



# Tobacco Dependence Treatment ToolKit

## Executive Summary

### Overview

This Tool Kit provides a practical approach to treating tobacco dependence effectively. The Tool Kit approaches tobacco dependence as a severe chronic illness, such as asthma, with exacerbations and remissions, and is based on the premise that chest physicians must be as actively and professionally engaged in treating tobacco dependence as they are with asthma. Effective tools, treatment algorithms, and strategies to obtain compensation for tobacco-dependence treatment services are provided.

Consensus recommendations in this Tool Kit are based both on the evidence in the literature and the extensive experience of the Committee members in tobacco-dependence treatment. Evidence on which we base our recommendations is described in the text and cited in the references. Because this product is a Tool Kit and not a guideline statement, we did not seek to formally grade evidence. For the interested reader, [US guidelines](#), [UK guidelines](#), and [ERS guidelines](#) are available. Treatment recommendations made in this Tool Kit are consistent with the recommendations in these guideline statements. However, the Tool Kit also includes practical information that is not part of the US Guideline due to the absence of studies in those areas, and useful tools to put your knowledge into practice. The tools in this Tool Kit include [treatment algorithms](#), [patient assessment tools](#), [patient management tools](#), [communication and patient education tools](#), [resources for healthcare practitioners](#), and [physician advocacy](#) information. Thus, this Tool Kit is more than a guideline; it is a bridge that provides the additional, practical information and tools you need to connect the knowledge base provided in the guidelines with what you need for day-to-day medical practice to provide effective tobacco-dependence treatment.

Please be advised that in certain instances, this Tool Kit includes treatment recommendations that are not approved in the US (so-called off-label uses of pharmaceutical products). For prescribing information, please see package inserts for all pharmacotherapeutics mentioned in this Tool Kit.

The Tool Kit opens with [Coding and Billing Principles](#), so that physicians can provide appropriate tobacco-dependence care to their patients and obtain fair compensation without undue financial hardship. The use of this Tool Kit places every chest physician at the forefront of preventive medicine and proactive treatment—a key component of every healthcare program.

### Principles of therapy

Approaching tobacco dependence as a chronic disease acknowledges the altered central nervous system (CNS) [neurobiology in tobacco-dependent patients](#). Therapy in asthma has the goal of achieving (near) normal airway function; similarly, the goal of therapy in tobacco dependence is to [normalize brain function](#)—so that the patient has minimal to no symptoms of nicotine withdrawal. Common nicotine withdrawal symptoms include:

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

The goal of tobacco-dependence therapy is to control and minimize these withdrawal symptoms through individualized treatment, thus allowing the patient to feel (near) normal while not using tobacco. The intensity of treatment should be based on the severity level of nicotine dependence. For highly nicotine-dependent patients, combination therapy is often needed.

In asthma, both long-acting Controllers and quick-acting Relievers are used; a similar approach can be used in tobacco-dependence treatment. Nicotine patches, bupropion, and varenicline can be thought of as Controllers. As in asthma, for those with moderate to severe disease, combination of Controller with Rescue or Reliever therapy is often needed to achieve therapeutic goals. Nicotine gum, lozenge, inhaler, and nasal spray can be thought of as Relievers, for as-needed use to relieve exacerbations (see [Treatment Process and Approach](#) and [Stepwise Treatment Guide](#)). A green-yellow-red zone [Action Plan](#) can be provided to the patient. Continuing the asthma analogy, medication is stepped down not according to a fixed time schedule, but as disease control permits. If the nicotine withdrawal symptoms are well-controlled, stepping down medication can be considered. If withdrawal symptoms are not well-controlled, consideration should be given to stepping up medications (see [Pharmacologic Treatment](#) and [Quick Reference Guide to Pharmacotherapy](#)).

### ARMR model

Based on a chronic disease model, we propose that tobacco-dependence treatment follows a proactive approach model that we call ARM<sup>R</sup>: **A**ssess and diagnose, **R**ecommend a treatment plan, **M**onitor the treatment plan's outcome, and **R**evise the treatment plan to improve effectiveness and minimize side effects.

- **A**ssess and diagnose (see [Patient Assessment Tools](#))
  - The [Fagerström Test for Nicotine Dependence \(FTND\)](#) is used to assess level of nicotine dependence. Pediatric assessment can be done with the [Modified Fagerström Tolerance Questionnaire \(mFTQ\)](#) to assess nicotine dependence and/or the [Hooked on Nicotine Checklist \(HONC\)](#) to assess autonomy over smoking behaviors.
  - Assess for previous history of or current psychiatric co-morbidities, such as depression, dysphoria, bipolar disorder, and post-traumatic stress disorder (PTSD) (see [Depression, Mood, Dyspnea, and Quality of Life Scales](#)).
- **R**ecommend a treatment plan (see [Pharmacologic Treatment](#))

- The treatment plan should be based on the level of nicotine dependence, with more dependent patients needing more aggressive therapy.
- Refer to the 2.2 Stepwise Tobacco-Dependence Treatment Guide, [Tables #1 & #2](#).
- For moderate to severe tobacco dependence, the combination of a Controller and Reliever medication is most beneficial. Very severe dependence often requires more aggressive pharmacotherapy, often with combination Controller or high-dose nicotine patch and for longer-than-typical treatment durations ([Tobacco-Dependence Treatment Process and Approach, Case Examples 1 & 2](#)).
- **Monitor** the treatment plan's outcome ([see Patient Management Tools](#))
  - The [Nicotine Withdrawal Symptom \(NWS\) Scale](#) is used to determine adequacy of control of withdrawal symptoms for patients already on treatment.
  - Depression, anxiety, suicidality, and other psychopathology are more common in smokers. Inadequate tobacco-dependence therapy may unmask these problems. Rarely, Controller medications (nicotine patch, bupropion, or varenicline) have been associated with depression and suicidality. Physicians treating tobacco dependence should routinely monitor for the development of psychiatric problems ([see Depression, Mood, Dyspnea, and Quality of Life Scales](#)) at each office visit, and, depending on the underlying cause, either increase nicotine replacement therapy, change control medications, or increase the doses of controller medications. In such cases, the treating physician should also consider psychiatric referral to determine whether these changes reflect an underlying or emergent psychiatric state or are merely nicotine withdrawal symptoms ([see Tobacco-Dependence Treatment Process and Approach](#)). Again, continuing the asthma analogy, this situation is very much like the controversy that revolves around the use of beta-agonists and increased mortality. Although over-use of beta agonists increases asthma mortality, so does poorly controlled asthma. Physician assessment and follow-up are key to better patient outcomes.
- **Revise** the treatment plan to improve its effectiveness and minimize side effects.
  - Base effectiveness on achieving control of nicotine withdrawal (rather than treating for a fixed time limit like 6 weeks). The patient and physician should decide together whether treatment needs to be escalated, can be stepped down, or can be discontinued. Just like any chronic disease, including asthma, re-exposures or exacerbations may occur that require a temporary increase or re-institution of medication.
  - If Reliever/Rescue medication is needed with high frequency (>10-15 times a day), consider escalation of the Controller medication regimen, such as by increasing the nicotine patch dose or by adding a second Controller medication.

### Reduction toward cessation

Tobacco-dependent patients who are not yet ready to stop smoking may benefit from use of a nicotine patch or bupropion to help them reduce their smoking and prepare for stopping completely.

### Relapse

Relapse is common in tobacco-dependent patients, particularly those whose treatment plan is inadequate. Relapse prevention strategies ([see Tobacco-Dependence Relapse-Prevention Checklist](#)) are best discussed 4-6 weeks after stopping smoking and when nicotine withdrawal symptoms are well-controlled. Triggers for relapse ([see Trigger Settings](#)) can include:

- Stress (or other negative mood states)
  - Particularly when that stress occurs in the presence of another smoker
  - Especially if stress occurs in the presence of another smoker along with mild alcohol consumption
- Sudden or unexpected re-appearance of nicotine withdrawal symptoms
- Celebrating or at a party
  - Particularly when consuming modest amounts of alcohol
- Plans to prevent relapse ([see Tobacco-Dependence Relapse-Prevention Checklist](#) and [see Behavioral Homework Worksheet](#)) in at-risk situations can include the following strategies:
  - Think something different
  - Do something different
  - Use nicotine Rescue Medication to prevent exacerbations, relapse, or re-exposure

### Tobacco dependence in pregnant women or women of childbearing age

Smoking is one of the most important modifiable causes of poor pregnancy outcomes in the United States.

- Ideally, women who smoke should be treated effectively for tobacco dependence BEFORE they become pregnant.
- Stopping smoking during pregnancy can still improve fetal outcomes.
- Behavioral counseling is advised as first-line therapy for tobacco-dependent pregnant women. If behavioral counseling alone is insufficient, pharmacotherapy for tobacco dependence, in most cases, poses less risk to the fetus than continued maternal smoking. As with any chronic disease, including asthma, working closely with the patient's obstetrician is advised. An algorithm for treatment of tobacco dependence in pregnancy is described in [Smoking and Tobacco-Dependence Treatment for Pregnant Women and Women of Childbearing Age](#).

### Tobacco dependence in parents

Pediatric healthcare providers have an important role in tobacco-dependence treatment and prevention ([see The Role of the Pediatric HealthCare Provider...](#)).

Tobacco dependence of parents can and should be addressed within the context of a child's health care. We endorse the American Academy of Pediatrics statement, "Pediatric health care providers should be knowledgeable about tobacco-dependence treatment and ROUTINELY offer help and referral to those who are tobacco dependent".

### Adolescents

Most adolescents who smoke consider themselves to be addicted to nicotine, recall withdrawal symptoms during previous attempts to stop smoking, and find it difficult to stop smoking. They often continue smoking well into adulthood. The [Hooked on Nicotine Checklist \(HONC\)](#) can be used to assess loss of autonomy over smoking in adolescents and young adults. There has been a dearth of research into effective tobacco-dependence treatment programs for youth. Given the

demonstrated effectiveness and safety of first-line tobacco-dependence treatments in adults and the grave harm of continued tobacco dependence, a trial of medically supervised pharmacotherapy plus close, ongoing follow-up is warranted in tobacco-dependent adolescents who are interested in stopping smoking ([see Management of the Child/Adolescent at Risk for Smoking](#)).

### **Intermittent, Non-Daily & Social Smoking**

Intermittent, non-daily smoking—frequently escalating to daily smoking and tobacco dependence in adolescents—may represent a low-incidence, stable form of chronic low-level use in adults. ([Intermittent, Non-Daily & Social Smoking](#)). Although it may not be associated with substantial tobacco dependence, it still subjects the individual to the adverse health consequences of smoking. Many of the above-noted triggers for relapse are also triggers for intermittent tobacco users. For these patients, focus should be on assessment of smoking behavior; behavior modification centering around trigger avoidance or, when not possible, use of nicotine rescue medication; counseling about the dangers of their active smoking and the effect of their smoke on friends and loved ones; encouragement of a smoke-free home and car; and behavioral counseling to negotiate reduction and elimination of smoking.

### **Conclusion**

In conclusion, the American College of Chest Physicians is committed to tobacco-dependence treatment and prevention. This Tool Kit will allow each of us to fully implement the College's Fellowship Pledge that we take upon induction into Fellowship. This Tool Kit provides the treating physician and other health care providers with an effective program that can be instituted immediately for every patient in your practice, no matter age or gender. It builds on published tobacco-dependence treatment guidelines, lessons learned from prior versions of this Tool Kit, and the experience and expertise of the Tool Kit Committee members. It attempts to increase your comfort in providing treatment by using your experience in the stepwise treatment of asthma as a foundation for effective tobacco-dependence treatment. This Tool Kit will enable you to help your patients to stop smoking successfully and remain tobacco free.

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## Suggested Citation

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The suggested citation is provided below:

Sachs DPL, Leone FT, Farber HJ, Bars MP, Prezant DJ, Schane RE, Glantz SA, Graham LM, Kletter AS, Pohlig C, Harrod CG, Lewis SZ. American College of Chest Physicians Tobacco-Dependence Treatment Tool Kit, 3rd Edition. Northbrook, IL: American College of Chest Physicians. November 2009. URL: <http://tobaccodependence.chestnet.org>, pp. 1-98.

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# Tobacco Dependence Treatment ToolKit

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### Acknowledgements

The committee gratefully acknowledges the contributions of the following individuals who provided invaluable assistance to this project:

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# Tobacco Dependence Treatment Tool Kit

## How To Use The ACCP Tool Kit

Treating patients with tobacco dependence is a medical responsibility. As with asthma, it requires the physician to accurately diagnose the state and severity of tobacco dependence, co-morbid conditions caused by tobacco use, and co-morbid conditions that could complicate the overall management and effective treatment of tobacco dependence. The chest physicians, in particular, but also primary care physicians, need to be on the vanguard, just as they have been for years in accurately diagnosing and effectively treating asthma. After all, tobacco use *causes* most of the lung diseases physicians treat. Those that it doesn't cause, it worsens. The *Tobacco-Dependence Treatment Tool Kit (3rd Edition)* Committee's [hereafter referred to as the Tool Kit Committee] aim is to provide physicians with proven tools and the scientific background necessary so that physicians and other professional healthcare colleagues can effectively treat tobacco dependence in their patients, and be appropriately paid for those skills, so that in another 10-15 years tobacco use will be fading into history.

### What is New in this Version of the Tool Kit

The Tobacco-Dependence Treatment Tool Kit (3rd Edition) was designed primarily for physicians, but also for nurses and tobacco dependence counselors to help their patients stop smoking. This is the 3<sup>rd</sup> edition produced by the American College of Chest Physicians (ACCP) since 2001. In this edition, clinical information and tools have been updated but many additional content sections and tools have been added, including advice on how to code for reimbursement, interpersonal approaches to yield the most successful partnerships with patients, protocols and tools for pediatricians to use for adolescent smokers and parents of their patients, and advice on treating pregnant women and non-daily smokers. Also new in this edition are sections on advocating for smoke free communities and increased taxes on cigarettes, locating endorsed performance measures, and slides to use for community and professional presentations. The patient education materials have been significantly revised, as have the sections on pharmacologic treatment.

### Tool Kit Overview

The Tool Kit contains a variety of [background content](#) and suggested [Treatment Algorithms](#) intended to provide the practitioner with relevant background information and practical insights into the treatment of tobacco dependence. Reviewing these sections and the video [introductory video] will improve your effectiveness by 1) making you more comfortable discussing tobacco-dependence treatment with your patients, 2) challenging potentially counterproductive pre-existing notions about treatment, and 3) presenting tips from the experts on identifying and dealing with commonly encountered conditions and challenges in stopping smoking.

**Section III** offers several [Patient Assessment Tools](#) that may be useful during the initial intake and evaluation phase of the tobacco-dependence treatment visit. We recommend you choose the instruments that make the most sense for patients within your practice. Several tools developed by other organizations and medical centers are presented as examples but permission has been granted for the owners of this Tool Kit to reproduce these tools for clinical or educational purposes only. In **Section IV**, the Tool Kit provides [Patient Management Tools](#) that may be used for your own organizational purposes, including chart stickers, checklists, a sample consultation report form, and special tools designed for pediatricians. Please modify and personalize these as necessary, so that they can be most useful and effective in *your* practice.

**Section V** presents several examples of [Communication and Patient Education Tools](#) including patient educational materials and systems instruments for improving communication within your practice and with insurance providers. Physicians and other healthcare providers are encouraged to use the Freedom From Tobacco Action Plan to help patients assess their own symptoms and follow prescribed treatments.

**Section VI**, [Additional Resources](#), includes a set of slides for presentations to patients, community groups, and professional meetings. This section also contains referral sources for national and state Quit Lines and contact information for other tobacco control organizations and resources.

The Tool Kit Committee encourages physicians and other healthcare providers to take an active role in advocating for smoke free ordinances and other means (e.g., increased tobacco taxes) that effectively prevent or reduce tobacco use and exposure. [Physician Advocacy](#), provides a guide for organizing grassroots advocacy at the local level and supporting references, annotated bibliographies, and talking points. Finally, Section VIII, on the [ACCP Role in Tobacco-Dependence Treatment](#), contains a historical timeline of the ACCP's efforts to reduce and prevent tobacco use and exposure and the ACCP No Smoking Pledge that all new Fellows of the College take at convocation.

### Where to look for the information you need

Within the background content of Section I, you will find the foundation of the entire Tool Kit. [Tobacco-Dependence Treatment Process and Approach](#), explains the recommended methods for managing chronic tobacco dependence. We encourage a multimodality approach, because treatment effectiveness, such as the proportion of patients who completely stop tobacco use and do not relapse, is higher when pharmacologic and behavioral management are combined. Further, a combination of long- and short-acting medications (Controller and Rescue, or Reliever, Medications) have resulted in even better gains, especially when combined with support and follow-up. [The Tobacco-Dependence Treatment Process and Approach](#) section also includes ideas for motivating the resistant patient to agree to a treatment plan for stopping smoking and for dealing with relapse. The [Treatment Algorithms](#) in this Tool Kit have been derived from the evidence-based recommendations in the guidelines published by the US Department of Health and Human Services in 2008<sup>1</sup>, the California Thoracic Society in 2005<sup>2</sup>, and supplemented by expert opinion and advice wherever necessary. These algorithms illustrate the process recommended by the Tool Kit Committee.

Section 1.7, [Pharmacologic Treatment](#), is designed to help the provider determine an appropriate, unique, individual treatment plan for each patient. The accompanying [Quick Reference Guide to Pharmacotherapy](#) provides critical facts about the use of available tobacco-dependence medications, as well as contraindications and side effects for both over-the-counter and prescription-only medications.

Pediatricians and others who provide services to children should read Section 1.10, [The Role of Pediatric Health Care Providers in Tobacco-Dependence Treatment and Secondhand Smoke Exposure Reduction](#). This section also covers identification and reduction of secondhand smoke exposure and the treatment of tobacco

dependence in the parents. The provision of healthcare services to children accompanied by their parents provides a very opportune and teachable discussion point about the adverse health effects of tobacco use, both primary and secondary, and for then initiating tobacco-dependence treatment in tobacco-dependent parents.

Section 1.3, [Coding and Reimbursement](#), may be one of the most important sections in the ACCP Tool Kit. It shows you how you can appropriately be reimbursed - **at your usual and customary fees** - for diagnosing and treating tobacco dependence, using standard, existing CPT and ICD-9-CM codes.

Section 6.3, [General & Referral Resources](#) includes addresses, telephone numbers, and Web sites of professional organizations that provide information and services that may be of use to your practice. Though the majority of listed resources are geared toward the clinician, a few sites also provide resources for patients and their families. A table of Quit Lines available in each state is also included.

### A word about using the ACCP Tool Kit tools

The remaining sections of this Tool Kit are consumable "tools" and the ACCP grants permission for these tools to be printed from this CD to assist you in the treatment and education of your patients and others. Materials may not be used for commercial purposes without the express written consent of the ACCP.

The ACCP Tool Kit Committee has designed most materials to be easily printed on standard 8 1/2" x 11" paper. You may print the chart stickers on standard Avery laser labels #5267. The [Patient Education Brochures](#) may also be downloaded from [www.chestnet.org/accp/patient-guides](http://www.chestnet.org/accp/patient-guides).

### Implementation

The physicians, nurses, and medical assistants within your practice, each with his or her defined role in encouraging the tobacco-dependence treatment process, should be able to easily implement the information and resources within this Tool Kit in regular office and hospital practice. *All of the tools provided in this Tool Kit have been used in actual clinical practice by at least one of the members of the ACCP Tool Kit Committee.*

Although this Tool Kit is written for the physician office setting, tobacco-dependence treatment counselors and hospital-based treatment programs can readily incorporate the concepts and most of the tools to work in these settings.

### The "1-2-3" Approach to Implementing this Tool Kit

The volume of material in this Tool Kit may seem overwhelming at first. However, realize that this is a comprehensive set of tools, not all of which you will use. The Tool Kit Committee chose to include multiple examples of resources so that all users of this Tool Kit can choose those most relevant to their practice. Also, some tools are only applicable to certain patient types.

Physician oversight is recommended for optimal integration of this Tool Kit into the office practice. However, the nurse or certified medical assistant also will use this Tool Kit on a day-to-day basis. Each physician will select those tools most appropriate for their practice and will need to assign the office staff the responsibility of ensuring those tools are available to the right personnel, as needed. For example, the receptionist and/or medical record managers should assure that the patients are provided with the appropriate assessment tools (e.g., the Fagerstrom Test of Nicotine Addiction) for completion in the reception area or early in the office visit.

The process of implementing this Treating Tobacco Dependence Tool Kit approach into your practice is as simple as 1-2-3:

Step 1 - Review the Treating Tobacco Dependence Tool Kit with your staff.

- Review your motivation for change - identify your current practice patterns: is there room to improve your practice efficiency in dealing with tobacco-dependence treatment?
- Discuss the proposed system changes and set some simple. Keep it simple, take baby steps, and reiterate the rationale for change.
- Think about how you can use the ACCP Tool Kit to help augment your existing tobacco-dependence treatment routines.

Step 2 - Identify roles.

- Make a list of the new tasks required of your team.
  - Two such examples follow:
    - Identify tobacco use status, give smoking patients an initial assessment form, e.g., the Fagerström Test for
    - Nicotine Dependence (FTND) or the Nicotine Withdrawal Symptom (NWS) scale
  - Deliver patient educational materials, including resource list
  - Decide who in your office will perform each of the critical tasks.
  - Discuss roles with office staff and make sure each staff member is comfortable with each assigned task.

Step 3 - Go for it!

- Just try it... see what happens!
- Remember to get feedback from your staff. Make modifications as necessary but do not give up on the goals.
- Give feedback to the American College of Chest Physicians. The College is always trying to improve services to its members. You may send your comments and suggestions to [Science@chestnet.org](mailto:Science@chestnet.org).

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# Tobacco Dependence Treatment ToolKit

## Introduction and Goals

### Introduction

Patients who use tobacco often represent a frustrating paradox for the chest physician and other healthcare providers. On the one hand, both physician and patient generally recognize the tremendous incentive to stop: Tobacco dependence is a fatal disease. If not treated, tobacco dependence kills 50% who suffer from it. Moreover, very few remain untouched by the tremendous toll on health and the human suffering tobacco use visits upon family and friends. As many as 90% of tobacco-dependent people identify tobacco use as harmful and want to reduce or stop using it.<sup>3, 4</sup>

On the other hand, the majority of tobacco-dependent people also experience a visceral reluctance to stop smoking, making only very brief and infrequent attempts to stop. Attempts to stop smoking are frequently private, even covert, for fear of not being able to stop. Few tobacco-dependent people seek a physician's advice on the best ways to use available over-the-counter medications and, in our experience, even fewer ask for help once their attempts begin to go awry. Unfortunately, since becoming available over-the-counter, Nicotine Replacement Therapy (NRT) has increasingly been used for too short a time and with too low a dose to be effective.<sup>5</sup> More than 95% of self-directed attempts to stop smoking will be doomed to fail without some form of additional help.

Physicians are in a powerful position to effect change. Most tobacco-dependent patients relate that physicians' advice was instrumental in aiding their attempts to stop smoking. Nearly 70% of tobacco-dependent patients see their physicians each year,<sup>1</sup> and even brief, 60-second advice from a physician can double to triple the spontaneous stop-smoking rates to 10%.<sup>3, 4</sup> One study<sup>6</sup> even showed that brief, 60-second advice from a physician increased 1-year, continuous stop-smoking rates from 0.3% to 5.1% (a 17-fold increase). Yet, despite this enormous potential, physicians often cite very significant concerns when it comes to the practical realities of treating tobacco use within their office practice, such as limited time available for a typical visit, poor reimbursement for tobacco-related services, limited knowledge and training specific to tobacco-dependence treatment, and a perceived ineffectiveness of therapy. Physicians and advance practice nurse practitioners generally have a working knowledge of treatment options and recognize the importance of patient intervention. However, patient measures of self-efficacy are generally poor, and relying on our patients' willpower and ineffective or misused over-the-counter aids is a Sisyphean endeavor. Therefore, most tobacco-dependent patients will be more successful in eliminating tobacco use with the help of a physician or advance practice nurse practitioner or other tobacco-dependence treatment specialist.

### Tool Kit Goals

The American College of Chest Physicians (ACCP) recognizes that this position remains untenable as long as the practical realities of tobacco-dependence treatment within medical practice remain unaddressed. To this end, the Tobacco-Dependence Treatment Tool Kit, 3rd Edition has been revised in an attempt to better serve the practicing physician interested in becoming more efficient and more effective in impacting this problem. In addition, in order to remove the negative connotations, stigma, or blame often associated with tobacco dependence, terms such as "tobacco-dependence treatment" and "stopping smoking" will be used in preference to "cessation;" "tobacco-dependent patient" or "tobacco user" instead of "smoker;" "continuous nonsmoking" instead of "abstinence;" and "stop smoking" instead of "quit."

By using the Tool Kit, clinicians will:

- *Get reimbursed for their efforts.* Clinicians should expect to be reimbursed for their interventions. Understanding the basic difference between a typical E&M visit and one focused on health counseling is the first step in successfully integrating tobacco-dependence treatment into your practice. Only modest adjustments in style and content are necessary to document the level of service provided. Attention should be paid to including all of the most appropriate ICD-9 codes for the reimbursement problems physicians face, including those that relate to tobacco-dependence treatment. This Tool Kit will help physicians and their billing managers understand how to increase the reimbursement rate associated with tobacco-dependence treatment.
- *Address tobacco dependence in the manner of a chronic disease, characterized by long-term relapse and remission.* We believe this approach will help relieve the typical awkwardness of "success" vs. "failure," encourage a medical model for tobacco-dependence treatment, and help engender a more therapeutic doctor-patient relationship. We frequently modeled the recommendations in this Tool Kit after the National Heart and Blood Institute's (NHLBI's) National Asthma Education and Prevention Program (NAEPP) Guidelines for the Diagnosis and Management of Asthma<sup>7</sup> to help make this Tool Kit's logic and style more familiar to chest physicians, although the target audience also includes primary care physicians, as well as hospital-based and out-patient nurses and cessation counselors.
- *Feel comfortable providing brief counseling.* The emotional burden of shame and guilt brought on by the diagnosis of a tobacco-related illness is often all too obvious in the strained examining room or during bedside conversations between physician and patient. Using the general principles and resources presented in this Tool Kit will help clinicians develop an effective approach to evaluation and management by providing useful patient education materials, practical tips, and evidence-based treatment recommendations.
- *Develop an aggressive prescribing philosophy for pharmacologic support.* The recommendations presented in this Tool Kit are intended to help clinicians make sound pharmacologic decisions based on available evidence and expert advice. In this 3<sup>rd</sup> edition of the Tool Kit, the Committee sought a model that would adequately guide the clinician while offering choice and individualization of treatment plan. By applying the concept of "Rescue/Reliever" and "Controller" medications (as in the stepwise asthma therapy model) to the treatment of tobacco dependence, we believe that we can increase the comfort level of both the treating healthcare professional and the patient for the use of these medications. Because the motivation to stop smoking is often fleeting, because treatment "failure" often means learned inefficacy, and because these treatments taken together are among the safest class of medications used by physicians, we support a model of therapy where physicians seek to effect control of withdrawal symptoms early, and taper or reduce treatment later based on feedback from the patient.

- *Develop efficiencies in practice, making intervention more feasible.* By utilizing the system tools, patient education resources, and practices available in this Tool Kit, physicians can reduce the variability in treatment approaches, improve documentation and compliance with evolving regulatory requirements, and be more effective in delivering care within the realistic constraints of a busy practice.

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# Tobacco Dependence Treatment ToolKit

## Correct Coding Principles For Tobacco-Dependence Treatment

***Contrary to popular misconceptions, mechanisms for compensating clinicians for tobacco dependence treatment services do exist.***

### Introduction

The use of imprecise language surrounding smoking and tobacco has led to several unfortunate misimpressions over the years. The prevailing notion that "smoking cessation is not paid for" is strictly true when referring to publicly provided lay counseling such as quit lines, community groups, etc. However, cognitive services provided by physicians are reimbursable, irrespective of the problem to which they are applied.

While the specifics of tobacco treatment reimbursement vary by both insurer and contract, as a general rule, clinicians should expect to be fairly compensated for tobacco use treatment services, in a manner similar to compensation for services delivered for other problems. Because tobacco use treatment represents a special circumstance with overlapping behavioral and biological dimensions, it is important to understand the basic structure of the compensation model in order to ensure that billing practices are consistent with prevailing requirements and definitions. This section of the Tool Kit provides a general framework of coding and billing principles relevant to tobacco use treatment, intended to help practice managers overcome practical obstacles to the provision of care.

In addition to describing the framework for compensation, this section offers sample cases and highlights caveats wherever appropriate. Though accurate in a general sense, the Tool Kit examples are intended only as a guide, and should not be interpreted as a guarantee of payment. When discrepancies exist, contact payer representatives for specific plan details and definitive guidance.

### First question: Is it counseling? Or is it management?

Because tobacco use treatment relies in large part on good communication and an effective therapeutic relationship, there can be substantial confusion over whether what we do in the office should be considered counseling or management. Imprecision in usage frequently leads to synonymous connotations. While either of these services can be provided within a clinical encounter, there is a typological distinction between these two services that may be useful in deciding which coding and documentation requirements apply.

**Evaluation** refers to the cognitive processes applied while determining the significance or status of a problem or condition. This is typically accomplished through careful appraisal and study. As an example, the elements of evaluation in general medical practice might include a careful history, a review of systems, X-ray testing, or the physical exam. Similarly, evaluation requirements for tobacco use often include a careful evaluation of variables such as severity of nicotine dependence, the severity of confounding co-morbidities, the likelihood of downstream toxic effects of prolonged exposure, the patient's insight into the problem and his or her confidence in abstinence, prior experience with cessation, or response to your recently prescribed interventions.

**Management** refers to the conduct or supervision of activities in pursuit of a pre-specified end. This often implies that the plan be based on the results of the evaluation, and that it includes the judicious use of multiple means to that end. As an example, the management plan for a severe asthmatic in exacerbation might include the decision to begin systemic steroids and the advice to avoid environmental triggers, and might be based on information garnered through historical, physical, and radiographic evaluation. Similarly, management decisions in the tobacco dependent patient might include medication or environmental modification recommendations, and are typically based on information garnered through historical, physical, or standardized instrument evaluation (e.g., screening for depression).

**Counseling** refers to the professional guidance provided to an individual. Though the typical connotation of counseling implies the utilization of psychological methods, counseling often happens in medical practice disguised as patient education. For example, physicians often use various techniques of personal interview during the collection of case data, including testing interest and aptitude, in an attempt to find the optimal way to transmit information or direction. In asthma, instruction on proper inhaler technique, or on environmental management, might be considered counseling. In tobacco use treatment, similar examples might include a discussion of potential triggers, or suggestions on stress management techniques.

Within this construct, counseling may be considered a subset of the cognitive services typically employed during management, such that:



Readers are referred to *Coding for Chest Medicine* 2009 published by the American College of Chest Physicians for specific coding details and definitions.<sup>8</sup> Counseling services (also referred to as Behavior Change Interventions) are services that are provided directly by a physician or other qualified healthcare professional for the purpose of promoting health or preventing injury. These are distinct from the more typical evaluation and management (E/M) services, and may be reported separately when performed. Behavior change interventions are for persons who have a condition that may be considered a disease unto itself,

including tobacco use, obesity, or substance abuse. Separate and distinct E/M services may be provided on the same day but, in this case, the time spent providing the counseling services may not be included as a basis for the E/M code selection.

#### Case Example 1: The Tobacco Dependence Evaluation and Management Visit

*Mrs. Smith presents to your office on referral from a colleague. She is referred for help with her current tobacco use, totaling approximately 20 cigarettes per day for over 30 years. Your history focuses on details of her tobacco use patterns to date, including a fuller understanding of previous quit attempts, triggers to smoking, and the nature of her reluctance to quit. The review of systems reveals that Mrs. Smith often feels short of breath with 1 flight of steps, and your exam reveals coarse rhonchi in bilateral lung fields. Office evaluation procedures are performed, including administration of Fagerstrom's test for nicotine dependence (FTND), administration of a depression screening instrument, and evaluation of spirometry before and after bronchodilator administration. By your evaluation, the patient appears to suffer from severe nicotine dependence, has a high likelihood of major depressive disorder in the recent past, and has mild irreversible airflow obstruction. Based on these insights, you determine the most appropriate pharmacologic and non-pharmacologic interventions, and begin developing a plan with the patient. After some discussion, the final plan is agreed upon and you confirm the patient's level of understanding and concurrence with the plan. You set a return visit appointment for 3 weeks from today in order to check response to medications, barriers to adherence, and any potential side effects.*

Though there is a modest amount of patient education and counseling integrated throughout the visit, the evaluative nature of the encounter is manifest in several ways. The results of this evaluation were used to formulate a plan that included an iterative reassessment of the effectiveness of the recommendations.

#### Case Example 2: The Tobacco Dependence Counseling Visit

*Last week, Mr. Jones presented to your office for evaluation and management of a mild COPD exacerbation. At that visit, he expressed an interest in quitting, but neither you nor he were prepared to engage in more than a superficial discussion of smoking at that time. Because Mr. Jones has smoked nearly 2 packs of cigarettes daily for 45 years, you decided to ask Mr. Jones to return for a more prolonged and meaningful discussion in about one week. Today, Mr. Jones returns to learn more about his cessation options. During today's visit, you reviewed the relevance of Mr. Jones' smoking to his current medical condition, offered him some advice on the proper use of the nicotine patch, and discussed available mechanisms for extra-treatment support, including calls to the national quit line 1 800 QUIT NOW. He was able to appropriately reflect back his understanding of the problem and expressed an actionable plan to attempt cessation. You arrange for a follow-up visit in your office in two weeks with the intention of assessing his progress and making further recommendations.*

This visit is characterized by the near exclusive focus on patient education and counseling. While it may have included a perfunctory assessment of his physical progress since last week, the purpose of the visit is clearly to address several manifest educational needs. The evaluative functions in this visit are limited to concepts such as testing of beliefs, assessment of understanding, and articulation of subsequent steps.

#### Case Example 3: Combined E/M and Tobacco Dependence Visit

*Mr. Doe presents to your office for follow-up evaluation and management of cough. The visit focuses on the progress made in the diagnosis and management of the cough, including an assessment of response to therapy and a review of relevant radiographs. During the visit, he is once again engaged in a discussion regarding the relevance of cessation to his overall health. He expresses an interest in quitting, but is not willing to commit to a stop date at this time. At the conclusion of the cough visit, you use the final five minutes to discuss the barriers to cessation, and make some recommendations on appropriate pharmacotherapeutic options for Mr. Doe to consider.*

The dominant theme of this visit is the evaluation and management of cough. During the visit, an opportunity to address smoking presented itself, and additional time was spent focused on tobacco use treatment.

### **Next question: What is the level of service?**

#### *Evaluation and Management (E/M) services*

For most Evaluation and Management visits, clinicians will refer to the American Medical Association CPT Guidelines and Procedures Manual (CPT)<sup>9</sup> to identify the correct level of service through the algorithms that relate elements of history, physical exam, and complexity of clinical decision making. When it comes to treating tobacco dependence however, the actual level of cognitive service provided to the patient during the visit may not be neatly reflected by the standard E/M rubric. For example, the clinician may actively choose to forgo evaluating several systems on physical exam in favor of gaining more insight into tobacco use patterns and obstacles to cessation. Irrelevant details of the family history may be omitted in favor of evaluating concurrent substance abuse potential.

#### Case Example 1: The Tobacco Dependence Evaluation and Management Visit

In the event that the primary goals of the visit relate directly to the diagnosis/confirmation and management of tobacco use and related complications, clinicians may elect to code the visit using the appropriate E/M service codes that relate to the type and duration of the visit, as long as the time dedicated to tobacco treatment counseling exceeds 50% of the total visit time. In this case, documentation is necessary to highlight the distinction between the behavioral change intervention and the more robust evaluation and management services. For example, comments should include reference to the subjective and/or objective evaluation of nicotine dependence ([Patient Assessment](#)), evaluation of potential concurrent co-morbidities (e.g., depression, treatment contraindications, etc.), as well as their potential impact on management decisions. Education efforts regarding the nature of tobacco use, treatment strategies, and possible side effects should be documented, as should the patient's response to the discussion. The plan for treatment should be outlined, including any contingency planning discussed with the patient. These details help to establish the evaluative nature of the visit, as well as the more complex and iterative nature of longitudinal management. The level of service can be determined using time thresholds (Table 1) as long as the note clearly documents 1) the time dedicated to counseling,

2) that the total time of the visit exceeded the threshold, 3) that counseling activities occupied more than 50% of the total visit time, and 4) counseling details. It is acceptable for clinicians to use clear and concise notation to document these facts instead of long or cumbersome prose, for example: "Total 25 min / counsel 15 min."

Table 1 - Time thresholds (in minutes) that define levels of service per visit category.

Visit Category	Code Range	Level 1	Level 2	Level 3	Level 4	Level 5
Outpatient Consultation	<b>99241 - 99245</b>	15	30	40	60	80
New Patient	<b>99201 - 99205</b>	10	20	30	45	60
Established Patient	<b>99211 - 99215</b>	5	10	15	25	40

#### Case Example 3: Combined E/M and Tobacco Dependence Visit

Frequently, clinicians are faced with a visit that starts off focused on a different problem, but comes to include a discrete focus on tobacco. In this case, two options are available for coding the level of service. For visits in which the overall counseling time exceeds 50% of the total time dedicated to the visit, the level of E/M service may be calculated based on the time thresholds listed in Table 1. In this case, all elements of counseling, including for example the time spent educating the patient on the diagnostic considerations of cough, should be included when calculating the proportion of counseling time for the visit. Conversely, if the time spent in counseling does not exceed 50% of the total visit time, the clinician may elect to code for the two component services separately. That is to say that the level of E/M services may be based on the standard CPT rubric, with the additional counseling service coded using the Behavior Change Intervention codes listed below.

**Caveat:** In many practices, the evaluation and management of cough may prompt a "referral" to the nurse practitioner at the conclusion of the visit for more complete counseling services. **Remember that smoking cessation counseling services can be provided on the same day as E/M services, either directly by the physician or by other qualified healthcare professionals.** However, the time spent providing the counseling services may not be included as a basis for a single E/M code selection. Report the E/M visit separately from the behavioral health intervention, if guidelines for each service are met. When an office visit (e.g., 99213) and smoking cessation counseling (e.g., 99407) are reported on the same day, append modifier 25 to the E/M (e.g., 99213-25)

#### *Counseling services - Behavior Change Interventions*

Medicare and Medicaid deem smoking cessation counseling to be reasonable and necessary for individuals who have evidence of conditions linked to tobacco. Clinicians should consider using the counseling codes when tobacco use treatment can be viewed as a portion of, or adjunct to, the primary purpose of the visit. For example, in a patient who presents for evaluation and management of COPD, cessation counseling would be considered a core component of their care, but may not be the main focus of the interaction.

Cessation counseling that lasts less than 3 minutes is considered to be part of the standard E/M service for the underlying condition. For patients who require additional counseling, the clinician may also report **intermediate** (3-10 minutes) or **intensive** (greater than 10 minutes) of service. Effective January 1, 2008 Medicare implemented two new CPT codes to reflect these services: **99406** for intermediate counseling, and **99407** for intensive. These codes replace the previous G codes.

#### Case Example 2: The Tobacco Dependence Counseling Visit

Medicare requires that the medical record include some documentation of the necessity of this service, which may include reference to a condition or therapeutic agent that is being adversely affected by tobacco use. Comments in the record should document both the time spent in counseling, as well as pertinent details of the cessation strategies discussed. Medicare has assigned intermediate counseling (99406) 0.24 work Relative Value Units (RVU), and intensive counseling (99407) 0.5 work RVU. 99406 cannot be reported in conjunction with 99407. Medicare will cover two attempts at smoking cessation each year, with each attempt consisting of a maximum of four sessions (any combination of intermediate and/or intensive).<sup>10</sup>

**Caveat:** Remember that Medicare covers and reimburses this service, while other payers may not. Private insurers may place Behavior Change Interventions within their behavioral health services carve out, in which case reimbursement for these services is not available to other clinicians. When the insurer denies payment for smoking cessation counseling, the financial responsibility for the charges may fall to the patient.

#### **Last question: Which diagnosis is which?**

Readers are referred to the *International Classification of Disease, Ninth Edition, Clinical Modification* (ICD-9-CM)<sup>11</sup> for complete descriptions of diagnostic codes relevant to tobacco use treatment.

#### *Selection of Primary Diagnosis:*

Healthcare providers are expected to determine the primary diagnosis based on the condition most related to the current plan of care. The diagnosis may or may not be related to the patient's chief complaint or reason for presentation. The primary diagnosis must relate to the services rendered, and to the documentation of the visit details.

#### *Selection of Secondary Diagnosis:*

Secondary diagnoses remain defined as "all conditions that coexisted at the time the plan of care was established, or which developed subsequently, or affect the treatment or care." Secondary diagnoses may include conditions actively addressed in the patient's plan of care as well as any co-morbid conditions that affect

treatment decisions. Avoid listing diagnoses that are of mere historical interest and without impact on patient progress or outcome, or for which the physician does not mention a course of action.

Is the visit about tobacco?				
Yes		No		
Is the service evaluative in nature?		Did counseling occupy >50% of the total visit time?		
Yes	No	Yes	No	
Service type: E/M service	Counseling service	E/M service	E/M service for the primary visit, PLUS Counseling service for tobacco portion	
Notes: ✓ Use time thresholds?	Level based on time	Level based on time	✓ Separate providers?	
1 <sup>st</sup> Dx Examples Toxic Effects of Tobacco (989.84)	Nicotine Dependence(305.1)	Asthma (493.00) COPD (496) Cough (786.2)	COPD (496) Cough (786.2) Fever (780.6)	
2 <sup>nd</sup> Dx Examples Shortness of breath (786.05) Angina (413)	Toxic Effects of Tobacco (989.84) Cough (786.2)	Toxic Effects of Tobacco (989.84)	Toxic Effects of Tobacco (989.84)	
Additional Counseling Code	N/A	N/A	Nicotine Dependence (305.1)	

**Caveat:** There is a subtle difference between Nicotine Dependence (305.1) and Toxic Effects of Tobacco (989.84). Nicotine dependence refers to the addictive nature of tobacco use. Strictly speaking, the evaluation and management of addiction may be considered the purview of behavioral health professionals, and may be subject to behavioral health contractual restrictions when used as the primary justification for the E/M visit. Toxic Effects of Tobacco (989.84) refers broadly to the set of untoward downstream consequences of tobacco use, within which dependence may be included. Within medical E/M encounters that relate primarily to tobacco, it may be most appropriate to list Toxic Effects of Tobacco (989.84) as the primary justification for the visit, and include the relevant related diagnoses and symptoms, for example Nicotine Dependence (305.1), COPD (496), or Cough (786.2), as the secondary diagnosis codes. It is best to note the related condition(s) as "resulting from" or "the toxic effect" of tobacco use. This best supports use of 989.84 when the documentation is internally or externally reviewed.

**Caveat:** Medicare guidelines allow Nicotine Dependence (305.1) to be used as the primary diagnosis code when reporting Behavioral Health Interventions, both intermediate (99406) and intensive (99407) services. Secondary diagnoses that reflect the related disorders or symptoms being affected by tobacco use should also be included to reflect the composite health concerns that prompted the counseling service. Current regulations prohibit Nicotine Dependence (305.1) from being used as the primary diagnosis for inpatient services.

**2009 Pulmonary PQRI performance measures**

The 2006 Tax Relief and Health Care Act (TRHCA) (P.L. 109-432) required the establishment of a physician quality reporting system, including an incentive payment for eligible professionals who satisfactorily report data on quality measures for covered services furnished to Medicare beneficiaries during the second half of 2007 (the 2007 reporting period). The Centers for Medicare and Medicaid Services (CMS) named this program the Physician Quality Reporting Initiative (PQRI). Pay for performance initiatives are developed in nearly all sites of service, and focus on the delivery of quality medical services. The ACCP encourages all eligible practices to participate in PQRI.<sup>12</sup>

In December 2008, CMS finalized the list of performance measure specifications for their 2009 initiative, which began January 1, 2009. Two measures specific to tobacco use are included in this initiative. Specifications for these measures are detailed on the CMS Web site and are available at [www.cms.hhs.gov/pqri] under "Codes/Measures." Denominator codes are the universe of eligible cases. The numerator quality-data codes (QDC) are the related CPT Category II codes listed below.

**PQRI Measure #114: Inquiry Regarding Tobacco Use**

**Description:** Percentage of patients aged 18 years or older who were queried about tobacco use one or more times within 24 months. Report a minimum of once per reporting period for all patients seen during the reporting period.

**Use codes:** CPT II **1000F** Tobacco use assessed (only modifier **8P**)

**AND**

CPT II **1034F** Current tobacco smoker, or

CPT II **1035F** Current smokeless tobacco user, or

CPT II **1036F** Current tobacco non-user

**PQRI Measure #115: Advising Smokers to Quit**

**Description:** Percentage of patients aged 18 years and older who are smokers and who received advice to quit smoking. Report a minimum of once per reporting period for all patients (whether or not they currently use tobacco) seen during the reporting period.

Use codes: CPT II **G8455** Current tobacco smoker

**AND**

CPT II **4000F** Tobacco use cessation intervention: counseling, or

CPT II **4001F** Tobacco use cessation intervention: pharmacologic therapy, or

CPT II **G8456** Current smokeless tobacco user, or

CPT II **G8457** Current tobacco non-user

**Examples of successful systems**

*Veterans Health Administration (VHA) Codes (Appendix A).*

Despite its effectiveness, tobacco-dependence counseling has been "widely underutilized in the VA healthcare system and other systems nationally."<sup>13, 14</sup> In an effort to increase the utilization of these services, the VA instituted several important policies intended to reduce or remove obstacles to care.

Beginning in 2003, the VA lifted prescribing restrictions on tobacco-dependence medications, making them more easily prescribed without the need for referral to a tobacco-dependence specialist.<sup>15</sup> Tobacco-dependence pharmaceuticals are available at the standard pharmacy benefit co-pay.

For outpatient tobacco-dependence treatment visits, VA physicians use the same standard diagnostic (ICD-9-CM) and procedural (CPT) codes as non-VA healthcare providers. Effective May 2, 2005, physicians have the ability to eliminate the visit co-payment requirement for these visits and provide group or individual counseling without cost to the patient.<sup>13, 14</sup> The physician or care provider uses the following STOP codes to remove the co-payment for counseling.<sup>13</sup>

**533707** Smoking Cessation Counseling - Individual

**566707** Smoking Cessation Counseling - Group

The elimination of the co-pay for patients receiving counseling removes a potential barrier for any tobacco-dependent patient who expresses interest in stopping smoking. Providing no-cost counseling increases patient use fourfold and those counseled are four times more likely to quit.<sup>14</sup>

Starting in January 2007, the Veterans Administration System revised its performance requirements, mandating that VA physicians not only advise all patients to stop smoking, but also offer and provide effective treatment, including counseling and pharmacotherapy, for tobacco dependence.<sup>15</sup>

*Kaiser Permanente of Northern and Southern California (Appendix B).*

Based on the cumulative evidence confirming a tremendous cost savings to health maintenance organizations, Kaiser Permanente of Northern California substantially liberalized its tobacco-dependence treatment formulary in 2003. Kaiser beneficiaries can now receive any FDA-approved tobacco-dependence medication in any dose and combination deemed necessary by the physician. Moreover, pharmacotherapy may be continued without restriction on treatment duration, if determined necessary for preventing relapse.

Tobacco-dependence medications currently on formulary include nicotine patch, nicotine gum, nicotine lozenge, and bupropion SR. Though non-formulary, the nicotine inhaler, nicotine nasal spray, and varenicline are available as a covered benefit if the physician enters the appropriate "exception code" on the prescription.

Patients receive the pharmacy benefit at the standard co-pay rates by enrolling in one of the many behavior modification options offered. Kaiser Permanente of Northern and Southern California effectively eliminated barriers to effective treatment by providing patients with access to resources including telephone counseling, web-based cessation, and multisession group counseling programs, based on individual preference.

*Caveat:* A 2005 Centers for Disease Control (CDC) survey found that 75% of state Medicaid plans will cover at least one form of tobacco-dependence treatment (i.e., medication or counseling) for their beneficiaries upon physician prescription at either no cost or a modest medication co-payment, although for close to one quarter of states, medication coverage depended on enrollment in a behavior-modification program or participation in smoking-cessation counseling.<sup>16</sup> In the 2006 CDC survey, the percentage of state Medicaid plans covering tobacco-dependence treatment increased to 76.5%; however, measures limiting their use also increased, "including measures that were inconsistent with the guideline (i.e., copayments, stepped-care approaches, requirements for enrollment in counseling to obtain medication, limitations on number of treatment courses, and not allowing combined treatments)."<sup>17</sup> Many commercial insurance carriers have similar programs. Pediatric health care providers can code for tobacco-dependence treatment services for children or their parents under the same diagnosis codes as adult health care providers.

**A call to action**

Insurers often adopt coverage policies similar to those of Medicare. With tobacco dependence however, there is variability in coverage detail. Policies that limit reimbursement, carve out tobacco use treatment to a small subset of clinicians, or otherwise obstruct access to effective therapies represent unsound medical policy. Physicians are in a powerful position to create change by acting at the public health and public policy levels.<sup>18</sup> Those interested in engaging in policy debates can do more than simply relay facts about tobacco and health to insurers. Engaging payers in discussion about coverage policies provides the opportunity to impact accessibility of tobacco use treatments, and is likely to be synergistic with efforts to help smokers quit within the office. Physicians who take steps to engage in local public health initiatives are likely to magnify the effects of their efforts at the bedside.<sup>19</sup>

*Cost Effectiveness*

Treating tobacco dependence is exceptionally cost-effective. As intensity of treatment goes up, the cost per quality adjusted life-year (QALY) saved goes down.

On average, it costs only \$3,539 per year of life saved, and as little as \$1,108 when intensive treatment is provided.<sup>20</sup> This compares favorably to other more expensive but common interventions, including HIV pharmacotherapy, renal transplantation, heart transplantation, treatment of hyperlipidemia, annual mammography, and even hypertension screening and pharmacotherapy.<sup>20, 21</sup> (e.g., See [Table 2](#)). Tobacco-dependence costs are recovered in approximately 9 months.<sup>22, 23</sup>

**TABLE 2**  
**Cost-Effectiveness Comparison of Tobacco–Dependence Treatment with Common Medical Tests and Interventions**

Medical Screening Tests or Interventions	Cost per Year of Life Saved <sup>20, 21</sup>
Tobacco-dependence pharmacotherapy and intensive physician involvement	\$1,108
Pneumovax	\$1,500
Tobacco dependence (minimal intervention)	\$4,329
AIDS pharmacotherapy	\$6,553
Renal transplantation	\$9,756
Heart transplantation	\$16,239
Hypertension screening	\$23,335
Hyperlipidemia pharmacotherapy	\$36,000
Postmyocardial infarction thrombolytic therapy	\$55,000
Annual mammography	\$61,744
Hypertension pharmacotherapy	\$72,100

### Summary recommendations

1. Create pre-printed encounter forms and fee slips that include the relevant tobacco dependence treatment codes alongside other common practice codes.
2. Encourage good communication on coding and reimbursement issues; monitor reimbursement by insurer and identify patterns / requirements early.
3. Query payer policies for varying coverage and coding instruction. Although Nicotine dependence (305.1) is the preferred ICD-9-CM diagnosis code for counseling services, other third party payers may reserve 300-level codes for behavioral health professionals. Using 305.1 as the primary diagnosis can result in claim denial if employed by a non-behavioral health clinician.
4. Keep good medical records. Review documentation of tobacco dependence E/M and counseling services to ensure that your notes meet documentation requirements for counseling time spent with the patient.
5. Continue to advocate for reimbursement from insurance carriers who do not currently support tobacco-dependence treatments.
6. Tobacco-dependence treatments are eligible expenses under many flexible spending account (FSA) plans, enabling patients to use pretax dollars to pay for health care expenses.

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- [Correct Coding Principles: Appendix A](#)

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# Tobacco Dependence Treatment ToolKit

## Correct Coding Principles: Appendix A

### Veterans Affairs/Veterans Health Administration

#### General Information

There are approximately 23.4 million veterans in the United States, and the Veterans Affairs (VA), also called the Veterans Health Administration (VHA), provides health care for nearly 7.9 million of them.<sup>24</sup> The VA currently has 153 medical centers and 909 ambulatory care and community outpatient centers in the United States.<sup>24</sup> The population of veterans who receive their medical care from the VHA has a slightly higher percentage of people who smoke (22% of approximately 7.2 million veterans, or 1.54 million people)<sup>25</sup> than the general U.S. adult population (20%, or 43.4 million people).<sup>26</sup> These numbers represent a significant decrease of smoking prevalence from 33% in the veterans population<sup>27</sup> vs. 24% in the general population<sup>28</sup> in 1999. Note that the smoking prevalence rate across Veterans Integrated Service Networks (VISNs) varies significantly, ranging from 16.5% to 27%.<sup>29</sup>

The VA offers and "encourages a comprehensive, evidence-based tobacco use screening and cessation counseling program"<sup>29</sup> as outlined in the United States Public Health Service *Treating Tobacco Use and Dependence: 2008 Update - Clinical Practice Guideline*<sup>1</sup> and the VA-Department of Defense (DoD) *Tobacco Use Cessation Clinical Practice Guideline* (TUC-CPG).<sup>30</sup> The most current version of the VA/DoD *Tobacco Use Cessation Clinical Practice Guideline* was updated in 2004, and will be updated to reflect the revised 2008 Public Health Service *Clinical Practice Guideline*. The VA provides tobacco-dependence treatment in the form of advice during normal appointments, free tobacco-dependence counseling, and pharmacotherapy with co-pay to all eligible veterans. In addition, tobacco-dependence specialty clinics provide more intensive counseling and treatment.<sup>31</sup> The VHA has required that VA physicians provide such treatment to veterans since 2007.

The key elements of treating tobacco dependence in the VA program are as follows:<sup>32</sup>

- **Every** tobacco user should be advised to quit.
- Tobacco use is a **chronic relapsing condition** that requires repeated interventions.
- Several **effective treatments are available** in assisting users to quit.
- It is essential to **provide access** to effective **evidence-based** tobacco use **counseling treatments and pharmacotherapy**.
- **Collaborative tailored treatment strategies** result in better outcomes.
- Quitting tobacco leads to **improved health and quality of life**.
- **Prevention strategies** aim at reducing initiation, decreasing relapse, and eliminating exposure to environmental tobacco smoke.

#### Tobacco-Dependence Treatment Policies and Performance Standards for VA Physicians

The VHA has taken steps over the past several years to promote tobacco-dependence treatment. The VA began systematic tobacco use screening - asking patients about tobacco use and advising them to stop smoking - as part of its performance measures in 1996.<sup>15</sup> In 2003, the VA lifted its restrictions on tobacco-dependence medications and mandated the availability of tobacco-dependence medications so that they could easily be prescribed to veterans.<sup>15</sup> The 2004 update to the VA/DoD *Tobacco Use Cessation Clinical Practice Guideline*<sup>30</sup> recommended "offering drugs and counseling to all smokers in the most intensive setting they are willing to attend."<sup>15</sup> The co-payment for tobacco-dependence counseling services, but not including pharmacotherapy co-pay, was removed in October 2005, in order to decrease financial barriers to treatment.<sup>15</sup> As of January 2007, the Veterans Administration System revised its performance requirements, mandating that VA physicians not only advise all patients to stop smoking, but also offer and provide effective treatment, including counseling and pharmacotherapy, for tobacco dependence.<sup>15</sup>

As of 2007, VA performance measures now require the VA physician to:

- Screen for tobacco use at least once per year and advise the patient who smokes to quit,
- Provide all current tobacco users with brief counseling for tobacco dependence, as described in the VA/DoD *Tobacco Use Cessation Clinical Practice Guideline*,
- Offer pharmacotherapy for tobacco-dependence treatment,
- Refer patients to a VA or community tobacco-dependence treatment clinic.

The electronic medical record system<sup>33</sup> is used as a tool to support performance measures, establishing a clinical reminder for the physician to assess tobacco usage by simply following the steps listed on screen. The health care provider documents directly into the electronic medical record the services and treatments that were provided. However, the time spent with the patient is not documented by this electronic system. (Further information about the Performance Measurement Program can be found at the Office of Quality and Performance Department of Veterans Affairs website.<sup>34</sup>)

The VA tobacco-dependence treatment programs (also referred to in the VA literature as tobacco or smoking cessation programs) support treatment for VA patients with either the primary care or mental health services provider, because the mental health provider is often the primary care provider as well. Any VA physician, however, can now provide tobacco-dependence treatment, including prescribing pharmacotherapy. The VA also has provided nationwide training programs on tobacco-dependence treatment for VA mental health care providers to keep them up to date on techniques and pharmacotherapy and enable them to train other providers at their local VA facilities.<sup>35</sup>

#### Approved Formulary

Physicians and care providers can prescribe tobacco-dependence medications (nicotine gum, patch, or lozenge, or bupropion, varenicline, or Combination Nicotine Replacement Therapy (CNRT)) that are listed in the VA-approved formulary pharmacotherapy table<sup>36</sup> and are available at pharmacy co-pay to veterans. All medications that are on the FDA approved list, and that are widely used outside of the VA, should also be available in the VA's formulary. Local VA pharmacies, however, at their sole discretion, may over-ride the physician's prescription and restrict the number of refills. Pharmacotherapy is also tied to the VA/DoD *Tobacco Use Cessation Clinical Practice Guideline* recommendations. Individual VA pharmacies may limit or restrict what medications they allow their VA physicians to prescribe for treating tobacco dependence. In such cases, the pharmacy may not provide sufficient resources to enable physicians to follow the recommended VA/DoD *Tobacco Use Cessation Clinical Practice Guideline* performance criteria. Therefore, although the VHA, as a health-care delivery system, is far more advanced and enlightened than private, third-party payers, there is still too much deviation from the mandated, national VA tobacco-dependence performance standards that is paradoxically dictated by the local VA pharmacy. Individual VA physicians, therefore, need to determine the pharmacological resources available to them at their specific VA and then work within their VA structure to improve those resources so that they are able to provide the level of care outlined by VA/DoD *Tobacco Use Cessation Clinical Practice Guideline* and this Tool Kit, and thus to fully comply with the medically appropriate and scientifically justified national VA performance standards for tobacco-dependence diagnosis and treatment.

### Veteran's Co-Payments

There are two main co-pay categories that are used for the tobacco-dependence treatment programs. There are no limits on number of office visits or counseling sessions.

- (1) No co-payment for tobacco screening and tobacco-dependence counseling (individual or group).
- (2) Basic \$15 co-payment for a basic outpatient primary care visit (for priority categories 7 and 8 only; no co-pay for other priority categories).

The co-payment for pharmacotherapy is \$8 for a 30-day supply of medication for outpatient treatment for those patients who have a medication co-pay.<sup>37</sup>

The VA uses special categories and priority groups for veterans and provides exceptions to the co-payments for them (e.g., for POWs, those with severe injuries sustained in the line of duty, etc.).<sup>38, 39</sup>

### Computer-Based Program for VA Care Providers

The Erie, PA VA Medical Center uses an enhanced computer-based program to support tobacco-dependence treatment. The program addresses both patient support and education. It automates tasks for the medical providers and allows them to order medications, provide ongoing education and counseling services, and arrange for follow-up visits immediately, during the patient visit. The first three months of using this program resulted in a 400% increase in the number of patients given smoking cessation treatment.<sup>33</sup> After further trial, this program could be easily ported to all other VA medical centers.

### VA Summary & Conclusions

The Veterans Administration Health Care System steadily and consistently increased the level, intensity, and effectiveness of tobacco-dependence treatment for its veterans between 1996 and 2007. In 1996 tobacco dependence became a priority for the VA system, nationwide. In 1996 the VA required physicians to ask each patient if that patient smoked and, if so, advise that patient to stop smoking. By January 2007, those physician performance standards had increased so that physicians were required to provide effective tobacco-dependence treatment including pharmacotherapy, as recommended by the 2004 VA/DoD *Tobacco Use Cessation Clinical Practice Guideline* and the 2000 US Public Health Service *Clinical Practice Guideline: Treating Tobacco Use and Dependence*.

Between 1999 and 2007, the smoking prevalence rate among veterans in the VA Health Care System fell from 33%<sup>27</sup> to 22%<sup>25</sup>. Also, between 1999 and 2007 the smoking prevalence rate among the US population, overall (men and women) fell from 24%<sup>28</sup> to 20%<sup>40</sup>. Thus, the VA smoking prevalence rate fell 33% between 1999 and 2007 while that in the civilian population fell only 17%. This is no accident and reflects the consistent increase in depth and breadth of tobacco-dependence treatment services that the Veterans Administration provided over those years to its veterans.

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# Tobacco Dependence Treatment ToolKit

## Correct Coding Principles: Appendix B

### Health Maintenance Organization (HMO) Capitated Managed Care Plans: Kaiser Permanente

HMO capitated managed care plans identify a specific budget and allow provider physicians to allocate the funds as they see fit. Tobacco-dependence treatment has proven highly cost effective (see [Table 2](#) in coding section) in reducing unexpected doctor's office visits; preventing, averting or resolving problems with other types of care; and reducing medication expenditures related to hypertension, asthma, and other pulmonary conditions.

Managed care organizations tend to encourage more healthful lifestyle changes and are generally willing to cover preventative services such as tobacco-dependence treatments. Kaiser Permanente (KP) of Northern and Southern California are examples of changes in HMO managed-care-plan formularies for tobacco-dependence treatment.

#### Kaiser Permanente's Tobacco-Dependence Pharmacotherapy Benefit

Before 2003, the lifetime pharmacy benefit for a patient suffering from tobacco dependence was a mere 42 "Step 1" nicotine patches (1 patch/day for 6 weeks). And that once-in-a-lifetime benefit could only be obtained if the Kaiser patient attended a one-day/week, 6-week group-counseling program. This changed in 2003 because the scientific literature compellingly showed that tobacco-dependence treatment was effective, tobacco dependence was a chronic medical disease, not one that was acute and self-limited, and that scientifically based tobacco-dependence treatment was highly cost-effective, enabling an HMO, such as Kaiser Permanente, to realize system-wide, real dollar savings within one year.

As of 2008, the Northern California Kaiser Permanente formulary for tobacco-dependence treatment includes nicotine patch, nicotine gum, nicotine lozenge, and bupropion. Nicotine inhaler, nicotine nasal spray, and varenicline, while not on-formulary, are available to the patient at standard co-pay rates if the prescribing physician enters an exception code on the prescription.<sup>41</sup> The medication dosages and combinations used and the duration of treatment are not proscribed by the Kaiser pharmacy. Rather the Permanente Medical Group physician determines individualized tobacco-dependence pharmacotherapy, just as that physician would if treating any chronic medical disease, such as hypertension or asthma. Treatment duration is not limited, because Kaiser Permanente recognizes tobacco dependence as a chronic disease.

Tobacco-dependence medications are available at drug benefit co-pay when received by prescription and in conjunction with participation in an approved tobacco-dependence treatment program.<sup>42</sup> The patient may select from an array of such programs, based on the patient preference. This can be as simple as using Kaiser Permanente's telephone counseling line, 1-800 NO BUTTS, or a Kaiser Permanente web-based behavioral intervention, Breathe Online Healthy Lifestyles program (available on kp.org), or using more intensive behavioral management programs provided by Kaiser Permanente, including individual counseling, single-session workshop, or multi-session, group-counseling classes.

Formulary management of medications can provide an increase in value relative to cost and clinical experts are using such programs as a way to optimize cost. It also helps primary care physicians who may not have the expertise in treating tobacco dependence rely on the experts to provide standardized formulary combinations.

In Northern California, Kaiser Permanente's Clinical Recommendations for Tobacco Cessation 2008<sup>43</sup> includes the following policies:

- Medications are available as often as medically necessary, at drug benefit co-pay, in conjunction with participation in a Kaiser Permanente-approved behavioral management program (see above).
- KP patients with Medicare Part D coverage do not need to attend smoking cessation program in order to receive medications member co-pay.
- Counseling (group or individual) is available at no added cost to KP members.

Kaiser Permanente also provides:

- Smoking as a Vital Sign<sup>44</sup> (assessing smoking status implemented in primary and specialty care visits, built into electronic medical record system)
- 100% Smoke Free Campuses (no smoking allowed on Kaiser Permanente-owned property)
- Quit Tobacco programs available at no extra cost for Kaiser Permanente members (Available in person, online, and by phone. Northern California partners with the CA Quit Line for phone counseling support, Southern California provides their own telephone support.)

#### Background and Motivation for Kaiser Permanente's Tobacco-Dependence Benefit Changes

In the year 2000, Kaiser Permanente Northern California reviewed the cost and disease burdens associated with tobacco use and the cost effectiveness of known treatments. Data showing Kaiser Permanente Northern California's performance on tobacco-dependence interventions from the standardized HEDIS (Health Plan Employer Data Information Set) tool, from the National Committee for Quality Assurance (NCQA), showed several opportunities for improvement. (More than 90% of America's health plans use HEDIS to measure performance on important dimensions of care and service.) Kaiser Permanente Northern California also conducted analyses and concluded that an expanded formulary benefit for tobacco-dependence treatment would pay for itself in less than one year.<sup>41</sup> Such compelling internal data led to a major change in the pharmacy benefits for tobacco-dependence treatment.

At the time, the demand for smoking cessation programs was widespread among consumers, purchasers, and regulators, as well as important to Kaiser Permanente's emphasis on wellness and healthful lifestyle changes. Kaiser Permanente realized that tobacco dependence is a chronic and relapsing condition, and that charging for tobacco-dependence programs, which frequently require multiple quit attempts to achieve long-term or lifetime continuous nonsmoking, constituted a barrier to access for many patients. Considering the burden of the disease, the costs of providing programs to members was relatively small.

In 2003, to improve patient access to effective (and cost-effective) pharmacotherapy, Kaiser Permanente Northern California removed the limitations on the use of tobacco-dependence medications. The behavioral change program became available at no additional cost to members and the formulary medications were made available at co-pay (with participation in a treatment program), with an unlimited treatment schedule, for as long as clinically indicated – not restricted to once a year. Kaiser Permanente of Southern California also enacted similar changes.<sup>41</sup>

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# Tobacco Dependence Treatment Tool Kit

## The Scientific & Clinical Basis for the Tool Kit Recommendations

### Overview

In 1996, the US Public Health Service published its first set of treatment guidelines for tobacco dependence.<sup>45</sup> A rich source of evidence-based recommendations, the guidelines firmly established that healthcare providers have an ethical obligation to treat tobacco dependence as a chronic illness, rather than approach it as a mere lifestyle choice. Updated in June of 2000, and again in May 2008, the guidelines provide the reader with dozens of meta-analytic recommendations regarding initial treatment decisions, utility of follow up, relative impact of treatment format, etc.<sup>4</sup> We refer all clinicians interested in tobacco-dependence treatment to this comprehensive and influential work. However, the guidelines are limited in terms of practical suggestions to guide specific treatment strategies pertinent to the office setting. The ACCP Tool Kit Committee recognized that, in order to be most useful, recommendations regarding tobacco-dependence treatment need to strike a balance between an open-ended educational approach, where the reader is left to explore the area as needed, and a prescriptive "program" approach, which users may find relatively restricted in application within their environment. The Committee sought a model that would adequately guide the clinician while maintaining relevance to the individualities of practice. We relied heavily on the model developed for the NHLBI's *Guidelines for the Diagnosis and Management of Asthma*,<sup>364</sup> and offer a Tool Kit that comprises a combination of US Public Health Service guideline recommendations, current standards of practice within the field, and expert consensus advice. The Tool Kit recommendations are guided by four significant assumptions which, taken together, may be equally applicable to virtually any chronic illness, including asthma.

1. Tobacco dependence is the clinical manifestation of altered central nervous system (CNS) neurobiology. Just as wheezing or shortness of breath is the outward manifestation of abnormal airway inflammation, the compulsion to smoke can be thought of as the outward manifestation of the altered CNS structure and function related to reward, survival, and learning.
2. Discontinuing tobacco use is the process of gaining control over the compulsion to administer nicotine via tobacco, a process marked by variability over time.
3. Several co-morbid factors may modify the range of possible treatment outcomes; it is the clinician's responsibility to identify and manage these co-morbidities in order to help patients achieve the best possible outcome.
4. As patient advocates, the clinician's role is not merely to encourage stopping smoking, but to minimize the symptoms of nicotine withdrawal while working toward establishing long-term control over the smoking behavior.

### Tobacco Dependence as a Chronic Illness

The brain is a dynamic organ, growing, changing, adapting, and integrating what it learns from the environment. With nicotine exposure, changes occur not only in primary pathways related to the exposure, but also in related modulating pathways such that, over time, irrespective of the inputs, the brain's output drives the person towards tobacco use and dependence.

The Tool Kit presents a basic outline of the neuropharmacologic effects of nicotine exposure. It is not intended as a complete review of the biologic basis of addictive behaviors, only as a starting point for clinicians to better understand both the nature of patient interventions and a patient's reluctance to stop using tobacco. It is our intention to provide the reader with a rational basis for the use of pharmacotherapy as well as a framework within which to refine the therapeutic approach to these patients.

### The Process of Establishing Control

In a general sense, the "process of stopping smoking" may be thought of as three overlapping phases of progressive control: the initiation of continuous nonsmoking, the struggle to prevent slips, and the avoidance of relapse.<sup>46</sup> While relapse has traditionally been viewed as the primary outcome of treatment trials, strategies that focus on the processes mediating progression from a minor slip to a resumption of smoking behaviors have had a substantial influence on treatment outcomes.<sup>47</sup> Tobacco-dependent patients attempting to stop smoking will pass through a "high risk period" following their Target Stop Date, during which they may sustain one or more slips, or lapses.<sup>48</sup> Most, but not all, tobacco-dependent patients stop smoking for at least one day on their chosen Target Stop Date. After this, the majority will go back to smoking if left unassisted and untreated. The incidence of relapse is depicted in the table below.

Time Since Target Stop Date (Days)	Incidence of Relapse (%)
3	30
7	50
14	75
30	97

Often, resumption of regular smoking begins with a minor lapse of just one or two cigarettes. At this critical juncture, tobacco-dependent patients will either reaffirm their desire to stop and adjust their approach accordingly, or will rapidly revert to regular smoking routines.<sup>49</sup> Smoking lapses therefore represent an important clinical juncture between stopping smoking and relapse. Tool Kit recommendations focus on effective tobacco-dependence treatment through an *active process* of managing lapses to minimize their frequency and reduce the likelihood that a lapse will progress to relapse.

The severity of craving for cigarettes and nicotine withdrawal symptoms directly predict cigarette lapse and complete treatment failure, i.e., relapse to regular cigarette smoking.<sup>50</sup> All FDA-approved tobacco-dependence medications, including nicotine medications,<sup>51-53</sup> bupropion,<sup>54</sup> and varenicline,<sup>55</sup> significantly reduce severity of craving for cigarettes and other nicotine withdrawal symptoms. The better craving for cigarettes and other nicotine withdrawal symptoms are suppressed, the better the treatment outcome, the less the likelihood of relapse, and the less the likelihood of a lapse progressing to complete treatment failure.<sup>50, 53, 56</sup>

### Preventing Lapses with Aggressive Pharmacotherapy (The "Controller" Paradigm)

Several observations led the Tool Kit Committee to adopt rather aggressive strategies for achieving control of withdrawal symptoms using Controller Medications. Given that absorption of nicotine from the patch delivery system is highly variable, the concept of individualized dosing of nicotine has been tested for efficacy. Findings from several independent studies suggest that individualizing patch dose to achieve targeted serum nicotine level during treatment can significantly improve treatment results, including control over withdrawal symptoms.<sup>57,58</sup> Accomplishing this, however, requires substantially higher patch doses than have been traditionally recommended, generally upwards of two or more patches.<sup>59-61</sup> The main barrier to individualizing patch recommendations is the infeasibility of measuring serum nicotine concentrations in a clinical setting. In lieu of laboratory guidance, the Tool Kit Committee advocates an approach wherein the main goal of aggressive therapy is the effective relief of withdrawal symptoms. High-dose NRT reduces withdrawal symptoms and craving,<sup>53</sup> can eliminate some symptoms entirely<sup>53</sup> and reduces lapses and treatment failure (relapse).<sup>50</sup>

The data guiding the use of multiple Controller Medications in combination are revealing, rapidly growing, and consistently robust (See [Pharmacologic Treatment, "Combination Pharmacotherapy - The Current Treatment Standard"](#)). In a large randomized clinical trial, designed specifically to answer this question, treatment with sustained-release bupropion in combination with a nicotine patch resulted in significantly higher long-term rates of continuous nonsmoking than use of either the nicotine patch alone or placebo. Continuous nonsmoking rates were higher with combination therapy than with bupropion alone.<sup>62</sup> The group receiving combination Controller therapy experienced better relief of their withdrawal and craving symptoms. This combination of two Controller medications - bupropion + nicotine patch - is both FDA-approved and is one of three combinations specifically recommended in the 2008 Public Health Service Guidelines with an "A" rating, for strength of evidence showing treatment effectiveness.

**Tobacco-Dependence Treatment of Schizophrenic Patients with Combination Medications:** In a separate study, subjects with schizophrenia were placed on bupropion + dual nicotine medications (patch and gum) and experienced a greater rate of smoking reduction at weeks 12 and 24, and a greater continuous nonsmoking rate at week 8 than the dual-nicotine medications, alone, control group.<sup>63</sup> Among patients who initially failed treatment, continued therapy with bupropion SR, either alone or in combination with the nicotine patch, resulted in significantly higher short- and long-term continuous nonsmoking rates than treatment with the nicotine patch alone or placebo.<sup>64</sup> The compelling similarity of these findings across trials suggests that combination Controllers, specifically bupropion + nicotine patch, can provide greater benefit to tobacco-dependent patients who have had difficulty stopping cigarette use with only one Controller, who are severely nicotine dependent, or who suffer from psychiatric co-morbidities that can influence treatment outcomes.

### Managing Lapses with Acute Nicotine Administration (The "Reliever" Paradigm)

Nicotine replacement therapy (NRT) has repeatedly been shown to improve smoking treatment outcomes in general. Aggressive use of NRT has also been shown to decrease the risk of progression from lapse to relapse. Active treatment appears to reduce the risk of both a second lapse (Hazard Ratio=0.54) and relapse (HR=0.22). This therapeutic effect might be mediated via decreased reinforcement experienced during a smoking lapse. Acute cravings, often provoked by exposure to smoking cues, can be effectively managed by using acute delivery forms of nicotine following exposure to smoking cues. Effective, "just-in-time" interventions should be offered to all patients and implemented as needed. Several studies have shown that combining two types of NRT - nicotine patch, as a controller medication that produces relatively steady levels of drug in the body, and ad libitum dosing, using reliever nicotine medication, such as gum or nasal spray, adjusted acutely by the patient in response to specific nicotine withdrawal symptoms - is more effective in promoting prolonged nonsmoking than providing either alone.<sup>66-70</sup> The 2008 US Public Health Service Guidelines recommends combining the nicotine patch with a self-administered form of NRT (Controller + Reliever medications), especially in those who have poorly controlled nicotine withdrawal symptoms with a single medication in the past (Strength of Evidence = A).<sup>1</sup> Encouraging patients to use such combined treatments is an important role for the physician, since patients often have preconceived reservations, particularly safety concerns, about using combination NRT.

### Preventing Relapse with Long-Term Pharmacotherapy (The "Step-Down" Approach)

Clearly, patients are best served by an approach to pharmacotherapy that neither unnecessarily prolongs the duration of treatment for patients who no longer require it, nor prematurely discontinues it in those who do. Because the relationship between effectiveness and duration of therapy for any chronic illness is not simple or linear, decisions regarding length of tobacco-dependence treatment should be a matter of clinical judgment rather than a fixed schedule. There is far more to be lost by too little treatment than there is by too much. None of the medications used for the treatment of tobacco dependence contain any of the pathogenic components found in tobacco smoke<sup>71</sup> or result in strong dependence.<sup>72</sup> Therefore, while it is certainly preferable to taper medications at a comfortable rate, clinicians should not feel compelled to discontinue medications if, in their judgment, that would undermine control of nicotine withdrawal symptoms. (See [Pharmacologic Treatment, "Duration of Use"](#) for further discussion on this topic.)

For varenicline in particular, converging lines of investigation suggest that prolonged periods of treatment help tobacco-dependent patients maintain continuous nonsmoking longer than "standard" treatment periods. For example, while the recommended treatment period for varenicline is 12 weeks, an additional 12 weeks of treatment confers an advantage, with continuous nonsmoking rates significantly higher than in those who did not receive the additional treatment.<sup>73</sup> Treatment with 52 weeks of varenicline 1 mg BID was generally safe and was associated with a continuous nonsmoking rate that maintained a plateau of nearly 40% throughout the treatment period.<sup>74</sup> The data concerning long-term use of nicotine replacement products is more mixed. Though clearly more effective than no treatment, it is less clear whether sustained use of NRTs results in improved long-term outcomes. It is important to note that the variability in effect may be confounded by other treatment variables, such as dose, route of administration, etc.<sup>75</sup> Observations made on data collected during the Lung Health Study suggest that a large portion of sustained nonsmoking tobacco-dependent patients, when left to make their own decisions about treatment duration, were still using NRT 12 months after starting treatment<sup>76</sup> and some for as long as 5 years, with no serious side effects.<sup>293</sup> More recent studies have unequivocally shown that longer

treatment - longer than typically suggested in the drug label - produces better treatment outcome and a higher percentage who are able to stop smoking. These observations led the 2008 US Public Health Service Guidelines to conclude that, "For some patients, it may be appropriate to continue medication treatment for periods longer than usually recommended" and that "continued use of such [tobacco-dependence] medications clearly is preferable to a return to smoking with respect to health consequences. Finally, it should be noted that the medication treatment that produced the largest effects on [nonsmoking] rates ... involved long-term nicotine patch therapy + *ad libitum* NRT Table 6.26."<sup>1</sup>

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# Tobacco Dependence Treatment ToolKit

## The Biological Basis for Tobacco Use

### Overview

Nearly all tobacco users are aware that tobacco use poses substantial health risks. Most know and will acknowledge tobacco use will shorten their lives and that they have a 50% chance of death secondary to a tobacco-caused disease. They may not have conceptualized this, though, as playing "Russian Roulette" with a 2-barreled revolver.

Appreciating the nature of tobacco dependence requires clinicians to first recognize the fundamental and powerful way that nicotine, particularly when delivered via the cigarette, influences behavior and causes nicotine dependence. (If nicotine dependence does not exist, tobacco dependence cannot be produced.)

Most people who are tobacco dependent believe that all it takes to stop smoking is enough willpower. However, in light of seminal advances in neuroscience of the past decade, this position is no longer valid. For example, adolescent smoking is commonly understood to be a child's simple, natural quest for independence and a manifestation of rebelliousness. We now understand that the adolescent's decision to initiate the behavior is generally made during a time of intense Central Nervous System (CNS) development. Exposing the developing brain to periodic surges of nicotine results in usually permanent alterations in brain structure and function. At the most basic level, nicotine-caused changes in brain receptor number, density, sensitivity, and permeability alter the brain's response to its normal neurotransmitters. More insidiously, nicotine exposure changes neuronal gene expression, second messenger system functions, modulation mechanisms, and even arborization patterns, creating an environment that is "engineered" to function best in the presence of nicotine, not the brain's endogenous ligands. While not absolutely deterministic, these changes substantively influence the *likelihood* that the individual will maintain tobacco use indefinitely.

With this understanding, discontinuing tobacco use and the smoking behavior requires stabilizing altered neuronal physiology to control the resulting compulsion to smoke; willpower, alone, generally is not sufficient. Effective tobacco-dependence treatment requires optimal medical management as well as patient and family education and support. Just like any other chronic disturbance in biology, effective management is often iterative, requiring long-term interventions characterized by adaptation and response to change.

### Neurobiology of Nicotine Addiction

Nicotine in tobacco smoke increases the number of nicotinic acetylcholine receptor sites in the brain by 2- to 3-fold.<sup>77-83</sup> Moreover, this nicotine receptor proliferation is not necessarily reversible in humans.<sup>84</sup> Nicotinic receptors are located in all areas of the mammalian brain, but they are particularly concentrated in both the mesolimbic dopaminergic pathway and the locus ceruleus. These sites are of critical importance to the organism's basic survival functions, cognitive processing, and memory. Because of nicotine's ability to "highjack" these fundamental functions - while simultaneously *improving* cognition and memory - it is one of the most potent neuropharmacologic drugs of dependence, exceeding the abuse potential heroin, cocaine, or d-amphetamine.<sup>85</sup> Nicotine's effects are potentiated by the rapidity with which it reaches the brain. Following a deep inhalation of tobacco smoke, as much as a ten-fold arterial-venous concentration difference can develop within just a few seconds.<sup>86</sup> Consequently, the brain can essentially "discern" individual puffs of a cigarette. The rapid surge in arterial nicotine concentration delivered to the brain is an important stimulus for neuronal alterations, and is the main determinant of the beneficial and rewarding effects of nicotine.

### The Beneficial Effects of Nicotine

The mesolimbic system is normally activated in response to drinking water, eating food, and engaging in sexual activity - activities essential for the survival of both the individual and the species. Sensory cortical and cognitive areas of the brain interface with the mesolimbic system through axonal projections that extend onto the ventral tegmental area, or VTA. Nerve terminals in the VTA are cholinergic, with the dominant form of post-synaptic cholinergic receptor of the  $\alpha 4\beta 2$  nicotinic subtype. Post-synaptic efferents extend outward to the nucleus accumbens, where the nerve terminals are dopaminergic. Dopamine release into the synaptic cleft activates accumbal  $D_2$  receptors on post-synaptic neurons, resulting in an action potential that is propagated toward the pre-frontal cortex, generally responsible for generating visceral emotions such as safety, threat, satisfaction, or fear. In this manner, sensory input from the outside world, for example, from the visual system, translates into "positive or negative" survival stimuli that are important to help keep the organism safe from harm. The nicotinic  $\alpha 4\beta 2$  acetylcholine receptors in the VTA are particularly sensitive to changes in nicotine concentration. Tobacco-dependent people modulate emotions and reward, in part, by modulating accumbal dopamine levels. When dopamine levels rise with nicotine intake, the individual becomes more cognitively aroused, feels more alert and vigorous, and perceives the sensation of pleasure, or gratification.<sup>87-94</sup> When brain dopamine levels fall, the opposite occurs. The individual no longer exposed to exogenous stimulation by nicotine may feel moody, depressed, and dysphoric.<sup>93</sup>

### Nicotine Withdrawal

Abrupt discontinuation of cigarette smoking (i.e. stopping "cold turkey") produces a number of profound physiologic effects. For example, EEG alterations are accompanied by slowing of cognitive performance and difficulty concentrating.<sup>95, 96</sup> By far the most common, and perhaps the most motivating, effects of withdrawal include anxiety, irritability, frustration, and depressed mood. Rather than a manifestation of weakness of character, these symptoms are a manifestation of altered nicotinic and dopaminergic physiology within survival pathways of the CNS.

All nicotine withdrawal symptoms are promptly reversed by resumption of tobacco use.<sup>97</sup> Fortunately, administration of pharmaceutical nicotine also relieves the adverse effects of withdrawal.<sup>96, 98-100</sup> Therapeutically, physicians are in a position to help patients achieve the same salutary effect without relying on the toxic tobacco smoke vehicle to do it.

### Medications to Treat Tobacco Dependence

Understanding tobacco use as the behavioral manifestation of a biological problem helps to inform a rational approach to the pharmacologic management of

tobacco use and dependence. The medications discussed in the Tool Kit should be thought of as members of three distinct classes: 1) Nicotine medications, such as patch, gum, or nasal. All nicotine medications are nicotinic acetylcholine receptor agonists. 2) Dopaminergic/ Noradrenergic reuptake inhibitors, of which there is only one at present, bupropion. 3)  $\alpha 4\beta 2$  nicotinic receptor partial agonists, of which there is only one at present, varenicline. See "[Pharmacologic Treatment](#)" for further information and details on all tobacco-dependence medications, including effectiveness, side effects, and safety. Case Examples, marked as "[Medication Prescribing Examples](#)", are available in [Tobacco-Dependence Treatment Process and Approach](#) to show how to use the [Stepwise Tobacco-Dependence Treatment Guide](#) in this Tool Kit to help select starting medication(s), dose(s), and combinations, depending on pre-treatment patient characteristics.) Though the exact mechanisms of action for each class are not fully understood, there are several generalities that prove useful when developing a treatment plan. Nicotine agonists act mainly through direct stimulation of the VTA, indirectly resulting in maintenance of accumbal dopamine levels, even in the absence of the dramatic nicotine surges produced by the cigarette. Tricyclic (nortriptyline) and tetracyclic (bupropion) antidepressants work primarily by improving the dopaminergic milieu within the nucleus accumbens.<sup>101</sup> The newest class of medications FDA approved for the treatment of tobacco dependence (varenicline) functions as a partial agonist for the  $\alpha 4\beta 2$  nicotinic receptors in the VTA. These medications should not be viewed as equivalent or interchangeable. Each has a specific pharmacology, with substantial differences in mechanism of action. Biologic variability within a population of tobacco-dependent patients likely accounts for the observed variability in effectiveness of these medications, and warrants an individualized approach to therapy, where treatment choices are evaluated for relevance, re-evaluated for effect, and adjusted as needed to achieve predefined targets.

The growing understanding of the biological basis for tobacco use, brought about by the neuroscience and neurogenetic research of the past 20 years, has led to radically revised concepts of tobacco use, changing it from a "bad habit" to what it really is: a chronic medical disease. This enhanced understanding of the biological basis for tobacco use, in turn, has led to totally new concepts in treatment, illustrating the imperative need to incorporate medications, if tobacco dependence is to be effectively treated. The sections [Tobacco-Dependence Treatment Process and Approach](#) and [Pharmacologic Treatment](#) cover this in depth and breadth.

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# Tobacco Dependence Treatment ToolKit

## Tobacco-Dependence Treatment Process and Approach

### Introduction

When physicians routinely identify tobacco use and dependence in their patients, they are more likely to treat it. Recurring, brief, friendly, unambiguous physician advice to stop smoking significantly increases long-term nonsmoking rates by 17-fold (0.3% to 5.1%).<sup>1, 6</sup> Adding only one medication increases the effect of physician advice another 2-fold (4.1% to 8.8%).<sup>102</sup> By applying basic medical management principles such as those used for asthma, tobacco-dependence treatment can be an additional 5 to 8 times more effective.

This 3rd Edition of the ACCP Treatment of Tobacco Dependence Tool Kit is built on the evidence base provided by the [U.S. Public Health Service Guideline](#) for the treatment of tobacco use and dependence, the [California Thoracic Society Position Paper](#), and the extensive clinical experience of the [Members of this Committee](#) treating tobacco dependence in their own clinical practice (aggregate number of patients diagnosed and treated for tobacco dependence one-on-one or in small groups by all Committee Members >> 20,000).

Based on the above evidence, one of the Tool Kit's core recommendations is that pulmonary specialists need to be far more proactive in diagnosing and treating tobacco dependence in a non-judgmental, "no-fault" manner, using one or more effective medications, just as we do routinely with asthma. We need to move beyond "5-A" mnemonic, Ask, Advise, Assess, Assist, and Arrange (<http://www.surgeongeneral.gov/tobacco/tobaqrg.htm>), replacing it with the proactive medical-model approach described in this Tool Kit - **ARMR**: **A**ssess and diagnose the patient, **R**ecommend a treatment plan, **M**onitor the treatment plan's outcome, **R**evise the treatment plan to improve its effectiveness, if necessary, and to reduce side-effects, if any. [1] ARMR acronym and concept developed by Reza Taheri, PharmD, Chair, Department of Pharmacotherapy & Outcomes Sciences, Loma Linda University School of Pharmacy, Linda H. Ferry, MD, Department of Preventive Medicine, Loma Linda University School of Medicine, and David P.L. Sachs, MD, Chair ACCP Tobacco-Dependence Tool-Kit Committee, at a meeting on May 6, 2008. This is precisely what we do with any other chronic medical disease, such as asthma or COPD.

You, the treating physician, should **ASSESS** and approach the patient in an objective, helpful manner, routinely quantify nicotine dependence using the [Fagerström Test for Nicotine Dependence \(FTND\)](#) and also routinely quantify [Nicotine Withdrawal Symptoms \(NWS\)](#), before you **RECOMMEND** any tobacco-dependence treatment. You should also measure NWS at each visit after starting treatment, in order to **MONITOR** the treatment plan for effectiveness and side effects. This kind of information will enable you to then rationally **REVISE** the patient's treatment plan, including behavioral or pharmacologic components as necessary, to improve tobacco-dependence treatment effectiveness and reduce side effects, if any. This Tool Kit provides several instruments to measure the severity of Nicotine Withdrawal Symptoms that can be downloaded and printed for use in your practice. Select and routinely use the ones that work best in your practice.

Suppression of nicotine withdrawal symptoms should be your primary treatment objective. Failure to suppress nicotine withdrawal symptoms can make it much more difficult for a patient to stop cigarette use and remain nonsmoking. The only way to objectively and quantitatively monitor a treatment plan's effectiveness is to quantitatively measure the patient's nicotine withdrawal symptoms (see [Nicotine Withdrawal Symptom Scale](#)) at each visit. The pivotal importance of nicotine withdrawal symptom suppression is supported by four independent lines of evidence.

1. At least two separate, randomized clinical trials have shown that 75%<sup>103</sup> to 90%<sup>49</sup> of tobacco users relapse within a mere 30 days, when trying to stop "cold turkey"-without any treatment.
2. At least three separate clinical trials have identified craving for cigarettes<sup>104, 105</sup> or other nicotine withdrawal symptom severity<sup>106</sup> as the cause for this precipitous relapse within the first 30 days after Target Stop Date.
3. At least two, non-randomized, open-label clinical trials have shown that relieving symptoms of nicotine withdrawal and mood disturbance with specific combinations of tobacco-dependence medications-at much higher-than-standard doses-improves treatment outcome and continuous non-smoking rates at the end of a 3-month treatment course,<sup>107, 108</sup> and even 9 months after treatment end.<sup>109</sup>
4. At least one controlled trial showed that an abrupt, several-fold increase in nicotine withdrawal symptoms and craving for cigarettes occurred one to two days before relapse.<sup>110</sup>

The collective clinical-treatment experience of this Committee also supports the necessity of suppressing Nicotine Withdrawal Symptoms as completely as possible, *from the Target Stop Date onward*, to maximize treatment effectiveness.

A second and corollary recommendation of this Tool Kit is to start tobacco-dependence treatment even before the patient is in the classic "Action Phase" (see Prochaska JO, et al. for a description of the Transtheoretical Model for the Stages-Of-Change<sup>111</sup>) and entirely ready to stop smoking. This Tool Kit will provide specific, concrete steps that you, the treating physician, can take to help your patient "get to yes".

### The Biology of Nicotine Addiction

Tobacco dependence is a **chronic** medical condition prone to relapse and recurrence over time, particularly in the absence of effective medical management or if the patient does not adhere to the treatment plan. Cigarette use is the primary symptom of tobacco dependence. Nicotine dependence leads to neurophysiologic alterations of brain structure and function, including cell receptor abnormalities, neuronal development changes, and increased dendritic connections. Tobacco dependence causes a proliferation of nicotine receptor sites in the central nervous system. Some receptor abnormalities may be reversible in some patients but not in others. In either case, the CNS pathophysiology of tobacco dependence can be stabilized with effective pharmacotherapy. Uptake of nicotine increases CNS

dopamine and norepinephrine synthesis and release, as well as increased synthesis and release of serotonin, b-endorphin, vasopressin, and glutamate, which cause feelings of pleasure, arousal, enhanced memory and intellect, increased problem-solving abilities, and reduced appetite.<sup>2, 112, 113</sup> See [The Biological Basis for Tobacco Use](#) section, for more details on the biology of nicotine addiction and resultant tobacco dependence.

### Nicotine Withdrawal Symptoms

Nicotine has a half-life of 2 hours, which is why tobacco-dependent people awaken with a significant urge to smoke. All nicotine is out of the body 8 hours after smoking the most recent cigarette. The physiological problem in stopping smoking is not having nicotine in the body and needing to get rid of it, as some people think. Rather, the physiological problem is that merely overnight, no nicotine is left in the circulation or the CNS. Consequently, sudden withdrawal from tobacco leaves brain nicotine receptor sites unfilled, thereby reducing CNS dopamine and norepinephrine levels, leading to craving for cigarettes and other nicotine withdrawal symptoms such as the ones listed below.

1. Dysphoric or depressed mood
2. Insomnia
3. Irritability, frustration or anger
4. Anxiety
5. Difficulty concentrating
6. Restlessness
7. Decreased heart rate
8. Increased appetite or weight gain

These symptoms are real, not imagined, and are readily reversible in a dose-responsive fashion with nicotine itself, bupropion, and varenicline. Stopping smoking "cold turkey" is not a treatment for tobacco dependence and frequently is not effective. Allowing a patient to try cold turkey is sub-standard tobacco-dependence care. It should no longer be used or even considered as a treatment option, any more than we would regard "no treatment" as satisfactory for management of mild persistent asthma. You should offer pharmacotherapeutic treatment *for all tobacco-dependent patients*, and explain to all patients how the treatments can be helpful in reducing Nicotine Withdrawal Symptoms and increase the likelihood of remaining cigarette-free. Refer to the section on [Pharmacologic Treatment](#) for specific guidance and decision support.

### A Chronic Disease

As discussed in [The Scientific and Clinical Basis for the Tool Kit Recommendations](#) section, the chronic nature of tobacco dependence demands a long-term treatment approach. Patient relapse and remission can be minimized, if not completely eliminated, when the physician and patient are attentive to medication needs and do not prematurely terminate all pharmacotherapy, particularly prn Rescue Medications. That said, treatment effectiveness and treatment response should not be judged only on the basis of permanent nonsmoking, but also on the progress and response to treatment over time. Relapse is a hallmark of any chronic medical disease and does not reflect the personal failure of either physician or patient. *Rather, it indicates failure of the treatment plan and the need to revise it.* The chronic, relapsing nature of tobacco dependence parallels that of asthma, hypertension, or any other chronic disease.

Patients with these disorders are treated with appropriate medications, support, and counseling. The same should be provided to patients with tobacco dependence.<sup>114-116</sup> Timely revision of the treatment plan can reduce the probability of a lapse, or slip, progressing to full-blown relapse. Tobacco dependence, like any other chronic medical condition, requires periodic treatment-plan adjustments, such as a change of medication, dosage, or attention to behavioral factors that are also a part of any chronic medical disease.

### Lapse vs. Relapse

"Relapse" denotes a return to full, baseline smoking rate, while "lapse" means smoking only 1, or a few cigarettes over 7 days, or less. Smoking a single cigarette, or even a few, does not define the patient as a smoker again. Try to determine the trigger (e.g., presence of unbearable nicotine withdrawal symptoms, sudden stress, alcohol consumption, presence of other smokers) and help the patient identify ways to treat, avoid, or effectively manage those trigger settings in the future. Make certain that nicotine withdrawal symptoms have been nearly or completely suppressed-90% suppression or better is your goal. Revise the patient's treatment plan, if necessary, so that nicotine withdrawal symptoms are better controlled. Ask your patient what strategies have worked well in the past with that particular trigger. Reinforce those approaches. Offer your support and provide follow up. Encourage and be positive. Do not focus on the lapse, per se, but learn what caused it, how to more effectively treat that cause or prevent it in the future, and focus on the successes.

### Relapse Prevention

Approximate 1-3 months after the patient has stopped smoking, the treating physician, or another trained healthcare professional in that medical office, should have a straightforward discussion with the patient to let the patient know the highest risk settings for relapse, based on well-designed scientific studies. That way, your patient can plan ahead and have a relapse-prevention plan in place. When you begin the discussion of relapse-prevention strategies, your patient should not have smoked anything for at least 4-6 weeks and should not have been bothered by any nicotine withdrawal symptoms for at least 4-6 weeks.

Relapse in this setting is most likely to occur when your patient experiences:

1. Stress (or other negative mood states)<sup>117-122</sup>
  - Particularly when that stress occurs in the presence of another smoker
    - And especially if these 2 conditions occur in the presence of mild alcohol consumption
2. Sudden or unexpected re-appearance of nicotine withdrawal symptoms

Relapse also commonly occurs when your patient is:

3. Celebrating or at a party
  - Particularly when consuming modest amounts of alcohol

The patient can blunt the risk of relapse by engaging in proactive behavior:[120-123](#)

- Think something different
- Do something different
- Use nicotine Rescue Medication, e.g., nicotine nasal spray[112](#)

To facilitate relapse prevention, physicians should ask their patient open-ended questions and actively engage the patient in dialogue on:

- accrued benefits of stopping smoking,
- patient investment in and length of time the patient has been tobacco-free,
- possible resurgence of nicotine withdrawal symptoms and methods for managing them,
- problems encountered to date or anticipated threats to maintaining nonsmoking.

Relapse is most likely when patients experience internal or external conditions that make them vulnerable. The chief internal cause of relapse is persistence or re-appearance of uncontrolled and intolerable nicotine withdrawal symptoms, including craving.[104-106](#) The most common external causes of relapse are being in a high-stress situation or while drinking alcohol or both.[117, 124](#) Additionally, lines of evidence indicate that relapse is more likely to occur when the patient encounters lack of support from health-care professionals, family, or friends, experiences weight gain, feels deprived, or becomes depressed or dysphoric. If the patient identifies lack of support as a threat, practitioners should consider how that can be addressed or remedied. For example, make sure all office staff from front-office staff, to you, to back-office staff are fully supportive. If some on your staff are not supportive and think cigarette smoking is merely a character flaw and that the tobacco-dependent patient is just bringing this all on himself or herself and this kind of patient is just wasting everybody's time and wasting medical resources, this should be correctable by appropriate in-service education. If the staff member refuses to read or learn from relevant scientific material or attend and learn from internal or external educational opportunities, such as the Annual CHEST International Scientific Assembly or that of the Society for Research on Nicotine and Tobacco, then that staff member should be transferred to a position that involves no patient contact or should be terminated. You would not tolerate a similar negative attitude that was impairing your office's care of an asthmatic or diabetic. You should not tolerate it in situations involving a tobacco-dependent patient under your care.

If you learn that the patient's family or friends are not supportive or are belittling the patient, work with your patient to develop ways to help those close to the patient to be helpful and supportive.

You may also consider referring the patient to appropriate treatment counseling or support groups in their area (see [General and Referral Resources](#)). However, before making such a referral, make certain that such a referral will, in fact, be helpful and not undermine the patient's efforts. For example, some widely available, national groups clearly state that use of any medication, particularly nicotine medications, to improve stopping smoking is a sign of weakness and a character flaw on the patient's part and that such medications should not be used. You or one of your staff should be able to determine the philosophy and practical aspects of such a referral by talking with someone at such a referral source that would be involved with your patient or by checking that referral source's Web site.

You should, of course, schedule follow-up visits or telephone calls from you or one of your office nurses to provide additional support, to make certain that nicotine withdrawal symptoms continue to be completely suppressed, and to make certain that your patient is not prematurely tapering or stopping tobacco-dependence medications.

If you uncover an underlying depression or other psychiatric states or find such a state emerging after you have commenced an adequate tobacco-dependence treatment plan, you should increase pharmacotherapy and refer your patient to a psychiatrist knowledgeable in treating psychiatric illness in the context of discontinuing tobacco use.

In all cases where your patient has lapsed or relapsed, *DO NOT* stop use of tobacco-dependence medications, such as nicotine patch. If your patient has lapsed or relapsed, this is *prima facie* evidence of an inadequate and insufficient treatment plan that you and your patient must revise, precisely as you would do if an asthmatic patient under your care had a breakthrough asthma attack. Also, use this opportunity to provide encouragement for *any* positive movement toward complete elimination of tobacco use.

## Stopping Smoking

Although nicotine withdrawal symptoms are at their peak 24-72 hours after stopping smoking, gradually decreasing over the next 4 weeks, they can last many months, remaining strong 6 or more months after stopping smoking.[84](#) In some patients, one or more nicotine withdrawal symptoms can remain strong and disabling for years to life. The time for withdrawal symptoms to resolve is variable from one patient to another, and not predictable a priori, even for a given patient. Time until symptom resolution can only be determined as tobacco-dependence treatment progresses. Moreover, not all tobacco-dependent patients experience the same withdrawal symptoms.

Your patients need to know that using pharmacotherapy to maintain continued suppression of nicotine withdrawal symptoms is crucial for tobacco-dependence treatment to be effective and enables them to stop smoking without the pain and discomfort that inadequately treated nicotine withdrawal symptoms cause. The patient education guide [You Deserve to Stop Smoking Comfortably](#) contains further helpful information.

The [Pharmacologic Treatment](#) section of this Tool Kit provides you with information you should share with your patients before they begin to use of any tobacco-dependence medications. You can provide necessary behavioral management using the principles provided in the [Communication and Patient Education Tools](#) section. Other potentially valuable resources you should consider include your state's Quit Line and well-run group-counseling or support programs, such as those provided by the American Lung Association's Freedom From Smoking Clinics Program, the Hawai'i Tobacco Education & Assistance Program, or the UCSF (University of California, San Francisco) Tobacco Education Center. Similarly, determine if there are specific local resources or a clinical psychologist in your area who could amplify your care of the tobacco-dependent patient. Some pulmonary specialists and members of your College have recruited a clinical psychologist, trained in tobacco-dependence behavioral management, specifically to provide the necessary behavioral management and support. You can also provide your patients with the [General and Referral Resources](#) for local, state, and national contacts. Before any referral, though, you or one of your office professionals should thoroughly evaluate the program(s) you are considering using as referral options for your patients, to make certain your patients will not receive messages that

conflict with the behavioral and pharmacological management principles in this Tool Kit.

### Pharmacotherapeutic Approach

A basic understanding of the science of nicotine addiction and tobacco dependence provides the foundation for a rational pharmacotherapeutic approach to treating tobacco dependence. Because numerous pharmacotherapies exist and have been shown to be effective, physicians should prescribe these to their tobacco-dependent patients, except in the presence of contraindications, which are very rare. Six (6) first-line pharmacotherapies have been proven to reliably increase long-term non-smoking. Two (2) second-line pharmacotherapies can be effective options in the unlikely event that the first-line medications are not effective or cause intolerable side effects. Refer to the sections labeled [Quick Reference Guide to Pharmacotherapy](#) and [Stepwise Tobacco-Dependence Treatment Guide](#) for more detailed information on formulating your own pharmacotherapy approach.

### The Necessity of Using the Fagerström Test for Nicotine Dependence (FTND), Assessing Nicotine Withdrawal Symptoms (NWS) Regularly, and Assessing for Previous and Treatment-Emergent Depression

#### The FTND

You cannot plan your pharmacotherapy plan for your patient without measuring nicotine dependence (see [Fagerström Test for Nicotine Dependence \(FTND\)](#)). You cannot determine your treatment plan's effectiveness for your patient, including the pharmacotherapy component, without measuring nicotine withdrawal state (see [Nicotine Withdrawal Symptom \(NWS\) Scale](#)). It is axiomatic in medical practice that you have to measure the right variable-FEV<sub>1</sub> to diagnose the severity of COPD, for example, or blood pressure, if you are diagnosing and treating hypertension. If you don't measure blood pressure initially, you have absolutely no way of even determining whether or not your patient is hypertensive, and if hypertensive, how severely. Initial disease severity determines your initial treatment plan and what, if any, further diagnostic tests are needed

The same is true in tobacco dependence diagnosis and treatment. The [Fagerström Test for Nicotine Dependence \(FTND\)](#) is analogous to measuring the FEV<sub>1</sub> the first time you see a COPD patient. In fact, the FTND is the single most important diagnostic test in diagnosing severity of tobacco dependence. All else comes after that. You need to make an initial measurement of FTND on *each* tobacco-dependent patient. Recent data show that the FTND for nearly three quarters of your tobacco-dependent patients will be high enough to place them at Step 3 (Severe) or Step 4 (Very Severe) disease severity.<sup>125</sup> (See [Stepwise Tobacco-Dependence Treatment Guide](#), [Table #1](#) & [Table #2](#) and [Pharmacologic Treatment, Medication Prescribing Examples #1, 2, and 4](#)). That means, just based on the FTND, 75% of your patients are going to need pharmacotherapy appropriate for tobacco-dependence severity of Step 3 or 4 (see [Stepwise Tobacco-Dependence Treatment Guide](#), [Table #2](#)). That means they will need to be prescribed multiple concomitant medications, both controller and reliever medications. This can only be done by you, the chest physician.

The number of cigarettes smoked per day is not a suitable proxy for the FTND. Its coefficient of variation is too high. Moreover, as the price of cigarettes has been increasing, patients have become much more efficient at extracting more nicotine from each puff and from each cigarette. Thus, in 2009 it is common to see patients who smoke 15-18 cigarettes per day, but have a high serum cotinine (> 300 ng/mL) and a high FTND (> 5/10 points). Ideally, you should obtain baseline measurement of both serum cotinine and the FTND while your patient is still smoking. While serum cotinine is the only accurate biomarker of 24-hour nicotine intake,<sup>126</sup> the FTND is a good proxy for measuring serum cotinine. Think of the FTND as the poor man's biomarker of nicotine intake. The FTND is the only physiologically validated question-based measurement of nicotine dependence.

However, you cannot use the FTND to determine how effective your treatment plan is, as you can by repeated measurement of blood pressure after initiating hypertension treatment. A quick look at the [FTND](#) tells you why: All 6 questions *assume the individual is smoking*. The questions in the instrument have no meaning at all after the patient has stopped smoking.

The [FTND Scoring Instructions](#) provides you the information you need to have to score and interpret the FTND. The FTND is a physiologically validated, linear scale producing a score from 0 to 10 points.<sup>127, 128</sup> A score of 0 out of 10 points means your patient has no physiological dependence on nicotine, while 10/10 points means your patient suffers from the severest degree of nicotine dependence. Less than 1% of your patients will have an FTND score of 0 points, while 5%-7% will have a score of 10 points. Over the last 15 years, the FTND has shown a shift toward more severe nicotine dependence. Whereas 15 years ago 50% of patients were highly nicotine dependent and 50% low, more than 75% are high-nicotine dependent now.<sup>113, 125</sup> The linearity of the FTND means that if your patient has an FTND score of 10 out of 10 points, that patient is 10% more physically dependent on nicotine than your patient with an FTND score of 9/10 points. Your patient with an FTND score of 9/10 points is 10% more physically addicted to nicotine than your patient with an FTND score of 8/10 points, and so on.

Knowing the severity of your patient's tobacco dependence enables you to plan a rational, appropriate treatment plan, just as you would with hypertension. For example, if you had a new hypertensive patient in your office and you knew from the data your nurse or medical assistant entered in the chart for that visit that the patient's blood pressure was 180/110, you would think in a very different direction regarding diagnostic work-up and initial treatment plan than if the blood pressure were 125/85. You would treat both. But the treatment intensity would be greater and the initial duration of intense treatment longer in the first case than the second. Likewise, you need to plan a more intensive and longer-duration initial treatment plan for tobacco dependence in a patient with a high FTND score, say 8, 9, or 10 points, compared to a patient with a score of only 2 or 3 points out of 10. Knowing the FTND score enables you to adequately conceptualize and frame your patient's treatment plan. The USPHS Clinical Practice Guidelines Update 2008 recommends that physicians prescribe at least one, and preferably more than one, of the first-line treatments listed in the [Quick Reference Guide to Pharmacotherapy](#) section to all patients who smoke.

The 2008 USPHS Guidelines recommends prescribing more than one first-line tobacco-dependence medication because the evidence shows that this generally produces better treatment outcome. Those with an FTND score of 5-6 points or higher will likely need two first-line medications and for a longer duration of time-6 to 12 months-or even longer. Patients who score below 6 points may only need one first-line medication and may only need it for 3-6 months to achieve permanent cure. Pay particular attention to those with a lower FTND score but whose prior tobacco-dependence treatment was not effective; whatever elements their treatment plan contained before, strengthen them this time around. Remember, they have relapsed-that is why they are smoking now. Therefore, their previous tobacco-dependence treatment plan was inadequate. Also, review the Factors that May Affect Treatment Choices (below) for other diagnostic criteria that would point to the need for treating a patient more intensively.

#### The Quantitative Nicotine Withdrawal Symptom (NWS) Scale

While you cannot assess your treatment plan's effectiveness by re-measuring the FTND, you can monitor how effective your treatment plan is for your patient by

measuring the suppression of nicotine withdrawal symptoms. And that you can do by using the [Nicotine Withdrawal Symptom \(NWS\) Scale](#) to quantitatively measure nicotine withdrawal symptom severity at baseline, while your patient is still smoking, and then at each visit thereafter. [Nicotine Withdrawal Symptom \(NWS\) Scale Instructions, Scoring, and Use](#) provides you the information you need to use, score, and interpret your patient's changes in nicotine withdrawal symptoms. Fundamentally, your treatment plan, and particularly its pharmacotherapy component, needs to suppress all nicotine withdrawal symptoms and keep them suppressed. If your patient's nicotine withdrawal symptoms are not close to fully suppressed at any time after stopping smoking, your patient will need treatment-plan change, more aggressive treatment, including increasing the dose(s) and/or combination(s) of medications, and closer follow-up, until NWS are well-suppressed. Nicotine withdrawal symptoms can cause relapse to smoking.

### Assessing Depression

Those who smoke cigarettes have a greater risk of depression and the more they smoke, the greater the depression risk. The same is true of suicide. Thus, as part of the basic medical history and physical exam for any new tobacco-dependent patient, the treating physician must also obtain an adequate history of depression, suicidal behavior, panic attacks, anxiety, and post-traumatic stress disorder (PTSD). Depression, in particular, also needs to be regularly assessed throughout treatment for tobacco dependence and especially after treatment has ended. The easiest and simplest way of doing so is to administer a simple, standard screening tool while the patient is in the waiting room. The tool most psychiatrists recommend for use in a medical office is the [Beck Depression Inventory®-II, or BDI®-II](#). This validated test takes only a few minutes for the patient to complete, readily identifies suicidality, and takes only about 10 seconds for the physician or staff to score. It is sensitive to detecting changes in depression or suicidality, so it is ideal to use in the medical context of treating tobacco dependence, where 5-10% of patients will demonstrate treatment-emergent depression or suicidality, if their pharmacotherapy for tobacco dependence is not adequate.

### Tapering Medications

Although never studied systematically, the clinical experience of the ACCP Tool Kit Committee Members indicates that once a patient's tobacco dependence has stabilized, the patient has been 100% tobacco free for at least 3-6 months, and the patient is not suffering from any nicotine withdrawal symptoms, then medication dose should be tapered, one medication at a time, to determine the lowest dose and the fewest number of medications necessary to continue tobacco-dependence control. The ultimate goal is to determine whether or not the patient can taper off all medications, with tobacco dependence remaining fully controlled. This approach, also developed applying principles we use in treating asthma, is described more fully in [Pharmacologic Treatment](#).

### Behavioral Management Principles

Providing appropriate behavioral management for your patients increases the likelihood of successfully terminating tobacco use. The more intense the behavioral treatment, the greater its effectiveness. Person-to-person treatment is more effective than group therapy, and the longer the duration, the better the results. Key behavioral management principles are straightforward and simple. As presented in the [Patient Management Tools](#), they involve: (1) having the patient identify triggers to smoke; (2) developing action plans for each trigger (e.g., how to handle stress-a dysphoric mood-without a cigarette, how to deal with wanting a cigarette after a meal-a conditioned-response situation, or how to turn down a proffered cigarette from a friend-skills training); and (3) anticipating relapse and how to manage that.

Another important part of the treatment plan is encouraging your patient to discuss the tobacco-dependence treatment plan with immediate family and close friends and obtain their support-social support. Finally, depending on the extent of behavioral management you and your professional staff provide your patients, you may want to recommend that your patients use the phone number for a well-run telephone quit line-available in most states-and other types of support outside of your office, such as tobacco-dependence treatment counselors or support groups (refer to the [General and Referral Resources](#) section). However, the treating physician should personally, or have one of the practice's nurses, carefully evaluate specifically what counseling and education will be provided from these referral services and resources to make certain the patient will not hear conflicting or contradictory messages from a telephone quit line, treatment counselor, or support group. Because content in these external programs differs from state to state and because they can change rapidly, content review by the ACCP is unfortunately not possible, which is why the physician (or staff) at the local level must do this. For example, many, if not nearly all, Nicotine Anonymous programs tend to regard all nicotine, whether from cigarettes or in a medication to help treat tobacco dependence, as "bad" and something to be overcome.<sup>129, 130</sup> This is a value system that is not compatible with the extensive data supporting rational pharmacotherapeutics and effective medical management of tobacco-dependence. Tobacco smoke kills, nicotine medications do not.

Programs that many patients find helpful and are generally readily available include those offered by the American Lung Association, local health departments, hospitals, and other voluntary health agencies; individual counseling from a medical provider or tobacco-treatment specialist; media resources (e.g., books, manuals, audiotapes and videotapes, and internet resources); and telephone counseling or hotlines. Some patients may also be able to benefit from workplace tobacco-dependence treatment programs. The treating physician or a trusted, knowledgeable staff member should evaluate the content and approach of *all* such potential referral resources, for the reasons already discussed, before having the patient consider the value of these methods of social and behavioral support.

### Lung Age-Its Value In Diagnosis and Treatment of Tobacco Dependence

A particularly valuable part of both medical management and improving motivation regarding stopping smoking is telling your tobacco-dependent patients their lung age, as determined from their FEV<sub>1</sub>.<sup>131</sup> Multiple studies have shown that this simple maneuver, by itself, significantly improves tobacco-dependence treatment outcome.<sup>132, 133</sup> Once a patient has stopped smoking, then the patient is going to want to know whether lung function and lung age have improved. The studies cited above show that your patient's knowledge of this information, independent of any other treatment component, including pharmacotherapy, improves stop smoking rates. Based on the rate of change in lung physiology and function, as reported in the Lung Health Study,<sup>134-136</sup> the ACCP Tool Kit Committee recommends obtaining spirometry on an annual basis as part of tobacco-dependence treatment.

*The ACCP Tool Kit Committee recommends routinely measuring the patient's Lung Age in diagnosing and treating tobacco-dependent patients and discussing this information with the tobacco-dependent patient.*

### The Multimodality Approach

An estimated 70% of users want to quit, but only 3% per year succeed in quitting permanently using the cold-turkey approach.<sup>49</sup> Providing the patient with the pharmacologic treatment and the behavioral management principles (see above), in addition to standard physician advice, improves the treatment plan and increases treatment effectiveness. Those who are dependent on nicotine but wish to quit can increase their chances of success by 2- to 3-fold, if not more, by

combining behavioral and pharmacologic therapy. Randomized clinical trials show that pharmacologic treatment of tobacco dependence with monotherapy, combined with standard, office-based behavioral support, will enable 50% of patients to remain nonsmokers at the end of a short, 6- to 12-week treatment course. Use of varenicline plus basic office-based behavioral management can boost 3-month, end-of-treatment non-smoking rates to as high as 65%,<sup>73</sup> while more individualized pharmacotherapy can boost 3-month, end-of-treatment non-smoking rates to as high as 80%.<sup>58</sup> Longer-duration treatment of 6 to 12 months from Target Stop Date (TSD) generally produces substantially and significantly better and long-term (6-month to 1-year), post-treatment, non-smoking rates.<sup>69, 73, 137-139</sup> Individualized, combination pharmacotherapy, including higher-than-standard nicotine medication doses, can boost 9-month, post-treatment non-smoking rates overall<sup>107, 108, 139</sup> and, in patients smoking > 40 cigarettes/day, to as high as 45%.<sup>107</sup> Longer-duration pharmacotherapy treatment produces better results than shorter treatment. Some patients will need treatment indefinitely to prevent resumption of tobacco use.<sup>2, 112, 113, 139</sup>

Most clinical trials to date, unfortunately, were designed from the scientifically inaccurate premise that tobacco dependence was merely a "bad habit" only requiring a relatively short treatment. As a profession, we have never designed asthma or COPD treatment trials measuring the major dependent outcome variable, for example FEV<sub>1</sub>, 9 months or 1 year *after* bronchodilator treatment ends. Similarly, no sound scientific basis exists for measuring the primary outcome variable in tobacco-dependence treatment trials-stopping cigarette use-*after* treatment has ended; relapse is the norm.

### Combination Pharmacotherapeutics

Effective treatment can be considerably higher when tobacco dependence is addressed in a manner similar to a chronic disease such as asthma. In asthma management, we think of medications as being "Controllers", i.e., controlling airway pathology, or "Relievers", i.e., relieving acute breakthrough asthma symptoms, such as cough, wheezing, chest tightness, or shortness of breath. Controller Medications also have a longer time to effect, while Relievers, or Rescue Medications, have a relatively fast onset of action. Similarly, tobacco-dependence medications can be thought of as being Controllers, controlling underlying CNS neuropathology, or short-acting Relievers, relieving acute, breakthrough, nicotine withdrawal symptoms, such as craving for a cigarette. Bupropion, nicotine patch, and varenicline are Controller-type medications; whereas the nicotine inhaler, lozenges, nasal spray, and gum are Reliever agents for immediate relief of breakthrough withdrawal symptoms. Bars, et al. reported a series of patients treated for only 3 months but with 1-year follow-up quit rates of 39% among those treated with combination nicotine medications,<sup>107</sup> and, remarkably, as high as 43% for those who had smoked >40 cigarettes/day, pre-treatment.<sup>107</sup> The use of bupropion seemed to increase compliance with the nicotine medications. In a review of five published studies, Sweeney, et al. examined the effectiveness of the nicotine combination therapy (nicotine patches used in conjunction with other nicotine delivery modes) compared to nicotine monotherapy.<sup>140</sup> This strategy also appears more effective than use of a single nicotine medication, and predictably doubles the treatment success rates compared to placebo. Several other recent clinical trials have confirmed significantly higher cessation rates with aggressive combination strategies.<sup>69, 141, 142</sup>

### Alternative Approaches

There are a number of alternative-medicine methods advocated by some for assisting the tobacco user to stop. These include hypnosis; acupuncture; laser treatment, which is merely a high-tech version of acupuncture; homeopathic medication; and herbal medication, amongst others. Published reports of a large series of consecutive patients treated with hypnosis would suggest it might be effective, but hypnosis has yet to be studied in a randomized, controlled fashion.<sup>1</sup> More evaluation research is needed before hypnosis can be recommended.<sup>1</sup>

Except for acupuncture, none of the other alternative-medicine approaches have ever been adequately tested scientifically.<sup>1</sup> In contrast, acupuncture has been tested in multiple, randomized, sham-acupuncture controlled trials, but has *not* been shown to be effective.<sup>1</sup> So-called laser treatment merely uses laser stimulation, instead of acupuncture needles, at acupuncture sites. Laser treatment has never been scientifically tested in any way. Because published scientific studies have not found acupuncture to be effective, there is no reason to think that laser treatment would be any more effective. No scientific studies support the use of homeopathic medications, herbal medication, or other alternative approaches.

### A "Reduction Toward Cessation" Approach

Complete cessation is the ultimate therapeutic goal. However, tobacco-dependent patients who are not quite ready to stop may benefit from pre-cessation treatment with nicotine patch in order to move toward eventual nonsmoking. Rose *et al.* demonstrated that a two-week "head start" treatment with nicotine patch *prior* to the target stop date more than doubles the chances of stopping smoking completely.<sup>143</sup>

### Harm Reduction

Even if a patient is unable to quit entirely, reducing tobacco use, while using any of the first-line tobacco-dependence medications (see [Quick Reference Guide to Pharmacotherapy](#) and [Stepwise Tobacco-Dependence Treatment Guide](#)), demonstrably reduces the risks and provides real medical benefits.<sup>144</sup> Although restriction in the number of cigarettes smoked has been hypothesized to lead to compensatory smoking (i.e., more intensive smoking in an effort to obtain the same level of nicotine intake), decrease in tobacco use has been associated with a reduction in mortality risk even when controlling for age and smoking rate.<sup>145</sup> The dose-response relationship between smoking and disease was examined in a Swedish study of cardiovascular risk.<sup>146</sup> This reduction in use was shown to result in improvements in levels of CO, hemoglobin, fibrinogen, and red and white blood cells. However, the Committee to Assess the Science Base for Tobacco Harm Reduction is more cautious. Although concluding that reducing exposure to many tobacco toxicants is feasible and can result in decreased disease incidence, the greatest benefit is associated with completely stopping smoking. This conclusion is based on the assumption (yet to be proven) that reduction in the number of cigarettes consumed does not lead to compensatory increase in exposure resulting from the method of use (e.g., long, deep drags to increase nicotine levels and possibly inflated exposures to other toxicants). Tobacco reduction is advised for those who absolutely cannot or will not stop smoking completely.<sup>147</sup> Reduction could be achieved by reducing the number of cigarettes smoked per day or the amount of each cigarette smoked.

### Factors that may affect treatment choices.

If smoking is the behavioral manifestation of complex disturbances in the biology of mood and motivation, it stands to reason that clinicians should expect to experience significant variability in treatment requirements and outcome among their patients. The treating physician can easily screen for several important indicators, alerting the physician that a particular patient may require more intense therapy. Though few *specific* treatment predictions can be made in response to these indicators, as a general rule, the presence of one or more of the following conditions should prompt a considered, individualized, and more intensive

approach to pharmacotherapy, including treatment for longer than 3 or 6 months and use of combination pharmacotherapy.

- **High FTND Score**-FTND scores of 6 or greater<sup>148</sup> or Fagerström Tolerance Questionnaire (FTQ) scores of 7 or greater<sup>149, 150</sup> have inferior treatment results during treatment, when treated with merely standard-dose pharmacotherapy and also have greater risk of relapse 6 to 9 months after treatment end. (The FTQ is the predecessor version of the FTND.) Patients with the most severe nicotine dependence generally benefit from more aggressive nicotine withdrawal symptom control, including higher doses of nicotine replacement, combination pharmacotherapy, or aggressive use of nicotine Rescue Medications in response to acute situational, or cue-induced, craving for cigarettes.<sup>107</sup>
- **High Daily Cigarette Consumption**-In addition to affecting the FTND score, the absolute number of cigarettes smoked daily independently and proportionately increases the risk of relapse. However, it is far less accurate than the FTND, in its totality. In addition, though not readily available in the office, smoking topography (i.e., the *intensity* of smoking, including number of puffs per cigarette, the volume of the puff, the duration of the puff, and the inter-puff interval) proportionately affects outcomes, especially in the young smoker.<sup>151</sup>
- **High Serum (or Salivary) Cotinine Level**-Cotinine has a 20-hour half-life.<sup>126</sup> Serum cotinine is the only biomarker of 24-hour nicotine intake and, fortunately, is a highly accurate measurement ( $r=0.82$ ;  $P<0.001$ ).<sup>126</sup> Therefore, it is the "gold-standard" for quantifying nicotine dependence. Several lines of published evidence from randomized, double-blind, placebo-controlled, clinical trials show that it is an inversely proportional and independent predictor of tobacco-dependence treatment effectiveness.<sup>58, 152, 153</sup> The higher the serum cotinine level while smoking, the less effective tobacco-dependence outcome, unless the patient is provided with higher medication dose.<sup>57, 58, 150, 152-154</sup> Also, data available tend to consistently show that standard or fixed-dose medication treatment plans produce poorer treatment outcomes the higher the measured cotinine level and can be substantially and significantly improved by increasing nicotine medication dose to attain a greater percent of cotinine replacement from treatment relative to smoking,<sup>57, 58, 154</sup> or simply by a higher medication dose in highly nicotine-dependent cigarette users, defined as having a high (or higher) serum cotinine level.<sup>57, 58, 150, 154, 155</sup> Serum cotinine is a potentially valuable predictor of the need for more intensive or longer-duration medical management but is underutilized in clinical tobacco-dependence treatment. Some, but not all, members of the Tool Kit Committee recommend routine, quantitative measurement of baseline serum (or saliva) cotinine levels to biologically determine nicotine dependence and, when using nicotine medications, measuring serum cotinine level at least one more time after the patient is on stable nicotine medication dose(s), to improve treatment effectiveness by attaining a percent cotinine replacement of  $\geq 100\%$  from medication treatment compared to cigarette smoking.<sup>58, 153</sup>
- **Psychiatric Co-Morbidity**-More than 50% of patients with underlying, previously diagnosed Major Depressive Disorder are regular cigarette users. Patients with depressive or anxiety symptoms smoke more than the population at large, and find it more difficult to stop tobacco use without medical intervention. Unfortunately, while they are not smoking, they are also more likely to suffer an exacerbation of their psychiatric symptoms.<sup>156</sup> Clinicians should consider using bupropion to treat tobacco dependence in these patients, including those on preexisting selective serotonin reuptake inhibitors.<sup>157</sup>
- Separately from the above, feelings of deprivation and loss of motivation are common following stopping smoking. The physician should probe to ensure that the patient is not using tobacco periodically to self-treat this problem, and emphasize that even a single puff will increase the urge to smoke and make stopping more difficult. Patients should be encouraged to reward themselves for incremental successes. Patients who are depressed or have negative affect state should be evaluated for severity and, if significant, provided with counseling, prescribed appropriate medications, or referred to a psychiatric or psychological specialist.
- Also, other recent studies clearly show that depressive risk and risk of successfully committing suicide, in those not even trying to stop smoking, is significantly and linearly proportional to the number of cigarettes smoked per day.<sup>158-160</sup> In other words, separate from other factors, the 2 pack-per-day cigarette smoker is significantly more likely to commit suicide than the 1 pack-per-day smoker. While it is not clear whether or not this is merely an association or a causal relationship, that is not really relevant to those of us who have cigarette smokers in our practice. We need to know that our patients who smoke more are more likely to commit suicide.
- **Concurrent Substance Abuse**-Contrary to widely held beliefs, substance abusers are in fact interested in stopping smoking, motivated to do so, and willing to accept treatment.<sup>161</sup> In fact, substance abuse treatment outcomes seem to be improved with concurrently stopping tobacco use.<sup>162</sup> In the typical clinical setting, it is important not to underestimate the likelihood that a substance-abusing patient will make a stop attempt with physician guidance. When they do however, they may well require additional support to maximize their likelihood of stopping tobacco use. With cocaine dependence in particular, treatment outcomes appear to be interdependent, with stopping smoking improving the likelihood of stopping cocaine use, and *vice-versa*.<sup>163-165</sup>
- **Female Gender**-While research results are mixed regarding the influence of gender on tobacco-dependence treatment outcomes, many studies show that women do less well than men with a standardized, fixed treatment regimen,<sup>150, 166-169</sup> and, as a consequence, may well benefit from more individualized and/or longer-duration medical management. While data are inadequate to draw firm conclusions, it appears that women may experience a smaller treatment effect in response to nicotine patch than do their male counterparts. However, it is important to note that this effect-difference may not hold true for other nicotine medication types<sup>167</sup> and some non-nicotine medications, e.g., varenicline,<sup>170</sup> but does hold true for bupropion.<sup>150</sup> In addition, women frequently cite concern over weight gain as a powerful disincentive to quitting. In fact, women who stop smoking are at higher risk for major weight gain ( $> 13\text{kg}$ ) as a result: 13.4% for women compared to 9.8% for men.<sup>171</sup> Therefore, clinicians should consider treatment with bupropion, given its effectiveness in women at risk for relapse and in minimizing weight gain.<sup>62, 172</sup>
- **Risk For Weight Gain**-Weight gain is not necessarily an *inevitable* consequence of stopping smoking. In fact, one third of smokers who stop experience some degree of *weight loss*. Instead, clinicians should view weight gain ( $>5\%$  of baseline) as a sign of poor control over the compulsion to smoke, prompting a reassessment of the pharmacologic and behavioral support methods being employed. A considerable amount of work is currently underway investigating novel pharmacologic approaches to preventing weight gain, including central nicotine antagonists and cannabinoid antagonists. Until these become available, however, physicians should respond to weight gain by evaluating whether higher doses or combinations of pharmacotherapeutics are warranted or also whether changes in behavioral management, such as increasing exercise or reducing calorie intake, should be discussed with the patient. Nicotine medications combined with bupropion SR resulted in less weight gain than placebo or either treatment alone (1.1kg vs. 2.1kg vs. 1.7kg respectively).<sup>62, 122</sup>

- Care should be taken when suggesting that patients should focus on quitting now and tackling weight gain later; while some may like this approach, others may perceive a tacit resignation to substantial weight gain. Young women may be especially reluctant to then even attempt stopping smoking because of weight-gain concerns, making it especially important for the physician to express support and an intent to manage this complication.

### Motivating the Resistant Patient To Stop Smoking

The physician should motivate patients who are resistant to stopping smoking by:

- Explaining the personal relevance to that patient;
- Advising them of the risks to self and family members (acute, long-term, and environmental);
- Explaining the rewards (improved health, improved senses of taste and smell, money saved, improved self-esteem, improved social acceptance, better-smelling environment, and setting a good example, particularly for children);
- Asking the patient to identify impediments to stopping smoking (withdrawal symptoms, fear of treatment failure, weight gain, lack of support, depression, etc.) and address each one;
- Reassuring the patient that with proper and effective use of medication(s), the patient can stop tobacco use, and avoid the pain and suffering brought about by nicotine withdrawal; and
- Repeating this discussion at each visit, as warranted.

### Special Population:

**Pregnant women** or those in the childbearing years should be advised of the risks that cigarette use poses to their developing fetuses. Everything in the maternal arterial circulation goes directly into the fetal circulation via the umbilical vein. Nicotine, carbon monoxide, and other toxins in tobacco smoke are absorbed into the maternal arterial bloodstream in extraordinarily high concentrations via the pulmonary capillary bed and flow not only to the maternal heart, brain, liver, and spleen, but also freely cross the placenta, traveling directly to the umbilical blood. Thus the fetal circulation received the same extraordinarily high levels of nicotine and carbon monoxide that the cigarette delivers to the maternal arterial circulation. In addition, cigarette toxins have been found in breast milk, cervical secretions, and amniotic fluid. Smoking mothers are more likely to miscarry or deliver low-birth-weight babies. Their infants are more likely to die of sudden infant death syndrome (SIDS) and their children have a higher risk of developing asthma, many types of solid cancers and lymphoma, and are more likely to become tobacco dependent later in childhood or adolescence than children born to nonsmoking mothers.

### Motivating Smoking Parents

Counsel parents that environmental tobacco smoke in the home has been shown to cause the following health problems in exposed children.

- Higher rates of sudden infant death syndrome (triple the normal risk);
- Asthma;
- Pneumonia;
- Bronchitis;
- Other respiratory diseases;
- Middle ear infections;
- Multiple different types of cancer; and
- Lymphoma.

The financial message can be motivating especially when the tobacco user is confronted by the total costs of their addiction.

### Daily, Monthly, and Yearly Tobacco Expenditure Smoking Is Expensive

Amount of Cigarettes Smoked per Day	Cost per Day	Cost per Month*	Cost per Year
1 Pack	\$5.50 to \$8.00	\$165 to \$240	\$2,008 to \$2,920
2 Packs	\$11.00 to \$16.00	\$330 to \$480	\$4,015 to \$5,840

*\*Relate the amount in this column to the cost/month of tobacco-dependence medications. For example, 1-month's supply of varenicline, 1 mg, q12h, costs \$112.99, and may be partially covered by medical insurance.*

Remember to be supportive, not judgmental. Tobacco dependence is a medical problem rather than a behavioral or psychological problem or a bad habit. The patient needs you to provide effective treatment and also be a supportive adviser, not be a disciplinarian.

If possible, encourage all family members who use tobacco to stop smoking at the same time. They can help support each other. Furthermore, exposure to tobacco smoke and the ready availability of cigarettes in the household decrease the likelihood of effective, successful tobacco-dependence treatment.

### Cost-Benefit Relationships

The benefits to society of stopping smoking are obvious. See [Coding and Reimbursement](#). Tobacco-dependence treatment is one of the cheapest forms of medical

management in our society.

However, physicians often think the cost to their practice is great, anticipating low reimbursements, extra time per patient and disrupted office flow. Although physicians and other providers want to help their patients stop using tobacco for the same reasons they want to treat other chronic medical conditions, there is a concern that treating tobacco dependence will not be cost-effective for their practices. For information on correct coding and information regarding reimbursement for tobacco-dependence treatment, go to [Coding and Reimbursement](#).

#### Rationale for Implementation of Tobacco Cessation Strategies in Office Encounters

Meta-analysis of recent research studies has shown that *brief physician advice significantly increases the chance of successful termination of tobacco use*. As individual providers, physicians already feel the sense of responsibility to address this topic and know they can improve the care given to their own patients. A simple, very-low-intensity intervention (*i.e. physician advice to quit*) can produce stop-smoking rates two to three times greater than the spontaneous ("cold turkey") rates. More intensive interventions (*i.e., combining behavioral counseling with pharmacologic treatment*) can produce stop smoking rates of 50%-65% at the end of 3 to 6 months' treatment. Research shows that the combination of active engagement on the part of the clinical provider, along with a multimodality approach to treatment, as described above, will achieve the best treatment success rates.

Physicians need to consider assessment of tobacco use to be a mandatory part of every patient encounter.<sup>173</sup> In fact, given the public expectation that physicians should provide the best treatments and prevent disease, whenever possible, they have a duty to provide information, counseling, and treatment for tobacco dependence.<sup>174</sup> The counseling involved for tobacco dependence is no more difficult than the counseling used for patients with diabetes or hypertension or asthma.

Documentation at each visit should include whether the patient is a current or former tobacco user or has never used tobacco products. This creates a "teachable moment" to discuss reasons for stopping, attempts to motivate the patient to stop, and could lead to additional details on strategies. The physician is encouraged to take an empathic and nonjudgmental tone so as not to alienate the patient, who is already well aware of the need to stop. A non-offensive request to inquire about usage shows your respect for the patient's autonomy while you are providing the care and concern that patients have come to expect.<sup>175</sup> At a minimum, it will document current tobacco use and serve as a marker for increased health risks. **Inquiries about tobacco use should become the fifth vital sign**-a routine component of every patient encounter.

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# Tobacco Dependence Treatment ToolKit

## Pharmacologic Treatment

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## Overview and Perspective

***Stopping smoking "is a struggle, but researchers have learned a lot about what works to help people [stop]. We need to make sure that effective [treatment] reaches the people who need them the most... To increase demand for treatments, we most motivate smokers to want them, expect them, and use them."***

David Ransohoff, MD  
Professor of Medicine, University of North Carolina  
&  
Chair, NIH Consensus Conference  
"Treating Tobacco Dependence"  
Wednesday, July 14, 2006

Tobacco dependence is a fatal disease.<sup>158</sup> Tobacco dependence kills half of its victims.<sup>176</sup> But stopping smoking by age 50 cuts the risk of death by half and stopping smoking at age 30 eliminates nearly all excess mortality risk.<sup>176</sup> In other words, tobacco dependence is a treatable disease, and, with the medications available today, a chronic disease that can be treated effectively. How to accomplish this is the topic of this section of the ACCP Tool Kit.

While it is true, in absolute numbers, that most cigarette smokers who have ever stopped smoking have done so without any treatment, this unfortunate approach – "cold turkey" – is the least effective available, causing most smokers who stop to relapse and resume smoking in less than 30 days. In fact over 50% resume smoking 14 days after stopping cold turkey; over 75% within in 30 days.<sup>103</sup>

For many people, the most effective treatments are pharmacologic and the tobacco user's physician should proactively offer them to all people who smoke,<sup>1, 2</sup> not merely those who ask for them. Then, the treating physician needs to regularly monitor treatment effectiveness and safety—just as we would do for asthma, a far less lethal medical disease.

Tobacco dependence is a chronic medical disease that may require pharmacological treatment for optimal treatment outcome.<sup>1, 2, 112, 113, 177</sup> Maximal health benefit results when the patient has been able to stop smoking completely and for long-term. Unfortunately, most clinical trials of pharmacotherapeutic agents have been based on a treatment paradigm that originated in the 1960s, when there were no medications available and before the neurogenetics, neuropathology, and neurobiology of nicotine addiction had become understood. Since the clinical psychology treatment paradigm of the mid-1960s was based on 6 weeks of group therapy sessions, the initial pharmacological research in the late 1960s and early 1970s used this same 6-week treatment paradigm. But at that time, the worth of such short-term tobacco-dependence treatment was and, in many circles, continues to be based upon long-term nonsmoking status, meaning percent not smoking at 1 year, or 10½ months *after treatment had ended*.

The asthma counterpart to this type of trial design would be testing a new inhaled corticosteroid in a randomized, double-blind, placebo-controlled trial, in which the new inhaled corticosteroid is administered for 3 months, but the value of the new medication is to be based on the improvement in FEV<sub>1</sub> *9 months after treatment had been stopped*. Studies of clinical efficacy of asthma medications are not designed that way. The lack of a carry-over therapeutic effect after its use has been stopped (e.g., Strunk RC, et al. 2009.<sup>178</sup>) does not negate the therapeutic value of the medication. Similar logic should have been applied in the design of pharmacologic tobacco-dependence clinical trials—not assuming a therapeutic carry-over effect.

We know now that tobacco dependence, like asthma, is a chronic medical disease.<sup>1, 2, 177</sup> We also know that tobacco dependence, like asthma, has a defined and described genetic, sub-cellular, and cellular basis and pathobiology.<sup>112, 179-185</sup> Based on their mechanisms of action, we have no reason to think, a priori, that any of the medications available to treat tobacco dependence — bupropion, nicotine, or varenicline — can reverse any of the underlying neuropathology

underpinning tobacco dependence. Indeed, the few published trials designed to provide treatment for 6-12 months or longer all show that longer treatment produces significantly better treatment results (i.e., stop-smoking rates).<sup>69, 73, 137, 138, 186</sup>

Therefore, most published clinical trials, placing emphasis on nonsmoking status *after* treatment has ended are flawed. This is not to say that these thousands of published, peer-reviewed, tobacco-dependence clinical trials do not contain useful information. They do. The most salient outcome is the *end-of-treatment results*.

Randomized, double-blind, placebo-controlled, fixed treatment trials show that, at the end of a 3-month treatment period, between 40-50% of study participants will have been 100% tobacco-free since their Target Stop Date.<sup>54, 55, 149</sup> Generally half relapse 9 months after treatment stops, most of those in the first several months after treatment ends.<sup>54, 55, 149</sup> The few studies that have specifically studied those individuals who are highly nicotine dependent on the Fagerström Tolerance Questionnaire (FTQ)<sup>127</sup> scale ( $\geq 7$  points out of 11) or the [Fagerström Test for Nicotine Dependence](#)<sup>128</sup> ( $\geq 5$  points out of 10) show that nearly 100% of highly nicotine dependent individuals relapse within a few months after a 3 months' treatment course has ended.<sup>149, 187</sup> Moreover, data relevant to the chest physician show that 75% of patients presenting for tobacco-dependence treatment today are highly nicotine dependent.<sup>125</sup> Thus, treatment for them will need to continue much longer than 3 months. How long has not been studied. Based on the fundamental neurobiology of nicotine addiction (see [Tobacco-Dependence Treatment Process and Approach](#)) and the clinical experience of Tool Kit Committee Members, most highly nicotine dependent patients need at least several years of treatment and many will need lifetime treatment. Thus, the gradual tapering approach based on level of disease control, as outlined in the previous section (§1.6) and this one, makes sense.

In addition, the U.S. Public Health Service *Clinical Practice Guideline: Treating Tobacco Use and Dependence, 2008 Update* recommends prescribing at least one medication, even for low-nicotine-dependent patients, those who score below 5 or 6 on the [Fagerström Test for Nicotine Dependence \(FTND\)](#) or smoke fewer than 10 cigarettes per day.<sup>1</sup> The reason for this recommendation is that all studies that have defined low nicotine dependent subgroups have shown up to 10-fold better treatment results from active medication compared to placebo.<sup>149, 187</sup> Moreover, for low FTND patients, unlike those with a high FTND, a short, 12-week treatment course can produce permanent cure for 75%-80%.<sup>149</sup>

The U.S. Public Health Service *Clinical Practice Guideline: Treating Tobacco Use and Dependence (2008 Update)* identifies seven first-line medications (bupropion, nicotine gum, nicotine inhaler, nicotine lozenge nicotine nasal spray, nicotine patch, and varenicline) and two second-line medications (clonidine and nortriptyline) for treating tobacco dependence.<sup>1</sup> First-line therapies have been found to be both safe and effective, with varenicline the most effective monotherapy (see [Table 2](#)).<sup>1</sup> The U.S. Public Health Service *Guideline* also states that the use of combination therapy is particularly effective and more effective than monotherapy (see [Table 1](#)).<sup>1</sup>

Second-line medications have been shown to be effective for treating tobacco dependence but are not FDA-approved for the tobacco-dependence indication and should only be used after first-line treatments have been attempted and have either not been tolerated (rare) or not been effective (even rarer). (see [Quick Reference Guide to Pharmacotherapy](#) and the [Stepwise Tobacco-Dependence Treatment Guide](#)).

### How Medications Will Be Presented in This Tool Kit

As is standard practice in journal articles, medication effectiveness will be discussed first, because if a medication is ineffective, there is little relevance to side effects. Second, we shall present a discussion of medication safety and side effects, starting with the most commonly occurring side effects. We shall conclude each section's discussion of medication safety with a discussion of potentially serious side effects, such as seizure and suicidality, that have a low incidence of occurrence.

Please be advised that in certain instances, this Tool Kit includes treatment recommendations that are not approved in the US (so-called off-label uses of pharmaceutical products). For prescribing information, please see package inserts for all pharmacotherapeutics mentioned in this Tool Kit.

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### Asthma Stepwise Therapy as a Model for Tobacco-Dependence Treatment

As discussed in previous sections of this Tool Kit, in the Third Edition of the Tool Kit, the ACCP Tool Kit Committee sought a model that would provide guidance to the clinician while also being flexible to adapt to individual practice style and needs. We realized that the model used in the NHLBI's *Guidelines for the Diagnosis and Management of Asthma* was also an appropriate model for determining tobacco-dependence disease severity and deciding on appropriate treatment (see [Stepwise Tobacco-Dependence Treatment Guide](#)). By applying the concept of using "reliever/rescue" and "controller" medications to improve asthma management to the treatment of tobacco dependence, ACCP Tool Kit Committee Members have found that we can substantially improve tobacco-dependence treatment outcome and make it nearly painless for the patient to be able to stop smoking. This requires applying rational pharmacotherapeutic principles to tobacco-dependence management.

Additionally, the use of nicotine medications, recommended in this ACCP Tool Kit, is fully consistent with the covered services by the United Kingdom's National Health Service, as of 2002, and changes to the official prescribing indications of the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA), as of 2006.<sup>188, 189</sup> These indications include extended use, combination medication use, and use of nicotine medications by cardiac patients, pregnant women, and pediatric patients.<sup>188, 189</sup> (See also: [New advice on use of nicotine replacement therapy](#) and [Smoking in England](#))

### Controller Medications

The foundation for tobacco-dependence treatment, as in asthma, is using at least one controller medication. There are three controllers: bupropion SR, nicotine patch, and varenicline. The three controller medications are discussed in detail below (see [Combination Pharmacotherapy](#)). Tobacco dependence is characterized by acute episodes of reversible nicotine withdrawal symptoms superimposed upon CNS  $\alpha_4\beta_2$  nicotinic receptor up-regulation and desensitization.  $\alpha_4\beta_2$  nicotinic receptors are part of the family of CNS nicotinic acetylcholine receptors (nAChR). The controller medications control

and stabilize the CNS  $\alpha_4\beta_2$  nicotinic receptor abnormalities, while the reliever medications relieve acute breakthrough nicotine withdrawal symptoms, such as increased irritability, short temperedness, or cigarette craving, literally rescuing the patient from relapsing to cigarette use.

This really is precisely the way we conceptualize and manage asthma. Asthma is characterized by acute episodes of reversible bronchoconstriction superimposed upon chronic airway inflammation, hyper-responsiveness, obstruction, and remodeling. The asthma controller medications control airway inflammation and remodeling, while the asthma reliever medications relieve bronchospasm and the hallmark asthma symptoms, such as shortness of breath, cough, chest tightness, or wheezing.

But do all tobacco-dependent patients need medications in order to be able to stop smoking and remain stopped? The overwhelming majority-about 90%-will. We all know individuals, however, who have successfully stopped smoking without using any medication. The large majority-65%-though, relapses within only 14 days after stopping smoking<sup>49, 103</sup> and 75% within 30 days<sup>49, 103</sup> because of nicotine withdrawal symptoms.<sup>104-106</sup> Those who don't relapse are generally low-nicotine-dependent smokers, with scores of 0, 1, or 2 on the FTND (see [Fagerström Test for Nicotine Dependence](#)), who have minimal nicotine withdrawal symptoms.

### "Reliever" or "Rescue" Medications

Nicotine's addictive potential is directly related to the speed and concentration with which nicotine is delivered to the brain. The cigarette is the most efficient drug-delivery system humanity has yet devised. It delivers nicotine more rapidly and in far higher concentration than any other device. Because of that, the cigarette is most efficient at creating impact and addiction. Conversely, because pharmaceutical nicotine sources achieve brain delivery rates that are considerably slower and with relatively low concentration, their addictive potential is quite low to nonexistent. Pharmaceutical nicotine has the additional advantage of being extremely safe. It is the 5,000 toxins contained in inhaled tar and gases, not nicotine, that cause tobacco's dangerous and serious health consequences. These toxins are absent from therapeutic nicotine sources. Nicotine medications lessen withdrawal symptoms, give patients a sense of control over the withdrawal process, and increase the likelihood of long-term nonsmoking. Nicotine medications can be used as "reliever" or "rescue medications" (nicotine gum, lozenge, nasal spray, and oral inhaler) and as a "controller" medication (nicotine patch).

There are 4 reliever, or rescue, medications available: Nicotine nasal spray, nicotine [oral] inhaler, nicotine polacrilex gum, and nicotine polacrilex lozenge. (Nicotine sub-lingual tablet is available in some countries, but not the United States.) The patient should use reliever medications on an as-needed (prn) basis to control acute, breakthrough nicotine withdrawal symptoms, often occurring because of an acute, severe stressor. The four reliever medications are discussed in detail below (see [Reliever Medications-Details](#), following the section on [Combination Pharmacotherapy](#)).

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### Efficacy and Effectiveness

Combination medication use is the currently recommended treatment standard for tobacco dependence, not only by the *2008 Update to the U.S. Public Health Service Clinical Treatment Guideline*<sup>1</sup> and the United Kingdom's National Health Service,<sup>189</sup> but also in the rapidly expanding body of scientific studies, including randomized, double-blind, placebo-controlled trials<sup>62, 68, 69, 141, 186, 190-194</sup> and studies involving consecutive patients in tobacco-dependence treatment clinics.<sup>107, 109</sup>

Varenicline is the most effective monotherapy<sup>1</sup> (see also [Table 1"Efficacy of Controller and Reliever Medications, Used in Combination"](#) in section below ; see also ["Safety"](#), below in this section). A recently published Phase II, open-label study indicates that the combination of varenicline and bupropion may be the most effective.<sup>193</sup> To get an idea of the combination effect, we can juxtapose the results from a 2009 study<sup>193</sup> to results from one of the original randomized, double-blind, placebo-controlled trials of varenicline and bupropion SR from 2006.<sup>55</sup> In the 2009 study, the varenicline + bupropion combination<sup>193</sup> demonstrated 71% not smoking at the end of 12 weeks treatment,<sup>193</sup> compared to 21% (placebo) or 51% (varenicline) from the earlier study<sup>55</sup> (approximate odds ratio of stopping smoking at 12 weeks for the varenicline + bupropion combination against placebo is 9.2; 95% Confidence Interval = 2.2-16.2). At 6 months, 3 months after treatment end, the varenicline + bupropion combination showed 58% not smoking,<sup>193</sup> compared to 17% (placebo) or 35% (varenicline) from the 2006 study.<sup>55</sup> This would approximate a varenicline + bupropion odds ratio against placebo of 6.7 (95% CI = 1.9-11.5). If confirmed by larger-scale, double-blind, head-to-head trials, this is a far higher stop-smoking rate than any other combination, let alone monotherapy. Given varenicline's and bupropion's mechanisms of action, this result is not surprising, because these two medications have mechanisms of action that should be complementary and synergistic.<sup>113, 195, 196</sup>

Theoretically, based on varenicline's mechanism of action as a nicotinic receptor partial agonist, we would think that adding any of the nicotine reliever medications (patch, gum, inhaler, lozenge, or nasal spray) to varenicline would *not* improve varenicline's effectiveness and would likely substantially increase varenicline's side effects, particularly nausea and vomiting. This turns out not to be the case. Both safety and efficacy of varenicline + nicotine medications (controller and relievers) used in combination have just been recently been shown in a series of 104 consecutive patients from the Mayo Clinic residential program.<sup>192</sup> Also, members of the ACCP Tool Kit Committee have found use of varenicline + nicotine reliever medications an effective and safe combination, with varenicline + bupropion + nicotine reliever medications being especially effective.

A recent study utilizing a randomized, double-blind, double-dummy, placebo-controlled, head-to-head design and a sample size of 1,504 study participants, presented at an international scientific conference just as this Tool Kit was going to press, showed that the combination of nicotine patch (controller) + nicotine lozenge (reliever) was significantly more effective at the end of the 8 weeks of treatment than nicotine patch alone, nicotine lozenge alone, or bupropion SR alone (54%, 45%, 40%, and 40%, respectively).<sup>194</sup> Also, the combination of bupropion SR (controller) + nicotine lozenge (reliever) showed 50% not smoking at 8 weeks, which was significantly more effective than the 3 monotherapies studied: nicotine patch, nicotine lozenge, and bupropion SR (45%, 40%, and 40%, respectively).<sup>194</sup> This unique study extends previous work that had shown that using bupropion SR + nicotine patch-two controllers-was significantly more effective than either medication alone, as monotherapy,<sup>1, 62</sup> to also show that bupropion SR + nicotine lozenge (controller + reliever) was significantly more effective than either medication alone.<sup>194</sup> Both combinations studied and all 3 monotherapies studied in this head-to-head study were significantly more effective than placebo treatment (double-dummy) at the end of the 8-week treatment phase (30%).<sup>194</sup> This single study, testing 2 novel combinations against 3 active monotherapies confirms what all, previous combination-studies have shown: combination therapy with at least 2 controllers or 1 controller + 1 reliever is significantly more effective than only one medication.

Essentially all studies included in the *2008 Update* to the Public Health Service *Clinical Practice Guideline* have deliberately excluded patients with underlying medical and psychiatric disease. The first study to specifically test a triple-medication, tobacco-dependence treatment regimen in a randomized study design also did so in 127 patients with 1 or more pre-defined chronic medical or psychiatric diseases.<sup>186</sup> The triple-medication intervention group could use any combination of the 3 medications (nicotine patch, nicotine inhaler, and bupropion [but at ½ standard dose]) for a flexible duration, up to 6 months, based on patient perception of nicotine withdrawal symptom control. The control group of similar, chronic disease patients received a fixed, standard-dose and fixed, standard-duration (10 weeks) nicotine patch treatment regimen, per package insert. The triple-medication regimen-2 controllers, nicotine patch + bupropion, + 1 reliever, nicotine oral inhaler-was significantly more effective than nicotine patch, only: 62% vs. 37% at the end of 8 weeks treatment and 35% vs. 19% at 6 months from Target Stop Date (OR=2.57 [95%CI=1.05-6.32]).<sup>186</sup>

**TABLE 1****Efficacy of Controller and Reliever Medications, Used in Combination**

Estimated odds ratio and 95% Confidence Interval (CI) for continuous nonsmoking at 6 months using medication combinations, when compared to placebo or nicotine patch, are from Fiore MC, et al.<sup>1</sup> and were based on studies using basically medically well, healthy study participants, unless otherwise noted:

Medication	Odds Ratio & 95% CI (vs. Placebo)	Odds Ratio & 95% CI (vs. Nicotine Patch)
Placebo	1.0	----
Nicotine patch (reference group)	----	1.0
COMBINATION MEDICATION TREATMENT		
Nicotine patch + Bupropion SR + Nicotine Inhaler*, <sup>230</sup>	No Placebo Condition	2.8 (1.1-6.3)
Varenicline + Bupropion SR <sup>192</sup>	6.7 (1.9-11.5)	2.6 (0.8-4.5)
Nicotine patch (Long-term: > 14 weeks + <i>ad lib</i> nicotine reliever medication (gum or nasal spray))	3.6 (2.5-5.2)	1.9 (1.3-2.7)
Individualized nicotine patch dose (up to 45-mg nicotine/16 hrs) to reach 100% nicotine replacement (from patch cf. smoking baseline) <sup>† 58</sup>	3.2 (0.9-11.7)	No Single-Patch Condition
Nicotine patch + Bupropion SR	2.5 (1.9-3.4)	1.3 (1.0-1.8)
Nicotine patch + Nicotine lozenge <sup>194</sup>	2.3 (1.4-3.3)	1.3 (0.8-1.7)
Nicotine patch + Nortriptyline	2.3 (1.3-4.2)	0.9 (0.6-1.4)
Nicotine patch + Nicotine inhaler	2.2 (1.3-3.6)	1.1 (0.7-1.9)
Nicotine patch + 2 <sup>nd</sup> -generation anti-depressant (paroxetine or venlafaxine)	2.0 (1.2-3.4)	1.0 (0.6-1.7)
Bupropion SR + Nicotine lozenge <sup>194</sup>	1.8 (1.0-2.5)	1.0 (0.6-1.3)

\*All study participants had 1 or more pre-defined chronic medical or psychiatric illnesses (see text).

† 12-week, end-of-treatment, continuous nonsmoking percent (placebo patch [n=31] vs. 100% replacement [n=31]) was 26% vs. 65% (odds ratio 5.2; 95% CI 1.8-15.6; P=0.0029)<sup>58</sup>

**TABLE 2****Efficacy of Controller and Reliever Medications, Used as Monotherapy**

Estimated odds ratio and 95% Confidence Interval (CI) for continuous nonsmoking at 6 months using first-line medications, when compared to placebo or nicotine patch, are from Fiore MC, et al.<sup>1</sup> and were based on studies using basically medically well, healthy study participants, unless otherwise noted:

Medication	Odds Ratio & 95% CI (vs. Placebo)	Odds Ratio & 95% CI (vs. Nicotine Patch)
Placebo	1.0	----
Nicotine patch (reference group)	----	1.0
<b>SINGLE MEDICATION TREATMENT</b>		
Varenicline (2 mg/day)	3.1 (2.5-3.8)	1.6 (1.3-2.0)
Nicotine nasal spray	2.3 (1.7-3.0)	1.2 (0.9-1.6)
Nicotine patch (High-dose: > 25 mg)	2.3 (1.7-3.0)	1.2 (0.9-1.6)
Nicotine gum (Long-term: > 14 weeks)	2.2 (1.5-3.2)	1.2 (0.8-1.7)
Varenicline (1 mg/day)	2.1 (1.5-3.0)	1.1 (0.8-1.6)
Nicotine inhaler	2.1 (1.5-2.9)	1.1 (0.8-1.5)
Clonidine	2.1 (1.2-3.7)	1.1 (0.6-2.0)
Bupropion SR	2.0 (1.8-2.2)	1.0 (0.9-1.2)
Nicotine patch (6-14 weeks treatment duration)	1.9 (1.7-2.2)	1.0 (N/A)
Nicotine patch (Long-term: > 14 weeks)	1.9 (1.7-2.3)	1.0 (0.9-1.2)
Nortriptyline	1.8 (1.3-2.6)	0.9 (0.6-1.4)
Nicotine gum (6-14 weeks treatment duration)	1.5 (1.2-1.7)	0.8 (0.6-1.0)

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### Practical Treatment Tips

Treating tobacco dependence using multiple drugs with different mechanisms of action or differing pharmacokinetic profiles, as discussed immediately above, is often necessary to achieve maximum treatment effectiveness, as is the case with many other chronic illnesses including asthma. The family of nicotine medications have identical mechanisms of action as nicotinic receptor agonists but all have quite different pharmacokinetic profiles. In fact, each type of nicotine patch has different pharmacokinetic delivery. The mechanisms of action for the nicotine medications, bupropion, and varenicline, at the cellular and sub-cellular levels, are different. Also, when treating tobacco dependence, as is the case with asthma, it is critical that you select the correct tools to monitor treatment efficacy and safety. To facilitate such measurement, this Tool Kit contains instruments that are standard in tobacco dependence treatment and that we on the Tool Kit Committee have used in clinical practice. These include a quantitative [Nicotine Withdrawal Symptom \(NWS\) Scale](#), based on the validated University of Minnesota, Hughes-Hatsukami scale and a reliable, validated tool for simply and accurately screening for depression. These should be used at each visit, particularly including the pre-stop-date visit(s). In this Tool Kit, for depression, we shall illustrate using the [PHQ-9](#). Other excellent, validated depression tools include the [Beck Depression Inventory \(BDI-II\) scale](#) and the [Centers for Epidemiologic Studies-Depression Scale \(CES-D\)](#).

The PHQ-9, developed in 2001 by Kroenke et al.,<sup>197</sup> contains 9 easy-to-answer questions, one of which deals specifically with suicidality, rated on a 0-3 Likert scale, for a maximum score of 27. The [BDI-II®](#), developed in 1996 by Beck, Steer, and Brown, is a validated improvement and second edition of their earlier, validated 1961 [Beck Depression Inventory \(BDI\)](#).<sup>198</sup> The BDI-II® contains 21 easy-to-answer questions, one of which deals specifically with suicidal ideation, another of which deals with irritability and takes 5 minutes to complete. Each question is rated on a 0-3 Likert scale, for a maximum score of 63 points.

In general, you should treat all patients in your practice who smoke with pharmacotherapy and with more than one medication, but at a minimum with at least one agent.<sup>1, 2, 188, 189</sup> Like stepwise therapy for asthma, the prevailing concept is to balance the use of controller medication(s) with reliever/rescue medication(s). (See [Stepwise Tobacco-Dependence Treatment Guide](#). We have designed the Stepwise Tobacco-Dependence Treatment Guide to help you pick a starting medication regimen for your patient based, on pre-diagnostic factors that you can readily determine with the tools provided in this Tool Kit. Like the NHLBI Asthma Treatment grid, *note that presence of any one factor indicating a higher level of disease severity places the patient at that more severe disease*

*state and thus intensifies therapy.* You need to see and re-assess the patient 3-5 days after the Target Stop Date and after the patient commences with the initial treatment plan so that you can evaluate treatment response to make certain that:

1. The patient has been able to readily stop smoking.
2. Nicotine withdrawal symptoms are suppressed.
3. The patient is not feeling depressed or dysphoric (occurs in only 10%-15% of patients stopping smoking, if treated with adequate pharmacotherapy for tobacco dependence).
4. In essence, the patient is feeling normal for himself or herself.

At each follow-up visit, if your patient is not already on a controller medication or your patient is using reliever/rescue medication(s) with high frequency (>10-15 times/day), then you should consider adding a controller to your patient's treatment regimen. This will simplify the treatment plan and facilitate treatment adherence. If your patient is already on a controller, e.g., nicotine patch, then either you should increase the patient's dose (say, go from applying 1, to 2, Step 1 patches each morning), or you should add a second controller, e.g., bupropion.

The combination of bupropion and 1, standard, Step 1 nicotine patch is the only combination approved by the FDA for treatment of tobacco dependence. However, as discussed in detail earlier in this section, every combination tested and published in the scientific literature shows benefit over and above each single medication, while still maintaining an excellent safety profile. This multimodality approach has yielded significantly higher treatment success rates than either medication alone. Each of these medications acts on a different site on the dopamine and norepinephrine neurons.<sup>112</sup> As noted above,<sup>194</sup> the combination of bupropion and nicotine lozenge has also recently been shown to be effective and safe. There is every reason to think that bupropion + any other nicotine reliever medication would be similarly effective.

Using a sustained-release controller, the nicotine patch, in combination with any near-immediate-delivery nicotine reliever medication is significantly more effective than any of the medications alone. Nicotine patch + gum,<sup>68, 190</sup> or lozenge,<sup>194</sup> or nasal spray,<sup>69</sup> or oral inhaler<sup>141</sup> is more effective than using a single form of nicotine medication. Only one study in the tobacco dependence literature has studied long-term follow-up for 5 years after 1 year of active-medication treatment. That study showed that even 6 years after the target stop date, patients who had received the combination of nicotine patch + nicotine nasal spray for the first year were 2 to 3 times more likely to remain nonsmokers.<sup>69</sup> These same studies have also shown these combinations to be safe.<sup>1</sup> *Regulation of nicotine intake is controlled at the CNS level; the brain literally will not let a person "overdose" with nicotine reliever medications.* Such combinations can be especially helpful in reducing, if not completely eliminating, breakthrough nicotine withdrawal symptoms and thereby preventing relapse.<sup>1, 113</sup>

*Following are several clinical examples to illustrate how you can use **Stepwise Tobacco-Dependence Treatment Guide** to determine initial pharmacotherapy and starting medication doses.*

#### Medication Prescribing Example #1:

**Using Stepwise Treatment Guide, Table #1:** This patient is a 45-year-old male, who smokes 15 cigarettes/day (**Step 2** for the first *Cigarette Use* factor), but smokes the first cigarette of the day within 15 minutes after awakening (**Step 3** for the third *Cigarette Use* factor). He has frequent nicotine withdrawal symptoms and a nicotine withdrawal symptoms (NWS) score of 27/48 points (**Step 2** for both *Nicotine Withdrawal Symptom* factors) and has a Fagerström Test for Nicotine Dependence (FTND) score of 6/10 points (**Step 3** for the first *Quantitative* factor) and a Serum Cotinine level of 325-ng cotinine/mL blood (**Step 3** for the second *Quantitative* factor). By either the *Cigarette Use* or *Quantitative* factor, you would classify this patient as **Step 3: Severe Tobacco Dependence**. However, he also has had a heart attack 6 months ago, has mild hypoxemia by pulse oximetry, and clinically has COPD. Thus, by the Medical component of the *Health Status* factor, this patient is **Step 4**. The patient denies any prior mental health or psychiatric problems and his PHQ-9 score is only 2 points out of a possible maximum score of 27 points (Normal range for the PHQ-9 is 0-4 points). Therefore, your final diagnostic classification for this patient is

#### **Step 4: Very Severe Tobacco Dependence.**

Then, armed with this diagnosis, go to [Stepwise Treatment Guide, Table #2](#) to determine the initial therapy for your patient. **Table #2**, based on published evidence to date and the clinical experience of the ACCP Tool Kit Committee in their clinical practices, recommends starting your patient on varenicline + bupropion SR. Initial varenicline dosing would be: 0.5 mg, each morning for 3 days; then, 0.5 mg, twice daily for 4 days; then, 1 mg, twice daily. Target Stop Date may be 1 week or longer after reaching the varenicline maintenance dose of 1 mg, q12h. The initial bupropion dose you should prescribe would be 150 mg, each morning for 3 days, then 150 mg, twice daily. Your initial therapy will then be intensified or relaxed, depending on the completeness of nicotine withdrawal symptom control that the initial therapy-varenicline, 1 mg, q12 h + bupropion SR, 150 mg, q12 h-provides.

Then, you can enable the patient to fine-tune withdrawal-symptom control by prescribing one or more reliever medications, such as nicotine oral inhaler and nicotine polacrilex gum, 4mg/piece dose. (See [varenicline's mechanism of action](#) for data validating the safety and efficacy of combining varenicline and nicotine medications.) Because the CNS self-regulates nicotine intake to control nicotine withdrawal symptoms, your patient will not overdose from nicotine reliever medications.

#### Medication Prescribing Example #2:

Another effective way to start treatment on the identical patient in Example #1, above, whom you have diagnosed as **Step 4: Very Severe Tobacco Dependence**, would be, from [Stepwise Tobacco-Dependence Treatment Guide, Table #2](#) to use high-dose, individualized nicotine patch dose (controller) and one or more reliever medications, such as nicotine nasal spray + nicotine polacrilex gum, 4 mg/piece dose. This can be a very valuable and also highly effective approach when physician, patient, or both do not want to use bupropion or varenicline or if the patient has had intolerable side-effects with either bupropion or varenicline.

The advantages include the fact that this approach is not exposing the patient to any chemical-nicotine that the patient is not already getting in much higher concentration from the cigarette. In addition, nicotine has been extensively studied for over 125 years; its medical strengths and toxicities are well-known and characterized. The disadvantage with this approach is that patients will need to be on multiple medications, and most likely at least two nicotine-reliever medications, which can be cumbersome and inconvenient, particularly if the patient travels frequently. Also, the average patient will need to be on more than 2, Step 1 nicotine patches, delivering >30-mg nicotine/16 hours of wear in order to adequately suppress nicotine withdrawal symptoms.<sup>192, 199</sup> Petite women, for example, can find it difficult to find enough skin surface area on which to apply more than 2 nicotine patches. In addition, this approach generally requires a higher nicotine replacement dose than necessary if other controllers, such as bupropion, are used along with an individualized nicotine patch dose.<sup>192, 199</sup>

If the patient is leaning in this direction solely because of the 7/1/09 FDA Black Box warning on bupropion and varenicline, the physician should counsel that emergence of serious psychiatric disorder or suicide occurs far more often in the absence of pharmacotherapy (up to 31% in tobacco-dependent individuals without any such prior history).<sup>200</sup> Perhaps more importantly, emergence of either serious psychiatric disorder or suicide on either of these medications is substantially and significantly lower than the incidence of these in the overall United States population<sup>201</sup> and that there does not appear to be an association between these medications and psychiatric disorder or suicide, far less a causal link, based on either US data or United Kingdom data<sup>202, 203</sup> (also see [Medication Safety](#))

#### Medication Prescribing Example #3:

**Using [Stepwise Tobacco-Dependence Treatment Guide, Table #1](#):** This 43-year-old male smokes 15 cigarettes/day (**Step 2 Cigarette Use** factor), and smokes the first cigarette of the day >60 minutes after awakening (**Step 1 Cigarette Use** factor). He has intermittent nicotine withdrawal symptoms and a nicotine withdrawal symptoms (NWS) score of 19/48 points (**Step 1** for both *Nicotine Withdrawal Symptom* factors) and has a Fagerström Test for Nicotine Dependence (FTND) score of 4/10 points (**Step 2 Quantitative** factor) and a Serum Cotinine level of 225-ng cotinine/mL blood (**Step 2 Quantitative** factor). By either

*Cigarette Use* (# cigarettes smoked/day) or *Quantitative* factor (FTND or Serum Cotinine), this patient would be classified as **Step 2: Moderate Tobacco Dependence**. He has no underlying medical problems; thus, the Medical component of *Health Status* is Healthy, which would be consistent with Step 2, Step 1, or Step 0. Also, when you take a basic psychiatric history, as part of your Review of Systems, he has no prior history of depression, panic disorder, or post-traumatic stress disorder (PTSD). His **Patient Health Questionnaire-9 (PHQ9)** is 4/27 points, which is within normal limits (normal  $\leq 4/27$  points). Thus, the Psychiatric component of *Health Status* is also "Healthy", which would also be consistent with Step 2, Step 1, or Step 0 for the *Health Status* factor. The items with the highest (worst) scores are number of cigarettes smoked/day (15), which is **Step 2** for the *Cigarette Use* factor; FTND of 4/10 points, also **Step 2** for *Quantitative* factor; and Serum cotinine of 225 ng/mL, which is also **Step 2** for *Quantitative* factor. Any one of these 3 factors-number cigarettes smoked/day, FTND, or Serum Cotinine level-would place this patient at **Step 2**. Therefore, your final diagnostic classification for this patient's tobacco dependence is **Step 2: Moderate Tobacco Dependence**.

Then, go to **Stepwise Tobacco-Dependence Treatment Guide, Table, #2** to determine the initial therapy for your patient. **Table #2**, based on published evidence to date and the clinical experience of the ACCP Tool Kit Committee in their clinical practices, recommends starting your patient on any one of the following regimens:

- 1) Nicotine patch, one Step 1 patch delivering 16-mg nicotine/16hrs or 21-mg nicotine/24 hrs, using reliever medications such as nicotine gum or nicotine nasal spray if needed to fully suppress nicotine withdrawal symptoms; after 3 or 4 days, you may need to increase the nicotine patch dose to 2 or 3 Step 1 patches, if nicotine withdrawal symptoms are not adequately controlled or if the patient is needing to use >16 pieces of the 4-mg dose of nicotine gum to adequately suppress nicotine withdrawal symptoms.
- 2) Bupropion SR or XL, 150 mg, qAM for the first 3 days, then increasing to either bupropion SR, 150 mg, q12h or bupropion XL, 300 mg, qAM, using reliever medications such as nicotine gum or nicotine nasal spray if needed to fully suppress nicotine withdrawal symptoms.
- 3) Varenicline, 0.5 mg, qAM for the first 3 days, then increasing to 0.5 mg, q12h for the next 4 days, then increasing to 1 mg, q12h. (NB: The Chantix "Starter Pak" provides this dose escalation automatically and also provides the first months' medication treatment.) This option is a simpler regimen, which should enhance adherence, and should be as effective as either of the first 2 options.

A 12- to 24-week course of treatment with any of the above 3 options might be all the treatment a patient at Step 2, Moderate will need.

#### Medication Prescribing Example #4:

##### Using **Stepwise Tobacco-Dependence Treatment Guide, Table #1**:

Patient is a 37-year-old, female, semi-skilled laborer earning \$35,000/year to support a family of 4. Her husband is a stay-at-home dad. She smokes 15 cigarettes/day (**Step 2 Cigarette Use** factor), and smokes the first cigarette of the day ~31 minutes after awakening (also, **Step 2 Cigarette Use** factor). The patient began smoking at age 14 and has smoked continuously since then, including through both pregnancies. (Her peak cigarette consumption 10 years ago was 2 packs per day.) The patient has frequent nicotine withdrawal symptoms and has a nicotine withdrawal symptoms (NWS) score of 26/48 points (**Step 2** for both *Nicotine Withdrawal Symptom* factors), and she has a Fagerström Test for Nicotine Dependence (FTND) score of 5/10 points and a Serum Cotinine level of 250-ng cotinine/mL blood (**Step 2** for both *Quantitative* factors). By either of the first three categories, *Cigarette Use*, *Nicotine Withdrawal Symptoms*, or *Quantitative*, this patient would be classified as **Step 2: Moderate Tobacco Dependence**. This patient has mild hypertension, treated with diet,

weight control, and exercise; thus, the Medical component of the *Health Status* factor is "≥ 1 Chronic Medical Disease," which would be consistent with Step 3 or Step 4. However, when you take a basic psychiatric history, as part of your Review of Systems, she tells you that she had severe post-partum depression after the birth of her second child 6 years ago, requiring a 1-year course of fluoxetine and weekly psychotherapy for 2 years. She feels fully recovered from that episode of depression, has not needed to see her psychiatrist in 4 years, and denies any current depressive symptoms. She has no history of panic disorder or post-traumatic stress disorder (PTSD). However, you look at the [Patient Health Questionnaire-9 \(PHQ9\)](#) that your office nurse had this new patient complete in the waiting room and note that it is 5/27 points. The diagnostic ranges for the Patient Health Questionnaire-9 (PHQ9) are: 0-4 points, normal; 5-9 points, mild depression; 10-14 points moderate depression; 15-19 moderately severe; and 20-27 points, severe depression. Thus, this patient is mildly depressed. Based on that, in conjunction with the significant past history of depression, the Psychiatric component of *Health Status* is "≥ 1 Psychiatric Disease." Thus, based on the *Health Status* factor, this patient's diagnostic category would be **Step 4**. Therefore, your final diagnostic classification for this patient's tobacco dependence is **Step 4: Very Severe Tobacco Dependence**.

Then, go to [Stepwise Tobacco-Dependence Treatment Guide, Table, #2](#) to determine the initial therapy for your patient, you consult [Table #2](#). Based on published evidence to date and the clinical experience of the ACCP Tool Kit Committee in their clinical practices, [Table 2](#) provides several recommended initial treatment approaches. Given this patient's history of severe post-partum depression 6 years ago and the mild depression shown on the PHQ-9, a particularly effective and appropriate initial treatment plan would be: 1) Bupropion SR or XL, 150 mg, qAM for the first 3 days, then increasing to either bupropion SR, 150 mg, q12h or bupropion XL, 300 mg, qAM, and 2) one standard Step 1 patch to be applied each morning and removed at bedtime, approximately 16 hours later, delivering 15-mg nicotine/16 hrs, and 3) Nicotine gum and/or nicotine nasal spray to be used as needed to keep nicotine withdrawal symptoms suppressed. This approach takes advantage of bupropion's dual therapeutic role: it is the only antidepressant that has been proven to be an effective tobacco-dependence medication, *independent* of its anti-depressant therapeutic effects, and independent of its effectiveness in treating tobacco dependence it is also an effective anti-depressant. While the physician always wants to clinically assess tobacco-dependent patients at each visit for depression and always checks a patient's NWS and PHQ-9 scores, because of this patient's history and minimal elevation in baseline PHQ-9 score, the physician naturally would want to be particularly attentive to these measures and assessments.

Separately from that, this treatment regimen gives you plenty of treatment flexibility to keep nicotine withdrawal symptoms, including treatment-emergent depression, controlled and suppressed. For example, because the baseline serum cotinine level is 250-ng cotinine/mL blood, which is the mean for US cigarette users, you could have started this patient on 2, Step 1 nicotine patches, both to be applied first thing in the morning and both to be removed at bedtime, thereby delivering 30-mg nicotine/16 hrs.<sup>57</sup>

Serum cotinine is far more accurate for medical decision making than number of cigarettes smoked per day. This has become particularly true over the past decade, as the cost of a pack of cigarettes has steadily increased from \$3-\$5/pack to \$6-\$10/pack. ACCP Tool Kit Committee Members have observed both in their clinical practices and in clinical research trials, that the serum cotinine levels have been remaining relatively constant over the past decade. Number of cigarettes of cigarettes smoked per day, on the other hand, has been steadily dropping from a mean of close to 30 cigarettes/day to as low as 15 cigarettes per day to <20 cigarettes per day. (Cigarette smokers become more efficient in extracting nicotine from their cigarettes by inhaling deeper and breath-holding longer.) If, at your regular medical assessment follow-up visits you are not fully happy with control of nicotine withdrawal symptoms you can:

- 1) Increase nicotine patch dose beyond 2 patches/day

(see [Medication Safety](#))

- 2) Increase bupropion SR to its maximum approved dose of 150 mg, q8h, for a total daily dose of 450 mg/day,
- 3) Instruct the patient to increase frequency of use of one or more nicotine reliever medications to completely suppress nicotine withdrawal symptoms.

In addition, in a patient with a prior psychiatric history, even one such as post-partum depression, you should consider recommending the patient also see the previous treating psychiatrist while you are treating the patient's tobacco dependence.

Depression occurring or worsening during tobacco-dependence treatment is rare but requires careful monitoring attention. We recommend that the PHQ-9 be administered at each patient visit. Most commonly, depression and its associated manifestations is a symptom of nicotine withdrawal and would then require an increase in medication dosages. However, given the recent FDA warnings concerning bupropion and varenicline (see below), the physician should be attentive to depression and suicidality as a possible, but rare, medication side-effect. Clinical suspicion for a medication side-effect would increase if the PHQ-9 score increased and if the depression occurring during tobacco-dependence treatment was out of proportion to any other nicotine withdrawal symptoms that the patient might be experiencing. If a medication side-effect is suspected, then the controller medication should be changed and consideration should be given for psychiatric evaluation, monitoring and, if needed, independent treatment of depression. And of course, suicidality, although very rare, should prompt the immediate discontinuation of any medication suspected as potentially causal and calls for immediate psychiatric evaluation.

With all patients, but particularly this woman, after the patient has been 100% tobacco-free for 6 or more months and has also been nicotine withdrawal symptom-free for 6 or more months and has also been depression-free for 6 or more months, you can begin medication tapering (see section later in this chapter headed, [Medication Tapering](#)) and you will want to regularly monitor the patient's nicotine withdrawal symptoms, using the [Nicotine Withdrawal Symptom Scale \(NWS\)](#) and the patient's depression, using the [Patient Health Questionnaire-9 \(PHQ9\)](#). That is the only way you can detect deterioration in withdrawal symptoms or depression in a timely way so that you can effectively intervene and increase the dose of medication last tapered back to where it had been and let the patient re-stabilize. Then, you can attempt a smaller dose reduction. The goal is to reduce the total number of medications necessary to control tobacco dependence to the fewest number possible and to reduce the dose of each medication to the lowest doses possible that will allow complete control of nicotine withdrawal symptoms, including depression and other mood disturbances. This tapering process, keeping dose and number of medications sufficient to suppress nicotine withdrawal symptoms, often can take several years. Pushing tapering too fast produces relapse. Some patients will need to be on one or more tobacco-dependence medications for the rest of their lives to avoid relapse.

**Clinical Pearl:** *Nicotine, particularly in the concentration and dose delivered by the cigarette, is a highly effective anxiolytic and antidepressant. The literature is quite clear that many cigarette users are using their cigarettes to control a sub-clinical depression or anxiolytic state but do not know they are doing that.<sup>200</sup> Additionally, the treating physician should be alert to the far lower risk of depression as a potential medication side-effect.*

**NB: "Correct Coding Principles for Tobacco-Dependence Treatment"** explains how you should employ ICD-9 and CPT E/M codes to be reimbursed for professional services you provide in all 4 of the illustrative examples, above.

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## Combination Pharmacotherapy Safety

Data regarding medication safety is discussed below for each individual medication.

### Controller Medications-Efficacy and Effectiveness Detail

**Bupropion SR (Sustained Release)**, first marketed as an antidepressant, received a second FDA indication for treatment of tobacco dependence in May 1997. Bupropion is only available by prescription and comes in three separate formulations: **Immediate Acting**, which should be dosed every 8 hours; **Sustained Release (SR)**, which should be dosed approximately every 12 hours; and **Extended Release (XL)**, which should only be dosed once per day, in the morning.\* A common misconception is that bupropion works by elevating mood in tobacco-dependent patients. Instead, bupropion works by slowing re-uptake of dopamine at the distal dopaminergic neuron and for some patients, filling the  $\alpha_4\beta_2$  nicotine receptors, thereby increasing dopaminergic neurotransmitter tone. This reduces the intensity of the compulsion to smoke and nicotine withdrawal-symptom severity. Indeed, the bupropion SR registration trials for the tobacco-dependence indication specifically *excluded* any one who was depressed.<sup>54, 62, 137</sup>

Bupropion has been shown to be effective tobacco-dependence treatment for non-depressed study participants;<sup>54</sup> depressed study participants;<sup>204</sup> low-income, poorly educated, African-American study participants;<sup>205</sup> adolescent study participants;<sup>206</sup> primary care patients (as distinct from study participants),<sup>207, 208</sup> and re-treating tobacco-dependent patients who used bupropion successfully in the past but relapsed after stopping bupropion.<sup>209</sup>

When used as monotherapy for non-depressed patients, bupropion SR shows classic, highly significant, dose-response outcome at the end of 6-weeks treatment from Target Stop Date; 44% not smoking with 300 mg, daily; 39% with 150 mg daily; 29% with 100 mg daily; and 19% with placebo.<sup>54</sup>

### Practical Treatment Tips

Treatment with bupropion should be initiated 1-2 weeks before the anticipated target stop date to allow for adequate CNS levels. Typically, start the patient with 150 mg of bupropion SR each morning for three days, and then increase to 150 mg b.i.d (or 300 mg, qAM, for the XL formulation).

*Combination treatment* with bupropion and nicotine medication is particularly effective<sup>1, 113</sup> and is recommended to help reduce withdrawal symptoms and also reduce the likelihood of weight gain. (Also, see above.)

**Nicotine transdermal system** has been available by prescription in the United States since late December 1991, and over-the-counter (OTC) since July 1996. The United States Food and Drug Administration (FDA) based its decision on moving the patch from prescription to OTC status primarily on the safety of the nicotine patch as a medication for treating tobacco dependence. The efficacy of the patch was definitive and unequivocal. The standard, over-the-counter nicotine patch dosing instructions, however, as printed on the box (only 1, Step 1 patch delivering 21-mg nicotine/24 hrs or 15-mg nicotine/16 hrs), inadequately treats about 80% of users, failing to suppress nicotine withdrawal symptoms and therefore causing the patient to relapse. Most tobacco-dependent individuals who smoke  $\geq 1$  pack per day or have a serum or saliva cotinine level  $\geq 250$ -ng cotinine/mL blood will need at least 2, Step 1 patches<sup>57, 210</sup> plus a second controller, i.e., bupropion SR (see "Combination Pharmacotherapy", above), plus prn use of one or more nicotine reliever/rescue medications (see above) in order to adequately suppress nicotine withdrawal symptoms. As discussed in §1.6 of

\*Although only one bupropion formulation, Zyban, which is bupropion SR, has FDA approval for the treatment of tobacco dependence, most experts in the field, including the ACCP Tool Kit Committee members regard all forms—immediate acting, sustained release, and extended release—as equivalently effective, pharmacologically. Treatment adherence for any disease seen in medical practice, of course, improves inversely in relation to dosing frequency. Thus, the specific bupropion formulation you prescribe should be that which will be easiest for the patient to use. All bupropion formulations are available generically.

this Tool Kit, this approach—providing effective pharmacotherapy—requires physician supervision and monitoring. (See also **Stepwise Tobacco-Dependence Treatment Guide**, in this Tool Kit.) Side effects such as sleep disturbance and bizarre dreams are reduced if the patient removes the prescribed nicotine patch dose at bedtime, approximately 16 hours after applying the patch(es) in the morning. Finally, remember that, despite similar amounts of available nicotine in a Step 1 patch compared to a pack of cigarettes, absorption differences between the routes of administration can profoundly affect blood levels achieved, making it necessary to adjust dose and frequency to effect rather than relying on a simple substitution calculation.

**Varenicline** tartrate was the first medication approved for treating tobacco dependence in almost a decade. In May 2006, the FDA approved varenicline, a sustained-release medication that is a selective  $\alpha_4\beta_2$  nicotinic receptor partial agonist and an  $\alpha_7$  nicotinic receptor full agonist.<sup>211, 212</sup> Varenicline blocks, but not completely, nicotine from binding to these receptors and prevents nicotine from producing the reinforcing and rewarding effects associated with tobacco use. On the agonist side, varenicline, binding into the  $\alpha_4\beta_2$  and  $\alpha_7$  nicotinic receptors, stimulates the dopaminergic neuron to release some dopamine at the distal terminus of the neuron, attenuating—but only partially—nicotine withdrawal symptoms. Varenicline is clearly the most effective monotherapy for tobacco dependence (see [Table 2](#)).<sup>1</sup> Three independent studies showed varenicline to be superior to bupropion SR in tobacco-dependence treatment efficacy.<sup>55, 170, 213</sup>

When used as monotherapy, varenicline shows classic, highly significant, dose-response outcome at the end of 6-weeks treatment from Target Stop Date; 41% not smoking with 1 mg, twice daily (2-mg total, daily dose); 31% with 1 mg, once daily; 25% with 0.3 mg, once daily; and 14% with placebo.<sup>213</sup> (This same trial also had a fifth arm, bupropion SR, 150 mg, twice daily [300-mg total, daily dose]. Percent not smoking, at the same time-point, was 29%, which was significantly better than placebo but not significantly better than varenicline, 1 mg, twice daily.<sup>213</sup>) In a series of larger trials specifically designed to compare treatment efficacy of varenicline head-to-head with bupropion SR, tobacco-dependent patients treated with varenicline had a biochemically confirmed quit rate of 50% at the end of 12-weeks treatment, superior to and significantly better than those patients treated with bupropion SR (36%) or placebo (21%).<sup>55, 170</sup> Thus, three independent trials show monotherapy with varenicline, 1 mg, twice daily, to be superior to monotherapy with bupropion SR, 150 mg, twice daily.<sup>55, 170, 213</sup>

## Practical Treatment Tips

Treatment with varenicline should be initiated a minimum of 7 days before the anticipated Target Stop Date to allow for development of adequate therapeutic CNS varenicline levels. Many clinical experts, including those on the ACCP Tool Kit Committee, start varenicline 2 or more weeks before the Target Stop Date, depending on patient response. (Some patients, within days after starting varenicline and before their Target Stop Date, see the number of cigarettes they are smoking daily falling, without any particular effort on their part and without any nicotine withdrawal symptoms.) Typically, start the patient with 0.5 mg of varenicline each morning for three days; then, increase to 0.5 mg, b.i.d., for four days; and then on treatment-day 8, increase the dose to 1.0 mg, b.i.d.

**Clinical Caveat:** Although FDA package labeling states that the Target Stop Date should be the very day that the varenicline total daily dose is increased from 1 mg daily to 2 mg daily, this makes no pharmacokinetic sense, because it takes *at least* 4 days after a dose change for varenicline serum (and presumably brain) levels to reach new steady-state equilibrium.<sup>211</sup> This is probably the reason why many clinical experts want their patients using varenicline for a total of 2 weeks before Target Stop Date.

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## Reliever (or Rescuer) Medications-Efficacy and Effectiveness Detail

**Nicotine polacrilex gum** was approved by the FDA in 1984, and has been available without prescription-over-the-counter (OTC)-since 1996 in both 2- and 4-mg dosage formulations and comes in several flavors. Nicotine is released through the chewing action and absorbed into the bloodstream through the lining of the mouth. To maintain the even flow of nicotine, it must be chewed slowly until a slight tingling occurs or a peppery taste is experienced. Then it must be placed between the cheek and the gingiva and parked until the peppery taste or tingling is gone. This cycle is repeated for about 30 minutes per piece. Technique is important; if chewed improperly, the gum loses effectiveness because absorption is compromised while the likelihood of gastrointestinal side effects such as nausea and hiccups increases.

In general, patients should not exceed 20 pieces per day, but some will need more, particularly if this is the only medication they are using. The ACCP Tool Kit Committee members' experience is that patients do better if they start with the 4-mg dose, even if this is being used with controller medications, such as nicotine patch or bupropion SR (see below). However, most people report that 9 to 12 pieces per day of the 4-mg dose controls their urge to smoke and suppresses nicotine withdrawal symptoms. Highly dependent users, for example those whose time to first cigarette after awakening is shorter than 30 minutes, should be encouraged to use the 4-mg rather than the 2-mg dose.

**Nicotine polacrilex lozenge** was approved by the FDA for OTC distribution in late 2002. It is available in 2- and 4-mg forms and comes in several flavors. The use strategy is much the same as with nicotine gum; at least 9 lozenges are required per day for initial, effective treatment (weeks 1-6), with 20 the probable maximum. The 4-mg dose is generally more effective at suppressing nicotine withdrawal symptoms, so patients should generally start with that strength, and particularly those patients who smoke their first cigarette of the day within 30 minutes of waking.<sup>214</sup> The 2-mg strength is more useful for tapering. Elderly or edentulous patients, or those with difficulty chewing may better tolerate lozenges than the gum. The nicotine lozenge should be placed between the cheek and gum, and allowed to dissolve slowly over a 20-30 minute period while occasionally moving the lozenge to a different place in the mouth. The lozenge should never be placed under the tongue, since that will stimulate excessive saliva production, causing the patient to swallow the nicotine-laden saliva and suffer side effects, such as nausea, abdominal cramping, or heartburn.

**Nicotine [oral] inhaler** was approved by the FDA in 1997. Only available by prescription, the inhaler works by releasing nicotine into the mouth and throat through a mouthpiece containing a plastic cartridge. The name "inhaler" is a misnomer; the nicotine is not inhaled into the lungs. Nicotine is absorbed only across the oral mucosa,<sup>215</sup> the same site as nicotine gum and lozenge. An important difference, though, is that the nicotine absorption from the oral inhaler is unaffected by oral pH. Release of nicotine from both the nicotine gum and lozenge is highly pH-dependent.<sup>216</sup> Thus, for social settings, such as at a bar or party, the oral inhaler and nasal spray would be a better reliever medications than gum or lozenge. In fact, deep inhalation from the oral inhaler can increase side effects (cough and sore throat) without adding to its efficacy. Nicotine that enters the bloodstream through the mucous membranes of the mouth or throat does so more slowly than the nicotine in cigarettes. The "dose" of the inhaler is determined by the frequency and intensity of puffing. Patients can use the inhaler alone or as an adjunct to the nicotine patch or bupropion, and can use it at scheduled time intervals to control cravings, or as a PRN reliever in response to acute, cue-induced cravings.

**Nicotine nasal spray**, approved by the FDA in 1996 and available by prescription only, reaches the bloodstream faster than any other nicotine medication. As a result, it has an impact more similar to the cigarette than other forms of nicotine replacement. Nicotine is sprayed into the nose where it is absorbed through the nasal mucosal lining. Effectiveness is maximized when used in conjunction with the nicotine patch.<sup>69</sup> Like the oral inhaler, nicotine absorption from in the nasal spray is not affected by pH, because the nicotine is not at all bound to a pH-dependent ion exchange molecule, as is the case with nicotine gum and lozenge.

**Nicotine water and nicotine lollipops** have no role in the treatment of tobacco use and are not currently recommended. In fact, many are concerned that they are being marketed not for their therapeutic efficacy but rather as early nicotine addiction systems for young children.

**E-Cigarette.** In 2009 an electronic device that vaporizes nicotine at high temperature and which contains no tobacco has been commercially marketed in the United States as the E-Cigarette. This device has not been approved by the FDA and no data of any kind are available.<sup>217</sup> No information defining the contents of the volatilized nicotine is available. No toxicology data are available. No safety data are available. No efficacy data are available. Because this device does not claim to be a cigarette or tobacco product, but a nicotine delivery system, it falls under the FDA's authority to regulate. As of this Tool Kit's press time, the manufacturer had not submitted any data for review to the FDA, so the FDA is likely going to require the manufacturer to pull the E-Cigarette from the market.<sup>217</sup> **The ACCP Tool Kit Committee cannot recommend use of the E-Cigarette at this time.**

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## Medication Safety

### Overview

- All FDA-approved tobacco-dependence medications-nicotine medications, bupropion, and varenicline-are generally safe and well tolerated. The safety record of nicotine medications and bupropion has been established over decades of use in tens of millions of tobacco-dependent patients. The most commonly occurring side effects (see [Quick Reference Guide to Pharmacotherapy](#)) are not of any significant medical consequence, are generally mild, and oftentimes either resolve within a few weeks, or can be readily treated so that the patient can continue to get the benefit of needed tobacco-dependence pharmacotherapy.
  - For example, insomnia, specifically difficulty remaining asleep, occurs in 30% of all bupropion users and is mild in about three fourths of those. Insomnia usually resolves in several weeks. If a continuing problem, though, **before** the Target Stop Date, switching the patient to the same dose, but in the once-daily XL formulation, taken in the morning, will usually solve the problem. Alternatively, if the patient is taking bupropion SR, 150 mg, q12h, the second dose can be taken earlier, 8 hours after the first dose.
  - Similarly, nausea is the most frequently occurring side effect from varenicline, occurring in 30%-40% of patients. For three-fourths of them nausea is mild and generally not a problem that warrants intervention. Such nausea usually resolves within 2-3 weeks. Once again, this is a good reason to delay the Target Stop Date so that the patient is feeling back to baseline before stopping smoking. Most patients find the benefits of varenicline far outweigh this side effect. If the nausea is more than mild and is not resolving before Target Stop Date, then you can lower the dose, because all of varenicline's side effects are dose-related. Its therapeutic effectiveness is also dose-related, so reducing the dose to control nausea may provide the patient with a sub-therapeutic dose of varenicline. In that case you and your patient could consider adding an anti-emetic, so that the patient can continue using a therapeutically effective dose of varenicline. Alternatively, you could switch to a completely different medication treatment plan. For many reasons, including your patient's sense of self-confidence and being in control of the situation, this is all best sorted out *before* the Target Stop Date.
- Medications with extensive cytochrome metabolism, such as theophylline and warfarin, or other medications, including insulin and thyroxin, may require dose adjustments after stopping smoking.
- Despite the well-established safety record of these medications and despite their effectiveness in treating the single leading cause of premature death and disability in the United States-tobacco dependence-physicians and patients underutilize them because of unfounded fears and concerns regarding their safety. We would never think of denying an asthmatic use of effective pharmacotherapy. We must approach treatment of tobacco dependence with same level of medical insight, sophistication, thoroughness, and urgency that we bring to the care of our asthmatic patients.
- Treatment-emergent depression, mood changes, and suicidality can occur whenever a person stops smoking, with or without medications, including bupropion, nicotine medications, and varenicline. If a tobacco-dependent patient is depressed, the physician should evaluate if the depression is due to nicotine withdrawal and therefore under-dosing of tobacco-dependence medication(s) or due to unmasked depression that requires a psychiatric evaluation. In rare cases, the changes in behavior or mood may be caused by the medication or inadequate dose of the medication. The physician should routinely monitor for the development of psychiatric problems at each office visit, using a tool such as the PHQ-9 discussed above, and, depending on the underlying cause, either increase nicotine medication dose, change controller medications, increase the doses of other controller medications, or add nicotine rescue medications. Also, the treating physician should consider psychiatric referral in such cases to determine whether these changes reflect an underlying psychiatric state, or are merely a manifestation of nicotine withdrawal. On July 1, 2009, the United States Food and Drug Administration (FDA) issued a Black Box warning for both the bupropion and varenicline prescribing labels, highlighting the apparent association of serious neuropsychiatric symptoms in patients using these medications.<sup>218</sup> These symptoms include changes in behavior, hostility, agitation, depressed mood, suicidal thoughts and behavior, and attempted suicide. The possible risks of serious adverse events occurring while using varenicline or bupropion should always be weighed against the "... health benefits of quitting smoking [which] are immediate and substantial."<sup>218</sup> Given our present state of knowledge, however, "it is impossible to know whether the psychiatric symptoms and suicidal behavior reported in patients taking varenicline or bupropion in order to stop smoking are due to the drugs, the smoke, the smoker, the cessation of smoking or simply the usual causes of such symptoms and behavior in the larger community."

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## Specific, Medication-Specific Side Effects

All FDA-approved tobacco-dependence medications-nicotine medications, bupropion, and varenicline-are exceptionally safe and well tolerated. The most commonly occurring side effects (see [Quick Reference Guide to Pharmacotherapy](#)) are not of any significant medical consequence, are generally mild, and oftentimes either resolve within a few weeks, or can be readily treated so that the patient can continue to get the benefit of needed tobacco-dependence pharmacotherapy.

### Bupropion

- The most common side effects when using bupropion are:
  - Headache (30%)
  - Insomnia, specifically difficulty remaining asleep (30%)
  - Xerostomia, or dry mouth (15%)

These side effects are generally mild and resolve within 2-4 weeks of starting bupropion.

- Bupropion SR has a reported seizure incidence of 0.1%. This is less than the reported seizure incidence of SSRI-type anti-depressants. Seizure has not turned out to be a problem in tobacco-dependence over the past 12 years. Patients with any of the following pre-existing conditions should not routinely be

prescribed bupropion. Doing so reduces the seizure probability to close to zero:

- History of grand mal or petit mal seizures
- History of brain surgery
- History of significant brain trauma
- History of anorexia nervosa
- History of bulimia
- Taking a medication known to lower seizure threshold
- Current alcoholic
- Hypertensive patients receiving combination bupropion and nicotine therapy should be monitored for treatment-induced blood pressure increase.
- Patients, especially those with a history of depression or suicidality, should be carefully monitored for nicotine withdrawal induced or bupropion-induced depression or suicidality (see below for details). That said, in 12 years of use in tobacco-dependence clinical practice, bupropion is a highly effective and safe medication, particularly for use in tobacco-dependent patients with psychiatric co-morbidities.

## Nicotine Medications

- The most common side effects of nicotine medications are generally related to the specific nicotine delivery system:
  - Patch
    - Erythema, edema, or pruritis at the patch application site.
  - Gum and Lozenge
    - Hiccups
    - Heartburn
    - Nausea
  - Nasal Spray
    - Nasal mucosal irritation
  - Oral Inhaler
    - Cough

Most of the side effects are secondary to incorrect usage of the delivery system and can be corrected by re-instruction in optimal use technique. In the case of cutaneous irritation at the nicotine patch application site, this is usually due to the adhesive of the specific patch brand. Switching brands frequently solves this problem. When it does not, treating the patch application with an appropriate topical steroid or prescribing a non-sedating anti-histamine or a leukotriene modulator will solve the problem.

- Nicotine medical products must be kept out of reach of children and pets. Don't forget, this includes *those that have been used and discarded, particularly nicotine patches*.
- Contrary to widespread belief and product insert disclaimers, smoking while using nicotine medications is not in any way a deadly combination.<sup>139,218</sup> While tobacco-dependent patients should be encouraged to stop smoking completely, the treating physician should emphasize that patients should continue their medications *particularly in the face of a lapse*. Patients should also realize that a lapse while using a given treatment combination means that their treatment plan is not completely adequate. Thus, they should call their treating physician promptly so that the treatment plan can be revised and effectiveness improved. (see **Treatment Process and Approach**, particularly the section describing the ARMR concept.)
- Overdose with nicotine medications is rare. It is more likely to occur with nicotine patch, since the patch has a fixed, pre-programmed amount of nicotine to deliver. Overdose is extraordinarily unlikely with the nicotine rescue medications, since the central nervous system self-regulates nicotine intake, just as it does when the person is smoking cigarettes. There is a large margin between achieving therapeutic effect, suppressing all nicotine withdrawal symptoms, and appearance of nicotine toxicity signs or symptoms. The first symptoms of nicotine overdose are abdominal queasiness, followed by nausea, then emesis. Serum nicotine level must get acutely much higher in order for tachycardia to occur, let alone tachyarrhythmias.
- Patients with heart disease or hypertension can safely use nicotine medications.<sup>218, 219</sup> Surveillance of blood pressure control and cardiac status is prudent, especially for patients on high-dose nicotine therapy.
- The decision to use nicotine medications in pregnant or breast-feeding patients should be individualized based on the relative risk-benefit of continued smoking. Use of any tobacco-dependence medications during pregnancy should proceed only under physician guidance. (See U.S. Public Health Service, *Clinical Practice Guideline: Treating Tobacco Use and Dependence (2008 Update)*,<sup>1</sup> Hodgkin JE, Celli BR, and Connors GL (Eds), *Pulmonary Rehabilitation: Guidelines for Success, 4<sup>th</sup> Edition*, 2009, Chapter 16,<sup>113</sup> and recent documents from the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA)<sup>188,220</sup> for more detailed discussion of this point.)
- Nicotine medications, including the controller nicotine patch (see below) are among the safest medications used in a pulmonary medicine practice.<sup>139</sup> It is important to remember that not one patient has died from therapeutic nicotine since nicotine gum was approved in 1984, while in that time over 8 million cigarette smokers have died from the myriad diseases caused by tobacco. Simply stated, these medications are woefully underutilized by physicians and by the patients who could benefit from them.

## Varenicline

As is the case with the nicotine medications and bupropion, varenicline is also safe for the vast majority of patients and generally well tolerated. The most common side effect is nausea, which occurred in 30% of study subjects, was mild in 75%, and tended to resolve by the Target Stop Date.<sup>55, 73, 170</sup> In those studies, nausea was also the most common cause of premature study withdrawal for an adverse event, with 3% withdrawing.

- The most common varenicline side effects, also generally mild, but occurring significantly more frequently than placebo, are:
  - Nausea (30%)
  - Abnormal Dreams (13%)
  - Headache (13%)
  - Constipation (9%)
  - Flatulence (6%)
  - Xerostomia (Dry Mouth) (6%)
  - Emesis (5%)
- Patients, especially those with a history of depression or suicidality, should be carefully monitored for nicotine withdrawal induced or varenicline-induced depression or suicidality (see below for details)
- Varenicline does not produce drowsiness or seizure disorder.

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## Depression, Suicidality and Tobacco Dependence

Suicide is associated with cigarette use<sup>159, 160</sup> and is unequivocally linked in a significant dose-response relation to number of cigarettes smoked per day.<sup>221-223</sup> For example, cigarette smokers have an increased odds ratio of committing suicide that is 2.6 compared to the non-smoker (95%CI = 1.6-4.2).<sup>224</sup> Moreover, the risk of committing suicide among cigarette smokers not trying to stop smoking increases significantly ( $P < 0.001$ ) with the number of cigarettes smoked/day,<sup>221</sup> with those smoking >20 cigarettes/day more than 2-fold more likely to commit suicide than those who have never smoked.<sup>221</sup> Cigarette use may also be an independent, dose-response risk factor predicting suicide.<sup>221-223</sup> In addition, suicide incidence is higher in cigarette users, independent of confounding factors, such as income, race, previous myocardial infarction, diabetes, alcohol use,<sup>224</sup> and also previous depression history or substance abuse.<sup>159</sup>

## Depression, Suicide, Cigarette Use and Pharmacotherapy

Major depressive disorder occurs in up to 31% of people without any prior history of depression if they attempt to stop cigarette use without the benefit of pharmacotherapy, and in up to 75% of those who have had a previous depressive episode even though not depressed when they tried to stop cigarettes.<sup>200</sup> ACCP Tool Kit Committee Members have observed this in clinical practice and have also observed acute suicidality when patients have attempted to stop smoking without pharmacotherapy. They have also observed psychiatric problems and suicidal ideation when the medication doses were sub-therapeutic. In all cases major depressive disorder or suicidality have promptly resolved upon either increasing the dose of nicotine medication, adding a rescue medication, such as nicotine nasal spray, to controller, such as nicotine patch or bupropion, using nicotine patch in combination with bupropion or increasing the dose of either until the depression or suicidality has come under control. Additionally, ACCP Tool Kit Committee Members have consistently observed that such acute psychiatric states resolve within minutes after the patient takes as few as 1 or 2 cigarette inhalations. This holds true whether the patient is on no medications or sub-therapeutic doses of tobacco-dependence medication.

On July 1, 2009, the United States Food and Drug Administration (FDA) issued a Black Box warning for both the bupropion and varenicline prescribing labels. This was based on the reporting of 37 tobacco-dependent patients taking varenicline who either made a suicide attempt or actually committed suicide. Of the 37, 18 were attempted suicides.<sup>225</sup> However, neither the prescribing information nor the FDA newsletter placed these 19 completed suicides into perspective, which could have been done by expressing them as the annualized number of suicides/100,000 varenicline users. For example, over approximately this same time period 5.5 million Americans used varenicline. This would then calculate as a completed suicide incidence rate of 0.49/100,000 varenicline users/year, which is far lower than the overall suicide incidence rate in the U.S. population of 11.01/100,000/year.<sup>226</sup>

Furthermore, in the largest published, peer-reviewed study to date, comparing 412 consecutive patients (64 of whom had diagnosed depressive disorder, 14 bipolar disorder, 24 psychosis and depression, 7 psychosis, only, and 2 eating disorders), 208 received varenicline and 204 nicotine medications, no patient in either treatment condition, with or without mental illness, committed suicide or experienced worsening or new onset of depression or other mental disorder.<sup>202</sup> Clearly, the risk benefit analysis favors the use of tobacco cessation medications when compared to the fact that each year 443,394<sup>227</sup> of the 43 million U.S. cigarette smokers<sup>40</sup> die of tobacco-caused illnesses. Over their lifetime, 50% of all cigarette smokers, if not provided effective tobacco-dependence treatment, will die of tobacco-caused diseases.<sup>158, 176</sup> That is an annualized death rate of 1,031.1 deaths/100,000 cigarette smokers per year.

Despite the fact that depression and suicide are rare and, when occurring, are far more commonly related to nicotine withdrawal than its treatment with bupropion or varenicline, all clinicians have a responsibility to carefully monitor this potential problem during tobacco cessation. For that reason we encourage the use of a validated depression questionnaire, such as the PHQ-9 or BDI-II, during the initial and all follow up clinical evaluations, particularly while any reductions in tobacco-dependence doses are being attempted. Clinical suspicion for a medication-induced side-effect would be higher if the PHQ-9 score increased and if the depression occurring during tobacco-dependence treatment was disproportionate to other nicotine withdrawal symptoms that the patient might be experiencing. If a medication side-effect was suspected, then the controller medication should be changed and consideration should be given for psychiatric evaluation, monitoring and, if needed, independent treatment of depression. And of course, suicidality, although extremely rare, should prompt immediate discontinuation of any suspected causal medication and immediate

psychiatric evaluation.

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## Second-Line Medications as Controller Medications

Second-line medications have variable efficacy in tobacco use treatment, and should be considered for use only after first-line treatments have failed. The primary reasons for this recommendation include: (1) they do not currently have FDA approval for treatment of tobacco dependence, and (2) there are more potential side effects than exist with the first-line treatments.

**Clonidine** is primarily used as an antihypertensive. Specific dosing regimens for use in cessation have not yet been determined. Its efficacy in cessation is limited by its rather significant side-effect profile. Abrupt discontinuation of clonidine can result in nervousness, agitation, headache, tremors, a rapid rise in blood pressure, and elevated catecholamine levels.

**Nortriptyline** is an antidepressant but published scientific studies show it to have comparable efficacy in tobacco dependence to bupropion SR.<sup>138, 228, 229</sup> However its TID dosing schedule and expanded side-effect profile make it less well tolerated and harder to use. It has therefore not received the same endorsement that bupropion has secured. Nortriptyline should be considered in smokers who are likely to benefit from the addition of an antidepressant, but for whom bupropion is contraindicated (i.e. seizure disorder, eating disorder, prior adverse reaction to bupropion, etc.).

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## Duration of Use and Medication Tapering

Longer-duration pharmacotherapy improves stopping smoking.<sup>1, 2, 69, 73, 137, 138, 230</sup> Six months or 1 year of treatment produces higher, continuous non-smoking rates than 6 weeks or 3 months of treatment. Most patients who want to stop smoking therefore should receive a minimum of 6 months of nicotine, bupropion, varenicline, or an appropriate combination. Most adverse events to any of the tobacco-dependence medications occur within the first few days or weeks of use. No evidence exists that extended medication use beyond 6 months or 1 year exposes the patient to any increased medical risk. In fact, the FDA specifically recommends a longer term (> 6 months) maintenance treatment for bupropion SR, in part because of the strong supporting clinical trial data showing improved effectiveness with longer treatment.<sup>137, 231, 232</sup>

Unfortunately, in general the manufacturers' recommendations for treatment duration with nicotine medications are not based on systematic research. Patients generally use nicotine medications for only 2 weeks<sup>5</sup> — not long enough to derive any clinical benefit. To obtain the best result, patients should receive at least a 3- to 6-month treatment course with nicotine medications.<sup>1, 2, 113, 233, 234</sup>

Patients who are especially likely to benefit from more intensive and longer-duration treatment, including more frequent office visits, and combination pharmacotherapy rather than monotherapy, include cigarette users who are highly nicotine dependent (as measured by the Fagerström Test for Nicotine Dependence (FTND)),<sup>52, 104, 149, 155, 235, 236</sup> have a higher serum cotinine level while still smoking,<sup>152, 153</sup> smoke more cigarettes per day,<sup>61, 237, 238</sup> are alcoholic,<sup>239</sup> depressed,<sup>200, 240</sup> unmarried (divorced, separated, never married, or widowed), female,<sup>58, 61, 69, 150, 241-243</sup> have another cigarette smoker in the household,<sup>150, 244</sup> previously tried to quit smoking,<sup>150, 244</sup> experienced nicotine withdrawal symptoms with previous quit attempts,<sup>104-106</sup> were <17 years old when they started smoking,<sup>153, 244</sup> or are younger at the start of treatment.<sup>150, 231, 245</sup>

Generally, after 3-6 months the patient should attempt to gradually reduce dosage of nicotine medications, one at a time, under medical supervision. It is crucial for the treating physician to closely monitor nicotine withdrawal symptoms and mood state, including depression and suicidality, after reducing or stopping any tobacco-dependence medication and reinstating the previous doses if withdrawal symptoms or dysphoria increase. Increased nicotine withdrawal symptoms generally account for most cases of relapse,<sup>113</sup> and must remain suppressed in order for the patient to remain tobacco free.

Long-term continuous use of pharmacotherapy may be appropriate in some patients. Although gradual reduction in doses and number of medications is the pharmacotherapeutic goal, protracted, indefinite use is obviously preferable to relapse. Occasionally, patients will express a concern that prolonged use of nicotine medications will delay abstinence; however this is a misconception. Unlike tobacco use, these medications do not contain toxins, the nicotine medications, specifically, do not produce nicotine surges in the bloodstream, or do not lead to dependence, and can be used for long periods without significant safety concerns.<sup>1, 2, 234, 246</sup>

Relapse is common following termination of medication, and is more likely to occur with higher FTND scores. This effect is seen irrespective of treatment approach. It is useful to think of the compulsion to smoke as the visible manifestation of a poorly controlled disturbance in nicotinic neurobiology, similar to the notion that wheeze is the audible manifestation of poorly controlled airway inflammation. As with asthma, there is no evidence that any of the pharmacotherapeutic agents reverse the underlying root cause of the abnormalities. Instead, medications should be intended to control the compulsion to smoke long enough to allow the patient to reverse the neuropathologic changes related to nicotine addiction. Nicotine dependence is a chronic condition, and some patients will require maintenance therapy of indefinite duration. Relapse should be anticipated and prevented but if it does occur, then it should be treated, as with any chronic condition.<sup>112, 113</sup> Patients may require lifetime treatment or repeated cycles of treatment. Therefore, the physician and patient should have a plan for regular follow-up visits, as would be done with asthma.

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## Conclusion

This Chapter presents a completely new concept in the pharmacologic management of tobacco dependence, based on rational, pharmacotherapeutic principles that the members of the ACCP Tool Kit Committee, as well as other physicians, have used in routine clinical practice for over 10 years. This approach is effective, it works, and it can be adopted and modified for any medical office or inpatient practice setting. The approach proffered by this Tool Kit changes the paradigm for tobacco-dependence treatment. As one of our Committee members accurately pointed out, "If we always do what we've always done, we'll always get what we've always gotten."

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<a href="#">&lt; Tobacco-Dependence Treatment Process and Approach</a>	<a href="#">up</a>	<a href="#">Quick Reference Guide to Pharmacotherapy &gt;</a>
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**TABLE 1: EFFECTIVE MEDICATIONS FOR TREATING TOBACCO DEPENDENCE**

Drug	Preparations	Usual, Daily Adult Maintenance Dose	Common Adverse Effects <sup>A</sup>	FDA Approved	PHS Recommended
<b>COMBINATION MEDICATIONS</b>					
3 or more medications <sup>2,107-109,192,199,230</sup>	See below under individual medications.	Dosages are the same per individual medication; see sections below.	No different than for individual medications, but such combinations usually provide better control of nicotine withdrawal symptoms, better tobacco-dependence treatment, and higher stop-smoking rates	Not Addressed	Not Addressed
Bupropion SR + a nicotine transdermal <sup>1,2</sup>	150-mg Bupropion SR + 15-mg nicotine/16 hr OR 21-mg nicotine/24 hr	Dosages are the same per individual medication; see above sections.	Bizarre dreams; insomnia; nausea; patch-site erythema or pruritus	Yes	Yes
Bupropion SR + a nicotine rescue medication <sup>1,2</sup>	See below under individual medications.	Dosages are the same per individual medication; see above sections.	Insomnia; xerostomia; side effects specific to the specific nicotine medication	Not Addressed	Yes
Nicotine transdermal + nicotine nasal spray <sup>1,2</sup>	See below under individual medications.	Dosages are the same per individual medication; see above sections.	Nasal irritation; pruritus and skin irritation at the patch site <sup>B</sup>	Not Addressed	Yes
Nicotine transdermal + nicotine oral inhaler <sup>1,2</sup>	See below under individual medications.	Dosages are the same per individual medication; see above sections.	Throat irritation and pruritus at the patch site <sup>B</sup>	Not Addressed	Yes
Nicotine transdermal + nicotine polacrilex gum <sup>1,2</sup>	See below under individual medications.	Dosages are the same per individual medication; see above sections.	Indigestion, nausea, flatulence, unpleasant taste, hiccups, sore mouth, sore throat, sore jaw; pruritus and skin irritation at the patch site <sup>B</sup>	Not Addressed	Yes
Nicotine transdermal + nicotine lozenge <sup>194</sup>	See below under individual medications.	Dosages are the same per individual medication; see above sections.	Indigestion, nausea, flatulence, unpleasant taste, hiccups, sore mouth, sore throat, sore jaw; pruritus and skin irritation at the patch site <sup>B</sup>	Not Addressed	Not Addressed
Varenicline + bupropion SR <sup>192,193</sup>	See below under individual medications.	Dosages are the same per individual medication; see above sections.	No serious side effects reported. No seizures or suicidal behavior reported.	Not Addressed	Not Addressed
<b>FIRST-LINE CONTROLLER MEDICATIONS</b>					
<b>α<sub>4</sub>-β<sub>2</sub> NICOTINIC RECEPTOR PARTIAL AGONISTS</b>					
Varenicline ( <i>Chantix</i> )	0.5- & 1.0-mg tablet	1 mg 2x/day	Nausea, vomiting, constipation, flatulence, abnormal dreams, headache, xerostomia, weight gain. See Note #2, below.	Yes	Yes
<b>DOPAMINERGIC-NORADRENERGIC RE-UPTAKE INHIBITORS</b>					
Bupropion HCl (immediate acting)	75- & 100-mg tablet	100 mg 3x/day	Insomnia, xerostomia, headache, all generally mild and transient. Seizure incidence in long-term, anti-depression, safety-surveillance studies was 0.4% for the immediate-acting formulation and 0.1% for the sustained-release formulation. Seizure has not occurred, even with daily usage of 300 mg up to 1 year, in the > 2,500 study participants double-blindly randomized to an active bupropion SR formulation in tobacco-dependence treatment trials. Exceeding rare incidence rate of Stevens-Johnson Syndrome, hyper-anxiety state, and elevated hepatic enzymes. <b>General Caution:</b> Bupropion should not be administered in conjunction with a MAO inhibitor. See Note #3, below.	Not Addressed	Yes
Bupropion SR ( <i>Wellbutrin SR, Zyban</i> )	100-, 150-, & 200-mg sustained-release tablet	150 mg 2x/day		Not Addressed	Yes ( <i>Wellbutrin SR</i> ); Yes ( <i>Zyban</i> )
Bupropion XL ( <i>Wellbutrin XL</i> )	150- & 300-mg extended-release tablet	300 mg 1x/day in AM		Not Addressed	Not Stated
<b>NICOTINIC-RECEPTOR AGONISTS</b>					
Nicotine transdermal ( <i>NicoDerm CQ, Nicotrol</i> ) <sup>C,D</sup>	7, 14, & 21 mg/24 hr 5, 10, & 15 mg/16 hr	1 patch/day <sup>F</sup>	Pruritus at the patch site; insomnia; bizarre dreams; ~2.5% incidence of cutaneous hypersensitivity reaction caused by 24-hour wear cycle. Neither nicotine overdose nor cardiac events increase with use of transdermal nicotine in conjunction with cigarette smoking beyond that seen with cigarette smoking, alone.	Yes	Yes

## FIRST-LINE RELIEVER (RESCUE) MEDICATIONS

### NICOTINIC-RECEPTOR AGONISTS

Nicotine-β-cyclodextrin sublingual tablet <sup>F</sup>	2-mg tablet	2 mg 8–16x/day	Hiccups; nausea; dyspepsia	Not Available in United States	Not Stated
Nicotine nasal spray ( <i>Nicotrol NS</i> )	0.5 mg/spray; 1 dose = 2 sprays	1 dose 8–40x/day	Minor burning and stinging of the nasal mucosa; minor throat irritation; cough; sneeze; increased lacrimation; rhinorrhea; nausea. (NB: All these side effects generally last only a few seconds.)	Yes	Yes
Nicotine oral inhaler ( <i>Nicotrol Inhaler</i> )	4-mg cartridge	4–16 cartridges/day	Minor mouth irritation; throat irritation; cough	Yes	Yes
Nicotine polacrilex gum ( <i>Nicorette</i> ) <sup>D</sup>	2 & 4 mg/piece	8–24 pieces/day	Side effects generally result from improper chewing technique and include indigestion, nausea, flatulence, unpleasant taste, hiccups, sore mouth, sore throat, sore jaw	Yes	Yes
Nicotine polacrilex lozenge ( <i>Commit</i> ) <sup>D</sup>	2 & 4 mg/lozenge	8–20 lozenges/day	Heartburn, hiccup, and nausea, due to swallowed nicotine; headache	Yes	Yes

## SECOND-LINE CONTROLLER MEDICATIONS (Options if First-Line Medications Not Tolerated)

### ALPHA<sub>2</sub> ADRENERGIC AGONISTS

Clonidine HCl ( <i>Catapres</i> ) <sup>G</sup>	0.1- & 0.2-mg tablet	0.2 or 0.3 mg 2x/day	From tobacco-dependence trials: <u>Dose-related</u> – Decreased heart rate; decreased systolic blood pressure; decreased diastolic blood pressure; xerostomia; drowsiness; spacey feeling; dizziness; postural hypotension. <u>Not necessarily dose-related</u> – Nausea; vomiting. <u>With transdermal only</u> – Pruritus; erythema; edema; vesicles; blisters, all at the patch application site, only.	No	Yes
Clonidine transdermal ( <i>Catapres-TTS</i> ) <sup>G</sup>	0.1, 0.2, & 0.3 mg/day/1-week patch	1 patch/week delivering 0.2–0.3 mg/day		No	Yes

### NORADRENERGIC-SEROTONERGIC RE-UPTAKE INHIBITORS

Nortriptyline HCl ( <i>Aventyl, Pamelor</i> )	25- & 75-mg capsule	25 mg 3–4x/day	From tobacco-dependence trials: constipation; xerostomia; lightheadedness; tremor; blurred vision. From anti-depression trials: rash; weight gain; xerostomia; lightheadedness; tremor; constipation, blurred vision; impotence; decreased libido; urinary retention; tachycardia; pedal edema; chest pain; shortness of breath; headache; agitation; nausea; vomiting; dizziness; insomnia; hyperhidrosis. <b>General Caution:</b> Nortriptyline should not be administered in conjunction with a MAO inhibitor.	Not Addressed	Yes
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### UNCERTAIN PHARMACOLOGIC CLASS

Topiramate ( <i>Topamax</i> )	25-, 50-, 100-, & 200-mg tablets	50 mg 2x/day	From migraine trials: dizziness, metabolic acidosis, somnolence, fatigue, nervousness, memory difficulty, ataxia, speech disturbance, nystagmus, anorexia, nausea, depression, confusion, diplopia, mood disturbances, insomnia, and anxiety, among others.	No	No
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#### Notes:

1. The ACCP Tool Kit Committee is aware of the existence of the so-called electronic cigarette, but does not recommend it at this time because of the complete absence of any data or scientific information – toxicologic, safety, or efficacy.

2. On July 1, 2009 the FDA issued a “Black-Box Warning” to the varenicline label because of the possibility of, particularly, treatment-emergent suicidality. In published data, the FDA reported 37 individuals who demonstrated suicidal behavior, 19 of whom killed themselves while taking varenicline.<sup>11</sup> These data were not presented in a normalized fashion, as a function of total varenicline users. There have been 5.5 million varenicline users since product launch on 8/1/06 (Data provided by Pfizer, Inc.). This produces an annual suicide completion rate of 0.49 suicides/100,000 varenicline users/year. To put this in perspective, based on CDC data, the annual suicide rate of the U.S. population, overall, is 11.01 suicides/100,000 people in the U.S. population.<sup>12</sup> The suicide rate of varenicline users is significantly *less* than that of the U.S. population at large (P<0.0001). Additionally, the FDA-reported death rate of varenicline users is also significantly *lower* than the death rate caused each year by tobacco-caused diseases: 0.49 suicide deaths/100,000 varenicline users/year vs. 1,031.2 tobacco-caused deaths/100,000 cigarette smokers/year (P<0.0001). The ACCP Tool Kit Committee does not see an association between varenicline and suicide, much less a causal link and suggests that the FDA re-evaluate the recent Black Box Warning in light of this broader perspective. (NB: Data from the United Kingdom also fail to show such an association or causal link.<sup>13</sup>) (See also [§1.7, Pharmacologic Treatment, sub-§ “Depression, Suicidality & Tobacco Dependence”](#) & sub-§ “Depression, Suicide, Cigarette Use, & Pharmacotherapy” for additional, pertinent information.)

3. On July 1, 2009 the FDA also issued a “Black-Box Warning” to the bupropion label because of the possibility of, particularly, treatment-emergent suicidality. In published data, the FDA reported 29 individuals who demonstrated suicidal behavior since bupropion launch for tobacco-dependence treatment in September 1997, 12 years ago.<sup>11</sup> Of the 29 bupropion users who made suicide attempts, 10 killed themselves while taking bupropion.<sup>11</sup> Were the ACCP Tool Kit Committee to have the time to determine the total number of bupropion users for tobacco-dependence treatment, only, from 9/1997 through 2009, that total would certainly be larger than the varenicline total, producing an even smaller suicide rate per year for bupropion than for varenicline. (See Note #2, above and [§1.7, Pharmacologic Treatment, sub-§ “Depression, Suicidality & Tobacco Dependence”](#) & sub-§ “Depression, Suicide, Cigarette Use, & Pharmacotherapy”.)

<sup>A</sup> Adverse effects listed are those reported in tobacco-dependence treatment trials, unless otherwise indicated, since some side effects frequently associated with a given drug (e.g., impotence with nortriptyline) did not occur significantly more often for active drug than placebo drug condition.

<sup>B</sup> No additive or synergistic side effects; side effects similar in incidence and severity to those seen with individual medications.

<sup>C</sup> See specific label for details regarding dose up-titration.

<sup>D</sup> Available without prescription, over-the-counter (OTC)

<sup>E</sup> Wearing the 24-hr patch for 16 hrs yields the same dosage as a 16-hr patch, 15-mg nicotine.

<sup>F</sup> Available in some European countries.

<sup>G</sup> Efficacy data are much less convincing for clonidine than for any of the First-Line medications or for nortriptyline.

TABLE 2: INEFFECTIVE MEDICATIONS FOR TOBACCO DEPENDENCE

Drug	FDA Approved	PHS Recommended
<b>ANXIOLYTICS/BENZODIAZEPINES/BETA-BLOCKERS</b>		
Buspirone (anxiolytic; <i>BuSpar</i> )	No	No
Diazepam (anxiolytic; <i>Valium</i> )	No	No
Propranolol (beta-blocker; <i>Inderal</i> )	No	No
<b>NICOTINIC RECEPTOR ANTAGONISTS</b>		
Mecamylamine ( <i>Inversine</i> )	No	No
<b>OPIOID PARTIAL AGONISTS/ANTAGONISTS</b>		
Buprenorphine (opioid partial agonist; <i>Buprenex</i> )	No	No
Naltrexone ( <i>Revia, Vivitrol</i> )	No	No
<b>SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs)</b>		
Fluoxetine ( <i>Prozac</i> )	No	No
Paroxetine ( <i>Paxil</i> )	No	No
Sertraline ( <i>Zoloft</i> )	No	No
Venlafaxine ( <i>Effexor</i> )	No	No
<b>OTHER</b>		
Lobeline (Nicotine Analog)	No	No
Silver Acetate	No	No

All of the above medications have been studied in clinical trials and found to be ineffective.<sup>8</sup>

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# Tobacco Dependence Treatment ToolKit

## Smoking and Tobacco-Dependence Treatment for Pregnant Women and Women of Childbearing Age

### Introduction

Smoking is one of the most important modifiable causes of poor pregnancy outcomes in the United States.<sup>247</sup> Women in the childbearing years should be informed of the risks to their babies and to themselves of smoking cigarettes. Ideally, women who smoke should be treated effectively for tobacco dependence BEFORE they become pregnant; however, stopping smoking during pregnancy can still improve fetal outcomes.<sup>248</sup>

### Risks of Maternal Smoking

#### Maternal Smoking and Fertility

Infertility is more common in women who smoke. Stopping smoking improves fertility.<sup>1, 248, 249</sup>

#### Risk for Complications of Pregnancy

Smoking during pregnancy increases rates of complications that can threaten the health of the mother and fetus, including ectopic pregnancy, placental abruption, placenta previa, premature rupture of membranes, bleeding, and maternal death.<sup>248</sup>

#### Risks to the Fetus

Nicotine, carbon monoxide, lead, and other toxins in tobacco smoke are rapidly absorbed into the mother's arterial bloodstream at concentrations about 10-fold higher than measured levels in maternal venous blood.<sup>86, 250</sup> Peak arterial nicotine levels after one cigarette puff will be in the range of 100- to 200-ng nicotine/mL arterial blood. Steady state, mixed venous nicotine concentration will only reach a maximum of 10- to 20-ng nicotine/mL blood. However, it is the contents of the maternal arterial (not venous) blood that rapidly cross the placenta, entering the developing fetus at maternal arterial concentrations.<sup>248, 249</sup> Fetal peak nicotine level, from maternal cigarette smoking, will be equivalent to the mother's peak arterial nicotine level.<sup>86, 250</sup>

Maternal smoking increases risk for preterm delivery, fetal demise, and low birth weight (for gestational age). These risks are prevented by stopping smoking prior to conception, and reduced by stopping smoking during pregnancy.<sup>249</sup>

#### Risks to the Infant and Child

Maternal smoking increases risk for Sudden Infant Death Syndrome (SIDS).<sup>248</sup> It also increases an infant's and child's risk for ear infections, acute respiratory infections, acute wheezing illness, and more severe asthma. Prenatal and postnatal tobacco smoke exposure increases risk for childhood cancers, including leukemia, lymphomas, and brain tumors.<sup>251</sup>

Breast-feeding has important health benefits for the newborn infant. Maternal smoking is associated with decreased breast milk production and decreased duration of breast-feeding.<sup>249</sup> Most tobacco-smoke toxins enter breast milk.

### Treatment of Tobacco Dependence During Pregnancy

Stopping smoking during pregnancy decreases all tobacco-caused risks to the baby and mother.

**Behavioral counseling** is the preferred treatment for pregnant mothers who smoke. Brief counseling interventions along with individually tailored self-help materials can increase quit rates over no intervention at all.<sup>252-254</sup> Individual counseling and group counseling programs are more effective than less intensive support.<sup>255-258</sup>

Many women are not able to stop smoking with behavioral counseling alone, because of intolerable nicotine withdrawal symptoms. Therefore, the clinician must monitor the patient closely, encourage her to contact the office with any questions or problems, and schedule frequent follow-up visits. Behavioral interventions have a higher risk of failure with higher levels of nicotine dependence.<sup>54, 55, 59, 149, 150, 235</sup> Escalation of therapy should be considered, including use of pharmacotherapy, if behavioral counseling fails or if there is relapse.

Although research is limited, tobacco-dependence **pharmacotherapy** presents a lower risk to the fetus than the significant harm caused by the mother's continued smoking.<sup>1, 259</sup> The physician needs to balance the risk (to both mother and fetus) of pharmacotherapy against the substantial risk of continued smoking. Refer to [Table 1](#) for a quick reference guide on tobacco-dependence treatment for pregnant women.

**TABLE 1: Tobacco-Dependence Treatment for Pregnant Women**

"Smoking is one of the most important modifiable causes of poor pregnancy outcomes in the United States"<sup>247</sup>

Treatment	Pros	Cons	FDA pregnancy category	When to use it
<b>Behavioral Counseling</b>	• No added medication.	• Not as effective as counseling + medication.		<b>Always; first choice.</b> If insufficient alone, consider risk vs. benefit of combination

				with one or more medications (see entries below).
<b>Bupropion</b>	<ul style="list-style-type: none"> <li>• More effective than counseling alone.</li> <li>• No major teratogenic effect.</li> </ul>	<ul style="list-style-type: none"> <li>• Cannot use if mother has a seizure disorder.</li> <li>• May increase risk for spontaneous abortion.</li> <li>• No long term follow-up studies available.</li> </ul>	C	<b>Second choice.</b> If counseling alone is insufficient, based on history and/or level of nicotine dependence.
<b>Nicotine Medications (e.g., Gum, Lozenge, Inhaler, Nasal Spray, Patch)</b>	<ul style="list-style-type: none"> <li>• No added substance; the fetus is already being exposed to nicotine.</li> <li>• Reduces fetal nicotine exposure by ~90%.</li> </ul>	<ul style="list-style-type: none"> <li>• Does not eliminate nicotine exposure for the fetus.</li> </ul>	D	<b>Third choice.</b> If counseling alone is insufficient, based on history and/or level of nicotine dependence AND if bupropion is not desired, not tolerated, or contraindicated. Advise mother to remove nicotine patch at bedtime to further reduce exposure of fetus.
<b>Combination Bupropion + Nicotine Medication(s)</b>	<ul style="list-style-type: none"> <li>• More effective than either medication alone.</li> </ul>	<ul style="list-style-type: none"> <li>• Exposes fetus to additional medication.</li> </ul>	D	<b>Fourth choice.</b> If single medication is insufficient. Combine Controller (bupropion) and Nicotine Rescue Medications for effective elimination of withdrawal symptoms.
<b>Varenicline</b>	<ul style="list-style-type: none"> <li>• Has been shown to be highly effective in studies of non-pregnant women who smoke.</li> </ul>	<ul style="list-style-type: none"> <li>• No data on safety in pregnancy.</li> </ul>	C	<b>Fourth choice.</b> If counseling alone is insufficient AND has failed or cannot use bupropion AND mother has a high level of nicotine dependence AND if potential benefits outweigh potential risks.
<b>Continued Tobacco Smoking</b>	None	<ul style="list-style-type: none"> <li>• Is the most dangerous way to deliver nicotine to mother and fetus.</li> <li>• Exposes mother and fetus to multiple toxins and teratogens.</li> <li>• Definite and well-documented adverse effects on mother and fetus.</li> </ul>	X*	* Currently, the FDA does not regulate or classify tobacco products; however, if it did, continued active tobacco smoking would meet criteria for Category X. (Studies in animals or human beings have demonstrated fetal abnormalities or risk which clearly outweigh any possible benefit.) Drugs in category X should NOT be taken by pregnant women for any reason.

**Bupropion** is often used as the first-line pharmacotherapy for treating tobacco dependence in pregnancy.<sup>1, 113, 167, 260</sup> Bupropion is classified as pregnancy category C (risk cannot be ruled out). A small observational study found bupropion to be effective for stopping smoking during pregnancy.<sup>261</sup> Human studies with bupropion have not found a link to major congenital malformations;<sup>262</sup> however, the risk of spontaneous abortions may be increased.<sup>263</sup> The major safety issue with bupropion is risk of seizures; it should not be prescribed to patients with a history of seizures.

**Nicotine** is classified as pregnancy category D (positive evidence of risk, potential benefits may outweigh the risk). Fetal nicotine toxicity and teratogenicity have been extensively studied, particularly in a variety of animal models, far more than bupropion or varenicline. Nicotine causes fetal malformation, spontaneous abortion, and premature birth.<sup>71</sup> However, nicotine's fetal toxicity is strictly dose-related: the greater the total nicotine or the higher the peak nicotine levels to which the fetus is exposed, the greater the fetal risk.<sup>71</sup>

Mothers who are moderately to heavily nicotine dependent are already delivering substantial amounts of nicotine to their unborn babies. Appropriately used nicotine medications, even in combination, deliver less nicotine than continued smoking<sup>113, 259</sup> and do not deliver any of the additional toxins contained in tobacco smoke, such as carbon monoxide and lead. To minimize fetal exposure when the nicotine patch is used, the patch can be removed at bedtime.

**Varenicline** is considered pregnancy category C (risk cannot be ruled out). It has not been studied in pregnancy and its safety profile in pregnancy is not

known.<sup>1, 264</sup> Varenicline should only be used if the other medication options fail.<sup>1, 113, 264</sup>

### Post-Partum Treatment

Minimal amounts of nicotine are excreted in breast milk when the mother is using nicotine medication(s) to stop smoking or maintain nonsmoking status.<sup>259</sup> Nicotine medications can be used by breast-feeding mothers as a better alternative to smoking.

After delivery of the baby, there is a substantial risk of relapse in the tobacco-dependent mother. It is important that any relapse or potential for relapse be recognized and treated promptly, as maternal smoking exposes the infant and child to massive amounts of toxins, both from breast milk and secondhand smoke exposure.<sup>265, 266</sup> Anticipatory guidance and close follow-up should be provided so that relapse can be prevented, or at least promptly recognized and treated.

### Conclusion

Because nicotine dependence is both physiological and psychological, many women of childbearing age continue to smoke, despite increased evidence and education about the risks of smoking during pregnancy. Effectively treating tobacco dependence in women of childbearing age, including during pregnancy and while breast-feeding, remains a paramount objective for healthcare providers.

[< Quick Reference Guide to Pharmacotherapy](#)      [up](#)      [The Role of the Pediatric Health-Care Provider in Tobacco-Dependence Treatment and Secondhand Smoke Exposure Reduction >](#)



# Tobacco Dependence Treatment ToolKit

## The Role of the Pediatric Health-Care Provider in Tobacco-Dependence Treatment and Secondhand Smoke Exposure Reduction

### Tobacco smoke exposure is an important health problem for children

The United States Surgeon General's report on the Health Consequences of Involuntary Exposure to Tobacco Smoke<sup>251</sup> documents the following:

1. Tobacco smoke exposure causes premature death and disease in children and adults who do not smoke.
2. Children exposed to secondhand smoke are at an increased risk for sudden infant death syndrome (SIDS), acute respiratory infections, ear problems, and more severe asthma.
3. The evidence suggests a relationship between prenatal and postnatal secondhand smoke exposure and childhood cancers, including leukemia, lymphomas, and brain tumors.
4. Smoking by parents causes respiratory symptoms and slows lung growth in their children.
5. There is no risk-free level of exposure to secondhand smoke.
6. A total ban on indoor smoking is the only way to eliminate secondhand smoke exposure in indoor environments. Exposure of nonsmokers to secondhand smoke cannot be controlled by air cleaning or mechanical air exchange

### Opportunities of the Pediatric Health Care Provider

Tobacco dependence starts in childhood. Most individuals who become tobacco addicted do so before high school graduation.<sup>267</sup> Pediatric health care providers have an important role in both preventing and treating tobacco dependence in their patients.<sup>268</sup>

Most parents who are tobacco dependent would accept treatment or referral from their child's health care provider.<sup>269</sup> Many young adult parents who smoke present more often to a pediatric health care provider (for care of their children) than to an internist or family physician for their own care. This situation provides a unique opportunity for intervention to address the tobacco dependence of the parents in the context of their child's illness. Routinely offering tobacco-dependence treatment to parents within the child health care setting will confer profound benefits to children and families.<sup>270</sup>

The American Academy of Pediatrics advises pediatricians to inquire about their patients' active and secondhand smoke exposure and recommends, "**Pediatric health care providers should be knowledgeable about tobacco-dependence treatment and ROUTINELY offer help and referral to those who are tobacco dependent**".<sup>271</sup>

Tobacco dependence and secondhand tobacco smoke exposure are among the most important preventable causes of morbidity and premature mortality. Pediatric health care providers need to seize available opportunities to 1) reduce secondhand smoke exposure of children, 2) reduce initiation of active tobacco smoking in children and adolescents, and 3) assist children and their parents who are active tobacco users to navigate the path to stopping smoking.

### Identifying and Reducing Children's Secondhand Smoke Exposure

Pediatric health care practitioners should routinely assess both their patients' active smoking and secondhand smoke exposure. (see [Assessment Specifics](#))

A child may be exposed to multiple sources of tobacco smoke both inside and outside of the primary home. Tobacco smoke exposure from a childcare provider can be as great as that from a parent.<sup>266</sup> In assessing a child's secondhand smoke exposure, it is important to examine all potential sources of exposure at all locations where the child regularly spends time.

Parental perception of an exposed child's level of tobacco smoke exposure is commonly inaccurate.<sup>272</sup> Even with a "smoke-free home", a parent may smoke outside, yet be close to a door or window so that the smoke re-enters the home. A child may be near the parent when they are smoking "outside". Lapses in keeping the home smoke free may occur during inclement weather, when the child is away from home, or when traveling.

### Biomarkers of tobacco smoke exposure:

Urine cotinine measurement reflects the child's previous 3 to 4 days of tobacco smoke exposure.<sup>273 274</sup> Urine cotinine measurement may help the physician address parental misperception about the level of a child's recent tobacco smoke exposure. When using a urine cotinine assay to assess for secondhand smoke exposure, it is important that the assay used detects cotinine levels  $\geq 5$  ng/ml. Some commercially available assays detect cotinine levels only in the range associated with active smoking ( $\geq 100$  ng/ml).

### Treating Tobacco Dependence in Pediatric Patients and their Parents

Pediatric health care providers should become skilled in treatment of tobacco dependence and seize the opportunity presented to them when meeting with their tobacco dependent patients and tobacco dependent parents of their patients.

Most parents who smoke are willing to consider stopping smoking. Most parents who smoke would accept referral from their child's physician to a telephone tobacco-dependence treatment program or Quit Line (see [General & Referral Resources](#)). The vast majority of parents who smoke and who are willing to consider use of medication to treat tobacco dependence would accept that recommendation and/or prescription from their child's doctor. The direct treatment of tobacco

dependence by the pediatric health care provider presents a unique opportunity to save the lives of tobacco-dependent adolescents and adults. Many young adults may not have their own primary provider and many may lack health insurance for themselves. For those parents, their child's doctor may be their only access to physician care and treatment of tobacco dependence.

The ARMR model discussed in section 1.6 applies to tobacco treatment in the pediatric health care setting. Anticipatory guidance is an important part of pediatric practice, and can help to prevent tobacco smoking in children and adolescents. Pediatric health care providers may wish to consider an additional "A" for anticipatory guidance.

#### **AARMR model for pediatrics:**

##### **Anticipate**

Give age appropriate messages on the dangers of tobacco smoking  
Ask the child to make a commitment to being a lifelong non-smoker

##### **Assess (in the child or parents, as appropriate)**

Level of tobacco-smoke exposure  
Level of tobacco dependence  
Social and psychological factors (role of smoking in their life).  
Patterns of smoking,  
Triggers of tobacco smoking  
Coping skills

##### **Recommend**

Appropriate pharmacotherapy  
Coping strategies  
Develop written tobacco-dependence treatment action plan. (see [Freedom From Tobacco Action Plan](#))  
Set Target Stop Date

##### **Monitor**

Treatment plan side effects  
Frequent follow-up is often needed

##### **Revise**

Treatment plan to improve effectiveness  
Treatment plan to reduce side effects  
How is the plan working, what changes are needed

The trans-theoretical model of behavior change assists the health care provider to offer messages tailored to the patient or parent's stage of change, thereby leading to more productive interactions. This model postulates five stages: pre-contemplation, contemplation, preparation, action-implementation, and maintenance.

To help patients and their families negotiate these stages, discussion should be stage-matched. Discovering why a patient is stuck at a particular stage may provide a window for progress to the next stage. See "[The Stages of Behavioral Change](#)" for more information.

#### **Parent is not ready to quit:**

If the parent or caregiver is not ready to consider stopping smoking at this time, discussion can focus on other ways to reduce the child's exposure. Helpful behavior changes include:

1. Make the home and car smoke free
  - a. Ask parents to make a no smoking rule for the home and car.
  - b. Limit smoking to 20 feet or more from a door or open window.
  - c. Ensure that the child is not near the tobacco-dependent person when s/he is smoking.
2. Keep the child away from places where tobacco smoking occurs.
3. Provide referral for quit smoking resources (such as 1 800 QUIT NOW) for when they are ready.

#### **Unique features in the treatment of tobacco dependence in adolescence**

Most adolescents who smoke consider themselves to be addicted to nicotine, recall withdrawal symptoms during previous attempts to stop smoking, and find it difficult to stop smoking. They often continue smoking well into adulthood.<sup>280</sup> Effective intervention with this group can dramatically attenuate the risk of tobacco-related morbidity and mortality. The teenage years present a critical window of opportunity for tobacco-dependence treatment to prevent decades of continued tobacco use and the severe morbidity and mortality that it causes. (see [Management of Child/Adolescent Tobacco Use](#))

Cigarette smoking is common among children; 23% of high school students and 8% of middle school students are current cigarette smokers. Non-cigarette tobacco products are frequently used. In national surveys, 13% of high school students and 5% of middle school students smoke cigars; 3% of high school students and 2% of middle school students smoke bidis and/or kreteks (flavored tobacco products); 10% of boys in high school and 4% of boys in middle school use

spit tobacco.<sup>281</sup>

In contrast to the situation with adults, there has been a relative dearth of research into effective tobacco-dependence treatment programs for youth.<sup>282</sup> Motivation enhanced, cognitive-behavioral, and social influence theory programs have shown modest benefit, even among tobacco-dependent adolescents. The most beneficial programs were school or classroom based and had multiple sessions (5 or more). The effect appears to be sustained over time.<sup>283</sup> More intensive tobacco-dependence treatment programs are more effective than brief interventions; however, brief interventions can show benefit, particularly with less tobacco-dependent adolescents.<sup>284</sup> A single randomized placebo controlled clinical trial demonstrated superior cessation rates with nicotine patch therapy compared to placebo when added to cognitive behavioral therapy among tobacco dependent adolescents who were motivated to quit.<sup>285</sup> Given the demonstrated effectiveness and safety of first line tobacco-dependence treatments in adults and the grave harm of continued tobacco dependence, a trial of medically supervised pharmacotherapy plus ongoing follow-up is warranted in tobacco-dependent adolescents who are interested in stopping smoking.

Nicotine dependence in adolescents can be assessed by the use of the Fagerström questionnaire, modified for adolescents.<sup>286, 287</sup> (see [Modified Fagerstrom Tolerance Questionnaire \(mFTQ\) for Adolescents](#)). Autonomy over smoking behavior can also be assessed by [The Hooked on Nicotine Checklist](#)<sup>288</sup> (HONC). Many youths become hooked before they even consider themselves to be smokers, because they don't smoke every day.

Level of nicotine dependence and history of experience with prior quit attempts can guide intensity of initial [pharmacotherapy](#). Frequent follow-up, especially in the days to weeks surrounding the target stop date, is important to successfully facilitate smoking cessation in adolescents.

Although nicotine addiction is common, it does not drive the smoking behavior of all adolescents. Relationships, activities, emotions, and social ramifications may drive intermittent smoking. (see [Intermittent, Non-Daily, Social Smoking](#)). For these patients, adolescent-specific school- or community-based programs that teach usable social, behavioral, and coping skills are helpful.<sup>289</sup> Intervention at this point is important, intermittent tobacco use in adolescents frequently progresses to regular tobacco use and long-term tobacco dependence.<sup>290</sup>

Once willingness to stop smoking is identified, develop a mutually agreed upon treatment plan. Building a strong partnership between patient and physician facilitates development of a realistic plan that the adolescent is interested in, invested in, and willing to implement.<sup>291</sup>

#### **Developing and implementing a mutually agreed upon plan for stopping smoking in the medical office setting (adapted from Adelman WP, 2006)<sup>291</sup>**

1. Determine willingness to stop smoking
2. Identify patterns of smoking, cigarettes smoked that may be most easily discarded, and triggers of tobacco smoking that may be avoided.
  - a. If patient smokes with friends before school or at parties, consider options to socialize without tobacco.
  - b. If patient smokes to manage boredom or anxiety, consider replacement activities where smoking is difficult, teach relaxation techniques, and encourage exercise.
3. Determine if pharmacotherapy for tobacco dependence is indicated and appropriate. If so, instruct on its appropriate use.
4. Teach coping skills.
5. Set a Target Stop Date. Develop a plan to inform friends and relatives and recruit their help. Give written instructions; consider the Freedom From Smoking Action Plan in this Tool Kit. (see [Freedom From Tobacco Action Plan](#))
6. Frequent follow-up, especially in the days to weeks surrounding the Target Stop Date, is important to successful facilitation of smoking cessation.

#### **Concerns about liability for treatment of tobacco dependence in a patient, parent or guardian by a pediatric health care provider**

Compared to nicotine medications cigarettes deliver higher levels of nicotine. Furthermore continued tobacco use causes severe illness and premature death. Nicotine medications are effective and not associated with serious adverse effects in adults with cardiovascular disease<sup>292</sup>, COPD<sup>293</sup>, the elderly<sup>294</sup>, and concurrent smokers<sup>295</sup>. According to a World Health Organization expert consensus report, "Virtually all potential users of nicotine replacement therapy are already consuming substantial quantities of the drug nicotine through its most addictive and toxic delivery system-tobacco smoke. Use of nicotine replacement therapy by a smoker can improve the chance that they will quit smoking tobacco, but will not introduce new risks not already faced by smokers and will greatly reduce or eliminate many smoking related risks."<sup>296</sup>

If bupropion is used, check for relative contraindications: seizure disorder, head trauma, heavy alcohol abuse, and anorexia/bulimia. (see [Developing a Medication Treatment Plan](#))

#### **Documentation of tobacco-dependence treatment offered to parents:**

Documentation can follow a similar model to other situations where the pediatrician prescribes for a parent of close family member due to a child's illness, such as when the child has meningococemia, pertussis, or scabies. Although specific requirements may vary by state, it is prudent to document the identity of the individual being prescribed or recommended the medication, the presence of indications for treatment (i.e., parental tobacco dependence adversely effecting the child's health), the absence of contraindications to treatment (see [Developing a Medication Treatment Plan](#)), and counseling about risks, benefits, and potential side effects of the medication. Documentation about the parent's treatment ideally would be placed in the parent's medical record; however if that is not possible it is acceptable to include the documentation of the parent's treatment in their child's medical record (as would be done if the child had meningococemia, pertussis, or scabies), with careful notation that this section applies to assessment and treatment offered to the parent.

#### **Health Insurance Concerns**

Pediatric health care providers can use the same diagnosis codes for tobacco-dependence treatment services for children or their parents as adult health care providers. For a discussion on coding and billing for tobacco-dependence treatment see [Coding and Reimbursement](#) section.

For pediatric practices that are not ready to offer tobacco dependence treatment assessment, assistance, and referral should be offered. The CEASE (Clinical Effort Against Secondhand Smoke Exposure) program is an example of a program to assess, assist, and refer treatment of parental tobacco dependence. As the CEASE Program points out, "36% of all children in the United States live with a household member who smokes. Children who live with a smoking parent are more likely to start smoking themselves. Secondhand tobacco smoke lingers long after the cigarette [is] extinguished, coats every surface inside the home with toxins, [and] kills three times more children than all childhood cancers combined." The CEASE program can be easily implemented in a busy pediatrician's office. CEASE program description and materials can be found at <http://www2.massgeneral.org/ceasetobacco>.

If a pediatrician does not wish to prescribe tobacco-dependence treatment medications, counseling about available medications and referral to cessation resources (including state or national quitlines such as 1 800 QUIT NOW) can empower effective action.

### Community based efforts and public policy

Involuntary tobacco smoke exposure is an important public health problem for children. The individual actions of a child's parents and care providers may reduce that child's tobacco smoke exposure, but elimination of a child's involuntary tobacco smoke exposure often requires community level interventions. Pediatric health care providers have a responsibility to promote tobacco-free policies in their offices and hospital campuses; to work with school boards to ban tobacco smoking on school property; and to urge state and local governments (if they have not already done so) to prohibit smoking in child care centers, restaurants, and other public places.<sup>297</sup>

The media and entertainment industries play an important role in promoting tobacco use among children and adolescents. The odds of becoming a tobacco user are more than doubled by exposure to marketing and media. Whether the outcome is initiation or increased tobacco use, the relationship between media and smoking behavior is robust, observed across time in different countries, in cross-sectional and prospective designs using a variety of measures of exposure.<sup>298</sup> A dose-response effect has been observed between exposure to smoking in movies and adolescent smoking initiation.<sup>299</sup> Smoking is common in popular movies viewed by children and adolescents. Amending the movie rating system to rate any movie depicting smoking as "R" would reduce the exposure of children and adolescents.

#### Public policy initiatives needed to decrease the likelihood of adolescents becoming tobacco addicted

1. Ban advertising for tobacco products
2. Reduce tobacco use and product placements in films, television, and videos
  - a. Require an "R" rating of films that depict tobacco use
3. Ban tobacco product sales from vending machines
4. Increase the excise tax on tobacco products
5. Support the development of anti-tobacco advertising
6. Improve enforcement of laws prohibiting youth from purchasing tobacco products
7. Ban smoking in indoor public places and outdoor public events

Greater availability of tobacco-dependence treatment programs for adolescents is needed. A recent national survey of tobacco-dependence treatment programs for youth found that many counties had none, with low socio-economic status counties disproportionately underserved (53 % vs. 31%). Most available programs were multi-session school-based group programs and did not involve use of medication. The majority of programs report that obtaining sufficient operating funds is challenging.<sup>300</sup>

As advocates for and guardians of children's respiratory health, pediatric health care providers, particularly pediatric pulmonologists, should actively promote legislation and regulation to protect children and adolescents from tobacco addictions and involuntary smoke exposure, as well as educate the public on the dangers of both active and secondhand smoking.<sup>271</sup>

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# Tobacco Dependence Treatment Toolkit

## The Stages of Behavior Change for Stopping Smoking

### Use of a Stages of Change Model

The trans-theoretical model of behavior change assists the health care provider by offering appropriate messages to facilitate smoking cessation and smoke exposure reduction.<sup>278, 279</sup> This model postulates five stages: pre-contemplation, contemplation, preparation, action-implementation, and maintenance.

To help patients and their families negotiate these stages, discussion should be stage-matched. Discovering why a patient is stuck at a particular stage may provide a window for progress to the next stage. Consideration of stage of change is consistent with the [ARMR model](#) (assess, recommend, monitor, revise) ([see Tobacco-Dependence Treatment Process and Approach](#)).

#### The Pre-contemplation Stage (Patient has no intention to change behavior):

Stage-matched interventions include:

1. Assess roadblocks (including level of nicotine dependence) to the proposed change.
2. Discuss the relevance, risks, and rewards of the proposed change.
3. Determine what action the patient and/or family is willing to take.

Motivational interviewing based on the "5 R's" (relevance, risks, rewards, roadblocks, and repetition) may help move smokers from pre-contemplation and contemplation towards preparation and action. Motivational interventions are most likely to be successful when the clinician is empathic, promotes patient autonomy (e.g., choice among options), avoids arguments, and supports the patient's self-efficacy (e.g., by identifying previous successes in behavior change efforts).<sup>301</sup>

Discussion of effective pharmacotherapy for tobacco dependence may help to move the nicotine dependent smoker from pre-contemplation to contemplation, preparation, or action. (see [Developing a medication Treatment Plan](#) Consider discussing the safety of nicotine replacement therapy relative to the risks of continued smoking.

#### The Contemplation Stage (Patient intends to make the behavior change within the next 6 months but makes no commitment to action)

Stage-matched interventions include:

1. Assess roadblocks, including level of nicotine dependence.
2. Assess opportunities to overcome roadblocks.
3. Recommend appropriate pharmacotherapy. See [Developing a medication Treatment Plan](#)
4. Build confidence that the patient can make a change that has beneficial results.

Assessment of level of tobacco dependence, patterns of smoking, triggers of tobacco smoking, and experience with prior quit attempts, and personal relevance of tobacco cessation may facilitate discussion of treatment options that may move the patient to pre-contemplation or action. (see [Tobacco-Dependence Treatment Process & Approach](#)).

#### The Preparation Stage (The intention is to implement the behavior change soon within one month)

Stage-matched interventions include:

1. Assess the specific changes needed, including level of nicotine dependence. level of nicotine dependence. (See [Nicotine Dependence Assessment - Adults.](#))
2. Recommend and/or prescribe appropriate pharmacotherapy.
3. Facilitate the development of specific plans for smoking cessation, including a quit date. [Freedom from Tobacco Action Plan](#)

Specific plans may include enrollment in a tobacco-dependence treatment program; determining what pharmacotherapy will be used; developing plans for how to identify and respond to withdrawal symptoms, how to respond to cravings and difficult situations, and how to prepare friends and family; and setting a Target Stop Date.

#### The Action-Implementation Stage (Patient has made the behavior change recently (within the past 6 months); relapse risk is at its highest)

Stage-matched interventions:

1. Monitor for difficulties and lapses.
2. Discuss strategies to recover from them.
3. If needed, revise the Action Plan, (see [Freedom from Tobacco Action Plan](#)), including adjusting pharmacotherapy. See [Developing a medication Treatment Plan](#)

- a. If nicotine withdrawal is not well-controlled, consider stepping up pharmacotherapy.
  - b. If nicotine dependence is well-controlled, consider if pharmacotherapy can be stepped down.
4. Discuss how to handle difficult situations, changes in routines, vacations, increases in stress, etc. Provide positive reinforcement.

**The Maintenance Stage** (Six months to life post change; the risk of relapse is still present, although not as high as during action-implementation. Relapse risk steadily and slowly falls over time but is always present)

Stage-matched interventions:

1. Monitor: Ask about lapses and temptations to lapse.
2. Revise: If nicotine withdrawal symptoms are in good control, consider if pharmacotherapy can be stepped down.

[< The Role of the Pediatric Health-Care Provider in Tobacco-Dependence Treatment and Secondhand Smoke Exposure Reduction](#) [up](#) [Intermittent, Nondaily, & Social Smoking](#) [>](#)



# Tobacco Dependence Treatment ToolKit

## Intermittent, Nondaily, & Social Smoking

### Nondaily Smoking Patterns

Treatment of tobacco dependence includes interventions for longstanding dependent cigarette users as well as therapy designed for individuals who consume tobacco products on a nondaily basis, smoking on some days but not every day. In the past, healthcare providers have viewed nondaily tobacco use as a transient smoking pattern associated with smoking initiation or stop smoking attempts.<sup>302-304</sup> However, new research on nondaily smoking shows that this pattern of tobacco use may represent a stable form of chronic low-level (fewer than 10 cigarettes per day on the days that they smoke) consumption.<sup>305, 306</sup> For example, longitudinal studies have shown that many nondaily smokers sustain their smoking patterns for 1 to 2 years, if not indefinitely.<sup>302, 303, 305</sup> Studies have also shown that nondaily smokers differ from daily smokers in that they tend not to self identify as smokers when asked by family, friends, or healthcare providers, and they appear to avoid cigarettes for days, weeks, and even months without exhibiting physiologic nicotine withdrawal symptoms.<sup>307, 308</sup> To date no formal trials have looked at the role of nicotine withdrawal among adult nondaily and social smokers once they stop using tobacco products. In a study of adolescent very light smokers (1-3 cigarettes per day), however, no evidence was found to suggest active signs of nicotine withdrawal, as measured by changes in heart rate and neuropsychological testing, after 24 hours of abstinence.<sup>309</sup>

Nondaily smoking is relevant to the practicing physician because its prevalence is increasing. In the United States, between 1996 and 2001, rates of nondaily smoking increased in 31 of the 50 states, going from 16% of current smokers in 1997 to 19% in 1999, and 24% in 2001.<sup>310</sup> Rates of nondaily smoking are likely to continue to increase as more laws pass limiting tobacco use in workplaces and public places. There are data that show that implementation of workplace restrictions increase the odds of a smoker being a light or intermittent user (OR= 1.28, 95% CI = 1.18-1.38).<sup>311</sup> Furthermore, smokers who enforce smoke-free policies at home are nearly three times as likely to be light or intermittent users (OR= 2.8, 95% CI = 2.60-3.04).<sup>311</sup> Accordingly, healthcare professionals will probably encounter these patients more frequently, highlighting the need for clinician education and training programs that will help this growing group become tobacco free.

Nondaily smokers also differ from everyday smokers in their demographic profile. Nondaily smokers tend to be younger, female, better educated, wealthier, and from minority backgrounds (African American and Hispanic)<sup>303, 305, 306</sup> when compared to everyday smokers. Hispanic/Latino smokers, for example, are more than three times as likely to smoke intermittently when compared to non-Hispanic Whites (OR = 3.2, 95% CI 2.75-3.74).<sup>312</sup> Nondaily smoking has also been associated with excessive alcohol consumption on U.S. college campuses.<sup>313, 314</sup>

### Health Risks Associated with Light and Nondaily Daily Smoking

Light smoking is defined as smoking fewer than 10 cigarettes per day, while nondaily smoking is defined as smoking on some days but not every day. Although there have been no formal trials that have looked at the dangers associated with social smoking, there are data that show that light and nondaily tobacco use are associated with increased risk of coronary artery disease (including ischemic heart disease and aortic aneurysm), cancer (esophageal, lung, gastric, and pancreatic), lower respiratory tract infections (increased frequency and prolonged symptoms), cataracts, compromised reproductive health (delayed time to conception in women), and poor bone mineral density leading to frequent ankle fractures in older women.<sup>315</sup> Light smokers (fewer than 15 cigarettes per day) also report lower health-related quality of life as measured by the SF-36 health status questionnaire than nonsmokers.<sup>316</sup> The risk of all-cause mortality in light or intermittent male smokers has been found to be 1.5 times that of nonsmoking men.<sup>317</sup> No association has been found yet for women between all-cause mortality and light or nondaily smoking.<sup>318</sup> It is pertinent to keep in mind, however, in this early stage of characterizing nondaily and light cigarette use, that initial research showed a relationship between regular cigarette smoking and lung cancer only in men, not in women.<sup>319</sup>

### Social Smoking: An Example of A Nondaily Smoking Pattern

"Social smoking" — smoking that is limited to social situations — is one example of a nondaily smoking behavior. The healthcare community first became aware of social smoking in the mid 1990s when a limited number of studies reported high rates of social smoking patterns on college campuses (up to 50%).<sup>320-322</sup> In these studies, social smokers are characterized as experimenting, affluent, Caucasian college students who only smoke socially to gain peer acceptance. Social smokers tend not to smoke alone and are described as restricting their tobacco use to parties, bars, or nightclubs.<sup>320-322</sup> Possible biological factors that separate social smokers from other nondaily or regular daily smokers, such as their genetics or physiology, have not been studied. Rather, what has been identified is that social smoking is primarily a behavioral phenomenon; social smokers may consume a similar volume of cigarettes as other nondaily smokers (smoking on some days but not every day) but their smoking is primarily initiated and driven by social contexts.<sup>320-322</sup>

Social smokers, like other nondaily smokers, refuse to categorize themselves as "smokers" when asked by family, friends, or healthcare providers and tend not view their smoking as a marker of personal addiction.<sup>320-322</sup> Social smokers often state that they could stop smoking anytime and under-recognize the health risks associated with their tobacco use.<sup>322</sup> At the same time, it is important for clinicians to realize that there are no formal trials that have looked at risks for nicotine withdrawal among this group once social smokers stop using tobacco products.

Although social smoking is relatively new to the medical community, it has been a focus of tobacco company research for over 30 years.<sup>323</sup> As early as the 1970s, confidential industry research found that social smokers represented as many as 20% to 25% of all smokers<sup>323, 324</sup> and that social smokers were observed among people of varying socioeconomic backgrounds, levels of education, and ethnicities — not just college students.<sup>323</sup> Social smokers purchased cigarettes primarily by the pack to limit consumption, smoking on average fewer than 10 cigarettes in a day, while commonly smoking more on weekends or at parties.<sup>323</sup> Industry marketers used their research to design cigarettes and advertising campaigns to attract and sustain social smoking patterns.<sup>323</sup> Tobacco companies further

discovered that social smokers did not identify themselves as smokers and denied nicotine dependence.<sup>323</sup>

In contrast to the low sensitivity to personal risks associated with their own smoking, tobacco companies discovered that social smokers were particularly concerned about the impact their smoking had upon others. Social smokers would often avoid situations where smoking was discouraged or would ask permission prior to lighting a cigarette.<sup>323</sup> Industry research showed that social smokers experiencing social pressure against smoking would either refrain from use in public or voluntarily relocate to minimize exposure to others. Social smokers supported smoking restrictions because these policies often designated areas that were acceptable to smoke without offending nonsmokers.

### Implications for Treatment Strategies

Because nondaily smokers, including social smokers, deny nicotine dependence, refuse to label themselves as smokers, and often under-recognize the harm associated with intermittent smoking, they pose a serious challenge to healthcare professionals. Existing tobacco-dependence treatment programs have been developed for daily, dependent cigarette users. The strategies recommended in the [Clinical Practice Guideline 2008 Update: Treating Tobacco Use and Dependence](#) to identify tobacco use, the 5A's ("Ask", "Advise", "Assess", "Assist", and "Arrange"), might not apply at all to either nondaily or to social smokers.<sup>325</sup> For example, when clinicians "Ask" patients "Are you a smoker?" they run the risk of missing tobacco users who self-categorize as nonsmokers. A better approach would be to "Ask", "Do you use tobacco products — ever?" If yes, "What products do you prefer to use?" And, finally, "Do you use cigarettes or any other tobacco product on a daily basis, intermittently, such as weekly or monthly, or do you smoke on a social basis, only when you are with friends or acquaintances who are smoking?" With focused, directed questions, healthcare professionals should be able to better identify the growing population of nondaily and social smokers. [Refer to box with suggested strategies]

#### Suggested Strategies:

- *Ask*: "Do you use tobacco products — ever?"
- *Ask*: "What products do you prefer to use?"
- *Ask*: "Do you use cigarettes or any other tobacco product on a daily basis, intermittently, such as weekly or monthly, or do you smoke on a social basis, only when you are with friends or acquaintances who are smoking?"
- *Advise*: patients about the dangers of secondhand smoke to friends and loved ones
- *Encourage*: personal smoke-free policies (such as smoke-free homes and cars)

Furthermore, treatment of tobacco dependence for the addicted daily smoker involves Advising patients about the personal health risk associated with their smoking.<sup>325</sup> While the harm associated with light and intermittent smoking is significant, at least for males, and emphasizes the need for clinicians to encourage stopping smoking completely, the psychological profile of nondaily and social smokers suggests that communicating these risks may not be an effective way to encourage them to stop smoking. Tobacco industry research suggests that clinicians should "Advise" their patients about the dangers of secondhand smoke to friends and loved ones<sup>317, 326</sup> and encourage personal smoke-free policies (such as smoke-free homes and cars). Although counseling nondaily and social smokers on the dangers of secondhand smoke as a treatment message has not been the subject of randomized clinical trials, concerns about the effects of secondhand smoke have been associated with intentions to quit and stopping smoking among young adult nondaily smokers.<sup>308</sup>

In conjunction with using an alternative counseling approach, healthcare professionals should also recognize that the pharmacotherapy options designed to treat tobacco dependence, such as nicotine medications, bupropion, and varenicline, were developed for regular, daily smokers who consume 10 or more cigarettes per day and suffer from nicotine addiction.<sup>325</sup> Because nondaily and social smokers consume less and tend not to show signs of nicotine dependence, Assisting patients with pharmacotherapies that are designed to counter withdrawal symptoms may not be relevant. The doses of nicotine found in commercially available nicotine medications may exceed that which nondaily smokers receive from smoking cigarettes or would need during treatment. Understanding what potential therapeutic approaches might be appropriate and effective for both nondaily and social smoking populations, including behavioral interventions and medications, such as nicotine medications, bupropion, and varenicline, will be a productive, future research area.

### Conclusions

Recent public health research indicates that nondaily smoking consists of a stable pattern of chronic low-level consumption and comprises about a quarter of all smokers (and growing) of varying age, ethnicity, socioeconomic status, and educational background. More importantly, public health research on nondaily smoking and internal, unpublished tobacco industry research on social smoking suggests that current tobacco-dependence treatment strategies based upon personal health risk and treatment of nicotine addiction may not be effective for this population of tobacco users. Both nondaily and social smokers may be more responsive to messages that focus on the harms their smoking poses to other nonsmoking friends or family members as a motivator to stop smoking.

Information on nondaily and social smoking patterns contained above in this Tool Kit will hopefully improve the way clinicians screen and identify these groups. Clinicians will recognize that taking detailed smoking histories of their patients with focused questions involving smoking frequency and volume of consumption will allow for better identification of nondaily and social smoking patterns. Once identified, clinicians should realize that social smokers may be motivated to stop smoking by messages stressing the harm of secondhand smoke and by encouragement to break associations between social activities and tobacco use, rather than by messages that only focus on personal health risk or with pharmacotherapy. Clinician training programs must recognize nondaily and social smoking patterns as examples of chronic tobacco use that require proper identification and most likely different treatment approaches as part of the healthcare community's commitment to providing effective treatments to enable our patients to become tobacco-free.

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# Tobacco Dependence Treatment ToolKit

## Introduction to Patient Management Tools

Most medical schools do not teach the basic pathology causing tobacco dependence, the mechanisms of action of effective tobacco-dependence medications, how to treat tobacco dependence effectively, or how to develop a clinical management plan for tobacco dependence and monitor the results. Classes cover asthma, diabetes, hypertension, and a long list of other diseases, but not tobacco dependence. Until medical school curricula, clinical clerkships, medical residency training programs, and pulmonary fellowship training programs rectify these omissions, this Tool Kit can provide Patient Assessment Tools and Patient Management Tools to guide your effective treatment of tobacco dependence. Members of the ACCP Tool Kit Committee have developed and have been using these tools in their clinical practice and treatment of tobacco dependence.

- [Trigger Settings](#)
- [Action Strategies](#)

It is not necessary to use all the tools for every patient. The clinician should evaluate the tools and use those that make sense and are most useful to effectively treat tobacco dependence in clinical practice. These tools can be modified to suit your personal practice needs and/or electronic medical records.

### Chart Identification Stickers

Printable [Chart Identification Stickers](#) (use AVERY Laser 5267 labels) clearly identify a patient as a *Current Smoker*, *Former Smoker*, *Never Smoker*, or *Secondhand Smoke Exposed* on their chart. These labels will alert the clinician in the future to the patient's tobacco use status as of the previous visit.

### Encounter Checklist

The [Encounter Checklist](#) is a means to track a patient's tobacco-use status and progress for each patient encounter, before and during treatment. It has been used in clinical tobacco-dependence practice for over 5 years.

### Tobacco-Dependence Pre-Treatment Checklist

The [Tobacco-Dependence Pre-Treatment Checklist](#) may be used to track topics to discuss with the patient, to ensure that you cover all the relevant topics that a patient needs to know about before the Target Stop Date (TSD), before treatment begins.

#### *Where to Find the Topical Information Listed in the Pre-Treatment Checklist*

Educational information that you or your nurse need to discuss with the patient can be found in this Tool Kit, as noted by the relevant "hot-linked" section number by each topic on the checklist. Also, the [Patient Education Brochures](#) can be helpful and save time in your office.

Some topics (such as reasons for stopping smoking, problems with past attempts, barriers to successful stopping, and concerns about weight gain) are part of the basic medical history. The information can be gathered using the [Assessment of Tobacco Use and Exposure](#) form, as a guided medical history, and/or via other [Patient Assessment Tools](#). The sections [Physician Notes and Treatment Planning](#) and [Tobacco-Dependence Consultation Report Form](#), described below, may be useful in recording this information and reporting it to referring or primary care physicians.

Some of the topics listed (such as destroying all tobacco products, anticipating challenges, and developing an action plan) are suggested actions for the patient to follow before the target stop date (TSD). The physician should discuss these suggestions with the patient and explain how to follow them. Tools that can help include the [Behavioral "Homework" Worksheet](#) and the [Freedom From Tobacco Action Plan](#).

The AAFP CD-ROM Audiobook (full title: [Dr. Art Ulene: How to Stop Smoking](#)) and the 30-minute Biology of Nicotine Addiction DVD are available directly from the [Palo Alto Center for Pulmonary Disease Prevention](#).

### Tobacco-Dependence Relapse-Prevention Checklist

The [Tobacco-Dependence Relapse-Prevention Checklist](#) may be used to track topics to discuss with the patient, 1-6 months after TSD, to ensure that you cover key relapse-prevention strategies with patients. Covering this information before TSD distracts the patient's attention from where it needs to be: identifying [Trigger Settings](#) and developing [Action Strategies](#) for each and every trigger. Revisit the patient's action plan to confirm that it addresses the patient's fears and disincentives to stop smoking, including any new concerns that may have arisen, then discuss these relapse prevention strategies. Again, refer to the [Behavioral "Homework" Worksheet](#) and the [Freedom From Tobacco Action Plan](#).

### How to Use the Pre-Treatment and Relapse-Prevention Checklists

Check the "Y" column when you have fully covered the topic, consistent with the patient's needs. Check the "±" column when you have partially covered the topic but have elected to defer completing the discussion to a later or better time (e.g., when the patient will be better able to actually hear the information and process it). Check the "N" column when you have decided that you do not need to cover the topic with that patient.

Y: topic fully covered  
 ±: topic partially covered and/or deferred  
 N: no need to cover topic

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**Other Tools**

The [Physician Notes and Treatment Planning](#) form and [Tobacco-Dependence Consultation Report Form](#) document preliminary patient encounters and aid the clinician in the development and communication of an effective treatment plan.

[Tools for the Pediatric Healthcare Provider](#) facilitates an assessment of secondhand smoke exposure in children, as well as an inquiry into adolescent tobacco use.

The [Carboxyhemoglobin versus Exhaled Carbon Monoxide Graph](#) shows the linear relationship between exhaled-air carbon monoxide levels, in parts per million (ppm), and blood levels of carboxyhemoglobin as %COHb. Exhaled air carbon monoxide is easily measured in the office and is a CPT-codeable service that is reimbursed by some insurance plans.

The section on [Performance Measures in Tobacco Dependence Treatment](#) describes initiatives taken by government and private entities, including the National Quality Forum (NQF), to develop and implement a national strategy for health care quality improvement through measurement and reporting. NQF has endorsed performance measures for tobacco dependence screening, treatment, and counseling.

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# Tobacco Dependence Treatment Toolkit

## Introduction to Treatment Algorithms: How to Use Them in Clinical Practice

This Tool Kit provides several treatment algorithms to aid the clinician in the care of the tobacco-dependent patient. These algorithms are listed below.

1. [Stepwise Therapy Guide](#) assists in targeting combination replacement therapies based on the tobacco user's degree of nicotine dependence.
2. [Recommended Visit Schedule for Diagnosing and Treating Tobacco Dependence](#) outlines activities and treatment algorithms to be employed during each treatment interval, from preparatory visits to long-term follow-up.
3. [Initial Evaluation](#) verifies the patient's smoking status and, if the patient is a smoker, assesses his or her willingness to begin treatment.
4. [Initial Management](#) assesses the severity of addiction, treatment modifiers, treatment contraindications, and patient preferences, and helps the clinician develop and record a medical treatment plan.
5. [Managing Patient Reluctance](#) identifies sources of reluctance, reframes goals, and evaluates the patient's willingness to accept treatment.
6. [Developing a Medication Treatment Plan](#) provides a logic model that assesses factors that influence treatment choices, aids in the choice of baseline controller and rescue (reliever) medications, and anticipates potential barriers to treatment.
7. [Long-Term Evaluation and Management](#) assesses the risk for relapse and includes a relapse risk reduction checklist.
8. [Managing Relapse](#) is a follow up to the assessment of risk for relapse; it includes an assessment of available support and reliever medication use and provides options for managing potential lapses.
9. [Tapering Pharmacologic Interventions](#) assesses the duration of the treatment plan and the ability of the patient to control the compulsion to smoke.
10. [Management of the Child/Adolescent at Risk for Smoking](#) assesses whether a child or adolescent smokes and, if so, assesses whether he or she is ready to stop. A list of options is provided to manage patients who are willing to stop.
11. [Management of the Smoke-Exposed Child](#) outlines strategies to mitigate exposure of a child to secondhand tobacco smoke.

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[up](#)

[Stepwise Tobacco-Dependence  
Treatment Guide: Table 1 >](#)



# Tobacco Dependence Treatment ToolKit

## Introduction to Treatment Algorithms: How to Use Them in Clinical Practice

This Tool Kit provides several treatment algorithms to aid the clinician in the care of the tobacco-dependent patient. These algorithms are listed below.

1. [Stepwise Therapy Guide](#) assists in targeting combination replacement therapies based on the tobacco user's degree of nicotine dependence.
2. [Recommended Visit Schedule for Diagnosing and Treating Tobacco Dependence](#) outlines activities and treatment algorithms to be employed during each treatment interval, from preparatory visits to long-term follow-up.
3. [Initial Evaluation](#) verifies the patient's smoking status and, if the patient is a smoker, assesses his or her willingness to begin treatment.
4. [Initial Management](#) assesses the severity of addiction, treatment modifiers, treatment contraindications, and patient preferences, and helps the clinician develop and record a medical treatment plan.
5. [Managing Patient Reluctance](#) identifies sources of reluctance, reframes goals, and evaluates the patient's willingness to accept treatment.
6. [Developing a Medication Treatment Plan](#) provides a logic model that assesses factors that influence treatment choices, aids in the choice of baseline controller and rescue (reliever) medications, and anticipates potential barriers to treatment.
7. [Long-Term Evaluation and Management](#) assesses the risk for relapse and includes a relapse risk reduction checklist.
8. [Managing Relapse](#) is a follow up to the assessment of risk for relapse; it includes an assessment of available support and reliever medication use and provides options for managing potential lapses.
9. [Tapering Pharmacologic Interventions](#) assesses the duration of the treatment plan and the ability of the patient to control the compulsion to smoke.
10. [Management of the Child/Adolescent at Risk for Smoking](#) assesses whether a child or adolescent smokes and, if so, assesses whether he or she is ready to stop. A list of options is provided to manage patients who are willing to stop.
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[Stepwise Tobacco-Dependence  
Treatment Guide: Table 1 >](#)

# Classification of Severity - Table #1

## CLASSIFY TOBACCO-DEPENDENCE SEVERITY Clinical Features Before Treatment\*

	Cigarette Use	Nicotine Withdrawal Symptoms	Quantitative	Health Status
<b>STEP 4 Very Severe</b>	- >40 CPD - Daily use - Time to 1st Cig:0-5 min	- Constant - NWS > 40	- FTND 8-10 - Se Cotinine > 400 ng/mL	- ≥1 Chronic Medical Dis. AND / OR - ≥1 Psychiatric Disease
<b>STEP 3 Severe</b>	- 20-40 CPD - Daily use - Time to 1st Cig:6-30 min	- Constant - NWS 31-40	- FTND 6-7 - Se Cotinine 250 - 400 ng/mL	- ≥1 Chronic Medical Dis. OR - ≥1 Psychiatric Disease
<b>STEP 2 Moderate</b>	- 6-19 CPD - Daily use - Time to 1st Cig:31-60 min	- Frequent - NWS 21-30	- FTND 4-5 - Se Cotinine 151-250 ng/mL	- Healthy medically - Healthy psychiatrically
<b>STEP 1 Mild</b>	- 1-5 CPD - Intermittent Use - Time to 1st Cig:>60 min	- Intermittent - NWS 11-20	- FTND 2-3 - Se Cotinine 51-150 ng/mL	- Healthy medically - Healthy psychiatrically
<b>STEP 0 Non-Daily/Social</b>	- Non-daily cigarette use - Social setting only - Time to 1st Cig:>>60 min	- None - NWS < 10	- FTND 0-1 - Se Cotinine < 50 ng/mL	- Healthy medically - Healthy psychiatrically

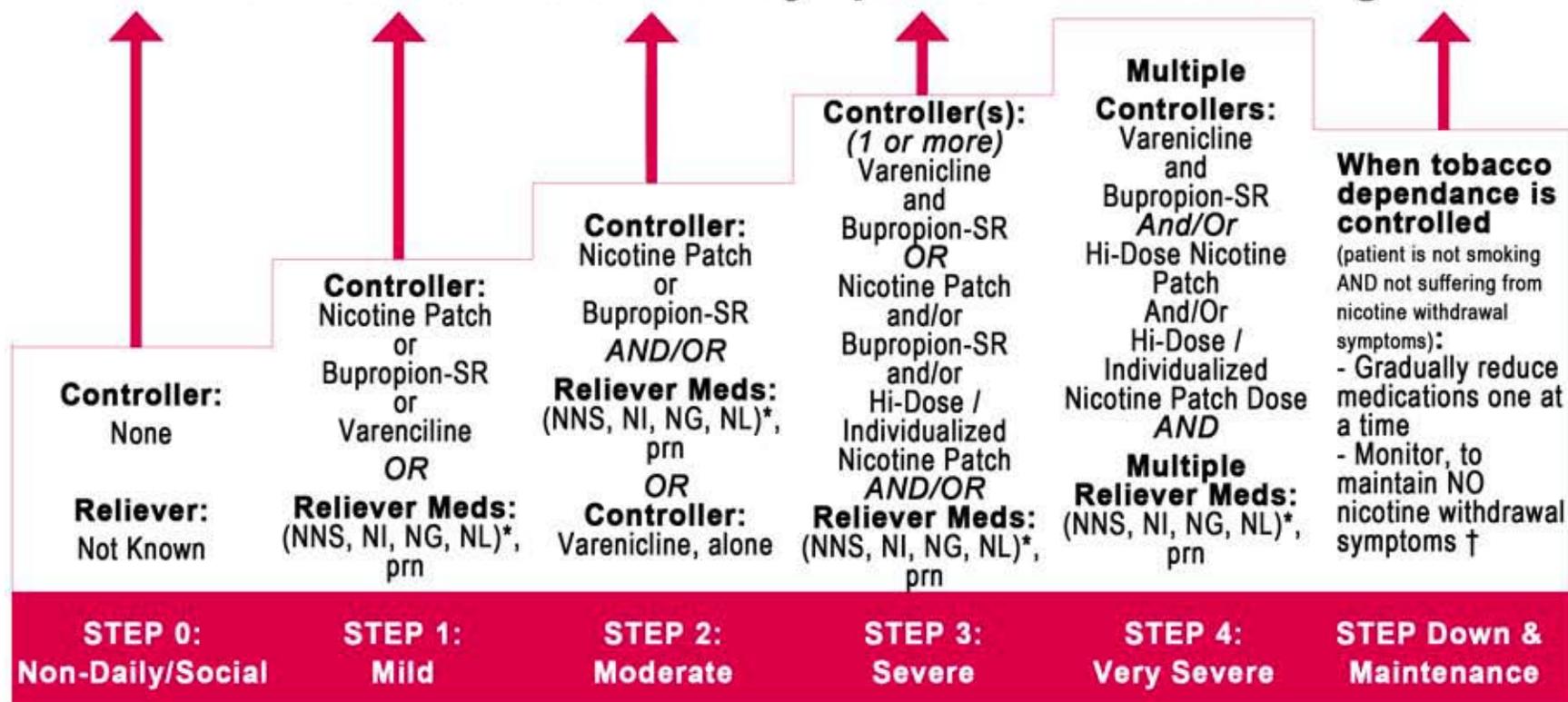
**\*The presence of one feature of severity is sufficient to place patient in that category.**

-CPD=Cigarettes Per Day -Time to 1st Cig=Time to First Cigarette after Awakening in the Morning  
-NWS=Nicotine Withdrawal Symptom Score -FTND=Fagerström Test for Nicotine Dependence Score  
-Se=Serum -Cotinine=First-pass, hepatic metabolite of nicotine; physiologically inactive

## Initial & Long-Term Tobacco-Dependence Management

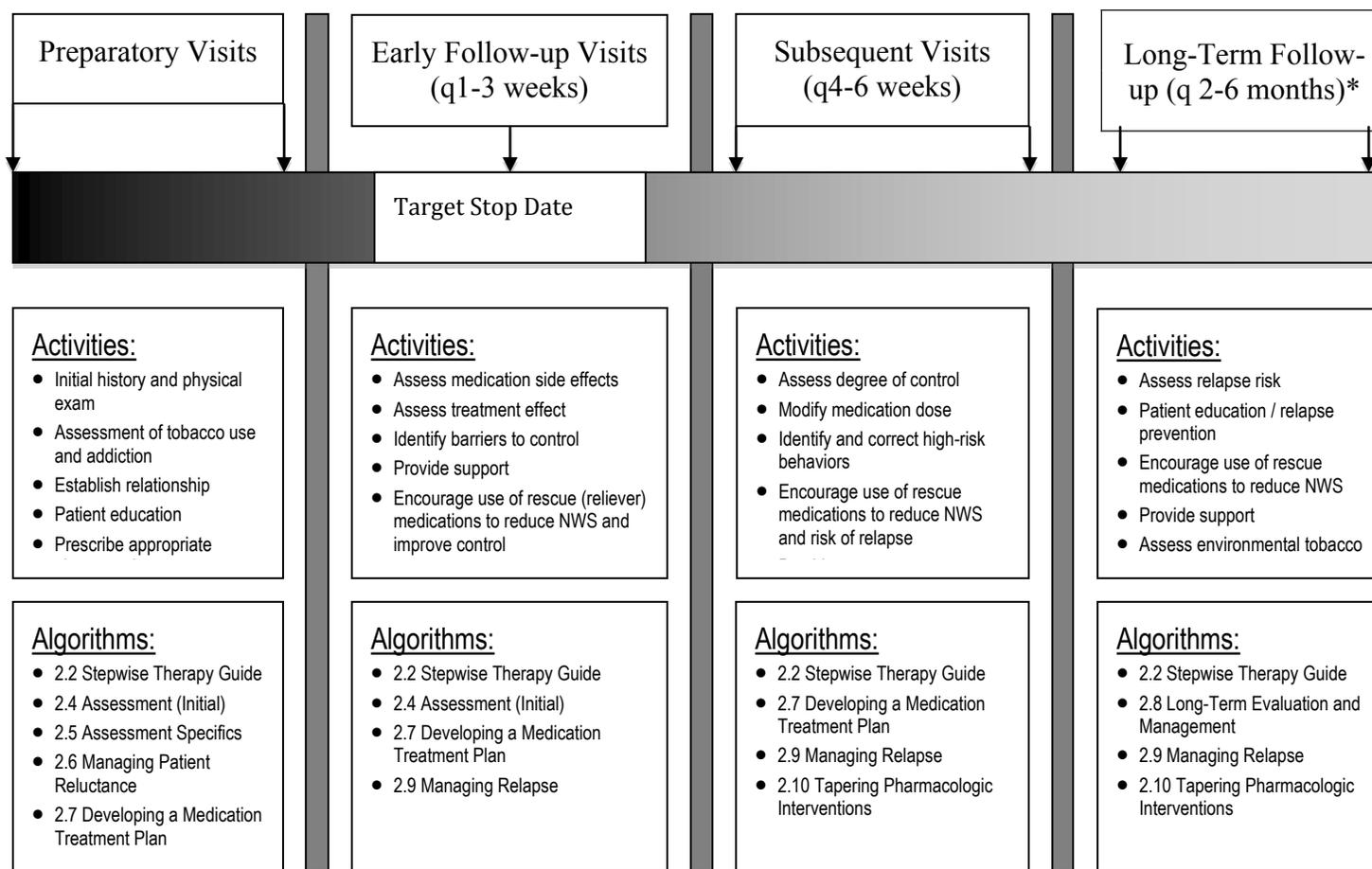
# Stepwise Approach to Tobacco-Dependence Therapy: Adults (Based on the Asthma Model) - Table #2

**Outcome: Tobacco-Dependence Control  
No Nicotine Withdrawal Symptoms and No Smoking**



\* **Reliever Medications (Rapid Acting Nicotine Agonists):** -NNS=Nicotine Nasal Spray -NI=Nicotine [Oral] Inhaler -NG=Nicotine Gum -NL=Nicotine Lozenge  
 † Some patients will need indefinite use of Controller or Reliever Medications to maintain zero nicotine withdrawal symptoms and no cigarette use.

## Recommended Visit Schedule for Diagnosing and Treating Tobacco Dependence



\*Continuing indefinitely, as for any chronic disease. Frequency of visits throughout treatment depends on individual clinical need.

NWS: nicotine withdrawal symptoms



# Tobacco Dependence Treatment ToolKit

## Algorithm Key

-  **Rounded Rectangle:** Clinical state or condition
-  **Hexagon:** Decision point requiring action; formulated as a question followed with Yes-No options. (Yes = vertical arrow; No = horizontal arrow)
-  **Rectangle:** Actions to be taken; process and treatment
-  **Oval:** (Algorithm) link to other sections within the Tool Kit
-  **Octagon:** End point
-  **Arrows:** flow of action; ordering the steps presented on the flow chart
-  **Horizontal Arrows:** next steps for NO response
-  **Vertical Arrows:** next steps for YES response

[Download Form \(PDF\)](#)

## Algorithm Format

The goal of the guideline for Management of Tobacco Use is to incorporate the information from several existing reports, recommendations, and statements into a format that facilitates clinical decision-making and maximizes the use of clinical tools. The algorithm format was chosen because of the evidence that such a format improves data collection, diagnostic and therapeutic decision-making and changes patterns of resource use. The algorithm format may help the clinician sort out the logic and sequence of the decision-making process for choosing the appropriate interventions.

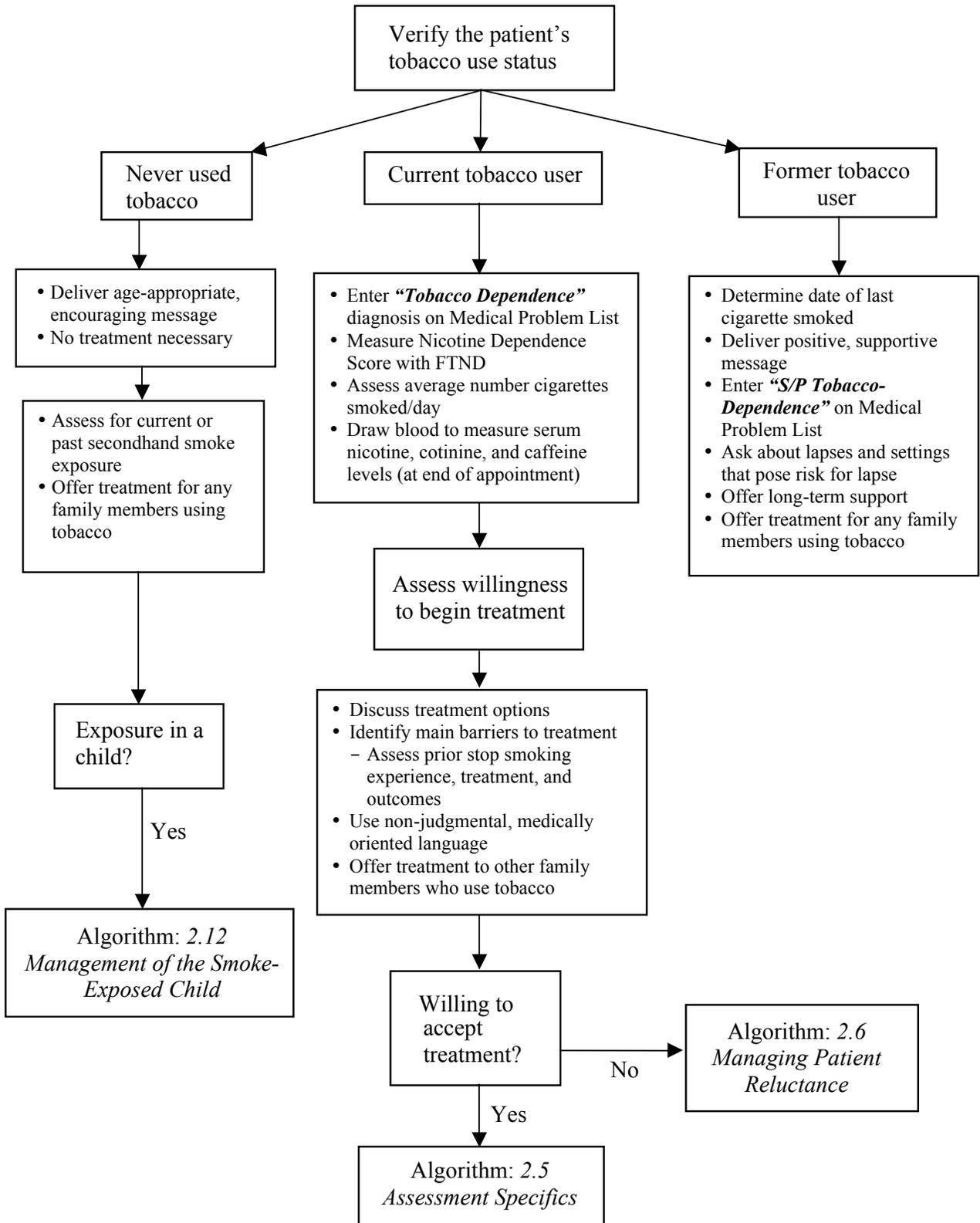
The algorithmic format allows the provider to follow a linear approach to critical information needed at the major decision points in the clinical process, and includes:

- An ordered sequence of steps of care
- Recommended observations
- Decisions to be considered
- Actions to be taken

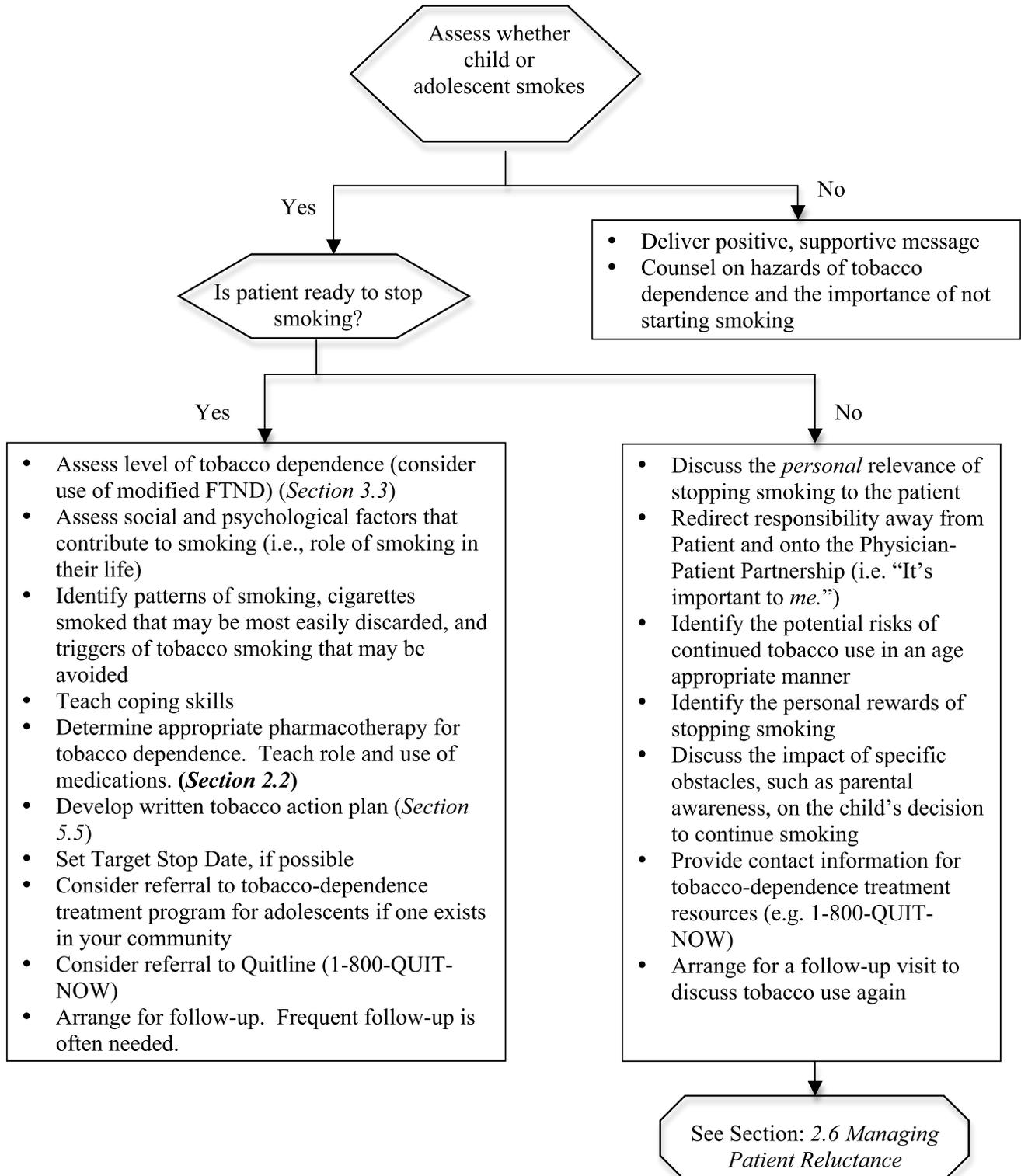
A clinical algorithm diagrams a guideline into a step-by-step decision tree. Standardized symbols are used to display each step in the algorithm. <sup>327</sup> ([Society for Medical Decision-Making Committee \[SMDMC\], 1992](#)). Arrows connect the numbered boxes, indicating the order in which the steps should be followed.

[< Management of the Smoke-Exposed Child](#) [up](#)

ASSESSMENT (INITIAL)



## Management of Child/Adolescent at Risk for Smoking





# Tobacco Dependence Treatment ToolKit

## Introduction to Patient Assessment Tools

Several tools have been included in this Tool Kit to assess tobacco use and exposure, nicotine dependence, nicotine withdrawal, depression, mood, dyspnea, and quality of life. The [Assessment of Tobacco Use and Exposure](#) tool gathers a history of tobacco use and exposure to environmental tobacco and evaluates a tobacco user's willingness to stop smoking. A *Nicotine Dependence Assessment* may be accomplished by employing one or more of the following tools:

- [Fagerstrom Test for Nicotine Dependence \(FTND\)](#) including [FTND Scoring Information](#)<sup>128</sup>
- [Modified Fagerstrom Tolerance Questionnaire \(FTQ\) for Adolescents](#) including [Modified FTQ Scoring Information](#)<sup>287, 328</sup>
- [Hooked on Nicotine Checklist \(HONC\)](#)<sup>329, 330</sup> including [HONC Instructions and Scoring Information](#)
- A [Nicotine Withdrawal Symptom \(NWS\) Scale](#) has been provided to assess the severity of withdrawal symptoms experienced during tobacco cessation, including [NWS Instructions and Scoring Information](#)<sup>331</sup>

Depression, mood, dyspnea, and quality-of-life assessment scales may also be employed and include the following:

- [Beck Depression Inventory®-II \(BDI®-II\)](#), including [BDI®-II Sample](#) and [BDI®-II Description and Ordering Information](#)<sup>332</sup>
- [Center for Epidemiologic Studies - Depression Scale \(CES-D\)](#)<sup>333</sup>
- [Profile of Mood States \(POMS\) Questionnaire](#)<sup>334</sup>
- [Borg Scale](#) for assessment of dyspnea<sup>335, 336</sup>
- [St. George's Respiratory Questionnaire \(SGRQ\)](#) for assessment of quality of life<sup>337</sup>
- [Visual Analog Scale](#) for assessment of dyspnea<sup>338</sup>

[< Patient Assessment Tools](#)      [up](#)      [Assessment of Tobacco Use and Exposure >](#)

## FAGERSTRÖM TEST FOR NICOTINE DEPENDENCE (FTND) \*

PATIENT NAME: \_\_\_\_\_ DATE: \_\_\_\_/\_\_\_\_/\_\_\_\_

PLEASE read each question below. Check only one box for each question that best describes your response.

1. How soon after you wake up do you smoke your first cigarette?
  - 3  Within 5 minutes
  - 2  6 – 30 minutes
  - 1  31 – 60 minutes
  - 0  After 60 minutes
2. Do you find it difficult to refrain from smoking in places where it is forbidden, e.g. in church, at the library, in cinemas, etc.?
  - 1  Yes
  - 0  No
3. Which cigarette would you hate most to give up?
  - 1  The first one in the morning
  - 0  Any other
4. How many cigarettes per day do you smoke? \_\_\_\_\_
  - 3  31 or more
  - 2  21 - 30
  - 1  11 - 20
  - 0  10 or less
5. Do you smoke more frequently during the first hours after awakening than during the rest of the day?
  - 1  Yes
  - 0  No
6. Do you smoke when you are so ill that you are in bed most of the day? (If you never get sick, give the most likely response.)
  - 1  Yes
  - 0  No

Total Score: \_\_\_\_\_

\_\_\_\_\_  
 Staff Member Signature

Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

\* From: Heatherton TF, et al. The Fagerström Test for Nicotine Dependence: A Revision of the Fagerström Tolerance Questionnaire. *Br J Addict.* 1991;86:1119-1127.

## The Fagerström Test for Nicotine Dependence (FTND) (Scoring Information)

1

*Prepared by:*

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**145 North California Avenue**

**Palo Alto, CA 94301-3911**

**PHONE: 650-833-7994**

**FAX: 650-833-7990**

Date of Preparation: 9/8/2008

- 
- ❖ The FTND is a *physiologically* validated scale
  - ❖ Easy to use in a clinic or office setting
    - ◆ 6 questions
    - ◆ Linear scale
      - 0-10 points
        - For Research Purposes, can be split:
          - Low Nicotine Dependence = 0-4 points
          - High Nicotine Dependence = 5-10 points
  - ❖ Use the FTND to diagnose severity of tobacco dependence as you would measure blood pressure to diagnose severity of hypertension
  - ❖ Measure immediately before you start treatment for tobacco dependence
  - ❖ *Not* useful to re-measure after a patient has stopped smoking
  - ❖ Useful to re-measure after a patient has relapsed
  - ❖ In Clinical Medical Practice:
    - ◆ Remember the FTND is linear
      - The higher the FTND score the more physically dependent is your patient on nicotine
      - A patient with an FTND score of 10 means that patient is 10% physically more dependent on nicotine than a different patient with an FTND score of 9
      - A patient with an FTND score of 9 or 10, for example, will need much more aggressive pharmacotherapy for tobacco dependence than a patient with an FTND score of 2 or 3 to suppress nicotine withdrawal symptoms and to keep them suppressed – meaning to have effective pharmacotherapy
        - The treating physician must use higher-than-standard doses of effective medication(s), and/or
        - Combine Controller - and Rescue -type tobacco-dependence medications
        - Treat tobacco dependence, including the pharmacotherapy component, for a much longer duration of time
          - Years to Decades to Lifetime

NB: This form and scoring instructions may be duplicated without restriction for patient -care or education purposes.

<sup>1</sup>Heatherton TF, et al. Brit J Addict 1991. 86:1119-27.

MODIFIED FAGERSTRÖM TOLERANCE QUESTIONNAIRE (mFTQ) FOR ADOLESCENTS \*

PATIENT NAME: \_\_\_\_\_ DATE: \_\_\_\_/\_\_\_\_/\_\_\_\_

PLEASE read each question below. Check only one box for each question that best describes your response.

1. How many cigarettes a day do you smoke?
  - 2  Over 26 cigarettes a day
  - 1  About 16 – 25 cigarettes a day
  - 0  About 1 – 15 cigarettes a day
  - 0  Less than 1 a day
2. Do you inhale?
  - 2  Always
  - 1  Quite often
  - 1  Seldom
  - 0  Never
3. How soon after you wake up do you smoke your first cigarette?
  - 1  Within the first 30 minutes
  - 0  More than 30 minutes after waking but before noon
  - 0  In the afternoon
  - 0  In the evening
4. Which cigarette would you hate to give up?
  - 1  First cigarette in the morning
  - 0  Any other cigarette before noon
  - 0  Any other cigarette after noon
  - 0  Any other cigarette in the evening
5. Do you find it difficult to refrain from smoking in places where it is forbidden (church, library, movies, etc.)?
  - 1  Yes, very difficult
  - 1  Yes, somewhat difficult
  - 0  No, not usually difficult
  - 0  No, not at all difficult
6. Do you smoke when you are so ill that you are in bed most of the day? (If you never get sick, give the most likely response.)
  - 1  Yes, always
  - 1  Yes, quite often
  - 0  No, not usually
  - 0  No, never
7. Do you smoke more during the first 2 hours after awakening than during the rest of the day?
  - 1  Yes
  - 0  No

Total Score: \_\_\_\_\_

Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

\_\_\_\_\_  
 Staff Member Signature

\* From: Prokhorov AV, et al. Measuring nicotine dependence among high-risk adolescent smokers. *Addict Behav.* 1996; 21:117-127.

## The Modified Fagerström Tolerance Questionnaire (mFTQ) for Adolescents<sup>1</sup> (Scoring Information)

*Based on:*

**Prokhorov, et al. and the NCI website**

*Finalized by:*

**Harold J. Farber, MD**

**David P.L. Sachs, MD**

Date of Preparation: 2/17/2009

- 
- ❖ This modified version of the FTQ<sup>2</sup> assesses the level of nicotine dependence among adolescents. The instrument uses a 5 -point Likert scale for all seven items, except for one item on smoking during the first two hours of the day. The original FTQ item, assessing nicotine content in the respondent's "usual" brand of cigarettes, was excluded from this adolescent version.
  - ❖ The mFTQ is a physiologically validated scale
  - ❖ Target Population: Adolescents aged 14 – 20
  - ❖ Easy to use in a clinic or office setting
    - ◆ 7 questions
    - ◆ Linear scale
      - 0 – 9 points
        - For Research Purposes, can be split:
          - No Nicotine Dependence = 0-2 points
          - Moderate Nicotine Dependence = 3-5 points
          - High Nicotine Dependence = 6-9 points
  - ❖ Use the mFTQ to diagnose severity of tobacco dependence as you would measure blood pressure to diagnose severity of hypertension
  - ❖ Measure immediately before you start treatment for tobacco dependence
  - ❖ Not useful to re-measure after a adolescent has stopped smoking
  - ❖ Useful to re-measure after adolescent has relapsed
  - ❖ In Clinical Medical Practice:
    - ◆ Remember the mFTQ is linear
      - The higher the mFTQ score the more physically dependent is your teen patient on nicotine
      - A teen patient with an mFTQ score of 9 means that patient is 11% physically more dependent on nicotine than a different teenager with an mFTQ score of 8
      - A teen patient with an mFTQ score of 8 or 9, for example, will need a much more comprehensive treatment plan for tobacco dependence than one with an mFTQ score of 2 or 3 to receive effective treatment

NB: This form and scoring instructions may be duplicated without restriction for patient -care or education purposes.

<sup>1</sup> Prokhorov AV, et al. Measuring nicotine dependence among high -risk adolescent smokers. *Addict Behav.* 1996; 21:117-127.

<sup>2</sup> Fagerström KO. Measuring degree of physical dependence to tobacco smoking with reference to individualization of treatment. *Addict Behav.* 1978; 3:235-241.

	NO	YES
1. Have you ever tried to quit, but couldn't?		
2. Do you smoke <u>now</u> because it is really hard to quit?		
3. Have you ever felt like you were addicted to tobacco?		
4. Do you ever have strong cravings to smoke?		
5. Have you ever felt like you really needed a cigarette?		
6. Is it hard to keep from smoking in places where you are not supposed to?		
<b>When you haven't used tobacco for a while ...</b> <b>OR</b> <b>When you tried to stop smoking ...</b>		
7. Did you find it hard to concentrate because you couldn't smoke?		
8. Did you feel more irritable because you couldn't smoke?		
9. Did you feel a strong need or urge to smoke?		
10. Did you feel nervous, restless or anxious because you couldn't smoke?		

## Introduction

The Hooked on Nicotine Checklist (HONC) is a validated measure of autonomy over adolescent tobacco use. It is useful for identifying when nicotine dependence has begun and for measuring the severity of dependence. The HONC may detect lower levels of nicotine dependence than the mFTQ detects. This sensitivity is particularly relevant for adolescent smokers. The construct measured by the HONC (loss of autonomy) is different from that measured by the mFTQ or FTND (physiologic withdrawal). The HONC and FTND scores are modestly correlated with each other. One study of adults smokers found 44% of the variability ( $r$ -square = 0.44) in the FTND score explained by the HONC score.

## Scoring

The HONC instrument is a 10-item checklist format with each item having dichotomous (yes/no) answers. The sum of the number of "yes" answers determines the HONC score. As the score increases from 1 to 10, it indicates increasing amounts of loss of autonomy over smoking.

## Use of the HONC

The HONC is useful in illustrating to adolescents that cigarette smoking can lead to nicotine addiction (i.e., loss of autonomy over smoking) and the degree of their addiction. This awareness may motivate adolescents to stop smoking, especially in the early stages of addiction development. Although we have not been able to identify research studies that used this score to guide treatment, it is reasonable to infer that individuals with a higher score would require more intensive tobacco-dependence treatment efforts. The mFTQ and FTND scores may be more sensitive than the HONC to higher levels of nicotine dependence and, therefore, can be used to differentiate between moderate and high levels of nicotine dependence for those with a high score on the HONC. On the other hand, for those with a low score on the FTND or mFTQ, it would be reasonable to evaluate a HONC score to better assess loss of autonomy over smoking behaviors.

The Hooked on Nicotine Checklist is included in this Tool Kit and it can be downloaded, with extensive supporting information, from <http://fmchapps.umassmed.edu/honc/>. It has been translated into seven languages.

**Quantitative NWS Scale**  
(To Be Administered By Program Staff)

FORM 10Ws  
WEEKLY FORM

PatientName: \_\_\_\_\_  
(LAST NAME) (FIRST NAME) (MIDDLE INITIALS)

Date Completed: \_\_\_\_\_ Time Completed: \_\_\_\_\_ AM/PM  
(MM/DD/YYYY)

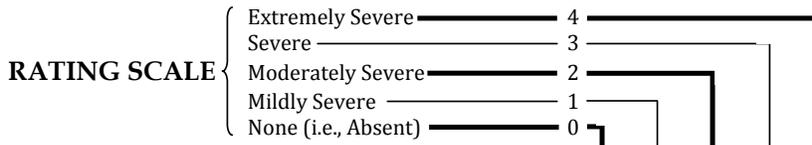
Date Last Cig. Smoked: \_\_\_\_\_ Time Last Cig. Smoked: \_\_\_\_\_ AM/PM Tobacco-Dependence Medication(s)  
Used: \_\_\_\_\_  
(MM/DD/YYYY)

Date Medication(s) Last Used: \_\_\_\_\_ Time Medication(s) Last Used: \_\_\_\_\_ AM/PM  
(MM/DD/YYYY)

Name of Staff Member Administering Form:  
\_\_\_\_\_  
(LAST NAME) (FIRST NAME) (MIDDLE INITIALS)

**STAFF INSTRUCTIONS:** After filling in the section above, give this form to the patient for completion of the symptom rating section below. This should be completed first thing in the morning.

**PATIENT INSTRUCTIONS:** Below you will find a series of symptoms and physical sensations that you might be feeling or experiencing. Based on how you have felt **during the LAST WEEK**, CIRCLE the appropriate number that best describes your symptom level for each of the symptoms listed below. Please answer ALL items. If you have any questions, just ask!



1. Craving/Desire to Smoke a Cigarette	0	1	2	3	4	
2. Constipation	0	1	2	3	4	
3. Restlessness/Impatience	0	1	2	3	4	
4. Increased Appetite (Excessive Hunger) or Weight Gain	0	1	2	3	4	
5. Depression/Sadness/Tearfulness/Moodiness	0	1	2	3	4	
6. Tension	0	1	2	3	4	
7. Bizarre/Vivid Dreams or Nightmares	0	1	2	3	4	
8. Frustration	0	1	2	3	4	
9. Psychological Need to Smoke a Cigarette	0	1	2	3	4	
10. Anger	0	1	2	3	4	
11. Difficulty Falling Asleep	0	1	2	3	4	
12. Difficulty Remaining Asleep	0	1	2	3	4	
13. Irritability	0	1	2	3	4	
14. Pimples	0	1	2	3	4	
15. Headache	0	1	2	3	4	
16. Anxiety	0	1	2	3	4	
17. Difficulty Concentrating	0	1	2	3	4	
18. Mouth Sores	0	1	2	3	4	
19. Other: _____	0	1	2	3	4	
20. Other: _____	0	1	2	3	4	



\*See separate instruction sheet prepared by David P.L. Sachs, MD. (4/1/2009) This form may be reproduced for patient care use.

**PALO ALTO CENTER FOR PULMONARY DISEASE PREVENTION  
 Nicotine Withdrawal Symptom (NWS) Scale\***

(Instructions, Scoring & Use)

*Quantitative NWS Scale Developed by & Scoring Information Prepared by:*

*David P.L. Sachs, MD*

*Director, Palo Alto Center for Pulmonary Disease Prevention*

*Palo Alto, CA*

\* Measure nicotine withdrawal symptom (NWS) severity score at each visit using this Scale.

\* Based on validated Hughes-Hatsukami University of Minnesota Scale.

\* This scale quantitatively measures nicotine withdrawal symptom severity. (**NB:** Professor Hughes advises that the scale NOT be "labeled a withdrawal scale because [patients can be] confused by filling out a 'nicotine withdrawal' scale prior to stopping smoking and will sometimes not report a symptom [after stopping smoking] if they do not believe it is due to withdrawal."343)

**Accordingly, this scale is named Medical Symptom Check-List.**

\* To calculate quantitative score:

o After patient has circled one, and only one, number in each item's Likert scale, copy the circled number into the open square to the far right.

\* Only "classic" DSM-III-R or DSM-IV nicotine withdrawal symptoms have an open square - p - for this purpose (there are 12 included on this scale).

\* The symptoms with a shaded square - - in the far right column are withdrawal signs or symptoms not classified as such in DSM-III-R or DSM-IV, but which most experts regard as highly likely to be valid nicotine withdrawal symptoms (e.g., #2. Constipation, #12 Difficulty Remaining Asleep, #14. Pimples, or #18. Mouth Sores). Others are potential medication side-effects (e.g., #7. Bizarre/Vivid Dreams or Nightmares or #11. Difficulty Falling Asleep).

\* Use this Medical Symptom Check-List to measure NWS severity for several visits before target stop date (TSD)

o Establishes baseline score out of 48-point max (the higher the score the more severe the patient's nicotine withdrawal)

o Use at each visit after TSD.

\* Adjust medication(s) and dose(s) to keep nicotine withdrawal symptom score <16/48 points, or <25% of baseline score, whichever is the lower score.

\* Optimal nicotine withdrawal symptom score <8/48 points or <5%-10% of baseline score after TSD, whichever is the lower score.

o With Craving/Desire to Smoke a Cigarette = 0 (to 1, *maximum*) out of 4 points.

o And no single withdrawal symptom item accounting for 3-4 points out of the <8/48 points.

*Violation of the above goals for suppressing nicotine withdrawal symptoms (NWS) dooms the patient to **treatment failure** (i.e., return to tobacco use).*

This form and scoring instructions may be duplicated without restriction for patient-care or educational purposes.

\*This is a quantitative modification of the validated Hughes-Hatsukami Scale that Dr. Sachs reviewed with Dr. Hughes on 2/28/2008. Dr. Sachs and others have used this scale in >600 patients in his clinical practice.



# Tobacco Dependence Treatment ToolKit

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### Acknowledgements

The committee gratefully acknowledges the contributions of the following individuals who provided invaluable assistance to this project:

**Gary A. Giovino, PhD**  
**Diane Krier-Marrow, MBA**  
**Rachel L. Gutterman**  
**Linda C. Kreger**  
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# Tobacco Dependence Treatment ToolKit

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