

Up in Smoke! New American Thoracic Society Guidelines for Pharmacologic Treatment in Tobacco-Dependent Adults

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Speaker/Mentor Conflicts of Interest

No conflicts of interest to disclose.



Learning Objectives

By the end of this presentation, pharmacist participants should be able to:

- Describe safe and effective pharmacotherapy options for smoking cessation.
- Explain evidence-based recommendations for initiating pharmacotherapy in tobacco-dependent adults.
- Discuss the safety and efficacy of varenicline and other smoking cessation pharmacotherapy in patients with comorbid psychiatric conditions.



Pre-Presentation Question #1

A 24-year-old patient has smoked 1 ppd for 8 years and smoked their first cigarette after breakfast, about 1.5 hours after waking. They have been using the 14 mg nicotine patch for the last 2 weeks but is having breakthrough cravings. They ask if the nicotine lozenge could help.

What dose should this patient take?

- A. 4 mg
- B. 2 mg
- C. None, this patient does not need short-acting nicotine replacement



Pre-Presentation Question #2

The American Thoracic Society released new guidelines in 2020 for Tobacco-Dependent Adults. They recommend:

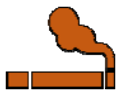
- A. Dual nicotine replacement therapy over varenicline
- B. Varenicline over bupropion
- C. Bupropion over dual nicotine replacement therapy
- D. Nicotine patch over bupropion

Pre-Presentation Question #3

Compared to placebo, what effects did varenicline demonstrate in patients with co-existing psychiatric conditions according to the EAGLES Trial (Anthenelli et al. 2016)?

- A. Significantly greater neuropsychiatric events
- B. Significantly fewer neuropsychiatric events
- C. No statistical difference in neuropsychiatric events

Cigarette Smoking



Leading cause of preventable disease, disability, and death in the US



In 2019, 14.0% of all adults currently smoked cigarettes



Each day, about 1,600 youth try their first cigarette

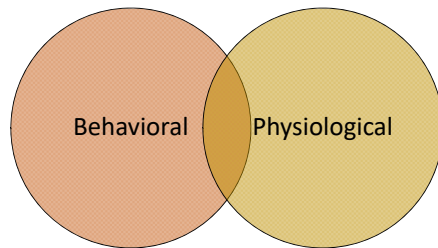


Smokers die 10 years earlier than non-smokers

Smoking Cessation

10% succeed

Disclaimer: Two Sides of Addiction



This presentation will focus on pharmacological aids – but both sides should be addressed when treating patients

Pharmacotherapy Options

Nicotine
patch

Nicotine
gum

Nicotine
lozenge

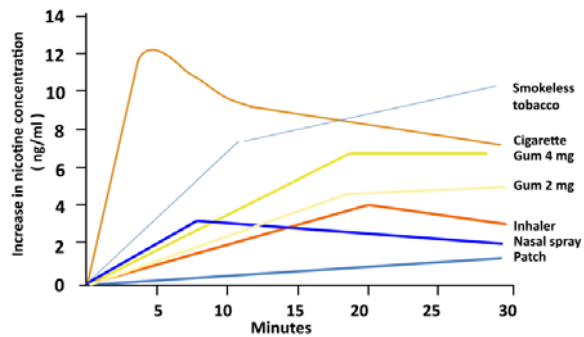
Nicotine
nasal spray

Nicotine
inhaler

Varenicline

Bupropion
SR

Nicotine Replacement Therapy (NRT)



Test Your Knowledge

A 45-year-old woman approaches the pharmacy counter and asks you about nicotine replacement therapy. Her friend quit smoking using the patch and lozenges, and she wants to do the same.

In order to dose the nicotine patch, what information about her smoking history should you ask?

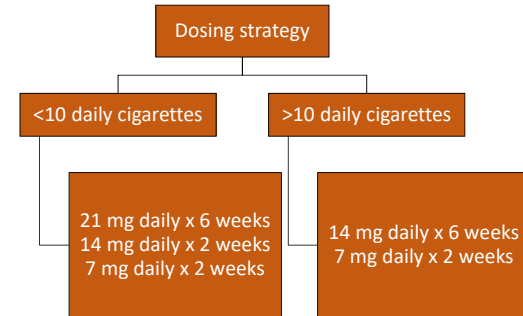
- How many years she has smoked cigarettes
- How many times she has tried to quit in the past
- How many cigarettes she smokes per day
- How long after waking she smokes her 1st cigarette

Patient Case Continued

The patient tells you she has smoked about 1 pack per day for the last 20 years. What daily nicotine patch dose should you recommend for her?

- A. 21 mg
- B. 14 mg
- C. 7 mg

Nicotine Patch

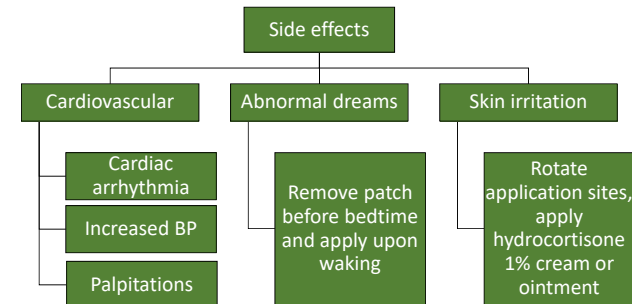


Patient Case Continued

It is about a week and a half later and your patient returns with good news that she has had fewer cravings and has not smoked since starting the patch. However, she has had vivid nightmares nearly every night for about a week. What should she do?

- A. Stop using the patch
- B. Only use the patch when she has cravings
- C. Take off the patch at night
- D. Get through the nightmares

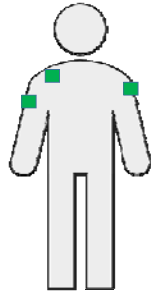
Nicotine Patch



Nicotine Patch Placement

DO:

- Place on dry, hairless area
- Remove previous day's patch before applying new one
- Wash hands after applying



DO NOT:

- Place on open or damaged skin
- Keep in reach of children or pets

Nicotine Patch

Pros

- Once daily dosing
- Delivers nicotine throughout the day

Cons

- Does not address cravings

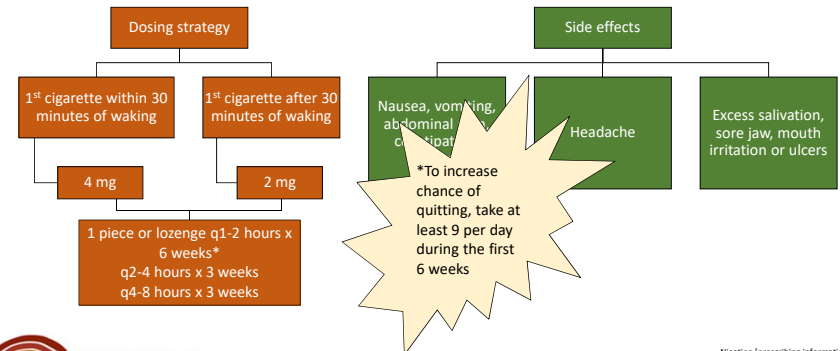
Test Your Knowledge

A 51-year-old patient has been using the 14 mg nicotine patch for the past 2 weeks to help him quit smoking, but he is still having breakthrough cravings. He would like to start using a nicotine lozenge to help.

In order to dose the nicotine lozenge, what information about his smoking history should you ask?

- How many years he has smoked cigarettes
- How many times he has tried to quit in the past
- How many cigarettes he smokes per day
- How long after waking he smokes his 1st cigarette

Nicotine Gum or Lozenge



Nicotine Gum or Lozenge

Gum

“Park” between gum and cheek

Stop when peppery taste appears

Chew slowly

Leave parked until peppery taste fades

Lozenge

Place in mouth and dissolve over 30 minutes.
Do not chew.

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Nicotine [prescribing information Barua 2018]

Nicotine Gum or Lozenge

Pros	Cons
<ul style="list-style-type: none"> Can address cravings/withdrawal 	<ul style="list-style-type: none"> Proper administration required Frequent dosing

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Other Nicotine Forms

Inhaler

- Delivers 4 mg nicotine per cartridge
- May address smoking behavior
- Less effective in cold weather

Nasal Spray

- 0.5 mg per spray
- May cause nasal irritation
- Avoid in chronic nasal disorders

Rx only – can be expensive
Used for cravings
Requires frequent dosing

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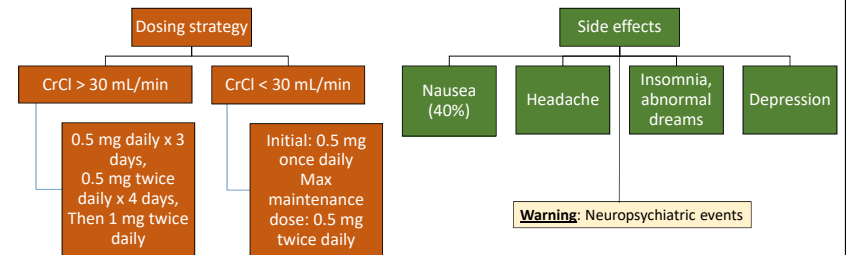
Varenicline

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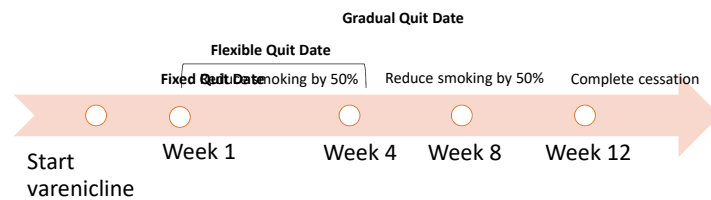
Varenicline Mechanism of Action

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<https://onlinelibrary.wiley.com/doi/10.1111/j.1368-5031.2006.00955.x>

Varenicline




Varenicline Quitting Strategies



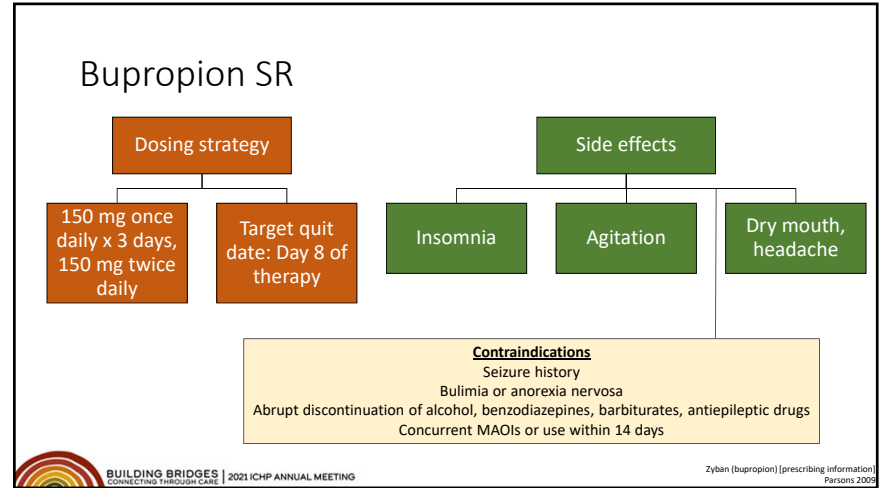
Varenicline

Pros	Cons
<ul style="list-style-type: none"> Twice daily dosing Variable quitting strategies 	<ul style="list-style-type: none"> Neuropsychiatric events

Bupropion SR




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Bupropion SR

Pros	Cons
<ul style="list-style-type: none"> • Can combine with NRT • Consider for patients with concurrent depression • Twice daily dosing 	<ul style="list-style-type: none"> • Many contraindications • Neuropsychiatric events



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How to Choose Pharmacotherapy



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Patient Case

A 43-year-old patient with history of HTN, depression, GAD, and prediabetes is seeking pharmacotherapy to help quit smoking.

What information do you want to know about the patient to help determine the next best step to take?

2020 American Thoracic Society Guidelines

AMERICAN THORACIC SOCIETY DOCUMENTS

Initiating Pharmacologic Treatment in Tobacco-Dependent Adults An Official American Thoracic Society Clinical Practice Guideline

Frank T. Leone*, Yuqing Zhang*, Sarah Evers-Casey, A. Eden Evins, Michelle N. Eakin, Joelle Fathi, Kathleen Fennig, Patricia Folan, Panagis Galiatsatos, Hyma Gogineni, Stephen Kantrow, Hasmeena Kathuria, Thomas Lamphere, Enid Neptune, Manuel C. Pacheco, Smita Pakhale, David Prezant, David P. L. Sachs, Benjamin Toll, Dona Upson, Dan Xiao, Luciane Cruz-Lopes, Izabela Fulone, Rachael L. Murray, Kelly K. O'Brien, Sureka Pavalagantharajah, Stephanie Ross, Yuan Zhang, Meng Zhu, and Harold J. Farber; on behalf of the American Thoracic Society Assembly on Clinical Problems

THIS OFFICIAL CLINICAL PRACTICE GUIDELINE WAS APPROVED BY THE AMERICAN THORACIC SOCIETY MAY 2020

Recommendation 1: Varenicline or Nicotine Patch?

Systematic review including 14 RCTs

7-day point-prevalence abstinence 6-mo follow up

- RR: 1.20 (95% CI, 1.09 to 1.32)
- ARR: 40 more per 1,000 patients (95% CI, 18 more to 65 more)
- High certainty in estimated effects

7-day point-prevalence abstinence during the treatment period

- RR: 1.40 (95% CI, 1.31 to 1.49)
- ARR: 101 more per 1,000 patients (95% CI, 79 more to 124 more)
- High certainty in estimated effects

Fewer serious adverse events than patch
Reduced relapse at the end of 6-mo follow-up
Cost-effectiveness analysis suggest varenicline is cost effective

Recommendation 2: Varenicline or Bupropion SR?

Systematic review including 7 RCTs

7-day point-prevalence abstinence 6-mo follow up

- RR: 1.30 (95% CI, 1.19 to 1.42)
- ARR: 77 more per 1,000 patients (95% CI, 40 more to 108 more)
- High certainty in estimated effects

7-day point-prevalence abstinence during the treatment period

- RR: 1.41 (95% CI, 1.32 to 1.52)
- ARR: 147 more per 1,000 patients (95% CI, 115 more to 187 more)
- High certainty in estimated effects

Reduced risk of serious adverse events, withdrawal symptoms, craving scores
Cost utility and cost effectiveness analysis suggest varenicline over bupropion

Recommendation 3: Varenicline + Nicotine Patch or Varenicline Alone?

3 treatment trials (n=776)

7-day point-prevalence abstinence 6-mo follow up

- RR: 1.36 (95% CI, 1.07 to 1.72)
- ARR: 105 more per 1,000 patients (95% CI, 21 more to 211 more)
- High certainty in estimated effects

7-day point-prevalence abstinence during the treatment period

- RR: 1.31 (95% CI, 1.11 to 1.54)
- ARR: 112 more per 1,000 patients (95% CI, 40 more to 196 more)
- High certainty in estimated effects

Slightly increased serious adverse events (1 more per 1000 patients)

Consider adherence, likelihood of coverage

Patient Case Revisited

43-year-old patient with history of HTN, depression, GAD, and prediabetes seeking pharmacotherapy to help quit smoking.

1.5 packs per day for 25 years

Medications (generally covered by private insurance):

- Lisinopril 30 mg daily
- Atorvastatin 10 mg daily
- Sertraline 100 mg daily

Based on the ATS 2020 Guidelines, what therapy do you recommend?

- Bupropion
- Varenicline monotherapy
- Nicotine patch
- Varenicline + nicotine patch

Therapy Duration

Patient Case - Test Your Knowledge

43-year-old patient with history of HTN, depression, GAD, and prediabetes seeking pharmacotherapy to help quit smoking.

1.5 packs per day for 25 years

Medications (generally covered by private insurance):

- Lisinopril 30 mg daily
- Atorvastatin 10 mg daily
- Sertraline 100 mg daily

How long should therapy last?

- 4 weeks
- 8 weeks
- 12 weeks
- 24 weeks

Therapy Duration



Active treatment should continue for at least 12 weeks



Extended duration (> 12 weeks)

- Increased abstinence at 1 year follow up compared to standard duration
- Varenicline, bupropion, and combination NRT
- 53 more per 1000 patients



Extended duration varenicline cost effective compared to standard duration varenicline

(No cost data for combination NRT or bupropion)

What If the Patient Doesn't Want to Quit Now?

Patient Case

A 34-year-old patient presents for their annual visit

Knowing that this patient has smoked 1 ppd for the last 10 years, you provide smoking cessation counseling.

The patient isn't ready to quit today but wants to quit in the near future.

Is there anything that can be done today to help this patient quit?

- No, the patient should wait until they're ready to quit to start pharmacotherapy
- Yes, start NRT anyway
- Yes, start varenicline anyway
- Yes, start bupropion anyway

Choosing Therapy: Smokers Less Committed to Quitting

Start varenicline before patient is ready to quit
4 RCTs evaluating initiation of tobacco-dependence pharmacotherapy
1 evaluating varenicline initiation


7-day point-prevalence abstinence 6-mo follow up

- RR: 2.00 (95% CI, 1.70 to 2.35)
- ARR: 173 more per 1,000 patients (95% CI, 121 more to 234 more)
- High certainty in estimated effects


Serious adverse effects

- RR: 1.75 (95% CI, 0.98 to 3.13)
- ARR: 12 more per 1,000 patients (95% CI, 0 fewer to 35 more)
- Moderate certainty in estimated effects


Other Considerations



Focus shift from the outcome (cessation) to the mediator (compulsion to smoke)



Cost-effectiveness estimates favor varenicline



Early initiation may increase health equity


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The Remaining Question...

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What About Dual NRT?

Long-acting



+


Short-acting



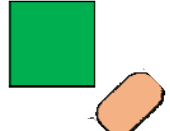
Not mentioned in guidelines
Still effective for smoking cessation

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Varenicline versus Dual NRT



OR



Guideline strengthens confidence in varenicline prescribing
Can recommend either to start according to patient preference

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What About Patients with Co-Existing Psychiatric Conditions (CPC)?

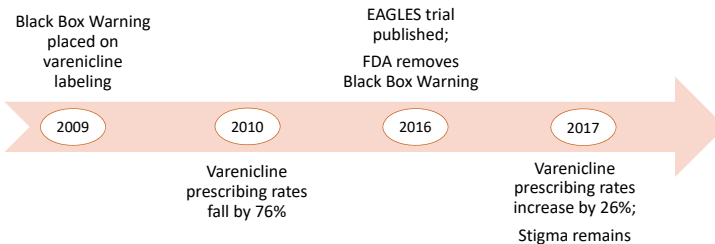
Gauge Your Comfort

39-year-old patient with PMH schizophrenia and HTN taking risperidone 2 mg by mouth twice daily and lisinopril 20 mg by mouth daily. The patient has smoked 2 ppd for the last 20 years and is interested in using varenicline to help quit smoking.

How comfortable would you feel prescribing varenicline for this patient?

- Completely uncomfortable
- Somewhat uncomfortable
- Neither uncomfortable nor comfortable
- Somewhat comfortable
- Completely comfortable

Why Are We Stratifying Those with CPC?



EAGLES Trial

Large (n=8,114), randomized, multicenter, double-blind, triple-dummy, placebo- and active-controlled trial

Safety and efficacy of NRT, varenicline, bupropion in psychiatric versus non-psychiatric patients

Mood disorders

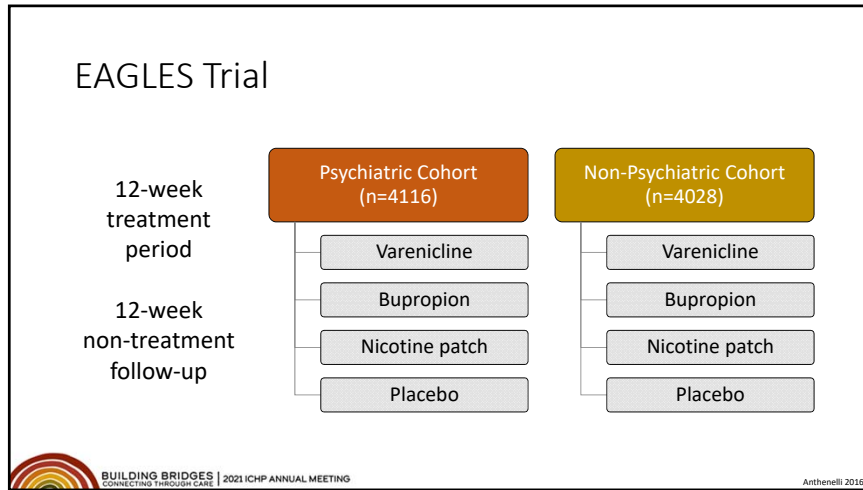
- Major depressive disorder
- Bipolar disorder

Anxiety disorders

- Panic disorder
- PTSD
- OCD
- Social phobia
- Generalized anxiety disorder

Psychotic disorders

- Schizophrenia
- Schizoaffective disorder
- Borderline personality disorder



EAGLES Trial Results

	Non-psychiatric cohort* (n=3984)				Psychiatric cohort* (n=4074)			
	Varenicline (n=990)	Bupropion (n=989)	Nicotine patch (n=1006)	Placebo (n=999)	Varenicline (n=1026)	Bupropion (n=1017)	Nicotine patch (n=1016)	Placebo (n=1015)
Primary composite neuropsychiatric endpoint	13 (1.3%)	22 (2.2%)	25 (2.5%)	24 (2.4%)	67 (6.5%)	68 (6.7%)	53 (5.2%)†	50 (4.9%)
Estimated primary composite neuropsychiatric adverse events (% [95% CI])	1.25% (0.60 to 1.90)	2.44% (1.52 to 3.36)	2.31% (1.37 to 3.25)	2.52% (1.58 to 3.46)	6.42% (4.91 to 7.93)	6.62% (5.09 to 8.15)	5.20% (3.84 to 6.56)	4.83% (3.51 to 6.16)
Difference in risk of composite primary endpoint (RD% [95% CI])								
Versus placebo	-1.28 (-2.40 to -0.15)	-0.08 (-1.37 to 1.21)	-0.21 (-1.54 to 1.12)	-	1.59 (-0.42 to 3.59)	1.78 (-0.24 to 3.81)	0.37 (-1.53 to 2.26)	-
Versus nicotine patch	-1.07 (-2.21 to 0.08)	0.13 (-1.19 to 1.45)	-	-	1.22 (-0.81 to 3.25)	1.42 (-0.63 to 3.46)	-	-
Versus bupropion	-1.19 (-2.30 to -0.09)	-	-	-	-0.20 (-2.34 to 1.95)	-	-	-

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EAGLES Trial

No statistical differences in neuropsychiatric adverse events in patients receiving any active treatment in comparison to placebo

All active treatments more effective than placebo

Varenicline more effective than bupropion or nicotine patch

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CPCs: Optimal controller for those without CPC or nicotine patch?

2 RCTs (n=2,194) comparing varenicline to nicotine patch

7-day point-prevalence abstinence 6-mo follow up	7-day point-prevalence abstinence during the treatment period
<ul style="list-style-type: none"> RR: 1.31 (95% CI, 1.12 to 1.53) ARR: 36 more per 1,000 patients (95% CI, 14 more to 62 more) High certainty in estimated effects 	<ul style="list-style-type: none"> RR: 1.78 (95% CI, 0.78 to 4.08) ARR: 108 more per 1,000 patients (95% CI, 31 fewer to 196 more) Moderate certainty in estimated effects

Use standard dosing of varenicline, bupropion, and NRT
Monitor patient especially within first 2 weeks of quitting

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Summary

- Smoking is the leading cause of preventable death in the US
- Varenicline is recommended over nicotine patch alone or bupropion
- Consider extending the duration of smoking cessation pharmacotherapy to reduce relapse
- Consider starting pharmacotherapy in patients less committed to quitting
- Varenicline may be safely used in patients with co-existing psychiatric conditions

Post-Presentation Question #1

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Compared to placebo, what effects did varenicline demonstrate in patients with co-existing psychiatric conditions according to the EAGLES Trial (Anthenelli et al. 2016)?

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- B. Significantly fewer neuropsychiatric events
- C. No statistical difference in neuropsychiatric events

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Thank You! Questions?

