

UNDERSTANDING AND ADDRESSING NICOTINE ADDICTION



A SCIENCE-BASED APPROACH TO POLICY AND PRACTICE

OCTOBER 2015

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Accompanying Statement by Samuel A. Ball, PhD, President and Chief Executive Officer

The fact that tobacco use, especially in the form of cigarettes, is one of the most costly and deadly health threats in the world is undisputed. Tobacco, tar and the many poisonous chemicals that are found in cigarettes and other combustible tobacco products cause immeasurable harm and contribute significantly to skyrocketing health care costs.

A critical determinant of the harms caused by smoking is nicotine, which reinforces the continued use of tobacco products. Nicotine is one of the most highly addictive substances, perpetuating cigarette and other tobacco product use, hindering smoking cessation efforts and increasing the risk of other substance use, addiction and a number of adverse health consequences.

Alternative, non-combustible products that contain nicotine but no tobacco--such as electronic cigarettes and other electronic nicotine delivery systems--are considered by most experts to be less harmful than tobacco products. They likely are a better alternative for those who already have a long-term addiction to nicotine, have made unsuccessful quit attempts, and would otherwise smoke cigarettes or use other tobacco products and not quit. However, the recent proliferation of these alternative nicotine products--especially their use among youth--is cause for serious concern. By some estimates, the prevalence of electronic cigarette use has seen a three-fold expansion over the course of one year among middle and high school students.

Emerging evidence indicates that non-combustible nicotine products are by no means harmless. They are not used exclusively as a substitute for cigarettes and have not shown clear proof of efficacy for tobacco cessation. Rather, they frequently are used in conjunction with cigarettes and by young people who do not yet smoke cigarettes and who might otherwise not have been susceptible to smoking. In addition, certain alternative nicotine products, like electronic cigarettes, also expose the user and nonusers to aerosols that contain numerous toxic chemicals. The fact that these products are unregulated by the government means that their nicotine content and emitted toxins are highly variable and difficult to determine, and that the companies that manufacture and distribute them have few restrictions on how and to whom they can be marketed. The assertive movement of "big tobacco" companies into this market is a cause for grave concern among public health experts.

The heated debate around nicotine products and the lack of certitude demonstrated by policymakers regarding their regulation reflects the deficient state of research evidence regarding their risks and potential benefits. Regardless of whether its delivery is through a combustible cigarette, an electronic cigarette, a hookah pipe or a cigar, nicotine remains one of our most addictive and potent "gateway drugs," associated with the later use of other addictive and dangerous substances. It is essential that the public be better informed about an addictive substance like nicotine that is seeing a resurgence in use, especially among youth. It also is critical for the actions taken by policymakers and health professionals to be informed by the research evidence, rather than by assumptions, misinformation, anecdote or industry interests.

To that end, CASAColumbia[®] has developed this white paper, *Understanding and Addressing Nicotine Addiction: A Science-Based Approach to Policy and Practice.* This paper summarizes the evidence regarding the prevalence and correlates of nicotine use and addiction, the effects of nicotine on the brain and body, the risk factors for nicotine addiction and the groups most at risk, current prevention and treatment efforts, and the implications of this research for policy and practice.

Public health and policy efforts have been remarkably successful in reducing rates of cigarette smoking in the United States over the past few decades. However, both the commercial interests of the tobacco industry and the natural human proclivity toward risk-taking, pleasure seeking and addictive behaviors require that we do not become complacent in allowing alternative nicotine products to undo decades of hard-won progress in reducing the enormous health and financial costs of tobacco and nicotine use. A rational and science-based approach to the regulation of all nicotine-containing products is required. Adequate attention must be paid to preventing the use of all addictive substances, including nicotine, and providing effective treatments that reduce or eliminate harm to those with addiction.

We extend special thanks to the Truth Initiative, formerly Legacy, for their generous financial support of this project.

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While many contributed to this effort, the opinions expressed herein are the sole responsibility of CASAColumbia.

Understanding and Addressing Nicotine Addiction: A Science-Based Approach to Policy and Practice

Introduction

The use of tobacco products is the primary cause of preventable disease and death in the United States.¹ The ingredient in all tobacco products that makes them addictive and that promotes continued use is nicotine.² As such, the main concern with regard to nicotine itself is its ability to perpetuate and reinforce unhealthy tobacco product use by engendering addiction to those products.³ However, research also indicates that nicotine use increases the risk of other substance use and addiction and may on its own have a number of adverse health consequences.⁴

Nicotine is a central nervous system stimulant and is one of the most highly addictive drugs, albeit one that is less euphoria inducing than other stimulants like cocaine, amphetamine or methamphetamine. Nicotine's mechanisms of action on the body contribute to its highly addictive nature. Once ingested, nicotine travels quickly to the brain where it precipitates the release of chemicals that ultimately trigger feelings of reward.⁵ The resulting pleasurable effects become associated with use of the substance and the environments in which it is used.⁶ The immediate physiological effects specific to nicotine, such as decreased appetite, elevated mood and increased concentration, decline rapidly when a person is not actively ingesting it.⁷ Regular use leads to uncomfortable withdrawal symptoms that occur soon after the last dose⁸ and perpetuates continued use.⁹ The relaxing and soothing feelings associated with nicotine use are thought to be due to relief from the symptoms of nicotine withdrawal that emerge after a period of nonuse rather than to the stimulating effects of nicotine itself.¹⁰

Although most studies of nicotine's effects have not examined nicotine in isolation, separate from the other toxic and cancer-causing ingredients in most tobacco and nicotine-containing products, research does suggest that nicotine itself is by no means a harmless drug.¹¹ It affects the nervous, cardiovascular and respiratory systems and there is some evidence, largely from animal studies, that it impairs cardiovascular¹² and lung¹³ function and may contribute to cancerous tumor development.¹⁴ Nicotine also is associated with poor reproductive health outcomes like preterm delivery and stillbirths, and exposure during fetal development and adolescence has lasting adverse effects on brain and lung development.¹⁵ A fatal human dose of nicotine is estimated to be approximately 0.5g or more of orally ingested nicotine (corresponding to an oral median lethal dose of 6.5–13.0 mg/kg).¹⁶

The risk of addiction and the health consequences associated with nicotine raise concerns about the proliferation of alternative (noncombustible) nicotine products, including those that do not contain tobacco, and underscore the importance of examining the short- and long-term effects of nicotine use, regardless of the mode of delivery, on addiction and other health problems.¹⁷

Cigarettes are the most frequently used nicotine-containing product. Cigarette smoking is harmful to nearly every part of the human body,¹⁸ contributing to premature deaths due to cancer, heart disease and lung disease¹⁹ and numerous other health conditions, including respiratory illness and chronic kidney disease.²⁰ An estimated 8.6 million Americans suffer from a serious smoking-related illness.²¹ Recent research demonstrates that the mortality rate among people who smoke cigarettes is two to three times the mortality rate among those who do not smoke.²² The economic costs associated with cigarette smoking are tremendous: an estimated \$300 billion each year is spent on smoking-related illness in the United States, with nearly \$170 billion in direct medical care for adults and more than \$156 billion in lost productivity.²³

Today's cigarettes are more addictive than in the past due to design changes that have increased the efficiency of nicotine delivery and the nicotine yield in tobacco products.²⁴ Additives found in traditional cigarettes--and in alternative (noncombustible) nicotine products--that facilitate nicotine delivery and increase the appeal of the products also may exacerbate their health consequences and the risk of nicotine addiction.²⁵

Despite significant declines in cigarette use over the past few decades, millions of Americans continue to smoke cigarettes. At the same time, the use of other nicotine-containing products such as cigars and hookah, as well as products newer to the market such as electronic cigarettes (e-cigarettes) and other electronic nicotine delivery systems (personal vaporizers, vape pens, e-cigars, e-hookahs, vaping devices), is on the rise.²⁶

Few people would dispute the fact that certain alternative nicotine products such as e-cigarettes, which do not contain tobacco, are less harmful than combustible cigarettes. Yet, a growing body of research suggests that such products are not harmless and often are used in addition to, rather than in place of, conventional cigarettes. Approximately 10 percent of all adults²⁷ and eight percent of all youth²⁸ (nearly two-thirds of youth who report having used such products in the past 30 days²⁹) use two or more nicotine-containing products. Those who use multiple nicotine/tobacco products are more likely to exhibit symptoms of addiction than those who use only one type.³⁰ A growing body of research also indicates that some users of these products are individuals--particularly youth--who have not engaged in and may never have taken up cigarette smoking.³¹ Finally, emerging evidence suggests that these products may not be particularly effective in deterring cigarette smoking and might actually perpetuate cigarette use, especially among young people.³²

Determining exactly how safe a nicotine-containing product may be is difficult because, other than combustible cigarettes, they largely are unregulated and the amount of nicotine each contains often is unknown.³³ A complete understanding of their health effects, addictive potential and association with the initiation or continued use of other nicotine-containing products, including cigarettes, awaits further research.³⁴ Therefore, the proliferation in the availability of alternative nicotine products and in their use, especially among youth, requires careful attention and a measured response informed by the research evidence, rather than by assumptions, misinformation, anecdote or industry interests.

Prevalence and Correlates of Nicotine Use and Addiction^{*}

One in four (25.4 percent) individuals aged 12 and older in the United States reported using a tobacco/nicotine product (21.1 percent used cigarettes) in the past 30 days[†] in 2013.[‡] That year, 37.0 percent of individuals aged 12 and older who reported smoking cigarettes[§] in the past 30 days met diagnostic criteria for nicotine addiction.^{** 35}

Rates of nicotine addiction among those aged 12 and older who reported current (past 30-day) cigarette smoking varied somewhat by demographic variables, with rates:

^{*} Based on analysis of data from the 2013 National Survey on Drug Use and Health (NSDUH).

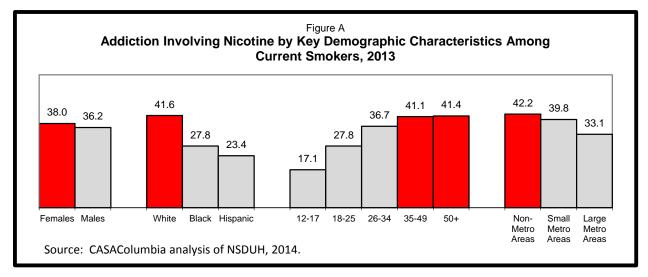
[†] Referred to as "current use."

[‡] Most recent available data.

[§] Nicotine addiction in the NSDUH is measured only in relation to cigarettes and not all tobacco/nicotine products.

^{**} The term "nicotine addiction" is used in this paper in reference to meeting diagnostic criteria for past-month "nicotine dependence," as measured by the Nicotine Dependence Syndrome Scale (NDSS), which is the measure of dependence used in the NSDUH. NDSS criteria generally parallel those for "tobacco use disorder" in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV).

- Similar among females and males (38.0 percent vs. 36.2 percent);
- Higher among white than black or Hispanic respondents (41.6 percent vs. 27.8 percent and 23.4 percent, respectively);*
- Higher among older than younger age groups (17.1 percent of 12-17 year olds; 27.8 percent of 18-25 year olds; 36.7 percent of 26-34 year olds; 41.1 percent of 35-49 year olds; and 41.4 percent of those aged 50 and older); and
- Higher among those living in non-metropolitan areas than among those living in small or large metropolitan areas (42.2 percent vs. 39.8 percent and 33.1 percent, respectively).³⁶ (Figure A)

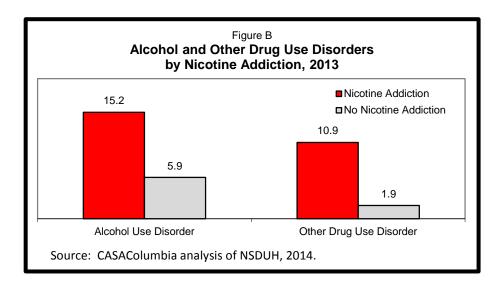


The use of tobacco/nicotine products not only is associated with an increased risk of nicotine addiction itself, but it also is associated with other substance use and addiction.³⁷ Specifically, those[†] who met criteria for nicotine addiction (vs. those who did not) had a higher rate of:

- Current alcohol use (58.3 percent vs. 51.4 percent) and meeting diagnostic criteria for a past-year alcohol use disorder (15.2 percent vs. 5.9 percent);
- Current use of other drugs (25.6 percent vs. 8.0 percent) and meeting diagnostic criteria for a past-year drug use disorder (10.9 percent vs. 1.9 percent): (Figure B)
 - Current marijuana use (21.4 percent vs. 6.4 percent) and meeting diagnostic criteria for a marijuana use disorder (5.9 percent vs. 1.2 percent);
 - Current misuse of controlled prescription drugs (7.9 percent vs. 2.0 percent) and meeting diagnostic criteria for a prescription drug use disorder (4.7 percent vs. 0.6 percent); and
 - Current use of any drug other than marijuana or controlled prescription drugs (3.6 percent vs. 1.0 percent) and meeting diagnostic criteria for a drug use disorder involving those other drugs (3.2 percent vs. 0.4 percent).³⁸

^{* 31.7} percent for 'other' which includes Native American/Alaskan Native (37.1 percent), Native Hawaiian/Other Pacific Islander/Asian (16.5 percent) and Multiracial (45.4 percent).

[†] In the total sample, aged 12 and older.



The differences in the rates of past-year alcohol and other drug use disorders among those with versus without nicotine addiction^{*} was more pronounced among younger than older respondents. Specifically, among youth aged 12-20, more than four times as many of those with versus without nicotine addiction had an alcohol use disorder (23.0 percent vs. 5.2 percent); among respondents aged 21 and older, more than twice as many of those with versus without nicotine addiction had an alcohol use disorder (14.7 percent vs. 6.0 percent). Similarly, among youth aged 12-20, seven times as many of those with versus without nicotine addiction had a drug use disorder (29.6 percent vs. 4.2 percent); among respondents aged 21 and older, approximately six times as many of those with versus without nicotine addiction had a drug use disorder (9.8 percent vs. 1.5 percent).^{† 39}

Characteristics of Nicotine Addiction

Nicotine addiction is a chronic and relapsing disease.⁴⁰ People who meet the diagnostic criteria for nicotine addiction[‡] typically report certain symptoms consistent with addiction involving other substances such as craving, impaired functioning without the substance and continued use despite adverse consequences.⁴¹

Mechanisms of Action

People who are addicted to tobacco products are addicted primarily to its main psychoactive ingredient, nicotine.⁴² Nicotine's mechanisms of action within the human body are very similar to the effects of other known addictive substances (e.g., stimulants) and highly rewarding addictive behaviors (e.g., gambling).⁴³

^{*} In the total sample; not just among current smokers.

[†] When the analyses were restricted to current smokers only, the differences in estimated rates of alcohol use disorders were not statistically significant between those with and without nicotine addiction (across age groups), but the differences remained statistically significant, although less pronounced, for estimated rates of drug use disorders.

[‡] Defined in accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for a "tobacco use disorder." Although the accepted term is "tobacco use disorder," it is nicotine specifically that leads to addiction, and addiction can occur in relation to non-tobacco products that contain nicotine. As such, a more accurate term for those who are addicted to the nicotine in tobacco and in non-tobacco products would be "nicotine use disorder" or "nicotine addiction."

Nicotine, an alkaline base, which passes easily through mucosal tissue in the human body,⁴⁴ can be lethal if ingested in concentrated doses.⁴⁵ When tobacco is chewed or smoked, nicotine is absorbed in the mouth by the oral mucosa that lines the cheeks and lips. When inhaled via tobacco smoke or e-cigarette aerosol, nicotine travels to the smallest branches of the lungs where it is absorbed into the bloodstream through the lining of the lungs.⁴⁶ After entering the bloodstream, it reaches the brain within seconds and triggers a cascade of biochemical reactions that are interpreted by the brain as rewarding.⁴⁷

Nicotine also acts on the adrenal glands, triggering the release of natural stimulants including adrenaline. The result is an increase in blood pressure, heart rate and respiration.⁴⁸ The physiological changes resulting from nicotine ingestion and the fast speed at which nicotine reaches the brain and triggers reward centers contribute to its high addictive potential.⁴⁹

The perceived benefits of nicotine use, such as decreased appetite, increased concentration and elevated mood,⁵⁰ primarily are due to its influence on neuronal receptors in the brain.⁵¹ These receptors, called nicotinic acetylcholine receptors, are specifically structured to receive acetylcholine--a biochemical very similar in structure to nicotine--which is responsible for muscle contraction⁵² and cognitive functions such as learning, memory and attention.⁵³

Acetylcholine is essential to normal physiological functioning, and the human body produces it naturally. Nicotine is not produced by the human body--it comes from external sources--but the body allows it to bind to acetylcholine receptors because it is similar in structure.⁵⁴ Nicotine is referred to as a nicotinic acetylcholine receptor agonist because it can mimic acetylcholine's structure and ultimately take over acetylcholine's binding sites. This is one reason for nicotine's high potential for addiction: it commandeers receptors meant for other important, naturally-occurring chemicals.⁵⁵

Once nicotine binds to receptors in the brain, the neurons (brain cells) undergo changes in their pattern of communication with other neurons in their networks. There are many of these neural networks in the brain, and each group is responsible for communicating signals to specific areas. Neurons stimulated by nicotine release excitatory electrical and chemical signals.⁵⁶ One chemical (neurotransmitter) released during this process is dopamine, which binds to receptors and triggers feelings of pleasure.⁵⁷ Dopamine also is strongly implicated in the experience of reward, cue salience, motivation and decision-making, and is a critical factor in addiction involving alcohol, other drugs and certain behaviors such as pathological gambling.⁵⁸

Nicotine's impact on dopamine, however, is not long lasting. Other neurotransmitters, called glutamate and GABA, which are critical for potentiating or attenuating (respectively) dopamine's rewarding effects, are affected differentially by nicotine. Nicotine activates glutamate, which further stimulates dopamine neurons in the brain, and it inhibits or maintains steady levels of GABA, which has the opposite effect on dopamine. These processes help to explain why dopamine levels in the brain remain elevated or amplified for longer periods than can be accounted for merely by the effects of dopamine alone, why even brief exposures to nicotine can result in long-term feelings of reward, and why nicotine use can result in addiction so quickly.⁵⁹

Dopamine communicates with several key areas in the brain. The mesostriatal pathway is composed of a tract of dopaminergic neurons that facilitate communication among structures such as the substantia nigra, related midbrain structures and ultimately the striatum, which is implicated in movement and reward salience.⁶⁰ The mesolimbocortical pathway comprises a tract of dopaminergic neurons that transmit signals from the ventral tegmental area in the midbrain to the limbic system and eventually to the cortex.⁶¹ The communication and reactions that occur along these pathways lead to changes in mood, increased concentration and decreased appetite.⁶² As a result, nicotine use becomes associated with these positive and performance-enhancing effects. Recent research also demonstrates the critical role of the endogenous

cannabinoid system in nicotine addiction, particularly in terms of its role in mediating nicotine's reinforcing effects through the dopamine system.⁶³

After continued use of nicotine, the body adjusts to its presence and increasing amounts of it are needed to produce the same rewarding effects (i.e., tolerance). Some studies have found that, depending on an individual's metabolism of nicotine,⁶⁴ nicotine receptors may become desensitized to the effects of nicotine.⁶⁵ Others have found that the number of available receptors in the brain increases in response to regular doses of nicotine.⁶⁶ These physiological changes can result in addiction and the key symptoms of irritability, craving and tolerance.⁶⁷ People who develop nicotine addiction begin to experience withdrawal symptoms such as anxiety, depression and cognitive deficits within minutes of their last dose, which make them susceptible to repeated use of the substance to avoid this discomfort.⁶⁸ Initially, withdrawal symptoms can be averted with minimal nicotine ingestion but, over time, as tolerance develops, nicotine ingestion must occur more frequently and at shorter and shorter intervals in order to alleviate the adverse withdrawal symptoms.⁶⁹

As a person enjoys the relaxed state, improved concentration or emotional ease seemingly caused by nicotine, the brain assigns increasing salience to the nicotine-containing product.⁷¹ This association is very powerful and, even when a person is not ingesting nicotine, he or she can experience physiological symptoms associated with craving and withdrawal merely by being exposed to cues that have become mentally linked with nicotine use.⁷² These cues--such as specific times of day, cigarette packaging and lighters, or certain social situations where nicotine use tends to occur--and their effects can be difficult to

manage when a person is attempting to abstain from nicotine. Indeed, these triggering factors, in addition to the uncomfortable withdrawal symptoms associated with smoking cessation, make it difficult for people to stop using nicotine.⁷³ Environmental cues become so strongly associated with nicotine use that they present a substantial risk for relapse.⁷⁴ People are particularly susceptible to triggering cues when they are experiencing stressful life events.⁷⁵

Symptoms

A person with nicotine addiction exhibits certain behaviors that are similar to those seen in people who are addicted to other substances or behaviors, such as using more of the substance (or engaging in the addictive activity to a greater extent) than was initially intended, disregarding physical hazards and other consequences related to use, and failed attempts at cessation.⁷⁶

According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)--the diagnostic tool published by

Tobacco Use Disorder (DSM-5)^{* 70}

Diagnostic Criteria: A problematic pattern of tobacco use leading to clinically significant impairment or distress, as manifested by at least two of the following occurring within a 12-month period:

- 1. Tobacco taken in larger amounts or over a longer period than intended.
- 2. Persistent desire or unsuccessful efforts to cut down or control use.
- 3. A great deal of time spent in activities necessary to obtain or use.
- 4. Craving, or a strong desire or urge to use.
- 5. Recurrent use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., interference with work).
- 6. Continued use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of tobacco.
- 7. Important activities given up or reduced because of use.
- 8. Recurrent use in physically hazardous situations.
- 9. Continued use despite knowledge of having a persistent or recurrent physical or psychological problem likely caused or exacerbated by tobacco.
- 10. Tolerance
- 11. Withdrawal

Specify severity: Mild (2-3 symptoms), Moderate (4-5 symptoms), Severe (6 or more symptoms)

^{*} This is the clinical term used in the DSM 5.

the American Psychiatric Association--a person has to have experienced several symptoms to be diagnosed with nicotine addiction, which the DSM-5 refers to as a Tobacco Use Disorder. This term is the official name of the diagnosis, despite the facts that nicotine, rather than tobacco, is the ingredient that leads to addiction and that it can arise from the use of products that contain nicotine but not tobacco. Still, the numerous adverse health effects of tobacco itself underlie much of the concern regarding the use of nicotine-containing products.

The number of symptoms experienced at any given time determines whether the diagnosis is deemed mild, moderate, or severe. Tolerance and withdrawal are not necessary for a diagnosis, but a history of withdrawal related to nicotine use may indicate a diagnosis of greater severity.⁷⁷

The diagnostic criteria related to nicotine addiction were introduced to the DSM in 1980 and were largely based on core features of addiction involving alcohol and other drugs.⁷⁸ In recent years, the relevance of some of these criteria for diagnosis has been questioned.⁷⁹ For example, three of the criteria (5, 6, and 7 in the DSM-5) focus on the social costs of smoking. However, these costs can vary significantly according to the individual's life circumstances (e.g., a person who smokes and works in a smoke-free setting vs. one who works in settings that allow smoking), and addiction can exist and be problematic even in the absence of such costs.⁸⁰ Nicotine, at least when delivered through smoked or chewed tobacco, does not cause behavioral intoxication and, therefore, the major harm from a Tobacco Use Disorder is from longer-term physical consequences rather than more immediate behavioral or social problems. As a result, many of the DSM criteria rarely are endorsed by those who use nicotine products regularly (e.g., use causing failure to fulfill role obligations, use in physically hazardous situations, use despite social problems).⁸¹ The DSM criteria also have relatively less predictive validity with regard to key consequences of nicotine addiction (e.g., relapse, lung cancer) than do other criteria such as the amount of time that passes before smoking the first cigarette after awakening and the number of cigarettes smoked per day.⁸² These measures predict ability to quit and response to treatment and yet have very little overlap with the DSM criteria.⁸³ Finally, the criteria were developed primarily with cigarettes in mind and are not necessarily applicable in equal measure to other nicotine-containing products.⁸⁴

A number of multi-item scales, such as the Fagerström Test for Nicotine Dependence (FTND),⁸⁷ the Heaviness of Smoking Index (HSI),⁸⁸ the Nicotine Dependence Symptom Scale (NDSS)⁸⁹ and the Wisconsin Inventory of Smoking Dependence Motives (WISDM),⁹⁰ have been developed that include items that are not in the DSM and that may better measure the unique aspects of nicotine addiction (rather than tobacco use itself). These scales have good predictive validity and tend to be used more extensively than the DSM in clinical practice and in research studies.⁹¹ Still, these scales primarily address cigarette smoking and have not been adapted and validated for measuring addiction involving alternative nicotine products, such as ecigarettes, which are growing in popularity and can lead to nicotine addiction. One recent study did test the validity of a brief, three-symptom index for measuring nicotine dependence across users of

The Fagerström Test for Nicotine Dependence (FTND)⁸⁵

- 1. How soon after you wake up do you smoke your first cigarette?
- 2. Do you find it difficult to refrain from smoking in places where it is forbidden (e.g., in church, at the library, etc.)?
- 3. Which cigarette would you hate most to give up? (the first one in the morning, all others)
- 4. How many cigarettes/day do you smoke?
- 5. Do you smoke more frequently during the first hours after waking than during the rest of the day?
- 6. Do you smoke if you are so ill that you are in bed most of the day?

Note: The Heaviness of Smoking Index (HSI)⁸⁶ is comprised of items 1 and 4 of the FTND.

different tobacco products, including cigarettes, cigars and smokeless tobacco. The three symptoms explored were "want to/try stop or cut down," "using just after getting up" and "using much more to get effect." This study found that this simple and brief measure of nicotine dependence was valid and useful

for assessing nicotine dependence; however, it did not measure the utility of this brief assessment among users of alternative nicotine products such as electronic nicotine delivery systems or hookah.⁹²

Risk Factors for Nicotine Use and Addiction

Several key risk factors contribute to nicotine addiction. Genetic factors influence whether and how quickly a person will become addicted to nicotine,⁹³ and play a role in the success of cessation efforts.⁹⁴ People who metabolize nicotine very quickly or who otherwise are more sensitive to the rewarding effects of nicotine are at increased risk of addiction.⁹⁵ These physiological risk factors often are present alongside developmental risk factors such as the increased impulsivity and significant brain plasticity that are characteristic of adolescence,⁹⁶ psychological risk factors such as depressed mood,⁹⁷ and environmental risk factors such as easy access to nicotine-containing products⁹⁸ and targeted marketing efforts by the tobacco/nicotine product industry.⁹⁹ It is important to note that, to date, the majority of the research on risk factors related to nicotine use and addiction has been conducted with regard to cigarettes rather than alternative nicotine products, but emerging research suggests that similar risk factors may predict other nicotine product use as well.¹⁰⁰

Genetics, Biological and Psychological Factors

Heritability is a significant risk factor for the development of nicotine addiction.¹⁰¹ Genetic variations play less of a role than environmental factors in predicting whether a person will initiate nicotine use,¹⁰² but once a person has begun to use nicotine products, notable genetic variants determine how the body processes the drug, which relates to the risk for developing addiction.¹⁰³

Particular genetic variants can help to predict the progression from nicotine use to addiction.¹⁰⁴ For example, nicotine metabolism is influenced by genetic inheritance,¹⁰⁵ and people who metabolize nicotine more slowly than others may be less likely to develop addiction.¹⁰⁶ Some people inherit genetic variants that are associated with specific smoking-related behaviors, such as the number of cigarettes smoked per day¹⁰⁷ and the ability to quit with ease,¹⁰⁸ and specific alleles--or variants in genetic code--have been found in those who smoke heavily.¹⁰⁹ Still, the exact nature of genetic contributions to the risk for developing nicotine addiction has yet to be firmly established.¹¹⁰

Some people are genetically predisposed to developing nicotine addiction, but other biological factors interact with these predispositions to exacerbate or mitigate risk. While this interplay makes it difficult to isolate genetic influences from other biological influences,¹¹¹ research does indicate that certain groups may be particularly vulnerable to addiction due to biological factors, such as how the brain produces and reacts to dopamine.¹¹² Faster nicotine metabolism, which is associated with an increased risk of developing addiction,¹¹³ is linked not only to specific genetic variants but also to the presence of female sex hormones.¹¹⁴ Pregnant women metabolize nicotine more quickly than those who are not pregnant,¹¹⁵ and women taking estrogen-only birth control pills metabolize nicotine more quickly than postmenopausal women or than men. Fast metabolism of nicotine has been associated with less successful quit attempts among women who use oral contraceptives and nicotine replacement therapies such as the nicotine patch or gum.¹¹⁶ Adolescents without variants in the gene for the nicotine-metabolizing enzyme^{*} progress to nicotine addiction faster than adolescents with variants in that gene.¹¹⁷ Variation in the genes that encode for nicotinic receptor subunits[†] are linked to increased risk of nicotine addiction and difficulty with tobacco cessation.¹¹⁸

^{*} CYP2A6.

[†] e.g., CHRNA5.

Finally, certain personality traits that have a strong genetic basis, such as risk-taking and sensation seeking,¹¹⁹ as well as cognitive difficulties involving concentration or memory,¹²⁰ can increase the risk of nicotine use and addiction.

Environmental Factors

Many variables within an individual's family, peer group and community, as well as the larger cultural climate, increase the likelihood that an individual will use tobacco/nicotine products and develop addiction. Prenatal exposure to nicotine can lead not only to behavioral problems later in life, but also to an increased likelihood of developing nicotine addiction.¹²¹ One study suggests that exposure to secondhand or passive smoke among nonsmoking children^{*} may be linked to subsequent symptoms of nicotine addiction.¹²² Growing up in a stressful home environment--for example due to poverty, illicit drug use in the home or an absent parent--is associated with an increased risk of developing addiction in general.¹²³ Childhood trauma increases the risk of developing nicotine addiction later in life, particularly among females.¹²⁴

The ways in which nicotine-containing products are marketed contribute to their use and may contribute to addiction and difficulty with cessation, especially among certain demographic groups. For example, nicotine products that contain menthol are more palatable, which makes them more appealing to those who are averse to the harsh taste of tobacco and nicotine.¹²⁵ Research suggests that smoking menthol cigarettes is associated with an increased risk of smoking initiation, greater smoking frequency, and nicotine addiction¹²⁶ and with decreased success in smoking cessation efforts.¹²⁷ Menthol in cigarettes appears to reduce the rate at which nicotine is metabolized, increasing exposure to the drug,¹²⁸ and alter the nicotine receptors in the brain in a way that increases the reinforcing value of nicotine and the risk of addiction.¹²⁹ Importantly, menthol-containing nicotine products disproportionately appeal to young people, blacks and women--groups historically singled out by the tobacco industry for targeted marketing of these products.¹³⁰

High Risk Groups

Certain groups are at increased risk of nicotine use and addiction relative to the general population and tend to have less success with cessation attempts.¹³¹ For example, young people who use any addictive substance are at a higher risk of developing addiction relative to adults, as are individuals with psychiatric symptoms or illness or other substance use disorders. Individuals, especially youth, who use multiple tobacco/nicotine products are at increased risk of addiction and are less likely to demonstrate successful cessation relative to those who use just one type of tobacco/nicotine product.¹³²

Early Initiators/Youth

The risk of becoming addicted to nicotine increases with earlier age of first use of nicotine-containing products.¹³³ The vast majority of people who are addicted to nicotine began smoking in adolescence or early adulthood: 83.6 percent of individuals aged 12 and older who meet criteria for nicotine addiction started smoking before the age of 18, and nearly all (95.0 percent) smoked before age 21.¹³⁴

National data also indicate that people who begin smoking before age 15 are more than twice as likely to develop addiction as those who begin at age 21 or older (17.9 percent vs. 7.3 percent). Among people who report current smoking, nearly half (48.5 percent) of those who initiated smoking before age 15 are addicted relative to about a quarter (23.5 percent) of those who initiated smoking at age 21 or older.¹³⁵

^{*} Aged 10 to 12.

For those who start young, symptoms of addiction can develop rapidly, making the notion of an "experimental smoker" inaccurate and potentially misleading.¹³⁶ Symptoms can appear within weeks or days after occasional nicotine use begins.¹³⁷ Even young people who engage in infrequent use of nicotine products may have symptoms of nicotine addiction.¹³⁸

Nearly half of adolescents who smoke will develop at least one symptom of addiction before the age of 18¹³⁹ and one in five will meet criteria for nicotine addiction.¹⁴⁰ Youth who use multiple nicotinecontaining products are at especially high risk of developing addiction, and twice as many youth in the U.S. use two or more of these products than use cigarettes alone.¹⁴¹ A study of middle and high school students found that among those who currently use cigarettes, cigars or smokeless tobacco, 21 percent to 42 percent reported symptoms of addiction, * even at relatively low levels of use.¹⁴²

The increased vulnerability to addiction among youth who engage in any substance use, including nicotine use, appears to be due both to biological and psychological risk factors to which this age group is especially sensitive.¹⁴³ In adolescence, the brain is undergoing essential developmental changes that allow young people to learn quickly and adapt rapidly. However, this also means that their brains are more responsive to and affected by addictive substances, including nicotine, and that these effects--particularly those related to neural connectivity and behavioral regulation--can persist into adulthood.¹⁴⁴ Research also suggests that nicotine use in young people primes the brain to be more susceptible to the addicting effects of alcohol and other drugs.¹⁴⁵

Those with Psychiatric Symptoms or Mental Illness

Rates of tobacco/nicotine use and addiction are highly prevalent among individuals with psychiatric or mental health symptoms and disorders, in large part due to shared neurobiological and psychosocial risk factors, the tendency to use nicotine-containing products as a means of self-medication, challenging life circumstances and a reduced ability to manage the difficult process of cessation.¹⁴⁶

The decline in cigarette smoking prevalence over the past decade seen in the general population generally has not been found in mentally ill populations.¹⁴⁷ One national study[†] found that an estimated 25 to 30 percent of individuals with a psychiatric disorder had nicotine addiction compared to 12.8 percent in the general population. The rates were similar among those with different psychiatric diagnoses--including mood, anxiety and personality disorders--with an approximate three-fold increase in the odds of nicotine addiction across these sub-groups. Specific psychiatric disorders with relatively higher rates of co-occurrence among those with nicotine addiction were major depression, phobia, obsessive-compulsive personality disorder, antisocial personality disorder and paranoid personality disorder.¹⁴⁸ The findings from another national study based on more recent data[‡] are consistent with these estimates: 21.2 percent of adults with any form of mental illness and 31.8 percent of adults with a serious mental illness[§] met clinical criteria for past month nicotine addiction compared to 12.0 percent of adults without a mental illness.¹⁴⁹ Research also indicates that, whereas individuals with nicotine addiction make up only 12.8 percent of the general U.S. population, they consume 57.5 percent of all the cigarettes smoked in the U.S.;

^{* 21} percent reported the symptom of wanting to use tobacco within 30 minutes of waking and 42 percent reported the symptom of recent strong cravings.

[†] Based on data from 2001-2002.

[‡] Based on data from 2008-2012.

[§] Participants were categorized as having any mental illness if they had a diagnosable mental disorder, excluding substance use disorders and developmental disorders, based on the DSM-IV, regardless of the level of functional impairment because of these disorders. Participants were defined as having a serious mental illness if they had a diagnosable mental disorder in the past 12 months that resulted in severe functional impairment, as assessed by the Global Assessment of Functioning scale in the DSM-IV.

those with a co-occurring psychiatric disorder make up 7.1 percent of the U.S. population yet consume 34.2 percent of all the cigarettes smoked.¹⁵⁰

Genetic, biological, psychological and environmental factors contribute to the heightened risk of nicotine addiction among those with a mental illness. For example, some people with schizophrenia have a gene associated with impaired sensory processing, and nicotine may help to compensate for this deficit.¹⁵¹ A national study of people who smoked cigarettes daily found that only those with active depression were at increased risk of developing nicotine addiction; the risk among those with past depression was no different from the risk among those who never had depression.¹⁵² Environmental factors also might help account for the link between mental illness and nicotine addiction. For example, the tobacco industry has provided free cigarette samples to psychiatric hospitals and homeless shelters and has engaged in other methods of targeted marketing to the homeless and seriously mentally ill populations.¹⁵³ Not having a stable living environment also is associated with increased risk: tobacco use is highly prevalent among the homeless (approximately three quarters of homeless adults smoke cigarettes¹⁵⁴), many of whom have severe mental illness and substance use disorders.¹⁵⁵

Young people with mental health problems are at particularly high risk of nicotine addiction. National data indicate that high school students who received treatment for a mental health problem were significantly more likely than those who had not received such treatment to meet criteria for nicotine addiction (5.1 percent vs. 1.7 percent).¹⁵⁶ One study found that individuals diagnosed with conduct disorder between ages 11 and 14 were four times as likely to have nicotine addiction by age 18 as adolescents without a diagnosed conduct disorder.¹⁵⁷ Other research finds that depressive symptoms in young people are a risk factor both for smoking initiation and the progression from initiation to regular smoking, and may increase the likelihood of nicotine addiction.¹⁵⁸

Prevention

The main way to prevent nicotine addiction is to prevent individuals from engaging in the use of products that contain nicotine. Because the majority of people who are addicted to nicotine began using nicotine products in adolescence or early adulthood,¹⁵⁹ preventive strategies that are implemented early and consistently throughout childhood, adolescence and young adulthood tend to work best. Effective approaches to prevention also are those that are comprehensive in nature and involve public education and awareness through mass media campaigns as well as school- and community-based initiatives that are grounded in prevention science, research-based policies and regulations that curb access and availability, early detection of risk, and health-based interventions to promote cessation.¹⁶⁰

Public Education and Awareness

Educating the public, and youth in particular, about nicotine and its effects is critical for prevention. Public awareness campaigns surrounding cigarette smoking have been tremendously successful in reducing the acceptability and desirability of smoking, and youth today are far less likely to initiate cigarette smoking relative to years ago, when smoking was promoted as a sophisticated and fun activity. Yet the current surge in the marketing of alternative nicotine products is threatening to undo decades of public health work that has stigmatized smoking and is beginning to normalize the use of nicotinecontaining products once again. In addition to educating the public about the risks and effects of tobacco and nicotine use, it is important to make people aware of the early signs of nicotine addiction (e.g., wanting or craving) so that they can obtain appropriate interventions to facilitate early cessation.¹⁶¹

Media Campaigns. Tobacco-related media campaigns seek to inform the public of the risks of tobacco use, prevent young people from initiating tobacco use and encourage those who already use to quit. Anti-

tobacco media campaigns have been implemented on national, state and local levels and many have demonstrated effectiveness, especially when they are part of a larger tobacco control program.¹⁶²

The Centers for Disease Control and Prevention's (CDC) Office of Smoking and Health provides antitobacco media campaign resources through its Media Campaign Resources Center (MCRC). The MCRC provides access to CDC-licensed tobacco-control advertisements--including television and radio commercials and print and outdoor ads, as well as brochures, press kits, flyers, testimony and talking points, blogs, text messaging and Web banners--that have been developed by state health departments, nonprofit health organizations and federal agencies.¹⁶³

In 2000, Truth Initiative (then known as Legacy), which was established as part of the 1998 tobacco *Master Settlement Agreement* (MSA),^{*} launched the *truth*® campaign--a nationwide counter-marketing campaign that provided adolescents with facts about the harms of smoking and about the tobacco industry's marketing practices.^{† 164} Its aims were to reduce youth susceptibility to tobacco marketing, challenge social norms around smoking and lower intentions to smoke.¹⁶⁵ Research suggests that the *truth*® campaign was effective (and cost-effective¹⁶⁶) in influencing adolescents' attitudes toward the tobacco industry and toward smoking,¹⁶⁷ attitudes that reliably predict young people's decisions about whether or not to smoke in the future.¹⁶⁸ In recent years, a new version of the campaign, called *FINISH IT*, was launched to leverage the influence of non-smoking youth on their peers and help them become the generation that "puts an end to smoking."¹⁶⁹

Certain cities and states also have implemented media campaigns to reduce tobacco product use and encourage those who do use these products to get help with cessation.¹⁷⁰ For example, New York State has had one of the largest and most effective state tobacco control programs in the United States, with a long history of implementing evidence-based media campaigns. These campaigns have played a significant role in New York's tobacco control efforts and have resulted in positive outcomes with regard to reducing smoking rates and increasing cessation rates.¹⁷¹ Likewise, the California Tobacco Control Program has been investing for many years in anti-tobacco media campaigns that include television, radio, print and billboard ads, online efforts, and advertisements targeted to specific populations that are at increased risk of tobacco use and its adverse effects.¹⁷²

School- and Community-Based Educational Prevention Programs. Most school- and communitybased education programs to prevent and reduce youth tobacco use lack the intensity or comprehensiveness needed to be effective. Programs should try to address all aspects of use, including health effects, reasons for use, negative social consequences, peer norms, resistance and refusal skills and media literacy related to marketing and advertising. It is not enough to offer anti-tobacco education only in middle school or early high school. Effective prevention programs are age sensitive, delivered repeatedly throughout the academic career--with greatest intensity in middle school--and reinforcement throughout high school and college, integrated into the curriculum, and bolstered by strong and consistent school policies that are health oriented rather than punitive in nature.¹⁷³

Policies and Regulations

Policy or regulatory approaches to preventing tobacco/nicotine use are aimed primarily at reducing the availability and accessibility of tobacco/nicotine products, particularly to youth. The 2009 Family Smoking Prevention and Tobacco Control Act gave the Food and Drug Administration (FDA) the authority to regulate tobacco products. Under this Act, the FDA has the authority to regulate the manufacture, distribution and marketing of tobacco products to protect public health; prohibit the sale of

^{*} See p.14 for a description of the MSA.

[†] The *truth*® campaign was modeled after an anti-smoking campaign implemented in Florida.

cigarettes with "characterizing flavors" (with the exception of menthol) in the hopes of limiting their attractiveness and appeal to youth; require bigger and more graphic warning labels on tobacco product packages and advertisements; prohibit "reduced harm" (e.g., low tar, light, or mild cigarettes) claims on tobacco products; and require tobacco companies to seek FDA approval for new tobacco products.¹⁷⁴ Still, the Act only covers cigarettes, loose tobacco, roll-your-own tobacco and smokeless tobacco, but does not give the FDA regulatory authority over all nicotine-containing products. In April 2014, the FDA announced a proposal to extend its regulatory authority to other, currently unregulated tobacco products including e-cigarettes, cigars, pipe tobacco, nicotine gels, water pipe (or hookah) tobacco and dissolvables.¹⁷⁵ As of September 2015, such regulation has yet to be implemented.

State and local governments also play a critical role in preventing and reducing tobacco/nicotine use. Evidence-based statewide programs improve health and save money in averted morbidity and mortality costs. Unfortunately, states rarely invest the recommended amount of money in prevention and tobacco control activities, as evidenced by a recent report by the CDC demonstrating that the total amount the 50 states and the District of Columbia spent in fiscal year 2011 was only 17.8 percent of the CDC's recommended amount for best practices.¹⁷⁶

Tobacco Taxes. Raising taxes on tobacco products increases their cost, which has been associated with reduced smoking¹⁷⁷ and increased smoking cessation,¹⁷⁸ especially among youth.¹⁷⁹ Youth tobacco use is more responsive than adult tobacco use to changes in tobacco prices.¹⁸⁰ Researchers have estimated that a 10 percent increase in the real price of cigarettes would decrease the number of adolescents and young adults who smoke by approximately 3.1 percent and reduce the average number of cigarettes they smoke by 5.2 percent.¹⁸¹ The American Cancer Society estimates that a \$1.00 per-pack increase in the cigarette tax in each state would help to prevent 1.7 million young people from taking up smoking.¹⁸²

Despite public support and evidence of their effectiveness with regard to teen tobacco control,¹⁸³ taxes on cigarettes generally are low and are not adjusted to keep pace with inflation.¹⁸⁴ States that produce and profit from tobacco are more likely to favor policies that increase tobacco revenues, rather than discourage tobacco use. The average tax in the major tobacco states that have extensive tobacco farming^{*} and cigarette manufacturing is \$0.49 per pack; the average tax in non-tobacco states is \$1.57 per pack.¹⁸⁵

Smoking Bans. Clean indoor/outdoor air laws in establishments such as workplaces, restaurants and other public places help to protect non-users from exposure to secondhand or passive environmental tobacco smoke or nicotine product aerosol exposure. In 2006, the Surgeon General concluded that there is no risk-free level of exposure to secondhand smoke and that such exposure leads to numerous health complications.¹⁸⁶ More recent research examining passive aerosol exposure from e-cigarettes found that such exposures were related to respiratory symptoms (e.g., asthma, bronchitis, cough, difficulty breathing, pneumonia), eye irritation, headache, nausea, sore throat, dizziness, and irregular heart rate.¹⁸⁷

In addition to protecting people from the physical harms of exposure to tobacco and other nicotinecontaining products, smoking bans also help to change social norms around smoking:¹⁸⁸ the less frequently young people are exposed to smoking and nicotine product use in their environment, the less likely they are to believe such use is normal and socially acceptable.¹⁸⁹

National data indicate the score for a state's clean indoor air laws,[†] which is inversely related to the proportion of young people who smoke in a state.¹⁹⁰ The higher the percentage of a state's population

^{*} Georgia, Kentucky, North Carolina, South Carolina, Tennessee and Virginia.

[†] The score is determined by summing each state's ratings on nine separate categories, including smoking bans in government worksites, private worksites, schools, childcare facilities, restaurants, retail stores and recreational/cultural facilities along with state policies related to enforcement and violation penalties.

covered by smoke-free air laws, the lower the rates of youth susceptibility to smoking, current smoking and established smoking.¹⁹¹ Adolescents who live in states with no or limited restrictions on smoking are approximately four times as likely to smoke daily as those living in states where smoking is restricted to separate and enclosed areas.¹⁹² Another study found that adolescents who live in towns with strong restaurant smoking restrictions have lower odds of progressing to regular smoking^{*} four years after baseline compared to those living in towns with weak regulations.¹⁹³

Bans on smoking in restaurants, bars and workplaces have been associated with a 20 percent decrease in hospital admission rates for heart attacks among Medicare beneficiaries aged 65 and older. Hospital admissions for chronic obstructive pulmonary disease declined by 11 percent in counties with workplace smoking bans and by 15 percent in counties with bar smoking bans.¹⁹⁴

Smoking bans also have benefited incarcerated individuals, particularly those with mental illness who are at increased risk of tobacco use, lending support for expanding smoke-free policies in prisons and jails. A recent study found that the mortality rate among incarcerated individuals with mental illness in New Jersey decreased by 48 percent between 2005 and 2014, during which time tobacco use was restricted and then ultimately banned.¹⁹⁵

Other research shows that the benefits of indoor smoking bans may extend to alcohol use: in states with smoking bans in bars, individuals had a lower likelihood of developing an alcohol use disorder and those with an alcohol use disorder were more likely to recover compared to individuals in states without these smoking bans.¹⁹⁶

Despite the evidence of the effectiveness of smoking bans, as of August 2015, only 28 states and the District of Columbia have passed comprehensive smoke-free air laws in which public places and workplaces, including restaurants and bars, are designated as smoke free.¹⁹⁷ The American Cancer Society estimates that if each state that does not currently have a comprehensive smoke-free law would adopt such a law, 398,700 fewer young people would begin smoking.¹⁹⁸

It is important to note that most clean indoor/outdoor air laws apply to cigarettes rather than all nicotinecontaining products. Although some state and local governments have included alternative nicotine products such as e-cigarettes in their policies, most have not.¹⁹⁹ The use of e-cigarettes in workplaces and public places poses a public health risk because it contributes to confusion regarding the acceptability and harms of smoking and because the adverse health impact of the aerosols emitted by e-cigarettes is still not well established.²⁰⁰

Restrictions on Advertising. Following the release of the 1964 U.S. Surgeon General's report on smoking and health, which concluded that smoking is a health hazard,²⁰¹ the federal government passed the *Federal Cigarette Labeling and Advertising Act* of 1965, which required that the Federal Trade Commission monitor methods of cigarette advertising and promotion. As of January 1, 1971, television and radio broadcast advertising of cigarettes was banned.²⁰²

In 1998, the four major U.S. cigarette manufacturers entered into an agreement, the *Master Settlement Agreement* (MSA), with the attorneys general of 46 states. The MSA prohibited manufacturers from directly or indirectly targeting underage youth in their advertisements, promotions or other marketing of tobacco products. The MSA also banned the use of cartoons in advertising; limited brand name sponsorships to one per year (and none at events that attract youth, like concert and sporting events); and eliminated outdoor (billboard) and transit advertising, brand name merchandise and giving gifts or free samples to underage youth.²⁰³ Two years after the MSA took effect, several of the leading cigarette

^{*} Smoking 100 or more cigarettes in a lifetime.

manufacturers voluntarily agreed to limit advertising to magazines that have less than an approximately15 percent youth readership.²⁰⁴ By 2008, all cigarette manufacturers were in compliance with this readership limit.²⁰⁵ Still, the American Academy of Pediatrics (AAP) recommends that tobacco advertising be banned in all media that is accessible to children.²⁰⁶

The current lack of regulatory authority of the FDA over alternative nicotine products has resulted in a resurgence of nicotine product advertising and marketing, particularly with regard to electronic nicotine delivery systems. Public health advocates are urging the FDA to improve regulation of these products and include them in the ban on television and radio advertising. However, to date, there are no restrictions on these marketing campaigns, which have revived many of the cigarette companies' old marketing strategies, many of which appeal to youth, nonusers and current cigarette users.²⁰⁷

Warning Labels. The Family Smoking Prevention and Tobacco Control Act of 2009 requires that cigarette packages and advertisements have larger and more visible graphic health warnings, and the FDA has required the implementation of these graphic warnings for cigarette packaging as of September 22, 2012.²⁰⁸ Although data are limited, there is some evidence that graphic warning labels are effective in producing negative reactions to smoking and increasing intentions to quit smoking.²⁰⁹ There is public support for this measure among both smoking and non-smoking adults.²¹⁰ Nevertheless, larger and more graphic warning label requirements, as well as rules requiring FDA approval of any new or changed warning label continue to be areas of dispute.²¹¹

Access Restrictions for Youth. There are two types of laws designed to restrict youth access to tobacco. The first is based on the Synar Amendment to the *Alcohol, Drug Abuse and Mental Health Administration Reorganization Act* of 1992 which requires all states, the District of Columbia and the U.S. territories to enact and enforce laws prohibiting the sale or distribution of tobacco products to individuals under age 18.²¹² The other type of laws that restrict youth access to tobacco/nicotine products are purchase and/or underage possession (PUP) laws, which target adolescents themselves. As of 2014, 41 states and the District of Columbia prohibit the purchase or attempted purchase of tobacco products by minors (28 states do so for electronic cigarettes and related products) and 37 states and the District of Columbia prohibit minors from possessing and/or using tobacco products (25 states do so for electronic cigarettes and related products).²¹³

Restricting youth access to tobacco through enforcement efforts such as local ordinances prohibiting the sale of tobacco products to minors have proven effective, according to a review of more than 400 articles and 400 government reports published from 1987-2010.²¹⁴ However, some have argued against PUP laws, which may unfairly punish or stigmatize children and adolescents, shifting the blame from adults who market and sell tobacco products to the youth who consume them.²¹⁵ These laws also do not address the reality that young people can access tobacco products from sources other than retail outlets--such as parents, friends or strangers--and continue to use these products even if retailers are in compliance with the laws.²¹⁶

Minimum Legal Purchase Age for Tobacco. While the current minimum legal purchase age for tobacco products in most of the U.S. is 18,²¹⁷ there have been proposals in state legislatures to increase it²¹⁸ and some states (Hawaii) and cities (New York City) already have done so. The Institute of Medicine recently released a report demonstrating the benefits of an increase to age 21, indicating that it would prevent or delay initiation of tobacco use by adolescents and young adults, particularly among youth aged 15 to 17 years.²¹⁹ In June 2015, the American Medical Association adopted a new policy calling for, among other things, the passage of laws and regulations that would set the minimum legal purchase age for electronic cigarettes and their liquid nicotine refills at 21 years old.²²⁰

School-Based Tobacco Policies. Under the *Pro-Children Act* of 1994, reauthorized under the *No Child Left Behind Act* of 2001, all schools receiving federal funding are required to prohibit indoor smoking.²²¹ Yet school districts may not have comprehensive tobacco-free policies that are well enforced and evidence regarding the effectiveness of these policies on reducing student smoking is not strong.²²²

Consistent enforcement of tobacco use policies is critical. One study found that, among middle and high school students, higher perceived levels of enforcement of school policies were related to lower rates of smoking.^{* 223} Another study found that high school students were less likely to smoke if they perceived that most or all students at their school obeyed the rules against smoking.²²⁴ Still another found that schools with greater enforcement of tobacco policies had fewer student reports of observed tobacco use by students on school grounds.²²⁵

Many schools take a punitive approach to the enforcement of anti-tobacco policies--such as reporting student violators to the principal, calling parents or suspending the students--rather than providing the student with evidence-based therapeutic interventions.²²⁶

Early Detection

Identifying tobacco use early is critical to preventing the progression to addiction as well as the many health consequences of tobacco and nicotine use.

A critical means of ensuring early detection as well as quality care for those who are addicted is the provision of comprehensive insurance coverage. Comprehensive coverage entails providing incentives to health care professionals to offer the full range of addiction care services--from prevention and early intervention to treatment and disease management--and removing the critical barrier of cost that prevents many patients from obtaining the services they need.

To detect use, health care professionals working in health care settings, schools, the justice system and social service settings should routinely screen for tobacco/nicotine use and intervene when necessary. Clinics and medical offices that have tobacco screening systems in place are approximately 1.7 times as likely to provide people who smoke with interventions as those that do not require tobacco screening.²²⁷ A single-item measure of current tobacco use[†] has been validated on adult populations for use in research protocols²²⁸ but also can be used clinically to determine if a patient currently smokes cigarettes. Comparable screening instruments for alternative nicotine products are not readily available, but those that screen for cigarette use should be adapted for these products.

Therapeutic Interventions and Treatment

The level of intervention required for tobacco/nicotine cessation varies by the quantity, frequency and intensity of use. Those at lower levels of severity of use typically have a good chance of successfully quitting by choosing a quit date, getting rid of tobacco/nicotine products and using available counseling and support services. Heavier tobacco users probably are addicted and tend to benefit from an approved smoking cessation aid in the form of nicotine replacement therapy (i.e., nicotine patch, gum, lozenge, inhaler or nasal spray) or a medication (e.g., bupropion, varenicline). Highly addicted, long-term users typically require more intensive counseling combined with pharmaceutical therapy.²²⁹

^{*} Past 30-day smoking, daily smoking, smoking at school and smoking a cigarette offered by a friend.

[†] Have you smoked one or more cigarettes in the past month?

There is reason to believe that nicotine serves different functions for different users. For example, although nicotine itself is physiologically rewarding, its self-medicating effects and alleviation of negative feelings, emotions and thoughts are strong motivators for use. Understanding the particular drivers of use is important for tailoring interventions and treatments to ensure their effectiveness.²³⁰

Brief Interventions

Brief interventions can be provided by trained health care professionals and generally occur in primary care or other clinical settings.²³¹ These interventions work best if they include a follow-up visit scheduled shortly after a patient's quit date.²³² According to clinical guidelines, health care professionals should provide brief interventions in accordance with the following "Five A's:"

- *Ask.* Inquire about tobacco/nicotine use during each visit.
- Advise. Advise individuals who use tobacco/nicotine in a clear, strong and personalized manner to quit.
- *Assess.* Determine whether a patient is willing to attempt to quit.
- Assist. Help patients who are willing to attempt to quit to create a quit plan, provide counseling and pharmaceutical treatment recommendations, offer problem solving and skills training, and distribute supplementary educational materials. One intervention approach for assisting patients in quitting is known as the "Five R's" which attempts to enhance motivation to quit via providers' use of an empathetic counseling style directed toward:
 - > *Relevance*: Encouraging patients to indicate why quitting is personally relevant.
 - > *Risks:* Helping patients identify the acute, long-term and environmental risks they take by continuing to use tobacco/nicotine products.
 - > *Rewards:* Pointing out the rewards that will come with cessation.
 - > *Roadblocks:* Asking patients to identify any roadblocks they may face during their attempt to quit and suggesting potential solutions for each.
 Repetition: Repeating this process at every patient visit.²³³
- Arrange. Schedule follow-up contact, either in person or by phone.²³⁴

A simpler approach is to restrict the brief intervention to the first two "A's"--Ask and Advise--and then refer the patient to a tobacco cessation service where the other three "A's" are performed.²³⁵ A recent review of research found that, compared to only providing advice, physicians who offer assistance in quitting^{*} to all patients regardless of their willingness to quit smoking could prompt an additional 40 to 60 percent of patients to make a quit attempt.²³⁶

A systematic review of 31 studies examining the effects of smoking interventions provided by nurses in hospital settings found that the smoking cessation rate of patients who received brief interventions was 1.3 times the cessation rate of control group patients.²³⁷ Another large-scale study found that people who smoked and reported that they had received a brief smoking cessation intervention from their primary care provider were more than three times as likely to quit smoking as those who did not receive such counseling.²³⁸ There is some evidence to suggest that shorter interventions for smoking cessation may be more successful than longer ones, perhaps because of the direct, instructional nature of the brief intervention.²³⁹

In the form of counseling or nicotine replacement therapy.

Smoking Cessation Quitlines

Smoking cessation quitlines are telephone-based programs aimed at helping tobacco users achieve successful cessation. An individual interested in getting help contacts the quitline and receives various services, including mailed information and self-help materials, brief counseling by trained counselors, access to cessation medication or a combination of these services; some quitline programs also make follow-up calls which enhance the effectiveness of the program.²⁴⁰ The services typically are free to the caller and are available in all 50 states, the District of Columbia and the U.S. territories.²⁴¹ Research indicates that quitline programs, offered as part of a larger tobacco control program, can be very effective in increasing cessation rates;²⁴² they enhance abstinence rates by approximately 30 percent.²⁴³ Recent research also indicates that tobacco quitlines can be effective in increasing cessation rates among smokeless tobacco users; one study found that at seven months follow-up, 43 percent of participants reported 30-day abstinence.²⁴⁴

Pharmaceutical Therapies

In addition to brief interventions and quitlines, evidence-based treatment for nicotine addiction may include pharmaceutical interventions, such as nicotine replacement therapy (NRT) and medications such as bupropion (Wellbutrin, Zyban) and varenicline (Chantix).

Nicotine Replacement Therapy (NRT). NRT--nicotine patches, gum, nasal spray, inhalers, lozenges and sub-lingual tablets--is a common pharmaceutical aid for smoking cessation. NRT, when used as directed, provides lower doses of nicotine at a slower rate than cigarette smoking,²⁴⁵ thereby easing nicotine withdrawal symptoms²⁴⁶ and reducing cravings.²⁴⁷ Some NRTs mimic the sensations of smoking (the inhaler) or otherwise occupy the mouth (gum, lozenges and sub-lingual tablets).²⁴⁸ Research indicates that the most effective use of NRT involves replicating the experience of smoking; for example, using nicotine patches to maintain a baseline serum nicotine level along with the gum or lozenges to produce a periodic boost of serum nicotine levels.²⁴⁹

Nicotine gum, lozenges, inhalers and nasal sprays deposit nicotine in the bloodstream through the lining of the mouth, nose or back of the throat,²⁵⁰ whereas the nicotine patch delivers the nicotine through the skin.²⁵¹ Nicotine gum and lozenges are over-the-counter medications; inhalers and sprays require prescriptions. The nicotine patch is available both over-the-counter and by prescription.²⁵²

Research indicates that use of nicotine gum, lozenges, inhalers, patches and nasal sprays approximately double abstinence rates over at least a six-month period, relative to a placebo.²⁵³

For many people who smoke, NRT works best as an aid to managing nicotine-related cravings when used in conjunction with psychosocial therapies. In most cases of acute care treatment, a therapeutic level of nicotine is reached and then use is reduced in order to eliminate the medication or reach a maintenance level.²⁵⁴ Because most patients who use NRT control their treatment regimen on their own, there is a risk that the nicotine intake from NRT products may be higher than intended for those who do not use them as directed or who use them while continuing to smoke.²⁵⁵ Nasal sprays have the highest potential for misuse: 15 to 20 percent of patients report using the spray for longer than the recommended period and five percent report using a higher dose than recommended.²⁵⁶

Contrary to the many controlled studies supporting the efficacy of NRT, a population-based survey of adults who smoked and who recently had quit casts doubt on its effectiveness in smoking cessation and relapse prevention. In this study, nearly one-third of those who smoked but had quit within the previous two years reported having relapsed, regardless of whether they used NRT for the recommended amount of time and regardless of whether the use of NRT was accompanied by professional behavioral counseling.

While this study appears to call into question the efficacy of NRT in achieving smoking cessation in the general population,²⁵⁷ it actually underscores the fact that, for many people who smoke, NRT is not a sufficient treatment approach on its own, but rather an aid to smoking cessation to be used in conjunction with other evidence-based approaches.

Bupropion. Bupropion-sustained release (brand names Wellbutrin or Zyban) is a prescription antidepressant medication that can be used alone or in combination with NRT for smoking cessation.²⁵⁸ It is believed to work by minimizing cravings and withdrawal symptoms during the early stages of tobacco cessation.²⁵⁹ Bupropion may be effective in relieving the negative moods and feelings that people who smoke may experience when going through smoking cessation.²⁶⁰ The neurological effects of bupropion that aid in its efficacy as a cessation medication may include blocking the re-uptake of two neurotransmitters that are active in nicotine addiction--dopamine and norepinephrine--and blocking nicotine receptors.²⁶¹ The medication reduces the severity of nicotine withdrawal and the depression that may accompany smoking cessation.²⁶² Bupropion also tends to lessen the weight gain that often accompanies (and sometimes derails) smoking cessation attempts.²⁶³

Patients generally are advised to begin daily bupropion treatment one to two weeks prior to quitting so that adequate blood levels of the medication can be reached.²⁶⁴ The standard course of treatment is seven to 12 weeks, although this period can be extended for up to six months if necessary.²⁶⁵

A meta-analysis of 24 bupropion studies found that the medication nearly doubles the chance of achieving abstinence that lasts longer than five months, compared to a placebo.²⁶⁶ Other analyses found similar results.²⁶⁷ The efficacy of bupropion does not appear to vary substantially as a function of the length of the follow-up period (e.g., six versus 12 months), treatment setting, dosage or the level of supplementary psychosocial therapy.²⁶⁸

Varenicline. The medication varenicline (brand name Chantix) is an effective therapy for smoking cessation that works by reducing the rewarding effects of nicotine among patients who smoke while on the medication and by reducing the craving and withdrawal symptoms that occur among those who are abstinent.²⁶⁹ Varenicline, compared with a placebo, can significantly increase the likelihood of continuous abstinence from smoking over the course of six months.²⁷⁰ One large-scale analysis of several randomized controlled trials found that the medication was significantly more effective than placebo or bupropion in relieving cravings and in increasing the likelihood of achieving continuous abstinence over a 12-month period.²⁷¹ A recent study of cigarette smokers attending a cessation clinic to receive treatment for nicotine dependence found that those who received varenicline had significantly higher cessation rates than those who received NRT.²⁷² Consistent with other findings showing the added benefits of combination therapy, another recent study found that varenicline plus NRT was even more effective than varenicline alone in achieving smoking cessation.²⁷³

Psychosocial Therapies

Psychosocial and behavioral therapies, commonly used in conjunction with medication, teach individuals to develop coping strategies that do not involve smoking, manage stress, improve problem-solving skills and increase social support.²⁷⁴ Some therapies focus on enhancing patients' motivations to change their tobacco use behaviors. Others focus on helping patients to alter their environments in order to reduce pressures and cues to engage in tobacco use, or provide positive or negative reinforcements to help people change their tobacco -related attitudes and behavior.²⁷⁵ Psychosocial therapies for cessation are similar to those used for other addiction treatment, and include motivational interviewing, cognitive-behavioral therapy and contingency management.²⁷⁶

The combination of NRT and psychosocial approaches to treating nicotine addiction increases patients' likelihood of quitting and long-term abstinence.²⁷⁷ One explanation for the improved results of combined therapies is that NRT is the primary mechanism behind patients' initial quitting success while the psychosocial therapies give patients the tools they need to avoid relapse over the longer term.²⁷⁸ Forms of pharmaceutical therapy other than NRT, such as antidepressants, also can enhance the benefits of psychosocial treatment for cessation.²⁷⁹

Electronic Nicotine Delivery Systems

With the relatively recent emergence of e-cigarettes and other forms of electronic nicotine delivery systems (ENDS), some researchers and health professionals have begun to explore their potential role in aiding cigarette-smoking cessation.²⁸⁰ However, the evidence regarding the efficacy of these products in smoking cessation remains inconclusive,²⁸¹ and some research finds no cessation benefits.²⁸² As a result, the United States Preventive Services Task Force (USPSTF), which makes recommendations about the effectiveness of preventive health care services based on available research evidence, recently concluded that there is not sufficient evidence to recommend the use of ENDS as a smoking cessation tool.²⁸³

A growing body of evidence indicates that e-cigarette and other ENDS use is not limited to cigarette smokers trying to quit. Rather, a significant proportion of youth who are not cigarette smokers are using these products,²⁸⁴ and their use among non-cigarette smoking youth has increased dramatically over the past few years.²⁸⁵ There also is emerging evidence of continued cigarette smoking (i.e., dual use) or new cigarette smoking among users of ENDS, particularly youth,²⁸⁶ and even among young people who had demonstrated no susceptibility to or intention of smoking cigarettes before they began to use these products.²⁸⁷

ENDS, which deliver nicotine along with other potentially toxic chemicals, additives and other ingredients (including those contained in the numerous appealing flavors that these products come in) may contribute to nicotine addiction and other adverse health effects.²⁸⁸ Although these products appear to pose less harm than conventional, combustible cigarettes, they expose users to nicotine--a highly addictive drug--and may convey pro-smoking messages to young people; therefore, their risks and benefits require further evaluation.²⁸⁹ Companies interested in developing such products for smoking cessation or reduction purposes specifically, should be required to subject their products to the established FDA regulatory review process that exists for bringing new drugs to market while assuring their safety and efficacy.²⁹⁰

Implications and Recommendations for Policy and Practice

Aside from its delivery through smoking tobacco, nicotine and nicotine addiction typically are not given the same attention as addiction involving alcohol and other drugs, primarily because nicotine use results in fewer psychosocial effects.²⁹¹ However, nicotine itself has adverse health effects, including increasing the risk of addiction and other substance use as well as relapse for those in recovery, and it contributes to the mounting health care costs associated with tobacco use and substance addiction. Therefore, addressing nicotine should be a significant part of any comprehensive approach to addiction prevention and treatment.²⁹²

To help encourage policymakers, health care professionals and researchers to attend adequately to nicotine use and addiction--in all its forms--CASAColumbia makes the following recommendations:

Strengthen Tobacco Control Regulations and Policies and Apply Them to All Nicotine-Containing Products

Policies and regulations are critical for reducing youth access to all nicotine-containing products and for preventing the initiation of nicotine use in all its forms. Effective policies include:

- Prohibiting the marketing of nicotine-containing products in any way that targets or appeals to youth;
- Restricting youth access to all nicotine-containing products;
- Including appropriate health warnings on all nicotine-containing products;
- Improved packaging to prevent accidental nicotine poisonings, especially by youth;
- Protecting of non-users from exposure to secondhand or passive smoke or to aerosols/vapors from electronic nicotine delivery systems (e.g., e-cigarettes);
- Increasing pricing (through higher taxes) to help minimize youth initiation and use;
- Establishing standards to ensure the transparency and consistency of ingredients, dosing and functioning of specific nicotine-containing products; and
- Reducing the addiction potential of nicotine-containing products, including reducing the nicotine content in cigarettes and other nicotine products.²⁹³

In 2009, the FDA was granted the authority to regulate the manufacture, distribution and marketing of tobacco products through the *U.S. Family Smoking Prevention and Tobacco Control Act.*²⁹⁴ However, this regulatory authority is limited and does not cover most alternative nicotine products.²⁹⁵ The FDA, which is considering regulating products not currently covered by the Act, should:

- Expand its regulation of the production, advertising and marketing of all nicotine-containing products, without exceptions. Because alternative nicotine products are not bound by the advertising restrictions that pertain to traditional combustible cigarettes, many marketing campaigns for these alternative products directly target youth (e.g., via cartoons), promote flavors that appeal to youth and generally glamorize their use.²⁹⁶ All nicotine-containing products should be subject to the same marketing restrictions as cigarettes, including prohibiting their advertisement on television and radio.
- Require all nicotine-containing products to carry a warning label that effectively informs the public, including youth, about their addictive nature.
- Follow through on the proposal introduced on June 30, 2015 to require warning labels and child-resistant packaging on bottles of liquid nicotine used in e-cigarettes and other electronic nicotine delivery systems.
- Ban all flavorings, including menthol, in all nicotine-containing products to reduce their appeal to youth and other at-risk groups.
- Require manufacturers to submit any new tobacco/nicotine product for federal approval.
- Prohibit alternative nicotine product manufacturers from making smoking cessation claims unless such claims are supported by research evidence and subject to the FDA review process.

State and local governments can do their part to reduce nicotine use and addiction by:

- Stepping up funding for comprehensive and evidence-based programming related to nicotine use prevention and cessation.
- Instituting or expanding the scope of tobacco retailer licensing laws to enforce tobacco tax and point-of-sale laws, control retail outlet density and location (e.g., restrict sales near schools or youth-oriented facilities) and promote responsible sale and distribution of tobacco/nicotine

products (e.g., restricting product sampling, banning sales in pharmacies, restricting flavored products, banning coupon redemption).

- Increasing enforcement of laws restricting the sale of nicotine-containing products to minors, conducting routine retailer compliance checks and strengthening penalties for violators.
- Enacting strong and comprehensive indoor and outdoor clean air laws that prohibit the use of all tobacco and nicotine products anywhere the use of conventional cigarettes is prohibited. This will help to limit exposure to environmental tobacco smoke and to aerosols and vapors from alternative nicotine products. It also will help to reduce the perceived acceptability and normalization of nicotine product use, especially among youth.
- Enacting zoning laws that restrict the density of tobacco and nicotine product retail outlets, which normalize their use.
- Raise the minimum legal purchasing age to 21 for all nicotine-containing products, including electronic nicotine delivery systems, combustible tobacco and smokeless tobacco products.
- Increasing taxes on all nicotine-containing products to help prevent youth initiation of use and reduce overall use. Higher taxes would generate revenues to help fund prevention and treatment services. The definition of "tobacco products" in state tobacco tax laws should be amended to include alternative nicotine products such as e-cigarettes that do not contain tobacco. The laws should establish a required minimum tax on smokeless and alternative nicotine products, including e-cigarettes, vaping devices and e-liquids.²⁹⁷
- Prohibiting the sale of alternative nicotine products in any venues where the sale of conventional cigarettes is prohibited and eliminating vending machines that sell these products.
- Mandating evidence-based tobacco cessation in addiction treatment and mental health care settings.

Improve Prevention, Early Intervention and Treatment Practice

Reducing the use of nicotine products in the U.S. requires the sustained implementation of populationwide research-based prevention programs, early interventions for those at risk, and timely and effective treatments for those with addiction. It also requires expansion of medical insurance coverage for tobacco/nicotine screening, brief interventions and treatment in all health insurance plans.

Certain groups who are at increased risk--including youth, pregnant women, those with other substance use disorders and the mentally ill--stand to benefit the most from a comprehensive and evidence-based public health approach to the prevention and treatment of nicotine use and addiction.

Prevention. Substance use prevention programming typically separates tobacco and nicotine use from other addictive substances, perpetuating the perception of nicotine addiction as a relatively harmless form of addiction and glossing over the fact that tobacco/nicotine use and addiction overlap considerably with alcohol and other drug use and addiction.²⁹⁸ Implementing comprehensive public awareness campaigns and prevention programming that include nicotine along with other addictive substances would educate the public about addiction in all its forms, help to delay initiation of substance use, and improve health and reduce costs.

Prevention efforts should alert parents, health care professionals, educators, clergy and others responsible for the health and well-being of young people about the importance of preventing youth nicotine use, intervening early with those who show signs of risk, and addressing psychological and behavioral problems that often co-occur with nicotine use and addiction.²⁹⁹

Screening and Early Intervention. Educators and health professionals have a critical role to play in identifying nicotine use through validated screening instruments and providing or connecting those who

use these products with evidence-based interventions. Routine screening for *all* forms of nicotine use should be conducted at initial visits to primary care or specialty care health professionals and routinely thereafter, and upon entry into a hospital, emergency department, trauma center or clinic. Although health care professionals are more likely to ask about smoking than other substance use, most do not provide smoking cessation advice or services.³⁰⁰ Nicotine use in all its forms should be included in all substance-related screening instruments and brief interventions and addressing it should be a routine part of mainstream medical and dental practice. Currently, most of the frequently used measures of tobacco product use, such as the FTND,³⁰¹ the HSI,³⁰² and the NDSS³⁰³ address cigarette use only and do not capture the unique characteristics of other forms of tobacco and nicotine use that are becoming more prevalent. Either new valid and reliable screening and assessment instruments should be developed to address all tobacco/nicotine products,³⁰⁴ or existing instruments should be adapted for use with alternative, non-cigarette nicotine products.

Treatment. All health care professionals should be well versed in evidence-based pharmaceutical and psychosocial interventions for tobacco cessation and provide these services directly to patients who use any tobacco or nicotine products, or refer patients to quitlines or other accessible and qualified providers of these services. To ensure that health care professionals have the necessary knowledge and capacity to address tobacco and nicotine use effectively, health care training institutions (including medical,³⁰⁵ graduate and professional schools and teaching hospitals), accrediting organizations and state professional boards should include core clinical competencies related to tobacco/nicotine (as well as other addictive substances) in health care curricula, professional licensing, board certification and continuing education requirements. The core competencies should include awareness of the risk factors and consequences of tobacco/nicotine use and addiction, information about how to screen for it and how to conduct brief interventions to promote cessation, and knowledge about available psychosocial and pharmaceutical treatments and how patients can access effective care.³⁰⁶

Although recognition is growing of the importance of integrating treatment for nicotine addiction into treatment for addiction involving alcohol and other drugs, actual practice lags behind.³⁰⁷ All addiction treatment programs, as well as criminal justice and social service settings, should be required to address addiction comprehensively--banning smoking and specifically including treatment for nicotine addiction in their services. Research has demonstrated that it is erroneous to assume that providing cessation services will compromise patients' ability to abstain from alcohol or other drug use.³⁰⁸

Invest in Quality Research

Despite the growth in alternative nicotine product use and an expanding scientific literature exploring the risk factors, effects, correlates and consequences of use, the current state of knowledge about their risks and potential benefits is still inconclusive.³⁰⁹

Part of the difficulty in ascertaining the health effects of alternative nicotine products and their role in the initiation of tobacco use, multiple nicotine product use or cessation is that most of the products are not regulated and so their nicotine content and concentrations may be highly variable.³¹⁰ A lack of available and current data also hampers our ability to fully understand the risks and benefits of alternative nicotine products. National data sets that track various forms of substance use are deficient in their inclusion of variables relevant to the full array of tobacco and alternative nicotine products. Even when studies do measure the use of these products, they often do so in a relatively superficial way and do not ask detailed questions about the frequency or quantity of use or the motivations for use. Insufficient available data thwarts efforts to gauge the prevalence, associated risks (including the risk of initiating other tobacco product use or the association with multiple tobacco product use and cessation success) and populations most susceptible to the use of these products. Likewise, data sets that measure variables associated with addiction treatment in the United States generally exclude measures related to nicotine addiction. This significant gap in national data hinders research efforts and precludes a comprehensive understanding of

the extent and nature of the risk factors, prevalence and consequences of nicotine addiction and how it is addressed. 311

Researchers should explore the full range of tobacco/nicotine products that are available and regularly update data collection methods to remain current with emerging products and trends. Policymakers should fund expansions to current data collection efforts to ensure the inclusion of all tobacco/nicotine products.

Conclusion

Nicotine is a highly addictive substance that not only perpetuates tobacco use,³¹² the leading cause of preventable morbidity and mortality in the United States,³¹³ but also has its own adverse effects.³¹⁴ Nicotine addiction is a chronic and relapsing disease³¹⁵ and the prevalence of nicotine addiction is higher than that of alcohol and other drug addiction.³¹⁶ The use of nicotine-containing products not only is associated with developing nicotine addiction, but also with using and becoming addicted to alcohol and other drugs.³¹⁷

Despite the decline in recent years in the use of cigarettes, the use of alternative, non-cigarette nicotine products has been rising dramatically.³¹⁸ While the overall harm of these products appears to be considerably lower than the harms associated with cigarette use, all nicotine-containing products carry the risk of addiction and other adverse health effects and, therefore, are a threat to the public health.³¹⁹

Public health and policy efforts have been remarkably successful in reducing rates of cigarette smoking in the United States over the past few decades. However, both the commercial interests of the tobacco industry and the natural human proclivity toward risk-taking, pleasure seeking, and addiction require that we do not become complacent in allowing alternative nicotine products to undo decades of hard-won progress in reducing the enormous health and financial costs of tobacco and nicotine use. A rational and science-based approach to the regulation of these products is required and adequate attention must be paid to preventing the use of all addictive substances, including nicotine, and providing effective treatments that reduce or eliminate harm to those with addiction.

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