? How would you manage Ms. Koff?

- 36 year old woman who presents to you asking for help to quit smoking. She tells you that her boyfriend is sick of her smoking and he won’t get married until she quits.
- HPI: A pack per day (20 cigarettes) for past 20 years. She tried to quit several times in the past cold turkey and has also tried the patch and the gum
- Vitals: 5’5”, 104 lbs, BP 110/60 mmHg, pulse 76
- Current Medications:
  - Depo-Provera (last shot 30 days ago)

Objectives

- **DESCRIBE** the primary health effects of tobacco use and the benefits of cessation
- **IDENTIFY** the latest drug treatments used in nicotine replacement therapy, their mechanisms of action, contraindications and delivery forms
- **DESCRIBE** the proactive role pharmacists can play in counseling patients on drug treatment strategies, medication adherence and means to enhance efforts to stop smoking
- **OUTLINE** strategies pharmacists may use to intervene with patients who have lapsed
Overview

- Epidemiology of cigarette smoking
- Impact of smoking
- Pharmacologic treatment options
- Case Review

Cigarette Smoking Overview

- Leading preventable cause of death in the United States (US)
  - Men lose an average of 13.2 years of life
  - Women lose an average of 14.5 years of life
- 20.9% of adult Americans smoke
  - Men - 23.9%
  - Women - 18.1%
- > 70% of smokers want to quit
- Only 2.5% of smokers quit annually

State-Specific Prevalence of Smoking Among Adults

- California 16.8%
- Kentucky 30.8%
- Nevada 25.2%
- New York 21.6%
- Texas 22.1%
- Utah 12.0%
- Illinois
- Maryland 20.2%

Health Effects of Smoking

- **Cardiovascular Disease**
  - Ischemic heart disease
  - Peripheral vascular disease
  - Stroke
  - Abdominal aortic aneurysm

- **Respiratory disease**
  - COPD
  - Asthma
  - Pneumonia

- **Cancer**
  - Lung, mouth, esophagus
  - Pancreatic, cervix, colorectal, bladder

- **Reproductive**
  - Reduced fertility
  - Erectile dysfunction
  - Pregnancy complications
  - Low birth weight, SIDS

- **Other**
  - Cataracts
  - Wound healing
  - Low bone density
  - Macular degeneration
  - Tooth decay

*Top 3 causes of smoking-related deaths

**Health Benefits of Smoking Cessation**

- **20 minutes**
  - Blood pressure, heart rate return to normal

- **8 - 12 hours**
  - O₂ level returns to normal; nicotine and CO levels reduced by half

- **2 weeks to 3 months**
  - Circulation improves and lung function increases

- **3 to 9 months**
  - Lung function increases by up to 10%; coughing, wheezing, breathing problems reduced

- **1 year**
  - Excess risk of coronary heart disease is half that of a smoker

- **5 years**
  - Stroke risk is reduced to that of a nonsmoker 5-15 years after quitting

- **10 years**
  - Lung cancer death rate is about half that of a continuing smoker

- **15 years**
  - Risk of coronary heart disease is that of a nonsmoker

**Life Cycle Effects of Smoking**

- SIDS
- RSV/Bronchiolitis
- Meningitis
- Infancy
- Low Birth Weight
- Stillbirth
- In utero
- Adolescence
- Adulthood
- Childhood
- Asthma
- Otitis Media
- Fire-related Injuries
- Cognitive Problems
- Influences to Start Smoking

**Treatment Overview**

- Nicotine Addiction
- Health Effects
- Cancer
- Cardiovascular Disease

---


Currently FDA-approved Agents Smoking Cessation

<table>
<thead>
<tr>
<th>Brand Name ®</th>
<th>Generic Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine Replacement Therapy (NRT)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commit</td>
<td>nicotine lozenge</td>
<td>Over the counter (OTC)</td>
</tr>
<tr>
<td>Nicotrol NS</td>
<td>nicotine nasal spray</td>
<td>Prescription</td>
</tr>
<tr>
<td>Habitrol, Nicoderm CQ, Nicotine®, Prostep</td>
<td>nicotine patch</td>
<td>OTC and Prescription*</td>
</tr>
<tr>
<td>Nicorette, Nicotine Polacrilex</td>
<td>nicotine gum</td>
<td>OTC</td>
</tr>
<tr>
<td>Nicotrol</td>
<td>nicotine oral inhaler</td>
<td>Prescription</td>
</tr>
</tbody>
</table>

Non-NRT Therapy

- Zyban: bupropion SR, Prescription
- Chantix: varenicline, Prescription

2000-Guidelines for Smoking Cessation Pharmacotherapy

Who should receive pharmacotherapy

- All smokers trying to quit
  - Except in the presence of medical contraindications
  - Based on clinical judgment: < 10 cigs/day; pregnant/breastfeeding women; and adolescent smokers

First-line pharmacotherapies

- 5 FDA approved pharmacotherapies for smoking cessation: NRT (gum, inhaler, nasal spray, patch) and sustained-release bupropion
  - Not included: NRT lozenge (FDA approved 10/30/02) and varenicline (FDA approved 5/10/06)

Second-line pharmacotherapies

- Clonidine (Catapres®) and nortriptyline (Pamelor®)


Comparison of NRTs

- Role of therapy
  - Replace some of the nicotine in blood from smoking without harmful chemicals
  - Helps reduce urges to smoke
  - Helps reduce withdrawal symptoms

- Class-wide precautions
  - Serious arrhythmias, serious or worsening angina pectoris, recent (< 2 week) myocardial infarction
  - Pregnancy category D

Comparison of NRTs

<table>
<thead>
<tr>
<th>NRT Form</th>
<th>Available Dosing</th>
<th>Primary Side Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine lozenge</td>
<td>Yes</td>
<td>hiccups, cough, heartburn</td>
<td>Do not eat or drink 15 mins before or during use</td>
</tr>
<tr>
<td>Nicotine nasal spray</td>
<td>Yes</td>
<td>nasal irritation</td>
<td>Not for pts w/ asthma, May cause dependence</td>
</tr>
<tr>
<td>Nicotine patch</td>
<td>No</td>
<td>topical skin rash</td>
<td>Not for pts w/ severe eczema or psoriasis</td>
</tr>
<tr>
<td>Nicotine gum</td>
<td>Yes</td>
<td>mouth soreness</td>
<td>Caution in pts with TMJ or dental problems</td>
</tr>
<tr>
<td>Nicotine oral inhaler</td>
<td>Yes</td>
<td>mouth and throat irritation</td>
<td>Do not drink acidic beverages during use, Unknown safety in pts w/ reactive airway disease Allows to mimic the use of cigarettes</td>
</tr>
</tbody>
</table>

Combination NRT

- Two different dosage forms
  - One type should be passive dosing
    - Produces relatively steady levels of drug in the body
    - Example: Nicotine patch
  - Second type should permit ad lib dosing
    - Allows user to adjust dosing on an acute basis
    - Example: Nicotine gum, nicotine nasal spray

A Meta-analysis of NRT Pharmacotherapies

<table>
<thead>
<tr>
<th>Cessation Pharmacotherapy</th>
<th>Number of Studies Included</th>
<th>Estimated Abstinence Rate (95% CI)</th>
<th>Estimated Odds Ratio (95% CI)</th>
<th>Number Needed to Treat (NNT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine gum</td>
<td>13</td>
<td>23.7 (20.6, 26.7)</td>
<td>1.5 (1.3, 1.8)</td>
<td>15</td>
</tr>
<tr>
<td>Placebo</td>
<td>17.1</td>
<td>1.0</td>
<td>1.0</td>
<td>8</td>
</tr>
<tr>
<td>Nicotine inhaler</td>
<td>4</td>
<td>22.8 (16.4, 29.2)</td>
<td>2.5 (1.7, 3.6)</td>
<td>8</td>
</tr>
<tr>
<td>Placebo</td>
<td>10.5</td>
<td>1.0</td>
<td>1.0</td>
<td>8</td>
</tr>
<tr>
<td>Nicotine nasal spray</td>
<td>3</td>
<td>30.5 (21.8, 39.2)</td>
<td>2.7 (1.8, 4.1)</td>
<td>6</td>
</tr>
<tr>
<td>Placebo</td>
<td>13.9</td>
<td>1.0</td>
<td>1.0</td>
<td>5</td>
</tr>
<tr>
<td>Nicotine patch</td>
<td>27</td>
<td>17.7 (16.0, 19.5)</td>
<td>1.9 (1.7, 2.2)</td>
<td>13</td>
</tr>
<tr>
<td>Placebo</td>
<td>10.0</td>
<td>1.0</td>
<td>1.0</td>
<td>10</td>
</tr>
</tbody>
</table>

Efficacy of Nicotine Lozenge

- Design: Double-blind, placebo controlled, randomized clinical trial
- Intervention: Low dependence smokers: 2mg lozenge (n=459) or placebo (n=458)
  - High dependence smokers: 4mg lozenge (n=450) or placebo (n=451)
- Population: Average age of 42 years w/ more than 20 yrs of smoking
  - Most had previously tried and failed to quit smoking and tried pharmacological treatment
- Outcomes: Abstinence at 24 and 52 weeks
- Results:
  - 24 wks: OR 1.96-2.76 (95% CI 1.39-4.02)
  - 52 wks: OR 2.14-2.69 (95% CI 1.43-4.29)
  - NNT range low dependence 8-12 (based on wks 24 & 52)
Bupropion SR (Zyban®)

- **First non-nicotine medication shown to be effective for smoking cessation**
- Block neuronal uptake of norepinephrine, serotonin, and dopamine
- Can be used in combination with NRT
- Effective in patients with depression


---

**Administration**

- Patient should set a quit date
- Start medication 1 week before quit date

- **Dose (duration for 7-12 weeks):**
  - 150mg/day (days 1-3)
  - 150mg twice/day

**Pregnancy Category: C**

**Cost:** $85*

*Cost for 30 days treatment rounded to nearest dollar based on most recent data available (June 30, 2006) from Wolters Kluwer Health.


---

**Contraindications**

- Seizure disorder
- Concomitant use with any form of bupropion
- Current or prior diagnosis of bulimia or anorexia
- Abrupt discontinuation of alcohol or sedatives
- Concurrent administration with MAO inhibitors

**Drug Interactions**

- Potential interactions with drugs that affect CYP2B6 (e.g. orphenadrine and cyclophosphamide)
- Potential interactions with drugs metabolized by CYP2D6 (e.g. nortriptyline, risperidone, type 1C antiarrhythmics)


---

**Adverse Effects**

- **Less common**
  - Dizziness, Disturbed Concentration
  - Nausea
  - Anxiety
  - Constipation

- **Most Common**
  - Insomnia
  - Dry mouth

Smoking Cessation - When Pharmacists Get Involved

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved. Reproduction in whole or in part without permission is prohibited.

Bupropion SR: Meta-Analysis 2 Studies

<table>
<thead>
<tr>
<th></th>
<th>Abstinence Rate (95% CI)</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>17.3</td>
<td>1.0</td>
</tr>
<tr>
<td>Bupropion SR</td>
<td>30.5 (23.2, 37.8)</td>
<td>2.1 (1.5, 3.0)</td>
</tr>
</tbody>
</table>

NNT = 8


Varenicline (Chantix®)

- Mechanism of Action
  - Binds with high affinity and selectivity at α4β2 neuronal nicotinic acetylcholine receptors

- No clinically meaningful interactions
- Most common adverse events
  - Nausea (most common adverse event) and is dose-dependent, 16-40% vs 8-10% placebo
  - Reduce dose if nausea is intolerable
  - Sleep disturbance
  - Constipation
  - Flatulence
  - Vomiting
- Pregnancy Category C


Varenicline (Chantix®)

- Administration
  - Patients should set a quit date
  - Start medication 1 week before Quit date
  - Take after eating with a glass of water
- Dosing Schedule (for 12 weeks)

<table>
<thead>
<tr>
<th>Day 1 to Day 3</th>
<th>Day 4 to Day 7</th>
<th>Day 8 to End of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>White tablet (0.5 mg), 1 tablet each day</td>
<td>White tablet (1.5 mg), twice a day</td>
<td>Blue tablet (1 mg) twice a day</td>
</tr>
<tr>
<td>1 in the morning and 1 in the evening</td>
<td>1 in the morning and 1 in the evening</td>
<td>1 in the morning and 1 in the evening</td>
</tr>
</tbody>
</table>

Varenicline (Chantix®)

- **Dosage Adjustment**
  - Severe renal impairment
    - Starting dose is 0.5 mg once daily
    - Titrate to max dose of 0.5 mg twice daily
  - End stage renal disease undergoing hemodialysis
    - Max dose of 0.5mg once daily


Varenicline: Phase 3 Studies (Gonzales et al.):
Efficacy Results

Continuous Abstinence Rates

- Varenicline vs. placebo (statistically significant at all three time points) (p<0.001)
- Varenicline vs. bupropion SR: significant at weeks 9-12 (P<0.001) and weeks 9-24 (P=0.007)

Continuous Abstinence Rates (%)

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Varenicline (P&lt;0.001)</th>
<th>Bupropion SR</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>9-12</td>
<td>44</td>
<td>29.5</td>
<td>21.9</td>
</tr>
<tr>
<td>9-24</td>
<td>29.5</td>
<td>20.7</td>
<td>6.1</td>
</tr>
<tr>
<td>9-52</td>
<td>21.9</td>
<td>8.4</td>
<td>17.7</td>
</tr>
</tbody>
</table>

Varenicline NNT= 5-7
Range based on Weeks 9-24, 9-52

Varenicline: Phase 3 Studies (Jorenby et al.):
Efficacy Results

Continuous Abstinence Rates

- Varenicline vs. placebo (statistically significant at all three time points) (P<0.001)
- Varenicline vs. bupropion SR (statistically significant at all three time points) weeks 9-12 (P<0.001); weeks 9-24 (P=0.003); weeks 9-52 (P=0.004)

Continuous Abstinence Rates (%)

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Varenicline (P&lt;0.001)</th>
<th>Bupropion SR</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>9-12</td>
<td>43.9</td>
<td>17.6</td>
<td>14.6</td>
</tr>
<tr>
<td>9-24</td>
<td>29.7</td>
<td>14.6</td>
<td>9.4</td>
</tr>
<tr>
<td>9-52</td>
<td>23</td>
<td>10.3</td>
<td>8.4</td>
</tr>
</tbody>
</table>

Varenicline NNT= 6-8
Range based on weeks 9-24, 9-52

Non-FDA Approved Agents
Smoking Cessation

- **Clonidine**
  - Dosage: 0.15 to 0.75mg/day
  - Precaution: Rebound hypertension
  - Less robust clinical data than other FDA approved agents
- **Nortriptyline**
  - Dosage: 75-100mg/day
  - Precaution: Risk of arrhythmias
  - Studies report additive effect on abstinence
- **Disadvantages:**
  - Lack of FDA-approved indication
  - Side effect profiles

Smoker committed to quitting and has set a quit date

Initiate smoking cessation program w/ focus on behavioral therapy and evaluate for pharmacotherapy

Pharmacotherapy initiated

Yes

Able to achieve/maintain abstinence

Yes

Select either NRT or bupropion SR or varenicline, based on patient factors and medical contraindications

No

Consider retrying or using another FDA approved agent and after multiple failed attempts consider 3rd line agents (clonidine or nortriptyline), or combination therapy

Maintain frequent contact to monitor success

No

How would you manage Ms. Koff?

- 36 year old woman who presents to you asking for help to quit smoking. She tells you that her boyfriend is sick of her smoking and he won’t get married until she quits.
- HPI: A pack per day (20 cigarettes) for past 20 years. She tried to quit several times in the past cold turkey and has also tried the patch and the gum
- Vitals: 5’5”, 104 lbs, BP 110/60 mmHg, pulse 76
- Current Medications:
  - Depo-Provera (last shot 30 days ago)