



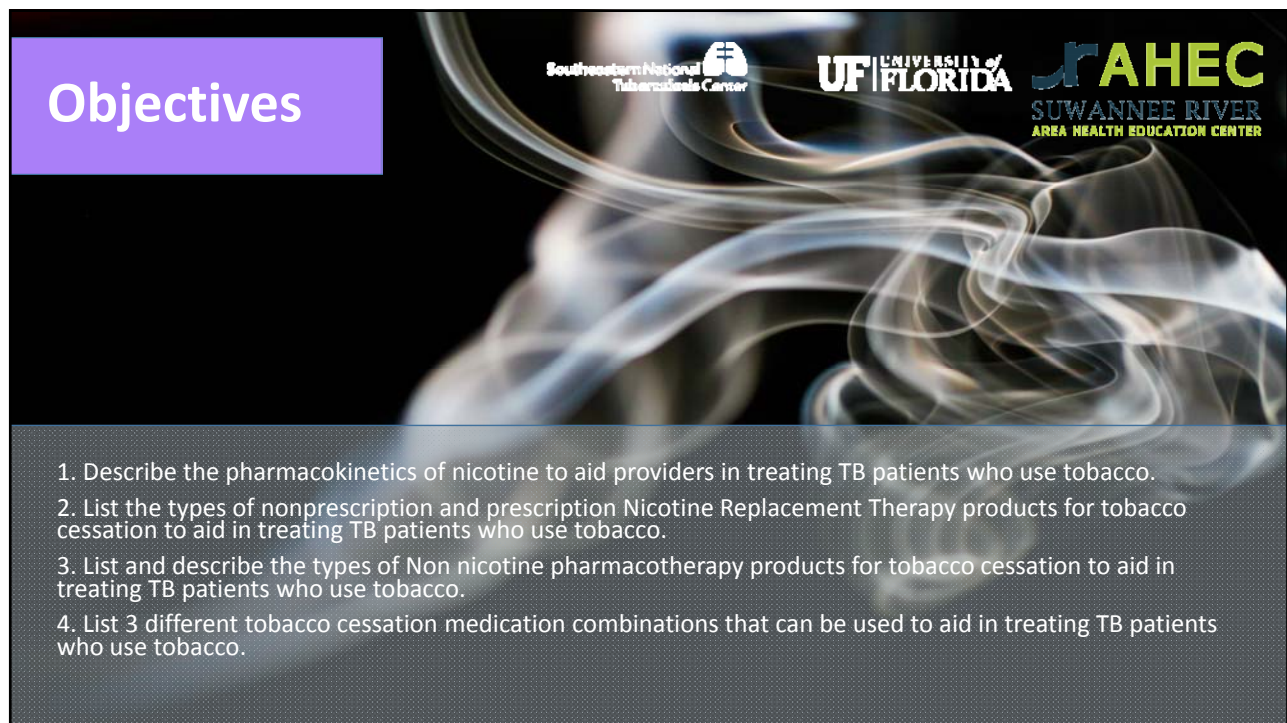
Southwestern National Tuberculosis Center

UF UNIVERSITY of FLORIDA

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# TB and Tobacco: Pharmacotherapy for Tobacco Cessation

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Southwestern National Tuberculosis Center

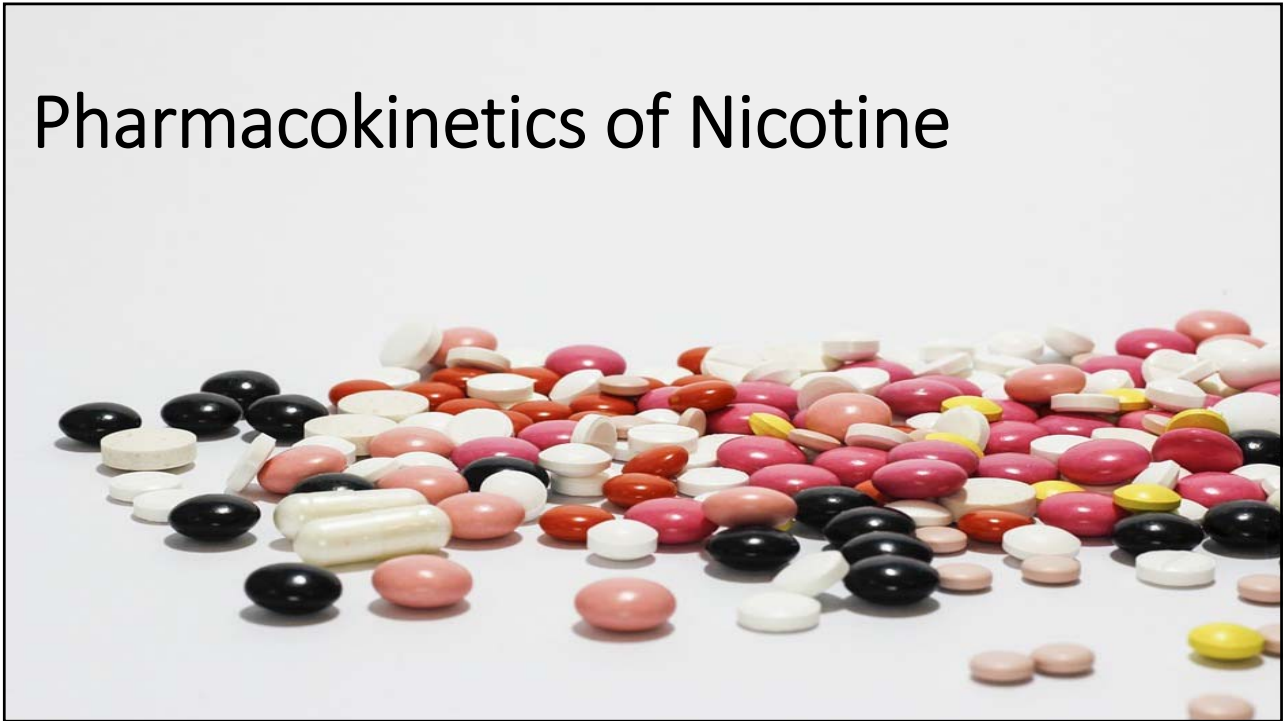
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## Objectives

1. Describe the pharmacokinetics of nicotine to aid providers in treating TB patients who use tobacco.
2. List the types of nonprescription and prescription Nicotine Replacement Therapy products for tobacco cessation to aid in treating TB patients who use tobacco.
3. List and describe the types of Non nicotine pharmacotherapy products for tobacco cessation to aid in treating TB patients who use tobacco.
4. List 3 different tobacco cessation medication combinations that can be used to aid in treating TB patients who use tobacco.

# Pharmacokinetics of Nicotine



## What is Nicotine

Chemical in tobacco that keeps users addicted

Structurally similar to other addictive substances

- Mimics Acetylcholine

One of the few natural alkaloids that exist in a liquid state

- Clear, volatile and turns brown on exposure to air.
- Has the smell of tobacco

## Nicotine in Tobacco

The amount of nicotine in tobacco products is not specified by manufacturers

- Standardized smoking machine tests can determine nicotine yield in brands

Differs by parts of the plant

- higher stalk positions = higher nicotine concentration
- lower stalk positions; ribs and stems of the leaves = lowest nicotine concentration

Combining different varieties of tobacco and different parts of the plant is a way to change the nicotine concentration of commercial tobacco

## Effects of Nicotine

Development  
of tolerance

Acute toxicity

Increased  
heart rate

Increased  
blood  
pressure

## Pharmacokinetics

Absorption

Distribution

Metabolism

Excretion

## Absorption

Absorption across biological membranes depends on pH.

- Weak base
- Ionized vs Non-ionized

When tobacco smoke reaches the small airways and alveoli of the lung, the nicotine is rapidly absorbed

- Surface area of alveoli and small airways

Concentrations of nicotine in blood rise quickly during cigarette smoking and peak at its completion

Smokeless tobacco

- Absorption through mucous membranes

## Distribution

Tissues rapidly uptake nicotine once inhaled

Organs with highest affinity for nicotine : liver, kidney, spleen, lung

- Lowest is adipose tissue

Nicotine accumulates in breast milk

- Crosses the placental barrier easily

Inhaled: Delivers nicotine rapidly to the pulmonary venous circulation, then to the left ventricle of the heart and to the systemic arterial circulation and brain.

- The lag time between a puff of a cigarette and nicotine reaching the brain is 10–20 seconds
- Rapid onset of effect provides optimal reinforcement for development of drug dependence

## Metabolism

Primary metabolites of nicotine:

- Cotinine
- Nicotine-N-oxide

Metabolized by the liver

- Lung metabolizes some nicotine

## Excretion

Nicotine is excreted by glomerular filtration and tubular secretion within the kidney

- Urinary pH and urine flow rate effects reabsorption of nicotine

Half life is ~2 hours

## Pharmacodynamics

- The relationship between nicotine levels in the body and their effects on behavior and physiological function
  - Dose-Response relationship
  - Level of tolerance

## Drug Interactions With Tobacco Cessation Medication



### Significant Pharmacokinetic Interactions with Smoking Cessation

- **Caffeine** – increased metabolism & clearance
- **Theophylline** (Theo Dur, etc.) – increased metabolism & clearance, decreased half-life; also, increased clearance with 2nd hand smoke
- **Insulin** requirements may drop notably within 1 day of quitting
- **Warfarin** requirements drop with smoking cessation – may need up to a 12% decrease of dosage
- **Blood pressure and/or antidepressant drugs** may also need to be adjusted

## Significant Pharmacokinetic Interactions with Smoking

- **Clozapine** (Clozaril) – increased metabolism & decreased plasma concentrations
- **Olanzapine** (Zyprexa) – increased metabolism & clearance, decreased serum concentrations
- **Fluvoxamine** (Luvox) – increased metabolism & clearance, decreased plasma and area-under-curve concentrations
- **Tacrine** (Cognex) – increased metabolism, decreased half-life and serum concentrations

## Significant Pharmacodynamic Interactions with Smoking

- **Inhaled corticosteroids** – asthmatic smokers may have a reduced response to these
- **Hormonal contraceptives** – increased risk of adverse cardiovascular effects (e.g., MI, stroke, thromboembolism)
  - This risk increases with age (especially 35 + YOA) and heavier smoking (15+ cig./day)
- **Beta-blockers** – less effective antihypertensive and heart rate control effects

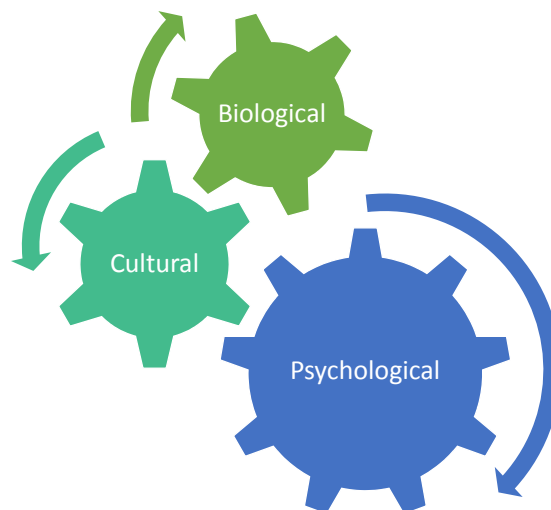


## Interactions with TB drugs

- No **significant** interactions
- **Bupropion** might have an interaction with linezolid
- **Cycloserine** and **bupropion** can both cause seizures-monitor the patient closely for any seizure activity
- Potential interaction with the **quinolones**

Overall, smoking cessation products have been used with TB patients and didn't have a problem with drug interactions

## Addiction Cycle



## Withdrawal Symptoms

- Tingling in hands/feet
- Sweating
- Nausea
- Headaches
- Coughing/Sore throat
- Insomnia
- Difficulty concentrating
- Irritability
- Weight gain



## Nicotine Withdrawal Timeline



# Nicotine Replacement Therapy



## Nicotine Replacement Therapy (NRT) & Non-nicotine pharmacotherapy (NNP)

There are 7 first-line medications available:

➤ 5 nicotine (NRT) and 2 non-nicotine (NNP)

- Prescription **ONLY**

- Nicotine Inhaler
- Nicotine Nasal Spray
- Bupropion SR (Wellbutrin, Zyban)
- Varenicline (Chantix)

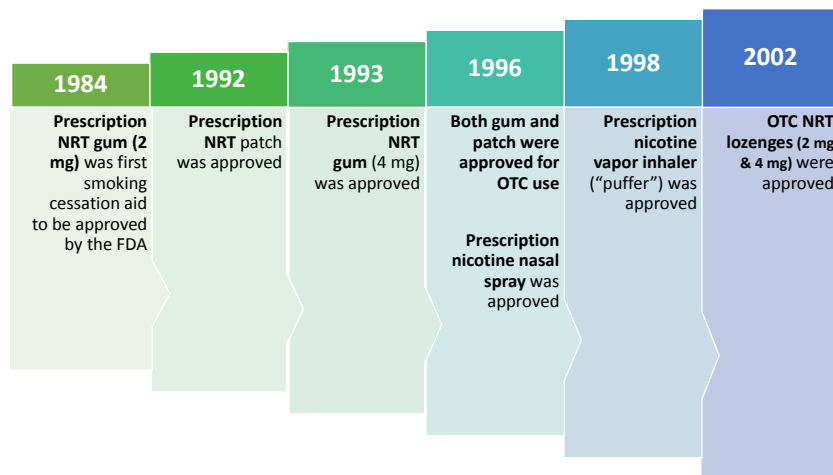


- OTC

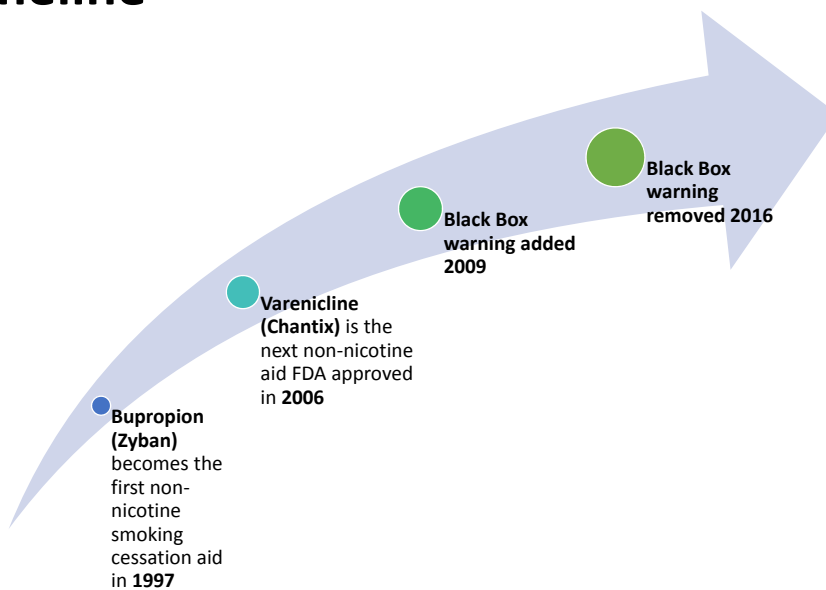
- Nicotine Patches
- Nicotine Gum
- Nicotine Lozenges



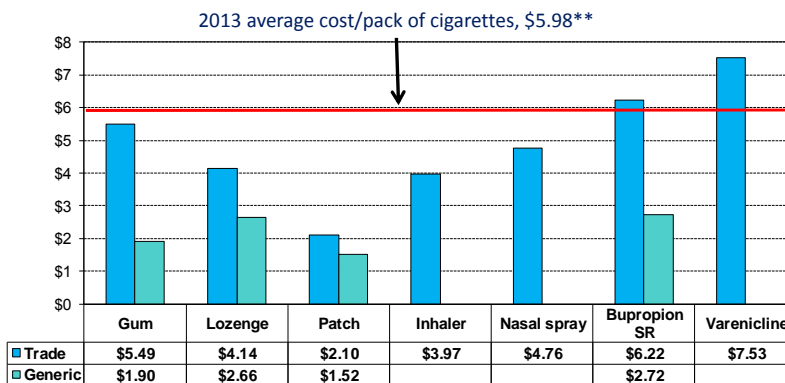
## NRT Timeline



## NNP Timeline



## Average Daily Costs of NRT/NNP



\*\* from Campaign for Tobacco Free Kids, avg. pack cost 2013 update

From Rx for Change, "Aids for Cessation" Power Point: <http://rxforchange.ucl.edu>, accessed 06/06/2014

Session 3031 Handout | November 9, 2012  
Essenmacher

### Nicotine Content in Tobacco Products

Product	Nicotine content	Suggested Rx
Cigarettes	1.1mg to 1.8mg per cigarette (22mg to 36mg/pack)	21mg patch QD x28 days <u>plus</u> NRT gum or NRT lozenge (4mg/2mg). Evaluate decrease patch dose monthly (PACT nurses to track?). <b>May add Bupropion if no contraindications.</b>
Cigars	13.3mg average	Patch and Short Acting NRT (4mg/2mg) based on # of cigars per day. <b>May add Bupropion if no contraindications.</b>
Mini-cigars (i.e. Swishers or Dark Horse)	3.8mg per mini-cigar = 76mg/pack	42mg to 21mg (depending on # smoked) <u>plus</u> Short Acting NRT (4mg/2mg). <b>May add Bupropion if no contraindications.</b>
Pipe	5.2mg average per bowl	Patch and Short Acting NRT (4mg/2mg) based on # of bowls smoked per day. <b>May add Bupropion if no contraindications.</b>
Chewing/dipping can (i.e. Skoal, Copenhagen)	88mg per can of dip/chew	42mg Patch and Short Acting NRT (4mg/2mg). <b>May add Bupropion if no contraindications.</b>
Loose leaf pouch (i.e. Redman)	144mg per pouch	42mg Patch and Short Acting NRT (4mg/2mg). <b>May add Bupropion if no contraindications.</b>
Hookah (water pipe)	One 45-60 minute session = approximately one pack of cigarettes in nicotine and tar content	21mg Patch and Short Acting NRT (4mg/2mg). <b>May add Bupropion if no contraindications.</b>
Bidi's (hand rolled cigarettes imported from India)	One bidi contains 3 to 5 times as much nicotine as a regular cigarette	Patch and Short Acting NRT (4mg/2mg) based on # of bidi's smoked per day. <b>May add Bupropion if no contraindications.</b>
Kretek (Clove cigarette)	Little research available. Increased risk of acute lung injury, especially with asthma or respiratory infections.	Short Acting NRT (4mg/2mg) based on # of Kretek's per day. <b>May add Bupropion if no contraindications.</b>
References available on request		

## Why NRT/NNP?

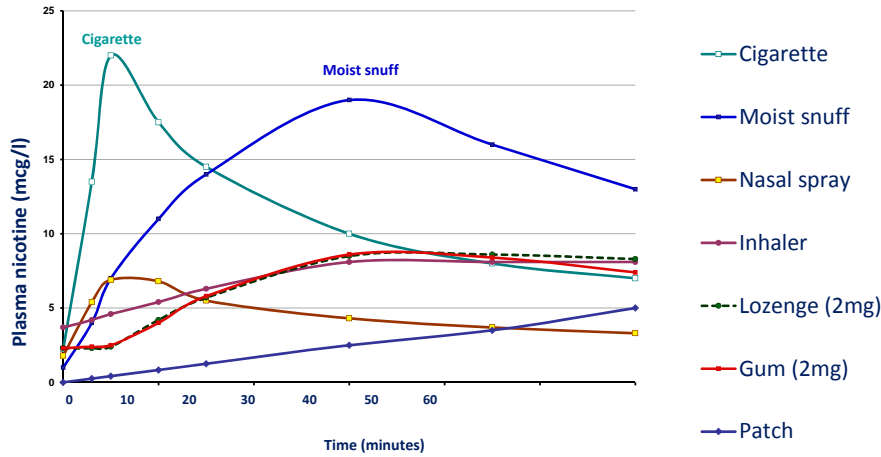
- More pharmacologic options **increase treatment-assisted quit attempts**
- Adding NRT/NNP to behavioral therapy greatly improves outcomes, **often doubling success rates**
- The World Health Organization **added NRT to its list of “essential medicines”** in March, 2009

MMWR July 28, 2000/49(29): 665-8 [http://www.who.int/tobacco/communications/Digitalize/quote\\_nrt\\_therapy/en/](http://www.who.int/tobacco/communications/Digitalize/quote_nrt_therapy/en/)

## NRT/NNP: To Use or Not?

USE	Talk to doctor first if...
<ul style="list-style-type: none"> <li>▪ <b>It works</b> – roughly <b>doubling</b> success rates</li> <li>▪ <b>Reduces severity of withdrawal symptoms</b></li> <li>▪ <b>Helps the patient feel more comfortable while they abstain</b></li> <li>▪ <b>It is very safe</b> <ul style="list-style-type: none"> <li>▪ Patient isn't getting any “new drug”, just the same one at lower dose, in a less addictive form, over a relatively short period of time</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Recent MI or arrhythmia</b></li> <li>▪ <b>Current pregnancy</b></li> <li>▪ <b>Under 18</b></li> <li>▪ <b>Bupropion</b> – seizure disorder, eating disorder, MAO use</li> <li>▪ <b>Concurrent medications</b></li> <li>▪ <b>Monitor psychiatric illness</b></li> <li>▪ <b>Varenicline</b> – kidney disease</li> </ul>

# Plasma Nicotine Concentrations for Nicotine-Containing Products



From Rx for Change, "Aids for Cessation" Power Point, <http://infoforchange.ucsf.edu>, accessed 07/01/2014

Tobacco Treatment Medication Dosing Chart							
Product	Nicotine Patch	Nicotine Gum	Nicotine Lozenge	Nicotine Nasal Spray	Nicotine Inhaler	Bupropion SR	Varenicline
Brand Name	Nicoderm CQ <sup>®</sup> Habitrol	Nicorette <sup>®</sup>	Nicorette <sup>®</sup>	Nicorette <sup>®</sup> NS <sup>®</sup>	Nicorette <sup>®</sup> Inhaler	Zyban <sup>®</sup>	Chantix <sup>®</sup>
Generic Available	Yes	Yes	Yes	No	No	Yes	No
Product Strength	21 mg, 14 mg, 7 mg	2 mg, 4 mg	2 mg, 4 mg	10 mg/mL, <i>varies by product</i>	10 mg/cartridge	150 mg SR	0.5 mg, 1 mg
Standard Dosing	1 patch/24 hours	Use one piece every 1-2 hours	Use one lozenge every 1-2 hours	1 spray each nostril/hour	6-16 cartridges/day	150 mg daily for 7 days & then twice daily	Begin 1 week before quit date
*Adjustments in dose and/or duration may be needed for optimal benefit and/or reducing risk of side effects	*11+ cigarettes per day, use 21 mg for 6 wks, 14 mg for 2 wks, 7 mg for 2 wks  *6-10 cigarettes per day, use 14 mg for 6 wks, 7 mg for 2 wks	If first cigarette within 30 min of waking—start with 4mg  Maximum 20 pieces/	If first cigarette within 30 min of waking—start with 4mg  Maximum 24 lozenges/	Do not exceed 5 doses per hour or 40 doses/day	Use for 6 months & taper over last 3 months	Start 7 days before target quit date	Starter Pack includes dose titration from 0.5 mg to 1 mg twice daily
Common Side Effects	Mild skin reactions; rotate site, apply 1% corticosteroid cream <u>Sleep disturbances (vivid dreams, insomnia not from withdrawal); may remove at night</u>	Mouth soreness, hiccups, jaw ache, indigestion.	Nausea, hiccups, heartburn, headache, coughing	Nose, throat or eye irritation; runny nose. Higher dependence potential compared to other NRT	Mouth or throat irritation, cough, taste change	Insomnia, dry mouth, gastrointestinal symptoms	Nausea, vomiting, gas, constipation, appetite change, headache, sleep disturbance, unusual dreams, drowsiness
Less common, Rare, or Serious Side Effects may include, but not limited to	Signs of excessive nicotine include: rapid heart rate, chest pain, dizziness, stomachache, diarrhea, nausea, vomiting, drooling, cold sweat, weakness, headache, confusion, shaking, seizure					Behavioral; include suicidality, agitation, violence, depressed or manic mood, confusion, hallucinations, impulsivity	Behavioral; include suicidality, agitation, violence, depressed mood, confusion, hallucinations, impulsivity <u>Cardiovascular</u> ; possible serious events like MI
Brief Instructions	Apply 1 patch to healthy, clean, dry, hairless skin like upper arm, upper back, shoulders, lower back, or hip. Replace daily after waking. Rotate skin site. Wash hands after handling. Avoid moisturizers under patch.	Chew gum until a peppery taste and slight tingle occurs, and park between cheek and gum. Repeat when taste fades, then park in another area of mouth. Avoid eating and drinking for 15 minutes before and after use.	Allow lozenge to dissolve slowly without chewing or swallowing. Occasionally move lozenge from the one side of mouth to the other. Avoid eating and drinking for 15 minutes before and after use.	Blow nose if not clear and tilt head back. Insert bottle tip as far as comfortable, angling toward wall of nostril. Do not sniff while spraying. Wait 2-3 minutes before blowing nose.	Inhale using short breaths or puffs to get vapor in mouth and throat but not lungs. Protect cartridges from excessive heat and light. Less effective if temperatures < 60 °F	Take with food	Swallow with water. Avoid taking at bedtime. Do not make up a missed dose by doubling up the next dose. Avoid using NRT with Chantix. May need dose reduction; renal disease, elderly, weight less than 100 lbs.
Relative Contraindications—partial list	Severe eczema or other skin disorder. Adhesive allergy.	Dental Disease, TMJ disease, dentures or other dental appliances, toothless.	Oral thrush, oral lesions.	Rhinitis, nasal polyps, sinusitis, asthma or other severe reactive airway disease.	Asthma or other severe reactive airway disease, COPD, allergy to menthol.	Seizure history or risk for seizures (e.g. bulimia, head injury, alcohol detox); some mental health conditions; uncontrolled hypertension	Suicidal, some serious mental health conditions (may be difficult to determine illness from adverse medication effect), recent cardiac event
Special Populations	Unstable cardiovascular disease and some acute post-op conditions—consult with a physician.  Must consider risks/benefits/alternatives to medication. <i>Pregnant/lactating women:</i> limited safety testing, no med FDA approved for tobacco treatment. <i>Truly:</i> no evidence for efficacy; probably safe, no FDA approved medication. <i>Cardiovascular disease:</i> NRT considered safe for most, but caution if recent MI or stroke, arrhythmias, unstable angina; 2011 CVD warnings with varenicline; bupropion may increase BP; consult with physician. <i>Psychiatric disorders:</i> all are generally safe, but potential for psychiatric destabilization with nicotine withdrawal, changes in psych med metabolism, and/or some of these medications, consider psychiatric consultation.						
Allergic Reactions	Possibly for any of these medications. Symptoms include: difficulty breathing or swallowing; swelling of face, mouth, tongue, lips, hives, blistering rash. Immediate medical assistance recommended.						
Rx Duration	Treatment is recommended for 3 months for most medications, but longer is appropriate for many people. Consultation with a health care provider is recommended for longer duration.						

## Tobacco Treatment Medication Dosing Chart

- **Suggests 3 months minimum length** of treatment for all medications
- **NRT/NNP use cautioned in:**
  - Pregnant women
  - Persons with unstable coronary syndrome (esp. heart attack within the past 2 weeks)
  - Persons under the age of 18
- **Chart for informational use only for patients and providers;** consult professional publications or manufacturers for more details

## NRT Usage: Nicotine Patch



3 patch strengths:	*If smoking >10 cigarettes/day:	If smoking ≤10 cigarettes/day:
<ul style="list-style-type: none"> <li>• 21mg</li> <li>• 14mg</li> <li>• 7mg</li> <li>• &lt;21mg*</li> </ul>	<ul style="list-style-type: none"> <li>• 21mg for 4 – 6 weeks</li> <li>• 14mg for 2 – 4 weeks</li> <li>• 7mg for 2 – 4 weeks</li> </ul>	<ul style="list-style-type: none"> <li>• 14mg for 6 weeks</li> <li>• 7mg for 2 weeks</li> </ul>

\* Product packaging slightly differs from chart



## NRT Usage: Nicotine Patch

- Apply to **clean, dry, hairless skin**
- **1 patch every 24 hours** – replace daily to prevent skin irritation
- Apply to **different areas of upper body**
- **Wash hands** after applying
- **DO NOT** cut the patch
- Skin irritation usually **caused by the adhesive, not the nicotine**



## NRT Usage: Nicotine Patch

- **Possible adverse reactions:**
  - Vivid dreams/sleep disturbance
  - Mild skin reactions (e.g. burning, itching)
- **Remove 1 – 2 hours before bed if sleep disturbance/vivid dreams occur;** apply new patch in the morning
- **Apply OTC cortisone cream or spray if rash occurs;** put cream under patch and reaffix to skin with medical tape
- Contraindicated in people with **severe eczema/skin disorders**

Tobacco Treatment Medication Dosing Chart, Center for Tobacco Independence

## NRT Usage: Nicotine Gum

**2 Strengths**

- 2mg
- 4 mg

**If first cigarette within 30 minutes of waking up:**

- 4mg
- 1 piece every 1-2 hours

**If first cigarette after 30 minutes:**

- 2mg
- 1 piece every 1-2 hours



Tobacco Treatment Medication Dosing Chart, Center for Tobacco Independence

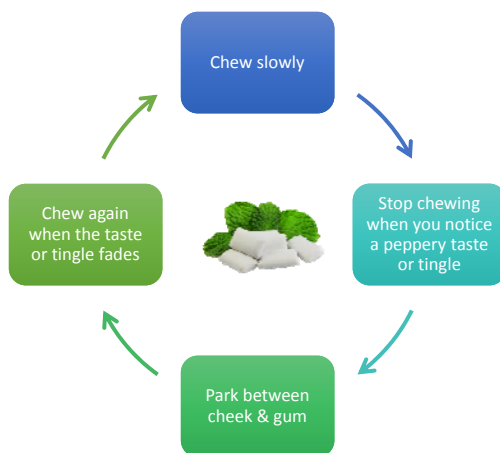
## NRT Usage: Nicotine Gum

- **Possible adverse reactions include:**
  - Mouth soreness
  - Hiccups
  - Indigestion
  - Jaw ache
  - Oral blistering (Sept. 2011 FDA packaging update)
- **Move gum around** to avoid mouth sores
- **Avoid chewing gum** too much to avoid jaw ache and indigestion
- **Caution** with peptic ulcers
- **Contraindicated with** TMJ disease or other jaw problems, dentures/other dental appliances or lack of teeth



Tobacco Treatment Medication Dosing Chart, Center for Tobacco Independence

## NRT Usage: Nicotine Gum



## NRT Usage: Nicotine Lozenge



**Strengths**

- 2mg
- 4 mg

**If first cigarette within 30 minutes of waking up:**

- 4mg
- 1 piece every 1-2 hours

**If first cigarette after 30 minutes:**

- 2mg
- 1 piece every 1-2 hours

Tobacco Treatment Medication Dosing Chart, Center for Tobacco Independence

## NRT Usage: Nicotine Lozenge

- **Allow to dissolve slowly for 10-30 minutes;** move from side to side of mouth
- **DO NOT** chew
- **DO NOT** use lozenge if oral thrush or oral lesions are present
- **Caution** with peptic ulcers
- **Avoid drinking acidic drinks 15 minutes** prior to and during lozenge use
- **Possible adverse side effects:**
  - Headache
  - Insomnia
  - Nausea
  - Indigestion
  - Hiccups

Tobacco Treatment Medication Dosing Chart, Center for Tobacco Independence

## Non-Nicotine Pharmacotherapy



## NRT Usage: Nasal Spray

- **1 – 2 doses/hour**
  - 1 dose = 1 spray/nostril
- **Do not exceed 5 doses/hour or 40 doses/day**
- **Prime pump** before first use
- **Blow nose prior** to application
- Insert bottle tip as far as comfortable, **angling away from septum**
- **Do not sniff** while spraying
- Used for **heavier smokers, dippers**
- **Higher dependence potential** compared to other NRT products
- Contraindications are **rhinitis, sinusitis or nasal polyps**



Tobacco Treatment Medication Dosing Chart, Center for Tobacco Independence

## NRT Usage: Nasal Spray

- **Possible adverse side effects** (usually short term):
  - Nose, throat or eye irritation
- **94% experience** these moderate to severe side effects within the first 2 days of starting the nasal spray:
  - Hot peppery feeling back of throat or nose
  - Sneezing
  - Coughing
  - Watery eyes
  - Runny nose



## NRT Usage: Nicotine Inhaler

- For use in any type smoker, but **generally not heavy smokers** due to slower administration
- **10mg/cartridge:**
  - 1 cartridge = 200 puffs
- **Use 6 – 16 cartridges/day**
- Pull top off, press cartridge in firmly until seal breaks; align marks on device to close
- **Not an actual inhaler** – nicotine is absorbed through oral lining
- To administer, use sipping or short puffing action
- **Satisfies handling habit** for some people

Tobacco Treatment Medication Dosing Chart, Center for Tobacco Independence

## NRT Usage: Nicotine Inhaler

- **Possible adverse reactions (usually short term):**
  - Mouth/throat irritation
  - Cough
- **Do NOT inhale into lungs**
- **Contraindicated in people** with asthma and/or allergy to menthol
  - Menthol is one of the ingredients in the cartridges



Tobacco Treatment Medication Dosing Chart, Center for Tobacco Independence  
Rx for Change, "Aids for Cessation" Power Point; <http://rxforchange.uscf.edu>, accessed 07/2014

## NNP: Bupropion SR

- Also known as **Zyban** or **Wellbutrin**
- **Produces mood elevating properties** and actually caused weight loss in some study participants
- Actual mechanism that promotes smoking cessation is unclear
- **Decreases withdrawal symptoms**



- **Bupropion differs** from other antidepressants in biochemical action in the brain:
  - Targets dopamine and to some extent noradrenaline – it reduces their re-uptake
  - **Does not alter** serotonin re-uptake
- **Decreases craving** for cigarettes

Tobacco Treatment Medication Dosing Chart, Center for Tobacco Independence  
Rx for Change, "Aids for Cessation" Power Point: <http://dx.doi.org/10.1186/1745-7214-10-104>, accessed 07/2014

## NNP: Bupropion SR

- Do not take bupropion with or within 14 days of discontinuing MAO inhibitor use – **bupropion lowers seizure threshold**
- **FDA recommends to discontinue meds and contact healthcare provider if experiencing:** agitation, hostility, atypical changes in behavior or thinking, suicidal thoughts or behavior

- **Possible adverse reactions include:**
  - Anxiety
  - Insomnia
  - Skin rash
  - Psychiatric symptoms
  - Depression
- **Off label use:** bupropion also used to treat ADD/ADHD

Tobacco Treatment Medication Dosing Chart, Center for Tobacco Independence

## NNP Usage: Bupropion SR

- 150 mg per dose
- Begin 3 – 7 days prior to quit date; **starting 7 – 10 days prior reduces side effects:**
  - 150 mg/day for first week
  - 150 mg twice/day until end of treatment (minimum 3 months) – **allow 8 hours between doses**
- Can reduce to once/day if adverse side effects occur
- **Contraindicated for people with** seizure history/risk, history of eating disorders, or if using MAO inhibitors

Tobacco Treatment Medication Dosing Chart, Center for Tobacco Independence

## NNP Usage: Varenicline

- Dose is 0.5 mg to 1 mg
- Begin 1 week before quit date
- **Starter pack used to titrate from 0.5 mg daily to 1.0 mg twice/day:**
  - 0.5 mg in morning only for 3 days
  - 0.5 mg twice/day for 4 days
  - 1mg twice/day until end of treatment (minimum 3 months)
- Can reduce to once/day if adverse side effects occur
- Take with food and water if possible



Tobacco Treatment Medication Dosing Chart, Center for Tobacco Independence



## NNP: Varenicline (Chantix)

- It is a **partial agonist** (activator) selective for the  $\alpha_4\beta_2$  nicotinic acetylcholine receptor subtype
- This partial activation is believed to **diminish nicotine withdrawal symptoms** by **enhancing mesolimbic** (“reward pathway”) **dopamine levels**, but at a lower level than nicotine would produce
- **Approved by FDA for monotherapy**; further studies needed to evaluate combination therapy



The Annals of Pharmacotherapy 2007 January, Volume 41 (pgs. 96-98)

## NNP Usage: Varenicline

- **Possible adverse reactions include:**
  - Nausea
  - Headache
  - Sleep disturbance/unusual dreams
  - Possible psychiatric symptoms/depression
- **FDA recommends to discontinue meds and contact healthcare provider if experiencing:** agitation, hostility, atypical changes in behavior or thinking, suicidal thoughts or behavior
- **Also reported: serious allergic/inflammatory reaction**
  - Swelling of face, lips, tongue, throat, neck
  - Hives
  - Breathing difficulties
  - Blistering rash in mouth or on skin
- **REMEMBER:** allergic reactions can happen with any medication

Tobacco Treatment Medication Dosing Chart, Center for Tobacco Independence

## Update: 2009 Varenicline Study

- October 2009 study in UK showed **Varenicline side effects are comparable to other cessation medications**
- Varenicline has **best cessation rates** of any NNP available and is **generally well tolerated**
- A two fold increase in risk of self harm cannot be ruled out due to the study parameters
- **REMEMBER:** depression and suicidal thoughts are also potential side effects of nicotine withdrawal

BMJ 2009;339:b3805

## 2009 FDA Update

- **July, 2009**--Varenicline (marketed as Chantix) and Bupropion (marketed as Zyban, Wellbutrin, and generics) received Boxed Warnings
- Highly publicized **reports of depression, suicidal thoughts/attempts, unusual changes in behavior**
- **Monitor patients** on these meds closely until symptoms resolve (during use and as needed after discontinuing use)
- **Small percentage** of patients experience serious adverse side effects
- **Benefits still outweigh risks**

<http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHealthcareProfessionals/ucm169986.htm>

## 2016 FDA Update

- EAGLES Trial published in The Lancet in April 2016
  - 8,144 participants between ages 18 and 75
  - Smoked more than ½ pack per day
  - Half with and half without psychiatric history
  - Neuropsychiatric symptoms with Varenicline just slightly more in psychiatric history
  - Benefit of Varenicline in smoking cessation outweighed the symptoms

## 2016 FDA Update

- FDA advisory board recommended that black box warning regarding neuropsychiatric symptoms be removed in September 2016
- Black Box warning was removed in December 2016
- Current recommendations
  - Clinicians should not prescribe Varenicline to smokers who have experienced suicidal ideation in the past year or those who are currently unstable regarding their mental health issues
  - If a smoker has a Mental Health provider, that provider should be consulted before initiating Varenicline

<http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHealthcareProfessionals/ucm169986.htm>

## Combination Therapy

- Patch +NRT gum
- Patch +NRT lozenge
- Patch +Bupropion SR
- Patch +Inhaler

## NRT for Other Tobacco Users



## NRT Usage For Smokeless/Other Tobacco Users

- Clinical Practice Guideline **does not recommend NRT** for smokeless/other tobacco users due to lack of studies proving efficacy
- Suggested dosages on dosing chart **based on cigarette equivalent of daily use**
- Doses should then be **self-titrated**



## NRT Usage For Smokeless Tobacco Users

- **1 can/week or more**  
(equals up to 4 packs of cigarettes )
  - 21 mg patch 4 – 6 weeks,  
14 mg 2 – 4 weeks, 7 mg 2 – 4 weeks
  - 4 mg gum or lozenge
- **Less than 1 can/week**
  - 14 mg patch 4 – 6 weeks,  
7 mg 2 – 4 weeks
  - 2 mg gum or lozenge
- High Dose Nicotine Patch
  - 21mg, 42mg, 53 mg



## Cigarette vs. Cigar



## NRT Suggestions For Cigar Users

- **2 medium cigars/day or more** (equals about 12 strong cigarettes)

- 21 mg patch 4 weeks, 14 mg 2 weeks, 7 mg 2 weeks
- 4 mg gum or lozenge
- Nicotine inhaler, 6 – 16 cartridges/day as needed



- **Less than 2 medium cigars/day**

- 14 mg patch 2 weeks, 7 mg 2 weeks
- 2 mg gum or lozenge
- Nicotine inhaler, 6 – 10 cartridges/day as needed
- **Little Cigars/One ppd** (one equals about four strong cigarettes)
- 42mg to 21mg patch (depending on # smoked) plus
- 4 mg gum or lozenge, depending on when first one is smoked



## Department of Health & Human Services Clinical Practice Guideline: 2008 Update

- **Off label discussion:**

- Using cessation medications in certain combinations **is more effective**



## Clinical Practice Guideline: 2008 Statements

- Many current studies show **combining therapies greatly increases success rates**
- FDA has yet to approve most combination usages: **it currently approves only NRT + bupropion**
- Some researchers recommend **continuing combination therapy for 3 – 6 months, or longer**

## Clinical Practice Guideline: 2008 Recommendations

- **Suggested combinations (as tolerated):**
  - Nicotine patch + nicotine gum or lozenge
  - Nicotine patch + nicotine nasal spray or inhaler (“puffer”)
  - Nicotine patch + Bupropion SR
- **Not recommended** to use NRT with Varenicline/Chantix (nicotine antagonist)
- If patient is using Wellbutrin, **DO NOT** prescribe Zyban/Bupropion SR & vice versa (same medication)

Treating Tobacco Use and Dependence: Clinical Practice Guideline, 2008 Update: pgs. 109, 114, 47

## Which product is BEST for my patient?

- **Double check** current medications being taken
- **Ensure** no contraindicated diseases/symptoms exist
- **Ask about** past cessation attempts and medications used
- **Ask if** patient is willing to try something new or revisit NRT/NNP



“Pharmacology of Smoking Cessation”, Arch Fam Med/vol. 9, Mar 2000



## Which product is best for my patient?

- **Method/ease of usage** can have impact on compliance
- **Patient Compliance Rates for NRT:**
  - **Patch** 82%
  - **Gum** 38%
  - **Spray** 15%
  - **Inhaler** 11%



Compliance can be increased by following up,  
and checking in with patients!

<http://www3.umn.edu/perio/tobacco/pharmacotherapy.html>  
Arch Intern Med. 1999; 159: 2033-2038

## Which product is best for my patient?

- **Usage rates in patients**
  - **5 – 20%** of nicotine gum users continue use after 1 year or more
  - **43%** of nicotine nasal spray users continue use at 1 year
  - Longer term use not typical with patch, inhaler and Zyban

**Note: recent studies have shown NO ADVERSE EVENTS  
with extended NRT/NNP use**

Treating Tobacco Use and Dependence: Clinical Practice Guideline, 2008 Update  
<http://www1.umn.edu/perio/tobacco/pharmacotherapy.html>

**Mark Your Calendar**

September 5:  
Treating Tobacco Dependence in Special Populations

Southeastern National Tuberculosis Center

UNIVERSITY OF FLORIDA

AHEC  
SUWANNEE RIVER  
AREA HEALTH EDUCATION CENTER