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

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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[SM]–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.
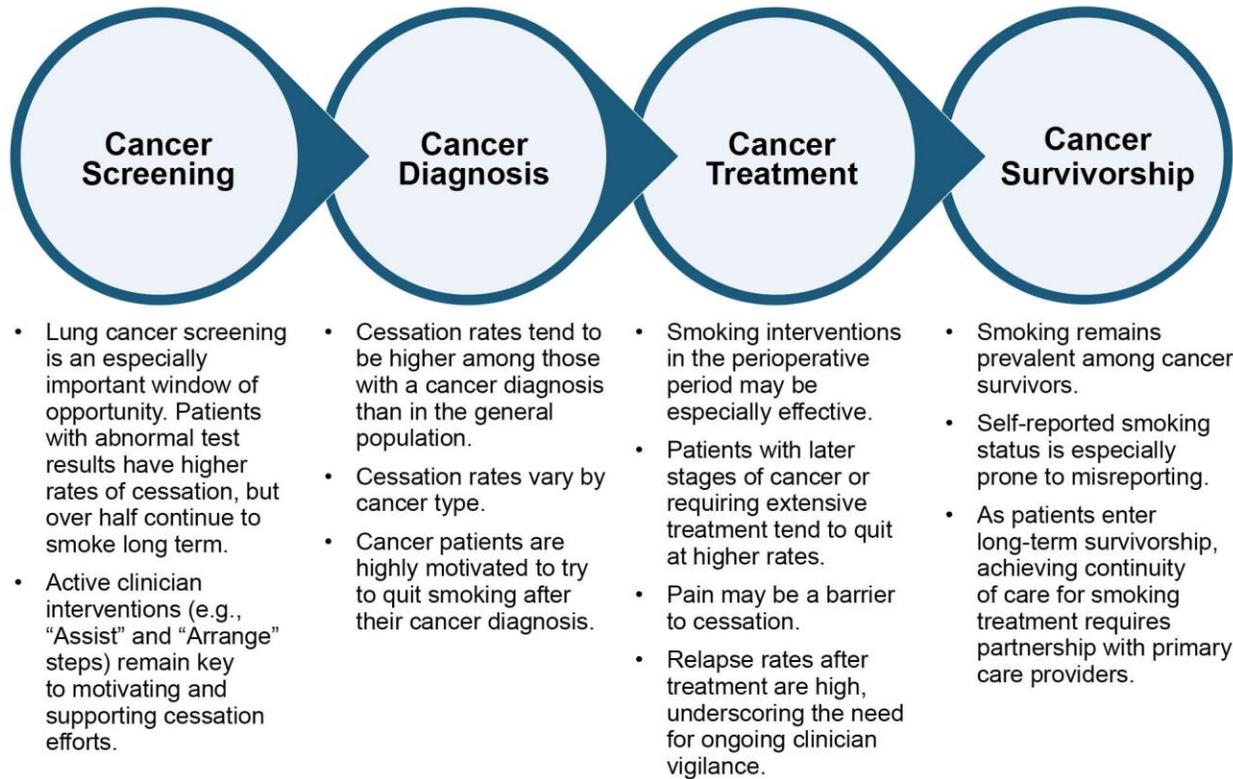
Addressing Smoking Cessation in Cancer Care Settings

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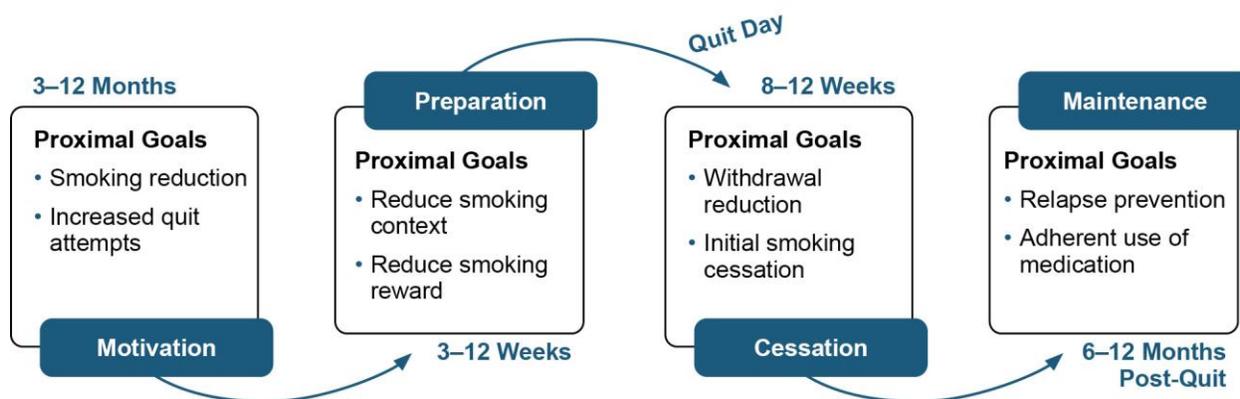
Note: Phases of smoking treatment, commonly used durations, and examples of their proximal goals. The durations of any of the phases of treatment can vary.

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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