

Smoking as a Chronic Disease

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Abstract Despite remaining the leading cause of preventable death in the United States, tobacco smoking does not garner the attention it deserves in the medical and public health communities. Smoking is often referred to merely as a “bad habit” that simply requires adequate willpower to conquer effectively. Fortunately, recent attitudes regarding smoking, as illustrated by the latest US Public Health Service Clinical Practice Guidelines, call for a “chronic disease model” for treating tobacco dependence. This article underscores the importance of viewing smoking as a chronic disease by illustrating the effects on morbidity and mortality, discussing the relapsing nature of addiction, outlining the need for continuum of care for different “severities” of illness, and describing the latest research regarding effective treatment components. Tobacco dependence treatments are safe, effective, and cost-saving, and their use should be encouraged and covered by health insurance analogous to other chronic conditions.

Keywords Smoking cessation · Tobacco dependence · Nicotine replacement · Cessation pharmacotherapy · Chronic disease model · Cardiovascular risk factor

Introduction

The concept of treating tobacco dependence as a chronic condition is not new. The US Public Health Service (PHS)

Clinical Practice Guidelines from 2000 stated this concept and explained that tobacco dependence often requires repeated interventions [1]. Instead of viewing smoking and tobacco use as a “bad habit” that can be cured with willpower, a more practical model describes smoking as a chronic relapsing condition that often requires ongoing medical and behavioral treatment. However, the manner in which our society discusses smoking and tobacco dependence treatment reveals several biases that underscore an agenda seeking to “cure” smoking in a defined period of time instead of treating it as a chronic condition. For example, smokers “quit” smoking, insurers reimburse a set number (if any) of counseling sessions or medication prescriptions per year, and the package labeling of over-the-counter nicotine medications contains a “cook book” treatment course of therapy. This emphasis may be one of the key reasons why our overall treatment success is suboptimal.

This article describes important topics related to treating tobacco use as a chronic condition and its impact on cardiovascular risk and disease. First, the review compares smoking and tobacco dependence treatment to other cardiovascular risk factors. Second, the spectrum of settings where tobacco dependence treatment can be instituted is discussed. Third, the article addresses the concepts of nicotine dependence and consideration of the risks and benefits of extended duration pharmacotherapy. Finally, an update of key pharmacologic advances that pertain to treating highly dependent smokers is provided.

Cardiovascular Consequences of Tobacco Dependence

Cardiovascular disease kills more people in the United States than any other condition, nearly 650,000 people per year [2], and tobacco use remains one of the most important

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risk factors in the development and progression of cardiovascular disease. Several components in tobacco smoke contribute to its cardiovascular harm. Substances such as carbon monoxide reduce the oxygen carrying capacity of red blood cells, thus forcing the circulatory system to increase its efforts to deliver needed oxygen to all cells of the body while also predisposing the heart to rhythm disturbances. Oxidizing chemicals, such as polycyclic aromatic hydrocarbons, cause inflammation and can lead to atherosclerosis. These same oxidizing chemicals can cause endothelial dysfunction and promote vascular damage. Other toxins in tobacco smoke are thrombogenic and can increase platelet adhesiveness, predisposing to clot formation within the vessel [3]. Nicotine itself has some modest physiologic effects on pulse, blood pressure, and vascular tone. However, these are mild in comparison with the other cardiovascular effects of the numerous other toxins [4]. However, despite the degree to which smoking leads to coronary artery disease and cerebrovascular disease, cessation treatment is still not widely implemented.

The concept of risk factor reduction identifies conditions that lead to serious medical outcomes and takes steps to minimize their impact. There are several major risk factors that contribute to cardiovascular disease, such as smoking, hypertension, diabetes, and hyperlipidemia. Physicians often have the impression that treatment success rates for tobacco dependence are inferior to those commonly seen in other chronic conditions, such as diabetes and hypertension. In fact, with 6-month to 1-year outcomes, the overall abstinence rates for comprehensive tobacco treatment are similar (25–30%) to those for successful treatment of hypertension (27%) or diabetes (40%) as assessed by standard clinical targets [1, 5, 6]. However, there are significant disparities in the level of health insurance coverage afforded each of these conditions, with hypertension and diabetes being almost universally covered and tobacco dependence coverage severely limited. Data from large cohort studies have been able to quantify the magnitude of risk that each of these factors plays in cardiovascular disease [7, 8]. A previous article written by the authors compared smoking with diabetes [9], so this article focuses on the other major risk factors.

In some models of predisposing factors, smoking carries with it the largest increase in cardiovascular risk. Based on Framingham data, one can look at the example of a 45-year-old man (Fig. 1). As a nonsmoker with a baseline total cholesterol of 200 mg/dL and systolic blood pressure of 120 mm Hg, this person has a 10-year risk of developing cardiovascular disease of 3%. However, while keeping all other variables constant, if he is a smoker, his risk of cardiovascular disease increases to 10%. Using the same model, with a nonsmoking individual, if his cholesterol levels are increased from 200 mg/dL to 300 mg/dL, then his

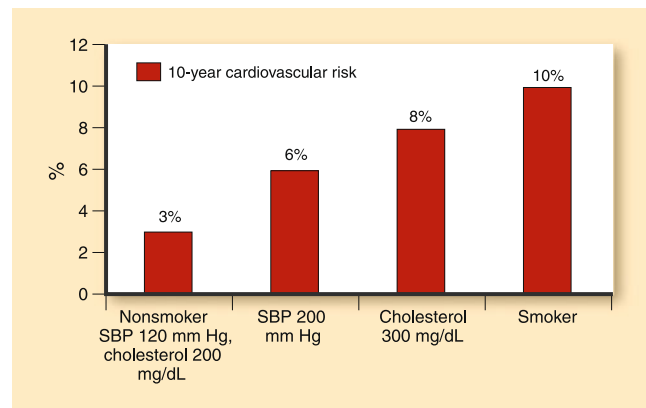


Fig. 1 Ten-year cardiovascular risk for varying cardiac risk factors. *SBP* systolic blood pressure

cardiovascular risk increases from 3% to 8%. If other factors were kept stable, an increase in systolic blood pressure from 120 to 200 mm Hg would increase his cardiovascular risk from 3% to 6%. Thus, the increase resulting from smoking is greater than other significant changes in risk factor status.

In addition to the higher cardiovascular risk of smoking as compared with other risk factors, treatment for tobacco dependence compares favorably with other risk factor reduction interventions from a cost-benefit standpoint. In some studies, treatment for smoking costs in the range of \$2,600 to \$8,000, whereas treating hypertension can cost from \$7,000 to \$127,000 and treating high cholesterol can cost from \$15,000 to \$1.7 million per year of life saved [10]. Other studies looking at secondary prevention show that effective tobacco treatment interventions typically cost \$2,000 per quality adjusted life-year (QALY) [11], whereas evaluation of cost-effectiveness of aspirin for secondary prevention in coronary heart disease estimated a ratio of about \$11,000 per QALY gained [12], and statin therapy for hyperlipidemia has demonstrated costs in the range of \$59,000 per life-year saved for persons in the highest-risk category [13].

Kahn et al. [14] studied the impact of a variety of prevention activities to reduce the burden of cardiovascular disease. These interventions, such as providing aspirin to high-risk individuals, lowering low-density lipoprotein (LDL) cholesterol in people with existing heart disease, or controlling pre-diabetes, are expensive as currently delivered. However, smoking cessation was the only strategy that provided cost-savings over the future 30 years [14]. Despite its importance for cardiovascular risk and the availability of cost-effective interventions, treatment for tobacco dependence does not receive the degree of insurance coverage for medical encounters or medications provided to the other risk factors. Medical office visits for diabetes, hypertension, or high cholesterol are reimbursed at the standard rate for

insurance payment. Visits for tobacco treatment are often not a covered diagnosis or only reimbursed as an “add-on” to an existing office visit. It is typical for people diagnosed with diabetes, hypertension, and high cholesterol to be on treatment medications for decades, if not for the patient’s lifetime. These medications are commonly reimbursed by most insurance plans. In contrast, tobacco cessation pharmacotherapies often are not covered at all, and if covered, often carry a limit in terms of the duration of allowable use. The differences in coverage for the leading risk factor of cardiovascular disease reflect the bias against treating smoking as a chronic disease and need to be corrected.

Continuum of Care for Treatment of Tobacco Dependence

Each smoker possesses a unique severity of dependence and need for treatment. As with other chronic diseases, smoking needs to be treated across a continuum of care. Tobacco dependence treatment can occur in a variety of settings, each of which contributes an important component to comprehensive care. The settings described in this section are not meant to be an exhaustive list of treatment opportunities. As tobacco treatment has expanded, so has the number of provider types and settings where this care can be delivered. For example, nurses, respiratory therapists, psychologists, physicians, social workers, dentists, addiction counselors, health educators, and pharmacists, just to name a few, can all be important components of tobacco treatment. In addition, tobacco treatment and education can be delivered outside of the traditional health care setting in such places as health fairs, workplaces, 12-step programs (eg, Nicotine Anonymous), correctional facilities, addiction treatment programs, day programs, halfway houses, and so forth. With this breadth of resources in mind, we discuss some of the common arenas where this type of care is typically found.

The primary care setting remains one of the most important delivery sites for tobacco treatment. Smokers continue to see their providers on a regular basis, multiple times each year, with the establishment of a provider–patient relationship. Smokers are seen for annual physical examinations or acute medical illnesses, both of which present opportunities to discuss tobacco use either as part of a comprehensive evaluation or as adjunctive treatment for a tobacco-caused illness, such as bronchitis or asthma. At these encounters, the provider has the opportunity to utilize the “5 A’s” as described by clinical practice guidelines (Ask, Advise, Assess, Assist, Arrange) [15••], or depending on the available resources, A-A-R (Ask, Advise, Refer for specialty treatment). The primary care setting allows for longitudinal care with familiar clinicians, regular follow-up,

and awareness of the patient’s full medical and psychiatric history. It also provides potential access to all cessation pharmacotherapies, including prescription-only medications, written by the patients’ provider at the time of the visit. However, the primary care setting does present barriers for tobacco treatment. Providers perceive tobacco treatment encounters as time consuming, so a lack of time is typically identified as an issue, as are competing priorities, lack of training, and poor reimbursement [16]. However, certain system interventions can help improve the delivery of tobacco treatment in primary care, such as a universal system for tobacco use identification, provider reminders, dedicated staff, proper training on effectively treating tobacco dependence, and referral systems.

Another important advance in primary care tobacco treatment has been the utilization of electronic medical record (EMR) systems. These systems have the ability to facilitate tobacco treatment in a primary care setting in a variety of ways. Most of these systems allow for the systematic identification of all smokers in a practice, as recommended by the Public Health Service (PHS) Guidelines [15••]. They also allow for establishing clinical protocols for appropriate medication use (ie, data from the EMR system can be used to automatically indicate or contraindicate certain cessation medications). Finally, technology exists to generate electronic referrals to specialty treatment services, such as face-to-face tobacco treatment clinics or telephone quitlines. These EMR applications have been shown to be effective in documenting smoking status and increasing counseling under these circumstances [17].

The general medical hospital is also a critical site for delivering tobacco treatment interventions. Smokers who are admitted both with tobacco-related illnesses or other illnesses benefit from interventions during their hospitalization. When followed by post-discharge counseling, these in-hospital interventions have been shown to increase abstinence rates following discharge [18], with the most important characteristics improving outcomes being the intensity of treatment and length of follow-up (ie, at least 1 month). Recent advances in treating hospitalized smokers have also utilized EMR components, which can effectively assist in bedside counseling, medication prescribing, and follow-up [19]. For surgical patients, intensive interventions during the pre-operative period can impact smoking cessation rates and surgical complications [20].

One of the most important changes that has the potential to dramatically improve the care of hospitalized smokers is the new standards proposed by the Joint Commission regarding tobacco treatment [21]. Under its 2005 standards, the Joint Commission had only required that hospitals identify and “intervene” with smokers admitted with one of three diagnoses: 1) acute myocardial infarction, 2) congestive heart failure, and 3) community-acquired pneumonia.

Often, hospitals would achieve full compliance by implementing universal measures that did not significantly change actual practices or impact outcomes (eg, a tobacco-specific hospital print-out sheet as part of a voluminous discharge packet provided to all patients, regardless of smoking status). The newly proposed standards would require hospitals to deliver more specific treatment and implement follow-up. The four proposed measures for tobacco would include: 1) tobacco screening, 2) tobacco dependence treatment documenting the offer of a cessation medication during hospitalization, 3) establishing a treatment plan including pharmacotherapy at discharge, and 4) conducting follow-up contact after discharge to determine smoking status and quit attempts. These new objectives have the potential to significantly increase the quality of care delivered to hospitalized smokers.

Although the proposed standards will dramatically improve the intensity of tobacco dependence treatment in hospitalized smokers, currently, the most intensive type of tobacco dependence intervention consist of specialty treatment. These treatment modalities typically include Internet-based resources, telephone-based treatment, and face-to-face treatment. Each of these modalities has its advantages and drawbacks as outlined in Table 1, and thus each contributes to an effective and comprehensive scope of care. Just as one would not simply offer all patients with cardiac disease the sole option of bypass surgery regardless of their specific disease severity or needs, these multiple tobacco treatment modalities provide an individualized level of care. Multiple treatment options exist for patients with cardiac disease, including primary prevention medications (eg, statins), secondary prevention medications

(eg, β -blockers, nitrates, aspirin), angioplasty, pacemaker/defibrillator, and bypass surgery. Just as cardiac disease is not a “one-size-fits-all” condition, a continuum of care is appropriate for all chronic conditions, including smoking.

Chronic Treatment of the Highly Dependent Smoker

The goal of tobacco dependence treatment seems fairly straightforward. However, debate still exists as to the objectives along the way. Most would agree that reducing tobacco-related death and disease is a universal objective in this field. However, there is still some debate about whether the benefit of medical cost reduction following abstinence is offset by the cost of those individuals living longer. These discussions usually exclude mention of improved quality of life for smokers who quit. Finally, as outlined below, one of the most contentious debates involves the discussion of implications for addiction to tobacco versus addiction to nicotine.

One of the cornerstones of pharmacologic treatment of tobacco dependence is the use of nicotine replacement therapies (NRT). These medications have been available for over 25 years and have a long track record of safety and efficacy [15••, 22]. There have been many barriers described in relation to the utilization of nicotine replacement medications [16], and recent efforts have been made to reduce these impediments to treatment [23].

One of the issues is the concern regarding the “harm” of nicotine. Many studies describe the safety of long-term use of NRT [24, 25•]. Compared with tobacco smoke, nicotine levels with NRT are lower, reach the brain more slowly, and

Table 1 Comparison of specialty tobacco treatment modalities

Treatment modality	Advantages	Limitations
Internet-based resources	National and state resource, wide distribution, ability to deliver large amounts of information at the user’s own pace, available 24 h/d 365 d/y, interaction with other users (chat rooms), ability to link to other related resources	Does not deliver “treatment” in the usual sense, inability to tailor interventions to individual needs (generic only), lack of “personal” aspect of information delivered, need for computer equipment and access
Telephone counseling	Fastest growing modalities for tobacco treatment over the past 5 years, National quitline and state quitlines exist, ability to serve a large population, convenience for rural areas, lower cost, moderate ability to deliver tailored treatment through individualized information, including mailing of medications to clients, evidence for effect on abstinence (12.7% quitline vs 8.5% self-help [15••])	Need telephone access, unable to confirm abstinence outcomes, lack of information and non-verbal cues from the client, limited ability to fully explore clinical history, less effective establishment of clinician-client relationship, lower level of intensity and inability to deliver group treatment
Face-to-face specialty counseling	Prolonged and detailed clinical encounter, higher quality patient–provider clinical relationships, ability to specifically tailor treatment plan including use of all FDA-approved medications, higher levels of treatment intensity (including group treatment), closer monitoring for adverse effects and withdrawal symptoms, including non-verbal clinical signs, evidence for effect on abstinence (16.8% vs 10.8% [15••])	Higher costs associated with more highly trained clinicians and a clinical site, need for clients to travel and attend on site (relatively local reach)

FDA US Food and Drug Administration.

contain none of the more than 4,000 toxins found in smoke that result in tobacco-caused diseases [3, 15••]. However, beliefs and misperceptions among smokers and health care professionals of nicotine's role in tobacco smoke have prevailed. Many smokers and health care professionals incorrectly believe that nicotine causes cancer and heart attacks, and that NRT is no safer than smoking. In one study, only 35% of individuals believed that the nicotine patch was less likely to cause a heart attack than smoking cigarettes, and only 33% disagreed that nicotine is a cause of cancer [26]. These beliefs impact the use of effective treatments, such as NRT. In fact, only 25% of smokers in the United States making a quit attempt in the past 6 months used NRT, compared with 36% in the United Kingdom and Canada [27].

There are several outcomes that are possible in tobacco dependence treatment. Abstinence by complete elimination of all tobacco-caused harm with no long-term risks is the best-case scenario. Alternatively, one can achieve tobacco use reduction. Depending on the degree of reduction, one can lower health risks from significant reduction of exposure to toxins. However, the smoker is still exposed to dangerous toxins. For many diseases (eg, cancer), there is a zero-safety threshold. Finally, a possible outcome could include elimination of tobacco use but via long-term nicotine substitution. In this case, the user has exposure to some small potential physiologic effect of nicotine, but a 95% or more reduction in overall health risk [28]. This modality could perpetuate addiction to nicotine, has some small cardiovascular effect, and costs more. However,

concerns have also been raised about increased risk for cancer on the basis of evidence from in vitro and in vivo studies showing that nicotine can result in tumor promotion through increased cell proliferation, inhibition of apoptosis, and angiogenesis [29, 30]. Although these data suggest that nicotine may act as a tumor promoter, these findings have not been demonstrated in over 25 years of human use, and nicotine supplementation is undoubtedly safer than the continuation of smoking.

Another issue is the concern regarding the “addiction” to nicotine, which may be interpreted and addressed very differently depending on the provider who is overseeing treatment. One of the unique aspects of tobacco dependence treatment is that it incorporates clinicians from a wide variety of disciplines. Each of these providers brings with them a different training, background, and orientation. Often, physicians will focus on the medical outcome (ie, “what will end up killing my patient?”). Psychologists and other behavioral health providers may focus on motivation and changing behavior (ie, “how can I help my patient change his/her behaviors?”). An addiction counselor may focus on the substance addiction (ie, “we need to break the addiction to nicotine”). So, depending on one's orientation, successful tobacco treatment goals might range from no smoking with allowance for life-long NRT to no use of nicotine in any form.

Tobacco dependence shares similar characteristics with other substance dependence. However, it also has some unique features (Table 2) [31]. One model that has become widely accepted is long-term use of methadone to treat

Table 2 Comparison of various substance dependence conditions

	Alcohol	Cocaine	Heroin	Tobacco
Intoxication	High	Moderate	High	Low
Physiologic dependence	Moderate	Moderate	High	High
Withdrawal	High (medically serious)	Moderate	High	High
Legal	Yes	No	No	Yes
Large industry influence	Yes	No	No	Yes
Number of users	100 million	5 million	500,000	60 million
Significant medical harm	Liver disease, heart disease, pancreatitis, cancer	Heart disease, stroke, nasal damage, infection, GI damage, kidney damage	Respiratory failure, infection	Heart disease, lung disease, multiple cancers, stroke, pulmonary infections
Deaths per year, <i>n</i>	150,000	2,000	2,000	400,000
Treatment	Detox, counseling, programs, 12-step program, medications	Detox, counseling, programs, 12-step programs	Detox, counseling, programs, 12-step program, medication	Programs, counseling, quit-lines, 12-step programs, medications
Medications	Naltrexone, disulfiram, acamprosate	None	Methadone	NRT, bupropion, varenicline

GI gastrointestinal; NRT nicotine replacement therapy. (Data from Brick [31].)

heroin abuse. The goals of methadone maintenance treatment are to decrease heroin use and the crime, death, and disease caused by heroin addiction. Methadone maintenance treatment is typically an option for heroin users with multiple failed attempts at other types of treatment such as detox, rehab, and outpatient treatment. Patients are given a daily dose of methadone which suppresses withdrawal from heroin, morphine, and other opioid drugs for about 24 to 36 h. The principal effects of methadone maintenance are to relieve narcotic craving, suppress the abstinence syndrome, and block the euphoric effects associated with heroin [32]. The patient becomes physically dependent on methadone but is no longer impaired by the uncontrollable and disruptive behavior seen in heroin addiction, allowing them to lead normal functioning lives.

The methadone maintenance treatment model for heroin-addicted people demonstrates a plausible model for long-term nicotine replacement treatment for cigarette smokers. Nicotine meets criteria for drug dependence in that it promotes compulsive use, has psychoactive effects, and reinforces its own use [33]. Smokers experience similar symptoms of other drug addictions such as tolerance, withdrawal, and loss of control. Nicotine replacement is an effective alternative to smoking because nicotine is the substance in tobacco that maintains the behavior. Although not yet approved by the US Food and Drug Administration, long-term use of nicotine replacement medications may still be considered for smokers who have tried other options and who have had numerous failed attempts to quit. Effective nicotine maintenance treatment has the potential to reduce mortality and morbidity, improve quality of life, and manage or eliminate withdrawal.

Advances in Pharmacotherapy

One of the breakthroughs of tobacco dependence treatment over the past 30 years has been the utilization of pharmacotherapy. Despite the numerous trials and thousands of successful patients, pharmacotherapy is vastly underutilized [34•]. However, there have been significant advances in the area of pharmacotherapy for tobacco dependence even over the past few years.

Combination therapy continues to be studied and its benefits demonstrated in various ways. The 2008 Public Health Service Guidelines summarized the data regarding trials of pharmacotherapy that suggest combinations of nicotine patch with gum, inhaler, and nasal spray, as well as combinations of NRT with bupropion, are effective [15••]. Other studies of combination medications included an assessment of five differing combinations in a primary care setting along with referral to telephone counseling [35•]. This study demonstrated that the combination of sustained-

release bupropion plus nicotine lozenge had the highest 6-month abstinence rate (29.9%), with the nicotine patch plus lozenge next (26.9%), and both were superior to single medications (16.8–19.9%). Another recent study of combination therapy demonstrated that in a sample of smokers with medical illnesses, the combination of nicotine patch, nicotine inhaler, and sustained-release bupropion was superior to patch alone (6-month abstinence rates of 35% for combination vs 19% for patch alone; $P=0.04$), with adjusted odds ratio for abstinence of 2.57 (95% CI, 1.05–6.32; $P=0.04$) [36•]. Recently, investigators have evaluated the combination of varenicline, the newest cessation medication, with other therapies. Ebbert et al. [37] reported a case series of smokers who used varenicline plus NRT ($n=104$) compared with usual care smokers who were treated prior to the release of varenicline ($n=135$). They found that the combination of varenicline with NRT was safe and well-tolerated in a residential tobacco treatment program [37]. An open-label trial was also conducted to evaluate the effectiveness and safety of varenicline combined with bupropion [38]. This small, non-randomized study suggested that this combination may be beneficial and was well tolerated. The two medications work through differing mechanisms of action, and thus could potentially have a cooperative effect.

In addition to new data regarding combination treatment, there have been recent studies looking at extended duration of treatment. One study examined the benefit of nicotine patch treatment for 24 weeks compared with standard 8 weeks and found a significant benefit on abstinence (31.6% vs 20.3%) and recovery from lapses in the longer-duration treatment [25•]. Additionally, an estimation of expanded use of NRT at the population level demonstrated that an increase in the proportion of NRT-assisted quit attempts to 100% would lead to approximately 40,000 avoided premature deaths over a 20-year period [39•].

Other studies evaluated the “pre-treatment” use of NRT prior to the target quit date. The first of these focused on the concept of using NRT in smokers who were not ready to set a quit date as a means to reduce consumption [40]. This review found that in trials that included regular behavioral support, use of NRT resulted in sustained abstinence in nearly 7% of smokers who had no intention or were unable to attempt an abrupt quit. Two other studies evaluated the benefit of pre-treatment with a nicotine patch [41] and nicotine gum [42] prior to quit date. The first of these studies found that smokers who received active nicotine patch 2 weeks prior to cessation had a 22% continuous abstinence rate at 10 weeks compared with 11% in those who received placebo patch during the pre-cessation period [41]. This concept is often used with non-nicotine pharmacotherapies (bupropion and varenicline), which are started 1 to 2 weeks prior to the target quit date. Perhaps similar

changes in brain chemistry that are observed with these non-nicotine medications could also explain the effect of nicotine replacement. However, the second of these studies found that pre-treatment for 4 weeks with nicotine gum did not increase abstinence rates [42].

Conclusions

Tobacco smoking remains one of the most important chronic conditions from a medical and public health perspective. It is a leading risk factor for cardiovascular disease, contributing to higher morbidity than most other risk factors. It is associated with a physiologically addictive component that makes it difficult to treat and evokes debate over the benefits of long-term pharmacologic replacement. Finally, tobacco dependence treatment can now be delivered by a variety of providers, under a variety of settings, and includes state-of-the-art medication advances, thus providing a continuum of care for all smokers. The idea of tobacco dependence as a chronic condition is one whose time has come and implies a need to rethink how society views and reimburses for these treatments as a means of delivering good quality and cost-effective healthcare to reduce the high burden of tobacco-caused diseases.

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