Chapter 1
Introduction, Conclusions, and the Evolving Landscape of Smoking Cessation

Introduction

Tobacco smoking is the leading cause of preventable disease, disability, and death in the United States (U.S. Department of Health and Human Services [USDHHS] 2014). Smoking harms nearly every organ in the body and costs the United States billions of dollars in direct medical costs each year (USDHHS 2014). Although considerable progress has been made in reducing cigarette smoking since the first U.S. Surgeon General's report was released in 1964 (USDHHS 2014), in 2018, 13.7% of U.S. adults (34.2 million people) were still current cigarette smokers (Creamer et al. 2019). One of the main reasons smokers keep smoking is nicotine (USDHHS 1988). Nicotine, a drug found naturally in the tobacco plant, is highly addictive, as with such drugs as cocaine and heroin; activates the brain's reward circuits; and reinforces repeated nicotine exposure (USDHHS 1988, 2010, 2014; National Institute on Drug Abuse [NIDA] 2018).

The majority of cigarette smokers (68%) want to quit smoking completely (Babb et al. 2017). The 1990 Surgeon General's report, *The Health Benefits of Smoking Cessation,* was the last Surgeon General's report to focus on current research on smoking cessation and to predominantly review the health benefits of quitting smoking (USDHHS 1990). Because of limited data at that time, the 1990 report did not review the determinants, processes, or outcomes of attempts at smoking cessation. Pharmacotherapy for smoking cessation was not introduced until the 1980s. Additionally, behavioral and other counseling approaches were slow to develop and not widely available at the time of the 1990 report because few were covered under health insurance, and programs such as group counseling sessions were hard for smokers to access, even by those who were motivated to quit (Fiore et al. 1990).

The purpose of this report is to update and expand the 1990 Surgeon General's report based on new scientific evidence about smoking cessation. Since 1990, the scientific literature has expanded greatly on the determinants and processes of smoking cessation, informing the development of interventions that promote cessation and help smokers quit (Fiore et al. 2008; Schlam and Baker 2013). This knowledge and other major developments have transformed the landscape of smoking cessation in the United States. This report summarizes this enhanced knowledge and specifically reviews patterns and trends of smoking cessation; biologic mechanisms; various health benefits; overall morbidity, mortality, and economic benefits; interventions; and strategies that promote smoking cessation.

From 1965 to 2017, the prevalence of current smoking declined from 52.0% to 15.8% (relative percent change: 69.6%) among men and from 34.1% to 12.2% (relative percent change: 64.2%) among women (Figure 1.1). These declines have been attributed, in part, to progress made in smoking cessation since the 1960s, which has continued since the 1990 Surgeon General's report. Specifically, clinical, scientific, and public health communities have increasingly embraced and acted upon the concept of tobacco use and dependence as a health condition that can benefit from treatment in various forms and levels of intensity. Accordingly, a considerable range of effective pharmacologic and behavioral smoking cessation treatment options are now available. As of October 16, 2019, the U.S. Food and Drug Administration (FDA) has approved five nicotine replacement therapies (NRTs) and two non-nicotine oral medications to help smokers quit, and the use of these treatments has expanded, including stronger integration with counseling support (Fiore et al. 2008).

In addition, the reach of smoking cessation interventions has increased substantially since 1990 with the emergence of innovative, population-level interventions and policies that motivate smokers to quit and raise awareness of the health benefits of smoking cessation (McAfee et al. 2013). This includes policies, such as comprehensive smokefree laws, that have been shown to promote cessation at the population level in addition to reducing exposure to secondhand smoke (USDHHS 2014). The development and subsequent expansion of telephone call centers ("quitlines"), mobile phone technologies, Internet-based applications, and other innovations have created novel platforms to provide behavioral and pharmacologic smoking cessation treatments (Ghorai et al. 2014). However, the continued diversification of the tobacco product landscape could have several different potential impacts, ranging from accelerating the rates of complete cessation among adult smokers to erasing progress in reducing all forms of use of tobacco products, especially among youth and young adults. For example, the increasing availability and rapidly increasing use of novel tobacco products, most notably electronic cigarettes (e-cigarettes), raise questions about the potential impact that such products could have on efforts to eliminate disease and death caused by tobacco use at the individual and population levels. Therefore, when considering the impact of e-cigarettes on public health, it is critical to evaluate their effects on both adults and youth.

Collectively, the changes cited in this report provide new opportunities and challenges for understanding and promoting smoking cessation in the United States. However, the evidence-based clinical-, health system-, and population-based tobacco prevention, control, and

Figure 1.1   Trends in prevalence (%) of current and former cigarette smoking among adults 18 years of age and older, by sex; National Health Interview Survey (NHIS) 1965–2017; United States
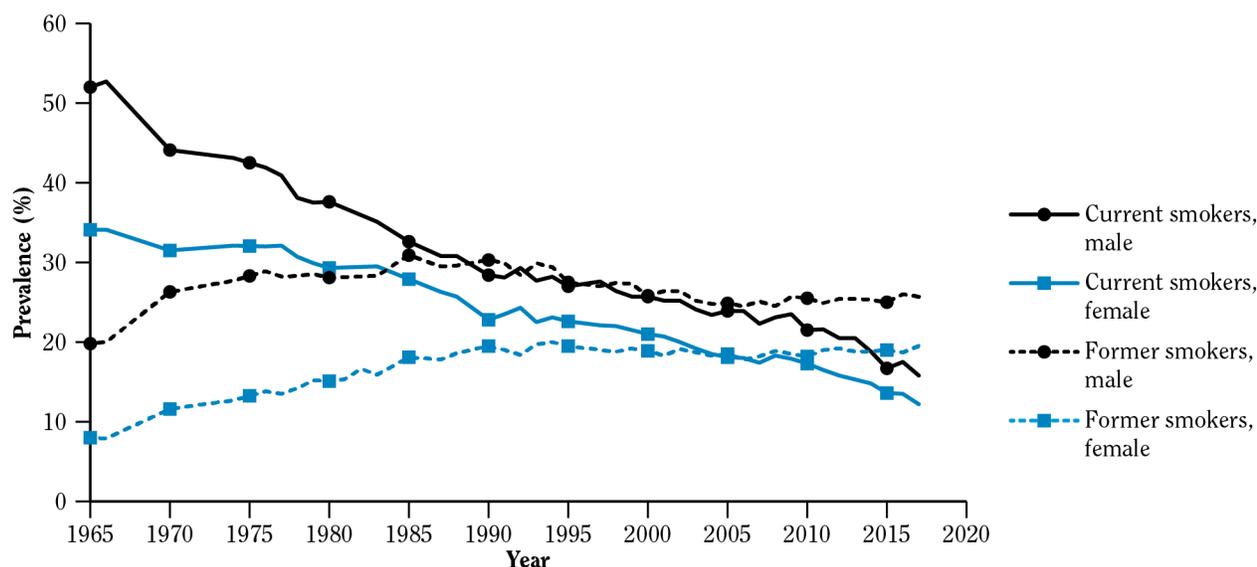
Source: NHIS, National Center for Health Statistics, public use data, 1965–2017.
Note: From 1965 to 2017, data were reported for the following years: 1965, 1966, 1970, 1974, 1976–1980, 1983, 1985, 1987, 1988, 1990–1995, and 1997–2017.

cessation strategies that are outlined in this report are a necessary but insufficient means to end the tobacco epidemic. Reaching the finish line will require coordination across federal government agencies and other government and non-government stakeholders at the national, state, and local levels. To achieve success, we must work together to maximize resources and coordinate efforts across a wide range of stakeholders.

Organization of the Report

This chapter summarizes the report, identifies its major conclusions, and presents the conclusions from each chapter. It also offers an overview of the evolving landscape of smoking cessation and key developments since the 1990 Surgeon General's report. Chapter 2 ("Patterns of Smoking Cessation Among U.S. Adults, Young Adults, and Youth") documents key patterns and trends in cigarette smoking cessation in the United States among adults overall (persons 18 years of age and older), young adults (18–24 years of age), and youth (12–17 years of age). The chapter also reviews the changing demographic- and smoking-related characteristics of cigarette smokers with a focus on how these changes may influence future trends in cessation. Chapter 3 ("New Biological Insights into Smoking Cessation") reviews several areas of intensive research since the 2010 Surgeon General's report on how tobacco smoke causes disease: cellular and molecular biology of nicotine addiction; vaccines and other immunotherapies as treatments for tobacco addiction; neurobiological insights into smoking cessation obtained from noninvasive neuroimaging; and genetics of smoking behaviors and cessation. Chapter 4 ("The Health Benefits of Smoking Cessation") reviews the more recent findings on disease risks from smoking and benefits after smoking cessation for major types of chronic diseases, including cardiovascular and respiratory systems, cancer, and a wide range of reproductive outcomes. Chapter 5 ("The Benefits of Smoking Cessation on Overall Morbidity, Mortality, and Economic Costs") discusses general indicators of health that change after smoking cessation, the health benefits of smoking cessation on all-cause mortality, and the economic benefits of smoking cessation. Chapter 6 ("Interventions for Smoking Cessation and Treatments for Nicotine Dependence") reviews the evidence on current and emerging treatments for smoking cessation, including research that has been conducted since the 2008 U.S. Public Health Service's

Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update* (Fiore et al. 2008). Chapter 7 ("Clinical-, System-, and Population-Level Strategies that Promote Smoking Cessation") focuses on clinical-, system-, and population-level strategies that combine individual components of treatment for smoking cessation with routine clinical care, making cessation interventions available and accessible to individual smokers and creating conditions whereby smokers are informed of these interventions and are motivated to use them. Chapter 8 ("A Vision for the Future") outlines broad strategies to accelerate the progress that has been made in helping smokers quit.

Preparation of the Report

This Surgeon General's report was prepared by the Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention (CDC), which is part of USDHHS. This report was compiled using a longstanding, peer-reviewed, balanced, and comprehensive process designed to safeguard the scientific rigor and practical relevance from influences that could adversely affect impartiality (King et al. 2018). This process helps to ensure that the report's conclusions are defined by the evidence, rather than the opinions of the authors and editors. In brief, under the leadership of a senior scientific editorial team, 32 experts wrote the initial drafts of the chapters. The experts were selected for their knowledge of the topics addressed. These contributions, which are summarized in Chapters 1–7, were evaluated by 46 peer reviewers. After this initial stage of peer review, more than 20 senior scientists and other experts examined the scientific integrity of the entire manuscript as part of a second stage of peer review. After each round of peer review, the report's scientific editors revised each draft based on reviewers' comments. Chapter 8, which summarizes and is founded upon the preceding content in the report, was written by the senior scientific editorial team once the content in Chapters 1–7 completed peer review. Subsequently, the report was reviewed by various institutes and agencies in the U.S. government, including USDHHS. Throughout the review process, the content of each chapter was revised to include studies and information that were not available when the chapters were first drafted; updates were made until shortly before the report was submitted for publication. These updates reflect the full scope of identified evidence, including new findings that confirm, refute, or refine the initial content. Conclusions are based on the preponderance and quality of scientific evidence.

Scientific Basis of the Report

The statements and conclusions throughout this report are based on an extensive review of the existing scientific literature. Thus, the report focuses primarily on cessation in the context of adults because this is the population for which the preponderance of scientific literature exists on this topic; however, data on youth and young adults are also presented, when available. The report primarily cites peer-reviewed journal articles, including reviews that integrate findings from numerous studies and books that were published between 2000 and 2018, which reflects a period after the last Surgeon General's report on the topic of cessation. This report also refers, on occasion, to unpublished research, such as presentations at professional meetings, personal communications from researchers, and information available in various media. These references are used when acknowledged by the editors and reviewers as being scientifically valid and reliable, and a critical addition to the emerging literature on a topic. Throughout the writing and review process, highest priority was given to peer-reviewed, scientific research that is free from tobacco industry interests. As noted in the 2014 Surgeon General's report, the tobacco industry has a well-documented record of manipulating scientific information about the extent of the harms from cigarette smoking (USDHHS 2014).

Following the model of the 1964 report, this Surgeon General's report includes comprehensive compilations of the evidence on smoking cessation. The evidence was analyzed to identify causal associations according to enunciated principles, sometimes referred to as the "Surgeon General's criteria" or the "Hill" criteria (after Sir Austin Bradford Hill) for causality. The criteria, offered in Chapter 3 of the 1964 report, included

- Consistency of the association,

- Strength of the association,

- Specificity of the association,

- Temporal relationship of the association, and

- Coherence of the association (U.S. Department of Health, Education, and Welfare [USDHEW] 1964, p. 20).

In the 2004 Surgeon General's report (USDHHS 2004), the framework for interpreting evidence on smoking and health was revisited in depth for the first time since the 1964 report. The 2004 report provided a four-level hierarchy of categories for interpreting evidence, and this current report follows the same model:

a. "Evidence is **sufficient** to infer a causal relationship.

b. Evidence is **suggestive but not sufficient** to infer a causal relationship.

c. Evidence is **inadequate** to infer the presence or absence of a causal relationship (which encompasses evidence that is sparse, of poor quality, or conflicting).

d. Evidence is **suggestive of no causal relationship**" (USDHHS 2004, p. 18).

Answers to several questions helped to guide judgment toward these categories:

- Do multiple high-quality studies show a consistent association between smoking and disease?

- Are the measured effects large enough and statistically strong?

- Does the evidence show that smoking occurs before the disease occurs (a temporal association)?

- Is the relationship between smoking and disease coherent or plausible in terms of known scientific principles, biologic mechanisms, and observed patterns of disease?

- Is there a dose-response relationship between smoking and disease?

- Is the risk of disease reduced after quitting smoking?

The categories acknowledge that evidence can be "suggestive but not sufficient" to infer a causal relationship, and the categories allow for evidence that is "suggestive of no causal relationship." This framework also separates conclusions about causality from the implications of such conclusions. Inference is sharply and completely separated from policy or research implications of the conclusions, thus adhering to the approach established in the 1964 report. However, consistent with past Surgeon General's reports on tobacco, conclusions are not limited to just causal determinations and frequently include recommendations for research, policies, or other actions.

Major Conclusions

1. Smoking cessation is beneficial at any age. Smoking cessation improves health status and enhances quality of life.

2. Smoking cessation reduces the risk of premature death and can add as much as a decade to life expectancy.

3. Smoking places a substantial financial burden on smokers, healthcare systems, and society. Smoking cessation reduces this burden, including smoking-attributable healthcare expenditures.

4. Smoking cessation reduces risk for many adverse health effects, including reproductive health outcomes, cardiovascular diseases, chronic obstructive pulmonary disease, and cancer. Quitting smoking is also beneficial to those who have been diagnosed with heart disease and chronic obstructive pulmonary disease.

5. More than three out of five U.S. adults who have ever smoked cigarettes have quit. Although a majority of cigarette smokers make a quit attempt each year, less than one-third use cessation medications approved by the U.S. Food and Drug Administration or behavioral counseling to support quit attempts.

6. Considerable disparities exist in the prevalence of smoking across the U.S. population, with higher prevalence in some subgroups. Similarly, the prevalence of key indicators of smoking cessation—quit attempts, receiving advice to quit from a health professional, and using cessation therapies—also varies across the population, with lower prevalence in some subgroups.

7. Smoking cessation medications approved by the U.S. Food and Drug Administration and behavioral counseling are cost-effective cessation strategies. Cessation medications approved by the U.S. Food and Drug Administration and behavioral counseling increase the likelihood of successfully quitting smoking, particularly when used in combination. Using combinations of nicotine replacement therapies can further increase the likelihood of quitting.

8. Insurance coverage for smoking cessation treatment that is comprehensive, barrier-free, and widely promoted increases the use of these treatment services, leads to higher rates of successful quitting, and is cost-effective.

9. E-cigarettes, a continually changing and heterogeneous group of products, are used in a variety of ways. Consequently, it is difficult to make generalizations about efficacy for cessation based on clinical trials involving a particular e-cigarette, and there is presently inadequate evidence to conclude that e-cigarettes, in general, increase smoking cessation.

10. Smoking cessation can be increased by raising the price of cigarettes, adopting comprehensive smoke-free policies, implementing mass media campaigns, requiring pictorial health warnings, and maintaining comprehensive statewide tobacco control programs.

Chapter Conclusions

Chapter 2: Patterns of Smoking Cessation Among U.S. Adults, Young Adults, and Youth

1. In the United States, more than three out of every five adults who were ever cigarette smokers have quit smoking.

2. Past-year quit attempts and recent and longer term cessation have increased over the past 2 decades among adult cigarette smokers.

3. Marked disparities in cessation behaviors, such as making a past-year quit attempt and achieving recent successful cessation, persist across certain population subgroups defined by educational attainment, poverty status, age, health insurance status, race/ethnicity, and geography.

4. Advice from health professionals to quit smoking has increased since 2000; however, four out of every nine adult cigarette smokers who saw a health professional during the past year did not receive advice to quit.

5. Use of evidence-based cessation counseling and/or medications has increased among adult cigarette smokers since 2000; however, more than two-thirds of adult cigarette smokers who tried to quit during the past year did not use evidence-based treatment.

6. A large proportion of adult smokers report using non-evidence-based approaches when trying to quit smoking, such as switching to other tobacco products.

Chapter 3: New Biological Insights into Smoking Cessation

1. The evidence is suggestive but not sufficient to infer that increasing glutamate transport can alleviate nicotine withdrawal symptoms and prevent relapse.

2. The evidence is suggestive but not sufficient to infer that neuropeptide systems play a role in multiple stages of the nicotine addiction process, and that modulating the function of certain neuropeptides can reduce smoking behavior in humans.

3. The evidence is suggestive but not sufficient to infer that targeting the habenulo-interpeduncular pathway with agents that increase the aversive properties of nicotine are a useful therapeutic target for smoking cessation.

4. The evidence is suggestive but not sufficient to infer that vaccines generating adequate levels of nicotine-specific antibodies can block the addictive effects of nicotine and aid smoking cessation.

5. The evidence is suggestive but not sufficient to infer that dysregulated brain circuits, including prefrontal and cingulate cortical regions and their connections with various striatal and insula loci, can serve as novel therapeutic targets for smoking cessation.

6. The evidence is suggestive but not sufficient to infer that the effectiveness of nicotine replacement therapy may vary across specific genotype groups.

Chapter 4: The Health Benefits of Smoking Cessation

Cancer

1. The evidence is sufficient to infer that smoking cessation reduces the risk of lung cancer.

2. The evidence is sufficient to infer that smoking cessation reduces the risk of laryngeal cancer.

3. The evidence is sufficient to infer that smoking cessation reduces the risk of cancers of the oral cavity and pharynx

4. The evidence is sufficient to infer that smoking cessation reduces the risk of esophageal cancer.

5. The evidence is sufficient to infer that smoking cessation reduces the risk of pancreatic cancer.

6. The evidence is sufficient to infer that smoking cessation reduces the risk of bladder cancer.

7. The evidence is sufficient to infer that smoking cessation reduces the risk of stomach cancer.

8. The evidence is sufficient to infer that smoking cessation reduces the risk of colorectal cancer.

9. The evidence is sufficient to infer that smoking cessation reduces the risk of liver cancer.

10. The evidence is sufficient to infer that smoking cessation reduces the risk of cervical cancer.

11. The evidence is sufficient to infer that smoking cessation reduces the risk of kidney cancer.

12. The evidence is sufficient to infer that smoking cessation reduces the risk of acute myeloid leukemia.

13. The evidence is sufficient to infer that the relative risk of lung cancer decreases steadily after smoking cessation compared with the risk for persons continuing to smoke, with risk decreasing to half that of continuing smokers approximately 10–15 years after smoking cessation and decreasing further with continued cessation.

Smoking Cessation After a Cancer Diagnosis

1. The evidence is suggestive but not sufficient to infer a causal relationship between smoking cessation and improved all-cause mortality in cancer patients who are current smokers at the time of a cancer diagnosis.

Cardiovascular Disease

1. The evidence is sufficient to infer that smoking cessation reduces levels of markers of inflammation and hypercoagulability and leads to rapid improvement in the level of high-density lipoprotein cholesterol.

2. The evidence is sufficient to infer that smoking cessation leads to a reduction in the development of subclinical atherosclerosis, and that progression slows as time since cessation lengthens.

3. The evidence is sufficient to infer that smoking cessation reduces the risk of cardiovascular morbidity and mortality and the burden of disease from cardiovascular disease.

4. The evidence is sufficient to infer that the relative risk of coronary heart disease among former smokers compared with never smokers falls rapidly after cessation and then declines more slowly.

5. The evidence is sufficient to infer that smoking cessation reduces the risk of stroke morbidity and mortality.

6. The evidence is sufficient to infer that, after smoking cessation, the risk of stroke approaches that of never smokers.

7. The evidence is suggestive but not sufficient to infer that smoking cessation reduces the risk of atrial fibrillation.

8. The evidence is suggestive but not sufficient to infer that smoking cessation reduces the risk of sudden cardiac death among persons without coronary heart disease.

9. The evidence is suggestive but not sufficient to infer that smoking cessation reduces the risk of heart failure among former smokers compared with persons who continue to smoke.

10. Among patients with left-ventricular dysfunction, the evidence is suggestive but not sufficient to infer that smoking cessation leads to increased survival and reduced risk of hospitalization for heart failure.

11. The evidence is suggestive but not sufficient to infer that smoking cessation reduces the risk of venous thromboembolism.

12. The evidence is suggestive but not sufficient to infer that smoking cessation substantially reduces the risk of peripheral arterial disease among former smokers compared with persons who continue to smoke, and that this reduction appears to increase with time since cessation.

13. The evidence is suggestive but not sufficient to infer that, among patients with peripheral arterial disease, smoking cessation improves exercise tolerance, reduces the risk of amputation after peripheral artery surgery, and increases overall survival.

14. The evidence is sufficient to infer that smoking cessation substantially reduces the risk of abdominal aortic aneurysm in former smokers compared with persons who continue to smoke, and that this reduction increases with time since cessation.

15. The evidence is suggestive but not sufficient to infer that smoking cessation slows the expansion rate of abdominal aortic aneurysm.

Smoking Cessation After a Diagnosis of Coronary Heart Disease

1. In patients who are current smokers when diagnosed with coronary heart disease, the evidence is sufficient to infer a causal relationship between smoking cessation and a reduction in all-cause mortality.

2. In patients who are current smokers when diagnosed with coronary heart disease, the evidence is sufficient to infer a causal relationship between smoking cessation and reductions in deaths due to cardiac causes and sudden death.

3. In patients who are current smokers when diagnosed with coronary heart disease, the evidence is sufficient to infer a causal relationship between smoking cessation and reduced risk of new and recurrent cardiac events.

Chronic Respiratory Disease

Chronic Obstructive Pulmonary Disease

1. Smoking cessation remains the only established intervention to reduce loss of lung function over time among persons with chronic obstructive pulmonary disease and to reduce the risk of developing chronic obstructive pulmonary disease in cigarette smokers.

2. The evidence is suggestive but not sufficient to infer that airway inflammation in cigarette smokers persists months to years after smoking cessation.

3. The evidence is suggestive but not sufficient to infer that changes in gene methylation and profiles of proteins occur after smoking cessation.

4. The evidence is inadequate to infer the presence or absence of a relationship between smoking cessation and changes in the lung microbiome.

Asthma

1. The evidence is suggestive but not sufficient to infer that smoking cessation reduces asthma symptoms and improves treatment outcomes and asthma-specific quality-of-life scores among persons with asthma who smoke.

2. The evidence is suggestive but not sufficient to infer that smoking cessation improves lung function among persons with asthma who smoke.

Reproductive Health

1. The evidence is sufficient to infer that smoking cessation by pregnant women benefits their health and that of their fetuses and newborns.

2. The evidence is inadequate to infer that smoking cessation before or during early pregnancy reduces the risk of placental abruption compared with continued smoking.

3. The evidence is inadequate to infer that smoking cessation before or during pregnancy reduces the risk of placenta previa compared with continued smoking.

4. The evidence is inadequate to infer that smoking cessation before or during pregnancy reduces the risk of premature rupture of the membranes compared with continued smoking.

5. The evidence is inadequate to infer that smoking during early or mid-pregnancy alone, and not during late pregnancy, is associated with a reduced risk of preeclampsia.

6. The evidence is sufficient to infer that women who quit smoking before or during pregnancy gain more weight during gestation than those who continue to smoke.

7. The evidence is suggestive but not sufficient to infer that women who quit smoking before or during pregnancy gain more weight during gestation than nonsmokers.

8. The evidence is inadequate to infer that smoking cessation during pregnancy increases the risk of gestational diabetes.

9. The evidence is sufficient to infer that smoking cessation during pregnancy reduces the effects of smoking on fetal growth and that quitting smoking early in pregnancy eliminates the adverse effects of smoking on fetal growth.

10. The evidence is inadequate to determine the gestational age before which smoking cessation should occur to eliminate the effects of smoking on fetal growth.

11. The evidence is sufficient to infer that smoking cessation before or during early pregnancy reduces the risk for a small-for-gestational-age birth compared with continued smoking.

12. The evidence is suggestive but not sufficient to infer that women who quit smoking before conception or during early pregnancy have a reduced risk of preterm delivery compared with women who continue to smoke.

13. The evidence is suggestive but not sufficient to infer that the risk of preterm delivery in women who quit smoking before or during early pregnancy does not differ from that of nonsmokers.

14. The evidence is inadequate to infer that smoking cessation during pregnancy reduces the risk of stillbirth.

15. The evidence is inadequate to infer that smoking cessation during pregnancy reduces the risk of perinatal mortality among smokers.

16. The evidence is inadequate to infer that women who quit smoking before or during early pregnancy have a reduced risk for infant mortality compared with continued smokers.

17. The evidence is inadequate to infer an association between smoking cessation, the timing of cessation, and female fertility or fecundity.

18. The evidence is suggestive but not sufficient to infer that smoking cessation reduces the risk of earlier age at menopause compared with continued smoking.

19. The evidence is inadequate to infer that smoking cessation reduces the effects of smoking on male fertility and sperm quality.

20. The evidence is suggestive but not sufficient to infer that former smokers are at increased risk of erectile dysfunction compared with never smokers.

21. The evidence is inadequate to infer that smoking cessation reduces the risk of erectile dysfunction compared with continued smoking.

Chapter 5: The Benefits of Smoking Cessation on Overall Morbidity, Mortality, and Economic Costs

1. The evidence is sufficient to infer that smoking cessation improves well-being, including higher quality of life and improved health status.

2. The evidence is sufficient to infer that smoking cessation reduces mortality and increases the lifespan.

3. The evidence is sufficient to infer that smoking exacts a high cost for smokers, healthcare systems, and society.

4. The evidence is sufficient to infer that smoking cessation interventions are cost-effective.

Chapter 6: Interventions for Smoking Cessation and Treatments for Nicotine Dependence

1. The evidence is sufficient to infer that behavioral counseling and cessation medication interventions increase smoking cessation compared with self-help materials or no treatment.

2. The evidence is sufficient to infer that behavioral counseling and cessation medications are independently

effective in increasing smoking cessation, and even more effective when used in combination.

3. The evidence is sufficient to infer that proactive quit-line counseling, when provided alone or in combination with cessation medications, increases smoking cessation.

4. The evidence is sufficient to infer that short text message services about cessation are independently effective in increasing smoking cessation, particularly if they are interactive or tailored to individual text responses.

5. The evidence is sufficient to infer that web or Internet-based interventions increase smoking cessation and can be more effective when they contain behavior change techniques and interactive components.

6. The evidence is inadequate to infer that smartphone apps for smoking cessation are independently effective in increasing smoking cessation.

7. The evidence is sufficient to infer that combining short- and long-acting forms of nicotine replacement therapy increases smoking cessation compared with using single forms of nicotine replacement therapy.

8. The evidence is suggestive but not sufficient to infer that pre-loading (e.g., initiating cessation medication in advance of a quit attempt), especially with the nicotine patch, can increase smoking cessation.

9. The evidence is suggestive but not sufficient to infer that very-low-nicotine-content cigarettes can reduce smoking and nicotine dependence and increase smoking cessation when full-nicotine cigarettes are readily available; the effects on cessation may be further strengthened in an environment in which conventional cigarettes and other combustible tobacco products are not readily available.

10. The evidence is inadequate to infer that e-cigarettes, in general, increase smoking cessation. However, the evidence is suggestive but not sufficient to infer that the use of e-cigarettes containing nicotine is associated with increased smoking cessation compared with the use of e-cigarettes not containing nicotine, and the evidence is suggestive but not sufficient to infer that more frequent use of e-cigarettes is associated with increased smoking cessation compared with less frequent use of e-cigarettes.

11. The evidence is sufficient to infer that certain life events—including hospitalization, surgery, and lung cancer screening—can trigger attempts to quit smoking, uptake of smoking cessation treatment, and smoking cessation.

12. The evidence is suggestive but not sufficient to infer that fully and consistently integrating standardized, evidence-based smoking cessation interventions into lung cancer screening increases smoking cessation while avoiding potential adverse effects of this screening on cessation outcomes.

13. The evidence is suggestive but not sufficient to infer that cytisine increases smoking cessation.

Chapter 7: Clinical-, System-, and Population-Level Strategies that Promote Smoking Cessation

1. The evidence is sufficient to infer that the development and dissemination of evidence-based clinical practice guidelines increase the delivery of clinical interventions for smoking cessation.

2. The evidence is sufficient to infer that with adequate promotion, comprehensive, barrier-free, evidence-based cessation insurance coverage increases the availability and utilization of treatment services for smoking cessation.

3. The evidence is sufficient to infer that strategies that link smoking cessation-related quality measures with payments to clinicians, clinics, or health systems increase the rate of delivery of clinical treatments for smoking cessation.

4. The evidence is sufficient to infer that tobacco quit-lines are an effective population-based approach to motivate quit attempts and increase smoking cessation.

5. The evidence is suggestive but not sufficient to infer that electronic health record technology increases the rate of delivery of smoking cessation treatments.

6. The evidence is sufficient to infer that increasing the price of cigarettes reduces smoking prevalence, reduces cigarette consumption, and increases smoking cessation.

7. The evidence is sufficient to infer that smokefree policies reduce smoking prevalence, reduce cigarette consumption, and increase smoking cessation.

8. The evidence is sufficient to infer that mass media campaigns increase the number of calls to quitlines and increase smoking cessation.

9. The evidence is sufficient to infer that comprehensive state tobacco control programs reduce smoking prevalence, increase quit attempts, and increase smoking cessation.

10. The evidence is sufficient to infer that large, pictorial health warnings increase smokers' knowledge about the health harms of smoking, interest in quitting, and quit attempts and decrease smoking prevalence.

11. The evidence is suggestive but not sufficient to infer that plain packaging increases smoking cessation.

12. The evidence is suggestive but not sufficient to infer that decreasing the retail availability of tobacco products and exposure to point-of-sale tobacco marketing and advertising increases smoking cessation.

13. The evidence is suggestive but not sufficient to infer that restricting the sale of certain types of tobacco products, such as menthol and other flavored products, increases smoking cessation, especially among certain populations.

The Evolving Landscape of Smoking Cessation

This section of the chapter reviews the history of smoking cessation, from its early origins to the modern era, including the changes that have occurred since publication of the 1990 Surgeon General's report. It also highlights developments that have shaped current initiatives in smoking cessation and will set the stage for the chapters that follow. Finally, this section highlights a broad set of interventions that have been implemented over the past three decades and are proven to be effective at helping people quit successfully. These interventions, which are now being integrated into clinical care and societal policies, include (a) low-intensity interventions, such as telephone quitlines; (b) brief but systematically repeated interventions in primary care settings; (c) over-the-counter medications; and (d) public policy approaches, such as increases in tobacco prices (e.g., through taxation), comprehensive policies to make indoor environments smokefree, and mass media campaigns that increase motivation to quit and may help sustain quit attempts (CDC 2014a; USDHHS 2014).

Historical Context of Smoking Cessation

Addiction Versus Habit

In 2017, a federal court ordered the major U.S. tobacco companies to run television and newspaper ads that tell the American public the truth about the dangers of smoking and secondhand smoke (U.S. Department of Justice 2017b). The ads included several statements related to the addictiveness of nicotine:

- "Smoking is highly addictive. Nicotine is the addictive drug in tobacco";

- "Cigarette companies intentionally designed cigarettes with enough nicotine to create and sustain addiction";

- "It's not easy to quit"; and

- "When you smoke, the nicotine actually changes the brain—that's why quitting is so hard" (U.S. Department of Justice 2017a; Farber et al. 2018, p. 128).

However, previously secret documents from the tobacco industry reveal that the tobacco industry was aware of the addictive nature of nicotine for decades, long before they publicly acknowledged it or were eventually ordered by the court to publicly acknowledge it (Elias et al. 2018). In fact, the tobacco industry had been engineering cigarettes for decades to improve the rapid delivery of nicotine (Proctor 2011). For years, the tobacco industry coordinated well-financed, systematic efforts to deny the addictiveness of nicotine and the need for users to quit smoking, thereby trivializing the harms of tobacco use while promoting the benefits of nicotine (Hirschhorn 2009; USDHHS 2014). The industry did this using well-documented tactics, including aggressive funding and support for academic, medical, and community organizations that were sympathetic to this perspective (Proctor 2011).

Addiction to any substance often brings on a variety of efforts to overcome or treat it. However, until the late twentieth century, clinical and public health approaches to smoking cessation often treated smoking as a habit rather than as an addiction (USDHEW 1964). The tobacco industry has asserted for many years in public messaging and litigation that smoking is a personal choice (Friedman et al. 2015). Indeed, both smoking and smoking cessation were considered personal choices; the idea was that

if persons started smoking cigarettes, they could quit if they truly wanted to, putting the onus on the individual smoker to quit using his or her own motivation and desire to do so. The Surgeon General first concluded in 1988 that "cigarettes and other forms of tobacco are addicting," and "nicotine is the drug in tobacco that causes addiction" (USDHHS 1988, p. 9). Eventually, intensive medical treatments and protocols—such as the use of multiple medications for long periods of time, long-term psychological counseling, and inpatient hospitalization—were developed to address the highly addictive nature of nicotine (Fiore et al. 2008). However, between 2000 and 2015, less than one-third of U.S. adult cigarette smokers reported using evidence-based cessation treatments, such as behavioral counseling and/or medication, when trying to quit smoking (Babb et al. 2017).

The first comprehensive clinical practice guideline for smoking cessation was produced by the federal government in 1996 and emphasized the role of healthcare providers in providing assessment and treatment interventions for smoking with patients who smoke (Fiore et al. 1996). In 2008, an updated federal guideline, *Treating Tobacco Use and Dependence: 2008 Update* (hereafter referred to as the *Clinical Practice Guideline*), was published (Fiore et al. 2008). This guideline uses language similar to that used in helping persons quit other addictive substances and is discussed in more detail in Chapter 7.

With the shift toward an improved understanding of the nature of nicotine addiction, terminology used to describe tobacco use has also shifted. The *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) is the primary clinical source of diagnostic criteria for mental health disorders. It provides diagnostic criteria for "tobacco use disorder," which includes physiologic dependence, impaired control, and social impairment, among others (American Psychiatric Association 2013). These diagnostic criteria align with those for other substance use disorders and acknowledge the physical, psychological, and environmental components of addiction. However, as noted in the *Clinical Practice Guideline,* although not all tobacco use results in tobacco use disorder, any tobacco use has risks and, therefore, warrants intervention (Fiore et al. 2008). Accordingly, throughout this report, the term "tobacco use and dependence" is used to be inclusive of all patterns of use and to acknowledge the multifactorial and chronic relapsing nature of nicotine addiction. The term "nicotine dependence" is used specifically to refer to physiologic dependence on nicotine. This terminology aligns with that used in the *Clinical Practice Guideline,* which further details why the term "tobacco use and dependence" is most appropriate when discussing cessation interventions (Fiore et al. 2008).

Coverage of Smoking Cessation, Nicotine, and Addiction in Surgeon General's Reports

Coverage of cessation, nicotine, and addiction in Surgeon General's reports has evolved greatly since 1964, reflecting the evolution of scientific understanding of addiction to nicotine and its treatment.

Coverage of Smoking Cessation

Of the 34 Surgeon General's reports on smoking and health published to date, this is the second to address smoking cessation as the main topic. Even so, beginning with the first report in 1964, evidence reviewed in various reports has supported some conclusions related to the health benefits of smoking cessation. Over time, as the epidemiologic findings from prospective cohort studies became more abundant and covered longer periods of time since quitting smoking, conclusions began to mount on the decline in risks for major smoking-caused diseases after cessation. In fact, declines in risk after cessation figured into the causal inference process presented in the reports, which documented a decrease in health risks after withdrawal of smoking—the presumptive causal agent.

The 1964 Surgeon General's report reviewed findings from seven prospective cohort studies that had included sufficient numbers of former smokers to provide estimates about cause-specific relative risk for mortality from selected diseases (USDHEW 1964). The data from the cohort studies were complemented by case-control studies for some cancer sites that had also addressed a change in risk after smoking cessation. For all-cause mortality, the 1964 report stated that compared with never smokers, relative mortality was 40% higher among former smokers and 70% higher among current smokers. For lung cancer, quantitative relationships with smoking patterns were described as follows: "The risk of developing lung cancer increases with duration of smoking and the number of cigarettes smoked per day, and is diminished by discontinuing smoking" (p. 37). In considering the causal nature of the association between smoking and lung cancer, the report stated, "Where discontinuance, time since discontinuance, and amount smoked prior to discontinuance were considered in either retrospective studies or, with more detail, in prospective studies, these all showed lower risks for ex-smokers, still lower risks as the length of time since discontinuance increased, and lower risks among ex-smokers if they had been light smokers" (p. 188). The report did not conclude that smoking caused cardiovascular disease, but it noted a lower risk of death from cardiovascular disease among former smokers compared with continuing smokers and stated, "Although the causative

role of cigarette smoking in deaths from coronary disease is not proven, the Committee considers it more prudent from the public health viewpoint to assume that the established association has causative meaning than to suspend judgment until no uncertainty remains" (p. 32).

In ensuing Surgeon General's reports through the 1970s, the health benefits of smoking cessation did not receive systematic attention, but the results identified a declining risk for some diseases after cessation. The 1979 report offered detailed reviews for major diseases, and it concluded that compared with smokers, risks were lower among former smokers for all-cause mortality, atherosclerosis and coronary heart disease, lung cancer, larynx cancer, lung function, and respiratory symptoms (USDHEW 1979). Three Surgeon General's reports released in the early 1980s focused on the health consequences of smoking on specific major disease categories: cancer (USDHHS 1982), cardiovascular disease (USDHHS 1983), and chronic lung disease (USDHHS 1984). Each report also examined the impact of smoking cessation on each of those disease categories. In 1988, the report reviewed the evidence to date on nicotine and drew major conclusions that nicotine was addictive (USDHHS 1988).

By 1990, the scope and depth of evidence on smoking cessation was sufficiently abundant to justify a full report, *The Health Benefits of Smoking Cessation.* The report's conclusions expanded on those of earlier reports, summarizing descriptions of the temporal course of declining risk for many of the diseases caused by smoking (USDHHS 1990). For example, the report concluded, "The excess risk of [coronary heart disease] caused by smoking is reduced by about half after 1 year of smoking abstinence and then declines gradually. After 15 years of abstinence, the risk of [coronary heart disease] is similar to that of persons who have never smoked" (p. 11).

Importantly, the 1990 report was the first to address smoking cessation and reproduction. That report offered strong conclusions with clinical implications related to reproduction and offered conclusions about the timing of cessation across gestation and implications for birthweight (USDHHS 1990).

The 2004 Surgeon General's report, *The Health Consequences of Smoking,* covered active smoking and disease; and the 2014 Surgeon General's report, *The Health Consequences of Smoking—Fifty Years of Progress,* again covered the full range of health consequences of smoking, providing conclusions that drew on data from long-running cohort studies that described how risks change in former smokers up to several decades after quitting. For example, the 2004 report concluded, "Even after many years of not smoking, the risk of lung cancer in former smokers remains higher than in persons who have never smoked" (USDHHS 2004, p. 25). In contrast, regarding the effect of smoking in

accelerating the decline of lung function, the report determined "[t]he evidence is sufficient to infer a causal relationship between sustained cessation from smoking and a return of the rate of decline in pulmonary function to that of persons who had never smoked" (p. 27). The 2014 report updated estimates of relative risks in former smokers, drawing on more contemporary cohorts, and used the estimates to calculate attributable mortality (USDHHS 2014). The extended follow-up of the cohort studies documented the benefits of cessation by early middle age for reducing the risk of death from any cause.

Coverage of Nicotine and Addiction

The 1964 Surgeon General's report suggested that smoking was a form of habituation, stating that "[e]ven the most energetic and emotional campaigner against smoking and nicotine could find little support for the view that all those who use tobacco, coffee, tea, and cocoa are in need of mental care even though it may at some time in the future be shown that smokers and nonsmokers have different psychologic characteristics" (USDHEW 1964, pp. 351–352). The report used such words as "compulsion" and "habit" but did not consider nicotine to be addicting: "Proof of physical dependence requires demonstration of a characteristic and reproducible abstinence syndrome upon withdrawal of a drug or chemical which occurs spontaneously, inevitably, and is not under control of the subject. Neither nicotine nor tobacco comply with any of these requirements" (USDHEW 1964, p. 352). Correspondingly, the report emphasized habituation and not addiction: "The habitual use of tobacco is related primarily to psychological and social drives, reinforced and perpetuated by the pharmacologic actions of nicotine on the central nervous system" (USDHEW 1964, p. 354). In 1977, the National Institute on Drug Abuse began to support studies of cigarette smoking as a "dependence process," comparing it to other drug addictions (Parascandola 2011). The monograph, *The Behavioral Aspects of Smoking* (Krasnegor 1979), reflected an advancing understanding of the power of nicotine as a pharmacologic agent: "Nicotine has been proposed as the primary incentive in smoking [Jarvik 1973, as cited in Krasnegor 1979] and may be instrumental in the establishment of the smoking habit. Whether or not it is the only reinforcing agent, it is still the most powerful pharmacological agent in cigarette smoke" (p. 12). The 1979 Surgeon General's report, *Smoking and Health,* devoted considerable attention to the behavioral aspects of smoking, but it still did not use the term "addiction" (USDHEW 1979). That report also concluded that there was general acceptance of the existence of a tobacco withdrawal syndrome, which was more prominent in heavy smokers.

The 1988 Surgeon General's report explored the clinical and public health implications of smoking, with

several major conclusions serving as an indictment of the addictiveness of nicotine in cigarettes. In fact, this report stated for the first time that cigarettes are addictive and function in a similar fashion to cocaine and heroin use. The three major conclusions of that report were:

- "Cigarettes and other forms of tobacco are addicting";

- "Nicotine is the drug in tobacco that causes addiction"; and

- "The pharmacologic and behavioral processes that determine tobacco addiction are similar to those that determine addiction to drugs such as heroin and cocaine" (USDHHS 1988, p. 9).

Later Surgeon General's reports on tobacco have addressed the subsequent scientific advances in the area of smoking and addiction, particularly the 2010 report on mechanisms by which smoking causes disease (USDHHS 2010).

Perspectives on Smoking Cessation

In 2015, most smokers stated that they wanted to quit smoking (68%), and about 56% of smokers made a serious attempt to quit; however, only about 7% of smokers reported that they had recently quit (Babb et al. 2017). Despite evidence demonstrating that using smoking cessation pharmacotherapy with behavioral support is more effective than quitting without these treatments, most smokers who had recently quit reported that they did not quit with medication or counseling assistance (see Chapter 6). Proponents of encouraging smokers to quit without treatment, often called quitting "cold turkey," point to data indicating that most smokers who quit successfully do so without medications or any type of formal assistance, as well as to population surveys suggesting that cold-turkey quitters do as well or better than those who use over-the-counter NRTs. Proponents of this approach also suggest that medicalization may disempower smokers and create artificial barriers to quitting (Alpert et al. 2013; Polito 2013). In contrast, others note that because of a lack of insurance coverage and other barriers, many smokers have little choice but to quit without formal treatment. Selection bias may also play a factor, as the most heavily addicted smokers are those most likely to use NRT, but these smokers also have a lower likelihood of success. In addition, most of those who use NRT do so for short periods of time or at lower-than-recommended doses and do not have adjunctive support available from tobacco cessation quitlines or other interventions (Amodei and

Lamb 2008). There are also issues of recall and attribution bias, which may make smokers more likely to report their most proximal experiences with use or nonuse of pharmacologic smoking cessation aids and/or behavioral supports and not to report previous quit attempts during which they used pharmacologic aids and/or behavioral support.

During most of the twentieth century, smokers who wanted to quit had limited resources to do so, especially smokers with mental health or substance use disorders. For example, the investment in research required for behavioral, pharmacologic, and systems-level interventions that increase successful cessation had been relatively limited given the magnitude of tobacco-related disease burden and the size of the population affected (Dennis 2004; Carter et al. 2015; Hall et al. 2016). Even when interventions developed in the 1980s and 1990s were clearly shown to be effective, most health insurers and health systems showed little interest in providing coverage for or integrating into regular practice any new pharmacologic, behavioral, or systems approaches to cessation (see Chapter 6). Additionally, many medical schools provide only a small amount of time, if any, in their academic curriculum or programs for developing clinical skills to train future physicians in addressing tobacco use and dependence in patients (Ferry et al. 1999; Montalto et al. 2004; Powers et al. 2004; Association of American Medical Colleges 2007; Geller et al. 2008; Richmond et al. 2009; Torabi et al. 2011; Griffith et al. 2013).

Development and Evolution of a Paradigm for Treating Nicotine Addiction

Clinicians' views on smoking cessation shifted toward the end of the twentieth century. Given the increasing amount of evidence and awareness of the robust and widespanning beneficial effects of smoking cessation on various chronic diseases (USDHHS 1990), clinicians began to understand that promoting smoking cessation was among the most powerful interventions for increasing health, while merely advising patients to quit was insufficient in promoting smokers to initiate quitting and sustain abstinence without relapsing. Concurrently, researchers began to better understand the powerfully addictive properties of nicotine and the complexities of the nicotine addiction process (USDHHS 1988). This knowledge was disseminated widely to health professionals and the community (Fiore et al. 1996).

Nicotine addiction is now increasingly emphasized as a main driver of both the initiation and continuation of smoking. Thus, the medical community sees

the morbidity and mortality associated with smoking as clinical endpoints and nicotine addiction as the cause. Correspondingly, a growing number of intensive behavioral and pharmacologic treatments have become available to promote sustained abstinence.

Epidemiologic Shifts in Smoking Cessation

Chapter 2 provides a detailed discussion of key patterns and trends in cigarette smoking cessation in the United States. It also reviews the changing demographic and smoking-related characteristics of cigarette smokers, with a focus on how these changes may influence future trends in cessation.

Changes in the Patterns of Smoking and Population Characteristics of Smokers

The typical profile of the smoker has evolved over the years. The "hardening hypothesis" suggests that adults who continue to smoke cigarettes in the face of strengthening tobacco control policies and the increasing availability of efficacious cessation interventions will tend to be heavier smokers who are more highly addicted, less interested in quitting, and likely to have more difficulty in quitting (National Cancer Institute [NCI] 2003). Only a limited amount of evidence supports this hypothesis (Hughes 2011). Instead of increases over time in the proportion of smokers with frequent or heavy patterns of smoking, as would be predicted by hardening, the proportion has actually decreased (Jamal et al. 2016). Furthermore, from 2005 to 2015, the percentage of current smokers who were daily smokers declined from 80.8% to 75.7%, and the proportion of current smokers who smoked on only some days (i.e., nondaily smokers) increased from 19.2% to 24.3% (Jamal et al. 2016). Similarly, among daily smokers, the average number of cigarettes smoked per day declined from 16.7 in 2005 to 13.8 in 2014. However, when considering other measures of dependence, some modest and preliminary support exists for hardening among treatment-seeking smokers. For example, in a summary review by Hughes and colleagues (2011), two of four studies showed increases in dependence and decreases in quit rates, but similar trends were not found among the general population of smokers who had quit.

Reductions in the frequency and heaviness of smoking do not necessarily suggest that a simple continuation of current approaches to increase smoking cessation will increase or even maintain progress in successful quitting. Nondaily or light smokers would be expected to be less addicted to nicotine and, therefore, when motivated to make a cessation attempt, would find it easier to quit than heavier smokers. Still, helping light and nondaily smokers to quit presents challenges. For example, some light and nondaily smokers do not self-identify as smokers, do not believe that they are addicted to nicotine, do not feel that they are at risk of smoking-related health effects, and do not expect quitting to be difficult (Berg et al. 2013; Scott et al. 2015; Chaiton et al. 2016). The 2008 *Clinical Practice Guideline* does not recommend cessation medications for use by light smokers, based on insufficient evidence of effectiveness in this population (Fiore et al. 2008). Ten years later, this gap in knowledge about treating light smokers is largely unchanged (Ebbert et al. 2016) (see Chapter 6) and presents a barrier for addressing this growing subpopulation of smokers.

The prevalence of smoking is increasingly concentrated in the United States in populations that may face barriers to quitting. These include persons with behavioral health conditions (including mental health conditions or substance use disorders); persons of low socioeconomic status; persons who are lesbian, gay, bisexual, or transgender; American Indians/Alaska Natives; recent immigrants from countries with a high prevalence of smoking; residents of the South and Midwest; and persons with a disability. Such populations have a markedly higher prevalence of cigarette smoking than their respective counterparts, and the decline in the prevalence of smoking in the United States as a whole has been slower among these groups, particularly those with behavioral health conditions and those of lower socioeconomic status (Grant et al. 2004; Schroeder and Morris 2010; CDC 2013b, 2016; Cook et al. 2014; Szatkowski and McNeill 2015) (see Chapter 2).

Changes in the Products Used by Smokers

The emergence of a wide array of new tobacco products and the increasing use of those products, combined with continued use of other conventional tobacco products, such as menthol cigarettes and smokeless tobacco, could complicate cessation efforts aimed at cigarette smoking (Trinidad et al. 2010; USDHHS 2014; Villanti et al. 2016; Wang et al. 2016). These products include hookahs (water pipes), little cigars and cigarillos, e-cigarettes, and heated tobacco products. Cigarette smokers who also use one or more other tobacco products, generally known as "dual" or "poly" use, have higher dependence on nicotine and greater difficulty quitting (Wetter et al. 2002; Bombard et al. 2007; Soule et al. 2015).

As of July 26, 2019, 11 states and the District of Columbia have passed laws legalizing nonmedical marijuana use (National Conference of State Legislatures [NCSL] 2019). Although not a tobacco product, marijuana is frequently used in combination with conventional

cigarettes or other tobacco products (e.g., cigars, e-cigarettes). For example, approximately 70% of adults who are current users of marijuana are also current users of tobacco (Schauer et al. 2016). Results from population-based surveys and some clinical studies indicate an association between the use of menthol-flavored cigarettes or marijuana and a lower probability of successful quitting (Ford et al. 2002; Patton et al. 2005; Gandhi et al. 2009; Schauer et al. 2017). The available longitudinal evidence from rigorously conducted studies is limited, so it is too soon to determine whether this association is correlational or causal.

Developments in Approaches to Smoking Cessation at the Individual Level

This section summarizes the landmark developments since the 1990 Surgeon General's report that have shaped treatment for tobacco dependence and corresponding breakthroughs in smoking cessation interventions at the individual level. Chapter 6 provides detailed evidence for current and emerging smoking cessation treatments, adding to the evidence presented in the *Clinical Practice Guideline* (Fiore et al. 2008). It also explores approaches to increasing the impact of tobacco cessation treatment through improved efficacy and increased reach.

Pharmacotherapy

The scientific understanding of the neurobiologic impact of chronic exposure to nicotine (USDHHS 2010) has stimulated research and development that focuses on identifying novel medications and improving existing medications. The only FDA-approved smoking cessation medication at the time of the 1990 Surgeon General's report was the gum form of NRT (USDHHS 1990). Since then, several additional NRT formulations (transdermal patch, lozenge, inhaler, and nasal spray) have been developed, with all but the inhaler and spray now approved for over-the-counter sale. Additionally, FDA has approved two non-NRT medications for smoking cessation: bupropion and varenicline (GlaxoSmithKline 2017; FDA 2017; Pfizer 2019).

Adding to the progress seen for individual agents, favorable developments in pharmacologic treatment have been seen in a variety of other areas over the past two decades. For example, because of the modest efficacy of monotherapy and the recognition that persons with nicotine addiction benefit from intensive treatments, a variety of combination pharmacotherapies have been studied (see Chapter 6).

Behavioral Interventions

Discoveries in the behavioral and social sciences have deepened our understanding of psychosocial influences on the nature and treatment of tobacco dependence, which has propelled new approaches to behavioral treatment. The evidence has clarified that during and long after the dissipation of acute pharmacologic withdrawal from nicotine during cessation, several factors—including vacillation of negative emotional states, repeated urges to smoke, diminished motivation, and having less confidence in the ability to successfully quit—can persist throughout the cessation process and undermine quitting (Liu et al. 2013; Ussher et al. 2013). Furthermore, encountering environments and situations previously associated with smoking, such as establishments that serve alcohol or interacting with friends who smoke, has been demonstrated to increase risk of relapse (Conklin et al. 2013). Fortunately, behavioral treatment models for mental health conditions and other substance use disorders have been translated and adapted for nicotine addiction to address these factors and have been shown to improve quit rates (Hall and Prochaska 2009).

In addition to quitlines, which have been a long-standing intervention to deliver population-based behavioral smoking cessation support, technological innovations have opened new service delivery platforms for sophisticated behavioral cessation interventions in other modalities. In the 1990s, computer-tailored, in-depth, personalized mailings based on answers to a lengthy questionnaire were developed and tested on smokers; the tailored or personalized mailings were more effective than mailings with standard text (Prochaska et al. 1993; Strecher et al. 1994). Receipt of personalized written feedback and self-help materials was also found to increase cessation rates (Curry et al. 1991). A systematic review by the U.S. Preventive Services Task Force (USPSTF) (2015) found self-help materials that were tailored to the individual patient to be effective cessation interventions. Interactive program modalities have been developed and tested (USPSTF 2015) for desktop and laptop computers, first via programs operated from a CD-ROM or hard drive, later via Internet downloads, and more recently from "the cloud" (Strecher et al. 2005; Haskins et al. 2017). The current state of science and technology also allows the leveraging of mobile phone technology and applications to deliver cessation interventions (Whittaker et al. 2016). These include applications involving standardized motivation-enhancing texts or quit-promoting strategies—some of which offer real-time, live-peer, or professional advising or counseling within the application (Smokefree.gov n.d.). Preliminary evaluations have suggested that these applications may be beneficial to users (Cole-Lewis et al. 2016; Squiers et al. 2016, 2017; Taber et al. 2016) and that the cost of delivery is low.

Treating Tobacco Use and Dependence

The 2000 and 2008 *Clinical Practice Guidelines* had marked impacts on increasing understanding of and operationalizing the current paradigm of treating tobacco use and dependence (Fiore et al. 2000, 2008). Until the 1990s, synopses of the state of the evidence on smoking cessation usually relied on a somewhat informal aggregation of clinical and population-based studies, an approach that is prone to author bias in the choice of studies included and in their interpretations. Markedly more formal review processes, such as systematic literature reviews, were applied to smoking cessation and treatment in the 1990s and 2000s, as thousands of cessation-related studies accumulated. These more formal reviews systematized the literature review process by using strict criteria for grading studies and employing meta-analyses where appropriate; they also included a more transparent and elaborate process for synthesizing evidentiary findings into conclusions and recommendations.

In addition, the standards and framing of cessation research have evolved over the past several decades, which is consistent with the increased sophistication of pharmaceutical and population-based trials in general. For example, clinical trials have evolved from examining the success rates of persons completing the trial, often examining only the point prevalence of abstinence, into using intent-to-treat, where all persons starting treatment are considered in the denominator and those lost to follow-up are counted as smokers or subject to data imputation techniques (Hall et al. 2001; Mermelstein et al. 2002; SRNT Subcommittee on Biochemical Verification 2002; Hughes et al. 2003; Shiffman et al. 2004). Definitions of successful abstinence often examine smoking status at 1 month, 6 months, and 1 year of abstinence after treatment.

Notably, some definitions of successful abstinence allow for brief lapses in smoking cessation to more accurately reflect the natural course of achieving long-term abstinence (Zhu et al. 1996). Similarly, population-level surveillance and research have evolved to include increasingly more complex questions and techniques to more accurately capture the nature of respondents' use of tobacco products and cessation behavior. For example, sets of questions have been developed to better categorize respondents' use of healthcare services and the nature of cessation support they received. In addition, new technologies have been deployed to better understand the patterns of behavior among smokers, such as ecological momentary assessment, which cues smokers to provide data on their smoking urges and other thoughts, emotions, and behaviors in real time (Shiffman 2009). Large clinical trials have also examined the interplay between multiple factors that affect quit success, such as different medications, dual-medication therapy, and different approaches

and intensities of behavioral interventions (Redmond et al. 2010).

The *Clinical Practice Guidelines* used formal scientific review processes to analyze thousands of studies produced in the 1990s and 2000s—analyses that included detailed evidence reviews that resulted in practical recommendations for clinicians (Fiore et al. 2000, 2008). Unlike most clinical guidelines, they also included recommendations at the health systems and policy levels based on evidence and tools designed specifically for clinicians to use in office practices. In addition, multiple Cochrane reviews have been performed on medications and counseling approaches (Hajek et al. 2013; Stead et al. 2013; Lindson-Hawley et al. 2015), and USPSTF has updated its literature on clinical preventive services (Siu and USPSTF 2015; USPSTF 2015). Based on the findings presented, the current paradigm for smoking cessation conceptualizes nicotine addiction as a chronic, relapsing disorder that benefits from long-term management and intensive treatment approaches, as do other chronic diseases. The major findings have shaped the way cessation is currently viewed:

- Any level of treatment is beneficial, and more intensive and longer behavioral and pharmacologic treatment is generally better.

- Physicians, psychologists, pharmacists, dentists, nurses, and numerous other healthcare professionals can treat nicotine addiction in smokers. Thus, by extension, the various settings in which such professionals work represent appropriate venues for providing these services.

- Behavioral interventions and FDA-approved pharmacotherapies are effective for treating nicotine dependence. A combination of behavioral interventions and pharmacotherapy is the optimal treatment based on overwhelming scientific evidence, with superiority in efficacy over either intervention alone.

Advances in research and technology have shaped how the clinical and scientific communities view and approach treatment for nicotine addiction in smokers, but this progress continues to lag the advances made in treating other chronic diseases. For instance, in cancer, cardiovascular disease, and other illnesses with multifactorial etiologies, major strides have been made toward precision treatment methods, which are based on the premise that clinical outcomes can be enhanced by selecting, adapting, and tailoring treatment on the basis of a patient's specific clinical profile and disease pathogenesis (Collins and Varmus 2015). Such approaches have been endorsed

and promoted as part of the Precision Medicine Initiative (Genetics Home Reference 2018), which reinforces that the future of clinical care lies in basic and clinical research and their translation to optimize health outcomes. Although precision treatment has not advanced for smoking cessation at the same rate as it has for treating certain other illnesses, emerging findings suggest that a personalized, precision approach has the potential to meaningfully improve smoking cessation outcomes (Allenby et al. 2016).

Evolution of Approaches to Smoking Cessation at the Population Level

More Intensity Versus Higher Reach of Support Services

Through the first decades in which cessation interventions were developed, most of the emphasis was on improved efficacy—specifically, increasing the probability that if smokers engaged and fully used an intervention service, their chances of success would be increased. As interventions, both behavioral or pharmacologic therapies and combination therapies have become increasingly effective, but despite the effectiveness of such therapies, they are not being used as designed by substantial numbers of smokers (Zhu et al. 2012). Several theoretical models suggested that efforts to develop interventions need to consider their population impact, not just their individual efficacy for those taking part in the intervention.

In the 1990s, the potential for smoking cessation interventions to make an impact on the tobacco epidemic was overshadowed by the low rate at which smokers actually used interventions. Several factors contributed to this phenomenon, and several other factors initially assumed to be the main drivers were eliminated. One assumption was that smokers were just not very interested in quitting or in accessing help to quit. However, population-level surveys over time and among diverse populations showed that not only were smokers interested in quitting, but more than half planned to quit in the next 6 months and had attempted to quit in the past year (Babb et al. 2017). In addition, when physicians or other healthcare providers systematically offered support for quitting, such as medications or follow-up, a much larger than expected fraction of smokers agreed to accept support. Even so, further examination revealed that helping smokers quit presented unique obstacles. Up to the 1990s,

- Almost no health insurers provided any coverage of smoking treatments—either medications, counseling, or physician intervention.

- Most physicians did not systematically address smoking in the course of clinical practice for multiple reasons, including lack of time, perception that patients are unready to quit, limited resources, and inadequate clinical skills related to cessation.

- Although smokers generally understood that smoking had unfavorable health effects, many did not fully understand or accept the magnitude or personal relevance of smoking's effects on various aspects of health and its dramatic overall effect on longevity (USDHHS 1989; Chapman et al. 1993). Even if smokers accept the theoretical possibility of risk, they often do not believe that the hypothetical future risk from smoking applies to them personally—for example, they believe they have "good genes" or other healthy habits, or they smoke in a less dangerous manner (Oakes et al. 2004).

- Smokers and physicians did not realize that effective treatments were available.

- Even when smokers wanted to quit and were potentially interested in getting help, evidence-based treatments were not readily available to them because of financial and practical barriers.

Thus, during the 1980s and 1990s, a series of system and policy innovations were developed and tested to address these barriers. These innovations included the use of organizational system change and quality improvement theory to systematically address opportunities to influence smokers during routine interactions with healthcare systems (Solberg et al. 1990; Manley et al. 1992); experiments providing different types of insurance coverage for cessation treatments (Curry et al. 1998); the development of more easily accessible treatments, such as phone-based quitlines (Orleans et al. 1991; Zhu et al. 2012); integrated promotion of cessation via mass media campaigns that encouraged the use of cessation services (McAfee et al. 2013); and easily accessible, in-person cessation clinics (Lee et al. 2016).

The lack of accessibility to cessation support was addressed in several ways. One approach attempted to bypass the lack of availability of support within healthcare services by creating easily accessible, low-intensity cessation supports, such as telephone quitlines or in-person clinics, that were generally operated and funded outside the healthcare system. Another approach attempted to integrate very brief but systematic, repeated support for cessation into primary care clinical practices while working to obtain insurance coverage and accessibility to more intense services for those interested in quitting. In

some instances, these approaches were combined synergistically (McAfee et al. 1998). A few U.S. states and some other countries, such as the United Kingdom, successfully developed—through funding from tobacco tax dollars or government healthcare—networks of freestanding, in-person cessation clinics that provided basic cessation counseling and medications (Gibson et al. 2010; West et al. 2013). However, this model has not been sustained in any geographic region of the United States, primarily because of limited resources to maintain it over time. Still, a higher intensity model, which includes more intensive and comprehensive cessation components, has continued to focus on markedly improving the chances of success by treating nicotine addiction via a tertiary treatment delivery model, akin to how a cancer center approaches patients who are referred for its services. For example, the Mayo Clinic and a handful of similar referral clinics use such strategies as in-depth evaluation by multidisciplinary staff; personalized treatment plans; recurrent follow-up; and, in some cases, admission to a residential facility or hospital (Hays et al. 2011). Although such programs often achieve high rates of smoking cessation, their utility is greatly limited by the high cost of implementation, unclear cost-effectiveness, and limited reach. For example, during a 7-year period, in a study of a large outpatient clinic, 2–3% of smokers used the available nicotine dependence services, even when the services were optimally promoted and delivered (Burke et al. 2015).

Population-Based Interventions

Historically, tobacco control efforts have focused on either helping smokers quit at the individual level, such as through clinical interventions, or on providing population-level interventions to decrease the prevalence of smoking. Potential synergies between these two approaches have become increasingly apparent over the past several decades. This section discusses four examples of attempts to combine individually delivered cessation support and population-based strategies to smoking cessation: quitlines, health systems transformation, mass media campaigns, and health insurance coverage of smoking cessation treatment. Chapter 7 provides a more in-depth review of the current literature on each of these topics and on other population-based interventions that have been shown to promote cessation, such as increasing the prices of tobacco products and the implementation of smokefree policies.

Quitlines

In the late 1980s and throughout the 1990s, researchers interested in helping large numbers of smokers quit smoking began to experiment with the provision of behavioral counseling support via telephone, in the hope of overcoming such barriers to utilization as cost and the reluctance of many smokers to attend face-to-face group or individual sessions. Providing counseling centrally was thought to provide more opportunities for systematically improving the quality of the counseling and the research infrastructures used to answer questions about the cessation process. Protocols were developed and tested in a variety of environments, ranging from academic centers (Ossip-Klein et al. 1991) to health systems (Orleans et al. 1991) to state health departments (Zhu et al. 1996). Multiple large, randomized trials have since established the effectiveness of the telephone modality (Stead et al. 2013). The availability of quitlines grew rapidly during the 1990s and the early 2000s.

The adoption of quitlines by state health departments was initially facilitated by the increased revenue provided to states from the Master Settlement Agreement in 1998 and higher taxes on tobacco products. In 2003, CDC provided supplemental funding to state health departments to establish quitlines in those that did not have them and to enhance quitline services and access in those with existing quitlines (Zhang et al. 2016). In 2004, a national network of state quitlines was created with a single national portal number (1-800-QUIT-NOW), which is serviced by NCI (Cummins et al. 2007; CDC 2014b). By 2006, residents in all 50 states, the District of Columbia, and U.S. territories had access to quitlines, and the North American Quitline Consortium had been developed to help set evaluation standards and enhance the collection of information, including an agreed-upon minimum dataset to be collected from all callers, with a data warehouse funded by CDC (North American Quitline Consortium 2007; Keller et al. 2010). Providers of quitline services grew from modest operations with a few dozen employees to multiple large providers based in a range of organizations, including for-profit and nonprofit national healthcare organizations and academic centers, some employing hundreds of "quit coaches."

Mass Media Campaigns

Mass media educational campaigns on the hazards of smoking have been used for decades, in part to motivate quit attempts in the general population of current smokers, and a considerable evidence base shows their effectiveness in promoting successful cessation at the population level (NCI 2008; USDHHS 2014). These campaigns are generally thought of as being unrelated to efforts to provide direct assistance and support to individual smokers in healthcare settings or through community initiatives. However, since 1990, numerous efforts have been made to create synergies and efficiencies between mass media campaigns and the provision of individual support for quit attempts. For example, CDC's *Tips From*

Former Smokers (Tips) media campaign features ads with real people (former smokers) who have suffered the health consequences of smoking to increase awareness of suffering caused by smoking. The ads are also tagged with a quitline number (CDC 2012, 2013a). Tagging the ads with an offer of assistance may help smokers absorb the message of the ad by making it actionable rather than simply negative. Chapter 7 discusses the effectiveness of mass media campaigns, including *Tips*.

Healthcare Systems

Clinic-Based Integration of Health Systems

In the 1980s, NCI funded primary care-based research showing that a systematic approach to addressing tobacco use could help individual smokers in a clinical practice to quit and could lower the prevalence of tobacco use in the population served by a clinic (Solberg et al. 1990; Manley et al. 1992). Out of this research grew the "4 A's model," a carefully crafted intervention for transforming the approach of primary care clinics to tobacco cessation that was developed and packaged for widespread dissemination. This model differed from previous efforts in that it emphasized a systems approach to effectively address tobacco use in the context of primary care clinical practice, rather than simply developing an intervention that required for delivery its own separate healthcare or community infrastructure. The model had four components:

- **Ask:** Systematically identify the smoking status of all patients flowing through a practice, usually by an assistant interviewing the patient rather than relying on physician recall of patients' smoking status at every visit;

- **Advise:** Provide at every encounter very brief, non-threatening recommendations to quit;

- **Assist:** Offer practical help for quitting, including tips to make it through the first few weeks and brief supportive counseling; and

- **Arrange:** Ensure that any smoker planning a quit attempt will receive follow-up (e.g., during future office visits and/or through off-site resources).

Despite being shown to have significant benefits to smokers in clinical practices in the 1980s and 1990s, the adoption, implementation, and subsequent maintenance of this systematic approach was slow and uneven (Ferketich et al. 2006).

Based on an additional review of the evidence (Fiore et al. 2008), a fifth step, "Assess," was added between the "Advise" and "Assist" components, thereby emphasizing the importance of determining a patient's level of interest in quitting so that assistance and follow-up could be tailored to that person's specific circumstances. For example, a brief interaction with a patient not interested in quitting would focus on enhancing motivation rather than providing quit advice.

The 5 A's model is an example of an intervention designed to maximize the probability of a smoker making a quit attempt and the probability that he or she will be successful during such an attempt. The model seeks to accomplish these two tasks for a population of smokers. Building on the effectiveness of the 5 A's model, the Ask, Advise, Refer (AAR) model was developed as a shorter alternative to the 5 A's model in clinical settings where there is less time afforded for the patient encounter (Schroeder 2005). In addition, a different model, termed Ask, Advise, Connect (AAC) (Vidrine et al. 2013) was developed to ameliorate the low rate of participation among persons passively referred to a smoking cessation treatment, usually a quitline, through the AAR model. In the AAC model, smokers who accept the referral are subsequently contacted by the provider of smoking cessation treatment, typically a quitline counselor. The referral or connection services, such as to quitlines, have very strong evidence for effectiveness (Vidrine et al. 2013; Adsit et al. 2014) (also see Chapter 7). However, fewer studies have assessed the overall population impact of the AAR and AAC models compared with the 4 A's and 5 A's models.

Although the identification of smoking status is now routine in most healthcare systems, providing assistance and follow-up to smokers occurs in only less than half of primary care visits (King et al. 2013; Bartsch et al. 2016). Health professionals have reported barriers to adopting and implementing these healthcare-based treatment protocols, including

- Lack of time;

- Lack of reliable reimbursement for provision of services;

- Lack of acceptance that addressing tobacco dependence is part of a physician's job;

- Lack of training and/or comfort addressing problems with substance abuse;

- Lack of reliable, accessible referral resources;

- High prevalence of smoking, meaning that even brief interventions significantly affect clinic flow, as the interventions may need to be implemented with a large number of patients (Vogt et al. 2005; Association of American Medical Colleges 2007; Blumenthal 2007); and

- Privacy concerns, fear of losing patients, the discouraging belief that most patients will not be able to stop, and concern about stigmatizing the smoker (Schroeder 2005).

Responding to these issues, several professional organizations, including the American Academy of Family Physicians, have recommended using the AAR model at the clinical level to address smoking behaviors.

In recent years, increased attention has also been paid to the importance of building linkages between public health and the healthcare system and between community and clinical healthcare resources. This draws on the recognition that public health and healthcare stakeholders have complementary strengths and perspectives; that ultimately achieving lasting improvements in population health will take the combined efforts of both; and that improved coordination efforts will hasten this outcome. As part of this broader trend, national public health organizations and state tobacco control programs have begun to engage with healthcare systems to encourage and help them integrate treatment for tobacco dependence into their workflows (CDC 2006). Some healthcare systems have broadened the scope of their interventions to address upstream factors that shape health outcomes. For example, some healthcare systems have championed evidence-based interventions that go beyond the clinical sphere, such as smokefree and tobacco-free policies, increases in the price of tobacco products, and policies raising the age of sale for tobacco products to 21 years (Campaign for Tobacco-Free Kids 2016). Predicting the evolution of cessation treatment in the United States and the various roles of different segments of the healthcare system is challenging because of the volatility and uncertain future structure of healthcare, especially the nature of healthcare insurance. Regardless of what type of delivery system emerges, efforts should continue to integrate evidence-based tobacco treatment and cessation supports into healthcare settings and expand those supports. This would require further embedding of smoking processes and outcomes in quality measures, adequate funding, and routinization of training. Such services could be provided in the general healthcare system, as well as through specialized cessation clinics. The ability to deliver services effectively would be aided by having sufficient geographic locations for delivering care, promoting services, and removing barriers to services.

Health Insurance Coverage

Comprehensive insurance coverage for evidence-based cessation treatments plays a key role in helping smokers quit by increasing their access to proven treatments that raise their chances of quitting successfully (Fiore et al. 2008; CDC 2014a). Research in multiple healthcare settings in the 1990s (Curry et al. 1998) and 2000s (Joyce et al. 2008; Hamlett-Berry et al. 2009; Smith et al. 2010; Fu et al. 2014; Fu et al. 2016) has demonstrated that comprehensive cessation coverage increases quit attempts, the use of cessation treatments, and successful quitting (Fiore et al. 2008). Accordingly, implementation of comprehensive cessation coverage is important in both private and public health insurance.

Significant milestones in the recognition that comprehensive insurance coverage for smoking cessation plays a key role in helping smokers quit include (a) the Community Preventive Services Task Force's finding that reducing tobacco users' out-of-pocket costs for proven cessation treatments increases the number of tobacco users who quit (Hopkins et al. 2001), and (b) the recommendation in each of the *Clinical Practice Guidelines* that health insurers cover the FDA-approved cessation treatments and the behavioral treatments that the *Guidelines* found to be effective (Fiore et al. 2000, 2008). These recommendations draw on a body of research that has documented the outcomes of insurance coverage for cessation, including its cost-effectiveness. This research has also helped to identify the levels of coverage that influence tobacco cessation. More recently, several studies have examined the utilization of cessation treatments covered by health insurance, especially cessation medications, and how this has changed over time. Initial findings from these analyses suggest that cessation treatments continue to be underused, especially among Medicaid populations, and utilization varies considerably across states (Babb et al. 2017).

Healthcare Insurance Policies

After 2010, several national levers were added to make tobacco use and dependence treatment a part of healthcare. Both Medicare and Medicaid required coverage of certain smoking cessation treatments, and the Affordable Care Act included several provisions that required non-grandfathered commercial health plans to provide in-network smoking cessation medications and counseling without financial barriers because those two treatments had "A" ratings from USPSTF (McAfee et al. 2015). Even with these new regulatory levers, many national plans are not yet providing the required coverage (Kofman et al. 2012). Chapter 7 provides an in-depth discussion of private and public health insurance coverage for the treatment of tobacco use and dependence.

E-Cigarettes: Potential Impact on Smoking Cessation

E-cigarettes (also called electronic nicotine delivery systems [ENDS], vapes, vape pens, tanks, mods, and pod-mods) are battery-powered devices designed to convert a liquid (often called e-liquid)—which contains a humectant (propylene glycol and vegetable glycerin) and also typically contains nicotine, flavorings, and other compounds—into aerosol for inhalation by the user. First introduced in the United States in 2007 (USDHHS 2016), the advent of e-cigarettes into the tobacco product marketplace was seen by some as a potential harm-reduction tool for current adult smokers if the products were used to transition completely from conventional cigarettes (Fagerstrom et al. 2015; Warner and Mendez 2019). E-cigarette aerosol has been shown to contain markedly lower levels of harmful constituents than conventional cigarette smoke (National Academies of Sciences, Engineering, and Medicine 2018). Accordingly, interest remains in policies and approaches that could maximize potential benefits of these devices while minimizing potential pitfalls posed by the devices at the individual and population levels, including concerns about initiation among young people. The 2016 Surgeon General's report, *E-Cigarette Use Among Youth and Young Adults,* examined many aspects of e-cigarettes related to young people; however, it did not address the potential impact of e-cigarettes on smoking cessation among adult smokers (USDHHS 2016). It is also important to note that the landscape of available e-cigarette products has rapidly diversified since their introduction in the United States in 2007, including the introduction of "pod mod" e-cigarettes that have dominated the e-cigarette marketplace in recent years (Barrington-Trimis and Leventhal 2018; Office of the U.S. Surgeon General n.d.). This section highlights salient issues about how e-cigarettes may influence cessation, which is reviewed in more depth in Chapter 6.

Implications of E-Cigarette Characteristics for Smoking Cessation

Nicotine delivery through inhalation, as is the case with cigarette smoking, results in rapid nicotine absorption and delivery to the brain. The pharmacokinetics of nicotine delivery varies across products and is influenced by user topography, with some, but not all, e-cigarette products providing nicotine delivery comparable to conventional cigarettes (National Academies of Sciences, Engineering, and Medicine 2018). By contrast, the nicotine inhaler, one of several FDA-approved NRTs, delivers nicotine primarily through the buccal mucosa; it is designed to reduce nicotine withdrawal and cravings while minimizing abuse liability (Schneider et al. 2001). For smokers of conventional cigarettes who seek a product with a rapid delivery of nicotine similar to cigarettes, e-cigarettes that deliver nicotine in a similar way to cigarettes may have greater appeal than NRTs. Although rapid boluses of nicotine could increase the appeal, as well as addiction and potential greater abuse liability, of e-cigarettes relative to NRTs, whether this pharmacokinetic profile produces an effective method of cessation is presently inconclusive from the emerging base of empirical evidence (Shihadeh and Eissenberg 2015).

Other features of e-cigarettes that may enhance their appeal to smokers of conventional cigarettes include the ways in which they mirror some of the sensorimotor features of conventional cigarette smoking, including stimulation of the airways, the sensations and taste of e-cigarette aerosol in the mouth and lungs, the hand-to-mouth movements and puffing in which e-cigarette users engage, and the exhalation of aerosol that may visually resemble cigarette smoking. Given the potentially important role of such sensorimotor factors in the reinforcing and addictive qualities of conventional cigarettes (Chaudhri et al. 2006), the presence of these attributes could make e-cigarettes more appealing to smokers as a substitute for cigarettes than NRTs because the NRTs either lack such sensorimotor features (e.g., the transdermal patch, nicotine gum) or offer only partial approximations (e.g., the inhaler).

However, when considering e-cigarettes as a potential cessation aid for adult smokers, it is also important to take into account factors related to both safety and efficacy. NRT has been proven safe and effective, but there is no safe tobacco product. Although e-cigarette aerosol generally contains fewer toxic chemicals than conventional cigarette smoke, all tobacco products, including e-cigarettes, carry risks.

As noted in the 2016 Surgeon General's report, many of the characteristics that distinguish e-cigarettes from conventional cigarettes increase the appeal of these new products to youth and young adults, particularly nonsmokers (USDHHS 2016). These factors include appealing flavors, high concentrations of nicotine, concealability of use, and widespread marketing through social media promotion and other channels (Barrington-Trimis and Leventhal 2018). Many e-cigarettes differ markedly in shape and feel compared with conventional cigarettes; e-cigarettes come in a variety of shapes, including rectangular tank-style and USB-shaped devices (as discussed in Chapter 6 and shown in Figure 6.1). For example, JUUL, the top-selling e-cigarette brand in the United States in 2018 (Wells Fargo Securities 2018), is shaped like a USB flash drive and offers high concentrations of nicotine in the cartridges, which are also known as "pods" (Huang et al. 2018). Notably, the novelty, diversity, and customizability of e-cigarettes appeal to youth (Chu et al. 2017; Office of the U.S. Surgeon

General n.d.). For example, there are numerous scientific reports documenting the appeal of, and dramatic rise in, JUUL use among youth and young adults (Chen 2017; Teitell 2017; Beal 2018; Bertholdo 2018; Coughlin 2018; Grigorian 2018; Saggio 2018; Suiters 2018; FDA 2018; Willett et al. 2018; Radding n.d.).

Of note, a growing number of e-cigarettes, including JUUL, also use nicotine salts, which have a lower pH than the freebase nicotine used in most other e-cigarettes and traditional tobacco products, and allow particularly high levels of nicotine to be inhaled more easily and with less irritation. Although this type of product may be appealing to adult smokers seeking e-cigarettes with potentially greater nicotine delivery, the potency and appeal of such products can also make it easier for young people to initiate the use of nicotine and become addicted (Office of the U.S. Surgeon General n.d.).

The final chapter of the 2014 Surgeon General's report concluded that the use of e-cigarettes could have both positive and negative impacts at the individual and population levels (USDHHS 2014). One of its conclusions was that "the promotion of noncombustible products is much more likely to provide public health benefits only in an environment where the appeal, accessibility, promotion, and use of cigarettes and other combusted tobacco products are being rapidly reduced" (USDHHS 2014, p. 874). Therefore, it is important to continue (a) monitoring the findings of research on the potential of e-cigarettes as a smoking cessation aid and (b) evaluating the positive and negative impacts that these products could have at the individual and population levels, so as to ensure that any potential benefits among adult smokers are not offset at the population level by the already marked increases in the use of these products by youth. It is particularly important to evaluate scientific evidence on the impact of e-cigarettes on adult smoking cessation in the current context of the high level of e-cigarette use by youth, which increased at unprecedented levels in recent years following the introduction of JUUL and other e-cigarettes shaped like USB flash drives (Cullen et al. 2019).

Summary

Once erroneously considered a habit that could be broken by simply deciding to stop, nicotine addiction is now recognized as a chronic, relapsing condition. The prevalence of cigarette smoking in the United States has declined steadily since the 1960s; however, as of 2017, there were still more than 34 million adult current cigarette smokers in the United States (Wang et al. 2018).

Proven smoking cessation treatments are widely available today. However, the reach and use of existing smoking cessation interventions remain low, with less than one-third of smokers using any proven cessation treatments (behavioral counseling and/or medication) (Babb et al. 2017). A majority of smokers still attempt to quit without using such treatments, contributing to a failure rate in excess of 90% (Hughes et al. 2004; Fiore et al. 2008).

Medications and behavioral interventions with increasing levels of efficacy and sophistication are becoming more widely available, but there is considerable room for improvement. Further, the challenge of getting behavioral and pharmacologic interventions to be used concurrently and disseminated more broadly to the public has only been partially solved.

Full integration of treatment for nicotine dependence into all clinical settings—including primary and specialty clinics, hospitals, and cancer treatment settings—can benefit from increases in barrier-free health insurance coverage. Combining health service systems and electronic media platforms for the delivery of smoking cessation interventions has emerged as one promising method to increase reach of smoking cessation treatment to smokers (e.g., evidence-based cessation interventions using phone lines and mobile phone applications, and use of electronic health records to promote more timely referral to cessation support services). Barrier-free health insurance coverage (e.g., copays, coverage limits, prior authorization) and access to services, coupled with the use of quality improvement metrics and methodologies, have been shown to increase smokers' use of evidence-based services.

Clinical-, system-, and population-level strategies are increasingly taking a more holistic approach to decreasing the prevalence of smoking, with interventions designed to increase quit attempts and enhance the chances of success. Examples include the national *Tips From Former Smokers* media campaign, which used ads featuring smokers who had suffered tobacco-related morbidity to increase awareness of individual suffering caused by smoking while simultaneously enhancing the capacity of the national quitline network to respond to upsurges in calls that were generated by tagging the ads with the phone number for the quitline. Millions of smokers made quit attempts as a result of exposure to the ads, and hundreds of thousands have successfully quit smoking. In addition, the development and dissemination of the carefully crafted and research-tested 5 A's model in healthcare settings, combined with public and private policy changes that encourage coverage of cessation, have systematically encouraged more smokers to try to quit and provided them with evidence-based support. Still, the potential of mass media campaigns, quitlines, and clinical support has been tapped only partially, leaving many opportunities for further adoption, dissemination, and extensions of these approaches.

Use of e-cigarettes could have varied impacts on different segments of the population, including potential benefits to current adult cigarette smokers who transition completely; however, potential efficacy may depend on many factors, such as type of devices and e-liquids used, reason for use, and duration of use. Well-controlled, randomized clinical trials and rigorous, large-scale observational studies with long-term follow-ups will be critical to better understand the impact of e-cigarettes on cessation under various conditions and settings. Nevertheless, the potential benefit of e-cigarettes for cessation among adult smokers cannot come at the expense of escalating rates of use of these products by youth. Accordingly, the current science base supports a number of actions to minimize population risks while continuing to explore the potential utility of e-cigarettes for cessation, including efforts to prevent e-cigarette use among young people, regulate e-cigarette products and marketing, and discourage long-term use of e-cigarettes as a partial substitute for conventional cigarettes rather than completely quitting.

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