

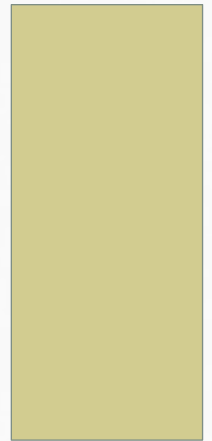
INSTITUTE FOR CLINICAL SYSTEMS IMPROVEMENT | ICSI

TOBACCO HEALTH SYSTEMS CHANGE: MEDICATION EDUCATION FOR TOBACCO DEPENDENCY

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DISCLOSURE

- Dr. Rouse has no relevant financial or nonfinancial relationships to disclose

LEARNING OBJECTIVES

- Summarize FDA approved pharmacotherapy for smoking cessation
- Recognize first-line pharmacotherapy options for the treatment of tobacco dependence
- Define current evidence and best-practice prescribing of pharmacotherapy for tobacco dependence
- Define patient-specific treatment options

BACKGROUND/SMOKING STATISTICS

- Smoking is the leading causes of preventable death in the United States
- Medical costs for smokers are >\$50 billion/year
- Many chronic diseases & medical complications are linked to smoking:
 - Adverse pregnancy outcomes
 - Aortic aneurysm
 - Asthma
 - Cancer
 - COPD
 - Coronary artery disease
 - Diabetes
 - Ectopic pregnancy
 - Erectile dysfunction
 - Hip fractures
 - Increase risk of pneumonia & other respiratory infections
 - Ocular implications
 - Blindness, cataracts, macular degeneration
 - Osteoporosis
 - Reduced fertility
 - Rheumatoid arthritis
 - Stroke
 - Mortality

BENEFITS OF QUITTING SMOKING

- Never-smokers are twice as likely to live to age 80 compared to current smokers
- 90% lower risk of death in those who quit smoking before age 40 compared to those who continue smoking
- Smokers who quit:
 - Age 25-34 years, gain 10 years of life
 - Age 35-44 years, gain 9 years of life
 - Age 45-54 years, gain 6 years of life

(N Engl J Med 2013; 368:341-50)

BENEFITS OF QUITTING SMOKING

- 50% lower risk of heart disease after 1 year of abstinence
- After 3-5 years of abstinence
 - 50% lower risk of bladder cancer
 - 50% lower risk of oral and esophageal cancer
- 50% lower risk of lung cancer at 10 year smoke free
- After 15 years, risk of heart disease is the same as those who never smoked

PHARMACOTHERAPY

WHY CHOOSE MEDICATIONS TO AID IN QUITTING?

USPHS CLINICAL PRACTICE GUIDELINES 2008

- Key Guidelines Recommendations:
 - Tobacco dependence is a chronic disease
 - Identify and document tobacco status - every patient, every time, every healthcare setting
 - Brief, repetitive interventions – individual, group, in person, by phone - are helpful and sometimes it takes multiple attempts to quit, but must provide practical counseling and social support to be successful
 - Seven first-line medications (5 nicotine and 2 non-nicotine) reliably increase long-term smoking abstinence rates
 - The combination of counseling and medication is more effective than either alone

FDA APPROVED MEDICATION OPTIONS FOR SMOKING CESSATION

- Nicotine Replacement Products
 - Skin patches
 - Gum
 - Lozenges
 - Inhaler
 - Nasal Spray
- Zyban (bupropion SR)
- Chantix (varenicline)

HOW DOES IT WORK?

- Block reinforcing effects
 - Positive reinforcement
 - Negative reinforcement
- Reduce urges to smoke
- Break the link between nicotine effects and environmental triggers
- Engage strategies to change smoking behavior

HOW DO WE KNOW PHARMACOTHERAPY WORKS?

WHERE'S THE EVIDENCE

<http://www.bing.com/images/search?view=detailV2&ccid=zGaxsZoR&id=52E6679FD186A5DE610FA55F4A0EDA9138F24BA0&q=show+me+the+money&simid=608035248713239848&selectedIndex=23&adlt=strict>

USPHS CLINICAL PRACTICE GUIDELINES 2008

Table 6.26 Meta-analysis (2008): Effectiveness and abstinence rates for various medications and medication combinations compared to placebo at 6-months postquit (n = 83 studies)^a

Medication	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Placebo	80	1.0	13.8
Monotherapies			
Varenicline (2 mg/day)	5	3.1 (2.5–3.8)	33.2 (28.9–37.8)
Nicotine Nasal Spray	4	2.3 (1.7–3.0)	26.7 (21.5–32.7)
High-Dose Nicotine Patch (> 25 mg) (These included both standard or long-term duration)	4	2.3 (1.7–3.0)	26.5 (21.3–32.5)
Long-Term Nicotine Gum (> 14 weeks)	6	2.2 (1.5–3.2)	26.1 (19.7–33.6)
Varenicline (1 mg/day)	3	2.1 (1.5–3.0)	25.4 (19.6–32.2)
Nicotine Inhaler	6	2.1 (1.5–2.9)	24.8 (19.1–31.6)
Clonidine	3	2.1 (1.2–3.7)	25.0 (15.7–37.3)
Bupropion SR	26	2.0 (1.8–2.2)	24.2 (22.2–26.4)
Nicotine Patch (6–14 weeks)	32	1.9 (1.7–2.2)	23.4 (21.3–25.8)
Long-Term Nicotine Patch (> 14 weeks)	10	1.9 (1.7–2.3)	23.7 (21.0–26.6)
Nortriptyline	5	1.8 (1.3–2.6)	22.5 (16.8–29.4)
Nicotine Gum (6–14 weeks)	15	1.5 (1.2–1.7)	19.0 (16.5–21.9)

USPHS CLINICAL PRACTICE GUIDELINES 2008

Table 6.26 Meta-analysis (2008): Effectiveness and abstinence rates for various medications and medication combinations compared to placebo at 6-months postquit (n = 83 studies)^a

Medication	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Placebo	80	1.0	13.8
Combination therapies			
Patch (long-term; > 14 weeks) + <i>ad lib</i> NRT (gum or spray)	3	3.6 (2.5–5.2)	36.5 (28.6–45.3)
Patch + Bupropion SR	3	2.5 (1.9–3.4)	28.9 (23.5–35.1)
Patch + Nortriptyline	2	2.3 (1.3–4.2)	27.3 (17.2–40.4)
Patch + Inhaler	2	2.2 (1.3– 3.6)	25.8 (17.4–36.5)
Patch + Second generation antidepressants (paroxetine, venlafaxine)	3	2.0 (1.2–3.4)	24.3 (16.1–35.0)
Medications not shown to be effective			
Selective Serotonin Re-uptake Inhibitors (SSRIs)	3	1.0 (0.7–1.4)	13.7 (10.2–18.0)
Naltrexone	2	0.5 (0.2–1.2)	7.3 (3.1–16.2)

NICOTINE REPLACEMENT THERAPY

(NRT)

NICOTINE REPLACEMENT THERAPY

- Match nicotine replacement to heaviness of smoking
- Most smokers will need combination NRT
- Single agent NRT may be appropriate for:
 - Light smokers (<10 cigarettes per day)
 - Non- daily smokers
 - Pregnant women
- NRT should be started on quit date
- Some NRT can be used while smoking
 - Aid to reduce smoking to lead to quitting

NICOTINE REPLACEMENT THERAPY

- Nicotine Replacement Products
 - Skin patches
 - Gum
 - Lozenges
 - Inhaler
 - Nasal Spray

NICOTINE PATCHES

- Transdermal nicotine delivery
- May be placed anywhere on the body including arms and back
 - Rotate sites each time
 - Can be worn up to 24 hours
- Available OTC
- Cost
 - ~\$3.86 per patch
 - Most often covered by insurance

NICOTINE PATCHES

- Advantages
 - Long acting, once daily
 - Achieve and maintain level of replacement
- Disadvantages
 - Less flexible dosing
 - Slower onset (3-4 hours)

NICOTINE PATCHES

- Dosing

Cigarettes per Day	Patch Dose
≥ 40	42 mg/day
21-39	28-35 mg/day
10-20	14-21 mg/day
<10	14 mg/day

- After 4-6 weeks smoking abstinence, taper every 2-4 weeks in 7-14mg steps
- Adjust based on withdrawal symptoms, urges and comfort

NICOTINE PATCH

- Adverse effects
 - Local skin reaction
 - Insomnia/vivid dreams (12%)
 - May be reduced or avoided by removing patch for 8 hours overnight

NICOTINE GUM

- Delivers nicotine through the lining of the mouth
- Not chewed like regular gum
 - “Bite & Park”
 - Bite/chew briefly and then “park” between gum and cheek
- Should not eat or drink 15 minutes before or during use
 - Especially acidic drinks (coffee, colas)
- Available OTC
- Cost
 - ~\$4 for 10 pieces
 - Often covered by insurance

NICOTINE GUM

- Advantages
 - Convenient, flexible dosing
 - Quick onset
 - 4mg strength can help delay weight gain
- Disadvantages:
 - Frequent dosing needed to maintain adequate nicotine levels
 - Caution in those with dental or TMJ issues
 - Caution if CV event in past 2 weeks, serious arrhythmias, unstable angina

NICOTINE GUM

- Dosing as monotherapy
 - Based on time of first cigarette of the day
 - < 30 minutes = 4mg
 - ≥ 30 minutes = 2mg
 - Based on cigarettes per day
 - > 20 = 4mg
 - ≤ 20 = 2mg
- Initial dosing: 1-2 pieces every 1-2 hours
 - 10-12 pieces per day, taper as tolerated

NICOTINE GUM

- Adverse effects:
 - Indigestion
 - Mouth soreness
 - Jaw ache
 - Hiccups

NICOTINE LOZENGE

- Delivers nicotine through the lining of the mouth as it dissolves
- Efficacy and side effects relates to amount used
- Mini lozenge is smaller and dissolves more rapidly
- Should not eat or drink 15 minutes before or during use
 - Especially acidic drinks (coffee, colas)
- Available OTC
- Cost
 - ~\$5.50 for 10 lozenges
 - Often covered by insurance

NICOTINE LOZENGE

- Advantages
 - Delivers doses of nicotine 25% higher than gum
 - Short acting, flexible dosing
 - 4mg strength delays weight gain
- Disadvantages
 - Should not be chewed or swallowed
 - Caution if CV event in past 2 weeks, serious arrhythmias, unstable angina

NICOTINE LOZENGE

- Dosing as monotherapy
 - Based on time of first cigarette of the day
 - < 30 minutes = 4mg
 - ≥ 30 minutes = 2mg
 - Based on cigarettes per day
 - > 20 = 4mg
 - ≤ 20 = 2mg
- Initial dosing: 1-2 lozenges every 1-2 hours
 - Minimum 9/day, taper as tolerated

NICOTINE LOZENGE

- Adverse effects
 - Nausea (most common, 12-15%)
 - Sore Throat
 - Hiccups
 - Heartburn

NICOTINE INHALER

- Delivers nicotine as a vapor absorbed through the lining of the mouth (not the lungs)
 - Do not have to inhale deeply for effects
- Should not eat or drink 15 minutes before or during use
 - Especially acidic drinks (coffee, colas)
- Cost
 - ~\$12.68 for 10 cartridges
 - Insurance coverage
 - Variable
 - Most difficult of NRT to get covered
 - Rx ONLY in US

NICOTINE INHALER

- Advantages
 - Flexible dosing, quick onset
 - Mimics hand-to-mouth motion
- Disadvantages
 - Requires frequent use to maintain nicotine levels
 - Decreased delivery if <40 degrees F in winter
 - Keep in a warm area
 - Caution if CV event in past 2 weeks, serious arrhythmias, unstable angina

NICOTINE INHALER

- Dosing
 - 6 to 16 cartridges per day
 - 1 cartridge = 80 puffs over 20 minutes
- Taper frequency as tolerated

NICOTINE INHALER

- Adverse effects:
 - Local irritation of mouth and throat (66 %)
 - Coughing (32 %)
 - Runny nose (23 %)
 - Headache (18-26 %)
 - Dyspepsia (18 %)
- Avoid in patients who have bronchospastic disease or other forms of airway irritation

NICOTINE NASAL SPRAY

- Delivers nicotine through nasal lining
 - Not meant to be sniffed
 - Do not sniff, inhale through the nose or swallow while spraying
 - Should spray against the lining of the nostril
- Rx ONLY
- Cost
 - ~\$7.77 for 12 doses
 - Insurance Coverage
 - Variable
 - Depend upon the plan

NICOTINE NASAL SPRAY

- Advantages
 - Fastest delivery system for NRT, rapid relief of withdrawal
 - Can be used in response to stress, urges to smoke
- Disadvantages
 - Highest dependence of any NRT
 - High frequency of use to maintain nicotine levels
 - Caution if CV event in past 2 weeks, serious arrhythmias, unstable angina
 - Avoid use in severe reactive airway disease

NICOTINE NASAL SPRAY

- Dosing: 1 spray each nostril 1-2 times/hr
 - Titrate to symptom relief
 - Max: 5 times/hour
- Can use 8-40 doses per day
 - Average initial dose: 14-15 times/day
- Doses should be tapered as tolerated

NICOTINE NASAL SPRAY

- May cause nasal irritation (1-10 % of pts)
 - Infrequently causes nosebleeds
- Nose/throat irritation common
 - Usually improves within a week of use
- Avoid in severe reactive airway disease, or patients who have chronic nasal disorders such as allergies, nasal polyps, or sinusitis

CAUTIONS/CONTRAINDICATIONS WITH NRT

- Recent MI (within 2 weeks)
- Serious Arrhythmias
- Serious or worsening angina
- Pregnancy

NRT IN PREGNANCY

- Pregnancy category C (gum) & D (patches)
 - Nicotine passes into the placenta and is found in both amniotic fluid and umbilical cord blood.
 - Fetus is actually exposed to higher nicotine concentrations than the mother
 - Decreased fetal breathing movements have been observed when nicotine is used during the last trimester

"If you are pregnant or breast-feeding, only use this medicine on the advice of your health care provider. Smoking can seriously harm your child. Try to stop smoking without using any nicotine replacement medicine. This medicine is believed to be safer than smoking. However, the risks to your child from this medicine are not fully known."

MONITORING WITH NRT

Discontinue if signs of nicotine toxicity occur:

- Severe headache
- Dizziness
- Mental confusion
- Disturbed hearing and vision
- Abdominal pain
- Rapid, weak or irregular pulse
- Salivation
- Nausea/Vomiting
- Diarrhea
- Cold sweats
- Weakness

Discontinue if patient experiences:

- Severe or intolerable myalgia
- Arthralgia
- Abnormal dreams
- Insomnia
- Nervousness
- Dry mouth
- Sweating

Monitor heart rate (HR) and blood pressure (BP) for all patient using NRT

OTHER SMOKING CESSATION PHARMACOTHERAPY

NON-NICOTINE REPLACEMENT THERAPIES

ZYBAN

BUPROPION SR

ZYBAN (BUPROPION SR)

- Blocks re-uptake of norepinephrine & dopamine
- Can be used in combo with NRT
- May be an option if patient has history of depression or schizophrenia
- Cost
 - ~\$1.17/day for generic
 - Often covered by insurance

ZYBAN (BUPROPION SR)

- Advantages
 - Easy to use, tablet form
 - Safer for patients with a history of CVD
 - Delays weight gain
- Disadvantages
 - Slight increase in seizure risk (1:1000)
 - Contraindicated with some medical conditions
 - Prior or current diagnosis of bulimia or anorexia
 - Abrupt discontinuation of alcohol, benzodiazepines, barbiturates, or antiepileptic drugs
 - Seizure disorders

ZYBAN (BUPROPION SR)

- Dosing: begin 1-2 weeks prior to quit date
 - 150 mg QAM x 3 days, then 150 mg BID
 - Then stop smoking on target quit date
 - Continue 150mg BID x 7-12 weeks
- Treat as long as 12 months to prevent relapse
- May stop abruptly – no taper needed

ZYBAN (BUPROPION SR)

- Contraindications
 - History of seizure
 - History of eating disorder
 - Use of MAOI within past 2 wks
 - Bipolar disorder (Caution not CI)
- Pregnancy Category C
- Adverse Effects
 - Insomnia (11-20 %)
 - Dry mouth (17-26 %)
 - Headache (25-34 %)

CHANTIX

VARENICLINE

CHANTIX (VARENICLINE)

- Partial nicotine agonist
- Can be used in patients with a history of CVD
- December 2016: FDA dropped black box warning for neuropsychiatric side effects
- Duration=12-24 weeks
- Cost
 - ~\$2.68/day
 - Often covered by insurance

CHANTIX (VARENICLINE)

- Advantages
 - Tablet form
 - Generally well tolerated
- Disadvantages
 - Nausea common, can be reduced by taking with food
 - May impair ability to drive or operate machinery
 - Renal dosing: adjust dose if $\text{CrCl} < 30 \text{ mL/min}$

CHANTIX (VARENICLINE)

- Dosing
 - Days 1-3 = 0.5 mg daily
 - Days 4-7 = 0.5 mg BID
 - Days 8-discontinuation = 1 mg BID
- Begin dosing 1 week before set quit date
- Continue for 12 weeks
- May be continued additional 12 weeks
 - If abstinent after first 12 weeks
 - May improve likelihood of long-term quitting

CHANTIX (VARENICLINE)

- Alternative dosing options
 - Flexible Quit Date
 - Following initial upward titration of dose over 7 days and then maintenance dose at day 8
 - Patient may set a quit date between days 8 and 35 of the regimen
 - Continue regimen for 12 weeks, add another 12 weeks if needed
 - Gradual Cessation
 - Helps patients not able or willing to quit abruptly
 - Begin dosing and reduce smoking by 50% within the first 4 weeks
 - Continue reduction by 50% every 4 weeks until reaching complete abstinence by 12 weeks or sooner
 - Continue treatment for an additional 12 weeks (24 weeks total)

CHANTIX (VARENICLINE)

- Adverse Effects
 - Nausea (16-40 %)
 - Insomnia (10-19 %)
 - Vivid/strange dreams (9-13 %)
 - Headaches (15-19 %)
 - Depressed mood/suicidal ideation (11 %)
 - Impairment of ability to drive and/or operate heavy machinery (3 % experience drowsiness)

VARENICLINE & BUPROPION

- Psychiatric Risk:
 - Depressed mood, behavior changes, hostility, agitation, and suicidal thoughts/behavior have been reported in patients using these medications
 - Clinicians should obtain information regarding psychiatric history and monitor for changes in mood or behavior
 - Patients should discontinue medication if they experience depressed mood, agitation, behavior change or suicidal thoughts
 - These are effective smoking cessation aids and FDA believes benefits outweigh risks

ALTERNATIVE THERAPIES

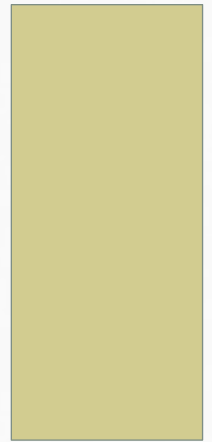
- Nortriptyline
 - Blocks NE reuptake
 - Similar efficacy to bupropion or NRT
 - Avoid in CVD or pts w/ arrhythmia risk
 - Dosing
 - Begin at 25mg daily 10-28 days before quit date
 - Increase to 75-100 mg daily
 - 12 week duration (up to 6 mo.)
 - Not FDA approved for smoking cessation
 - Cost/day: \$0.43
 - AE: sedation, dry mouth, urinary retention, lightheadedness, blurred vision, shaky hands

ALTERNATIVE THERAPIES

- Clonidine
 - Centrally acting alpha 2 agonist
 - Not FDA approved for smoking cessation
 - Duration of use = 3-10 wks
 - Begin 3 days before or on quit date
 - 0.15-0.75 mg po daily
 - 0.1-0.2 mg/24 hr patch
 - Cost/day = \$0.22 PO and \$7.50 patch
 - Adverse effects: dry mouth, drowsiness, dizziness, sedation, constipation

CLINICAL DECISION MAKING

HOW TO CHOOSE THE RIGHT PHARMACOTHERAPY



FIRST LINE OPTIONS

- First line Therapies:
 - Nicotine Replacement Products
 - Skin patches, chewing gum, lozenges, inhaler, nasal spray
 - Zyban (bupropion SR)
 - Chantix (varenicline)
- According to the AHRQ Guidelines

“Because of the lack of sufficient data to rank-order these [...] medications, choice of a specific first-line pharmacotherapy must be guided by factors such as clinician familiarity with the medications, contraindications for selected patients, patient preference, previous patient experience with a specific pharmacotherapy (positive or negative), and patient characteristics (e.g., history of depression, concerns about weight gain).”

SPECIAL POPULATIONS

- Light smokers (<10 cigarettes per day)
 - Behavioral therapy is 1st Line
- Adolescents
 - Behavioral therapy alone or in combination with NRT are first line
 - Bupropion and Chantix are not recommended as first line treatments in this group

SPECIAL POPULATIONS

- Pregnant women
 - Counseling/behavioral therapy are 1st Line
 - NRT or Bupropion are options in women at higher risk of continued smoking
 - women who smoke over 10 cigarettes/day
 - women smoking later in pregnancy
 - Women who have already tried to stop and failed
 - Consider waiting until the 2nd trimester to begin therapy to avoid the period of embryogenesis
 - Also, consider use of intermittent dosing products such as gum or lozenges rather than patches

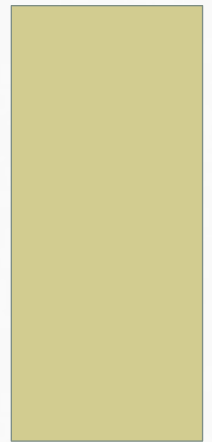
SMOKING AFTER INITIATION OF PHARMACOTHERAPY

- NRT
 - Patients should be advised to completely stop smoking upon initiation of therapy
- Bupropion
 - Begin therapy at least one week before target quit date
 - Target quit date generally during 2nd week of treatment
- Chantix
 - Start therapy one week before quit date
 - Alternatively patients may set quit date up to 35 days after beginning therapy

NON-PHARMACOLOGIC TIPS

- Behavioral counseling
- Manage stress
 - Massage, yoga, meditation, relaxing music
- Avoid triggers like alcohol or coffee
- For post-meal smokers chew gum or brush teeth
- Exercise
- Throw out ashtrays and lighters
- Use money saved to buy a reward

PATIENT CASES



BOB PATIENT CASE

- Bob is a 62 y.o. man who had a heart attack 4 years ago. He smokes “a little more than a pack” each day. He wants to start a medication to help him quit smoking and he has tried using gum alone in the past which “did not work.” What would you recommend for him today in addition to counseling support?

BOB PATIENT CASE CT' D

- A. Nicotine lozenges + Nicotine gum
- B. Bupropion alone
- C. Nicotine patches
- D. Chantix + Nicotine gum
- E. Nicotine patches + Nicotine gum

BOB PATIENT CASE CT' D

- What else would you recommend Bob do?
 - A. Remove the patch for 8 hours overnight to help with sleep
 - B. Get rid of all cigarettes, ashtrays, and lighters in his home and car
 - C. Rotate sites of patch placement
 - D. Chew the gum for about 30 min using the “bite and park” method
 - E. All of the above

SARAH PATIENT CASE

- Sarah is a 29 y.o. female who is about 4 months pregnant. She typically smokes 15 cigarettes per day. She has tried quitting 3 times because she did not want to smoke once she became pregnant. She is determined to quit smoking now that she is expecting a baby and wants to start some type of medication. What would you recommend for her?

SARAH CT' D

- A. Counseling alone
- B. Counseling combined with nicotine gum or lozenges
- C. Chantix + counseling
- D. Nicotine patches + gum + counseling
- E. None of the above

SUMMARY

- It is important to ask every patient about smoking cessation at every visit
- There are many resources for patients who want to quit smoking such as face-to-face support/encouragement, phone support, hotlines, text message, etc.
- Chantix, bupropion OR combination nicotine replacement therapy (patch + gum/lozenge) are first line options in most patients

SUMMARY

- It is important to think about patient factors such as CVD, history of depression, history of an eating or seizures disorders in selecting medication therapy
- There are also special populations to consider such as pregnant women, adolescents, and light smokers
- Patients who use counseling + pharmacotherapy together have better outcomes than either alone

THANK YOU

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QUESTIONS

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