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NCI TOBACCO CONTROL
MONOGRAPH SERIES

23

Treating Smoking in Cancer Patients: An Essential Component of Cancer Care

U.S. Department of Health & Human Services | National Institutes of Health

About the National Cancer Institute Tobacco Control Monograph Series

The National Cancer Institute established the Tobacco Control Monograph series (formerly the Smoking and Tobacco Control Monograph series) in 1991. The series provides comprehensive scientific reviews of tobacco use, treatment, and prevention topics to inform the work of researchers, clinicians, and public health practitioners working to reduce cancer morbidity and mortality. All 23 Tobacco Control Monographs and their supplemental materials can be downloaded from cancercontrol.cancer.gov/monographs.

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Foreword

The National Cancer Institute's (NCI's) role in tobacco control has been long, broad, and deep. The uniqueness of NCI's role is due, in part, to the National Cancer Act of 1971, which granted special authorities and responsibilities to the institute, including a determination that NCI's director be appointed directly by the President—the only institute director at the National Institutes of Health with this special status.

The recognition of the 50th anniversary of the National Cancer Act in 2021 illustrated that the dissemination mission assigned by Congress to NCI continues to be manifested in a variety of ways. In the case of tobacco control, the Tobacco Control Monograph series is one key vehicle that NCI uses to disseminate research evidence to a global audience. The monograph series leverages the scientific independence afforded by NCI's authorities with the institute's firmly established credibility throughout the international biomedical and public health communities. In an era plagued by rampant misinformation, the value of authoritative, peer-reviewed summaries of the research literature has never been higher. The rigorously transparent, data-driven, and self-corrective nature of the scientific enterprise enables both medicine and public health to evolve and adapt to ever-changing threats, but only if the latest scientific evidence is provided in a clear and actionable manner to those in a position to use it. This monograph seeks to fulfill that goal by providing clinicians with the latest knowledge concerning smoking among their patients, while providing scientists with clear descriptions of research gaps remaining to be filled.

This monograph describes a variety of research efforts conducted over a span of decades that have sought to describe, explain, and address the nature and consequences of smoking among patients with cancer. Long-standing, recalcitrant problems in medicine and public health can persist for many years until a catalyst (often in the form of a person or people) meets a special opportunity (often in the form of new funding). In the case of tobacco use among patients with cancer, the catalysts were two members of NCI's advisory boards, Karen Emmons, Ph.D., and Graham Colditz, M.D., Dr.P.H. The opportunity was the Beau Biden Cancer Moonshot℠, a special 7-year initiative supported by the 21st Century Cures Act, which was passed by Congress in 2016. During a discussion at a meeting of the NCI advisory boards, Emmons and Colditz suggested that addressing the lack of tobacco use assessment and treatment among all patients treated for cancer at NCI-Designated Cancer Centers would be a worthy goal of the Cancer Moonshot. This author, then serving as the Director of NCI's Division of Cancer Control and Population Sciences, was charged by the then-Acting NCI Director, Douglas R. Lowy, M.D., to propose a major effort to support the enhancement and evaluation of research-based smoking cessation programs within NCI-Designated Cancer Centers. This led to NCI's funding of the Cancer Center Cessation Initiative (C3I), the largest-ever effort to evaluate and improve the quality of care for patients with cancer who use tobacco products.

Although C3I is only one of many research initiatives discussed in this monograph, its launch led to a broader revitalization of NCI's efforts concerning tobacco use among patients with cancer. This monograph is an important component of this broader set of efforts, that have included the strengthening of collaborations with other agencies and organizations; sustained support for Smokefree.gov, the federal government's primary digital health resource for tobacco cessation; and expanded support through research grants to study tobacco cessation program implementation in clinical settings.

The slow rate of progress in providing all patients with cancer with high-quality smoking cessation services is the result of a complex set of barriers at the level of the practitioner, the health care organization, the payer, and the policymaker. Both institutional and sociological barriers are discussed within the chapters that follow. However, it is clear that the lack of financial incentives (i.e., low reimbursement rates for these services) and an insufficient appreciation of the importance of smoking cessation among clinicians and their service line managers have played a role. We hope that the compilation of evidence provided by this monograph will serve as an important catalyst to action through enhancements in payment incentives, professional training, the structure of healthcare systems, and through underscoring the moral imperative of providing the highest quality cancer care to every patient. It is never too late to quit, nor is it too late for all of us to complete the task of enabling every patient with cancer to rid themselves of the most devastating carcinogen known to humanity.

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Table of Abbreviations and Acronyms

Abbreviation/Acronym	Definition
AACR	American Association for Cancer Research
ASCO	American Society of Clinical Oncology
BRFSS	Behavioral Risk Factor Surveillance System
C3I	Cancer Center Cessation Initiative
CBT	Cognitive behavioral therapy
CDC	U.S. Centers for Disease Control and Prevention
EHR	Electronic health record
ENDS	Electronic nicotine delivery systems
FDA	U.S. Food and Drug Administration
IASLC	International Association for the Study of Lung Cancer
NCCN	National Comprehensive Cancer Network
NCI	U.S. National Cancer Institute
NHIS	National Health Interview Survey
NRT	Nicotine replacement therapy
USPSTF	U.S. Preventive Services Task Force

Glossary

Term	Definition
Cancer survivors	A population with a history of a cancer diagnosis, referring to individuals who have completed treatment for active cancer, who have metastatic disease, or who require intermittent treatment.
EHR problem list	A list used within electronic health records (EHR) that outlines the illnesses, injuries, and other factors affecting the health of a patient, usually identifying symptoms, time of occurrence, diagnosis, and treatment or resolution.
Electronic nicotine delivery systems	Electronic nicotine delivery systems (ENDS) represent a rapidly changing class of tobacco products known by many different names, including e-cigarettes, e-cigs, vapes, mods, and tank systems. ENDS deliver an aerosol to the user that typically contains nicotine, propylene glycol, vegetable glycerin, and flavoring chemicals.
Long-term abstinence	Typically refers to 6 or more months without tobacco product use.
Medically underserved and vulnerable populations	Populations who experience disparities in cancer burden, smoking prevalence, access to smoking cessation treatment, and/or smoking cessation treatment success. For the purposes of this monograph, 'vulnerable' refers to a heightened risk for cancer or a higher cancer burden relative to the general population. Medically underserved and vulnerable populations discussed in this monograph include socioeconomically disadvantaged populations, racial and ethnic minority populations, rural populations, sexual and gender minority (SGM) populations, individuals with co-occurring substance use disorders, and individuals with serious mental illness (SMI).
Pack year	A way to measure the amount a person has smoked over a period of time. It is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked. For example, 1 pack year is equal to smoking 1 pack per day for 1 year, or 2 packs per day for half a year.
Patients with cancer	Refers to those newly diagnosed with cancer and in treatment for active or recurrent cancer.
Smoking	Refers to cigarette use.
Smoking cessation treatment	Encompasses treatment aimed at smoking reduction, smoking cessation, and relapse prevention after treatment.
Tobacco use	Refers to use of tobacco products including cigarettes, cigars, hookah, ENDS, and smokeless tobacco.

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Monograph 23
Treating Smoking in Cancer Patients:
An Essential Component of Cancer Care

Chapter 1
Introduction and Overview

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Chapter 1
Introduction and Overview

Introduction

Patients with cancer deserve the highest level of care from their clinicians and health care systems. As described in the 2020 Surgeon General's report, smoking cessation may result in improved all-cause mortality in patients with cancer who quit smoking. The evidence presented in the report strengthens the rationale for "aggressively promoting and supporting smoking cessation in cancer patients and survivors."[1,p.213] Unfortunately, patients with cancer who smoke often do not receive the appropriate level of care needed to adequately address their tobacco use.[2]

Evidence also documents that continued tobacco use can adversely influence the effectiveness of cancer treatment, including chemotherapy and radiotherapy.[3] It is important for clinicians treating patients with cancer, and for patients themselves, to realize that quitting smoking improves cancer outcomes, that it is never too late to quit smoking at any stage of the cancer care continuum, and that benefits to doing so are clear,[4–6] regardless of cancer type.

The purpose of this monograph is to build upon the conclusions of the 2014 and 2020 Surgeon General's reports and recent research findings, including from the National Cancer Institute's (NCI) Cancer Moonshot℠–supported Cancer Center Cessation Initiative (C3I) program, to heighten the focus on smoking cessation in patients with cancer. The 2020 Surgeon General's report offers a powerful impetus for intervening with cancer patients who smoke. This monograph expands upon that prior work to inform clinicians and their patients with cancer about the science and practice of quitting smoking. It provides an up-to-date synthesis of evidence that clarifies the need to intervene with smoking in cancer care, informs decision-making about such intervention, identifies effective smoking cessation intervention methods, and describes how such methods can be implemented effectively in cancer care. To this end, this monograph presents evidence on:

- Smoking and the biology of cancer.
- The effectiveness of smoking cessation treatment in the general population of individuals who smoke and in cancer populations specifically.
- How smoking cessation treatments can be modified to address the special challenges and needs of individuals with cancer.
- How smoking cessation treatment can be implemented in health care contexts generally and in cancer care contexts specifically.
- The opportunities for and challenges to enhancing smoking cessation success in medically underserved and vulnerable populations with cancer who smoke.

This monograph is intended to provide a strong evidence base for treating smoking in people with cancer by helping health care systems, clinicians, health insurers, funding agencies, patients with cancer, and policymakers optimize and prioritize the treatment of smoking in cancer care.

This monograph also identifies important research gaps to assist in the development, evaluation, and implementation of smoking cessation interventions for people with cancer who smoke. The monograph affirms for patients and their cancer care team that addressing smoking cessation in the cancer care setting has the potential to yield multiple benefits, including better tolerance of cancer treatment, better cancer treatment outcomes, reduced development of second primary tumors, reduced all-cause and cancer-specific mortality, and a better quality of life.

For more than half a century, tobacco use has been known to cause a broad range of cancers and other adverse health outcomes.[7,8] Although multiple forms of tobacco cause cancer, cigarette smoking is responsible for most of the cancer burden caused by tobacco use. As a result, cigarette smoking, herein referred to as "smoking," holds the distinction of being the leading cause of preventable disease and premature death overall[8] and accounts for about 30% of all cancer deaths in the United States.[9,10] Moreover, factors such as gender, race and ethnicity, and place of residence affect the cancer burden attributed to smoking. For example, one study noted that smoking accounted for nearly 40% of cancer deaths among men in five Southern states.[11]

In terms of cancer type, cigarette smoking is most strongly associated with the development of lung cancer; smoking increases the risk of lung cancer approximately 20-fold.[8,12] Smoking is also causally associated with an increased risk of many other types of cancers, including those of the oral cavity and pharynx, larynx, esophagus, stomach, kidney, pancreas, liver, bladder, cervix, colon and rectum, and acute myeloid leukemia.[8,9] Within this monograph, chapter 2 briefly reviews the relationship between smoking and the biology of cancer, including studies of the effects of tobacco smoke exposure on cancer cells.

Smoking Among Cancer Patients and Survivors

There are relatively few nationally representative data sets on rates of smoking or cessation across the cancer care continuum, from the prevention of cancer, to screening for and treatment of cancer, through survivorship. Among patients seen at the Roswell Park Comprehensive Cancer Center between 1982 and 1998, more than 60% reported that they were ever smokers (i.e., they were current or former smokers).[13] Based on data from the 2020 National Health Interview Survey (NHIS), 9,575,944, or 48.7%, of adults ever diagnosed with cancer reported ever having smoked cigarettes, with 12.2% reporting that they currently smoked (11.5% of male respondents and 12.4% of female respondents reported currently smoking) (Table 1.1).[14,15] In addition to gender, the prevalence of current smoking also varies by multiple factors, including age. For example, older cancer survivors are less likely to report current smoking than younger cancer survivors (Table 1.1).

Table 1.1 Current and Former Smoking Among Adult Cancer Survivors, 2020

	Current Smoking Weighted % (95% CI)	Former Smoking Weighted % (95% CI)
Total	12.2% (10.7–13.9)	36.4% (34.4–38.4)
Sex		
Male	11.5% (9.4–14.1)	43.0% (39.7–46.3)
Female	12.4% (10.5–14.6)	30.8% (28.3–33.4)

Table 1.1 (continued)

	Current Smoking Weighted % (95% CI)	Former Smoking Weighted % (95% CI)
Age		
18–44 years	21.3% (15.4–28.6)	20.0% (13.8–27.9)
45–64 years	18.0% (14.8–21.7)	27.9% (24.5–31.7)
65 years and older	7.4% (6.1–8.9)	44.0% (41.5–46.6)

Note: Estimates are weighted to the civilian, noninstitutionalized U.S. population and age-adjusted based on the age distribution of cancer patients' diagnoses in 2000 in the Surveillance, Epidemiology, and End Results Program (SEER) Registry, using the following age groups: 18–24, 25–34, 35–44, 45–54, 55–64, 65–74, 75–84, 85 and older. Cancer survivors are defined as any person with a history of cancer, not including nonmelanoma skin cancer. Abbreviations: CI = confidence interval.
Sources: National Center for Health Statistics 2020,[14] National Cancer Institute 2020.[15]

Rates of current smoking and successful smoking cessation also vary considerably by cancer site. As expected, smoking prevalence is higher among people diagnosed with tobacco-related cancers compared with those with non–tobacco-related cancers.[16,17] Regarding cessation outcomes, an analysis of 2009 Behavioral Risk Factor Surveillance System survey data found that 27% of survivors with a tobacco-related cancer smoked, compared with 16% of survivors with non–tobacco-related cancers and 18% of people with no history of cancer.[16] In general, people who smoke who are diagnosed with cancer tend to have high nicotine dependence, suggesting a need for more intensive intervention in this population.[2,18,19]

Patients with cancer often are motivated to quit smoking following a cancer diagnosis, and many make quit attempts; however, not all of these attempts are successful. Using data from the 2017 NHIS, Gritz and colleagues[20] found that, among cancer survivors, 309 (44%) reported having successfully quit smoking while 372 (56%) reported that they continued to smoke. Similarly, a 2019 review found that although most patients with lung cancer who smoke cigarettes attempt to quit smoking after a lung cancer diagnosis, only about half succeed.[21] Even among those who successfully quit smoking following a lung cancer diagnosis, it is estimated that between 13% and 60% will relapse to cigarette smoking after treatment.[21]

Nicotine dependence is a major factor in relapse, but it is not the only contributor.[1] People with cancer are often less motivated to quit if their disease is advanced or if they believe that their prognosis is poor.[22] The presence of depression, pain, anxiety, or cancer treatment side effects may complicate both the motivation to quit and maintenance of cessation for a patient following a cancer diagnosis.[21] Failure to address these specific challenges of tobacco cessation among patients with cancer contributes to continued smoking.

The Consequences of Continued Smoking After a Cancer Diagnosis

Smoking at the time of a cancer diagnosis increases the risk of mortality caused by cancer and the risk of mortality due to other causes, such as heart disease, noncancer pulmonary disease, and stroke.[8] Further, smoking increases risk of second primary cancers and can increase the risk of cancer recurrence and adverse treatment-related outcomes, including postoperative pulmonary complications, poor surgical healing, and decreased response to chemotherapeutic medications and radiation.[23] A 2019 study examined the effects of smoking abstinence following cancer diagnosis on quality of life over time (baseline and 2, 6, and 12 months after baseline). In this sample of 332 cancer patients, longer abstinence from smoking was associated with higher overall quality of life.[24]

Improved treatments for some cancers, including several of the most common cancers, have resulted in increased long-term survivorship.[25] For patients with these types of cancers, continued smoking can increase overall mortality by increasing risk for cardiovascular and pulmonary disease, in addition to increasing cancer-specific mortality. On the other hand, cancers with poor survival rates and aggressive tumor biology may result in relatively shorter life expectancy, making it difficult to observe the effects of smoking on survival. However, evidence showing that smoking is associated with poor outcomes across a range of smoking definitions, durations of observation, and cancer sites suggests a consistent and negative effect on overall mortality for cancer survivors, as described in the 2014 Surgeon General's report.[8]

Cancers, and tobacco-related cancers in particular, impose a high burden on individuals, families, and society; this burden is particularly onerous in certain patient populations such as socioeconomically disadvantaged populations and racial and ethnic minority populations.[9] Chapter 5 of this monograph addresses these and other medically underserved and vulnerable populations that experience disparities in cancer outcomes related to smoking.

Continued smoking after a cancer diagnosis not only affects the health of the patient but results in a substantial added financial burden; it is estimated to increase the costs of cancer treatment by nearly $11,000 per patient.[26] These additional expenses could increase cancer-related financial stress to patients and their caregivers, resulting in increased psychosocial distress, diminished patient health outcomes, and poorer quality of life. Warren and colleagues[26] estimated an overall annual burden of approximately $3.4 billion in added cancer treatment costs in the United States for continued smoking after a cancer diagnosis. Chapter 4 of this monograph further discusses the economics of smoking cessation treatment for patients with cancer.

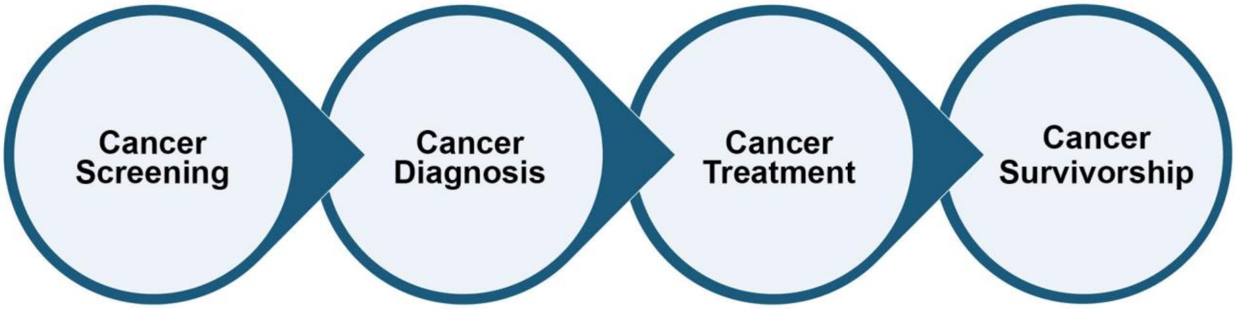
Addressing Smoking Cessation in Cancer Care Settings

Quitting smoking is important for patients with all types of cancer, both those that are tobacco-related and those that are not. It is also important for patients across the cancer care continuum. This monograph is focused on the stages of the cancer care continuum where there are substantial data on addressing smoking specifically; specifically addressing smoking among individuals being screened for, diagnosed with, and treated for cancer; and addressing it among those who have survived a cancer diagnosis. There is not yet consensus in the scientific literature on the effects of smoking cessation for patients with advanced cancer or who are receiving hospice care. This monograph does not address these specific patient populations in depth; some studies are described in chapter 4, and additional related research needs are discussed in chapter 6.

Patients across the cancer care continuum interact with clinicians in multiple health care settings (Figure 1.1) and each of these clinical encounters offers the opportunity to integrate smoking cessation treatment into routine cancer care. Such "health systems change" opportunities to integrate smoking cessation treatment into clinical care were defined in the Public Health Service (PHS) Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*[27]:

"Systems strategies are intended to ensure that tobacco use is systematically assessed and treated at every clinical encounter."

Figure 1.1 Opportunities for Smoking Intervention Across the Cancer Care Continuum



Cancer Screening

- Lung cancer screening is an especially important window of opportunity. Patients with abnormal test results have higher rates of cessation, but over half continue to smoke long term.
- Active clinician interventions (e.g., "Assist" and "Arrange" steps) remain key to motivating and supporting cessation efforts.

Cancer Diagnosis

- Cessation rates tend to be higher among those with a cancer diagnosis than in the general population.
- Cessation rates vary by cancer type.
- Cancer patients are highly motivated to try to quit smoking after their cancer diagnosis.

Cancer Treatment

- Smoking interventions in the perioperative period may be especially effective.
- Patients with later stages of cancer or requiring extensive treatment tend to quit at higher rates.
- Pain may be a barrier to cessation.
- Relapse rates after treatment are high, underscoring the need for ongoing clinician vigilance.

Cancer Survivorship

- Smoking remains prevalent among cancer survivors.
- Self-reported smoking status is especially prone to misreporting.
- As patients enter long-term survivorship, achieving continuity of care for smoking treatment requires partnership with primary care providers.

Notes: Intervention to promote smoking cessation is critical across the cancer care continuum. Cancer screening, diagnosis, treatment, and survivorship are all candidate stages for "teachable moments" that hold the potential for positive behavior change. Specific challenges to smoking cessation treatment implementation may vary by stage.

Chapters 3 and 4 describe opportunities and strategies to expand smoking cessation treatment in cancer care. These strategies include electronic health record (EHR) referral to state tobacco cessation quitlines or text-message based interventions, such as NCI's SmokefreeTXT; use of trained tobacco treatment specialists to work collaboratively with the oncology team[28]; expanded access to cessation counseling and medications; reimbursement for smoking cessation treatment; and others.[29] NCI's C3I is described in chapter 4 of this monograph and furnishes real-world scientific evidence and examples of how to address the multilevel challenges involved in integrating smoking cessation treatment into cancer care.

The case for consistent and effective tobacco use treatment in cancer care settings rests on two complementary bodies of research: 1) that continued smoking after a cancer diagnosis imposes significant harms, such as poorer treatment efficacy and adverse health outcomes, including mortality, and 2) that smoking cessation markedly decreases those harms, thereby improving cancer prognosis and other health outcomes. The evidence base documenting both the risks of smoking among patients with cancer and the benefits of cessation on cancer outcomes was first included in the 2014 Surgeon General's report on the health consequences of smoking and then expanded upon in the 2020 Surgeon General's report on smoking cessation (Table 1.2).

Table 1.2 Findings From the 2014 and 2020 Surgeon General's Reports

Findings regarding smoking and cancer outcomes from the 2014 Surgeon General's report	
In patients with cancer, the evidence is sufficient to infer a causal relationship between:	• Cigarette smoking and adverse health outcomes. Quitting smoking improves the prognosis of patients with cancer. • Cigarette smoking and increased all-cause mortality. • Cigarette smoking and increased cancer-specific mortality. • Cigarette smoking and increased risk for second primary cancers known to be caused by cigarette smoking, such as lung cancer.
In patients with cancer, the evidence is suggestive, but not sufficient, to infer a causal relationship between:	• Cigarette smoking and risk of recurrence. • Cigarette smoking and poorer response to cancer treatment. • Cigarette smoking and increased treatment-related toxicity.
Findings regarding smoking and cancer outcomes from the 2020 Surgeon General's report	
The evidence is sufficient to infer that:	• Smoking cessation reduces the risk of lung cancer, laryngeal cancer, cancers of the oral cavity and pharynx, esophageal cancer, pancreatic cancer, bladder cancer, stomach cancer, colorectal cancer, liver cancer, cervical cancer, kidney cancer, and acute myeloid leukemia.
In patients with cancer, the evidence is suggestive, but not sufficient, to infer a causal relationship between:	• Smoking cessation and improved all-cause mortality in patients who are currently smoking at the time of a cancer diagnosis.

Sources: USDHHS 2014,[8] USDHHS 2020.[1]

The 2014 Surgeon General's report concluded that there was sufficient evidence to infer a causal relationship between cigarette smoking and adverse health outcomes among patients with cancer and cancer survivors.[8] The 2020 Surgeon General's report formally evaluated the evidence comparing all-cause mortality between patients who quit smoking versus patients who continue to smoke after diagnosis.[1] The 2020 Surgeon General's report concluded that the evidence was suggestive, but not sufficient, to infer a causal relationship between smoking cessation and improved all-cause mortality among patients currently smoking at the time of their diagnosis.[1] The latter conclusion was based on 10 studies published between 2000–2016 that compared the risk of all-cause mortality among cancer patients who continued smoking after diagnosis or treatment with that of patients who quit.

Research on this topic has continued to expand. This monograph includes an additional 8 studies, published between 2017 and 2020, that examined the association between quitting smoking and all-cause mortality (Table 1.3).[5,30–36] These studies, which included patients with lung,[5,32] head and neck,[31] ovarian,[33,36] or any type of cancer,[30,34,35] expand upon the conclusions of the 2020 Surgeon General's report. Two studies of ovarian cancer patients indirectly compared those who quit after diagnosis with those who continued smoking after diagnosis. Wang and colleagues[36] compared each of these groups with those who never smoked. Hansen and colleagues[33] compared each of these groups with a reference group consisting of both those who had never smoked and those who had quit smoking prior to diagnosis. In both analyses, patients who continued smoking had a significantly increased risk of all-cause mortality compared with the referent group, while patients who quit smoking had a similar risk of all-cause mortality as the referent group.[33,36]

Six studies directly compared all-cause mortality between patients who quit smoking after diagnosis and those who continued to smoke. Of these, one compared mean survival time between the two groups and found that patients who quit smoking lived significantly longer (i.e., an average of 7 years) than patients who continued to smoke.[35] The remaining five studies compared all-cause mortality between the same two groups using multivariable-adjusted models. Two studies found that risk of all-cause mortality was significantly lower among patients who quit after diagnosis compared with patients who continued smoking.[5,34] A third study grouped patients according to the stage of cancer at diagnosis; it found that, among patients with Stage I or II cancer, but not among patients with Stage III or IV cancer, quitting after diagnosis was associated with significantly lower risk of all-cause mortality.[31]

In summary, evidence continues to mount that smoking cessation improves outcomes in patients with cancer compared with continued smoking after a cancer diagnosis. For this reason, cessation should be a high priority for patients and their clinicians.

Table 1.3 Studies That Compare All-Cause Mortality in Patients Who Quit Smoking After a Cancer Diagnosis With Patients Who Continued After Diagnosis (2017–2021)

Study	Design/population	Follow-up period	Definition of groups	All-cause mortality findings
Barnett et al. 2020[30]	• Retrospective cohort • 369 patients with nonmetastatic cancer who were current smokers at time of diagnosis • United States	3 years	• *Quit:* Smoking cessation within 6 months of diagnosis • *Continued smoking:* No smoking cessation within 6 months of diagnosis	Adjusted RR: • Quit: 0.72 (95% CL, 0.37–1.4) • Continued smoking: 1.0 (referent)
Day et al. 2020[31]	• Prospective cohort • 117 patients with head and neck squamous cell carcinoma who were current smokers and enrolled in a tobacco treatment program • United States	Median follow-up of 5.2 years (among survivors)	• *Quit:* Abstinence (7-day point prevalence) at 9 months after tobacco treatment program enrollment • *Continued smoking:* Nonabstinence at 9 months	Adjusted HR, Stage I-II patients: • Quit: 0.15 (95% CI, 0.03–0.82) • Continued smoking: 1.0 (referent) Adjusted HR, Stage III-IV patients: • Quit: 1.51 (95% CI, 0.75–3.07) • Continued smoking: 1.0 (referent)
Gemine et al. 2019[32]	• Prospective cohort • 1,124 patients with newly diagnosed non-small cell lung cancer, including 364 patients who were current smokers at the time of diagnosis • United Kingdom	1 year	• *Quit:* Smoking cessation within 3 months of diagnosis and sustained abstinence during the follow-up period • *Continued smoking:* No smoking cessation within 3 months of diagnosis	Adjusted HR: • Quit: 0.75 (95% CI, 0.46–1.20) • Continued smoking: 1.0 (referent)
Hansen et al. 2020[33]	• Prospective cohort • 678 patients with invasive epithelial ovarian cancer, including 512 patients with postdiagnosis data available • Australia	4 years	• *Quit:* Smoking cessation after diagnosis • *Continued smoking:* No smoking cessation after diagnosis • *Never or former smoking:* Never or former smoking before and after diagnosis	Adjusted HR: • Quit: 0.99 (95% CI, 0.57–1.72) • Continued smoking: 1.90 (95% CI, 1.08–3.37) • Never or former smoking: 1.0 (referent)

Table 1.3 (continued)

Study	Design/population	Follow-up period	Definition of groups	All-cause mortality findings
Hawari et al. 2019[34]	• Retrospective cohort • 2,387 cancer patients who were current smokers with survival data available • Jordan	2 years	• *Quit at two or more time points:* More than one visit to smoking cessation clinic and smoking abstinence at two or more follow-up points (3, 6, and 12 months) • *Quit at one time point:* More than one visit to smoking cessation clinic and abstinence at only one-follow-up point • *Continued smoking:* More than one visit to smoking cessation clinic and no abstinence recorded at any follow-up point • *No follow-up:* No visits or only one visit to smoking cessation clinic, or smoking cessation clinic visit occurred more than a year after diagnosis	Adjusted HR: • Quit at two or more time points: 1.0 (referent) • Quit at one time point: 1.3 (95% CI, 0.65–2.6) • Continued smoking: 2.7 (95% CI, 1.4–5.0) • No follow-up: 2.8 (95% CI, 1.7–4.6)
Romaszko-Wojtowicz et al. 2018[35]	• Retrospective cohort • 111 patients with multiple primary malignancies, including 108 ever-smokers • Poland	Survival assessed for eligible patients identified from 2013 to 2017	• *Quit:* Quit smoking after first cancer and before new cancer • *Continued smoking:* Continued to smoke after first cancer • *Nonsmoking:* Never smoking or smoked fewer than 100 cigarettes in lifetime	Average survival time after first cancer: • Quit: 13.75 years • Continued smoking: 6.57 years
Sheikh et al. 2021[5]	• Prospective cohort • 517 patients with non-small cell lung cancer who were current smokers • Russia	Average 7 years	• *Quit:* Smoking cessation during follow-up period (annual follow-ups) • *Continued smoking:* No smoking cessation during follow-up	Adjusted HR: • Quit: 0.67 (95% CI, 0.53–0.83) • Continued smoking: 1.0 (referent)

Table 1.3 (continued)

Study	Design/population	Follow-up period	Definition of groups	All-cause mortality findings
Wang et al. 2020[36]	• Prospective cohort (Nurses' Health Study [NHS] and NHSII) • 1,279 patients with ovarian cancer, including 1,133 patients with postdiagnosis data • United States	Median survival time of 4.5 years in NHS and 6.6 years in NHSII	• *Quit smoking:* Smoking status of current smoking before diagnosis and former smoking after diagnosis • *Continued smoking:* Smoking status of current smoking at both pre- and post-diagnosis assessments • *Never smoking:* Never smoking at both pre- and post-diagnosis assessments • *Former smoking:* Former smoking at both pre- and post-diagnosis assessments	Adjusted HR: • Quit: 0.91 (95% CI, 0.62–1.35) • Continued smoking: 1.43 (95% CI, 1.11–1.86) • Former smoking: 1.19 (95% CI, 1.01–1.40) • Never smoking: 1.0 (referent)

Note. CI = confidence interval, CL = confidence limit, HR = hazard ratio, NHS = Nurses' Health Study, RR = risk ratio

Chapter 3 of this monograph uses evidence from cancer populations and the general population to evaluate the effectiveness of smoking cessation treatments with a goal of identifying those that might be especially effective in cancer care. Importantly, many national and international cancer organizations recommend treating tobacco use among patients with cancer, including the International Association for the Study of Lung Cancer, the American Society of Clinical Oncology, the American Association for Cancer Research, and the National Comprehensive Cancer Network (Table 1.4).[37–40]

Table 1.4 Summary of Recommendations for Addressing Tobacco Use Among Cancer Patients

Organization	Recommendation Title	Date	Focus	Recommendation
National Comprehensive Cancer Network (NCCN)	NCCN Guidelines: Smoking Cessation	2021	Resource that serves as a standard for oncologists to address smoking cessation.	Ask every patient with cancer at every visit about smoking status and document responses in the electronic medical record (EMR).
International Association for the Study of Lung Cancer (IASLC)	Declaration from IASLC: Tobacco Cessation After Cancer Diagnosis	2019	Smoking cessation is critical to increase the efficacy of cancer treatment.	All patients should be screened for tobacco use and advised on the benefits of tobacco cessation. Evidence-based tobacco cessation assistance should be routinely and integrally incorporated into multidisciplinary cancer care. Smoking status should be a required data element for all prospective clinical studies, and clinical trials of patients with cancer should be designed to determine the most effective tobacco cessation interventions.
National Cancer Institute (NCI)/American Association for Cancer Research (AACR)	Research Priorities, Measures, and Recommendations for Assessment of Tobacco Use in Clinical Cancer Research	2016	Standardized approaches for assessing tobacco use in clinical cancer research trials.	Includes the recommended measures, protocol for measurement, and priority research areas for assessing tobacco use.

Table 1.4 (continued)

Organization	Recommendation Title	Date	Focus	Recommendation
AACR	Assessing Tobacco Use by Cancer Patients and Facilitating Cessation: An American Association for Cancer Research Policy Statement	2013	Improved provision of cessation assistance to all patients with cancer who use tobacco or have recently quit.	Universal assessment and documentation of tobacco use as standard of care, and cancer care providers should receive training in tobacco treatment and be incentivized for treatment referral and delivery. Further study of the deleterious effects of tobacco use and benefits of tobacco cessation on cancer progression and treatment are needed and recommended.
American Society of Clinical Oncology (ASCO)	Tobacco Cessation Guide for Oncology Providers and Tobacco cessation and control a decade later: American Society of Clinical Oncology policy statement update	2012 and 2013	Goal is smoking cessation intervention as an integrated element of care.	Oncology providers should be provided with the evidence-based and practical information they need to successfully integrate tobacco cessation activities into their practices.

Sources: ASCO 2012,[64] Hanna 2013,[37] IASLC 2019,[38] Land 2016,[65] NCCN 2022,[39] Toll 2013.[40]

Consistent with these many recommendations to address smoking in cancer care, in a 2019 *JAMA Oncology Commentary*, Fiore and colleagues[41] called for the designation of smoking cessation as the "Fourth Pillar of Cancer Care," joining surgery, chemotherapy, immunotherapy, and radiation therapy as an essential treatment component for patients with cancer who smoke. Fiore and colleagues called on all cancer care clinical settings to implement a set of specific actions that would lead to the universal delivery of evidence-based smoking cessation services so that every patient who smokes and is diagnosed with cancer receives effective smoking cessation treatment.

Chapter 3 identifies multiple smoking cessation treatments that have been shown to be consistently effective in promoting smoking cessation in the general population. This evidence strongly suggests that smoking cessation treatment will be effective and yield important benefits in cancer patients. However, chapter 3 also identifies important gaps in the research evidence with regard to smoking interventions in cancer care. For example, while it is clear that quitting smoking can greatly benefit cancer patients, too little is currently known about which smoking cessation treatments are most effective and cost-effective (chapter 4) in cancer patient populations and how they affect cancer outcomes, such as cancer treatment effectiveness, toxicity, and survival. The differences between cancer patients and the general population emphasize the importance of gathering additional data on smoking cessation treatment effectiveness and outcomes in cancer patients (see chapter 6).

Additional research that demonstrates the benefits of smoking cessation treatment for cancer outcomes may also increase the consistency with which cancer care clinicians and programs intervene with smoking. At present, effective smoking cessation treatments are too rarely implemented in oncologic care,[42,43] and tobacco use is not consistently treated in cancer treatment settings.[44,45] For example, tobacco cessation treatments are not consistently offered in hospitals providing oncology services.[46] This lack of consistency highlights the need to identify and address barriers to the adoption of evidence-based tobacco treatment guidelines.[27] In a 2019 review, Price and colleagues[47] found that cancer care clinicians are not adequately addressing smoking cessation with their patients as recommended by the PHS Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*, and other guidelines. The reviewed studies revealed that, although more than 75% of cancer care clinicians assess tobacco use during an intake visit and more than 60% typically advise patients to quit, a substantially lower percentage recommend or arrange smoking cessation treatment or follow-up after a quit attempt. Less than 30% of cancer care clinicians report adequate training in cessation interventions.[47] Other surveys of cancer care clinicians demonstrate low rates of intervening among cancer patients who smoke.[48,49] Below are strategies to support the identification of tobacco users and the delivery of smoking cessation treatment in cancer care settings.

Strategies That Support the Dissemination, Adoption, and Reach of Smoking Cessation Treatment Programs in Cancer Care Settings

- Establish an evidence-based standard of smoking cessation care across cancer clinical delivery systems that includes tobacco user identification, advice to quit, provision of or referral to evidence-based tobacco treatment, and patient follow-up.
- Measure and report the delivery of smoking cessation treatment as performance metrics for clinicians, hospitals, and health care system leadership.
- Emphasize the delivery of smoking cessation treatment as an important evaluation criterion for oncologists and cancer clinics by professional oncology organizations.
- Implement changes in health care systems, such as using electronic health record tools and other workflow adaptations that facilitate the consistent delivery of smoking cessation interventions in cancer care.
- Develop resources that enable universal implementation of smoking cessation treatment programs in cancer care settings, including strategies that:
  - Reduce clinician burden,
  - Enhance clinical workflow integration, and
  - Provide patients with easy access to multiple treatment options.

This monograph affirms that all patients with cancer should have access to evidence-based smoking cessation treatment as a standard component of their care. However, additional research is needed to understand the effectiveness of specific cessation treatment strategies for cancer patients who smoke and how best to deliver them in various cancer care settings. Chapter 6 of this monograph summarizes future directions for research that may enhance cessation interventions for all patients with cancer who smoke.

Purpose of the Monograph

This monograph is the 23rd volume in the series of monographs on tobacco control produced by the NCI of the National Institutes of Health, an agency of the U.S. Department of Health and Human Services. Other recent topics addressed as part of the Tobacco Control Monograph Series include tobacco-related health disparities (volume 22), the economics of tobacco control (volume 21), genetic studies of nicotine use and dependence (volume 20), and the role of the media in promoting and reducing tobacco use (volume 19). The goals of this tobacco control monograph are to: 1) give a brief overview of the relationship of smoking to the biology of cancer, 2) review and evaluate the evidence that smoking cessation interventions enhance cessation rates for patients who smoke in general and for patients with cancer in particular, 3) identify health care strategies that have the potential to enhance the delivery of smoking cessation treatment in the cancer care context, 4) discuss medically underserved and vulnerable populations that typically have higher cancer burdens and face unique challenges in quitting smoking, and 5) identify important research gaps related to these topics. The monograph is intended to inform clinicians, health care systems, cancer patients who smoke, researchers, policymakers, funding agencies, community-based organizations, caregivers who support cancer patients and survivors, and other stakeholders with interests in cancer and cancer care. It is intended to present these audiences with a rigorous summary of the science regarding effective smoking cessation treatments, implementation models for those treatments, and clear research needs that can enhance smoking cessation treatment in cancer care.

The Role of Public Health Practitioners

While directed primarily at oncology clinicians and researchers, this monograph recognizes the important role that state and local public health practitioners, as well as other public and private sector organizations, can play in improving the health of patients with cancer who smoke. Those working in tobacco control can significantly enhance the health and welfare of patients with cancer and survivors by: (1) improving data collection related to tobacco use and cancer outcomes, (2) improving public knowledge of the benefits of quitting tobacco for patients with cancer, (3) increasing access to evidence-based smoking cessation treatments, and (4) implementing evidence-based tobacco prevention and control policies. Ongoing monitoring of cancer incidence and outcomes, as well as tobacco use patterns, can help identify populations who experience disproportionately high rates of tobacco-related cancers and who may require enhanced access to smoking cessation treatments. Such data collection will also inform efforts to evaluate the effectiveness of tobacco control programs and policies for populations with cancer. Public health practitioners can emphasize to cancer patients and survivors how important quitting can be to the success of their cancer treatment and life beyond cancer. Consistently asking survivors whether they use tobacco products, encouraging those who do to quit, and offering cessation support and resources all serve to underscore for patients and their families that cessation is an important aspect of their cancer care.

State and local public health practitioners can work to ensure equitable access to evidence-based cessation treatments, including U.S. Food and Drug Administration (FDA)–approved medications and counseling services. Multiple strategies can support treatment utilization and successful cessation, leading to improvements in the prognosis for patients with cancer and survivors who smoke. Such strategies include promoting cessation resources and programs such as telephone quitlines and web- and text-based programs in health systems and communities, increasing reimbursement rates for tobacco cessation services for clinicians, and removing patient-level treatment barriers (such as co-pays, prior authorization requirements, or limits on quit attempts). Additionally, implementing evidence-based policies that lower tobacco use rates in the general population (e.g., increasing the price of tobacco products, enacting comprehensive smokefree laws) are also likely to reduce tobacco use rates among people diagnosed with cancer and their families.

Specifically, the monograph examines the following areas:

- **Smoking in Patients With Cancer: Biological Factors:** Chapter 2 provides a brief overview of the relationship of smoking to the biological aspects of cancer, including the relationship between cigarette smoke and tumorigenesis, biological characteristics of lung cancers in smokers and never-smokers, and the effects of cigarette smoke exposure on cancer cells.
- **Treating Tobacco Use and Dependence in Cancer Populations:** Chapter 3 describes the evidence regarding smoking cessation treatment effectiveness. It draws from literature on the general population of people who smoke as well as studies that examine cessation among patients with cancer who smoke to identify effective counseling and medication treatments. It also reviews evidence on the specific needs of cancer patients and potential modifications of smoking cessation treatment to address such needs.
- **Implementing Smoking Cessation Treatment Programs in Cancer Care Settings: Challenges, Strategies, Innovations, and Models of Care:** Chapter 4 evaluates evidence on health care system strategies that can be used to implement smoking cessation treatment in cancer care settings, building on the extant literature, the 2020 Surgeon General's report, and published findings from C3I. Topics reviewed include extending the reach of smoking cessation treatment and enhancing its effectiveness, ease of implementation, and maintenance over time.
- **Addressing Smoking in Medically Underserved and Vulnerable Cancer Populations:** Chapter 5 identifies populations that experience especially high levels of harm from both cancer and smoking. For example, some racial groups (e.g., American Indian or Alaska Native), people of lower socioeconomic status, sexual and gender minority communities, and individuals with mental health conditions and/or co-occurring substance use disorders have significantly higher rates of tobacco use. This chapter reviews evidence on smoking cessation in these populations, the challenges to cessation, and considers strategies to treat members of these and other vulnerable populations who smoke.
- **Monograph Conclusions and Future Research Directions:** Chapter 6 describes the monograph's major conclusions and the conclusions from each chapter. It also outlines

key research needs to clarify the challenges and opportunities to intervening with smoking in cancer care settings.

Some redundancy across the chapters of this monograph is intentional. This redundancy supplies appropriate context for each topic of discussion and is designed for readers who may be interested in focusing on a particular chapter or section of the volume.

Preparation of the Monograph

This monograph underwent a rigorous development process led by three senior editors. These editors were joined by two experts with extensive experience in tobacco control and oncology to form the Scientific Editorial Committee (SEC). The SEC developed a shared vision of the monograph's purpose and focus. Given responsibility for specific topics, SEC members were joined by chapter leads to develop chapter outlines; identify chapter contributors and reviewers; and contribute to the development, writing, reviewing, and editing of the monograph. Chapter leads and contributors drafted chapters in accordance with the outlines and under the guidance of the SEC. Literature searches were generally restricted to studies conducted in the United States and those in English, typically among adults 18 years and older. The individuals who contributed to this monograph are listed on pages xiv–xix.

In addition to multiple internal reviews by the editorial team, each chapter was reviewed by external expert peer reviewers, followed by an extensive review of the full monograph volume. The NCI also conducted a final review of the monograph before publication. In all, 52 reviewers participated in this process.

Key Terminology and Concepts

While several terms in the tobacco control and oncology literature are used interchangeably, a concerted effort was made to review the nomenclature and come to a consensus on the various terms used in this monograph. Table 1.5 presents some of those key terms. Additional terms can be found in the glossary on page xxi.

Table 1.5 Monograph Terminology

Term(s)	Use in This Monograph
Tobacco use vs. smoking	"Smoking" is used when referring to cigarette use. "Tobacco use" is used when referring to tobacco product use more generally.
Smoking cessation treatment	"Smoking cessation treatment" is used to encompass treatment aimed at smoking reduction, smoking cessation, and relapse prevention after treatment.
Electronic nicotine delivery systems (ENDS)	"Electronic Nicotine Delivery Systems (ENDS)" is used when referring to e-cigarettes and related products.

Table 1.5 (continued)

Term(s)	Use in This Monograph
Patients with cancer vs. cancer survivors	"Patients with cancer" refers to those newly diagnosed with cancer and in treatment for active or recurrent cancer; "cancer survivors" refers to individuals who have completed treatment for active cancer, have metastatic disease, or are receiving intermittent treatment. The term "long-term survivor" is used, where applicable, to distinguish between those who recently completed cancer treatment versus those in a later phase.
Medically underserved and vulnerable populations	Populations who experience disparities in cancer burden, smoking prevalence, access to smoking cessation treatment, and/or smoking cessation treatment success. "Vulnerable" refers to a heightened risk for cancer or a higher cancer burden relative to the general population.

The cancer care continuum described previously in Figure 1.1 includes people undergoing screening for cancer, diagnosed with cancer, in treatment for cancer, and those who, at some time in the past, received a diagnosis of cancer or were treated for cancer. As explained in Table 1.5, in general, this monograph will use the term "patients with cancer" or "cancer patients" to refer to those newly diagnosed with cancer and in treatment for active or recurrent cancer. In some instances, the monograph will also use the term "cancer survivors" when the reviewed studies used this specific terminology, recognizing that the use of this term could result in some overlap of populations along the cancer continuum. In addition, where possible and appropriate, the monograph identifies the location along the cancer care continuum where smoking cessation treatments are delivered or where smoking status is determined (e.g., at or near diagnosis, during cancer screening, 10 years post-diagnosis). Further, this monograph attempts to characterize samples based upon important individual and clinical factors (e.g., age, type and stage of cancer, time since diagnosis).

This monograph focuses primarily on addressing cigarette smoking because it is the most common form of tobacco use among adults, and the type of tobacco use for which the most cessation data exist. Nonetheless, it is important to note that other forms of tobacco, such as cigars[50] and smokeless tobacco,[51] also play an important role in the etiology of certain cancers such as head, neck, and oral cavity cancers and their continued use is likely to be detrimental to cancer patients. Therefore, the use of other tobacco products is discussed where possible. To date, little evidence exists on the relationship of noncigarette tobacco product use among patients with cancer and their cancer outcomes or their ability to quit tobacco use. This monograph identifies these topics as areas in need of additional research.

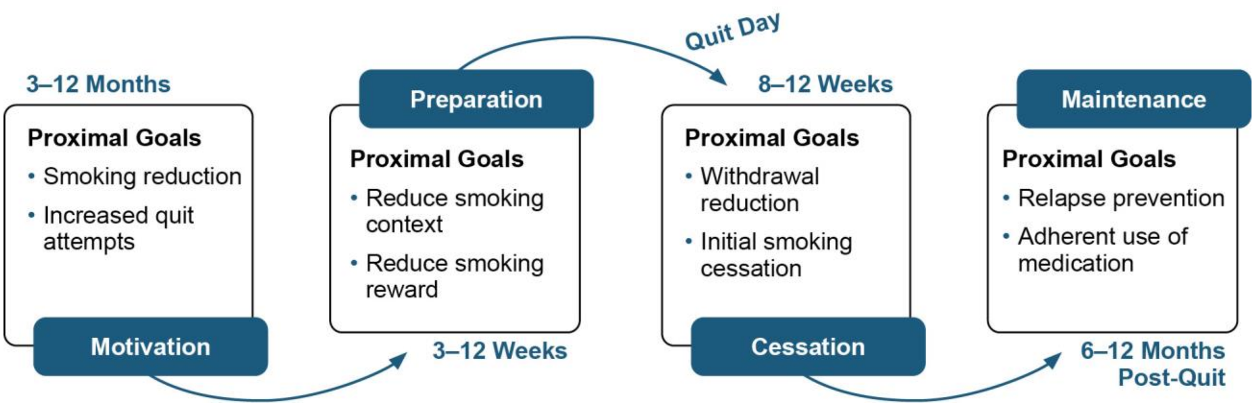
The Multiple Phases of Smoking Cessation Treatment

In this monograph, the term "smoking cessation treatment" is used to refer to a variety of interventions for cigarette dependence and use, interventions that can differ substantially in their methods and goals. The diversity of smoking treatments is conceptualized in the *Phase-Based Model* of smoking treatment,[52,53] which recognizes that individuals who smoke vary in their receptivity to and involvement in smoking treatment. The model identifies phases along the continuum of treatment and links these phases with distinct proximal goals, challenges, and opportunities. The model holds that treatments for smoking should be developed and validated to address the particular challenges and opportunities that are relevant for each phase. Figure 1.2 shows four "phase-based" treatment types that have been widely researched and used clinically. These treatment types are sometimes used alone in smoking treatment programs, such as when only cessation treatment is offered, but can also be combined, for example, when cessation and maintenance interventions are combined.

The four major types of smoking treatments are described below:

1. **Motivation-phase treatments** are delivered to individuals who are not yet ready to make a cessation attempt. These treatments typically involve medication, usually nicotine replacement therapy (NRT), and smoking reduction counseling and are often intended to help the patient decrease the amount they smoke and the contexts in which they smoke. Offering motivation-phase treatment increases the portion of a smoking population that enters evidence-based smoking treatment in comparison with the offer of cessation treatment alone.[54]
2. **Preparation-phase or "preloading treatments"** are designed for individuals who are willing to make a quit attempt. These treatments usually provide smoking cessation medication over 3 to 12 weeks prior to the targeted quit day: typically NRT,[55,56] or varenicline.[57,58] Counseling may also be delivered[59] to help prepare the person for their quit attempt, for instance, by helping them adopt a smoke-free home policy. There is some evidence that preparation treatment increases smoking abstinence once patients use cessation treatment but the size of the effect is modest.[55,56,59,60]

Figure 1.2 Phases of Smoking Treatment



Note: Phases of smoking treatment, commonly used durations, and examples of their proximal goals. The durations of any of the phases of treatment can vary.

3. **Cessation-phase treatments** are provided to individuals who are willing to make a quit smoking attempt and are delivered beginning on either the target quit day or shortly before it. Cessation treatment is most effective when it combines smoking cessation medication and cessation counseling. Multiple cessation medications have been shown

to be effective, but combination NRT (e.g., the patch with either nicotine gum or lozenge) and varenicline are the most effective. Cessation counseling typically involves training the person to cope with urges and nicotine withdrawal symptoms and avoid smoking triggers as well as providing intra-treatment support.[61] Cessation treatment is consistently effective; combining cessation counseling with the most effective medications typically doubles or triples smoking abstinence rates compared with minimal treatment.

4. **Maintenance-phase treatments** typically start once a cessation treatment has ended, usually 8–12 weeks after the patient's target quit day. Some treatments combine cessation and maintenance treatment elements and do not formally distinguish between them. Maintenance treatment typically involves both pharmacotherapy and counseling, with the latter often intended to sustain patients' quitting motivation and to encourage adherence to medication.[62] Unfortunately, there is little evidence that such counseling is effective.[63] The evidence is mixed as to whether very extended maintenance pharmacotherapy improves long-term smoking abstinence rates; there is some evidence that extended NRT or varenicline may sustain abstinence when given to those who are initially successful in quitting.[62,63]

Using treatments aimed at different phases of quitting can have advantages. For instance, offering motivation-phase treatment to those unwilling to enter cessation treatment can increase the proportion of patients who use evidence-based treatment, defined by use of either motivation treatment itself or later use of cessation treatment. Moreover, motivation-phase treatment ultimately increases the likelihood of long-term abstinence from smoking. However, providing multiple types of treatment to individuals who smoke has disadvantages, such as increased complexity. If only one type of treatment is offered, it should be cessation treatment, which results in the largest increases in long-term abstinence rates if an individual is willing to use it.

Major Conclusions

Based on the evidence reviewed, the monograph makes the following eight overall conclusions regarding smoking cessation treatment across the cancer care continuum:

1. **Smoking cessation after the diagnosis of cancer is highly likely to reduce all-cause mortality and cancer-specific mortality.** Evidence continues to mount that quitting smoking after a cancer diagnosis is causally associated with reduced all-cause mortality and cancer-specific mortality, in comparison with continued smoking. The studies reviewed in this monograph confirm and expand upon findings of the 2014 and 2020 Surgeon General's reports regarding this topic. Laboratory studies provide insight into the mechanisms by which smoking may increase tumor aggressiveness and decrease cancer treatment effectiveness.
2. **Research from the general population indicates that patients with cancer who smoke will benefit from smoking cessation treatments, including both counseling and U.S. Food and Drug Administration (FDA)–approved medications.** Smoking cessation counseling and medication have been shown to be effective in diverse populations of people who smoke. This substantial evidence, including some studies with cancer patients, clearly supports the delivery of evidence-based smoking cessation treatment as an essential component of cancer care.

3. **Effective strategies exist to increase the delivery of smoking cessation treatment in cancer care settings.** Barriers identified by cancer care clinicians include lack of time, lack of specialized training to deliver smoking cessation treatment options, misconceptions about patients' intentions to quit, and difficulties with health insurance reimbursement. Multiple strategies, including use of EHR-based clinical workflow tools, can be adopted to address tobacco use for every patient across the cancer care continuum, including those who are screened for or diagnosed with cancer. These strategies can improve the identification of patients who smoke, the offer of smoking cessation treatment, and the delivery of or referral for smoking cessation treatment and can do so in a low-burden, efficient manner.
4. **Evidence-based smoking cessation treatment should be systematically provided to all patients with cancer, regardless of the type of cancer. However, patients with cancer are not consistently offered and provided such treatment.** Many national and international cancer organizations recommend addressing smoking among patients with cancer and provide guidance to cancer care clinicians for effectively delivering smoking cessation treatment. However, the implementation of these evidence-based recommendations has been inconsistent and incomplete, highlighting the need to identify and address barriers to providing smoking cessation intervention that exist for both cancer care clinicians and health care systems.
5. **Continued smoking after a cancer diagnosis is associated with higher health care utilization and greater health care costs in comparison with quitting smoking.** Direct non–health care costs, such as transportation and caregiving, may also be increased with continued smoking after a cancer diagnosis. Smoking cessation interventions in patients with cancer are highly likely to be cost-effective.
6. **Medically underserved and vulnerable populations of cancer patients who smoke are very likely to benefit from using the evidence-based smoking cessation treatments identified as effective in the general population of people who smoke.** Medically underserved and vulnerable populations are faced with multiple factors at the individual, community, institutional or health care system, and societal levels that may impede access to smoking cessation treatment and cessation success. Importantly, substantial evidence indicates that medically underserved and vulnerable populations overall (i.e., noncancer populations) benefit from evidence-based smoking cessation treatment, providing evidence that these populations with cancer will benefit as well.
7. **The tobacco product marketplace and consumer use patterns are changing for both the general population and for patients with cancer, posing challenges for researchers and cancer care clinicians.** Research is needed to monitor the use and effects of diverse tobacco products, both conventional and new, by patients with cancer, including their effects on smoking cessation and relapse and their potential deterrence of patients' using evidence-based smoking cessation treatments such as counseling and FDA-approved medications.
8. **Continued research is needed to identify effective cessation interventions for patients with cancer who smoke and to better understand the effects of smoking cessation on cancer outcomes.** Relatively few well-powered randomized controlled trials of smoking cessation treatments in patients with cancer have been conducted. Additional research is needed to identify: the effectiveness of smoking cessation

interventions in increasing abstinence among patients with cancer, including which intervention strategies are most effective; the effects of smoking cessation treatment and resulting abstinence on cancer-related outcomes (e.g., all-cause and cancer-specific mortality); and health care system changes and implementation strategies that are especially effective in engaging patients with cancer in evidence-based smoking cessation treatment.

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NCI Monograph 23
Treating Smoking in Cancer Patients:
An Essential Component of Cancer Care

Chapter 2
Smoking in Patients With Cancer: Biological Factors

Chapter Contents

Figures and Tables

Chapter 2
Smoking in Patients With Cancer: Biological Factors

Introduction

Enormous progress has been achieved over the past several decades in researchers' understanding of the biology that underlies cancer.[1] As a result, many cancers are now prevented or are diagnosed at an earlier stage, and fewer patients who develop cancer die from their disease. In terms of clinical care, revolutionary advances in treatment strategies, including minimally invasive surgery, highly conformal radiotherapy, targeted biologic therapeutics, and immunotherapy, have markedly improved patient outcomes.[2–4] These advances, along with successes in prevention and screening, have contributed to a 31% reduction in cancer death rates between 1991 and 2017,[5] dramatically increasing the number of patients who survive cancer.[5–7] As a result, morbidity from cancer treatment sequelae as well as noncancer-related morbidity and mortality are more important determinants of overall patient outcomes than ever before.

As described in chapter 1, a strong clinical evidence base demonstrates the adverse effects of smoking on clinical cancer outcomes. The 2014 Surgeon General's report, *The Health Consequences of Smoking—50 Years of Progress*, was the first Surgeon General's report to comprehensively review the effects of cigarette smoking on health outcomes in cancer patients and survivors. This report, which reviews more than 400 studies, concluded that quitting smoking improves the prognosis of patients with cancer, and that smoking is causally linked with adverse health outcomes, including all-cause mortality, cancer-specific mortality, and increased risk for second primary cancers caused by smoking.[8] In aggregate, among studies that included relative risks (RR), risk of all-cause mortality increased by a median of 51% among patients with cancer who smoked compared with never-smoking patients with cancer, while former smoking was associated with a median increased risk of 22% compared with never smoking. Current smoking also increased risk of cancer-specific mortality by a median of 61% while former smoking did not appear to increase risk relative to never smoking (increasing risk by only a median of 3%). Current smoking increased risk of recurrence by a median of 42% compared with never smoking, while former smoking increased median risk by 15%. Finally, there was a strong association between current smoking and the risk of developing a second primary cancer (median RR of 2.2).[8] The 2020 Surgeon General's report, *The Health Benefits of Smoking Cessation*, built on these findings by reviewing the effects of smoking cessation on risk of all-cause mortality among patients with cancer. This report reviewed 10 studies, representing 10,975 patients with cancer, which were published on this topic between 2000 and 2016. Among the 7 prospective cohort studies reviewed, continued smoking was associated with a median increased risk in all-cause mortality of 82% compared with quitting smoking.[9]

The clinical effects of smoking on cancer treatment outcomes are mirrored by biological observations that smoking increases tumor promotion and is associated with decreased efficacy of cancer treatment.[10,11] Studies of cigarette smoking and cancer contribute to the understanding of the biology of cancer and to developing treatments for cancer; they also provide a compelling rationale for addressing tobacco use by patients with cancer. This chapter will first provide a brief discussion of the numerous mechanisms by which cigarette smoking causes cancer. It will then discuss studies of the molecular characteristics of lung cancers occurring in smokers compared with never-smokers before turning to a discussion of experimental studies of the effects of tobacco smoke exposure on cancer cells. A comprehensive review of the mechanisms by which cigarette smoking causes disease, including cancer, is available in the 2010 report of the Surgeon General, *How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease*.[12] This chapter will focus on the biological effects of cigarette smoking because it is the predominant form of tobacco used by adults. Additionally, there are not yet sufficient studies of the biological effects of newer forms of tobacco, such as electronic nicotine delivery systems, on cancer.

Tobacco Smoke and Tumorigenesis

Chemical Composition of Tobacco Smoke

The causal relationship between cigarette smoking and numerous cancers has been well documented.[8] Tobacco smoke contains more than 7,000 chemical compounds, of which approximately 70 cause cancer in either laboratory animals or humans.[8,12,13] This complex mixture of carcinogens causes at least 12 types of cancer in humans.[8,12] The U.S. National Toxicology Program and the International Agency for Research on Cancer (IARC) have determined that tobacco smoke is carcinogenic.[13,14] Similar to other IARC Group 1 carcinogens (known human carcinogens), tobacco smoke exhibits 1 or more of the 10 key characteristics of carcinogens shown in Table 2.1.[13,15] Although the biological effects of tobacco smoke on tumorigenesis have been well studied, some knowledge gaps remain, including whether the route of exposure to tobacco smoke influences the site-specific biology of the resultant tumors. For example, tissues that come into direct contact with tobacco smoke (e.g., lung) are exposed to the whole mixture of chemical compounds, whereas other organs are exposed only to those chemical compounds or their metabolites that reach the tissue through the circulatory system. As a result, there may be biological differences between tobacco-related tumors based on whether they receive exposure to tobacco smoke directly, through the circulatory system, or a combination of both.

Table 2.1 Key Characteristics of Carcinogens

Characteristic	Examples of relevant evidence
1. Is electrophilic or can be metabolically activated	Parent compound or metabolite with an electrophilic structure (e.g., epoxide, quinone), formation of DNA and protein adducts
2. Is genotoxic	DNA damage (DNA strand breaks, DNA–protein cross-links, unscheduled DNA synthesis), intercalation, gene mutations, cytogenetic changes (e.g., chromosome aberrations, micronuclei)
3. Alters DNA repair or causes genomic instability	Alterations of DNA replication or repair (e.g., topoisomerase II, base-excision, or double-strand break repair)
4. Induces epigenetic alterations	DNA methylation, histone modification, microRNA expression
5. Induces oxidative stress	Oxygen radicals, oxidative stress, oxidative damage to macromolecules (e.g., DNA, lipids)
6. Induces chronic inflammation	Elevated white blood cells, myeloperoxidase activity, altered cytokine and/or chemokine production

Table 2.1 (continued)

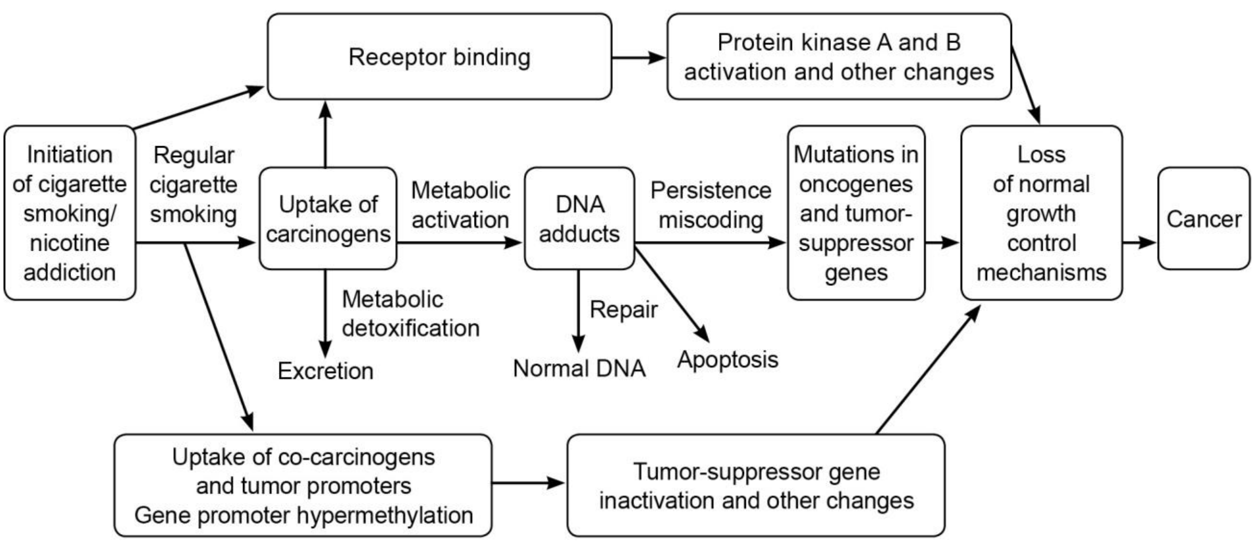
Characteristic	Examples of relevant evidence
7. Is immunosuppressive	Decreased immunosurveillance, immune system dysfunction
8. Modulates receptor-mediated effects	Receptor in/activation (e.g., ER, PPAR, AhR) or modulation of endogenous ligands (including hormones)
9. Causes immortalization	Inhibition of senescence, cell transformation
10. Alters cell proliferation, cell death, or nutrient supply	Increased proliferation, decreased apoptosis, changes in growth factors, energetics and signaling pathways related to cellular replication or cell cycle control, angiogenesis

Note: Any of the 10 characteristics in this table could interact with any other (e.g., oxidative stress, DNA damage, and chronic inflammation), which when combined provides stronger evidence for a cancer mechanism than would oxidative stress alone. DNA = deoxyribonucleic acid. RNA = ribonucleic acid. ER = estrogen receptor. PPAR = peroxisome proliferator-activated receptor. AhR = aryl hydrocarbon receptor.
Source: Smith et al. 2016.[15] Reproduced from *Environmental Health Perspectives* with permission from corresponding author, Martyn T. Smith.

Tobacco Smoke: DNA Damage

Many chemical compounds in tobacco smoke damage deoxyribonucleic acid (DNA) either directly or via their metabolic by-products.[12] This damage can lead to both small and large genetic alterations.[12,16] These alterations accumulate from prolonged exposure to tobacco smoke chemical compounds over time to increase the level of mutations within exposed tissues and can result in loss of normal function of proteins involved in the control of cell growth and DNA damage repair, thus contributing to tobacco-related tumor formation.[12] Figure 2.1 depicts the major pathways by which the carcinogens in tobacco smoke cause cancer or tumor development.[12] Former smokers are at reduced risk of many cancers relative to current smokers.[9] However, the genetic changes accrued during the time they smoked contributes to their increased cancer risk relative to never-smokers.

Figure 2.1 Major Pathways of Cancer Causation by Cigarette Smoking



Note: DNA = deoxyribonucleic acid.
Source: USDHHS 2010.[12]

Tobacco Smoke: Mutational Burden

Analyses of the genetic changes associated with tobacco smoke exposure can provide insight into molecular changes occurring in cancers among smokers. The types of genetic changes include single base substitutions (SBS), insertions or deletions (indels), or copy number variations, as well as larger chromosomal alterations.[17–20] Sequencing of tumor DNA from current and former smokers reveals significant smoking-related mutation patterns that vary by organ site.[17,20–22] The organs that come in direct contact with tobacco smoke chemical compounds have the highest number of total mutations per cancer DNA region or mutational burden.[17] Lung cancer has the highest overall mutation levels of smoking-related cancers; elevated mutation levels are also observed in head and neck, bladder, liver, and kidney tumors from smokers compared with nonsmokers.[17,20–22] In addition, the extent of mutations can be lower in former smokers relative to current smokers, depending on the organ site.[21,22]

Studies of normal bronchial cells from current, former, and never-smokers indicate that smoking causes mutations in these cells, with current smokers having the highest mutation burden; the mutational burden of former smokers is intermediate between that of current smokers and never-smokers.[23] Additionally, the fraction of cells without mutations is higher in the bronchial epithelium of former smokers than in current smokers, suggesting that following smoking cessation, the damaged cells within the bronchial epithelium are replaced by cells that avoided mutagenesis.[23]

The types of mutations associated with tobacco smoke exposure shift depending on the tumor location.[17,20,24] This may be due to the susceptibility of different tissues to the variety of chemical compounds present in tobacco smoke, to differences in tissue-specific metabolic activities that activate or inactivate mutagens, or to the extent to which different tissues are exposed to the various chemical compounds in tobacco smoke. Furthermore, there may be organ differences in how the tissues respond to tobacco smoke-related DNA damage, given that there are cancers (e.g., pancreatic or cervical cancer) for which smoking-related DNA damage has been detected but the mutational burden is not significantly different between smokers and nonsmokers.[17]

Tobacco Smoke: Mutational Signatures

Somatic mutations contribute to carcinogenesis by altering the activity of proteins involved in cell cycle control as well as other important cellular processes. Mutational signatures are distinctive patterns, or footprints, caused by specific mutagenic processes, such as exposure to individual DNA-damaging chemical compounds or defective endogenous processes like DNA repair pathways. These signatures are identified by bioinformatics analysis of genomic DNA from thousands of tumors that focuses on extracting characteristic somatic mutation patterns and, where possible, attributing them to individual mutagenic sources.[25] Researchers have compiled the mutational signatures extracted from thousands of cancer genomes in the Catalogue of Somatic Mutations in Cancer (COSMIC).[26] These patterns are based on SBS, doublet base substitutions, indels, and large-scale genomic structural alterations.[27] As numerous mutational signatures are associated with specific exposures, their presence provides evidence that a given exposure plays a role in the carcinogenic process.

Multiple signature mutations are elevated in tumors in smokers, including COSMIC mutation signatures 2, 4, 5, 13, and 16.[17] Some of these signatures are present in all tumor cells, indicating that they likely occurred early in the tumorigenesis process. These signatures reveal valuable mechanistic information about the carcinogenic process. For example, signature 4 involves GC to TA transversion mutations in patterns similar to those produced by the tobacco smoke chemical benzo[a]pyrene in model systems.[28] This signature is mainly detected in tumors located at sites that come in direct contact with tobacco smoke chemical compounds, such as the lung, larynx, oral cavity, pharynx, and esophagus.[17] On the other hand, signature 5 is thought to derive from an endogenous mutation process.[17] Because this signature is more abundant in cancers occurring in smokers compared with never-smokers for lung, larynx, pharynx, oral cavity, esophagus, bladder, liver, and kidney tumors,[17] it is thought that indirect effects of tobacco smoke trigger an endogenous mutation process responsible for this signature. Similarly, the higher levels of signatures 2 and 13 in tobacco-related cancers are thought to be derived from indirect effects of tobacco smoke, as these signatures are associated with the APOBEC enzyme family (apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like)[17]; APOBEC members can be overexpressed in some cancers and cause mutations by converting DNA cytosine bases to uracil.[29]

Tobacco Smoke: Cancer Driver Genes

Genetic analyses have shown that there are dramatic differences in somatic mutation patterns between and within cancer subtypes.[30–32] These analyses led to the identification of gene sets that drive carcinogenesis when they are mutated; the specific genes that house these mutations are defined as cancer driver genes.[33] These mutations give an advantage to the cells containing them and have been selected for during the cancer's evolution.[33,34] The combination of cancer driver genes mutated in the carcinogenic process varies with tumor subtype, stage, and the etiological factors leading to tumor formation (e.g., smoking status).[33] Identification of the specific genes mutated in a patient's tumor can inform the selection of appropriate cancer therapies and help predict patient survival, the risk of recurrence, and response to therapy.[35] Because smoking impacts the number and type of mutations, depending on the organ site, the cancers formed in ever-smokers can be biologically distinct from those in never-smokers, requiring different approaches for cancer treatment.[18,36,37]

Tobacco Smoke: Epigenetic Changes

Tobacco smoke also causes nonmutational structural changes in DNA that affect gene expression (epigenetic changes, e.g., levels of 5-methylcytosine). Consequently, the epigenetic landscape of tumors from patients with a history of smoking can differ from those of patients without a history of smoking, depending on the tumor type.[17,38–45] The most extensive effects of smoking on epigenetic markers are observed in lung tumors.[17] Similarly, smoking, particularly current smoking, has been shown to alter gene expression in some tumors.[46–55] These changes can affect the biology of the tumor, influencing tumor behavior, such as the aggressiveness of tumor growth or responsiveness to cancer therapies.

Biological Characteristics of Lung Cancers in Smokers and Never-Smokers

Lung cancers are classified as small cell lung cancers or non-small cell lung cancers (NSCLCs) by the presence or absence of neuroendocrine characteristics.[56] NSCLC, which represents approximately 85% of lung cancer in the United States,[57] is further categorized into adenocarcinoma (40% of lung cancers), squamous cell carcinoma (25% of lung cancers), and large cell carcinoma (10% of lung cancers).[58] In the United States, the vast majority of lung cancers (~80%–90%), regardless of histologic subtype, occur in current or former smokers; lung cancers that occur in never-smokers are predominantly adenocarcinoma.[59–62] An understanding of the molecular characteristics of lung cancers contributes to the understanding of their etiology as well as to their diagnosis and treatment. To highlight how tobacco smoke exposure can influence the molecular characteristics of cancer, characteristics of lung cancer in smokers and never-smokers are discussed below.

It is important to note that studies do not always distinguish between never-smokers and former smokers, instead comparing current smokers with "nonsmokers." In addition, some studies compare never-smokers to "ever-smokers," a category that comprises both current and former smokers. The categories of current, former, and ever-smoker may include individuals with a wide range of smoking histories and patterns; in particular, the category of former smokers may include individuals who quit decades ago as well as those who quit very recently. Furthermore, it is not always possible to accurately distinguish between never-smokers, current smokers, and former smokers based on patient report or medical record. In the section below, results are reported based on the categories used in the literature cited.

Lung Cancer: Driver Genes

Studies show that lung cancers in smokers are molecularly distinct from lung cancers in never-smokers, particularly in mutations in the cancer driver genes.[62,63] The driver genes vary with histological tumor type and smoking status.[64–66] There are data indicating that the genesis of lung tumors in current smokers, former smokers, and never-smokers follow different pathways with distinct patterns of driver mutations.[67] For example, the frequency of epidermal growth factor receptor (*EGFR*) mutations is significantly higher in lung cancers in nonsmokers compared with smokers; *EGFR* is the most frequent mutation in lung adenocarcinomas in never-smokers but is relatively rare in heavy smokers.[64,68–79] The frequency of *EGFR* mutations drops with increasing pack years smoked.[69,71–73,76] In contrast, Kirsten rat sarcoma viral oncogene homolog (*KRAS*) and tumor protein p53 (*TP53*) mutations are more prevalent in adenocarcinomas in current and former smokers, compared with never-smokers.[24,64,68,69,75,80–82] Former smoker NSCLC patients had more *EGFR* mutations and fewer *KRAS* mutations than patients who currently smoke.[69,83]

Differences in driver genes are significant because they can affect the responsiveness of the tumor to different therapeutic approaches, with implications for prognosis and survival.[18,36,75] Targeted therapies have been developed to treat tumors with specific driver genes, such as *ALK*, *EGFR*, *BRAF*, *ROS1*, *RET*, and *MET*. Targeted therapies increase the life expectancy of patients with these specific mutations relative to patients who lack those mutations; this increase in survival is independent of smoking history, which emphasizes the importance of molecular genetic testing of lung adenocarcinoma specimens for targetable driver mutations regardless of smoking history.[84–86]

Lung Cancer: Mutational Burden

The mutational burden in lung tumors from smokers is higher than that in lung tumors from nonsmokers.[17,21,36,37,65] Genome-wide comparison of lung adenocarcinomas from smokers and never-smokers indicated that the average mutation frequency is more than 10 times higher in smokers than in never-smokers.[36] This is consistent with the high mutational activity of the chemical compounds in tobacco smoke, which drives tumorigenesis.

Mutational burden includes both small and large genetic changes.[17,19,21,65] Mutated genes in lung cancers from smokers often have a different spectrum of mutations than occurs in lung cancers from never-smokers.[69,80,81,87] Genome-wide analysis of genomic aberrations in lung adenocarcinomas from smoking and nonsmoking patients indicates that these two populations have both global and regional differences in their tumor genome. Tumors from never-smokers were more likely to have gene copy number gains on chromosomes 5q, 7p, and 16p and were more likely to have a larger fraction of their genome altered. In comparison, tumors from ever-smokers were more likely to have more regions of focal DNA amplifications and deletion.[65] Another study indicated that the significant copy number gains in heavy smokers were especially frequent in 8q and 12q, whereas focal copy number losses in never-smokers or light smokers tended to occur in areas not associated with genes.[19] The overall mutational complexity of tumors in smokers may contribute to the difficulty in treating such tumors.

Lung Cancer: Epigenetic Modifications

In addition to mutations, smoking causes structural changes to DNA which, in turn, affect how the tumor grows and responds to therapy. For example, DNA methylation, an epigenetic modification, controls the expression of specific genes; there are distinct differences in the patterns of gene methylation or methylation status in lung tumor DNA from smokers compared with nonsmokers.[17,38,39,45,88–91] The methylation status of specific genes is associated with tumor aggressiveness and patient outcomes.[92,93] A meta-analysis of studies conducted in patients with lung cancer found a positive association between cigarette smoking and hypermethylation of *p16* in tumor tissues from both adenocarcinomas and squamous cell carcinomas. The meta-analysis, which included 19 studies conducted in several countries, found a stronger association between smoking and *p16* hypermethylation in studies conducted in Asian countries compared with those conducted in North America.[91] Methylation of *p16* and *MGMT* genes is elevated in NSCLC tumors in ever-smokers versus never-smokers.[39] Similarly, a meta-analysis of 97 studies of NSCLC found a significant association between cigarette smoking and hypermethylation of 7 genes (including *CDKN2A, RASSF1, MGMT, RARB, DAPK, WIF1, FHIT*).[38]

Lung Cancer: Variation in Gene Expression

Smoking-related variations in gene expression as measured by variations in ribonucleic acid (RNA) levels have also been reported for lung cancers and, in some cases, associated with patient prognosis. Smoking-associated expression networks of messenger RNA (mRNA) and a variety of noncoding RNAs have been reported.[48–50,53–55,94] In all cases, researchers observed marked differences between tumors from smoking and nonsmoking patients, with tumors from smoking patients exhibiting a more complex disease with greater dysregulation of gene expression. Studies focused on specific genes also showed differences between smokers and nonsmokers. For example, never-smokers were more likely to have down-regulation of expression of *p14*, but not *p16*, than were ever-smokers (63% vs. 35%, $p = .008$).[74] In addition, expression of a variety of receptor genes was altered in tumors as a function of smoking status. Progesterone and androgen receptor gene expression was lower in NSCLC than in normal tissues with levels being lower for smokers than for never-smokers. Aryl hydrocarbon receptor (*AHR*) gene expression was also lower in tumors in smokers compared with never-smokers.[95] The expression patterns of genes encoding nicotinic acetylcholine receptor subunits (*CHRN*) were different depending on histological tumor type and smoking behavior. The expression of *CHRNA7* gene, which encodes a CHRN subunit, was elevated in squamous cell carcinoma in smokers relative to nonsmokers and was associated with poor survival.[96]

Therapeutic Implications of Molecular Differences in Lung Cancers

With the development of targeted therapies and immunotherapies, the molecular differences between lung cancer in smokers and never-smokers contribute to differences in treatment options, prognosis, and survival. As noted above, *EGFR* mutations are predominantly found in lung cancers in never-smokers. The presence of *EGFR* mutations strongly predicts a positive response to therapy with the *EGFR* tyrosine kinase inhibitors gefitinib, erlotinib, and osimertinib.[97,98] Lung cancers arising in never-smokers are more likely to contain *ALK* mutations than those arising in smokers; targeted therapies that improve progression-free survival, such as alectinib and crizotinib, for this subset of lung cancer are also available.[99–101] Targeted therapies now exist for several additional molecular abnormalities, including *ROS1*, *RET*, and *NTRK*, among others.[102,103]

Expression of programmed death-1 ligand (PD-L1) is a means by which cancer cells can evade normal immune surveillance. This protein is a target for immunotherapy drugs, known as immune checkpoint inhibitors, which have had a major impact on the care of patients with lung cancer; in some patients with advanced lung cancer, their use has produced long-term survival.[85,104] PD-L1 positivity is linked to checkpoint inhibitor responses and multiple studies show higher expression in patients with NSCLC who are smokers than in those who are nonsmokers.[105–107] Checkpoint inhibitors are generally not effective for cancers driven by molecular abnormalities such as *EGFR* mutations typically found in never-smokers, irrespective of PD-L1 status.[108]

The Effects of Tobacco Smoke Exposure on Cancer Cells

Tobacco smoke can have both systemic and local effects on cancer cells in experimental models. As an example of its systemic effects, tobacco smoke suppresses the immune system, which allows cancer to develop and to expand without the normal immune system checks on cell growth.[12,21,109] There are many potential local effects of tobacco smoke that may promote the continued growth and transformation of cancer cells to more advanced stages and may cause cancers to be resistant to therapeutic strategies. These may include:

1. DNA damage
2. Changes in gene expression
3. Alteration of cell cycle control
4. Promotion of epithelial-mesenchymal transition associated with metastasis
5. Promotion of angiogenesis
6. Alterations of the tumor microenvironment
7. Promotion of dedifferentiation
8. Inhibition of response to chemotherapeutic agents

This section describes studies examining the effect of tobacco smoke on cancer cells; most of the studies were performed *in vitro* with cancer cells exposed to tobacco smoke extract or individual tobacco smoke chemical compounds and may not reflect *in vivo* occurrences.

DNA Damage

Continued exposure to tobacco smoke chemical compounds may result in additional damage to cancer cell DNA.[110,111] This damage provides the opportunity for further evolution of the cancer, because of additional aberrant cellular function, such as decreased DNA repair, increased genetic instability, increased rates of cell division, as well as cellular dedifferentiation.[12] Consistent with this hypothesis, the mutations per genome in some tobacco-related cancers increased with cumulative exposure to tobacco smoke.[17]

Changes in Gene Expression

Chronic exposure of lung cancer cell lines to cigarette smoke leads to significant changes in RNA and protein levels in directions that are consistent with those observed in lung cancers and are associated with dysregulation of normal cellular function.[112,113]

Alteration of Cell Cycle Control

Tobacco smoke promotes cell proliferation (increased rate of cell division) through interaction with cell-surface receptors and activation of a variety of signaling pathways.[11] Tumor cells that express these receptors are sensitive to the cell proliferation effects of tobacco smoke chemical compounds. For example, activation of nicotinic acetylcholine receptors by tobacco smoke chemical compounds, such as nicotine and nicotine-derived nitrosamine ketone, an important tobacco-specific n-nitrosamine, increases the rate of cell proliferation by increasing the rate of cell division and blocking cell death through activation of signaling pathways; the exact signaling pathway is dependent on the cancer type.[114–116]

Promotion of Epithelial-Mesenchymal Transition Associated With Metastasis

Epithelial-mesenchymal transition (EMT) is a complex molecular process in which epithelial cells lose cell–cell adhesion and develop motility characteristics of mesenchymal cells.[117] By increasing the invasiveness and metastatic potential of tumor cells, EMT contributes to cancer progression.[118] The ability of cigarette smoke to promote EMT and increase the invasive nature of cancer cells has been explored in a wide variety of cancer cell lines.[119–129] These effects were achieved through changes in expression of metastasis-associated proteins.[123,124,127,128] In oral cancer cell lines, cigarette smoke extract increased the levels of cathepsins, protease enzymes that facilitate metastasis.[126] Mechanistic studies in lung cancer cell lines indicated that cigarette smoke extract–induced invasive activity was triggered by the increased expression of a key prometastatic gene, *SNCG* (synuclein-γ).[130] Similarly, cigarette smoke–induced EMT, migration, and invasion resulted from a series of epigenetic changes leading to reduced levels of E-cadherin, an intercellular adhesion protein, in lung cancer cells.[131] This study also found that loss of E-cadherin is an unfavorable prognostic factor in patients with lung cancer and that downregulation of this protein is associated with number of pack years of smoking.[131]

Promotion of Angiogenesis

Cigarette smoke may also increase angiogenesis, which is the ability of cancer cells to induce the formation of new blood vessels. Interaction of tobacco smoke chemical compounds with nicotinic acetylcholine receptors is linked to the increased production of vascular endothelial growth factor, a major factor in the generation of new blood vessels within tumor cells.[132] Cigarette smoke extracts trigger this production in a variety of cancer cell lines including those derived from NSCLC, pancreatic cancer, and colon cancer.[114,133,134]

Alterations Within the Tumor Microenvironment

Tumor cells alter their microenvironment, the surrounding tissue in which they reside, to inhibit antitumor processes and promote functions crucial for tumor maintenance and growth. The tumor microenvironment consists of cells and components that surround and infiltrate the tumor, which include extracellular matrix, fibroblasts, blood vessels, diverse immune cells, and other cells.[135,136] A number of studies show that tobacco smoke may enhance tumor growth and metastasis through alteration of the tumor microenvironment. For example, cigarette smoke chemical compounds alter the fibroblasts that surround the tumor, causing premature aging and mitochondrial dysfunction in these cells.[137] As a consequence, the fibroblasts secrete energy-rich compounds (e.g., L-lactate, ketone bodies) into the tumor microenvironment, which promotes tumor growth. Exposure of fibroblast cell lines to cigarette smoke leads to increased tumor growth of cancer cell lines in coculture conditions.[137,138] Cigarette smoke exposure leads to metabolic coupling between the two cell types, increases cancer cells' resistance to cell death, and causes increased cancer cell migration.[138]

Promotion of Stem Cell–Like Properties

Cancer stem cells are a subpopulation of tumor cells that have adopted stem-like properties (low in abundance, high proliferative potential, and sufficient to reconstitute all the cell types of the tumor) and are implicated in tumor formation, growth, progression, and metastasis; they also play a role in resistance to therapy, relapse, and prognosis.[139–141]

Tobacco smoke extracts or condensates have been shown to cause the development of stem cell-like subpopulations in breast and lung cancer cell lines.[121,142] Additionally, a study found that administration of nicotine to mice altered normal homeostasis of pancreatic tissue, promoted pancreatic carcinogenesis, and induced pancreatic acinar cell dedifferentiation.[143] Cigarette smoke extract–exposed renal cancer cell lines develop characteristics of cancer stem cells that are mediated through activation of the Sonic Hedgehog (SHH) pathway and express increased levels of multiple cancer stem cell markers. The observation that renal tumor tissue from smokers had higher levels of cancer stem cell markers and SHH pathway–related proteins than tumor tissue from nonsmokers suggests that this mechanism may act in renal cancers in patients.[144]

Inhibition of Response to Chemotherapeutic Agents

In vitro studies demonstrate that continued exposure to tobacco smoke reduces the ability of chemotherapeutic agents to kill cancer cells through a variety of different mechanisms. One mechanism involves the upregulation of xenobiotic transporters, which is associated with an increased removal of chemotherapeutic agents out of the cancer cell.[145,146] Mechanistic studies suggest that the upregulation of the xenobiotic transporter ABCG2 occurs through an AhR-mediated process, and that this transporter is also important for cigarette smoke–mediated increase in malignancy.[147] Expression of this gene is correlated with chemoresistance, and the presence of cells with stem-like features in lung and esophageal cancers[148–152] and poor prognosis in these patients.[146,153,154]

Tobacco smoke may also promote chemoresistance through disruption of signal transduction pathways. In some cases, this disruption allows cancer cells to resist programmed cell death (apoptosis). For example, long-term exposure of lung cancer cell lines to cigarette smoke condensate alters apoptotic processes resulting in resistance to chemotherapy drugs, such as carboplatin.[155,156] In other cases, tobacco smoke increases the signaling pathway targeted by the therapeutic agent. For example, cigarette smoke extract reduced the sensitivity of *EGFR*-mutant cell lines to the inhibitory effects of gefitinib (an anti-EGFR tyrosine kinase inhibitor [TKI]) by increasing EGFR signaling and inducing EMT; smoking also negatively affected the progression-free survival of patients with lung cancer with mutated *EGFR* receiving EGFR-TKI treatment.[157] Nicotine may contribute to these observed effects.[158]

Summary

Tobacco smoke contains thousands of chemical compounds, including approximately 70 known carcinogens. These chemical compounds and/or their metabolic by-products may cause DNA damage, epigenetic changes, and other cellular alterations that lead to the development of cancer by altering normal cellular growth control mechanisms. Cancers in patients with and without a history of smoking can exhibit biological differences, particularly in tissues that come into direct contact with tobacco smoke. Some of these biological differences have important therapeutic consequences. For example, NSCLCs characterized by mutations of the *EGFR* gene and the *ALK* gene are highly responsive to tyrosine kinase inhibitor therapies. *In vitro* exposure of cancer cells to tobacco smoke causes them to display characteristics associated with cancer aggressiveness, metastasis, and resistance to therapy, which is consistent with clinical evidence of an association between continued smoking and reduced life expectancy and decreased response to therapies for most cancers.

Conclusions

1. Tobacco smoke contains more than 7,000 chemical compounds including approximately 70 that are carcinogenic. Continued exposure to tobacco smoke after a cancer diagnosis may promote the continued growth and transformation of tumor cells through a variety of mechanisms.
2. Tumors in smokers are often biologically distinct from tumors in nonsmokers. In the case of lung cancer, these differences have important implications for cancer treatment and prognosis.
3. Laboratory studies of cancer cells exposed to tobacco smoke or tobacco smoke constituents provide experimental evidence that continued smoking by patients with cancer increases tumor aggressiveness and reduces therapeutic response.

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NCI Monograph 23
Treating Smoking in Cancer Patients:
An Essential Component of Cancer Care

Chapter 3
Treating Tobacco Use and Dependence in Cancer Populations

Chapter Contents

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Chapter 3
Treating Tobacco Use and Dependence in Cancer Populations

Introduction

Smoking by patients with cancer is causally associated with all-cause and cancer-specific mortality.[1] Although some patients with cancer who smoke at the time of their diagnosis may quit after learning of their illness,[2,3] a substantial proportion of patients will continue to smoke after receiving a cancer diagnosis or relapse back to smoking shortly thereafter.[4] For these patients, access to evidence-based behavioral and pharmacological treatments to quit smoking is a critical priority.

Effective smoking cessation treatments exist but are too rarely implemented in oncologic care,[4–9] and tobacco use has not been consistently addressed by cancer centers.[13,14] However, the National Cancer Institute (NCI) Cancer Moonshot[SM] Cancer Center Cessation Initiative (C3I)[10] has propelled more cancer centers to address this treatment gap (see chapter 4), emphasizing the need to evaluate the effectiveness of smoking cessation treatments in cancer populations.

This chapter discusses current treatments to quit smoking and considerations that may affect successful smoking cessation. The discussion of smoking cessation treatments primarily focuses on cigarette smoking because it is the type of tobacco use that is most prevalent among adults,[15] and is the most frequent target of cessation research. First, the chapter addresses motivation to quit smoking, a key construct that determines a person's willingness to enter treatment for smoking. Second, the chapter reviews the current scientific evidence regarding the elements of effective smoking cessation treatment approaches. The relevant scientific literature reviewed includes studies of patients with cancer as well as those of the general population in order to broaden the evidence base for this evaluation. However, it is noted that smoking cessation research on people without cancer diagnoses may not generalize fully to patients with cancer. The smoking cessation treatment approaches evaluated include medications and behavioral interventions, with the latter including discussions of delivery via quitlines and internet/mobile devices. Third, the chapter discusses unique issues and challenges concerning the treatment of cigarette smoking among patients with cancer, including patient- (e.g., psychiatric comorbidity, treatment engagement); clinician- (e.g., training in and beliefs about treating tobacco use); and systems- (e.g., infrastructure, policy) level factors that can critically affect the success of smoking cessation treatments (systems-level factors are covered more extensively in chapter 4). Fourth, this chapter addresses special topics related to effective treatments for smoking including personalized treatment and chronic care models and the need to consider gender, race and ethnicity, and socioeconomic status in the provision of smoking cessation treatment (which is addressed more fully in chapter 5). Fifth, electronic nicotine delivery systems (ENDS) are discussed with regard to their prevalence, short- and long-term health effects, and potential relevance to smoking cessation treatment approaches, with an emphasis on patients with cancer.

This chapter, along with the rest of this monograph, evaluates and characterizes the current research literature on its targeted topics. It is not intended to provide specific treatment recommendations as would be contained in a clinical practice guideline, nor is it intended to provide fine-grained or "how to" information on intervention methods, which are available elsewhere.[16,17]

Motivation to Quit

Quitting motivation, measured using self-report questionnaires like readiness rulers or ladders[18] or by recorded quit attempts, is an important marker of eventual tobacco cessation. In the general population, engaging in steps toward smoking cessation by making a quit attempt and expressing motivation to quit increases the probability of smoking cessation.[19–22]

Data from the general population show that the great majority of individuals who smoke exhibit meaningful levels of quitting motivation and such motivation often predicts making quit attempts,[23,24] although success in those quit attempts appears to be more highly determined by factors such as nicotine dependence.[20,25,26] With regard to quitting motivation, national surveys[27,28] consistently show that more than two-thirds of individuals who smoke in the general population report interest in quitting smoking. Although quit rates can vary by socioeconomic status, a readiness or interest in quitting cuts across socioeconomic strata with one study showing past-year quit attempts of 66%, 68%, and 72% for those with no insurance, private insurance, or Medicaid, respectively.[29] Data from the 2017 Behavioral Risk Factor Surveillance System show a past-year quit attempt rate with a median of 65.4%.[30] Further, analyses of nationally representative data suggest that the prevalence of quit attempts has increased over the past 25 years among individuals who smoke in the general population.[31]

In the context of cancer care, patients may exhibit higher levels of readiness to quit smoking and attempts to quit than those in the general population as suggested by cancer patients' high quit rates.[2] Indeed, the cancer diagnosis itself is thought of as a teachable moment, meaning that motivation to quit and receptivity to smoking cessation treatment is unusually strong at this time.[32] Studies of patients with cancer who smoke indicate high levels of readiness to quit and quit attempts.[33] One study found that more than two-thirds of patients with smoking-related cancers report that they were ready to quit smoking in the next 30 days and a quarter of patients reported that they have made a quit attempt in the past year.[34] A study of patients with head and neck cancer reported that, among those who continued using tobacco after surgery, 92% were considering quitting and 84% made at least 1 quit attempt following surgery.[35] Gritz and colleagues found that almost 90% of a sample of patients with head and neck cancer enrolled in a smoking cessation trial (N = 186) had tried to quit smoking at least once since their diagnosis.[36] In a sample of 74 patients with head and neck or lung cancer participating in an observational study, 38% of those who were currently smoking reported having made a quit attempt in the previous 6 months.[37] Cooley and colleagues reported that more than 40% of a sample of 37 patients with lung cancer who smoked expressed an interest in smoking cessation intervention.[38] Little and colleagues examined quitting motivation in a retrospective cross-sectional survey.[39] Results showed that one-third of a sample of 110 cancer survivors reported being ready to quit in the next 30 days and another third reported being ready to quit in the next 6 months; 46% of the overall sample reported trying to quit when they were diagnosed. In a national study with more than 2,500 cancer survivors identified in the 2015 National Health Interview Survey (NHIS), 57% of individuals currently smoking reported wanting to quit smoking and 49% reported making a quit attempt in the past year.[8] Likewise, in a sample of close to 1,700 patients with cancer who reported smoking, more than 90% reported that they were ready to quit.[40] Finally, using 2017 NHIS data, Gritz and colleagues found that among the 681 cancer survivors who were smoking at the time of cancer diagnosis, 309 (43.96%) reported having successfully quit smoking and 372 (56%) reported continuing smoking.[41] Among continuing smokers, more than half (N = 176, 57%) reported an unsuccessful quit attempt in the last 12 months.

Elements of Effective Smoking Cessation Treatments

Cigarette smoking can produce nicotine dependence, a chronic, relapsing condition.[1] Dependence arises, in part, because cigarette companies intentionally designed cigarettes to maximally exploit the addictive properties of nicotine.[1,42] Despite the intransigence of nicotine dependence, multiple types of treatments can increase an individual's chances of quitting smoking successfully two- to threefold.[17] Dependence is a condition in which heavy or regular use of a drug or agent is associated with compulsive use, tolerance, and withdrawal symptoms when drug use is discontinued. Dependence is often associated with addiction, which occurs when heavy or compulsive drug use exacts significant costs in important life spheres such as health, social and vocational status, and functioning.[17] This section reviews evidence on the nature of nicotine dependence and reviews evidence on the effectiveness of treatments for smoking generally (i.e., within the general population of people who smoke cigarettes).

The prevailing therapeutic approach to treating cigarette smoking involves the use of medication to reduce the withdrawal associated with nicotine abstinence, along with psychosocial interventions to address the behavioral aspects of nicotine dependence and cessation.[17,31,43–46] The U.S. Food and Drug Administration (FDA) has approved seven medications for treating nicotine dependence, which include nicotine replacement therapies (NRTs), bupropion, and varenicline.[31] These were developed to alleviate the symptoms of nicotine withdrawal and craving, which peak soon after smoking has ceased and may persist or recur long after that time.[47,48] Withdrawal and associated craving are major causes of smoking relapse.[49,50] The psychological influences of nicotine dependence are addressed through counseling that teaches strategies that foster quitting and reduce the risk of relapse. This treatment model is rooted in scientists' understanding of the neurobiological, behavioral, and motivational processes associated with nicotine use. This chapter will focus on approaches to smoking cessation treatment that are supported by the research literature (e.g., Table 3.1)[17,46,51] and will also discuss the use of ENDS, with a focus on cancer patients and survivors.

Table 3.1 Findings Regarding Interventions for Smoking Cessation and Treatments for Nicotine Dependence From the 2020 Surgeon General's Report on Smoking Cessation

The evidence is sufficient to infer that:	• Behavioral counseling and cessation medication interventions increase smoking cessation compared with self-help materials or no treatment. • Behavioral counseling and cessation medications are independently effective in increasing smoking cessation, and even more effective when used in combination. • Proactive quitline counseling, when provided alone or in combination with cessation medications, increases smoking cessation. • Short text message services about cessation are independently effective in increasing smoking cessation, particularly if they are interactive or tailored to individual text responses. • Web- or internet-based interventions increase smoking cessation and can be more effective when they contain behavior-change techniques and interactive components.
The evidence is inadequate to infer that:	• Smartphone apps for smoking cessation are independently effective in increasing smoking cessation. • Electronic nicotine delivery systems (ENDS), in general, increase smoking cessation.
The evidence is suggestive but not sufficient to infer that:	• The use of ENDS containing nicotine is associated with increased smoking cessation compared with the use of ENDS not containing nicotine. • More frequent use of ENDS is associated with increased smoking cessation compared with less frequent use of ENDS.

Note: The Surgeon General's report refers to e-cigarettes, which are also known as ENDS.
Source: USDHHS 2020.[31]

Neurobiological and Behavioral-Motivational Dimensions of Cigarette Smoking: Relevance to Treatment

Neurobiological Dimensions of Cigarette Smoking

Nicotine induces increased dopamine activity in the ventral striatum (e.g., the shell of the nucleus accumbens)[52] and the prefrontal cortex.[53] Such increased dopaminergic activity is experienced as rewarding and pleasurable, which is thought to be a critical mechanism in nicotine dependence development.[54,55] Dopamine can also inflate the incentive value of nicotine cues, leading to a heightened positive anticipation or wanting to use an addictive agent such as nicotine.[56,57] Both nicotine reward and its incentive effects build with repeated use, greatly increasing the appeal of nicotine use in the chronic user. Numerous animal studies[58,59] and neuroimaging studies[60,61] have documented the important role of dopamine as a key mechanism of nicotine dependence. Within this conceptualization, nicotine's addictive properties are rooted in the positive-reinforcing and incentive effects that arise from chronic use and the consequent enhancement of dopamine levels. In turn, FDA-approved medications for nicotine dependence affect key nicotine receptors and augment endogenous levels of dopamine, as well as other neurotransmitters.[54] Thus, use of such medications with dopaminergic effects may allow individuals to experience positive anticipation of and reward from non-drug stimuli or events without the use of nicotine.

Chronic use of nicotine (from cigarettes or other tobacco products) produces physical dependence in addition to sensitization to its rewarding and incentive effects.[54,62] Physical dependence manifests as a characteristic withdrawal syndrome when nicotine levels in the body decrease after chronic exposure, a syndrome that is associated with activation of the extrahypothalamic corticotrophin-releasing factor system.[54] Withdrawal symptoms include hunger, anxiety, and irritability,[50,63] and people report strong cravings to resume nicotine use during withdrawal.[64–66] Anhedonia, an inability to experience pleasure from normally rewarding stimuli, also occurs following decreased nicotine use after chronic exposure.[67,68] This inability may arise from the loss of anticipatory excitement in response to incentive stimuli[56] or from actual decrements in reward processing that occur with disuse of nicotine.[59,68] Anhedonia, along with other withdrawal symptoms, is alleviated by agents that increase dopaminergic activity, including FDA-approved smoking cessation medications.[67,69–71]

Behavioral-Motivational Dimensions of Cigarette Smoking

In parallel with research on the neurobiological effects of nicotine, behavioral research shows that nicotine reward, incentive effects, and negative reinforcement play crucial roles in sustaining nicotine use. For instance, neuropharmacologic and neuroimaging studies of brain regions and neurocircuitry involved in nicotine use have documented that nicotine can enhance fine motor functions, attention, concentration, and working and episodic memory in the short term.[73,74] Such effects may account, in part, for the rewarding effects of nicotine, along with the direct experience of rush, enjoyment, or pleasure and the speed and consistency of nicotine's effects. Research also suggests that withdrawal from nicotine can decrease function in some cognitive domains.[74,75] Smoking is reinforced by the reversal of multiple types of withdrawal symptoms associated with stopping tobacco use, including concentration difficulties, negative affect, craving, anhedonia, and hunger.[67,76,77]

Behavioral research, including both human and animal studies, suggests that negative affective states or distress may increase the motivation to smoke and motivate relapse or a resumption in nicotine self-administration.[77–81] Indeed, there is evidence that just the expectation of smoking reduces anxiety.[82] Perceptions among those dependent on nicotine may account for the strong relationship between stressor exposure and smoking urges and self-administration.[81,83] As of this writing, whether nicotine reduces affective distress arising from external stressors is unresolved.[84,85] If nicotine produces any stress relief, it is short lived; evidence suggests that former smokers experience less stress, anxiety, and depression after quitting smoking than they did before quitting.[86,87]

Behavioral research also shows that exposure to smoking-related cues significantly heightens the motivation to smoke.[88–90] In fact, research indicates that point-of-sale tobacco displays, tobacco industry advertising, and promotions heighten urges to smoke and increase tobacco use.[91–95] Thus, cues such as seeing others smoking, consuming alcohol, or the perceived opportunity to smoke, can elicit powerful urges to smoke and lead to a resumption of nicotine use in rats[96,97] and people previously dependent on nicotine.[80,98] In addition, over time, the ritual of smoking or any nicotine administration ritual can become automatic and reflexively elicited by smoking-related cues.[99–101]

Summary: Neurobiological and Behavioral-Motivational Dimensions of Cigarette Smoking

Regular cigarette smoking can produce dependence, which is accompanied by changes in affect, cognition, and physiology. As a result, smoking is repeatedly reinforced, becoming automatic and refractory, especially in contexts in which it has frequently occurred. Additionally, discontinuing smoking acutely results in negative moods, craving for nicotine, a loss of pleasure, and adverse cognitive effects that may impede decision-making. These symptoms decline over time with long-term quitters reporting improved mood and reduced stress. Moreover, FDA-approved medications and behavioral interventions are effective at reducing the physical and psychological symptoms of nicotine withdrawal even early in the quitting period when symptoms would otherwise be at their highest.

Smoking Cessation Treatments in the General Population

Approach

This section reviews the state of the science with regard to pharmacological, counseling, and digital/internet treatments for cigarette smoking within the general population. This section relies heavily upon prior systematic reviews[17,31,102–109] and several highly relevant and informative individual studies. The intent here is to extrapolate from the existing literature to identify approaches that might be most effective with cancer patient populations. An intervention approach is deemed effective if supported by meta-analyses or consistent findings from randomized controlled trials (RCTs), and preferably both, in synthesizing the evidence. Information on sample size, significance levels, certainty of evidence, and magnitude of effects is strategically presented for key studies where it is especially important to assess the generalizability of findings, their magnitude, their statistical significance, and whether an effect was tested with sufficient statistical power. Certain interventions are also deemed promising if supported by a consistent body of nonexperimental evidence, such as observational studies. Observational studies have value because they yield evidence, though not definitive, on smoking cessation treatments in real-world conditions, including treatment delivery by clinical staff to a broad representative range of patients. Clear instructions for the use and dosing of pharmacotherapies are available in the Public Health Service (PHS) Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update,*[17] and the American College of Cardiology Expert Consensus Decision Pathway on Tobacco Cessation Treatment.[110]

Finally, it is important to note that the majority of RCTs that evaluated medications for smoking also provided counseling or behavioral support in the active-treatment and placebo or control arms. Medications for smoking cessation are typically less effective when used without any behavioral support.[111]

Medications for Smoking Cessation

The 2020 Surgeon General's report concluded that behavioral counseling and cessation medications are independently effective in increasing smoking cessation.[31] The PHS Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*, recommends the use of FDA-approved smoking cessation medications, which include nicotine gums, nicotine inhalers, nicotine lozenges, nicotine nasal sprays, nicotine patches, bupropion, and varenicline.[17] Medication adherence (using the medication for the prescribed or indicated amounts and duration) is positively associated with smoking cessation.[112]

This section will discuss the effectiveness of medications as they are used for smoking cessation in the general population (see Table 3.2). In addition, several specialized pharmacotherapy strategies will also be discussed. Two such strategies are designed to extend smoking abstinence.[105,113] These will be discussed because the majority of individuals who smoke, including patients with cancer,[114] will relapse back to smoking after making an aided or unaided quit attempt. One of these pharmacologic approaches is the extended use of medication (beyond the standard 8–12 weeks) among all who start it. The second pharmacologic approach is relapse prevention (i.e., providing a longer course of medication to those who have already become abstinent). Other strategies include providing medication to those who are not yet motivated to quit smoking and providing medication for an extended period prior to a person's target quit date (i.e., preloading).

Table 3.2 Effectiveness and Abstinence Rates for Various Medications and Medication Combinations Compared to Placebo at 6-Months Post-quit

Medication	Number of arms	Estimated odds ratio (95% CI)	Estimated abstinence rate (95% CI)
Placebo	80	1.0	13.8
Monotherapies			
Varenicline	5	3.1 (2.5–3.8)	33.2 (28.9–37.8)
Nicotine nasal spray	4	2.3 (1.7–3.0)	26.7 (21.5–32.7)
High-dose nicotine patch (> 25 mg) (these included both standard or long-term duration)	4	2.3 (1.7–3.0)	26.5 (21.3–32.5)
Long-term nicotine gum (>14 weeks)	6	2.2 (1.5–3.2)	26.1 (19.7–33.6)
Varenicline (1 mg/day)	3	2.1 (1.5–3.0)	25.4 (19.6–32.2)
Nicotine inhaler	6	2.1 (1.5–2.9)	24.8 (19.1–31.6)
Clonidine	3	2.1 (1.2–3.7)	25.0 (15.7–37.3)
Bupropion SR	26	2.0 (1.8–2.2)	24.2 (22.2–26.4)
Nicotine patch (6–14 weeks)	32	1.9 (1.7–2.2)	23.4 (21.3–25.8)
Long-term nicotine patch (> 14 weeks)	10	1.9 (1.7–2.3)	23.7 (21.0–26.6)
Nortriptyline	5	1.8 (1.3–2.6)	22.5 (16.8–29.4)
Nicotine gum (6–14 weeks)	15	1.5 (1.2–1.7)	19.0 (16.5–21.9)

Table 3.2 (continued)

Medication	Number of arms	Estimated odds ratio (95% CI)	Estimated abstinence rate (95% CI)
Combination Therapies			
Patch (long-term; >14 weeks) + ad lib NRT (gum or spray)	3	3.6 (2.5–5.2)	36.5 (28.6–45.3)
Patch + bupropion SR	3	2.5 (1.9–3.4)	28.9 (23.5–35.1)
Patch + nortriptyline	2	2.3 (1.3–4.2)	27.3 (17.2–40.4)
Patch + inhaler	2	2.2 (1.3– 3.6)	25.8 (17.4–36.5)
Patch + second generation antidepressants (paroxetine, venlafaxine)	3	2.0 (1.2–3.4)	24.3 (16.1–35.0)
Medications not shown to be effective			
Selective serotonin re-uptake inhibitors	3	1.0 (0.7–1.4)	13.7 (10.2–18.0)
Naltrexone	2	0.5 (0.2–1.2)	7.3 (3.1–16.2)

Note: *N* = 86 studies. Visit https://www.ahrq.gov/prevention/guidelines/tobacco/clinicians/references/meta/meta03.html#t626 for the studies used in this meta-analysis. NRT = nicotine replacement therapy.
Source: Adapted from Fiore et al. 2008: Table 6.26.[17]

Nicotine Replacement Therapies (NRTs). NRT agents occupy nicotine receptors, as does nicotine contained in cigarette smoke, but their pharmacodynamics cause them to reduce withdrawal symptoms and craving (e.g., hunger, negative affect) without the highly rewarding effects that would sustain dependence or relapse. The FDA has approved five forms of NRT for smoking cessation: patch, gum, lozenge (and mini lozenge), nasal spray, and inhaler; the first three are available over the counter or by prescription, while the last two are available only by prescription. The safety of NRTs has been well-established in numerous studies consisting of people who smoke differing in age, gender, race and ethnicity, psychiatric status, and other important factors.[17] Moreover, there are few contraindications for the use of NRTs, with some of the more common ones being an allergy to the nicotine patch adhesive, temporomandibular joint disease for the nicotine gum, and gastric or duodenal ulcer for the nicotine nasal spray.[115] Other contraindications can be found in the package inserts for each product. Systematic reviews show that NRTs can increase quit rates compared with placebo,[17] yielding long-term (i.e., 6–12 months) quit rates of about 20%–25% (Table 3.2). Further, systematic reviews have shown that individual types of NRTs are similarly effective to one another but that combination NRT (e.g., combining a long-acting NRT like the nicotine patch with a short-acting NRT like nicotine gum) yields significantly higher rates of long-term abstinence than does a single type of NRT (i.e., NRT monotherapy)[17,116] (Table 3.2). Because research shows that the different NRT medications produce very similar effects of smoking abstinence, this chapter rarely distinguishes among the different NRT types in evaluating the evidence.

Evidence also suggests that NRT effectiveness can be increased by specialized use strategies.[31] These include adjusting the NRT dose based on the individual's level of nicotine dependence (e.g., time to first cigarette of the day) and initiating NRT prior to a designated quit attempt (i.e., preloading),[116–118] an effect that may be greatest with the nicotine patch.[31,116]

NRT can increase smoking cessation rates even among those not motivated to make quit attempts (see section "Patient-Level Barriers to Treating Tobacco Use in Cancer Care Settings"). A systematic review and meta-analysis indicate that long-term use of NRT (6–18 months) and behavioral support can double the likelihood of smoking cessation compared with placebo even in individuals who initially report no intention to quit smoking.[119,120] In addition, there is evidence that medication sampling with NRT products, or the provision of 2–4 weeks of NRT with minimal accompanying instructions, prior to the quit attempt, can increase the likelihood of long-term abstinence; this finding applies to people who smoke and who are willing or unwilling to make a quit attempt.[121]

Extended Use. The evidence regarding the effects of extending NRT beyond its standard period of use (typically 8–12 weeks) is mixed.[31] Thus, no firm conclusions regarding the efficacy of extended medication use can be drawn as of this writing.

Relapse Prevention. A Cochrane Review meta-analysis showed that providing nicotine gum significantly reduced relapse likelihood in individuals who were abstinent at study start and who had previously quit smoking without using formal smoking cessation treatment (2 studies, N = 2,261, risk ratio [RR] = 1.24, 95% confidence interval [CI] = 1.04–1.47). However, additional NRT did not significantly increase long-term abstinence among those who initially became abstinent in response to formal smoking cessation treatment (2 studies, N = 553, RR = 1.04, 95% CI = 0.77–1.40, low certainty evidence).[105] Thus, it is difficult to draw conclusions about the ability of NRT to prevent relapse given the small number of relevant studies and the modest effect sizes obtained.[105]

Bupropion. Bupropion was originally introduced as an antidepressant and was later found to increase the likelihood of smoking cessation. Bupropion increases dopamine and norepinephrine activity in the brain; the former is likely responsible, in part, for its ability to reduce nicotine withdrawal. Bupropion is also a nicotinic receptor antagonist, which may reduce smoking reward.[54] Meta-analyses of clinical trials of bupropion show that its impact on long-term abstinence is similar to NRTs (e.g., yielding abstinence in about 25% of users, an increase in abstinence of about 50% to nearly 80% relative to placebo)[17,104,122,123] (Table 3.2).

Preloading. Only a single small study (N = 95) has been done to determine whether extended preloading with bupropion prior to the targeted quit date (4 weeks of prequit use) increases abstinence rates when compared with a normal course of bupropion treatment (1 week of prequit use).[124] Further study is needed regarding the effectiveness of extended preloading with bupropion.

Extended Use. The limited available data indicate that extending the duration of use of bupropion does not reliably increase its efficacy.[125]

Relapse Prevention. A Cochrane Review meta-analysis of six studies evaluating relapse prevention with bupropion showed no significant effect. Livingstone-Banks and colleagues noted that there was considerable variation in key study characteristics (e.g., the nature of the smoking cessation treatment, the length of the extended bupropion treatment), which may have increased error in effect estimates.[105]

Safety. Due to early reports of serious changes in mood and behavior related to bupropion use, the FDA required a boxed warning for bupropion and required a large clinical trial to be conducted to address bupropion safety. The double-blinded, triple-dummy, randomized trial involving 8,144 people who smoked found no significant increase in neuropsychiatric adverse events attributable to bupropion relative to nicotine patch or placebo. Therefore, the evidence suggested that bupropion was safe and effective and the product labeling was revised accordingly.[31,126]

Varenicline. The FDA approved varenicline for treating smoking cessation in 2006, and it is now approved for up to 6 months of treatment.[31,127] Varenicline, a nicotine acetylcholine $\alpha 4\beta 2$ receptor partial agonist, is one of the most efficacious medications for nicotine dependence, with most evidence suggesting that it yields long-term quit rates of about 19%–30%.[17,128,129] The drug's presumed mechanisms of action involve preventing nicotine from binding with nicotinic acetylcholine receptors and stimulating dopamine release. These actions reduce smoking reward and abstinence-induced withdrawal symptoms.[130] There may also be a secondary agonist effect on $\alpha 7$ nicotinic receptors, which alter the reinforcing capacity of salient stimuli.[131] Varenicline also mitigates adverse psychological effects, including depressive symptoms and the temporary cognitive impairment associated with quitting smoking.[130,132–135]

Several systematic reviews and meta-analyses indicate that varenicline can more than double the likelihood of smoking cessation compared with placebo and is more effective than single NRT or bupropion[17,128] (Table 3.3). Evidence of the relatively greater effectiveness of varenicline led the American Thoracic Society to recommend varenicline over nicotine patch and bupropion monotherapy as a first-line smoking cessation treatment in their clinical practice guideline.[136] Two factors that moderate varenicline's effectiveness are an individual's rate of nicotine metabolism and whether an individual is adherent to the medication. Individuals who metabolize nicotine relatively rapidly tend to achieve higher smoking abstinence rates than those who metabolize nicotine more slowly, a relation that has led to a medication treatment algorithm.[137] As has been found with other smoking cessation medications, individuals who are adherent to varenicline tend to achieve significantly higher long-term abstinence rates than are those who are only partially adherent or nonadherent.[138]

Preloading. One small study ($N = 60$) suggests that preloading with varenicline, extending its pre-cessation use for 4 weeks before the quit date,[139] may increase its effectiveness. Similarly, a study with a large sample ($N = 1,510$) showed that prolonged varenicline use prior to the quit date (i.e., 12 weeks) increases abstinence rates among people who smoke and who are not willing to make an immediate quit attempt.[140]

Extended Use. There are limited data about whether extended treatment with varenicline after the quit day enhances outcomes. The normal course of varenicline treatment is 12 weeks (1 week pre-quit and 11-weeks post-quit). One study with a large sample (*N* = 1,251) showed no benefit of 24 weeks of varenicline versus the standard 12-week duration.[141]

Relapse Prevention. A meta-analysis suggests that varenicline is an effective relapse prevention intervention for individuals who have recently become abstinent in response to a prior smoking cessation treatment. This meta-analysis included 2 studies (*N* = 1,297) and yielded a small but significant effect of varenicline on abstinence at 12-month follow-up (RR = 1.23, 95% CI = 1.08–1.41).[105]

Safety. Substantial evidence supports the safety of varenicline. At one time, the FDA required boxed warning labels for varenicline due to concern over neuropsychiatric side effects. However, considerable evidence shows that varenicline produces no greater rates of such side effects than does placebo.[31,126] Concerns were also raised that varenicline might increase the occurrence of major cardiovascular events.[142] However, multiple studies subsequently have shown no meaningful increase in such events related to varenicline use.[31,110]

In June 2021, Pfizer Pharmaceuticals voluntarily recalled varenicline tablets because some batches were found to contain a nitrosamine impurity (N-nitroso-varenicline) at levels above FDA's acceptable intake limit. N-nitroso-varenicline may increase cancer risk if exposure exceeds the acceptable limit (37 ng/day) over a long period of time.[143] However, as of September 2021, varenicline that met FDA criteria for safety became available from other manufacturers.

Medication Combination. Given the efficacy of individual FDA-approved medications for smoking cessation, researchers have examined the potential for increased efficacy by combining these medications. A review of four studies reported that the combination of bupropion and varenicline yields significant benefits compared with varenicline alone,[144] although this has not been a consistent finding.[145] Studies have also examined the combination of NRT (nicotine patch) and varenicline versus varenicline alone. Although two small studies reported no significant benefit from combination therapy,[146,147] one study reported that adding NRT to varenicline significantly increased long-term abstinence rates versus varenicline alone.[148] A 2020 meta-analysis by a committee of the American Thoracic Society conditionally recommended the use of varenicline and nicotine patch over varenicline alone based on the available data.[136] However, a subsequent large sample study (*N* = 1,251) showed that there was no difference in long-term abstinence rates produced by the combination of varenicline and the nicotine patch versus varenicline alone.[141] Therefore, it is unclear that the combination of varenicline and the nicotine patch enhances long-term smoking abstinence in comparison with varenicline only.

Meta-analytic evidence shows that adding NRT to bupropion does not significantly improve long-term abstinence rates relative to either medication alone.[104] Several studies have shown that combination NRT is more effective than a single form of NRT or bupropion alone and is similar to varenicline monotherapy.[17,104,149,150]

Summary: Medications for Smoking Cessation. All seven FDA-approved medications improve long-term smoking abstinence rates relative to placebo. Moreover, varenicline and combination NRT are the two most effective pharmacotherapies available. Either therapy is more effective than placebo and NRT monotherapy. Varenicline and combination NRT are similarly considered first-line treatments in cancer populations.

Table 3.3 Odds of Smoking Cessation Using Medications

Comparison	Odds ratio (95% credible interval)	Number of studies with a direct comparison[a]
Treatments vs. placebo		
Patch vs. placebo	1.91 (1.71–2.14)	43
Gum vs. placebo	1.68 (1.51–1.88)	56
Other NRT vs. placebo	2.04 (1.75–2.38)	16
Combination NRT vs. placebo	2.73 (2.07–3.65)	2
Bupropion vs. placebo	1.85 (1.63–2.10)	36
Varenicline vs. placebo	2.89 (2.40–3.48)	15
Treatments vs. patch		
Gum vs. patch	0.88 (0.75–1.03)	0
Other NRT vs. patch	1.07 (0.91–1.26)	6
Combination NRT vs. patch	1.43 (1.08–1.91)	3
Bupropion vs. patch	0.97 (0.83–1.13)	6
Varenicline vs. patch	1.51 (1.22–1.87)	0
Treatments vs. gum		
Other NRT vs. gum	1.21 (1.01–1.46)	0
Combination NRT vs. gum	1.63 (1.21–2.20)	1
Bupropion vs. gum	1.10 (0.93–1.30)	0
Varenicline vs. gum	1.72 (1.38–2.13)	0
Other inter-treatment comparisons		
Combination NRT vs. other NRT	1.34 (1.00–1.80)	1
Bupropion vs. other NRT	0.91 (0.75–1.09)	2
Varenicline vs. other NRT	1.42 (1.12–1.79)	0
Varenicline vs. bupropion	1.56 (1.26–1.93)	3

Note: Smoking cessation duration varied by study. NRT = nicotine replacement therapy.
[a]When direct comparisons were not available for two medications, effect sizes were estimated based on their effects relative to comparison medications they had in common. Medications were typically tested with the same level and type of behavioral intervention in all treatment arms that were compared.
Source: Adapted from Cahill et al. 2013.[104]

Behavioral Interventions for Smoking Cessation

In addition to medications, which address the physiological components of nicotine dependence, behavioral interventions provide people who smoke with strategies to overcome the effects of nicotine withdrawal and other threats to their smoking abstinence (e.g., smoking cues). Counseling is the predominant behavioral or psychosocial intervention, and different types of counseling and their effectiveness are reviewed in this section. In addition, telephone and video-based interventions receive additional, focused review because the mode or conduit of behavioral intervention delivery could influence its effectiveness. These intervention delivery routes may hold advantages over in-person delivery modes in terms of efficiency, cost, and patient burden (e.g., travel); therefore, data on their effectiveness may be of great interest to health care systems. Additionally, contingency management (CM) and digital approaches are reviewed. Table 3.4 provides information derived from systematic reviews on the effectiveness of different types of behavioral interventions. The discussion of treatment approaches provided below briefly describes therapy types and their research support based upon smoking cessation studies among the general population (i.e., not restricted to individuals with cancer).

Table 3.4 Odds of Smoking Cessation Using Behavioral Interventions

Comparison	Odds ratio, risk ratio, or *g* (95% CI)	Number of studies included in the respective review
Counseling treatments		
Cognitive behavioral therapy vs. control (Fiore et al. 2008)[17]	1.5 (1.3–1.8)[a]	64
Mindfulness vs. control (Maglione et al. 2017)[165]	2.52 (0.76–8.29)	6
Acceptance and commitment therapy vs. control (Lee et al. 2015)[171]	0.42 (0.19–0.64)[b]	5
Behavioral activation	N/A	N/A
Motivational interviewing vs. control (Lindson et al. 2019)[189]	0.84 (0.63–1.12)	4
Contingency management vs. control (Notley et al. 2019)[200]	1.49 (1.28–1.73)[a]	30
Digital treatments		
Website interventions vs. control (McCrabb et al. 2019)[249]	1.19 (1.06–1.35)[a,c]	31
Text message intervention vs. control (Whittaker et al. 2019)[107]	1.54 (1.19–2.0)[a]	13

Note: N/A = not applicable. Smoking cessation measure varied by study.

[a]Indicates benefit for active treatment vs. control. [b]*g* statistic indicating benefit of acceptance and commitment therapy vs. control. [c]*N* and effect estimate for the study by McCrabb and colleagues are for all long-term (6-month) outcomes (prolonged abstinence, 7-day point-prevalence abstinence, and 30-day point-prevalence abstinence). Variation was found by outcome measure, with significant effects for prolonged abstinence, but no significant effects for 7- and 30-day point-prevalence abstinence determined at 6-month follow-up.
Sources: Adapted from systematic reviews and meta-analyses from Fiore et al. 2008,[17] Maglione et al. 2017,[165] Lee et al. 2015,[171] Lindson et al. 2019,[189] Notley et al. 2019,[200] McCrabb et al. 2019,[249] and Whittaker et al. 2019.[107]

Cognitive Behavioral Therapy (CBT). CBT is the most thoroughly researched and commonly used behavioral approach to treating nicotine dependence. CBT is sometimes referred to as problem solving, skills training, or behavior therapy,[17] and because of their overlap,[113] this chapter includes all of these interventions as CBT. Such therapies focus on clinician–patient collaboration to improve coping skills; boost self-efficacy; modify cognitions that serve as barriers to smoking cessation; provide support; and develop, modify, and improve cognitive and behavioral skills (i.e., learning how to avoid smoking triggers, contexts, and reframing thoughts about smoking).[151] Key elements include establishing a quit date, identifying potential risks for relapse, developing skills to manage smoking urges, and learning how to elicit and rely on social support during the quit attempt. In addition, CBT is often delivered with other counseling components such as intra-treatment social support and suggestions on the use of smoking cessation medications.[17] These adjuvant counseling elements would typically be added to any of the other counseling approaches reviewed below (see Table 3.5 for examples of representative content delivered in a CBT counseling intervention).[17] There is little evidence regarding which of these elements are especially determinant of cessation success,[109,113,152] and it may be that a good portion of their effectiveness is due to general features of therapy (e.g., support). However, CBT treatments have produced meaningful and reliable benefits across many different populations of people who smoke.[17] CBT can be delivered effectively by telephone (e.g., via a quitline) and in-person, via video or telehealth,[153] and individually or in a group.[17]

Table 3.5 Elements of Brief Tobacco-Cessation Counseling Based on the PHS Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*

Action	Strategies for implementation
Help the patient with a quit plan.	*A patient's preparations for quitting*: • ***S****et* a quit date. Ideally, the quit date should be within 2 weeks. • ***T****ell* family, friends, and co-workers about quitting, and request understanding and support. • ***A****nticipate* challenges to the upcoming quit attempt, particularly during the critical first few weeks. These include nicotine withdrawal symptoms. • ***R****emove* tobacco products from your environment. Prior to quitting, avoid smoking in places where you spend a lot of time (e.g., work, home, car). Make your home smokefree.
Recommend the use of approved medication, except when contraindicated or with specific populations for which there is insufficient evidence of effectiveness.	Recommend the use of medications found to be effective. Explain how these medications increase quitting success and reduce withdrawal symptoms. The first-line medications include: bupropion sustained release (SR), nicotine gum, nicotine inhaler, nicotine lozenge, nicotine nasal spray, nicotine patch, and varenicline.
Provide practical counseling (problem-solving/skills training).	Abstinence. Emphasize that the ultimate goal is abstinence. Past-quit experience. Identify what helped and what hurt in previous quit attempts. Build on past success. Anticipate triggers or challenges in the upcoming attempt. Discuss challenges/triggers and how the patient will successfully overcome them (e.g., avoid triggers, alter routines). Alcohol. Because alcohol is associated with relapse, the patient should consider limiting/abstaining from alcohol while quitting. Other people who smoke in the household. Quitting is more difficult when there is another person who smokes in the household. Patients should encourage housemates to quit with them or not to smoke in their presence.

Table 3.5 (continued)

Action	Strategies for implementation
Provide intra-treatment social support.	Provide a supportive clinical environment while encouraging the patient in his or her quit attempt. "My office staff and I are available to assist you." "I'm recommending treatment that can provide ongoing support."
Provide supplementary materials, including information on quitlines.	*Sources*. Federal agencies, nonprofit agencies, national quitline network (1-800-QUIT-NOW, Text QUITNOW to 333888, or local/state/tribal health departments/quitlines).

Source: Adapted from Fiore et al. 2008.[17]

Meta-analytic studies of CBT skills-based behavioral smoking cessation treatments indicate that this counseling model can increase smoking cessation rates by about 50% compared with no-intervention controls.[17] RCTs have demonstrated the efficacy of CBT-based smoking cessation treatments in hospitalized patients who smoke[154] and African-American people who smoke.[155] There is evidence that even relatively brief exposures to CBT can significantly increase long-term abstinence rates. The PHS Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update,* presented meta-analyses that related counseling intensity to its effectiveness. These meta-analyses suggest that CBT counseling lasting between 4–30 minutes of total contact time may increase long-term abstinence rates from about 11% to almost 19% in the general population.[17] It is unclear if increasing total contact time of cessation counseling beyond 30–90 minutes increases long-term abstinence.[17,45] However, there is evidence that more contacts or sessions are associated with increased long-term abstinence with the greatest increase in abstinence observed with up to four contacts or more.[17] Some evidence suggests that neither extending CBT beyond the amounts noted above nor use of CBT for relapse prevention significantly boosts long-term abstinence[31,45,105,108]; although a very small number of studies have reported a benefit of highly intense, extended CBT.[156]

Mindfulness-Based Therapy. In the 1990s, mindfulness-based stress reduction (MBSR)[157] gained prominence as a treatment for a range of conditions, including stress. Rooted in a Buddhist tradition, MBSR is a structured, multisession counseling model that is intended to train individuals to learn to focus on the present and assume an open acceptance of thoughts and emotions. Mindfulness-based counseling (mindfulness meditation) for nicotine dependence focuses on increasing self-awareness, decreasing smoking urges, and reducing the risk of relapse.[158,159] To date, four RCTs have evaluated mindfulness-based counseling for smoking cessation, using appropriate control arms, long-term follow-up of smoking, and biochemical verification of abstinence. A meta-analysis of 4 RCTs[160–163] indicated significant benefits on long-term abstinence, with a near doubling of the quit rates (i.e., 25.2% vs. 13.6%).[164] A second meta-analysis (N = 10) concluded that mindfulness-based smoking cessation treatments were not more effective than comparator treatments or no treatment.[165] As of this writing, the efficacy of mindfulness-based smoking cessation treatment, particularly relative to CBT, remains uncertain. Further, the level of counselor training required for this approach and its lack of appeal to some individuals who smoke may limit its translation potential.

Acceptance and Commitment Therapy (ACT). Another novel counseling smoking cessation treatment developed and tested over the past decade is ACT, an approach with established efficacy for treating depression and substance use.[166,167] The central focus of ACT is to help the individual manage "experiential avoidance," which underlies ineffective attempts to exert control over unwanted behaviors like smoking and to help them commit to basing their behaviors upon intrinsically valued goals. ACT focuses on identifying and accepting aversive thoughts and feelings, such as cravings or withdrawal during a quit attempt, to mitigate the threat and negative affective and cognitive reactions to such symptoms.[168] In an early clinical trial that compared ACT to CBT in 7 weekly small group (N = 81) sessions, ACT yielded more than a twofold greater quit rate than CBT.[169] Other small sample studies and a 2015 meta-analysis provide some evidence that ACT may be effective as a tobacco use intervention.[170,171] However, most relevant studies are limited by small sample sizes and self-reported cessation without biochemical confirmation. A large RCT found nonsignificantly lower long-term abstinence rates in an ACT condition than in a CBT condition when both were delivered via group counseling.[172] In sum, the available evidence is consistent with the 2020 Surgeon General's report, which notes that ACT may be promising but that more research is needed to determine the effectiveness for this counseling approach.[31]

Behavioral Activation Therapy (BA). Negative affect, including depressed mood and anhedonia, and a lack of positive affect are widely recognized, critical barriers to the successful treatment of nicotine dependence.[173–176] Developed as a treatment for depression,[177–179] BA focuses on increasing engagement in rewarding activities by reducing patterns of avoidance, withdrawal, and inactivity.[178,180] BA is effective in treating depression[181,182] and may be well-suited for those who smoke as a primary means of reducing or avoiding negative affect.[183] However, studies of this approach have tended to have relatively small sample sizes, have lacked biochemical confirmation of follow-up self-report, and have yielded mixed findings.[184–186] Thus, the supportive evidence for CBT is much stronger than it is for BA. More research is needed to determine the effectiveness of BA as a treatment for smoking.

Motivational Interviewing (MI). MI is a client-centered, directive counseling technique that aims to encourage readiness for behavior change by helping clients explore and resolve ambivalence about such change.[187,188] Its core techniques include expressing empathy, active listening, reflecting on the patient's thoughts and emotions, and supporting self-efficacy. A Cochrane Review meta-analysis of 4 studies using the longest follow-up outcome provided by the studies showed no benefit of MI versus no treatment (RR = 0.84, 95% CI = 0.63–1.12, adjusted N = 684, 4 studies).[189] There was also no evidence that MI added significantly to the effectiveness of other forms of behavioral intervention for tobacco use (RR = 1.07, 95% CI = 0.85–1.36, adjusted N = 4,167, 12 studies) or that it was relatively more effective than other behavioral interventions (RR = 1.24, 95% CI = 0.91–1.69, N = 5,192, 19 studies). The studies involved a wide range of populations, clinicians (including counselors), and settings. Thus, there is little evidence that MI significantly increases the likelihood of long-term smoking abstinence relative to no treatment, brief treatment, or self-help material. It is also unclear that MI reliably increases motivation to quit.[190]

Contingency Management (CM). The effectiveness of financial rewards for smoking cessation (cash payments or vouchers) has been demonstrated among adolescents,[191] pregnant women,[192–194] hospitalized patients,[195] Medicaid recipients,[196] employees,[197,198] and in the general population.[199] In a 2019 meta-analysis that included 33 studies (of which 2 involved patients with cancers of the head and neck), CM smoking interventions yielded a 40%–50% increase in the likelihood of smoking cessation versus control conditions, a difference that was maintained at follow-up once the incentives were discontinued[200]; however, some studies used multiple additional treatment components (e.g., brief advice, MI, and/or self-help material) which may have added to the CM effects.

In addition, multiple studies have explored the use of financial incentives to increase engagement with smoking cessation treatment rather than smoking abstinence itself.[31] These trials demonstrated that financial incentives for engagement in smoking cessation treatment by low-income populations not only increase treatment engagement but also increase smoking cessation success.[201–205] As such, the evolving literature on CM-based interventions shows their effectiveness, although rigorous comparisons with other behavioral approaches are lacking.

The 2020 Surgeon General’s report noted that the effects of CM interventions may largely dissipate once the contingency is no longer in force.[31] However, a meta-analytic review of behavioral approaches to treating tobacco use found that the use of financial incentives increased long-term abstinence rates with a high degree of certainty.[109] Also, the effects of CM may be sustained by incentivizing treatment engagement as opposed to smoking cessation, and the former has increased long-term abstinence.[202,203] Digital or technologic strategies may enhance the feasibility or reach of CM approaches by monitoring smoking and providing incentives as individuals go about their daily lives.[206,207]

The 2020 Surgeon General’s report acknowledges that it may be difficult to institute financial incentives outside the research setting and notes the need for more research on the long-term effects of CM interventions and how they might be best implemented in real-world settings.[31] However, the report also notes that the use of financial incentives to promote quitting during pregnancy may be appealing to insurers and policymakers, given the high costs of adverse birth outcomes and the short-term cost savings of providing pregnant women with help to quit. The use of financial incentives to assist patients with cancer to quit may also appeal to insurers and policymakers, given the likely financial benefits to doing so.

Relapse Prevention and Chronic Care. Although smoking cessation counseling is clearly effective in increasing initial success, the majority of individuals who make a quit attempt ultimately relapse.[208] In fact, about two-thirds or more of individuals who try to quit smoking with and without counseling relapse in the first month after their quit attempt.[209–211] For this reason, many smoking cessation treatment programs arrange for counseling sessions to start early in the quit attempt. The high rate of relapse has led to the development and evaluation of relapse-prevention treatments (i.e., treatments added to smoking cessation treatments intended to reduce the likelihood of future relapse). Such treatments typically teach people to recognize situations that confer a high risk for relapse and train them on strategies to cope with such challenges.[105] The weight of evidence from RCTs suggests that counseling interventions, either in the form of extended treatment or relapse-prevention interventions, do not consistently and meaningfully increase long-term abstinence rates among those already abstinent. For instance, a Cochrane Review meta-analysis addressed the effectiveness of behavioral relapse prevention interventions, focusing on studies that had randomized relapse prevention interventions among individuals who had previously established abstinence.[105] The authors conducted several meta-analyses that focused on different populations, such as pregnant women, hospital inpatients, and the general population. The number of studies reviewed ranged from 4 to 15 depending on the population involved. None of the meta-analyses found significant relapse prevention effects of behavioral interventions. The types of interventions used in these studies included support groups, group skill-training sessions, tailored counseling calls, and social media interventions, as well as low-intensity interventions, such as booklets. Although the authors note that different formats of relapse prevention were used in the studies analyzed, the major therapy content in most of the studies involved CBT emphasizing training skills for coping with relapse precipitants (e.g., smoking cues, stressors).[105] Therefore, most available evidence as of this writing does not support the effectiveness of psychosocial interventions for relapse prevention across different populations of people who smoke.[109]

Because smoking is a chronically relapsing condition,[31] chronic care approaches, such as those commonly used to treat asthma, high blood pressure, high cholesterol, and diabetes, have been used to address smoking relapse. Chronic care strategies involve periodically reaching out to people who smoke (via calls, letters, or electronic health record [EHR] messages sent out approximately every 6 months) to offer them re-treatment if they have relapsed. This strategy has been shown to increase both treatment re-entry and smoking cessation rates, albeit to a modest extent.[212–219]

Combinations of Medications With Behavioral Interventions for Smoking Cessation. Combining medication and counseling is more effective than the use of either alone.[17,31,149] A 2019 meta-analysis of 83 studies found that adding counseling to the provision of medication increased the likelihood of smoking cessation by about 10%–20% versus medication alone and that this effect was consistent across the FDA-approved medications.[220] This increased effect was present when counseling was conducted either in-person or via telephone, and the incremental effect increased modestly as a function of counseling intensity. A meta-analysis of 49 trials compared the provision of individual counseling alone with the combination of individual counseling and an FDA-approved medication; the combination treatment produced significantly higher long-term abstinence rates, typically 6 months or longer.[108] The combination of counseling with an FDA-approved medication has also been shown to be more effective than usual care and brief smoking cessation advice.[45,149] Lastly, some evidence suggests that the combination of varenicline with counseling is more effective than are other medications when used with counseling,[221] although not all reviews have reported this.[220]

Summary: Behavioral Interventions for Smoking Cessation. Counseling interventions play a key role in promoting smoking cessation. Of the counseling approaches examined, CBT has the most robust support as its effectiveness has been demonstrated in numerous, different populations of people who smoke. Evidence also shows that abstinence rates increase up to a point, as the dose of CBT counseling (e.g., number or duration of sessions) increases; intensities of at least 30 minutes of total contact time for a quit attempt and multiple treatment contacts are needed to optimize benefit. Counseling approaches such as ACT and BA require more experimental evaluation before their effectiveness can be adequately gauged, especially their effects relative to comparably intensive CBT. Similarly, further evaluation is needed to understand whether engagement approaches such as MI will be effective to include in smoking cessation interventions. Substantial evidence indicates that combining counseling with pharmacotherapy produces higher long-term abstinence rates than is produced by either type of intervention when used by itself. CM or incentive treatments appear to be effective in producing high initial smoking cessation rates; one promising use of this approach is to incentivize engagement in smoking cessation treatment. In sum, data from the general population suggest that among the various types of counseling approaches, CBT, especially when paired with smoking cessation medication, produces the most reliable and robust benefits and can be effective when delivered via a variety of routes, including in-person, via videoconferencing, or by phone.

Beyond In-Person Counseling: Telephone, Telehealth, and Digital Approaches for Smoking Cessation

Telephone Counseling. In 2002, a subcommittee of the U.S. Department of Health and Human Services Interagency Committee on Smoking and Health recommended the establishment of a national network of tobacco cessation quitlines—a single nationwide 1-800 portal providing uniform access to state quitlines.[222] The National Network of Tobacco Cessation Quitlines launched in 2004, with funding from the Centers for Disease Control and Prevention and the National Institutes of Health via NCI, to provide telephone-based cessation services to individuals in all states, Washington DC, and U.S. Territories. Quitlines are a commonly used resource; the National Network of Tobacco Cessation Quitlines (1-800-QUIT-NOW) received its 10 millionth call in 2019.[222,223]

Quitline services can include telephone-based coaching and counseling, referrals, mailed materials, training for clinicians, mobile phone–based and web-based services, and free smoking cessation medications.[224] The level and types of services vary across states. For instance, some quitlines offer text message services while others do not; also, the individual state quitlines offer different amounts and types of medication.[225,226] In general, state quitlines provide counseling comprising CBT and adjuvant intra-treatment social support and motivational content, and most provide some amount of smoking cessation medication.[113,227] Access to other adjuvants such as web resources may be offered in addition to this base treatment. Users can receive support by proactively calling the quitline or by registering online (not universally available) or through health care program or clinician referral via fax or EHR-mediated referral.[9,228] Referred patients are called by the quitline and the patient must answer the call to register for service. Quitlines strive to match a client with services that reflect their preferences and needs, but clients are generally offered both counseling and a range of other resources.[225,229] Quitlines often have intervention protocols designed for special populations such as youth and pregnant women.

Quitlines receive approximately half a million direct calls annually,[226,230] reflecting the advantages to their use: they require no travel or health insurance and are free to the user. These features also make them especially appropriate for populations that have a dearth of other treatment options. Almost half of quitline users had a GED degree or less than a high school education.[226] One limitation of referring patients to quitlines is that only half or fewer of referred patients ultimately accept a quitline call and receive treatment.[9,228] In addition, the intensity of the smoking cessation treatment offered by many state quitlines is modest, in some cases consisting of only 1 counseling call and a 2–4 week starter supply of medication (although individuals can recontact the quitline).[226,231]

A 2019 Cochrane Review evaluated the effects of multisession counseling in 14 trials among individuals from the general population who called a quitline.[232] This analysis compared experimental conditions that differed in counseling intensity but not in other treatment factors such as medication. The results indicated that multisession counseling increased long-term abstinence relative to control conditions that provided self-help or briefer counseling contact (RR = 1.38, 95% CI = 1.19–1.61, *N* = 32,484). Thus, smoking cessation counseling appears similarly effective when delivered via phone as it is in face-to-face contexts. Other analyses in this report found mixed evidence regarding the relative effectiveness of more versus less intense counseling on long-term abstinence. In sum, studies showed that individuals from the general population who called a quitline and received multisession quitline counseling had modestly higher long-term abstinence rates than did individuals who received only self-help or a single quitline call. The magnitude of this effect was to increase the chances of long-term abstinence on average from about 7% to 10% relative to the control conditions.

The 2019 Cochrane Review cited above also indicated that proactive phone counseling (where treatment personnel call individuals to deliver treatment) is effective among the general population.[232] Proactive telephone counseling was evaluated in 35 trials in which it was compared with minimal intervention (e.g., self-help). The resulting meta-analysis yielded a significant effect (RR = 1.35, 95% CI = 1.16–1.57, *N* = 22,917). Importantly, a 2018 RCT with patients with cancer compared intense (4 weekly sessions plus 4 biweekly and monthly sessions and FDA-approved smoking cessation medication for 12 weeks) versus less intense (4 weekly sessions and medication advice) smoking counseling delivered by phone to patients with cancer.[233] This study showed significant benefit of telephone counseling (see "Behavioral Interventions for Smoking Cessation Among Patients With Cancer" for an extended discussion of this study).

Video-Based Counseling. Audiovisual (video) counseling (or telehealth) can be delivered to patients through a smartphone, tablet, or computer. In such treatment, the health care program typically contacts a patient in response to clinician referral or because a patient responded to health system outreach. The treatment is largely determined by each health care system; however, if it follows clinical practice recommendations,[17] it should include CBT, motivational intervention, intra-treatment support, and medication recommendation and provision.

Video counseling can expand access to evidence-based smoking cessation treatment and improve treatment adherence. Video delivery allows clinicians to respond to nonverbal cues that may improve the communication and the therapeutic alliance achieved during counseling sessions, allowing patients to feel better supported by their clinician.[234] However, there are also challenges with video counseling. Some patients may not have access to necessary resources, such as reliable, high-speed internet, or they may lack the knowledge to use needed resources effectively. For these patients, phone counseling may be more appropriate. Video counseling also requires that a health system or program provide the technologic and personnel support to make routine intervention feasible.

Video counseling for smoking cessation treatment has not been evaluated extensively in either the general population or in patients with cancer. A Cochrane Review identified two studies that compared real-time video counseling for smoking cessation with telephone counseling in individuals from the general population.[235] The meta-analysis revealed no significant difference between the 2 counseling types (RR = 2.15, 95% CI = 0.38–12.04, *N* = 608). However, the authors of the meta-analysis rated the certainty of this finding as very low due to methodologic limitations and imprecision in the effect estimate. Another systematic review also found mixed evidence regarding the effectiveness of video counseling for smoking cessation treatment versus telephone counseling or face-to-face counseling.[236] Carlson and colleagues compared group video counseling treatment delivery to rural residents with in-person group tobacco cessation treatment to urban residents in a nonrandomized study.[237] The two approaches yielded similar long-term abstinence rates.

Evidence suggests that video counseling is acceptable, feasible, and yields encouraging engagement rates in cancer patient populations.[238] LeLaurin and colleagues used a pragmatic design, giving patients with cancer who smoke (median age 58; one-third rural residents) a choice of traditional quitline (N = 39), in-person group counseling (N = 14), or individual video counseling via smartphone (N = 37).[239] The video counseling patients gave especially favorable ratings to their intervention, mainly due to the treatment's convenience. In another study, patients with cancer undergoing radiation treatment completed surveys appraising their smoking cessation treatment delivered during office (N = 726) or video (N = 351) visits. Patients gave similarly high satisfaction ratings to the two types of interventions.[240]

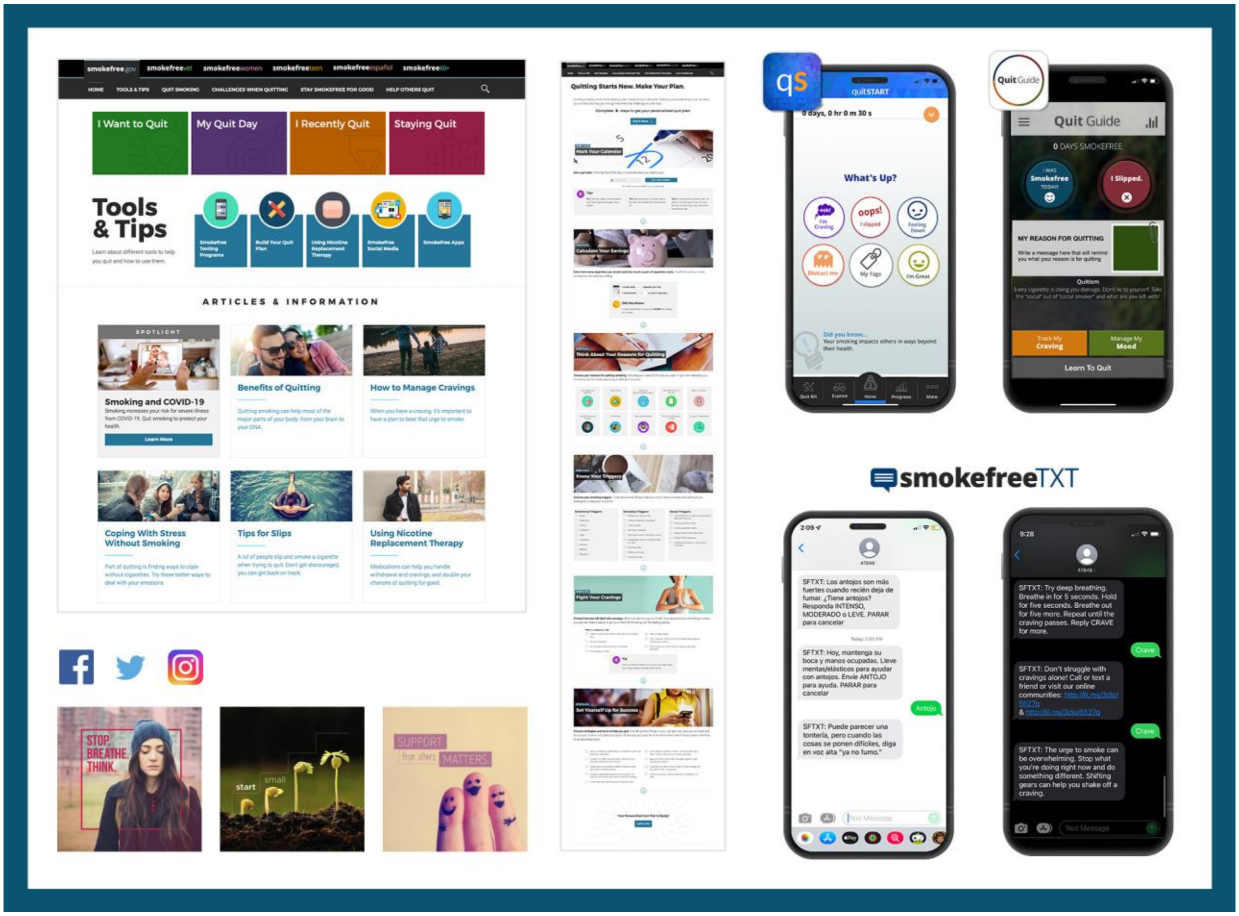
In sum, limited evidence suggests that video counseling may be similar in effectiveness to phone counseling when used with the general population. Further research is needed to establish its effectiveness relative to phone counseling as well as to other behavioral treatment approaches. Similar comparative effectiveness research is clearly needed to establish its effectiveness in cancer patient populations.

Digital Interventions. Digital interventions include web-based and mobile phone delivery of smoking cessation treatment. These web- and mobile-based interventions have tremendous promise because of their potential population reach given that cell and/or smartphones are widely available.[241] In addition, they can often be delivered at relatively low cost once the needed infrastructure is implemented, permit easy tailoring, allow for good quality control of content, are continuously available to the user, and permit easy collection of data on use.[31,242] They may be especially beneficial for groups that have limited access to other forms of treatment (e.g., in-person counseling), health care, or transportation resources.[243] Additionally, digital interventions may align with recent trends in telehealth and help reach rural smokers,[244] although internet access remains lower among rural residents than among suburban and urban residents.[245,246]

Evaluating digital interventions for smoking cessation treatment is difficult because of their diversity, rapid development, and continuous evolution.[31] For example, websites vary with regard to interactivity, personalization, recruitment route (search engines, advertising, health care referral), whether their content is evidence based, and their goals (i.e., an intervention vs. a referral resource). What follows is a summary of the current literature on three types of digital channels for delivering smoking cessation interventions: website, short message service (SMS), and smartphone app. The present review of these intervention strategies is brief, relies on prior authoritative reviews, and is focused on the potential for these interventions to benefit patients with cancer who smoke. In addition, this review tries to address whether such interventions are effective relative to no treatment or minimal treatment controls and how they compare with other forms of treatment such as person-to-person counseling and pharmacotherapy. These comparisons are relevant to decisions about whether to use such interventions and whether to use them in lieu of other types of interventions. Again, these data arise from research on the general population but may be relevant to patients with cancer as well.

The National Cancer Institute's Smokefree.gov Initiative (SFGI) provides free, evidence-based cessation support to the public through a multimodal suite of digital interventions (Figure 3.1), including six mobile-optimized websites, seven text messaging programs (in English and Spanish), and two mobile applications. In addition to digital resources directed at the general population, the SFGI includes population-targeted resources for adolescents, women, military veterans, Spanish speakers, and older adults. All SFGI resources are free for use or download; data fees may apply for some text message subscribers. Additional details about SFGI interventions are provided in the subsections below as examples of resources available to clinicians and public health professionals.

Figure 3.1 Smokefree.gov Initiative Digital Interventions



Website/Web-Based Interventions. A website or web-based intervention can present either (or both) static content that is the same for every user or interactive content so that user performance influences the nature of the material that is presented or available. Early evidence on the effectiveness of web-based interventions shows a mixed picture,[31] in part because of the range of web-based interventions and combinations that have been evaluated in studies,[247,248] which makes it difficult to isolate the effects of any individual component (e.g., a website). Taylor and colleagues conducted a meta-analysis comprising 8 studies (N = 6,786) that showed a modest but significant benefit of web-based interventions on long-term abstinence, compared with no treatment (6–12 months) (RR = 1.15, 95% CI = 1.01–1.30).[248] On the other hand, one meta-analysis of 5 trials that compared web-based interventions with active comparison conditions (such as face-to-face or telephone counseling) found that the pooled effect estimate was not significant (RR = 0.92, 95% CI = 0.78–1.09, N = 3,806, I^2 = 0%).[248] Another meta-analysis compared web-based interventions (with interactivity and tailoring) with more basic or comparison conditions (no intervention, usual care, more basic web-based interventions, or non-web interventions).[249] About half of the active or web-based intervention conditions included other types of interventions so data on effectiveness might not reflect the effects of web-based interventions alone. The evidence showed a significant effect of web-based intervention on long-term (6-months or more) abstinence when assessed with pooled outcome measures (e.g., measures of prolonged and point-prevalence abstinence [PPA]: odds ratio [OR] = 1.19, 95% CI = 1.06–1.35, p = .004, 34 trials). However, significant effects were not found for standard outcomes such as 30-day PPA (OR = 0.87, 95% CI = 0.76–1.00, p = .054, 8 studies), or 7-day PPA (OR = 1.20, 95% CI = 0.93–1.55, p = .155, 17 studies).[249] Thus, like the Taylor meta-analysis, the McCrabb and colleagues' meta-analyses suggest that web-based interventions can significantly increase long-term smoking abstinence, but the effect may not be wholly attributable to the web-based intervention and is not robust across different sets of studies or outcomes. Also, many digital interventions (including web-based) experience retention problems or high dropout rates, which might reduce the effectiveness of the intervention or challenge outcome ascertainment.

Smokefree.gov Websites

Smokefree.gov (https://smokefree.gov) is the National Cancer Institute's (NCI's) public-facing smoking cessation website. The website provides information, support, motivational enhancement, and interactive tools to assist people who smoke in quitting. The website serves as an entry point for all Smokefree.gov Initiative (SFGI) digital resources and tools, as well as the NCI's telephone and online smoking cessation counseling services (https://smokefree.gov/tools-tips/speak-expert). A quit plan–builder tool guides users through the steps to prepare for making a quit attempt. Quizzes allow users to assess factors such as their level of nicotine dependence and perceived stress level to inform their quit experience. SFGI social media platforms offer inspiration and encouragement to support people during their quit attempts and beyond.

Other meta-analyses have found that more active and complex web-based interventions can yield significantly higher long-term abstinence rates than do various control conditions. Graham and colleagues found that interactive interventions were more effective than no-treatment controls and assessment controls or print-based smoking cessation materials.[247] McCrabb and colleagues performed meta-analyses on many of the same web-based internet interventions analyzed by Graham and colleagues and found that the effectiveness of the web-based interventions was positively related to certain content that addressed active treatment elements such as making goals and planning and obtaining social support.[249]

In sum, there is meaningful evidence that web-based interventions, such as interactive websites, can be more effective than no intervention. However, the benefits of web-based interventions tend to be modest in size compared with the effects of medication and person-to-person counseling,[103,109,248,250] and static or simple website interventions composed of few components may impart little benefit.[31,247–249] Thus, some care must be taken in assessing the nature and quality of such interventions. This task is challenging because many of the web-based interventions that were evaluated and reported in the literature no longer exist.[249] However, it is important to note that even small benefits from web-based interventions may be important because they are highly accessible, can be provided at low cost, and require no clinical personnel.

SMS Interventions. In SMS text messaging interventions, individuals are sent automated smoking intervention text messages for an extended time period (typically starting prior to the target quit date and extending for multiple weeks thereafter). Text message–based interventions may also have bidirectional functionality, which enables individuals to send or respond to messages (i.e., request on-demand help or provide information about withdrawal symptoms, smoking status, and desire for additional or tailored interventions). The potential reach of texting interventions is considerable given that 85% of Americans owned a smartphone as of 2021 and 97% of Americans owned a cell phone of some kind.[241] Further, texting is common among smartphone users in the United States.[251]

Meta-analyses suggest that SMS interventions significantly enhance long-term smoking cessation rates.[107,252] A Cochrane Review meta-analysis of 13 studies showed that the effects of the SMS interventions were significant when using both point prevalence and continuous measures of abstinence and when abstinence reports were biochemically confirmed.[107] In these meta-analyses, the SMS interventions were compared with control conditions that typically involved no or minimal intervention (reduced-intensity texts); only one study compared the SMS intervention to counseling and pharmacotherapy.

Smokefree.gov Initiative's Text Messaging Programs

SmokefreeTXT is Smokefree.gov Initiative's (SFGI) text messaging−based cessation program. The fully automated service provides people who smoke with up to 8 weeks of encouragement, advice, and quitting tips. SmokefreeTXT users are asked to set a quit date within the next 2 weeks. Subscribers who are ready to quit right away can begin receiving cessation support immediately; those not yet ready can receive up to 2 weeks of preparation messages. Text messages are delivered daily (approximately 3−5 messages per day) and are timed around the quit date selected by the user. In addition to the main SmokefreeTXT program, SFGI offers text messaging-based cessation programs for pregnant women, adolescents, Spanish speakers, military veterans, and other populations.

The 2020 Surgeon General's report concluded that SMS interventions are effective at increasing smoking cessation, particularly if the text messages are interactive or tailored to the user's responses.[31] The Community Preventive Services Task Force similarly noted that mobile phone text messaging interventions are effective when implemented alone or with other interventions, especially when an intervention delivers tailored content, interactive features, or both.[102] However, the 2020 Surgeon General's report[31] noted that although the effects of SMS interventions are often significant in the short term (less than 6 months), their long-term effects tend to be highly variable across studies[253] and recommended additional research to increase understanding of the effect of various treatment aspects of these interventions. In sum, SMS interventions can be effective relative to no treatment, but the effectiveness of SMS interventions can vary meaningfully across different versions of the interventions (e.g., content, tailored vs. untailored, nature of the comparison condition) or populations studied (e.g., age, race and ethnicity), suggesting a need for research on factors that influence their effectiveness.[31]

Smartphone Applications (Apps). Apps are integrated software units designed to run on mobile devices such as smartphones or tablets. They are typically highly interactive and can present information in multiple different formats, monitor data, and provide feedback to users in the service of some goal. There are hundreds of apps for smoking cessation,[254] and these vary greatly in their content and the approaches they take to promote smoking cessation.[254,255] A 2019 Cochrane Review meta-analysis of five studies compared smoking cessation smartphone apps with either a less intense app or minimal support. The evidence was deemed of very low certainty and yielded no evidence that smartphone apps improved the likelihood of smoking cessation (RR = 1.00, 95% CI = 0.66–1.52, $I^2 = 59\%$, $N = 3{,}079$).[107] The uncertainty of the evidence may arise from the great variability among apps. A 2020 study shows evidence of such variability in app effectiveness. Bricker and colleagues completed a large randomized clinical trial ($N = 2{,}415$) that compared an ACT-based smoking cessation smartphone app with NCI's smoking cessation smartphone app (i.e., QuitGuide).[256] The latter was designed based on the treatment recommendations in the PHS Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*.[17] The primary smoking cessation outcomes were based on unconfirmed self-report; the 30-day PPA rates at 12-month follow-up were significantly greater for the ACT app than for the NCI QuitGuide app (28.2% vs. 21.1%, OR = 1.49, 95% CI = 1.22–1.83).[256]

Smartphone Apps

The Smokefree.gov Initiative supports two smartphone-based mobile apps (https://smokefree.gov/tools-tips/apps), accessible on both iPhone and Android platforms, designed to guide people who smoke through quitting and to help them build skills to maintain cessation. QuitGuide was developed for a general adult audience; quitSTART was developed for adolescents and young adults who smoke. These mobile apps provide real-time monitoring of cessation progress, including tracking of cigarettes, cravings, mood, triggers, and lapses.

Apps can be provided to patients at relatively low cost, and they create little burden for clinical staff. However, the selection of a smartphone app is critical because they can differ meaningfully in guiding theoretical model and change strategies[257,258]; such differences could substantially affect their effectiveness. This variability also makes it difficult to make general statements about their effectiveness.[31] Also, as with websites and SMS interventions, it is unclear that they have the same level of effectiveness as relatively intense interventions including person-to-person counseling and pharmacotherapy.

Summary: Digital Interventions for Smoking Cessation. There is strong evidence that phone counseling delivered by quitlines or delivered proactively by smoking cessation treatment programs increases long-term abstinence rates in individuals in the general population. In addition, an RCT conducted with patients with cancer who smoke showed that more intense telephone-based smoking cessation treatment counseling is more effective than less intense telephone-based smoking cessation treatment counseling. Two drawbacks of quitline treatment are that patients often do not take quitline calls even when they previously accepted a referral to it, and patients with cancer may need more intense treatment than is typically provided by quitlines.

There is little research evidence on the effectiveness of video-based smoking cessation counseling. Telehealth (i.e., video counseling) remains an understudied model of delivering smoking cessation treatment; however, limited evidence from the general population suggests that it is similar in effectiveness to phone counseling for smoking cessation. Video counseling for smoking cessation appears to be quite acceptable to patients and feasible for use in health care settings, including in cancer treatment programs. These features increase the importance of establishing its effectiveness in cancer patient populations.

Digital interventions for smoking cessation hold considerable promise given their potential reach and there is evidence that they can be effective (Table 3.3), which has led the U.S. Preventive Services Task Force (USPSTF) to recommend them for the treatment of nicotine dependence.[46] The evidence of their effectiveness is greatest and most robust when they are being compared with control conditions involving little or no treatment. Most data suggest that they are less effective than the combination of moderately intense person-to-person counseling and pharmacotherapy. Furthermore, there is evidence of substantial variability within the different types of digital interventions (i.e., among web-based, SMS interventions, and smartphone apps). Thus, such interventions must be selected with care. Moreover, more data are needed to guide decisions about whether such interventions are best used as adjuvants to, or substitutes for, other types of evidence-based smoking cessation treatments. Finally, health care systems using such resources must consider how to encourage patients to use digital interventions (e.g., after referral), a topic addressed in chapter 4. In sum, there is some evidence of effectiveness for both web-based and SMS interventions, which, given their great potential reach, encourages their consideration for use as smoking cessation strategies.

Smoking Cessation Treatments Among Patients With Cancer

Many patients with cancer are motivated to quit smoking and are receptive to smoking cessation treatment. This section reviews pharmacological, behavioral, and program-level treatments for smoking among patients with cancer. This section includes results from individual RCTs and some nonexperimental studies (e.g., single-arm trials) with the former permitting stronger inference regarding causality.

Patients with cancer who smoke differ from the general population of people who smoke in several ways: They are often more nicotine dependent and face challenges related to their cancer diagnosis, including anxiety, stress, pain, and the demanding nature of cancer treatment.[7,259] Many also feel ashamed that they smoke, and experience stigma related to their smoking.[260] These and other factors could complicate cessation treatment in this population.

Medications for Smoking Cessation Among Patients With Cancer

Table 3.6 describes the smoking cessation studies conducted with patients with cancer. Many of the trials included small sample sizes and relied on the self-report of smoking abstinence, rather than on biochemically confirmed abstinence. Several reviews summarize smoking cessation studies among patients with cancer.[261–264] Trials that have experimentally evaluated FDA-approved smoking cessation medications in patients with cancer are rare and only one such trial has used a placebo-controlled clinical trial design.[265] Further, most trials involving smoking cessation medication also involve adjuvant counseling so the effects of medication and counseling cannot be accurately distinguished.

Cancer patient populations often have high levels of nicotine dependence,[7,33,266] so there is a strong rationale for using smoking cessation medications with this population. No study has tested the use of NRTs, or combination NRT, with patients with cancer using a placebo-controlled design. Two RCTs compared a usual-care treatment arm (i.e., smoking cessation advice and referral) with a treatment arm that included NRT and counseling,[267,268] and neither trial found a significant difference in biochemically confirmed quit rates at 6–12 months. A pilot study by Pollak and colleagues compared an active condition involving NRT (type unspecified) and four 60-minute sessions of counseling with a waiting-list control condition.[269] This study reported somewhat higher short-term (2-month) abstinence rates in the active treatment condition than in the control condition (14% vs. 6%). However, the sample size was quite small ($N = 30$) and no long-term (≥6 month) follow-up outcomes were reported. Also, waiting-list control conditions may encourage individuals to wait to make a quit attempt until treatment is available. A 2020 single-cohort observational study provided patients with cancer who smoke with brief counseling and a free 4-week supply of nicotine patches. Among patients with complete follow-up data, 35% reported smoking cessation, although self-reported quit rates were not biochemically confirmed.[270]

A placebo-controlled RCT of bupropion found no overall smoking cessation effect for the medication, but bupropion increased abstinence rates more for patients with depressive symptoms versus those without depressive symptoms.[265]

Four studies have evaluated the use of varenicline for treating tobacco use among patients with cancer. One nonrandomized cohort-type study compared patients with cancer who received counseling and varenicline with those who previously received usual care (historical controls; no smoking cessation treatment). The quit rate for the counseling and varenicline arm was higher than for usual care (34% vs. 14%), but this difference was not significant likely due in part to the small sample size ($N = 49$).[271] An open-label study in which all patients were given varenicline ($N = 132$) found a quit rate of 40% after 12 weeks of treatment.[12] The placebo-controlled randomized phase of one study examined the effects of extended varenicline (24 weeks) versus standard duration varenicline therapy (12 weeks of varenicline plus 12 weeks of placebo). The 2 varenicline treatments did not differ significantly in abstinence rates at 24-week follow-up (30% in both groups).[272] The last study was a very small study that randomized patients with cancer ($N = 29$) to either: (1) a control arm that received a single counseling session, educational material, and a referral to a smoking cessation program; or (2) an intervention arm that received 8 weekly MI sessions; CM ($5 per report of biochemically verified abstinence); and the choice of combined NRT, varenicline, or bupropion. At week 8, a significantly greater proportion of intervention-arm patients had quit smoking (biochemically confirmed) than was found in the control arm (74% vs. 30%).[273]

One study with patients with cancer as participants evaluated the effect of access to multiple FDA-approved smoking cessation medications. Duffy and colleagues compared a usual-care intervention with an intervention comprising counseling and access to either NRT or bupropion (N = 184) and reported significantly increased quit rates for the active-treatment arm.[274] This effect is difficult to interpret because a portion of the participants who were treated in this study were not currently smoking at the beginning of their participation in the study. A second study also involved use of multiple FDA medications[233] but differences in the medication condition were confounded with different counseling intensities. This study is discussed in the section, "Behavioral Interventions for Smoking Cessation Among Patients With Cancer."

Table 3.6 reveals that only 3 RCTs have a sample size >100 and had measures of biochemically confirmed abstinence at long-term follow-up (>6 months).[265,268,272] None of these three studies showed a significant benefit of medication in whole sample analyses.

It is important to note that smoking cessation medications have been judged to be quite safe when used by patients with cancer, consistent with their being recommended for the treatment of smoking in patients with cancer by the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology.[16] However, clinicians should ensure that smoking cessation pharmacotherapies are appropriate given the patient's cancer, their existing pharmacologic regimens, and the effects of their cancer treatment. For example, use of oral NRT may be contraindicated for patients with cancers of the oral cavity.[275]

Table 3.6 Studies of Smoking Cessation Interventions Among Patients With Cancer

Study	Sample size	Intervention arm	Control arm	Timing of quit rate assessment[a]	Quit rate[b] intervention arm	Quit rate control arm	Methodological comments
Studies of smoking cessation medications (with or without counseling)[c]							
Randomized studies							
Rettig et al. 2018[273]	29	Combined NRT, bupropion, or varenicline; counseling	Counseling, referral	8 weeks from baseline	74%	30%	Randomized, biochemical confirmation
Schnoll et al. 2019[272]	207	24 weeks varenicline, counseling	12 weeks varenicline, counseling	24 weeks from baseline	61% (adherent patients), 10% (nonadherent)	45% (adherent patients), 13% (nonadherent)	Randomized, biochemical confirmation
Duffy et al. 2006[274]	184	NRT or bupropion, counseling	Counseling, referral	6 months from baseline	31%	15%	Randomized, self-reported cessation
Schnoll et al. 2010[265]	246	Bupropion, patch, counseling	Placebo, patch, counseling	12 and 27 weeks from baseline	27% (12wk), 18% (27wk)	24% (12wk), 17% (27wk)	Randomized, biochemical confirmation
Pollak et al. 2018[269]	30	NRT, counseling	Waitlist control (received NRT and counseling 2 months after randomization)	2 months after randomization	14%	6%	Randomized, biochemical confirmation
Thomsen et al. 2010[267]	130	NRT, counseling	Advice, referral	12 months postoperative	13%	9%	Randomized, self-reported cessation
Wakefield et al. 2004[268]	137	NRT, counseling	Advice, referral	6 months from baseline	5%	6%	Randomized, biochemical confirmation
Nonrandomized studies							
Park et al. 2011[271]	49	Varenicline, counseling	Varenicline	12 weeks from baseline	34%	14%	Quasi-experimental, biochemical confirmation

Table 3.6 (continued)

Study	Sample size	Intervention arm	Control arm	Timing of quit rate assessment[a]	Quit rate[b] intervention arm	Quit rate control arm	Methodological comments
Arifin et al. 2020[270]	117	NRT, counseling	None	Median 9 months from baseline (interquartile range, 5.7—11.6 months)	35%	N/A	Single-cohort observational, self-reported cessation
Studies of behavioral smoking interventions (with or without medications)[d]							
Randomized studies							
Stanislaw and Wewers 1994[278]	26	Counseling	Advice	5 weeks after hospital discharge	75%	43%	Randomized, biochemical confirmation
Gritz et al. 1993[36]	186	Counseling	Advice	1, 6, and 12 months from baseline	69% (1m), 71% (6m), 69% (12m)	76% (1m), 74% (6m), 79% (12m)	Randomized, biochemical confirmation
Schnoll et al. 2005[280]	109	Tailored counseling (cognitive behavioral therapy, including 3 phone sessions and 1 in-person session), NRT	Standard counseling (general health education), NRT	1 and 3 months after intervention completion	45% (1m), 43% (3m)	47% (1m), 39% (3m)	Randomized, self-reported cessation
Park et al. 2020[233]	303	Extended counseling 11 counseling sessions over about 24 weeks) and NRT, bupropion, or varenicline	Counseling (4 counseling sessions over 4 weeks) and medication advice	6 months from baseline	35%	22%	Randomized, biochemical confirmation
Wewers et al. 1994[279]	80	Counseling	Advice	5 to 6 weeks after hospital discharge	38%	26%	Randomized, self-reported cessation
Ostroff et al. 2014[290]	185	Counseling, NRT, scheduled smoking reduction	Counseling, NRT	6 months after hospitalization	32%	32%	Randomized, biochemical confirmation

Table 3.6 (continued)

Study	Sample size	Intervention arm	Control arm	Timing of quit rate assessment[a]	Quit rate[b] intervention arm	Quit rate control arm	Methodological comments
Ghosh et al. 2016[289]	14	CM	Advice, smoking cessation classes	6 months from baseline	33%	0%	Randomized, biochemical confirmation
Griebel et al. 1998[277]	28	Counseling	Advice	6 weeks after intervention completion	21%	14%	Randomized, self-reported cessation
Bricker et al. 2020[291]	59	Quit2Heal (smartphone app)	NCI QuitGuide	2 months from baseline	20%	7%	Randomized, self-reported cessation
Schnoll et al. 2003[281]	432	Counseling	Advice, referral	6 and 12 month from baseline	14% (6m), 13% (12m)	12% (6m), 14% (12m)	Randomized, self-reported cessation
Nonrandomized studies							
Browning et al. 2000[276]	25	Counseling	Advice	6 months from baseline	71%	55%	Quasi-experimental, biochemical confirmation
Charlot et al. 2019[288]	18	Mindfulness-based group visits	None	3 months from baseline	0%	N/A	No control arm, self-reported cessation
Cinciripini et al. 2019[334]	3,245	CBT/MI counseling 8 visits	N/A	6 months	46%	N/A	Prospective cohort with no control arm, self-reported cessation

Note: NRT = nicotine replacement therapy. NCI = National Cancer Institute. CBT = cognitive behavioral therapy. CM = contingency management. MI = motivational interviewing. N/A = not applicable. [a]"Baseline" refers to study enrollment or start of cessation treatment. Some studies have deceased patients removed from the sample (e.g., Arifin et al. 2020) in determining abstinence percentage. [b]Quit rates are rounded to nearest integer. [c]Studies of smoking cessation medications are those in which medication varied across trial arms. [d]Studies of behavioral smoking interventions are those in which the counseling intervention varied across trial arms.

Summary: Medications for Smoking Cessation Among Patients With Cancer. At present, strong conclusions about the level of effectiveness and optimal regimen of cessation medications in patients with cancer are difficult to draw because of a paucity of adequately powered, well-controlled clinical trials in this population. Patients with cancer who smoke may differ in multiple and important ways from the general population. Patients with cancer, for instance, may achieve higher quit rates in the absence of smoking cessation treatment due to their greater motivation to quit, they may experience greater affective distress, and the burden of imminent and taxing medical treatment may increase their level of stress. This suggests that it is possible that FDA-approved medication treatments for tobacco use may differ in effectiveness for patients with cancer compared with the general population. Demonstrating a benefit for cessation medications among patients with cancer can also be challenging because many patients quit without assistance after being diagnosed with cancer; patients who either do not attempt to quit or do not succeed in quitting are likely to have the most difficulty doing so, even when receiving smoking cessation treatment.

Some evidence indicates that smoking cessation medications may be effective for patients with cancer. Specifically, one study showed significant benefit in a subset of participants.[272] Further, some of the studies presented in Table 3.6 show modestly better abstinence rates in the active-medication arms than in the control arms. However, as noted, most of these studies had small samples and, thus, were under-powered, of questionable generalizability, and may not be reproducible.

The PHS Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*,[17] concluded that counseling and medication treatments found effective for patients in general are likely to be effective when used in a variety of subpopulations who smoke. This underlies guideline recommendations that all patients with cancer be encouraged to use evidence-based smoking cessation counseling and medication.[16] More evidence on the effectiveness of smoking cessation treatment in cancer patient populations is needed to identify the optimal cessation medication regimens for patients with cancer, including the optimal combination of medication with different levels of counseling (e.g., brief vs. intense).

Behavioral Interventions for Smoking Cessation Among Patients With Cancer

This section addresses two key questions: (1) is behavioral intervention, or counseling, for smoking cessation effective in increasing abstinence rates among patients with cancer, and (2) is there evidence that adapting behavioral intervention for patients with cancer makes it more effective?

To address these questions, studies should ideally permit causal inferences about counseling intensity; for example, RCTs where participants are randomized to intense counseling versus no or minimal counseling. In such studies, smoking cessation medication should either not be used or should be the same across the treatment arms. Counseling interventions for smoking in patients with cancer have been researched more extensively than have medication treatments, although many of the counseling studies are small, underpowered, and lack methodological rigor.[263]

Counseling studies have typically used standard cognitive behavioral frameworks and psychoeducational approaches to guide counseling. Very early studies compared usual care to nurse-led, multiweek counseling treatments.[276–279] These were very small studies (<50 participants each) that used self-reported smoking cessation outcomes without biochemical confirmation. Although quit rates were often higher among patients in the intervention arm, the effects in these studies were not significant (Table 3.6), likely due in part to small sample sizes that reduced power.

However, studies with larger sample sizes have also not found significant effects. For example, a study with 96 patients randomized to usual care or a multiweek counseling intervention found no significant effect for the counseling intervention after 12 months.[36] Although this study was larger, it was still underpowered given the likely effect sizes expected from counseling. Later studies used counseling models that were more tailored to address specific barriers to smoking cessation among patients with cancer, such as emphasizing the benefits of smoking cessation for reducing recurrence, managing psychological distress, and/or reducing fatalism. A study using a randomized trial design to compare CBT-based smoking cessation counseling tailored to the needs of patients with cancer who smoke (e.g., addressing fatalistic beliefs) to a general health education intervention found no significant differences between the two groups; both intervention arms produced quit rates close to 40%.[280] One of the largest studies (N = 432) compared a physician-based counseling intervention with usual care and found low overall quit rates for both arms at the 12-month follow-up assessment (< 15%) and no difference between treatment arms in self-reported cessation.[281]

More recently, Park and colleagues used a randomized clinical trial design to compare standard smoking cessation treatment (four weekly counseling phone calls and medication advice) with a more intensive treatment that included seven additional counseling calls over 3 months and the choice of an FDA-approved smoking cessation medication provided at no charge. Thus, conditions differed in both counseling intensity and medication. However, this study is best conceptualized as one comparing 2 levels of counseling because participants in both arms used medication (77.0% in the intensive arm and 59.1% in the standard arm). Smoking cessation counseling was delivered by certified tobacco treatment counselors. Participants had recently been diagnosed with cancer (breast, gastrointestinal, genitourinary, gynecological, head and neck, lung, lymphoma, or melanoma cancers). At a 6-month follow-up, there was a significant increase in the biochemically confirmed PPA rate for the intensive treatment versus standard care (34.5% vs. 21.5%)[233] (Table 3.6). In all, this study is important because of its sample size (N = 303) and long-term biochemically confirmed follow-up. Therefore, it provides important evidence on the effectiveness of intense versus less intense smoking cessation counseling on long-term smoking abstinence in patients with cancer where many patients in both conditions use medication.

Two meta-analyses included studies using combinations of counseling and pharmacotherapy treatments delivered to patients with cancer.[282,283] Klemp and colleagues conducted a systematic review and meta-analysis of smoking cessation treatment studies with patients with head and neck cancer.[282] They found that counseling can help such patients quit smoking, compared with various control conditions (i.e., brief advice, general health education, or no cessation treatment). However, this meta-analysis may not provide a sensitive test of counseling effects because only three of the eight studies analyzed were RCTs and counseling differed among the eight studies;

only one of the RCTs found a significant effect. Furthermore, participants in the cohort and case series studies received pharmacotherapy in addition to counseling. Thus, the effects of these different types of interventions cannot be disentangled.

Sheeran and colleagues analyzed 21 RCTs that were intended to evaluate smoking cessation treatments in cancer populations.[283] The trials analyzed comprised a mixture of pharmacologic and/or behavioral smoking cessation treatments. Also, the trials involved diverse samples; some included recently diagnosed patients and others included long-term survivors of childhood and adolescent/young adult (AYA) cancer (additional discussion on childhood and AYA cancer survivors is below). This meta-analysis did not find evidence of a significant benefit of smoking cessation treatment, compared with the control condition, in terms of increased smoking cessation at follow-up. This negative outcome may largely reflect limitations of the analyzed studies. One paper evaluated in the meta-analysis by Sheeran and colleagues was not evaluated in this chapter because it was reported only as an abstract and provided insufficient information on the treatments and outcomes.[284] Additionally, two of the papers in the meta-analysis were not evaluated in this chapter because only a very small proportion (12% or fewer) of the sample smoked[285,286]; results for only the subsample that smoked were broken out by Sheeran and colleagues. In one of the studies,[287] only a portion of the sample had cancer diagnoses (i.e., 29%) and the authors reported that no smoking cessation treatment was provided in the study (the study tested the effects of providing genetic cancer susceptibility information on smoking cessation). Finally, this meta-analysis did not include the RCT by Park and colleagues[233] previously discussed (Table 3.6), which suggested that large, well-designed RCTs, with guideline-recommended smoking cessation treatment delivered with high treatment fidelity can support the effectiveness of smoking cessation treatment in cancer populations.

Smoking Cessation Intervention Effectiveness Among Childhood, Adolescent, and Young Adult Cancer Survivors

In the U.S., an estimated 10,470 children (age 0–14) will be diagnosed with cancer and 1,050 will die from their disease in 2022.[483] Additionally, in 2020, an estimated 89,500 U.S. adolescents and young adults (AYA: age 15–39 years) were diagnosed with cancer and an estimated 9,270 died from their disease.[483] The population of childhood and AYA cancer survivors varies widely with regard to cancer site, age at diagnosis, type and intensity of treatment, and survival. Due to advances in diagnosis, treatment, and supportive care, most childhood and AYA cancer survivors are expected to be cured.[484–486] Yet, childhood and AYA cancer survivors often experience acute, chronic, and late adverse effects from their cancer and its treatment,[486] including "cardiovascular disease, renal dysfunction, severe musculoskeletal problems, and endocrinopathies."[487,p.1580] Additionally, both childhood and AYA cancer survivors are at risk for developing second primary malignancies due to their cancer history.[488] Smoking increases the risk of long-term negative health outcomes among survivors of childhood cancer[489] and among survivors of AYA cancer.[490]

Two studies provide nationally representative estimates of the prevalence of tobacco use among survivors of AYA cancers, relative to their same-age peers who have not had cancer. Kaul and colleagues analyzed data from the 2012–2014 NHIS to determine the prevalence of cigarette smoking among adults (18 and older) who had been diagnosed with cancer between the ages of 15 and 39, and who were at least 5 years post-diagnosis, compared with an age-matched comparison group of adults who had not been diagnosed with cancer.[491] This analysis found that 32.9% of cancer survivors currently smoked compared with 22.1% in the comparison group ($p < .001$). Current smoking among survivors was associated with a higher number of comorbid health conditions (e.g., heart disease) and with a greater likelihood of reporting only fair or poor health. Similarly, a study using data from the 2015–2018 National Survey of Drug Use and Health (NSDUH), found that past-year tobacco use was higher among AYA cancer survivors age 12–34, compared with their non-cancer age-matched peers (38.4% vs. 32.9%, $p = .02$).[492] The Childhood Cancer Survivors Study (CCSS) is a large cohort study of survivors who were diagnosed with cancer before the age of 21.[493] A CCSS follow-up study compared the smoking rates of adult (18 years and older) CCSS participants to siblings without cancer and with the general population, matched for age, sex, and race, using 2007 NHIS data.[494] At an average of 12.5 years after enrollment in the CCSS, survivor participants had a smoking prevalence of 14%, compared with 16% among siblings without cancer, and 20% in the U.S. general population. Differences in smoking prevalence between the CCSS participants compared with the other cancer survivor populations may be related to younger age at diagnosis, cognitive impairment, or other sample differences.

As described above, despite the serious health risks, smoking is not uncommon among survivors of childhood and AYA cancer and warrants focused attention from oncologists and other clinicians. The effectiveness of smoking cessation treatments may differ in survivors of childhood and AYA cancer in comparison with patients who develop cancer later in life. These groups may differ in important ways, including emotional reaction to their health status, engagement in active cancer treatment, stress of making multiple life changes in response to their illness, and perception of an imminent threat of smoking. For this reason, research on smoking cessation treatment with other populations with cancer might not generalize to the child and AYA survivor population and vice-versa.

The Partnership for Health (PFH) study is one of the few large-scale studies focused on addressing smoking cessation among childhood and AYA cancer survivors. The PFH-1 randomized 796 currently smoking CCSS participants to either a self-help condition, involving receipt of a cessation brochure ($N = 398$) or to telephone counseling provided by counselors who were themselves childhood cancer survivors ($N = 386$).[495] Participants in the peer-delivered telephone counseling group received a written report that provided feedback tailored to their smoking status, cancer type, treatment regimen, and other survivorship topics; peer-counselors worked with participants over the course of the intervention, providing up to six calls over a 7-month intervention period. Telephone counseling group participants were able to receive free NRT for themselves and spouses/partners; the self-help group was advised of the utility of NRT but were required to purchase it themselves. At both 8- and 12-month follow-up, the peer-delivered telephone counseling condition had significantly higher quit rates than the self-help group (16.8% vs. 8.5% at 8 months and 15% vs. 9% at 12 months, respectively; at 12 months, OR = 1.99, 95% CI = 1.27–3.14). In a subsequent long-term assessment of the PFH study (2–6 years post baseline), cessation rates continued to be significantly higher among the peer-delivered telephone counseling group than in the self-help control group (20.6% vs. 17.6%; $p < .0003$).[496] The authors attribute the higher quit rates seen at the later follow-up time point to both sustained cessation among participants who had quit previously and additional quitting efforts made by participants in the study. Especially high long-term abstinence rates were associated with high levels of self-efficacy for smoking cessation at baseline and by NRT use during treatment.

A follow-up study, PFH-2, designed to enhance scalability of the intervention, tested a web-based version (*N* = 230) and a print version (*N* = 144) of the original PFH intervention among childhood or AYA cancer survivors who were currently smoking.[497] Participants were recruited from 5 cancer centers in the U.S. and Canada, as well as from survivorship websites; all had been diagnosed with cancer before age 35 and had completed their cancer treatment at least 2 years before the study. Both study arms received a letter from an oncologist encouraging smoking cessation, pharmacotherapy for themselves and their spouse/partner, and tailored and targeted content based on PFH-1 delivered either in print (organized into a series of manuals) or via the web (in discrete sessions). A procedure intended to lead participants to believe that smoking status was being biochemically verified (bogus pipeline) was used to encourage accurate self-report. At the final assessment at 15-months post-randomization, 16.5% of web participants (22/132) and 15.5% of print participants (20/127) reported being abstinent from smoking for the previous 30 days. No differences in smoking cessation (OR = 1.07, 95% CI = 0.50–2.26) and intervention satisfaction were found between conditions suggesting that the more scalable web-based version was similar in effectiveness to the print version.

However, another study raises questions about the effectiveness of evidence based treatments to significantly increase long-term cessation among survivors of childhood and AYA cancer. A study of adult survivors of childhood cancer (*N* = 519) who were enrolled in either the CCCS or the St. Jude Lifetime Cohort study and reported they were "regular smokers" were randomized to receive either a proactive quitline intervention or a reactive quitline intervention.[498] In the proactive condition the quitline called the participant and offered 6 sessions of counseling and 4 weeks of NRT with additional NRT if the participant became abstinent. In the reactive quitline condition, participants who called the quitline were offered the same 6-session counseling intervention as well as 2 weeks of NRT and were encouraged to seek more NRT. These conditions were chosen to mirror "real life" quitline services. The counseling intervention provided to both groups discussed preparing to quit, the quitting process, and short- and long-term relapse prevention strategies tailored to survivors of childhood cancer. Proactive calls were much more effective at increasing counseling treatment engagement than were the invitations to call that occurred in the reactive condition. Of those in the reactive condition, 84% attended ≤1 session while about 75% of participants in the proactive condition attended 2 or more sessions. At 12-month follow-up, the study found only very low and nonsignificant differences in biochemically verified smoking cessation (<2%) in the two study arms. Thus, although the proactive group received more NRT and had a much greater exposure to counseling, the two conditions did not differ in terms of long-term abstinence. Although not all participants were able to be tested for cotinine, the study also documented extremely high rates of inaccurate disclosure of smoking status (80%) among those who were tested.

To better understand inaccurate disclosure of smoking status in this population, a study was conducted among adult survivors of childhood cancer (*N* = 287) enrolled in the St. Jude Lifetime Cohort Study.[499] In addition to assessing tobacco use (both self-reported and cotinine verified) the study also asked participants about marijuana use. The authors found that a substantial portion of both self-reported never and past smokers had biochemical evidence of active smoking (2.5%–6.7% and 19.7%–36.9%, respectively). Inaccurate disclosure was more common among younger survivors, men, and those who were either past or current marijuana users.

In summary, there is evidence from one RCT with long-term follow-up that a peer counseling intervention is more effective than self-help in treating smoking among childhood and AYA cancer survivors. A second study suggests that this intervention may also be effective when implemented using either a print or web-based format. Confidence in the effectiveness of this peer counseling treatment would be bolstered by replication. However, another RCT found little evidence of long-term (12-month) benefit of providing adult survivors of childhood cancer more intensive counseling and longer NRT versus less counseling and a shorter duration of NRT. Studies also indicate that self-reported smoking status among childhood cancer survivors is often inaccurate and that co-occurring substance use (e.g., marijuana) should also be assessed. More research is needed to determine the effectiveness of widely available evidence-based treatments in this population, such as those recommended in the PHS Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*,[17] the Community Preventive Service Task Force reports,[102,103] and the NCCN Guideline.[16] Research questions that should be addressed with this population include how to increase engagement and adherence to smoking cessation treatments and whether particularly effective pharmacotherapies such as varenicline and combination NRT increase long-term abstinence rates. All such research should include biochemical assessment of smoking status, given the unreliability of self-report in this population.

In the past several years, researchers have focused on evaluating behavioral smoking interventions targeted specifically to patients with cancer. Charlot and colleagues conducted a single-arm study with 18 patients with cancer to obtain pilot data on a mindfulness-based smoking intervention.[288] Smoking intensity (cigarettes per day) declined significantly over time among participants in the study, but there was no apparent effect on smoking cessation. Likewise, a small study of CM with 14 patients with cancer yielded long-term cessation among just 2 participants.[289] A relatively large RCT randomized 185 presurgical patients with cancer to either a handheld computer intervention or to NRT plus standard CBT-based counseling.[290] The handheld computer intervention was intended to guide the patient in a scheduled, progressive smoking reduction program to support eventual smoking cessation. Both groups received phone counseling, plus one hospital bedside visit delivered by nurse practitioners over 5 weeks; the majority of participants used smoking cessation medications. At 6 months, the biochemically confirmed quit rate for both groups was 32%. A small pilot study evaluated a smartphone app-based behavioral intervention in 59 patients with cancer.[291] Patients were randomized to the NCI QuitGuide app or to Quit2Heal, an app adapted for patients with cancer, which provided behavioral support for smoking cessation treatment by addressing internalized shame, cancer stigma, depression, and anxiety. At a 2-month follow-up, self-reported cessation was 7% for the QuitGuide app and 20% for the Quit2Heal app. No study has directly evaluated the effects of ACT on smoking abstinence among patients with cancer. However, several small studies have found that ACT significantly improves their emotional well-being and quality of life.[292]

Summary: Behavioral Interventions for Smoking Cessation Among Patients With Cancer. As with studies of smoking cessation pharmacotherapy for patients with cancer, there is a dearth of high-quality research evidence about the effectiveness of smoking cessation counseling or other types of behavioral interventions on long-term smoking abstinence among patients with cancer (follow-up ≥6 months). That is, few large studies used experimental designs that randomized the presence, type, or intensity of counseling so that causal inferences could be made. In addition, there is little evidence that identifies the features or dimensions of counseling that might be especially effective in this population (e.g., targeted to cancer patient's concerns, duration, content, timing). These study characteristics lead to an inability to determine how effective behavioral or counseling interventions are when delivered to patients with cancer and how to deliver them optimally.

In sum, RCTs evaluating counseling in cancer populations have not yielded clear and consistent evidence of counseling effectiveness. However, the consistent effectiveness of smoking cessation counseling with many other populations supports providing patients with cancer with smoking cessation treatments found to be beneficial in the general population.

Relapse Prevention and Chronic Care for Cancer Populations

Little evidence exists regarding relapse prevention interventions in cancer populations. Simmons and colleagues have evaluated the potential use of the Forever Free© relapse prevention self-help guides for use with cancer patients and survivors.[293] Initial work used qualitative methods to inform the development of relapse prevention interventions in the cancer context and to provide specific feedback on the redesign of the guide.[294] A subsequent prospective study with 154 patients with cancer identified predictors of relapse including psychiatric comorbidity, low self-efficacy, fears of cancer recurrence, and low risk perceptions associated with continued smoking.[114] This work led to the development of the Surviving Smokefree® DVD relapse prevention intervention.[295] The DVD was developed with patient and clinician input, embedding patient and clinician testimonials into the program. Initial usability assessments ensured that the program was appealing, promoted comprehension, and was relatable and acceptable to patients.[295] However, an RCT of the Surviving Smokefree relapse prevention program (N = 412) did not show benefit of this self-help treatment versus usual care.[296]

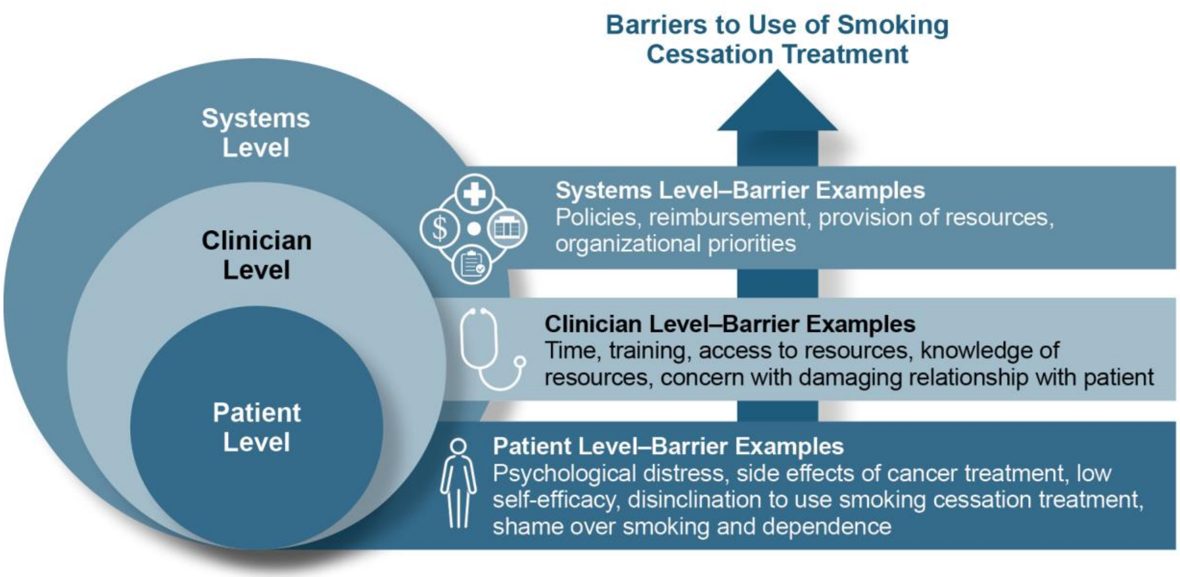
Another approach to the problem of smoking relapse after treatment is the use of chronic care interventions. These interventions are designed to offer treatment opportunities repeatedly over time to those who continue to smoke or who have relapsed after prior quit attempts. Although there have been no studies of chronic care interventions for cancer populations, data from studies of the general population suggest that this approach has promise. A chronic care approach might be feasible in cancer care because cancer treatment often involves extended contact over time, during which renewed offers of smoking cessation treatment and treatment delivery could be provided. In addition, because research in the general population shows that certain pharmacotherapies, such as varenicline, can sustain abstinence in those who have quit successfully,[105] this approach should be evaluated in patients with cancer who have recently succeeded in quitting. Finally, the development of effective relapse prevention or chronic care treatments might be informed by research that reveals factors that predict a decreased likelihood of patients with cancer quitting successfully or staying quit.[297]

Summary: Relapse Prevention and Chronic Care for Cancer Populations. Little is known about how to sustain smoking cessation among patients with cancer or how to increase renewed quitting efforts among those who have relapsed. Strategies that have shown promise in the general population include provision of varenicline to those who have recently quit successfully and chronic care approaches that periodically offer smoking cessation treatment over time to individuals who have not attained stable abstinence.

Special Considerations and Barriers Concerning Smoking Cessation Treatment in Cancer Care Settings

It has long been clear that effective smoking cessation treatments exist but that these are too rarely implemented in the cancer care setting.[10,11] NCI has made substantial investments in implementation science efforts to increase the use of evidence-based treatments in general and for risk behaviors such as tobacco use across the cancer care continuum.[298] Such efforts are guided by established conceptual models and utilize implementation strategies[299,300] that prioritize the identification of patient-, clinician-, and systems-level determinants of implementation success[301] (Figure 3.2). The discussion that follows addresses the first two of these influences on implementation success in order to inform future efforts to develop effective methods for treating tobacco use in the cancer care context. Systems-level barriers are discussed briefly in this chapter but are discussed at length in chapter 4.

Figure 3.2 Examples of Patient-, Clinician-, and Systems-Level Barriers to the Use of Smoking Cessation Treatment in Cancer Care Settings



Patient-Level Barriers to Treating Tobacco Use in Cancer Care Settings

When considering the design of studies of smoking interventions for patients with cancer or when considering the implementation of a smoking cessation treatment program within the context of cancer care, it is vital to consider patient characteristics that might influence treatment effectiveness. Patient factors such as psychiatric comorbidity, oncology treatment–related challenges, and willingness to engage in and adhere to smoking cessation treatment, can be key determinants of treatment effectiveness.

Psychiatric Comorbidity

A cancer diagnosis and its medical treatment can lead to clinically significant psychological distress[302] that typically involves symptoms of depression and/or anxiety[303,304] as well as anhedonia.[305] For example, a study of the tobacco cessation treatment program at the University of Texas MD Anderson Cancer Center found that more than 40% of patients with cancer enrolled in tobacco use treatment had a current psychiatric disorder, including depression and anxiety.[306] Such symptoms have been extensively examined as important correlates of smoking behavior.

With regard to research on individuals in the general population, a systematic review and meta-analysis of smoking cessation treatment outcomes among people who smoke with and without past major depressive disorder (MDD) examined 42 RCTs published between 2000 and 2008. This review found that people who smoke with past MDD had 17% lower odds of short-term abstinence and 19% lower odds of long-term abstinence than people who smoke without past MDD.[307] Research has also explored the relationship between anxiety and smoking cessation. Systematic reviews have demonstrated that anxiety disorders are associated with an increased risk of both initiating tobacco use[308] and developing nicotine dependence.[309] Studies indicate that individuals with anxiety disorders tend to have less smoking cessation success than other people who smoke[310] and relapse at higher rates even when provided evidence-based smoking cessation treatment.[311,312] In sum, and as also discussed in chapter 5, psychiatric comorbidities, particularly depressive symptoms and active substance use disorders, are associated with a lower likelihood of quitting after a cancer diagnosis and with an increased risk of relapse.[313–317]

The reasons for the reduced quitting success of people with anxiety and depression diagnoses are unclear. Some evidence suggests that individuals with anxiety and depressive disorders have stronger withdrawal symptoms than individuals without these disorders[318] but other evidence counters this explanation.[319]

Few studies have evaluated the relationship between depression and anxiety symptoms and smoking cessation outcomes in patients with cancer. However, the available literature shows that greater symptoms of depression and anxiety are associated with continued smoking following a cancer diagnosis.[114,313,320,321] In a prospective study with 175 patients with cancer, higher levels of baseline depressive symptoms predicted a greater likelihood of smoking relapse at follow-up.[322] In an analysis of more than 2,000 patients with cancer who received smoking cessation counseling and medication, patients with a history of panic attacks were significantly less likely to quit smoking than those without a history of panic attacks.[323] Research is needed to develop additional treatment strategies that mitigate some of the risk posed by the psychiatric comorbidities that are common among patients with cancer. Conceptual frameworks that focus on the link between affect and smoking are leading to new treatment approaches that may mitigate the effects of psychiatric disorders and symptoms on smoking cessation success.[324,325] Chapter 5 reviews evidence regarding the relationship between severe mental illness and smoking and smoking cessation success.

Oncology Treatment–Related Challenges

A cancer diagnosis is often also accompanied by stress due to physical and other challenges related to debilitating surgeries and prolonged adjuvant chemotherapeutic and radiation therapies. The stress related to cancer and its treatment can make quitting smoking more difficult.[326] For clinicians, these challenges can make it difficult to prioritize and deliver smoking cessation treatment; they also make it difficult for patients to engage in smoking cessation treatment themselves. More significantly, these challenges can undermine the patient’s hope for recovery and promote fatalism, casting doubt on the benefits of smoking cessation or the effort needed to attain it.[32,37] These challenges need to be considered when developing models of smoking cessation treatment in cancer care settings.

Physical Concerns

Several practical, physical challenges facing patients with cancer should also be considered. Patients with head and neck cancer, in particular, may experience impaired swallowing, which could make it difficult to take oral medications like varenicline and certain NRTs. Similarly, some phases of cancer treatment may also make it difficult to take oral medications for tobacco cessation (i.e., chemotherapy and radiation often cause xerostomia [dry mouth]).[327] Chemotherapy often causes nausea and vomiting, which are also common side effects of varenicline and bupropion,[328,329] so their use may exacerbate such symptoms and reduce use. Indeed, nausea reactions from varenicline are associated with discontinuation of its use.[330] Pain is also a very common complication of both cancer and cancer treatment; pain has been associated with a higher rate of smoking among patients with cancer[331] and in the general population.[332] Further, although patients may make frequent visits to the clinical setting for medical care, cancer treatment–related complications may impair the patient's ability to attend in-person counseling visits for smoking cessation treatment. Phone and video counseling may be used to address this barrier.

Psychological Aspects

There are also broader psychological aspects of cancer treatments and their associated complications, symptoms, and side effects that create challenges for smoking cessation treatment. Lack of sleep and feelings of hopelessness may contribute to stress, which can interfere with participation in treatment programs.[34,333] Further, for patients with advanced disease and limited life expectancy, the effects of smoking cessation treatment on the patient's quality of life, either negatively or positively, should be considered when exploring patients' goals regarding quitting smoking. Cancer and its treatment entail considerable stress; striving to quit smoking and engage in smoking cessation treatment may add to this stress in the short-term.

Therefore, addressing the physical and psychological factors associated with the treatment of cancer should be part of planning for smoking cessation treatment in cancer care settings. Patients with cancer often report thinking that smoking will help them manage their stress, so clinicians need to consider how best to help patients find healthy methods to cope with stress. In addition, the clinician needs to help the patient focus on the long-term benefits of quitting smoking and to counter any sense of guilt or self-blame the patient may have regarding their smoking.[259] The provision of support and treatments that address cancer-related stress during the patient's smoking cessation and cancer treatment may be needed to optimize patient outcomes.[233,290,334]

Treatment Engagement and Adherence

A wealth of evidence derived from the general population shows that using FDA-approved smoking cessation medications increases the likelihood of smoking cessation success during aided quit attempts.[17,21,149,335] Unfortunately, the vast majority of those who smoke and who try to quit do not use FDA-approved medications in their attempts. Data from Medicaid,[336] Medicare,[337] and outpatient health care settings[338] show that fewer than 30% of patients interested in quitting use medication in their quit attempt.[27] Likewise, although research suggests that patients with cancer are very receptive to treatment referral,[339] only about one-third to one-half of patients with cancer report using FDA-approved medication in previous quit attempts.[340,341] Indeed, an analysis using data from the Population Assessment of Tobacco and Health (PATH) study showed that, among 331 participants with a cancer history, one-half attempted smoking cessation without any form of treatment, only 36.5% used medication and/or counseling, and 13.2% used e-cigarettes in lieu of treatment (see "ENDS Use and Cessation From Cigarettes in Cancer Populations").[342] Importantly, medication use was associated with a greater likelihood of tobacco cessation in this study. Another study suggested that providing cessation treatment by tobacco treatment specialists to patients with cancer via smartphone video may be preferred by patients and may increase overall treatment engagement.[239]

This avoidance of treatment can also occur in tobacco users in the general population.[27] This preference for unassisted smoking cessation attempts may reflect patient guilt about their smoking, depression, poor self-efficacy, or a lack of appreciation that evidence-based smoking cessation treatments can mitigate withdrawal symptomatology and enhance quitting success.[341,343] Lung cancer, in particular, is associated with stigma emanating from the perception that the patient's cancer is a self-induced disease[344]; this frequently leads to guilt, negative judgment, isolation, and defensiveness,[345] which may impede patients from seeking appropriate intervention.[346,347]

In addition to low levels of use of evidence-based treatments for smoking, low rates of treatment adherence are also a concern. There is a growing literature from studies conducted in the general population that shows that adherence to smoking cessation medication is a critical determinant of treatment efficacy.[348–350] Reviews show that rates of nonadherence to varenicline (i.e., taking <80% of medication) and the nicotine patch (i.e., using the patch <5/6 days per week) are very high (~40% or higher in many studies), and nonadherence significantly diminishes the likelihood that people who smoke will successfully quit.[348,351] For example, in the general population, 55% of patients receiving varenicline in a primary care setting were adherent and quit rates were nearly doubled for these patients versus those who were nonadherent or partially adherent.[138] Additionally, evidence using electronic monitoring of smoking cessation medication supports a causal model in which decreases in medication use precede the occurrence of lapses in smoking cessation.[352] Such findings appear to be highly relevant to patients with cancer.

Additional studies have shown that adherence to varenicline among patients with cancer is about 43%–55% and greater adherence is associated with improved quit rates.[12,272,353] Thus, strategies that enhance adherence to smoking cessation medication have the potential to increase smoking cessation rates both among the general population and among patients with cancer. Several studies point to the rate and intensity of side effects as important factors associated with nonadherence, which argues for efforts to monitor side effects in patients with cancer and adjust medication accordingly.[330,349,354,355] The above evidence suggests that medication adherence be monitored and encouraged when medication is used in smoking cessation treatment with cancer patients. This is consistent with the NCCN clinical practice guidelines in oncology.[16] Kotsen and colleagues discuss the need for tailoring medication usage, medication effectiveness and side effects, and behavioral interventions in the context of multisession counseling treatment.[356]

Clinician-Level Barriers to Treating Tobacco Use in Cancer Care Settings

Leveraging the Opportunity for Intervention

Oncology clinicians are well positioned to refer or to initiate the treatment for nicotine dependence for their patients with cancer who continue to smoke, given the frequency with which they typically interact with patients and patients' willingness to follow their treatment advice. Indeed, ample evidence from the general population suggests that clinicians can boost smoking cessation rates if they deliver smoking cessation treatment.[17,106] As such, several professional organizations such as the American Association for Cancer Research,[6] the NCCN,[16] the American Society of Clinical Oncology,[357] and the International Association for the Study of Lung Cancer[358] have developed and disseminated tobacco use treatment guidelines to help clinicians incorporate cessation intervention into their oncology workflow. Unfortunately, consistently addressing tobacco use among patients with cancer is a clinical practice gap at the clinician and systems levels.[10,11,13,14,281,359,360] Although more than 80% of patients are routinely screened for tobacco use during oncology visits, fewer than half of oncology clinicians provide formal assistance with smoking cessation, including referral, medications, or counseling.[361,362] This is consistent with observations in other practice settings such as in primary care, where identification of smoking status often exceeds 95% and recommendations to quit exceed 65%, but performance of the more complex, second-order components of delivering smoking cessation treatments and providing follow-up remain suboptimal.[17,31,363,364]

Barriers to Intervention and Strategies to Overcome Them

Oncology clinicians generally understand that continued tobacco use during cancer care significantly affects treatment outcomes and recognize their potential role in promoting abstinence.[361] Close to 90% of oncologists agree that tobacco cessation treatment should be a standard part of cancer care. However, several practical factors impede the integration of tobacco cessation treatment into practice workflows. For example, almost half of oncology clinicians report limited available time during the visit for counseling or for arranging referrals.[361,362,365] Oncologists must balance competing priorities in cancer care, including cancer therapy decisions, cancer therapy side effects, treating and managing medical comorbidities, infection control, psychological distress, and sometimes acute life-threatening issues that demand immediate attention. Further, many clinicians report having too little time to intervene with smoking, having too few tobacco cessation treatment resources for their patients or being unaware of those that exist, and having too little training to deliver nicotine dependence treatment effectively.[361,362,365,366] All of these factors or beliefs likely discourage oncology clinicians from delivering smoking cessation treatment with their patients who smoke. Finally, a perceived lack of reimbursement for tobacco intervention or billing difficulties are also cited as obstacles to care by oncology clinicians.[361,362,365]

Importantly, advances have been made over the past 2 decades that can help clinicians overcome the barriers noted above. These include mechanisms for direct reimbursement for both the evaluation and management of tobacco dependence[136] and a national quitline portal (see "Telephone Counseling"). Chapter 4 contains additional information on strategies that clinicians can use to provide their patients with smoking cessation resources.

Despite advances, more progress is needed. For example, despite the availability of computerized reminders, comparative feedback, and even direct payments for meeting performance metrics, referral to smoking quitlines remains low.[9,113,367] The NCI C3I (see chapter 4) has provided funding to develop programs designed to increase the availability of onsite tobacco cessation treatment resources in 52 NCI-Designated Cancer Centers. Though screening rates for tobacco use are fairly high at many cancer centers,[368] one center reported that, despite implementation of an opt-out referral process designed specifically to minimize oncology workflow interruption (i.e., a standard default order in the EHR to a tobacco cessation treatment program for all patients who smoke), up to 60% of automated orders for referral were canceled by the treatment team.[369] These orders were cancelled due to factors such as clinician concerns about low patient interest, the appropriateness of addressing tobacco use at a given point in time, a perceived lack of smoking cessation treatment efficacy, caseload, and patient characteristics (e.g., treatment stage, cancer type). Such findings suggest that clinician education should be a part of any smoking cessation treatment program implementation. This accords with other evidence that identifies clinician factors that impede tobacco use intervention in cancer care.

Common myths among oncology clinicians that may reduce the likelihood that they would provide smoking cessation treatment to patients include: (1) it is too late to quit once a person has cancer, (2) the time of diagnosis is not suited to addressing tobacco use, (3) patients with cancer lack interest in quitting, (4) quitting smoking among patients with advanced disease is unimportant, and (5) it is not the oncologist's job to address tobacco use.[370,371] In addition, clinician surveys have found that at least 58% of oncologists queried felt they would be unable to get patients to quit using tobacco, and more than two-thirds believed their patients would be resistant to cessation treatment.[361,362,365] This therapeutic nihilism appears to stem from the influence of several key cognitive biases, one of which is a focus solely on immediate medical needs rather than on the long-term benefits of quitting smoking.[372] In addition, culpability bias (i.e., the illness is implicitly interpreted as the result of a controllable decision) may negatively influence the willingness of some clinicians to offer help to patients (with cancer or other diseases) and has been identified among general practice clinicians caring for people who smoke.[373] This bias may, in part, be responsible for the differences in patterns of referral to and use of tobacco cessation treatment observed in patients with advanced lung cancer compared to patients with advanced breast cancer.[374]

Changing Clinician Approaches to Smoking Cessation Treatment

A patient's diagnosis and treatment of cancer are teachable moments when the patient and the patient's family members may be receptive to information about the heightened risks of smoking and the benefits of quitting.[375] There are approaches that clinicians can take to better leverage such opportunities for intervention. The literature supports adoption of several simple practice changes in the oncologic approach to smoking cessation. First, clinicians can help patients feel less defensive by reframing smoking cessation treatment as treating an underlying illness (dependence) rather than focusing on smoking as a personal behavior.[376] This approach gives clinicians the opportunity to focus their discussion on the nature of dependence and on anticipated pharmacotherapeutic effects to achieve their goal.[377] Second, adopting an empathic communication strategy wherein the clinician actively seeks to understand the patient's experience and point of view is associated with higher rates of patient satisfaction with treatment and lower levels of psychological distress.[378,379] Lastly, clinicians' model of care should incorporate treating tobacco use as a means of improving the effectiveness of their medical approach to cancer treatment, which is relevant to all patients with cancer regardless of whether their tumor is tobacco-related (see chapter 4).

Care teams can facilitate smoking cessation by adopting a proactive outreach approach.[380] Developing an approach that automates or routinely identifies tobacco use status as an important topic of discussion before the clinical care visit can increase the patient's comfort with the tobacco discussion. Such a proactive approach has the additional advantage of being independent of the clinician's estimation of the patient's ability to quit. Chapter 4 provides more information on strategies to incorporate smoking cessation treatment into oncology workflows and contexts.

Systems-Level Barriers to Treating Tobacco Use in Cancer Care Settings

Ensuring the consistent and comprehensive delivery of evidence-based treatments for tobacco use requires consideration of the broader systems or organizations within which cancer care is delivered[381] (see also chapter 4). Leadership, policies and protocols, and infrastructure can play critical roles in influencing the delivery and uptake of evidence-based smoking cessation treatments for patients with cancer (see chapter 4). In particular, institutional commitment, organization-wide policies, and the availability of critical resources to support smoking cessation treatment in cancer care can influence patient engagement in such services.[369,382]

Systems-wide changes can have a significant impact on the provision of smoking cessation treatment in the clinic. Leadership teams can explicitly support smoking cessation treatment; direct financial support of personnel, medications, and equipment can meaningfully increase smoking cessation treatment in a cost-effective way[383] and may enhance patient satisfaction.[384] Evidence from primary care contexts suggests that EHR enhancements that promote smoking cessation treatment engagement can also lead to a greater likelihood of smoking intervention with medically underserved and vulnerable populations.[9,228] Integrating smoking cessation treatment into existing service-line quality metrics creates new norms and can have a powerful influence on organizational change.[31,385] Finally, the language used in promotional materials and patient communications should impart a supportive, destigmatizing message and normalize conversations around tobacco use.[376]

Chapter 4 further discusses systems-level challenges, opportunities to deliver smoking cessation treatment, and provides information on the costs of smoking and the cost-effectiveness of smoking cessation treatment in cancer populations.

Summary: Special Considerations and Barriers Concerning Smoking Cessation Treatment in Cancer Care Settings

The success of coordinated efforts to address smoking by patients with cancer largely depends on the ability to overcome a range of patient-, clinician-, and systems-level barriers. Patient-level barriers include competing demands related to their cancer treatment, pain, psychological distress, and guilt regarding their tobacco use. Clinician-level barriers include limited time per encounter, clinicians' beliefs that FDA-approved cessation medications are ineffective, an actual or perceived lack of training in providing smoking cessation treatment, and beliefs that the patient will be uninterested or unable to quit smoking successfully. Systems-level barriers include a lack of clear and consistent emphasis on tobacco intervention by organizational leadership and a lack of policies, protocols, and infrastructure that support smoking cessation treatment. Remaining mindful of these issues as cancer care programs adopt new policies and actions to address patient tobacco use will help increase the ultimate impact of these efforts.

Special Topics in the Treatment of Smoking in Patients With Cancer

This section discusses two special topics relevant to the treatment of smoking in the cancer care setting. First, it is important to identify and address patient motivation to quit smoking and engage in evidence-based smoking cessation treatment. Second, a discussion about whether smoking cessation treatments require targeting or adaptation with regard to biological factors and sociodemographic variables (including race and ethnicity and gender) is included. Research on the general population is reviewed in these sections and the potential relevance to cancer populations is considered.

Addressing Motivation to Quit

As discussed at the beginning of this chapter, data indicate that many patients with cancer are motivated to quit smoking and are receptive to offers of smoking cessation treatment. However, some patients will not express interest in quitting, and these patients should be offered specific motivational interventions. Some interventions have shown promising effects in increasing smoking cessation motivation in the general population literature and may be useful in promoting quitting motivation in patients with cancer. These include NRT sampling[386,387] and the use of varenicline or NRT in the context of a smoking reduction effort.[119,140] These approaches have not been tested with patients with cancer, but other approaches such as opt-out referral strategies[388,389] have been used successfully to increase patient engagement (see chapter 4).

Relevance of Pharmacogenetic Intervention: Steps Toward Personalized Medicine

Multiple factors influence the likelihood of smoking cessation (e.g., exposure to others smoking),[390] and it is now widely acknowledged that genetic factors do so as well.[391,392] Twin studies have concluded that as much as two-thirds of the variability in the ability to quit smoking may be attributable to genetic factors,[393–395] including the results of smoking cessation attempts,[395] the duration of smoking cessation,[396] and the self-reported level of withdrawal symptoms.[395] The heritable dimensions of smoking cessation have also been suggested by adoption studies, which have shown that a person's ability to quit smoking is strongly associated with their adopted-away, biological sibling's ability to quit smoking.[397] A greater understanding of the neurobiology of nicotine dependence, and a growing recognition of the genetic influences on both dependence and the ability to quit smoking, have prompted researchers to explore specific genetic polymorphisms, or groups of genetic polymorphisms, linked with smoking-related phenotypes, such as the ability to quit smoking and the response to specific treatments. For instance, one polygenic model applied to longitudinal, developmental smoking data predicted the escalation of smoking, the development of dependence, and the likelihood of smoking cessation.[398]

Genetic markers, such as variants in nicotinic acetylcholine receptors and variants in the dopaminergic, serotonergic, or opioid pathways, have been examined as potential moderators of response to treatments for nicotine dependence.[399,400] Candidate gene studies, genome-wide association studies, and linkage analysis studies have evaluated variability in nicotinic receptors (e.g., *ChAT* or the *CHRNA5* gene) and nicotine metabolizing genes (*CYP2A6*),[401] variability in dopaminergic genes (e.g., *ANKK1*, *DRD2*), variability in serotonergic genes (e.g., *5-HTTLPR*), variability in the opioid pathway (e.g., *OPRM1* gene), and variability in markers of bupropion metabolism (*CYP2B6*) as potential moderators of response to NRT, bupropion, and varenicline; however, results have been mixed thus far.[399,400,402]

In contrast, studies of the nicotine metabolite ratio (NMR), a biomarker of individual differences in nicotine metabolism, affected by both genetic variation from *CYP2A6* variants and other factors that influence nicotine metabolism (e.g., race, sex), have yielded more consistent effects and suggest a method for personalized treatment for nicotine dependence.[137] More specifically, four studies have shown that individuals who smoke and have slower nicotine metabolism report higher quit rates with NRT compared to individuals who smoke and have faster (i.e., normal) nicotine metabolism.[403–406] A secondary analysis of a placebo-controlled bupropion study showed that bupropion significantly enhanced quit rates for fast metabolizers of nicotine, but not for slow metabolizers,[407] and a prospective study showed that varenicline was more effective at treating nicotine dependence for faster nicotine metabolizers than was NRT.[408]

The studies cited above using retrospective analysis linking NMR to treatment response led to the first prospective NMR-stratified pharmacogenetic trial of treatments for nicotine dependence, in which 1,246 individuals who smoked were characterized as slow or fast (i.e., normal) metabolizers of nicotine. These individuals were randomized to placebo patch and placebo pill, nicotine patch and placebo pill, or varenicline and placebo patch.[409] The results showed that, at both end-of-treatment and 6 months after the target quit date, faster metabolizers had significantly higher quit rates if treated with varenicline versus the nicotine patch and that slow metabolizers exhibited similar quit rates across the two treatments but reported more severe side effects if treated with varenicline. In a number-needed-to-treat (NNT) analysis, there was little difference in the NNT to yield 1 successful quitter (10.3 for patch vs. 8.1 for varenicline) among slow metabolizers. However, among fast metabolizers, the NNT to yield 1 successful quitter was 26 for the patch versus 4.9 for varenicline. Thus, treating slow nicotine metabolizers with the patch and fast nicotine metabolizers with varenicline may maximize effectiveness, minimize side effects, and reduce costs (e.g., versus treating all individuals with varenicline). Future studies might examine the possibility that translating this NMR-based treatment algorithm into clinical practice improves quit rates.[137] This approach may have heightened relevance for patients with cancer because some evidence suggests that faster nicotine metabolism is associated with a greater cancer risk, presumably because faster metabolism leads to higher levels of nicotine intake and consequently greater carcinogen exposure.[399,410–412] Studies are needed to examine the potential use of the NMR to personalize treatment for tobacco use in the cancer context as a way to improve treatment effectiveness. In addition, a quick and inexpensive assay of NMR might increase research use and clinical application of this approach to smoking cessation treatment personalization.[31]

Future research may also reveal the potential for genetic data to enhance patient activation or readiness to quit. Information on the relationship between nicotine metabolism and cancer risk might be used to motivate quitting by patients with cancer, cancer survivors, and any individual who smokes. Similarly, education about the high-risk variants in *CHRNA5* on chromosome 15q25 may be used to enhance quitting motivation. Status of the *CHRNA5* variant rs16969968 has been shown to predict delayed smoking cessation among the general population; smokers with the high-risk genotype quit at mean age 56 versus age 52, the mean age at which individuals with the low-risk genotype variant quit.[413] Similarly, those with the high-risk genotype had a 4-year earlier age of lung cancer diagnosis (61 years) compared to those with the low-risk genotypes (65 years).[413,414] The use of genetic risk feedback for people with cancer who smoke remains an understudied but potentially useful intervention tool.

Treatment Effectiveness and Access Across Different Populations

Although smoking prevalence has declined significantly in the general population over the past half-century, it is disproportionally higher among some populations.[93,415,416] In addition, differences exist in the likelihood of successful smoking cessation across sexes,[417] racial and ethnic groups,[418,419] and by socioeconomic status.[93,420–423] Some racial and ethnic minority groups and people of lower socioeconomic status may be less likely to receive advice to quit smoking, use evidence-based smoking cessation treatments, and be successful in their quit attempts.[27,418,424,425]

Differences in smoking patterns, smoking effects, and cessation success among different populations may raise the question as to whether evidence-based smoking cessation treatments are effective in these populations. For example, sex differences in the effects of nicotine, reactivity to smoking cues, abstinence-induced withdrawal, and response to smoking cessation intervention have been documented.[426–430] A 2017 meta-analysis examined the efficacy of pharmacotherapy in women compared with men. Compared with placebo, medications improved quit rates for both sexes. There was a statistically significant difference in 6-month abstinence among women treated with varenicline compared with women treated with transdermal nicotine or sustained-release bupropion, suggesting that clinicians may wish to prescribe varenicline as a first treatment option for female patients.[431] There are also smoking cessation treatments that have been adapted for certain populations. For instance, a group-based culturally specific CBT for smoking cessation among low-income African Americans has been shown to be effective.[432] However, there is substantial evidence that smoking cessation treatments for the general population are effective in women, different racial and ethnic minority groups, and groups with lower incomes.[17,433–435] Such interventions are widely available and therefore can achieve high reach in different populations of persons who smoke. Considerations for delivering smoking cessation treatment to vulnerable and medically underserved populations are further discussed in chapter 5.

The Use of Electronic Nicotine Delivery Systems (ENDS) in Patients With Cancer

ENDS comprise a rapidly changing class of tobacco products (e.g., e-cigarettes, vapes, mods, tank systems). Despite their heterogeneity, all ENDS deliver an aerosol to the user that typically contains a mixture of nicotine, propylene glycol, vegetable glycerin, and flavoring chemicals. Over the past decade, the prevalence of ENDS use has dramatically increased, particularly among youth and young adults.[436] ENDS use has increased both in the general population and in cancer patients and survivors.[437,438] In the United States, ENDS are classified as tobacco products and no ENDS product has been approved by the FDA for use as a smoking cessation aid. However, patients often ask oncologists and other clinicians about ENDS as an alternative to cigarette smoking and whether they can be used as a smoking cessation aid.[439,440] This section provides a brief overview of the current literature on the prevalence of use, the health effects, and the effects of ENDS on smoking cessation, with specific attention to patients with cancer.

The literature on ENDS is complicated by several factors. For example, many of the studies discussed below were conducted before 2018 and involved early-generation ENDS products (e.g., cig-a-likes). Compared to ENDS devices available as of 2022, these earlier products, particularly the cig-a-likes, tended to have lower nicotine yield profiles than that of cigarettes.[441] Newer ENDS products contain nicotine salt formulation and/or have customizable design features that can facilitate increased nicotine delivery that more closely mimics cigarette smoking.[441,442] Therefore, many of the studies discussed below do not reflect the design features and nicotine delivery efficiencies of newer ENDS products. Also, many studies are heterogeneous regarding the type of ENDS devices used and their characteristics (e.g., settings, nicotine content, and formulation), or do not measure these factors. The literature also includes both RCTs as well as observational studies; as discussed below, both study types have strengths and limitations.

Prevalence of ENDS Use

As of 2019, 4.5% of U.S. adults reported current (every day or some days) ENDS use. Among adult current ENDS users, 36.9% were also current cigarette smokers, 39.5% were former cigarette smokers, and 23.6% were never cigarette smokers. Young adults (ages 18–24 years) had the highest prevalence of ENDS use of all age groups (9.3%); more than half of young adult ENDS users (56%) reported they had never smoked cigarettes.[443] The primary reasons that adult dual users (i.e., individuals who report current use of both cigarettes and ENDS) offer for using ENDS are to mitigate withdrawal symptoms during times when smoking is not permitted, to reduce the number of cigarettes smoked and exposure to the harmful constituents in cigarettes, and as a way to quit smoking.[31,444–446] Indeed, more than one-half of dual users report using ENDS as a way to quit smoking[444,446,447] and about 80% indicate that they perceive ENDS to be less harmful than cigarettes.[446,448]

Several studies have reported the prevalence of ENDS use among patients with cancer and/or among those with a history of cancer; across these studies, the overall prevalence of current ENDS use ranged from 1.6% to 4.1%.[449–454] Across samples of patients with cancer or those with a history of cancer who report current use of cigarettes, the prevalence of current ENDS use ranged from 11.6% to 23.1%.[452–458] Similar to ENDS users without a cancer diagnosis, the majority of cancer patients and cancer survivors who use ENDS report doing so to help them quit smoking and because they perceive them to be less harmful than cigarettes.[454,457–459] Additionally, Correa and colleagues found that patients with cancer believed that ENDS were less addictive, less expensive, less stigmatizing, and less likely to affect cancer treatment than cigarettes.[459]

Health Effects of ENDS

Research has demonstrated that the exposure to toxicants in ENDS aerosols varies by device type, e-liquid composition, user behavior, and other factors.[445] In general, ENDS expose users to fewer toxicants and lower levels of toxicants than cigarettes. For example, a report of the National Academies of Sciences, Engineering, and Medicine concluded that, "taken together, the evidence in support of these conclusions suggests that e-cigarette aerosol contains fewer numbers and lower levels of toxicants than smoke from combustible tobacco cigarettes."[445,p.6] However, while noting the relatively lower toxicant exposure from ENDS, this report also noted that ENDS emit numerous harmful and potentially harmful substances, including carcinogens and metals, and that the amounts vary greatly across different types of ENDS products. Preclinical and clinical, as well as epidemiological, studies published after the National Academies of Sciences, Engineering, and Medicine report demonstrate that ENDS products can have adverse respiratory, cardiovascular, and immunological effects.[460] Moreover, as noted above, some ENDS users also smoke cigarettes (i.e., engage in dual use), often employing ENDS as a mechanism to cope with settings in which cigarette smoking is not allowed. Some studies indicate that dual use of cigarettes and ENDS may lead to greater toxicant exposure and risks of health harms than use of cigarettes alone[461–463]; however, other studies do not find such effects.[464,465]

A recent nationally representative longitudinal study analyzed the association of ENDS use with any self-reported cardiovascular disease, using data collected in five waves of the PATH study from 2013 to 2019.[466] Participants (N = 24,027) were categorized as nonusers (no current use of ENDS or cigarettes), exclusive cigarette smokers, exclusive ENDS users, or dual users of ENDS and cigarettes. In this study, the risk of cardiovascular disease was similar among dual users (of ENDS and cigarettes) and exclusive cigarette smokers; exclusive ENDS use was associated with a small, nonsignificant increase in risk of any cardiovascular disease, relative to individuals who used neither ENDS nor cigarettes. These authors' findings accord with the uncertainty regarding the harms of exclusive ENDS use but clear and significant risk of dual use of ENDS and cigarettes.

An appraisal of the net health effects of ENDS is currently limited by the fact that many studies are preclinical in nature, assess only short-term or acute ENDS use, or are nonrandomized, cross-sectional studies that do not permit strong inference. Rigorous assessment of the health effects of long-term ENDS use remains a critical priority; assessment of existing and novel biomarkers of cardiovascular harm and cancer-related progression and outcomes can increase researchers' understanding of long-term health risks.[460] Finally, it is also important to note that ENDS use will serve to increase harm if it delays complete cessation from cigarette products.[31]

ENDS Use and Cessation From Cigarettes in the General Population

Most of the research on the relationship between ENDS use and smoking cessation comes from cross-sectional and prospective cohort studies conducted in the general population. This research provides mixed evidence that the use of ENDS may help or hinder adult smoking cessation.[467–471] Some studies and meta-analyses found no statistically significant association between ENDS use and quitting smoking.[31,470,472] The 2020 Surgeon General's report concluded that "the evidence is inadequate to infer that e-cigarettes, in general, increase smoking cessation."[31,p.11] In addition, the report found suggestive but not sufficient evidence that "more frequent use of e-cigarettes is associated with increased smoking cessation compared with less frequent use of e-cigarettes."[31,p.11] Consistent with this, a meta-analysis published after the 2020 Surgeon General's report found evidence that daily use of ENDS was positively associated with increased smoking cessation in observational or population studies; less than daily use was associated with reduced smoking cessation.[473] Finally, some cohort studies show that former smokers may relapse back to smoking if they use ENDS following cigarette cessation.[474–476] A 2017–2019 analysis of data from the nationally representative PATH Study found that among individuals attempting to quit smoking cigarettes, those who used ENDS in their quit attempt were less likely to be successful.[471]

Inferences from nonrandomized cross-sectional and prospective cohort studies about the effects on ENDS on smoking cessation can be limited by: (1) potential selection biases in sampling; (2) intrinsic differences in those who choose to use ENDS and those who do not, differences that can be difficult to control for statistically; (3) imprecise measurement of ENDS product characteristics and use behavior, which may affect the observed relation between ENDS use and smoking cessation[31]; and (4) heterogeneity in ENDS use (type, intensity) over time and across individuals. Therefore, observational studies do not afford as strong a level of inference about the effects of ENDS on cessation as do RCTs designed to test the efficacy of ENDS as cessation aids.[31] However, an important potential limitation of RCTs is that their results reflect the ENDS product used in the study, with the chosen device characteristics, and not the effects of ENDS products in general. Also, volunteers for such studies might not reflect the effects of ENDS in nonvolunteers. For instance, volunteers may be much more motivated to stop smoking and therefore achieve higher cessation rates when provided ENDS devices. Therefore, generalizability of RCT findings may not translate to the plethora of ENDS products on the market, nor the context of real-world use.

Randomized Controlled Trials

A 2021 Cochrane Review evaluated RCTs that compared interventions using nicotine-containing ENDS against several different comparison conditions.[477] The authors identified 34 RCTs with follow-up data for at least a 6-month period. A meta-analysis of 4 RCTs (N = 1,924) found that individuals who were randomized to nicotine-containing ENDS achieved higher long-term smoking abstinence rates than did those assigned to use NRT (RR = 1.53, 95% CI = 1.21–1.93). The estimate is that this effect would yield three more cigarette abstainers per 100 (95% CI = 1–6) than would occur with NRT use. This finding was rated with a moderate level of certainty of the evidence, limited by imprecision. In addition, 5 studies randomized people to nicotine-containing ENDS or placebo (non-nicotine) ENDS (N = 1,447). A meta-analysis of these studies yielded moderate-certainty evidence, limited by imprecision, that long-term cigarette abstinence rates were higher in individuals randomized to nicotine-containing ENDS than placebo ENDS (RR = 1.94, 95% CI = 1.21–3.13). In absolute terms, this might lead to an additional 7 more abstainers per 100 (95% CI = 2–16) than would occur with placebo ENDS. Finally, the authors conducted a meta-analysis of 6 studies (N = 2,886) in which individuals assigned to ENDS use were compared with individuals who received only behavioral support or no behavioral support (with no pharmacologic or ENDS provision). Compared to the group receiving behavioral support or no behavioral support, the long-term abstinence rates were statistically significantly higher for participants who were randomized to nicotine-containing ENDS (RR = 2.61, 95% CI = 1.44–4.74). It was estimated that 6 more cigarette abstainers per 100 (95% CI = 2–15) would be found if ENDS were used in the quit attempt as opposed to behavioral support only or no support. However, this finding was of very low certainty due to imprecision and risk of bias. The authors of this Cochrane Review concluded that, under the conditions of an experimental trial, nicotine-containing ENDS versus non-nicotine-containing ENDS or NRT helps more people attain long-term abstinence from cigarette smoking.

The authors found little evidence of harm from ENDS use but noted that the longest follow-up period used in the studies they analyzed was 2 years.[477] The authors also acknowledged several limitations including: (1) the small number of studies for some analyses; (2) that the type of ENDS used varied across time and study; and (3) that the trials primarily include data from disposable and refillable ENDS tank devices rather than from pod devices, which may deliver nicotine more efficiently due to their frequent inclusion of high nicotine content in the nicotine salt formulation, which facilitates inhalation. In addition, the proportion of participants who become dual users or who become long-term exclusive ENDS users should also be considered in weighing the overall benefits and harms of this approach.

An additional meta-analysis of ENDS effects on smoking cessation involved nine RCTs in which individuals were randomized to either ENDS use to aid smoking cessation or to a control condition that did not include ENDS use.[473] In seven of the nine studies, the control condition received some form of smoking intervention, typically NRT or a means to access it easily. Like the 2021 Cochrane Review,[477] this meta-analysis also found that the provision of ENDS significantly increased the likelihood of long-term smoking abstinence (RR = 1.555, 95% CI = 1.173–2.061, $p = .002$).[473] The proportions of participants who became dual users were not reported in this meta-analysis.

Eisenberg and colleagues conducted a study in which individuals motivated to quit smoking (N = 376) were randomized to 1 of 3 conditions: nicotine-containing ENDS (N = 128), non-nicotine ENDS (N = 127), and no ENDS (N = 121).[478] Participants in all study arms also received counseling; outcomes included biochemically confirmed PPA from smoking at 12 and 24 weeks after the target quit day. The authors stated that the study had to be terminated early due to ENDS product manufacturing delays and is only adequately powered for the 12-week PPA analyses rather than the planned 52-week PPA analyses. Participants assigned to nicotine-containing ENDS had significantly higher abstinence rates than did those in the counseling-only condition at 12-weeks follow-up (21.9% vs. 9.1%, risk difference [RD] = 12.8, 95% CI = 4.0–21.6), but not at 24-weeks follow-up (17.2% vs. 9.9%, RD = 7.3, 95% CI = –1.2–15.7). Participants assigned to the non-nicotine ENDS condition did not have higher abstinence rates than did those in the counseling-only condition at 12-weeks follow-up (17.3% vs. 9.1%, RD = 8.2, 95% CI = –0.1–16.6), but did have significantly higher abstinence rates at 24-weeks follow-up (20.5% vs. 9.9%, RD = 10.6, 95% CI = 1.8–19.4). This study suggests that nicotine-containing ENDS plus counseling can produce higher short-term abstinence rates than counseling only, but that the effect diminishes with time. It also suggests that some of the benefit of ENDS use regarding smoking cessation may be due to the self-administration ritual rather than to nicotine delivery alone. Finally, Eisenberg and colleagues reported that there was significant e-cigarette use in the post-intervention follow-up period (by 24 weeks) among all 3 study groups, with 37% of the nicotine-containing ENDS plus counseling group, 23% of the non-nicotine ENDS plus counseling group, and 17% of the counseling-only group reporting non-study ENDS use.

The 2020 Surgeon General’s report noted that the evidence from RCTs suggests that the use of nicotine-containing ENDS increases the likelihood of smoking cessation relative to comparison conditions.[31] Research published since that Surgeon General’s report is consistent with this statement.[477,478] However, the 2020 Surgeon General’s report noted that more studies are needed to increase confidence in conclusions drawn on this issue and that findings from RCTs might not generalize to real world ENDS use.[31] Also, any potential benefit of ENDS for smoking cessation must consider the potential for ENDS use to become long term, which may have negative health effects and/or lead to relapse back to smoking. For example, Hajek and colleagues found that of those assigned ENDS use as a cessation strategy and who had become abstinent from cigarettes, 80% were still using ENDS 1 year later.[479] In addition, the evaluation of ENDS effects on cessation should consider the potential for prolonged dual use of cigarettes and ENDS. As described above, dual use may do little to reduce the harms of cigarette smoking if it does not lead to smoking cessation and may confer additional risk above that of exclusive smoking.[31,461–463]

ENDS Use and Cessation From Cigarettes in Cancer Populations

Several studies have examined the use of ENDS for smoking cessation in cancer populations. Borderud and colleagues examined the use of ENDS among patients with cancer referred to the tobacco cessation program (N = 1,074) at an NCI-Designated Cancer Center from January 2012 to December 2013.[480] At enrollment in cessation treatment, approximately one-fourth (26.5%) of patients reported they had used ENDS in the past 30 days; most ENDS users (92%) were dual users of ENDS and cigarettes. ENDS use increased substantially over time from 10.6% in early 2012 to 38.5% in 2013. ENDS users smoked more cigarettes per day, had higher cigarette dependence scores, and were more likely to be highly nicotine dependent compared with nonusers. The authors reported that the relationship between ENDS use at baseline and smoking status at 6-month follow-up differed by type of analysis. Using a complete case analysis, ENDS users and nonusers were equally likely to be abstinent from smoking at 6-month follow-up (44.4% vs. 43.1%, self-reported 7-day point prevalence). However, using an intent-to-treat model, patients who did not use ENDS had twice the rate of smoking abstinence as ENDS users (30% vs. 14.5%, self-reported 7-day point prevalence). The study authors note several limitations: the findings represent a clinical cohort at a single comprehensive cancer center, abstinence data were self-reported, the two use populations were not randomly assigned, and a substantially higher percentage of ENDS users were lost to follow-up compared with nonusers.

Akinboro and colleagues analyzed 2014–2017 data from the NHIS, a nationally representative survey of the U.S. civilian noninstitutionalized adult population.[455] The study sample consisted of NHIS participants who reported having ever received a diagnosis of a smoking-related cancer (N = 3,162) (68% of whom were long-term survivors, defined as 5 or more years since initial cancer diagnosis). In addition to sociodemographic variables, participants were asked about their use of cigarettes and quit attempts in the past year, their ENDS use (current and ever), and their alcohol use. The weighted prevalence of ENDS use in the overall study sample was 3.2%. The use of ENDS was higher among current smokers (11.6%), compared with former smokers (2.2%) and never-smokers (0.2%). Current ENDS use did not differ between smokers who had made a quit attempt in the past year (11.6%) and those who had not (11.3%). The authors concluded that “e-cigarette use among patients and survivors of smoking-related cancers was not associated with increased quit attempts in the prior year.”[455,p.2093]

Finally, Salloum and colleagues analyzed data from the 2013-2014 (Wave 1) PATH Study, which asked participants about their smoking status, quit attempts, and cancer diagnosis.[342] Among the 565 adult smokers who reported they had received a cancer diagnosis, more than half (57.1%) had tried to quit smoking in the past year. Reported quitting methods included medication only (22.7%); e-cigarettes only (13.2%); medication and e-cigarettes (6.7%); medication, e-cigarettes, and counseling (2.6%); e-cigarettes and counseling (0.2%); as well as attempting to quit without assistance (49.5%). The authors conducted logistic regression analyses to examine the association between smoking cessation methods and quitting success with statistical adjustment for potential confounders. They found that participants who used FDA-approved smoking cessation medications had higher odds of success, compared with all other cessation methods (adjusted odds ratio [aOR] = 3.77, 95% CI = 1.04–13.68).

Published Guidelines on ENDS Use Among Patients With Cancer

Several organizations have published position statements and guidelines for clinicians regarding the use of ENDS in the oncology context, including the American Society of Clinical Oncology, the American Association for Cancer Research,[481] the NCCN,[16] and the International Association for the Study of Lung Cancer.[482] As of this writing, no professional organization recommends the use of ENDS as a smoking cessation strategy for patients with cancer. USPSTF commissioned a review, published in 2021, to evaluate the benefits and harms of primary care–based smoking cessation interventions.[46] Although aimed at clinicians caring for the general population, USPSTF guidelines represent up-to-date clinical guidance regarding ENDS use and smoking cessation. Similar to the current guidance provided by oncology professional associations, the USPSTF review concluded that "the current evidence is insufficient to assess the balance of benefits and harms of electronic cigarettes (e-cigarettes) for tobacco cessation in adults, including pregnant persons. The USPSTF recommends that clinicians direct patients who use tobacco to other tobacco cessation interventions with proven effectiveness and established safety."[46,p.266]

Summary: The Use of ENDS in Patients With Cancer

Evidence from RCTs conducted among the general population suggests that ENDS use may increase the likelihood of smoking cessation among adults who smoke and who are sufficiently motivated to make a quit attempt and participate in a cessation study. However, this might not reflect the effects of ENDS use outside of the clinical trial setting. In addition, the potential harms of ENDS use as a smoking cessation aid are not well understood but may include persistent ENDS use (both alone and in combination with cigarettes) and short-term and long-term negative health effects including an increased risk of relapse back to smoking. Moreover, the available observational studies do not present a clear or consistent picture of the relationship of ENDS use with smoking cessation. Finally, the specific health effects of ENDS use for patients with cancer are unknown; however, available data on the respiratory, cardiovascular, and immunological effects raises concerns that warrant additional study in the context of cancer and its treatment. Cessation from ENDS use is also an important topic for study in the context of cancer patients and survivors.

A small number of observational studies have been conducted among patients with cancer; these found no association between ENDS use and increased smoking cessation in cancer populations. Additional high-quality, longitudinal, observational studies and RCTs are needed to understand the short- and long-term health effects of ENDS use and to better understand their effects on smoking cessation in the general population and in patients with cancer. Further studies of ENDS use among patients with cancer are important because studies have reported moderate to high levels of ENDS use among patients with cancer who smoke. It is important to determine whether ENDS use undermines the motivation of patients with cancer to use FDA-approved smoking cessation medications and/or cessation counseling, which are safe and effective evidence-based smoking cessation treatments.

Patients who have been diagnosed with cancer and who continue to use tobacco products—especially cigarettes—are at high risk for disease caused by tobacco use, as well as from risks related to their cancer and its treatment. For this reason, assisting patients with cancer to quit smoking should be a very high priority for all cancer care programs and clinicians. The potential utility of ENDS to improve tobacco cessation in this medically vulnerable population must be weighed against the limited data regarding both short- and long-term adverse health effects of these products, as well as the potential for other effects including prolonged exclusive ENDS use or dual use of ENDS and cigarettes and a heightened vulnerability to smoking relapse. Fortunately, as described in this monograph, many effective treatments for tobacco cessation are currently available, and have a strong safety profile, including for use in the oncology setting.

Summary

Regular cigarette smoking can produce dependence, which is accompanied by changes in affect, cognition, and physiology. All seven FDA-approved smoking cessation medications improve long-term smoking abstinence rates relative to placebo as shown in research using multiple, diverse populations. Varenicline and combination NRT are the two most effective pharmacotherapies available. Data from the general population suggest that smoking cessation counseling produces reliable and robust increases in long-term abstinence from cigarette smoking, and that it adds significantly to the benefits of FDA-approved smoking cessation medications. CBT or skills training counseling has received the greatest level of experimental support. Smoking cessation counseling can be effective when delivered via a variety of routes, including in-person, via videoconferencing, or by phone. Digital interventions such as websites and texting interventions have also been shown to significantly increase long-term abstinence rates in the general population of individuals who smoke. Patients diagnosed with cancer differ from other individuals in ways that may affect their likelihood of quitting smoking. Although patients diagnosed with cancer who smoke may have especially great motivation to quit smoking, they may experience greater affective distress, and the burden of imminent and taxing medical treatment may constitute competing demands for their time and attention. Such differences suggest that the effectiveness of smoking cessation treatments may differ when used by patients with cancer in comparison with other patients who smoke. RCTs evaluating smoking cessation medications and counseling in cancer populations have not yielded clear and consistent evidence of effectiveness. However, research with the general population of individuals who smoke strongly suggests that smoking cessation counseling and medication can be effective with patients with cancer. Little is known about how to sustain smoking cessation among patients with cancer or how to increase renewed quitting efforts among those who have relapsed. However, research from the general population suggests that chronic care approaches that periodically re-offer smoking cessation treatment over time can increase smoking quit attempts and abstinence. When considering the effectiveness of smoking cessation treatment, it is important to acknowledge and address challenges and opportunities that can occur at the patient-, clinician-, and health systems-levels. Finally, ENDS use is becoming increasingly common among patients with cancer. ENDS use appears to increase smoking cessation rates in RCTs conducted among the general population, but this may not reflect real-world use patterns. Additionally, no research demonstrates that ENDS help patients with cancer quit smoking. Moreover, ENDS use may entail risk, as these products can deliver potentially harmful chemicals to the user, may sustain nicotine dependence resulting in prolonged ENDS use or dual use of cigarettes and ENDS, and may increase the likelihood that individuals will relapse back to cigarette smoking after a quit smoking attempt. More research is needed before the harms and benefits of this diverse category of products can be accurately assessed.

Conclusions

1. Despite the heightened risks for adverse cancer-related outcomes due to continued smoking after a cancer diagnosis, too few patients with cancer who smoke are offered evidence-based smoking cessation treatment and too few engage in such treatment.
2. Patients with cancer who smoke generally have strong motivation to quit, and a high percentage make one or more quit attempts during their cancer treatment.
3. Research with the general population of individuals who smoke has identified effective smoking cessation intervention strategies, including counseling, medications, and web-based and short message service (SMS) (text) digital interventions.
4. Although more research on the effectiveness of smoking cessation treatments in cancer populations is needed, the consistent effects of these treatments across diverse populations who smoke suggests that they are likely effective in cancer populations as well. Smoking cessation treatments may benefit from adaptation (e.g., addressing fatalism and depression) to best meet the needs of cancer populations and provide optimal benefit.
5. The combination of cognitive behavioral therapy (CBT) counseling with either nicotine replacement therapy (NRT) or varenicline is an especially effective smoking cessation treatment among the general population of people who smoke. CBT counseling has been shown to be effective in the general population when delivered via several different routes, such as in-person, in groups, and by phone. These treatments are recommended for use with patients who smoke in the Public Health Service (PHS) Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*, and for patients with cancer who smoke in the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology.
6. Patients who have been diagnosed with cancer face significant patient-level barriers to smoking cessation that include competing demands due to their cancer treatment, complications and side effects of cancer treatment, pain, psychological distress, and guilt regarding tobacco use. These barriers should be assessed and addressed in strategies used to offer and deliver smoking cessation treatment to patients with cancer.
7. Clinician-level barriers to providing smoking cessation treatment to patients with cancer include limited time per encounter, clinicians' beliefs that FDA-approved cessation medications are ineffective, and lack of confidence or training in providing smoking cessation treatment.
8. The efficacy of electronic nicotine delivery systems (ENDS) as an aid for smoking cessation for patients with cancer is not established. Additionally, the short- and long-term health effects of ENDS use (alone or in combination with cigarettes) by patients with cancer remain to be determined.
9. Many patients with cancer who try to quit smoking will relapse. Data from the general population suggest that periodic, repeated offers of additional smoking cessation treatment to patients with cancer diagnoses who have relapsed will lead to increased quit attempts and quitting success.

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An Essential Component of Cancer Care

Chapter 4
Implementing Smoking Cessation Treatment Programs in Cancer Care Settings: Challenges, Strategies, Innovations, and Models of Care

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Appendices

Chapter 4 Implementing Smoking Cessation Treatment Programs in Cancer Care Settings: Challenges, Strategies, Innovations, and Models of Care

The Importance of a Systematic Approach to Treating Tobacco Use in Cancer Care Settings

Introduction

Patients with cancer who smoke deserve high-quality, evidence-based treatment of their tobacco use as part of comprehensive cancer care. The need for integrating smoking cessation treatment in the cancer care setting is multifactorial. First, the past decade has seen an extensive and growing body of evidence that continued smoking after a cancer diagnosis can markedly worsen oncology treatment side effects, cancer outcomes, cancer mortality, and all-cause mortality[1,2] (see chapters 1 and 2). Second, a cancer diagnosis does not preclude the myriad of other adverse health effects resulting from smoking. Cancer is often diagnosed in patients with other chronic diseases caused by smoking, including cardiovascular and pulmonary diseases.[2] Including smoking cessation treatment as an integral part of cancer care can help address such comorbidities, which is particularly important given the high rates of co-occurrence of cancer and cardiopulmonary diseases.[1,2] Third, the treatment of cancer is frequently associated with compromised immune function and increased risk of upper and lower respiratory tract infections that are exacerbated by smoking; quitting smoking can help protect against such sequelae, given the deleterious impact of smoking on immune function.[2] Fourth, patients with cancer who smoke often feel responsible for their cancer diagnosis. Therefore, assisting them with successful smoking cessation may help ease the guilt, shame, and/or responsibility that they may feel.[3,4] Finally, a cancer diagnosis and/or cancer treatment can serve as a teachable moment for patients who smoke.[5,6] By offering smoking cessation treatment during cancer care, clinicians may seize an opportunity to intervene when motivation to quit could be high.[5,6] Thus, a strong argument can be made for viewing smoking cessation treatment as the "fourth pillar" of cancer treatment, one that could affect cancer treatment outcomes as powerfully as surgery, chemotherapy, or radiation therapy.[7]

Pharmacologic and behavioral smoking cessation treatment strategies and their effectiveness are addressed in chapter 3. In contrast, this chapter focuses on implementing such treatments. Comprehensive cancer care is delivered within acute care, ambulatory, and inpatient hospital settings, and spans the continuum of screening, diagnosis, treatment, and survivorship. Each of these clinical settings serves as an intervention point and provides opportunities to facilitate smoking cessation as part of the delivery of comprehensive cancer care.

The importance of integrating smoking cessation into cancer care is highlighted by the Cancer Center Cessation Initiative (C3I), launched by the National Cancer Institute (NCI) in 2017. As part of the Cancer Moonshot℠ program, C3I represents a new focus for NCI-Designated Cancer Centers.[8] Specifically, C3I aims to help cancer centers build and implement sustainable tobacco treatment programs so that they consistently address tobacco cessation among patients with cancer who smoke.[9] The implementation of tobacco treatment at 52 NCI-Designated Cancer Centers, as part of C3I, offers substantial promise to advance the science of tobacco cessation among patients with cancer by evaluating various clinical and health care system approaches to reducing tobacco use.

Clinical, research, and patient organizations have joined NCI in calling on cancer care settings to address tobacco use when treating patients with cancer who smoke (Table 4.1). For example, the National Comprehensive Cancer Network (NCCN) issued guidelines for smoking cessation.[10] The NCCN guidelines emphasize a population health perspective, establishing the clinical expectation that all patients with cancer should be systematically assessed for tobacco use during cancer care visits, and that all patients identified as currently smoking should be advised to quit and prompted to engage in evidence-based smoking cessation treatment. In addition, the American Association for Cancer Research (AACR),[11] the American Society of Clinical Oncology,[12] the International Society of Nurses in Cancer Care,[13] the Oncology Nursing Society,[14] and the International Association for the Study of Lung Cancer[15] all advocate for providing smoking cessation services as a part of cancer care. These guidelines reflect widespread momentum and recognition of the importance of reaching all tobacco users in cancer care settings.

Table 4.1 Selected Guidelines and Recommendations from Clinical and Research Organizations for Addressing Tobacco Use in Cancer Care Settings

Organization	Guidelines/recommendations
National Comprehensive Cancer Network (NCCN)	• Combining pharmacologic therapy and behavior therapy is the most effective approach and leads to the best results for smoking cessation. • Smoking status should be documented in the patient's health record. Patient health records should be updated at regular intervals to indicate changes in smoking status, quit attempts made, and interventions utilized. • Smoking relapse and brief slips are common and can be managed. Clinicians, the health care team, and tobacco treatment specialists should discuss this and provide guidance and support to encourage continued smoking cessation attempts. Smoking slips are not necessarily an indication to try an alternative method. It may take more than one quit attempt with the same therapy to achieve long-term cessation. • Smoking cessation should be offered as an integral part of cancer treatment and continued throughout the entire cancer care continuum, including surgery, radiation therapy, systemic therapy, and end-of-life care. An emphasis should be put on patient preferences and values when considering the best approach to fostering smoking cessation during end-of-life care.

Table 4.1 (continued)

Organization	Guidelines/recommendations
American Association for Cancer Research (AACR)	• Patients with cancer from all clinical settings, patients in therapeutic cancer clinical trials, and cancer-screening patients who use tobacco or have recently quit (past 30 days) should be provided with evidence-based tobacco cessation assistance. Ideally, that assistance capacity should be within or associated with the oncology practice. Even if the assistance is provided through an external service, the cancer patient's oncology clinician should assume responsibility for ensuring that the patient receives appropriate care. That capacity can also be supplemented by telephone cessation quitlines in all 50 states that can be reached via a common toll-free telephone number (1-800-QUIT-NOW). • Tobacco use should be comprehensively and repeatedly documented for all patients so that the confounding effects of tobacco on cancer treatment, disease progression, comorbid events, and survival can be evaluated in all oncology clinical trials, from registration to survival endpoints, and in all clinical cancer settings. • To provide all patients with tobacco cessation assistance and facilitate improved research into the confounding effects of tobacco, the following objectives should be pursued: – Universal assessment and documentation of tobacco use by patients with cancer in all clinical settings, participants in therapeutic cancer clinical trials, and cancer-screening patients; – Development of universal standards for measurement of tobacco use and exposure in clinical and research settings; – Incorporation of evidence-based tobacco interventions into review criteria used by research and health care quality and accreditation bodies; and – Recognition and support of the value of tobacco cessation interventions by health care systems, payers, and research funders through provision of appropriate incentives for infrastructure development and intervention delivery.
American Society of Clinical Oncology (ASCO)	• Treat tobacco dependence as aggressively and compassionately as cancer, discussing the causal relationship between tobacco use and cancer and assisting the patient and family members to end tobacco dependency. • Help to ensure tobacco cessation services are widely available.
International Society of Nurses in Cancer Care (ISNCC)	• Nurses must ensure that tobacco use assessment, documentation, and dependence treatment is an expected part of care in all cancer inpatient and outpatient treatment programs and protocols, including addressing the stigma faced by many patients affected by a tobacco-related cancer and specifically highlighting the benefits of smoking cessation in the context of a cancer diagnosis.
Oncology Nursing Society (ONS)	• ONS endorsed the ISNCC Tobacco Position Statement in 2014.
International Association for the Study of Lung Cancer (IASLC)	• All patients with cancer should be screened for tobacco use and advised on the benefits of tobacco cessation. • In patients who continue smoking after diagnosis of cancer, evidence-based tobacco cessation assistance should be routinely and integrally incorporated into multidisciplinary cancer care for the patients and their family members. • Educational programs regarding cancer management should include tobacco cessation training, empathetic communication around history of tobacco use and cessation, and utilization of existing evidence-based tobacco cessation resources. • Smoking cessation counseling and treatment should be a reimbursable service.

Note: The guidelines/recommendations are taken directly from the sources and the terminology used reflects that of the source.
Sources: NCCN 2022,[10] Toll et al. 2013,[11] Hanna et al. 2013,[12] Bialous and Sarna 2016,[13] International Society of Nurses in Cancer Care (ISNCC)[14] and Jassem 2019.[15]

This chapter discusses the science regarding the implementation of smoking cessation treatment programs in cancer care settings. Moreover, it provides guidance on implementation strategies by sharing models of care and relevant findings from C3I and elsewhere. This information is designed to foster the efficient and effective implementation of comprehensive smoking cessation treatment programs across multiple types of cancer care settings. This chapter refers to both tobacco use and smoking, recognizing that (a) other forms of tobacco use, beyond cigarette smoking, bear a significant burden on cancer and cancer care, but (b) cigarette smoking is by far the predominant form of tobacco use and dependence in adults, thus giving rise to the importance of smoking cessation. Finally, there are multiple evidence-based options that cancer care settings might implement to deliver smoking cessation treatment more effectively and consistently to patients with cancer who smoke. This chapter describes a broad array of approaches to implementing smoking cessation treatment in cancer care settings that aim to ensure all patients who smoke are provided with effective smoking cessation treatment as part of their cancer care.

Application of the Reach, Effectiveness, Adoption, Implementation, Maintenance (RE-AIM) Evaluation Framework

The RE-AIM framework[16] is used to inform the evaluation of implementation approaches in this chapter. RE-AIM has been applied broadly to structure the planning, implementation, and evaluation of a variety of health care initiatives,[17] including smoking cessation treatment delivery in cancer care.[18] This well-established evaluation framework consists of five key elements: (1) *Reach* (the absolute number, proportion, and representativeness of targeted individuals who are willing to participate in a given intervention), (2) *Effectiveness* (how well an intervention affects a specific outcome), (3) *Adoption* (evidence of organizational support for an intervention and its initiation by relevant clinicians and health care staff), (4) *Implementation* (the degree to which an intervention is consistently delivered across patients, clinicians, and settings), and (5) *Maintenance* (how well an implemented intervention or its effects are maintained across time). Of these five elements, Reach and Effectiveness are particularly important in determining overall treatment impact or, in this case, net quit rates within a population. The goal is to broadly reach and engage individuals who smoke in the use of evidence-based smoking cessation treatments, thereby producing the highest possible cessation impact. The RE-AIM evaluation framework fits well within established guidelines for delivery of smoking cessation treatment, most notably the 5A's (Ask, Advise, Assess, Assist, and Arrange).[19] Oncologists and other clinicians can help patients who use tobacco by embracing this fundamental 5A's-based approach in cancer care settings by *Asking* all patients if they smoke; *Advising* patients who smoke to quit; *Assessing* their willingness to quit or reduce their smoking on the way to quitting; *Assisting* them by offering brief counseling, prescribing smoking cessation medications, and connecting them to additional resources (such as a call-based quitline, a text-based quitting program, or local tobacco treatment specialists); and *Arranging* follow-up with continued support and additional treatment as needed.[19] Streamlined variations on the 5A's, including the clinical referral models "Ask, Advise, Refer" (AAR) and "Ask, Advise, Connect" (AAC), discussed below, recognize that clinicians may be unable to provide a comprehensive cessation intervention during oncology office visits. The following sections detail each component of the RE-AIM framework by reviewing literature pertaining to the implementation of smoking cessation treatment and suggesting efficient strategies for integrating such treatment into cancer care.

Reach

Reach represents the number and proportion of individuals who participate in a given initiative and how representative participants are compared with the target population. In the context of this chapter, Reach refers to the proportion of patients with cancer who participate in health care system–delivered smoking cessation treatment. Among cancer patients and survivors, uptake of evidence-based smoking cessation treatments tends to be low.[20] Low uptake of evidence-based smoking cessation treatments is also seen among people who smoke in the general population in which those motivated to quit tend to make quit attempts without using proven quit aids.[21] As reported in the 2020 Surgeon General's report, although most people who smoke cigarettes make a quit attempt each year, less than one-third report use of smoking cessation medications approved by the U.S. Food and Drug Administration (FDA) or engage in behavioral counseling to support quit attempts.[1] Furthermore, less than 5% of people who smoke, in the general and cancer patient populations,[20,21] report using both evidence-based counseling and medication, the standard of care recommended by the Public Health Service (PHS) Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*.[19,21]

Several innovative strategies have been developed over the past decade to improve reach at the health care system level. These include:

- **Leveraging the electronic health record (EHR)** to track tobacco use status and prompt smoking cessation treatment delivery using chronic disease management approaches.[22]
- **Using clinical referral models** (e.g., AAR and AAC), which are designed to expand reach by efficiently connecting patients who smoke to existing smoking cessation treatment resources within or outside of the health care system after initial clinician advice to quit.[23]
- **Referring patients to "treatment extenders,"** namely evidence-based tobacco cessation treatment options that can expand upon what the clinician provides directly to the patient who uses tobacco (e.g., state tobacco quitlines, SmokefreeTXT). Such treatment extenders would be provided to the patient via EHR electronic referral (eReferral) or via other referral mechanisms (fax or other referral modalities).[19]
- **Utilizing interactive voice response (IVR)** or automated call systems to provide follow-up to patients after a clinic or hospital visit.[24–28]
- **Implementing opt-out** (versus opt-in) approaches where patients who use tobacco receive cessation treatment unless they explicitly indicate that they do not want to receive it.[29]
- **Telehealth**, or virtual treatment services, provides an additional way to expand the reach of tobacco cessation treatment delivery to patients with cancer who smoke.[30]

The following sections review each of these strategies in more detail.

Enhancing Reach via Leveraging the Electronic Health Record (EHR)

The EHR can serve as an essential resource in the implementation of high-quality, clinically based interventions for nicotine dependence, although it may not be available for every setting that may care for patients with cancer who smoke. Fortunately, more than 95% of U.S. nonfederal acute care hospitals have adopted EHRs.[31] The lack of a universal EHR poses challenges to implementation due to the use of different EHR platforms across different health care settings and the need for site-based customizations even among sites that share a common EHR. Nevertheless, numerous clinical trials and observational studies have demonstrated the utility of EHR-facilitated screening, referral, and treatment for nicotine dependence.[22,32–35] For instance, enhanced EHRs can now prompt clinicians to identify tobacco users, refer them for behavioral support, and order pharmacotherapy. Importantly, while such functionalities exist, not all clinicians, clinics, and/or health care systems use them or keep them up to date.

Increasingly, the EHR can also enable clinicians to electronically refer individuals who use tobacco to treatment resources, such as state quitlines and text-based quitting programs including NCI's SmokefreeTXT or automated call systems (e.g., IVR). These EHR-based referrals can support both opt-in and opt-out treatment approaches. All of these can extend the impact of the clinical encounter by providing patients with ongoing smoking cessation treatment and support. These treatment extenders[36] also frequently include Health Insurance Portability and Accountability Act of 1996 (HIPAA)-compliant, closed-loop referral components that promote continuity of care by automatically returning information on referral outcomes to clinicians and the EHR.[32,37]

A Cochrane review[22] concluded that EHR enhancements can facilitate smoking cessation treatment by increasing rates of both tobacco use screening and delivery of cessation assistance in clinical settings. The interventions in this Cochrane review included use of the EHR to improve both documentation of smoking status and smoking cessation assistance for patients who use tobacco, including by direct action or by providing feedback on clinical performance.[22]

Clinical decision support systems for smoking cessation treatment that are integrated into the EHR (e.g., alerts, order sets, care summary dashboards) can guide clinicians to deliver guideline-recommended tobacco use interventions and patient-specific assessments during clinical encounters and thereby increase medication orders, counseling, and referrals to additional treatment services, such as state quitlines for telephone counseling.[38,39] The EHR can also provide sample text in multiple languages to help guide clinicians to intervene.[40] Importantly, clinicians and administrators need to work closely with information technology (IT) staff/informatics teams to harmonize and universalize the routine assessment and documentation of tobacco use status as well as its treatment.

EHRs not only help identify people who smoke and systematically deliver smoking cessation treatment to them but can also document the short- and long-term outcomes of treatment. Such outcomes can include treatment side effects; rates of relapse to smoking; and other adverse events such as cancer recurrence, second primary cancers, and other illnesses caused by smoking, such as cardiovascular or pulmonary disease. Assessing short- and long-term outcomes is particularly important given the persistent elevation in risk of illnesses caused by smoking (both cancer and noncancer), underscoring the need for continued monitoring of patients once they successfully quit smoking.[41,42]

Enhancing Reach via Use of Clinical Referral Models Including "Ask, Advise, Refer" (AAR) and "Ask, Advise, Connect" (AAC)

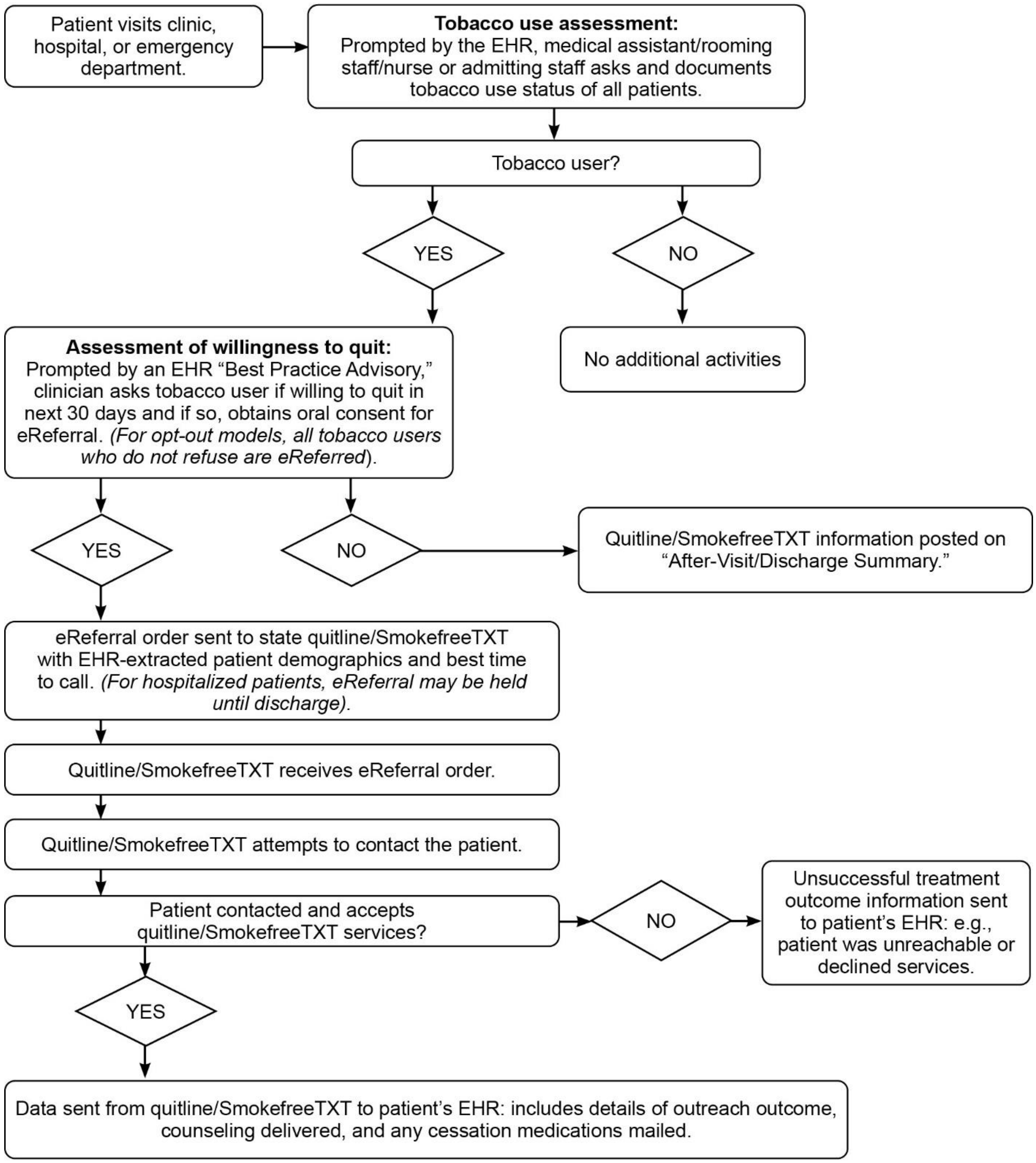
The EHR can also expand reach by facilitating the use of evidence-based clinical models that trigger core steps in the smoking cessation treatment process, such as the 5A's-based AAR and AAC interventions.[23] These models adapt the 5A's treatment approach[19] for encounters when clinicians are unable to personally deliver all components of the 5A's smoking cessation treatments during clinic visits. These referral models are designed to prompt clinicians and other clinical staff to initiate smoking cessation treatment ("Ask and Advise") and then connect patients who smoke with other treatment resources that are either within or outside of the clinical setting ("Refer" or "Connect"). The AAC model may be even more effective than AAR in increasing the reach of smoking cessation treatment because the treatment team proactively connects the patient who smokes to a treatment program rather than relying on the patient to make the connection.[23] Importantly, these models also guide clinicians to prescribe smoking cessation medications. This guidance is a strength of clinical referral models as clinicians retain the ability to prescribe, monitor medication use, and adjust pharmacotherapy as needed. In practice, treating oncologists may be too busy and/or have little training in nicotine dependence counseling or prescribing pharmacotherapy. This argues for a systems-based approach[19] that utilizes additional members of the treatment team (e.g., health educators, counselors, nurses, rooming staff) to augment those responsible for delivering smoking cessation treatment. In this way, such clinical models may increase the likelihood that patients receive recommended courses of pharmacotherapy rather than the brief courses typically available through quitlines. Prescription of smoking cessation medication also fosters the integration of the patient's smoking cessation treatment into their cancer care.[43] Although there is little published data specific to the cancer care setting as of this writing, clinical referral models hold promise to enhance the implementation of smoking cessation treatment during cancer care visits.

Treatment Extender: State Quitlines

State quitlines offer evidence-based, clinically effective, and cost-effective smoking cessation treatment to a wide range of individuals who smoke, thereby enhancing reach.[44] Quitlines are toll-free telephone services available throughout the United States and Canada and constitute the largest population-based network of smoking cessation treatment in North America.[45–47] They provide services, typically in multiple languages, to approximately 500,000 people who smoke each year, typically reaching about 1% of people who smoke in the United States annually.[48] As of 2019, 15 years after the National Network of Tobacco Cessation Quitlines was launched by the Centers for Disease Control and Prevention (CDC) and NCI, more than 10 million calls had been made to quitlines in the United States.[49,50] Although vastly underutilized, state quitlines have been documented as effective smoking cessation interventions for the general population of people who smoke.[19]

In the United States, each state manages its own quitline services, usually via a contract with a quitline vendor; for example, Optum™ and National Jewish Health™ provide services to more than 30 states and territories. Some states provide their own quitline services or contract with a university in their state (e.g., California). Typically, people who smoke contact a quitline on their own (via phone or website) but increasingly, they are referred by a clinician or other clinic staff during a health care visit (via EHR-based eReferral) (Figure 4.1). Trained tobacco cessation treatment counselors are often available by phone 7 days a week and typically offer counseling in multiple languages. Most quitlines offer both free counseling and limited quantities of FDA-approved smoking cessation medications (primarily starter packs [e.g., 2-week supplies] of over-the-counter nicotine replacement products) that are typically delivered via U.S. mail. Some quitlines offer ancillary text messaging programs, and most offer web-based services and print materials.[50] However, due to budget constraints, quitline service intensity varies by state.

Figure 4.1 Typical EHR-Guided Staff Workflow for eReferral of a Patient who Smokes From a Clinical Setting to a State Quitline or NCI SmokefreeTXT



Note: Aspects of the eReferral process may vary by clinical care setting and institution. The eReferral employs standardized data elements as determined by the Office of the National Coordinator for Health Information Technology to maximize interoperability, or efficient exchange of information, between health care service providers. For more detailed descriptions of workflow and technical specifications for eReferral to quitlines, please see Adsit and colleagues[32] (outpatient clinical setting) and Tindle and colleagues[60] (inpatient clinical setting). For a detailed description of workflow and technical specifications for eReferral to NCI SmokefreeTXT, see McCarthy and colleagues.[37]
EHR = Electronic health record.
Source: Society of Behavioral Medicine 2014, 2020.[32,37]

A large body of evidence supports the effectiveness of quitlines to promote smoking cessation,[19,51] though none of these studies focused specifically on cancer populations, which may need a more intensive dose of treatment, including counseling interventions combined with pharmacotherapy over multiple session visits.[30] A 2002 study by Zhu and colleagues[52] of 3,282 people who smoke who called the California quitline found that the 12-month, self-reported abstinence rate was 9.1% among those randomized to proactive quitline calls (i.e., calls initiated from the quitline) versus 6.9% for those who did not receive proactive calls ($p < .001$). Additional studies support the integration of nicotine replacement therapy (NRT) into quitline care.[53–55] Importantly, the 2020 Surgeon General's report concluded that "the evidence is sufficient to infer that tobacco quitlines are an effective population-based approach to motivate quit attempts and increase smoking cessation."[1,p.11]

Individuals have typically connected with the national quitline by calling a toll-free telephone number (1-800-QUIT-NOW) to obtain assistance with tobacco or smoking cessation. Because more than 70% of individuals who smoke visit a clinician each year,[21] such visits provide additional opportunities to link patients with quitline services. Health care systems initially attempted to link patients via paper fax referrals to the quitline call center. However, with the decrease in use of fax machines, this practice does not fit easily into current clinical practices. The advent of near-universal use of EHRs has provided a new means of referring patients during clinic visits. In response, researchers and health care systems have more recently focused on developing EHR-based quitline eReferral capacity (Figure 4.1). A growing body of evidence shows that eReferral to quitlines is an effective means of expanding the reach of smoking cessation treatment into health care settings. Such eReferral has also been facilitated by the North American Quitline Consortium (NAQC), which has produced a technical guide to support its implementation.[56] Multiple studies have explored EHR-embedded automated referral to a state tobacco quitline in primary care[32–34,57] and hospital settings.[38,58–60] Adsit and colleagues,[32] in the first eReferral demonstration study, programmed a closed-loop referral to the quitline into the EHR at two Wisconsin clinics. Closed-loop referral (also referred to as bidirectional referral) is a term used to describe the process whereby clinics use the EHR to refer a patient to the state quitline, which then attempts to reach and treat the patient. The quitline then electronically transmits back to the EHR the outcome of the referral, typically both to the patient's chart and to the referring clinician (Figure 4.1). Compared with a baseline period of fax referral only (0.3% quitline referral), this closed-loop approach significantly increased quitline referral (to 13.9%), while actual quitline usage increased from 0.15% to 4.9%.[32] Later research comparing fax and eReferral in primary care clinics in Wisconsin similarly found increased reach after the implementation of closed-loop eReferral.[33,34] In a randomized trial in 2 health care systems, average rates of referral and quitline connection were at least 13% and 3% higher, respectively, in clinics using eReferral compared with those using fax referral.[34] An observational study assessing the reach of closed-loop eReferral in 30 primary care clinics that previously used fax referral observed increases in both assessment of readiness to quit (24.8% 4 months pre-launch compared with 93.2% 8 months post-launch) and referral rates (1.7% pre-launch compared with 11.3% post-launch) after eReferral implementation.[33]

Tindle and colleagues[60] demonstrated the feasibility of quitline eReferral among hospitalized patients at discharge, through which 36% of hospitalized patients who smoke accepted eReferral, generating 818 eReferrals to the quitline over 8 months. These 818 eReferrals constituted more than one-fifth of all quitline referrals from the entire state of Pennsylvania during that period.

However, only 24% of those referred were reached by the quitline, and only 21% of those reached enrolled in quitline services, thus underscoring the persistent challenge of engaging patients in smoking cessation treatment.

Hood-Medland and colleagues[59] embedded a prompt into the EHR of a large university hospital system to eRefer people who smoke to a state tobacco quitline. The eReferral was initially installed within the EHR of ambulatory sites, and, later, expanded as an order set for use with hospitalized patients who smoke at discharge. From 2013 to 2015, 16,083 encounters with patients who smoked led to 1,137 (7.1%) eReferrals. For all encounters, the reach of the eReferral system with regard to quitline connection was 1.6% (the percentage of identified patients who smoked who were ultimately connected with the quitline). At 6 to 12 months, first-time eReferral patients had a documented cessation rate of 12.2%. This study demonstrated the feasibility of implementing eReferral for both ambulatory and hospitalized patients, although reach rates were quite low.

Bernstein and colleagues[38,58] designed an EHR-embedded package of decision-support resources to identify people who smoke who are admitted to the hospital and link them with treatment, including quitlines. The "Electronic Support Tool and Orders for the Prevention of Smoking" (E-STOPS) package was developed and tested in a cohort of adults who smoke and were admitted to the inpatient medical services of a large U.S. university hospital; 254 physicians were randomized to receive the E-STOPS tool or usual care (control) conditions. The E-STOPS tool consisted of an electronic prompt that appeared when the inpatient physician opened the chart of a person who smokes, offering five components in opt-out fashion, four of which were automated in addition to a medication order that required a physician signature. Physicians in the control condition could choose to carry out all of the above five functions but had to execute them manually.[58]

E-STOPS was found to be effective in improving the delivery of smoking cessation treatment components. Among 10,939 people who smoke and were assigned based on the physician who had initially treated them (5,391 intervention and 5,548 control), intervention physicians were more likely than control physicians to complete 3 of the prompted actions: ordering smoking cessation medication (34% vs. 29%; $p < .0001$), populating the patient's problem list (42% vs. 2%; $p < .0001$), and referring to the quitline (29% vs. 0%; $p < .0001$). Ninety-nine percent of intervention physicians notified the patient's primary care provider (PCP) via email (no data available for control physicians).[38] However, in a subset of 1,044 patients followed for 1 year, quit rates for intervention and control patients were 11.5% and 11.6%, ($p = .94$), respectively, after controlling for age, sex, race, ethnicity, and insurance status.[58] Hence, while E-STOPS was widely implemented, it did not enhance long-term abstinence. This could reflect inadequate follow-up with and transfer of care from the inpatient team to primary care physicians, and that hospitalization may have led to fairly high abstinence rates among patients in both intervention and control arms.

Overall, quitlines are a promising tool to improve reach, especially in health care settings when referrals can be made electronically via EHRs. Closed-loop, or bidirectional, referral capacity further supports continuity of care through automatic follow-up communication back to the patient's medical record. While limited research has specifically addressed eReferral to quitlines in cancer care settings,[61] 59% of Cohort 1 C3I sites (22 NCI-Designated Cancer Centers) have adopted the use of quitline eReferral.[9] Additional research is needed to establish the effectiveness of quitline referrals for increasing rates of smoking cessation in cancer patient populations.

Treatment Extenders: National Cancer Institute's (NCI) SmokefreeTXT

The EHR has also been used to electronically refer patients who smoke to a mobile phone–based resource, SmokefreeTXT, a freely available text messaging program for smoking cessation treatment operated by NCI.[62] Once a patient is eReferred to SmokefreeTXT by their clinician, the patient will receive a text message from SmokefreeTXT inviting them to enroll in the program.[62] McCarthy and colleagues[37] first demonstrated the feasibility of integrating an EHR-enabled, closed-loop eReferral into the outpatient clinic setting. Overall, 12% of eligible patients who smoked were eReferred to SmokefreeTXT. Of those eReferred, 25.7% enrolled, set a quit smoking date, and received text messages, for an overall 3.1% connection rate among all people who smoke cigarettes. Like eReferral to state quitlines, eReferral to SmokefreeTXT may extend reach by facilitating referral, thereby decreasing the burden on clinicians and clinical staff.[37] Also, some patients could prefer technology-delivered, digital interventions that do not entail person-to-person contact. Additional research is needed to optimize the implementation of eReferral to SmokefreeTXT to determine its effects on smoking cessation among patients with cancer.

Utilizing Interactive Voice Response (IVR) Systems

Among the technological innovations that have been added to the array of tools to connect patients who smoke to cessation resources and interventions is IVR outreach via automated calls.[27] IVR allows individuals to interact with a computer via voice detection mechanisms (or keypad entry) and is an important component of the inpatient Ottawa Model of bedside counseling and follow-up calls.[63] A similar model has also been tested in the United States in two randomized controlled trials (RCTs) conducted in large tertiary care medical centers. In the first of these 2 studies, Rigotti and colleagues[64] reported that among 198 hospitalized patients who wanted to quit smoking, receipt of IVR calls + smoking cessation medication upon discharge resulted in statistically significant higher 6-month post-discharge biochemically confirmed quit rates (26%) than those who received a standard recommendation to use counseling + medication (15%) ($p < .009$). In the second study, using a similar design (N = 1,357), Rigotti and colleagues[65] reported that those who received IVR calls + cessation medications upon discharge did not achieve statistically significant higher 6-month post-discharge biochemically confirmed abstinent rates (17%) versus those who received a standard recommendation upon discharge to use counseling + smoking cessation medication (16%). In a subsequent publication, Rigotti and colleagues[28] described IVR characteristics and use patterns among those randomized to the IVR condition in the two RCTs, finding that participants completed a median of three to five calls, and that higher IVR utilization was associated with higher odds of smoking abstinence at 6-months' follow-up. Evidence has documented that, in addition to positive effects on reach and engagement, the combination of bedside counseling with post-discharge IVR follow-up was cost-saving (i.e., overall adjusted mean health care charges for people who smoke who were exposed to the program were $7,299 lower than for those who did not receive the tobacco cessation treatment services, $p = .047$) and resulted in reduced readmissions and fewer total number of hospital days.[66,67] However, there are no specific studies evaluating IVR for smoking cessation in patients with cancer.

Opt-Out Versus Opt-In Models of Smoking Cessation Treatment Delivery

Many health care systems have used an opt-in approach to delivering smoking cessation treatment. Using this approach, patients must request (or accept) a referral for smoking cessation treatment from their oncology clinicians or other clinicians; without this, referral or treatment is not provided. An opt-out model, sometimes referred to as a proactive model, has been recommended in a manner such that all patients who smoke are automatically referred for evidence-based smoking cessation treatment[29] unless they specifically refuse such a referral. Approaches that seek to provide opt-out smoking cessation treatment hold promise to increase treatment reach in ambulatory,[68–70] acute care/emergency,[71] and hospital settings,[27,72,73] and, as with other proactive treatment approaches, could enhance smoking cessation treatment engagement among individuals with lower motivation to quit.[74] Researchers have argued that opt-out approaches may be ethically superior to opt-in services that rely on clinician referral for treatment[29] because of their potential for equitable delivery of such treatment services broadly and to different populations.[73,75,76] Opt-out approaches are based on psychological responses to defaults and have been found in several domains to increase preference-consistent and public health promoting behaviors such as organ donation.[77] Such approaches are not viewed as representing coercion but rather a form of "soft paternalism" in which the freedom of choice is maintained and yet the audience is "nudged" in the direction of a desirable choice.[78]

The NCCN Smoking Cessation Guidelines, a consensus document established in 2016 and reviewed annually by a panel of smoking cessation treatment and oncology experts, recommends the opt-out model for patients with cancer who have used tobacco in the past 30 days.[10] While an opt-out model does not guarantee acceptance of smoking cessation treatment by the patient, it has been shown to increase treatment reach and engagement, including in studies of patients with cancer.[79] An opt-out approach can be used to refer patients to an internal health care system smoking cessation treatment program or to an external community resource, such as a quitline. Another study suggests that an opt-out referral approach can be effective for encouraging referral to smoking cessation support.[80] Patients with cancer who screened positively for smoking via an EHR-based assessment were automatically referred (an opt-out strategy) to smoking cessation treatment. Half of the referred patients were called by the smoking cessation treatment program and half were mailed a letter inviting them to contact that program. The automatic (opt-out) referral with direct phone outreach by the smoking cessation treatment program successfully contacted 81.3% of patients; in contrast, only 1.2% of patients who received a letter contacted the program. The research suggests that an opt-out referral strategy when paired with follow-up phone outreach can be highly effective in linking patients with cancer with smoking cessation treatment.[80] Nolan and colleagues[79] also used an opt-out approach, in this case, to link patients with breast cancer who smoked with smoking cessation treatment. They implemented an opt-out referral process whereby all patients with breast cancer who smoked were referred for smoking cessation treatment. This study showed that the reach of the smoking cessation treatment increased from a baseline rate of 29% to a post-intervention rate of 74%. Among patients referred, treatment engagement (defined as keeping an initial tobacco cessation treatment consultation appointment) increased from 41% to 75% after implementing the opt-out referral method.[79]

In an additional assessment of the opt-out model for patients with cancer, Taylor and colleagues[81] described the implementation of a smoking cessation treatment program that used proactive telephone outreach to patients with cancer identified as currently smoking. They reported reaching 69% of eligible people who smoke, and of those reached, 43% engaged in smoking cessation treatment. Gali and colleagues[82] reported that implementing an opt-out referral process in cancer care settings increased referrals from less than 10% to 100%, and increased smoking cessation treatment engagement from 1% to 33%. Himelfarb-Blyth and colleagues[83] similarly reported an increase in reach after implementing an opt-out referral model at a cancer center where accepted referrals to quit support increased from 11.5% under the previous opt-in model to 34.7% under the new opt-out referral process. Jose and colleagues[84] piloted an EHR-based opt-out referral of all tobacco users (regardless of intention to quit) as they were being "roomed" (i.e., the process of taking the patient to the exam room and collecting essential information [e.g., vital signs, medications used] by a medical assistant, nurse, or other staff member prior to the treating clinician seeing the patient) in the cancer clinic. Staff who roomed the patients made the eReferral, which did not require a clinician co-signature. Over 70% of patients who smoked were referred to smoking cessation treatment via this opt-out approach, supporting the potential for broad reach. However, only 17% of patients kept the smoking cessation treatment appointment, underscoring ongoing challenges with engagement.[84]

Lastly, the Michigan Oncology Quality Consortium designed an opt-out approach for identifying people who smoke in Michigan oncology practices and referring them to the state quitline. From 2012 to 2017, they found that annual referrals from oncology practices increased from 364 at baseline (5% of all quitline callers) to 876 (17% of quitline callers).[61] This program achieved a self-reported quit rate of 26% at 6 months. This population-based initiative demonstrates the feasibility of increasing access to evidence-based smoking cessation treatment for patients with cancer using existing statewide resources.

Using Telehealth

Delivering tobacco cessation treatments to patients with cancer who smoke via telehealth provides an additional opportunity to expand the reach of these treatments, overcoming travel and other challenges. Access to telehealth treatment opportunities expanded during the COVID-19 pandemic, including smoking cessation treatment to patients with cancer who use tobacco.[1,30,34,85]

Summary: Reach

To maximize population impact, smoking cessation treatment programs must achieve high rates of reach. Multiple promising strategies to enhance reach have been identified, including: (1) leveraging EHRs to track tobacco use status, offer treatment delivery using a chronic disease management approach, and make eReferrals to external resources, such as state quitlines and NCI's SmokefreeTXT; (2) promoting clinical referral models, including AAR and AAC, to increase patient engagement in smoking cessation treatment and also offload front-line clinician responsibilities for delivering smoking cessation treatments, given that clinicians might not have the time or training to provide a comprehensive smoking cessation intervention; (3) promoting IVR or automated call systems to follow patients after a clinic or hospital visit and provide treatment offers and support; (4) implementing opt-out (versus opt-in) treatment approaches that automatically refer or connect patients who smoke with smoking cessation treatment unless they explicitly decline; and (5) implementing cancer center–based telehealth smoking cessation treatment delivered to patients directly through smartphones, tablets, and computers in their homes, which offers flexibility and patient convenience. While these strategies hold great promise for patients with cancer who smoke, additional research is needed in clinical cancer care settings.

Effectiveness

Effectiveness in this chapter refers to changes in smoking behavior, typically quit rates, across clinic and health care system populations who smoke after implementing a smoking cessation treatment program. Chapter 3 provides an in-depth discussion of smoking cessation treatment effectiveness among the general population and those with cancer. While few well-powered RCTs have been conducted among patients with cancer, the totality of evidence from RCTs across the general population of individuals who smoke, often comprising large samples of diverse types of patients, including patients with cancer, provides strong support for the use of evidence-based smoking cessation treatments. Specifically, evidence has found counseling and medication to be effective across patients differing on a host of important characteristics, including age, gender, socioeconomic status, physical health status, and affective/psychiatric status. This suggests that counseling and medication smoking cessation treatments are effective for patients with cancer.[19] The NCCN Guidelines for Smoking Cessation recommends the provision of both smoking cessation pharmacotherapy and counseling to patients with cancer who smoke.[10] This section summarizes some of the evidence synthesized in chapter 3.

For example, a multisite RCT among patients recently diagnosed with cancer who smoke tested the effectiveness of sustained (four weekly telephone sessions followed by four biweekly sessions followed by three monthly sessions) telephone counseling sessions and choice of FDA-approved cessation medication provided without charge.[86] This treatment arm was compared with standard care, consisting of four weekly telephone counseling sessions and cessation medication advice. The sustained treatment arm produced a statistically significant higher 6-month, biochemically verified 7-day point-prevalence abstinence (34.5% of patients, $N = 153$) than did the standard care arm (21.5% of patients, $N = 150$). It is worth noting that participants in both study arms used cessation medication (77.0% in the intensive arm and 59.1% in the standard care arm). Thus, the results suggest that sustained smoking cessation counseling and medication can be both feasible and effective for recently diagnosed patients with cancer.[86]

In addition to the experimental study described above, observational cohort studies have shown that providing evidence-based smoking cessation treatment produces high rates of cessation in patients with cancer who smoke (see chapter 3). For example, Cinciripini and colleagues[87] reported 3-, 6-, and 9-month point-prevalence abstinence rates from a large, prospective cohort of people who smoke ($N = 3{,}245$) treated at the University of Texas MD Anderson Cancer Center. The authors found that overall self-reported abstinence was 45.1% at 3 months and 45.8% at 6 months. The same high quit rates were seen in patients without cancer who received intensive cognitive behavioral therapy (CBT) treatment. Such high quit rates might reflect, in part, the experience of the MD Anderson Cancer Center smoking cessation program, a long-standing program first established in 2006[88] that offers intensive multisession CBT treatment delivered by tobacco treatment specialists who work with a team of nurses, physician assistants, or nurse practitioners able to prescribe cessation medication. Observational studies limit the ability to assess effectiveness due to the absence of a control group; however, this study suggests that patients with cancer are highly motivated to quit and can achieve effective treatment outcomes. This evidence, along with the results of the study by Park and colleagues,[86] suggests a role for relatively intense smoking cessation treatments for patients with cancer.

Summary: Effectiveness

Delivery of intensive CBT counseling along with combination NRT or with varenicline are especially effective smoking cessation treatments in the general population of people who smoke. Relatively few well-powered RCTs have evaluated the effectiveness of implementing smoking cessation treatments in patients with cancer. However, large observational cohort studies have shown that smoking cessation treatment programs can be successfully implemented consistently in cancer care settings and are associated with high long-term rates of abstinence from tobacco. Further research is needed to evaluate the effectiveness of smoking cessation treatments that are targeted and tailored to meet the needs of patients with cancer across the care continuum. Clinically important questions remain about the ideal dose, duration, timing, and delivery of counseling and the acceptability and effectiveness of cessation pharmacotherapy among patients with cancer who smoke.

Adoption

In the context of this chapter, Adoption refers to evidence of commitment or support to implement a smoking cessation treatment program by health care systems, clinics, clinicians, or staff. Adoption might be indicated by program leadership providing necessary resources or by clinicians and staff initiating relevant service delivery.[89] Despite the known risks of continued smoking for patients with cancer,[2] the availability of Clinical Practice Guidelines that encourage smoking cessation treatment for such patients,[10,19] and strong endorsement by leading professional organizations, such as the AACR, the NCCN, the American Society of Clinical Oncology, and the International Association for the Study of Lung Cancer,[10–12,15,90,91] tobacco use screening and evidence-based treatment delivery have not been consistently adopted in many cancer care settings. For example, in 2013, a survey of 58 NCI-Designated Cancer Centers found that only about one-half had mechanisms to identify their patients with cancer who smoked and only one-half had a dedicated smoking cessation treatment program embedded within the cancer center.[92] Furthermore, a 2019 review by Price and colleagues[93] found that, although 75% of cancer care clinicians assess tobacco use during an intake visit and more than 60% typically advise patients to quit, a substantially lower percentage recommend or arrange smoking cessation treatment or follow-up after a quit attempt, and less than 30% of oncology care clinicians reported adequate training in cessation interventions.

Large national surveys of cancer care clinicians have demonstrated low rates of clinician provision of smoking cessation treatments. An online survey of 1,507 thoracic cancer clinicians conducted by the International Association for the Study of Lung Cancer revealed low levels of smoking cessation treatment adoption with just 39% of respondents indicating that they actively provide smoking cessation assistance.[94] Another online survey of 1,197 clinicians conducted by the American Society of Clinical Oncology revealed that 90% of clinicians asked about tobacco use and 84% of clinicians advised their patients to quit, but only 44% of clinicians discussed medications and 39% of clinicians provided cessation support.[95] Similarly, a national survey of urologists that inquired about the provision of smoking cessation assistance for their patients with bladder cancer reported that about 56% of urologists never discussed smoking cessation.[96] A survey of the American College of Surgeons' Commission on Cancer programs, published in 2018, examined the adoption of smoking cessation treatment by participating academic and community cancer programs.[97] This survey found that most cancer treatment programs did not have comprehensive, institutional programs to identify patients with cancer who smoke and to provide systematic smoking cessation treatment. Few programs had developed resources that aided clinicians in providing smoking cessation pharmacotherapy. Collectively, these data suggest that both cancer health care systems and cancer care clinicians have often underdeveloped or underutilized smoking cessation treatment resources.[9] However, several types of policy and regulatory actions can encourage the adoption of smoking cessation treatment in health care systems in general and in cancer care programs in particular.

Payment Models, Quality Metrics, and Regulation

Payment models, quality metrics, and regulatory and legislative actions all have the potential to spur greater adoption of smoking cessation treatment by health care systems and clinicians. Reports on patient safety and quality by the National Academy of Medicine (formerly the Institute of Medicine) catalyzed the quality revolution in health care in the United States.[98,99] These reports identified six domains of health care quality: safety, effectiveness, timeliness, patient-centeredness, equity, and efficiency. Health care policymakers, clinicians, and organizations have recognized that tobacco control could contribute to improving multiple domains of quality. Notably, effective smoking cessation treatment can also improve outcomes obtained across a broad range of health conditions.[2,19]

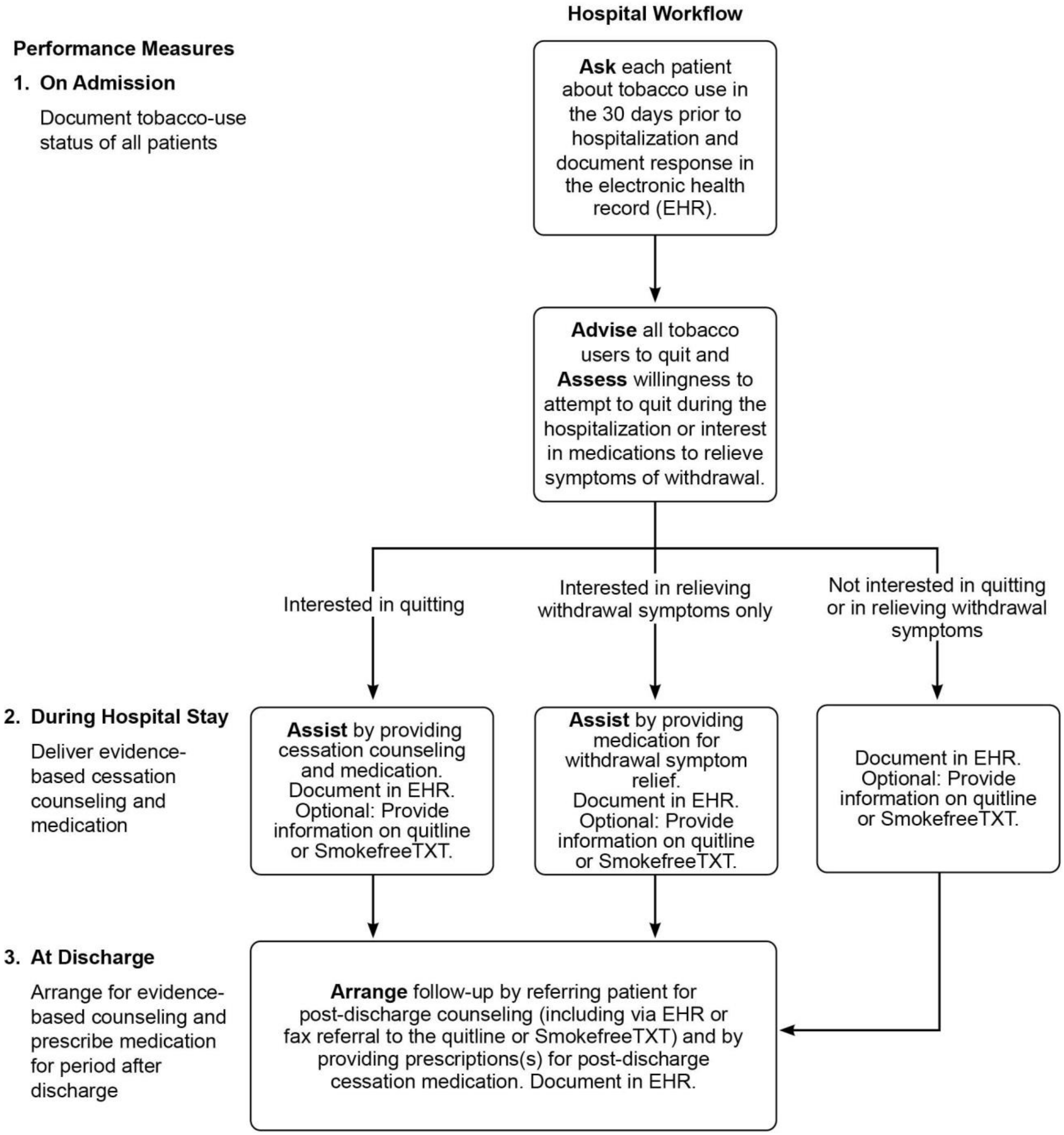
The ongoing transformation of payment models from rewarding volume to rewarding value has further catalyzed the adoption of quality measures that include tobacco control.[1] These policy developments, regulations, and payment models might be highlighted by clinicians and practices who are asking their institutions to enhance the quality and quantity of treatment for nicotine dependence and thereby spur adoption. Four key reporting and payment models that might be used are (1) the Joint Commission performance measure set around smoking cessation treatment, (2) the Oncology Care Model (OCM), (3) other Centers for Medicare and Medicaid Services (CMS) payment models, and (4) outpatient clinical quality measures included in Medicaid and the State Children's Health Insurance Program (CHIP).

For years, numerous regulatory and accreditation agencies, including CMS, the Joint Commission, and the National Quality Forum, have recognized that the delivery of smoking cessation treatments requires assessment of tobacco use during inpatient and outpatient clinical encounters, with reimbursement partially contingent on its documentation.[100,101] In addition to the OCM, several other CMS payment models include tobacco measures. These models include measure sets designed to assess health plans (the Healthcare Effectiveness Data and Information Set, or HEDIS); patient-reported measures of tobacco interventions (the Consumer Assessment of Healthcare Providers and Systems, or CAHPS); and a 2015 update of the basic Medicare value-based program, known as the Medicare Access and CHIP Reauthorization Act (MACRA).[102,103] Collectively, these measures have resulted in a marked increase in the documentation of smoking status in EHRs and referral at discharge to smoking cessation treatment programs and quitlines.[22,32,34,38,58–60]

In 2012, the Joint Commission created an optional performance measure set addressing nicotine dependence in inpatient clinical encounters.[100] This measure set initially had four components: (1) screening all patients age 18 years and older for tobacco use, (2) offering counseling and cessation/withdrawal mitigation medications during hospitalization for all patients who smoke, (3) creating a plan at discharge to continue smoking cessation treatment (i.e., counseling and medications) in the post-hospitalization period, and (4) following up within 1 month of hospital discharge. Psychiatric facilities were required to attest to these quality measures, with resultant increases in documentation of tobacco use assessment and treatment, based on their effectiveness in augmenting smoking cessation treatment in clinical populations.[104,105] The National Quality Forum did not ratify the 1-month post-discharge measure and the Joint Commission subsequently dropped it. Additionally, because of near-universal compliance, the screening measure was retired in 2017 for psychiatric facilities.[1] The current Joint Commission Tobacco Dependence Performance Measures are described in more detail in Figure 4.2.

Hospitals have the option of selecting which 4 Joint Commission Performance Measure Sets to complete from the 10 to 15 sets available each year for Joint Commission accreditation.[1,106,107] Regrettably, the rate of adoption of the tobacco performance measure set has been very low; in 2019, only about 2% of 5,000 hospitals elected to report on these measures.[106] This context illustrates that the low rates of addressing tobacco use in cancer care are reflective of a broader challenge. Encouraging such reporting can serve a key role in maintaining smoking cessation treatment delivery to hospitalized patients, including patients with cancer. In part to encourage such Joint Commission reporting, Sarna and colleagues[106] called on *U.S. News and World Report* to withhold designating a hospital as being among the “Nation’s Best” unless they report on the Joint Commission Tobacco Measure set.

Figure 4.2 Joint Commission Tobacco Cessation Measures



Source: Version 2021A Specifications Manual, The Joint Commission,[304] Fiore et al. 2012.[100]

The OCM was created in 2015 when CMS launched an episode-based payment model for cancer care.[108] The OCM provides enhanced payment for oncology practices that adhere to certain quality measures and deliver certain services, such as patient navigation and care coordination. As of July 2021, 126 practices and 5 commercial payers, a small proportion of cancer care settings nationwide, participate in the OCM.[109] Although assessing rates of tobacco use and treatment is not an OCM quality measure, incorporating tobacco-related measures into such payment models would serve to enhance the adoption of cessation efforts. This incorporation might also focus the clinical enterprise on providing services that improve the patient experience or health outcomes, rather than on appointments or procedures for which a clinician typically bills. Moreover, treating tobacco use has the potential to improve other OCM outcomes, including reduced cancer treatment-related side effects and improved cancer outcomes, which should increase the appeal of such treatment.

Regarding outpatient quality measures, the CMS Child and Adult Core Sets support federal and state efforts to collect, report, and use a standardized set of measures to drive improvement in the quality of care provided to Medicaid and State CHIP beneficiaries.[110] Beginning in fiscal year 2024, states will be required to report on the core set of health care quality measures for children enrolled in Medicaid and CHIP and on the core set of behavioral health measures for adults enrolled in Medicaid. The core sets allow states, the public, and CMS to monitor trends in performance on standardized indicators of quality of care provided to Medicaid and CHIP beneficiaries under both fee-for-service and managed care arrangements and examine performance across states. The Child and Adult Core Performance Measure Sets in 2022 include the following tobacco- and smoking-related performance measures:

- **Preventive Care and Screening: Tobacco Use: Screening and Cessation Intervention** (National Quality Forum Number 0028/0028e). The percentage of patients aged 18 years and older who were screened for tobacco use one or more times within 12 months and who received tobacco cessation intervention if identified as a tobacco user.[111]
- **Tobacco Use and Help with Quitting Among Adolescents** (National Quality Forum Number 2803). The percentage of adolescents ages 12–20 with a primary care visit during the measurement year for whom tobacco use status was documented and who received help with quitting if identified as a tobacco user.[112]
- **Medical Assistance With Smoking and Tobacco Use Cessation** (National Quality Forum Number 0027). The three components of this measure assess different facets of providing medical assistance with smoking and tobacco use cessation and include advising smokers and tobacco users to quit, discussing cessation medications, and discussing cessation strategies with patients aged 18 and older who were current smokers or tobacco users.[113]

Legislative Action

Passed in 2009, the Health Information Technology for Economic and Clinical Health (HITECH) Act accelerated the adoption of the EHR by nearly all U.S. health care systems.[114,115] The HITECH Act required hospitals and health care systems to adopt a set of measures designed to encourage the "meaningful use" of EHRs. Included in the initial meaningful use criteria was a measure requiring the recording of smoking status for all patients aged 13 and older. However, the HITECH Act did not require the systematic clinical assessing, recording, and documenting of tobacco use status.

Passage of the Patient Protection and Affordable Care Act (ACA) in 2010 has also enhanced health care systems' adoption of tobacco interventions.[116] The ACA did this by (1) requiring coverage of A- or B-level U.S. Preventive Services Task Force recommendations (USPSTF),[117] (2) expanding eligibility for Medicaid, (3) mandating coverage by Medicaid and private insurance of nicotine dependence medications and counseling, and (4) creating new value-based payment models via the Center for Medicare and Medicaid Innovation.[118] The value-based models include the OCM (discussed previously), as well as the Medicare Shared Savings Program (MSSP).[109]

The MSSP encourages clinicians in health care systems to create Accountable Care Organizations (ACOs) in which payment is conditioned on the ACO accepting some financial risk to encourage adoption of coordinated high-value care practices. In the MSSP, adoption of tobacco screening and treatment of identified people who smoke is required to realize full financial benefits. While the effects of the MSSP on the provision of smoking cessation treatment are not yet known, one study suggests that it increases the number of beneficiaries with diabetes mellitus who refrain from smoking.[119]

Of note, the ACA resulted in a substantial increase in the proportion of Medicaid recipients who received pharmacologic treatment for nicotine dependence.[116] A 2017 paper found that expanded Medicaid coverage was associated with a 36% increase in the number of prescriptions for smoking cessation medications.[120] Another study found that states that expanded Medicaid coverage had a 2.1% greater increase in smoking cessation among adults who smoke, ages 18–64, than states that did not expand Medicaid.[121] Similarly, coverage of prescription smoking cessation medication remains incomplete for Medicare patients, even with Part D plans, that do not cover over-the-counter medications and which could still charge co-pays for FDA-approved smoking cessation medication. While the ACA requires expanded Medicaid programs to provide tobacco cessation services with no cost-sharing requirements, it does not require state programs to remove all barriers to accessing these treatments and services. State Medicaid programs have different tobacco cessation coverage requirements resulting in considerable differences in the availability of tobacco cessation treatment across states.[118] Also, according to estimates from the CDC,[122] many states still have high levels of uninsured people (about 11% of the total U.S. population), preventing access to insurance-covered cessation medications. Private insurers could also require prior authorization and co-pays. These restrictions continue to hinder delivery of evidence-based care for people who smoke, including patients with cancer.

Summary: Adoption

The adoption of evidence-based smoking cessation treatment delivery in cancer care settings has lagged behind the evidence of its benefit. This lack of adoption appears to be due, at least in part, to health care systems failing to support implementation of smoking cessation treatment programs,[123] as well as many clinicians not providing such treatment. Improved adoption will require focused attention to the factors that influence decisions to adopt smoking cessation treatments, including barriers and facilitators at the patient, clinician, health care system, and health insurance system level (discussed in detail later in this chapter in "Challenges to Implementing Smoking Cessation Treatment in Cancer Care Settings at the Patient, Clinician, and Health Care System Level"). Fortunately, payment models, quality metrics, and regulatory and legislative actions show promise for increasing adoption of smoking cessation treatment in cancer care settings and making it a required standard of clinical care for all patients with cancer who smoke.

Implementation

In the RE-AIM framework, Implementation refers to the consistency and fidelity with which elements of an intervention protocol or plan are delivered.[16] Evaluation of implementation can include assessing the consistency of the delivery of discrete intervention elements, whether interventions are delivered as recommended, whether adaptations are made in delivery, and the time and cost of the intervention. There are relatively few assessments of the implementation of smoking cessation treatment in the context of cancer care. However, the existing data suggest that the implementation of screening and treatment for nicotine dependence in patients with cancer is inadequate. A survey of 28 cancer treatment programs located in the northeastern United States accredited by the American College of Surgeons Committee on Cancer reported data on the consistency of implementation of key elements of smoking cessation treatment.[97] This study revealed that while 75% of responding programs linked people who smoke to outside treatment programs (such as quitlines) to "some" extent or a "great" extent, 60% of programs reported that they provided decision aids to support the prescription of smoking cessation medications "very little" or "not at all," and 78% of programs provided prompt follow-up and re-evaluation of patients' cessation goals "very little" or "not at all." These results are consistent with those of another study assessing whether the 5A's of smoking cessation treatment were delivered as recommended in cancer care. In that study by Simmons and colleagues,[124] investigators queried patients about whether their oncologist or the oncology staff delivered the full 5A's or a reduced set. Results showed that full implementation of the 5A's was rare. More than 90% of patients reported that their physician or a staff member asked whether they smoked and 76.1% of patients reported being advised to quit. However, less than one-half reported being asked about their interest in quitting and being helped with quitting, and less than 5% of patients reported follow-up support for their quitting. Overall, patients reported that clinicians executed only the first two of the 5A's.[124] These data are consistent with the level of tobacco intervention implementation found in oncology programs in other studies. For instance, Ramsey and colleagues[125] examined rates of tobacco intervention at a large cancer center prior to the implementation of an enhanced point-of-care smoking cessation treatment program. These authors found the following rates of baseline intervention elements (prior to the point-of-care program): health care clinicians assessed 48% of patients for tobacco use, referred less than 1% of patients to smoking cessation counseling, and provided smoking cessation medication to only 3% of patients.

Summary: Implementation

Research on the implementation of smoking cessation treatment programs in cancer care settings is limited. Existing data indicate that there is a need to increase referrals to smoking cessation counseling or other cessation support, provision of smoking cessation medication, and follow-up support. Important strides have been made in the implementation of comprehensive treatment of smoking in cancer care settings through NCI's C3I initiative (see "Disseminating and Implementing Tobacco Cessation Treatment in Cancer Care Settings: The National Cancer Institute's Cancer Center Cessation Initiative").

Maintenance

Maintenance addresses the extent to which a new program or policy becomes institutionalized and integrated into routine clinical workflows or policies that are sustained over time. This is a critical issue, insofar as sustained organizational change is difficult, and policies and practices often revert to prior states after the initial energy and enthusiasm that is invested in a new program begins to wane. In fact, there is clear evidence that clinicians and health care systems tend to implement smoking cessation treatment less consistently over time.[33]

Several strategies have been shown to maintain the delivery of tobacco interventions in the general health care context.[1,19] These include (1) securing support from health care system leadership for maintaining a smoking cessation treatment program, as organizational and financial support is crucial to mobilize clinicians and administrative staff, including IT specialists who are likely to be involved; (2) embedding the intervention in a multilevel fashion into the usual workflows, policies, and practices of clinicians, ancillary staff, practices, clinics, hospitals, health care systems, and communities; (3) leveraging health information technologies including the EHR, patient-facing mobile health strategies, and other emerging approaches such as wearables and sensors[126]; and (4) leveraging tobacco-relevant quality metrics, payment models, and regulatory policies by accrediting agencies, governmental agencies, payers, and professional societies.

Below are some examples of how these four maintenance strategies can be implemented and maintained in cancer care clinical settings.

Secure Support From Health Care System Leadership

Leadership engagement and support is crucial to both initiating and sustaining any substantial organizational change.[92,127–129] Leadership may be persuaded to implement organizational changes because smoking cessation treatment is clinically effective, cost-effective, and helps institutions comply with numerous external regulatory requirements and financial incentives.[1] Value-based payment models, rather than fee-for-service billing, may incentivize smoking cessation treatment for health care leadership.[1] Salloum and colleagues[130] conducted a study to evaluate system-level implementation costs across 15 NCI-Designated Cancer Centers participating in C3I. In 2020, the median cost-per-participant was $466 (range: $70–$2,093) and cost-per-quit was $2,688 (range: $330–$9,628). These real-world data help inform leadership as they contemplate maintaining smoking cessation treatment programs for patients with cancer.[130]

Integrate Tobacco Screening and Treatment Strategies Into Clinical Workflows

There is a dearth of evidence on specific health care system changes that enhance maintenance of smoking cessation treatment in cancer care settings. However, strategies that have been effective in other health care contexts, such as primary care,[19,131,132] are likely to be beneficial in cancer care. Thus, routine screening of tobacco use among patients with cancer can be performed at multiple sites and throughout the continuum of cancer care. Such screening and treatment delivery can be incorporated into clinical workflows of practices, clinics, and centers that specialize in the treatment of individuals with cancer and can be performed at intake; at routine follow-up visits; and before procedures, such as chemotherapy infusions and radiation treatments. One strategy that can facilitate the re-engineering of cancer care to better address smoking cessation treatment might be to expand the capacity of the cancer care clinical workforce to deliver evidence-based smoking cessation treatment. This facilitation can be achieved through training and education, and by embedding tobacco treatment specialists into multidisciplinary oncology teams. The wide-scale implementation of such tobacco treatment specialists has frequently been limited by their inability to bill independently for cessation treatments provided. Finally, tobacco use status and treatment can become an expected part of the care plan discussed at meetings of tumor boards.

Leverage EHRs

As discussed earlier, several mechanisms exist to leverage the EHR to maintain the delivery of smoking cessation treatments. In addition to their capacity to enhance maintenance, these mechanisms can also be used to enhance the adoption and implementation elements of this framework.

These include:

- Building order sets that guide clinicians in delivering evidence-based counseling and medication;
- Using EHR-based referrals to quitlines and texting programs;
- Scripting clinicians for brief motivational or cessation counseling;
- Automating electronic orders to facilitate prescribing smoking cessation medication; and
- Designing macros to facilitate the identification of and intervention with people who smoke.[32,34]

Macros are EHR text—a phrase, sentence, or series of sentences—that prompt a set of actions. Macros are recorded and saved with the capacity to retrieve and paste for future and repeated ease of use. Such EHR capacities could promote maintenance by reducing the burden for clinical staff (including reducing their counseling responsibilities) and by making smoking cessation treatment an integral part of service delivery. Despite these benefits of the EHR, challenges exist in realizing its full potential, including those related to optimizing the clinical workflow through vendor customizations, clinician engagement, and training. Overcoming these challenges requires an institutional commitment to the effective use of the EHR.[14,133,134]

Leveraging Tobacco-Relevant Quality Metrics, Payment Models, and Regulatory Policies

The use of such metrics, policies, and payment models can incentivize the leadership of oncology practices and cancer centers to prioritize the treatment of nicotine dependence; their use can also prompt clinicians and other oncology staff to adopt and maintain such treatment.[98–100,120]

Summary: Maintenance

Once a health care system decides to implement a smoking cessation treatment program, key strategies can help ensure its maintenance. These strategies include securing health care system leadership support; engineering tobacco use screening and treatment into clinical workflows, making them an integrated, routine element of health care; and leveraging the power of the EHR to reduce clinician burden and facilitate delivery of cessation interventions. These steps, plus adoption of payment models and regulatory requirements that enhance maintenance, should help sustain tobacco intervention in cancer care settings.

Assessing and Verifying Tobacco Use Status

Screening for tobacco use status and updated documentation of that status for all patients with cancer is a critical first step in initiating cessation interventions across the cancer care continuum. However, some cancer patients and survivors report a reluctance to acknowledge ongoing tobacco use,[135,136] likely due to the stigma associated with continued tobacco use after a cancer diagnosis.[137–139] Consistent with this, studies have found that misreporting of current tobacco use among cancer patients and survivors ranges from 39% to 48%.[135,136,140–142] The accurate identification of tobacco use by patients with cancer is a necessary first step to providing them with effective treatment. As with all measurement approaches, an optimal solution balances the validity of the assessment with its expense and the staff and patient burden required for implementation.

NCI and AACR convened the NCI–AACR Cancer Patient Tobacco Use Assessment Task Force to develop recommendations for tobacco use measurement and for research priorities regarding tobacco use after a cancer diagnosis.[143,144] The Task Force's consensus measures form the Cancer Patient Tobacco Use Questionnaire (C-TUQ) (Table 4.2; available at https://cancercontrol.cancer.gov/ctuq). The C-TUQ includes four core items that assess current and past cigarette smoking, as well as a more extensive library that includes items designed for cancer patients and survivors (e.g., assessing tobacco use relative to the timeline of cancer diagnosis and treatment). In addition, the Task Force recommended the use of validated procedures to biochemically confirm self-reported tobacco abstinence (e.g., cotinine or breath carbon monoxide tests) when feasible (see "Appendix B: Biochemical Confirmation Reasons and Methods").[145] Biochemical confirmation of self-reported tobacco use status is likely to provide a more accurate index of cessation treatment effects than self-report alone. However, the routine use of biochemical assessment may not be feasible in some clinical practice and research settings. For instance, time constraints and the cost of the tests can affect feasibility. Also, the clinical team must have a clear idea of the actions to be taken if a test result indicates smoking. The Task Force recommended C-TUQ assessment (self-report with or without biochemical confirmation) at diagnosis or at the point of study entry and at the end of treatment, at a minimum. The C-TUQ can also be administered at Day 1 of each chemotherapy cycle, at the onset and conclusion of radiation therapy, at the onset and conclusion of any other systemic cancer therapy, and 6–12 months after the end of cancer treatment.

Table 4.2 Consensus Assessment Instrument for Tobacco Use in Oncology (C-TUQ, Selected Items)

Section 1. Basic Tobacco Use Information (C-TUQ Core)
1) Have you smoked at least 100 cigarettes (5 packs = 100 cigarettes) in your <u>entire life</u>? ☐ Yes ☐ No ☐ Don't know/Not sure
4) How many total years have you smoked (or did you smoke) cigarettes? Do not count any time you may have stayed off cigarettes. _____ Years *If you smoked less than one year, write "1."*

Table 4.2 (continued)

5) On average when you smoked, about how many cigarettes do you (or did you) smoke a day? A pack usually has 20 cigarettes in it. _____ Number of cigarettes per day.
6) How long has it been since you last smoked a cigarette (even one or two puffs)? *First check which one of the following choices applies to you. Then, if applicable, write a number on the line for how many days, weeks, months, or years it has been since your last cigarette.* ☐ I smoked a cigarette today (at least one puff). ☐ 1-7 days. → Number of days since last cigarette: _____ ☐ Less than 1 month. → Number of weeks since last cigarette: _____ ☐ Less than 1 year. → Number of months since last cigarette: _____ ☐ More than 1 year. → Number of years since last cigarette: _____ ☐ Don't know/Don't remember
Section 2. Cigarette Smoking in Relation to Cancer Diagnosis and Treatment
During each of the following time frames, please indicate whether you smoked cigarettes every day, some days, or not at all. a. The year before you were first told you had cancer b. After diagnosis, and before treatment started c. From 2 days before your last cancer surgery to 2 days after d. During the course of treatment e. After treatment ended f. Since your last visit to this clinic

Note: C-TUQ = Cancer Patient Tobacco Use Questionnaire.
Sources: Land et al. 2016,[144] National Cancer Institute 2017.[305]

Advances in the design and use of EHRs, particularly given the influence of meaningful use measures included in the HITECH Act of 2009,[146] have greatly increased the frequency of tobacco use assessments in the clinical setting.[147,148] While not addressing the limitations of relying on self-report, EHR-based assessments of smoking by patients with cancer have been shown to increase rates of tobacco use assessment and referral to tobacco cessation treatment,[149] even when such assessment depends upon a single question about current tobacco use.[150] Burris and colleagues[151] recommend the use of a single measure assessing 30-day point-prevalence tobacco use. Further, misreporting of tobacco use because of embarrassment, worry, or shame may be overcome either via the use of empathetic and nonjudgmental approaches to information collection[139] or by using assessment methods that reduce perceived adverse evaluations, such as electronic screening devices.[152] While relatively simple measures of smoking status could be appropriate in the context of routine clinical care, tobacco cessation treatment programs should consider more comprehensive measures of tobacco use status and biochemical validation of self-reported tobacco use status. Across both clinical and research activities, the use of standardized assessments of tobacco use as recommended by the NCI–AACR Cancer Patient Tobacco Use Assessment Task Force, along with procedures to reduce the likelihood of misreporting, can improve the quality of patient care and facilitate research by allowing data pooling and comparisons across different studies and populations.

Challenges to Implementing Smoking Cessation Treatment in Cancer Care Settings at the Patient, Clinician, and Health Care System Levels

Health care systems, including cancer care settings, are well-positioned to address tobacco use and dependence at a population level because most U.S. adults who smoke self-report that they see a clinician each year, want to quit smoking, and have made a quit attempt in the past.[21,153] Moreover, as discussed in chapter 1, smoking cessation clearly reduces overall tobacco-related morbidity and mortality in cancer care populations. Despite this patient receptivity and the benefits of smoking cessation, oncology practice often falls short of addressing the behaviors that could lead to reduced smoking and its resultant harms.[92] This has led to a call for cancer care settings to implement a systematic approach to delivering smoking cessation treatment and overcoming challenges to such delivery.[154]

Among the factors responsible for the inadequate treatment of smoking in cancer centers are the multiple barriers at the patient, clinician, and health care systems levels.[154] Understanding barriers at each of these levels can aid health care systems in their efforts to reach, engage, and effectively treat patients with cancer who smoke. In particular, it is critical to understand how to engage patients in smoking cessation treatment and how to re-engage them if they relapse. This knowledge can also assist health care systems in allocating resources to best meet the needs of their patient population. Health care systems must similarly address barriers to clinicians' delivery of effective smoking cessation treatment to ensure patients are offered and able to access high-quality smoking cessation treatment. This section summarizes patient, clinician, and health care systems barriers to implementing smoking cessation treatment in cancer centers, as well as potential strategies to address these barriers, summarized in Table 4.3.

Table 4.3 Challenges to Implementing Smoking Cessation Treatment in Cancer Care Settings at the Patient, Clinician, and Health Care System Levels

Challenges	Potential strategies
Patient level	
Sociodemographic differences in smoking rates by age, sex, race and ethnicity, educational attainment, income level, comorbid psychiatric or substance abuse diagnoses, and medical/physical challenges.	Groups that are disproportionately affected by smoking can be targeted for intervention to equitably reach all populations. Research is needed to improve equitable delivery of smoking cessation treatments, and health care systems should be mindful of these factors when designing and delivering interventions to the patients they serve within their community.
Lack of knowledge or misconceptions about cancer-related risks of smoking and benefits of quitting.	Clinicians can educate patients on how smoking increases the risk of cancer and emphasize the benefits of cessation for cancer patients, including improved response to cancer treatments and quality of life. Health care systems can disseminate educational resources for clinicians and patients.
Low rates of engagement in smoking cessation treatment components (e.g., counseling sessions, medication use) even when they have been offered to and accepted by the patient.	Simplify access and remove barriers to engagement including offering treatments at point of care, providing counseling via multiple modalities (e.g., telehealth, phone), and eliminating copays and other costs.

Table 4.3 (continued)

Challenges	Potential strategies
Low motivation and/or confidence to quit smoking.	Clinicians can use brief intervention strategies to build motivation and confidence to quit. Referral to specialized smoking cessation treatment resources, such as an internal smoking cessation treatment program or the state quitline, may be especially helpful.
Psychological distress related to cancer diagnosis and treatment, including depression, anxiety, stress, shame, guilt, stigma, and other factors that may hinder treatment engagement. Smoking or other tobacco use may also be used as a coping strategy.	Patients can be connected with mental health clinicians as part of their cancer care to manage psychological distress.
Misperceptions about the quitting process including the following: fears that medications are unsafe, do not work, or are addictive; that severe withdrawal symptoms will not dissipate over time; and/or a fatalism that it is too late to quit and that the benefits of quitting only accrue for those who quit early in life.	Correct misconceptions about medications and highlight their potential to reduce withdrawal symptoms. Emphasize that most individuals feel better when they quit with improvements in health typically experienced within days of quitting (e.g., reducing breathlessness) and that such improvements in health are typically experienced irrespective of the age at which an individual quits.
Clinician level	
Limited knowledge of or confidence in delivering smoking cessation treatment or lack of awareness of available resources.	Training clinicians can improve knowledge and confidence to provide smoking cessation treatment.[214] Health care systems can promote educational resources to make clinicians aware of available treatment resources.
Perceptions of patients as unwilling or unmotivated.	Opt-out referral methods may help overcome reluctance or bias on the part of clinicians to address smoking with patients.
Concerns about alienating patients by addressing the topic of smoking.	Communicate that evidence supports higher patient satisfaction when clinicians address tobacco use during the visit. Training clinicians to use gain-framed messages that are personalized may further reduce alienation concerns (i.e., people who quit smoking feel better due to fewer pulmonary symptoms such as reduced breathlessness, less, pain, quicker recovery from surgery).
Awareness that patients may be discouraged by their past failures to successfully quit tobacco use and, as a result, may be unwilling to try to quit again.	Frame the treating of tobacco use as a chronic disease,[19] often requiring repeated interventions similar to treating other chronic diseases (e.g., hypertension, diabetes, even cancer). Highlight modest successes by patients (e.g., brief period off cigarettes, reduced number of cigarettes smoked per day).
Health care system level	
Institutional commitment and accountability (e.g., recognition of smoking cessation treatment as a core component of cancer care).	Health care systems including cancer care settings can formally recognize and promote smoking cessation treatment as a clinical priority, report on the optional Joint Commission tobacco cessation performance measure, and highlight smoking cessation treatment activities as part of reporting for NCI-designation status.

Table 4.3 (continued)

Challenges	Potential strategies
Time (e.g., clinician time constraints, poor workflow integration).	EHR systems that are well-integrated with easy-to-use cessation treatment functionalities can facilitate documentation and automated referral processes of patients who smoke without disrupting workflows or requiring significant additional time from clinicians.
Referral options (e.g., lack of dedicated, stable smoking cessation treatment programs).	Dedicated smoking cessation staff prioritized by leadership, clinical champions, and opinion leaders can increase smokin cessation treatment.
Funding and reimbursement (e.g., lack of stable funding for smoking cessation treatment resources, inadequate clinician and institutional reimbursement).	A health care system commitment to stable funding can help maintain dedicated smoking cessation treatment programs. Reimbursement for clinicians can increase provision of smoking cessation treatment at point-of-care. At the policy level, reimbursement programs such as the Medicare Shared Savings Program that prioritize population-level health outcomes can promote smoking cessation interventions. Also, including the provision of nicotine dependence treatment as part of certification for health care systems (e.g., Joint Commission[106]) can encourage implementation of cessation programs.

Note: NCI = National Cancer Institute. EHR = Electronic health record.

Patient-Level Barriers to Delivering Smoking Cessation Treatment in Cancer Care Settings

Sociodemographic Differences in Smoking Rates

Several studies have used large, nationally representative samples to examine rates of current and former smoking among patients with cancer and cancer survivors compared with those without a cancer diagnosis, revealing sociodemographic factors that are consistently associated with smoking behavior among people with a history of cancer (see chapter 5). Underlying reasons for these patterns are myriad, but may, in part, reflect a failure of health care systems to offer certain populations smoking cessation treatment. For example, among people with a cancer history, current smoking (versus not smoking currently) is associated with younger age,[155–162] female sex,[155,157,159–162] lower levels of educational attainment,[155,157–159,162,163] lower income,[155,161,162] and lack of health insurance.[155,157–159,163,164] Therefore, it is important that health care systems and cancer care settings attempt to ensure that such populations are offered smoking cessation treatment.

Similarly, prospective studies of patients with lung cancer have found younger age and lower income are associated with shorter time to relapse and higher rates of current smoking in the months following surgery.[165,166] Other cancer populations that have especially high levels of current smoking include individuals who report being divorced, separated, widowed, single, or not living with their partner.[158,159,163,167] The causes of these relatively high rates of smoking are unclear, but could involve knowledge gaps, affective or motivational susceptibilities, stress, the presence of comorbid conditions (mental health and/or substance use), or a lack of social support. Regardless, these relationships identify patient groups that are especially likely to smoke and experience harms caused by smoking.

Data on regional variation in smoking rates among people with a cancer history are limited, although one study using nationally representative Behavioral Risk Factor Surveillance System data suggested that rates may be higher among those living in the Midwestern and Southern U.S. states.[155] This finding is consistent with trends in the general population. Smoking rates and tobacco-related disease, including cancer incidence and mortality, vary widely by state and are significantly higher than the national average in a cluster of 13 Southern and Midwestern states.[168–170] These states are less likely to have implemented effective tobacco control policies such as comprehensive smokefree laws than other states,[170] and people living in this region tend to have lower knowledge of the risks of smoking than those in other U.S. regions.[169]

Health care systems can use these data to inform efforts to extend their reach to diverse patient populations. For example, systems serving higher proportions of low-income patients or those living in Southern and Midwestern U.S. states could require that additional resources be allocated to smoking cessation treatment. As discussed in greater detail in chapter 5, it is important that health care systems utilize strategies to increase the representativeness of their reach, to include disproportionately affected patient populations, and to help promote equity in smoking cessation treatment delivery in cancer care. An analysis of reach across NCI-Designated Cancer Centers selected as part of Cohort 1 of NCI's C3I documented improved cessation program reach among racial and ethnic minority groups who smoked over the 2 years of the initiative.[171] Presumably this occurred due to health care system changes that were widely implemented in these programs, such as EHR enhancements that were compatible with clinical workflows, staff training, clear allocation of clinical responsibilities, and facilitation of smoking cessation treatment referral. Moreover, overall cessation program reach among such racial and ethnic minority groups was similar to majority population rates of reach.[171]

Knowledge of Risks of Smoking and Benefits of Quitting

Individuals with cancer who smoke often do not understand the cancer-related risks of continued smoking and the benefits of quitting. For example, many bladder and cervical cancer survivors indicated that they were unaware that smoking was a risk factor for their cancer.[172–175] In general, people who currently smoke perceive themselves to be at higher risk of developing lung cancer than never and former smokers, though only about 15% perceive themselves to be at "very high" risk (response options: very low, somewhat low, moderate, somewhat high, very high).[176] This is consistent with the finding that people who smoke tend to underestimate their personal likelihood of developing lung cancer and other diseases caused by smoking.[177] People who smoke who articulate these optimistically biased (i.e., unrealistically low) risk perceptions are in turn more likely to endorse inaccurate beliefs about smoking and are less likely to quit smoking.[178,179] Others could believe that quitting smoking is not important because life is inherently risky.[180]

One prospective study of people receiving care for acute or chronic illness who smoke, including patients with cancer, found that among those with an illness caused by smoking, optimism bias[181] was associated with lower motivation to quit and lower odds of smoking cessation.[178] In an additional analysis, patients with cancer with higher perceived risk of developing another cancer 3 months after surgical resection were more likely to have quit smoking by 12 months,[182] suggesting that perceived cancer risk could motivate smoking cessation among people with cancer. Qualitative and survey research suggests that patients with cancer are receptive to information about the effects of continued smoking on their health and how quitting smoking would benefit their cancer treatment.[173,183] Evidence suggests that conversations between patients and clinicians can increase patients' awareness of the effects of smoking on their cancer treatment.[139,184,185]

Motivation and Confidence to Quit

Greater motivation, or readiness to quit smoking, is a consistent predictor of smoking cessation abstinence, including among patients with cancer.[186,187] However, once diagnosed with cancer, demographic and psychological factors likely influence patients' motivation to quit. For example, motivation to quit is lower among older and less educated cancer survivors.[157] In addition, lower motivation is observed among those living with other people who smoke, those with lower self-efficacy, lower perceived benefits of quitting, lower risk perceptions, more emotional distress, and more fatalistic beliefs (i.e., believing that there is no benefit to quitting).[188] A qualitative investigation among patients with gastrointestinal cancer suggested several possible reasons for lower motivation to quit, including fatalistic beliefs and lack of confidence in one's ability to quit based on past failed quit attempts.[189]

It is also likely that the nature and intensity of quitting motivations affect the willingness to engage in and benefit from smoking cessation treatment. For example, people with chronic conditions caused by smoking who reported that health concerns were their primary motivation to quit were twice as likely to quit as those reporting other (unspecified) primary motivations.[190] One qualitative study found that the patients who had remained abstinent after their cancer diagnosis tended to be internally motivated; while those who cited external motivation for their quit attempts, such as lack of opportunity to smoke during a hospital stay or influence from friends and family, tended to have relapsed.[139] Still, nearly half of people with a cancer history who currently smoke report having made a quit attempt in the past year,[157] a rate similar to the general adult population of individuals who smoke,[21] and many patients report a desire for help with quitting smoking and cite the importance of doctors' advice in motivating them to quit.[157,190–192] These data suggest that many patients with cancer are already motivated to quit smoking. However, some patients with cancer who smoke certainly lack motivation to quit. There is a great deal of evidence, however, that clinicians can increase patients' motivation to quit by discussing the patient's personal risk of continued smoking (including the heightened risks of adverse cancer outcomes) and offering to help them in the quitting process.[19,193,194]

Psychological Distress

As discussed in chapters 3 and 5, psychiatric comorbidities, particularly depressive symptoms and active substance use disorders, are associated with a lower likelihood of quitting after a cancer diagnosis and with an increased risk of relapse.[192,195–200] Berg and colleagues[192] found that about 64% of patients who continued to smoke after their cancer diagnosis had significant depressive symptoms, compared with only about 27% of those who had quit smoking. Feelings of depression, stress, and anxiety may be barriers to successful smoking cessation,[19] while stress management skills and more adaptive coping could facilitate smoking cessation.[173] Two model programs describe treating psychological distress symptoms while addressing nicotine dependence.[86,87]

Coping

Smoking or other tobacco use can be perceived by patients as an important coping strategy during a difficult life experience. Thus, many individuals could be highly likely to be more nicotine dependent and continue using tobacco in response to the anxiety, stress, and pain that often accompanies cancer diagnosis and treatment.[189,201–203] Indeed, the thought of stopping tobacco use can itself be very stressful. These feelings of distress can be compounded by feelings of guilt, shame, or stigma patients experience related to continued tobacco use.[204] One qualitative investigation in the cancer care setting found that about one-half of relapsed patients were uncomfortable discussing smoking with their clinicians, fearing that they would be judged negatively.[139] These concerns about stigma or feelings of guilt and shame may contribute to patients not being completely truthful about their tobacco use.[139] Addressing patients' depressive symptoms and approaching tobacco use cessation with an empathic, nonjudgmental attitude is an important component of successful smoking cessation treatment for people with cancer who smoke.

Summary: Patient-Level Barriers

Numerous patient-level factors challenge the effective and equitable implementation of smoking cessation treatment in cancer care settings. The observed sociodemographic differences in tobacco use among patients with cancer underscore the importance of consistently offering smoking cessation treatment and monitoring treatment reach for all patients with cancer who smoke, including those in medically underserved and vulnerable populations. Variability in patients' knowledge about the risks of continued smoking after a cancer diagnosis, motivation to quit, and confidence in quitting suggest a need for systems to integrate informational and motivation-building tools into standard care for patients with cancer who smoke. Challenges associated with comorbid distress symptoms, such as depression, anxiety, and worry, and limited capacity to cope with psychological stressors support the potential benefit of integrating smoking cessation treatment with comprehensive mental health treatment. As health care systems design and implement smoking cessation treatment programs in cancer care settings, attention to these patient-level barriers is needed to promote treatment engagement and maximize reach.

Clinician-Level Barriers to Delivering Smoking Cessation Treatment in Cancer Care Settings

Lack of Smoking Cessation Knowledge and Training

Although the importance of smoking cessation for patients with cancer is well understood, cancer care clinicians and staff frequently report that they lack the confidence and training to provide smoking cessation treatment (see chapter 3).[92–95,205–211] Surveys of members of the American Society of Clinical Oncology and the International Association for the Study of Lung Cancer revealed that most members agreed that smoking affects cancer outcomes, and that smoking cessation treatment should be a standard part of clinical care.[94,95,210] However, only about one-third of members in each group reported they were adequately trained to provide smoking cessation services to their patients who smoked. A survey of Arkansas clinicians caring for general primary care populations, predominantly Medicaid- and Medicare-covered, found that nearly 75% reported that they had no training in the treatment of tobacco use, as well as very limited knowledge of free treatment programs available in their state.[212] Further, cancer care clinicians could be concerned about smoking cessation medication side effects or their potential interactions with cancer treatments.[207,213] Training efforts should include educating clinicians on the safety and efficacy of smoking cessation medications for patients with cancer and how to prescribe them.[19]

Perceptions of inadequate knowledge and/or training can stem from uncertainty about the clinician's role in smoking cessation treatment.[203,205] In the United Kingdom, participants in focus groups of radiographers (health professionals delivering radiation therapy for cancer treatment) noted that they did not think smoking cessation was part of their role as it was not part of standard practice, and their departments had no clear policy or process for addressing smoking.[205] One survey of oncologists in Australia found that only 4% of the medical oncologists and none of the radiation oncologists preferred treating patients for tobacco use themselves and instead preferred to refer patients to external services like quitlines, PCPs, or dedicated specialists in their own institutions.[207] These survey results are consistent with qualitative data from interviews with patients with cancer and their clinicians that indicate that cancer care clinicians play a limited role in smoking cessation treatment. Most cancer care clinicians reported that they referred patients to their PCPs for smoking cessation medication prescriptions and other assistance due to feeling unprepared to treat tobacco use themselves or being hesitant to take on the responsibility of long-term follow-up for tobacco use care.[139]

Cancer care settings may vary in their expectations for individual cancer care clinicians, and these expectations should be reflected in health care system policies and processes that clarify clinicians' role in integrating smoking cessation treatment into their patients' care (i.e., whether to provide smoking cessation treatment themselves or to refer patients to other clinicians or treatment-extender programs such as quitlines). The paramount goal is to offer evidence-based smoking cessation treatment that is integrated into patients' cancer care.

Building clinician confidence and competency to address tobacco use is a key component of successfully implementing smoking cessation treatment programs in health care settings, including cancer care. Training programs tested both in primary care[19] and in cancer care settings[214] have significantly improved clinicians' knowledge of smoking cessation treatment and confidence in its provision. Academic detailing—peer-to-peer education, training, technical assistance, and feedback to improve clinical practice in a particular area[215]—has been shown to increase rates of tobacco use assessment and treatment by clinicians and/or clinic staff.[19,216] In one study, 49 primary care outpatient clinics were randomized to a fax-to-quit program only (N = 25) or to a fax-to-quit program with academic detailing (N = 24). Over a 13-month period, academic detailing greatly increased the average number of quitline referrals per clinician compared with usual-care fax-to-quit instruction only (8.5 vs. 1.6 referrals).[216] In another study, one peer-to-peer training program was aimed at increasing clinicians' (predominantly radiation therapists and registered nurses) support of patients with cancer in smoking cessation. Clinicians were trained to identify people who currently smoke, provide a basic smoking cessation intervention, and document such interventions for other members of the care team. Of those who completed the post-training survey (30% response rate), most clinicians (88%) agreed that the training had impacted their patients' smoking cessation attempts and many clinicians (67%) reported they had opportunities in their daily practice to use the training to support patients' smoking cessation efforts.[206] Finally, a brief, 1-hour educational program among nurses in several clinical practice settings, including cancer care settings, significantly improved smoking cessation treatment provision, resulting in increased rates of assessment of patients' interest in quitting, assistance with quit attempts, and quitline referrals.[217]

Memorial Sloan Kettering Cancer Center has developed a tobacco treatment training program to increase the competency of cancer care clinicians to intervene with their patients who use tobacco (Tobacco Treatment Training-Oncology [TTT-O]).[214] Since 2017, more than 200 individuals from across the nation have completed the TTT-O training at Memorial Sloan Kettering, which consists of a 2-day workshop followed by 6 monthly, 1-hour collaborative videoconference calls designed to support workshop attendees in implementing NCCN guidelines for smoking cessation in their cancer care settings. The TTT-O workshop training format includes didactic presentations and experiential small group role-play exercises. Enhanced training is likely to play an important role in increasing the reach and effectiveness of smoking cessation treatment services targeting patients with cancer.

In a national survey of Australian oncologists, most of the surveyed oncologists preferred online tobacco cessation skills training, though many also supported face-to-face training in their institutions, training at regional meetings, and via professional society guidelines.[207] Understanding the preferences and logistical constraints facing U.S. oncology clinicians is an important consideration for future tobacco cessation training efforts.

There is growing recognition that increasing access to evidence-based smoking cessation treatment in oncologic practice requires increasing the percentage of the health care workforce that has received sufficient training to effectively intervene with patients who smoke. Certification or accreditation programs can also enhance the quality of training, increase its breadth, and serve as a training quality metric. The Council for Tobacco Treatment Training Programs[218] accredits tobacco treatment training programs. Clinicians who complete one of these programs can receive certification as Certified Tobacco Treatment Specialists (CTTS).[219] Program use has increased markedly, with almost 8,000 clinicians trained from 2016 to 2019.[220] These programs teach clinicians effective counseling skills and core competencies[219] needed to work with tobacco users within health care settings and other settings. Expanding the multidisciplinary cancer care team to include individuals who have obtained tobacco treatment specialist training likely improves the delivery of smoking cessation treatment in cancer care settings. Importantly, a wide array of clinicians can and have obtained CTTS training including health educators, nurses, and other treating clinicians (e.g., physicians, nurse practitioners). Clinicians with advanced tobacco treatment training, compared with those without specialty tobacco treatment training, have been shown to provide treatment of higher fidelity and/or to result in higher quit rates among their patients trying to quit.[86,87,221–225]

Clinician Perceptions of Patients With Cancer

Clinicians' perceptions of their patients with cancer can also influence their provision of smoking cessation treatment. For example, clinicians could perceive their patients with cancer who smoke as unwilling to engage in or unlikely to benefit from smoking cessation treatment.[94,95,208,209,211,226] One survey of oncology clinicians and midlevel clinicians reported the presence of multiple misperceptions of patients that would likely discourage clinicians from intervening with their patients who smoke. The most common responses were that patients were unmotivated, uninterested in quitting, and unwilling to listen to smoking cessation advice. In addition, one-third of clinicians believed that their efforts to help patients quit smoking were never successful, and none believed they were very successful.[211] Similarly, more than 70% of site coordinators at 93 surveyed lung cancer screening (LCS) sites reported patients' lack of motivation and resistance to smoking cessation advice and treatment as barriers to providing smoking cessation treatment to patients enrolled in screening programs.[208] In contrast, studies of patients with cancer typically report high rates of interest in quitting. For example, Conlon and colleagues[227] reported that more than 85% of patients with head and neck cancer who smoked were interested in quitting and more than 70% were seriously considering quitting smoking within the subsequent 30 days. Meadows-Taylor and colleagues,[228] in a study of patients with thoracic cancer, reported that, among people who currently smoke, 60% were very interested in quitting and 37% would participate in a smoking cessation program.

Clinician perceptions of patients' motivation or readiness to quit can also differ depending on stage of care or treatments. For example, one qualitative study of smoking cessation treatment in the LCS context found that some clinicians believed that referring patients for LCS could increase motivation, whereas others doubted that referral alone would influence smoking behavior. Most agreed that receiving LCS results could be impactful, with many believing that abnormal results could motivate behavior change, while also fearing that normal results could decrease motivation.[185] Some clinicians mentioned that they were especially likely to discuss smoking cessation with people receiving normal LCS results to help them to quit smoking.[185]

Despite believing that key events, such as abnormal LCS results, cancer diagnosis, and cancer treatment initiation can motivate patients, clinicians could still hesitate to encourage smoking cessation at these times because they are concerned about adding to patients' distress.[185,203,229] In the case of LCS, clinicians expressed concern that patients with an abnormal scan might be too overwhelmed by the possibility of a cancer diagnosis to engage in a discussion about smoking cessation.[185] Similarly, radiographers felt the time of diagnosis was a bad time to discuss smoking cessation, citing concerns that patients would be overwhelmed.[205] Clinicians can be especially unwilling to initiate smoking cessation discussions with patients diagnosed with advanced disease, perhaps, due to uncertainty about the usefulness of recommending smoking cessation in this context.[127,203,211]

Clinicians have also expressed concern that smoking cessation treatment discussions could damage their relationships with patients, despite study results reporting that patients who smoke feel that they receive better health care when their clinicians offer to help them quit.[230–233] Some clinicians worry that their patients will feel stigmatized or judged if they are encouraged to quit smoking.[139,203,205,209] In qualitative interviews with clinicians treating patients with cancer, many expressed concerns that addressing smoking around the time of diagnosis could induce feelings of guilt in their patients, adding to their distress in an already overwhelming and difficult time. Rather than risk appearing judgmental to their patients, many avoided the topic unless patients brought it up themselves or clearly indicated they were open to quitting smoking.[203]

In response to staff members' reluctance to approach smoking cessation treatment with patients, Cancer Care Ontario introduced an opt-out approach wherein patients who smoke were automatically referred to an available smoking cessation treatment.[127,128] This approach resulted in improved referral rates, suggesting that integrating an opt-out approach into smoking cessation treatment for cancer care can help clinicians overcome concerns about if, how, or when to initiate it. In addition, multiple C3I sites in the United States have implemented similar opt-out approaches.[18,84,125,128,150] It is worth noting that concerns about adding to patients' feelings of stigma and distress can be well-founded, as patients have described these feelings themselves.

Providing support and treatments that address patients' feelings of cancer-related stress could be warranted to optimize patient outcomes.[86,87,223] These data suggest a need for additional training and research to support appropriate, empathetic, and equitable communication about smoking cessation treatment and stress management in the cancer context rather than avoiding the topic.

Summary: Clinician-Level Barriers

Building capacity for expanding smoking cessation treatment delivery within cancer care settings should include addressing cancer care clinicians' concerns about lack of training to accomplish these goals. Academic detailing is one promising strategy to train clinicians; provide performance feedback; and promote the use of treatment extenders, such as eReferral to state quitlines during cancer care visits. Implementing opt-out programs also has the potential to increase rates of smoking cessation treatment delivery and to normalize the delivery of smoking cessation treatment in cancer care settings. Finally, educating clinicians about the safety and efficacy of smoking cessation treatment options, including medications, is essential and can be reinforced by clinician champions.

Health Care System–Level Barriers to Delivering Smoking Cessation Treatment in Cancer Care Settings

Since health care system institutional changes were first recognized as essential for smoking cessation treatment delivery more than two decades ago,[234] there has been substantial progress in refining and advancing such changes at multiple levels (clinician practice, informatics, hospital policies). However, many barriers remain within health care and health insurance reimbursement systems broadly that can hinder the systematic delivery of smoking cessation treatment in cancer care settings.

Institutional Commitment and Accountability

A 2009 NCI conference on treating nicotine dependence at NCI-Designated Cancer Centers identified barriers and challenges at the clinician, health care system, institutional, policy, and research levels.[154] At that time, a key institutional barrier was the failure of cancer care settings to recognize smoking cessation treatment as a core component of cancer care. A subsequent survey conducted in the same year was the first to document tobacco cessation treatment services offered by NCI-Designated Cancer Centers.[92] Among the 58 centers, 12 (21%) reported no tobacco cessation services or were unsure whether there were cessation services, and only 48% reported having designated personnel to deliver or coordinate tobacco cessation treatment delivery (in contrast, 78% reported having a designated nutritionist). Slightly more than one-half (62%) of these centers reported identification of tobacco use in the outpatient and inpatient settings. Finally, only 28% reported that they had selected tobacco use as a quality improvement metric.

The participants in the 2009 conference made four key recommendations for NCI-Designated Cancer Centers[92]:

1. All cancer centers who treat patients should have a tobacco use treatment program.
2. NCI should facilitate the incorporation of tobacco use treatment services into cancer center clinical care.

3. All cancer centers should adopt quality improvement measures and other opportunities to enhance the delivery of tobacco use treatment services.
4. Institutional funding should support tobacco use treatment services in these cancer centers.

Achieving these four milestones would position NCI-Designated Cancer Centers to lead by example in delivering evidence-based tobacco cessation treatment that is fully integrated with cancer care.

A 2014 National Academy of Medicine (formerly the Institute of Medicine) workshop entitled “Reducing Tobacco-Related Cancer Incidence and Mortality” suggested that tobacco cessation treatment would be rapidly implemented if this was a requirement for accreditation by the Commission on Cancer or other accrediting bodies, or for receiving designation as a cancer center by the NCI.[235] However, this landscape has changed substantially over the past decade, including efforts by NCI designed to heighten awareness of the importance of tobacco cessation treatment in cancer centers. For example, C3I encourages a population-based approach to increase the reach and effectiveness of tobacco cessation treatment delivery within and beyond cancer centers.[8] While C3I was a competitive supplement limited to NCI-Designated Cancer Centers, the initiative has made its data and resources available to all cancer centers to help accelerate availability and uptake of cessation services for patients with cancer.

Limitations of Clinician Time and Referral Options

Even when oncology clinicians are trained in smoking cessation and health care systems recognize its value, smoking cessation treatment may not be prioritized amid other vital components of patients’ cancer care. A variety of constraints inhibit health care systems’ emphasis on providing smoking cessation treatment.[9,91,94,95,185,226] Oncology clinicians are typically overburdened, and express concern about increasing their workload with smoking cessation.[127,128] Nearly one-half of oncology clinicians report having limited time available during patient visits for counseling or making referrals.[94,95,210] As a result, health care systems report that smoking cessation treatment is a lower priority.[211] Indeed, oncology clinical workflows offer health care systems little opportunity to integrate smoking cessation treatment into clinical care. For example, results of LCS are often delivered through written messages or voicemail, leaving health care system staff without a natural opening for a discussion of smoking cessation.[185]

Several systems-level resources can help enable clinicians to provide smoking cessation treatment. Communication regarding such resources is essential given that over a third of surveyed oncology clinicians reported that they did not know where to refer patients for smoking cessation assistance.[211] Moreover, dedicated smoking cessation staff can facilitate treatment and relieve some of the burden on oncology clinicians and advanced practice clinicians.[92,185,236] Having referral systems well-integrated into the EHR can facilitate connections to available smoking cessation treatment resources both internal and external to the health care system.[9,80] Easy-to-use EHR functionalities can facilitate smoking cessation treatment in other ways as well. For example, direct-entry mandatory EHR fields, often completed by rooming staff, can facilitate documentation of smoking status and prompt treatment delivery to either an internal (e.g., oncology clinic-based tobacco treatment specialist) or external (e.g., state tobacco quitline) smoking cessation resource.[9,18,57,125,127,150,237]

At the Siteman Cancer Center of the Washington University School of Medicine, the Electronic Health Record-Enabled Evidence-Based Smoking Cessation Treatment Program was designed as part of NCI's C3I to facilitate tobacco cessation treatment at the point of cancer care, rather than relying on referral to specialists or dedicated treatment programs.[125] After its implementation, tobacco use assessment of patients with cancer increased from 48% to 90%, and the percentage of people with cancer who smoke who were prescribed smoking cessation medication increased from 3% to 17%.[125] These results support the potential of highly functional EHR systems to increase reach and help sustain smoking cessation treatment programs in cancer care settings via improved implementation support for cancer care staff and clinicians. Importantly, such systems-based approaches are most effective when they do not disrupt the clinical workflow.[125]

Support from health care system leaders is critical to obtaining and sustaining the resources and infrastructure necessary for smoking cessation treatment programs' success in the cancer context.[92,127–129] The importance of such senior support was highlighted by the previously mentioned 2009 survey of key staff of 58 NCI-Designated Cancer Centers that found that fewer than one-half believed their center's leadership was committed to smoking cessation treatment.[92] The 2009 survey also identified additional factors that respondents perceived as likely to improve smoking cessation treatment in their centers, including stable funding, tobacco treatment specialists on staff, adequate space, additional staff training, a clinician champion, technical assistance for system enhancements, links to available resources, and support from their administrations.[92]

Interviews with smoking cessation staff in cancer centers also suggested that a lack of strong health care system commitment to smoking cessation services hindered their ability to provide effective smoking cessation treatment, and several staff suggested that leadership support would enhance the integration of smoking cessation treatment services into routine cancer care.[203] The importance of tobacco cessation program leadership was highlighted in a C3I program evaluation that found the identification of tobacco cessation program champions who take ownership of initiatives designed to develop, train, and implement tobacco intervention services in clinical settings was associated with enhanced tobacco cessation treatment program delivery.[18] Such champions may be opinion leaders or influencers within institutions who are committed to developing and sustaining tobacco cessation treatment programs. These individuals should be identified and included in implementation plans to facilitate broad staff engagement and to help lead training efforts.[92,128]

Funding and Reimbursement for Smoking Cessation Treatment Programs

Financial considerations also affect smoking cessation treatment delivery at the clinician and health care system levels.[1] Specifically, stable funding for smoking cessation treatment programs within cancer centers facilitates their ability to deliver smoking cessation treatment consistently as part of cancer care. More than 80% of key staff at 58 surveyed NCI-Designated Cancer Centers believed that stable tobacco cessation treatment program funding was likely to improve tobacco cessation treatment delivery in their centers.[92] Options for tobacco treatment specialists to bill payers for their efforts could also increase these programs' sustainability.[92]

In addition, billing and reimbursement options for clinicians can further facilitate smoking cessation treatment at the point of care.[208] However, only 10% of outpatient oncology clinicians surveyed reported that reimbursement was a barrier to them giving smoking cessation advice.[211] In contrast, in a survey of members of the International Association for the Study of Lung Cancer (including members in the United States), 32% reported that reimbursement was a barrier to providing smoking cessation care, care that is typically more intensive than brief smoking cessation advice.[94,95,210]

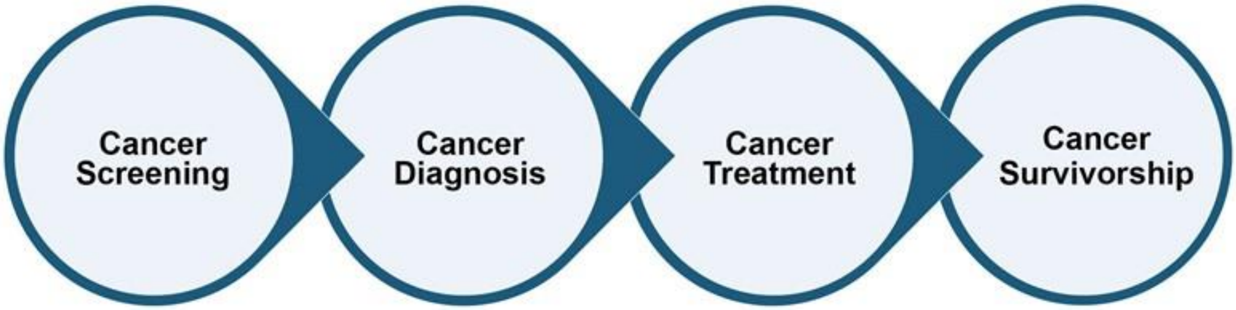
Summary: Health Care System–Level Barriers

While health care systems offer unequaled opportunities to systematically address smoking in patients with cancer, this potential requires an institutional approach to maximize success. Multiple health care systems–level barriers constrain effective smoking cessation treatment delivery, including a lack of support and accountability of the smoking cessation treatment program by health care system leaders or champions; competing demands for clinician time; lack of training of clinicians; a perceived lack of referral options; a failure to embed the intervention into clinical workflows; inadequate leveraging of health information technologies including the EHR; inadequate leveraging of tobacco-relevant quality metrics, payment models, and regulatory policies by accrediting agencies, governmental agencies, payers, and professional societies; and inadequate funding for smoking cessation treatment programs and reimbursement for clinicians. Addressing these barriers would likely facilitate the effective integration of smoking cessation treatment into cancer care. A key first institutional step is to expand the health care system's standard of care such that every patient with cancer who smokes can expect to receive evidence-based smoking cessation treatment as part of his or her cancer care. This foundation can help ensure that health care systems provide opportunities to quit tobacco use to all such patients with cancer who smoke and visit cancer care settings.

A Systems Approach to Providing Smoking Cessation Treatment Across the Cancer Care Continuum

The cancer care continuum is a useful framework to understand the stages at which smoking cessation treatment can be particularly effective. This continuum spans cancer prevention, screening, diagnosis, treatment, survivorship, and end-of-life care, and can be thought of as a circular process rather than a linear one with cancer survivors engaged in cancer prevention. This chapter focuses more narrowly on cancer screening, diagnosis, treatment, and survivorship as phases that represent times when the patient can be especially receptive to smoking cessation treatment (Figure 4.3). Moreover, these moments can be integrated into health care system changes that increase the likelihood that individuals who smoke will receive evidence-based smoking cessation treatments. Some of these cancer continuum stages could be better suited for smoking cessation than others (e.g., smoking cessation rates might be higher at the time of new cancer diagnosis).[6,185,238–241] While intervention to promote smoking cessation is important across the cancer care continuum, specific challenges at each stage may require adaptation of smoking cessation treatment strategies. The following section highlights characteristics of patients, diagnoses, and treatments that can guide health care systems in maximizing the reach and effectiveness of their smoking cessation treatment programs from screening through long-term survivorship.

Figure 4.3 Smoking Cessation Treatment Across the Cancer Care Continuum, From Screening to Long-Term Survivorship



Cancer Screening

- Lung cancer screening is an especially important window of opportunity. Patients with abnormal test results have higher rates of cessation, but over half continue to smoke long term.
- Active clinician interventions (e.g., "Assist" and "Arrange" steps) remain key to motivating and supporting cessation efforts.

Cancer Diagnosis

- Cessation rates tend to be higher among those with a cancer diagnosis than in the general population.
- Cessation rates vary by cancer type.
- Cancer patients are highly motivated to try to quit smoking after their cancer diagnosis.

Cancer Treatment

- Smoking interventions in the perioperative period may be especially effective.
- Patients with later stages of cancer or requiring extensive treatment tend to quit at higher rates.
- Pain may be a barrier to cessation.
- Relapse rates after treatment are high, underscoring the need for ongoing clinician vigilance.

Cancer Survivorship

- Smoking remains prevalent among cancer survivors.
- Self-reported smoking status is especially prone to misreporting.
- As patients enter long-term survivorship, achieving continuity of care for smoking treatment requires partnership with primary care providers.

Note: Intervention to promote smoking cessation is critical across the cancer care continuum. Cancer screening, diagnosis, treatment, and survivorship are all candidate stages for teachable moments that hold the potential for positive behavior change. Specific challenges to smoking cessation treatment implementation may vary by stage.

Smoking Cessation Treatment at Cancer Screening

Individuals with a history of cigarette smoking are at increased risk for developing a range of malignancies,[2,149] including those of the aerodigestive tract (e.g., lung, throat, and oral cancers). This increased risk creates the potential for early detection strategies that target individuals at increased risk for cancer who are likely to benefit from screening and early detection.[242] This section focuses on LCS via low-dose computed tomography (LDCT), which represents an important opportunity to offer people who smoke assistance to quit with evidence-based strategies. Health care systems can also integrate addressing tobacco use into other cancer screenings, including mammography and colorectal cancer screening.

Findings from the National Lung Screening Trial (NLST) offered the first substantial evidence for the utility of LDCT to reduce lung cancer mortality.[243] In 2001, Ostroff and colleagues used data from the Early Lung Cancer Action Project (ELCAP) trial[244] to examine the association between LDCT screening and smoking status.[245] Based on self-report, nearly a quarter of participants reported smoking cessation following screening, while another quarter reduced their smoking rate. These promising observational data suggested that LDCT LCS is a teachable moment[6,246] to engage individuals who smoke in evidence-based smoking cessation treatment strategies.

Eligibility, Guidelines, and Policy for Lung Cancer Screening (LCS)

Following publication of results from the NLST, several organizations provided guidance for LCS implementation. The USPSTF and CMS[247] upgraded LCS using LDCT to a grade B recommendation, making it a covered insurance benefit in the United States under the ACA.[248] LDCT screening guidelines include a strong recommendation for pairing it with evidence-based smoking cessation treatment. During shared decision-making visits to discuss the need for LCS, CMS requires that patients receive counseling on the importance of smoking cessation and abstinence and information about smoking cessation interventions. As of 2015, CMS also requires that radiology imaging facilities make smoking cessation treatment available to people who currently smoke.[248]

Impact of LCS on Smoking

Ostroff and colleagues[245] found that nearly one-half of all participants tried to modify their smoking behavior following participation in the ELCAP program, which offered no formal smoking cessation treatment. Data from subsequent studies have shown more modest and varied associations between LCS and changes in smoking.[240,246,249–259]

Ostroff and colleagues[245] also noted the possibility that normal/clear/negative LCS results could incorrectly communicate an invulnerability to the consequences of smoking and might result in individuals continuing to smoke or former smokers to relapse.

Slatore and colleagues[254] conducted a systematic review of LCS trials that reported smoking behavior change outcomes. In contrast with previous studies, this systematic review found little evidence that supported an overall impact of screening program participation on smoking behavior. However, receiving abnormal or suspicious results was associated with increased abstinence. Consistent with results from the NLST, both the number and suspiciousness of abnormal results contributed to an increased likelihood of smoking reduction or cessation.[254] These findings underscore the complexity of risk perceptions and the potential impact of risk perception biases on quit attempts.[179]

Enhancing Smoking Cessation Treatment Reach and Effectiveness in the Context of LCS

While LCS can be a “teachable moment,”[260] little is known about how to most efficiently and effectively engage individuals in smoking cessation treatment in the LCS context or process. Extant evidence suggests that the most effective methods could involve clinician interventions that directly facilitate smoking cessation treatment entry. Park and colleagues[261] found that smoking cessation rates among NLST participants were meaningfully higher when PCPs delivered the “Assist” and “Arrange” components of the 5A’s after LCS, whereas “Ask, Advise, and Assess” did not significantly influence smoking cessation rates.

It is important to note that early LCS trials tended to test the efficacy of screening combined with only minimal smoking cessation treatment (e.g., brochures).[256] It is certainly possible that higher smoking cessation rates might be observed if more intensive treatment was used. Unfortunately, most published studies in this area have significant limitations. Some have evaluated minimal smoking cessation interventions,[249,259] others had small sample sizes,[241,251,252] and others used nonexperimental designs.[261–263]

More recently, additional efforts have been made to identify effective smoking cessation treatments for this population. For example, the Smoking Cessation at Lung Examination (SCALE) Collaboration comprises seven NCI-funded and one VA-funded clinical trials of smoking cessation interventions for LDCT participants designed to test various smoking cessation interventions in the screening context.[264,265] This work could reveal intervention approaches that are especially effective in the provision of LCS.

Importantly, in 2021, the USPSTF issued an updated recommendation on screening for lung cancer that expanded the eligible age range from 55 to 80 years old to 50 to 80 years old and decreased the required smoking history from 30 pack years to 20 pack years. This expands the eligible pool of patients by about 50%[117] relative to the previous USPSTF recommendations and these changes are expected to expand screening access, especially among women and racial and ethnic minority groups.[247,266] In 2022, CMS issued a national coverage determination that provides Medicare coverage for LDCT screening for patients ages 50 to 77 years old with smoking history of at least 20 pack years.[267]

Incorporating cessation into LCS has high potential benefit. Using the Cancer Intervention and Surveillance Modeling Network (CISNET) and the 2021 USPSTF recommended eligibility, Meza and colleagues[268] demonstrated that smoking cessation with LDCT screening would substantially reduce lung cancer deaths and increase life-years. For example, adding a cessation intervention of modest effectiveness (15%) to LDCT screening results in life-year gains that are comparable to increasing screening uptake from 30% to 100%. Based on these results, the authors concluded that “incorporating cessation programs into screening practice should be a priority as it can maximize overall benefits.”

There are fundamental differences that distinguish the cancer screening context from traditional smoking cessation treatment contexts.[269] First, the patients are older than the general population of individuals who smoke. Second, many of those screened are not seeking and may not even be expecting smoking cessation treatment interventions. Third, as required by the eligibility criteria for screening, this group has, on average, a longer history of smoking and greater nicotine dependence. These characteristics may require a different treatment approach, perhaps one that emphasizes chronic care and motivational interventions.

While data regarding the effectiveness of smoking cessation treatments offered in the context of LCS remain limited and mixed, the Association for the Treatment of Tobacco Use and Dependence (ATTUD) and the Society for Research on Nicotine and Tobacco (SRNT) have recommended the integration of smoking cessation treatment into LCS.[270] Table 4.4 highlights the six key recommendations. This guidance is informed by evidence from multiple care settings and populations[19] and provides initial recommendations on smoking cessation treatment in the LCS context.[270]

Table 4.4 Guidance from the Association for the Treatment of Tobacco Use and Dependence (ATTUD)/the Society for Research on Nicotine and Tobacco (SRNT) Regarding Smoking Cessation Treatment and Smoking Cessation Within Lung Cancer Screening Programs

1)	Screening program participants who smoke should be encouraged to quit at each visit, regardless of lung cancer screening results.
2)	Screening program participants who smoke should be assisted with cessation using evidence-based interventions that combine pharmacotherapy and behavioral intervention as outlined in the PHS Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*.[19]
3)	Screening program participants who smoke should receive follow-up contacts (from the referring clinician or the screening program) to support their smoking cessation efforts.
4)	For screening program participants who smoke but are not motivated to quit or are not interested in evidence-based interventions, behavioral interventions like the 5R's model[a] are recommended at each visit to motivate patients to change their smoking.
5)	Screening programs are encouraged to generate data regarding the optimal intensity, delivery platforms, and overall approaches to guide future efforts.
6)	Screening programs are also encouraged to generate data regarding the potential adverse effects of screening on smoking cessation interventions within lung cancer screening programs as well as the barriers to optimal implementation and outcomes.

Note: PHS = Public Health Service.
[a]5R's model: The clinician should engage the patient in a discussion of the personal *relevance* of smoking cessation, the *risks* of smoking, the potential *rewards* of smoking cessation, and the potential *roadblocks* to quitting (and treatment to address these, if relevant). The fifth step is to *repeat* these steps at subsequent visits.
Source: Fucito et al. 2016.[270]

Cancer Diagnosis

The evidence demonstrates that a cancer diagnosis can increase smoking cessation rates, perhaps by motivating quit attempts. A large U.S. prospective cohort study found that 2-year unaided quit rates were higher among people who were diagnosed with cancer compared with those who were not (31.3% vs. 19.5%), with similar differences also observed at the 4-year follow-up point.[271] An observational study of the tobacco cessation treatment program at MD Anderson Cancer Center that included 2,652 people with a cancer history and 593 without a cancer history found that abstinence rates did not differ between groups.[87] In this study, participants without a cancer history included a substantial number of cancer center employees and patients who were being screened for cancer. Thus, they could have been more motivated to quit smoking than members of the general population (see "Smoking Cessation Treatment at Cancer Screening"). Further, participants with a cancer diagnosis had a history of having smoked more cigarettes over a longer time and demonstrated higher nicotine dependence than those without a cancer diagnosis, factors that can hinder smoking cessation success.[188,202] One review suggested that smoking cessation treatment within 3 months of diagnosis yields higher smoking cessation rates than those occurring more than 3 months after diagnosis,[201] underscoring the importance of timely smoking cessation treatment, ideally at or soon after a cancer diagnosis and the initiation of cancer care.[188,201]

Park and colleagues[86] compared the effects of sustained smoking cessation counseling and provision of medication ("intense treatment") versus shorter-term counseling and medication advice ("standard treatment") on smoking abstinence rates among patients recently diagnosed with cancer in two NCI-Designated Cancer Centers. These authors observed a statistically significantly higher biochemically confirmed 6-month quit rate among those in the intensive treatment group (34.5%) versus those in the standard treatment group (21.5%). This study demonstrated that integrating evidence-based, sustained tobacco cessation treatment into the care of newly diagnosed patients with cancer can be effective. Overall, these data highlight the potential of a cancer diagnosis to motivate smoking cessation, across a range of cancer types and stages, though more research is needed to understand how to most effectively leverage this teachable moment.

Cancer Treatment

The initiation of cancer treatment is another opportunity to offer and provide smoking cessation treatment. An analysis of a large, nationally representative longitudinal sample suggested that having major surgery was associated with a doubling of the chances of quitting for a person who smokes, with higher quit rates observed when surgeries were performed to treat diseases caused by tobacco, including cancer, versus diseases not caused by tobacco.[272] While a systematic review and meta-analysis of 10 RCTs and 3 prospective cohort studies found smoking cessation treatment did not significantly increase smoking cessation rates overall in cancer populations, interventions delivered in the perioperative setting were associated with more than a doubling of the odds of smoking cessation compared with those delivered in other settings (e.g., clinic, postoperative).[273] On the other hand, prospective studies following patients in the months following surgery for lung cancer find high rates of relapse, especially among people who quit smoking shortly before their surgeries.[165,274] In 2020, the Society for Perioperative Assessment and Quality Improvement released a Consensus Statement on Perioperative Smoking Cessation based on studies of people who smoke across multiple clinical settings endorsing the delivery of smoking cessation treatment in the perioperative setting.[275] Together, these data suggest that initiation of cancer surgical treatment could be especially conducive to tobacco cessation. However, additional efforts to arrange smoking cessation treatment follow-up post-surgery could be needed to assist people who were able to quit to avoid relapse.

Smoking Cessation Treatment for Patients With Advanced Cancer

Patients with cancer who are terminally ill or who have been diagnosed with advanced cancer (i.e., cancer that is unlikely to be controlled with treatment) represent a special population regarding smoking cessation treatment. These patients could be receiving cancer treatment to slow the progression of their disease or could be receiving palliative care to relieve symptoms related to their diagnosis. There has been little research on smoking cessation treatment among patients with cancer with terminal illness or advanced disease. However, oncologists’ and other clinicians’ attitudes toward advising patients with cancer who are receiving curative or palliative care to quit smoking were examined in a study conducted in 16 European countries.[276] An invitation sent to 6,235 members of European medical or clinical oncology societies gleaned 544 eligible responses (response rate = 8.7%). For patients with cancer in palliative settings, 74% of respondents agreed that tobacco use negatively affects treatment outcomes, and 63% of those agreed that smoking cessation should be standard treatment in this setting. Only 14% responded that smoking cessation after diagnosis was a waste of time. However, 43% of oncologists reported “not feeling comfortable taking something away patients enjoy doing” when they are receiving palliative care.[276]

Patients with advanced cancer who quit smoking may experience benefits that include improved oxygenation, lower blood pressure, improved blood circulation and respiration, improved appetite, and less fatigue.[277] However, these benefits can be modest, leading Leventakos and colleagues[277] to conclude that, before advising smoking cessation in patients with advanced cancer, clinicians should consider both the potential negative emotional consequences of this effort, including frustration caused by unsuccessful quit attempts, and patients' personal preferences and goals of care. Although the limited available evidence suggests that smoking cessation could provide short-term physical benefits to patients with a diagnosis of advanced cancer, these benefits could also be outweighed by the potential negative effects of cessation on patients' quality of life. Decisions about smoking cessation treatment for patients with terminal cancer should thus be made on an individual basis, based on discussions between the clinician and the patient, and considering the appropriate goals of care for the patient. For those patients wanting to quit, clinicians should link them to evidence-based treatment. Additional research can focus on how clinicians can best engage in these types of discussions or tailor the approach to smoking cessation treatment for individuals with advanced cancer and limited life expectancy.

Post-Treatment and Long-Term Survivorship

A longitudinal study of adult survivors of childhood cancer (mean age = 28 years) found that 19% smoked at baseline, and that smoking rates remained high (14%) over several years of follow-up.[278] While data regarding the persistence of smoking among adult survivors of childhood cancer are limited, these rates reflect a need for more effective smoking cessation treatment in this population. An RCT of a peer-to-peer phone counseling intervention among childhood cancer survivors indicated higher long-term self-reported quit rates among those who had been assigned a peer counselor, compared with those who had received only self-help materials consisting of the "Clearing the Air" manual and a letter from the study physicians about the importance of quitting smoking (quit rates were 20.6% vs. 17.6%, respectively; $p < .0003$).[279]

However, other evidence suggests that achieving cessation and maintaining quitting success for cancer survivors can be challenging. In 2 prospective trials of quitline interventions for adult survivors of childhood cancer, self-reported smoking cessation rates at 12 months were comparable to rates observed in other smoking cessation trials (i.e., 19%–26%).[280] However, biochemically verified abstinence rates at 12-month follow-up were less than 2% among adult survivors of childhood cancer and less than 5% among adult-onset cancer survivors, indicating that nearly 50% of adult-onset cancer survivors and more than 80% of childhood cancer survivors misreported their smoking status.[280] These results strongly suggest that self-reported smoking status among cancer survivors is prone to misreporting.[281]

Thus, there is mixed evidence regarding the effectiveness of smoking cessation treatment among individuals after they have received cancer treatment. Some have suggested that higher quit rates might be achieved with the use of guideline-recommended treatment, such as the use of both pharmacotherapy and behavioral support.[273,282] In addition, interventions can be made more effective if tailored to the individual's readiness to quit smoking and if intensive treatments are paired with sustained follow-up.[282]

Summary: Cessation Across the Cancer Care Continuum

Evidence supports a need for smoking cessation treatment across the cancer care continuum from screening to cancer care to cancer survivorship. Importantly, such interventions can be particularly effective when initiated as early as possible after a cancer diagnosis. Systems that integrate smoking cessation treatment into perioperative workflows hold promise for helping people who smoke quit, although relapse risk remains a concern postoperatively. Finally, as patients with cancer enter the post-treatment phase, continuity of care for smoking cessation treatment can be facilitated through communication between cancer clinicians and those who care for the patient after their cancer care, including primary care clinicians.

The Economic Rationale for Implementing Smoking Cessation Treatment in Cancer Care

The financial burden of cancer care on the patient is considerable; in 2019, this cost for U.S. patients was estimated to be more than $21 billion.[283] The annual direct medical care costs for illnesses caused by smoking among adults in the United States, including cancer, were estimated to be more than $225 billion[284] in 2014. The average annual value of lost productivity due to early mortality from cigarette smoking among adults ages 35–79 years old in the United States was estimated at approximately $150.7 billion for the period of 2005–2009.[2] The substantial costs of smoking, the economic impact, and the cost-effectiveness of smoking cessation treatment have been investigated for decades.[285] However, only recently has research focused on the economic effects of smoking and on the economics of smoking cessation treatment among individuals with cancer.

Incremental Costs Associated With a Smoking History Among Patients With Cancer

Warren and colleagues[286] modeled the incremental cost of additional cancer treatment or re-treatment required because of patients' smoking in the United States. The model was developed in 2018 using data from the 2014 Surgeon General's report and considered smoking prevalence in patients with cancer, likelihood of first-line cancer treatment failure attributed to smoking compared with nonsmoking, and cost of cancer treatment after failure of first-line cancer treatment. The model did not incorporate costs associated with noncancer comorbid disease management, end-of-life care, and complications associated with cancer treatment. Assuming a 20% smoking prevalence, a 60% increased risk of treatment failure attributed to smoking, and $100,000 mean added cost per cancer treatment failure, the analysis estimated an additional $10,678 in average costs per patient with cancer who smokes. The authors extrapolated this finding to 1.6 million patients with cancer each year to project a potential $3.4 billion incremental cost of treating cancer failures associated with continued smoking among patients with cancer in the United States each year.[286]

In another study, Isaranuwatchai and colleagues[287] investigated the impact of smoking on health care system costs among patients with cancer using administrative data from a population-based cohort in Ontario, Canada, between 2014 and 2016. The health services incorporated into the analysis were hospitalizations, emergency room visits, drugs, home care services, and physician services. Patients who smoked (defined as patients who smoked at the time of diagnosis or who had smoked in the past 6 months prior to their first ambulatory care visit) were more likely to have advanced cancer stages than nonsmokers. Overall, the unadjusted estimated total monthly health care costs were almost 20% higher in people who smoked (2016 CAN$5,649) compared with nonsmokers (2016 CAN$4,704). From the adjusted regression model estimates controlling for age, sex, income, rurality, stage, cancer site, geographical region, and comorbidity, people who smoked still had significantly higher monthly health care costs (2016 CAN$5,091) than nonsmokers (2016 CAN$4,847).

Similarly, Salloum and colleagues[130] evaluated the costs of implementing tobacco cessation treatment programs in 15 cancer centers funded by NCI's C3I between 2018 and 2020. The study calculated the total operating costs for each center within a 6-month period, expressed in local market terms, and taking the perspective of the health care system. The study focused on operating costs to maintain the program after it was developed, as they are most relevant to decision-makers. These costs included program personnel type (e.g., oncologists vs. nurses) and effort (with fringe benefits estimated at 30% of total salary costs), medications covered by the program, educational and training materials, software and technology services, equipment, and office space. Median total monthly operating costs in 2020 were $11,045 (range: $5,129–$20,751), dominated by personnel costs. Median cost-per-participant was $466 (range: $70–$2,093) and cost-per-quit was $2,688 (range: $330–$9,628), with sites offering different combinations of program components.

Kaul and colleagues[288] examined annual health care utilization and expenditures among adult cancer survivors in the 2010–2014 Medical Expenditures Panel Survey. Cancer survivors who were currently smoking, compared with nonsmokers, had significantly fewer office-based/outpatient visits (marginal effect = −3.44, 95% CI = −5.02 to −1.86), significantly more emergency department visits (marginal effect = 0.11, 95% CI = 0.05–0.18), but no significant difference in total health care expenditures.[288]

In addition to studies that estimated health care utilization and costs broadly among all patients with cancer, other economic studies have been limited in scope to the cost of treating patients with a specific cancer site diagnosis. Murphy and colleagues[289] examined pretreatment predictors of total cost and length of stay among patients with locally advanced esophageal adenocarcinoma who underwent esophagectomy between 2002 and 2008. While they did not separate current smoking from former smoking in their cohort, the researchers found that number of pack years smoked was significantly associated with increased inpatient cost of esophagectomy ($\beta = 0.0022$, $p = .028$). Sari and colleagues[290] evaluated the effects of smoking on the cost of hospitalization and length of stay among patients with lung cancer in Iran between 2014 and 2015. Compared with never-smokers, current and former smokers in this study showed a 48% and 35% increase ($p = .0001$) in hospitalization costs, respectively.

Two studies using 2007–2014 U.S. Department of Defense (TRICARE) administrative claims data examined the association of tobacco use with medical care costs among head and neck cancer survivors.[291,292] Both studies found that patients with a history of tobacco use had significantly increased medical care costs. Tobacco use was associated with an increased number of ambulatory visits, but no significant change in number of hospitalizations.[291,292]

Cost-Effectiveness of Smoking Cessation Treatment for Individuals With Cancer

To assess the utility of smoking cessation treatment from an economic standpoint among people with cancer who continue to smoke, it is vital to conduct appropriate cost-benefit analyses. Smoking can lead to increases in direct health care costs (e.g., hospitalization costs), direct non-health care costs (e.g., transportation and caregiving costs), and indirect costs (e.g., lost productivity due to illness).[2,293] With the mounting evidence on the health benefits of quitting smoking after a cancer diagnosis, economic evaluations have begun to determine increased cancer medical care utilization rates and treatment costs for patients who continue to smoke compared with those who do not currently smoke. This section examines information from published studies on economic outcomes associated with smoking among individuals diagnosed with cancer and the integration of smoking cessation treatment into cancer care.

Smoking cessation treatment provides substantial economic benefits at both the individual and population levels, and tobacco cessation interventions are cost-effective compared with many other disease prevention interventions.[285] Cost-effectiveness is a form of economic analysis used to compare the change in costs between two scenarios (either two different interventions or between an intervention and "doing nothing") relative to the change in health outcomes between the two scenarios. Cost-effectiveness of smoking cessation has been measured using several different health outcomes, including cost per stop (quit rate), cost per life-year gained, and cost per quality-adjusted-life-year (QALY) saved.[1] Estimates of the incremental cost-effectiveness of smoking cessation treatment have ranged across settings from several hundred to several thousand dollars per life-year or QALY saved and have varied according to the age group quitting smoking, the economic perspective employed, the smoking cessation treatment type, and the baseline (control) intervention used for comparison.[1] The 2020 Surgeon General's report concluded that smoking cessation interventions are cost-effective.[1] However, this report did not examine the economic impacts of smoking cessation treatment among individuals diagnosed with cancer.

One of the first published studies to evaluate the cost-effectiveness of smoking cessation treatment in cancer treatment was a model by Slatore and colleagues[294] examining the implementation of a smoking cessation treatment program at the time of surgery for lung cancer. Initiating a smoking cessation treatment program before surgical lung resection was found to be cost-effective (compared with usual care that omitted offer of a smoking cessation treatment program) at both 1 year and 5 years post-surgery. The incremental cost per QALY and cost per life-year were $16,415 and $45,629 at 1 year post-surgery and $2,609 and $2,703 at 5 years post-surgery, respectively. Djalalov and colleagues[295] conducted an economic evaluation of smoking cessation programs in the regional cancer programs of the Canadian province of Ontario. The study modeled the potential cost-effectiveness of two smoking cessation treatment approaches: the current-practice smoking cessation treatment program established in 2012 consisting of screening for tobacco use, advice, and referral,[128] and a best-practice smoking cessation treatment program that included the current basic program with the addition of pharmacological therapy, counseling, and follow-up. For the modeled population (people with cancer who smoke), the best-practice smoking cessation treatment program was both more effective and more costly than the basic smoking cessation treatment program. The incremental cost-effectiveness ratio of the best-practice smoking cessation treatment program compared with the basic smoking cessation treatment program (in 2015 dollars) was CAN$3,367 per QALY gained and CAN$5,050 per life-year gained for men, and CAN$2,050 per QALY gained and CAN$4,100 per life-year gained for women—suggesting that a best-practice smoking cessation treatment program could be a highly cost-effective option.[295]

In addition to studies examining the cost-effectiveness of smoking cessation treatment within the context of active cancer treatment, there has been at least one economic evaluation of smoking cessation treatment in cancer survivorship. Emmons and colleagues[296] tested a smoking cessation treatment intervention consisting of peer-delivered counseling for people who smoke in the Childhood Cancer Survivors Study. Participants (mean age = 31 years) were randomly assigned to either a self-help or a peer-counseling program that included up to 6 telephone calls from a trained adult survivor of childhood cancer, tailored and targeted materials, and free NRT. The smoking cessation rate at 12 months was significantly higher in the counseling program (15%) compared with self-help (9%), and the cost of delivering the peer-counseling intervention was approximately $300 per participant. The incremental cost-effectiveness of the peer-counseling intervention compared with the self-help program was $5,371 per additional quit.[296]

Cost-Effectiveness of Smoking Cessation Treatment in the Context of LCS

Patients who are eligible for LCS represent a population that is at high risk for cancer due to their smoking history. The prospect of preventing cancers and other illnesses caused by smoking in this high-risk population has led to the development of smoking cessation treatment interventions for such individuals. Villanti and colleagues[297] modeled the cost-utility (i.e., incremental cost per QALY gained) of annual LCS with no smoking cessation treatment versus LCS with a light or an intensive smoking cessation treatment intervention. In a hypothetical cohort of current and former smokers between the ages of 50 and 64 years with a smoking history of at least 30 pack years, adding a smoking cessation treatment intervention to annual LCS improved the cost-utility. Cost-utility ratios versus no screening (using 2012 dollars) ranged from $28,240 per QALY gained for annual screening without any smoking cessation treatment intervention to $23,185 per QALY gained for annual screening with a light intervention to $16,198 per QALY gained for screening with an intensive intervention. The authors concluded that repeat annual LCS in a high-risk cohort of adults ages 50–64 is highly cost-effective and offering smoking cessation interventions with the annual screenings improves the cost-effectiveness by 20%–45%.[297] Another study by Goffin and colleagues[298] compared the outcomes and costs between annual and biennial LDCT screening in Canada using a simulation modeling approach. Relative to no screening, either annual or biennial screening that included smoking cessation treatment was more cost-effective; however, the cost-effectiveness of annual compared with biennial screening did not differ. Additional studies have found that offering smoking cessation treatment in the context of LCS could provide several benefits (e.g., more people quitting smoking, thus preventing some lung cancers as well as other diseases and resulting in life-years saved) at reasonable costs.[299–301]

Summary: Economic Outcomes Related to Smoking in Patients With Cancer

The small number of published studies suggests that individuals who continue smoking after a cancer diagnosis have increased health care costs. In addition, smoking cessation treatment interventions among patients with cancer are highly likely to be cost-effective. As with smoking cessation treatment interventions among individuals without a cancer diagnosis, the cost-effectiveness of smoking cessation treatment interventions among individuals diagnosed with cancer will likely vary by type of intervention and economic perspective, as well as the clinical characteristics of the patient (e.g., type and stage of cancer diagnosed).

Disseminating and Implementing Tobacco Cessation Treatment in Cancer Care Settings: The NCI Cancer Center Cessation Initiative (C3I)

Despite clear recommendations from national and international cancer organizations, tobacco use screening and delivery of/referral to smoking cessation services have been inconsistently implemented in NCI-Designated Cancer Centers and other cancer care settings.[92] While there are clear guidelines for what types of smoking cessation services are most effective for helping people who smoke to quit, how to implement these services within the context of cancer care delivery is less well understood. Although hundreds of research studies have been conducted to identify the most effective smoking cessation treatments,[19] less research has addressed RE-AIM strategies to foster Reach, Adoption, Implementation, and Maintenance of these treatments in health care generally. Even fewer have addressed these challenges in the context of cancer care.

In 2017, NCI established the C3I as part of the Cancer Moonshot Initiative to help NCI-Designated Cancer Centers build and implement sustainable tobacco cessation treatment. The overall goal was to improve the delivery of evidence-based tobacco cessation treatment services to every patient with cancer who smokes. This initiative was developed in response to a critical unmet need identified for cancer care—the routine assessment of tobacco use and provision of assistance in quitting.[7] The implementation and progress of C3I since 2017 provides real-world examples and lessons learned for how to address the multilevel challenges in integrating tobacco cessation treatment into clinical cancer care. In addition to C3I in the United States, Cancer Care Ontario designed its own program to improve the quality of cancer care by implementing evidence-based tobacco cessation treatment delivery for patients newly diagnosed with cancer who use tobacco.[127]

In 2017, the first cohort of 22 NCI-Designated Cancer Centers received 2 years of funding[8]; in 2018, a second cohort of 20 additional cancer centers was funded. Finally, in 2020, a third cohort of 10 additional centers was funded and 11 previously funded centers received 1 additional year of support (52 total NCI-Designated Cancer Centers funded, as of October 2020 – Figure 4.4). To increase the likelihood of ensuring that programs had an impact across the cancer center patient population that was sustained after NCI support ended, the initiative encouraged systems-level changes to prompt tobacco cessation treatment delivery. Importantly, while not prescriptive in terms of the type of tobacco cessation programs provided, C3I sites were mandated to evaluate outcomes every 6 months including rates of (a) screening of all patients with cancer for smoking, (b) referral for treatment of patients who smoked, (c) the proportion of patients referred who received tobacco cessation treatment, and (d) abstinence rates of those treated.

Figure 4.4 National Cancer Institute (NCI) Cancer Center Cessation Initiative (C3I) Sites

Cohort 1 (2017–2019)
1. Baylor College of Medicine
2. Case Western Reserve University
3. Duke University
4. Georgetown University
5. Indiana University
6. Medical University of South Carolina
7. New York University
8. University of California Davis
9. University of Chicago
10. University of Colorado
11. University of Iowa
12. University of Kansas
13. University of Kentucky
14. University of Minnesota
15. University of New Mexico
16. University of North Carolina at Chapel Hill
17. University of Pennsylvania
18. University of Utah
19. University of Virginia
20. Vanderbilt University
21. Washington University
22. Yale University

Cohort 2 (2018–2020)
1. Columbia University
2. Dana-Farber/Harvard Cancer Center
3. Dartmouth College
4. Emory University
5. Mayo Clinic
6. Memorial Sloan Kettering
7. Moffitt
8. Mount Sinai
9. Northwestern University
10. Oregon Health and Science University
11. Roswell Park
12. Stanford University
13. University of Arizona
14. University of California San Francisco
15. University of Michigan
16. University of Texas Southwestern
17. UPMC Hillman
18. Virginia Commonwealth University
19. Wake Forest University
20. Wayne State University

Cohort 3 (2020–2021)
1. City of Hope Comprehensive Cancer Center
2. Fox Chase Cancer Center
3. Rutgers Cancer Institute of New Jersey
4. Thomas Jefferson University
5. University of Alabama at Birmingham
6. University of California, San Diego
7. University of Maryland
8. University of Southern California
9. University of Texas
10. University of Washington

= C3I Coordinating Center, University of Wisconsin Carbone Cancer Center

In addition to funding the 52 cancer centers, NCI established the C3I Coordinating Center at the University of Wisconsin Carbone Cancer Center to provide scientific and technical assistance and to serve as a knowledge hub for implementing tobacco cessation treatment programs in cancer care settings. The Coordinating Center's responsibilities include facilitating program implementation and assisting the 52 funded sites in the modification of their EHRs, with a goal of systematizing the universal identification and delivery/referral of patients with cancer who smoke to tobacco cessation treatment. C3I grantees provide data to the Coordinating Center twice annually including tobacco cessation treatment program characteristics, such as services offered, staff hired, implementation strategies and progress, tobacco use screening rates, and the reach and effectiveness of their tobacco cessation treatment programs.

As noted, cancer centers participating in C3I designed their programs by taking a population-based approach to delivering evidence-based tobacco cessation treatment to every patient with cancer who smokes. Publications from cancer centers participating in C3I are included in Appendix A. As a result, the interventions implemented at various C3I sites comprise a variety of clinical practices designed to provide evidence-based smoking cessation treatments to patients with cancer who smoke. Three general categories of programs were implemented by C3I sites with many sites using a combination of these program types (Figure 4.5):

1. Point-of-Care Delivery of Tobacco Cessation Treatment Programs, which includes internal programs, such as counseling and pharmacotherapy provided at the point of cancer care;
2. Refer Patients to Internal Tobacco Cessation Treatment Programs, which includes counseling and medication delivered via health care system personnel; and
3. Refer Patients to External Tobacco Cessation Treatment Programs, which includes referring patients who smoke to external cessation treatment options such as state quitlines and text/mobile programs like NCI's SmokefreeTXT.

Centers were strongly encouraged to use the EHR to facilitate the identification of patients with cancer who smoke, to support treatment delivery, to refer tobacco users for cessation services, and to report on program reach and effectiveness. As of mid-2019, 40 of the 42 C3I centers funded at that time offered in-person counseling services, with 24 of those delivering advice to quit at the point of care; 28 centers offered connections to the state quitline via a fax or EHR referral. Some centers engineered their EHRs to streamline both the identification of tobacco users and their referral to tobacco cessation treatment via automatic EHR-based referral systems (i.e., eReferral). eReferral has been shown to be a promising method for increasing the reach of tobacco cessation treatment programs implemented in cancer care.[302] Prior to receiving C3I funding, only 7 of the 22 centers in the first cohort used eReferral to facilitate tobacco cessation treatment delivery[9]; by mid-2019, all 22 had implemented eReferral EHR functionalities. One innovative component of eReferral is that it sometimes provides closed-loop referral capacity (based on whether such closed-loop functionality is programmed into the EHR). This capacity both facilitates EHR-based referral of patients to cessation services, often to outside service providers such as a state quitline or NCI's SmokefreeTXT, and also feedback on the outcome of the referral (e.g., successfully contacted, patient quit) to the patient's EHR and/or the referring clinician in a HIPAA-compliant way.[32,37]

Prior to receiving C3I funding, only 10 of the 22 cancer centers in the first C3I cohort had the ability to report on the proportion of patients screened for tobacco use, the proportion of people who smoke who engaged in or were connected with smoking cessation treatment (i.e., reach), or the proportion of people who smoke who received specific evidence-based tobacco cessation treatment components (e.g., counseling, pharmacotherapy, quitline/text to quit referrals). C3I Coordinating Center biannual data showed that among those 10 centers, 81% of patients were screened for tobacco use in 2017; this increased to 93% in 2019, 2 years after receiving funding. These 10 cancer centers also reported that their tobacco cessation treatment programs reached an average of 19% of people who identified as currently smoking prior to C3I funding. After 2 years of funding, all 22 centers in Cohort 1 had developed capacities to report on reach. Across those 22 centers, mean reach was 36% (range: 0.5%–100%), demonstrating that C3I funding increased funded centers' capacity to track treatment engagement accurately and with an increased likelihood that individuals would engage in tobacco cessation treatment.

Models of Tobacco Cessation Treatment Employed by C3I Sites

Depending on the resources available and site preferences, three broad models of tobacco cessation treatment were implemented across the C3I sites (Figure 4.5). Sites frequently combined components and treatment elements from the three models. Regardless of which model or which combination of models was used, all patients with cancer who smoke were offered at least the minimum standard of care for treatment, which included a combination of brief smoking cessation counseling and FDA-approved smoking cessation medication.[19] Typically, this goal was accomplished through a combination of point-of-care treatment, such as advice to quit and a medication prescription from the oncologist at the time of the clinic visit followed by referral to an internal or external program. Such a scenario exemplifies precisely how clinical referral models such as the 5A's, AAR, and AAC can be applied in cancer care settings. The following section describes in more detail the three models of care shown in Figure 4.5.

Figure 4.5 Elements of Exemplar Tobacco Cessation Treatment Programs: Three Models Used Successfully in Cancer Care Settings

Common Elements for All Tobacco Treatment Programs (TTPs)

- Screen all patients for tobacco use and document status in EHR.
- Offer all tobacco users both counseling and medication for smoking cessation via one or more of the three treatment models below.
- Leverage the EHR to facilitate delivery of program elements and to monitor program utilization and outcomes.

Oncology clinics and their health systems can adapt one of the three treatment models below or combine elements of these models.

Model 1
Point-of-Care Delivery of Tobacco Cessation Treatment Programs

- Oncology clinicians:
  - Advise tobacco cessation.
  - Prescribe cessation medication.
  - May provide counseling.
  - Emphasize the impact of continued tobacco use on both cancer and non-cancer outcomes.
- Nurse or health educator in oncology clinic:
  - Typically delivers bulk of counseling care.
  - Sometimes including referral to internal/external TTPs (see models 2 and 3).
- Point-of-care treatment occurs as part of cancer care visits.

Model 2
Refer Patients to an Internal TTP

- Oncology clinicians and/or clinic staff:
  - Advise tobacco cessation.
  - Refer patients to dedicated TTP within the cancer center health care system.
- Internal TTPs are staffed by trained tobacco treatment specialists or other trained clinicians. Such staff typically:
  - Provide feedback, usually via the EHR, to the oncology care clinicians.
  - Oversee cessation follow-up care (e.g., continuing counseling, troubleshooting medication problems, renewals, changes).
- Internal TTPs also typically include (either via opt-in or opt-out system):
  - EHR-based outreach to all patients within the cancer care setting identified as patients who smoke (e.g., via the EHR Tobacco User Registry function).
- Internal TTPs cessation services are typically delivered apart from oncology care visits.

Model 3
Refer Patients to an External TTP

- Oncology clinicians and/or clinic staff:
  - Refer patients to TTPs outside of the cancer center/ health care system, such as state quitline or SmokefreeTXT.
- Outcomes of external TTP referral and care are shared with oncology care team:
  - Ideally, via closed-loop e-Referral capacities that now exist for state quitline and SmokefreeTXT to inform treating clinicians of referral outcomes.
- Prescribing of cessation medications may be delivered by the oncology care clinical team or by the external TTP referral.
- Referral to external TTPs can be offered via EHR-based outreach to all patients who smoke within the cancer care setting, typically via the EHR Tobacco User Registry function.
- External TTP cessation services are typically delivered apart from oncology care.

Note: EHR = electronic health record.

Point-of-Care Treatment Models

Point-of-care treatment models typically utilize the EHR to prompt a variety of clinic staff members (e.g., medical assistants, nurses, health educators, treating clinicians) to deliver evidence-based treatment components themselves, including smoking cessation counseling. The use of multiple team members helps reduce the time burdens on busy cancer care clinicians (physicians, physician assistants, nurse practitioners) whose charge is focused on highlighting the importance of tobacco cessation and prescribing or endorsing the use of tobacco cessation medications. Such multi-clinician-delivered care was a frequent choice for C3I health care systems and may be particularly helpful for cancer care settings that (1) have an in-house tobacco cessation "specialist program" that is underutilized, (2) have tobacco cessation programs without dedicated tobacco treatment specialists, or (3) want to increase patient engagement using existing internal program resources. For example, the C3I-supported Siteman Cancer Center at the Washington University School of Medicine implemented a full point-of-care treatment model where the health care delivery team together delivered the 5A's.[125] The clinical workflow was modified so that the nurse or medical assistant taking patient vital signs was prompted by the EHR to ask about tobacco use, provide brief advice to quit, assess interest in cessation counseling and medication, and connect the patient to external cessation counseling resources via eReferrals. During the cancer care encounter, based on clinical data collected by the nurse or medical assistant, the prescribing clinician was prompted with a best practice alert to address tobacco use with the patient who smokes. Additional EHR tools (e.g., "smart sets") then provided guidance options for the clinician to prescribe appropriate tobacco cessation medications.

Internal Referral Treatment Models

Internal referral treatment models typically identify patients who smoke during the rooming process and then refer those patients to an internal tobacco cessation counseling program, either in person, telephone based, or both. This model was also commonly implemented at C3I Cancer Centers. It requires additional staff, often in the form of trained tobacco treatment specialists or other health care professionals trained in tobacco cessation counseling. Many centers opted to train nurse practitioners or physician assistants to serve as tobacco treatment specialists, to see patients specifically for tobacco cessation (because of their capacity to provide counseling, write prescriptions, and bill for treatment services provided). However, many programs also use tobacco treatment specialists, professionals typically with bachelor's- or master's-level education who receive extensive training on tobacco cessation treatment options including a variety of evidence-based counseling approaches to become certified in this role.[219] Referrals to these specialists could be initiated by rooming staff or treating clinicians via an EHR referral during cancer care encounters.[150] Alternatively, tobacco cessation treatment program staff could use the EHR to target patients who smoke using the EHR registry function and by providing outreach to all people who smoke who visit the cancer care setting regardless of their interest in quitting (i.e., opt-out treatment delivery).[82]

External Referral Treatment Models

External referral treatment models typically refer patients who smoke to external programs such as state tobacco quitlines, an IVR telephone program, and/or a text/mobile program, such as NCI's SmokefreeTXT, designed to aid in smoking cessation or to increase motivation to quit.

Such programs often utilize the EHR and an opt-out approach, designed to increase the proportion of patients who are offered treatment. While such programs have the potential to enhance reach, some of these interventions (IVR, text programs) may have lower quit rates.[303] As noted, many of the C3I sites implemented components of more than one model.

Lessons Learned From Implementation of C3I

The 52 funded C3I sites identified important lessons regarding integration of evidence-based tobacco cessation treatment into cancer care settings that should be relevant to implementing tobacco cessation programs in cancer care settings broadly, although they were not necessarily tested via randomized trials. These lessons were compiled via C3I Coordinating Center site visits when funding ended for funded centers and are described in detail below.

Secure Organizational Buy-In Through Clinical, Administrative, and IT Champions. C3I sites highlighted the key role that champions play in facilitating implementation. Effective champions were typically knowledgeable about the health benefits of smoking cessation for patients with cancer, enthusiastic about the initiative, viewed as trusted clinicians, and influential within the cancer care setting. C3I centers with clinical champions reported that these individuals facilitated interactions between the clinical staff and the tobacco cessation treatment program staff, including helping both to implement changes to the clinical workflow and to facilitate training of clinical staff in the new workflow. Effective champions were also identified in other areas.[18] While clinical champions helped to obtain clinical staff agreement to alter their responsibilities and workflows, administrative and IT champions were critical for obtaining the necessary organizational and EHR modification approvals and implementation. For most cancer care settings, modifying the clinical workflow, including adapting EHR changes to support that workflow, typically requires several levels of approval. Thus, champions can help pave the way for the implementation of an effective tobacco cessation treatment program—both within cancer centers and within community cancer care clinical settings.

Systematically Implement Workflow and EHR Changes. After determining which workflow changes are both necessary and possible, it is essential to work with health care system and clinician leadership, as well as front-line clinicians, to communicate these changes prior to implementation. It is vital to provide information, such as why the changes are necessary, the expected benefits resulting from the changes, and efforts made to minimize extra burden. Adoption can be further enhanced by systematizing the changes via simple EHR adaptations.

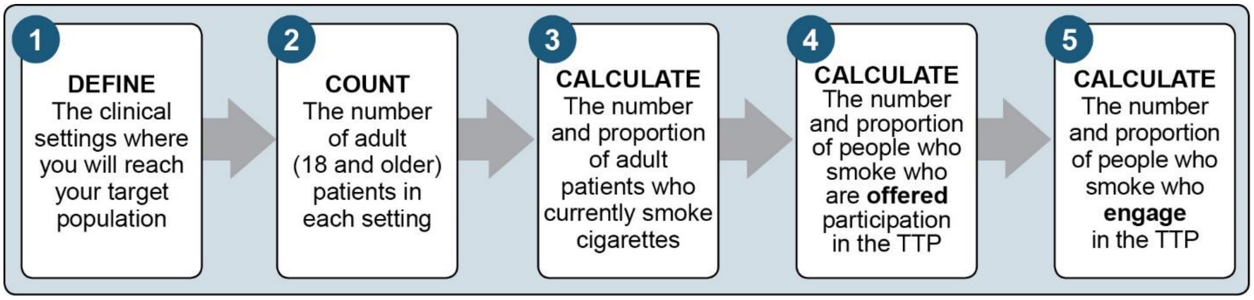
Once the new clinical workflow has been determined and the necessary EHR changes identified, the timeline for IT staff to make those changes needs to be included in the project implementation timeline. All clinicians, including medical assistants, nurses, oncologists, and others with a role in the identification, treatment, and referral of patients who smoke must be trained on the new workflow. C3I sites have used a variety of instructional methods for training, including in-person and video-based demonstrations and simulated patient encounters using test records in the EHR.[18] Progress in implementing a tobacco cessation treatment program can be enhanced if training and EHR adaptations occur in tandem (i.e., training occurs contemporaneously with the implementation of planned EHR changes by IT staff).

Reduce Barriers for Patients to Participate. For models of care that provide tobacco cessation treatment counseling at separate appointments, coordinating these visits with other patient oncology appointments can increase attendance and, thereby, reach. Alternatively, telehealth/telephone visits can be offered to patients for whom travel is a barrier. Cost can also present a barrier for patients, whether it is an insurance co-pay for counseling, surcharges based on smoking status, or the cost of smoking cessation pharmacotherapy. Working with patients to find low- or no-cost options for tobacco cessation treatment and pharmacotherapy can reduce barriers to participation. Cancer centers often have integrated patient support resources, such as social workers, who may be able to assist tobacco cessation treatment programs and patients with finding resources.

Monitor Program and Patient Outcomes Using the EHR. The EHR can be utilized to track whether patients are screened for smoking, advised to quit, and have received treatment from either a cancer center–based cessation program or via referral to external cessation treatment services. Developing functionalities that can provide reports on these measures is critical for evaluating implementation outcomes of the program, including program reach. As discussed earlier in this chapter, reach refers to the proportion of people who currently smoke who engage in or are connected with evidence-based tobacco cessation treatment. Each C3I site first defined the target population of its current tobacco cessation treatment, such as the cancer center as a whole or specific clinical settings such as hospitalized patients with cancer.

As part of its reporting requirements, C3I sites counted the number of adult patients in each setting, reported the number and proportion who were identified as people who currently smoke, and evaluated the number and proportion of people who currently smoke who were offered treatment and who engaged in it (Figure 4.6). The EHR can be used for this purpose, or programs could develop databases where follow-up visits and smoking cessation outcomes are documented for program participants. A challenge to measuring smoking cessation outcomes is that it relies on both program-level resources to contact patients, and on the patient completing follow-up assessments. Conducting follow-up assessments via telephone can possibly increase rates of follow-up. Moreover, utilizing the EHR during subsequent clinic visits to track patient smoking status can provide additional data to assess outcomes when resources are not available for dedicated patient follow-up.[18] Additionally, program reach and effectiveness should be examined as a function of patient sociodemographics in order to ensure effective implementation for the entire patient population and to monitor whether there are sociodemographic disparities in smoking cessation rates.

Figure 4.6 Methods Used by Cancer Center Cessation Initiative (C3I) Sites to Track Program Reach and Effectiveness



Note: As part of the C3I program, “Reach” is defined as the proportion of people who currently smoke who engage in or are connected with evidence-based tobacco treatment. TTP = Tobacco Treatment Program.

Summary

The C3I program and other research has demonstrated that health care systems can successfully and effectively integrate smoking cessation treatment into cancer care settings. Applying findings from implementation science can enhance that integration. Each clinical setting, whether an acute care, ambulatory, or inpatient site, can provide smoking cessation treatment as part of comprehensive cancer care. Guidelines put forth by clinical, research, and patient organizations, such as the NCCN, reflect the growing momentum and recognition of the importance of providing evidence-based smoking cessation treatment to all patients with cancer who smoke.

The RE-AIM framework has been applied broadly to structure the planning, implementation, and evaluation of smoking cessation treatment delivery in cancer care. Specific strategies that have been shown to facilitate such treatment delivery at the health care system level include leveraging EHRs to enhance current smoking identification and treatment delivery, implementing opt-out approaches to expand population reach, utilizing IVR systems to automate follow-up, and using telehealth to connect clinicians with patients who smoke. Payment models, quality metrics, and regulatory and legislative actions all have the potential to spur greater adoption of smoking cessation treatment by health care systems and clinicians. Strategies to promote maintenance of smoking cessation treatment programs in clinical care settings include securing support from health care system leadership, integrating tobacco screening and cessation treatment strategies into clinical workflows, and leveraging tobacco-relevant quality metrics, payment models, and regulatory policies. These components can provide a foundation for the use of evidence-based smoking cessation treatment models such as the 5A’s in the PHS Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update.*

Much can be learned from the models of care identified as part of NCI’s C3I program. The real-world experiences of C3I can help guide the successful implementation of comprehensive smoking cessation treatment programs across multiple types of cancer care settings. Applying the findings of C3I, along with the research reviewed in this chapter, provide effective and practical evidence-based examples for health care systems and cancer care settings that aim to implement smoking cessation treatment programs to assist patients with cancer who smoke to quit.

Conclusions

1. Challenges to implementing smoking cessation treatment in cancer care settings persist at the patient, clinician, and health care system levels. It is important that these multilevel barriers be understood and addressed so that health care systems can provide cessation treatment equitably and effectively to all patients with cancer who smoke.
2. Successful implementation of smoking cessation treatment in cancer care settings requires health care system changes designed to increase the reach, effectiveness, adoption, implementation, and maintenance (i.e., the RE-AIM framework) of smoking cessation treatment interventions.
3. Effective strategies to improve smoking cessation treatment reach and engagement in oncology care start with the consistent and accurate assessment of tobacco use status for all patients across the cancer care continuum. Assessment of tobacco use for all patients with cancer needs to be empathic and nonjudgmental to reduce patient anxiety, embarrassment, or guilt, and to encourage accurate disclosure of tobacco use status.
4. Clinic-wide opt-out (as opposed to opt-in) smoking cessation treatment engagement strategies show promise as a means of enhancing the reach and delivery of smoking cessation treatments to patients with cancer who smoke.
5. Clinical decision supports, prompts, and order sets embedded in electronic health records (EHRs) can improve the rate of both screening for tobacco use and delivering smoking cessation treatments. Such EHR tools can aid in the delivery of smoking cessation treatment, either as part of the cancer care or via a referral to an internal health care system tobacco treatment specialist or to an external option, such as a state tobacco quitline, state quitline-provided texting program, or the National Cancer Institute's (NCI) SmokefreeTXT.
6. Health care system accreditation guidelines, publicly reported quality metrics, and pay-for-performance programs can encourage health care systems to improve the frequency of tobacco use screening and treatment for all patients who smoke, including those with cancer.
7. Research has identified multiple smoking cessation treatment program models (e.g., smoking cessation treatment delivered during cancer care or via referral to internal or external smoking cessation treatment services) that can be effectively implemented in a variety of cancer clinical settings.
8. Continued smoking after a cancer diagnosis is associated with increased health care costs relative to not smoking. Smoking cessation interventions provided to patients with cancer are highly likely to be cost-effective.
9. The NCI Cancer Center Cessation Initiative (C3I) has developed a variety of implementation strategies to enhance the reach and effectiveness of smoking cessation treatment delivery in NCI-Designated Cancer Centers. These approaches exemplify how smoking cessation treatment strategies can be implemented broadly in cancer care settings.
10. Strategies to reduce system-level barriers to cessation among patients with cancer who smoke include ensuring that evidence-based cessation treatments are provided as a covered benefit by health insurers and other payers, without barriers to access and/or use.

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Appendix A. C3I Grantee Publications

Below is a selected list of C3I Grantee Publications that may be useful for cancer centers to refer to. Further information and an extended list of publications, presentations, and posters may be found on the National Cancer Institute's C3I website (https://cancercontrol.cancer.gov/c3i) and the University of Wisconsin-Madison C3I website (https://c3i.wiscweb.wisc.edu/publications/).

Year Published	Title	Authors	Site	Publication Information
2022	*Increased reach and effectiveness with a low-burden point-of-care tobacco treatment program in cancer clinics*	Ramsey, A.T., Baker, T.B., Stoneking, F., Smock, N., Chen, J., Pham, G., James, A.S., Colditz, G. A., Govindan, R., Bierut, L.J., & Chen, L.S.	Alvin J. Siteman Cancer Center—Washington University	Journal of the National Comprehensive Cancer Network, 20(5), 488-495.e4. doi:10.6004/jnccn.2021.7333
2022	*Reach and effectiveness of the NCI Cancer Moonshot-funded Cancer Center Cessation Initiative*	D'Angelo, H., Hohl, S.D., Rolland, B., Adsit, R.T., Pauk, D., Fiore, M.C., & Baker, T.B.	C3I Coordinating Center	Translational Behavioral Medicine, ibac009. doi:10.1093/tbm/ibac009
2022	*The tragic triad of tobacco dependence, cancer, and COVID-19 pandemic: An urgent call for attention by health care systems and professionals*	Presant, C.A., Macalintal, J., Ashing, K.T., Yeung, S., Tiep, B., West, H., Merla, A., & Phillips, T.	City of Hope Comprehensive Cancer Center	Journal of Clinical Oncology Practice, 18, 99-105. doi:10.1200/OP.21.00625
2022	*Changes in cigarette smoking behavior in cancer survivors during diagnosis and treatment*	Jose, T., Schroeder, D.R., & Warner, D.O.	Mayo Clinic Cancer Center—Mayo Clinic	Nicotine & Tobacco Research, ntac072, Advance online publication. doi:10.1093/ntr/ntac072
2022	*Assessment and counseling gaps among former smokers eligible for lung cancer screening in U.S. adults: A cross-sectional analysis of National Health and Nutrition Examination Surveys (NHANES), 2013-2018*	Hood-Medland, E.A., Dove, M.S., & Tong, E.K.	UC Davis Comprehensive Cancer Center—University of California Davis	Journal of General Internal Medicine, Advance online publication. doi:10.1007/s11606-022-07542-0
2022	*Proposing a model of proactive outreach to advance clinical research and care delivery for patients who use tobacco*	Burris, J.L., Borger, T N., Baker, T. B., Bernstein, S L., Ostroff, J.S., Rigotti, N.A., & Joseph, A.M.	N/A	Journal of General Internal Medicine, Advance online publication. doi:10.1007/s11606-022-07553-x

Year Published	Title	Authors	Site	Publication Information
2021	*Introduction to the Cancer Center Cessation Initiative Working Groups: Improving oncology care and outcomes by including tobacco treatment*	The Cancer Center Cessation Initiative Coordinating Center and Expert Advisory Panel	C3I Coordinating Center	Journal of the National Comprehensive Cancer Network, 19(Suppl_1), S1-S3. doi:10.6004/jnccn.2021.7095
2021	*Achieving equity in the reach of smoking cessation services within the NCI Cancer Moonshot-funded Cancer Center Cessation Initiative*	D'Angelo, H., Webb Hooper, M., Burris, J.L., Rolland, B., Adsit, R., Pauk, D., Rosenblum, M., Fiore, M.C., & Baker, T.B.	C3I Coordinating Center	Health Equity, 5(1):424-430. doi:10.1089/heq.2020.0157
2021	*Time to put it out—nurse-facilitated tobacco treatment in a comprehensive cancer center*	Katz, D.A., Mott, S.L., Utech, J.A., Bahlmann, A.C., Dukes, K.A., Seaman, A.T., Laux, D.E., Furqan, M., Pollack, Z.J., & Vander Weg, M.W.	Holden Comprehensive Cancer Center—University of Iowa	Translational Behavioral Medicine, 11(9):1726-1738. doi:10.1093/tbm/ibab073
2021	*Presumed consent with opt-out: an ethical consent approach to automatically refer patients with cancer to tobacco treatment services*	Ohde, J., Master, Z., Tilbert, J., & Warner, D.	Mayo Clinic Cancer Center—Mayo Clinic	Journal of Clinical Oncology, 39(8):876-880. doi:10.1200.
2021	*Nicotine addiction and its treatment*	Prochaska, J.J., & Benowitz, N.L.	Stanford Cancer Institute	In S. Hecht & D. Hatsukami (Eds.), Tobacco and cancer: The science and the story. Singapore: World Scientific Publishing
2021	*Integrating diversity, equity, and inclusion approaches into treatment of commercial tobacco use for optimal cancer care delivery*	The Cancer Center Cessation Initiative Diversity, Equity, and Inclusion Working Group	N/A	Journal of the National Comprehensive Cancer Network, 19(Suppl_1), S4-S7. doi:10.6004/jnccn.2021.7091
2021	*Involving family and social support systems in tobacco cessation treatment for patients with cancer*	The Cancer Center Cessation Initiative Family and Social Support Systems Working Group	N/A	Journal of the National Comprehensive Cancer Network, 19(Suppl_1), S8-S11. doi:10.6004/jnccn.2021.7090
2021	*Implementation science to improve tobacco cessation services in oncology care*	The Cancer Center Cessation Initiative Implementation Science Working Group	N/A	Journal of the National Comprehensive Cancer Network, 19(Suppl_1), S12-S15. doi:10.6004/jnccn.2021.7094
2021	*Sustainability of tobacco treatment programs in the Cancer Center Cessation Initiative*	The Cancer Center Cessation Initiative Sustainability Working Group	N/A	Journal of the National Comprehensive Cancer Network, 19(Suppl_1), S16-S20. doi:10.6004/jnccn.2021.7093

Year Published	Title	Authors	Site	Publication Information
2021	*Telehealth delivery of tobacco cessation treatment in cancer care: An ongoing innovation accelerated by the COVID-19 pandemic*	The Cancer Center Cessation Initiative Telehealth Working Group	N/A	Journal of the National Comprehensive Cancer Network, 19(Suppl_1), S21-S24. doi:10.6004/jnccn.2021.7092
2021	*Mixed-methods economic evaluation of the implementation of tobacco treatment programs in National Cancer Institute-designated cancer centers*	Salloum, R.G., D'Angelo, H., Theis, R.P., et al.	N/A	Implementation Science Communications, 2(41). doi:10.1186/s43058-021-00144-7
2020	*Low burden strategies are needed to reduce smoking in rural healthcare settings: a lesson from cancer clinics*	Ramsey, A.T., Baker, T.B., Pham, G., Stoneking, F., Smock, N., Colditz, G.A., James, A.S., Liu, J., Bierut, L.J., & Chen, L.S.	Alvin J. Siteman Cancer Center—Washington University	International Journal of Environmental Research and Public Health, 17(5), 1728. doi:10.3390/ijerph17051728
2020	*Implementation of tobacco cessation services at a comprehensive cancer center: A qualitative study of oncology providers' perceptions and practices*	Rodgers-Melnick, S.N., & Webb Hooper, M.	Case Comprehensive Cancer Center—Case Western Reserve University	Supportive Care in Cancer. doi:10.1007/s00520-020-05749-7
2020	*Health benefits and economic advantages associated with increased utilization of a smoking cessation program*	Datta, S.K., Dennis, P.A., & Davis, J.M.	Duke Cancer Center—Duke University	Journal of Comparative Effectiveness Research, 9(11), 817-828. doi:10.2217/cer-2020-0005
2020	*Comparison of referral methods into a smoking cessation program*	Davis, J.M., Thomas, L.C., Dirkes, J.E., Datta, S.K., & Dennis, P.A.	Duke Cancer Center—Duke University	Journal of Comparative Effectiveness Research, 9(11), 807-815. doi:10.2217/cer-2020-0004
2020	*Strategies for referring cancer patients in a smoking cessation program*	Davis, J.M., Thomas, L.C., Dirkes, J.E., & Swartzwelder, H.S.	Duke Cancer Center—Duke University	International Journal of Environmental Research and Public Health, 17(17), 6089. doi:10.3390/ijerph17176089
2020	*Implementation of the Smoking Treatment and Recovery (STAR) program: Healthy cancer survivorship through integrated tobacco control*	Taylor, K.L., Fallon, S., Subramaniam, D., Davis K.M., To, C., Lobo, T., Tercyak, K.P., Friberg, J., Tynan, M., Russell, E., Ahmed, W., Ponder, M.C., Cusaac, L., Thompson, J., Gardner, K., Kim, C., & Weiner, L.M.	Georgetown Lombardi Comprehensive Cancer Center—Georgetown Lombardi	Journal of Cancer Survivorship, 14(1), 53–58. doi:10.1007/s11764-019-00826-1

Year Published	Title	Authors	Site	Publication Information
2020	*Design and pilot implementation of an electronic health record-based system to automatically refer cancer patients to tobacco use treatment*	Jose, T., Ohde, J.W., Hays, J.T., Burke, M.V., & Warner, D.O.	Mayo Clinic Cancer Center—Mayo Clinic	International Journal of Environmental Research and Public Health. 17(11). doi:10.3390/ijerph17114054
2020	*Improved documentation of electronic cigarette use in an electronic health record*	Jose, T., Hays, J.T., & Warner, D.O.	Mayo Clinic Cancer Center—Mayo Clinic	International Journal of Environmental Research and Public Health, 17(16), 5908. doi:10.3390/ijerph17165908
2020	*Integration of tobacco treatment services into cancer care at Stanford*	Gali, K., Pike, B., Kendra, M.S., Tran, C., Fielding-Singh, P., Jimenez, K., Mirkin, R., & Prochaska, J.J.	Stanford Cancer Institute	International Journal of Environmental Research and Public Health, 17(6), 2101. doi:10.3390/ijerph17062101
2020	*Special issue: tobacco use and treatment among cancer survivors*	Goldstein, A. & Warren, G.	N/A	Special Issue of the International Journal of Environmental Research and Public Health, guest edited by Dr. Goldstein and Dr. Warren
2020	*Effect of sustained smoking cessation counseling and provision of medication vs shorter-term counseling and medication advice on smoking abstinence in patients recently diagnosed with cancer: A randomized clinical trial*	Park, E.R., Perez, G.K., Regan, S., Muzikansky, A., Levy, D.E., Temel, J.S., Rigotti, N.A., Pirl, W.F., Irwin, K.E., Partridge, A.H., Cooley, M.E., Friedman, E.R., Rabin, J., Ponzani, C., Hyland, K.A., Holland, S., Borderud, S., Sprunck, K., Kwon, D., Peterson, L., Miller-Sobel, J., Gonzalez, I., Whitlock, C.W., Malloy, L., de León-Sanchez, S., O'Brien, M., & Ostroff, J.S.	N/A	JAMA, 324(14):1406-1418. doi:10.1001/jama.2020.14581
2020	*Leveraging patient reported outcomes measurement via the electronic health record to connect patients with cancer to smoking cessation treatment*	May, J.R., Klass, E., Davis, K., Pearman, T., Rittmeyer, S., Kircher, S., & Hitsman, B.	Robert H. Lurie Comprehensive Cancer Center—Northwestern University	International Journal of Environmental Research and Public Health, 17(14), 5034. doi:10.3390/ijerph17145034

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2020	*Tobacco dependence treatment in oncology: initial patient clinical characteristics and outcomes from Roswell Park Comprehensive Cancer Center*	Sheffer, C.E., Stein, J.S., Petrucci, C., Mahoney, M.C., Johnson, S., Giesie, P., Carl, E., Krupski, L., Tegge, A.N., Reid, M.E., Bickel, W.K., & Hyland, A.	Roswell Park Comprehensive Cancer Center	International Journal of Environmental Research and Public Health, 17(11):E3907. doi:10.3390/ijerph17113907.
2020	*Engagement and effectiveness of a smoking cessation quitline intervention in a thoracic surgery clinic*	Mustoe, M.M., Clark, J.M., Huynh, T.T., Tong, E.K., Wolf, T.P., Brown, L.M., & Cooke, D.T.	UC Davis Comprehensive Cancer Center—University of California Davis	JAMA Surgery, 155(9), 816-822. doi:10.1001/jamasurg.2020.1915
2020	*The emergence of a sustainable tobacco treatment program across the cancer care continuum: A systems approach for implementation at the University of California Davis Comprehensive Cancer Center*	Tong, E.K., Wolf, T., Cooke, D., Fairman, N., & Chen Jr., M.S.	UC Davis Comprehensive Cancer Center—University of California Davis	International Journal of Environmental Research and Public Health Special Issue Tobacco Use and Treatment among Cancer Survivors, 17(9), 3241. doi:10.3390/ijerph17093241
2020	*Using a family systems approach to treat tobacco use among cancer patients*	Ruebush, E., Mitra, S., Meyer, C., Sisler, L., & Goldstein, A.O.	UNC Lineberger Comprehensive Cancer Center—University of North Carolina at Chapel Hill	International Journal of Environmental Research and Public Health, 17(6), 2050 doi:10.3390/ijerph17062050
2020	*Intensive smoking cessation counseling for patients with cancer*	Goldstein, A.O., Shoenbill, K.A., & Jolly, T.A.	UNC Lineberger Comprehensive Cancer Center—University of North Carolina at Chapel Hill	JAMA, 324(14):1401-1403. doi:10.1001/jama.2020.13102
2019	*Building systems to address tobacco use in oncology: Early benefits and opportunities from the Cancer Center Cessation Initiative*	Jenssen, B.P., Leone, F., Evers-Casey, S., Beidas, R., & Schnoll, R.	Abramson Cancer Center—University of Pennsylvania	Journal of the National Comprehensive Cancer Network, 17(6), 638-643. doi:10.6004/jnccn.2019.7312
2019	*Care-paradigm shift promoting smoking cessation treatment among cancer center patients via a low-burden strategy, electronic health record-enabled evidence-based smoking cessation treatment*	Ramsey, A.T., Chiu, A., Baker, T., Smock, N., Chen, J., Lester, T., Jorenby, D.E., Colditz, G.A., Bierut, L.J., & Chen, L.S.	Alvin J. Siteman Cancer Center—Washington University	Translational Behavioral Medicine, 10(6):1504-1514. doi:10.1093/tbm/ibz107
2019	*Addressing a core gap in cancer care—The NCI Moonshot program to help oncology patients stop smoking*	Croyle, R., Morgan, G., & Fiore, M.	C3I Coordinating Center	New England Journal of Medicine, 380: 512-515. doi:10.1056/NEJMp1813913

Year Published	Title	Authors	Site	Publication Information
2019	*Tobacco treatment program implementation at NCI Cancer Centers: Progress of the NCI Cancer Moonshot-funded Cancer Center Cessation Initiative*	D'Angelo, H., Rolland, B., Adsit, R., Baker, T., Rosenblum, M., Pauk, D., Morgan, G., & Fiore, M.	C3I Coordinating Center	Cancer Prevention Research, 12(11):735-740. doi:10.1158/1940-6207.CAPR-19-0182
2019	*Effective cessation treatment for patients with cancer who smoke—The fourth pillar of cancer*	Fiore, M., D'Angelo, H., & Baker, T.	C3I Coordinating Center	JAMA Network Open Oncology, 2(9):e1912264. doi:10.1001/jamanetworkopen.2019.12264
2019	*Mitigating the adverse health effects and costs associated with smoking after a cancer diagnosis*	Warren, G.W.	Hollings Cancer Center—Medical University of South Carolina	Translational Lung Cancer Research, 8(Suppl 1), S59-S66. doi:10.21037/tlcr.2019.04.07
2019	*Association of a comprehensive smoking cessation program with smoking abstinence among patients with cancer*	Cinciripini, P.M., Karam-Hage, M., Kypriotakis, G., Robinson, J.D., Rabius, V., Beneventi, D., Minnix, J.A., & Blalock, J.A.	MD Anderson Cancer Center—The University of Texas	JAMA Network Open Oncology. doi:10.1001/jamanetworkopen.2019.12251

Appendix B. Biochemical Confirmation Reasons and Methods: Evidence Based on the Society for Research on Nicotine and Tobacco (SRNT) Working Group on Biochemical Verification

In 2020, the Society for Research on Nicotine and Tobacco (SRNT) provided updated recommendations on whether and how to use biochemical markers in determining tobacco use and abstinence. The following information is relevant to both the research and clinical treatment contexts.

1. Rationale for use of biochemical confirmation. There is evidence of significant levels of misreporting of smoking status.
   a) Misreporting appears to be increasing over time.
   b) Misreporting appears to be especially common in patients who have smoking-related diseases.
   c) Some evidence suggests that as many as one-third to one-half of patients with cancer who smoke deny it.[135,142]
2. Purposes
   a) Use of biochemical assessment will likely detect more smokers in the patient population so that smoking cessation treatment can be offered and encouraged and to aid treatment planning (e.g., the scheduling of surgery).
   b) Use of regular biochemical assessments will help determine whether a patient has successfully quit smoking after a quit attempt.
3. Types of biochemical verification and relevant information
   a) Carbon monoxide (CO) via a breath sample
      i) CO can be measured quickly and accurately with a relatively inexpensive device that requires little training for clinic staff to use routinely.
      ii) Provides immediate information about smoking status.
      iii) Smoking levels are typically over 4–5 ppm CO but nonsmokers may sometimes exceed these levels due to environmental exposure or marijuana smoking.[306]
      iv) In the case of high levels of CO in a person who denies the use of combustible tobacco, the clinician should inquire about other forms of exposure in a nonleading manner.
      v) CO assessment detects elevated CO due to combustion products and therefore will not show high values due to use of NRT.
      vi) CO assessment has a relatively short half-life of about 4 hours, it is influenced by pulmonary ventilation and exercise, and may reach a “non-smoking” value in a regular smoker after 6–24 hours of non-smoking.
   b) Cotinine from laboratory assay
      i) Is a relatively stable, major proximate metabolite of nicotine.
      ii) Can be determined from a blood sample serum, plasma, or whole blood routinely collected as part of clinical care or can be determined from saliva or urine.
      iii) Serum levels of free cotinine in individuals who smoke typically range from 100–250 ng/ml; those not using nicotine should have values <15 ng/ml.[307,308]
      iv) Detection in urine is less sensitive than in blood; a cut-point for regular nicotine use is ≥30 ng/ml.[309]

   v) Individual variation in cotinine level is influenced by environmental exposure, pregnancy status, and metabolic rate.
   vi) Cotinine half-life can vary from 8–30 hours; typically, it would take about 2 days or more for cotinine levels to fall to nonsmoking levels after nicotine intake is discontinued (from a blood level of 200 ng/ml).
   vii) Cotinine reflects the use of NRT; therefore, individuals with high values who deny smoking should be queried in a nonleading manner about use of noncombustible nicotine products (NRT, ENDS).

c) Cotinine (from commercially available dip sticks)
   i) These are relatively inexpensive, widely available, and provide immediate feedback as to smoking status.
   ii) They provide easily interpreted evidence of cotinine level from urine or saliva.
   iii) They are less sensitive than laboratory assays using blood or urine and provide only nonquantitative (categorical) evidence.
   iv) Lateral flow immunoassay cotinine strips for urine are inexpensive, provide a binary outcome (smoking vs. nonsmoking), and are meaningfully associated with total cotinine in urine.[310]
   v) As with any cotinine assay, dip-stick cotinine tests will reflect the use of nicotine from any source (NRT, ENDS).

Note: NRT = nicotine replacement therapy. ENDS = electronic nicotine delivery systems.
Source: Benowitz et al. 2020.[145]

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NCI Monograph 23
Treating Smoking in Cancer Patients:
An Essential Component of Cancer Care

Chapter 5
Addressing Smoking in Medically Underserved and Vulnerable Cancer Populations

Chapter Contents

Figures and Tables

Chapter 5
Addressing Smoking in Medically Underserved and Vulnerable Cancer Populations

Introduction

Although cigarette smoking prevalence and cancer deaths caused by tobacco have declined over the past several decades,[1] disparities in tobacco use and tobacco-related cancer burden persist among various populations in the United States.[2] Greater knowledge of health disparities caused by tobacco can provide useful information to health care systems and clinicians about population-specific needs for cigarette smoking cessation treatment, especially among patients with cancer. Such knowledge has the potential to enhance patient care and smoking cessation treatment effectiveness, reduce cancer-related health disparities, and promote population health. This chapter reviews research regarding medically underserved and vulnerable populations who experience disparities in cancer burden, smoking prevalence, access to smoking cessation treatment, and/or smoking cessation treatment success.

For the purposes of this monograph, "vulnerable" refers to a heightened risk for cancer or a higher cancer burden relative to the general population. Medically underserved and vulnerable populations discussed in this chapter include:

- Socioeconomically disadvantaged populations;
- Racial and ethnic minority populations;
- Individuals residing in rural areas (rural populations);
- Sexual and gender minority (SGM) populations (e.g., lesbian, gay, bisexual, transgender individuals);
- Individuals with co-occurring substance use disorders; and
- Individuals with serious mental illness (SMI), specifically those with schizophrenia spectrum disorders and bipolar disorder.

The intent of this chapter is to inform relevant stakeholders of the challenges medically underserved and vulnerable populations face, especially concerning enhancing treatment of cigarette smoking. This chapter characterizes the targeted populations regarding their status across multiple domains (e.g., individual, social, economic, cancer burden) that are associated with cigarette smoking and response to smoking cessation treatment. The characteristics reviewed were gleaned largely from empirical associations with a primary focus on characteristics seen as relevant to the clinical encounter and treatment of patients with cancer. Given the nature of the available evidence, there was no attempt to rank order such influences or to evaluate the validity of particular causal or theoretical frameworks, although some frameworks are discussed as background information. The chapter begins with a discussion of the challenges faced by medically underserved and vulnerable patients with cancer, both those who smoke and those who do not. The chapter reviews available data on the cancer burden (incidence, prevalence, and mortality) of these groups to underscore the observed health disparities. The chapter then explores smoking patterns, cessation patterns, and barriers to care among medically underserved and vulnerable populations and seeks to apply lessons learned from the general population when data from patients with cancer are unavailable or limited.

The Socioecological Model

Health disparities among medically underserved and vulnerable groups have been conceptualized via the socioecological model (SEM),[3,4] which posits that health is determined and reinforced by multiple factors at the individual, interpersonal, community, and societal levels. These same factors may also result in health inequities.

- The individual, which encompasses characteristics such as race and ethnicity, income, educational attainment, sexual orientation, and gender identity; affective or psychiatric status; attitudes, knowledge, perceptions, and motivation of the members of medically underserved and vulnerable populations; and characteristics of clinicians, such as knowledge level, behaviors, or biases;
- Interpersonal social context, such as family systems and intimate relationships, experiences of discrimination or stigma, exposure to smoking in social networks, social norms, and clinician practice patterns (e.g., the offer of smoking cessation treatment);
- The community and health care system, which includes the availability of smoking cessation treatment services and resources; barriers to accessibility; policies, such as protocols for clinical screening for tobacco use and the cost of services, adaptation, and utilization/engagement; and shared attitudes among clinicians; and
- The societal level, including cultural and social norms; health, economic, educational, and social policies; discrimination; tobacco industry marketing patterns; educational opportunities; public service campaigns; and disparities in health care resources or health insurance coverage.

As explained by the National Cancer Institute’s (NCI) Tobacco Control Monograph 22:

> The socioecological model underscores the interrelationships between tobacco use and multiple disparate circumstances—social, educational, health, residential, economic, and political disparities—and how each influences the other. This model makes it possible to critically examine the dynamic influences of factors (e.g., stressors, social or financial difficulties) on tobacco–disease trajectories, the timing of exposure to these factors, and the clustering of these factors at different points in relationship to disease outcomes. The socioecological model calls attention to the chronicity and incidence of disadvantages (e.g., discrimination, disenfranchisement, low SES) and how these disadvantages influence disparities.[5,p.9]

Thus, the SEM suggests that factors, such as stressors, arise and are expressed at multiple levels and contexts in a person’s life[6] and therefore encourages consideration of a broad range of potential influences on cancer and smoking disparities.

Many medically underserved and vulnerable populations share exposure to potential barriers to smoking cessation, such as resource constraints; lower educational attainment; limited health care access; social barriers, such as stigmatization; exposure to high levels of smoking in their environments; exposure to targeted tobacco industry marketing for menthol cigarettes and other tobacco products (e.g., little cigars); discrimination; stress; lack of or inadequate health insurance; and lack of access to effective smoking cessation treatment. Complex interactions among such factors, occurring at multiple levels and during the life course, could contribute to the high rates of cancer, cancer mortality, and/or tobacco use observed among medically underserved and vulnerable populations.[2,7,8]

Combinatorial Effects on Vulnerabilities

It is possible or likely that factors that affect cancer, smoking, and treatment disparities could exert effects in complex, multifactorial ways. Indeed, evidence indicates that combinations of identities or characteristics can produce effects on health outcomes that differ from those produced by single influences. Therefore, when evaluating possible influences on disparities in health outcomes, it is important such influences are not viewed as producing orthogonal or isolated effects. For example, data from the 2012–2013 National Epidemiologic Survey of Alcohol and Related Conditions-III show that tobacco use is especially high among sexual minority individuals who also report experiences of racial discrimination.[9] Perceptions of inequities and discrimination could exacerbate the effects of chronic stress,[10] which can affect health via psychological or physiological mechanisms.[11,12] This chronic stress could exacerbate the additional stress caused by cancer and could increase negative reactions to it, including reduced cancer treatment adherence, cancer fatalism (i.e., the belief that a cancer is uncontrollable and a death sentence),[13,14] and reduced likelihood of engagement with smoking cessation treatment and successful cessation.

This chapter identifies multiple factors that can be related to smoking behaviors by medically underserved or vulnerable individuals with cancer; however, the many possible causal pathways of such factors are not explored.

Stigma in Medically Underserved and Vulnerable Populations

Certain characteristics or experiences are likely to be relevant to all medically underserved and vulnerable populations, and these experiences could affect their willingness to engage in smoking cessation treatment and quit smoking. One such shared experience is stigma, a factor that might affect both access to and use of health care resources, including smoking cessation treatment.[6] Although stigma could affect any individuals who smoke, stigma could be especially pronounced for medically underserved and vulnerable populations.

The effect of stigma is particularly relevant because patients with cancer, medically underserved and vulnerable populations, and people who smoke can all experience varying degrees of stigma. For example, individuals with SMI, such as bipolar disorder, report significant concern about being devalued or discriminated against because of their mental health condition, and such concern is positively related to their level of symptomatic impairment.[15]

Stigma has two components. The internalized components are the individual’s anticipation, experience, and subsequent internalization of negative appraisals from others or from generally held beliefs. The externalized components include the negative attitudes and behaviors that occur in reaction to another person’s characteristics (e.g., poverty, ethnicity, race, substance use, disability). Externalized beliefs can be primary determinants of internalized stigma, although a person's own attributions can also affect felt stigma.[6,16] There is evidence that stigma associated with smoking or with having a cancer caused by smoking can affect a patient's communication with their clinicians, including disclosure of smoking behavior; their pursuit of, or engagement in, smoking cessation treatment; their adherence to cancer treatment; and their likelihood of seeking cancer screening.[6,17]

Stigma is relevant to medically underserved and vulnerable populations in several ways. Some members of medically underserved and vulnerable populations, including racial and ethnic minority groups, low-income individuals, and SGM individuals, report high levels of discrimination,[18–20] which could affect their internalization of stigma. For example, members of SGM populations report discrimination related to their sexual/gender behaviors or identification, which could be responsible, in part, for their low rate of health care engagement and high levels of subjective distress.[19,21–25] Moreover, many medically underserved and vulnerable populations have especially high smoking prevalence rates,[26] and as such they are likely to experience stigma related to smoking or having cancer caused by smoking, such as lung cancer.[6,27–29]

In the cancer context, stigma connotes that those using cigarettes often feel "guilty" for continuing to smoke despite knowing the health risks of smoking, they could have "brought it [their cancer] on themselves," and are not worthy of help.[27] Public health messages intended to inform the public that cigarette smoking causes many types of cancers could have the unintended consequence of appearing to assign personal blame for these cancers, thus generating subsequent negative perceptions of those with cancers caused by smoking among the general public or clinicians, as well as negative internalized self-perceptions among patients with cancer.[6,16]

Stigma, both internalized and expressed, can contribute to multiple clinical challenges and present barriers to smoking cessation among patients with cancer. Stigma can trigger guilt and self-blame and, thus, affect willingness to enter smoking cessation treatment or disclose smoking status to one's clinician.[6,17] Stigma can also lead to defensive reactions, including a decreased desire to quit smoking.[30,31] Further, stigma can be expressed by clinicians in the form of reduced empathy and pessimistic assumptions about patients' interest in or ability to quit; such reactions might serve as a barrier to effective patient–clinician communication.[6,29] With respect to medically underserved and vulnerable groups, the effects of stigmatization of smoking should also be considered within the context of other factors faced by these individuals, including economic hardships, stress, and discrimination.[6]

Prevalence and Trends in Smoking: Relevance to Medically Underserved and Vulnerable Populations With Cancer

The number of individuals within the different medically underserved and vulnerable populations in the United States varies; some communities are quite large and, collectively, these populations constitute a large portion of the U.S. population. For example, SGM populations constitute an estimated 3%–11% of the U.S. population,[32,33] and about 20% of the U.S. population reside in rural areas.[34] When considered in totality, the prevalence of medically underserved and vulnerable groups in the United States, as well as their elevated cancer burden, suggests that they constitute a large portion of the patient population seeking cancer care. Further, although smoking prevalence has generally fallen across medically underserved and vulnerable populations, many continue to smoke at high rates (Table 5.1), resulting in a potentially disproportionate smoking-associated cancer burden and need for cessation treatment by those receiving cancer treatment.[1,2]

Table 5.1 Prevalence of Current Cigarette Smoking Among U.S. Adults Aged 18 and Older, by Sex, Race and Ethnicity, Poverty Status, Income, Educational Attainment, and Sexual Orientation, 1994–2020

Category	1994	1998	2002	2006	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Total	25.5	24.1	22.5	20.8	19.3	19.0	18.1	17.8	16.8	15.1	15.5	14.0	13.7	14.0	12.5
Sex															
Male	28.2	26.4	25.2	23.9	21.5	21.6	20.5	20.5	18.8	16.7	17.5	15.8	15.6	15.3	14.1
Female	23.1	22.0	20.0	18.0	17.3	16.5	15.8	15.3	14.8	13.6	13.5	12.2	12.0	12.7	11.0
Race/ethnicity[a]															
White	26.3	25.0	23.6	21.9	21.0	20.6	19.7	19.4	18.2	16.6	16.6	15.2	15.0	15.5	13.3
Black	27.2	24.7	22.4	23.0	20.6	19.4	18.1	18.3	17.5	16.7	16.5	14.9	14.6	14.9	14.4
Latino or Hispanic	19.5	19.1	16.7	15.2	12.5	12.9	12.5	12.1	11.2	10.1	10.7	9.9	9.8	8.8	8.0
American Indian or Alaska Native	42.2	40.0	40.8	32.4	31.4	31.5	21.8	26.1	29.2	21.9	31.8	24.0	22.6	20.9	27.1
Asian or Pacific Islander	13.9	13.7	—	—	—	—	—	—	—	—	—	—	—	—	—
Asian	—	—	13.3	10.4	9.2	9.9	10.7	9.6	9.5	7.0	9.0	7.1	7.1	7.2	8.0
Multiple races	—	—	—	—	25.9	27.4	26.1	26.8	27.9	20.2	25.2	20.6	19.1	—	—
Poverty status															
At or above	24.1	23.5	22.2	20.4	18.3	17.9	17.0	16.2	15.2	13.9	14.3	—	—	—	—
Below	34.7	32.3	32.9	30.6	28.9	29.0	27.9	29.2	26.3	26.1	25.3	—	—	—	—
Unknown	28.8	22.5	19.7	18.3	16.0	15.0	13.6	16.0	16.4	10.5	12.0	—	—	—	—
Income (USD)															
<35,000	—	—	—	—	—	—	—	—	—	—	—	21.4	21.3	21.4	20.2
35,000–74,999	—	—	—	—	—	—	—	—	—	—	—	15.3	14.9	15.7	14.1
75,000–99,999	—	—	—	—	—	—	—	—	—	—	—	11.8	13.3	11.4	10.5
≥100,000	—	—	—	—	—	—	—	—	—	—	—	7.6	7.3	7.1	6.2
Educational attainment[b]															
0–12 years (no diploma)	—	—	27.6	26.7	25.1	25.5	24.7	24.2	22.9	24.2	24.1	23.1	21.8	21.6	21.5
≤8th grade	23.7	21.9	19.3	17.4	16.2	15.0	15.2	15.4	13.7	14.4	16.2	—	—	—	—
9th–11th grade	38.2	36.8	34.1	35.4	33.8	34.6	32.1	33.2	29.5	31.6	30.7	—	—	—	—
12th grade (no diploma)	—	—	31.0	25.6	21.7	25.1	24.7	19.7	25.7	26.3	24.8	—	—	—	—
GED certificate	—	—	42.3	46.0	45.2	45.3	41.9	41.4	43.0	34.1	40.6	36.8	36.0	35.3	32.0

Table 5.1 (continued)

Category	1994	1998	2002	2006	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
High school graduate	29.8	27.4	25.6	23.8	23.8	23.8	23.1	22.0	21.7	19.8	19.7	18.7	19.7	19.6	17.6
Some college (no degree)	—	—	23.1	22.7	23.2	22.3	20.9	20.9	19.7	18.5	18.9	17.4	18.3	17.7	14.4
Associate degree	—	—	21.5	21.2	18.8	19.3	17.9	17.8	17.1	16.6	16.8	15.5	14.8	14.0	12.7
Undergraduate degree	—	—	12.1	9.6	9.9	9.3	9.1	9.1	7.9	7.4	7.7	7.1	7.1	6.9	5.6
Graduate degree	—	—	7.2	6.6	6.3	5.0	5.9	5.6	5.4	3.6	4.5	4.1	3.7	4.0	3.5
13–15 years	25.7	24.6	—	—	—	—	—	—	—	—	—	—	—	—	—
≥16 years	12.3	11.3	—	—	—	—	—	—	—	—	—	—	—	—	—
Sexual orientation[c]															
Straight	—	—	—	—	—	—	—	17.6	16.6	14.9	15.3	13.7	13.5	13.8	12.3
Gay/lesbian/ bisexual	—	—	—	—	—	—	—	26.6	23.9	20.6	20.5	20.3	20.6	19.2	16.1

Note: Numbers are percentages. Em dash (—) = data not collected in a category for a particular year. Current smoking includes individuals who smoked at least 100 cigarettes in their lifetime and who smoked every day or some days. The National Health Interview Survey (NHIS) was redesigned in 1997 and 2019, and trend analysis and comparison with prior years should be conducted with caution.

[a]All racial and ethnic groups are non-Hispanic except those categorized as Hispanic. In 1997, the Office of Management and Budget changed its data collection guidelines to require that Native Hawaiian and Other Pacific Islander data be collected separately from Asian populations. Limited data were collected on American Indian or Alaska Native people, and data for a single year could be unstable or unreliable due to a small sample size. Data on current smoking among Native Hawaiian or other Pacific Islander people are not reported. [b]Additional categories were added to education in 1999. Educational attainment data are provided for individuals aged 25 years or older. GED = general educational development certificate. [c]Response options provided on the NHIS were “straight, that is, not gay” for men, and “straight, that is, not gay or lesbian” for women.

Sources: National Health Interview Survey, 1994–2019: Agaku et al. 2014[362]; Centers for Disease Control and Prevention (CDC) 1996,[363] 2000,[364] 2004,[365] 2007,[366] 2012[367]; Cornelius et al. 2020,[368] 2022[41]; Creamer et al. 2019[369]; Jamal et al. 2014,[370] 2015,[371] 2016,[372] 2018[373]; Wang et al. 2018.[374]

In particular, smoking prevalence remains high among socioeconomically disadvantaged populations,[5,35–37] as well as among members of certain racial and ethnic minority groups,[5] residents of rural areas,[38] and those with SMI.[39]

As noted, it could be helpful to consider the effects of potential influences in combination rather than in isolation. Thus, there is evidence that smoking prevalence varies with different intersections of medically underserved and vulnerable populations. For example, smoking prevalence is especially high among individuals who are both socioeconomically disadvantaged and who experience mental illness.[40] In addition, smoking prevalence is higher among Black or African-American and Latino or Hispanic individuals living in rural areas compared with those living in urban areas.[41] As stated in the 1998 Surgeon General’s Report on Smoking and Health:

> No single factor determines patterns of tobacco use among racial/ethnic groups; these patterns are the result of complex interactions of multiple factors, such as socioeconomic status, cultural characteristics, acculturation, stress, biological elements, targeted advertising, price of tobacco products, and varying capacities of communities to mount effective tobacco control initiatives.[42,p.6]

It is important for researchers and clinicians to increase understanding of these factors and others that drive tobacco-related disparities, such as contextual effects, education, discrimination, economic opportunities, and stress, and explore how this information can be used to enhance the reach and effectiveness of clinical and population-based smoking interventions among medically underserved and vulnerable populations. Clinicians attempting to intervene to effect smoking cessation by cancer patients who are members of these populations need to be prepared to recognize these attendant complexities.

Heterogeneity Among Medically Underserved and Vulnerable Populations

It is vital to recognize that medically underserved and vulnerable populations are not homogeneous, and any broad characterizations discussed in this chapter are likely to be inaccurate in describing many members of such groups. For example, there is not only inevitable variation among individuals in such groups, but there are also diverse subgroups within each population group. For example, SGM populations include lesbian, gay, bisexual, and transgender people, and include individuals of all races, ages, socioeconomic statuses (SES), and geographic locations, each of which can have somewhat distinct smoking patterns and cancer burden.[43–45] In Asian populations, who overall have higher levels of income and educational attainment compared with other racial and ethnic minority groups, some subgroups, including Cambodian and Hmong individuals, have lower levels of education and higher levels of poverty.[46–48] Recognition that subgroups within larger populations can have very distinct health profiles and outcomes has led to suggestions for research designs that focus on factors or dimensions within subpopulations that confer heightened vulnerability.[49] Such variation should be kept in mind when collecting, analyzing, and disseminating data on medically underserved and vulnerable populations and in the consideration or formulation of clinical or public health actions.

In sum, the individual who is a member of a medically underserved and vulnerable group is likely affected by influences that span individual to societal strata, with one possible influence being stigmatization. The complex nature of such influences could be increased by the fact that individuals can belong to multiple medically underserved and vulnerable groups and the fact that such groups are heterogeneous. Thus, researchers and clinicians should be aware of and sensitive to a person's membership in a medically underserved and vulnerable group, as well as unique individual features that can affect their health.

Cancer Burden

The medically underserved and vulnerable populations discussed in this chapter can be considered vulnerable, in part, because many of them have higher cancer incidence and mortality rates than the general population, although these figures vary by population and cancer site. This section will not attempt to thoroughly characterize the cancer burden of the populations reviewed in this chapter. Rather, specific examples will be offered to support two points: (1) multiple medically underserved and vulnerable populations face especially high levels of cancer incidence and mortality, and (2) the burden varies across populations in level and type of cancer so that the risk of each population warrants focused evaluation.

Socioeconomically disadvantaged groups have higher incidences of cancer and cancer-related mortality than do higher SES groups.[1,50] Substantial disparities by SES exist among patients diagnosed with cancers caused by smoking, including lung, colorectal, cervical, stomach, and liver cancer.[1,8,51,52] For example, a study found that among individuals with fewer than 12 years of education or living below the poverty threshold, lung cancer incidence rates were 1.5 to 3 times greater than in college graduates or individuals with higher incomes.[51] Such evidence speaks to the important role of smoking in cancer incidence across medically underserved and vulnerable populations (see "Factors Associated with Cancer Burden" below).

In addition, some racial and ethnic groups in the United States face relatively high levels of cancer burden. For example, while the disparity between cancer mortality of Black or African-American and White individuals has narrowed over time, Black or African-American men and women in 2019 had the highest cancer mortality rate overall and for most cancer sites compared with all other racial and ethnic groups.[53] Black or African-American individuals have relatively high lung cancer incidence rates, especially among males, and they also have the worst survival rates.[54–56] Some racial and ethnic populations also exemplify the variation in the burden of specific cancers that occur across medically underserved and vulnerable populations. Latino or Hispanic and Asian or Pacific Islander individuals, for example, have lung cancer rates that are about half of those of White individuals, yet these two groups have a higher incidence of and mortality from liver cancers compared with White individuals.[57]

Individuals residing in rural areas provide further evidence of the variability in cancer burden that occurs across medically underserved and vulnerable populations. Rural populations have a lower incidence of cancer overall,[58] yet they tend to have a greater incidence and mortality from cancers caused by smoking, including lung and laryngeal cancers, compared with individuals living in urban areas.[58,59] In addition, a 2019 report found that lung cancer incidence rates were higher and decreased more slowly in nonmetropolitan than in metropolitan counties.[60]

Some SGM populations face a heightened cancer burden. For example, compared with heterosexual men, gay men are more likely to be diagnosed with cancer, even after controlling for demographic and socioeconomic factors.[61] In addition, bisexual women have a greater likelihood of being diagnosed with cancer compared with heterosexual women.[61]

Individuals who use tobacco along with other substances also tend to have especially high rates of cancer. For instance, the use of both cigarettes and alcohol can increase the risk of cancer synergistically.[62] A study using data from the International Head and Neck Cancer Epidemiology Consortium found a greater than multiplicative joint effect of tobacco and alcohol use on the risk of head and neck cancer.[63] In addition, the use of both tobacco and alcohol is also associated with increased risk of second primary cancer.[64,65] Abundant evidence indicates that alcohol use is associated with an elevated risk of multiple forms of cancer regardless of smoking status.[66–68]

With regard to SMI, a retrospective cohort study comparing Maryland Medicaid beneficiaries diagnosed with schizophrenia or bipolar disorder (N = 3,317) with the general population found a standardized incidence rate (SIR) of 2.6 for cancers of all types (95% confidence interval [CI], 2.2–3.0 for schizophrenia and 2.0–3.2 for bipolar disorder). Lung cancer SIRs among participants with schizophrenia and bipolar disorder were 4.7 (95% CI, 3.1–6.8) and 4.1 (95% CI, 2.2–7.2), respectively.[69]

Factors Associated With Cancer Burden

As noted above, there is variability not only in the level of cancer burden in medically underserved and vulnerable populations, but also in the likely causes of cancer risk. For instance, populations of lower SES or those living in rural areas tend to have less access to health care, including cancer screening,[70–72] less health insurance coverage,[73,74] and greater exposure to environmental toxicants.[70,72] These factors could contribute to heightened cancer mortality. Some SGM populations appear to incur greater cancer risk due to exposure to human immunodeficiency virus (HIV) or human papillomavirus (HPV) infection via sexual practices. Consistent with this, gay or bisexual men are over-represented among men with Kaposi sarcoma and anal cancer.[75,76] SGM populations, and other medically underserved and vulnerable populations, could also avoid accessing health care for fear of stigmatization and discrimination.[19,44] Finally, a major factor in the increased cancer burden of many medically underserved and vulnerable populations is higher rates of smoking. There is strong evidence that smoking contributes to differential cancer incidence and mortality rates in some racial and ethnic groups,[42,77–79] some SGM groups,[80] groups with low SES,[8,70,72] persons with SMI,[81,82] and individuals in some substance-using groups.[62,63,83]

Summary: Cancer Burden

Cancer risk among medically underserved and vulnerable populations defies simple characterization. However, evidence suggests that many of these populations experience higher risks of cancer relative to nonmedically underserved or vulnerable groups, and that in many cases, this risk is attributable, in part, to smoking. This disproportionate elevation in cancer burden underscores the need to encourage smoking cessation in these groups, increase their access to smoking cessation treatment, and understand the effectiveness of such treatment within specific populations. It also underscores the need to ensure that health care settings are perceived as welcoming to diverse population groups.

Smoking Cessation Treatment for Medically Underserved and Vulnerable Populations in the Clinical Cancer Care Context

The following section reviews the evidence on smoking cessation treatment within the context of cancer care for each of the following medically underserved and vulnerable groups: (1) socioeconomically disadvantaged populations; (2) racial and ethnic minority populations; (3) rural populations; (4) SGM populations; (5) individuals with co-occurring substance use disorders and smoking; and (6) individuals with SMI. Where possible, data on cancer populations are used, but relevant data from noncancer populations are also considered, largely due to the paucity of research on smoking cessation treatment among cancer populations.

Smoking Among Socioeconomically Disadvantaged Populations With Cancer

Epidemiology

Smoking is especially prevalent among socioeconomically disadvantaged populations with cancer, similar to populations without cancer.[36,37,84] Smoking prevalence overall has decreased among all populations over time, including among those living below the poverty threshold and with lower levels of educational attainment (Table 5.1), which reflects the influence over time of policies intended to prevent and control tobacco use and secondhand smoke (SHS) exposure, along with steps taken to increase access to smoking cessation treatment (e.g., nationwide access to free tobacco cessation quitlines).[85] However, smoking prevalence remains substantially higher among socioeconomically disadvantaged populations with cancer or a cancer history than among higher-SES populations with a similar cancer status. This disparity occurs across cancer types and multiple measures of SES including poverty level, income, educational attainment, and health insurance status.[86–91]

Smoking Cessation

Observational studies show that socioeconomically disadvantaged individuals are more likely than higher-SES individuals to continue to smoke after a cancer diagnosis.[92,93]A study by Talluri and colleagues assessed factors that were associated with smoking cessation among adults with an initial cancer diagnosis in a cross-sectional study based on the National Health Interview Survey (NHIS) that captured data from 2006 to 2018.[94] This population-based survey of U.S. residents who were 18 or older included 381,989 respondents of whom 35,524 (8.8%) had a cancer diagnosis. The data revealed a strong association between measures of SES and smoking cessation success; having an undergraduate degree or a post-graduate degree was associated with greater success, while living below the poverty threshold was associated with much poorer success. The association between socioeconomic disadvantage and lower likelihood of cessation has also been found in studies of patients with cancers caused by smoking.[95–97]

Research with both patients with cancer and populations without cancer suggests that socioeconomic disadvantage is typically associated with poorer cessation outcomes both when making unaided quit attempts and when using formal treatment (i.e., medication and/or counseling).[93,98–108] This association does not appear to be due to fewer attempts to quit smoking.[104,106] For example, past-year quit attempts were similar among those living below the poverty threshold and those living at or above the poverty threshold in 2015 (55.5% and 55.2%, respectively).[85] However, adults living below the poverty threshold have less success in quitting. In 2017, the quit ratio (the number of former smokers divided by the number of ever-smokers) among those living below the poverty threshold was 42.2% (95% CI, 38.7%–45.7%) while it was 64.5% (95% CI, 63.2%–65.8%) for those living above the poverty threshold.[85] Unfortunately, little is known about smoking cessation treatment and success among low-SES cancer populations who smoke.

Barriers to Smoking Cessation

Socioeconomically disadvantaged patients with cancer face multiple barriers to smoking cessation. These barriers include low rates of health insurance and/or poor access to both health care and smoking cessation treatment resources,[109–116] as well as high levels of psychological distress, competing priorities, nicotine dependence, high levels of exposure to smoking in the environment, and relatively low perceived social support.[117,118]

There is also compelling evidence that socioeconomically disadvantaged populations have been targeted by tobacco companies through advertising and promotions. Such advertising is based on extensive research that characterizes the needs and motivations of these populations and tobacco companies develop tobacco products, advertising, and promotions to appeal to this audience.[5] Moreover, socioeconomically disadvantaged individuals often reside in neighborhoods that have dense concentrations of tobacco retailers; this is especially true in neighborhoods with predominantly racial and ethnic minority residents.[119–121] Socioeconomically disadvantaged individuals could perceive smoking as more normative due to greater exposure to it in their social environments,[117,122,123] which could affect their motivation to quit smoking or to seek smoking cessation treatment.

Knowledge barriers might interfere with smoking cessation treatment engagement or motivation to quit, including those for socioeconomically disadvantaged patients with cancer. In the general population, individuals who smoke and who are of lower SES tend to have less awareness about the harms of smoking and the availability of effective smoking cessation treatments.[124–127] Consistent with this, a qualitative study conducted among lower-SES cervical cancer patients revealed a lack of awareness that smoking was associated with cervical cancer.[128]

While incomplete knowledge can serve as barriers to cessation treatment engagement in socioeconomically disadvantaged populations, there is evidence from the general population that such barriers can be effectively addressed. For example, quitlines attract a disproportionate number of people of lower SES who smoke.[129] Furthermore, evidence indicates that media campaigns are especially effective in attracting socioeconomically disadvantaged individuals to quitlines[130–132]; use of quitlines could therefore have utility when extended to patients with cancer who are socioeconomically disadvantaged.

Summary: Smoking Among Socioeconomically Disadvantaged Populations With Cancer

Socioeconomically disadvantaged populations have high smoking prevalence and are more likely than non-disadvantaged populations to continue smoking after a cancer diagnosis. Further, lower-SES individuals, in general, tend to be less successful in quitting compared with higher-SES individuals who smoke. Socioeconomically disadvantaged individuals who smoke face multiple barriers to successful smoking cessation, including relatively poor access to smoking cessation treatment resources, greater exposure to smoking in their environments, knowledge barriers, and greater exposure to tobacco advertising and promotion. These findings should encourage cancer care clinicians and programs to ensure that socioeconomically disadvantaged patients with cancer have access to smoking cessation treatment and are informed about the benefits of cessation in relation to their cancer.

Smoking Among Racial and Ethnic Minority Populations With Cancer

Epidemiology

In the general population, there are notable differences in smoking prevalence within and between different racial and ethnic minority groups. For example, although overall smoking prevalence among Latino or Hispanic individuals in the United States is lower than among people who are not Latino or Hispanic (Table 5.1), significant differences in prevalence exist within the U.S. Latino or Hispanic population (e.g., smoking prevalence is typically higher among men than women and among certain subgroups).[133] Similarly, while smoking prevalence is somewhat higher among Black or African-American men than among White men, Black or African-American women have a lower smoking prevalence than do White women.[26,134–136]

Smoking patterns among racial and ethnic groups also differ. For example, while Black or African-American individuals tend to smoke fewer cigarettes per day than White Americans, it has also been reported that they have lower rates of cessation[137] and derive more nicotine from each cigarette smoked.[138] These differences could account, at least in part, for higher rates of lung cancer at equivalent rates of cigarettes smoked per day.[55,139] Further, Black or African-American men have been reported to have higher prevalence of smoking nondaily (as opposed to daily) than White men.[135] Latino or Hispanic individuals are especially likely to have light and intermittent smoking patterns.[140,141] Additionally, Black or African-American individuals are significantly more likely to be exposed to SHS than are White individuals. Among nonsmoking individuals aged 3 years or older, the prevalence of SHS exposure was 50.3% for Black or African-American individuals and 21.4% for White individuals in 2013–2014.[142] Although SHS exposure has decreased over time, exposures remained higher among Black or African-American adults compared with White adults in 2015–2018 (39.7% vs. 18.4%, respectively).[143]

A striking characteristic of the smoking patterns of Black or African-American individuals is their high prevalence of menthol cigarette use.[144–146] Data from the 2019 National Survey on Drug Use and Health (NSDUH) indicate that, among Black or African-American adults who smoke, the majority (85%) use menthol cigarettes.[147] Menthol cigarette use is associated with reduced likelihood of smoking cessation, particularly among Black or African-American individuals who smoke.[148–154] A 2020 meta-analysis of 19 studies found that among Black or African-American individuals who smoked cigarettes, those who smoked menthol cigarettes had 12% lower odds of smoking cessation, which may be due in part to targeted tobacco industry marketing in Black or African-American communities.[153] In addition, an analysis of 2013–2018 data from the Population Assessment of Tobacco and Health (PATH) Study compared the quitting success of individuals who switched from smoking menthol cigarettes to non-menthol cigarettes versus the quitting success of those who continued to smoke menthol cigarettes. The results showed that switching to nonmenthol cigarettes was associated with a 58% increased probability of later abstinence from smoking when abstinence was defined as 30-days of no smoking, and was associated with a 97% increased probability of abstinence when abstinence was defined as 12 months of no smoking.[155] Patterns of menthol cigarette use among cancer patients are not available, but are likely to reflect those observed in the general population.

Several studies have used nationally representative data sources to examine racial and ethnic differences in cigarette smoking prevalence among populations with a cancer history. These studies have produced mixed results, but overall suggest that Black or African-American and Latino or Hispanic cancer survivors have a similar or lower likelihood of current smoking compared with White cancer survivors. According to data from the 2009 Behavioral Risk Factor Surveillance System (BRFSS), American Indian or Alaska Native and multiracial adults diagnosed with cancers caused by tobacco had the highest smoking prevalence after a cancer diagnosis (near 50%) compared with other racial and ethnic groups. Black or African-American and Latino or Hispanic survivors of cancers caused by tobacco had the lowest smoking prevalence (around 20%).[96] A study by Azagba and colleagues used longitudinal data from the Population Assessment of Tobacco and Health (PATH) study from 2013 to 2016 to examine 1,527 individuals with a history of a cancer diagnosis.[156] Among those with a cancer diagnosis, Latino or Hispanic individuals had lower odds of current smoking (OR = 0.58, 95% CI = 0.37–0.92) than White individuals; neither Black or African-American individuals nor other racial groups differed from White individuals with regard to odds of current smoking.[156] An analysis of data from 3,672 cancer survivors who participated in the Health Information National Trends Survey (HINTS) from 2003 to 2014 found that both Latino or Hispanic and Black or African-American cancer survivors had lower odds of current smoking than White survivors.[157] A separate analysis of HINTS data (limited to the time period of 2003–2007) found no difference in current smoking prevalence when comparing Black or African-American and Latino or Hispanic survivors with White survivors, but found lower odds of current smoking among those of other races when compared with White survivors.[158] However, other studies that have examined BRFSS and PATH data have found no racial or ethnic differences among cancer survivors in terms of current cigarette use[87] or current use of any tobacco products.[159]

Additional information on smoking prevalence among patients with cancer can be gleaned from studies with smaller sample sizes or of specific, geographically defined groups. Blair and colleagues examined the correlation of ethnicity with current smoking in 283 survivors of colorectal cancer who resided in New Mexico. The study found that the prevalence of smoking was greater among Latino or Hispanic survivors than among those who were not Latino or Hispanic (28.5% and 18.1%, respectively).[160] However, in a study of adolescent and young adult survivors of childhood cancer,[161] Latino or Hispanic survivors reported less lifetime cigarette smoking than did White survivors. Therefore, more information on the smoking patterns of ethnic minority individuals in cancer populations is needed.

One limitation to the reliable assessment of racial and ethnic differences in cessation is that researchers' categorization of racial and ethnic groups can vary, sometimes making it difficult to compare smoking prevalence across studies. For example, two studies examined smoking prevalence in adult long-term cancer survivors using data gathered in 2009 via the population-based BRFSS. One used four racial and ethnic categories (White, African-American, Latino or Hispanic, and other)[87] while the other used a seven-category grouping of racial and ethnic groups.[96] The study using four categories showed that the "other" category had the highest smoking rate, while the study using seven categories showed that the highest smoking rate occurred among American Indian/Alaska Native individuals and those in the "other" category had midrange smoking rates. Clearly, the approach to categorizing race and ethnicity can affect the findings and subsequent interpretations of the data.

Smoking Cessation

Smoking Cessation and Black or African-American Individuals. Evidence about the association between Black or African-American race, cancer history, and smoking cessation is mixed. Among those who reported ever having had cancer and who were currently smoking (N = 877) in the 2015 BRFSS, Black or African-American cancer survivors had higher odds of having made a quit attempt in the past year than White survivors.[104] Data from the 2015 NHIS found that Black or African-American cancer survivors who reported current smoking had a slightly higher prevalence of past-year quit attempts (67.4%, 95% CI = 48.4%–82.0%) compared with White survivors (48.2%, 95% CI = 40.8%–55.6%).[88] These findings are consistent with data from the general population suggesting that Black or African-American individuals have high interest in smoking cessation; in 2017, 72.8% of Black or African-American NHIS respondents who smoked were interested in quitting, similar to White individuals (67.5%).[162] In another study, Black or African-American adults were more likely to quit smoking after a bladder cancer diagnosis than were adults of other racial groups.[108] However, Black or African-American race was not significantly associated with quitting after a cancer diagnosis in a study of patients recently diagnosed with lung or colorectal cancer,[93] among 2017 NHIS participants with smoking-related and non-smoking-related cancer diagnoses,[163] or among cancer survivors who participated in the National Health and Nutrition Examination Survey (NHANES) from 1998 to 2008.[164]

In populations not diagnosed with cancer, Black or African-American individuals who smoke are less likely to quit smoking than White individuals who smoke.[85,165,166] Thus, additional research is needed to understand factors that could account for differences in quitting success between Black or African-American adults with and without cancer. Identification of such factors could inform efforts to enhance interventions across populations.

Smoking Cessation and Latino or Hispanic Individuals. Tseng and colleagues explored racial and ethnic differences in the likelihood of quitting smoking among individuals who smoked at the time of their cancer diagnosis, using data from NHANES 1999–2008 surveys.[164] Of the 2,374 cancer survivors aged 20 and over for whom data were available, 566 had regularly smoked at the time of their cancer diagnosis and were included in the analyses. Analyses showed that Latino or Hispanic survivors were significantly less likely to have quit smoking compared with White survivors, but the sample of Latino or Hispanic individuals was relatively small ($N = 58$). Other studies have found no association between Latino or Hispanic ethnicity and quitting[163] or making a quit attempt[104] among cancer survivors.

Evidence-Based Smoking Cessation Treatment. Little research exists on racial and ethnic differences in response to formal smoking cessation treatment. There is some evidence from the general population that Black or African-American individuals tend to achieve lower rates of long-term cessation (6 months or more) than do White individuals when engaged in a formal smoking cessation treatment program.[167–172] Although some studies have not found racial and ethnic differences in treatment response,[173,174] it is uncommon for Black or African-American individuals to achieve higher rates of smoking cessation in population-based data or after formal treatment compared with White individuals.[175] Despite this disparity in smoking cessation treatment efficacy across racial and ethnic subgroups, there is substantial evidence that Black or African-American adults benefit from treatment,[171,176] highlighting the importance of increasing their access via health care and other population-based delivery routes. Nollen and colleagues conducted a study investigating the effects of formal treatment (medication and counseling) in individuals from the general population and found lower cessation success among Black or African-American than White individuals. Secondary analyses suggested that this difference appeared to be related to socioeconomic factors and smoking characteristics, not race and ethnicity.[166] Another study by Nollen and colleagues suggested that differential response to cessation pharmacotherapy did not drive racial differences in smoking cessation treatment efficacy, as researchers also observed the difference in individuals who received placebo treatment.[171] Importantly, of the three pharmacotherapies evaluated in these analyses—varenicline, nicotine replacement therapy (NRT), and bupropion—only varenicline produced a significantly higher long-term cessation rate than did placebo among Black or African-American adults. However, both NRT and bupropion increased short-term abstinence relative to placebo, leading Nollen and colleagues to recommend research into extended pharmacotherapy strategies with Black or African-American individuals.[171]

While evidence-based smoking cessation treatment is effective across racial and ethnic groups,[176] more research is needed on effective interventions to promote smoking cessation among racial and ethnic minority individuals diagnosed with cancer. Targeted or culturally specific treatments have produced promising short-term results in noncancer populations,[175,177,178] although significant improvements in cessation and sustained abstinence in the long-term (≥6-month follow-up) remain an important goal. It is possible that targeted smoking cessation treatments could attract more individuals in minority racial and ethnic groups into treatment (i.e., improve reach) even if they do not consistently produce superior cessation outcomes in those treated.

Barriers to Smoking Cessation

There is a paucity of research on factors that hinder smoking cessation treatment use and effectiveness in racial and ethnic minority cancer populations. However, members of racial and ethnic minority populations frequently report experiences of discrimination and bias,[179] and many Black or African-American individuals live in environments that expose them to frequent encounters with smoking[180] and point-of-sale tobacco marketing.[120,181,182] One study found that the density of tobacco retailers in the United States was significantly higher in low-income neighborhoods and in neighborhoods with greater percentages of Black or African-American residents or Latino or Hispanic residents than in neighborhoods with lower percentages of those groups.[183] Such factors could affect either smoking cessation treatment use or effectiveness. In addition, data from the general population show that some racial and ethnic minority groups experience barriers related to availability of health insurance coverage and/or health care resources, lack of culturally competent care, clinician biases, health literacy, economic factors, patient–clinician communication barriers, and clinician assumptions that lead to the delivery of substandard care.[5,70,184,185]

Data derived from cancer populations suggest that lack of awareness of the benefits of evidence-based treatment and the potential harms of continued smoking might also limit treatment participation for some racial and ethnic minority groups. For example, compared with nonimmigrants, some immigrant cancer patients are less likely to perceive continued smoking as harmful.[186] However, this finding requires more investigation.

Racial and ethnic differences have been found in the provision of smoking cessation treatment in the general population. For example, some evidence suggests that clinicians are less likely to offer smoking cessation treatment, such as pharmacotherapy, to Black or African-American individuals than to White individuals.[187,188] There is also evidence that Black or African-American individuals are less likely to receive advice to quit smoking than are White individuals[189–191]; however, some studies report no differences related to race in rates of advice to quit or provision of counseling in the healthcare context.[192,193] It remains a possibility that decreased access to treatment or decreased clinician intervention rates could contribute to disparities in use of smoking cessation treatment as a function of race.[193,194] In addition, there is evidence that Black or African-American individuals have substantial concerns about the safety or addictiveness of smoking cessation medications[194] and such concerns might also affect their decisions to use such medications. In addition, Latino or Hispanic individuals are also less likely to use evidence-based smoking cessation treatment (counseling or medication) in quit attempts,[162,193,194] which could be related to their low rates of insurance coverage.[195]

While it is clear that the reach of smoking cessation treatment has been especially low among certain racial and ethnic groups in the past, findings from the NCI Center Cessation Initiative (C3I) suggest that enhanced health care systems changes could increase the reach of tobacco cessation treatment for racial and ethnic minority patients with cancer.[196] Seventeen participating NCI-Designated Cancer Centers that received funding in the first funding cohort implemented enhanced tobacco intervention system changes over a 1-year period. These changes included electronic health record (EHR) enhancements that connected patients with cancer directly with smoking cessation treatment resources, such as telephone counseling, text messaging, and web-based resources. The reach of the smoking cessation treatment was compared over the first 6-month period (Time 1) to the second 6-month period (Time 2) as a means of ascertaining the benefits of such enhanced treatment delivery. At Time 1, means computed across cancer centers showed that smoking cessation treatment reach occurred at the following percentages of those smoking in the various racial and ethnic groups: Latino or Hispanic = 19.0%; Black or African-American = 18.8%; White = 17.6%; Asian, Native Hawaiian, or Pacific Islander = 7.3%; American Indian or Alaska Native = 6.6%. Thus, even before the enhanced smoking interventions were fully implemented, reach was roughly equivalent across White, Latino or Hispanic, and Black or African-American groups. Time 2 data showed large increases in reach for all racial and ethnic groups with the increases being greatest for American Indian or Alaska Native (6.6%–24.7%, p = .07); Asian, Native Hawaiian, or Pacific Islander (7.3%–19.4%, p = .04); and Black or African-American (18.8%–25.9%, p = .11) individuals (although, only the increase for Asian, Native Hawaiian, or Pacific Islander groups reached statistical significance). Smaller gains in reach were observed among Latino or Hispanic individuals (19.0%–22.8%, p = .56) and White individuals (17.6%–23.4%, p = .16). These results suggest that considerable motivation to participate in smoking cessation treatment occurs across racial and ethnic groups, and health care systems can reach all races and ethnicities by using efficient strategies to facilitate the provision of evidence-based smoking cessation treatment. Similar results are observed in populations that do not have cancer.[197] Nonetheless, there remains an opportunity for improving the reach of smoking cessation treatment for all those who smoke (see chapter 4).

Very little evidence is available on the factors that influence quitting success among racial and ethnic minority patients with cancer. However, one study used data from the Detroit Research on Cancer Survivors study, a cohort of Black or African-American people with breast, prostate, lung, or colorectal cancer to identify factors associated with successful smoking cessation among Black or African-American adult cancer survivors.[198] Survivors diagnosed between 2013 and 2019 who had completed a baseline survey within 18 months of their cancer diagnosis were included in the analysis (N = 1,145). In this group, 18% (N = 356) smoked at the time of their cancer diagnosis and of these individuals, 57% (N = 203) continued smoking after they were diagnosed. Factors that were associated with continued smoking included living with someone who smokes (odds ratio [OR] = 2.78, 95% CI = 1.64–4.70), more cumulative years of smoking (OR = 1.03, 95% CI = 1.01–1.05), and having relatively low levels of social well-being (social support) (inverted OR = 1.04, inverted 95% CI = 1.00–1.08).

Greater diversity and inclusion in smoking cessation treatment clinical trials, including in the cancer context, are needed. Racial and ethnic minority groups tend to be underrepresented in smoking cessation clinical trials (as well as in cancer treatment trials), which could be due, in part, to restrictive trial inclusion criteria, mistrust of researchers and health care systems, and barriers to attending in-person sessions.[199–202] Strategies are needed that encourage and provide equitable opportunities for individuals in racial and ethnic minority groups to participate in smoking cessation treatment research.

Summary: Smoking Among Racial and Ethnic Minority Populations With Cancer

In general, racial and ethnic minority populations have different patterns of smoking prevalence and cessation likelihood, and they appear to face different types and intensities of obstacles to their engagement in smoking cessation treatment than do other populations. Further, smoking patterns of minority racial and ethnic groups following a cancer diagnosis are not well documented, and responses to smoking cessation treatment and factors that influence cessation likelihood are vastly understudied relative to noncancer populations. However, some research shows that some racial and ethnic minority cancer populations, such as Black or African-American individuals, could be highly motivated to quit as indicated by their relatively high rates of quit attempts. Nonetheless, racial and ethnic minority individuals, like their nonminority counterparts, often continue to smoke after their cancer diagnoses, highlighting the need for additional research into factors that influence cessation attempts and the success of those attempts.

Smoking Among Rural Populations With Cancer

Epidemiology

Evidence from populations without cancer indicates that rural residents have significantly greater prevalence of tobacco use compared with residents of metropolitan areas.[35,41,203,204] Some studies have also shown that patients with cancer who live in rural areas have higher smoking prevalence than patients with cancer who reside in non-rural areas. Weaver and colleagues used 2006–2010 NHIS data to examine rural–urban differences in smoking among cancer survivors.[205] This study found that the prevalence of smoking was higher among survivors living in rural counties (25.3%) than survivors living in urban counties (15.8%). Further, 2009–2010 BRFSS data indicate that cancer survivors in Missouri living in rural counties had a higher smoking prevalence (24.9%) than cancer survivors in urban Missouri counties (14.8%).[206]

Smoking Cessation

While few reports of rural versus non-rural smoking cessation data among cancer populations exist, some evidence does exist for the general population. NHIS data from 2018 indicate that adult rural residents differ from adults living in metropolitan areas in prevalence of current cigarette smoking (20.4% vs. 13.0%)[207] and quit attempts (51.6% vs. 56.8%, respectively).[208]

Very few trials have examined the effectiveness of smoking cessation treatments as a function of rural residence.[209] However, one observational study provided group smoking cessation treatments via videoconferencing to residents of rural areas in Canada and compared this with in-person counseling delivered to residents of an urban area. Continuous abstinence rates at 12 months revealed no statistically significant differences in long-term (12-months) quit rates: 21.1% for urban residents (N = 370) and 25.5% for rural residents (N = 184).[210] No studies have examined the likelihood of quitting smoking among rural patients with cancer compared with non-rural patients with cancer. The effectiveness of evidence-based smoking cessation treatments in multiple smoking populations[176] suggests that such interventions should be effective with rural residents. However, randomized controlled trials comparing cessation in rural cancer patients with urban cancer patients in response to evidence-based smoking cessation treatments have not been conducted.

Barriers to Smoking Cessation

Information on barriers to smoking cessation treatment for rural populations is largely available from populations without cancer. Rural residents face obstacles regarding access to both cancer care and smoking cessation treatment. Data on rural residents show that they are more likely to report exposure to smoking in their environments and are less likely to report smokefree policies at home and at work compared with individuals who reside in urban and suburban environments.[211] Frequent exposure to smoking could produce a variety of effects that undercut cessation: It contributes to smoking being viewed as normative, it could stimulate urges to smoke, and could provide easier access to cigarettes. Also, rural areas often have fewer financial resources and limited capacity to implement local cessation programs,[212] and often face shortages of health care professionals and facilities.[213] Individuals in rural communities could also have limited health resources, including a lack of health insurance or limited access to employer-sponsored health insurance, lack of consistent clinician availability, and difficulty covering costs of medical visits.[73,74] An American Society of Clinical Oncology (ASCO) workforce analysis revealed that only 3% of medical oncologists practice in rural areas, while nearly 20% of the total U.S. population resides in such areas.[214] As a result, rural cancer patients must often travel long distances to receive care.[215] Further, lack of access to care resources means that these patients often do not receive key elements of oncology care, such as radiotherapy and access to hospice.[216–218] Such obstacles likely reduce cancer control and prevention efforts in rural populations related to smoking cessation relative to urban dwellers.[74]

In addition, access to technology could affect rural residents' ability to engage in smoking cessation treatment. In 2021, around three-quarters of rural Americans (72%) said they had a broadband internet connection at home. While this is a notable increase from the 35% reporting a broadband internet connection in 2007, it is still lower than the level of broadband access reported among urban and suburban Americans (77% and 79%, respectively).[219] Further, in a 2018 survey, 24% of adults living in rural areas reported that access to high-speed internet was a major problem in their local community compared with only 13% of adults living in urban areas.[220] This lack of access could affect the availability of smoking cessation treatment delivery via telehealth for some of these populations.

Research suggests that smoking is just one element in a constellation of factors shared by many rural residents that might serve as obstacles to seeking smoking cessation treatment and achieving success in quitting smoking. Compared with residents of metropolitan areas, rural residents have higher levels not only of smoking, but also obesity and physical inactivity.[221] Data from the 2013 BRFSS showed that adults residing in nonmetropolitan counties, compared with those in metropolitan counties, had a lower prevalence of self-reporting four health behaviors important for avoiding chronic disease and injury: current nonsmoking, maintaining normal body weight, nondrinking or moderate drinking, and meeting aerobic leisure time physical activity recommendations.[203] Such health behaviors could serve as proxies for general risk factors that might thwart health-related behavior change. These factors might include treatment access, risk awareness, economic factors, social and structural determinants of health (e.g., educational and social policies), cultural factors, stress, and social network influences.

Summary: Smoking Among Rural Populations with Cancer

Research shows that rural residents have especially high smoking prevalence and could be less likely to attempt to quit smoking compared with non-rural residents. Little research exists regarding the effectiveness of evidence-based smoking cessation treatment in rural compared with non-rural populations. Barriers to smoking cessation in this population include high levels of exposure to smoking in their daily environments, relatively poor access to health care, and barriers to accessing cessation support resources. The same factors could present challenges to smoking cessation among rural residents with cancer.

Smoking Among Sexual and Gender Minority (SGM) Populations with Cancer

Epidemiology

Data from populations without cancer or a cancer history suggest a relatively high prevalence of smoking in SGM populations.[41,45,222] The nationally representative NHIS conducted in 2020 showed that the prevalence of any tobacco product use was greater in sexual minority individuals than in heterosexual individuals (25.1% [95% CI, 21.4%–29.1%] compared with 18.8% [95% CI, 18.2%–19.5%]), although prevalence of cigarette smoking was only slightly higher among sexual minority individuals (16.1%, 95% CI = 12.7%–19.9%) in comparison with heterosexual individuals (12.3%, 95% CI = 11.7%–12.8%).[41] There is also evidence from the 2009–2010 National Adult Tobacco Survey that, compared with heterosexual women, bisexual women initiate smoking at a younger age, exhibit greater nicotine dependence, and make fewer quit attempts.[223]

Transgender people appear to have especially high smoking prevalence. In a cross-sectional survey of 241 transgender women in the San Francisco area, Gamarel and colleagues reported prevalence estimates of 83% for past 30-day smoking and 62% for daily smoking.[21] However, differences in smoking prevalence between transgender and cisgender populations could be due in part to sociodemographic differences. Data from the 2014–2015 PATH survey indicate that transgender individuals had a higher prevalence of current use of any tobacco product (33.0%) compared with cisgender individuals (23.8%). However, after adjusting for sociodemographic variables including race and income, transgender identity was not significantly associated with current tobacco use.[45]

Little evidence exists regarding smoking prevalence among SGM cancer populations. Some data regarding sexual minority cancer survivors are available from California Health Interview Survey data pooled across 2001, 2003, and 2005.[224] This survey identified respondents who reported cancer of any kind after age 18; it asked respondents to categorize their behavior concerning ever smoking, past smoking, and current smoking; and allowed respondents to identify as either heterosexual, gay, bisexual, or lesbian. Among female cancer survivors, heterosexual women were significantly less likely to have ever smoked 100 cigarettes in their lifetime (47.7%) than lesbian (54.6%) or bisexual women (65.3%). Heterosexual women were also less likely to be currently smoking (15.8%) than were lesbian (21.1%) or bisexual women (37.4%). Among male cancer survivors, heterosexual men were significantly less likely to be currently smoking (12.0%) than were gay (23.0%) or bisexual (22.8%) men. In addition, in a study using 2010 BRFSS data, Kamen and colleagues analyzed cigarette smoking among cancer survivors in five states (Alaska, California, Massachusetts, New Mexico, and Wisconsin).[225] The analysis, which included 248 heterosexual respondents and 124 lesbian, gay, or bisexual respondents, found a higher lifetime history of smoking (57.7% vs. 51.2%), as well as a higher prevalence of current smoking (17.2% vs. 10.7%) among sexual minority cancer survivors than among heterosexual cancer survivors. These findings suggest higher prevalence of current smoking among sexual minority cancer populations, but the small size of the sexual minority samples limits interpretation and generalizability.

Smoking Cessation

Only one study has examined quitting behavior among a sexual minority cancer population. In the previously discussed study by Kamen and colleagues (the five-state sample of BRFSS respondents who were cancer survivors in 2010), there was no statistically significant difference in past-year quit attempts when comparing sexual minority and heterosexual cancer survivors.[225] Additional information on cessation must be derived from noncancer SGM groups. Observational studies have reported fairly high quit rates (e.g., nearly 40% at 6 months) when SGM individuals have undergone smoking cessation treatment.[226–228] Most of this research has involved interventions that targeted the needs of a specific SGM population. One challenge in evaluating interventions designed for SGM populations is that such interventions differ meaningfully regarding the SGM subpopulation and in the nature of the content.[226–228] Interventions have been targeted or adapted based on smoking characteristics in these communities,[229,230] including SGM-specific health concerns, bar culture and smoking,[230] tobacco company targeted marketing, coping with chronic stressors related to factors such as prejudice and discrimination,[231,232] and strategies to increase social support.[230]

Targeted interventions are intended to increase the effectiveness of smoking cessation treatment in the focal populations.[231] As noted above, these studies have generally led to fairly high smoking quit rates,[226,229] but they include few randomized control conditions and have other methodologic limitations, such as small samples and substantial attrition, and often lack biochemical confirmation.[226] Such features limit inferences that can be made about the utility of targeting and the effectiveness of the smoking interventions.

SGM populations can also benefit from smoking interventions designed for the general population (i.e., nontargeted interventions).[233,234] For example, Vogel and colleagues examined the effectiveness of a Facebook intervention with general population content and found very similar 12-month quit rates among SGM and heterosexual/cisgender individuals (i.e., 20.0% and 21.6%, respectively).[231] In addition, Matthews and colleagues conducted a randomized controlled trial that evaluated the effectiveness of culturally targeted smoking cessation treatment compared with a standard control condition in 345 SGM individuals who smoked.[235] The study randomly assigned participants to six sessions of targeted counseling plus NRT or a standard (i.e., general population) intervention based upon recommendations of the Public Health Service (PHS) Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*.[176] There were no differences in cessation between conditions through the 12-month follow-up period, with overall cessation rates ranging from 31.9% at 1 month to 22.3% at 12 months.[235] Finally, in a randomized controlled trial of two web-based cessation interventions, Heffner and colleagues also found no difference in 12-month smoking cessation outcomes between sexual minority and heterosexual participants (24% vs. 25%, respectively).[236] Such studies suggest that generally available smoking cessation treatments are similarly effective in SGM and heterosexual and cisgender individuals; use of such widely available treatments could enhance the reach of smoking cessation treatment in SGM populations.

There is virtually no information on the level of benefit that SGM populations derive from evidence-based smoking cessation treatment compared with placebo or inactive control conditions. Therefore, meaningful estimates of the amount of benefit produced by active treatment are unavailable. However, there is evidence that SGM groups achieve quit rates that are similar to those of non-SGM populations when both use nontargeted, evidence-based smoking interventions.[227]

Barriers to Smoking Cessation

Systematic reviews indicate that SGM individuals report high levels of discriminatory experiences in health care settings.[19,237] Perceived discrimination has been found to be negatively correlated with both attempts to quit smoking and smoking cessation success among transgender women in San Francisco.[21] Also, the HINTS 5 (cycle 1) revealed that, compared with other respondents, sexual minority respondents were less likely to seek medical information from a physician as their first choice of a health information resource.[238]

Further, compared with heterosexual individuals, sexual minority individuals tend to report higher levels of depression and mental distress and to have especially high levels of health risk factors such as obesity, chronic medical conditions, binge drinking, and overall poor physical health.[236,239] Such challenges might reduce the likelihood that SGM individuals with cancer would seek smoking cessation treatment. One study with sexual minority individuals in the general population showed that they reported being much less likely to call a tobacco quitline than were other individuals who smoked.[240]

Inadequate clinician training or biases could reduce SGM populations' access to high-quality health care. A survey of medical clinicians, including oncologists, found that only 54% reported competence to provide care for SGM patients, and oncology clinicians reported lower competence to care for this population than did primary care clinicians.[241] Among oncology clinicians at an NCI-Designated Cancer Center ($N = 108$), only 26% assessed patients' sexual orientation and only 28% reported knowledge of SGM health concerns.[242] A survey of 149 oncologists from 45 NCI-Designated Cancer Centers reported that many oncologists reported positive experiences working with SGM patients (e.g., positive communication, compassion) but also identified several barriers to providing care to SGM patients: lack of experience with transgender patients and knowledge of their needs, and fear of offending patients in asking for sexual orientation and gender identity information.[243] More than two-thirds of respondents (70.4%) indicated interest in receiving education regarding the health needs of SGM patients, and 43.7% agreed there should be mandatory education about SGM patients' health needs.[244]

It is important that oncology clinicians gain knowledge about the needs of SGM patients, as clinician discomfort and bias can impede patient care.[241] In fact, clinicians rarely receive formal education in the health risks and disparities experienced by SGM people.[241,245] In-depth clinician training and continuing education in cultural competence have the potential to increase equitable cancer care to SGM people,[246] including their engagement in smoking cessation treatments. Moreover, greater adoption of enhanced EHR-based health care system improvements, such as those that have increased smoking cessation treatment reach among racial and ethnic minority groups,[196,197] might similarly increase smoking cessation treatment reach in SGM populations.

Summary: Smoking Among SGM Populations With Cancer

Data from the general and cancer survivor populations show that SGM groups have especially high smoking prevalence compared with heterosexual and cisgender individuals. Other evidence from the general population shows that when SGM individuals receive evidence-based smoking cessation treatment, they are as likely to quit smoking as are those who are not members of an SGM group. While targeted smoking interventions have been developed for SGM populations, there is insufficient evidence to determine their effectiveness relative to nontargeted interventions. Barriers to smoking cessation success in some segments of the SGM population include high rates of discrimination, lack of access to treatment resources, high levels of depression and negative affect, mistrust of clinicians, and health care systems and personnel that are not trained to deliver high-quality care to them.

Smoking Among People With Co-Occurring Substance Use Disorders and Cancer

People who use tobacco and who have co-occurring substance use disorders are a medically underserved and vulnerable population; they tend not to receive evidence-based smoking cessation treatment as part of their substance use disorder treatment,[247] and they are at elevated risk for cancer and its harms.[248] People with substance use disorders also tend to differ from those without substance use disorders in that they smoke more cigarettes per day and are more likely to begin smoking earlier in life,[249–254] possibly amplifying the negative health effects of substance use.

This section discusses evidence on the use of alcohol, cannabis, and/or opioids along with smoking among cancer populations. Most of the research on patients with cancer focuses on the use of both tobacco and alcohol, with a small number of studies focusing on tobacco use together with opioid and cannabis use. However, many studies provide little information on the types of substances used or do not distinguish the use of illicit substances from the use of prescription drugs or alcohol.[255] Thus, it is often difficult to identify the particular substances being studied. Also, while studies on alcohol often describe the amount of alcohol use of participants (albeit often via broad, imprecise categories), the use of other substances is typically characterized only in terms of presence or absence of use disorder. When possible, this section attempts to characterize the population in each study by the substances being used and by the heaviness or frequency of use.

Cannabis, Tobacco, and Cancer

The National Institute on Drug Abuse (NIDA) explains that “marijuana [also referred to as cannabis] is the most commonly used addictive drug after tobacco and alcohol.”[375] In 2020, 17.9% of people aged 12 or older (49.6 million) reported use of marijuana in the past year.[376] Use of cannabis is more common among people who smoke cigarettes than among those who do not. For example, an analysis of 2013–2014 data from the Population Assessment of Tobacco and Health (PATH) study found that, compared with noncurrent tobacco use, the current use of any tobacco product was associated with far higher likelihood (AOR = 4.4, 95% CI = 4.0–4.9) of past-year marijuana use; the study also found higher levels of marijuana use among users of cigars, pipes, waterpipe, ENDS, and smokeless tobacco products.[377]

Studies have shown that marijuana use could have a negative influence on tobacco cessation. Tobacco users who also use cannabis could be less motivated to quit using tobacco,[378] less likely to try to quit,[378,379] less likely to successfully quit,[380,381] and could score higher on cigarette dependence measures than tobacco users who do not also use cannabis.[382]

Over the past decade, there have been rapid changes in state and local-level laws regulating cannabis sales and marketing.[383] These laws have increased access to cannabis in many jurisdictions, as well as the types of cannabis products available for sale. These changes could influence cannabis-use patterns in the general population, as well as among cancer patients and survivors.

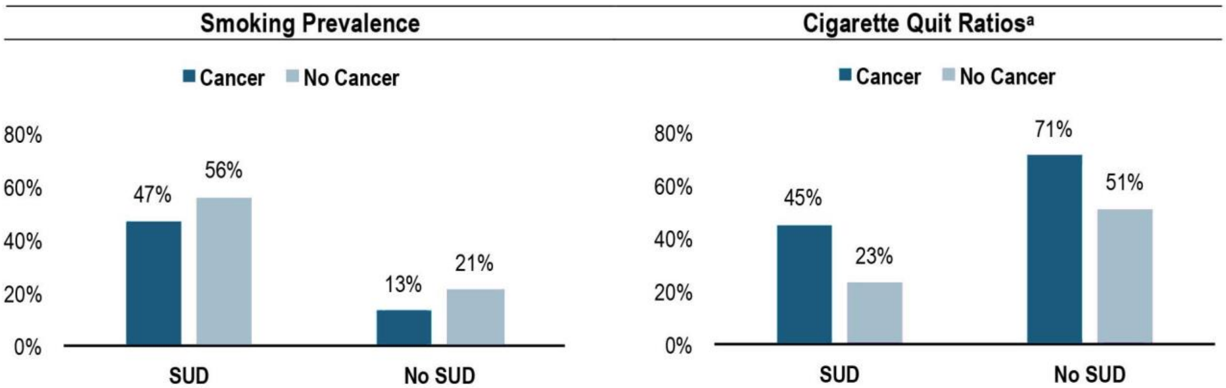
Few studies have examined the patterns of cannabis and tobacco use in patients with cancer. An analysis of 2013–2018 data from the PATH study reported that 8% of cancer survivors reported past-year cannabis use, compared with 15% of respondents without a history of cancer.[384] Some evidence suggests that medicinal cannabis could provide relief (e.g., antiemetic effects, appetite stimulation, pain relief, and improved sleep) from some common symptoms of cancer treatment.[385,386] However, whether used for symptom relief or for non-medicinal use, cannabis use is likely to make quitting tobacco more difficult for cancer populations.

This monograph recognizes that the use of cannabis is common among people who smoke cigarettes, and that cannabis use is likely to have implications for cessation among patients with cancer who use tobacco. However, in the absence of a robust body of evidence, this topic is not addressed further in the monograph. Studies of patterns of cannabis use among oncology patients and subsequent health effects, including the potential to interfere with tobacco cessation treatment, are urgently needed. Research is also needed to guide clinical management of oncology patients who smoke and also use cannabis products, including counseling patients on the efficacy and harms of cannabis for symptom management.

Epidemiology

Smoking and Any Substance Use. Estimates of substance use (other than tobacco) among cancer populations range from 2% to 35%.[255] Data from the National Survey on Drug Use and Health (NSDUH) gathered during 2015–2018 show that adults with substance use disorders, both with and without cancer, have higher prevalence of cigarette smoking than do adults without substance use disorders.[256] In this population-based research, adults reporting a past-year cancer diagnosis (*N* = 1,571) and those without a past-year cancer diagnosis (*N* =168,540) were categorized according to current (past month) smoking and past-year substance use, which included use of alcohol, cannabis, methamphetamines, hallucinogens, inhalants, tranquilizers, cocaine, heroin, prescription pain relievers, simulants, and sedatives. Current smoking was more common among those without a past-year cancer diagnosis (24%) than in those with a past-year cancer diagnosis (15%), which the study authors attribute to smoking cessation in response to a cancer diagnosis. Current (past-year) substance use was also more common among those without a past-year cancer diagnosis (7.9%) than in those with a past-year cancer diagnosis (4.6%). Further, among those with a past-year cancer diagnosis, individuals with a current substance use disorder were more likely to smoke (47%) than were those who did not report current substance use (13%, $p < .001$ across survey years: Figure 5.1). A similar pattern was observed in those without a past-year cancer diagnosis (56% compared with 21% across years, $p < .001$).

Figure 5.1 Current Cigarette Smoking Prevalence and Quitting by Past-Year Substance Use Disorder Status and Past-Year Cancer Diagnosis Among U.S. Adults Aged 18 and Older, 2015–2018



[a]Cigarette quit ratios were defined as the ratio of those with former smoking to those with ever smoking at each survey year.
Source: Adapted from Streck et al. 2020,[256] based on data from the National Survey on Drug Use and Health, 2015–2018.

As shown in Table 5.2, individuals with a past-year cancer diagnosis were more likely to use alcohol than other substances (excluding tobacco use). They were also significantly less likely to use alcohol, cannabis, or stimulants than were individuals without a past-year cancer diagnosis. It is important to note that this study could have underestimated substance use among the respondents because substance abuse and/or dependence within the past year was required in order to be characterized as having a substance use disorder.

Table 5.2 Substance Use Disorders Among U.S. Adults Aged 18 and Older With and Without a Past-Year Cancer Diagnosis, 2015–2018

Substance use disorder (SUD)[a]	Cancer (unweighted *N* = 1,571)	No cancer (unweighted *N* = 168,540)	*p* value[b]
Any past-year SUD	4.6%	7.9%	<.001
1 SUD	4.0%	6.6%	
2+ SUDs	0.4%	1.2%	
Alcohol use disorder	3.4%	6.0%	.001
Cannabis use disorder	0.2%	1.4%	<.001
Opioid use disorder	0.8%	0.8%	.87
Stimulant use disorder[c]	0.2%	0.5%	.01
Other use disorder[d]	0.4%	0.7%	.11
Past-month cigarette smoking	5.0%	24.0%	<.001

Note: Percentages are weighted and unadjusted for demographic characteristics. Percentages may not sum to 100% due to rounding. [a]Nontobacco substance use disorders were defined as diagnosis of abuse and/or dependence within the past year. [b]*p* values compare characteristic values for respondents with a past-year cancer diagnosis with those without a past-year cancer diagnosis. [c]Includes prescription stimulant and cocaine use disorder. [d]Includes hallucinogen, inhalant, methamphetamine, tranquilizer, or sedative use disorder.
Source: Adapted from Streck et al. 2020,[256] based on data from the National Survey on Drug Use and Health, 2015–2018.

A study based on 2007–2016 data from the Canadian Community Health Survey examined the co-occurrence of smoking and both alcohol and illicit drug use among 15,168 adults with cancer.[257] This study found significant associations between current smoking and heavy alcohol use (no heavy drinking compared with heavy drinking: OR = 0.41, 95% CI = 0.29–0.58) and the use of illicit drugs (OR = 2.42, 95% CI = 1.96–2.98). These associations are consistent with data from the 2020 NSDUH showing high prevalence of comorbid substance use disorders in the general population.[258] Thus, among patients with cancer, as well as in the general population, smoking is highly associated with greater likelihood of use of a variety of other substances, including alcohol and illicit drugs.

Other observational studies of patients with cancer have also demonstrated a positive association among smoking, alcohol, and/or illicit drug use.[259–262] For example, a retrospective chart review of patients with advanced cancers (*N* = 300) found that those who currently smoked were more likely to report a history of alcoholism and illicit substance use compared with those who never smoked.[262]

Smoking and Opioid Use. Opioids include illicit drugs, such as heroin, as well as prescription pain relievers such as oxycodone, hydrocodone, codeine, fentanyl, and morphine. Opioids are often used to reduce pain related to cancer or its treatment. Several studies have focused on the use of both tobacco and opioids among patients with cancer. A 2021 meta-analysis of seven studies examining chronic opioid use after treatment for head and neck cancer found that 35% of patients who smoked later developed chronic opioid use disorder.[263] In a separate study of patients being treated for cancer-related pain (*N* = 486) at a cancer pain management center, those currently smoking (*N* = 94) did not differ from nonsmokers (*N* = 392) in terms of opioid use (measured by morphine equivalency daily dose).[264] However, individuals who currently smoked had more risk factors for opioid misuse (as measured by the short form of the Screener and Opioid Assessment for Patients with Pain) compared with nonsmokers, including more frequent mood swings, taking medications in a nonindicated manner, history of illegal drug use, and history of legal problems. Patients who smoked also reported greater pain during a 6-month follow-up after their initial pain center visit than those who did not smoke.

Another study examined differences in opioid self-administration by smoking status among patients diagnosed with gastric cancer, following distal gastrectomy with gastroduodenostomy ($N = 236$).[265] Results demonstrated that patients who smoked administered a greater quantity of patient-controlled intravenous analgesic for postoperative pain compared with patients who were nonsmokers. This greater rate of analgesia self-administration could be due to the association of smoking status with pain sensitivity. A cross-sectional study examined associations between smoking status and several pain-related outcomes in patients with cancer ($N = 224$) about to begin chemotherapy.[266] This study found that patients who continued to smoke after their cancer diagnosis reported more severe pain than those who never smoked. Those who continued to smoke after diagnosis also reported that pain interfered more with their daily routine than those who had never smoked or who had smoked in the past. The authors of this research acknowledge that the directionality of the pain-smoking association in patients with cancer is unclear; greater pain could motivate smoking or continued smoking could increase pain.

Data from the general population also show an association of smoking with opioid use. Nearly half of people with prescription opioid use disorder also have nicotine dependence (NIDA 2020).[267] A meta-analysis of 10 observational studies published through 2017 found increased odds of opioid use disorder among people who smoked compared with nonsmokers (OR = 8.23, 95% CI = 3.07–22.09).[268]

Smoking and Alcohol. Sanford and colleagues used NHIS data from 2000 to 2017 to examine alcohol use patterns among adults reporting a cancer diagnosis.[269] The sample included 34,080 respondents with a cancer diagnosis; 56.5% of respondents reported current drinking, including 34.9% who reported heavy drinking (defined as more than 1 drink per day for women and 2 drinks per day for men). Further, 21.0% reported a history of binge drinking (defined as consuming $\geq$5 drinks on at least 1 day during the past year, for both men and women). Heavy drinking was more common among those who currently smoked; for example, binge drinking was reported by 8.0% of people who never smoked compared with 23.6% of those currently smoking.

These findings by Sanford and colleagues[269] show a high prevalence of heavy drinking compared with previously discussed research by Streck and colleagues,[256] which found a 6% prevalence of past-year alcohol use disorder among individuals with a past-year cancer history. The study by Streck and colleagues restricted its examination to recent (past-year) cancer occurrence, which could explain the discrepancy. Additionally, Streck and colleagues used DSM-IV criteria for diagnosis of substance use disorder in the past year, whereas the study by Sanford and colleagues examined the number of drinks per day.

One study showed that, among survivors of childhood cancers, those who reported current smoking at the time of the survey were significantly more likely to report current drinking than were those without a smoking history.[86] Similar findings were reported among patients diagnosed with non-B, non-C hepatocellular carcinoma who underwent curative surgical treatment.[270]

Smoking Cessation

Substance Use and Smoking Cessation. The analysis of NSDUH data by Streck and colleagues, discussed previously, examined quit rates of individuals with a cancer diagnosis in the past year in relation to past-year substance use disorder.[256] The quit rate outcome was based on the ratio of those who reported former smoking relative to ever-smoking in each survey year. The data showed that among those with a past-year cancer diagnosis, individuals who smoked had a lower quit ratio if they also had a substance use disorder (45%) than if they did not (71%, $p = .002$: Figure 5.1). A similar pattern was seen for those without cancer (23% compared with 51% across years, $p < .001$). The quit ratio was higher for adults with a past-year cancer diagnosis than in those without such a history, regardless of substance use disorder, perhaps reflecting the teachable moment provided by a cancer diagnosis.

Other research among the general population suggests that the use of illicit drugs is associated with reduced cessation likelihood. Data from the 1997 National Household Survey on Drug Abuse ($N = 16{,}661$) found that adult illicit drug users had a history of successful quitting that was half that of nonuser respondents (23% compared with 56%).[253] Further, a structured review of 29 epidemiologic studies of the general population concluded that, among people who smoke, those with alcohol or substance use disorders had lower smoking quit rates, greater withdrawal symptoms, and greater nicotine dependence than did those without alcohol or substance use disorders.[271] Thus, multiple studies have found that substance use is associated with a lower likelihood of smoking cessation.

Alcohol Use and Smoking Cessation. Studies conducted in the United States,[272,273] Canada,[274] and Australia[275] have found that alcohol consumption is negatively associated with smoking cessation among cancer populations. One study in Korea found that alcohol dependence was associated with continued smoking compared with cessation in adult cancer survivors who smoked at the time of their cancer diagnosis.[276] As noted previously, a study using data from the Detroit Research on Cancer Survivors Study identified factors associated with continued smoking in Black or African-American cancer survivors at about 18 months post cancer diagnosis.[198] This study identified a higher prevalence of any alcohol use in the past month (57.4%) among survivors who continued smoking compared with those who quit. In sum, most research suggests that current or proximal alcohol use is associated with continued smoking versus successful quitting in patients with cancer.

Research with the general population yields a pattern of findings similar to that obtained with cancer populations. That is, current alcohol use is associated with a reduced likelihood of smoking cessation with either aided or unaided quit attempts.[271,277–281]

In contrast, a considerable body of evidence suggests that past alcohol use or even past alcohol dependence often does not significantly reduce the likelihood of later cessation, especially when evidence-based smoking cessation treatments are used.[282,283]

Evidence-Based Smoking Cessation Treatment. Research with the general population shows that evidence-based treatment can significantly increase quit rates among those with a variety of substance use disorders.[283–286] A Cochrane Review examined the effectiveness of smoking cessation treatment in people in treatment or in recovery for substance use disorders.[284] This research, which included 35 randomized controlled trials, showed that 2 treatments significantly increased the likelihood of long-term abstinence from tobacco: smoking cessation pharmacotherapy and the combination of smoking cessation pharmacotherapy and counseling. This research showed that smoking cessation treatment significantly increased smoking quit rates for both people with alcohol use disorders as well as other substance use disorders. Another systematic review of smoking cessation interventions for individuals in substance use disorder treatment or recovery similarly found that pharmacotherapy and combination pharmacotherapy and counseling were effective for this population.[287] The review also concluded that contingency management, along with counseling and relapse prevention or counseling and pharmacotherapy, was effective in increasing smoking abstinence.

The effectiveness of smoking cessation treatment among individuals with substance use disorders could apply to cancer populations, as well. In the Smokefree Support Study, a randomized controlled trial that compared intensive (N = 153) and standard treatment (N = 150) for smoking cessation in newly diagnosed patients with cancer, problematic alcohol use (defined as binge drinking or a score of two or greater on the Cut-down, Annoyed, Guilty, Eye-opener [CAGE] questionnaire) did not have a statistically significant effect on biochemically confirmed 6-month abstinence, although participants in the study frequently identified the use of alcohol, drugs, or other substances as barriers to quitting smoking.[288]

In sum, research among populations with and without cancer shows that current drinking and substance use are associated with reduced likelihood of quitting smoking. However, there is strong evidence that individuals who drink heavily or engage in other forms of substance use can benefit from the receipt of evidence-based smoking cessation treatment. Thus, the evidence supports the recommendation of the PHS Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*,[176] that patients who use alcohol or who have other substance use disorders be provided evidence-based smoking cessation treatment. This recommendation is also supported by the available evidence for cessation success among patients with cancer who have current or past substance use disorders.

Barriers to Smoking Cessation

Research conducted among the general population suggests that those with substance use disorders face unique barriers to quitting smoking. Such populations are typically exposed to multiple factors that could undermine smoking cessation: high prevalence of smoking in the social network, high levels of life stress due to social and vocational upheaval, decreased cognitive control and self-regulation due to intoxication, and psychiatric comorbidities.[289–291] These challenges suggest that individuals with substance use disorders need intensive smoking cessation treatment and, ideally, treatment for their comorbid drinking or other substance use[284,287] to maximize the likelihood of smoking cessation.

There has been a long-standing supposition that people with substance use disorders are uninterested in trying to quit smoking.[283] However, research on noncancer populations shows that more than 60% of individuals with alcohol or other substance use disorders are interested in quitting tobacco use.[254,292,293] This is similar to the general population of those in the United States who smoke, where about 70% of individuals express interest in quitting,[162,176] and reflects a clinically significant opportunity to intervene. Also, clinicians might increase the percentage of those willing to try to quit smoking by clearly articulating the benefits of smoking cessation with regard to cancer treatment and outcomes.

Although evidence suggests that treatment for smoking does not worsen patterns of alcohol or substance use or reduce recovery from such disorders among the general population,[283,284] some clinicians have assumed that an attempt to quit smoking might exacerbate a substance use disorder and interfere with recovery from it. In a survey of 2,067 substance use treatment counselors, 16% believed that smoking cessation interventions would have a negative effect on clients' chances of achieving sobriety.[294] Smoking cessation treatment is often not provided in substance use disorder treatment settings; less than half of substance use treatment programs provide counseling for smoking cessation, and only about one-quarter provide pharmacotherapy.[247] For example, the 2016 National Survey of Substance Abuse Treatment Services indicated that, although 64% of substance use treatment facilities screened patients for tobacco, just 47% offered cessation counseling, 26% offered NRT, and 20% offered varenicline or bupropion.[295]

The available research therefore strongly supports the assessment of alcohol and substance use because people with such disorders may need additional encouragement and may benefit from more intense treatment in order to quit successfully.[283] The use of alcohol and other substances could also be a target of treatment because their use could precipitate relapse back to smoking. Finally, there is substantial evidence that people who use alcohol and other substances can quit smoking successfully when given evidence-based treatment, which supports strong efforts to provide such treatment to these individuals within the context of cancer care.

Summary: Smoking Among People With Co-Occurring Substance Use Disorders and Cancer

Data on people with substance use disorders are often difficult to interpret because relevant studies sometimes do not provide information on the specific type of substance or amounts used, and the diagnostic codes used in this area have changed over time. In populations with and without a cancer diagnosis, data show that those who use alcohol or other substances tend to have higher smoking prevalence than those who do not use such substances. Further, current alcohol use is associated with reduced smoking cessation success when making unaided cessation attempts in studies of general and cancer populations. Data from the general population show that individuals using illicit drugs also have a lower likelihood of quitting successfully in unaided quit attempts. However, evidence-based smoking cessation treatment can significantly increase smoking cessation success among both alcohol- and substance-abusing individuals in the general population. Such treatment does not appear to jeopardize their status regarding recovery from their alcohol or drug use condition. Barriers to successful smoking cessation include a high level of smoking in social networks, stress due to social and vocational upheaval, low rates of provision of smoking cessation treatment in substance use treatment programs, and psychiatric comorbidities.

Smoking Among Individuals With Serious Mental Illness (SMI) and Cancer

This section discusses patients with a variety of psychiatric disorders but will focus particularly on bipolar and schizophrenia spectrum disorders, given their serious health and social consequences,[296] the availability of extant research, and the high cancer burden. Depression and anxiety disorders and their associated symptoms are discussed in more detail in chapter 3.

Epidemiology

Little evidence is available on smoking prevalence as a function of psychiatric condition among cancer populations and most of the extant data arise from populations outside the United States. Some of this evidence suggests similar levels of mental health problems or disorders in cancer populations and whole-population prevalence rates,[297] while other data from Australia indicate higher rates among cancer populations relative to the respective whole-population prevalence.[298] However, it is difficult to draw firm conclusions from these data because the studies differ not only on geographical region but also on definitions of mental health problems and means of defining cancer status.

Research in the general population shows that the prevalence of smoking is higher in virtually all psychiatric populations.[5] Based on pooled data from the 2009–2011 NSDUH, Gfroerer and colleagues estimated that individuals with any mental illness account for 30.9% of all cigarettes smoked by adults.[299] Individuals who currently smoked and had mental illness also smoked more cigarettes in the past month (mean = 331) compared with those without mental illness (mean = 310). Estimates are that as many as 46%–70% of people with bipolar disorder smoke.[300–302] The smoking prevalence of individuals with schizophrenia is estimated to be between 60% and 90%.[83,296,301,303] A meta-analysis of 42 studies found higher odds of current smoking in people with schizophrenia compared with those without schizophrenia (OR = 5.9, 95% CI = 4.9–5.7), with the odds of current smoking being substantially higher among men with schizophrenia (OR = 7.2, 95% CI = 6.1–8.3) than among women (OR= 3.3, 95% CI = 3.0–3.6).[83] Moreover, individuals living with schizophrenia tend to smoke especially heavily, puffing with greater frequency and intensity than other individuals who smoke.[302,304–306]

Data from the 2009–2011 NSDUH were used to estimate the past-year prevalence of cigarette smoking among adults who had any mental illness based on distress and disability assessments; developmental and substance use disorders were not included in this estimate.[40] Results showed that an average of 19.9% of adults had a past-year diagnosis; among these respondents, 36.1% were currently smoking, compared with 21.4% of adults with no mental illness.

In summary, evidence demonstrates that individuals with SMI are much more likely to smoke and smoke heavily than those without such disorders.

Smoking Cessation

There is abundant evidence that smoking cessation rates tend to be lower for those with psychiatric diagnoses than for those without psychiatric diagnoses.[5,85,307] This pattern has been observed across individuals with depression, bipolar disorder, post-traumatic stress disorder, and schizophrenia spectrum disorders.[5,307]

Among adults in the general population who have ever smoked daily in the 2012–2014 NSDUH, about 50% of individuals with no mental illness have quit smoking, compared with about 40% among people with any past-year mental illness.[39] Evidence from population-based studies suggests that individuals with SMI are more likely to become heavily nicotine dependent and to have particularly low quitting rates,[308–311] although there is clear evidence that they can be aided by evidence-based smoking cessation treatment.[312–314]

Kalkhoran and colleagues analyzed data from adults sampled in the nationally representative 2014 Health Center Patient Survey (*N* = 5,592), which includes data on patients seen at health centers funded by any of four types of Health Resources and Services Administration (HRSA) grant programs: Community Health Center Programs, Migrant Health Center Programs, Health Care for the Homeless Programs, and Public Housing Primary Care Programs.[315] They examined prevalence of current and ever smoking in those with and without SMI diagnoses and calculated quit ratios (current-smoking prevalence divided by ever-smoking prevalence) for both. In the SMI sample (*N* = 1,376), the prevalence of ever smoking was 68%; the comparable rate for individuals without an SMI diagnosis was 41%. The prevalence of current smoking was 48% and 22% for participants with and without an SMI diagnosis, while the quit ratios were 30% and 46%, respectively. This disparity in quitting success occurred despite people with and without an SMI diagnosis not differing in number of quit attempts.

Evidence-based treatments significantly increase smoking cessation rates among individuals with psychiatric diagnoses, including anxiety and mood disorders, among others.[289,316,317] For example, multiple randomized controlled trials have shown that evidence-based treatment can significantly increase smoking cessation rates among individuals with depression.[318–321]

As noted above, individuals diagnosed with schizophrenia can also quit smoking successfully with evidence-based treatment.[296] Multiple studies using combined counseling and medication for smoking cessation suggest positive effects when used with populations with schizophrenia and other SMI diagnoses.[322–326]

As discussed in chapter 3, varenicline appears to be an especially effective smoking cessation intervention in the general population.[85,176,327,328] There is substantial evidence that supports both the safety and efficacy of this agent in the treatment of smoking among individuals with SMI diagnoses,[323–325,329–331] with the EAGLES trial (Evaluating Adverse Events in a Global Smoking Cessation Study) producing the strongest evidence to date. The EAGLES trial included individuals with psychotic disorders who smoked (*N* = 390) and compared several FDA-approved cessation medications with placebo; all subjects received counseling in addition to pharmacotherapy. The 4-week continuous abstinence rate at the end of treatment was 23.2% for varenicline, 13.1% for the nicotine patch, 11.2% for bupropion, and 4.1% for placebo.[296,330]

Significant concerns were once raised about the safety of varenicline, especially for those with psychiatric disorders, which resulted in an FDA black box warning related to such use. The FDA removed that warning in December 2016 based on the EAGLES trial in addition to other evidence.[331]

While the evidence of efficacy is strongest for varenicline, there is positive evidence for the effectiveness of both bupropion and the nicotine patch in SMI populations as well.[296,331,333–337]

However, in interpreting this information, it is important to note that most trials included only participants who were motivated to quit and whose psychiatric disorder was stable.

Virtually all of the evidence attesting to the effectiveness of smoking cessation medications comes from studies that included adjuvant counseling: often repeated, multisession, high-intensity counseling visits. While such counseling likely contributed to the effectiveness of the pharmacotherapies, there is evidence that brief advice or minimal counseling alone is not meaningfully effective with individuals experiencing SMI.[296,331] This evidence is consistent with the results from the EAGLES trial, which found that participants with SMI had very low cessation rates when given placebo (all arms received minimal counseling). Thus, it is important that patients with SMI diagnoses be encouraged to use pharmacotherapy in their smoking cessation attempts and perhaps relatively intensive counseling support.

Finally, most of the data reviewed above were derived from formal randomized controlled efficacy trials that do not resemble real world clinical practice (e.g., in that efficacy trials typically employ specially trained counselors, provide intense counseling, and include highly motivated participants). However, a 2019 pragmatic, randomized controlled trial conducted in the United Kingdom suggests that smoking cessation treatment for SMI populations can be effectively implemented in real world settings.[338] In this study, intensive smoking cessation treatment, which included pharmacotherapy and counseling, was delivered to individuals with SMI diagnoses (schizophrenia, schizoaffective disorder, bipolar disorder, and other psychotic disorders) in primary care clinics or community-based mental health centers. Compared with usual care, individuals who received the relatively intense smoking cessation treatment had significantly higher smoking cessation rates at 6 months (6% in usual care group vs. 14% in intervention group), although there was no difference in smoking cessation at 12 months.

Barriers to Smoking Cessation

Information on barriers to smoking cessation treatment engagement and success in SMI populations comes almost exclusively from the general population, rather than from studies of cancer populations. People diagnosed with SMI, and to some extent other psychiatric disorders, face numerous barriers to quitting smoking successfully and to receiving treatment. Important barriers to quitting smoking include a high level of nicotine dependence, socioeconomic disadvantage, unemployment, and social isolation.[339–343] There is clear evidence that these factors are associated with an increased likelihood of smoking or a reduced likelihood of quitting smoking in the general population.[85,98,344,345]

Some people with psychiatric disorders could be less motivated to quit smoking than those without psychiatric disorders who smoke. While some psychiatric populations show evidence of quitting motivation that is comparable to levels seen in those without psychiatric disorders,[283,289,346] there is evidence of lower motivation in individuals with SMI diagnoses.[347–349] Some evidence suggests that motivational interventions can enhance the motivation to quit smoking among SMI-diagnosed individuals.[350]

Weinstein and colleagues noted additional characteristics of psychiatric populations that might interfere with smoking cessation success and possibly treatment engagement.[351] These include exposure to chronic stressors, medication side effects, and lack of financial and health care resources. Systemic barriers in the U.S. health care system prevent many SMI-diagnosed individuals from getting the evidence-based tobacco cessation treatment that they need. Weinstein and colleagues noted that much of the disparity in mortality associated with psychiatric illness is due to disparities in health insurance coverage, health care access, and utilization. Such disparities also occur regarding smoking cessation treatment.[351] While some evidence shows that individuals with schizophrenia are as likely as other individuals to receive physician advice to quit smoking,[315,352] advice alone could be ineffective.[353] There is evidence that those with SMI diagnoses are unlikely to receive evidence-based smoking cessation treatment in the course of normal psychiatric or health care contacts,[283,354–356] although Srivastava and colleagues found that, among hospitalized patients, psychiatric patients were more likely to be prescribed pharmacotherapy than patients hospitalized for other reasons.[357] Clinicians in cancer care settings cannot expect that clinicians in other settings will address smoking with patients with SMI or other psychiatric diagnoses.

Insufficient efforts to engage patients in smoking cessation treatment are just one manifestation of SMI patients' inadequate receipt of health care. In the context of cancer care, SMI patients are relatively unlikely to undergo surgical resection and they tend to receive fewer chemotherapy treatments.[351,358] In short, SMI patients receive an inadequate level of health care across a wide range of health domains. This emphasizes the need for health care systems and clinicians to examine obstacles that reduce health care delivery for this population, including clinician biases and suboptimal screening and intervention within health care systems.

Summary: Smoking Among Individuals With SMI and Cancer

Data from populations without cancer suggest that individuals with psychiatric disorders, especially those in SMI populations, tend to have especially high smoking prevalence relative to those without such disorders. Data from the general population also show that individuals with psychiatric diagnoses tend to be less successful at quitting smoking when making unaided quit attempts than are non-SMI diagnosed individuals who smoke. However, evidence-based smoking cessation treatments significantly increase the likelihood of successful cessation among individuals with psychiatric disorders, including SMIs. There is also evidence that smoking cessation pharmacotherapy, varenicline in particular, is especially effective for the SMI population. This complements evidence that varenicline is an especially effective pharmacotherapy for the general population. Barriers to successful smoking cessation among the SMI population include high levels of physical dependence on cigarettes, socioeconomic disadvantage, and inadequate referral or access to evidence-based smoking cessation treatment. The provision of relatively intense treatment that includes smoking cessation pharmacotherapy is likely to be extremely important for SMI populations given their low rates of quitting success and the many barriers this population faces that reduce the chances of quitting. The relatively high rates of cancer and cancer-related mortality in the SMI population buttress this recommendation.

Smokeless Tobacco and Medically Underserved and Vulnerable Populations

Although smokeless tobacco products, such as chewing tobacco, dip, snuff, or snus, are not as widely used as cigarettes, these products are commonly used by some medically underserved and socioeconomically disadvantaged groups. According to data from the 2020 National Health Interview Survey (NHIS), 4.5% of men and 0.3% of women reported using some form of smokeless tobacco "every day" or "some days" during the past month. This indicates that there are approximately 5.7 million smokeless tobacco users aged 18 or older in the United States.[41] Additionally, in 2020, according to the National Youth Tobacco Survey, 3.1% of high school students (4.8% of male students and 1.4% of female students) reported current use of smokeless tobacco.[387] Data from the Population Assessment of Tobacco and Health (PATH) study indicate that 1.6% of cancer survivors reported using smokeless tobacco in 2013–2014, and 4.7% of cancer survivors who currently smoked cigarettes also reported smokeless tobacco use.[159] In general, trends in smokeless tobacco use have shown little change over the past 20 years.[388]

Smokeless tobacco products contain nicotine and are addictive, and their use is causally associated with oral cancer, esophageal cancer, and pancreatic cancer. At least 28 carcinogens have been identified in smokeless tobacco products.[389] An expert group convened by the International Agency for Research on Cancer concluded that there is sufficient evidence that smokeless tobacco, along with two tobacco-specific nitrosamines present in smokeless tobacco (NNN and NNK), are carcinogenic to humans (Group 1).[390,391] A study using nationally representative data from the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2012 found higher concentrations of serum cotinine and urinary NNAL, a tobacco-specific nitrosamine, among smokeless tobacco users, compared with cigarette smokers.[392]

Higher prevalence of smokeless tobacco use is associated with younger age, White race, living in rural areas, residence in the South, lower education, and unemployment.[393] Smokeless tobacco use, and dual use with cigarettes, have also been reported to be high among Alaska Native individuals.[394] According to the 2020 National Survey on Drug Use and Health (NSDUH), adults living in a large or small metropolitan area (2.2% and 4.2%, respectively) were less likely to report past-year smokeless tobacco use than adults living in a nonmetropolitan area (6.7%).[38] NHIS data from 2020 show that adults with lower educational attainment, including those with a GED (3.8%) or high school diploma (3.3%) were more likely to use smokeless tobacco than those with higher levels of education, such as those with undergraduate or graduate degrees (1.3% and 0.8%, respectively).[41] Smokeless tobacco use is also associated with blue-collar employment; for example, one study reported a prevalence of 35% among construction workers.[395]

Smokeless tobacco also warrants concern because of its association with cigarette smoking and other tobacco use behaviors. National surveys have shown that nondaily use of smokeless tobacco is strongly associated with cigarette smoking among male adolescents and young adults.[396,397] Dual users of smokeless tobacco and cigarettes also exhibit higher levels of nicotine dependence compared with those who use only cigarettes.[397]

People who use smokeless tobacco are less likely to try to quit than people who smoke cigarettes.[398] At the same time, current evidence-based interventions for smoking cessation have had limited success among smokeless tobacco users. Clinical trials provide some evidence that behavioral interventions in particular settings, such as cessation counseling in dental offices, could increase abstinence rates among users of smokeless tobacco.[399] However, trials of pharmacotherapies in users of smokeless tobacco have shown limited impact on long-term (i.e., longer than 6 months) rates of abstinence.[399,400] There is also a lack of interventions targeted at smokeless tobacco use among patients with cancer. However, a large, randomized trial conducted in India found a reduction in oral cancer mortality from repeated visual screening in tobacco and alcohol users.[401]

In summary, smokeless tobacco products pose novel challenges to public health and tobacco control, are a cause of several types of cancers, and contribute to tobacco-related health disparities. In addition to presenting a significant challenge for cancer prevention and control in the U.S., smokeless tobacco is also a global health problem; worldwide, more than 300 million people across 127 countries consume smokeless tobacco products.[402]

Effectiveness of Smoking Cessation Treatment

The literature reviewed above shows that many members of medically underserved and vulnerable populations face significant challenges in terms of generally high smoking prevalence, reduced likelihood of smoking cessation, and barriers to receiving smoking cessation treatment and its benefits. However, research suggests that evidence-based smoking cessation treatment is effective across a wide variety of populations.[5,85,176,359] There is evidence supporting smoking cessation treatment for medically underserved and vulnerable populations, such as individuals with psychotic disorders,[296,330] socioeconomically disadvantaged individuals,[360] and those with substance use disorders.[283] Based on such evidence, the PHS Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*, concluded that evidence-based treatment was effective for men and women, racial and ethnic minority groups, and those who are socioeconomically disadvantaged.[176] In sum, the weight of this evidence strongly supports the provision of evidence-based smoking cessation treatment for all individuals who smoke, regardless of their membership in a medically underserved and vulnerable population (see also chapter 3 for additional supporting evidence).

Although smoking cessation treatments are generally effective for medically underserved and vulnerable populations overall, quit rates achieved could be lower among specific sub-groups. For example, there is evidence that socioeconomically disadvantaged populations and Black or African-American adults tend to have lower quit rates than other smoking populations.[166,171,361] In addition, smoking populations with comorbid substance use disorders could be more prone to relapse after achieving initial smoking cessation than are other smoking populations.[283]

While evidence-based smoking cessation treatments are effective across diverse populations of individuals who smoke, some targeted interventions have been developed for especially vulnerable smoking populations. While some of these have produced promising effects on short-term abstinence (at the end of treatment and at 3 months),[178] at present, experimental evaluations of targeted smoking interventions have not shown that they consistently increase long-term smoking abstinence over and above evidence-based smoking interventions (pharmacotherapy and counseling) shown to be effective in the general population.[227] However, it is possible that targeted interventions could be more attractive to members of some populations and thereby increase treatment reach and engagement. Importantly, to the extent that nontargeted evidence-based smoking cessation treatment is effective in medically underserved and vulnerable populations, it could increase the efficiency, cost-effectiveness, and reach of smoking cessation treatment in such populations.

A notable limitation is that the great majority of studies on smoking cessation treatment in medically underserved and vulnerable populations were conducted in the general population and not in patients with cancer.

Summary

This chapter shows that diverse, medically underserved, and vulnerable populations face both shared and unique challenges that affect the likelihood that such individuals will smoke and have greater difficulty in quitting. For many of these populations, inadequate reach of evidence-based smoking cessation treatment is a major impediment to smoking cessation in cancer care settings. Some evidence suggests that smoking cessation treatment reach could be improved by embracing EHR-based smoking assessment and referral strategies. In addition, medically underserved and vulnerable populations commonly report distrust or concern about how they are perceived or treated by clinicians, and clinicians report a lack of knowledge or training about working with some populations. Efforts to explore each patient's concerns or views regarding their health care could uncover such concerns and allow clinicians to build rapport with these patients. Also, prior research suggests an interest in further training and educational experiences that could allow oncology clinicians to better address such issues.

Each medically underserved and vulnerable population experiences multiple factors at the individual, community, institutional or health care system, and societal levels that can serve as obstacles to both treatment access and cessation success. There is considerable overlap of these factors across populations (e.g., high levels of stress, discrimination, lack of access) and individuals in these populations will differ in the extent to which such factors apply to them. Therefore, knowledge about the obstacles facing medically underserved and vulnerable populations with regard to smoking cessation success should not encourage generalizations and broad assumptions about individuals. Rather, such knowledge is intended to raise awareness of the challenges that individuals in these populations could face and underscores the need for focused efforts to engage them in effective smoking cessation treatment. Moreover, this chapter emphasizes that members of every medically underserved and vulnerable population can benefit from evidence-based smoking cessation treatment. This underscores the need to provide smoking cessation treatment to cancer patients from medically underserved and vulnerable populations who smoke, given the strong association between smoking cessation and improved health outcomes for these patients.

Conclusions

1. Medically underserved and vulnerable populations face challenges at the individual, community, health care system, and societal levels that affect the likelihood that individuals will smoke, that they will develop cancer, and/or that they will receive effective smoking cessation treatment.
2. Challenges shared by many medically underserved and vulnerable individuals who smoke, including those with cancer, include poverty, high levels of stress, discrimination, lack of health insurance coverage, competing priorities, inadequate access to health care

and smoking cessation treatment, and frequent exposure to smoking in their social networks and to tobacco industry marketing.

3. Patients with cancer who are also members of medically underserved and vulnerable populations are motivated to quit smoking but some of these groups tend to be less likely to be successful in their attempts to quit smoking than are cancer patients from the general population. More research is needed regarding the effectiveness of smoking cessation treatment among medically underserved and vulnerable groups of cancer patients who smoke and regarding strategies for increasing the reach and cost-effectiveness of such treatment.

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NCI Monograph 23
Treating Smoking in Cancer Patients:
An Essential Component of Cancer Care

Chapter 6
Monograph Conclusions and Future Research Directions

Chapter Contents

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Chapter 6
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Introduction

This monograph provides an up-to-date review of the effects of smoking cessation on cancer outcomes; smoking cessation treatments for patients with cancer who smoke; challenges of and strategies for implementing smoking cessation in cancer care settings; and tobacco use, cancer burden, and smoking cessation among medically underserved and vulnerable populations. The first section of this chapter synthesizes the evidence reviewed in this monograph into eight major conclusions; these are followed by chapter-specific conclusions that provide a more fine-grained summary of the research reviewed for the monograph. Next, the chapter highlights areas where additional research is warranted. Finally, it describes two key National Cancer Institute (NCI) initiatives designed to meet the cessation treatment needs of individuals at high risk of lung cancer, patients with cancer, and cancer survivors who smoke.

Major Conclusions

The eight overall conclusions that emerge from this monograph are:

1. **Smoking cessation after the diagnosis of cancer is highly likely to reduce all-cause mortality and cancer-specific mortality.** Evidence continues to mount that quitting smoking after a cancer diagnosis is causally associated with reduced all-cause mortality and cancer-specific mortality, in comparison with continued smoking. The studies reviewed in this monograph confirm and expand upon findings of the 2014 and 2020 Surgeon General's reports regarding this topic. Laboratory studies provide insight into the mechanisms by which smoking may increase tumor aggressiveness and decrease cancer treatment effectiveness.
2. **Research from the general population indicates that patients with cancer who smoke will benefit from smoking cessation treatments, including both counseling and U.S. Food and Drug Administration (FDA)–approved medications.** Smoking cessation counseling and medication have been shown to be effective in diverse populations of people who smoke. This substantial evidence, including some studies with cancer patients, clearly supports the delivery of evidence-based smoking cessation treatment as an essential component of cancer care.
3. **Effective strategies exist to increase the delivery of smoking cessation treatment in cancer care settings.** Barriers identified by cancer care clinicians include lack of time, lack of specialized training to deliver smoking cessation treatment options, misconceptions about patients' intentions to quit, and difficulties with health insurance reimbursement. Multiple strategies, including use of EHR-based clinical workflow tools, can be adopted to address tobacco use for every patient across the cancer care continuum, including those who are screened for or diagnosed with cancer. These strategies can improve the identification of patients who smoke, the offer of smoking cessation

treatment, and the delivery of or referral for smoking cessation treatment and can do so in a low-burden, efficient manner.

4. **Evidence-based smoking cessation treatment should be systematically provided to all patients with cancer, regardless of the type of cancer. However, patients with cancer are not consistently offered and provided such treatment.** Many national and international cancer organizations recommend addressing smoking among patients with cancer and provide guidance to cancer care clinicians for effectively delivering smoking cessation treatment. However, the implementation of these evidence-based recommendations has been inconsistent and incomplete, highlighting the need to identify and address barriers to providing smoking cessation intervention that exist for both cancer care clinicians and health care systems.
5. **Continued smoking after a cancer diagnosis is associated with higher health care utilization and greater health care costs in comparison with quitting smoking.** Direct non–health care costs, such as transportation and caregiving, may also be increased with continued smoking after a cancer diagnosis. Smoking cessation interventions in patients with cancer are highly likely to be cost-effective.
6. **Medically underserved and vulnerable populations of cancer patients who smoke are very likely to benefit from using the evidence-based smoking cessation treatments identified as effective in the general population of people who smoke.** Medically underserved and vulnerable populations are faced with multiple factors at the individual, community, institutional or health care system, and societal levels that may impede access to smoking cessation treatment and cessation success. Importantly, substantial evidence indicates that medically underserved and vulnerable populations overall (i.e., noncancer populations) benefit from evidence-based smoking cessation treatment, providing evidence that these populations with cancer will benefit as well.
7. **The tobacco product marketplace and consumer use patterns are changing for both the general population and for patients with cancer, posing challenges for researchers and cancer care clinicians.** Research is needed to monitor the use and effects of diverse tobacco products, both conventional and new, by patients with cancer, including their effects on smoking cessation and relapse and their potential deterrence of patients' using evidence-based smoking cessation treatments such as counseling and FDA-approved medications.
8. **Continued research is needed to identify effective cessation interventions for patients with cancer who smoke and to better understand the effects of smoking cessation on cancer outcomes.** Relatively few well-powered randomized controlled trials of smoking cessation treatments in patients with cancer have been conducted. Additional research is needed to identify: the effectiveness of smoking cessation interventions in increasing abstinence among patients with cancer, including which intervention strategies are most effective; the effects of smoking cessation treatment and resulting abstinence on cancer-related outcomes (e.g., all-cause and cancer-specific mortality); and health care system changes and implementation strategies that are especially effective in engaging patients with cancer in evidence-based smoking cessation treatment.

Chapter Summaries and Conclusions

The following section summarizes each chapter within this monograph and presents the chapters' conclusions.

Chapter 1: Introduction and Overview

Chapter 1 introduces the monograph, describes its framework, and explains how it was prepared and organized. The chapter also presents the evidence base regarding smoking and cancer outcomes from the 2014 and 2020 Surgeon General's reports as well as studies conducted since then that have examined the association between quitting smoking and all-cause mortality.

Chapter 2: Smoking in Patients With Cancer: Biological Factors

A strong body of research documents the biological rationales for addressing tobacco use in cancer care. Chapter 2 provides a brief overview of the relationship of smoking to the biological aspects of cancer, including the relationship between cigarette smoke and tumorigenesis, biological characteristics of lung cancers in smokers and never-smokers, and the effects of cigarette smoke exposure on cancer cells.

Conclusions

1. Tobacco smoke contains more than 7,000 chemical compounds including approximately 70 that are carcinogenic. Continued exposure to tobacco smoke after a cancer diagnosis may promote the continued growth and transformation of tumor cells through a variety of mechanisms.
2. Tumors in smokers are often biologically distinct from tumors in nonsmokers. In the case of lung cancer, these differences have important implications for cancer treatment and prognosis.
3. Laboratory studies of cancer cells exposed to tobacco smoke or tobacco smoke constituents provide experimental evidence that continued smoking by patients with cancer increases tumor aggressiveness and reduces therapeutic response.

Chapter 3: Treating Tobacco Use and Dependence in Cancer Populations

This chapter extracts evidence from cancer populations and from the general smoking population literature to identify elements of effective smoking cessation treatments that can be applied to patients across the cancer care continuum who smoke.

Conclusions

1. Despite the heightened risks for adverse cancer-related outcomes due to continued smoking after a cancer diagnosis, too few patients with cancer who smoke are offered evidence-based smoking cessation treatment and too few engage in such treatment.
2. Patients with cancer who smoke generally have strong motivation to quit, and a high percentage make one or more quit attempts during their cancer treatment.

3. Research with the general population of individuals who smoke has identified effective smoking cessation intervention strategies, including counseling, medications, and web-based and short message service (SMS) (text) digital interventions.
4. Although more research on the effectiveness of smoking cessation treatments in cancer populations is needed, the consistent effects of these treatments across diverse populations who smoke suggests that they are likely effective in cancer populations as well. Smoking cessation treatments may benefit from adaptation (e.g., addressing fatalism and depression) to best meet the needs of cancer populations and provide optimal benefit.
5. The combination of cognitive behavioral therapy (CBT) counseling with either nicotine replacement therapy (NRT) or varenicline is an especially effective smoking cessation treatment among the general population of people who smoke. CBT counseling has been shown to be effective in the general population when delivered via several different routes, such as in-person, in groups, and by phone. These treatments are recommended for use with patients who smoke in the Public Health Service (PHS) Clinical Practice Guideline, *Treating Tobacco Use and Dependence: 2008 Update*, and for patients with cancer who smoke in the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology.
6. Patients who have been diagnosed with cancer face significant patient-level barriers to smoking cessation that include competing demands due to their cancer treatment, complications and side effects of cancer treatment, pain, psychological distress, and guilt regarding tobacco use. These barriers should be assessed and addressed in strategies used to offer and deliver smoking cessation treatment to patients with cancer.
7. Clinician-level barriers to providing smoking cessation treatment to patients with cancer include limited time per encounter, clinicians' beliefs that FDA-approved cessation medications are ineffective, and lack of confidence or training in providing smoking cessation treatment.
8. The efficacy of electronic nicotine delivery systems (ENDS) as an aid for smoking cessation for patients with cancer is not established. Additionally, the short- and long-term health effects of ENDS use (alone or in combination with cigarettes) by patients with cancer remain to be determined.
9. Many patients with cancer who try to quit smoking will relapse. Data from the general population suggest that periodic, repeated offers of additional smoking cessation treatment to patients with cancer diagnoses who have relapsed will lead to increased quit attempts and quitting success.

Chapter 4: Implementing Smoking Cessation Treatment Programs in Cancer Care Settings: Challenges, Strategies, Innovations, and Models of Care

Chapter 4 evaluates evidence on health care system strategies that can be used to implement smoking cessation treatment programs in cancer care settings. Strategies are reviewed regarding the reach and effectiveness of treatment, ease of implementation, and maintenance over time. The chapter presents an organizational framework for planning, implementing, and evaluating smoking cessation treatments within oncology health care delivery systems and describes effective models of care, highlighting findings from the NCI Cancer Moonshot[SM]-supported Cancer Center Cessation Initiative (C3I).

Conclusions

1. Challenges to implementing smoking cessation treatment in cancer care settings persist at the patient, clinician, and health care system levels. It is important that these multilevel barriers be understood and addressed so that health care systems can provide cessation treatment equitably and effectively to all patients with cancer who smoke.
2. Successful implementation of smoking cessation treatment in cancer care settings requires health care system changes designed to increase the reach, effectiveness, adoption, implementation, and maintenance (i.e., the RE-AIM framework) of smoking cessation treatment interventions.
3. Effective strategies to improve smoking cessation treatment reach and engagement in oncology care start with the consistent and accurate assessment of tobacco use status for all patients across the cancer care continuum. Assessment of tobacco use for all patients with cancer needs to be empathic and nonjudgmental to reduce patient anxiety, embarrassment, or guilt, and to encourage accurate disclosure of tobacco use status.
4. Clinic-wide opt-out (as opposed to opt-in) smoking cessation treatment engagement strategies show promise as a means of enhancing the reach and delivery of smoking cessation treatments to patients with cancer who smoke.
5. Clinical decision supports, prompts, and order sets embedded in electronic health records (EHRs) can improve the rate of both screening for tobacco use and delivering smoking cessation treatments. Such EHR tools can aid in the delivery of smoking cessation treatment, either as part of the cancer care or via a referral to an internal health care system tobacco treatment specialist or to an external option, such as a state tobacco quitline, state quitline-provided texting program, or the National Cancer Institute's (NCI) SmokefreeTXT.
6. Health care system accreditation guidelines, publicly reported quality metrics, and pay-for-performance programs can encourage health care systems to improve the frequency of tobacco use screening and treatment for all patients who smoke, including those with cancer.
7. Research has identified multiple smoking cessation treatment program models (e.g., smoking cessation treatment delivered during cancer care or via referral to internal or external smoking cessation treatment services) that can be effectively implemented in a variety of cancer clinical settings.
8. Continued smoking after a cancer diagnosis is associated with increased health care costs relative to not smoking. Smoking cessation interventions provided to patients with cancer are highly likely to be cost-effective.
9. The NCI Cancer Center Cessation Initiative (C3I) has developed a variety of implementation strategies to enhance the reach and effectiveness of smoking cessation treatment delivery in NCI-Designated Cancer Centers. These approaches exemplify how smoking cessation treatment strategies can be implemented broadly in cancer care settings.

10. Strategies to reduce system-level barriers to cessation among patients with cancer who smoke include ensuring that evidence-based cessation treatments are provided as a covered benefit by health insurers and other payers, without barriers to access and/or use.

Chapter 5: Addressing Smoking in Medically Underserved and Vulnerable Cancer Populations

Chapter 5 describes the cancer burden, smoking prevalence, and difficulties medically underserved and vulnerable populations face when making a quit attempt. The chapter specifically focuses on racial and ethnic minority populations, socioeconomically disadvantaged populations, sexual and gender minority (SGM) populations, rural populations, individuals with serious mental illness (SMI), and people who use alcohol or other substances.

Conclusions

1. Medically underserved and vulnerable populations face challenges at the individual, community, health care system, and societal levels that affect the likelihood that individuals will smoke, that they will develop cancer, and/or that they will receive effective smoking cessation treatment.
2. Challenges shared by many medically underserved and vulnerable individuals who smoke, including those with cancer, include poverty, high levels of stress, discrimination, lack of health insurance coverage, competing priorities, inadequate access to health care and smoking cessation treatment, and frequent exposure to smoking in their social networks and to tobacco industry marketing.
3. Patients with cancer who are also members of medically underserved and vulnerable populations are motivated to quit smoking but some of these groups tend to be less likely to be successful in their attempts to quit smoking than are cancer patients from the general population. More research is needed regarding the effectiveness of smoking cessation treatment among medically underserved and vulnerable groups of cancer patients who smoke and regarding strategies for increasing the reach and cost-effectiveness of such treatment.

Future Research Directions

This monograph has emphasized the importance of clinicians and oncology health care systems delivering smoking cessation treatment to all patients with cancer who smoke. However, key research questions remain regarding identifying, implementing, and maintaining effective smoking cessation treatments across cancer care settings; and prompting oncologists and other cancer care clinic staff to use these treatments. While not exhaustive, the research questions identified in this monograph are presented thematically below and summarized in Table 6.1.

Table 6.1 Summary of Research Needs

Topic	Specific Needs for Further Study	Monograph Chapter(s) With Related Content
Clarifying the effects of continued smoking and smoking cessation treatment on cancer outcomes	• Effects of smoking cessation on cancer site–specific and treatment-specific health outcomes • Data collection on smoking status after a cancer diagnosis and tracking smoking status longitudinally through survivorship • Effects of smoking cessation on outcomes other than all-cause mortality • Biological differences between smoking-related tumors based on how exposure to cigarette smoke is received	Chapter 2
Assessing the economic effects of continued smoking and cessation after a cancer diagnosis	• Cost-effectiveness studies specific to cancer populations • Studies of smoking-attributable mortality in patients with cancer to improve the validity of parameters used in economic models • Economic studies to better understand the value of evidence-based smoking cessation programs in cancer care settings • The impact of continued smoking on the economic burden of cancer from the patient perspective	Chapter 4
Achieving better tobacco use assessment in cancer care	• Methods that achieve consistent assessment of tobacco use in clinical practice and in cancer treatment clinical trials • Objective measures of tobacco exposure and promotion of standard definitions of current smoking status for cancer patients and survivors to improve tobacco use assessment	Chapter 4
Addressing barriers to the implementation of effective treatment of tobacco use in cancer care	• Well-powered randomized controlled trials that provide additional experimental evidence on the effectiveness of smoking cessation treatments in patients with cancer • Barriers that discourage patient involvement in smoking cessation treatment in cancer care • Identification and tests of acceptable, effective, and scalable strategies to improve implementation of smoking cessation treatment in cancer care settings • Strategies that improve adherence to smoking cessation pharmacotherapy among patients with cancer • System-wide barriers, including payer barriers, that reduce clinician involvement in smoking cessation treatment in cancer settings	Chapters 3 and 4
Understanding the effects of new tobacco products and other drug use in patients with cancer	• Whether use of electronic nicotine delivery systems (ENDS) or other new tobacco products poses unique risks to patients with cancer and affects the success of their cancer treatment • Whether the use of ENDS has an impact on the motivation of patients with cancer to use U.S. Food and Drug Administration (FDA)–approved smoking cessation medications and/or cessation counseling • Expansion of current assessment measures to include other tobacco products • Evaluation of the effectiveness of evidence-based smoking cessation treatments for cancer patients and survivors who engage in dual and co-occurring substance use • Characterization of patterns of cannabis use among patients with cancer and the health effects of such use, and studies to guide the clinical management of patients with cancer who smoke and also use cannabis products	Chapter 3

Table 6.1 (continued)

Topic	Specific Needs for Further Study	Monograph Chapter(s) With Related Content
Optimizing smoking cessation treatment for medically underserved and vulnerable populations with cancer	• Methods to enhance the reach and engagement of smoking cessation treatment for such populations in cancer care settings • Effects of training cancer care clinicians in social and cultural competencies on the reach and effectiveness of smoking cessation treatment • Factors that discourage smoking cessation treatment participation in these populations and evaluation of strategies that address such barriers • Facilitators of quitting success among patients with cancer with different types of psychiatric disorders	Chapter 5

Clarifying the Effects of Continued Smoking and Smoking Cessation Treatment on Cancer Outcomes

Studies included in this monograph advance the understanding of the effects of smoking on cancer patient outcomes. Evidence suggests that smoking increases tumor aggressiveness and decreases cancer treatment effectiveness for therapies such as radiotherapy and chemotherapy. The monograph also adds to evidence that smoking cessation after a diagnosis of cancer is highly likely to improve overall mortality. However, additional research is needed on the effects of smoking cessation on cancer site–specific and treatment-specific health outcomes. Relatively few studies on outcomes of cancer treatment have collected data on smoking status after a cancer diagnosis or tracked smoking status longitudinally, and there is a dearth of research on the effects of smoking cessation on outcomes other than all-cause mortality. Similarly, more research is needed to understand whether there are biological differences between smoking-related tumors based on whether they receive exposure to cigarette smoke directly, through the circulatory system, or a combination of both. Much of the research to date has also focused on earlier stages of cancer, and it is important to understand how cessation versus continued smoking affect advanced stages of cancer. Such research would yield more informative data on the relationship between smoking cessation and improved outcomes among patients with cancer.

Assessing the Economic Effects of Continued Smoking and Cessation After a Cancer Diagnosis

Similarly, as detailed in chapter 4, further research on the economic effects of continued smoking and cessation after a cancer diagnosis would be useful. As part of such analyses, additional information is needed on smoking-attributable mortality in patients with cancer to improve the validity of the parameters used in economic models. Although a few modeling studies provide estimates of the impact of continued smoking by patients with cancer, more studies are needed to assess the economic effects of smoking cessation among patients with cancer. Further, it is vital to conduct economic evaluations to better understand the value of evidence-based smoking cessation programs. Cost-effectiveness studies in the general smoking population may not provide accurate cost-effectiveness and cost-benefit data for cancer populations. Patients with cancer, for instance, may differ from the general population on factors such as higher quit rates in the absence of smoking cessation treatment, greater stress and affective distress, greater relapse rates over time, costs associated with cancer treatment, and the burden of imminent and taxing medical treatment. Any of these factors might affect smoking cessation treatment success or the costs and cost-effectiveness associated with it.

More studies are also needed to evaluate the effects of different types and intensities of smoking cessation interventions on outcomes in patients with cancer, including the use of less costly intervention modalities (e.g., technology-based interventions). Additionally, future research should investigate the impact of continued smoking on the economic burden of cancer from the patient perspective.

Achieving Better Tobacco Use Assessment in Cancer Care

Additional research is needed to identify methods that achieve consistent assessment of tobacco use in clinical practice and in cancer treatment clinical trials. Research should also focus on identifying methods to measure smoking, how to implement those methods in clinical settings, and how the accuracy of smoking status assessment in cancer care settings affects the reach of smoking cessation treatment. Assessment should include objective measures of tobacco exposure and standard definitions of current smoking status. A detailed assessment of smoking behavior after a cancer diagnosis should include assessment of recent quitting status, short-term abstinence (e.g., during hospitalization, chemotherapy treatment), relapse, amount smoked, type of tobacco product(s) used, and current smoking status of others within the patient's household. Further, assessing short- and long-term health outcomes is particularly important given the persistent elevation in risk of illnesses caused by smoking (both cancer and noncancer), underscoring the need for continued monitoring of patients once they successfully quit smoking. Researchers may make use of the Cancer Patient Tobacco Use Questionnaire (C-TUQ), developed jointly by NCI and the American Association for Cancer Research.[1]

Addressing Barriers to the Implementation of Effective Treatment of Tobacco Use in Cancer Care

Most research evaluating smoking cessation treatments in patients with cancer has involved small samples or nonrandomized trials. Despite some evidence that indicates that smoking cessation treatment can be effective in patients with cancer, there is a need for well-powered randomized controlled trials that provide additional experimental evidence on the effectiveness of smoking cessation treatments in patients with cancer. Studies that examine the effectiveness of different types of smoking cessation treatments will help clarify those that are especially effective and cost-effective with cancer populations. Studies are also needed to ensure that such cessation treatment strategies are effective with medically underserved and vulnerable populations who constitute a large percentage of the cancer patient population and typically have high smoking rates. Also, while many patients with cancer are motivated to quit using tobacco, many are reluctant to engage in formal treatment. Further exploration of the barriers that discourage patient involvement in smoking cessation treatment in cancer care are warranted.

Further research is needed to identify and test acceptable, effective, and scalable strategies to improve implementation of smoking cessation treatment in cancer care settings. One approach would be to use highly efficient and pragmatic research designs and methods to explore different approaches to smoking cessation treatment delivery in cancer care settings. Also, telehealth and digital strategies may be particularly helpful approaches when travel or time constraints are barriers to patients receiving in-clinic treatment. The ability of digital interventions to enhance the effects of other treatment approaches (i.e., serve as adjuvants or treatment extenders) should also be explored. Similarly, additional research is needed to optimize implementation of eReferral to programs such as NCI's SmokefreeTXT to determine their effects on smoking cessation among patients with cancer. Finally, it is important that researchers explore the role of the entire cancer care clinical team in delivering smoking cessation treatment. For instance, involving the patient's cancer care team can often increase the reach and effectiveness of smoking cessation treatment.

Adherence to smoking cessation pharmacotherapy is a frequent problem among people in the general population who smoke. It may be especially problematic for patients with cancer who smoke given their additional challenges (e.g., cancer treatment side effects, time pressures, distraction by cancer treatment needs). Research on strategies that improve adherence to smoking cessation pharmacotherapy among patients with cancer would address an important impediment to greater smoking cessation success in this population. Additionally, research on effective strategies to prompt clinicians to prescribe evidence-based smoking cessation pharmacotherapy for all patients with cancer who smoke, including an opt-out provision of cessation medications, is needed. These strategies could build on the foundation of evidence-based referral approaches such as "Ask, Advise, Connect" that can be implemented via EHR enhancements such as eReferral.

While the evidence base is still developing for cancer patient–specific approaches to smoking cessation treatment, a robust evidence base exists for the general population of people who smoke that can guide intervention. While basic cognitive behavioral or skills-based training approaches have been demonstrated to be effective with multiple populations of individuals who smoke, other approaches might be even more effective in the cancer care setting. Patients with cancer may be especially likely to experience feelings of guilt over their smoking, as well as fear and depression resulting from their cancer diagnosis. Interventions such as mindfulness training or cognitive behavioral interventions for negative affect might be helpful adjuvants to smoking cessation treatment.

The considerable research reviewed in chapter 4 has identified health care system changes that can significantly enhance smoking assessment, as well as patient engagement and cessation treatment success in cancer care settings. Further research is needed to explore how such approaches can be used to improve implementation of smoking cessation treatment in the cancer care context. Specific issues pertaining to cancer populations include: 1) how to best use the EHR to enhance tobacco use assessment, treatment engagement, and treatment success; 2) what implementation strategies result in high and sustained levels of tobacco intervention engagement and cessation success; and 3) how different intervention models such as point-of-service clinician approaches can be integrated with models that refer patients with cancer who smoke to an internal or external treatment program, with the goal of enhancing treatment engagement and cessation success.

Understanding the system-wide barriers that reduce clinician involvement in smoking cessation treatment in cancer care settings is an important first step toward addressing such barriers. For example, additional implementation studies on sustainable funding approaches for smoking cessation treatment under various reimbursement models may shed light on the most feasible options.

Understanding the Effects of New Tobacco Products and Other Drug Use in Patients With Cancer

The tobacco product landscape is expected to continue to change over time, and it is anticipated that new products will enter the marketplace. Researchers and clinicians alike need to be vigilant and nimble regarding the impact of changing tobacco product use patterns in cancer populations. For example, most patients with cancer and those with a cancer history who use ENDS report doing so to help them quit smoking and because they perceive them to be safer than cigarettes (similar to people without a cancer diagnosis). The short- and long-term health effects of ENDS and other new tobacco products (such as heated tobacco products) for patients with cancer is an important understudied topic. More research is warranted to determine whether use of ENDS or other new tobacco products poses unique risks to patients with cancer and affects the success of their cancer treatment. Research findings on the risks and potential benefits of ENDS and other new tobacco product use can inform communication between clinicians and patients.

It is also important to determine whether the use of ENDS has an impact on the motivation of patients with cancer to use FDA-approved smoking cessation medications and/or cessation counseling. This research could help shed light as to whether ENDS or ENDS marketing strategies negatively influence the uptake and successful use of safe and effective evidence-based smoking cessation treatments.

Although cigarette smoking remains the predominant form of tobacco use among cancer patients and survivors, cigarettes may be used in conjunction with other tobacco products, as well as with alcohol and other drugs. Polytobacco use, defined as the use of multiple tobacco products, is common,[2] highlighting the need to evaluate such use among cancer patients and survivors. Specifically, two areas for future research include the following: 1) expanding current assessment measures to include other tobacco products (e.g., ENDS, heated tobacco products, cigars, little cigars and cigarillos, smokeless tobacco, dissolvable tobacco, waterpipes) as well as alcohol and other drug use; and 2) evaluating the effectiveness of evidence-based smoking cessation treatments for cancer patients and survivors who engage in dual and co-occurring substance use.

As briefly discussed in chapter 5, the use of cannabis may affect smoking cessation among patients with cancer who smoke. There is limited research evidence regarding cannabis use among patients with cancer who smoke. Research is urgently needed that characterizes patterns of cannabis use among patients with cancer and the health effects of use, including the potential to interfere with smoking cessation treatment. Research is also needed to guide the clinical management of patients with cancer who smoke cigarettes and use cannabis products, including counseling patients on the efficacy and harms of cannabis for symptom management.

Optimizing Smoking Cessation Treatment for Medically Underserved and Vulnerable Populations With Cancer

Chapter 5 concludes that certain sociodemographic groups suffer disproportionately from smoking-related cancers, are especially unlikely to receive evidence-based smoking cessation treatment, and experience high levels of stress and other challenges that can reduce smoking cessation success. Research is needed to explore methods to enhance the reach and engagement of smoking cessation treatment for such populations in the cancer care context and to increase their success in quitting. Innovative methods are needed to inform these populations about the effects of continued tobacco use on their cancer and to increase their knowledge of the effectiveness and importance of smoking cessation treatment as part of their cancer care. Similarly, randomized controlled trials evaluating evidence-based smoking cessation treatments in rural patients with cancer could identify opportunities to improve cessation treatment reach and effectiveness among this population. Research efforts with medically underserved and vulnerable populations may need to consider the following subgroups.

Racial and Ethnic Populations. Far too little is known about the smoking patterns of specific racial and ethnic groups following a cancer diagnosis, or their responses to smoking cessation treatment. It is important to note that researchers' categorization of racial and ethnic groups can vary, sometimes making it difficult to compare smoking prevalence across studies. More research is needed on the use and effects of different smoking cessation treatment approaches with such groups in cancer populations and how such treatment affects cancer recovery and outcomes. Future research should develop multilevel ecological and system-wide models that can help researchers and clinicians understand and intervene to address tobacco-related health disparities, including those among cancer patients and survivors. Appropriate and standardized tobacco product use assessment, such as use of EHR-enabled prompts and surveillance strategies, could be used to enhance the accurate assessment of smoking among cancer patients and survivors from diverse racial and ethnic populations and to monitor their inclusion in smoking cessation treatment programs and clinical trials. Exploration of the effects of training cancer care clinicians in social and cultural competencies on the reach and effectiveness of smoking cessation treatment is also warranted.

Sexual and Gender Minority (SGM) Populations. SGM populations experience poorer health outcomes, including cancer-related outcomes, compared with the general population. At present, there is limited research focused on tobacco use among patients with cancer who identify as SGM. In particular, very little is known about how tobacco use affects cancer and its treatment among transgender people, representing a major gap in the literature. Improved and expanded measures, including EHR tools, to better assess and document sexual orientation and gender identity should be explored as a means of alerting clinicians to SGM status and to help promote the equitable inclusion of all SGM groups in smoking cessation programs. There is a need for increased attention to the smoking cessation treatment needs of SGM patients with cancer, and more robust empirical findings to support health system initiatives aimed at health equity for this population. Additionally, it is important to determine the acceptability and effectiveness of evidence-based smoking cessation treatments in SGM groups.

Childhood and Adolescent and Young Adult (AYA) Cancer Survivors. There is limited research on evidence-based cessation interventions for adult survivors of childhood and AYA cancer. These populations are at substantial risk for delayed effects from their cancer treatment, many of which are exacerbated by tobacco use. Despite the serious risks, smoking is not uncommon among survivors of childhood and AYA cancer, indicating a need to further examine the personal factors as well as the interpersonal, community, and organizational factors that influence their smoking.

Serious Mental Illness (SMI) and Cancer-Related Psychological Distress. Research is needed to better define the prevalence of psychiatric disorders in cancer patients and survivors and the smoking prevalence among cancer populations with psychiatric disorders. It is also vital to determine the reach of smoking cessation treatments in this population and whether such individuals are equitably offered such treatment in cancer care settings. This research need is especially great for those with SMI. Research is also needed to identify the factors that discourage smoking cessation treatment participation in this population and to evaluate strategies that address such barriers. In addition, research to evaluate the facilitators of quitting success in those with different types of psychiatric disorders in the cancer patient population is needed. Psychological distress is very common among patients who have cancer. As noted in chapter 5, the evidence base in this area is dated and could benefit from additional studies.

NCI Initiatives to Support Implementation of Smoking Cessation Treatment in Cancer Care and Screening Settings

As described above, several topics require further research and consideration to improve the identification and delivery of smoking cessation treatment to those at high risk of cancer, patients with cancer, and cancer survivors. To address some of these challenges, NCI established two initiatives to further the implementation of tobacco use assessment and interventions for smoking cessation treatment.

Cancer Center Cessation Initiative (C3I)

As discussed in detail in chapter 4, as part of the Cancer Moonshot^{SM}, NCI launched an effort to promote smoking cessation treatment at NCI-Designated Cancer Centers. The goal of C3I is to ensure that every patient with cancer is asked about their tobacco use status during cancer care and that all patients with cancer who smoke are provided with smoking cessation treatment. Since 2017, 52 NCI-Designated Cancer Centers have received C3I funding. An additional goal of the initiative is to identify and summarize best practices to enhance smoking cessation treatment interventions in cancer care settings that can be shared with cancer treatment facilities across the United States.

Key features of C3I include:

- Funded centers must take a population-based approach; that is, the aim is that every patient with cancer who smokes and presents to the cancer center will be identified, urged to quit, offered evidence-based tobacco treatment, and tracked in terms of treatment outcomes.
- Centers must take a systems-based approach, integrating evidence-based tobacco treatment into cancer care workflows and utilizing EHR technology to facilitate that integration.
- Centers are required to address program sustainability; that is, have a plan that sustains the program after NCI funding ends.

A key component of C3I is identifying strategies to effectively implement tobacco cessation treatment in cancer care settings. Each funded cancer center was provided with the flexibility to establish its own approach to tobacco treatment, thus creating an opportunity to determine how a variety of intervention models can affect smoking interventions in cancer care settings.[3]

Smoking Cessation at Lung Examination (SCALE) Collaboration

Integrating smoking cessation treatment across the cancer care continuum entails integrating such interventions into lung cancer screening settings. The lung cancer screening setting differs from traditional smoking cessation treatment settings in multiple ways. For example, patients who smoke and present for lung cancer screening are typically older with a longer history of tobacco use than tobacco users in the general population. Many are not seeking or expecting smoking cessation treatment intervention efforts as part of their screening. The screening context presents the opportunity to tailor treatment based on screening results. Studies should pursue this opportunity, capitalizing on the teachable moment framework (see chapter 4), but with attention to potential unintended consequences of a negative screening test. Efforts should also focus on reducing the possibility of relapse among former smokers who receive normal screening results; proactive efforts to curtail relapse will likely enhance the individual and population health benefits of lung cancer screening.

The expanded U.S. Preventive Services Task Force (USPSTF) low-dose computed tomography (LDCT) lung cancer screening recommendations[4] increased the number of screening-eligible patients, which may accelerate screening and lead to earlier identification of some lung cancers and lower mortality rates. Many of the eligible patients are current or former smokers at risk of relapse and will need continuing treatment over time.

In response to these needs, NCI has funded seven trials of smoking cessation treatment for people undergoing LDCT lung cancer screening. The investigators of these trials form the SCALE Collaboration, created to support the sharing of methods and data to facilitate cross-project research on lung cancer screening and cessation outcomes. SCALE collaborators also share best practices for measuring feasibility, cost, and other implementation outcomes. Collaborators work together to disseminate the results of their findings and related resources.[5]

Conclusion

Tobacco use remains prevalent among patients across the cancer care continuum. Importantly, patients with cancer who smoke can experience multiple benefits of quitting, regardless of the severity of disease or time since diagnosis. Quitting smoking improves the likelihood of survival, quality of life, and overall health of people with cancer, highlighting the importance of identifying tobacco use status and providing smoking cessation treatment to every patient with cancer who smokes. Many cancer patients and survivors, as well as their clinicians, underestimate the risks of continued smoking after a cancer diagnosis. Clinicians and cancer care teams can play an important role in assessing tobacco use and providing evidence-based smoking cessation treatment to their patients who smoke as a means of improving their health outcomes.

More research is needed to determine how to better assess and intervene with individuals who smoke across the cancer care continuum. Additional research is also needed to evaluate whether smoking cessation treatments documented as effective in the general population are also effective in patients with cancer. Addressing the research gaps described in this chapter will contribute to improving the treatment of tobacco use among cancer patients and survivors. This monograph describes multiple evidence-based smoking cessation treatment interventions that have been shown to be highly effective across a range of populations and settings. The monograph provides strategies to overcome patient-, clinician-, and systems-level challenges to implement smoking cessation treatment efficiently, equitably, and sustainably in cancer care settings. Providing patients with cancer who smoke with smoking cessation treatment holds great promise to improve both the length and quality of their lives.

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