

Treating Tobacco Use and Dependence: A Focus on the Pharmacotherapy Options



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CME Information and Disclosures



I have no real or perceived vested interests that relate to this presentation nor do I have any relationships with pharmaceutical companies, and/or other corporations whose products or services are related to pertinent therapeutic areas.

Overview

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- Review the pathophysiology of tobacco addiction and the recommended treatment approach
- Review the pharmacotherapy options to assist in the quit process
- Describe how clinicians can ask about tobacco use and advise patients to quit

Clinician-Assisted Tobacco Cessation: Why Bother?

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- Single-most effective strategy to lengthen and improve patients' lives
- Quitting tobacco has immediate and long-term benefits for all patients
- It is inconsistent to provide health care and, at the same time, remain silent (or inactive) about a major health risk.

**TOBACCO CESSATION
is a significant component of PATIENT
CARE.**

Tobacco Addiction

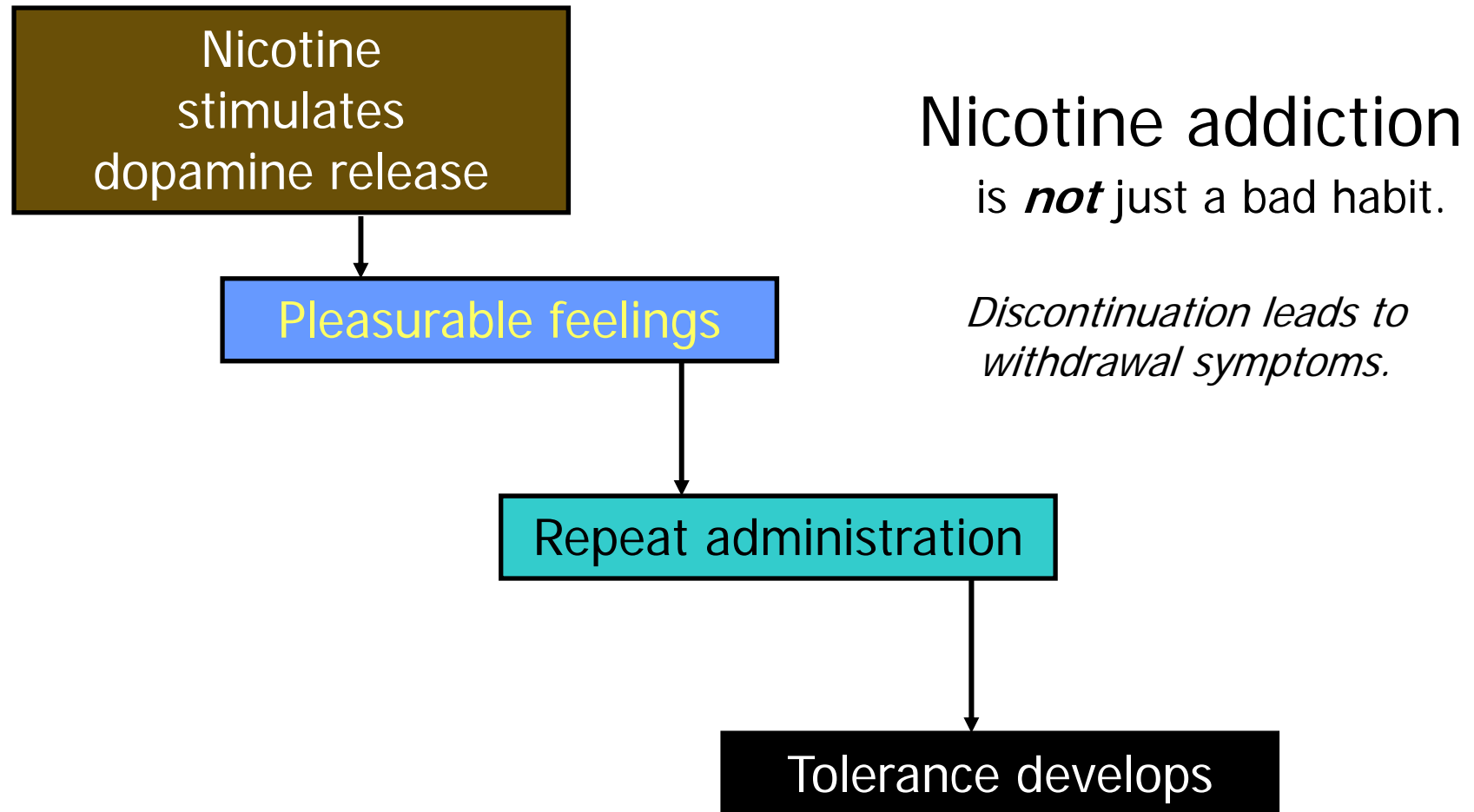
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What is Addiction?

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

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

Biology of Nicotine Addiction: Role of Dopamine



Tobacco Use Behavior



Tobacco Use Behavior

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- Physical addiction
- Habit
- Psychological dependence

Addiction

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- Reinforcer
 - Nicotine reaches the brain within 11 sec
- Withdrawal syndrome
 - Irritability, anxiety, impatience, etc.
- Individuals self-titrate nicotine delivery:
 - Smoking more frequently
 - Smoking more intensely
 - Obstructing vents on low nicotine/cigs



Habit

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- “Automatic smoking”
 - Repeatedly pairing smoking with other situations or behaviors
 - The paired behavior creates unconscious urges to smoke
 - “Pavlovian” response

Psychological Dependence

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- The mistaken belief that cigarettes are doing something positive for the smoker
- The additional belief that this positive impact is something the smoker cannot do on his or her own

Treatment Approach and Pharmacotherapy Options

2000 and 2008 Clinical Practice Guideline Update

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- 2000 Clinical practice guideline
 - Promoted 5 **A's** and 5 **R's**
 - Recommended medications and behavioral changes to assist in the quit process
 - 5 First line agents
- 2008 Clinical practice guideline

5 A's and 5 R's

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- 5 A's
 - Ask
 - Advise
 - Assess
 - Assist
 - Arrange

- 5 R's
 - Relevance
 - Risks
 - Rewards
 - Roadblocks
 - Repetition

2000 and 2008 Clinical Practice Guideline Update

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- 2000 Clinical practice guideline
 - Promoted 5 A's and 5 R's
 - Recommended medications and behavioral changes to assist in the quit process
 - 5 First line agents
- 2008 Clinical practice guideline
 - Reinforced 5A's and 5R's
 - Counseling and the use of medications are more effective than either intervention alone
 - 7 First line agents (Addition of the nicotine lozenge and varenicline)
 - Specific considerations when counseling special populations

2008 Clinical Practice Guideline Update

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- Special populations
 - Pregnant patients
 - Light smokers
 - Adolescents
 - Smokeless tobacco users
- Recommendation:
 - To utilize counseling cessation interventions rather than medications to assist in the quit process

Case # 1

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- JS is a 30 year old Caucasian female who comes to your Clinic for a follow up visit. She is currently 8 weeks pregnant.
- PMH/SH: Significant for Tobacco use (1 ppd x 7 years)
- She reports that she has never tried to quit in the past but is interested in quitting now that she is pregnant. JS has identified 1 week from today as her quit date.

Case # 1

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- What is your recommended treatment approach for JS today?
 - A. Encourage JS to wait until her second trimester to quit
 - B. Discuss behavioral strategies as the primary quit approach
 - C. Initiate Varenicline
 - D. Initiate NRT in addition to behavioral strategies

Targets of Tobacco Cessation

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Environment/Habit

- Coping strategies
- Modifying daily routines
- Social interactions

Psychological

- Healthy alternatives
 - Stress
 - Weight control
 - Pleasure/relaxation

**Tobacco
Use**

Physical Addiction

- Alleviation of withdrawal symptoms
- Use of Medications
- Additional focus on behavioral changes

Tobacco Cessation Treatments

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- **Nicotine Replacement Therapies (NRTs)**

- Nicotine Gum
- Nicotine Patch
- Nicotine Lozenge
- Nicotine Nasal spray
- Nicotine Inhaler

- Bupropion SR
(Zyban®)

- Varenicline
(Chantix®)

Nicotine Replacement Therapies: Mechanism of Action

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- Reduces withdrawal symptoms
- Allows patient to focus on the behavioral and psychological aspects of tobacco use

Nicotine Replacement Therapies: Efficacy

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Nicotine Replacement Therapies	Estimated Abstinence Rate at 6 months vs. Placebo	Estimated Odds Ratio (95% CI)
Nicotine patch	23.4%	1.9 (1.7- 2.2)
Nicotine gum	19%	1.5 (1.2- 1.7)
Nicotine lozenge	23.6- 24.2%	2.0 (1.4- 2.8) 2.8 (1.9- 4.0)
Nicotine inhaler	24.8%	2.1 (1.5- 2.9)
Nicotine spray	26.7%	2.3 (1.7- 3.0)

Source: Fiore MC, Jaén CR, Baker TB, et al. *Treating Tobacco Use and Dependence: 2008 Update*. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. May 2008; www.rxforchange.ucsf.edu

Nicotine Gum

- Resin complex
 - Nicotine
 - Polacrillin
- Sugar-free chewing gum base
- Contains buffering agents to enhance buccal absorption of nicotine
- Available: 2 mg, 4 mg; original, cinnamon, fruit, mint (various), and orange flavors
- Dosing based on the number of cigarettes the patient smokes



Nicotine Gum: Dosing

Recommended Usage Schedule for Nicotine Gum		
Weeks 1–6	Weeks 7–9	Weeks 10–12
1 piece q 1–2 h	1 piece q 2–4 h	1 piece q 4–8 h
DO NOT USE MORE THAN 24 PIECES PER DAY.		

Nicotine Lozenge

- Nicotine polacrilex formulation
 - Delivers ~25% more nicotine than equivalent gum dose
 - Sugar-free mint (various), cappuccino or cherry flavor
 - Contains buffering agents to enhance buccal absorption of nicotine
- Available: 2 mg, 4 mg
- Dosing based on the time to the first cigarette



Nicotine Lozenge: Dosing

Recommended Usage Schedule for Commit Lozenge

Weeks 1–6	Weeks 7–9	Weeks 10–12
1 lozenge q 1–2 h	1 lozenge q 2–4 h	1 lozenge q 4–8 h

DO NOT USE MORE THAN 20 LOZENGES PER DAY.

Nicotine Patch

- Nicotine is well absorbed across the skin
- Delivery to systemic circulation avoids hepatic first-pass metabolism
 - Plasma nicotine levels are lower and fluctuate less than with smoking
- Step-down dosing



Source: www.rxfchange.ucsf.edu; Fiore MC, Jaén CR, Baker TB, et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service; Gore AV, Chien YW. (1998). The nicotine transdermal system. *Clin Dermatol* 16:599–615; Palmer KJ, Buckley MM, Faulds D. (1992). Transdermal nicotine: A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy as an aid to smoking cessation. *Drugs* 44:498–529.

Nicotine Patch: Dosing

Product	Heavy Smoker
NicoDerm CQ	>10 cigarettes/day Step 1 (21 mg x 6 weeks) Step 2 (14 mg x 2 weeks) Step 3 (7 mg x 2 weeks)

Source: www.rxforchange.ucsf.edu; Fiore MC, Jaén CR, Baker TB, et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service; Gore AV, Chien YW. (1998). The nicotine transdermal system. *Clin Dermatol* 16:599–615; Palmer KJ, Buckley MM, Faulds D. (1992). Transdermal nicotine: A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy as an aid to smoking cessation. *Drugs* 44:498–529.

Nicotine Nasal Spray

- 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
- For best results, use about 8 doses/day



Nicotine Nasal Spray: Dosing

- One dose = 1 mg nicotine
(2 sprays, one 0.5 mg spray in **each** nostril)
- Start with 1–2 doses per hour
- For best results, patients should use at least 8 doses daily for the first 6–8 weeks
- Termination:
 - Gradual tapering over an additional 4–6 weeks

Nicotine 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
- Patients should use about 6-8 cartridges/day



Nicotine Inhaler: Dosing

- Start with at least 6 cartridges/day during the first 3-6 weeks of treatment
 - Increase prn to *maximum* of 16 cartridges/day
- Recommended duration of therapy is 3 months
- Gradually reduce daily dosage over the following 6–12 weeks

Case # 2

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- LW is a 64 year old Caucasian male admitted to the hospital secondary to a myocardial infarction.
- PMH: Hyperlipidemia
- SH: Tobacco use (1- 1 ½ ppd x 49 years)
- Meds: Simvastatin 40mg QHS, Daily Multivitamin (Patient reports difficulty remembering to take his medications)
- LW reports:
 - He is interested in quitting utilizing one of the over the counter options (he identifies his quit date as his birthday- 3 ½ weeks from today)
 - He is concerned since his wife is also a smoker

Case # 2

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- What is your recommended pharmacotherapy option for LW today?
 - A. Nicotine patch 21 mg
 - B. Nicotine gum 4 mg
 - C. Nicotine lozenge 4 mg
 - D. Bupropion 150 mg po bid

Tobacco Cessation Treatments

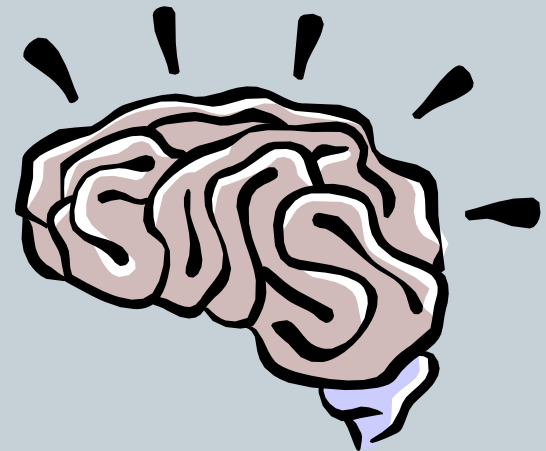
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- Nicotine Replacement Therapies (NRTs)
 - Nicotine Gum
 - Nicotine Patch
 - Nicotine Lozenge
 - Nicotine Nasal spray
 - Nicotine Inhaler
- **Bupropion SR (Zyban®)**
- Varenicline (Chantix®)

Bupropion: Mechanism of Action

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- Atypical antidepressant
 - Dopamine
 - Norepinephrine
- Clinical effects
 - ↓ craving for cigarettes
 - ↓ symptoms of nicotine withdrawal



Bupropion: Efficacy

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Pharmacotherapy	Estimated Abstinence Rate at 6 months vs. Placebo	Estimated Odds Ratio (95% CI)
Bupropion	24.2%	2.0 (1.8- 2.2)

Bupropion: Dosing

❖ Patients should begin therapy 1 to 2 weeks PRIOR to their quit date to ensure therapeutic plasma levels.

Initial treatment

- 150 mg po q AM x 3 days

Then...

- 150 mg po bid
- Duration, 7–12 weeks

Tobacco Cessation Treatments

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- Nicotine Replacement Therapies (NRTs)
 - Nicotine Gum
 - Nicotine Patch
 - Nicotine Lozenge
 - Nicotine Nasal spray
 - Nicotine Inhaler
- Bupropion SR (Zyban®)
- **Varenicline (Chantix®)**

Varenicline: Mechanism of Action

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- Nicotinic receptor partial agonist
 - Stimulates low-level agonist activity
 - Competitively inhibits binding of nicotine
- Clinical effects
 - ↓ craving for cigarettes
 - ↓ symptoms of nicotine withdrawal

Varenicline: Efficacy

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Pharmacotherapy	Estimated Abstinence Rate at 6 months vs. Placebo	Estimated Odds Ratio (95% CI)
Varenicline	33.2%	3.1 (2.5- 3.8)

Varenicline: Dosing

❖ Patients should begin therapy 1 week PRIOR to their quit date while increasing gradually to minimize treatment-related nausea and insomnia.

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



* Up to 12 weeks

Bupropion and Varenicline Warnings

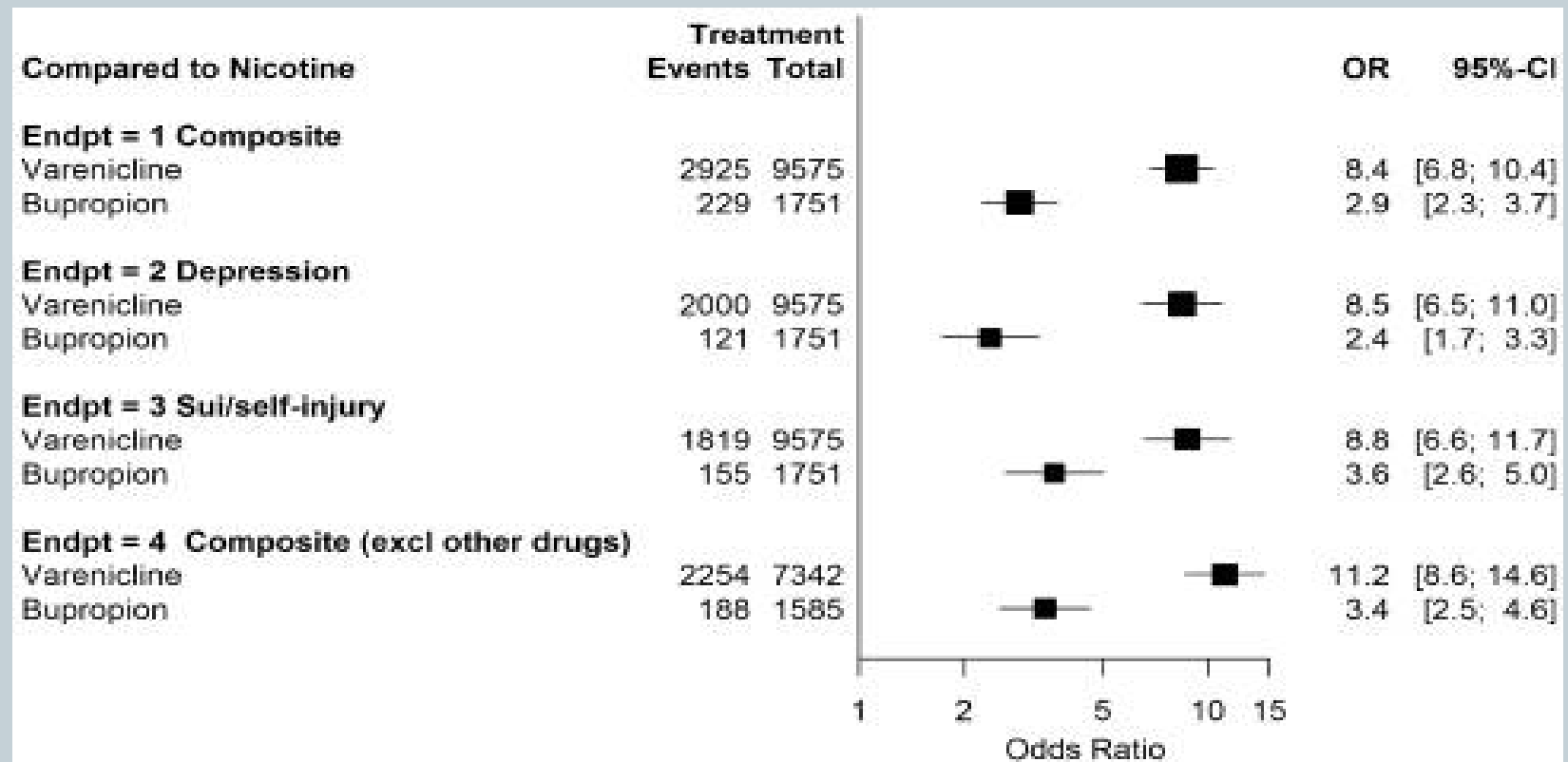
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- Bupropion and Varenicline:
 - FDA is requiring a boxed warning to highlight the risk of serious neuropsychiatric symptoms
 - ✦ Changes in behavior
 - ✦ Hostility
 - ✦ Agitation
 - ✦ Suicidal thoughts and behavior or attempted suicide
 - Assess the risk to benefit
- Varenicline in the news:
 - Singh et. al.
 - Moore et. al.

Source: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm170100.htm>; Singh S, Loke YK, Spangler JG, Furberg CD. Risk of serious adverse cardiovascular events associated with varenicline: a systematic review and meta-analysis. CMAJ. 2011 Sep 6;183(12):1359-66. Moore TJ, Furberg CD, Glenmullen J, Maltzberger JT, Singh S. Suicidal behavior and depression in smoking cessation treatments. PLoS One. 2011;6(11):e27016.

Moore et.al.

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Use of Combination Treatments

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Pharmacotherapy Combinations	Estimated Abstinence Rate at 6 months vs. Placebo	Estimated Odds Ratio (95% CI)
Nicotine patch + gum or nasal spray	36.5%%	3.6 (2.5- 5.2)
Nicotine patch + Bupropion	28.9%	2.5 (1.9- 3.4)
Nicotine patch + Inhaler	25.8%	2.2 (1.3- 3.6)

Case # 3

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- JM is a 59 year old African American male who comes to your office for an annual exam.
- PMH: HTN, Hyperlipidemia
- SH: Tobacco use (1 ½- 2 ppd x 41 years)
- Meds:
 - Norvasc 10 mg once daily
 - Crestor 10 mg once daily
- JM reports:
 - He was recently diagnosed with lung cancer (approximately 5 weeks ago) and reports he is ready to quit now
 - He has tried the nicotine inhaler and the nasal spray during previous quit attempts but “didn’t like using these products” and states he is not interested in trying them again.

Case # 3

48

- What is your recommended pharmacotherapy option for JM today?
 - A. Nicotine patch 21 mg
 - B. Nicotine lozenge 4 mg
 - C. Nicotine patch 21 mg daily + Nicotine gum 4 mg when needed for cravings
 - D. Nicotine patch 21 mg daily + Varenicline 1 mg po twice daily

Case # 4

49

- AB is a 22 year old Hispanic female presents to the Clinic for her annual exam.
- PMH/SH: Significant for Tobacco use (1 ppd x 8 years)
- Meds: Norethindrone (Micronor)
- AB reports:
 - She is interested in quitting but her main concern is gaining weight after she quits.

Case # 4

50

- What is your recommended pharmacotherapy option for AB today?
 - A. Nicotine patch 21 mg
 - B. Nicotine gum 4 mg
 - C. Nicotine nasal spray (Initiate 10 doses daily to start)
 - D. Varenicline 1 mg po bid

How can Clinicians get involved?



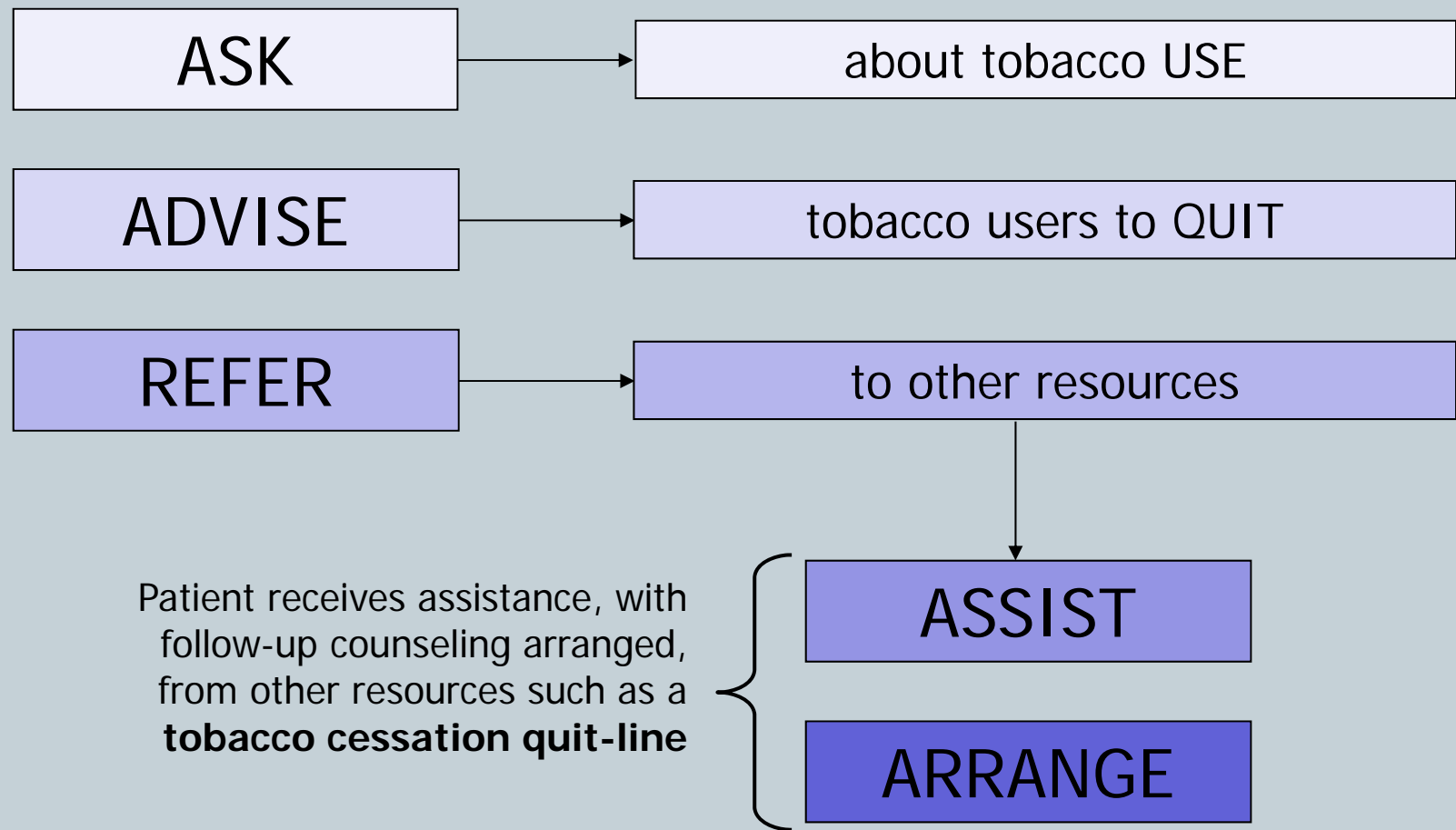
What can you DO?

- If you are unable to lead the smoking cessation visit:
 - Clinicians can play a vital role initiating the quitting process and then referring the patient to available resources.



Brief Counseling: Ask, Advise, Refer

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Make a Commitment...

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- **Address tobacco use** with ALL patients at every visit.
 - Make a commitment to incorporate brief tobacco interventions as part of routine patient care.
- **Ask, Advise, and Refer**

Questions?

