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Target Audience

This educational activity is designed for primary care physicians and those physicians who manage patients with tobacco dependence.

Learning objectives:

Upon completion of this activity, physicians should be able to:

- Describe approaches determining the level of tobacco dependence and assessment of the patient's readiness to attempt smoking cessation
- Utilize pharmacologic treatment approaches for smoking cessation that are evidence-based.

CME Information

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Treatment of Tobacco Dependence

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Scope of the Problem

Tobacco use remains the leading cause of preventable death in our society. It is a major cause of numerous deadly diseases including heart disease, COPD, stroke, and multiple cancers. The latest Surgeon General's Report states^{1,2} that there is *no safe level* of tobacco smoke exposure, indicating that the best strategy is abstinence from tobacco use. Since the first Surgeon General's Report regarding the harms of tobacco use in 1964, there had been a dramatic decline in tobacco use prevalence over the past 5 decades. Unfortunately, this decline has stalled in the most recent years.³

Tobacco use is a particularly important issue among certain subgroups of the population. Higher smoking prevalence is associated with lower education levels, lower socioeconomic status, and among people with certain comorbidities such as medical illness, psychiatric illness, and concurrent substance abuse. This population represents a high priority for delivery of tobacco dependence treatment. The assessment of medical conditions is critical as they can be a motivating factor or can influence a treatment plan. Heart disease, pulmonary disease, seizure disorders, kidney and liver disease, dental conditions, and pregnancy are important considerations in choosing pharmacotherapy. However, some concerns of certain medications (*e.g.*, use of nicotine replacement in patients with coronary artery disease) are overstated as evidence supports their safety.⁴ Additionally, since people with mental health issues and other substance abuse concerns tend to use tobacco at higher rates than people without these comorbidities, providers who care for these patients should be adept at treating their tobacco use.

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Clinical Characteristics of Tobacco Dependence

Nicotine is one of the most addictive substances in our society. Therefore, tobacco users who attempt to quit experience a constellation of cravings and withdrawal symptoms (DSM IV diagnosis 292.0) that can result in relapse. These common withdrawal symptoms are shown in **Table 1**.

Clinically, one can measure the level of dependence in many ways. A standardized instrument to measure nicotine dependence is the Fagerstrom Test for Nicotine Dependence (FTND)⁶, that generates a point value for specific criteria (**Table 2**).

Table 1. Nicotine Withdrawal Symptoms (4 or more of the following to meet criteria)⁵

- Depressed mood
- Insomnia
- Irritability, frustration, or anger
- Anxiety
- Difficulty concentrating
- Restlessness
- Decreased heart rate
- Increased appetite/weight gain

Table 2. Fagerstrom Test for Nicotine Dependence

Questions	Answers	Points
1) How soon after you wake up do you have your first cigarette?	Within 5 minutes 6 to 30 minutes 31-60 minutes after 60 minutes	3 2 1 0
2) Do you find it difficult to refrain from smoking in places where it is forbidden such as church, the library or movie theaters?	Yes No	1 0
3) Which cigarette would you hate most to give up?	The first one in the morning All others	1 0
4) How many cigarettes do you smoke each day?	10 or less 11-20 21-30 31 or more	0 1 2 3
5) Do you smoke more frequently during the first hours after waking than the rest of the day?	Yes No	1 0
6) Do you smoke if you are so ill that you are in bed most of the day?	Yes No	1 0
SCORING	0-2 points: Very Low Addiction 3-4 points: Low Addiction 5 points: Medium Addiction 6-7 points: High Addiction 8-10 points: Very High Addiction	

Other simpler scales include the Heaviness of Smoking Index (HSI) which is a modification of the FTND⁷ (**Table 3**) and may be more clinically practical considering its ease of use.

Table 3. Heaviness of Smoking Index

Questions	Answers	Points
1) How soon after waking do you smoke your first cigarette?	Within 5 minutes Within 30 minutes Within 1 hour	3 2 1
2) How many cigarettes do you smoke per day?	More than 30 per day 21 to 30 per day 11 to 20 per day	3 2 1
SCORING	5-6 points: Heavy nicotine dependence 3-4 points: Moderate nicotine dependence 0-2 points: Light nicotine dependence	

Motivation

In addition to dependence and withdrawal, another important consideration in tobacco cessation is motivation to stop. There is some misperception among providers that tobacco users do not want to stop using tobacco. In fact, surveys generally demonstrate that as many as 70% of tobacco users have made a serious attempt to quit.⁸ Despite this figure, not everyone who wants to quit is ready at any given time. One tool that is used to determine readiness to change is based on the Transtheoretical Model of Behavior Change or the Stages of Change (Figure 1).⁹

Tobacco users may not believe that their behavior is a concern for them or have no desire to consider quitting (Precontemplation). Others may be considering quitting, but are unsure. They weigh the pros and cons of continued tobacco use and could consider quitting, but just not right now (Contemplation). There are some tobacco users who have decided that this is the right time for them to quit and are ready to take steps to do so, typically within the next month (Preparation), and there are those who are in the active process of quitting (Action). Maintenance is when the new behavior pattern (not using tobacco) is sustained and consolidated into the lifestyle of the individual. Population-based estimates suggest that in a 1-year, cross-sectional period, 59% of daily smokers were precontemplators, 33% were contemplators, and 8% were in preparation.¹⁰

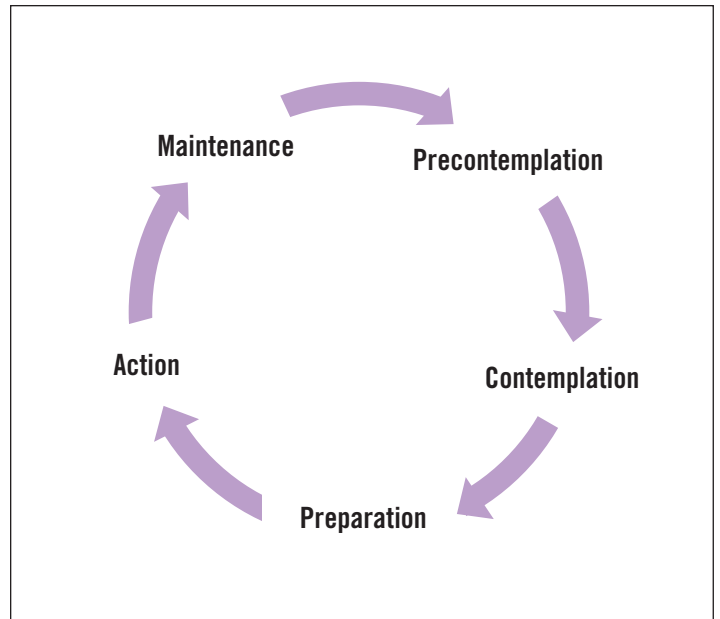


Figure 1. Stages of Change

Recognizing where an individual stands on this stage of change continuum is important as interventions are best tailored to that specific stage. Smokers who are not even considering quitting would not respond well to a prescription for nicotine replacement medications. Additionally, someone who has decided to quit and is in Preparation does not need to be lectured as to the health benefit of stopping. Instead, for those ready to make a quit attempt, clinical practice guidelines exist to help implement a treatment plan.

Clinical Practice Guidelines

The clinical practice guideline, *Treating Tobacco Use and Dependence: 2008 Update* provides state-of-the-art, evidence-based recommendations for treating tobacco dependence.⁴ This update is the third Public Health Service Clinical Practice Guideline published on tobacco use. The first Guideline, the 1996 Smoking Cessation Clinical Practice Guideline No. 18, was sponsored by the Agency for Healthcare Policy and Research. The second Guideline, published in 2000, *Treating Tobacco Use and Dependence*, was sponsored by a consortium of U.S. Public Health Service agencies (AHRQ; CDC; NCI; NHLBI; NIDA, as well as the Robert Wood Johnson Foundation and the University of Wisconsin Center for Tobacco Research and Intervention). The current 2008 update addresses literature published from 1975 to 2007.

The overarching goal of these recommendations is that clinicians strongly recommend the use of effective tobacco dependence counseling and medication treatments to their patients who use tobacco, and that health systems, insurers, and purchasers assist clinicians in making such effective treatments available. The highlighted points include:

1. Tobacco dependence is a chronic disease that often requires repeated intervention and multiple attempts to quit. Effective treatments exist, however, that can significantly increase rates of long-term abstinence.

Recently, it has been recognized that tobacco dependence is not merely a “bad-habit” that can be cured with a single course of treatment. The view of tobacco dependence as a chronic condition has gained favor in the treatment community.⁴ In this sense, treatment should focus on comprehensive approaches that incorporate behavioral, environmental, and pharmacological aspects of care. Tobacco dependence is a condition characterized by relapse and remission, and as with other chronic conditions (e.g., diabetes), treatment should be ongoing and utilize effective, evidence-based therapies. Unfortunately, many barriers exist for tobacco dependence treatments that do not exist to the same extent for conditions such as diabetes.¹¹

2. It is essential that clinicians and health care delivery systems consistently identify and document tobacco use status and treat every tobacco user seen in a health care setting.

One of the best ways to incorporate these interventions into clinical practice is to “institutionalize” them or fully integrate them into the organizational system. For example, instead of relying on individual physicians to ask every patient their tobacco use status, it should be made part of the routine intake system (e.g., tobacco status as a vital sign). Other components of tobacco dependence treatment can also be integrated and/or reminders for the provider can be generated for advising abstinence and assisting cessation.

3. Brief tobacco dependence treatment is effective. Clinicians should offer every patient who uses tobacco at least the brief treatments shown to be effective in the Guideline.

For busy clinicians, the Guideline recommends objectives to deliver brief clinical interventions, as could be implemented in a medical office setting. These interventions are described as the “5 A’s” (Table 4).⁴

Table 4. The “5 A’s” Model for Treating Tobacco Use and Dependence⁴

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.

4. Numerous effective medications are available 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. The effectiveness of these medications is provided in **Table 5**. As a prescriber, physicians can utilize proven pharmacotherapy as part of a comprehensive treatment plan.

Individual Medications

Cigarettes are the most efficient, highly-engineered nicotine delivery device known. They deliver high doses of nicotine to the brain within 10 seconds of inhaling; quicker than intravenous administration.

The medications discussed below deliver nicotine at much lower doses and much less rapidly than when smoking tobacco. Therefore, it is very important that tobacco users be given realistic expectations for all of the pharmacotherapies available, and the nicotine effects they will experience from using them. The purpose of these medications is to reduce cravings and withdrawal symptoms so that the person can feel more comfortable and more easily deal with the difficult behavioral aspects of quitting tobacco. The medications do not make it so a tobacco user will “magically” never want another cigarette again. They are simply one component of a comprehensive treatment plan.

• Patch

The nicotine transdermal patch is probably the most well-known and most commonly used nicotine replacement therapy (NRT). In the U.S., the patch is an over-the-counter (OTC) medication. It has the advantages of being easy to use and once placed, it delivers a slow and steady amount of nicotine throughout the day. The main barrier with the patch is that it is passive, not active, so there is nothing pharmacologically to do if a craving occurs while wearing the patch. It is suggested that the patch be placed in a different location each day to reduce the skin irritation side effect, and it can be removed at bedtime if wearing the patch at night results in sleep problems.

• Gum

The gum is also an OTC medication that comes in 2 and 4 mg doses based on number of cigarettes smoked each day. The gum is an active medication that can be used on an as needed schedule or on a fixed-schedule, such as chew 1 piece every 30 minutes throughout the day. The gum provides nicotine that is absorbed through the oral mucosa. Therefore, the gum must be “chewed and parked” to regulate the amount of nicotine released to allow for proper absorption. If chewed constantly, much of the nicotine released will be swallowed, rendered ineffective by gastric acidity, and simply produce nausea. In addition, since most foods and beverages are acidic, it is suggested that they be avoided around the time of gum use. One can use up to approximately 20 pieces per day. Recently, the gum has become available in a wide variety of improved flavors. Therefore, those smokers who had previously used the gum and were not satisfied with the taste can be encouraged to try again with these new products.

Table 5. Effectiveness of Pharmacotherapies with FDA-Approved Labeling for Smoking Cessation

Medication	Odds Ratio	Abstinence rate
Placebo	1.0	13.8%
Varenicline	3.1	33.2%
Nicotine nasal spray	2.3	26.7%
Nicotine inhaler	2.1	24.8%
Bupropion SR	2.0	24.2%
Nicotine patch	1.9	23.4%
Nicotine gum	1.5	19.0%
Patch + Gum/Spray	3.6	36.5%
Patch + Bupropion SR	2.5	28.9%

Adapted from Fiore MC, Jaén CR, Baker TB, et al. Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. 2008.

- ***Lozenge***

The nicotine lozenge is also OTC and functions similarly to the gum, available in 2 and 4 mg doses based on time to first cigarette smoked in the morning, and providing orally absorbed nicotine. The lozenge, however, should not be chewed, but instead allowed to dissolve in the mouth. As with the gum, food and beverages should be avoided around lozenge use. One can use up to approximately 20 lozenges per day. Recently, mini-lozenges have become available as an option and may be more acceptable than the original formulation.

- ***Inhaler***

The nicotine inhaler is a prescription medication that also delivers a dose of nicotine when puffed. The device consists of a plastic tube into which one inserts a cartridge that contains a nicotine-infused sponge. When the cartridge is inserted and the inhaler puffed on, nicotine vapor is absorbed through the oral mucosa. The product's name is a bit of a misnomer as the inhaler's vapor is not truly inhaled into the lungs. Therefore, pharmacologically, the inhaler works similarly to the gum and lozenge. The advantage of the inhaler is that in addition to delivering orally absorbed nicotine, it also provides a behavioral, hand-to-mouth substitution for smoking. The inhaler should be puffed as needed or on a fixed-schedule and when the "peppery" taste disappears, the cartridge should be changed. The suggested dose is up to 16 cartridges per day.

- ***Nasal Spray***

The nicotine nasal spray is also a prescription medication that delivers a slightly higher level of nicotine per dose and a bit more rapidly than other short-acting nicotine medications. Therefore, it may be especially useful in tobacco users with strong cravings, severe withdrawal symptoms, or high levels of dependence. Unfortunately, the nasal spray is not as well tolerated as some of the other nicotine medications due to nasal irritation. Patients should be advised not to inhale the nasal spray deeply, but to instead simply tilt their head back, spray into the nose, and keep their head tilted back for 1 minute to allow absorption. One dose can be used up to approximately 40 times per day.

- ***Bupropion SR***

Bupropion has been in use for the treatment of depression for many years. In 1997, it was approved for use in smoking cessation. This medication acts to reduce reuptake of dopamine in the brain, and results in a decrease in cravings and nicotine withdrawal symptoms, and improved abstinence rates. The clinical effect of bupropion for tobacco cessation is independent of its antidepressant effects. Bupropion is typically started 1-2 weeks prior to the target quit date, and titrated during the initial few days. The standard dose is 150 mg daily for 3 days and then 150 mg twice daily. The most common side effect is insomnia, but it can also produce headache and rarely rashes. Users of this medication may experience anxiety during the first few days of taking it. This medication is contraindicated in people with seizures, eating disorders, or those on MAO inhibitors. Duration of treatment is typically up to 12 weeks.

- ***Varenicline***

Varenicline is the latest medication to become available and was specifically developed for tobacco dependence treatment. Varenicline acts at the $\alpha 4$ - $\beta 2$ nicotine receptor in the brain and acts as a partial agonist and an antagonist. Therefore, as a partial agonist, when binding to the receptor, varenicline results in release of a modest amount of dopamine, less than that from nicotine, but enough to reduce cravings and withdrawal symptoms. In addition, through its antagonist activity, varenicline binds to the receptor and blocks nicotine from binding. Therefore, if someone uses tobacco while on varenicline, nicotine is unable to bind the receptor, and tobacco use does not have its rewarding effect. Varenicline has been proven effective in improving abstinence rates in numerous clinical trials. Dosing includes a titration period during the first week: standard dosing is 0.5 mg daily for 3 days, then 0.5 mg twice daily for 4 days, then 1 mg twice daily, with the typical target quit date being on Day 8 of treatment. The most common side effects of varenicline include nausea, which occurs in about 30% of users and is typically mild and improved with food; sleep disturbances and gastrointestinal effects also occur. There have been reports of severe neuropsychiatric effects in the postmarketing surveillance of varenicline including erratic behavior, depressed mood, and suicidality. Therefore, the FDA has placed a warning on varenicline and patients who experience these symptoms should stop the medication and contact their physician.¹² In contrast to these case reports, clinical trials of varenicline have not demonstrated adverse effects on mood, behavior, or suicidality.¹³ Varenicline is

exclusively metabolized in the kidney and therefore should be used with caution or at a reduced dose in patients on dialysis or with severe renal impairment. The standard duration of treatment is 12 weeks; however, benefit in those who are abstinent at 12 weeks has been seen with an additional 12 weeks of treatment.¹⁴

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

Combination pharmacotherapy for tobacco dependence (*i.e.*, multiple NRTs or NRT plus bupropion) may have several advantages. First, the simultaneous use of nicotine medications with bupropion addresses tobacco withdrawal through different mechanisms of action. Second, the combination of a passive, continuous form of nicotine medication (patch) with an active, shorter-acting form (gum, lozenge, inhaler, spray) to be used in response to cravings, allows for more individualized delivery of medication as needed by the patient, giving them more control over their dosing. Finally, patients may wish to use certain forms of NRT in different settings. For example, some tobacco users prefer to use the inhaler while driving, but at work would prefer to use a more discreet medication, such as the lozenge. Combination therapy continues to be studied and its benefits demonstrated in various ways. The 2008 PHS Guidelines suggest that combinations of nicotine patch with gum, inhaler, and nasal spray, as well as combinations of NRT with bupropion are effective.⁴ However, it should be noted that NRT combinations currently do not have FDA-approved labeling for smoking cessation. An overview table of all agents to treat tobacco dependence is provided in **Table 6**.

Table 6. FDA-Approved Drugs for the Treatment of Tobacco Dependence

Product	Use	Advantages	Disadvantages	Precaution	Side Effects	Cost (estimates)
Long-Acting Medications						
Nicotine Patch	Apply each day to clean, dry, hairless skin; Start 21 mg patch if > 10 cig per day; can taper to 14 mg in 4-6 weeks then 7 mg in 2 weeks if <u>no cravings</u>	Place and forget; Over the counter; can decrease morning cravings if worn at night	Passive - No action to take when craving occurs	Not recommended to use while smoking; caution within 2 weeks of heart attack	Skin reaction (50% of patients) (usually mild); Rotate sites; hydrocortisone cream; vivid dreams or sleep disturbances possible at night	\$25 / 2 week supply (generics available and effective) at big discount stores
Bupropion Zyban Wellbutrin SR Wellbutrin XL Generic	150 mg each morning for 3-7 days, then may increase to 300 mg/day if desired (OK to maintain 150 mg dose) Start prior to quit date (If Zyban or SR, doses must be at least 8 hours apart; take second pill in early evening to reduce insomnia)	Less weight gain while using; can smoke while initiating treatment	Side effects not uncommon; Passive-no action to take with cravings; Prescription required	Do not use with: Seizure disorders; current use of Wellbutrin or MAO inhibitors; electrolyte abnormalities; eating disorders; Monitor blood pressure	Insomnia (40%); dry mouth, headache, anxiety, rash Flexible dosing (keeping at 150 mg/day) helpful if side-effects	\$40 / month (Generic) \$100 / month (Brand)
Varenicline Chantix	0.5 mg once daily Days 1-3 0.5 mg twice daily Days 4-7 then 1 mg twice daily Use up to 12 weeks; Additional 12 weeks recommended if effective	Reduces withdrawal and may prevent relapse	Passive - no action to take with cravings; Prescription required	Do not use if you have severe kidney disease Evaluate mental illness and monitor mood	Nausea (30%) usually mild – can reduce to 0.5 mg level; Take with food; insomnia.Caution for neuropsych effects (<i>e.g.</i> depression, suicidal ideation). Need good follow-up	\$100 / month

(cont'd)

Table 6. FDA-Approved Drugs for the Treatment of Tobacco Dependence (cont'd)

Product	Use	Advantages	Disadvantages	Precaution	Side Effects	Cost (estimates)
Short Acting Medications						
Nicotine Gum	Chew every 1-2 hours as needed; chew and park; 2 and 4 mg strength (4 mg if around 1 pack)	Use as needed; can self-dose; Over the counter	Difficult to chew, taste (newer flavors improved)	Avoid food and acidic drinks 15 minutes before and while using (decreases absorption); caution within 2 weeks of heart attack	Jaw pain; nausea if swallowing saliva	\$35-50 / 2 week supply - Generic brands are less expensive
Nicotine Inhaler	Puff as needed; use up to 16 cartridges/day; less needed if using combination therapy; oral absorbed-no need to inhale deeply	Use as needed; mimics hand-mouth behavior	Costly, visible; Requires prescription	Avoid food and acidic drinks before and while using; caution within 2 weeks of heart attack	Cough, throat irritation (usually mild)	\$150 / 168 cartridges Wide variation in price—shop for best price
Nicotine Nasal Spray	1-2 sprays per hour; do not sniff/inhale; tilt head back and spray	Use as needed; rapid relief of symptoms	Cost; Requires prescription	Caution with asthma, nasal/sinus problems; caution within 2 weeks of heart attack	Nasal irritation; Possible dependence	\$45 / 1 bottle Dispensed in 4 bottle packs
Nicotine Lozenge	2 and 4 mg (4 mg if smoke within 30 min of waking); dissolve in mouth; do not chew; use 9-15 per day for 6 weeks then taper; Mini-lozenges new	Ease of use, over the counter; flexible dosing	Cost vs. gum	Avoid food and acidic drinks before and while using; caution within 2 weeks of heart attack	Hiccups, nausea, heartburn	\$45 (or less) for 72 lozenges Generic brand may be cheaper

6. Counseling and medication are effective when used by themselves for treating tobacco dependence. The combination of counseling and medication, however, is more effective than either alone. Thus, clinicians should encourage all individuals making a quit attempt to use both counseling and medication.

7. 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 (problem solving/skills training)
- Social support delivered as part of treatment

• **Comprehensive Treatment Plan**

The most effective tobacco dependence treatment includes components of behavioral treatment (counseling and skills learning), social support (as part of treatment and outside of treatment), and pharmacotherapy to reduce cravings and withdrawal symptoms (as listed above).

• Behavioral Therapy

Evidence indicates that behavioral treatment is effective in achieving tobacco abstinence. These interventions can take the form of practical skills training (*e.g.*, what should I do in this difficult situation), managing stressful environments, and changing rituals and associations. This type of treatment can be delivered in an individual setting or in a group setting. The advantage to employing group treatment is that it provides the additional resource of tobacco users going through the quitting process together, sharing what has worked for them with the others in the group, and supporting each other in this activity. In addition, group treatment is more efficient as one clinician can treat several people in one session.

• Support

As stated above, support has been proven to increase success in quitting. Both support as a component of treatment (*i.e.*, group counseling) and support outside of treatment (*i.e.*, social support from friends, family, peers) is beneficial. One should work on changing the environment at home, work, and in social settings to reduce exposure to other tobacco users and high-risk situations for the patient. The increase in smoke-free policies to limit locations where others can smoke has helped.

8. Telephone quitline counseling is effective with diverse populations and has broad reach. Therefore, both clinicians and health care delivery systems should ensure patient access to quitlines and promote quitline use (1-800-QUIT NOW).

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

For those tobacco users who are not ready to make a quit attempt, the Guidelines suggest using the “5 R’s” to increase motivation (Table 7).

Table 7. The 5 R’s for Tobacco Users not Ready to Quit⁴

Relevance	Why is quitting personally relevant?
Risks	Identify negative consequences of tobacco use
Rewards	Identify potential benefits of stopping tobacco use
Roadblocks	Identify barriers to quitting
Repetition	Repeat these at each visit

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 the Guideline as covered benefits.

Current Tobacco Dependence Treatment Utilization

Barriers to Utilizing Pharmacotherapy

Despite the enormous impact that tobacco use has on public health, there exist significant barriers to the receipt of treatment for this chronic condition. These include low self-efficacy for quitting, high levels of tobacco dependence, a belief that tobacco use is not a condition that usually requires treatment, unawareness of tobacco treatment resources, lack of intervention by healthcare providers, cost or access to effective treatments, and competing medical priorities.¹⁵ A recent study showed that only a small minority of tobacco users accessed effective treatments in their recent quit attempts. Specifically, only 25% of smokers in the U.S. making a quit attempt in the past 6 months used NRT, compared with 36% in the UK and Canada.¹⁶

Despite evidence demonstrating the effectiveness of tobacco dependence treatment medications, studies have consistently shown low levels of utilization. Nationally representative data of tobacco dependence pharmacotherapy utilization reveal some interesting findings. It should be noted that 3 of the 7 FDA-approved pharmacotherapies are OTC products, and therefore may not be fully accounted for in certain database analyses.

Figure 2 shows that among over 8 million patients with a diagnosis of tobacco dependence from July 2009 to June 2010, only a fraction (17%) of them received cessation medications. It should be noted that as described earlier based on the stages of change model, only a certain proportion of tobacco users are ready to make a quit attempt at any given point. Despite this fact, the data presented still represent a low number for treatment utilization.

As stated earlier, the PHS Guidelines indicate that each of the 7 FDA-approved medications is safe and effective for treating tobacco dependence. Varenicline may have slightly higher rates of abstinence at the present time compared to other single agents, although it has been on the market for the shortest time. Data reported in **Figure 3** suggest that the most commonly utilized medication is varenicline, followed by bupropion, nicotine patch, nicotine oral inhaler and nicotine gum.

Evidence indicates that smokers of all ages can be successful in quitting. The “quit-ratio”, or proportion of former smokers divided by ever smokers, is an indicator of successful quitting. The quit-ratio has traditionally been actually lowest for younger smokers and highest for older smokers, despite commonly held perceptions of the inability of people who have smoked for many years to quit; this does not turn out to be the case. Unfortunately, data from the current analysis (**Figure 4**) indicate that both younger and older smokers are not receiving the same level of pharmacotherapy support as middle-aged smokers. The actual low quit-ratio for young smokers may be influencing prescribing practices. However, this misperception of older smokers’ lower success may result in less support for them and should be addressed with educational efforts.

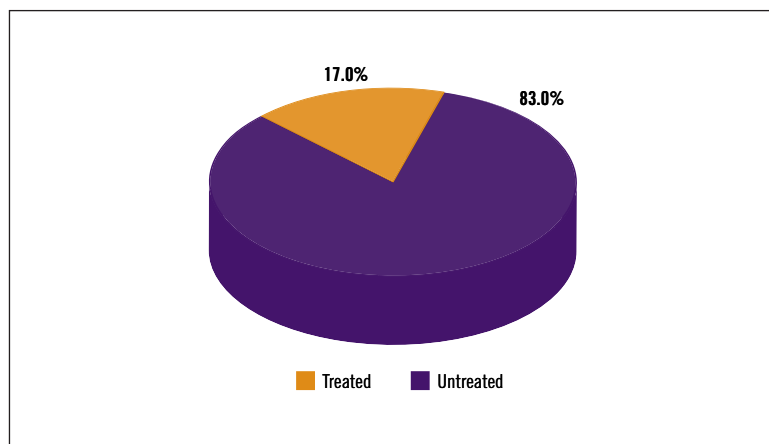


Figure 2. Patients Diagnosed With Tobacco Dependence: Treated vs. Untreated

Source: IMS Lifelink™ Health Plan Claims Data. Time period: 12 months ending June 2010. The category of diagnosed/untreated is derived for those patients with a diagnosed tobacco dependence/tobacco use disorder (ICD-9: 305.1) but who did not receive a prescription for a smoking cessation agent or an over-the-counter nicotine replacement agent for a period of twelve months since being diagnosed.

*Treated means pharmacologically treated with a prescription agent of interest used for tobacco dependence: varenicline, bupropion, nicotine patch, nicotine inhaler, nicotine nasal spray, nicotine gum, nicotine lozenge. The “untreated” category may include nonpharmacological treatment.

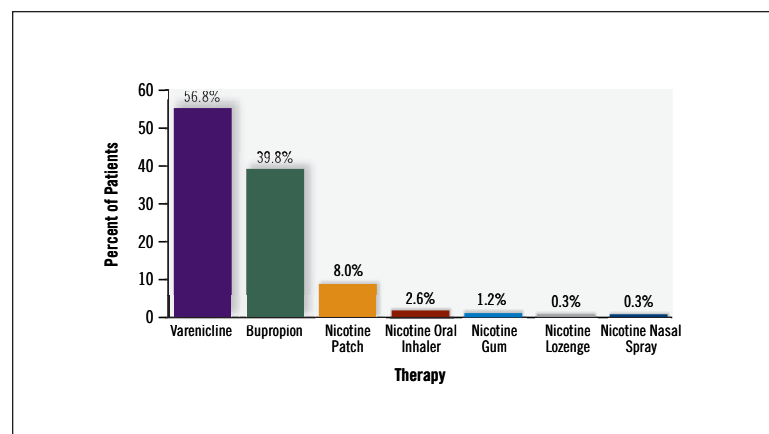


Figure 3. Patients Diagnosed with Tobacco Dependence—Treated with Drugs for Smoking Cessation

Source: IMS Lifelink™ Health Plan Claims Data. Time period: 12 months ending June 2010. Smoking cessation agents of interest: varenicline, bupropion, nicotine patch, nicotine inhaler, nicotine nasal spray, nicotine gum, nicotine lozenge

Previous evidence indicates that there are differences among medical specialties regarding treating tobacco users. In general, providers who treat a high proportion of tobacco-caused disease tend to have higher awareness and utilization of treatment resources.^{17,18} In the current data (Figure 5), it is also the case that some specialties who treat a high proportion of tobacco-caused disease have higher rates of pharmacological treatment (e.g., primary care and pulmonology). Interestingly and encouragingly, psychiatrists whose patients include very high proportions of smokers, have the highest utilization of therapy in the current sample. This result has not been seen in some other studies.¹⁷

It appears that as fewer people are using tobacco throughout the country, those who continue to use tobacco have higher levels of comorbidity, both physical and psychological. The current data presented here (Figure 6) indicate that a significant proportion of those tobacco users who received pharmacotherapy have comorbidities such as lung disease, heart disease, diabetes, and cancer. In addition, over one-quarter of these patients have depression. What is somewhat encouraging is that recent studies indicate that even tobacco users with these comorbidities can safely use these medications, so even though caution is sometimes warranted, prescribers should not be overly cautious in utilizing them.

As expected, the majority of prescriptions dispensed for tobacco treatment medications nationally was for varenicline followed by the nicotine patch. Similar data are found in several individual states.

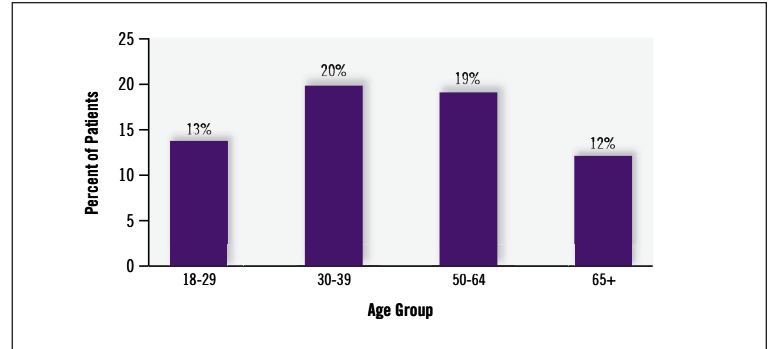


Figure 4. Tobacco Dependence Patients Treated by Age Group

Source: IMS Lifelink™ Health Plan Claims Data. Time period: 12 months ending June 2010.

The category of diagnosed/treated means pharmacologically treated. Smoking cessation drugs of interest: varenicline, bupropion, nicotine patch, nicotine inhaler, nicotine nasal spray, nicotine gum, nicotine lozenge

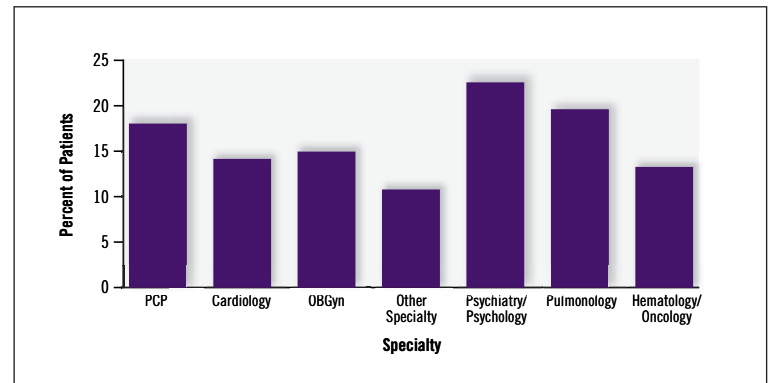


Figure 5. Pharmacologic Therapy in Patients with Tobacco Dependence by Medical Specialty

Source: IMS Lifelink™ Health Plan Claims Data. Time period: 12 months ending June 2010. Proportion of healthcare providers who prescribed smoking cessation agents for patients diagnosed with tobacco dependence.

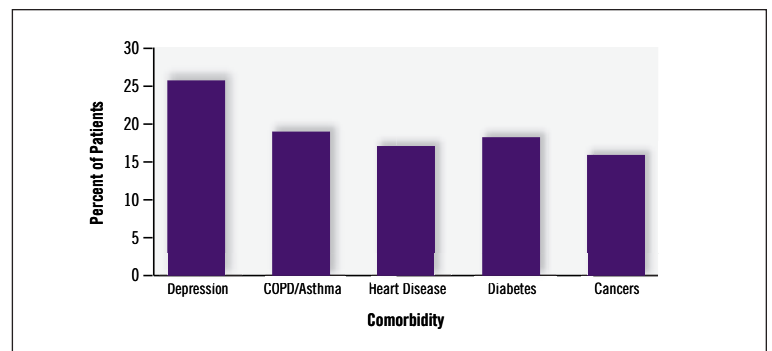


Figure 6. Pharmacologic Treatment of Tobacco Dependence Patients with Comorbidities

Source: IMS Lifelink™ Health Plan Claims Data. Time period: year ending June 2010.

Derived from national patient claim data on 1.42 million patients treated with smoking cessation prescription pharmacotherapy using ICD-9-CM diagnostic codes for depression, COPD/asthma, heart disease, diabetes and cancer.

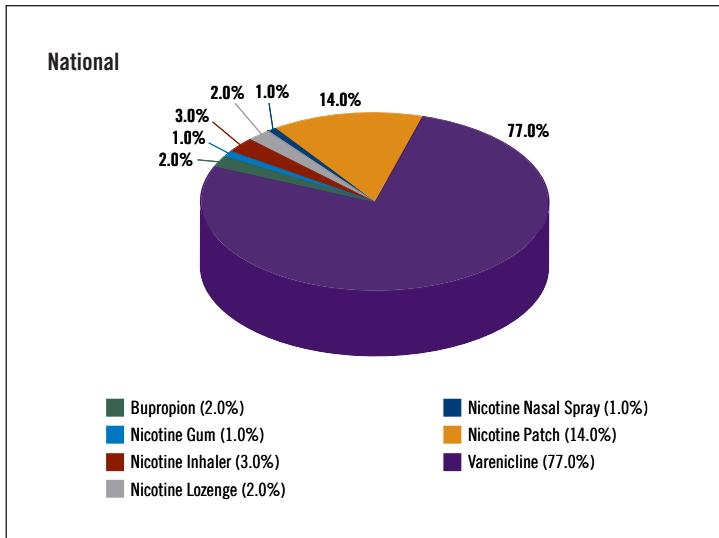


Figure 7a. Proportion of Prescriptions for Smoking Cessation Drugs at Retail Pharmacies Nationally

Source: IMS Health, National Retail Prescription Data.
 Time Period: 12 months ending December 2010. Bupropion: these data are for Buproban and Zyban only. Bupropion HCL SR Z is not included

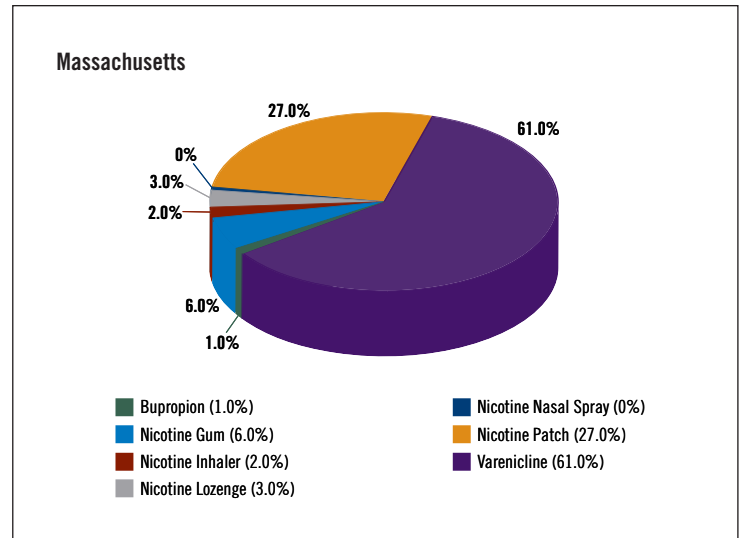


Figure 7b. Proportion of Prescriptions for Smoking Cessation Drugs at Retail Pharmacies in the State of Massachusetts

Source: IMS Health, National Retail Prescription Data.
 Time Period: 12 months ending December 2010. Bupropion: these data are for Buproban and Zyban only. Bupropion HCL SR Z is not included

Outpatient prescription patterns for smoking cessation agents from a National Retail Prescription database of more than 800,000 individual prescribers provides additional information on the use of these agents. **Figures 7a and 7b** show the national and state level data. Prescriptions dispensed for varenicline represented by far the most common smoking cessation agent followed by the nicotine patch. National retail prescription data show a lower use (between 1%-3%) of all other nicotine replacement agents.

Summary

Tobacco use remains the leading cause of preventable death in our society and thus warrants the utmost consideration as a treatment priority. This is not merely a “bad habit” but a chronic condition characterized by neurochemical dependence, multi-billion dollar tobacco industry marketing, and previously unrecognized medical and psychiatric comorbidity. Evidence-based clinical practice guidelines are clear on the most effective ways to help tobacco users stop, which includes a comprehensive approach consisting of behavioral counseling, social support, and effective pharmacotherapy. Although not a cure by itself, the FDA-approved tobacco treatment medications have been demonstrated to be vital in helping reduce cravings and nicotine withdrawal symptoms.

Despite this, the national data presented here indicate that tobacco treatment medications may be underutilized. Significant barriers to optimal pharmacologic treatment include variations in insurance coverage as well as smokers’ and providers’ misperceptions about medication treatment. The healthcare system as a whole would do well to expand the emphasis, coverage, and thus utilization of tobacco dependence treatments that have been proven safe and effective for countless tobacco users throughout the world.

Self-Assessment Questions

You may receive your CME certificate online by going to www.ama-assn.org/go/therapeuticinsights and completing the self-assessment and program evaluation. Alternatively, you may use the answer sheet provided with the AMA Therapeutic Insights newsletter to record your answers, and either fax to 312-464-4849 or mail to:

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Therapeutic Insights—Treatment of Tobacco Dependence
American Medical Association
515 N State Street
Chicago, IL 60654

If faxing or mailing, you will receive your CME certificate in 3-4 weeks.
(circle one)

1. Which of the following provides evidence-based, clinical practice guidelines for treating tobacco dependence:
 - a. Diagnostic and Statistical Manual of Mental Disorders version IV
 - b. International Classification of Diseases 10th revision
 - c. 2010 US Surgeon General's Report on Harms of Tobacco Use
 - d. 2008 US Public Health Service – Treating Tobacco Use and Dependence
 - e. All of the above
 1. a
 2. b
 3. c
 4. d
 5. e
2. Which of the following is NOT a DSM-IV nicotine withdrawal symptom?
 - a. Dysphoric/depressed mood
 - b. Irritability
 - c. Headache
 - d. Insomnia
 - e. Decreased concentration
 1. a
 2. b
 3. c
 4. d
 5. e
3. According to the Clinical Practice Guidelines, the “5A’s” brief intervention should be used:
 - a. When a person wants to make a serious quit attempt
 - b. Primarily for relapse prevention
 - c. Only by a primary care doctor
 - d. Only when the patient has medical complications from smoking
 - e. Routinely and consistently with every patient
 1. a
 2. b
 3. c
 4. d
 5. e
4. In which stage of change would it be appropriate to set a “Quit Date”?
 - a. Precontemplation
 - b. Contemplation
 - c. Preparation
 - d. Avoidance
 - e. Reluctance
 1. a
 2. b
 3. c
 4. d
 5. e
5. Which of the following recommendations for treating tobacco dependence is NOT found in the Clinical Practice Guidelines?
 - a. Tobacco dependence is a chronic disease that often requires repeated intervention and multiple attempts to quit.
 - b. Lowering morbidity through switching to low-tar or low-nicotine cigarettes is a reasonable goal for some smokers.
 - c. Numerous effective medications are available for tobacco dependence, and clinicians should encourage their use by all patients attempting to quit smoking, except when medically contraindicated.
 - d. 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.
 - e. If a tobacco user currently is unwilling to make a quit attempt, clinicians should use the motivational treatments to increase future quit attempts.
 1. a
 2. b
 3. c
 4. d
 5. e

Program Evaluation

1. As a result of participating in this activity, I am better able to describe approaches determining level of tobacco dependence and assessment of the patient's readiness to attempt smoking cessation.
2. As a result of participating in this activity, I am better able to utilize pharmacologic treatment approaches for smoking cessation that are evidence-based.
3. Overall, the program effectively met my educational needs.
4. As a result of participating in this educational activity I plan to change my treatment of tobacco dependence.
5. The program was free of commercial bias. (yes or no) If “no” what was the perceived bias?
6. Based on the information in this program, what likely changes do you anticipate making in your treatment of tobacco dependence?

If no changes are planned, why not? (e.g., currently diagnosing and managing patients with tobacco dependence as described or not currently practicing).

Self-Assessment Responses

(Please circle your response, one response per question)

Q.1	1	2	3	4	5
Q.2	1	2	3	4	5
Q.3	1	2	3	4	5
Q.4	1	2	3	4	5
Q.5	1	2	3	4	5

Name: _____

Address: _____

City/State/Zip _____

Phone: _____ Fax: _____

Evaluation Responses *(Please circle)*

	<i>Strongly Disagree</i>		<i>Agree</i>		<i>Strongly Agree</i>
Q.1	1	2	3	4	5
Q.2	1	2	3	4	5
Q.3	1	2	3	4	5
Q.4	1	2	3	4	5
Q.5	yes	no			

E-mail address: _____

*M.E.# _____

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Date of Birth: _____

Mo/day/year

Medical School: _____

Yr. Graduation: _____

Total AMA PRA Category 1 Credits™ claimed: _____

Signature: _____

Date: _____

If no, explain _____

Q.6 _____

Would you like to be notified of new AMA CME programs on other topics?

yes no

Additional Comments _____

When completed, please fax to 312.464.4849 or mail to:

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References

1. U.S. Department of Health and Human Services: The Consequences of Smoking: A Report of the Surgeon General. 2004, US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
2. U.S. Department of Health and Human Services. How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2010.
3. Centers for Disease Control and Prevention. State-specific prevalence of cigarette smoking and smokeless tobacco use among adults - United States, 2009. *MMWR*. 2010;59(43):1400-1406.
4. Fiore MC, Jaén CR, Baker TB, et al. Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. 2008.
5. American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision. Washington DC, American Psychiatric Association, 2000; page 266.
6. Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. *Br J Addict*. 1991; 86(9):1119-1127.
7. Heatherton TF, Kozlowski LT, Frecker RC, Rickert WS, Robinson J. Measuring the heaviness of smoking using self-reported time to first cigarette of the day and number of cigarettes smoked per day. *Br J Addict*. 1989;84:791-800.
8. Cory S, Ussery-Hall A, Griffin-Blake S, Easton A, Vigeant J, Balluz L, Garvin W, Greenlund K. Prevalence of selected risk behaviors and chronic diseases and conditions-steps communities, United States, 2006-2007. *MMWR*. 2010;59(8):1-37.
9. Prochaska JO, DiClemente CC. Stages and processes of self-change of smoking: toward an integrative model of change. *J Consult Clin Psychol*. 1983;51:390-395.
10. Wewers ME, Stillman FA, Hartman AM, Shopland DR. Distribution of daily smokers by stage of change: Current Population Survey results. *Prev Med*. 2003;36(6):710-720.
11. Steinberg MB, Schmelzer AC, Richardson DL, Foulds J. The case for treating tobacco dependence as a chronic disease. *Ann Int Med*. 2008;148(7):554-557.
12. U.S. Food and Drug Administration-Consumer updates. 2008; <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm170356.htm>; accessed March 2011.
13. Tonstad S, Davies S, Flammer M, Russ C, Hughes J. Psychiatric adverse events in randomized, double-blind, placebo-controlled clinical trials of varenicline: a pooled analysis. *Drug Safety*. 2010; 33(4),289-301.
14. Tonstad S, Tonnesen P, Hajek P, Williams KE, Billing CB, Reeves KR. Effect of maintenance therapy with varenicline on smoking cessation. *JAMA*. 2006;296,64-71.
15. Gundersen DA, Steinberg MB, Jordan HM, Delnevo CD, Berger HF, Hrywna M. The 2008 New Jersey Health Care Provider Tobacco Survey: A Statewide Report for the New Jersey Department of Health and Senior Services. New Brunswick, NJ: University of Medicine and Dentistry of New Jersey-School of Public Health; 2008.
16. Hyland A. Perceptions of NRT safety and efficacy: results from the International Tobacco Control (ITC) Four C Country Survey. In: Society for Research on Nicotine and Tobacco (SRNT) Pre-conference Symposium, Increasing Access to Effective Treatments: The Case for More Flexible Regulatory Policy; Austin, TX; 2007 Feb 21.
17. Steinberg MB, Alvarez MS, Delnevo CD, Kaufman I, Cantor JC; Disparity of Physicians' Utilization of Tobacco Treatment Services; *Am J Health Behaviors* 2006;30(4);375-386.
18. Thorndike AN, Rigotti NA, Stafford RS, Singer DE. National patterns in the treatment of smokers by physicians. *JAMA*. 1998; 279(8):604-608.

IMS Health Data Sources. National Retail Prescription data is sourced from the IMS Xponent family of products. Xponent™ is based on actual prescription activity within the retail, mail service, long-term care, specialty retail, and Puerto Rico markets. Based on complex algorithms Xponent projects prescriptions generated across all prescription channels and payment types (cash, Medicaid and third-party) for more than 800,000 individual prescribers every month. IMS collects over 75% of the retail prescription data. The IMS LifeLink™ Health Plan Claims Data is fully HIPAA-compliant assuring anonymous data collection, and is used to provide the diagnostic and treatment information for this newsletter. This source is comprised of fully adjudicated medical and pharmaceutical claims for over 60 million unique anonymous patients from over 90 health plans across the US. The database includes both inpatient and outpatient diagnoses and treatment. The database is representative of the national, commercially insured population on a variety of demographic measures including age, gender, and plan type.

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