

SMOKING CESSATION TREATMENT INTERVENTIONS



Smoking and Health



- Tobacco is the single most preventable cause of death in the world today.
- kills more than five million people
- By 2030, the death toll will exceed eight million a year.
- The only legal consumer product that can harm everyone exposed to it.

Smoking and Health



- **Cigarette smoking increases the risk of**
 - **Cardiovascular diseases such as stroke, sudden death, and heart attack.**
 - **Nonmalignant respiratory diseases including emphysema, asthma, chronic bronchitis, and chronic obstructive pulmonary disease.**
 - **Lung cancer.**
 - **Other cancers (e.g., mouth, pharynx, larynx, esophagus, stomach, pancreas, uterus, cervix, kidney, ureter, and bladder).**



Passive smoking and children:

Babies and children exposed to tobacco smoke are at serious risk of:

- Sudden infant death syndrome (SIDS).
- Bronchitis, pneumonia and other lung or airway infections.
- Worsening of asthma.
- Respiratory symptoms such as coughing and wheezing.
- Middle ear disease ('glue ear')



Smoking kills your profits even faster than it kills your employees.

- * If 30% of employees are smokers,
- * Each smoker smokes 6 cigarettes during work duty,
- * 5 minutes per cigarette wasted time, which results in 30 minutes total daily wasted time,
- * If average work hour costs SR25,
- * A company with 100 smokers, the profit loss is not less than SR302,500 annually not including medical expenses.

[SR25X0.5HoursDailyX22daysMonthlyX11MonthsYearlyX100Employees]

Nicotine



- Nicotine is a ganglionic cholinergic receptor agonist with pharmacologic effects that are highly dependent on dose.
- Pharmacological effects: central and peripheral nervous system stimulation and depression, respiratory stimulation, skeletal muscle relaxation, catecholamine release by the adrenal medulla, peripheral vasoconstriction, and increased blood pressure, heart rate, cardiac output, and oxygen consumption.
- Cigarette smoking or low doses of nicotine produce an increased alertness and increased cognitive functioning by stimulating the cerebral cortex.
- At higher doses, nicotine stimulates the “reward” center in the limbic system of the brain.

Nicotine

- Chronic nicotine ingestion can lead to physical and psychologic dependence and tolerance to some of its pharmacologic effects.
- Abrupt smoking cessation in physically dependent smokers results in withdrawal symptoms

TABLE 65–4. Withdrawal Symptoms of Nicotine

Anxiety	Gastrointestinal disturbances
Craving for tobacco	Headache
Decreased blood pressure and heart rate	Hostility
Depression	Increased appetite and weight gain
Difficulty concentrating	Increased skin temperature
Drowsiness	Insomnia
Frustration, irritability, impatience	Restlessness

TREATMENT



TREATING TOBACCO USE AND DEPENDENCE

2008 UPDATE

U.S. Public Health Service
Clinical Practice Guideline



10 Key Guideline Recommendations

10 Key Guideline Recommendations

1. Tobacco dependence is a chronic disease that often requires repeated intervention and multiple attempts to quit. However, effective treatments exist that can significantly increase rates of long-term abstinence.
2. It is essential that clinicians and healthcare delivery systems consistently identify and document tobacco use status and treat every tobacco user seen in a healthcare setting.

10 Key Guideline Recommendations



3. Tobacco dependence treatments are effective across a broad range of populations. Clinicians should encourage every patient willing to make a quit attempt to use the counseling treatments and medications recommended in this Guideline.

10 Key Guideline Recommendations



4. Brief tobacco dependence treatment is effective.

Clinicians should offer every patient who uses tobacco at least the brief treatments shown to be effective in this Guideline.

5. Individual, group and telephone counseling are effective, and their effectiveness increases with treatment intensity. Two components of counseling are especially effective and clinicians should use these when counseling patients making a quit attempt.

- Practical counseling (problemsolving/skills training)
- Social support delivered as part of treatment

10 Key Guideline Recommendations

6. There are numerous effective medications for tobacco dependence and clinicians should encourage their use by all patients attempting to quit smoking, except when medically contraindicated or with specific populations for which there is insufficient evidence of effectiveness (i.e., pregnant women, smokeless tobacco users, light smokers and adolescents).

- Seven first-line medications (5 nicotine and 2 non-nicotine) reliably increase long-term smoking abstinence rates:

Bupropion SR	Nicotine nasal spray
Nicotine gum	Nicotine patch
Nicotine inhaler	Varenicline
Nicotine lozenge	

- **Clinicians should also consider the use of certain combinations of medications identified as effective in this Guideline.**

10 Key Guideline Recommendations



7. Counseling and medication are effective when used by themselves for treating tobacco dependence. However, the combination of counseling and medication is more effective than either alone. Thus, clinicians should encourage all individuals making a quit attempt to use both counseling and medication.
8. Telephone quitline counseling is effective with diverse populations and has broad reach. Therefore, clinicians and healthcare delivery systems should both ensure patient access to quitlines and promote quitline use.

10 Key Guideline Recommendations



9. If a tobacco user is currently unwilling to make a quit attempt, clinicians should use the motivational treatments shown in this Guideline to be effective in increasing future quit attempts.

10. Tobacco dependence treatments are both clinically effective and highly cost-effective relative to interventions for other clinical disorders. Providing coverage for these treatments increases quit rates. Insurers and purchasers should ensure that all insurance plans include the counseling and medication identified as effective in this Guideline as covered benefits.

Combinations: Medication and Counseling

Effectiveness of and estimated abstinence rates for the combination of counseling and medication versus medication alone (n = 18 studies)

Treatment	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Medication alone	8	1.0	21.7
Medication and counseling	39	1.4 (1.2, 1.6)	27.6 (25.0, 30.3)

Combinations: Medication and Counseling

Effectiveness of and estimated abstinence rates for the combination of counseling and medication versus counseling alone (n = 9 studies)

Treatment	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Counseling alone	11	1.0	14.6
Medication and counseling	13	1.7 (1.3, 2.1)	22.1 (18.1, 26.8)

Treatment Recommendations – Counseling

Combining Counseling and Medication

Recommendation: The combination of counseling and medication is more effective for smoking cessation than either medication or counseling alone. Therefore, whenever feasible and appropriate, both counseling and medication should be provided to patients trying to quit smoking. (Strength of Evidence = A).

Recommendation: There is a strong relation between the number of sessions of counseling when it is combined with medication, and the likelihood of successful smoking cessation. Therefore, to the extent possible, clinicians should provide multiple counseling sessions, in addition to medication, to their patients who are trying to quit smoking. (Strength of Evidence = A).

Strength of Evidence for Recommendations

20

Classification	Criteria
Strength of Evidence = A	Multiple well-designed randomized clinical trials, directly relevant to the recommendation, yielded a consistent pattern of findings.
Strength of Evidence = B	Some evidence from randomized clinical trials supported the recommendation, but the scientific support was not optimal. For instance, few randomized trials existed, the trials that did exist were somewhat inconsistent, or the trials were not directly relevant to the recommendation.
Strength of Evidence = C	Reserved for important clinical situations where the panel achieved consensus on the recommendation in the absence of relevant randomized controlled trials.

Pro-Active Quitlines

Effectiveness of and estimated abstinence rates for quitline counseling compared to minimal interventions, self-help or no counseling (n = 9 studies)

Intervention	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Minimal or no counseling or self-help	11	1.0	8.5
Quitline counseling	11	1.6 (1.4, 1.8)	12.7 (11.3, 14.2)

Pro-Active Quitlines

22

Effectiveness of and estimated abstinence rates for quitline counseling and medication compared to medication alone (n = 6 studies)

Intervention	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Medication alone	6	1.0	23.2
Medication and quitline counseling	6	1.3 (1.1, 1.6)	28.1 (24.5, 32.0)

Medication



Seven first-line medications shown to be effective and recommended for use by the Guideline Panel:

- ▣ Bupropion SR
- ▣ Nicotine Gum
- ▣ Nicotine Inhaler
- ▣ Nicotine Lozenge
- ▣ Nicotine Nasal Spray
- ▣ Nicotine Patch
- ▣ Varenicline

Varenicline

Effectiveness and abstinence rates for various medications and medication combinations compared to placebo at 6-months post-quit (n = 86 studies)

Medication	Number of arms	Estimated odds ratio (95% C. I.)	Estimated abstinence rate (95% C. I.)
Placebo	80	1.0	13.8
Varenicline (2 mg/day)	5	3.1 (2.5, 3.8)	33.2 (28.9, 37.8)

Nicotine Lozenge

Effectiveness of the nicotine lozenge: Results from the single randomized controlled trial.

Lozenge Dose	N for active/ N for placebo	Odds Ratio (95% C.I.)	Continuous abstinence rates at 6 months (Active/Placebo)
2 mg	459/458	2.0 (1.4, 2.8)	24.2/14.4
4 mg	450/451	2.8 (1.9, 4.0)	23.6/10.2

Relative Efficacy

Medication	Number of arms	Estimated odds ratio (95% C. I.)
Nicotine Patch (reference group)	32	1.0
Varenicline (2 mg/day)	5	1.6 (1.3, 2.0)
Patch (long-term; >14 weeks) + NRT (gum or spray)	3	1.9 (1.3, 2.7)
Patch + Bupropion SR	3	1.3 (1.0, 1.8)

Medication Recommendation

Recommendation: Certain combinations of first-line medications have been shown to be effective smoking cessation treatments. Therefore, clinicians should consider using these combinations of medications with their patients who are willing to quit. Effective combination medications are:

- * Long-term (> 14 weeks) nicotine patch + other NRT (gum and spray)
- * The nicotine patch + the nicotine inhaler
- * The nicotine patch + bupropion SR.

(Strength of Evidence = A)

Specific Populations



- Children and Adolescent Smokers
- Light Smokers
- Noncigarette Tobacco Users
- Pregnant Smokers

Systems Interventions: Clinician Training and Chart Reminders



Clinician Training and Reminder Systems:

Recommendation: All clinicians and clinicians-in-training should be trained in effective strategies to assist tobacco users willing to make a quit attempt and to motivate those unwilling to quit. Training appears to be more effective when coupled with systems changes.
(Strength of Evidence = B).

The "5 A's" Model for Treating Tobacco Use and Dependence - 2008

Ask about tobacco use. Identify and document tobacco use status for every patient at every visit.

Advise to quit. In a clear, strong and personalized manner urge every tobacco user to quit.

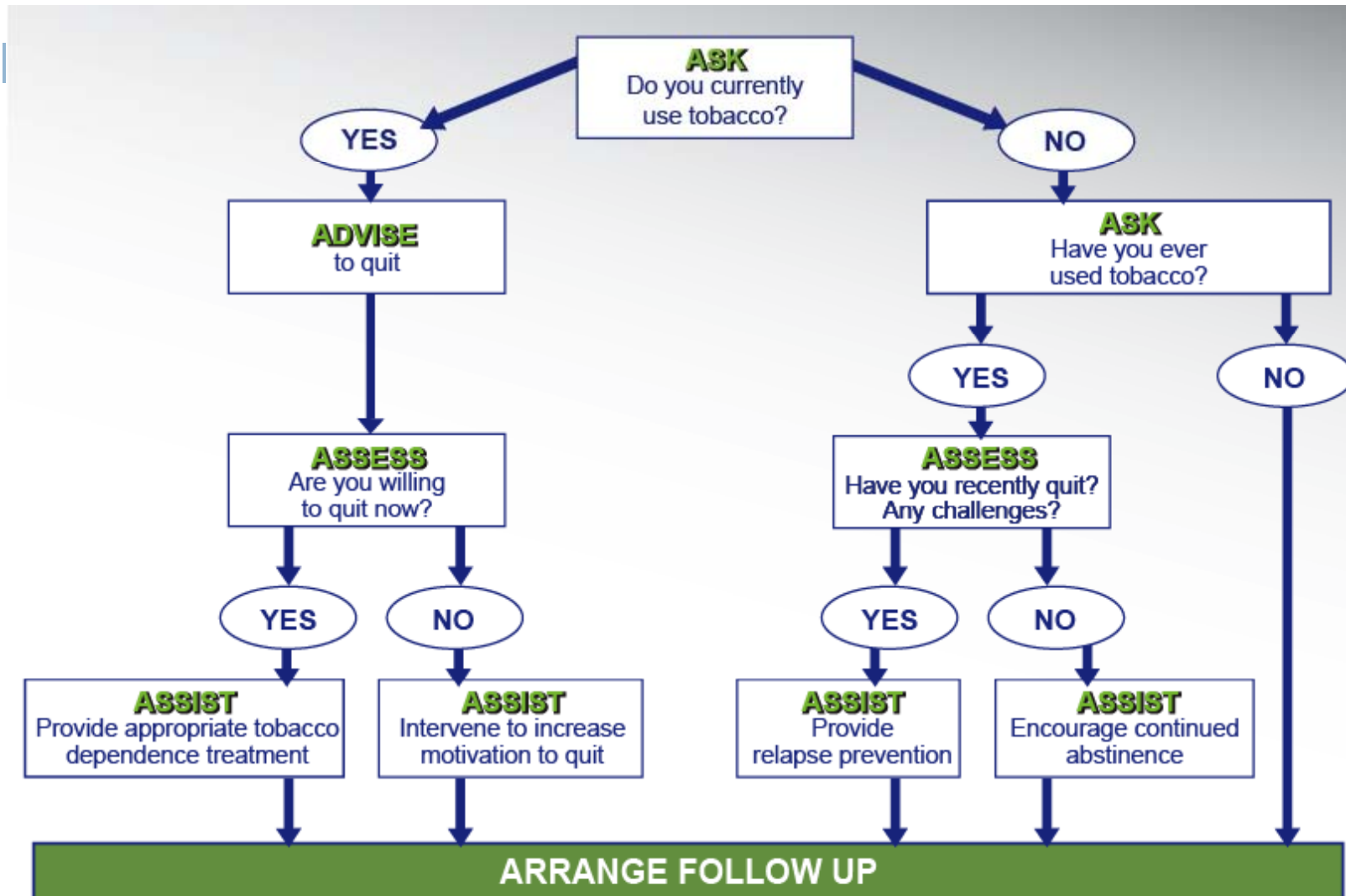
Assess willingness to make a quit attempt. Is the tobacco user willing to make a quit attempt at this time?

Assist in quit attempt. For the patient willing to make a quit attempt, offer medication and provide or refer for counseling or additional treatment to help the patient quit. **For patients unwilling to quit at the time, provide interventions designed to increase future quit attempts.**

Arrange follow-up. For the patient willing to make a quit attempt, arrange for follow-up contacts, beginning within the first week after the quit date.

For patients unwilling to make a quit attempt at the time, address tobacco dependence and willingness to quit at next clinic visit.

The "5 A's" Model for Treating Tobacco Use and Dependence - 2008



Treatment Recommendations - Medication

Treatment Recommendations – Medications



Recommendation: Clinicians should encourage all patients attempting to quit to use effective medications for tobacco dependence treatment except where contraindicated or for specific populations for which there is insufficient evidence of effectiveness (i.e., pregnant women, smokeless tobacco users, light smokers and adolescents).
(Strength of Evidence = A).

Treatment Recommendations – Medications

Coding rules for medication duration and dose

Medication	Coding	Meaning
Nicotine Patch	Usual duration	6-14 weeks
	Long duration	> 14 weeks
	Usual dose/day	15mg/16 hours/day 21mg/24 hours/day
	High dose	> 25 mg/day
Nicotine Gum	Usual duration	6-14 weeks
	Long duration	> 14 weeks

Treatment Recommendations – Medications

Coding rules for medication duration and dose (cont.)

Nicotine Inhaler and Nasal Spray	Usual duration	Up to 6 months
	Long duration	> 6 months
Bupropion SR	Usual duration	Up to 14 weeks
	Usual dose/day	150 mg once daily or twice daily
Varenicline	Usual duration	Up to 14 weeks
	Usual dose/day	1 mg daily or 1 mg twice daily

Bupropion SR



- Bupropion inhibits neuronal reuptake and potentiates the effects of norepinephrine and dopamine.
- Withdrawal symptoms can be decreased by virtue of bupropion inhibition of norepinephrine uptake.
- **Recommendation:** Bupropion SR is an effective smoking cessation treatment that patients should be encouraged to use. (Strength of Evidence = A).

Bupropion SR

Patient selection	Appropriate as a first-line medication for treating tobacco use.
Precautions, warnings, contraindications and side effects	<p>Pregnancy – Pregnant smokers should be encouraged to quit without medication. Bupropion has not been shown to be effective for tobacco dependence treatment in pregnant smokers. (Bupropion is an FDA pregnancy Class C agent.) Bupropion has not been evaluated in breast-feeding patients.</p> <p>Cardiovascular diseases – Generally well-tolerated; occasional reports of hypertension.</p> <p>Side effects – The most common reported side effects were insomnia (35-40%) and dry mouth (10%).</p> <p>Contraindications – Bupropion SR is contraindicated in individuals who have a history of seizures or eating disorder, who are taking another form of bupropion, or who have used an MAO inhibitor in the past 14 days.</p> <p>Warning - In July, 2009, the FDA issued a boxed warning regarding the use of bupropion. Specifically, the use of bupropion has been associated with reports of changes in behavior such as hostility, agitation, depressed mood and suicidal thoughts or actions. The FDA is requiring the manufacturer of this product to add a new Boxed Warning to the product labeling to alert healthcare professionals to this important new safety information. People who are taking bupropion and experience any serious or unusual changes in mood or behavior or who feel like hurting themselves or someone else should stop taking the medicine and call their healthcare professional right away. In light of these FDA recommendations, clinicians should consider eliciting information on their patients' psychiatric history and monitoring for changes in mood and behavior.</p>
Dosage	Patients should begin bupropion SR treatment 1-2 weeks before they quit smoking. Patients should begin with a dose of 150 mg every morning for 3 days, then increase to 150 mg twice daily. Dosage should not exceed 300 mg per day. Dosing at 150 mg twice daily should continue for 7-12 weeks. For long-term therapy, consider use of bupropion SR 150 mg for up to 6 months post-quit.
Availability	Prescription only
Prescribing instructions	<p>Stopping smoking prior to quit date – Recognize that some patients may lose their desire to smoke prior to their quit date, or will spontaneously reduce the amount they smoke.</p> <p>Dosing information – If insomnia is marked, taking the PM dose earlier (in the afternoon, at least 8 hours after the first dose) may provide some relief.</p>

Nicotine Gum



Recommendation: Nicotine gum is an effective smoking cessation treatment that patients should be encouraged to use. (Strength of Evidence = A).

Recommendation: Clinicians should offer 4 mg rather than 2 mg nicotine gum to highly dependent smokers. (Strength of Evidence = B).

Nicotine Gum

Patient selection	Appropriate as a first-line medication for treating tobacco use.
Precautions, warnings, contraindications and side effects	<p>Pregnancy – Pregnant smokers should be encouraged to quit without medication. Nicotine gum has not been shown to be effective for treating tobacco dependence in pregnant smokers. (Nicotine gum is an FDA pregnancy Class D agent.) Nicotine gum has not been evaluated in breast-feeding patients.</p> <p>Cardiovascular diseases – NRT is not an independent risk factor for acute myocardial events. NRT should be used with caution among particular cardiovascular patient groups: those in the immediate (within 2 weeks) post myocardial infarction period, those with serious arrhythmias, and those with unstable angina pectoris.</p> <p>Side effects – Common side effects of nicotine gum include mouth soreness, hiccups, dyspepsia, and jaw ache. These effects are generally mild and transient, and often can be alleviated by correcting the patient’s chewing technique.</p>
Dosage	Nicotine gum (both regular and flavored) is available in 2 mg and 4 mg (per piece) doses. The 2 mg gum is recommended for patients smoking less than 25 cigarettes per day, while the 4 mg gum is recommended for patients smoking 25 or more cigarettes per day. Smokers should use at least 1 piece every 1 to 2 hours for the first six weeks and the gum should be used for up to 12 weeks with no more than 24 pieces/day.
Availability	OTC only

Nicotine Gum (cont.)

Prescribing instructions	<p>Chewing technique – Gum should be chewed slowly until a “peppery” or “flavored” taste emerges, then “parked” between cheek and gum to facilitate nicotine absorption through the oral mucosa. Gum should be slowly and intermittently “chewed and parked” for about 30 minutes or until the taste dissipates.</p> <p>Absorption – Acidic beverages (e.g., coffee, juices, soft drinks) interfere with the buccal absorption of nicotine, so eating and drinking anything except water should be avoided for 15 minutes before or during chewing.</p> <p>Dosing information – Patients often do not use enough prn NRT medicines to obtain optimal clinical effects. Instructions to chew the gum on a fixed schedule (at least one piece every 1-2 hours) for at least 1-3 months may be more beneficial than <i>ad libitum</i> use.</p>

Nicotine Inhaler



Recommendation: The nicotine inhaler is an effective smoking cessation treatment that patients should be encouraged to use. (Strength of Evidence = A).

Nicotine Inhaler

42

Patient selection	Appropriate as a first-line medication for treating tobacco use.
Precautions, warnings, contraindications and side effects .	<p>Pregnancy – Pregnant smokers should be encouraged to quit without medication. The nicotine inhaler has not been shown to be effective for treating tobacco dependence in pregnant smokers. (The nicotine inhaler is an FDA pregnancy Class D agent.) The nicotine inhaler has not been evaluated in breast-feeding patients.</p> <p>Cardiovascular diseases – NRT is not an independent risk factor for acute myocardial events. NRT should be used with caution among particular cardiovascular patient groups: those in the immediate (within 2 weeks) post myocardial infarction period, those with serious arrhythmias, and those with unstable angina pectoris.</p> <p>Local irritation reactions – Local irritation in the mouth and throat was observed in 40% of patients using the nicotine inhaler. Coughing (32%) and rhinitis (23%) also were common. Severity was generally rated as mild, and the frequency of such symptoms declined with continued use.</p>
Dosage	<p>A dose from the nicotine inhaler consists of a puff or inhalation. Each cartridge delivers a total of 4 mg of nicotine over 80 inhalations. Recommended dosage is 6-16 cartridges/day. Recommended duration of therapy is up to 6 months. Instruct patient to taper dosage during the final 3 months of treatment.</p>

Nicotine Inhaler (cont.)

Availability	Prescription only
Prescribing instructions	<p>Ambient temperature – Delivery of nicotine from the inhaler declines significantly at temperatures below 40°F. In cold weather, the inhaler and cartridges should be kept in an inside pocket or other warm area.</p> <p>Absorption – Acidic beverages (e.g., coffee, juices, soft drinks) interfere with the buccal absorption of nicotine, so eating and drinking anything except water should be avoided for 15 minutes before or during use of the inhaler.</p> <p>Dosing information – Patients often do not use enough prn NRT medicines to obtain optimal clinical effects. Use is recommended for up to 6 months with gradual reduction in frequency of use over the last 6-12 weeks of treatment. Best effects are achieved by frequent puffing of the inhaler and using at least 6 cartridges/day.</p>

Nicotine Lozenge



Recommendation: The nicotine lozenge is an effective smoking cessation treatment that patients should be encouraged to use.
(Strength of Evidence = B).

Nicotine Lozenge

45

Patient selection	Appropriate as a first-line medication for treating tobacco use.
Precautions, warnings, contraindications and side effects	<p>Pregnancy – Pregnant smokers should be encouraged to quit without medication. The nicotine lozenge has not been shown to be effective for treating tobacco dependence for pregnant smokers. The nicotine lozenge has not been evaluated in breast-feeding patients. Because the lozenge was approved as an over-the-counter agent, it was not evaluated by the FDA for teratogenicity.</p> <p>Cardiovascular diseases – NRT is not an independent risk factor for acute myocardial events. NRT should be used with caution among particular cardiovascular patient groups: those in the immediate (within 2 weeks) postmyocardial infarction period, those with serious arrhythmias, and those with unstable angina pectoris.</p> <p>Side effects – The most common side effects of the nicotine lozenge are nausea, hiccups, and heartburn. Individuals on the 4 mg lozenge also had increased rates of headache and coughing (less than 10% of participants).</p>
Dosage	Nicotine lozenges are available in 2 mg and 4 mg (per piece) doses. The 2 mg lozenge is recommended for patients who smoke their first cigarette more than 30 minutes after waking, while the 4 mg lozenge is recommended for patients who smoke their first cigarette within 30 minutes of waking. Generally, smokers should use at least 9 lozenges per day in the first six weeks. The lozenge should be used for up to 12 weeks with no more than 20 lozenges/day.

Nicotine Lozenge (cont.)

Availability	OTC only
Prescribing instructions	<p>Lozenge use – The lozenge should be allowed to dissolve in the mouth rather than chewing or swallowing it.</p> <p>Absorption – Acidic beverages (e.g., coffee, juices, soft drinks) interfere with the buccal absorption of nicotine, so eating and drinking anything except water should be avoided for 15 minutes before or during use of the nicotine lozenge.</p> <p>Dosing information – Patients often do not use enough prn NRT medicines to obtain optimal clinical effects. Generally, patients should use one lozenge every 1-2 hours during the first six weeks of treatment, using a minimum of 9 lozenges/day, then decrease lozenge use to one lozenge every 2-4 hours during Weeks 7-9, and then to one lozenge every 4-8 hours for Weeks 10-12.</p>

Nicotine Nasal Spray



Recommendation: Nicotine nasal spray is an effective smoking cessation treatment that patients should be encouraged to use.
(Strength of Evidence = A).

Nicotine Nasal Spray

48

Patient selection	Appropriate as a first-line medication for treating tobacco use.
Precautions, warnings, contraindications and side effects	<p>Pregnancy – Pregnant smokers should be encouraged to quit without medication. Nicotine nasal spray has not been shown to be effective for treating tobacco dependence in pregnant smokers. (Nicotine nasal spray is an FDA pregnancy Class D agent.) Nicotine nasal spray has not been evaluated in breast-feeding patients.</p> <p>Cardiovascular diseases – NRT is not an independent risk factor for acute myocardial events. NRT should be used with caution among particular cardiovascular patient groups: those in the immediate (within 2 weeks) postmyocardial infarction period, those with serious arrhythmias, and those with unstable angina pectoris.</p> <p>Nasal/airway reactions – Some 94% of users report moderate to severe nasal irritation in the first 2 days of use; 81% still reported nasal irritation after 3 weeks, although rated severity was typically mild to moderate. Nasal congestion and transient changes in sense of smell and taste also were reported. Nicotine nasal spray should not be used in persons with severe reactive airway disease.</p> <p>Dependency – Nicotine nasal spray produces higher peak nicotine levels than other NRTs and has the highest dependence potential of the nicotine replacement therapies. About 15-20% of patients report using the active spray for longer periods than recommended (6-12 months), and 5% used the spray at a higher dose than recommended.</p>

Nicotine Nasal Spray (cont.)

Dosage	A dose of nicotine nasal spray consists of one 0.5 mg dose delivered to each nostril (1 mg total). Initial dosing should be 1-2 doses per hour, increasing as needed for symptom relief. Minimum recommended treatment is 8 doses/day, with a maximum limit of 40 doses/day (5 doses/hr). Each bottle contains approximately 100 doses. Recommended duration of therapy is 3-6 months.
Availability	Prescription only
Prescribing instructions	Dosing information – Patients should not sniff, swallow, or inhale through the nose while administering doses as this increases irritating effects. The spray is best delivered with the head tilted slightly back.

Nicotine Patch



Recommendation: The nicotine patch is an effective smoking cessation treatment that patients should be encouraged to use.
(Strength of Evidence = A).

Nicotine Patch

<p>Patient selection</p>	<p>Appropriate as a first-line medication for treating tobacco use.</p>
<p>Precautions, warnings, contraindications and side effects</p>	<p>Pregnancy – Pregnant smokers should be encouraged to quit without medication. The nicotine patch has not been shown to be effective for treating tobacco dependence treatment in pregnant smokers. (The nicotine patch is an FDA pregnancy Class D agent.) The nicotine patch has not been evaluated in breast-feeding patients.</p> <p>Cardiovascular diseases – NRT is not an independent risk factor for acute myocardial events. NRT should be used with caution among particular cardiovascular patient groups: those in the immediate (within 2 weeks) postmyocardial infarction period, those with serious arrhythmias, and those with unstable angina pectoris.</p> <p>Skin reactions – Up to 50% of patients using the nicotine patch will experience a local skin reaction. Skin reactions are usually mild and self-limiting, but occasionally worsen over the course of therapy. Local treatment with hydrocortisone cream (1%) or triamcinolone cream (0.5%) and rotating patch sites may ameliorate such local reactions. In less than 5% of patients, such reactions require the discontinuation of nicotine patch treatment.</p> <p>Other side effects – insomnia and/or vivid dreams.</p>
<p>Dosage</p>	<p>Treatment of 8 weeks or less has been shown to be as efficacious as longer treatment periods. Patches of different doses are sometimes available as well as different recommended dosing regimens. The doses and durations recommendations in this table are examples. Clinicians should consider individualizing treatment based on specific patient characteristics such as previous experience with the patch, amount smoked, degree of dependence, etc.</p>

Nicotine Patch (cont.)

Availability	OTC or prescription.	
Type	Duration	Dosage
Step-Down Dosage	4 weeks then 2 weeks then 2 weeks	21 mg/24 hours 14 mg/24 hours 7 mg/24 hours
Single Dosage	Both a 22 mg/24 hours and an 11 mg/24 hours (for lighter smokers) are available in a one-step patch regimen.	
Prescribing instructions	<p><i>Location</i> – At the start of each day, the patient should place a new patch on a relatively hairless location, typically between the neck and waist, rotating the site to reduce local skin irritation.</p> <p><i>Activities</i> – No restrictions while using the patch.</p> <p><i>Dosing information</i> – Patches should be applied as soon as the patient wakes on their quit day. With patients who experience sleep disruption, have the patient remove the 24-hour patch prior to bedtime or use the 16-hour patch (designed for use while patient is awake).</p>	

Instructing Patients in the Use of NRT

- Compliance with NRT improves when the patient is presented a clear rationale for its use and a realistic expectation about the response.
- It should be explained to the patient that nicotine is responsible for addiction and that discontinuation of the nicotine causes craving for cigarettes, tension, irritability, sadness, problems with sleep, and difficulty concentrating. These are partly because of nicotine withdrawal.
- The patient should be told that using the patch results in less desire to smoke and provides an opportunity for a new nonsmoker to practice all the new nonsmoking skills without being burdened by craving.

Instructing Patients in the Use of NRT

- The patient should understand that with smoking, there are naturally peaks and valleys in the amount of nicotine in the bloodstream.
- With the patch there is a steady gradual rise in the blood nicotine concentration that levels off and remains constant for much of the day and then gradually decreases while the person is asleep.
- Maintaining an adequate blood level of nicotine lessens withdrawal symptoms.
- A similar rationale can be used if patients are using gum. It should be emphasized that NRT is not a “magic bullet” and that the use of coping skills is essential for abstinence.
- The patch or the gum only buys time by reducing withdrawal symptoms and giving individuals a chance to figure out alternatives that they can use in place of smoking.

Varenicline



Recommendation: Varenicline is an effective smoking cessation treatment that patients should be encouraged to use.
(Strength of Evidence = A).

Varenicline

- Varenicline is a partial agonist that binds selectively to $\alpha 4$ - $\beta 2$ -nicotinic acetylcholine receptors with a greater affinity than nicotine.
- When bound to the receptor, the drug blocks nicotine from binding and also evokes a response but to a lesser degree than nicotine.
- The stimulation of the receptor that occurs results in release of dopamine and thus provides a type of “reward” that can decrease craving and withdrawal symptoms.

Varenicline

57

Patient selection	Appropriate as a first-line medication for treating tobacco use.
Precautions, warnings, contraindications and side effects	<p>Pregnancy – Pregnant smokers should be encouraged to quit without medication. Varenicline has not been shown to be effective for treating tobacco dependence in pregnant smokers. (Varenicline is an FDA pregnancy Class C agent.) Varenicline has not been evaluated in breast-feeding patients.</p> <p>Cardiovascular diseases – Not contraindicated</p> <p>Precautions – Use with caution in patients with significant kidney disease (creatinine clearance < 30mL/min) or who are on dialysis. Dose should be reduced with these patients. Patients taking varenicline may experience impairment of the ability to drive or operate heavy machinery.</p> <p>Warning - In July, 2009, the FDA issued a boxed warning regarding the use of varenicline. Specifically, the use of varenicline has been associated with reports of changes in behavior such as hostility, agitation, depressed mood and suicidal thoughts or actions. The FDA is requiring the manufacturer of this product to add a new Boxed Warning to the product labeling to alert healthcare professionals to this important new safety information. People who are taking varenicline and experience any serious or unusual changes in mood or behavior or who feel like hurting themselves or someone else should stop taking the medicine and call their healthcare professional right away clinicians should consider eliciting information on their patients' psychiatric history and monitoring for changes in mood and behavior.</p> <p>Side effects – Nausea, trouble sleeping, abnormal/vivid/strange dreams.</p>

Varenicline (cont.)

Dosage	Start varenicline one week before the quit date at 0.5 mg once daily for 3 days followed by 0.5 mg twice daily for 4 days followed by 1 mg twice daily for 3 months. Varenicline is approved for a maintenance indication for up to 6 months. Note: patient should be instructed to quit smoking on day 8 when dosage is increased to 1 mg twice daily.
Availability	Prescription only
Prescribing instructions	<i>Stopping smoking prior to quit date</i> – Recognize that some patients may lose their desire to smoke prior to their quit date, or will spontaneously reduce the amount they smoke. <i>Dosing information</i> –To reduce nausea, take on a full stomach. To reduce insomnia, take second pill at supper rather than bedtime.

Second line medication – Clonidine



Recommendation: Clonidine is an effective smoking cessation treatment. It may be used under a physician's supervision as a second-line agent to treat tobacco dependence. (Strength of Evidence = A).

Clonidine

<p>Patient selection</p>	<p>Appropriate as a second-line medication for treating tobacco use.</p>
<p>Precautions, warnings, contraindications and side effects</p>	<p>Pregnancy – Pregnant smokers should be encouraged to quit without medication. Clonidine has not been shown to be effective for tobacco cessation in pregnant smokers. (Clonidine is an FDA pregnancy Class C agent.) Clonidine has not been evaluated in breast-feeding patients.</p> <p>Activities – Patients who engage in potentially hazardous activities, such as operating machinery or driving, should be advised of a possible sedative effect of clonidine.</p> <p>Side effects – Most commonly reported side effects include dry mouth (40%), drowsiness (33%), dizziness (16%), sedation (10%), and constipation (10%). As an antihypertensive medication, clonidine can be expected to lower blood pressure in most patients. Therefore, clinicians should monitor blood pressure when using this medication.</p> <p>Rebound hypertension – When stopping clonidine therapy, failure to reduce the dose gradually over a period of 2-4 days may result in a rapid increase in blood pressure, agitation, confusion, and/or tremor.</p>
<p>Dosage</p>	<p>Doses used in various clinical trials have varied significantly, from 0.15-0.75 mg/day by mouth and from 0.10-0.20 mg/day transdermal (TTS), without a clear dose-response relation to treatment outcomes. Initial dosing is typically 0.10 mg bid. PO or 0.10 mg/day TTS, increasing by 0.10 mg/day per week if needed. The dose duration also varied across the clinical trials, ranging from 3-10 weeks.</p>

Clonidine (cont.)

Availability	Oral – Prescription only. Transdermal – Prescription only.
Prescribing instructions	Initiate – Initiate clonidine shortly before (up to 3 days), or on, the quit date. Dosing information – If the patient is using transdermal clonidine, at the start of each week, he or she should place a new patch on a relatively hairless location between the neck and waist. Users should not discontinue clonidine therapy abruptly.

Second line medication - Nortriptyline



Recommendation: Nortriptyline is an effective smoking cessation treatment. It may be used under a physician's supervision as a second-line agent to treat tobacco dependence. (Strength of Evidence = A).

Nortriptyline

Patient selection	Appropriate as a second-line medication for treating tobacco use.
Precautions, warnings, contraindications and side effects	<p>Pregnancy – Pregnant smokers should be encouraged to quit without medication. Nortriptyline has not been shown to be effective for tobacco cessation in pregnant smokers. (Nortriptyline is an FDA pregnancy Class D agent.) Nortriptyline has not been evaluated in breast-feeding patients.</p> <p>Side effects – Most commonly reported side effects include sedation, dry mouth (64-78%), blurred vision (16%), urinary retention, lightheadedness (49%), and shaky hands (23%).</p> <p>Activities – Nortriptyline may impair the mental and/or physical abilities required for the performance of hazardous tasks, such as operating machinery or driving a car; therefore, the patient should be warned accordingly.</p> <p>Cardiovascular and other effects – Because of the risk of arrhythmias and impairment of myocardial contractility, use with caution in patients with cardiovascular disease. Do not co-administer with MAO inhibitors.</p>
Dosage	Doses used in smoking cessation trials have initiated treatment at a dose of 25 mg/day, increasing gradually to a target dose of 75-100 mg/day. Duration of treatment used in smoking cessation trials has been approximately 12 weeks, although clinicians may consider extending treatment for up to 6 months.

Treatment Recommendations – Medications – Nortriptyline (cont.)

Availability	Nortriptyline HCl – Prescription only.
Prescribing instructions	<p>Initiate – Therapy is initiated 10-28 days before the quit date to allow nortriptyline to reach steady state at the target dose.</p> <p>Therapeutic monitoring – Although therapeutic blood levels for smoking cessation have not been determined, therapeutic monitoring of plasma nortriptyline levels should be considered under American Psychiatric Association Guidelines for treating patients with depression. Clinicians may choose to assess plasma nortriptyline levels as needed.</p> <p>Dosing information - Users should not discontinue nortriptyline abruptly due to withdrawal effects.</p> <p>Overdose may produce severe and life-threatening cardiovascular toxicity, as well as seizures and coma. Risk of overdose should be considered carefully before using nortriptyline.</p>

Treatment Recommendations – Medications



Combination Medications

Recommendation: Certain combinations of first-line medications have been shown to be effective smoking cessation treatments. Therefore, clinicians should consider using these combinations of medications with their patients who are willing to quit.

Effective combination medications are:

- Long-term (> 14 weeks) nicotine patch + other NRT (gum and spray)
- The nicotine patch + the nicotine inhaler
- The nicotine patch + bupropion SR. (Strength of Evidence = A)

Treatment Recommendations – Medications – Relative Effectiveness

Meta-analysis (2008): Effectiveness and abstinence rates of medications relative to the nicotine patch (n = 86 studies)

Medication	Number of arms	Estimated odds ratio (95% C. I.)
Nicotine Patch (reference group)	32	1.0
Monotherapies		
Varenicline (2 mg/day)	5	1.6 (1.3, 2.0)
Nicotine Nasal Spray	4	1.2 (0.9, 1.6)
High Dose Nicotine Patch (> 25 mg; standard or long-term)	4	1.2 (0.9, 1.6)
Long-Term Nicotine Gum (> 14 weeks)	6	1.2 (0.8, 1.7)
Varenicline (1 mg/day)	3	1.1 (0.8, 1.6)
Nicotine Inhaler	6	1.1 (0.8, 1.5)

Treatment Recommendations – Medications – Relative Effectiveness

67

**Meta-analysis (2008): Effectiveness and abstinence rates of medications relative to the nicotine patch
(n = 86 studies)**

Medication	Number of arms	Estimated odds ratio (95% C. I.)
Nicotine Patch (reference group)	32	1.0
Monotherapies		
Clonidine	3	1.1 (0.6, 2.0)
Bupropion SR	26	1.0 (0.9, 1.2)
Long-Term Nicotine Patch (> 14 weeks)	10	1.0 (0.9, 1.2)
Nortriptyline	5	0.9 (0.6, 1.4)
Nicotine Gum	15	0.8 (0.6, 1.0)

Treatment Recommendations – Medications –

Relative Effectiveness

68

Meta-analysis (2008): Effectiveness and abstinence rates of medications relative to the nicotine patch (n = 86 studies)

Medication	Number of arms	Estimated odds ratio (95% C. I.)
Nicotine Patch (reference group)	32	1.0
Combination therapies		
Patch (long-term; > 14 weeks) + NRT (gum or spray)	3	1.9 (1.3, 2.7)
Patch + Bupropion SR	3	1.3 (1.0, 1.8)
Patch + Nortriptyline	2	0.9 (0.6, 1.4)
Patch + Inhaler	2	1.1 (0.7, 1.9)
Second-generation antidepressants & Patch	3	1.0 (0.6, 1.7)
Medications not shown to be effective		
Selective Serotonin Reuptake Inhibitors (SSRIs)	3	0.5 (0.4, 0.7)
Naltrexone	2	0.3 (0.1, 0.6)

Treatment Recommendations – Medications

Meta-analysis (2008): Effectiveness and abstinence rates for smokers not willing to quit (but willing to change their smoking patterns or reduce their smoking) after receiving nicotine replacement therapy compared to placebo (n = 5 studies)

Intervention	Number of arms	Estimated odds ratio (95% C.I.)	Estimated Abstinence rate (95% C.I.)
Placebo	5	1.0	3.6
Nicotine replacement (gum, inhaler or patch)	5	2.5 (1.7, 3.7)	8.4 (5.9, 12.0)

Treatment Recommendations – Medications – Over the Counter Medications



Recommendation: Over-the-counter nicotine patch therapy is more effective than placebo and its use should be encouraged.
(Strength of evidence =B).

Treatment Recommendations – Medications – Over the Counter Medications

Meta-analysis (2000): Effectiveness and estimated abstinence rates for over-the-counter nicotine patch therapy (n = 3 studies)

OTC therapy	Number of arms	Odds Ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Placebo	3	1.0	6.7
Over-the-counter nicotine patch therapy	3	1.8 (1.2, 2.8)	11.8 (7.5, 16.0)

Future Treatments

- Work has begun to develop a vaccine that would be used in treating nicotine addiction.
- One such product is called NicVAX (nicotine conjugate vaccine) and is designed to cause the immune system to produce antibodies that bind to nicotine and prevent it from entering the brain.
- As a result, the positive stimulus in the brain that is normally caused by nicotine is no longer present, thereby taking away the physical motivation for smoking, consequently helping people to quit

THE END

Questions?