz Answers

1. False – Any introduction of something into the mouth starts the digestive process which creates an acidic environment.
2. False – Nicotine increases both blood sugar and insulin production

Nicotine in Tobacco Products

1 cigarette = 1 - 2mg (12 - 14 mg)

1 can spit tobacco = approx. 60 - 80mg

1 average size dip = approx. 3 - 5mg

1.5 ounce stogie = 12 - 24mg the same as a
one pack cigarettes

Some up to 50mg for one cigar



NRT: Rationale for Use

- Reduces physical withdrawal from nicotine
- Allows patient to focus on behavioral and psychological aspects of tobacco cessation

IMPROVES SUCCESS RATES

Best Treatment Practices in Nicotine Addiction

- Use of nicotine replacement therapy and/or bupropion
- Cognitive-behavioral intervention
- High level of motivation
- Implementation of exercise program

Clinical Practice Guidelines: 2000

Treating Tobacco Use and Dependence

- *First-line Medications*
 - Bupropion SR
 - Varenicline
 - Nicotine Replacement
 - Nicotine Gum
 - Nicotine Lozenge
 - Nicotine Inhaler
 - Nicotine Nasal Spray
 - Nicotine Patch
- *Second-line Medications*
 - Clonidine
 - Nortriptyline

Typical Smoking Pattern

*Nicotine level
before bedtime*



NRT: Indicators

- Any one who smokes > 10 cigarettes a day
- Anyone who reports withdrawal symptoms during a previous quit attempt
- Each quit attempt is different; if NRT didn't help before, it's OK to try it again; motivation may have shifted
- All NRTs are better than placebo

Effects of NRT

- Reduces withdrawal symptoms and craving
- Allows patient time to relearn life w/o tobacco
- May provide positive effects of nicotine – desirable mood, improved attention
- Replaces oral/handling aspects of habit
- Can keep patient away from smoking due to fear of smoking and using NRT

NRT: Contraindications

- Post MI
- Uncontrolled arrhythmias
- Severe or worsening angina
- Accelerated or severe hypertension
- Severe PV
- Poorly controlled insulin dependent Diabetes
- Active peptic ulcer
- Renal Insufficiency

NRT: Contraindications

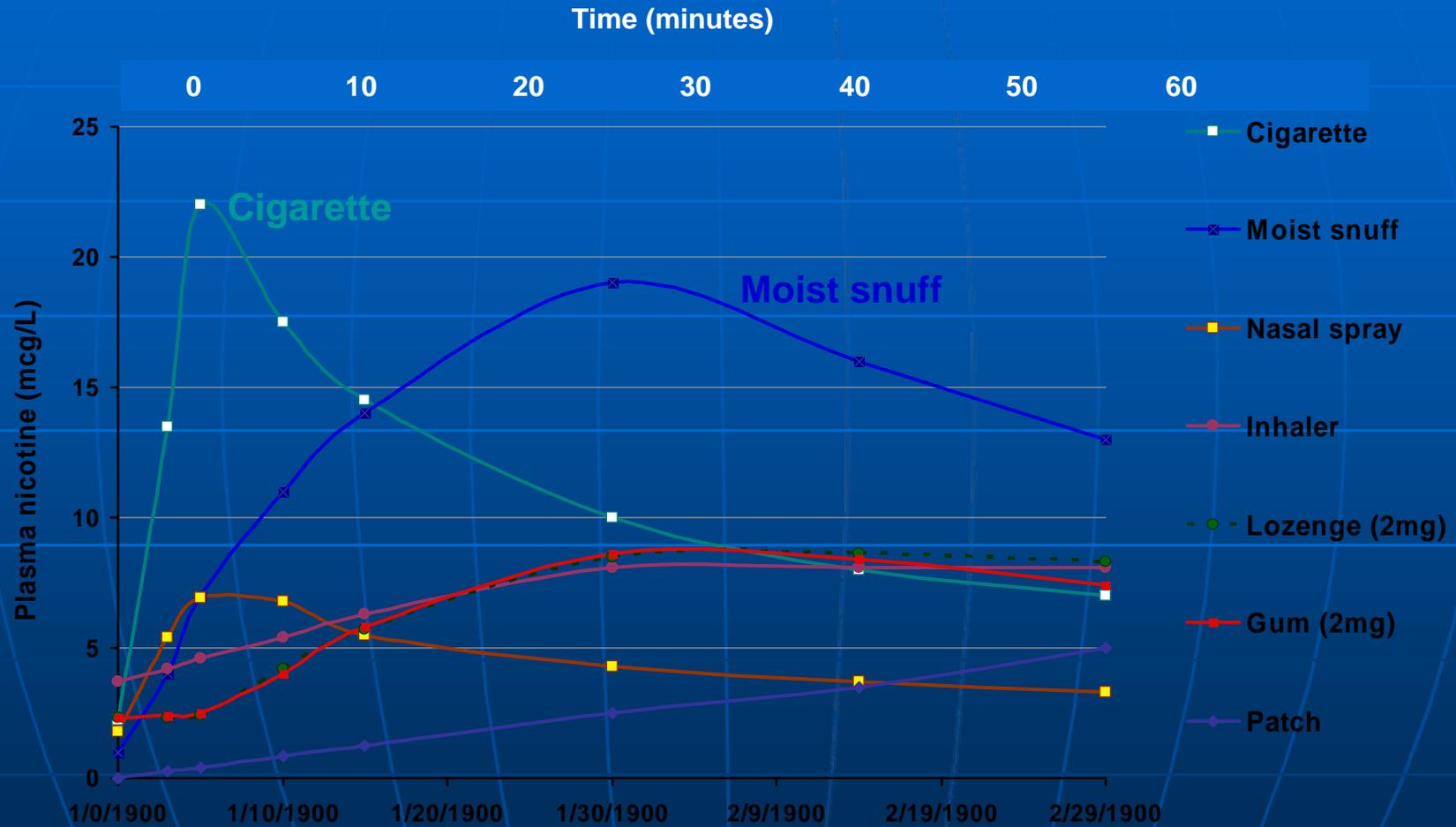
- Hepatic insufficiency
- Uncontrolled Hyperthyroidism
- Pregnancy - Few studies have addressed the safety of NRT, varenicline or bupropion in pregnancy
- Children and adolescents



NRT: PRECAUTIONS

- Patients with underlying cardiovascular disease
 - Recent myocardial infarction
 - Life-threatening arrhythmias
 - Severe or worsening angina
- Patients with other underlying conditions
 - Active temporomandibular joint disease (gum only)
 - Lactation
 - Peptic Ulcer Disease

PLASMA NICOTINE CONCENTRATIONS



Fant et al., 1999; Schneider et al., 2001; Choi et al., 2003).

Nicotine Gum/Lozenge

- Nicotine absorbed in mucosa
- 2mg and 4mg doses
 - Insert recommendations < 24 cigarettes 2mg; >24 cigarettes 4mg
- Each piece is good for 20-30 minutes
- Chew gum until “peppery” taste; “park” between gum and cheek until peppery taste is gone, repeat process

Nicotine Gum/Lozenge

Pros:

- Easily imitate individual's nicotine loading pattern
- Nicotine reaches brain 5-10 minutes
- Can be prescribed on regular schedule and/or PRN use
- Flexibility of use

Nicotine Gum/Lozenge

Cons:

- Not user friendly; must follow instructions
- For gum - Difficult with dental work & gum chewers
- For Lozenge – Chalky build-up in patients with dry mouth
- Makes saliva; GI problems
- Restrictions with eating and drinking
- OTC, expensive
- Difficulties getting off the gum/lozenge

Nicotine Patch

- Six dosages: 21mg, 14mg, 7mg
- Both OTC
- 24 hour doses
- Place on non-hairy area above the waist
- Passive dosing
- Can be used while swimming or showering

Nicotine Patch Delivery



Typical Smoking Pattern

*Nicotine level
before bedtime*



Nicotine Patch

Pros:

- User friendly, just stick and go
- Once a day dosage & different dosages

Cons:

- Steady state dosing
- Passive aid
- \approx 2 hrs to reach therapeutic level
- Skin reactions
- Sleep disturbance if worn at night
- Can cause "dull" pain if applied on "boney" area

Nicotine Spray

- Nicotine absorbed through nasal mucosa
- 1 spray to each nostril after exhale - SHOULD NOT BE INHALED
- Each bottle contains 100 doses (200 sprays)
- Recommend to not be used more than 5 times an hour or 40 times in 24 hours

Nicotine Spray

Pros:

- Fastest absorption (< 5 minutes)
- Rx
- Flexibility

Cons:

- First week difficult; burning eyes, throat, nasal discharge, sneezing
- Poor compliance or problems getting off
- Expensive without insurance

Nicotine Inhaler

- Absorbed in mucosa
- Mouthpiece with 10mg cartridge
- User “sucks” on mouthpiece to deliver nicotine – use like a straw
- Each cartridge good for 80 puffs or 20 minutes
- Minimum use 6 cartridges, maximum 16 cartridges per day

Nicotine Inhaler

Pros:

- Flexible dosing
- Hand to mouth behavior
- Relative quick delivery, 5-10 minutes

Cons:

- Frequent use to achieve adequate dosing
- Throat irritation
- Prescription medication, expensive; not always covered by insurance plans



Bupropion: Mechanism of Action

- Atypical antidepressant thought to affect levels of various brain neurotransmitters
 - Dopamine
 - Norepinephrine
- Clinical effects
 - ↓ craving for cigarettes
 - ↓ symptoms of nicotine withdrawal



bupropion hydrochloride

- Similar effects on brain as nicotine (60% people)
- Rx
- Begin 7-10 days before quit date
- 3-6 days 150mg; 150mg bid
- Contraindications: Seizure disorder, active eating disorder, recent MI, unstable angina, MAOs, abrupt cessation of alcohol or sedatives

bupropion hydrochloride

Pros:

- Easy to use
- Can be used in combination with NRT
- Effective with large number of people
- Covered by most insurance plans
- Cheap without insurance as generic

Cons:

- Most common side effects: Sleep disorder, dry mouth, sense of discomfort

Combination Nicotine Therapy

- Use of a “passive” and “*ad libitum*” NRT product
 - Increases long-term abstinence rates than did use of only one NRT
 - More studies are being completed on combination therapy

Varenicline

- Oral tablet delivery
- Non-nicotine tobacco cessation aid
- Partial agonist/antagonist
 - Increases the brain's response to nicotine
 - Blocks the brain's natural response to nicotine
- Release of dopamine but blocks response to nicotine
 - Lower dose but longer lasting

Varenicline

- Prescription required
- Monotherapy
- Begin treatment 7-10 days before quit date
- Dosing: 0.5 mg daily for three days, then 0.5 mg BID for four days, then 1 mg BID

Varenicline

Pros:

- Easy to use
- Alternative to bupropion and NRT
- Non-nicotine medication – surgery, MI patients, plastics
- Initial research looks promising
- Covered by most insurance plans

Cons:

- Most common side effects: Nausea, insomnia, and unusual dreams
- Expensive without insurance (\$355/3 months)

Varenicline

- FDA Boxed Warning –
All patients being treated with Chantix should be observed for neuropsychiatric symptoms including changes in behavior, hostility, agitation, depressed mood and suicide-related events including ideation, behavior, attempted suicide.

Summary

- Consider pharmacological interventions for all smokers making quit attempts
- Gather history
- Get involved in the process of choosing meds
- Nicotine patch is the recommended first aid – bupropion next
- Use guidelines for dose and tapering
- Consider combination therapy for those who have failed NRT/bupropion alone
- Counseling and pharmacotherapy have additive effects

Questions

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Training Evaluation

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