Clinical Management Review

A Comprehensive Approach to Tobacco Dependence Interventions

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Tobacco smoking remains the leading preventable cause of death and illness in the United States. Smoking cessation is particularly relevant for individuals with chronic obstructive pulmonary disease because it is known from multiple studies that individuals who quit smoking experience an initial improvement in pulmonary function, a decreased rate of normal age-related decline in FEV_1, a lower risk of hospital admission, and improved survival. Tobacco dependence must be recognized as a chronic disease, and comprehensive treatment for the tobacco-dependent patient with chronic obstructive pulmonary disease begins with a physician's inquiry into smoking and encouragement to quit, followed by an assessment of the level of dependence and the severity of withdrawal symptoms during previous quit attempts. Combination pharmacotherapy is recommended for the initial treatment of most smokers, especially those with moderate to high baseline levels of tobacco dependence. The patient's history, combined with his or her personal preference, can guide the clinician in initiating an appropriate treatment regimen. Given the chronic nature of tobacco dependence, clinicians must anticipate relapses and the need for recurrent, long-term follow-up. Comprehensive tobacco treatment consultation should be sought whenever possible for patients with high levels of tobacco dependence and multiple relapses or failed quit attempts.   © 2015 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2015;3:481-8)

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The use of combustible tobacco products is causally linked to chronic obstructive pulmonary disease (COPD), lung cancer, tuberculosis, pneumonia, asthma, and cardiovascular disease, as well as many other noncardiopulmonary diseases.[1] Since 1965, there have been more than 20 million estimated premature deaths caused by smoking and exposure to secondhand smoke. Similarly, the Surgeon General estimates that if current trends continue, an additional 5.6 million US individuals currently younger than 18 years will die prematurely as a result of smoking.[1] Despite a significant decline in the number of adult smokers in the US over the past 50 years, approximately 18% of the US population continues to smoke.[2] The Centers for Disease Control and Prevention estimated that between 2000 and 2004 there were 443,000 premature deaths, 5.1 million years of potential life lost, and $96.8 billion annual productivity losses in the United States.[3] Moreover, the most recent evidence suggests that the health toll of smoking is even worse than previously noted, with links to deaths from renal failure, breast and prostate cancer, infections, and various other respiratory diseases.[4]

Smoking cessation is particularly relevant for individuals with COPD because it is known from multiple studies that individuals who quit smoking experience an initial improvement in pulmonary function, a decreased rate of normal age-related decline in FEV_1, a lower risk of hospital admission, and improved survival.[5-9] Despite being equally motivated to quit smoking compared with healthy smokers, patients with COPD typically suffer from a higher degree of tobacco dependence, smoke more cigarettes per day, and have a more difficult time quitting smoking.[10] Consequently, they represent a unique population that may require intensive treatment to gain control over the compulsion to smoke.

This review will discuss standard therapies for tobacco addiction, will provide the clinician with a relevant approach to evaluation and treatment, and will briefly consider areas of uncertainty, including the public health controversy surrounding the use of electronic cigarettes (e-cigs) and snus.

CHRONIC DISEASE MODEL FOR TOBACCO DEPENDENCE

One of the greatest challenges in treating tobacco dependence is the degree to which cigarettes are addictive. Nicotine, the major addictive component of tobacco, is delivered to the pulmonary circulation and reaches the arterial circulation and brain within seconds after inhalation.[11,12] After reaching the brain, nicotine binds to nicotinic cholinergic receptors and causes release of multiple neurotransmitters including dopamine, glutamate, and gamma-aminobutyric acid. The net biologic effects are feelings of pleasure, satisfaction, heightened mood and concentration, and relief from stress and anxiety. Furthermore,

Abbreviations used
COPD- chronic obstructive pulmonary disease
* e-cigs- electronic cigarettes*
*   FDA- Food and Drug Administration*
FTND- Fagerström Test for Nicotine Dependence
*   NRT- nicotine replacement therapy*

other additives and constituents of smoke such as monoamine oxidase inhibitors produced from acetaldehydes potentiate the level of tobacco addiction by reducing the metabolism of dopamine.[13,14] Following prolonged and recurrent tobacco smoking, tolerance, desensitization, and upregulation of nicotine receptors occurs, which leads to craving, addiction, and withdrawal symptoms when nicotine is no longer present.[15,16]

Multiple studies have shown high relapse rates among smokers attempting to quit.[17-19] Strong and long-lasting cravings and other symptoms of withdrawal are commonly implicated in disrupting quit attempts and causing relapses.[20,21] Given the difficulty of quitting and the frequency of relapses, tobacco dependence must be viewed as a chronic disease. Just as conditions such as COPD, asthma, diabetes, and hypertension are chronic conditions prone to exacerbation, tobacco dependence is a long-term condition that must be managed through episodes of relapse and remission. Recognition that relapses are not indicative of patient or provider failure, but instead reflect a common part of the course of the illness, can allow patients and health care providers to focus on refining the treatment plan and arranging regular follow-up.

CLINICAL INTERVENTIONS FOR SMOKING CESSATION
Brief clinician interventions

Brief physician advice is the most important first step in promoting smoking cessation and has been shown to significantly increase long-term quit rates.[22,23] Utilizing smoking status as a vital sign is recommended because it has been shown to significantly increase recognition of smokers in the clinical setting.[24] The advice provided and the approach to initiating management will differ depending on whether a smoker is willing to quit or not. For smokers who are unwilling to quit, motivational interviewing is a technique that has been shown to be effective in assisting smokers in quitting, either alone or in combination with pharmacotherpy.[25-27] Motivational interviewing uses nonconfrontational counseling and expression of empathy to encourage smokers to consider changing their behaviors.[22,28] The purpose of this counseling is to assist smokers in moving from a precontemplative stage to a contemplative stage of change by highlighting the benefits of quitting and empathizing with the smoker's ambivalence. An acknowledgment and exploration of patient concerns regarding quitting such as fear of weight gain or withdrawal symptoms may help ease fears of making a quit attempt and address barriers to quitting.

Another concept that has gained recognition is the calculated "lung age," which has shown promise in motivating smokers with chronic lung disease to stop smoking.[29,30] *Lung age* is defined as the age of the average person who has an FEV_1 equal to that of the individual. Because people who smoke experience a more rapid decline in FEV_1 than do nonsmokers, a smoker's lung age will be higher than his or her chronologic age. A

multicenter randomized controlled trial provided smokers with spirometry results either as a raw number or as measured by their lung age.[29] Participants were then advised to quit smoking and given access to a local smoking cessation service. Those randomized to the lung age group had a significantly higher quit rate at 12 months than did the FEV_1 raw number group. The mechanism by which this effect occurred was not entirely clear because subjects with worse lung age were no more likely to quit than were subjects with normal lung age in either group. However, the study was not powered to detect differences among people with varying severity of lung disease. A more recent meta-analysis of 15 clinical trials studied the efficacy of providing additional biomarkers to motivate individuals to quit smoking.[31] There was no evidence that providing carbon monoxide level, spirometry, or genetic susceptibility to lung cancer increased smoking cessation rates in this meta-analysis.

More recent evidence has begun to emerge that initiating treatment and encouraging a more gradual reduction in smoking among patients willing to cut down but not yet ready to quit may also be beneficial and improve long-term quit rates.[32-39] Counseling and pharmacotherapy can be effective for this group of smokers, and consequently these patients should be approached and treated in a similar manner as those who are ready to stop smoking.[27,32,37,40]

For smokers who are ready to quit, the clinician should offer support and facilitate setting a quit date, ideally within the next 2 weeks.[22] An evaluation of the level of tobacco dependence and the history of withdrawal symptoms is useful in determining a treatment plan, followed by a discussion of treatment options (reviewed below) and arrangement of follow-up.

Assessing the level of tobacco dependence and withdrawal symptoms

Assessment of a smoker's severity of tobacco dependence is one of the most important steps taken before initiating appropriate treatment. Individuals with higher levels of dependence will require more intensive interventions to achieve smoking cessation and need to be identified before treatment is started. The Fagerström Test for Nicotine Dependence (FTND) is one of the most commonly used tools for assessing the severity of tobacco dependence (see Table I).[41] The test is a 6-item scale, and its total score is closely related to biochemical measures of intensity of smoking.[41] The questions from this scale focus on how quickly a person smokes after waking ("time-to-first cigarette"), intensity of smoking, and smoking patterns during the day. An analysis of the relationship between smoking cessation success and the FTND in individuals enrolled across multiple smoking cessation clinical trials found that the "time-to-first cigarette" in the morning item was the strongest predictor of cessation outcome.[42] These findings suggest that those who smoke their first cigarette within 5 minutes of waking have the highest levels of tobacco dependence and are likely to require the most intensive treatment to ensure a successful attempt at cessation. Assessing the patient's level of dependence is a critical step in determining the appropriate initial therapy because those with higher levels of dependence are less likely than those with lower levels of dependence to succeed without combination therapy.

A second important step is assessing the severity of withdrawal symptoms from previous quit attempts, and on each subsequent visit after a quit attempt is made. Common symptoms include