Medication Management to Aid in Smoking Cessation

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Learning Objectives:

• Review the prevalence of tobacco use.
• Describe tools and resources to assist with smoking cessation.
• Discuss pharmacotherapy used for smoking cessation and recognize clinical pearls for each agent.
• Assess patient cases to determine appropriate treatment options.
Disclosure Statement

• I have no actual or potential conflict of interest in relationship to this presentation
Why is smoking cessation important?

- Tobacco smoking adversely affects all phases of the atherothrombotic disease process which culminates in acute cardiovascular events:
  - Endothelial dysfunction
  - Plaque development and destabilization
  - Imbalances of antithrombotic and prothrombotic factors
Epidemiology

• 14.1% of Americans which equates to over 30 million people, smoked in 2017
• 7 out of 10 smokers reported they wanted to quit in 2015
• 5 out of 10 smokers reported attempting to quit smoking in 2015
• Nearly 1/3 of US deaths attributed to cigarette smoking are due to cardiovascular disease
• Tobacco use is a major risk factor for cardiovascular morbidity and mortality and is the leading preventable cause of death worldwide
• Tobacco use is the leading preventable cause of morbidity and mortality worldwide, responsible for over 6 million deaths annually
Tools to assist with smoking cessation:

**The 5 A’s to Quit Tobacco**

- **Ask** _____ to quit at every visit.
- **Advise** _____ to quit tobacco at every visit.
- **Assess** _____ willingness to quit at every visit.
- **Assist** _____ quitting within 2 weeks with pharmacotherapy or counseling.
- **Arrange** _____ follow-up contact in 1st week after quitting.

**The 5 R’s to the Patient Unwilling to Quit Tobacco**

- **Relevance** _____ why quitting is important to them.
  (second hand exposure, overall health, etc.)
- **Risks** _____ negative consequences of ongoing habit.
- **Rewards** _____ benefits of tobacco cessation.
- **Roadblocks** ____ identify impediments to quitting.
  (withdrawal symptoms, fear, weight gain)
- **Repetition** _____ repeat every time the patient comes to the clinic.
Pathway for tobacco cessation treatment
Algorithm for patients not ready to quit at this present time

Current smoker not ready to quit now

Treatments
- Motivational interviewing (risks, rewards, roadblocks)
- Prescribe and/or offer free medication samples of stop smoking medications and encourage to reduce quantity smoked
- Discuss the use of non-combustible tobacco product if not interested in using stop smoking medications
- Advise patient to adopt smoke-free home and car policy

Follow-up
Reassess+ with patients within 1 month

If ready to quit, refer/connect to stop smoking treatments
If not ready to quit, repeat provision of treatment

+ Reassess by connecting with the patient within ~ 1 month through the following: face-to-face contact during an office visit, sending MyChart query, e-mail or text message, or calling the patient on the phone.
Former smoker treatment algorithm according to risk

Former smoker

Assess risk of relapse based upon time since last smoked

<table>
<thead>
<tr>
<th>Highest risk (no smoking for less than 1 month)</th>
<th>Moderately high risk (no smoking for at least 1 month to 6 months)</th>
<th>Lower risk (no smoking for 6 months or longer)</th>
</tr>
</thead>
</table>
| Treatment options
  - Ask about smoking status on follow-up visits
  - Start and/or intensify pharmacotherapy to address nicotine withdrawal
  - Connect patients to behavioral/psychosocial treatment program
  - Monthly follow-up contact* with referral to treatment if relapsed |
| Treatment options
  - Ask about smoking status on follow-up visits
  - Continue/adjust pharmacotherapy as needed
  - Monthly follow-up contact* with referral to treatment if relapsed |
| Treatment options
  - Ask about smoking status on follow-up visits
  - Offer treatment if requested |

Assess all former smokers for SHS exposure and advise adopting smoke-free policy for home and car

Routine follow-up
  - 6-month and 12-month
  - Referral to treatment if relapsed

* Assesses by connecting with the patient within ~1 month via either a face-to-face contact during an office visit, or by sending MyChart query, e-mail or text message, or calling the patient on the phone.
Outpatient Services: Simplified Workflow and Quality Measures

TABLE 7
National Quality Forum Tobacco Treatment Outpatient Quality Measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part A</td>
<td>Percentage of patients age 18 years and older who were screened for tobacco use 1 or more times within 24 months AND who received tobacco cessation intervention if identified as a tobacco user.</td>
</tr>
<tr>
<td>Part B</td>
<td>Percentage of patients age 18 years and older who were screened for tobacco use and identified as a tobacco user who received tobacco cessation intervention.</td>
</tr>
<tr>
<td>Part C</td>
<td>Percentage of patients age 18 years and older who were screened for tobacco use 1 or more times within 24 months AND who received tobacco cessation intervention if identified as a tobacco user.</td>
</tr>
</tbody>
</table>
Among hospitalized smokers, starting smoking cessation counseling in the hospital and continuing it for at least 1 month after discharge increases long-term quit rates by 37%.
Resources

• Local:
  – Smoking cessation clinic at Baptist Health Corbin
    • Call: 606-526-4647

• National:
  – 1-800-QUIT-NOW
  – BeTobaccoFree.gov
  – Smokefree.gov
  – Women.smokefree.gov
  – Becomeanex.org
Smoking cessation pharmacotherapy agents

- Pharmacotherapy acts synergistically with behavioral counseling to increase quit rates and should be encouraged for virtually all daily smokers and considered on a case-by-case basis for non-daily smokers.

- Meta-analyses and a recent large randomized controlled trial indicate that each of these medications is more effective than placebo in promoting smoking cessation for ≥ 6 months and is safe for use in patients with CVD.
FDA approved medications

Nicotine replacement therapies (NRT)
• Nicotine patch: OTC or Rx
• Nicotine lozenge: OTC or Rx
• Nicotine gum: OTC or Rx
• Nicotine inhaler: Rx only

Bupropion SR (Wellbutrin SR) • Rx only

Varenicline (Chantix) • Rx only
# NRT Overview

<table>
<thead>
<tr>
<th>Gum</th>
<th>Lozenge</th>
<th>Transdermal Patch</th>
<th>Nasal Spray</th>
<th>Oral Inhaler</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Nicorette</em>¹, ZONNIC², Generic OTC 2 mg, 4 mg original, cinnamon, fruit, mint</td>
<td><em>Nicorette Lozenge</em>,¹ 2 mg, 4 mg; cherry, mint</td>
<td><em>NicoDerm CQ</em>, Generic OTC (NicoDerm CQ, generic) 7 mg, 14 mg, 21 mg (24-hr release)</td>
<td><em>Nicotrol NS</em>³ Rx Metered spray 10 mg/mL aqueous solution</td>
<td><em>Nicotrol Inhaler</em>³ 10 mg cartridge delivers 4 mg inhaled vapor</td>
</tr>
</tbody>
</table>

## Dosing

<table>
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<tr>
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<tbody>
<tr>
<td>1st cigarette ≤30 minutes after waking: 4 mg 1st cigarette &gt;30 minutes after waking: 2 mg</td>
<td>1st cigarette ≤30 minutes after waking: 4 mg 1st cigarette &gt;30 minutes after waking: 2 mg</td>
<td>&gt;10 cigarettes/day: 21 mg/day x 4–6 weeks 14 mg/day x 2 weeks 7 mg/day x 2 weeks</td>
<td>1–2 doses/hour (8–40 doses/day) One dose = 2 sprays (one in each nostril); each spray delivers 0.5 mg of nicotine to the nasal mucosa</td>
<td>6–16 cartridges/day Individualize dosing; initially use 1 cartridge q 1–2 hours</td>
</tr>
</tbody>
</table>

- Maximum, 24 pieces/day
- Chew each piece slowly
- Park between cheek and gum when peppery or tingling sensation appears (~15–30 chews)
- Resume chewing when tingle fades
- Repeat chew/park steps until most of the nicotine is gone (tingle does not return; generally 30 min)
- Park in different areas of mouth
- No food or beverages 15 minutes before or during use
- Duration: up to 12 weeks

- Maximum, 20 lozenges/day
- Allow to dissolve slowly (20–30 minutes for standard; 10 minutes for mini)
- Nicotine release may cause a warm, tingling sensation
- Do not chew or swallow
- Occasionally rotate to different areas of the mouth
- No food or beverages 15 minutes before or during use
- Duration: up to 12 weeks

- Rotate patch application site daily; do not apply a new patch to the same skin site for at least one week
- May wear patch for 16 hours if patient experiences sleep disturbances (remove at bedtime)
- Duration: 8–10 weeks

- Maximum – 5 doses/hour or 40 doses/day
- For best results, initially use at least 8 doses/day
- Do not sniff, swallow, or inhale through the nose as the spray is being administered
- Duration: 3–6 months

- Nicotine in cartridge is depleted after 20 minutes of active puffing
- Inhale into back of throat or puff in short breaths
- Do NOT inhale into the lungs (like a cigarette) but “puff” as if lighting a pipe
- Open cartridge retains potency for 24 hours
- No food or beverages 15 minutes before or during use
- Duration: 3–6 months
## NRT Overview:

<table>
<thead>
<tr>
<th>GUM</th>
<th>LOZENGE</th>
<th>TRANSDERMAL PATCH</th>
<th>NASAL SPRAY</th>
<th>ORAL INHALER</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Mouth/jaw soreness</td>
<td>- Mouth irritation</td>
<td>- Local skin reactions (erythema, pruritus, burning)</td>
<td>- Nasal and/or throat irritation (hot, peppery, or burning sensation)</td>
<td>- Mouth and/or throat irritation</td>
</tr>
<tr>
<td>- Hiccups</td>
<td>- Nausea</td>
<td>- Headache</td>
<td>- Rhinitis</td>
<td>- Cough</td>
</tr>
<tr>
<td>- Dyspepsia</td>
<td>- Hiccups</td>
<td>- Sleep disturbances (insomnia, abnormal/vivid dreams); associated with nocturnal nicotine absorption</td>
<td>- Tearing</td>
<td>- Headache</td>
</tr>
<tr>
<td>- Hypersalivation</td>
<td>- Heartburn</td>
<td></td>
<td>- Sneezing</td>
<td>- Rhinitis</td>
</tr>
<tr>
<td>- Effects associated with incorrect chewing technique:</td>
<td>- Headache</td>
<td></td>
<td>- Cough</td>
<td>- Dyspepsia</td>
</tr>
<tr>
<td>- Lightheadedness</td>
<td>- Sore throat</td>
<td></td>
<td></td>
<td>- Hiccups</td>
</tr>
<tr>
<td>- Nausea/vomiting</td>
<td>- Dizziness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Throat and mouth irritation</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

### Adverse Effects

- Recent (≤ 2 weeks) myocardial infarction
- Serious underlying arrhythmias
- Serious or worsening angina pectoris
- Temporomandibular joint disease
- Pregnancy and breastfeeding
- Adolescents (<18 years)

### Precautions

- Recent (≤ 2 weeks) myocardial infarction
- Serious underlying arrhythmias
- Serious or worsening angina pectoris
- Pregnancy (Rx formulations, category D) and breastfeeding
- Adolescents (<18 years)
Nicotine Gum Advantages

- Might serve as an oral substitute for tobacco
- Might delay weight gain
- Can be titrated to manage withdrawal symptoms
- Can be used in combination with other agents to manage situational urges
- Relieve withdrawal symptoms more quickly than the patch and provide some satisfaction associated with smoking
Nicotine Gum Disadvantages

• Need for frequent dosing can compromise adherence
• Might be problematic for patients with significant dental work
• Proper chewing technique is necessary for effectiveness and to minimize adverse effects
• Gum chewing might not be acceptable or desirable for some patients
• Need to avoid drinking acidic drinks such as orange juice, coffee, beer, and soda 15 minutes prior and while chewing nicotine gum
Lozenge Advantages:

• Might serve as an oral substitute for tobacco
• Might delay weight gain
• Can be titrated to manage withdrawal symptoms
• Can be used in combination with other agents to manage situational urges
• Relieve withdrawal symptoms more quickly than the patch and provide some satisfaction associated with smoking
Lozenge Disadvantages

• Need for frequent dosing can compromise adherence
• Gastrointestinal side effects (nausea, hiccups, heartburn) might be bothersome
• Need to avoid drinking acidic drinks such as orange juice, coffee, beer, and soda 10 minutes prior and while using the lozenges
Transdermal Patch Advantages

• Once-daily dosing associated with fewer adherence problems
• Of all NRT products, its use is least obvious to others
• Can be used in combination with other agents; delivers consistent nicotine levels over 24 hours
Transdermal Patch Disadvantages

• When used as monotherapy, cannot be titrated to acutely manage withdrawal symptoms
• Not recommended for use by patients with dermatologic conditions (e.g. psoriasis, eczema, atopic dermatitis)
Nasal Spray Advantages

• Can be titrated to rapidly manage withdrawal symptoms
• Can be used in combination with other agents to manage situational urges
• Relieve withdrawal symptoms more quickly than the patch and provide some satisfaction associated with smoking
Nasal Spray Disadvantages

• Need for frequent dosing can compromise adherence
• Nasal administration might not be acceptable or desirable for some patients; nasal irritation often problematic
• Not recommended for used by patients with chronic nasal disorders or severe reactive airway disease
Oral Inhaler Advantages

• Might serve as an oral substitute for tobacco
• Can be titrated to manage withdrawal symptoms
• Mimics hand-to-mouth ritual of smoking
• Can be used in combination with other agents to manage situational urges
• Relieve withdrawal symptoms more quickly than the patch and provide some satisfaction associated with smoking
Oral Inhaler Disadvantages

• Need for frequent dosing can compromise adherence
• Cost of treatment
• Cartridges might be less effective in cold environments (≤ 60°F)
Preference of NRT

• Similar efficacy exists between agents

• Compliance ranked: patch >>> gum = lozenge > inhaler = spray

• Combination of the nicotine patch with a more rapidly absorbed NRT is more effective than using a single product
## Bupropion SR Overview

### PRODUCT
- **Bupropion SR**
  - Zyban®, Generic Rx
  - 150 mg sustained-release tablet

### DOSING
- 150 mg po q AM x 3 days, then 150 mg po bid
  - Do not exceed 300 mg/day
  - Begin therapy 1–2 weeks prior to quit date
  - Allow at least 8 hours between doses
  - Avoid bedtime dosing to minimize insomnia
  - Dose tapering is not necessary
  - Duration: 7–12 weeks, with maintenance up to 6 months in selected patients

### ADVERSE EFFECTS
- Insomnia
- Dry mouth
- Nervousness/difficulty concentrating
- Nausea
- Dizziness
- Constipation
- Rash
- Seizures (risk is 0.1%)
- Neuropsychiatric symptoms (rare; see PRECAUTIONS)

### PRECAUTIONS
- Concomitant therapy with medications/conditions known to lower the seizure threshold
- Hepatic impairment
- Pregnancy (category C) and breastfeeding
- Adolescents (<18 years)
- Treatment-emergent neuropsychiatric symptoms¹: BOXED WARNING REMOVED 12/2016

**Contraindications:**
- Seizure disorder
- Concomitant bupropion (e.g., Wellbutrin) therapy
- Current or prior diagnosis of bulimia or anorexia nervosa
- Simultaneous abrupt discontinuation of alcohol or sedatives/benzodiazepines
- MAO inhibitors in preceding 14 days; concurrent use of reversible MAO inhibitors
Bupropion SR Mechanism of Action

• Stimulates some of nicotine’s effects on the brain by blocking neuronal uptake of dopamine and to a lesser extent, norepinephrine
Bupropion SR Advantages

- Twice-daily oral dosing is simple and associated with fewer adherence problems
- Might delay weight gain
- Might be beneficial in patients with depression
- Can be used in combination with NRT agents
- May be beneficial in patients with CVD
Bupropion SR Disadvantages

- Seizure risk is increased
- No benefit seen in smokers who are hospitalized
- Several contraindications and precautions preclude use in some patients
  - **Precautions:** Concomitant therapy with medications/conditions known to lower the seizure threshold
  - **Contraindications:** Seizure disorder, concomitant bupropion (Wellbutrin) therapy, current or prior diagnosis of bulimia or anorexia nervosa, simultaneous abrupt discontinuation of alcohol or sedatives/benzodiazepines, MAO inhibitors in preceding 14 days/concurrent use of reversible MAO inhibitors
- Patients should be monitored for potential neuropsychiatric symptoms
  - Clinicians should advise patients to stop taking bupropion SR and contact a health care provider immediately if they experience agitation, depressed mood, or any changes in behavior that are not typical of nicotine withdrawal, or if they experience suicidal thoughts or behavior. If treatment is stopped due to neuropsychiatric symptoms, patients should be monitored until the symptoms resolve.
Bupropion SR Role in Smoking Cessation

• Combination therapy with bupropion SR and nicotine patch is more effective than either alone

• Bupropion SR plus Chantix showed significantly enhanced quit rates at both 12 and 26 weeks, but not at 52 weeks.
Varenicline Overview

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>VARENICLINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chantix®</td>
<td>Rx</td>
</tr>
<tr>
<td>0.5 mg, 1 mg tablet</td>
<td></td>
</tr>
</tbody>
</table>

**Dosage**
- Days 1–3: 0.5 mg po q AM
- Days 4–7: 0.5 mg po bid
- Weeks 2–12: 1 mg po bid

- Begin therapy 1 week prior to quit date
- Take dose after eating and with a full glass of water
- Dose tapering is not necessary
- Dosing adjustment is necessary for patients with severe renal impairment
- Duration: 12 weeks; an additional 12-week course may be used in selected patients
- May initiate up to 35 days before target quit date OR may reduce smoking over a 12-week period of treatment prior to quitting and continue treatment for an additional 12 weeks

**Adverse Effects**
- Nausea
- Sleep disturbances (insomnia, abnormal/vivid dreams)
- Constipation
- Flatulence
- Vomiting
- Neuropsychiatric symptoms (rare; see PRECAUTIONS)

**Precautions**
- Severe renal impairment (dosage adjustment is necessary)
- Pregnancy (category C) and breastfeeding
- Adolescents (<18 years)
- Treatment-emergent neuropsychiatric symptoms

*Boxed Warning Removed 12/2018*
Varenicline Mechanism of Action

• A partial agonist at the α4β2 nicotinic cholinergic receptor that mediates brain dopamine release
Varenicline Advantages

• Twice-daily oral dosing is simple and associated with fewer adherence problems
• Offers a different mechanism of action for patients who have failed other agents
Varenicline Disadvantages

• Cost of treatment
• Patients should be monitored for potential neuropsychiatric symptoms
  – Clinicians should advise patients to stop taking varenicline and contact a health care provider immediately if they experience agitation, depressed mood, or any changes in behavior that are not typical of nicotine withdrawal, or if they experience suicidal thoughts or behavior. If treatment is stopped due to neuropsychiatric symptoms, patients should be monitored until the symptoms resolve.
Varenicline Role in Smoking Cessation

- Varenicline is proven to be more effective in promoting smoking cessation than single NRT or bupropion SR.

- Meta-analyses suggest varenicline and combination NRT are similarly efficacious alone and are 1st line treatment options in patients with CVD.

- Combination of NRT and Varenicline is utilized only after unsuccessful attempts with each agent alone.
Other non-FDA approved smoking cessation agents

Nortriptyline

Clonidine
Summary of Recommended Pharmacotherapy for Smoking Cessation in Patients with CVD

<table>
<thead>
<tr>
<th></th>
<th>Outpatient With Stable CVD</th>
<th>Inpatient With ACS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st line</td>
<td>Varenicline OR combination NRT*</td>
<td>In-hospital to relieve nicotine withdrawal: Nicotine patch OR combination NRT* At discharge: Combination NRT or varenicline†</td>
</tr>
<tr>
<td>2nd line</td>
<td>Bupropion OR single NRT product</td>
<td>At discharge: Single NRT product</td>
</tr>
<tr>
<td>3rd line</td>
<td>Nortriptyline‡</td>
<td>Bupropion§</td>
</tr>
</tbody>
</table>

If single agent is insufficient to achieve abstinence
Combine categories of FDA-approved drugs:
- Varenicline + NRT (single agent)
- Varenicline + bupropion
- Bupropion + NRT (single agent)

n/a
# Summary of when to avoid smoking cessation agents

<table>
<thead>
<tr>
<th>Conditions</th>
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</thead>
<tbody>
<tr>
<td>History of seizure disorder</td>
</tr>
<tr>
<td>History of mental illness</td>
</tr>
<tr>
<td>History of eating disorder</td>
</tr>
<tr>
<td>Use of MAO inhibitor within 14 days</td>
</tr>
<tr>
<td>Serious cardiac arrhythmias, recent history of MI (within 14 days), serious cardiac arrhythmias or severe or unstable angina</td>
</tr>
<tr>
<td>Abrupt discontinuation of alcohol, benzodiazepine, barbiturates or antiepileptic drugs</td>
</tr>
<tr>
<td>Severe renal impairment</td>
</tr>
<tr>
<td>Moderate renal impairment</td>
</tr>
<tr>
<td>Moderate to severe hepatic impairment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Agents To Avoid</th>
<th>Bupropion SR</th>
<th>Varenicline</th>
<th>Nicotine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
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</tbody>
</table>
## Summary slide of relative cost of each agent

<table>
<thead>
<tr>
<th>Agent</th>
<th>Gum</th>
<th>Lozenge</th>
<th>Transdermal patch</th>
<th>Nasal spray</th>
<th>Oral inhaler</th>
<th>Bupropion SR</th>
<th>Varenicline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>2mg or 4mg: $3.33 – $3.60 (9 piece)</td>
<td>2mg or 4mg: $3.33 – $3.60 (9 piece)</td>
<td>$1.52 - $2.90 (1 patch)</td>
<td>$7.30 (8 doses)</td>
<td>$12.42 (6 cartridges)</td>
<td>$2.58 - $8.25 (2 tablets)</td>
<td>$11.88 (2 tablets)</td>
</tr>
</tbody>
</table>
Case 1

Mr. White is ready to quit smoking. He currently smokes 1 PPD and smokes within the first 5 minutes of waking up in the morning. What would be the most appropriate NRT for this patient?

A. Nicotine patch + nicotine lozenge 2mg
B. Nicotine patch
C. Nicotine patch + nicotine gum 4 mg
D. Nicotine gum
Case 2

Mrs. Smith is ready to quit smoking. She has previously tried to quit in the past and was successful for 3 months with bupropion SR last year. She smokes 1.5 PPD Her PMH is significant for depression. Which of the following is the most appropriate regimen for her?

A. Bupropion SR 150mg
B. Chantix
C. NRT
D. A and C
E. B and C
Case 3

Ms. Carter is ready to quit smoking and currently smokes 2 PPD. She has heard great things about Chantix and wants to know if you would recommend this for her. She has PMH significant for depression, eating disorder, and suicide ideation. Would you recommend this for her, if not what would be the most appropriate treatment for her?

A. Chantix
B. Bupropion SR
C. NRT
D. Chantix + NRT
E. Bupropion + NRT
References


• CDC. URL: https://www.cdc.gov. Accessed 15 February 2019