NIH NATIONAL CANCER INSTITUTE

NCI TOBACCO CONTROL MONOGRAPH SERIES

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

Cessation Strategie

Medications Counse

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

About the National Cancer Institute 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.

Citation

To cite this monograph in other works, please use the following format:

U.S. National Cancer Institute. *Treating Smoking in Cancer Patients: An Essential Component of Cancer Care.* National Cancer Institute Tobacco Control Monograph 23. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute; 2022.

Contents

About the National Cancer Institute Monograph Series	ii
Foreword	xi
Acknowledgments	xiii
Table of Abbreviations and Acronyms	XX
Glossary	xxi

Chapter 1. Introduction and Overview

Introduction	3
Smoking Among Cancer Patients and Survivors	4
The Consequences of Continued Smoking After a Cancer Diagnosis	5
Addressing Smoking Cessation in Cancer Care Settings	6
Purpose of the Monograph	16
Preparation of the Monograph	18
Key Terminology and Concepts	18
The Multiple Phases of Smoking Cessation Treatment	19
Major Conclusions	21
References	24

Chapter 2. Smoking in Patients with Cancer: Biological Factors

Introduction	31
Tobacco Smoke and Tumorigenesis	32
Chemical Composition of Tobacco Smoke	32
Tobacco Smoke: DNA Damage	33
Tobacco Smoke: Mutational Burden	34
Tobacco Smoke: Mutational Signatures	34
Tobacco Smoke: Cancer Driver Genes	35
Tobacco Smoke: Epigenetic Changes	35
Biological Characteristics of Lung Cancers in Smokers and Never-Smokers	35
Lung Cancer: Driver Genes	36
Lung Cancer: Mutational Burden	36
Lung Cancer: Epigenetic Modifications	37
Lung Cancer: Variation in Gene Expression	37
Therapeutic Implications of Molecular Differences in Lung Cancers	38
The Effects of Tobacco Smoke Exposure on Cancer Cells	38
DNA Damage	39
Changes in Gene Expression	39
Alteration of Cell Cycle Control	39
Promotion of Epithelial-Mesenchymal Transition Associated With Metastasis	39
Promotion of Angiogenesis	40
Alterations Within the Tumor Microenvironment	40
Promotion of Stem Cell-Like Properties	40
Inhibition of Response to Chemotherapeutic Agents	40
Summary,,	,,, 41

Conclusions	41
References	42
Chapter 3. Treating Tobacco Use and Dependence in Cancer Populations	
Introduction	54
Motivation to Quit	55
Elements of Effective Smoking Cessation Treatments	56
Neurobiological and Behavioral-Motivational Dimensions of Cigarette Smoking:	
Relevance to Treatment	57
Neurobiological Dimensions of Cigarette Smoking	57
Behavioral-Motivational Dimensions of Cigarette Smoking	58
Summary: Neurobiological and Behavioral-Motivational Dimensions of Cigarette	
Smoking	58
Smoking Cessation Treatments in the General Population	59
Approach	59
Medications for Smoking Cessation	59
Behavioral Interventions for Smoking Cessation	65
Beyond In-Person Counseling: Telephone, Telehealth, and Digital Approaches for	
Smoking Cessation	72
Smoking Cessation Treatments Among Patients With Cancer	79
Medications for Smoking Cessation Among Patients With Cancer	80
Behavioral Interventions for Smoking Cessation Among Patients With Cancer	85
Relapse Prevention and Chronic Care for Cancer Populations	91
Special Considerations and Barriers Concerning Smoking Cessation Treatment in Cancer	
Care Settings	92
Patient-Level Barriers to Treating Tobacco Use in Cancer Care Settings	92
Psychiatric Comorbidity	92
Oncology Treatment–Related Challenges	93
Physical Concerns	94
Psychological Aspects	94
Treatment Engagement and Adherence	04

Treatment Engagement and Adherence	
Clinician-Level Barriers to Treating Tobacco Use in Cancer Care Settings	
Leveraging the Opportunity for Intervention	
Barriers to Intervention and Strategies to Overcome Them96	
Changing Clinician Approaches to Smoking Cessation Treatment97	
Systems-Level Barriers to Treating Tobacco Use in Cancer Care Settings	
Summary: Special Considerations and Barriers Concerning Smoking Cessation	
Treatment in Cancer Care Settings	
Special Topics in the Treatment of Smoking in Patients With Cancer	
Addressing Motivation to Quit	
Relevance of Pharmacogenetic Intervention: Steps Toward Personalized Medicine	
Treatment Effectiveness and Access Across Different Populations101	
The Use of Electronic Nicotine Delivery Systems (ENDS) in Patients With Cancer101	
Prevalence of ENDS Use	
Health Effects of ENDS102	

ENDS Use and Cessation From Cigarettes in the General Population	103
Randomized Controlled Trials	104
ENDS Use and Cessation From Cigarettes in Cancer Populations	106
Published Guidelines on ENDS Use Among Patients With Cancer	107
Summary: The Use of ENDS in Patients With Cancer	107
Summary	108
Conclusions	109
References	110

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	139
Introduction	139
Application of the Reach, Effectiveness, Adoption, Implementation, Maintenance (RE-	
AIM) Evaluation Framework	142
Reach	143
Enhancing Reach via Leveraging the Electronic Health Record (EHR)	143
Enhancing Reach via Use of Clinical Referral Models Including "Ask, Advise,	
Refer" (AAR) and "Ask, Advise, Connect" (AAC)	145
Treatment Extender: State Quitlines	145
Treatment Extenders: National Cancer Institute's (NCI) SmokefreeTXT	150
Utilizing Interactive Voice Response (IVR) Systems	150
Opt-Out Versus Opt-In Models of Smoking Cessation Treatment Delivery	151
Using Telehealth	152
Summary: Reach	152
Effectiveness	153
Summary: Effectiveness	154
Adoption	154
Payment Models, Quality Metrics, and Regulation	155
Legislative Action	158
Summary: Adoption	159
Implementation	160
Summary: Implementation	160
Maintenance	160
Secure Support From Health Care System Leadership	161
Integrate Tobacco Screening and Treatment Strategies Into Clinical Workflows	161
Leverage EHRs	162
Leveraging Tobacco-Relevant Quality Metrics, Payment Models, and Regulatory	
Policies	162
Summary: Maintenance	162
Assessing and Verifying Tobacco Use Status	163
Challenges to Implementing Smoking Cessation Treatment in Cancer Care Settings at the	
Patient, Clinician, and Health Care System Levels	165
Patient-Level Barriers to Delivering Smoking Cessation Treatment in Cancer Care	
Settings	167

Sociodemographic Differences in Smoking Rates	167
Knowledge of Risks of Smoking and Benefits of Quitting	168
Motivation and Confidence to Quit	169
Psychological Distress	169
Coping	170
Summary: Patient-Level Barriers	170
Clinician-Level Barriers to Delivering Smoking Cessation Treatment in Cancer Care	
Settings	170
Lack of Smoking Cessation Knowledge and Training	170
Clinician Perceptions of Patients With Cancer	172
Summary: Clinician-Level Barriers	174
Health Care System–Level Barriers to Delivering Smoking Cessation Treatment in	
Cancer Care Settings	174
Institutional Commitment and Accountability	174
Limitations of Clinician Time and Referral Options	175
Funding and Reimbursement for Smoking Cessation Treatment Programs	176
Summary: Health Care System–Level Barriers	177
A Systems Approach to Providing Smoking Cessation Treatment Across the Cancer Care	
Continuum	177
Smoking Cessation Treatment at Cancer Screening	178
Eligibility, Guidelines, and Policy for Lung Cancer Screening (LCS)	179
Impact of LCS on Smoking	179
Enhancing Smoking Cessation Treatment Reach and Effectiveness in the Context of	
LCS	179
Cancer Diagnosis	
Cancer Treatment	
Smoking Cessation Treatment for Patients With Advanced Cancer	
Post-Treatment and Long-Term Survivorship	
Summary: Cessation Across the Cancer Care Continuum	
The Economic Rationale for Implementing Smoking Cessation Treatment in Cancer Care	184
Incremental Costs Associated With a Smoking History Among Patients With Cancer.	
Cost-Effectiveness of Smoking Cessation Treatment for Individuals With Cancer	
Cost-Effectiveness of Smoking Cessation Treatment in the Context of LCS	187
Summary: Economic Outcomes Related to Smoking in Patients With Cancer	
Disseminating and Implementing Tobacco Cessation Treatment in Cancer Care Settings:	
The NCI Cancer Center Cessation Initiative (C3I)	188
Models of Tobacco Cessation Treatment Employed by C3L Sites	191
Point-of-Care Treatment Models	193
Internal Referral Treatment Models	193
External Referral Treatment Models	193
Lessons Learned From Implementation of C31	194
Summary	196
Conclusions	197
References	108

Appendix A. C3I Grantee Publications	214
Appendix B. Biochemical Confirmation Reasons and Methods: Evidence Based on the	
Society for Research on Nicotine and Tobacco (SRNT) Working Group on Biochemical	
Verification	220

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

Introduction	226
The Socioecological Model	227
Combinatorial Effects on Vulnerabilities	228
Stigma in Medically Underserved and Vulnerable Populations	228
Prevalence and Trends in Smoking: Relevance to Medically Underserved and	
Vulnerable Populations With Cancer	229
Heterogeneity Among Medically Underserved and Vulnerable Populations	232
Cancer Burden	232
Factors Associated With Cancer Burden	234
Summary: Cancer Burden	234
Smoking Cessation Treatment for Medically Underserved and Vulnerable Populations in	
the Clinical Cancer Care Context	234
Smoking Among Socioeconomically Disadvantaged Populations With Cancer	234
Epidemiology	234
Smoking Cessation	235
Barriers to Smoking Cessation	235
Summary: Smoking Among Socioeconomically Disadvantaged Populations With	
Cancer	236
Smoking Among Racial and Ethnic Minority Populations With Cancer	236
Epidemiology	236
Smoking Cessation	238
Barriers to Smoking Cessation	240
Summary: Smoking Among Racial and Ethnic Minority Populations With Cancer	242
Smoking Among Rural Populations With Cancer	242
Epidemiology	242
Smoking Cessation	242
Barriers to Smoking Cessation	243
Summary: Smoking Among Rural Populations with Cancer	244
Smoking Among Sexual and Gender Minority (SGM) Populations with Cancer	244
Epidemiology	244
Smoking Cessation	245
Barriers to Smoking Cessation	246
Summary: Smoking Among SGM Populations With Cancer	247
Smoking Among People With Co-Occurring Substance Use Disorders and Cancer	247
Epidemiology	248
Smoking Cessation	252
Barriers to Smoking Cessation	253
Summary: Smoking Among People With Co-Occurring Substance Use Disorders	
and Cancer	254

Smoking Among Individuals With Serious Mental Illness (SMI) and Cancer	255
Epidemiology	255
Smoking Cessation	255
Barriers to Smoking Cessation	257
Summary: Smoking Among Individuals With SMI and Cancer	258
Effectiveness of Smoking Cessation Treatment	
Summary	
Conclusions	
References	

Chapter 6. Monograph Conclusions and Future Research Directions

Introduction	287
Major Conclusions	287
Chapter Summaries and Conclusions	289
Chapter 1: Introduction and Overview	289
Chapter 2: Smoking in Patients With Cancer: Biological Factors	289
Conclusions	289
Chapter 3: Treating Tobacco Use and Dependence in Cancer Populations	289
Conclusions	289
Chapter 4: Implementing Smoking Cessation Treatment Programs in Cancer Care	
Settings: Challenges, Strategies, Innovations, and Models of Care	290
Conclusions	291
Chapter 5: Addressing Smoking in Medically Underserved and Vulnerable Cancer	
Populations	292
Conclusions	292
Future Research Directions	292
Clarifying the Effects of Continued Smoking and Smoking Cessation Treatment on	
Cancer Outcomes	294
Assessing the Economic Effects of Continued Smoking and Cessation After a Cancer	
Diagnosis	294
Achieving Better Tobacco Use Assessment in Cancer Care	295
Addressing Barriers to the Implementation of Effective Treatment of Tobacco Use in	
Cancer Care	295
Understanding the Effects of New Tobacco Products and Other Drug Use in Patients	
With Cancer	297
Optimizing Smoking Cessation Treatment for Medically Underserved and Vulnerable	
Populations With Cancer	297
NCI Initiatives to Support Implementation of Smoking Cessation Treatment in Cancer	
Care and Screening Settings	299
Cancer Center Cessation Initiative (C3I)	299
Smoking Cessation at Lung Examination (SCALE) Collaboration	
Conclusion	
References	302

Figures and Tables

Figures

Figure 1.1 Figure 1.2	Opportunities for Smoking Intervention Across the Cancer Care Continuum Phases of Smoking Treatment	7 20
Figure 2.1	Major Pathways of Cancer Causation by Cigarette Smoking	33
Figure 3.1 Figure 3.2	Smokefree.gov Initiative Digital Interventions Examples of Patient-, Clinician-, and Systems-Level Barriers to the Use of Smoking Cessation Treatment in Cancer Care Settings	75 92
Figure 4.1	Typical EHR-Guided Staff Workflow for eReferral of a Patient who Smokes From a Clinical Setting to a State Quitline or SmokefreeTXT	147
Figure 4.2 Figure 4.3	Joint Commission Tobacco Cessation Measures Smoking Cessation Treatment Across the Cancer Care Continuum, From Screening to Long-Term Survivorship	.157
Figure 4.4	National Cancer Institute (NCI) Cancer Center Cessation Initiative (C3I) Sites	
Figure 4.5	Elements of Exemplar Tobacco Cessation Treatment Programs: Three Models Used Successfully in Cancer Care Settings	192
Figure 4.6	Methods Used by Cancer Center Cessation Initiative (C3I) Sites to Track Program Reach and Effectiveness	.196
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	249
Tables		
Table 1.1 Table 1.2 Table 1.3	Current and Former Smoking Among Adult Cancer Survivors, 2020 Findings From the 2014 and 2020 Surgeon General's Reports Studies That Compare All-Cause Mortality in Patients Who Quit Smoking After a Cancer Diagnosis With Patients Who Continued After Diagnosis (2017–2021)	4 8
Table 1.4	Summary of Recommendations for Addressing Tobacco Use Among Cancer Patients	13
Table 1.5	Monograph Terminology	18
Table 2.1	Key Characteristics of Carcinogens	32
Table 3.1	Findings Regarding Interventions for Smoking Cessation and Treatments for Nicotine Dependence From the 2020 Surgeon General's Report on Smoking Cessation	57
Table 3.2	Effectiveness and Abstinence Rates for Various Medications and Medication Combinations Compared to Placebo at 6-Months Post-guit	
Table 3.3	Odds of Smoking Cessation Using Medications	65

Table 3.4	Odds of Smoking Cessation Using Behavioral Interventions	66
Table 3.5	Elements of Brief Tobacco-Cessation Counseling Based on the PHS Clinical	
	Practice Guideline, Treating Tobacco Use and Dependence: 2008 Update	67
Table 3.6	Studies of Smoking Cessation Interventions Among Patients With Cancer	82
Table 4.1	Selected Guidelines and Recommendations from Clinical and Research	
	Organizations for Addressing Tobacco Use in Cancer Care Settings	140
Table 4.2	Consensus Assessment Instrument for Tobacco Use in Oncology (C-TUQ,	
	Selected Items)	163
Table 4.3	Challenges to Implementing Smoking Cessation Treatment in Cancer Care	
	Settings at the Patient, Clinician, and Health Care System Levels	165
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	181
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	230
Table 5.2	Substance Use Disorders Among U.S. Adults Aged 18 and Older With and	
	Without a Past-Year Cancer Diagnosis, 2015–2018	250
Table 6.1	Summary of Research Needs	293

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 MoonshotSM, 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.

Robert T. Croyle, Ph.D. Former Director Division of Cancer Control and Population Sciences National Cancer Institute

Acknowledgments

Scientific Editorial Committee (SEC)

Chairs

Timothy Baker, Ph.D.

Director of Research University of Wisconsin Center for Tobacco Research and Intervention University of Wisconsin-Madison Madison, Wisconsin

Michael Fiore, M.D., M.P.H., M.B.A.

Director University of Wisconsin Center for Tobacco Research and Intervention University of Wisconsin-Madison Madison, Wisconsin

Gordon Willis, Ph.D.

Program Director Tobacco Control Research Branch Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Members

Monica Webb Hooper, Ph.D.

Deputy Director National Institute on Minority Health and Health Disparities National Institutes of Health Bethesda, Maryland

Anne Joseph, M.D., M.P.H.

Wexler Professor of Medicine Division of General Internal Medicine Department of Medicine University of Minnesota Medical School Minneapolis, Minnesota

Managing Editor

Kristen Mangold, M.S.W. Public Health Advisor

Tobacco Control Research Branch Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Chapter Leads

Lisa A. Peterson, Ph.D.

Professor, Division of Environmental Health Sciences
Program Co-Leader, Carcinogenesis and Chemoprevention, Masonic Cancer Center
School of Public Health
University of Minnesota
Minneapolis, Minnesota

Robert A. Schnoll, Ph.D.

Director, Center for Interdisciplinary Research on Nicotine Addiction, Department of Psychiatry, Perelman School of Medicine
Professor, Department of Psychiatry, Perelman School of Medicine
Associate Director for Population Science, Abramson Cancer Center
Senior Fellow, Center for Public Health Initiatives
University of Pennsylvania
Philadelphia, Pennsylvania

Vani N. Simmons, Ph.D.

Co-Director, Tobacco Research and Intervention Program Senior Member, Department of Health Outcomes and Behavior Moffitt Cancer Center Tampa, Florida

Hilary A. Tindle, M.D., M.P.H.

Associate Professor of Medicine, School of Medicine and Vanderbilt Ingram Cancer Center William Anderson Spickard Jr., M.D., Chair in Medicine Founding Director of ViTAL, the Vanderbilt Center for Tobacco, Addiction and Lifestyle Vanderbilt University Nashville, Tennessee

Graham Warren, M.D., Ph.D.

Professor and Mary M. Gilbreth Endowed Chair of Clinical Oncology
Vice Chairman for Research in Radiation Oncology
Department of Radiation Oncology
Department of Cell and Molecular Pharmacology and Experimental Therapeutics
Hollings Cancer Center
Medical University of South Carolina
Charleston, South Carolina

Contributors

Rob Adsit, M.Ed.

Director of Education and Outreach Center for Tobacco Research and Intervention School of Medicine and Public Health University of Wisconsin-Madison Madison, Wisconsin

Steven L. Bernstein, M.D.

Chief Research Officer Dartmouth-Hitchcock Medical Center Senior Associate Dean for Clinical and Translational Research Geisel School of Medicine at Dartmouth Director, C. Everett Koop Institute Professor of Emergency Medicine Lebanon, New Hampshire

Paul M. Cinciripini, Ph.D.

Professor and Chair, Department of Behavioral Science Division of Cancer Prevention and Population Sciences University of Texas MD Anderson Cancer Center Houston, Texas

Heather D'Angelo, Ph.D., M.H.S.

Program Director Health Communication and Informatics Research Branch Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Nicole Senft Everson, Ph.D.

Program Director Health Communication and Informatics Research Branch Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Michael T. Halpern, M.D., Ph.D., M.P.H.

Medical Officer Healthcare Assessment Research Branch Healthcare Delivery Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Brian L. Hitsman, Ph.D.

Associate Professor of Preventive Medicine Feinberg School of Medicine Northwestern University Chicago, Illinois

Frank T. Leone, M.D., M.S.

Professor, Medicine Director, Comprehensive Smoking Treatment Programs University of Pennsylvania, Perelman School of Medicine Philadelphia, Pennsylvania

Margaret Mayer, Ph.D., M.P.H.

Program Director Tobacco Control Research Branch Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

LaTrice Montgomery, Ph.D.

Research Associate Professor Psychiatry and Behavioral Neuroscience University of Cincinnati, College of Medicine Cincinnati, Ohio

Mark Parascandola, Ph.D., M.P.H.

Chief, Research and Training Branch Center for Global Health National Cancer Institute National Institutes of Health Bethesda, Maryland

Jamie S. Ostroff, Ph.D.

Chief, Behavioral Sciences Service and Vice Chair of Research
Department of Psychiatry and Behavioral Sciences
Memorial Sloan Kettering Cancer Center
Professor of Population Health Sciences
Weill Medical College of Cornell University
New York, New York

Ramzi G. Salloum, Ph.D.

Associate Professor, Health Outcomes and Biomedical Informatics, College of Medicine University of Florida Gainesville, Florida

Christine E. Sheffer, Ph.D.

Professor of Oncology, Department of Health Behavior Roswell Park Comprehensive Cancer Institute Buffalo, New York

Jamie L. Studts, Ph.D.

Professor Division of Medical Oncology Department of Medicine University of Colorado School of Medicine Co-Leader of Cancer Prevention and Control University of Colorado Cancer Center Aurora, Colorado

Reviewers

Brian S. Armour, Ph.D.

Associate Director for Science Office on Smoking and Health Centers for Disease Control and Prevention Atlanta, Georgia

Julia T. Arnold, Ph.D., M.S.

Program Director Translational Research Program Division of Cancer Treatment and Diagnosis National Cancer Institute National Institutes of Health Bethesda, Maryland

David Berrigan, Ph.D., M.P.H.

Program Director Health Behaviors Research Branch Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Kelly D. Blake, Sc.D.

Program Director Health Communication and Informatics Research Branch Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Michele Bloch, M.D., Ph.D.

Chief, Tobacco Control Research Branch Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Thomas H. Brandon, Ph.D.

Department Chair and Program Leader, Health Outcomes and Behavior Moffitt Distinguished Scholar Director, Tobacco Research & Intervention Program Moffitt Cancer Center Professor, University of South Florida Departments of Psychology and Oncologic Sciences Tampa, Florida

Alexandra R. Budenz, Dr.P.H., M.A.

Social Scientist Office of Health Communication and Education Center for Tobacco Products Food and Drug Administration Silver Spring, Maryland

Priscilla Callahan-Lyon, M.D.

Senior Science Advisor Office of the Center Director Center for Tobacco Products Food and Drug Administration Silver Spring, Maryland

Matthew J. Carpenter, Ph.D.

Professor, College of Medicine, Department of Psychiatry and Behavioral Sciences Co-Leader, Cancer Control Program Hollings Cancer Center Medical University of South Carolina Charleston, South Carolina

Frank J. Chaloupka, Ph.D.

Distinguished Professor Emeritus University of Illinois Chicago Chicago, Illinois

David Chambers, DPhil

Deputy Director for Implementation Science Office of the Director Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Srikumar Chellappan, Ph.D.

Moffitt Distinguished Scholar, Professor, and Chair Department of Tumor Biology Moffitt Cancer Center Tampa, Florida

Joseph T. Ciccolo, Ph.D.

Program Director Tobacco Control Research Branch Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

JoyAnn (Rohan) Courtney, Ph.D.

Health Scientist Administrator Office of Disease Prevention National Institutes of Health Bethesda, Maryland

Elizabeth A. Courtney-Long, M.A., M.S.P.H.

Deputy Associate Director for Science Office on Smoking and Health Centers for Disease Control and Prevention Atlanta, Georgia

K. Michael Cummings, Ph.D., M.P.H.

Professor, College of Medicine, Department of Psychiatry and Behavioral Sciences
Department of Psychiatry and Behavioral Sciences
Medical University of South Carolina
Co-Leader Tobacco Research Program
Hollings Cancer Center
Charleston, South Carolina

Carolyn Dresler, M.D., M.P.A.

Volunteer, Action on Smoking and Health Thoracic Surgical Oncologist, Retired Western Colorado

Kristie Foley, Ph.D., M.S.

Professor and Chair, Department of Implementation Science Acting Senior Associate Dean for Research Wake Forest University School of Medicine Winston-Salem, North Carolina

Neal D. Freedman, Ph.D., M.P.H.

Senior Investigator Metabolic Epidemiology Branch Division of Cancer Epidemiology and Genetics National Cancer Institute National Institutes of Health Bethesda, Maryland

Kya Grooms, Ph.D., M.P.H.

ORISE Post-Doctoral Fellow Oak Ridge Institute for Science and Education Office on Smoking and Health Centers for Disease Control & Prevention Atlanta, Georgia

Jaimee Heffner, Ph.D.

Associate Professor, Cancer Prevention Program Public Health Sciences Division Fred Hutchinson Cancer Research Center Seattle, Washington

Nadia Howlader, Ph.D., M.S.

Program Director and Cancer Epidemiologist Data Analytics Branch Surveillance Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Leah Hubbard, Ph.D.

Program Director, Brain, Skin, and Head & Neck/Thyroid Specialized Programs of Research Excellence Translational Research Program Division of Cancer Treatment and Diagnosis National Cancer Institute National Institutes of Health Bethesda, Maryland

Maki Inoue-Choi, Ph.D., M.S., R.D.

Staff Scientist Metabolic Epidemiology Branch Division of Cancer Epidemiology and Genetics National Cancer Institute National Institutes of Health Bethesda, Maryland

Paul Jacobsen, Ph.D.

Associate Director Healthcare Delivery Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Ron Johnson, Ph.D.

Program Director DNA and Chromosome Aberrations Branch Division of Cancer Biology National Cancer Institute National Institutes of Health Bethesda, Maryland

William M. P. Klein, Ph.D.

Associate Director Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Chris Kotsen, Psy.D., NCTTP

Associate Professor of Psychology in Clinical Psychiatry Weill Cornell Medical College Associate Director, Tobacco Treatment Program Department of Psychiatry & Behavioral Sciences Memorial Sloan Kettering Cancer Center New York, New York

Igor A. Kuzmin, Ph.D.

Program Director Translational Research Program Division of Cancer Treatment and Diagnosis National Cancer Institute National Institutes of Health Rockville, Maryland

Gabriel Y. Lai, Ph.D.

Program Director Environmental Epidemiology Branch Epidemiology and Genomics Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Stephanie R. Land, Ph.D.

Program Director and Statistician Tobacco Control Research Branch Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Natasha Buchanan Lunsford, Ph.D., M.A.

Associate Director for Health Equity Office on Smoking and Health Centers for Disease Control and Prevention Atlanta, Georgia

Ann Malarcher, Ph.D., M.S.P.H.

Senior Public Health Analyst Katmai Government Services Office on Smoking and Health Centers for Disease Control and Prevention Atlanta, Georgia

Candace Maynard, M.P.A.

Deputy Associate Director, Office of Program Management Branch Chief, NCI's Cancer Information Service Office of Communication and Public Liaison National Cancer Institute Bethesda, Maryland

Rachel Grana Mayne, Ph.D., M.P.H.

Program Director Tobacco Control Research Branch Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Steven F. Nothwehr, Ph.D.

Program Director Translational Research Program Division of Cancer Treatment and Diagnosis National Cancer Institute National Institutes of Health Rockville, Maryland

Orestis A. Panagiotou, M.D., Ph.D.

Assistant Professor Department of Health Services, Policy and Practice Brown University School of Public Health Legorreta Cancer Center Providence, Rhode Island

Elyse R. Park, Ph.D., M.P.H.

Clinical Associate in Psychology Program Director, Cancer Center Smokefree Support Service Professor, Psychiatry & Medicine Director, Health Promotion and Resiliency Intervention Research Program Massachusetts General Hospital Harvard Medical School Boston, Massachusetts

Yvonne Prutzman, Ph.D., M.P.H.

Program Director Tobacco Control Research Branch Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Carolyn Reyes-Guzman, Ph.D., M.P.H.

Program Director and Epidemiologist Tobacco Control Research Branch Behavioral Research Program Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Kimber P. Richter, Ph.D., M.P.H., NCTTP

Director, UKanQuit at the University of Kansas Hospital Professor, Population Health Co-founder, University of Kansas Tobacco Treatment Specialist Training Program University of Kansas School of Medicine

Kansas City, Kansas

Erin Rogers, Dr.P.H., M.P.H.

Assistant Professor Department of Population Health NYU Grossman School of Medicine NYU Langone Health New York, New York

Isabel C. Scarinci, Ph.D., M.P.H.

Professor Vice-Chair for Global and Rural Health Department of Obstetrics and Gynecology Heersink School of Medicine Senior Advisor for Globalization and Cancer O'Neal Comprehensive Cancer Center University of Alabama at Birmingham Birmingham, Alabama

Peter G. Shields, M.D.

Deputy Director, Comprehensive Cancer Center Professor, Epidemiology College of Public Health The Ohio State University Columbus, Ohio

Eva Szabo, M.D.

Chief, Lung and Upper Aerodigestive Cancer Research Group Division of Cancer Prevention National Cancer Institute National Institutes of Health Bethesda, Maryland

Kathryn L. Taylor, Ph.D.

Professor, Department of Oncology Cancer Prevention and Control Program Lombardi Comprehensive Cancer Center Georgetown University Medical Center Washington, D.C.

Cheryll C. Thomas, M.S.P.H.

Deputy Associate Director for Science Division of Cancer Prevention and Control Centers for Disease Control and Prevention Atlanta, Georgia

Randi Tolstyk, M.S.Ed.

Public Health Analyst Office on Smoking and Health Centers for Disease Control and Prevention Atlanta, Georgia

Emily S. Tonorezos, M.D., M.P.H.

Director Office of Cancer Survivorship Division of Cancer Control and Population Sciences National Cancer Institute National Institutes of Health Bethesda, Maryland

Peter Ujhazy, M.D., Ph.D.

Deputy Associate Director Translational Research Program Division of Cancer Treatment and Diagnosis National Cancer Institute National Institutes of Health Bethesda, Maryland

Brenna VanFrank, M.D., M.S.P.H.

Medical Officer Office on Smoking and Health Centers for Disease Control and Prevention Atlanta, Georgia

Robert E. Vollinger, Jr., Dr.P.H., M.S.P.H.

Senior Policy Analyst Office on Smoking and Health Centers for Disease Control and Prevention Washington, D.C.

Editorial and Publication Support

Laura Baker, M.P.H. Senior Public Health Associate The Bizzell Group New Carrollton, Maryland

Dana Chomenko, M.A., PMP

Vice President, Public Health Research and Evaluation BLH Technologies, Inc. Rockville, Maryland

Megan Keil, M.P.H.

Public Health Associate The Bizzell Group New Carrollton, Maryland

Cailey Muñana, M.P.H.

Public Health Associate The Bizzell Group New Carrollton, Maryland **Jenny Twesten, M.P.H.** Managing Director, Health Research The Bizzell Group New Carrollton, Maryland

K. Ceres Wright, M.A.

Scientific Publications Manager/Writer–Editor The Bizzell Group New Carrollton, Maryland The team acknowledges the editing, design, and project management support from the following:

Lisa Adams, BLH Technologies, Inc. Pam Grimes, BLH Technologies, Inc. Terry Head, BLH Technologies, Inc. Sarah Ashley Jolly, BLH Technologies, Inc. Susan Long, The Bizzell Group Jolie A. Mandelbaum, BLH Technologies, Inc. Srila Sen, The Bizzell Group Stephanie Siekierka, BLH Technologies, Inc.

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 (ENDS)	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.

This page left blank intentionally.

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

Chapter 1 Introduction and Overview

Chapter Contents

Introduction	3
Smoking Among Cancer Patients and Survivors	4
The Consequences of Continued Smoking After a Cancer Diagnosis	5
Addressing Smoking Cessation in Cancer Care Settings	6
Purpose of the Monograph	16
Preparation of the Monograph	18
Key Terminology and Concepts	18
The Multiple Phases of Smoking Cessation Treatment	19
Major Conclusions	21
References	24

Figures and Tables

Figure 1.1	Opportunities for Smoking Intervention Across the Cancer Care Continuum	7
Figure 1.2	Phases of Smoking Treatment	20
Table 1.1	Current and Former Smoking Among Adult Cancer Survivors, 2020	4
Table 1.2	Findings From the 2014 and 2020 Surgeon General's Reports	8
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)	10
Table 1.4	Summary of Recommendations for Addressing Tobacco Use Among Cancer	
	Patients	13
Table 1.5	Monograph Terminology	18

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 MoonshotSM–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 overall⁸ 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).

	Current Smoking Weighted % (95% CI)	Former Smoking Weighted % (95% Cl)
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 Current and Former Smoking Among Adult Cancer Survivors, 2020

Table 1.1 (continued)

	Current Smoking Weighted % (95% CI)	Former Smoking Weighted % (95% Cl)
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 cancer smoked, compared with 16% of survivors with non–tobacco-related cancer smoked, compared with 16% of survivors with non–tobacco-related 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 colleagues²⁰ 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 colleagues²⁶ 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

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 team²⁸; 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 cance	r 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 colleagues³⁶ compared each of these groups with those who never smoked. Hansen and colleagues³³ 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	 <i>Quit:</i> Smoking cessation within 6 months of diagnosis <i>Continued smoking:</i> 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)	 <i>Quit:</i> Abstinence (7-day point prevalence) at 9 months after tobacco treatment program enrollment <i>Continued smoking:</i> 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	 <i>Quit:</i> Smoking cessation within 3 months of diagnosis and sustained abstinence during the follow-up period <i>Continued smoking:</i> 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)

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, 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	 <i>Quit:</i> Quit smoking after first cancer and before new cancer <i>Continued smoking:</i> Continued to smoke after first cancer <i>Nonsmoking:</i> Never smoking or smoked fewer than 100 cigarettes in lifetime 	Average survival time after first cancer:Quit: 13.75 yearsContinued smoking: 6.57 years
Sheikh et al. 2021⁵	 Prospective cohort 517 patients with non-small cell lung cancer who were current smokers Russia 	Average 7 years	 <i>Quit:</i> Smoking cessation during follow-up period (annual follow-ups) <i>Continued smoking:</i> 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	 <i>Quit smoking:</i> Smoking status of current smoking before diagnosis and former smoking after diagnosis <i>Continued smoking:</i> Smoking status of current smoking at both pre- and post-diagnosis assessments <i>Never smoking:</i> Never smoking at both pre- and post-diagnosis assessments <i>Former smoking:</i> 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}

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 Summary of Recommendations for Addressing Tobacco Use Among Cancer Patients

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 colleagues⁴¹ 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 colleagues⁴⁷ 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 xiii–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.

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 Monograph Terminology

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.

Table 1.5 (continued)

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 cigars⁵⁰ 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 delivered⁵⁹ 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.

References

- 1. U.S. Department of Health and Human Services (USDHHS). Smoking cessation. A report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2020.
- 2. Chang EH, Braith A, Hitsman B, Schnoll RA. Treating nicotine dependence and preventing smoking relapse in cancer patients. Expert Rev Qual Life Cancer Care. 2017;2(1):23-39. doi: 10.1080/23809000.2017.1271981.
- 3. Warren GW, Sobus S, Gritz ER. The biological and clinical effects of smoking by patients with cancer and strategies to implement evidence-based tobacco cessation support. Lancet Oncol. 2014;15(12):e568-80. doi: 10.1016/s1470-2045(14)70266-9.
- 4. Gritz ER, Vidrine DJ, Lazev AB. Smoking cessation in cancer patients: never too late to quit. In: Given CW, Given B, Champion VL, Kozachik S, DeVoss DN, editors. Evidence based cancer care and prevention: behavioral interventions. New York: Springer Publishing Company; 2003. p. 107-40.
- Sheikh M, Mukeriya A, Shangina O, Brennan P, Zaridze D. Postdiagnosis smoking cessation and reduced risk for lung cancer progression and mortality: A prospective cohort study. Ann Intern Med. 2021;174(9):1232-9. doi: 10.7326/M21-0252.
- 6. Simmons VN, Litvin EB, Jacobsen PB, Patel RD, McCaffrey JC, Oliver JA, et al. Predictors of smoking relapse in patients with thoracic cancer or head and neck cancer. Cancer. 2013;119(7):1420-7. doi: 10.1002/cncr.27880.
- 7. U.S. Department of Health, Education, and Welfare (USDHEW). Smoking and health: report of the Advisory Committee to the Surgeon General of the Public Health Service. Washington: U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control and Prevention; 1964.
- 8. U.S. Department of Health and Human Services (USDHHS). The health consequences of smoking: 50 years of progress. A report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.
- American Cancer Society (ACS). Cancer facts & figures 2021 [Internet]. Atlanta: The Society; 2021 [cited 2022 Feb 17]. Available from: <u>https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2021/</u> cancer-facts-and-figures-2021.pdf.
- Islami F, Sauer AG, Miller KD, Siegel RL, Fedewa SA, Jacobs EJ, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA Cancer J Clin. 2018;68(1):31-54. doi: 10.3322/caac.21440.
- 11. Lortet-Tieulent J, Sauer AG, Siegel RL, Miller R, Islami F, Fedewa S, et al. State-level cancer mortality attributable to cigarette smoking in the United States. JAMA Intern Med. 2016;176(12):1792-8. doi: 10.1001/jamainternmed.2016.6530.
- Alberg AJ, Brock MV, Ford JG, Samet JM, Spivack SD. Epidemiology of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based Clinical Practice Guidelines. Chest. 2013;143(5 Suppl):e1S-29S. doi: 10.1378/chest.12-2345.
- 13. Warren GW, Kasza KA, Reid ME, Cummings KM, Marshall JR. Smoking at diagnosis and survival in cancer patients. Int J Cancer. 2013b;132(2):401-10. doi: 10.1002/ijc.27617.
- National Center for Health Statistics. National Health Interview Survey, 2020. Public-use data file and documentation, September 30, 2021 [cited 13 June 2022]. Available from: <u>https://www.cdc.gov/nchs/nhis/2020nhis.htm</u>
- 15. National Cancer Institute (NCI). Cancer trends progress report: cancer survivors and smoking, March 2020 [cited 14 Feb 2022]. Available from: <u>https://progressreport.cancer.gov/after/smoking</u>.
- Underwood JM, Townsend JS, Tai E, White A, Davis SP, Fairley TL. Persistent cigarette smoking and other tobacco use after a tobacco-related cancer diagnosis. J Cancer Surviv. 2012;6(3):333-44. doi: 10.1007/s11764-012-0230-1.
- 17. Westmaas JL, Alcaraz KI, Berg CJ, Stein KD. Prevalence and correlates of smoking and cessation-related behavior among survivors of ten cancers: findings from a nationwide survey nine years after diagnosis. Cancer Epidemiol Biomarkers Prev. 2014;23(9):1783-92. doi: 10.1158/1055-9965.Epi-14-0046.
- 18. Karam-Hage M, Cinciripini PM, Gritz ER. Tobacco use and cessation for cancer survivors: an overview for clinicians. CA Cancer J Clin. 2014;64(4):272-90. doi: 10.3322/caac.21231.

- 19. Morgan G, Schnoll RA, Alfano CM, Evans SE, Goldstein AO, Ostroff J, et al. National Cancer Institute conference on treating tobacco dependence at cancer centers. J Oncol Pract. 2011;7(3):178-82. doi: 10.1200/JOP.2010.000175.
- Gritz ER, Talluri R, Domgue, JF, Tami-Maury I, Shete S. Smoking behaviors in survivors of smoking-related and non-smoking-related cancers. JAMA Network Open. 2020;3(7):e209072. doi: 10.1001/jamanetworkopen.2020.9072.
- 21. Jassem J. Tobacco smoking after diagnosis of cancer: clinical aspects. Transl Lung Cancer Res. 2019;8(Suppl 1):S50-8. doi: 10.21037/tlcr.2019.04.01.
- 22. Duffy SA, Louzon SA, Gritz ER. Why do cancer patients smoke and what can providers do about it? Community Oncol. 2012;9(11):344-52. doi: 10.1016/j.cmonc.2012.10.003.
- 23. Shields PG, Herbst RS, Arenberg D, Benowitz NL, Bierut L, Luckart JB, et al. Smoking cessation, version 1.2016: NCCN Clinical Practice Guidelines in oncology. J Natl Compr Canc Netw. 2016;14(11):1430-68. doi: 10.6004/jnccn.2016.0152.
- 24. Martínez Ú, Brandon KO, Sutton SK, Brandon TH, Simmons VN. Does smoking abstinence predict cancer patients' quality of life over time? Psychooncology. 2019;28(8):1702-11. doi: 10.1002/pon.5145.
- 25. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA Cancer J Clin. 2021 Jan;71(1):7-33. doi: 10.3322/caac.21654. Erratum in: CA Cancer J Clin. 2021 Jul;71(4):359.
- 26. Warren GW, Cartmell KB, Garrett-Mayer E, Salloum RG, Cummings KM. Attributable failure of first-line cancer treatment and incremental costs associated with smoking by patients with cancer. JAMA Netw Open. 2019;2(4):e191703. doi: 10.1001/jamanetworkopen.2019.1703.
- 27. Agency for Healthcare Research and Quality (AHRQ). Systems change: treating tobacco use and dependence [Internet]. Rockville, MD: The Agency; December 2012 [cited 2022 May 17]. Available from: https://www.ahrq.gov/prevention/guidelines/tobacco/decisionmakers/systems/index.html.
- 28. Sheffer CE, Al-Zalabani A, Aubrey A, Bader R, Beltrez C, Bennett. S, et al. The emerging tobacco treatment workforce: characteristics of tobacco treatment specialists trained in council-accredited training programs from 2017 to 2019. Int J Environ Res Public Health. 2021;18(5):2416. doi: 10.3390/ijerph18052416.
- 29. Goldstein AO, Shoenbill KA, Jolly TA. Intensive smoking cessation counseling for patients with cancer. JAMA. 2020;324(14):1401-3. doi: 10.1001/jama.2020.13102.
- 30. Barnett TE, Lu Y, Gehr AW, Ghabach B, Ojha RP. Smoking cessation and survival among people diagnosed with non-metastatic cancer. BMC Cancer. 2020;20(1):726. doi: 10.1186/s12885-020-07213-5.
- 31. Day AT, Dahlstrom KR, Lee R, Karam-Hage M, Sturgis EM. Impact of a tobacco treatment program on abstinence and survival rates among current smokers with head and neck squamous cell carcinoma. Head Neck. 2020;42(9):2440-52. doi: 10.1002/hed.26268.
- 32. Gemine RE, Ghosal R, Collier G, Parry D, Campbell I, Davies G, et al. Longitudinal study to assess impact of smoking at diagnosis and quitting on 1-year survival for people with non-small cell lung cancer. Lung Cancer. 2019;129:1-7. doi: 10.1016/j.lungcan.2018.12.028.
- 33. Hansen JM, Nagle CM, Ibiebele TI, Grant PT, Obermair A, Friedlander ML, et al. A healthy lifestyle and survival among women with ovarian cancer. Int J Cancer. 2020;147(12):3361-9. doi: 10.1002/ijc.33155.
- 34. Hawari FI, Obeidat NA, Rimawi D, Jamal K. Smoking cessation care can translate to lower hazard of death in the short-run in cancer patients a retrospective cohort study to demonstrate the value of smoking cessation services within the treatment phase of cancer. BMC Cancer. 2019;19(1):580. doi: 10.1186/s12885-019-5778-v.
- 35. Romaszko-Wojtowicz A, Buciński A, Doboszyńska A. Impact of smoking on multiple primary cancers survival: a retrospective analysis. Clin Exp Med. 2018;18(3):391-7. doi: 10.1007/s10238-018-0498-1.
- Wang T, Townsend MK, Simmons VN, Terry KL, Matulonis UA, Tworoger SS. Prediagnosis and postdiagnosis smoking and survival following diagnosis with ovarian cancer. Int J Cancer. 2020;147(3):736-46. doi: 10.1002/ijc.32773.
- Hanna N, Mulshine J, Wollins DS, Tyne C, Dresler C. Tobacco cessation and control a decade later: American Society of Clinical Oncology policy statement update. J Clin Oncol. 2013;31:3147-57. doi: 10.1200/JCO.2013.48.8932.
- International Association for the Study of Lung Cancer (IASLC). Declaration from IASLC: Tobacco cessation after cancer diagnosis, September 4, 2019 [cited 14 Feb 2022]. Available from: <u>https://www.iaslc.org/iaslc-news/press-release/declaration-iaslc-tobacco-cessation-after-cancer-diagnosis</u>.
- 39. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in oncology (NCCN Guidelines®). Smoking cessation, version 1.2021. Plymouth Meeting, PA: NCCN; 2022.

- 40. Toll BA, Brandon TH, Gritz ER, Warren GW, Herbst RS. Assessing tobacco use by cancer patients and facilitating cessation: an American Association for Cancer Research policy statement. Clin Cancer Res. 2013;19(8):1941-8. doi: 10.1158/1078-0432.CCR-13-0666.
- 41. Fiore MC, D'Angelo H, Baker T. Effective cessation treatment for patients with cancer who smoke—the fourth pillar of cancer care. JAMA Netw Open. 2019;2(9):e1912264. doi: 10.1001/jamanetworkopen.2019.12264.
- 42. Croyle RT, Morgan GD, Fiore MC. Addressing a core gap in cancer care—the NCI moonshot program to help oncology patients stop smoking. N Engl J Med. 2019;380(6):512-5. doi: 10.1056/NEJMp1813913.
- 43. Peters EN, Torres E, Toll BA, Cummings KM, Gritz ER, Hyland A, et al. Tobacco assessment in actively accruing National Cancer Institute cooperative group program clinical trials. J Clin Oncol. 2012;30(23):2869-75. doi: 10.1200/JCO.2011.40.8815.
- 44. Cooley ME, Poghosyan H, Sprunck-Harrild K, Winickoff JP, Edge SB, Emmons KM. Tobacco treatment implementation within 28 commission on cancer accredited programs in the Northeast region of the USA: a pilot study. Transl Behav Med. 2018;8(5):706-13. doi: 10.1093/tbm/ibx024.
- 45. Day AT, Tang L, Karam-Hage M, Fkhry C. Tobacco treatment programs at National Cancer Institutedesignated cancer centers. Am J Clin Oncol. 2019;42(4):407-10. doi: 10.1097/COC.00000000000522.
- 46. Gallaway MS, Tai E, Rohan EA. Smoking cessation treatment programs offered at hospitals providing oncology services. J Smok Cessat. 2019;14(1):65-71. doi: 10.1017/jsc.2018.15.
- 47. Price SN, Studts JL, Hamann HA. Tobacco use assessment and treatment in cancer patients: a scoping review of oncology care clinician adherence to Clinical Practice Guidelines in the U.S. oncologist. 2019;24(2):229-38. doi: 10.1634/theoncologist.2018-0246.
- Schnoll RA, Zhang B, Montserrat R, Krook J, Spears WT, Marcus AC, et al. Brief physician-initiated quitsmoking strategies for clinical oncology settings: a trial coordinated by the Eastern Cooperative Oncology Group. J Clin Oncol. 2003;21:355-65. doi: 10.1200/JCO.2003.04.122.
- 49. Warren GW, Marshall JR, Cummings KM, Toll BA, Gritz ER, Hutson A, et al. Addressing tobacco use in patients with cancer: a survey of American Society of Clinical Oncology members. J Oncol Pract. 2013a;9(5):258-62. doi: 10.1200/JOP.2013.001025.
- 50. National Academies of Sciences, Engineering, and Medicine. Premium cigars: patterns of use, marketing, and health effects. Washington: The National Academies Press; 2022. doi: 10.17226/26421.
- Wyss AB, Hashibe M, Lee YA, Chuang SC, Muscat J, Chen C, et al. Smokeless tobacco use and the risk of head and neck cancer: pooled analysis of US studies in the INHANCE Consortium. Am J Epidemiol. 2016;184(10):703-16. doi: 10.1093/aje/kww075.
- 52. Baker TB, Mermelstein R, Collins LM, Piper ME, Jorenby DE, Smith SS, et al. New methods for tobacco dependence treatment research. Ann Behav Med. 2011;41(2):192-207. doi: 10.1007/s12160-010-9252-y.
- 53. Baker TB, Collins LM, Mermelstein R, Piper ME, Schlam TR, Cook JW, et al. Enhancing the effectiveness of smoking treatment research: conceptual bases and progress. Addiction. 2016;111(1):107-16. doi: 10.1111/add.13154.
- 54. Petersen A, Mermelstein R, Berg KM, Baker TB, Smith SS, Jorenby D, et al. Offering smoking treatment to primary care patients in two Wisconsin healthcare systems: who chooses smoking reduction versus cessation? Prev Med. 2017;105:332-6.
- 55. Aveyard P, Lindson N, Tearne S, Adams R, Ahmed K, Alekna R, et al. Nicotine preloading for smoking cessation: the Preloading RCT. Health Technology Assess. 2018;22(41):1-84. doi: 10.3310/hta22410.
- 56. Lindson N, Aveyard P. An updated meta-analysis of nicotine preloading for smoking cessation: investigating mediators of the effect. Psychopharmacology (Berl). In: Gale Academic OneFile [Internet]. 2011 Apr [cited 14 May 2022];214(3):579 92. Springer. Available from: <u>https://go.gale.com/ps/i.do?p=AONE&u=oregon_oweb&id=GALE|A354183520&v=2.1&it=r&sid=googleScholar&asid=99ff4c06</u>.
- 57. Ebbert JO, Hughes JR, West RJ, Rennard SI, Russ C, McRae TD, et al. Effect of varenicline on smoking cessation through smoking reduction: a randomized clinical trial. JAMA. 2015 Feb 17;313(7):687-94.
- 58. Hajek P, McRobbie HJ, Myers KE, Stapleton J, Dhanji AR. Use of varenicline for 4 weeks before quitting smoking: decrease in ad lib smoking and increase in smoking cessation rates. Arch Intern Med. 2011;171(8):770-7.
- 59. Piper ME, Fiore MC, Smith SS, Fraser D, Bolt DM, Collins LM, et al. Identifying effective intervention components for smoking cessation: a factorial screening experiment. Addiction. 2016;111(1):129-41.
- 60. Lindson N, Chepkin SC, Ye W, Fanshawe TR, Bullen C, Hartmann-Boyce J. Different doses, durations and modes of delivery of nicotine replacement therapy for smoking cessation. In: The Cochrane Database of

Systematic Reviews [Internet]. 2019 Apr 18;(4). John Wiley & Sons, Ltd. Art. No.: CD013308. doi: 10.1002/14651858.CD013308.

- 61. Fiore MC, Jaen CR, Baker TB, Bailey WC, Benowitz NL, Curry SJ, et al. Treating tobacco use and dependence: 2008 update. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service; 2008. Available from: <u>https://www.ahrq.gov/sites/default/files/wysiwyg/professionals/clinicians-providers/guidelines-</u> recommendations/tobacco/clinicians/update/treating_tobacco_use08.pdf.
- 62. Schlam TR, Fiore MC, Smith SS, Fraser D, Bolt DM, Collins LM, et al. Comparative effectiveness of intervention components for producing long-term abstinence from smoking: a factorial screening experiment. Addiction. 2016;111(1):142-55.
- 63. Livingstone-Banks J, Norris E, Hartmann-Boyce J, West R, Jarvis M, Hajek P. Relapse prevention interventions for smoking cessation. In: The Cochrane Database of Systematic Reviews [Internet]. 2019;(2). John Wiley & Sons, Ltd. Art. No.: CD003999. doi: 10.1002/14651858.CD003999.pub5.
- 64. American Society of Clinical Oncology (ASCO). Tobacco cessation guide for oncology providers [Internet]. American Society of Clinical Oncology; 2012 [cited 2022 May 26]. Available from: <u>https://www.asco.org/sites/new-www.asco.org/files/tobacco-cessation-guide.pdf</u>.
- 65. Land SR, Toll BA, Moinpour CM, Mitchell SA, Ostroff JS, Hatsukami DK, et al. Research priorities, measures, and recommendations for assessment of tobacco use in clinical cancer research. Clin Cancer Res. 2016;22(8):1907-13. doi: 10.1158/1078-0432.CCR-16-0104.

This page left blank intentionally.

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

Introduction	31
Tobacco Smoke and Tumorigenesis	32
Chemical Composition of Tobacco Smoke	32
Tobacco Smoke: DNA Damage	33
Tobacco Smoke: Mutational Burden	34
Tobacco Smoke: Mutational Signatures	34
Tobacco Smoke: Cancer Driver Genes	35
Tobacco Smoke: Epigenetic Changes	35
Biological Characteristics of Lung Cancers in Smokers and Never-Smokers	35
Lung Cancer: Driver Genes	36
Lung Cancer: Mutational Burden	36
Lung Cancer: Epigenetic Modifications	37
Lung Cancer: Variation in Gene Expression	37
Therapeutic Implications of Molecular Differences in Lung Cancers	38
The Effects of Tobacco Smoke Exposure on Cancer Cells	
DNA Damage	39
Changes in Gene Expression	39
Alteration of Cell Cycle Control	
Promotion of Epithelial-Mesenchymal Transition Associated With Metastasis	
Promotion of Angiogenesis	40
Alterations Within the Tumor Microenvironment	40
Promotion of Stem Cell–Like Properties	40
Inhibition of Response to Chemotherapeutic Agents	40
Summary	41
Conclusions	41
References	42

Figures and Tables

Figure 2.1	Major Pathways of Cancer Causation by Cigarette Smoking	
Table 2.1	Key Characteristics of Carcinogens	

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 allcause 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.

Characteristic	Examples of relevant evidence
 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 Key Characteristics of Carcinogens

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

Table 2.1 (continued)

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.





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 neversmokers, 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 p16in 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 AhRmediated 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.

References

- 1. The 'war on cancer' isn't yet won. Nature. 2022;601(7893):297. doi: 10.1038/d41586-022-00109-3.
- 2. American Association for Cancer Research. AACR cancer progress report 2021. Philadelphia: American Association for Cancer Research; 2021. 202 pages. Available from: <u>https://cancerprogressreport.aacr.org/wp-content/uploads/sites/2/2021/10/AACR_CPR_2021.pdf</u>.
- 3. DeVita VT Jr, Lawrence TS, Rosenberg SA. DeVita, Hellman, & Rosenberg's cancer: principles & practice of oncology. 11th ed. Philadelphia: Wolters Kluwer Health; 2018. 2432 p.
- 4. Islami F, Ward EM, Sung H, Cronin KA, Tangka FK, Sherman RL, et al. Annual report to the nation on the status of cancer, part 1: national cancer statistics. J Natl Cancer Inst. 2021;113(12):1648-69. doi: 10.1093/jnci/djab131.
- 5. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020;70(1):7-30. doi: 10.3322/caac.21590.
- 6. Bluethmann SM, Mariotto AB, Rowland JH. Anticipating the "silver tsunami": prevalence trajectories and comorbidity burden among older cancer survivors in the United States. Cancer Epidemiol Biomarkers Prev. 2016;25(7):1029-36. doi: 10.1158/1055-9965.EPI-16-0133.
- 7. Miller KD, Nogueira L, Mariotto AB, Rowland JH, Yabroff KR, Alfano CM, et al. Cancer treatment and survivorship statistics, 2019. CA Cancer J Clin. 2019;69(5):363-85. doi: 10.3322/caac.21565.
- 8. U.S. Department of Health and Human Services (USDHHS). The health consequences of smoking—50 years of progress: a report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.
- 9. U.S. Department of Health and Human Services (USDHHS). Smoking cessation: a report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2020.
- Sobus SL, Warren GW. The biologic effects of cigarette smoke on cancer cells. Cancer. 2014;120(23):3617-26. doi: 10.1002/cncr.28904.
- 11. Warren GW, Sobus S, Gritz ER. The biological and clinical effects of smoking by patients with cancer and strategies to implement evidence-based tobacco cessation support. Lancet Oncol. 2014;15(12):e568-80. doi: 10.1016/s1470-2045(14)70266-9.
- 12. U.S. Department of Health and Human Services (USDHHS). How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease: a report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2010.
- 13. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Tobacco smoke and involuntary smoking. IARC Monogr Eval Carcinog Risks Hum. 2004;83:1-1438.
- 14. National Toxicology Program (NTP). Report on carcinogens. 15th ed. Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service; 2021. Available from https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html.
- 15. Smith MT, Guyton KZ, Gibbons CF, Fritz JM, Portier CJ, Rusyn I, et al. Key characteristics of carcinogens as a basis for organizing data on mechanisms of carcinogenesis. Environ Health Perspect. 2016;124(6):713-21. doi: 10.1289/ehp.1509912.
- Hecht SS. Lung carcinogenesis by tobacco smoke. Int J Cancer. 2012;131(12):2724-32. doi: 10.1002/ijc.27816.
- Alexandrov LB, Ju YS, Haase K, Van Loo P, Martincorena I, Nik-Zainal S, et al. Mutational signatures associated with tobacco smoking in human cancer. Science. 2016;354(6312):618-22. doi: 10.1126/science.aag0299.
- 18. Cancer Genome Atlas Research Network. (2014). Correction: corrigendum: comprehensive molecular profiling of lung adenocarcinoma. Nature. 2014;514(7521):262. doi: 10.1038/nature13879.
- Huang YT, Lin X, Liu Y, Chirieac LR, McGovern R, Wain J, et al. Cigarette smoking increases copy number alterations in nonsmall-cell lung cancer. Proc Natl Acad Sci U S A. 2011;108(39):16345-50. doi: 10.1073/pnas.1102769108.
- Pickering CR, Zhang J, Neskey DM, Zhao M, Jasser SA, Wang J, et al. Squamous cell carcinoma of the oral tongue in young non-smokers is genomically similar to tumors in older smokers. Clin Cancer Res. 2014;20(14):3842-8. doi: 10.1158/1078-0432.Ccr-14-0565.

- 21. Desrichard A, Kuo F, Chowell D, Lee KW, Riaz N, Wong RJ, et al. Tobacco smoking-associated alterations in the immune microenvironment of squamous cell carcinomas. J Natl Cancer Inst. 2018;110(12):1386-92. doi: 10.1093/jnci/djy060.
- 22. South AP, den Breems NY, Riche T, Nwagu U, Zhan T, Poojan S, et al. Mutation signature analysis identifies increased mutation caused by tobacco smoke associated DNA adducts in larynx squamous cell carcinoma compared with oral cavity and oropharynx. Sci Rep. 2019;9:19256. doi: 10.1038/s41598-019-55352-y.
- 23. Yoshida K, Gowers KH, Lee-Six H, Chandrasekharan DP, Coorens T, Maughan EF, et al. Tobacco smoking and somatic mutations in human bronchial epithelium. Nature. 2020;578(7794):266-72. doi: 10.1038/s41586-020-1961-1.
- 24. Porta M, Crous-Bou M, Wark PA, Vineis P, Real FX, Malats N, et al. Cigarette smoking and K-ras mutations in pancreas, lung and colorectal adenocarcinomas: etiopathogenic similarities, differences and paradoxes. Mutat Res. 2009;682(2-3):83-93. doi: 10.1016/j.mrrev.2009.07.003.
- 25. Alexandrov LB, Nik-Zainal S, Wedge DC, Aparicio SA, Behjati S, Biankin AV, et al. Signatures of mutational processes in human cancer. Nature. 2013;500(7463):415-21. doi: 10.1038/nature12477.
- 26. COSMIC: catalogue of somatic mutations in cancer [Internet]. COSMIC: mutational signatures; [about 3 screens]. Available from: <u>https://cancer.sanger.ac.uk/cosmic/signatures</u>.
- 27. Alexandrov LB, Kim J, Haradhvala NJ, Huang MN, Tian Ng AW, Wu Y, et al. The repertoire of mutational signatures in human cancer. Nature. 2020;578(7793):94-101. doi: 10.1038/s41586-020-1943-3.
- 28. Nik-Zainal S, Kucab JE, Morganella S, Glodzik D, Alexandrov LB, Arlt VM, et al. The genome as a record of environmental exposure. Mutagenesis. 2015;30(6):763-70. doi: 10.1093/mutage/gev073.
- Roberts SA, Lawrence MS, Klimczak LJ, Grimm SA, Fargo D, Stojanov P, et al. An APOBEC cytidine deaminase mutagenesis pattern is widespread in human cancers. Nat Genet. 2013;45(9):970-6. doi: 10.1038/ng.2702.
- Clinical Lung Cancer Genome Project (CLCGP); Network Genomic Medicine (NGM). A genomics-based classification of human lung tumors. Sci Transl Med. 2013;5(209):209ra153. doi: 10.1126/scitranslmed.3006802.
- 31. Hammerman PS, Lawrence MS, Voet D, Jing R, Cibulskis K, Sivachenko A, et al. Comprehensive genomic characterization of squamous cell lung cancers. Nature. 2012;489(7417):519-25. doi: 10.1038/nature11404.
- 32. Kim J, Akbani R, Creighton CJ, Lerner SP, Weinstein JN, Getz G, et al. Invasive bladder cancer: genomic insights and therapeutic promise. Clin Cancer Res. 2015;21(20):4514-24. doi: 10.1158/1078-0432.Ccr-14-1215.
- 33. Martinez-Jimenez F, Muinos F, Sentis I, Deu-Pons J, Reyes-Salazar I, Arnedo-Pac C, et al. A compendium of mutational cancer driver genes. Nat Rev Cancer. 2020;20(10):555-72. doi: 10.1038/s41568-020-0290-x.
- 34. Stratton MR, Campbell PJ, Futreal PA. The cancer genome. Nature. 2009;458(7239):719-24. doi: 10.1038/nature07943.
- 35. Berger MF, Mardis ER. The emerging clinical relevance of genomics in cancer medicine. Nat Rev Clin Oncol. 2018;15(6):353-65. doi: 10.1038/s41571-018-0002-6.
- 36. Govindan R, Ding L, Griffith M, Subramanian J, Dees ND, Kanchi KL, et al. Genomic landscape of non-small cell lung cancer in smokers and never-smokers. Cell. 2012;150(6):1121-34. doi: 10.1016/j.cell.2012.08.02.
- 37. Nagahashi M, Sato S, Yuza K, Shimada Y, Ichikawa H, Watanabe S, et al. Common driver mutations and smoking history affect tumor mutation burden in lung adenocarcinoma. J Surg Res. 2018;230:181-5. doi: 10.1016/j.jss.2018.07.007.
- 38. Huang T, Chen X, Hong Q, Deng Z, Ma H, Xin Y, et al. Meta-analyses of gene methylation and smoking behavior in non-small cell lung cancer patients. Sci Rep. 2015;5:8897. doi: 10.1038/srep08897.
- 39. Liu Y, Lan Q, Siegfried JM, Luketich JD, Keohavong P. Aberrant promoter methylation of p16 and MGMT genes in lung tumors from smoking and never-smoking lung cancer patients. Neoplasia. 2006;8(1):46-51. doi: 10.1593/neo.05586.
- 40. Marsit CJ, Karagas MR, Andrew A, Liu M, Danaee H, Schned AR, et al. Epigenetic inactivation of SFRP genes and TP53 alteration act jointly as markers of invasive bladder cancer. Cancer Res. 2005;65(16):7081-5. doi: 10.1158/0008-5472.CAN-05-0267.
- 41. Marsit CJ, Karagas MR, Danaee H, Liu M, Andrew A, Schned AR, et al. Carcinogen exposure and gene promoter hypermethylation in bladder cancer. Carcinogenesis. 2006;27(1);112-6. doi: 10.1093/carcin/bgi172.
- 42. Marsit CJ, Houseman EA, Schned AR, Karagas MR, Kelsey KT. Promoter hypermethylation is associated with current smoking, age, gender and survival in bladder cancer. Carcinogenesis. 2007;28(8):1745-51. doi: 10.1093/carcin/bgm116.

- 43. Conway K, Edmiston SN, Parrish E, Bryant C, Tse CK, Swift-Scanlan T, et al. Breast tumor DNA methylation patterns associated with smoking in the Carolina Breast Cancer Study. Breast Cancer Res Treat. 2017;163(2):349-61. doi: 10.1007/s10549-017-4178-8.
- 44. Shui IM, Wong CJ, Zhao S, Kolb S, Ebot EM, Geybels MS, et al. Prostate tumor DNA methylation is associated with cigarette smoking and adverse prostate cancer outcomes. Cancer. 2016;122(14):2168-77. doi: 10.1002/cncr.30045.
- 45. Tan Q, Wang G, Huang J, Ding Z, Luo Q, Mok T, et al. Epigenomic analysis of lung adenocarcinoma reveals novel DNA methylation patterns associated with smoking. Onco Targets Ther. 2013;6:1471-9. doi: 10.2147/ott.S51041.
- Andres SA, Bickett KE, Alatoum MA, Kalbfleisch TS, Brock GN, Wittliff JL. Interaction between smoking history and gene expression levels impacts survival of breast cancer patients. Breast Cancer Res Treat. 2015;152(3):545-56. doi: 10.1007/s10549-015-3507-z.
- 47. Fantini D, Seiler R, Meeks JJ. Molecular footprints of muscle-invasive bladder cancer in smoking and nonsmoking patients. Urol Oncol. 2019;37(11):818-25. doi: 10.1016/j.urolonc.2018.09.017.
- 48. Li Y, Xiao X, Ji X, Liu B, Amos CI. RNA-seq analysis of lung adenocarcinomas reveals different gene expression profiles between smoking and nonsmoking patients. Tumour Biol. 2015;36(11):8993-9003. doi: 10.1007/s13277-015-3576-y.
- 49. Liu Y, Ni R, Zhang H, Miao L, Wang J, Jia W, et al. Identification of feature genes for smoking-related lung adenocarcinoma based on gene expression profile data. Onco Targets Ther. 2016;9:7397-407. doi: 10.2147/ott.S114230.
- 50. Nogueira Jorge NA, Wajnberg G, Ferreira CG, de Sa Carvalho B, Passetti F. snoRNA and piRNA expression levels modified by tobacco use in women with lung adenocarcinoma. PLoS One. 2017;12(8):e0183410. doi: 10.1371/journal.pone.0183410.
- Ortega-Gomez A, Rangel-Escareno C, Molina-Romero C, Macedo-Perez EO, Aviles-Salas A, Lara-Garcia A, et al. Gene-expression profiles in lung adenocarcinomas related to chronic wood smoke or tobacco exposure. Respir Res. 2016;17:42. doi: 10.1186/s12931-016-0346-3.
- 52. Prueitt RL, Wallace TA, Glynn SA, Yi M, Tang W, Luo J, et al. An immune-inflammation gene expression signature in prostate tumors of smokers. Cancer Res. 2016;76(5):1055-65. doi: 10.1158/0008-5472.Can-14-3630.
- 53. Staaf J, Jonsson G, Jonsson M, Karlsson A, Isaksson S, Salomonsson A, et al. Relation between smoking history and gene expression profiles in lung adenocarcinomas. BMC Med Genomics. 2012;5:22. doi: 10.1186/1755-8794-5-22.
- Wu C, Zhu J, Zhang X. Network-based differential gene expression analysis suggests cell cycle related genes regulated by E2F1 underlie the molecular difference between smoker and non-smoker lung adenocarcinoma. BMC Bioinformatics. 2013;14:365. doi: 10.1186/1471-2105-14-365.
- 55. Yao Y, Zhang T, Qi L, Liu R, Liu G, Wang X, et al. Competitive endogenous RNA network construction and comparison of lung squamous cell carcinoma in smokers and nonsmokers. Dis Markers. 2019;2019: 5292787. doi: 10.1155/2019/5292787.
- 56. Lemjabbar-Alaoui H, ul Hassan O, Yang YW, Buchanan P. Lung cancer: biology and treatment options. Biochim Biophys Acta. 2015;1856(2):189-210. doi: 10.1016/j.bbcan.2015.08.002.
- 57. Molina JR, Yang P, Cassivi SD, Schild SE, Adjei AA. Non-small cell lung cancer: epidemiology, risk factors, treatment, and survivorship. Mayo Clin Proc. 2008;83(5):584-94. doi: 10.4065/83.5.584.
- 58. PDQ Adult Treatment Editorial Board. PDQ non-small cell lung cancer treatment (PDQ®): health professional version [Internet]. Bethesda, MD: National Cancer Institute; updated 2022 Feb 7 [cited 2022 Feb 10]. Available from: https://www.cancer.gov/types/lung/hp/non-small-cell-lung-treatment-pdq.
- 59. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424. doi: 10.3322/caac.21492.
- 60. PDQ Screening and Prevention Editorial Board. Lung cancer prevention (PDQ®): health professional version. [Internet]. Bethesda, MD: National Cancer Institute; updated 2022 Apr 22 [cited 2022 Feb 25]. Available from: <u>https://www.cancer.gov/types/lung/hp/lung-prevention-pdq/</u>.
- 61. Subramanian J, Govindan R. Lung cancer in never smokers: a review. J Clin Oncol. 2007;25(5):561-70. doi: 10.1200/jco.2006.06.8015.
- 62. Sun S, Schiller JH, Gazdar AF. Lung cancer in never smokers—a different disease. Nat Rev Cancer. 2007;7(10):778-90. doi: 10.1038/nrc2190.

- 63. Zhang T, Joubert P, Ansari-Pour N, Zhao W, Hoang PH, Lokanga R, et al. Genomic and evolutionary classification of lung cancer in never smokers. Nat Genet. 2021;53(9):1348-59. doi: 10.1038/s41588-021-00920-0.
- 64. An SJ, Chen ZH, Su J, Zhang XC, Zhong WZ, Yang JJ, et al. Identification of enriched driver gene alterations in subgroups of non-small cell lung cancer patients based on histology and smoking status. PLoS One. 2012;7(6):e40109. doi: 10.1371/journal.pone.0040109.
- 65. Thu KL, Vucic EA, Chari R, Zhang W, Lockwood WW, English JC, et al. Lung adenocarcinoma of never smokers and smokers harbor differential regions of genetic alteration and exhibit different levels of genomic instability. PLoS One. 2012;7(3):e33003. doi: 10.1371/journal.pone.0033003.
- 66. Toyooka S, Tokumo M, Shigematsu H, Matsuo K, Asano H, Tomii K, et al. Mutational and epigenetic evidence for independent pathways for lung adenocarcinomas arising in smokers and never smokers. Cancer Res. 2006;66(3):1371-5. doi: 10.1158/0008-5472.Can-05-2625.
- 67. Yu XJ, Chen G, Yang J, Yu GC, Zhu PF, Jiang ZK, et al. Smoking alters the evolutionary trajectory of nonsmall cell lung cancer. Exp Ther Med. 2019;18(5):3315-24. doi: 10.3892/etm.2019.7958.
- 68. Cho J, Choi SM, Lee J, Lee CH, Lee SM, Kim DW, et al. Proportion and clinical features of never-smokers with non-small cell lung cancer. Chin J Cancer. 2017;36:20. doi: 10.1186/s40880-017-0187-6.
- 69. Dogan S, Shen R, Ang DC, Johnson ML, D'Angelo SP, Paik PK, et al. Molecular epidemiology of EGFR and KRAS mutations in 3,026 lung adenocarcinomas: higher susceptibility of women to smoking-related KRAS-mutant cancers. Clin Cancer Res. 2012;18(22):6169-77. doi: 10.1158/1078-0432.Ccr-11-3265.
- 70. Huang YS, Yang JJ, Zhang XC, Yang XN, Huang YJ, Xu CR, et al. Impact of smoking status and pathologic type on epidermal growth factor receptor mutations in lung cancer. Chin Med J (Engl). 2011;124(16):2457-60. doi: 10.3760/cma.j.issn.0366-6999.2011.16.011.
- 71. Jain A, Lim C, Gan EM, Ng DZ, Ng QS, Ang MK, et al. Impact of smoking and brain metastasis on outcomes of advanced EGFR mutation lung adenocarcinoma patients treated with first line epidermal growth factor receptor tyrosine kinase inhibitors. PLoS One. 2015;10(5):e0123587. doi: 10.1371/journal.pone.0123587.
- 72. Jida M, Toyooka S, Mitsudomi T, Takano T, Matsuo K, Hotta K, et al. Usefulness of cumulative smoking dose for identifying the EGFR mutation and patients with non-small-cell lung cancer for gefitinib treatment. Cancer Sci. 2009;100(10):1931-4. doi: 10.1111/j.1349-7006.2009.01273.x.
- 73. Lee YJ, Shim HS, Kang YA, Hong SJ, Kim HK, Kim H, et al. Dose effect of cigarette smoking on frequency and spectrum of epidermal growth factor receptor gene mutations in Korean patients with non-small cell lung cancer. J Cancer Res Clin Oncol. 2010;136(12):1937-44. doi: 10.1007/s00432-010-0853-4.
- 74. Mounawar M, Mukeria A, Le Calvez F, Hung RJ, Renard H, Cortot A, et al. Patterns of EGFR, HER2, TP53, and KRAS mutations of p14(arf) expression in non-small cell lung cancers in relation to smoking history. Cancer Res. 2007;67(12):5667-72. doi: 10.1158/0008-5472.Can-06-4229.
- 75. Paik PK, Johnson ML, D'Angelo SP, Sima CS, Ang D, Dogan S, et al. Driver mutations determine survival in smokers and never-smokers with stage IIIB/IV lung adenocarcinomas. Cancer. 2012;118(23):5840-7. doi: 10.1002/cncr.27637.
- 76. Pham D, Kris MG, Riely GJ, Sarkaria IS, McDonough T, Chuai S, et al. Use of cigarette-smoking history to estimate the likelihood of mutations in epidermal growth factor receptor gene exons 19 and 21 in lung adenocarcinomas. J Clin Oncol. 2006;24(11):1700-4. doi: 10.1200/jco.2005.04.3224.
- 77. Ren JH, He WS, Yan GL, Jin M, Yang KY, Wu G. EGFR mutations in non-small-cell lung cancer among smokers and non-smokers: a meta-analysis. Environ Mol Mutagen. 2012;53(1):78-82. doi: 10.1002/em.20680.
- 78. Sonobe M, Manabe T, Wada H, Tanaka F. Mutations in the epidermal growth factor receptor gene are linked to smoking-independent, lung adenocarcinoma. Br J Cancer. 2005;93(3):355-63. doi: 10.1038/sj.bjc.6602707.
- 79. Sugio K, Uramoto H, Ono K, Oyama T, Hanagiri T, Sugaya M, et al. Mutations within the tyrosine kinase domain of EGFR gene specifically occur in lung adenocarcinoma patients with a low exposure of tobacco smoking. Br J Cancer. 2006;94(6):896-903. doi: 10.1038/sj.bjc.6603040.
- Halvorsen AR, Silwal-Pandit L, Meza-Zepeda LA, Vodak D, Phuong V, Sagerup C, et al. TP53 mutation spectrum in smokers and never smoking lung cancer patients. Front Genet. 2016;7:85. doi: 10.3389/fgene.2016.00085.
- 81. Le Calvez F, Mukeria A, Hunt JD, Kelm O, Hung RJ, Taniere P, et al. TP53 and KRAS mutation load and types in lung cancers in relation to tobacco smoke: distinct patterns in never, former, and current smokers. Cancer Res. 2005;65(12):5076-83. doi: 10.1158/0008-5472.Can-05-0551.
- 82. Tam IY, Chung LP, Suen WS, Wang E, Wong MC, Ho KK, et al. Distinct epidermal growth factor receptor and KRAS mutation patterns in non-small cell lung cancer patients with different tobacco exposure and clinicopathologic features. Clin Cancer Res. 2006;12(5):1647-53. doi: 10.1158/1078-0432.Ccr-05-1981.

45

- 83. Zheng S, Wang R, Zhang Y, Pan Y, Cheng C, Zheng D, et al. Former smokers with non-small-cell lung cancers: a comprehensive investigation of clinicopathologic characteristics, oncogenic drivers, and prognosis. Cancer Med. 2016;5(8):2117-25. doi: 10.1002/cam4.764.
- 84. Aisner DL, Sholl LM, Berry LD, Rossi MR, Chen H, Fujimoto J, et al. The impact of smoking and TP53 mutations in lung adenocarcinoma patients with targetable mutations—the Lung Cancer Mutation Consortium (LCMC2). Clin Cancer Res. 2018;24(5):1038-47. doi: 10.1158/1078-0432.Ccr-17-2289.
- 85. Howlader N, Forjaz G, Mooradian MJ, Meza R, Kong CY, Cronin KA, et al. The effect of advances in lungcancer treatment on population mortality. N Engl J Med. 2020;383(7):640-9. doi: 10.1056/NEJMoa1916623.
- 86. Gridelli C, Rossi A, Carbone DP, Guarize J, Karachaliou N, Mok T, et al. Non-small-cell lung cancer. Nat Rev Dis Primers. 2015;1:15009. doi: 10.1038/nrdp.2015.9.
- 87. Takamochi K, Oh S, Suzuki K. Differences in EGFR and KRAS mutation spectra in lung adenocarcinoma of never and heavy smokers. Oncol Lett. 2013;6(5):1207-12. doi: 10.3892/ol.2013.1551.
- 88. Freeman JR, Chu S, Hsu T, Huang YT. Epigenome-wide association study of smoking and DNA methylation in non-small cell lung neoplasms. Oncotarget. 2016;7(43):69579-91. doi: 10.18632/oncotarget.11831.
- Kikuchi S, Yamada D, Fukami T, Maruyama T, Ito A, Asamura H, et al. Hypermethylation of the TSLC1/IGSF4 promoter is associated with tobacco smoking and a poor prognosis in primary nonsmall cell lung carcinoma. Cancer. 2006;106(8):1751-8. doi: 10.1002/cncr.21800.
- Wu XM, Chen Y, Shao Y, Zhou XL, Tang WR. Association between cigarette smoking and RASSF1A gene promoter hypermethylation in lung cancer patients: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(19):8451-4. doi: 10.7314/apjcp.2014.15.19.8451.
- 91. Zhang B, Zhu W, Yang P, Liu T, Jiang M, He ZN, et al. Cigarette smoking and p16INK4 alpha gene promoter hypermethylation in non-small cell lung carcinoma patients: a meta-analysis. PLoS One. 2011;6(12):e28882. doi: 10.1371/journal.pone.0028882.
- 92. SatoT, Arai E, Kohno T, Takahashi Y, Miyata S, Tsuta K, et al. Epigenetic clustering of lung adenocarcinomas based on DNA methylation profiles in adjacent lung tissue: its correlation with smoking history and chronic obstructive pulmonary disease. Int J Cancer. 2014;135(2), 319-34. doi: 10.1002/ijc.28684.
- 93. Sun R, Li J, Wang B, Guo Y, Ma L, Quan X, et al. Liver kinase B1 promoter CpG island methylation is related to lung cancer and smoking. Int J Clin Exp Med. 2015;8(8):14070-4.
- 94. Chen Y, Pan Y, Ji Y, Sheng L, Du X. Network analysis of differentially expressed smoking-associated mRNAs, lncRNAs and miRNAs reveals key regulators in smoking-associated lung cancer. Exp Ther Med. 2018;16(6):4991-5002. doi: 10.3892/etm.2018.6891.
- 95. Szymanowska-Narloch A, Jassem E, Skrzypski M, Muley T, Meister M, Dienemann H, et al. Molecular profiles of non-small cell lung cancers in cigarette smoking and never-smoking patients. Adv Med Sci. 2013;58(2):196-206. doi: 10.2478/ams-2013-0025.
- 96. Bordas A, Cedillo JL, Arnalich F, Esteban-Rodriguez I, Guerra-Pastrian L, de Castro J, et al. Expression patterns for nicotinic acetylcholine receptor subunit genes in smoking-related lung cancers. Oncotarget. 2017;8(40):67878-90. doi: 10.18632/oncotarget.18948.
- 97. D'Angelo SP, Pietanza MC, Johnson ML, Riely GJ, Miller VA, Sima CS, et al. Incidence of EGFR exon 19 deletions and L858R in tumor specimens from men and cigarette smokers with lung adenocarcinomas. J Clin Oncol. 2011;29(15):2066-70. doi: 10.1200/jco.2010.32.6181.
- Soria JC, Ohe Y, Vansteenkiste J, Reungwetwattana T, Chewaskulyong B, Lee KH, et al. Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer. N Engl J Med. 2018;378(2):113-25. doi: 10.1056/NEJMoa1713137.
- 99. Peters S, Camidge DR, Shaw AT, Gadgeel S, Ahn JS, Kim DW, et al. Alectinib versus crizotinib in untreated ALK-positive non-small-cell lung cancer. N Engl J Med. 2017;377(9):829-38. doi: 10.1056/NEJMoa1704795.
- 100. Shaw AT, Engelman JA. ALK in lung cancer: past, present, and future. J Clin Oncol. 2013;31(8):1105-11. doi: 10.1200/jco.2012.44.5353.
- 101. Solomon BJ, Mok T, Kim DW, Wu YL, Nakagawa K, Mekhail T, et al. First-line crizotinib versus chemotherapy in ALK-positive lung cancer. N Engl J Med. 2014;371(23):2167-77. doi: 10.1056/NEJMoa1408440. Corrected and republished from: N Engl J Med. 2015 Oct 15;373(16):1582.
- 102. D'Angelo A, Sobhani N, Chapman R, Bagby S, Bortoletti C, Traversini M, et al. Focus on ROS1-positive nonsmall cell lung cancer (NSCLC): crizotinib, resistance mechanisms and the newer generation of targeted therapies. Cancers (Basel). 2020;12(11):3293. doi: 10.3390/cancers12113293.
- 103. Harada G, Santini FC, Wilhelm C, Drilon A. NTRK fusions in lung cancer: from biology to therapy. Lung Cancer. 2021;161:108-13. doi: 10.1016/j.lungcan.2021.09.005.

- 104. Onoi K, Chihara Y, Uchino J, Shimamoto T, Morimoto Y, Iwasaku M, et al. Immune checkpoint inhibitors for lung cancer treatment: a review. J Clin Med. 2020;9(5):1362. doi: 10.3390/jcm9051362.
- 105. Ng TL, Liu Y, Dimou A, Patil T, Aisner D, Dong Z, et al. Predictive value of oncogenic driver subtype, programmed death-1 ligand (PD-L1) score, and smoking status on the efficacy of PD-1/PD-L1 inhibitors in patients with oncogene-driven non-small cell lung cancer. Cancer. 2019;125(7):1038-49.
- 106. Rangachari D, VanderLaan PA, Shea M, Le X, Huberman MS, Kobayashi SS, et al. Correlation between classic driver oncogene mutations in EGFR, ALK, or ROS1 and 22C3-PD-L1 ≥50% expression in lung adenocarcinoma. J Thorac Oncol. 2017;12(5):878-83.
- 107. Pan Y, Zheng D, Li Y, Cai X, Zheng Z, Jin Y, et al. Unique distribution of programmed death ligand 1 (PD-L1) expression in East Asian non-small cell lung cancer. *J Thorac Dis.* 2017;9(8):2579-86. doi: 10.21037/jtd.2017.08.61.
- 108. Schoenfeld AJ, Rizvi H, Bandlamudi C, Sauter JL, Travis WD, Rekhtman N, et al. Clinical and molecular correlates of PD-L1 expression in patients with lung adenocarcinomas. Ann Oncol. 2020;31(5):599-608. doi: 10.1016/j.annonc.2020.01.065. Epub 2020 Feb 6.
- 109. de la Iglesia JV, Slebos RJ, Martin-Gomez L, Wang X, Teer JK, Tan AC, et al. Effects of tobacco smoking on the tumor immune microenvironment in head and neck squamous cell carcinoma. Clin Cancer Res. 2020;26(6):1474-85. doi: 10.1158/1078-0432.CCR-19-1769. Corrected and republished from: Clin Cancer Res. 2021 Sep 1;27(17):4941.
- 110. Gyorffy E, Anna L, Gyori Z, Segesdi J, Minarovits J, Soltesz I, et al. DNA adducts in tumour, normal peripheral lung and bronchus, and peripheral blood lymphocytes from smoking and non-smoking lung cancer patients: correlations between tissues and detection by P-postlabelling and immunoassay. Carcinogenesis. 2004;25(7):1201-9. doi: 10.1093/carcin/bgh131.
- 111. Szyfter K, Hemminki K, Szyfter W, Szmeja Z, Banaszewski J, Yang K. Aromatic DNA adducts in larynx biopsies and leukocytes. Carcinogenesis. 1994;15(10):2195-9. doi: 10.1093/carcin/15.10.2195.
- 112. Advani J, Subbannayya Y, Patel K, Khan AA, Patil AH, Jain AP, et al. Long-term cigarette smoke exposure and changes in miRNA expression and proteome in non-small-cell lung cancer. OMICS. 2017;21(7):390-403. doi: 10.1089/omi.2017.0045.
- 113. Babu N, Advani J, Solanki HS, Patel K, Jain A, Khan AA, et al. miRNA and proteomic dysregulation in nonsmall cell lung cancer in response to cigarette smoke. Microrna. 2018;7(1):38-53. doi: 10.2174/2211536607666180103165343.
- 114. Ma X, Jia Y, Zu S, Li R, Jia Y, Zhao Y, et al. α5 nicotinic acetylcholine receptor mediates nicotine-induced HIF-1α and VEGF expression in non-small cell lung cancer. Toxicol Appl Pharmacol. 2014;278(2):172-9. doi: 10.1016/j.taap.2014.04.023.
- 115. Mucchietto V, Fasoli F, Pucci S, Moretti M, Benfante R, Maroli A, et al. α9- and α7-containing receptors mediate the pro-proliferative effects of nicotine in the A549 adenocarcinoma cell line. Br J Pharmacol. 2018;175(11):1957-72. doi: 10.1111/bph.13954.
- 116. Schuller HM. Is cancer triggered by altered signalling of nicotinic acetylcholine receptors? Nat Rev Cancer. 2009;9(3):195-205. doi: 10.1038/nrc2590.
- 117. Yang J, Antin P, Berx G, Blanpain C, Brabletz T, Bronner M, et al. Guidelines and definitions for research on epithelial–mesenchymal. Nat Rev Mol Cell Biol. 2020;21(6):341-52. doi: 10.1038/s41580-020-0237-9. Corrected and republished from: Nat Rev Mol Cell Biol. 2021 Dec;22(12):834.
- 118. Ribatti D, Tamma R, Annese T. Epithelial-mesenchymal transition in cancer: a historical overview. Transl Oncol. 2020;13(6):100773. doi: 10.1016/j.tranon.2020.100773.
- Allam E, Zhang W, Al-Shibani N, Sun J, Labban N, Song F, et al. Effects of cigarette smoke condensate on oral squamous cell carcinoma cells. Arch Oral Biol. 2011;56(10):1154-61. doi: 10.1016/j.archoralbio.2011.03.008.
- 120. Chapman S, Mick M, Hall P, Mejia C, Sue S, Abdul Wase B, et al. Cigarette smoke extract induces oral squamous cell carcinoma cell invasion in a receptor for advanced glycation end-products-dependent manner. Eur J Oral Sci. 2018;126(1):33-40. doi: 10.1111/eos.12395.
- 121. Di Cello F, Flowers VL, Li H, Vecchio-Pagan B, Gordon B, Harbom K, et al. Cigarette smoke induces epithelial to mesenchymal transition and increases the metastatic ability of breast cancer cells. Mol Cancer. 2013;12:90. doi: 10.1186/1476-4598-12-90.
- 122. Dino P, D'Anna C, Sangiorgi C, Di Sano C, Di Vincenzo S, Ferraro M, et al. Cigarette smoke extract modulates E-Cadherin, Claudin-1 and miR-21 and promotes cancer invasiveness in human colorectal adenocarcinoma cells. Toxicol Lett. 2019;317:102-9. doi: 10.1016/j.toxlet.2019.09.020.

- 123. Jeon SY, Go RE, Heo JR, Kim CW, Hwang KA, Choi KC. Effects of cigarette smoke extracts on the progression and metastasis of human ovarian cancer cells via regulating epithelial-mesenchymal transition. Reprod Toxicol. 2016;65:1-10. doi: 10.1016/j.reprotox.2016.06.012.
- 124. Kim CW, Go RE, Lee HM, Hwang KA, Lee K, Kim B, et al. Cigarette smoke extracts induced the colon cancer migration via regulating epithelial mesenchymal transition and metastatic genes in human colon cancer cells. Environ Toxicol. 2017;32(2):690-704. doi: 10.1002/tox.22271.
- 125. Kispert S, Marentette J, McHowat J. Cigarette smoke induces cell motility via platelet-activating factor accumulation in breast cancer cells: a potential mechanism for metastatic disease. Physiol Rep. 2015;3(3):e12318. doi: 10.14814/phy2.12318.
- 126. Nagaraj NS, Zacharias W. Cigarette smoke condensate increases cathepsin-mediated invasiveness of oral carcinoma cells. Toxicol Lett. 2007;170(2):134-45. doi: 10.1016/j.toxlet.2007.02.014.
- 127. Park GB, Kim D. PI3K catalytic isoform alteration promotes the LIMK1-related metastasis through the PAK1 or ROCK1/2 activation in cigarette smoke-exposed ovarian cancer cells. Anticancer Res. 2017;37(4):1805-18. doi: 10.21873/anticanres.11515.
- 128. Sun X, Deng Q, Liang Z, Liu Z, Geng H, Zhao L, et al. Cigarette smoke extract induces epithelialmesenchymal transition of human bladder cancer T24 cells through activation of ERK1/2 pathway. Biomed Pharmacother. 2017;86:457-65. doi: 10.1016/j.biopha.2016.12.022.
- 129. Yang S, Long M, Tachado SD, Seng S. Cigarette smoke modulates PC3 prostate cancer cell migration by altering adhesion molecules and the extracellular matrix. Mol Med Rep. 2015;12(5):6990-6. doi: 10.3892/mmr.2015.4302.
- Liu H, Zhou Y, Boggs SE, Belinsky SA, Liu J. Cigarette smoke induces demethylation of prometastatic oncogene synuclein-gamma in lung cancer cells by downregulation of DNMT3B. Oncogene. 2007;26(40):5900-10. doi: 10.1038/sj.onc.1210400.
- 131. Nagathihalli NS, Massion PP, Gonzalez AL, Lu P, Datta PK. Smoking induces epithelial-to-mesenchymal transition in non-small cell lung cancer through HDAC-mediated downregulation of E-cadherin. Mol Cancer Ther. 2012;11(11):2362-72. doi: 10.1158/1535-7163.Mct-12-0107.
- 132. Carmeliet P. VEGF as a key mediator of angiogenesis in cancer. Oncology. 2005;69 Suppl 3:4-10. doi: 10.1159/000088478.
- 133. Birrane G, Li H, Yang S, Tachado SD, Seng S. Cigarette smoke induces nuclear translocation of heme oxygenase 1 (HO-1) in prostate cancer cells: nuclear HO-1 promotes vascular endothelial growth factor secretion. Int J Oncol. 2013;42(6):1919-28. doi: 10.3892/ijo.2013.1910.
- 134. Ye YN, Wu WK, Shin VY, Cho CH. A mechanistic study of colon cancer growth promoted by cigarette smoke extract. Eur J Pharmacol. 2005;519(1-2):52-7. doi: 10.1016/j.ejphar.2005.07.009.
- 135. Baghban R, Roshangar L, Jahanban-Esfahlan R, Seidi K, Ebrahimi-Kalan A, Jaymand M, et al. Tumor microenvironment complexity and therapeutic implications at a glance. Cell Commun Signal. 2020 Apr 7;18(1):59. doi: 10.1186/s12964-020-0530-4.
- 136. Whiteside TL. The tumor microenvironment and its role in promoting tumor growth. Oncogene. 2008;27(45):5904-12. doi: 10.1038/onc.2008.271.
- 137. Salem AF, Al-Zoubi MS, Whitaker-Menezes D, Martinez-Outschoorn UE, Lamb R, Hulit J, et al. Cigarette smoke metabolically promotes cancer, via autophagy and premature aging in the host stromal microenvironment. Cell Cycle. 2013;12(5):818-25. doi: 10.4161/cc.23722.
- 138. Domingo-Vidal M, Whitaker-Menezes D, Martos-Rus C, Tassone P, Snyder CM, Tuluc M, et al. Cigarette smoke induces metabolic reprogramming of the tumor stroma in head and neck squamous cell carcinoma. Mol Cancer Res. 2019;17(9):1893-909. doi: 10.1158/1541-7786.Mcr-18-1191.
- Cheng L, Alexander R, Zhang S, Pan CX, MacLennan GT, Lopez-Beltran A, et al. The clinical and therapeutic implications of cancer stem cell biology. Expert Rev Anticancer Ther. 2011;11(7):1131-43. doi: 10.1586/era.11.82.
- 140. Clarke MF. Clinical and therapeutic implications of cancer stem cells. N Engl J Med. 2019;380(23):2237-45. doi: 10.1056/NEJMra1804280.
- 141. Franco SS, Szczesna K, Iliou MS, Al-Qahtani M, Mobasheri A, Kobolak J, et al. In vitro models of cancer stem cells and clinical applications. BMC Cancer. 2016;16 Suppl 2:738. doi: 10.1186/s12885-016-2774-3.
- 142. Hussain M, Rao M, Humphries AE, Hong JA, Liu F, Yang M, et al. Tobacco smoke induces polycombmediated repression of Dickkopf-1 in lung cancer cells. Cancer Res. 2009;69(8):3570-8. doi: 10.1158/0008-5472.Can-08-2807.

- 143. Hermann PC, Sancho P, Canamero M, Martinelli P, Madriles F, Michl P, et al. Nicotine promotes initiation and progression of KRAS-induced pancreatic cancer via Gata6-dependent dedifferentiation of acinar cells in mice. Gastroenterology. 2014;147(5):1119-33.e4. doi: 10.1053/j.gastro.2014.08.002.
- 144. Qian W, Kong X, Zhang T, Wang D, Song J, Li Y, et al. Cigarette smoke stimulates the stemness of renal cancer stem cells via Sonic Hedgehog pathway. Oncogenesis. 2018;7(3):24. doi: 10.1038/s41389-018-0029-7.
- 145. An Y, Kiang A, Lopez JP, Kuo SZ, Yu MA, Abhold EL, et al. Cigarette smoke promotes drug resistance and expansion of cancer stem cell-like side population. PLoS One. 2012;7(11):e47919. doi: 10.1371/journal.pone.0047919.
- 146. Chen YJ, Huang WC, Wei YL, Hsu SC, Yuan P, Lin HY, et al. Elevated BCRP/ABCG2 expression confers acquired resistance to gefitinib in wild-type EGFR-expressing cells. PLoS One. 2011;6(6):e21428. doi: 10.1371/journal.pone.0021428.
- 147. Zhang M, Mathur A, Zhang Y, Xi S, Atay S, Hong JA, et al. Mithramycin represses basal and cigarette smokeinduced expression of ABCG2 and inhibits stem cell signaling in lung and esophageal cancer cells. Cancer Res. 2012;72(16):4178-92. doi: 10.1158/0008-5472.Can-11-3983.
- 148. Bertolini G, Roz L, Perego P, Tortoreto M, Fontanella E, Gatti L, et al. Highly tumorigenic lung cancer CD133+ cells display stem-like features and are spared by cisplatin treatment. Proc Natl Acad Sci U S A. 2009;106(38):16281-6. doi: 10.1073/pnas.0905653106.
- 149. Ho MM, Ng AV, Lam S, Hung JY. Side population in human lung cancer cell lines and tumors is enriched with stem-like cancer cells. Cancer Res. 2007;67(10):4827-33. doi: 10.1158/0008-5472.CAN-06-3557.
- 150. Huang D, Gao Q, Guo L, Zhang C, Jiang W, Li H, et al. Isolation and identification of cancer stem-like cells in esophageal carcinoma cell lines. Stem Cells Dev. 2009;18(3):465-73. doi: 10.1089/scd.2008.0033.
- 151. Li H, Gao Q, Guo L, Lu SH. The PTEN/PI3K/Akt pathway regulates stem-like cells in primary esophageal carcinoma cells. Cancer Biol Ther. 2011;11(11):950-8. doi: 10.4161/cbt.11.11.15531.
- 152. To KK, Yu L, Liu S, Fu J, Cho CH. Constitutive AhR activation leads to concomitant ABCG2-mediated multidrug resistance in cisplatin-resistant esophageal carcinoma cells. Mol Carcinog. 2012;51(6):449-64. doi: 10.1002/mc.20810.
- 153. Li F, Zeng H, Ying K. The combination of stem cell markers CD133 and ABCG2 predicts relapse in stage I non-small cell lung carcinomas. Med Oncol. 2011;28(4):1458-62. doi: 10.1007/s12032-010-9646-5.
- 154. Tsunoda S, Okumura T, Ito T, Kondo K, Ortiz C, Tanaka E, et al. ABCG2 expression is an independent unfavorable prognostic factor in esophageal squamous cell carcinoma. Oncology. 2006;71(3-4):251-8. doi: 10.1159/000106787.
- 155. Samanta D, Kaufman J, Carbone DP, Datta PK. Long-term smoking mediated down-regulation of Smad3 induces resistance to carboplatin in non-small cell lung cancer. Neoplasia. 2012;14(7):644. doi: 10.1593/neo.12548.
- 156. Samanta D, Gonzalez AL, Nagathihalli N, Ye F, Carbone DP, Datta PK. Smoking attenuates transforming growth factor-beta-mediated tumor suppression function through downregulation of Smad3 in lung cancer. Cancer Prev Res (Phila). 2012;5(3):453-63. doi: 10.1158/1940-6207.Capr-11-0313.
- 157. Liu M, Zhou C, Zheng J. Cigarette smoking impairs the response of EGFR-TKIs therapy in lung adenocarcinoma patients by promoting EGFR signaling and epithelial-mesenchymal transition. Am J Transl Res. 2015;7(10):2026-35.
- 158. Li H, Wang S, Takayama K, Harada T, Okamoto I, Iwama E, et al. Nicotine induces resistance to erlotinib via cross-talk between α 1 nAChR and EGFR in the non-small cell lung cancer xenograft model. Lung Cancer. 2015;88(1):1-8. doi: 10.1016/j.lungcan.2015.01.017. Epub 2015 Jan 25.

This page left blank intentionally.
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

Introduction	54
Motivation to Quit	55
Elements of Effective Smoking Cessation Treatments	56
Neurobiological and Behavioral-Motivational Dimensions of Cigarette Smoking:	
Relevance to Treatment	57
Neurobiological Dimensions of Cigarette Smoking	57
Behavioral-Motivational Dimensions of Cigarette Smoking	58
Summary: Neurobiological and Behavioral-Motivational Dimensions of Cigarette	
Smoking	58
Smoking Cessation Treatments in the General Population	59
Approach	59
Medications for Smoking Cessation	59
Behavioral Interventions for Smoking Cessation	65
Beyond In-Person Counseling: Telephone, Telehealth, and Digital Approaches for	
Smoking Cessation	72
Smoking Cessation Treatments Among Patients With Cancer	79
Medications for Smoking Cessation Among Patients With Cancer	80
Behavioral Interventions for Smoking Cessation Among Patients With Cancer	85
Relapse Prevention and Chronic Care for Cancer Populations	91
Special Considerations and Barriers Concerning Smoking Cessation Treatment in Cancer	
Care Settings	92
Patient-Level Barriers to Treating Tobacco Use in Cancer Care Settings	92
Psychiatric Comorbidity	92
Oncology Treatment–Related Challenges	93
Physical Concerns	94
Psychological Aspects	94
Treatment Engagement and Adherence	94
Clinician-Level Barriers to Treating Tobacco Use in Cancer Care Settings	96
Leveraging the Opportunity for Intervention	96
Barriers to Intervention and Strategies to Overcome Them	96
Changing Clinician Approaches to Smoking Cessation Treatment	97
Systems-Level Barriers to Treating Tobacco Use in Cancer Care Settings	98
Summary: Special Considerations and Barriers Concerning Smoking Cessation	
Treatment in Cancer Care Settings	98
Special Topics in the Treatment of Smoking in Patients With Cancer	99
Addressing Motivation to Quit	99
Relevance of Pharmacogenetic Intervention: Steps Toward Personalized Medicine	99
Treatment Effectiveness and Access Across Different Populations	101
The Use of Electronic Nicotine Delivery Systems (ENDS) in Patients With Cancer	101
Prevalence of ENDS Use	102
Health Effects of ENDS	102
ENDS Use and Cessation From Cigarettes in the General Population	103
Randomized Controlled Trials	104
ENDS Use and Cessation From Cigarettes in Cancer Populations	106
Published Guidelines on ENDS Use Among Patients With Cancer	.107

Summary: The Use of ENDS in Patients With Cancer	107
Summary	108
Conclusions	109
References	110

Figures and Tables

Figure 3.1 Figure 3.2	Smokefree.gov Initiative Digital Interventions Examples of Patient-, Clinician-, and Systems-Level Barriers to the Use of	75
8	Smoking Cessation Treatment in Cancer Care Settings	92
Table 3.1	Findings Regarding Interventions for Smoking Cessation and Treatments for	
	Nicotine Dependence From the 2020 Surgeon General's Report on Smoking	
	Cessation	57
Table 3.2	Effectiveness and Abstinence Rates for Various Medications and Medication	
	Combinations Compared to Placebo at 6-Months Post-quit	60
Table 3.3	Odds of Smoking Cessation Using Medications	65
Table 3.4	Odds of Smoking Cessation Using Behavioral Interventions	66
Table 3.5	Elements of Brief Tobacco-Cessation Counseling Based on the PHS Clinical	
	Practice Guideline. Treating Tobacco Use and Dependence: 2008 Update	67
Table 3.6	Studies of Smoking Cessation Interventions Among Patients With Cancer	82

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 MoonshotSM 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 ladders¹⁸ 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 guit 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 guit 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 guit 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 3.1Findings Regarding Interventions for Smoking Cessation and Treatments for Nicotine
Dependence From the 2020 Surgeon General's Report on Smoking Cessation

 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. 	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 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. 	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:* U.S. Department of Health and Human Services 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 stimuli⁵⁶ 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).

Medication	Number of arms	Estimated odds ratio (95% Cl)	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	
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	
Nicotine gum (6–14 weeks)	15	1.5 (1.2–1.7)	19.0 (16.5–21.9)

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% Cl)	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)

Table 3.2 (continued)

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 "<u>Patient-Level Barriers to Treating Tobacco Use in Cancer Care Settings</u>"). 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 α 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 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.

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

Table 3.3 Odds of Smoking Cessation Using Medications

Note: Smoking cessation duration varied by study. NRT = nicotine replacement therapy.

^aWhen 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).

Comparison	Odds ratio, risk ratio, or <i>g</i> (95% Cl)	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

Table 3.4 Odds of Smoking Cessation Using Behavioral Interventions

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

^aIndicates 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. *Source*: 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 inperson, 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: Set a quit date. Ideally, the quit date should be within 2 weeks. Tell family, friends, and co-workers about quitting, and request understanding and support. Anticipate challenges to the upcoming quit attempt, particularly during the critical first few weeks. These include nicotine withdrawal symptoms. Remove 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.

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.	<i>Sources</i> . Federal agencies, nonprofit agencies, national quitline network (1-800-QUIT-NOW, Text QUITNOW to 333888, or local/state/tribal health departments/quitlines).

Table 3.5 (continued)

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 nointervention controls.¹⁷ RCTs have demonstrated the efficacy of CBT-based smoking cessation treatments in hospitalized patients who smoke¹⁵⁴ and African-American people who smoke.¹⁵⁵ There is evidence that even relatively brief exposures to CBT can significantly increase longterm 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 treatments were not more effective than comparator 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 discontinued²⁰⁰; 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 metaanalyses 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 "<u>Behavioral Interventions for Smoking Cessation Among Patients With Cancer</u>" 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., inperson 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 nonweb 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 longterm (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 metaanalysis, 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 (<u>https://smokefree.gov</u>) 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 (<u>https://smokefree.gov/tools-tips/speak-expert</u>). 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 report³¹ 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 studies²⁵³ 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 (<u>https://smokefree.gov/tools-tips/apps</u>), 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 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 placebocontrolled 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 followup 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 medications²³³ 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

Timing of quit Quit rate^b Sample Quit rate Methodological Study Intervention arm Control arm size rate assessment^a intervention arm control arm comments Studies of smoking cessation medications (with or without counseling) Randomized studies Rettig et al. 2018²⁷³ 29 Combined NRT. Counseling, referral 8 weeks from 74% 30% Randomized. baseline biochemical bupropion, or varenicline; confirmation counseling 61% (adherent Schnoll et al. 2019²⁷² 207 24 weeks 24 weeks from 45% 12 weeks Randomized. varenicline. baseline biochemical varenicline. patients), 10% (adherent (nonadherent) confirmation counseling counseling patients), 13% (nonadherent) Randomized, self-Duffy et al. 2006274 184 NRT or bupropion, Counseling, referral 6 months from 31% 15% counseling baseline reported cessation Schnoll et al. 2010²⁶⁵ 246 12 and 27 weeks 24% (12wk), Bupropion, patch, Placebo, patch, 27% (12wk), Randomized, 18% (27wk) counseling counselina from baseline 17% (27wk) biochemical confirmation 14% 6% Pollak et al. 2018269 30 NRT, counseling Waitlist control 2 months after Randomized, (received NRT and randomization biochemical counseling 2 months confirmation after randomization) Thomsen et al. 2010²⁶⁷ 130 NRT, counseling Advice, referral 12 months 13% 9% Randomized. selfpostoperative reported cessation Wakefield et al. 2004²⁶⁸ 137 NRT, counseling Advice, referral 6 months from 5% 6% Randomized, baseline biochemical confirmation Nonrandomized studies 49 Varenicline, Varenicline 12 weeks from 34% 14% Quasi-experimental, Park et al. 2011271 counseling baseline biochemical confirmation

Table 3.6 Studies of Smoking Cessation Interventions Among Patients With Cancer

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 smokin	g interven	tions (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	СМ	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. ^bQuit rates are rounded to nearest integer. ^cStudies of smoking cessation medications are those in which medication varied across trial arms. ^dStudies 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 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 colleagues²³³ 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 cancer⁴⁸⁹ 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 ($p < 10^{-10}$.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 guit 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 guit previously and additional guitting 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 guitline intervention or a reactive guitline 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 guitline 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 appbased 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 \geq 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 success³⁰¹ (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 distress³⁰² 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 metaanalysis 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 use³⁰⁸ and developing nicotine dependence.³⁰⁹ Studies indicate that individuals with anxiety disorders tend to have less smoking cessation success than other people who smoke³¹⁰ 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 disorders³¹⁸ 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 cancer³³¹ 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 settings³³⁸ 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 disease³⁴⁴; 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 Cancer³⁵⁸ 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 guit 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 dependence¹³⁶ and a national quitline portal (see "<u>Telephone Counseling</u>"). 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 guit 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 delivered³⁸¹ (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; 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 way³⁸³ 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 and the response 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 4year 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 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 ecigarettes is associated with increased smoking cessation compared with less frequent use of ecigarettes".^{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 cessation³¹; 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 in nonvolunteers. For instance, 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 nicotinecontaining 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 nicotinecontaining 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 followup (20.5% vs. 9.9%, RD = 10.6, 95% CI = 1.8–19.4). This study suggests that nicotinecontaining 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 nonnicotine ENDS plus counseling group, and 17% of the counseling-only group reporting nonstudy 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 FDAapproved 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.

References

- 1. U.S. Department of Health and Human Services (USDHHS). The health consequences of smoking—50 years of progress: a report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.
- Westmaas JL, Newton CC, Stevens VL, Flanders WD, Gapstur SM, Jacobs EJ. Does a recent cancer diagnosis predict smoking cessation? An analysis from a large prospective U.S. cohort. J Clin Oncol. 2015;33(15):1647-52. doi: 10.1200/JCO.2014.58.3088.
- Luo SJ, Choi E, Aredo JV, Wilkens LR, Tammemagi MC, LeMarchand L, et al. Smoking cessation after lung cancer diagnosis and the risk of second primary lung cancer: the Multiethnic Cohort Study. JNCI Cancer Spectr. 2021 Oct;5(5):pkab076. doi: 10.1093/jncics/pkab076.
- 4. Goldstein AO, Ripley-Moffitt CE, Pathman DE, Patsakham KM. Tobacco use treatment at the U.S. National Cancer Institute's designated cancer centers. Nicotine Tob Res. 2013;15(1):52-8. doi: 10.1093/ntr/nts083.
- 5. Toll BA, Brandon TH, Gritz ER, Warren GW, Herbst RS. AACR subcommittee on tobacco and cancer. Clin Cancer Res. 2013;19(8):1941-8. doi: 10.1158/1078-0432.CCR-13-0666.
- 6. Gritz ER, Toll BA, Warren GW. Tobacco use in the oncology setting: advancing clinical practice and research. Cancer Epidemiol Biomarkers Prev. 2014;23(1):3-9. doi: 10.1158/1055-9965.EPI-13-0896.
- 7. Chang EHE, Braith A, Hitsman B, Schnoll RA. Treating nicotine dependence and preventing smoking relapse in cancer patients. Expert Rev Qual Life Cancer Care. 2017;2(1):23-39. doi: 10.1080/23809000.2017.1271981.
- Gallaway MS, Glover-Kudon R, Momin B, Puckett M, Lunsford NB, Ragan KR, et al. Smoking cessation attitudes and practices among cancer survivors—United States, 2015. J Cancer Surviv. 2019;13(1):66-74. doi: 10.1007/s11764-018-0728-2.
- 9. Fiore M, Adsit R, Zehner M, McCarthy D, Lundsten S, Hartlaub P, et al. An electronic health record–based interoperable eReferral system to enhance smoking quitline treatment in primary care. J Am Med Inform Assoc. 2019;26(8-9):778-86. doi: 10.1093/jamia/ocz044.
- 10. Croyle RT, Morgan GD, Fiore MC. Addressing a core gap in cancer care—the NCI moonshot program to help oncology patients stop smoking. N Engl J Med. 2019;380(6):512-5. doi: 10.1056/NEJMp1813913.
- 11. Peters EN, Torres E, Toll BA, Cummings KM, Gritz ER, Hyland A, et al. Tobacco assessment in actively accruing National Cancer Institute cooperative group program clinical trials. J Clin Oncol. 2012;30(23):2869-75. doi: 10.1200/JCO.2011.40.8815.
- Price S, Hitsman B, Veluz-Wilkins A, Blazekovic S, Brubaker TR, Leone F, et al. The use of varenicline to treat nicotine dependence among cancer patients. Psychooncology. 2017;26(10):1526-34. doi: 10.1002/pon.4166.
- 13. Cooley ME, Poghosyan H, Sprunck-Harrild K, Winickoff JP, Edge SB, Emmons KM. Tobacco treatment implementation within 28 commission on cancer accredited programs in the Northeast region of the USA: a pilot study. Transl Behav Med. 2018;8(5):706-13. doi: 10.1093/tbm/ibx024.
- 14. Day AT, Tang L, Karam-Hage M, Fkhry C. Tobacco treatment programs at National Cancer Institutedesignated cancer centers. Am J Clin Oncol. 2019;42(4):407-10. doi: 10.1097/COC.00000000000522.
- Creamer MR, Wang TW, Babb S, Cullen KA, Day H, Willis G, et al. Tobacco product use and cessation indicators among adults—United States, 2018. MMWR Morb Mortal Wkly Rep. 2019;68:1013-9. doi: 10.15585/mmwr.mm6845a2.
- 16. National Comprehensive Cancer Network® (NCCN®). NCCN clinical practice guidelines in oncology (NCCN guidelines®): smoking cessation, version 1.2022 [Internet]. Plymouth Meeting, PA: The Network; 2022 [cited 2022 Jun 22]. Available from: <u>https://www.nccn.org/professionals/physician_gls/pdf/smoking.pdf</u>.
- 17. Fiore MC, Jaen CR, Baker TB, Bailey WC, Benowitz NL, Curry SJ, et al. Treating tobacco use and dependence: 2008 update [Internet]. Bethesda, MD: USDHHS; 2008 [cited 2022 Jan 30]. Available from: https://www.ahrq.gov/prevention/guidelines/tobacco/index.html.
- 18. Boudreaux ED, Sullivan A, Abar B, Bernstein SL, Ginde AA, Camargo CA Jr. Motivation rulers for smoking cessation: a prospective observational examination of construct and predictive validity. Addict Sci Clin Pract. 2012;7(1):8. doi: 10.1186/1940-0640-7-8.
- 19. Hartmann-Boyce J, Stead LF, Cahill K, Lancaster T. Efficacy of interventions to combat tobacco addiction: Cochrane update of 2013 reviews. Addiction. 2014;109(9):1414-25. doi: 10.1111/add.12633.
- 20. Klemperer EM, Mermelstein R, Baker TB, Hughes JR, Fiore MC, Piper ME, et al. Predictors of smoking cessation attempts and success following motivation-phase interventions among people initially unwilling to quit smoking. Nicotine Tob Res. 2020;22(9):1446-52. doi: 10.1093/ntr/ntaa051.

- 21. Kotz D, Brown J, West R. 'Real-world' effectiveness of smoking cessation treatments: a population study. Addiction. 2014;109(3):491-9. doi: 10.1111/add.12429.
- 22. Silfen SL, Cha J, Wang JJ, Land TG, Shih SC. Patient characteristics associated with smoking cessation interventions and quit attempt rates across 10 community health centers with electronic health records. Am J Public Health. 2015;105(10):2143-9. doi: 10.2105/AJPH.2014.302444.
- 23. Borland R, Yong HH, Balmford J, Cooper J, Cummings KM, O'Connor RJ, et al. Motivational factors predict quit attempts but not maintenance of smoking cessation: findings from the International Tobacco Control Four country project. Nicotine Tob Res. 2010;12 Suppl(Suppl 1):S4-11. doi: 10.1093/ntr/ntq050.
- 24. Vangeli E, Stapleton J, Smit ES, Borland R, West R. Predictors of attempts to stop smoking and their success in adult general population samples: a systematic review. Addiction. 2011;106(12):2110-21. doi: 10.1111/j.1360-0443.2011.03565.x.
- 25. Hyland Å, Borland R, Li Q, Yong HH, McNeill A, Fong GT, et al. Individual-level predictors of cessation behaviours among participants in the International Tobacco Control (ITC) Four Country Survey. Tob Control. 2006;15(Suppl 3):iii83-94. doi: 10.1136/tc.2005.013516.
- 26. Ussher M, Kakar G, Hajek P, West R. Dependence and motivation to stop smoking as predictors of success of a quit attempt among smokers seeking help to quit. Addict Behav. 2016;53:175-80. doi: 10.1016/j.addbeh.2015.10.020.
- 27. Babb S, Malarcher A, Schauer G, Asman K, Jamal A. Quitting smoking among adults—United States, 2000–2015. MMWR Morb Mortal Wkly Rep. 2017;65(52):1457-64. doi: 10.15585/mmwr.mm6552a1.
- Wang TW, Walton K, Jamal A, Babb SD, Schecter A, Prutzman YM, et al. State-specific cessation behaviors among adult cigarette smokers—United States, 2014–2015. Prev Chronic Dis. 2019;16:e26. doi: 10.5888/pcd16.180349.
- 29. Naavaal S, Malarcher A, Xu X, Zhang L, Babb S. Variations in cigarette smoking and quit attempts by health insurance among us adults in 41 states and 2 jurisdictions, 2014. Public Health Rep. 2018;133(2):191-9. doi: 10.1177/0033354917753120.
- 30. Walton K, Wang TW, Schauer GL, Hu S, McGruder HF, Jamal A, et al. State-specific prevalence of quit attempts among adult cigarette smokers—United States, 2011–2017. MMWR Morb Mortal Wkly Rep. 2019;68(28):621-6. doi: 10.15585/mmwr.mm6828a1\.
- 31. U.S. Department of Health and Human Services (USDHHS). Smoking cessation: a report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2020.
- 32. McBride CM, Ostroff JS. Teachable moments for promoting smoking cessation: the context of cancer care and survivorship. Cancer Control. 2003;10(4):325-33. doi: 10.1177/107327480301000407.
- 33. Karam-Hage M, Cinciripini PM, Gritz ER. Tobacco use and cessation for cancer survivors: an overview for clinicians. CA Cancer J Clin. 2014;64(4):272-90. doi: 10.3322/caac.21231.
- 34. Berg CJ, Carpenter MJ, Jardin B, Ostroff JS. Harm reduction and cessation efforts and interest in cessation resources among survivors of smoking-related cancers. J Cancer Surviv. 2013;7(1):44-54. doi: 10.1007/s11764-012-0243-9.
- 35. Ostroff JS, Jacobsen PB, Moadel AB, Spiro RH, Shah JP, Strong EW, et al. Prevalence and predictors of continued tobacco use after treatment of patients with head and neck cancer. Cancer. 1995;75(2):569-76. doi: 10.1002/1097-0142(19950115)75:2<569::aid-cncr2820750221>3.0.co;2-i.
- 36. Gritz ER, Carr CR, Rapkin D, Abemayor E, Chang LJ, Wong WK, et al. Predictors of long-term smoking cessation in head and neck cancer patients. Cancer Epidemiol Biomarkers Prev. 1993;2(3):261-70.
- Schnoll RA, Malstrom M, James C, Rothman RL, Miller SM, Ridge JA. Correlates of tobacco use among smokers and recent quitters diagnosed with cancer. Patient Educ Couns. 2002;46(2):137-45. doi: 10.1016/s0738-3991(01)00157-4.
- 38. Cooley ME, Finn KT, Wang Q, Roper K, Morones S, Shi L, et al. Health behaviors, readiness to change, and interest in health promotion programs among smokers with lung cancer and their family members: a pilot study. Cancer Nurs. 2013;36(2):145-54. doi: 10.1097/NCC.0b013e31825e4359.
- 39. Little MA, Klesges RC, Bursac Z, Ebbert JO, Halbert JP, Dunkle AN, et al. Why don't cancer survivors quit smoking? An evaluation of readiness for smoking cessation in cancer survivors. J Cancer Prev. 2018;23(1):44-50. doi: 10.15430/JCP.2018.23.1.44.
- 40. Sampson L, Papadakos J, Milne V, Le LW, Liu G, Abdelmutti N, et al. Preferences for the provision of smoking cessation education among cancer patients. J Cancer Educ. 2018;33(1):7-11. doi: 10.1007/s13187-016-1035-0.

- Gritz E, Talluri R, Domgue JF, Tami-Maury I, Shete S. Smoking behaviors in survivors of smoking-related and non-smoking-related cancers. JAMA Netw Open. 2020;3(7):e209072. doi: 10.1001/jamanetworkopen.2020.9072.
- 42. U.S.A. v. Philip Morris USA Inc. et al., final opinion, United States District Court for the District of Columbia, 2006 Aug 17.
- Bozinoff N, Le Foll B. Understanding the implications of the biobehavioral basis of nicotine addiction and its impact on the efficacy of treatment. Expert Rev Respir Med. 2018;12(9):793-804. doi: 10.1080/17476348.2018.1507736.
- 44. Kathuria H, Leone FT, Neptune ER. Treatment of tobacco dependence: current state of the art. Curr Opin Pulm Med. 2018;24(4):327-34. doi: 10.1097/MCP.00000000000491.
- Stead LF, Koilpillai P, Fanshawe TR, Lancaster T. Combined pharmacotherapy and behavioural interventions for smoking cessation. Cochrane Database Syst Rev. 2016;3:CD008286. doi: 10.1002/14651858.CD008286.pub3.
- U.S. Preventive Services Task Force. Interventions for tobacco smoking cessation in adults, including pregnant persons: U.S. Preventive Services Task Force recommendation statement. JAMA. 2021;325(3):265-79. doi: 10.1001/jama.2020.25019.
- 47. Piasecki TM, Jorenby DE, Smith SS, Fiore MC, Baker TB. Smoking withdrawal dynamics: I. Abstinence distress in lapsers and abstainers. J Abnorm Psychol. 2003;112(1):3-13.
- 48. Piasecki TM, Jorenby DE, Smith SS, Fiore MC, Baker TB. Smoking withdrawal dynamics: II. Improved tests of withdrawal-relapse relations. J Abnorm Psychol. 2003;112(1):14.
- 49. Piper ME, Federmen EB, McCarthy DE, Bolt DM, Smith SS, Fiore MC, et al. Using mediational models to explore the nature of tobacco motivation and tobacco treatment effects. J Abnorm Psychol. 2008;117(1):94. doi: 10.1037/0021-843X.117.1.94.
- 50. Piper ME, Schlam TR, Cook JW, Sheffer MA, Smith SS, Loh W-Y, et al. Tobacco withdrawal components and their relations with cessation success. Psychopharmacology (Berl). 2011;216(4):569-78. doi: 10.1007/s00213-011-2250-3.
- 51. Fiore MC, Baker TB. Clinical practice. Treating smokers in the health care setting. N Engl J Med. 2011 Sep 29;365(13):1222-31.
- 52. Rice ME, Cragg SJ. Nicotine amplifies reward-related dopamine signals in striatum. Nat. Neurosci. 2004;7:583-84. doi: 10.1038/nn1244.
- 53. Rao TS, Correa LD, Adams P, Santori EM, Sacaan AI. Pharmacological characterization of dopamine, norepinephrine and serotonin release in the rat prefrontal cortex by neuronal nicotinic acetylcholine receptor agonists. Brain Res. 2003;990(1-2):203-8. doi: 10.1016/s0006-8993(03)03532-7.
- 54. Benowitz, N. Pharmacology of nicotine: addiction, smoking-induced disease, and therapeutics. Annu Rev Pharmacol Toxicol. 2009;49:57-71. doi: 10.1146/annurev.pharmtox.48.113006.094742.
- 55. Nestler EJ. Is there a common molecular pathway for addiction? Nat Neurosci. 2005;8(11):1445-9. doi: 10.1038/nn1578.
- 56. Berridge KC. The debate over dopamine's role in reward: the case for incentive salience. Psychopharmacology (Berl). 2007;191(3):391-431. doi: 10.1007/s00213-006-0578-x.
- 57. Brunzell DH, Picciotto MR. Molecular mechanisms underlying the motivational effects of nicotine. Nebr Symp Motiv. 2009;55:17-30. doi: 10.1007/978-0-387-78748-0_3.
- David V, Besson M, Changeux JP, Granon S, Cazala P. Reinforcing effects of nicotine microinjections into the ventral tegmental area of mice: dependence on cholinergic nicotinic and dopaminergic D1 receptors. Neuropharmacology. 2006 Jun;50(8):1030-40.
- 59. Epping-Jordan MP, Watkins SS, Koob GF, Markou A. Dramatic decreases in brain reward function during nicotine withdrawal. Nature. 1998;393(6680):76-9. doi: 10.1038/30001.
- 60. Cosgrove KP, Esterlis I, Sandiego C, Petrulli R, Morris ED. Imaging tobacco smoking with PET and SPECT. Curr Top Behav Neurosci. 2015;24:1-17. doi: 10.1007/978-3-319-13482-6_1.
- 61. Ray R, Loughead J, Wang Z, Detre J, Yang E, Gur R, et al. Neuroimaging, genetics, and the treatment of nicotine addiction. Behav Brain Res. 2008;193(2):156-69. doi: 10.1016/j.bbr.2008.05.021.
- 62. Benowitz NL. Nicotine addiction. N Engl J Med. 2010;362(24):2295-303. doi: 10.1056/NEJMra0809890.
- 63. Hughes JR, Hatsukami D. Signs and symptoms of tobacco withdrawal. *Arch Gen Psychiatry*. 1986;43(3):289-94. doi: 10.1001/archpsyc.1986.01800030107013.
- 64. Javitz HS, Lerman C, Swan GE. Comparative dynamics of four smoking withdrawal symptom scales. Addiction. 2012;107(8):1501-11. doi: 10.1111/j.1360-0443.2012.03838.x.

- 65. Javitz HS, Swan GE, Lerman C. The dynamics of the urge-to-smoke following smoking cessation via pharmacotherapy. Addiction. 2011;106(10):1835-45. doi: 10.1111/j.1360-0443.2011.03495.x.
- 66. McCarthy DE, Piasecki TM, Fiore MC, Baker TB. Life before and after quitting smoking: an electronic diary study. J Abnorm Psychol. 2006;115(3):454-66. doi: 10.1037/0021-843X.115.3.454.
- 67. Cook JW, Piper ME, Leventhal AM, Schlam TR, Fiore MC, Baker TB. Anhedonia as a component of the tobacco withdrawal syndrome. J Abnorm Psychol. 2015;124(1):215-25. doi: 10.1037/abn0000016.
- 68. Bruijnzeel AW. Reward processing and smoking. Nicotine Tob Res. 2017;19(6):661-2. doi: 10.1093/ntr/ntw303.
- 69. Paterson NE, Balfour DJ, Markou A. Chronic bupropion attenuated the anhedonic component of nicotine withdrawal in rats via inhibition of dopamine reuptake in the nucleus accumbens shell. Eur J Neurosci. 2007;25(10):3099-108. doi: 10.1111/j.1460-9568.2007.05546.x.
- Shiffman S, Ferguson SG, Gwaltney CJ, Balabanis MH, Shadel WG. Reduction of abstinence-induced withdrawal and craving using high-dose nicotine replacement therapy. Psychopharmacology (Berl). 2006;184(3-4):637-44. doi: 10.1007/s00213-005-0184-3.
- 71. West R, Shiffman S. Effect of oral nicotine dosing forms on cigarette withdrawal symptoms and craving: a systematic review. Psychopharmacology (Berl). 2001;155(2):115-22.
- 72. Ashare RL, Falcone M, Lerman C. Cognitive function during nicotine withdrawal: implications for nicotine dependence treatment. Neuropharmacol. 2014;76 Pt B(0 0):581-91. doi: 10.1016/j.neuropharm.2013.04.034.
- 73. Valentine G, Sofuoglu M. Cognitive effects of nicotine: recent progress. Curr Neuropharmacol. 2018;16(4):403-14. doi: 10.2174/1570159X15666171103152136.
- 74. Evans DE, Maxfield ND, Van Rensburg KJ, Oliver JA, Jentink KG, Drobes DJ. Nicotine deprivation influences P300 markers of cognitive control. Neuropsychopharmacology. 2013;38(12):2525-31. doi: 10.1038/npp.2013.159.
- Loughead J, Wileyto EP, Valdez JN, Sanborn P, Tang K, Strasser AA, et al. Effect of abstinence challenge on brain function and cognition in smokers differs by COMT genotype. Mol Psychiatry. 2009;14(8):820-6. doi: 10.1038/mp.2008.132.
- Hall FS, Der-Avakian A, Gould TJ, Markou A, Shoaib M, Young JW. Negative affective states and cognitive impairments in nicotine dependence. Neurosci Biobehav Rev. 2015;58:168-85. doi: 10.1016/j.neubiorev.2015.06.004.
- 77. Baker TB, Piper ME, McCarthy DE, Majeskie MR, Fiore MC. Addiction motivation reformulated: an affective processing model of negative reinforcement. Psychol Rev. 2004;111(1):33-51. doi: 10.1037/0033-295X.111.1.33.
- 78. Buczek Y, Lê AD, Wang A, Stewart J, Shaham Y. Stress reinstates nicotine seeking but not sucrose solution seeking in rats. Psychopharmacology (Berl). 1999;144(2):183-8.
- 79. Grella SL, Funk D, Coen K, Li Z, Lê AD. Role of the kappa-opioid receptor system in stress-induced reinstatement of nicotine seeking in rats. Behav Brain Res. 2014;265:188-97. doi: 10.1016/j.bbr.2014.02.029.
- Shiffman S, Paty JA, Gnys M, Kassel JA, Hickcox M. First lapses to smoking: within-subjects analysis of realtime reports. J Consult Clin Psychol. 1996;64(2):366-79. doi: 10.1037//0022-006x.64.2.366.
- Yu G, Sharp BM. Basolateral amygdala and ventral hippocampus in stress-induced amplification of nicotine self-administration during reacquisition in rat. Psychopharmacology (Berl). 2015;232(15):2741-9. doi: 10.1007/s00213-015-3911-4.
- 82. Bradford DE, Curtin JJ, Piper ME. Anticipation of smoking sufficiently dampens stress reactivity in nicotinedeprived smokers. J Abnorm Psychol. 2015;124(1):128-36. doi: 10.1037/abn0000007.
- 83. Minami H, Frank BE, Bold KW, McCarthy DE. Ecological momentary analysis of the relations among stressful events, affective reactivity, and smoking among smokers with high versus low depressive symptoms during a quit attempt. Addiction. 2018;113(2):299-312. doi: 10.1111/add.13964.
- 84. Cook JW, Baker TB, Beckham JC, McFall M. Smoking-induced affect modulation in nonwithdrawn smokers with posttraumatic stress disorder, depression, and in those with no psychiatric disorder. J Abnorm Psychol. 2017;126(2):184-98. doi: 10.1037/abn0000247.
- 85. Perkins KA, Karelitz JL, Conklin CA, Sayette MA, Giedgowd GE. Acute negative affect relief from smoking depends on the affect situation and measure but not on nicotine. Biol Psychiatry. 2010;67(8):707-14. doi: 10.1016/j.biopsych.2009.12.017.
- Piper ME, Kenford S, Fiore MC, Baker TB. Smoking cessation and quality of life: changes in life satisfaction over three years following a quit attempt. Ann Behav Med. 2012;43(2):262-70. doi: 10.1007/s12160-011-9329-2.

- 87. Taylor G, McNeill A, Girling A, Farley A, Lindson-Hawley N, Aveyard P, et al. Change in mental health after smoking cessation: systematic review and meta-analysis. BMJ. 2014;348:g1151. doi: 10.1136/bmj.g1151.
- Stoker AK, Markou A. Neurobiological bases of cue- and nicotine-induced reinstatement of nicotine seeking: implications for the development of smoking cessation medications. Curr Top Behav Neurosci. 2015;24:125-54. doi: 10.1007/978-3-319-13482-6_5.
- 89. Ferguson SG, Shiffman S. The relevance and treatment of cue-induced cravings in tobacco dependence. J Subst Abuse Treat. 2009;36(3):235-43. doi: 10.1016/j.jsat.2008.06.005.
- 90. Shiffman S, Dunbar M, Kirchner T, Li X, Tindle H, Anderson S, et al. Smoker reactivity to cues: effects on craving and on smoking behavior. J Abnorm Psychol. 2013;122(1):264-80. doi: 10.1037/a0028339.
- 91. U.S. National Cancer Institute. The role of the media in promoting and reducing tobacco use. National Cancer Institute Tobacco Control Monograph 19. NIH Publication No. 07-6242. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute; June 2008.
- 92. U.S. National Cancer Institute and World Health Organization. The economics of tobacco and tobacco control. National Cancer Institute Tobacco Control Monograph 21. NIH Publication No. 16-CA-8029A. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute; and Geneva, CH: World Health Organization; 2016.
- 93. U.S. National Cancer Institute. A socioecological approach to addressing tobacco-related health disparities. National Cancer Institute Tobacco Control Monograph 22. NIH publication no. 17-CA-8035A. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute; 2017.
- 94. U.S. Department of Health and Human Services. Preventing tobacco use among youth and young adults: a report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2012.
- Siahpush M, Shaikh RA, Cummings KM, Hyland A, Dodd M, Carlson L, et al. The association of point-of-sale cigarette marketing with cravings to smoke: results from a cross-sectional population-based study. Tob Control. 2016;25(4):402-5. doi: 10.1136/tobaccocontrol-2015-052253.
- 96. Markou A, Li J, Tse K, Li X. Cue-induced nicotine-seeking behavior after withdrawal with or without extinction in rats. Addict Biol. 2018;23(1):111-9. doi: 10.1111/adb.12480.
- 97. Liu X, Caggiula AR, Yee SK, Nobuta H, Poland RE, Pechnick RN. Reinstatement of nicotine-seeking behavior by drug-associated stimuli after extinction in rats. Psychopharmacology (Berl). 2006;184(3-4):417-25. doi: 10.1007/s00213-005-0134-0.
- 98. Ferguson SG, Shiffman S, Blizzard L. Triggers of smoking lapses over the course of a quit attempt. J Smok Cessat. 2017;12(4):205-12. doi: 10.1017/jsc.2016.21.
- 99. Baker TB, Piper ME, Schlam TR, et al. Are tobacco dependence and withdrawal related among heavy smokers? Relevance to conceptualizations of dependence. J Abnorm Psychol. 2012;121(4):909-21. doi: 10.1037/a0027889.
- Everitt BJ, Robbins TW. Neural systems of reinforcement for drug addiction: from actions to habits to compulsion [published correction appears in Nat Neurosci. 2006;9(7):979]. Nat Neurosci. 2005;8(11):1481-9. doi: 10.1038/nn1579.
- 101. Tiffany ST. A cognitive model of drug urges and drug-use behavior: role of automatic and nonautomatic processes. Psychol Rev. 1990;97(2):147-68. doi: 10.1037/0033-295x.97.2.147.
- 102. Guide to Community Preventive Services. Tobacco use: mobile phone text messaging cessation interventions [Internet]. Atlanta: Community Preventive Services Task Force; 2020 Jul [updated 2021 Nov 12]. Available from: <u>https://www.thecommunityguide.org/findings/tobacco-use-mobile-phone-text-messaging-cessationinterventions</u>.
- 103. Guide to Community Preventive Services. Tobacco use: internet-based cessation interventions [Internet]. Atlanta: Community Preventive Services Task Force; 2019 Dec [updated 2021 Nov 12]. Available from: https://www.thecommunityguide.org/findings/tobacco-use-internet-based-cessation-interventions.
- 104. Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database Syst Rev. 2013;5:CD009329. doi: 10.1002/14651858.CD009329.pub2.
- 105. Livingstone-Banks J, Norris E, Hartmann-Boyce J, West R, Jarvis M, Hajek P. Relapse prevention interventions for smoking cessation. Cochrane Database Syst Rev. 2019;2:CD003999. doi: 10.1002/14651858.CD003999.pub5.
- 106. Stead LF, Buitrago D, Preciado N, Sanchez G, Hartmann-Boyce J, Lancaster T. Physician advice for smoking cessation. Cochrane Database Syst Rev. 2013;5:CD000165. doi: 10.1002/14651858.CD000165.pub4.

- 107. Whittaker R, McRobbie H, Bullen C, Rodgers A, Gu Y, Dobson R. Mobile phone text messaging and appbased interventions for smoking cessation. Cochrane Database Syst Rev. 2019;10:CD006611. doi: 10.1002/14651858.CD006611.pub5.
- 108. Lancaster T, Stead LF. Individual behavioural counselling for smoking cessation. Cochrane Database Syst Rev. 2017;3:CD001292. doi: 10.1002/14651858.CD001292.pub3.
- 109. Hartmann-Boyce J, Livingstone-Banks J, Ordóñez-Mena JM, Fanshawe TR, Lindson N, Freeman SC, et al. Behavioural interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database Syst Rev. 2021;1:CD013229. doi: 10.1002/14651858.CD013229.pub2.
- 110. Barua RS, Rigotti NA, Benowitz NL, Cummings KM, Jazayeri MA, Morris PB, et al. 2018 ACC expert consensus decision pathway on tobacco cessation treatment: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol. 2018;72(25):3332-65.
- 111. Leas EC, Pierce JP, Benmarhnia T, White MM, Noble ML, Trinidad DR, et al. Effectiveness of pharmaceutical smoking cessation aids in a nationally representative cohort of American smokers. J Natl Cancer Inst. 2018;110(6):581-87. doi: 10.1093/jnci/djx240.
- 112. Hays JT, Leischow SJ, Lawrence D, Lee TC. Adherence to treatment for tobacco dependence: association with smoking abstinence and predictors of adherence. Nicotine Tob Res. 2010;12(6):574-81. doi: 10.1093/ntr/ntq047.
- 113. Baker TB, McCarthy DE. Smoking treatment: a report card on progress and challenges. Annu Rev Clin Psychol. 2021;17:1-30.
- 114. Simmons VN, Litvin EB, Jacobsen PB, Patel RD, McCaffrey JC, Oliver JA, et al. Predictors of smoking relapse in patients with thoracic cancer or head and neck cancer. Cancer. 2013;119(7):1420-7. doi: 10.1002/cncr.27880.
- 115. Giulietti F, Filipponi A, Rosettani G, Giordano P, Iacoacci C, Spannella F, et al. Pharmacological approach to smoking cessation: an updated review for daily clinical practice. High Blood Press Cardiovasc Prev. 2020;27(5):349-62.
- 116. Lindson N, Chepkin SC, Ye W, Fanshawe TR, Bullen C, Hartmann-Boyce J. Different doses, durations and modes of delivery of nicotine replacement therapy for smoking cessation. Cochrane Database Syst Rev. 2019;4:CD013308. doi: 10.1002/14651858.CD013308.
- 117. Aveyard P, Lindson N, Tearne S, Adams R, Ahmed K, Alekna R, et al. Nicotine preloading for smoking cessation: the Preloading RCT. Health Technol Assess. 2018;22(41):1-84. doi: 10.3310/hta22410.
- 118. Fucito LM, Bars MP, Forray A, Rojewski AM, Shiffman S, Selby P, et al. Addressing the evidence for FDA nicotine replacement therapy label changes: a policy statement of the Association for the Treatment of Tobacco Use and Dependence and the Society for Research on Nicotine and Tobacco. Nicotine Tob Res. 2014;16(7):909-14. doi: 10.1093/ntr/ntu087.
- 119. Moore D, Aveyard P, Connock M, Wang D, Fry-Smith A, Barton P. Effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking: systematic review and meta-analysis. BMJ. 2009;338:b1024. doi: 10.1136/bmj.b1024.
- 120. Lindson-Hawley N, Hartmann-Boyce J, Fanshawe TR, Begh R, Farley A, Lancaster T. Interventions to reduce harm from continued tobacco use. Cochrane Database Syst Rev. 2016;(10):CD005231. doi: 10.1002/14651858.CD005231.pub3.
- 121. Carpenter MJ, Wahlquist AE, Dahne J, Gray KM, Garrett-Mayer E, Cummings KM, et al. Nicotine replacement therapy sampling for smoking cessation within primary care: results from a pragmatic cluster randomized clinical trial. Addiction. 2020;115(7):1358-67. doi: 10.1111/add.14953.
- 122. Hughes JR, Stead LF, Hartmann-Boyce J, Cahill K, Lancaster T. Antidepressants for smoking cessation. Cochrane Database Syst Rev. 2014;1:CD000031. doi: 10.1002/14651858.CD000031.pub4.
- 123. Howes S, Hartmann-Boyce J, Livingstone-Banks J, Hong B, Lindson N. Antidepressants for smoking cessation. Cochrane Database Syst Rev. 2020;4:CD000031. doi: 10.1002/14651858.CD000031.pub5.
- 124. Hawk LW Jr, Ashare RL, Rhodes JD, Oliver JA, Cummings KM, Mahoney MC. Does extended pre quit bupropion aid in extinguishing smoking behavior? Nicotine Tob Res. 2015;17(11):1377-84. doi: 10.1093/ntr/ntu347.
- 125. Killen JD, Fortmann SP, Murphy GM Jr., Hayward C, Arredondo C, Cromp D, et al. Extended treatment with bupropion SR for cigarette smoking cessation. J Consult Clin Psychol. 2006;74(2):286-94. doi: 10.1037/0022-006X.74.2.286.
- 126. Anthenelli RM, Benowitzr NL, West R, St. Aubin L, McRae T, Lawrence D, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders

(EAGLES): a double-blind, randomised, placebo-controlled clinical trial. Lancet. 2016;387(10037):2507-20. doi: 10.1016/S0140-6736(16)30272-0

- 127. Gonzales D, Rennard S, Nides M, Oncken C, Azoulay S, Billing CB, et al. Varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs sustained-release bupropion and placebo for smoking cessation: a randomized controlled trial. JAMA. 2006;296(1):47-55. doi: 10.1001/jama.296.1.47.
- Cahill K, Lindson-Hawley N, Thomas KH, Fanshawe TR, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database Syst Rev. 2016;5:CD006103. doi: 10.1002/14651858.CD006103.pub7.
- 129. Chen LS, Baker TB, Miller JP, Bray M, Smock N, Chen J, et al. Genetic variant in CHRNA5 and response to varenicline and combination nicotine replacement in a randomized placebo-controlled trial. Clin Pharmacol Ther. 2020;108(6):1315-25. doi: 10.1002/cpt.1971.
- Rollema H, Hajós M, Seymour PA, Kozak R, Majchrzak MJ, Guanowsky V, et al. Preclinical pharmacology of the alpha4beta2 nAChR partial agonist varenicline related to effects on reward, mood and cognition. Biochem Pharmacol. 2009;78(7):813-24. doi: 10.1016/j.bcp.2009.05.033.
- 131. Mihalak KB, Carroll FI, Luetje C. Varenicline is a partial agonist at $\alpha 4\beta 2$ and a full agonist at $\alpha 7$ neuronal nicotinic receptors. Mol Pharmacol. 2006;70(3):801-5. doi: 10.1124/mol.106.025130.
- Patterson F, Jepson C, Strasser AA, Loughead J, Perkins KA, Gur RC, et al. Varenicline improves mood and cognition during smoking abstinence. Biol Psychiatry. 2009;65(2):144-9. doi: 10.1016/j.biopsych.2008.028.
- 133. Philip NS, Carpeter LL, Tyrka AR, Whiteley LB, Price LH. Varenicline augmentation in depressed smokers: an 8-week, open-label study. J Clin Psychiatry. 2009;70(7):1026-31. doi: 10.4088/jcp.08m04441.
- 134. Smith RC, Lindenmayer JP, Davis JM, Cornwell J, Noth K, Gupta S, et al. Cognitive and antismoking effects of varenicline in patients with schizophrenia or schizoaffective disorder. Schizophr Res. 2009;110(1-3):149-55. doi: 10.1016/j.schres.2009.02.001.
- 135. Sofuoglu M, Herman AI, Mooney M, Waters AJ. Varenicline attenuates some of the subjective and physiological effects of intravenous nicotine in humans. Psychopharmacology (Berl). 2009;207(1):153-62. doi: 10.1007/s00213-009-1643-z.
- 136. Leone FT, Zhang Y, Evers-Casey S, Evins A, Eakin M, Fathi J, et al. Initiating pharmacologic treatment in tobacco-dependent adults: an official American Thoracic Society clinical practice guideline. Am J Respir Crit Care Med. 2020; 202(2):e5-e31. doi: 10.1164/rccm.202005-1982ST.
- 137. Siegel S, Lerman C, Flitter A, Schnoll R. The use of the nicotine metabolite ratio as a biomarker to personalize treatment for nicotine dependence: current evidence and future directions. Cancer Prev Res. 2020;13(3):261-72. doi: 10.1158/1940-6207.CAPR-19-0259.
- Liberman JN, Lichtenfeld MJ, Galaznik A, Mastey V, Harnett J, Zou KH, et al. Adherence to varenicline and associated smoking cessation in a community-based patient setting. J Manag Care Pharm. 2013;19(2):125-31. doi: 10.18553/jmcp.2013.19.2.125.
- Hawk LW Jr., Ashare RL, Lohnes SF, Schlienz NJ, Rhodes JD, Tiffany ST, et al. The effects of extended prequit varenicline treatment on smoking behavior and short-term abstinence: a randomized clinical trial. Clin Pharmacol Ther. 2012;91(2):172-80. doi: 10.1038/clpt.2011.317.
- Ebbert JO, Hughes JR, West RJ, Rennard SI, Russ C, McRae TD, et al. Effect of varenicline on smoking cessation through smoking reduction: a randomized clinical trial. JAMA. 2015;313(7):687-94. doi: 10.1001/jama.2015.280.
- 141. Baker TB, Piper ME, Smith SS, Bolt DM, Stein JH, Fiore MC. Effects of combined varenicline with nicotine patch and of extended treatment duration on smoking cessation: a randomized clinical trial. JAMA. 2021;326(15):1485-93. doi: 10.1001/jama.2021.15333.
- 142. Singh S, Loke YK, Spangler JG, Furberg CD. Risk of serious adverse cardiovascular events associated with varenicline: a systematic review and meta-analysis. CMAJ. 2011;183(12):1359-66. doi: 10.1503/cmaj.110218.
- 143. U.S. Food and Drug Administration (FDA) [Internet]. Silver Spring, MD: FDA; 2021 [cited 26 Feb 2012]. Laboratory analysis of varenicline products; [about 2 screens]. Available from: https://www.fda.gov/drugs/drug-safety-and-availability/laboratory-analysis-varenicline-products.
- 144. Vogeler T, McClain C, Evoy KE. Combination bupropion SR and varenicline for smoking cessation: a systematic review. Am J Drug Alcohol Abuse. 2016;42(2):129-39. doi: 10.3109/00952990.2015.1117480.
- 145. Cinciripini PM, Minnix JA, Green CE, Robinson JD, Engelmann JM, Versace F, et al. An RCT with the combination of varenicline and bupropion for smoking cessation: clinical implications for front line use [published online ahead of print]. Addiction. 2018;10.1111/add.14250. doi: 10.1111/add.14250.
- 146. Hajek P, Smith KM, Dhanji AR, McRobbie H. Is a combination of varenicline and nicotine patch more effective in helping smokers quit than varenicline alone? A randomised controlled trial. BMC Med. 2013;11:140. doi: 10.1186/1741-7015-11-140.

- 147. Ramon JM, Morchon S, Baena A, Masuet-Aumatell C. Combining varenicline and nicotine patches: a randomized controlled trial study in smoking cessation. BMC Med. 2014;12:172. doi: 10.1186/s12916-014-0172-8.
- 148. Koegelenberg CF, Noor F, Bateman ED, van Zyl-Smit RN, Bruning A, O'Brien JA, et al. Efficacy of varenicline combined with nicotine replacement therapy vs varenicline alone for smoking cessation: a randomized clinical trial. JAMA. 2014;312(2):155-61. doi: 10.1001/jama.2014.7195.
- 149. Patnode CD, Henderson JT, Coppola EL, Melnikow J, Durbin S, Thomas RG. Interventions for tobacco cessation in adults, including pregnant persons: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2021;325(3):280-98. doi: 10.1001/jama.2020.23541.
- 150. Tulloch HE, Pipe AL, Els C, Clyde MJ, Reid RD. Flexible, dual-form nicotine replacement therapy or varenicline in comparison with nicotine patch for smoking cessation: a randomized controlled trial. BMC Med. 2016;14:80. doi: 10.1186/s12916-016-0626-2.
- 151. Vidrine JI, Cofta-Woerpel L, Daza P, Wright KL, Wetter DW. Smoking cessation 2: behavioral treatments. Behav Med. 2006;32(3):99-109. doi: 10.3200/BMED.32.3.99-109.
- 152. McCarthy DE, Piasecki TM, Jorenby DE, Lawrence DL, Shiffman S, Fiore MC, et al. A multilevel analysis of nonsignificant counseling effects in a randomized smoking cessation trial. Addiction. 2010;105(12):2195-208. doi: 10.1111/j.1360-0443.2010.03089.x.
- 153. The Cancer Center Cessation Initiative Telehealth Working Group, Telehealth delivery of tobacco cessation treatment in cancer care: an ongoing innovation accelerated by the COVID-19 pandemic. Natl Compr Canc Netw. 2021;19(Suppl 1):S21-4. doi: 10.6004/jnccn.2021.7092.
- 154. Simon JA, Carmody TP, Hudes ES, Snyder E, Murray J. Intensive smoking cessation counseling versus minimal counseling among hospitalized smokers treated with transdermal nicotine replacement: a randomized trial. Am J Med. 2003;114(7):555-62. doi: 10.1016/s0002-9343(03)00081-0.
- 155. Webb MS, de Ybarra DR, Baker EA, Reis IM, Carey MP. Cognitive-behavioral therapy to promote smoking cessation among African American smokers: a randomized clinical trial. J Consult Clin Psychol. 2010;78(1):24-33. doi: 10.1037/a0017669.
- 156. Hall SM, Humfleet GL, Muñoz RF, Reus VI, Prochaska JJ, Robbins JA. Using extended cognitive behavioral treatment and medication to treat dependent smokers. Am J Public Health. 2011;101(12):2349-56. doi: 10.2105/AJPH.2010.300084.
- 157. Ludwig DS, Kabat-Zinn J. Mindfulness in medicine. JAMA. 2008;300(11):1350-2. doi: 10.1001/jama.300.11.1350.
- 158. Cropley M, Ussher M, Charitou E. Acute effects of a guided relaxation routine (body scan) on tobacco withdrawal symptoms and cravings in abstinent smokers. Addiction. 2007;102(6):989-93. doi: 10.1111/j.1360-0443.2007.01832.x.
- 159. De Souza IC, de Barros VV, Gomide HP, Miranda TC, Menezes Vde P, Kozasa EH, et al. Mindfulness-based interventions for the treatment of smoking: a systematic literature review. J Altern Complement Med. 2015;21(3):129-40. doi: 10.1089/acm.2013.0471.
- Brewer JA, Mallik S, Babuscio TA, Nich C, Johnson HE, Deleone CM, et al. Mindfulness training for smoking cessation: results from a randomized controlled trial. Drug Alcohol Depend. 2011;119(1-2):72-80. doi: 10.1016/j.drugalcdep.2011.05.027.
- Davis JM, Goldberg SB, Anderson MC, Manley AR, Smith SS, Baker TB. Randomized trial on mindfulness training for smokers targeted to a disadvantaged population. Subst Use Misuse. 2014;49(5):571-85. doi: 10.3109/10826084.2013.770025.
- 162. Davis JM, Manley AR, Goldberg SB, Smith SS, Jorenby DE. Randomized trial comparing mindfulness training for smokers to a matched control. J Subst Abuse Treat. 2014; 47(3):213-21. doi: 10.1016/j.jsat.2014.04.005.
- 163. Davis JM, Mills DM, Stankevitz KA, Manley AR, Majeskie MR, Smith SS. Pilot randomized trial on mindfulness training for smokers in young adult binge drinkers. BMC Complement Altern Med. 2013;13:215. doi: 10.1186/1472-6882-13-215.
- 164. Oikonomou MT, Arvanitis M, Sokolove RL. Mindfulness training for smoking cessation: a meta-analysis of randomized-controlled trials. J Health Psychol. 2017;22(14):1841-50. doi: 10.1177/1359105316637667.
- 165. Maglione MA, Maher AR, Ewing B, Colaiaco B, Newberry S, Kandrack R, et al. Efficacy of mindfulness meditation for smoking cessation: a systematic review and meta-analysis. Addict Behav. 2017;69:27-34. doi: 10.1016/j.addbeh.2017.01.022.

- 166. Dindo L, Van Liew JR, Arch JJ. Acceptance and commitment therapy: a transdiagnostic behavioral intervention for mental health and medical conditions. Neurotherapeutics. 2017;14(3):546-53. doi: 10.1007/s13311-017-0521-3.
- Zhang CQ, Leeming E, Smith P, Chung PK, Hagger MS, Hayes SC. Acceptance and commitment therapy for health behavior change: a contextually-driven approach. Front Psychol. 2018;8:2350. doi: 10.3389/fpsyg.2017.02350.
- 168. Hayes SC, Luoma JB, Bond FW, Masuda A, Lillis J. Acceptance and commitment therapy: model, processes and outcomes. Behav Res Ther. 2006;44(1):1-25. doi: 10.1016/j.brat.2005.06.006.
- Hernández-López M, Luciano MC, Bricker JB, Roales-Nieto JG, Montesinos F. Acceptance and commitment therapy for smoking cessation: a preliminary study of its effectiveness in comparison with cognitive behavioral therapy. Psychol Addict Behav. 2009;23(4):723-30. doi: 10.1037/a0017632.
- 170. Bricker JB, Bush T, Zbikowski SM, Mercer LD, Heffner JL. Randomized trial of telephone-delivered acceptance and commitment therapy versus cognitive behavioral therapy for smoking cessation: a pilot study. Nicotine Tob Res. 2014;16(11):1446-54. doi: 10.1093/ntr/ntu102.
- 171. Lee EB, An W, Levin ME, Twohig MP. An initial meta-analysis of acceptance and commitment therapy for treating substance use disorders. Drug Alcohol Depend. 2015;155:1-7. doi: 10.1016/j.drugalcdep.2015.08.004.
- 172. McClure JB, Bricker J, Mull K, Heffner JL. Comparative effectiveness of group-delivered acceptance and commitment therapy versus cognitive behavioral therapy for smoking cessation: a randomized controlled trial. Nicotine Tob Res. 2020;22(3):354-62. doi: 10.1093/ntr/nty268.
- 173. Berlin I, Covey LS. Pre-cessation depressive mood predicts failure to quit smoking: the role of coping and personality traits. Addiction. 2006;101(12):1814-21. doi: 10.1111/j.1360-0443.2006.01616.x.
- 174. Cook J, Spring B, McChargue D, Doran N. Effects of anhedonia on days to relapse among smokers with a history of depression: a brief report. Nicotine Tob Res. 2010;12(9):978-82. doi: 10.1093/ntr/ntq118.
- 175. Heffner JL, Mull KE, Watson NL, McClure JB, Bricker JB. Smokers with bipolar disorder, other affective disorders, and no mental health conditions: comparison of baseline characteristics and success at quitting in a large 12-month behavioral intervention randomized trial. Drug Alcohol Depend. 2018;193:35-41. doi: 10.1016/j.drugalcdep.2018.08.034.
- 176. Ziedonis D, Hitsman B, Beckham JC, Zvolensky M, Adler L, Audrain-McGovern J, et al. Tobacco use and cessation in psychiatric disorders: National Institute of Mental Health report. Nicotine Tob Res. 2008;10(12):1691-715. doi: 10.1080/14622200802443569.
- 177. Cuijpers P, van Straten A, Warmerdam L. Behavioral activation treatments of depression: a meta-analysis. Clin Psychol Rev. 2007;27(3):318-26.
- Dimidjian S, Barrera M Jr, Martell C, Munoz RF, Lewinsohn PM. The origins and current status of behavioral activation treatments for depression. Annu Rev Clin Psychol. 2011;7:1-38. doi: 10.1146/annurev-clinpsy-032210-104535.
- 179. Lejuez CW, Hopko DR, Hopko SD. A brief behavioral activation treatment for depression. Treatment manual. Behav Modif. 2001;25(2):255-86. doi: 10.1177/0145445501252005.
- 180. Rhodes S, Richards D, Ekers D, McMillan D, Byford S, Farrand PA, et al. Cost and outcome of behavioural activation versus cognitive behaviour therapy for depression (COBRA): study protocol for a randomised controlled trial. Trials. 2014;15(1):29. doi: 10.1186/1745-6215-15-29.
- 181. Dobson KS, Hollon SD, Dimidjian S, Schmaling KB, Kohlenberg RJ, Gallop RJ, et al. Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the prevention of relapse and recurrence in major depression. J Consult Clin Psychol. 2008;76(3):468-77. doi: 10.1037/0022-006X.76.3.468.
- Jacobson NS, Dobson KS, Truax PA, Addis ME, Koerner K, Gollan JK, et al. A component analysis of cognitive-behavioral treatment for depression. J Consult Clin Psychol. 1996;64(2):295-304. doi: 10.1037//0022-006x.64.2.295.
- 183. Kahler CW, Brown RA, Strong DR, Lloyd-Richardson EE, Niaura R. History of major depressive disorder among smokers in cessation treatment: associations with dysfunctional attitudes and coping. Addict Behav. 2003;28(6):1033-47. doi: 10.1016/s0306-4603(02)00234-4.
- 184. Busch AM, Tooley EM, Dunsiger S, Chattillion EA, Srour JF, Pagoto SL, et al. Behavioral activation for smoking cessation and mood management following a cardiac event: results of a pilot randomized controlled trial. BMC Public Health. 2017;17(1):323. doi: 10.1186/s12889-017-4250-7.
- 185. MacPherson L, Tull MT, Matusiewicz AK, Rodman S, Strong DR, Kahler CW, et al. Randomized controlled trial of behavioral activation smoking cessation treatment for smokers with elevated depressive symptoms. J Consult Clinical Psychol. 2010;78(1):55-61. doi: 10.1037/a0017939.

- 186. Martínez-Vispo C, Martínez Ú, López-Durán A, Fernández Del Río E, Becoña E. Effects of behavioural activation on substance use and depression: a systematic review. Subst Abuse Treat Prev Policy. 2018;13(1):36. doi: 10.1186/s13011-018-0173-2.
- 187. Hettema J, Steele J, Miller WR. Motivational interviewing. Annu Rev Clin Psychol. 2005;1:91-111. doi: 10.1146/annurev.clinpsy.1.102803.143833.
- 188. Miller WR, Rollnick S. Motivational interviewing: helping people change. New York: Guilford Press; 2013.
- 189. Lindson N, Thompson TP, Ferrey A, Lambert JD, Aveyard P. Motivational interviewing for smoking cessation. Cochrane Database Syst Rev. 2019;7(7):CD006936. doi: 10.1002/14651858.CD006936.pub3.
- 190. Engle JL, Mermelstein R, Baker TB, Smith SS, Schlam TR, Piper ME, et al. Effects of motivation phase intervention components on quit attempts in smokers unwilling to quit: a factorial experiment. Drug Alcohol Depend. 2019;197:149-57. doi: 10.1016/j.drugalcdep.2019.01.011.
- 191. Krishnan-Sarin S, Cavallo DA, Cooney JL, Schepis TS, Kong G, Liss TB, et al. An exploratory randomized controlled trial of a novel high-school-based smoking cessation intervention for adolescent smokers using abstinence-contingent incentives and cognitive behavioral therapy. Drug Alcohol Depend. 2013;132(1-2):346-51. doi: 10.1016/j.drugalcdep.2013.03.002.
- 192. Higgins ST, Bernstein IM, Washio Y, Heil SH, Badger GJ, Skelly JM, et al. Effects of smoking cessation with voucher-based contingency management on birth outcomes. Addiction. 2010;105(11):2023-30. doi: 10.1111/j.1360-0443.2010.03073.x.
- 193. Higgins ST, Nighbor TD, Kurti AN, Heil SH, Slade EP, Shepard DS, et al. Randomized controlled trial examining the efficacy of adding financial incentives to best practices for smoking cessation among pregnant and newly postpartum women. Prev Med. Epub 2022 Mar 3. doi: 10.1016/j.ypmed.2022.107012.
- 194. Berlin I, Berlin N, Malecot M, Breton M, Jusot F, Godzahl L. Financial incentives for smoking cessation in pregnancy: multicentre randomised controlled trial. BMJ. 2021;375:e065217.
- 195. Ladapo JA, Tseng CH, Sherman SE. Financial incentives for smoking cessation in hospitalized patients: a randomized clinical trial. Am J Med. 2020;133(6):741-49. doi: 10.1016/j.amjmed.2019.12.025.
- 196. Witman A, Acquah J, Alva M, Hoerger T, Romaire M. Medicaid incentives for prevention chronic disease: effects of financial incentives for smoking cessation. Health Serv Res. 2018;53(6 Pt I):5016-34.
- 197. Halpern SD, French B, Small DS, Saulsgiver K, Harhay MO, Audrain-McGovern J, et al. Randomized trial of four financial-incentive programs for smoking cessation. N Engl J Med. 2015;372:2108-17. doi: 10.1056/NEJMoa1414293.
- 198. Volpp KG, Troxel AB, Pauly MV, Glick HA, Puig A, Asch DA, et al. A randomized, controlled trial of financial incentives for smoking cessation. N Engl J Med. 2009;360:699-709. doi: 10.1056/NEJMsa0806819.
- 199. Ledgerwood DM, Arfken CL, Petry NM, Alessi SM. Prize contingency management for smoking cessation: a randomized trial. Drug Alcohol Depend. 2014;140:208-12. doi: 10.1016/j.drugalcdep.2014.03.032.
- 200. Notley C, Gentry S, Livingstone-Banks J, Bauld L, Perera R, Hartmann-Boyce J. Incentives for smoking cessation. Cochrane Database Syst Rev. 2019;7:CD004307. doi: 10.1002/14651858.CD004307.pub6.
- 201. Anderson CM, Cummins SE, Kohatsu ND, Gamst AC, Zhu SH. Incentives and patches for Medicaid smokers: an RCT. Am J Prev Med. 2018;55(6 Suppl 2):S138-47. doi: 10.1016/j.amepre.2018.07.015.
- 202. Baker TB, Fraser DL, Kobinsky K, Adsit R, Smith SS, Khalil L, et al. A randomized controlled trial of financial incentives to low income pregnant women to engage in smoking cessation treatment: effects on postbirth abstinence. J Consult Clin Psychol. 2018:86(5)464-73.
- 203. Fraser DL, Fiore MC, Kobinsky K, Adsit R, Smith SS, Johnson ML, et al. A randomized trial of incentives for smoking treatment in Medicaid members. Am J Prev Med. 2017;53(6):754-63. doi: 10.1016/j.amepre.2017.08.027.
- 204. Mundt MP, Baker TB, Piper ME, Smith SS, Fraser DL, Fiore MC. Financial incentives to Medicaid smokers for engaging tobacco quit line treatment: maximising return on investment. Tob Control. 2020;29(3):320-5. doi: 10.1136/tobaccocontrol-2018-054811.
- 205. Tong EK, Stewart SL, Schillinger D, Vijayaraghavan M, Dove MS, Epperson AE, et al. The medical incentives to quit smoking project: impact of statewide outreach through health channels. Am J Prev Med. 2018;55:S159-69. doi: 10.1016/j.amepre.2018.07.031.
- 206. Dallery J, Raiff BR, Kim SJ, Marsch LA, Stitzer M, Grabinski MJ. Nationwide access to an internet-based contingency management intervention to promote smoking cessation: a randomized controlled trial. Addiction. 2017;112(5):875-83. doi: 10.1111/add.13715.
- 207. Dallery J, Raiff BR. Contingency management in the 21st century: technological innovations to promote smoking cessation. Subst Use Misuse. 2011;46(1):10-22. doi: 10.3109/10826084.2011.521067.
- 208. Piasecki TM. Relapse to smoking. Clin Psychol Rev. 2006;26(2):196-215. doi: 10.1016/j.cpr.2005.11.007.

- 209. Hughes JR, Keely J, Naud S. (2004). Shape of the relapse curve and long-term abstinence among untreated smokers. Addiction. 2004;99(1):29-38. doi: 10.1111/j.1360-0443.2004.00540.x.
- 210. Kenford SL, Fiore MC, Jorenby DE, Smith SS, Wetter D, Baker TB. Predicting smoking cessation. Who will quit with and without the nicotine patch. JAMA. 1994;271(8):589-94. doi: 10.1001/jama.271.8.589.
- Zhu SH, Pierce JP. A new scheduling method for time-limited counseling. Prof Psychol Res Pr . 1995;26(6):624-25. doi: 10.1037/0735-7028.26.6.624.
- Carlini BH, Zbikowski SM, Javitz HS, Deprey TM, Cummins SE, Zhu SH. Telephone-based tobacco-cessation treatment: re-enrollment among diverse groups. Am J Prev Med. 2008; 35(1):73-6. doi: 10.1016/j.amepre.2008.03.025.
- 213. Carlini BH, McDaniel AM, Weaver MT, Kauffman RM, Cerutti B, Stratton RM, et al. Reaching out, inviting back: using interactive voice response (IVR) technology to recycle relapsed smokers back to Quitline treatment—a randomized controlled trial. BMC Public Health. 2012;12:507. doi: 10.1186/1471-2458-12-507.
- 214. Carlini B, Miles L, Doyle S, Celestino P, Koutsky J. Using diverse communication strategies to re-engage relapsed tobacco quitline users in treatment, New York State, 2014. Prev Chronic Dis. 2015;12:E179. doi: 10.5888/pcd12.150191.
- 215. Ellerbeck EF, Mahnken JD, Cupertino AP, Cox LS, Greiner KA, Mussulman LM, et al. Effect of varying levels of disease management on smoking cessation: a randomized trial. Ann Intern Med. 2009;150(7):437-46. doi: 10.7326/0003-4819-150-7-200904070-00003.
- 216. Fu SS, Partin MR, Snyder A, An LC, Nelson DB, Clothier B, et al. Promoting repeat tobacco dependence treatment: are relapsed smokers interested? Am J Manag Care. 2006;12(4):235-43.
- 217. Joseph AM, Fu SS, Lindgren B, Rothman AJ, Kodl M, Lando H, et al. Chronic disease management for tobacco dependence: a randomized, controlled trial. Arch Intern Med. 2011;171(21):1894-900. doi: 10.1001/archinternmed.2011.500.
- 218. Partin MR, An LC, Nelson DB, Nugent S, Snyder A, Fu SS, et al. Randomized trial of an intervention to facilitate recycling for relapsed smokers. Am J Prev Med. 2006;31(4):293-9. doi: 10.1016/j.amepre.2006.06.021.
- Vickerman KA, Keller PA, Deprey M, Lachter RB, Jenssen J, Dreher M. Never quit trying: reengaging tobacco users in statewide cessation services. J Public Health Manag Pract. 2018;24(3):e25-33. doi: 10.1097/PHH.00000000000635.
- 220. Hartmann-Boyce J, Hong B, Livingstone-Banks J, Wheat H, Fanshawe TR. Additional behavioural support as an adjunct to pharmacotherapy for smoking cessation. Cochrane Database Syst Rev. 2019;6:CD009670. doi: 10.1002/14651858.CD009670.pub4.
- 221. Windle SB, Filion KB, Mancini JG, Adye-White L, Joseph L, Gore GC, et al. Combination therapies for smoking cessation: a hierarchical bayesian meta-analysis. Am J Prev Med. 2016;51(6):1060-71. doi: 10.1016/j.amepre.2016.07.011.
- 222. Fiore MC, Baker TB. Ten million calls and counting: progress and promise of tobacco quitlines in the U.S. Am J Prev Med. 2021;60(3 Suppl 2):S103-6. doi: 10.1016/j.amepre.2020.06.021.
- 223. Centers for Disease Control and Prevention (CDC) [Internet]. Atlanta: CDC; 2021 [cited 2022 Feb 26]. 1-800-Quit-Now: 15 years of helping people quit; [about 5 screens]. Available from: <u>https://www.cdc.gov/tobacco/features/quitlines/index.html#:~:text=1%2D800%2DQUIT%2DNOW%20is%20</u> <u>the%20national%20portal%20to,who%20want%20to%20quit%20tobacco</u>.
- 224. North American Quitline Consortium (NAQC). Adoption of recommended best practices among state quitlines [Internet]. Phoenix: NAQC; 2018 [cited 2022 Feb 10]. Available from:
- https://cdn.ymaws.com/www.naquitline.org/resource/resmgr/issue_papers/QLBestPracticesReport_mredit.pdf. 225. North American Quitline Consortium (NAQC). Evolving quitline practices: technology-mediated services, youth cessation and vaping cessation [Internet]. Phoenix: NAQC; 2020 [cited 2022 Feb 11]. Available from:
- <u>https://cdn.ymaws.com/www.naquitline.org/resource/resmgr/reports-naqc/LC-Brief Sept 2020 FINAL2.pdf</u>.
 226. North American Quitline Consortium (NAQC). 2020 survey [Internet]. Phoenix: NAQC; 2021 [cited 2022 Feb 10]. Available from: <u>https://www.naquitline.org/page/2020survey</u>.
- 227. Lichtenstein E, Zhu SH, Tedeschi GJ. Smoking cessation quitlines: an underrecognized intervention success story. Am Psychol. 2010;65(4):252-61. doi: 10.1037/a0018598.
- 228. Baker TB, Berg KM, Adsit RT, Skora AD, Swedlund MP, Zehner ME, et al. Closed loop eReferral from primary care clinics to a state tobacco cessation quitline: an implementation and maintenance evaluation. Am J Prev Med. 2021;60(3 Suppl 2):S113-22.

- 229. North American Quitline Consortium (NAQC). What is a quitline? Phoenix: NAQC; 2021 [cited 2022 Feb 26]. Available from: <u>https://www.naquitline.org/page/whatisquitline</u>.
- 230. Schauer GL, Malarcher AM, Zhang L, Engstrom MC, Zhu SH. Prevalence and correlates of quitline awareness and utilization in the United States: an update from the 2009-2010 national adult tobacco survey. Nicotine Tob Res. 2014;16:544-53. doi: 10.1093/ntr/ntt181.
- 231. North American Quitline Consortium (NAQC). Quitline services: current practice and evidence base [Internet]. Phoenix, AZ: The Consortium; 2016 [cited 2022 June 5]. Available from:
- <u>https://cdn.ymaws.com/www.naquitline.org/resource/resmgr/issue_papers/Quitline_Services_issue_pape.pdf.</u> 232. Matkin W, Ordóñez-Mena JM, Hartmann-Boyce J. Telephone counselling for smoking cessation. Cochrane
- Database Syst Rev. 2019;5:CD002850. doi: 10.1002/14651858.CD002850.pub4. 233. Park ER, Perez GK, Regan S, Muzikansky A, Levy DE, Temel JS, et al. Effect of sustained smoking cessation
- 233. Park ER, Perez GK, Regan S, Muzikansky A, Levy DE, Temel JS, et al. 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. JAMA. 2020;324(14):1406-18. doi: 10.1001/jama.2020.14581.
- 234. American Academy of Family Physicians (AAFP). Tobacco cessation telehealth guide [Internet]. Leawood, KS: AAFP; 2020 [cited 2022 Feb 26]. Available from: https://www.aafp.org/dam/AAFP/documents/patient_care/tobacco/tobacco-cessation-telehealth-guide.pdf.
- 235. Tzelepis F, Paul CL, Williams CM, Gilligan C, Regan T, Daly J, et al. Real-time video counselling for smoking cessation. Cochrane Database Syst Rev. 2019;10:CD012659. doi: 10.1002/14651858.CD012659.pub2.
- 236. Byaruhanga J, Atorkey P, McLaughlin M, Brown A, Byrnes E, Paul C, et al. Effectiveness of individual realtime video counseling on smoking, nutrition, alcohol, physical activity, and obesity health risks: systematic review. J Med Internet Res. 2020;22(9):e18621.
- 237. Carlson LE, Lounsberry JJ, Maciejewski O, Wright K, Collacutt V, Taenzer P. Telehealth-delivered group smoking cessation for rural and urban participants: feasibility and cessation rates. Addict Behav. 2012;37(1):108-14.
- 238. Kotsen C, Dilip D, Carter-Harris L, O'Brien M, Whitlock CW, de Leon-Sanchez S, et al. Rapid scaling up of telehealth treatment for tobacco-dependent cancer patients during the COVID-19 outbreak in New York City. Telemed J E Health. 2021;27(1):20-9. doi: 10.1089/tmj.2020.0194.
- 239. LeLaurin JH, Dallery J, Silver NL, Markham MJ, Theis RP, Chetram DK, et al. An implementation trial to improve tobacco treatment for cancer patients: patient preferences, treatment acceptability and effectiveness. Int J Environ Res Public Health. 2020;17(7):2280. doi: 10.3390/ijerph17072280.
- 240. Shaverdian N, Gillespie EF, Cha E, Kim SY, Benvengo S, Chino F, et al. Impact of telemedicine on patient satisfaction and perceptions of care quality in radiation oncology. J Natl Compr Canc Netw. 2021;19(10):1174-80. doi: 10.6004/jnccn.2020.7687.
- 241. Pew Research Center [Internet]. Washington: Pew Research Center; 2021 [cited 2022 Jan 30]. Mobile fact sheet; [about 7 screens]. Available from: <u>https://www.pewresearch.org/internet/fact-sheet/mobile/</u>.
- 242. Kreps GL, Neuhauser L. New directions in eHealth communication: opportunities and challenges. Patient Educ Couns. 2010;78(3):329-36. doi: 10.1016/j.pec.2010.01.013.
- 243. Griffiths F, Lindenmeyer A, Powell J, Lowe P, Thorogood M. Why are health care interventions delivered over the internet? A systematic review of the published literature. J Med Internet Res. 2006;8(2):e10. doi: 10.2196/jmir.8.2.e10.
- 244. Amato MS, Graham AL. Geographic representativeness of a web-based smoking cessation intervention: reach equity analysis. J Med Internet Res. 2018;20(10):e11668. doi: 10.2196/11668.
- 245. Anderson M. About a quarter of rural Americans say access to high-speed internet is a major problem [Internet]. Washington: Pew Research Center; 2018; [about 7 screens]. Available from: <u>https://www.pewresearch.org/fact-tank/2018/09/10/about-a-quarter-of-rural-americans-say-access-to-high-speed-internet-is-a-major-problem/</u>.
- 246. Pew Research Center [Internet]. Washington: Pew Research Center; 2021 [cited 2022 Jan 30]. Internet/broadband fact sheet; [about 7 screens]. Available from: <u>https://www.pewresearch.org/internet/fact-sheet/internet-broadband/</u>.
- 247. Graham AL, Carpenter KM, Cha S, Cole S, Jacobs MA, Raskob M, et al. Systematic review and meta-analysis of internet interventions for smoking cessation among adults. Subst Abuse Rehabil. 2016;7:55-69. doi: 10.2147/SAR.S101660.

- 248. Taylor GMJ, Dalili MN, Semwal M, Civljak M, Sheikh A, Car J. Internet-based interventions for smoking cessation. Cochrane Database Syst Rev. 2017;9(9):CD007078. doi: 10.1002/14651858.CD007078.pub5.
- 249. McCrabb S, Baker AL, Attia J, Skelton E, Twyman L, Palazzi K, et al. Internet-based programs incorporating behavior change techniques are associated with increased smoking cessation in the general population: a systematic review and meta-analysis. Ann Behav Med. 2019;53(2):180-95. doi: 10.1093/abm/kay026.
- 250. Do HP, Tran BX, Le Pham Q, Nguyen LH, Tran TT, Latkin CA, et al. Which eHealth interventions are most effective for smoking cessation? A systematic review. Patient Prefer Adherence. 2018;12:2065-84. doi: 10.2147/PPA.S169397.
- 251. Pew Research Center [Internet]. Washington: Pew Research Center; 2015 [cited 2022 Jan 30]. U.S. smartphone use in 2015; [about 10 screens]. Available from: https://www.pewresearch.org/internet/2015/04/01/us-smartphone-use-in-2015/.
- 252. Ybarra ML, Jiang Y, Free C, Abroms LC, Whittaker R. Participant-level meta-analysis of mobile phone-based interventions for smoking cessation across different countries. Prev Med. 2016;89:90-7. doi: 10.1016/j.ypmed.2016.05.002.
- 253. Scott-Sheldon LA, Lantini R, Jennings EG, Thind H, Rosen RK, Salmoirago-Blotcher E, et al. Text messaging-based interventions for smoking cessation: a systematic review and meta-analysis. JMIR Mhealth Uhealth. 2016;4(2):e49. doi: 10.2196/mhealth.5436
- 254. Abroms LC, Lee Westmaas J, Bontemps-Jones J, Ramani R, Mellerson J. A content analysis of popular smartphone apps for smoking cessation. Am J Prev Med. 2013;45(6):732-6. doi: 10.1016/j.amepre.2013.07.008.
- 255. Abroms LC, Padmanabhan N, Thaweethai L, Phillips T. iPhone apps for smoking cessation: a content analysis. Am J Prev Med. 2011;40(3):279-85. doi: 10.1016/j.amepre.2010.10.032.
- 256. Bricker JB, Watson NL, Mull KE, Sullivan BM, Heffner JL. Efficacy of smartphone applications for smoking cessation: a randomized clinical trial. JAMA Intern Med. 2020:e204055. doi: 10.1001/jamainternmed.2020.4055.
- 257. Haskins BL, Lesperance D, Gibbons P, Boudreaux ED. A systematic review of smartphone applications for smoking cessation. Transl Behav Med. 2017 Jun;7(2):292-9. doi: 10.1007/s13142-017-0492-2.
- 258. Vilardaga R, Casellas-Pujol E, McClernon JF, Garrison KA. Mobile applications for the treatment of tobacco use and dependence. Curr Addict Rep. 2019;6:86-97. doi: 10.1007/s40429-019-00248-0.
- 259. Wells M, Aitchison P, Harris F, Ozakinci G, Radley A, Bauld L, et al. Barriers and facilitators to smoking cessation in a cancer context: a qualitative study of patient, family and professional views. BMC Cancer. 2017;17(1):348. doi: 10.1186/s12885-017-3344-z.
- 260. Warner ET, Park ER, Luberto CM, Rabin J, Perez GK, Ostroff JS. Internalized stigma among cancer patients enrolled in a smoking cessation trial: the role of cancer type and associations with psychological distress [published online ahead of print, Nov. 19, 2021]. Psychooncology. 2021;10.1002/pon.5859. doi: 10.1002/pon.5859.
- 261. Kaiser EG, Prochaska JJ, Kendra MS. Tobacco cessation in oncology care. Oncology. 2018;95(3):129-37. doi: 10.1159/000489266.
- 262. McCarter K, Martínez Ú, Britton B, Baker A, Bonevski B, Carter G, et al. Smoking cessation care among patients with head and neck cancer: a systematic review. BMJ Open. 2016;6(9):e012296. doi: 10.1136/bmjopen-2016-012296.
- 263. Nayan S, Gupta KM, Strychowsky JE, Sommer DD. Smoking cessation interventions and cessation rates in the oncology population: an updated systematic review and meta-analysis. Otolaryngol Head Neck Surg. 2013;149(2):200-11. doi: 10.1177/0194599813490886.
- 264. Zeng L, Yu X, Yu T, Xiao J, Huang Y. Interventions for smoking cessation in people diagnosed with lung cancer. Cochrane Database Syst Rev. 2015;(12):CD011751. doi: 10.1002/14651858.CD011751.pub3.
- 265. Schnoll RA, Martinez E, Tatum KL, Weber DM, Kuzla N, Glass M, et al. A bupropion smoking cessation clinical trial for cancer patients. Cancer Causes Control. 2010;21(6):811-20. doi: 10.1007/s10552-010-9507-8.
- 266. Morgan G, Schnoll RA, Alfano CM, Evans SE, Goldstein AO, Ostroff J, et al. National Cancer Institute conference on treating tobacco dependence at cancer centers. J Oncol Pract. 2011;7(3):178-82. doi: 10.1200/JOP.2010.000175.
- 267. Thomsen T, Tønnesen H, Okholm M, Kroman N, Maibom A, Sauerberg ML, et al. Brief smoking cessation intervention in relation to breast cancer surgery: a randomized controlled trial. Nicotine Tob Res. 2010;12(11):1118-24. doi: 10.1093/ntr/ntq158. Epub 2010 Sep 20.
- 268. Wakefield M, Olver I, Whitford H, Rosenfeld E. Motivational interviewing as a smoking cessation intervention for patients with cancer: randomized controlled trial. Nurs Res. 2004;53(6):396-405. doi: 10.1097/00006199-200411000-00008.
- 269. Pollak KI, Fish LJ, Sutton LM, Gao X, Lyna P, Owen L, et al. A smoking cessation and pain management program for cancer survivors. J Cancer Surviv. 2018;12(6):821-7. doi: 10.1007/s11764-018-0719-3.
- 270. Arifin AJ, McCracken LC, Nesbitt S, Warner A, Dinniwell RE, Palma DA, et al. Does free nicotine replacement improve smoking cessation rates in cancer patients? Curr Oncol. 2020;27(1):14-8.
- 271. Park ER, Japuntich S, Temel J, Lanuti M, Pandiscio J, Hilgenberg J, et al. A smoking cessation intervention for thoracic surgery and oncology clinics: a pilot trial [published correction appears in J Thorac Oncol. 2011;6(8):1454]. J Thorac Oncol. 2011;6(6):1059-65. doi: 10.1097/JTO.0b013e318215a4dc.
- 272. Schnoll R, Leone F, Veluz-Wilkins A, Miele A, Hole A, Jao NC, et al. A placebo-controlled randomized clinical trial testing the efficacy and safety of 24-weeks of varenicline to treat nicotine dependence among cancer patients. Psychooncology. 2019;8:561-9. doi: 10.1002/pon.4978.
- 273. Rettig EM, Fakhry C, Hales RK, Kisuule F, Quon H, Kiess AP, et al. Pilot randomized controlled trial of a comprehensive smoking cessation intervention for patients with upper aerodigestive cancer undergoing radiotherapy. Head Neck. 2018;40(7):1534-47. doi: 10.1002/hed.25148.
- 274. Duffy SA, Ronis DL, Valenstein M, Lambert MT, Fowler KE, Gregory L, et al. A tailored smoking, alcohol, and depression intervention for head and neck cancer patients. Cancer Epidemiol Biomarkers Prev. 2006;15(11):2203-8. doi: 10.1158/1055-9965.EPI-05-0880.
- 275. Gritz ER, Fingeret MC, Vidrine DJ, Lazev AB, Mehta NV, Reece GP. Successes and failures of the teachable moment: smoking cessation in cancer patients. Cancer. 2006;106(1):17-27.
- 276. Browning K, Ahijevych K, Ross P. Implementing the Agency for Health Care Policy and Research's smoking cessation guideline in a lung cancer surgery clinic. Oncol Nurs Forum. 2000;27:1248-54. doi: 10.1016/j.soncn.2007.11.008.
- 277. Griebel B, Wewers ME, Baker CA. The effectiveness of a nurse-managed minimal smoking-cessation intervention among hospitalized patients with cancer. Oncol Nurs Forum. 1998;25(5):897-902.
- 278. Stanislaw AE, Wewers ME. A smoking cessation intervention with hospitalized surgical cancer patients: a pilot study. Cancer Nurs. 1994;17(2):81-6.
- Wewers ME, Bown JM, Stanislaw AE, Desimone VB. A nurse-delivered smoking cessation intervention among hospitalized postoperative patients: influence of a smoking-related diagnosis: a pilot study. Heart Lung. 1994;23(2):151-6.
- 280. Schnoll RA, Rothman RL, Wielt DB, Lerman C, Pedri H, Wang H, et al. A randomized pilot study of cognitive-behavioral therapy versus basic health education for smoking cessation among cancer patients. Ann Behav Med. 2005;30(1):1-11. doi: 10.1207/s15324796abm3001_1.
- 281. Schnoll RA, Zhang B, Rue M, Krook JE, Spears WT, Marcus AC, et al. Brief physician-initiated quit-smoking strategies for clinical oncology settings: a trial coordinated by the Eastern Cooperative Oncology Group. J Clin Oncol. 2003;21(2):355-65. doi: 10.1200/JCO.2003.04.122.
- Klemp I, Steffenssen M, Bakholdt V, Thygesen T, Sørensen JA. Counseling is effective for smoking cessation in head and neck cancer patients-a systematic review and meta-analysis. J Oral Maxillofac Surg. 2016;74(8):1687-94. doi: 10.1016/j.joms.2016.02.003.
- 283. Sheeran P, Jones K, Avishai A, Symes YR, Abraham C, Miles E, et al. What works in smoking cessation interventions for cancer survivors? A meta-analysis. Health Psychol. 2019;38(10):855. doi: 10.1037/hea0000757.
- 284. Weaver KE, Urbanic JJ, Case D, Kaplan SG, Lesser GJ, Zbikowski S, et al. Preliminary efficacy of an enhanced quitline smoking cessation intervention for cancer patients. J Clin Oncol. 2015;33(15 Suppl):e20671. doi: 10.1200/jco.2015.33.15_suppl.e20671.
- 285. Kanera IM, Bolman CA, Willems RA, Mesters I, Lechner L. Lifestyle-related effects of the web-based Kanker Nazorg Wijzer (Cancer Aftercare Guide) intervention for cancer survivors: a randomized controlled trial. J Cancer Surviv. 2016t;10(5):883-97. doi: 10.1007/s11764-016-0535-6.
- 286. Hawkes AL, Chambers SK, Pakenham KI, Patrao TA, Baade PD, Lynch BM, et al. Effects of a telephonedelivered multiple health behavior change intervention (CanChange) on health and behavioral outcomes in survivors of colorectal cancer: a randomized controlled trial. J Clin Oncol. 2013;31(18):2313-21. doi: 10.1200/JCO.2012.45.5873.
- 287. Ito H, Matsuo K, Wakai K, Saito T, Kumimoto H, Okuma K, et al. An intervention study of smoking cessation with feedback on genetic cancer susceptibility in Japan. Prev Med. 2006;42(2):102-8. doi: 10.1016/j.ypmed.2005.10.006.

- Charlot M, D'Amico S, Luo M, Gemei A, Kathuria H, Gardiner P. Feasibility and acceptability of mindfulness-based group visits for smoking cessation in low-socioeconomic status and minority smokers with cancer. J Altern Complement Med. 2019;25(7):762-9. doi: 10.1089/acm.2019.0016.
- 289. Ghosh A, Philiponis G, Bewley A, Ransom ER, Mirza N. You can't pay me to quit: the failure of financial incentives for smoking cessation in head and neck cancer patients. J Laryngol Otol. 2016;130(3):278-83. doi: 10.1017/S0022215116000037.
- 290. Ostroff JS, Brukhalter JE, Cinciripini PM, Li Y, Shiyko MP, Lam CY, et al. Randomized trial of a presurgical scheduled reduced smoking intervention for patients newly diagnosed with cancer. Health Psychol. 2014;33(7):737-47. doi: 10.1037/a0033186.
- 291. Bricker JB, Watson NL, Heffner JL, Sullivan B, Mull K, Kwon D, et al. A smartphone app designed to help cancer patients stop smoking: results from a pilot randomized trial on feasibility, acceptability, and effectiveness. JMIR Form Res. 2020;4(1):e16652. doi: 10.2196/16652.
- 292. Fashler SR, Weinrib AZ, Azam MA, Katz J. The use of acceptance and commitment therapy in oncology settings: a narrative review. Psychol Rep. 2018;121(2):229-52. doi: 10.1177/0033294117726061.
- 293. Moffitt Cancer Center [Internet]. Tampa: Moffitt Cancer Center; 2018 [cited 2022 Feb 26]. Forever free self-help; [about 12 screens]. Available from: <u>https://moffitt.org/research-science/research-teams/tobacco-research-and-intervention-program-trip/trip-research/forever-free-self-help/</u>.
- 294. Simmons VN, Litvin EB, Patel RD, Jacobsen PB, McCaffrey JC, Bepler G, et al. Patient-provider communication and perspectives on smoking cessation and relapse in the oncology setting. Patient Educ Couns. 2009;77(3):398-403. doi: 10.1016/j.pec.2009.09.024.
- 295. Meltzer LR, Meade CD, Diaz DB, Carrington MS, Brandon TH, Jacobsen PB, et al. Development of a targeted smoking relapse-prevention intervention for cancer patients. J Cancer Educ. 2018;33(2):440-7. doi: 10.1007/s13187-016-1089-z.
- 296. Simmons VN, Sutton SK, Meltzer LR, Martinez U, Palmer AM, Meade CD, et al. Preventing smoking relapse in patients with cancer: a randomized controlled trial. Cancer. 2020;126(23):5165-72. doi: 10.1002/cncr.33162.
- 297. Park ER, Japuntich SJ, Rigotti NA, Traeger L, He Y, Wallace RB, et al. A snapshot of smokers after lung and colorectal cancer diagnosis. Cancer. 2012;118(12):3153-64. doi: 10.1002/cncr.26545.
- Chambers DA, Vinson CA, Norton WE. Advancing the science of implementation across the cancer continuum. Oxford, England: Oxford University Press; 2019.
- 299. Powell BJ, Fernandez ME, Williams NJ, Aarons GA, Beidas RS, Lewis CC, et al. Enhancing the impact of implementation strategies in healthcare: a research agenda. Front Public Health. 2019;7:3. doi: 10.3389/fpubh.2019.00003.
- 300. Skolarus T, Tabak R, Sales A. Theories, frameworks, and models in implementation science in cancer. Advancing the science of implementation across the cancer continuum. In: Chambers DA, Vinson CA, Norton WE, editors. Advancing the science of implementation across the cancer continuum. Oxford, England: Oxford University Press; 2019.
- 301. U.S. National Cancer Institute. Guiding the future of cancer control [Internet]. Bethesda, MD: National Cancer Institute; 2021 [cited 30 Jan. 2022]. Available from: <u>https://cancercontrol.cancer.gov/overview-highlights/docs/NCI-DCCPS-Overview-and-Highlights-2021.pdf</u>.
- 302. Pirl WF. Evidence report on the occurrence, assessment, and treatment of depression in cancer patients. J Natl Cancer Inst Monogr. 2004;(32):32-9. doi: 10.1093/jncimonographs/lgh026.
- 303. Holland JC, Alici Y. Management of distress in cancer patients. J Support Oncol. 2010;8(1):4-12.
- 304. Kash KM, Mago R, Kunkel EJ. Psychosocial oncology: supportive care for the cancer patient. Semin Oncol. 2005;32(2):211-8. Doi: 10.1053/j.seminoncol.2004.11.011.
- Sharpley CF, Bitsika V, Christie DH. Do prostate cancer patients suffer more from depressed mood or anhedonia? Psychooncology. 2013;22(8):1718-23. doi: 10.1002/pon.3203.
- 306. Karam-Hage M, Oughli HA, Rabius V, Beneventi D, Wippold RC, Blalock JA, et al. Tobacco cessation treatment pathways for cancer patients: 10 years in the making. J Natl Compr Canc Netw. 2016;14(11):1469-77. doi: 10.6004/jnccn.2016.0153.
- 307. Hitsman B, Papandonatos GD, McChargue DE, DeMott A, Herrera MJ, Spring B, et al. Past major depression and smoking cessation outcome: a systematic review and meta-analysis update. Addiction. 2013;108(2):294-306. doi: 10.1111/add.12009.
- 308. Fluharty M, Taylor AE, Grabski M, Munafò MR. The association of cigarette smoking with depression and anxiety: a systematic review. Nicotine Tob Res. 2017;19(1):3-13. doi: 10.1093/ntr/ntw140.

- 309. Jiang F, Li S, Pan L, Zhang N, Jia C. Association of anxiety disorders with the risk of smoking behaviors: a meta-analysis of prospective observational studies. Drug Alcohol Depend. 2014;145:69-76. doi: 10.1016/j.drugalcdep.2014.10.022.
- 310. Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: a population-based prevalence study. JAMA. 2000;284(20):2606-10.
- 311. Piper ME, Smith SS, Schlam TR, Fleming MF, Bittrich AA, Brown JL, et al. Psychiatric disorders in smokers seeking treatment for tobacco dependence: relations with tobacco dependence and cessation. J Consult Clin Psychol. 2010;78(1):13-23. doi: 10.1037/a0018065.
- 312. Zvolensky MJ, Stewart SH, Vujanovic AA, Gavric D, Steeves D. Anxiety sensitivity and anxiety and depressive symptoms in the prediction of early smoking lapse and relapse during smoking cessation treatment. Nicotine Tob Res. 2009;11(3):323-31. doi: 10.1093/ntr/ntn037.
- Berg CJ, Thomas AN, Mertens AC, Schauer GL, Pinsker EA, Ahluwalia JS, et al. Correlates of continued smoking versus cessation among survivors of smoking-related cancers. Psychooncology. 2013b;22(4):799-806. doi: 10.1002/pon.3077.
- 314. Blalock JA, Lam C, Minnix JA, Karam-Hage M, Gritz ER, Robinson JD, et al. The effect of mood, anxiety, and alcohol use disorders on smoking cessation in cancer patients. J Cogn Psychother. 2011;25(1):82-96. doi: 10.1891/0889-8391.25.1.82.
- 315. Boyes AW, Girgis A, D'Este C, Zucca AC. Flourishing or floundering? Prevalence and correlates of anxiety and depression among a population-based sample of adult cancer survivors 6 months after diagnosis. J Affect Disord. 2011;135(1-3):184-92. doi: 10.1016/j.jad.2011.07.016
- 316. Martinez E, Tatum KL, Weber DM, Kuzla N, Pendley A, Campbell K, et al. Issues related to implementing a smoking cessation clinical trial for cancer patients. Cancer Causes Control. 2009;20(1):97-104. doi: 10.1007/s10552-008-9222-x.
- 317. Schnoll RA, Martinez E, Langer C, Miyamoto C, Leone F. Predictors of smoking cessation among cancer patients enrolled in a smoking cessation program. Acta Oncol. 2011;50(5):678-84. doi: 10.3109/0284186X.2011.572915.
- 318. Weinberger AH, Desai RA, McKee SA. Nicotine withdrawal in U.S. smokers with current mood, anxiety, alcohol use, and substance use disorders. Drug Alcohol Depend. 2010;108(1-2):7-12. doi: 10.1016/j.drugalcdep.2009.11.004.
- 319. Kaye JT, Baker TB, Beckham JC, Cook JW. Tobacco withdrawal symptoms before and after nicotine deprivation in veteran smokers with posttraumatic stress disorder and with major depressive disorder. Nicotine Tob Res. 2021;23(7):1239-47. doi: 10.1093/ntr/ntaa242.
- 320. Bloom EL, Oliver JA, Sutton SK, Brandon TH, Jacobsen PB, Simmons VN. Post-operative smoking status in lung and head and neck cancer patients: association with depressive symptomatology, pain, and fatigue. Psychooncology. 2015;24(9):1012-9. doi: 10.1002/pon.3682.
- 321. Hopenhayn C, Christian WJ, Christian A, Studts J, Mullet T. Factors associated with smoking abstinence after diagnosis of early stage lung cancer. Lung Cancer. 2013;80(1):55-61. doi: 10.1016/j.lungcan.2012.12.013.
- 322. Guimond AJ, Croteau VA, Savard MH, Bernard P, Ivers H, Savard J. Predictors of smoking cessation and relapse in cancer patients and effect on psychological variables: an 18-month observational study. Ann Behav Med. 2017;51(1):117-27. doi: 10.1007/s12160-016-9834-4.
- 323. Farris SG, Robinson JD, Zvolensky MJ, Hogan J, Rabius V, Cinciripini PM, et al. Panic attacks and smoking cessation among cancer patients receiving smoking cessation treatment. Addict Behav. 2016;61:32-9. doi: 10.1016/j.addbeh.2016.05.011.
- 324. Leventhal AM, Zvolensky MJ. Anxiety, depression, and cigarette smoking: a transdiagnostic vulnerability framework to understanding emotion-smoking comorbidity. Psychol Bull. 2015;141(1):176-212. doi: 10.1037/bul0000003.
- 325. Mathew AR, Hogarth L, Leventhal AM, Cook JW, Hitsman B. Cigarette smoking and depression comorbidity: systematic review and proposed theoretical model. Addiction. 2017;112(3):401-12. doi: 10.1111/add.13604.
- 326. Matulewicz RS, Sherman S, Bjurlin MA. Smoking cessation and cancer survivorship. JAMA. 2020;324(14):1475. doi: 10.1001/jama.2020.16277.
- 327. Scarpace SL, Brodzik FA, Mehdi S, Belgam R. Treatment of head and neck cancers: issues for clinical pharmacists. Pharmacotherapy. 2009;29(5):578-92. doi: 10.1592/phco.29.5.578.
- 328. Fava M, Rush AJ, Thase ME, Clayton A, Stahl SM, Pradko JF, et al. 15 years of clinical experience with bupropion HCl: from bupropion to bupropion SR to bupropion XL. Prim Care Companion J Clin Psychiatry. 2005;7(3):106-13. doi: 10.4088/pcc.v07n0305.

- 329. Peng AR, Swardfager W, Benowitz NL, Ahluwalia JS, Lerman C, Nollen NL, et al. Impact of early nausea on varenicline adherence and smoking cessation. Addiction. 2020;115(1):134-44. doi: 10.1111/add.14810.
- Drovandi AD, Chen CC, Glass BD. Adverse effects cause varenicline discontinuation: a meta-analysis. Curr Drug Saf. 2016;11(1):78-85. doi: 10.2174/1574886311207040282.
- 331. Aigner CJ, Cinciripini PM, Anderson KO, Baum GP, Gritz ER, Lam CY. The association of pain with smoking and quit attempts in an electronic diary study of cancer patients trying to quit. Nicotine Tob Res. 2016;18(6):1449-55. doi: 10.1093/ntr/ntv118.
- 332. LaRowe LR, Ditre JW. Pain, nicotine, and tobacco smoking: current state of the science. [published online ahead of print Mar. 20, 2020]. Pain. 2020;161(8):1688-93. doi: 10.1097/j.pain.000000000001874.
- 333. Duffy SA, Louzon SA, Gritz ER. Why do cancer patients smoke and what can providers do about it? Community Oncol. 2012;9(11):344-52. doi: 10.1016/j.cmonc.2012.10.003.
- 334. Cinciripini PM, Karam-Hage M, Kypriotakis G, Robinson JD, Rabius V, Beneventi D, et al. Association of a comprehensive smoking cessation program with smoking abstinence among patients with cancer. JAMA Netw Open. 2019;2(9):e1912251. doi: 10.1001/jamanetworkopen.2019.12251.
- 335. Hartmann-Boyce J, Chepkin SC, Ye W, Bullen C, Lancaster T. Nicotine replacement therapy versus control for smoking cessation. Cochrane Database Syst Rev. 2018;5:CD000146. doi: 10.1002/14651858.CD000146.pub5.
- 336. Ku L, Bruen BK, Steinmetz E, Bysshe T. Medicaid tobacco cessation: big gaps remain in efforts to get smokers to quit. Health Aff (Millwood). 2016;35(1):62-70. doi: 10.1377/hlthaff.2015.0756.
- Jarlenski M, Hyon Baik S, Zhang Y. Trends in use of medications for smoking cessation in Medicare, 2007–2012. Am J Prev Med. 2016;51(3):301-8. doi: 10.1016/j.amepre.2016.02.018.
- 338. Jamal A, Dube SR, King BA. Tobacco use screening and counseling during hospital outpatient visits among US adults, 2005–2010. Prev Chronic Dis. 2015;12:E132. doi: 10.5888/pcd12.140529.
- 339. Tang MW, Oakley R, Dale C, Purushotham A, Møller H, Gallagher JE. A surgeon led smoking cessation intervention in a head and neck cancer centre. BMC Health Serv Res. 2014;14:636. doi: 10.1186/s12913-014-0636-8.
- 340. Nightingale CL, Sterba KR, Tooze JA, King JL, Weaver KE. Cessation attitudes and preferences in head and neck cancer patients and implications for cessation program design: a brief report. Glob Adv Health Med. 2019;8:2164956119847117. doi: 10.1177/2164956119847117.
- 341. Schnoll RA, Rothman RL, Newman H, Lerman C, Miller SM, Movsas B, et al. Characteristics of cancer patients entering a smoking cessation program and correlates of quit motivation: implications for the development of tobacco control programs for cancer patients. Psychooncology. 2004;13(5):346-58. doi: 10.1002/pon.756.
- 342. Salloum RG, Lee J, Lee JH, Boeckmann M, Xing C, Warren GW. Smoking-cessation methods and outcomes among cancer survivors. Am J Prev Med. 2020;59(4):615-17. doi: 10.1016/j.amepre.2020.03.016.
- 343. Leone FT, Evers-Casey S, Toll BA, Vachani A. Treatment of tobacco use in lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013;143(5 Suppl):e61S-77S. doi: 10.1378/chest.12-2349.
- 344. Williamson TJ, Kwon DM, Riley KE, Shen MJ, Hamann HA, Ostroff JS. Lung cancer stigma: does smoking history matter? Ann Behav Med. 2020;54(7):535-40. doi: 10.1093/abm/kaz063.
- 345. Evans-Polce RJ, Castaldelli-Maia JM, Schomerus G, Evans-Lacko SE. The downside of tobacco control? Smoking and self-stigma: a systematic review. Soc Sci Med. 2015;145:26-34. doi: 10.1016/j.socscimed.2015.09.026.
- 346. Bell J, McCullough L. Smoking, stigma and tobacco 'denormalization': Further reflections on the use of stigma as a public health tool. A commentary on Social Science & Medicine's Stigma, Prejudice, Discrimination and Health Special Issue (67:3). Soc Sci Med. 2010;70(6):795-9.
- 347. Scott N, Crane M, Lafontaine M, Seale H, Currow D. Stigma as a barrier to diagnosis of lung cancer: patient and general practitioner perspectives. Prim Health Care Res Dev. 2015;16(6) 618-22. doi: 10.1017/S1463423615000043.
- 348. Pacek LR, McClernon FJ, Bosworth HB. Adherence to pharmacological smoking cessation interventions: a literature review and synthesis of correlates and barriers. Nicotine Tob Res. 2018;20(10):1163-72. doi: 10.1093/ntr/ntx210.
- 349. Schlam TR, Cook JW, Baker TB, Hayes-Birchler T, Bolt DM, Smith SS, et al. Can we increase smokers' adherence to nicotine replacement therapy and does this help them quit? Psychopharmacology (Berl). 2018;235(7):2065-75. doi: 10.1007/s00213-018-4903-y.

- 350. Shiffman S, Sweeney CT, Ferguson SG, Sembower MA, Gitchell JG. Relationship between adherence to daily nicotine patch use and treatment efficacy: secondary analysis of a 10-week randomized, double-blind, placebo-controlled clinical trial simulating over-the-counter use in adult smokers. Clin Ther. 2008;30(10):1852-58. doi: 10.1016/j.clinthera.2008.09.016.
- 351. Mersha AG, Eftekhari P, Bovill M, Tollosa DN, Gould GS. Evaluating level of adherence to nicotine replacement therapy and its impact on smoking cessation: a systematic review and meta-analysis. Arch Public Health. 2021;79(1):26. doi: 10.1186/s13690-021-00550-2.
- 352. Schlam TR, Baker TB, Smith SS, Bolt DM, McCarthy DE, Cook JW, et al. Electronically monitored nicotine gum use before and after smoking lapses: relationship with lapse and relapse. Nicotine Tob Res. 2020;22(11):2051-8. doi: 10.1093/ntr/ntaa116.
- 353. Crawford G, Weisbrot J, Bastian J, Flitter A, Jao NC, Carroll A, et al. Predictors of varenicline adherence among cancer patients treated for tobacco dependence and its association with smoking cessation. Nicotine Tob Res. 2019;21(8):1135-9. doi: 10.1093/ntr/nty133.
- 354. Balmford J, Borland R, Hammond D, Cummings KM. Adherence to and reasons for premature discontinuation from stop-smoking medications: data from the ITC Four-Country Survey. Nicotine Tob Res. 2011;13(2):94-102. doi: 10.1093/ntr/ntq215.
- 355. Yingst JM, Veldheer S, Hrabovsky S, Sciamanna C, Foulds J. Reasons for non-adherence to nicotine patch therapy during the first month of a quit attempt. Int J Clin Pract. 2015;69(8):883-8. doi: 10.1111/ijcp.12644.
- 356. Kotsen C, Ostroff J, Carter-Harris L. e-Health interventions for tobacco cessation. In: Breitbart WS, Butow PN, Jacobsen PB, Lam W, Lazenby M, and Loscalzo MJ, editors. Psychooncology. 4th ed. New York: Oxford University Press; 2021.
- 357. American Society of Clinical Oncology. American Society of Clinical Oncology policy statement update: tobacco control—reducing cancer incidence and saving lives. J Clin Oncol. 2003;21(14):2777-86.
- 358. International Association for the Study of Lung Cancer [Internet]. Denver: IASLC; 2019 [cited 30 Jan. 2012]. Declaration from IASLC: tobacco cessation after cancer diagnosis; [about 2 screens]. Available from: <u>https://www.iaslc.org/About-IASLC/News-Detail/declaration-from-iaslc-tobacco-cessation-after-cancer-diagnosis</u>.
- 359. Bjurlin MA, Goble SM, Hollowell CM. Smoking cessation assistance for patients with bladder cancer: a national survey of American urologists. J Urol. 2010;184(5):1901-06. doi: 10.1016/j.juro.2010.06.140.
- Simmons VN, Litvin EB, Unrod M, Brandon TH. Oncology healthcare providers' implementation of the 5A's model of brief intervention for smoking cessation: patients' perceptions. Patient Educ Couns. 2012;86(3):414-19. doi: 10.1016/j.pec.2011.06.016.
- Warren GW, Marshall JR, Cummings KM, Toll B, Gritz ER, Hutson A, et al. Practice patterns and perceptions of thoracic oncology providers on tobacco use and cessation in cancer patients. J Thorac Oncol. 2013;8(5):543-8. doi: 10.1097/JTO.0b013e318288dc96.
- 362. Warren GW, Marshall JR, Cummings KM, Toll BA, Gritz ER, Hutson A, et al. Addressing tobacco use in patients with cancer: a survey of American Society of Clinical Oncology members. J Oncol Pract. 2013;9(5):258-62. doi: 10.1200/JOP.2013.001025.
- 363. Solberg L, Asche SE, Boyle RG, Boucher JL, Pronk NP. Frequency of physician-directed assistance for smoking cessation in patients receiving cessation medications. Arch Intern Med. 2005;165(6):656-60. doi: 10.1001/archinte.165.6.656.
- 364. Tong EK, Strouse R, Hall J, Kovac M, Schroeder SA. National survey of U.S. health professionals' smoking prevalence, cessation practices, and beliefs. Nicotine Tob Res. 2010 1;12(7):724-33. doi: 10.1093/ntr/ntq071.
- 365. Warren GW, Dibaj S, Hutson A, Cummings KM, Dresler C, Marshall JR. Identifying targeted strategies to improve smoking cessation support for cancer patients [published correction appears in J Thorac Oncol. 2015;10(12):1702]. J Thorac Oncol. 2015;10(11):1532-37. doi: 10.1097/JTO.000000000000659.
- 366. Price SN, Studts JL, Hamann HA. Tobacco use assessment and treatment in cancer patients: a scoping review of oncology care clinician adherence to clinical practice guidelines in the U.S. Oncologist. 2019;24(2):229-38. doi: 10.1634/theoncologist.2018-0246.
- 367. Adsit RT, Fox BM, Tsiolis T, Ogland C, Simerson M, Vind LM, et al. Using the electronic health record to connect primary care patients to evidence-based telephonic tobacco quitline services: a closed-loop demonstration project. Trans Behav Med. 2014;4:324-32.
- 368. D'Angelo H, Rolland B, Adsit R, Baker TB, Rosenblum M, Pauk D, et al. Tobacco treatment program implementation at NCI cancer centers: progress of the NCI Cancer Moonshot-Funded Cancer Center Cessation Initiative. Cancer Prev Res (Phila). 2019;12(11):735-40. doi: 10.1158/1940-6207.CAPR-19-0182.

- 369. Jenssen BP, Leone F, Evers-Casey S, Beidas R, Schnoll R. Building systems to address tobacco use in oncology: early benefits and opportunities from the Cancer Center Cessation Initiative. J Natl Compr Canc Netw. 2019;17(6):638-43. doi: 10.6004/jnccn.2019.7312.
- 370. Giuliani M, Brual J, Cameron E, Chaiton M, Eng L, Haque M, et al. Smoking cessation in cancer care: myths, presumptions and implications for practice. Clin Oncol (R Coll Radiol). 2020;32(6):400-6. doi: 10.1016/j.clon.2020.01.008.
- 371. Rodgers-Melnick SN, Hooper MW. Implementation of tobacco cessation services at a comprehensive cancer center: a qualitative study of oncology providers' perceptions and practices. Support Care Cancer. 2021;29(5):2465-74. doi: 10.1007/s00520-020-05749-7.
- 372. Leone FT, Evers-Casey S, Graden S, Schnoll R, Mallya G. Academic detailing interventions improve tobacco use treatment among physicians working in underserved communities. Ann Am Thorac Soc. 2015;12(6):854-8. doi: 10.1513/AnnalsATS.201410-466BC.
- 373. Evers-Casey S, Schnoll R, Jenssen BP, Leone FT. Implicit attribution of culpability and impact on experience of treating tobacco dependence. Health Psychol. 2019;38(12):1069-74. doi: 10.1037/hea0000784.
- 374. Wassenaar TR, Eickhoff JC, Jarzemsky DR, Smith SS, Larson ML, Schiller JH. Differences in primary care clinicians' approach to non-small cell lung cancer patients compared with breast cancer. J Thorac Oncol. 2007;2(8):722-8. doi: 10.1097/JTO.0b013e3180cc2599.
- 375. McBride CM, Blocklin M, Lipkus IM, Klein WM, Brandon TH. Patient's lung cancer diagnosis as a cue for relatives' smoking cessation: evaluating the constructs of the teachable moment. Psychooncology. 2017;26(1):88-95. doi: 10.1002/pon.4011.
- 376. Woods SS, Jaén CR. Increasing consumer demand for tobacco treatments: ten design recommendations for clinicians and healthcare systems. Am J Prev Med. 2010;38(3 Suppl):S385-92. doi: 10.1016/j.amepre.2009.12.003.
- 377. Leone FT, Evers-Casey S. Developing a rational approach to tobacco use treatment in pulmonary practice: a review of the biological basis of nicotine addiction. Clin Pulm Med. 2012;19(2):53-61. doi: 10.1097/CPM.0b013e318247cada.
- 378. Kim SS, Kaplowitz S, Johnston MV. The effects of physician empathy on patient satisfaction and compliance. Eval Health Prof. 2004;27(3):237-51. doi: 10.1177/0163278704267037.
- 379. Lelorain S, Brédart A, Dolbeault S, Sultan S. A systematic review of the associations between empathy measures and patient outcomes in cancer care. Psychooncology. 2012;21(12):1255-64. doi: 10.1002/pon.2115.
- 380. Joseph A, Fu S. Proactive outreach strategies to connect smokers with tobacco cessation treatment. JAMA Intern Med. 2015;175(2):226-7. doi: 10.1001/jamainternmed.2014.5291.
- Birken SA, Bunger AC, Powell BJ, Turner K, Clary AS, Klaman SL, et al. Organizational theory for dissemination and implementation research. Implement Sci. 2017;12(1):62. doi: 10.1186/s13012-017-0592-x.
- 382. Warren GW, Sobus S, Gritz ER. The biological and clinical effects of smoking by patients with cancer and strategies to implement evidence-based tobacco cessation support. Lancet Oncol. 2014;15(12):e568-80. doi: 10.1016/S1470-2045(14)70266-9.
- 383. Trapero-Bertran M, Leidl R, Muñoz C, Kulchaitanaroaj P, Coyle K, Präger M, et al. Estimates of costs for modelling return on investment from smoking cessation interventions. Addiction. 2018;113(S1):32-41. doi: 10.1111/add.14091.
- 384. Conroy M, Majchrzak N, Regan S, Silverman C, Schneider LI, Rigotti N. The association between patientreported receipt of tobacco intervention at a primary care visit and smokers' satisfaction with their health care. Nicotine Tob Res. 2005;7 Suppl 1:S29-34. doi: 10.1080/14622200500078063.
- 385. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci. 2009;4(1):50. doi: 10.1186/1748-5908-4-50.
- 386. Carpenter MJ, Hughes JR, Gray KM, Wahlquist AE, Saladin ME, Alberg AJ. Nicotine therapy sampling to induce quit attempts among smokers unmotivated to quit: a randomized clinical trial. Arch Intern Med. 2011;171(21):1901-07. doi: 10.1001/archinternmed.2011.492.
- 387. Jardin BF, Cropsey KL, Wahlquist AE, Gray KM, Silvestri GA, Cummings KM, et al. Evaluating the effect of access to free medication to quit smoking: a clinical trial testing the role of motivation. Nicotine Tob Res. 2014;16(7):992-9. doi: 10.1093/ntr/ntu025.
- 388. Jose T, Ohde JW, Hays JT, Burke MV, Warner DO. Design and pilot implementation of an electronic health record-based system to automatically refer cancer patients to tobacco use treatment. Int J Environ Res Public Health. 2020;17(11):4054. doi: 10.3390/ijerph17114054.

- 389. Ohde JW, Master Z, Tilburt JC, Warner DO. Presumed consent with opt-out: an ethical consent approach to automatically refer patients with cancer to tobacco treatment services. J Clin Oncol. 2021;39(8):876-80. doi: 10.1200/JCO.20.03180.
- 390. Bolt DM, Piper ME, McCarthy DE, Japuntich SJ, Fiore MC, Smith SS, et al. The Wisconsin Predicting Patients' Relapse questionnaire. Nicotine Tob Res. 2009;11(5):481-92.
- 391. Hopfer CJ, Crowley TJ, Hewitt JK. Review of twin and adoption studies of adolescent substance use. J Am Acad Child Adolesc Psychiatry. 2003;42(6):710-9. doi: 10.1097/01.CHI.0000046848.56865.54.
- 392. Li MD, Cheng R, Ma JZ, Swan, GE. A meta-analysis of estimated genetic and environmental effects on smoking behavior in male and female adult twins. Addiction. 2003;98(1):23-31. doi: 10.1046/j.1360-0443.2003.00295.x.
- 393. Hamilton AS, Lessov-Schlaggar CN, Cockburn MG, Unger JB, Cozen W, Mack TM. Gender differences in determinants of smoking initiation and persistence in California twins. Cancer Epidemiol Biomarkers Prev. 2006;15(6):1189-97. doi: 10.1158/1055-9965.EPI-05-0675.
- 394. Sullivan PF, Kendler KS. The genetic epidemiology of smoking. Nicotine Tob Res. 1999;1 Suppl 2:S51-7;discussion S69-70.
- 395. Xian H, Scherrer JF, Madden PA, Lyons MJ, Tsuang M, True WR, et al. The heritability of failed smoking cessation and nicotine withdrawal in twins who smoked and attempted to quit. Nicotine Tob Res. 2003;5(2):245-54.
- 396. Hardie TL, Moss HB, Lynch KG. Genetic correlations between smoking initiation and smoking behaviors in a twin sample. Addict Behav. 2006;31(11):2030-37. doi: 10.1016/j.addbeh.2006.02.010.
- 397. Osler M, Holst C, Prescott E, Sorensen TI. Influence of genes and family environment on adult smoking behavior assessed in an adoption study. Genet Epidemiol. 2001;21(3):193-200. doi: 10.1002/gepi.1028.
- 398. Belsky DW, Moffitt TE, Baker T, Biddle AH, Evans JP, Harrington HL, et al. Polygenic risk accelerates the developmental progression to heavy smoking and nicotine dependence: evidence from a 4-decade longitudinal study. JAMA Psychiatry. 2013;70(5):534-42.
- 399. Tanner JA, Tyndale RF. Variation in CYP2A6 activity and personalized medicine. J Pers Med. 2017;7(4):18. doi: 10.3390/jpm7040018jpm7040018.
- 400. Schnoll RA, Leone F. Biomarkers to optimize the treatment of nicotine dependence. Biomark Med. 2011:5(6);745-61. doi: 10.2217/bmm.11.91.
- 401. Styn MA, Nukui T, Romkes M, Perkins KA, Land SR, Weissfeld JL. CYP2A6 genotype and smoking behavior in current smokers screened for lung cancer. Subst Use Misuse. 2013;48(7):490-4. Epub 2013 Mar 25. doi: 10.3109/10826084.2013.778280.
- 402. Chenoweth MJ, Tyndale RF. Pharmacogenetic optimization of smoking cessation treatment. Trends Pharmacol Sci. 2017;38(1):55-66. doi: 10.1016/j.tips.2016.09.006.
- 403. Ho MK, Mwenifumbo JC, Al Koudsi N, Okuyemi KS, Ahluwalia JS, Benowitz NL, et al. Association of nicotine metabolite ratio and CYP2A6 genotype with smoking cessation treatment in African-American light smokers. Clin Pharmacol Ther. 2009;85(6):635-43. doi: 10.1038/clpt.2009.19.
- 404. Kaufmann A, Hitsman B, Goelz PM, Veluz-Wilkins A, Blazekovic S, Powers L, et al. Rate of nicotine metabolism and smoking cessation outcomes in a community-based sample of treatment-seeking smokers. Addict Behav. 2015;51:93-9. doi: 10.1016/j.addbeh.2015.07.019.
- 405. Lerman C, Tyndale R, Patterson F, Wileyto EP, Shields PG, Pinto A, et al. Nicotine metabolite ratio predicts efficacy of transdermal nicotine for smoking cessation. Clin Pharmacol Ther. 2006;79(6):600-8. doi: 10.1016/j.clpt.2006.02.006
- 406. Schnoll RA, Patterson F, Wileyto EP, Tyndale RF, Benowitz N, Lerman C. Nicotine metabolic rate predicts successful smoking cessation with transdermal nicotine: a validation study. Pharmacol Biochem Behav. 2009;92(1):6-11. doi: 10.1016/j.pbb.2008.10.016.
- 407. Patterson F, Schnoll RA, Wileyto EP, Pinto A, Epstein LH, Shields PG, et al. Toward personalized therapy for smoking cessation: a randomized placebo-controlled trial of bupropion. Clin Pharmacol Ther. 2008;84(3):320-5. doi: 10.1038/clpt.2008.57.
- 408. Glatard A, Dobrinas M, Gholamrezaee M, Lubomirov R, Cornuz J, Csajka C, et al. Association of nicotine metabolism and sex with relapse following varenicline and nicotine replacement therapy. Exp Clin Psychopharmacol. 2017;25(5):353-62. doi: 10.1037/pha0000141.
- 409. Lerman C, Schnoll RA, Hawk LW Jr., Cinciripini P, George TP, Wileyto EP, et al. Use of the nicotine metabolite ratio as a genetically informed biomarker of response to nicotine patch or varenicline for smoking cessation: a randomised, double-blind placebo-controlled trial. Lancet Respir Med. 2015;3(2):131-8. doi: 10.1016/S2213-2600(14)70294-2.

- 410. Carroll DM, Murphy SE, Benowitz NL, Strasser AA, Kotlyar M, Hecht SS, et al. Relationships between the nicotine metabolite ratio and a panel of exposure and effect biomarkers: findings from two studies of U.S. commercial cigarette smokers. Cancer Epidemiol Biomarkers Prev. 2020;29(4):871-9. doi: 10.1158/1055-9965.EPI-19-0644.
- 411. Jalas JR, Hecht SS, Murphy SE. Cytochrome P450 enzymes as catalysts of metabolism of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone, a tobacco specific carcinogen. Chem Res Toxicol. 2005;18(2):95-110. doi: 10.1021/tx049847p.
- 412. Yuan JM, Nelson HH, Carmella SG, Wang R, Kuriger-Laber J, Jin A, et al. CYP2A6 genetic polymorphisms and biomarkers of tobacco smoke constituents in relation to risk of lung cancer in the Singapore Chinese Health Study. Carcinogenesis. 2017;38(4):411-8. doi: 10.1093/carcin/bgx012.
- 413. Chen LS, Hung RJ, Baker T, Horton A, Culverhouse R, Saccone N, et al. CHRNA5 risk variant predicts delayed smoking cessation and earlier lung cancer diagnosis-a meta-analysis. J Natl Cancer Inst. 2015;107(5). doi: 10.1093/jnci/djv100.
- 414. Chen LS, Baker TB, Hung RJ, Horton A, Culverhouse R, Hartz S, et al. Genetic risk can be decreased: quitting smoking decreases and delays lung cancer for smokers with high and low CHRNA5 risk genotypes, a meta-analysis. EBioMedicine. 2016;11:219-26. doi: 10.1016/j.ebiom.2016.08.012.
- 415. Garrett BE, Dube SR, Trosclair A, Caraballo RS, Pechacek TF, Centers for Disease Control and Prevention. Cigarette smoking—United States, 1965–2008. MMWR Suppl. 2011;60(1):109-13.
- 416. Hiscock R, Bauld L, Amos A, Fidler JA, Munafo M. Socioeconomic status and smoking: a review. Ann N Y Acad Sci. 2012;1248(1):107-23. doi: 10.1111/j.1749-6632.2011.06202.x.
- 417. Smith PH, Bessette AJ, Weinberger AH, Sheffer CE, McKee SA. Sex/gender differences in smoking cessation: a review. Prev Med. 2016;92:135-40. doi: 10.1016/j.ypmed.2016.07.013.
- 418. Kulak JA, Cornelius ME, Fong GT, Giovino GA. Differences in quit attempts and cigarette smoking abstinence between whites and African Americans in the United States: literature review and results from the international tobacco control US survey. Nicotine Tob Res. 2016;18(Suppl 1):S79-87. doi: 10.1093/ntr/ntv228.
- 419. Nollen NL, Mayo MS, Sanderson Cox L, Benowitz NL, Tyndale RF, Ellerbeck EF, et al. Factors that explain differences in abstinence between black and white smokers: a prospective intervention study. J Natl Cancer Inst. 2019;111(10):1078-87. doi: 10.1093/jnci/djz001.
- 420. Businelle MS, Kendzor DE, Reitzel LR, Costello TJ, Cofta-Woerpel L, Li Y, et al. Mechanisms linking socioeconomic status to smoking cessation: a structural equation modeling approach. Health Psychol. 2010;29(3):262-73. doi: 10.1037/a0019285.
- 421. Kendzor DE, Businelle MS, Costello TJ, Castro Y, Reitzel LR, Cofta-Woerpel LM, et al. Financial strain and smoking cessation among racially/ethnically diverse smokers. Am J Public Health. 2010;100(4):702-6. doi: 10.2105/AJPH.2009.172676.
- 422. Reitzel LR, Mazas CA, Cofta-Woerpel L, Li Y, Cao Y, Businelle MS, et al. Subjective social status affects smoking abstinence during acute withdrawal through affective mediators. Addiction. 2010;105(5):928-36. doi: 10.1111/j.1360-0443.2009.02875.x.
- 423. Wetter DW, Cofta-Gunn L, Fouladi RT, Irvin JE, Daza P, Mazas C, et al. Understanding the associations among education, employment characteristics, and smoking. Addict Behav. 2005;30(5):905-14. doi: 10.1016/j.addbeh.2004.09.006.
- 424. Reid RD, Mullen K-A, D'Angelo MES, Aitken DA, Papadakis S, Haley PM, et al. Smoking cessation for hospitalized smokers: an evaluation of the "Ottawa model." Nicotine Tob Res. 2010;12(1):11-18. doi: 10.1093/ntr/ntp165.
- 425. Shiffman S, Brockwell SE, Pillitteri JL, Gitchell JG. Individual differences in adoption of treatment for smoking cessation: demographic and smoking history characteristics. Drug Alcohol Depend. 2008;93(1-2):121-31. doi: 10.1016/j.drugalcdep.2007.09.005.
- 426. Perkins, KA. Smoking cessation in women. Special considerations. CNS Drugs. 2001;15(5):391-411. doi: 10.2165/00023210-200115050-00005.
- 427. Perkins KA, Donny E, Caggiula AR. Sex differences in nicotine effects and self-administration: review of human and animal evidence. Nicotine Tob Res. 1999;1(4):301-15. doi: 10.1080/14622299050011431.
- Perkins KA, Jacobs L, Sanders M, Caggiula AR. Sex differences in the subjective and reinforcing effects of cigarette nicotine dose. Psychopharmacology (Berl). 2002;163(2):194-201. doi: 10.1007/s00213-002-1168-1.
- 429. Perkins KA, Karelitz JL. Sex differences in acute relief of abstinence-induced withdrawal and negative affect due to nicotine content in cigarettes. Nicotine Tob Res. 2015;17(4):443-8. doi: 10.1093/ntr/ntu150.
- 430. Perkins KA, Scott J. Sex differences in long-term smoking cessation rates due to nicotine patch. Nicotine Tob Res. 2008;10(7):1245-50. doi: 10.1080/14622200802097506.

- 431. Smith PH, Weinberger AH, Zhang J, Emme E, Mazure CM, McKee SA. Sex differences in smoking cessation pharmacotherapy comparative efficacy: a network meta-analysis. Nicotine Tob Res. 2017 Mar 1;19(3):273-81. doi: 10.1093/ntr/ntw144.
- 432. Webb Hooper M, Antoni MH, Okuyemi K, Dietz NA, Resnicow K. Randomized controlled trial of groupbased culturally specific cognitive behavioral therapy among African American smokers. Nicotine Tob Res. 2017;19(3):333-41. doi: 10.1093/ntr/ntw181.
- 433. Burgess DJ, Van Ryn M, Noorbaloochi S, Clothier B, Taylor BC, Sherman S, et al. Smoking cessation among African American and white smokers in the Veterans Affairs health care system. Am J Public Health. 2014;104(S4):S580-7.
- 434. McKee SA, Smith PH, Kaufman M, Mazure CM, Weinberger AH. Sex differences in varenicline efficacy for smoking cessation: a meta-analysis. Nicotine Tob Res. 2016;18(5):1002-11. doi: 10.1093/ntr/ntv207.
- 435. Smith CE, Hill SE, Amos A. Impact of specialist and primary care stop smoking support on socio-economic inequalities in cessation in the United Kingdom: a systematic review and national equity analysis. Addiction. 2020;115(1):34-46. doi: 10.1111/add.14760.
- 436. Stanton CA, Sharma E, Seaman EL, Kasza KA, Edwards KC, Halenar MJ, et al. Initiation of any tobacco and five tobacco products across 3 years among youth, young adults and adults in the USA: findings from the PATH Study Waves 1-3 (2013–2016). Tob Control. 2020;29(Suppl 3):s178-90. doi: 10.1136/tobaccocontrol-2019-055573.
- 437. Jackson I, Osaghae I, Etuk A, Jackson N. Prevalence and factors associated with electronic cigarette use among young adult cancer survivors using Behavioral Risk Factor Surveillance System, 2016–2018. J Adolesc Young Adult Oncol. 2021;10(5):588-98. doi: 10.1089/jayao.2020.0104.
- 438. Sanford NN, Sher DJ, Xu X, Aizer AA, Mahal BA. Trends in smoking and e-cigarette use among U.S. patients with cancer, 2014–2017. JAMA Oncol. 2019;5(3):426-8. doi: 10.1001/jamaoncol.2018.6858.
- 439. Fiore MC, Schroeder SA, Baker TB. Smoke, the chief killer—strategies for targeting combustible tobacco use. N Engl J Med. 2014;370(4):297-9. doi: 10.1056/NEJMp1314942.
- 440. Nickels AS, Warner DO, Jenkins SM, Tilburt J, Hays JT. Beliefs, practices, and self-efficacy of US physicians regarding smoking cessation and electronic cigarettes: a national survey. Nicotine Tob Res. 2017;19(2):197-207. doi: 10.1093/ntr/ntw194.
- 441. El Hourani M, Shihadeh A, Talih S, Eissenberg T; CSTP Nicotine Flux Work Group. Comparison of nicotine emissions rate, 'nicotine flux', from heated, electronic and combustible tobacco products: data, trends and recommendations for regulation. Tob Control. Epub 2022 Jan 27. doi: 10.1136/tobaccocontrol-2021-056850.
- 442. Barrington-Trimis, Leventhal AM. Adolescents' use of "pod mod" e cigarettes—urgent concerns. N Engl J Med. 2018;379:1099-102.
- 443. Cornelius ME, Wang TW, Jamal A, Loretan CG, Neff LJ. Tobacco product use among adults—United States, 2019. MMWR Morb Mortal Wkly Rep. 2020;69:1736-42. doi: 10.15585/mmwr.mm6946a4.
- 444. Mayer M, Reyes-Guzman C, Grana R, Choi K, Freedman ND. Demographic characteristics, cigarette smoking, and e-cigarette use among US adults. JAMA Netw Open. 2020;3(10):e2020694. doi: 10.1001/jamanetworkopen.2020.20694.
- 445. National Academies of Sciences, Engineering, and Medicine. Public health consequences of e-cigarettes. Washington, DC: The National Academies Press; 2018.
- 446. Yong HH, Borland R, Cummings KM, Gravely S, Greenhalgh B, Thrasher J, et al. Reasons for regular vaping and for its discontinuation among smokers and recent ex-smokers: findings from the 2016 ITC Four Country Smoking and Vaping Survey. Addiction. 2019;114 Suppl 1:35-48. doi: 10.1111/add.14593. PMC6717696.
- 447. Vickerman KA, Carpenter KM, Altman T, Nash CM, Zbikowski SM. Use of electronic cigarettes among state tobacco cessation quitline callers. Nicotine Tob Res. 2013;15(10):1787-91. doi: 10.1093/ntr/ntt061.
- 448. Romijnders KAGJ, van Osch L, de Vries H, Talhout R. Perceptions and reasons regarding e-cigarette use among users and non-users: a narrative literature review. Int J Environ Res Public Health. 2018;15(6):1190. doi: 10.3390/ijerph15061190.
- 449. Azagba S, Shan L, Manzione L. Cigarette, e-cigarette, alcohol, and marijuana use by cancer diagnosis status: a longitudinal analysis. Subst Abuse. 2020;14:1178221820980470. doi: 10.1177/1178221820980470.
- 450. Bjurlin MA, Basak R, Zambrano I, Schatz D, El Shahawy O, Sherman S, et al. Patterns and associations of smoking and electronic cigarette use among survivors of tobacco related and non-tobacco related cancers: a nationally representative cross-sectional analysis. Cancer Epidemiol. 2021;101913. doi: 10.1016/j.canep.2021.101913.

- 451. Boyd P, Lowry M, Morris KL, Land SR, Agurs-Collins T, Hall K, et al. Health behaviors of cancer survivors and population controls from the National Health Interview Survey (2005-2015). JNCI Cancer Spectr. 2020;4(5):pkaa043. doi: 10.1093/jncics/pkaa043.
- 452. Fahey MC, Bursac Z, Ebbert JO, Klesges RC, Little MA. Prevalence and correlates of dual tobacco use in cancer survivors. Cancer Causes Control. 2019;30(3):217-23. doi: 10.1007/s10552-019-1132-6.
- 453. Salloum RG, Getz KR, Tan ASL, Carter-Harris L, Young-Wolff KC, George TJ Jr., et al. Use of electronic cigarettes among cancer survivors in the U.S. Am J Prev Med. 2016;51(5):762-66. doi: 10.1016/j.amepre.2016.04.015.
- 454. Salloum RG, Huao J, Lee J, Dallery J, George T, Warren G. Tobacco and e-cigarette use among cancer survivors in the United States. PLoS One. 2019;14(2):e0226110. doi: 10.1177/0194599815613279.
- 455. Akinboro O, Nwabudike S, Elias R, Balasire O, Ola O, Ostroff JS. Electronic cigarette use among survivors of smoking-related cancers in the United States. Cancer Epidemiol Biomarkers Prev. 2019;28(12):2087-94. doi: 10.1158/1055-9965.EPI-19-0105.
- 456. Antwi GO, Lohrmann DK, Jayawardene W, Chow A, Obeng CS, Sayegh AM. Associations between ecigarette and combustible cigarette use among U.S. cancer survivors: implications for research and practice. J Cancer Surviv. 2019;13(2):316-25. doi: 10.1007/s11764-019-00753-1.
- 457. Kalkhoran S, Kruse GR, Rigotti NA, Rabin J, Ostroff JS, Park ER. Electronic cigarette use patterns and reasons for use among smokers recently diagnosed with cancer. Cancer Med. 2018;7(7):3484-91. doi: 10.1002/cam4.1585.
- 458. Symes YR, Ribisl KM, Boynton MH, Westmaas JL, Mayer DK, Golden SD. Dual cigarette and e-cigarette use in cancer survivors: an analysis using population assessment of tobacco health (PATH) data. J Cancer Surviv. 2019;13(2):161-70. doi: 10.1007/s11764-019-0735-y.
- 459. Correa JB, Brandon KO, Meltzer LR, Hoehn HJ, Piñeiro B, Brandon TH, et al. Electronic cigarette use among patients with cancer: reasons for use, beliefs, and patient-provider communication. Psychooncology. 2018;27(7):1757-64. doi: 10.1002/pon.4721.
- 460. Gotts J, Jordt SE, McConnell R, Tarran R. What are the respiratory effects of e-cigarettes? BMJ 2019;366:15275 doi: 10.1136/bmj.15275.
- 461. Goniewicz ML, Smith DM, Edwards KC, Blount BC, Caldwell KL, Feng J, et al. Comparison of nicotine and toxicant exposure in users of electronic cigarettes and combustible cigarettes. JAMA Netw Open. 2018;1(8):e185937.
- 462. Kim CY, Paek YJ, Seo HG, Cheong YS, Lee CM, Park SM, et al. Dual use of electronic and conventional cigarettes is associated with higher cardiovascular risk factors in Korean men. Sci Rep. 2020;10:5612.
- 463. Wang JB, Olgin JE, Nah G, Vittinghoff E, Cataldo JK, Pletcher MJ, et al. Cigarette and e-cigarette dual use and risk of cardiopulmonary symptoms in the Health eHeart Study. PLoS One. 2018 Jul 25;13(7):e0198681.
- 464. Smith DM, Christensen C, van Bemmel D, Borek N, Ambrose B, Erives G, et al. Exposure to nicotine and toxicants among dual users of tobacco cigarettes and e-cigarettes: Population Assessment of Tobacco and Health (PATH) Study, 2013–2014. Nicotine Tob Res. 2021 May 4;23(5):790-7.
- 465. Dai H, Benowitz NL, Achutan C, Farazi PA, Degarege A, Khan AS. Exposure to toxicants associated with use and transitions between cigarettes, e-cigarettes, and no tobacco. JAMA Netw Open. 2022;5(2):d2147891.
- 466. Berlowitz JB, Xie W, Harlow AF, Hamburg NM, Blaha MJ, Bhatnagar A, et al. E-cigarette use and risk of cardiovascular disease: a longitudinal analysis of the PATH Study (2013–2019). Circulation. 2022 May 17;145(20):1557-9. doi: 10.1161/CIRCULATIONAHA.121.057369.
- 467. Abrams LR, Kalousova L, Fleischer NL. Gender differences in relationships between sociodemographic factors and e-cigarette use with smoking cessation: 2014-15 current population survey tobacco use supplement. J Public Health (Oxf). 2020;42(1):e42-e50.
- 468. Beard E, West R, Michie S, Brown J. Association of prevalence of electronic cigarette use with smoking cessation and cigarette consumption in England: a time-series analysis between 2006 and 2017. Addiction. 2020;115(5):961-74.
- 469. Kalkhoran S, Glantz SA. E cigarettes and smoking cessation in real world and clinical settings: a systematic review and meta analysis. Lancet Respir Med. 2016 Feb;4(2):116-28.
- 470. El Dib R, Suzumura EA, Akl EA, Gomaa H, Agarwal A, Chang Y, et al. Electronic nicotine delivery systems and/or electronic non-nicotine delivery systems for tobacco smoking cessation or reduction: a systematic review and meta-analysis. BMJ Open. 2017;7(2):e012680. Erratum in: BMJ Open. 2020;10(1):e012680corr1. doi: 10.1136/bmjopen-2016-012680.

- 471. Chen R, Pierce JP, Leas EC, Benmarhnia T, Strong DR, White MM, et al. Effectiveness of e cigarettes as aids for smoking cessation: evidence from the PATH Study cohort, 2017–2019. Tob Control. Epub 2022 Feb 7. doi: 10.1136/tobaccocontrol-2021-056901.
- 472. Jackson SE, Shahab L, West R, Brown J. Associations between dual use of e-cigarettes and smoking cessation: a prospective study of smokers in England. Addict Behav. 2020;103:106230. doi: 19.1016/j.addbeh.2019.106230.
- 473. Wang RJ, Bhadriraju S, Glantz SA. E-cigarette use and adult cigarette smoking cessation: a meta-analysis. Am J Public Health. 2021;111(2):230-46. doi: 10.2105/AJPH.2020.305999.
- 474. Everard CD, Silveira ML, Kimmel HL, Marshall D, Blanco C, Compton WM. Association of electronic nicotine delivery system use with cigarette smoking relapse among former smokers in the United States. JAMA Netw Open. 2020;3(6):e204813. doi: 10.1001/jamanetworkopen.2020.4813.
- 475. Liu X, Lugo A, Davoli E, Gorini G, Pacifici R, Fernández E, et al. Electronic cigarettes in Italy: a tool for harm reduction or a gateway to smoking tobacco? Tob Control. 2020;29(2):148-52. doi: 10.1136/tobaccocontrol-2018-054726.
- 476. Pierce JP, Chen R, Kealey S, Leas EC, White MM, Stone MD, et al. Incidence of cigarette smoking relapse among individuals who switched to e cigarettes or other tobacco products. JAMA Netw Open. 2021;4(10):e2128810.
- 477. Hartmann-Boyce J, McRobbie H, Butler AR, Lindson N, Bullen C, Begh R, et al. Electronic cigarettes for smoking cessation. Cochrane Database Syst Rev. 2021;9:CD010216. doi: 10.1002/14651858.CD010216.pub6.
- 478. Eisenberg MJ, Hébert-Losier A, Windle SB, Greenspoon T, Brandys T, Fülöp T, et al. Effect of e-cigarettes plus counseling vs counseling alone on smoking cessation: a randomized clinical trial. JAMA. 2020;324(18):1844-54. doi: 10.1001/jama.2020.18889.
- 479. Hajek P, Phillips-Waller A, Przulj D, Pesola F, Myers Smith K, Bisal N, et al. A randomized trial of ecigarettes versus nicotine-replacement therapy. N Engl J Med. 2019;380(7):629-37. doi: 10.1056/NEJMoa1808779.
- 480. Borderud SP, Li Y, Burkhalter JE, Sheffer CE, Ostroff JS. Electronic cigarette use among patients with cancer: characteristics of electronic cigarette users and their smoking cessation outcomes [published correction appears in Cancer. 2015;121(5):800]. Cancer. 2014;120(22):3527-35. doi: 10.1002/cncr.28811.
- 481. Brandon TH, Goniewicz MJ, Hanna NH, Hatsukami DK, Herbst RS, Hobin JA, et al. Electronic nicotine delivery systems: a policy statement from the American Association for Cancer Research and the American Society of Clinical Oncology. Clin Cancer Res. 2015;21(3):514-25. doi: 10.1200/JCO.2014.59.4465.
- 482. Cummings KM, Dresler CM, Field JK, Fox J, Gritz ER, Hanna NH, et al. E-cigarettes and cancer patients. J Thorac Oncol. 2014;9(4):438-41. doi: 10.1097/JTO.000000000000129.
- 483. American Cancer Society (ACS) [Internet]. Atlanta: The Society. [cited 2022 Jun 22]. Annual cancer facts & figures [about 5 screens]. Available from: <u>https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures.html</u>.
- 484. van der Meer DJ, Karim-Kos HE, van der Mark M, Aben KK, Bijlsma RM, Rijneveld AW, et al. Incidence, survival, and mortality trends of cancers diagnosed in adolescents and young adults (15–39 Years): a population-based study in the Netherlands 1990–2016. Cancers (Basel). 2020 Nov 18;12(11):3421. doi: 10.3390/cancers12113421.
- 485. Close AG, Dreyzin A, Miller KD, Seynnaeve BK, Rapkin LB. Adolescent and young adult oncology—past, present, and future. CA Cancer J Clin. 2019;69(6):485-96. doi: 10.3322/caac.21585.
- 486. National Academies of Sciences, Engineering, and Medicine. Childhood cancer and functional impacts across the care continuum. Washington: The National Academies Press; 2021. doi: 10.17226/25944.
- 487. Oeffinger KC, Mertens AC, Skla CA, Kawashima T, Hudson MM, Meadows AT, et al. Chronic health conditions in adult survivors of childhood cancer. N Engl J Med. 2006;355(15):1572 82. doi: 10.1056/NEJMsa060185.
- 488. Inskip P, Ries L, Cohen R, Curtis R. New malignancies following childhood cancer. In: Curtis R, Freedman D, Ron E, Ries L, Hacker D, Edwards B, et al., editors. New malignancies among cancer survivors: SEER cancer registries, 1973-2000. Bethesda, MD: National Cancer Institute; 2006. p. 465-479.
- 489. Nathan PC, Ford JS, Henderson TO, Hudson MM, Emmons KM, Casillas JN, et al. Health behaviors, medical care, and interventions to promote healthy living in the Childhood Cancer Survivor Study cohort. J Clin Oncol. 2009;27(14):2363-73. doi: 10.1200/JCO.2008.21.1441.
- 490. Antwi GO, Lohrmann DK, Jayawardene W, Chow A, Obeng CS, Sayegh AM. Associations between cigarette smoking and health-related quality of life in adult survivors of adolescent and young adult cancer. J Cancer Educ. Epub 2020 Jul 29. doi: 10.1007/s13187-020-01837-8.

- 491. Kaul S, Veeranki SP, Rodriguez AM, Kuo YF. Cigarette smoking, comorbidity, and general health among survivors of adolescent and young adult cancer. Cancer. 2016;122(18):2895 905. doi: 10.1002/cncr.30086.
- 492. Ji X, Cummings JR, Mertens AC, Wen H, Effinger KE. Substance use, substance use disorders, and treatment in adolescent and young adult cancer survivors—results from a national survey. Cancer. 2021;127(17):3223-31. doi: 10.1002/cncr.33634.
- 493. Robison LL, Mertens AC, Boice JD, Breslow NE, Donaldson SS, Green DM, et al. Study design and cohort characteristics of the Childhood Cancer Survivor Study: a multi-institutional collaborative project. Med Pediatr Oncol. 2002;38(4):229-39. doi: 10.1002/mpo.1316.
- 494. Gibson TM, Liu W, Armstrong GT, Srivastava DK, Hudson MM, Leisenring WM, et al. Longitudinal smoking patterns in survivors of childhood cancer: an update from the Childhood Cancer Survivor Study. Cancer. 2015;121(22):4035-43. doi: 10.1002/cncr.29609.
- 495. Emmons KM, Puleo E, Park E, Gritz ER, Butterfield RM, Weeks JC, et al. Peer-delivered smoking counseling for childhood cancer survivors increases rate of cessation: the partnership for health study. J Clin Oncol. 2005;23(27):6516-23. doi: 10.1200/JCO.2005.07.048.
- 496. Emmons KM, Puleo E, Mertens A, Gritz ER, Diller L, Li FP. Long-term smoking cessation outcomes among childhood cancer survivors in the Partnership for Health Study. J Clin Oncol. 2009;27(1):52-60. doi: 10.1200/JCO.2007.13.0880.
- 497. Emmons KM, Puleo E, Sprunck-Harrild K, Ford J, Ostroff JS, Hodgson D, et al. Partnership for health-2, a web-based versus print smoking cessation intervention for childhood and young adult cancer survivors: randomized comparative effectiveness study. J Med Internet Res. 2013;15(11):e218. doi: 10.2196/jmir.2533.
- 498. Klesges RC, Krukowski RA, Klosky JL, Liu W, Srivastava DK, Boyett JM, et al. Efficacy of a tobacco quitline among adult survivors of childhood cancer. Nicotine Tob Res. 2015;17(6):710-8. doi: 10.1093/ntr/ntu216.
- 499. Huang IC, Klosky JL, Young CM, Murphy SE, Krull KK, Srivastava D, et al. Misclassification of self-reported smoking in adult survivors of childhood cancer. Pediatr Blood Cancer. 2018 Sep;65(9):e27240. Epub 2018 Jun 1. doi: 10.1002/pbc.27240.

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

Chapter 4

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

Chapter Contents

The Importance of a Systematic Approach to Treating Tobacco Use in Cancer Care	
Settings	139
Introduction	139
Application of the Reach, Effectiveness, Adoption, Implementation, Maintenance (RE-	
AIM) Evaluation Framework	142
Reach	143
Enhancing Reach via Leveraging the Electronic Health Record (EHR)	143
Enhancing Reach via Use of Clinical Referral Models Including "Ask, Advise,	
Refer" (AAR) and "Ask, Advise, Connect" (AAC)	145
Treatment Extender: State Quitlines	145
Treatment Extenders: National Cancer Institute's (NCI) SmokefreeTXT	150
Utilizing Interactive Voice Response (IVR) Systems	150
Opt-Out Versus Opt-In Models of Smoking Cessation Treatment Delivery	151
Using Telehealth	152
Summary: Reach	152
Effectiveness	153
Summary: Effectiveness	154
Adoption	154
Payment Models, Quality Metrics, and Regulation	155
Legislative Action	158
Summary: Adoption	159
Implementation	160
Summary: Implementation	160
Maintenance	160
Secure Support From Health Care System Leadership	161
Integrate Tobacco Screening and Treatment Strategies Into Clinical Workflows	161
Leverage EHRs	162
Leveraging Tobacco-Relevant Quality Metrics, Payment Models, and Regulatory	
Policies	162
Summary: Maintenance	162
Assessing and Verifying Tobacco Use Status	163
Challenges to Implementing Smoking Cessation Treatment in Cancer Care Settings at the	
Patient, Clinician, and Health Care System Levels	165
Patient-Level Barriers to Delivering Smoking Cessation Treatment in Cancer Care	
Settings	167
Sociodemographic Differences in Smoking Rates	167
Knowledge of Risks of Smoking and Benefits of Quitting	168
Motivation and Confidence to Quit	169
Psychological Distress	169
Coping	170
Summary: Patient-Level Barriers	170
Clinician-Level Barriers to Delivering Smoking Cessation Treatment in Cancer Care	
Settings	170
Lack of Smoking Cessation Knowledge and Training	170
Clinician Perceptions of Patients With Cancer	172

Summary: Clinician-Level Barriers	174
Health Care System–Level Barriers to Delivering Smoking Cessation Treatment in	
Cancer Care Settings	174
Institutional Commitment and Accountability	174
Limitations of Clinician Time and Referral Options	175
Funding and Reimbursement for Smoking Cessation Treatment Programs	176
Summary: Health Care System–Level Barriers	177
A Systems Approach to Providing Smoking Cessation Treatment Across the Cancer Care	
Continuum	177
Smoking Cessation Treatment at Cancer Screening	178
Eligibility, Guidelines, and Policy for Lung Cancer Screening (LCS)	179
Impact of LCS on Smoking	179
Enhancing Smoking Cessation Treatment Reach and Effectiveness in the Context of	
LCS	179
Cancer Diagnosis	181
Cancer Treatment	182
Smoking Cessation Treatment for Patients With Advanced Cancer	182
Post-Treatment and Long-Term Survivorship	183
Summary: Cessation Across the Cancer Care Continuum	184
The Economic Rationale for Implementing Smoking Cessation Treatment in Cancer Care	184
Incremental Costs Associated With a Smoking History Among Patients With Cancer	184
Cost-Effectiveness of Smoking Cessation Treatment for Individuals With Cancer	186
Cost-Effectiveness of Smoking Cessation Treatment in the Context of LCS	187
Summary: Economic Outcomes Related to Smoking in Patients With Cancer	187
Disseminating and Implementing Tobacco Cessation Treatment in Cancer Care Settings:	
The NCI Cancer Center Cessation Initiative (C3I)	188
Models of Tobacco Cessation Treatment Employed by C3I Sites	191
Point-of-Care Treatment Models	193
Internal Referral Treatment Models	193
External Referral Treatment Models	193
Lessons Learned From Implementation of C3I	194
Summary	196
Conclusions	197
References	198

Figures and Tables

Figure 4.1	Typical EHR-Guided Staff Workflow for eReferral of a Patient who Smokes	
-	From a Clinical Setting to a State Quitline or SmokefreeTXT	147
Figure 4.2	Joint Commission Tobacco Cessation Measures	157
Figure 4.3	Smoking Cessation Treatment Across the Cancer Care Continuum, From	
-	Screening to Long-Term Survivorship	178
Figure 4.4	National Cancer Institute (NCI) Cancer Center Cessation Initiative (C3I)	
-	Sites	189
Figure 4.5	Elements of Exemplar Tobacco Cessation Treatment Programs: Three	
C	Models Used Successfully in Cancer Care Settings	192
	J 8	-

Figure 4.6	Methods Used by Cancer Center Cessation Initiative (C3I) Sites to Track Program Reach and Effectiveness	196
Table 4.1	Selected Guidelines and Recommendations from Clinical and Research	
	Organizations for Addressing Tobacco Use in Cancer Care Settings	140
Table 4.2	Consensus Assessment Instrument for Tobacco Use in Oncology (C-TUQ,	
	Selected Items)	163
Table 4.3	Challenges to Implementing Smoking Cessation Treatment in Cancer Care	
	Settings at the Patient, Clinician, and Health Care System Levels	165
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	181

Appendices

Appendix A. C3I Grantee Publications	214
Appendix B. Biochemical Confirmation Reasons and Methods: Evidence Based on the	
Society for Research on Nicotine and Tobacco (SRNT) Working Group on	
Biochemical Verification	220

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 (see chapters 1 and 2).^{1,2} 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 MoonshotSM 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 Cancer¹⁵ 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.

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

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.

Table 4.1 (continued)

Note: The guidelines/recommendations are taken directly from the sources and the terminology used reflects that of the source. *Source*: Adapted from 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 framework¹⁶ 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 5Å'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 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 followup 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 extenders³⁶ 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 review²² 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 approach¹⁹ 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 approach¹⁹ 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, OptumTM and National Jewish HealthTM 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 overthe-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 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 colleagues³² (outpatient clinical setting) and Tindle and colleagues⁶⁰ (inpatient clinical setting). For a detailed description of workflow and technical specifications for eReferral to 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 colleagues⁵² 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 guitline 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 colleagues⁶⁰ 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 colleagues⁵⁹ 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 NCL.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 colleagues³⁷ 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 colleagues⁶⁴ reported that among 198 hospitalized patients who wanted to guit 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 colleagues⁶⁵ reported that those who received IVR calls + cessation medications upon discharge did not achieve statistically significant higher 6-month postdischarge 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 colleagues²⁸ 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 treatment²⁹ 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 treatment²⁹ 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 colleagues⁷⁹ 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 colleagues⁸¹ 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 colleagues⁸² 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 colleagues⁸³ 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 colleagues⁸⁴ 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 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 FDAapproved 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 6month, 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 colleagues⁸⁷ 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 2006⁸⁸ 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 colleagues⁹³ 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 colleagues¹⁰⁶ 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 Children's Health Insurance Program (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 "<u>Challenges to</u> <u>Implementing Smoking Cessation Treatment in Cancer Care Settings at the Patient, Clinician, and Health Care System Level</u>"). 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 reevaluation 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 colleagues¹²⁵ 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 sensors¹²⁶; 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 colleagues¹³⁰ 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 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.

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>		
	□ 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.
 - \Box I smoked a cigarette today (at least one puff).
 - \Box 1-7 days. \rightarrow Number of days since last cigarette: _
 - \Box Less than 1 month. \rightarrow Number of weeks since last cigarette: ____
 - \Box Less than 1 year. \rightarrow Number of months since last cigarette: ____
 - \Box More than 1 year. \rightarrow 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. *Source*: 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 colleagues¹⁵¹ 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 collection¹³⁹ 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 selfreported 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.

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

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 delivered 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 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 bias¹⁸¹ 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 colleagues¹⁹² 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 care¹⁹ and in cancer care settings²¹⁴ 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 area²¹⁵—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 Programs²¹⁸ 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 competencies²¹⁹ 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 colleagues²²⁷ 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 Centers⁹²:

- 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 evidencebased 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 longterm survivorship.

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



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) trial²⁴⁴ 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 CMS²⁴⁷ 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 colleagues²⁴⁵ 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 colleagues²⁴⁵ 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 colleagues²⁵⁴ 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 colleagues²⁶¹ 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 colleagues²⁶⁸ 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 populations¹⁹ and provides initial recommendations on smoking cessation treatment in the LCS context.²⁷⁰

Table 4.4Guidance 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

- Screening program participants who smoke should be encouraged to quit at each visit, regardless of lung cancer screening results.
- 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.

^a5R'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 colleagues⁸⁶ 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 colleagues²⁷⁷ 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 billion²⁸⁴ 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 colleagues²⁸⁶ modeled the incremental cost of additional cancer treatment or retreatment 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 colleagues²⁸⁷ 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 colleagues¹³⁰ 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 colleagues²⁸⁸ 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 colleagues²⁸⁹ 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 colleagues²⁹⁰ 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 colleagues²⁹⁴ 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 postsurgery, respectively. Djalalov and colleagues²⁹⁵ 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 costeffectiveness 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 colleagues²⁹⁶ 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 colleagues²⁹⁷ 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 costutility. 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 colleagues²⁹⁸ 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 funding⁸; 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

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 populationbased 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 <u>Appendix A</u>. 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 delivery⁹; 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 optout 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-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 realworld 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 payfor-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.

References

- U.S. Department of Health and Human Services (USDHHS). Smoking cessation: a report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2020.
- 2. U.S. Department of Health and Human Services (USDHHS). The health consequences of smoking—50 years of progress: a report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.
- Hamann HA, Ver Hoeve ES, Carter-Harris L, Studts JL, Ostroff JS. Multilevel opportunities to address lung cancer stigma across the cancer control continuum. J Thorac Oncol. 2018;13(8):1062-75. doi: 10.1016/j.jtho.2018.05.014.
- 4. Lehto RH. Patient views on smoking, lung cancer, and stigma: a focus group perspective. Eur J Oncol Nurs. 2014;18(3):316-22. doi: 10.1016/j.ejon.2014.02.003.
- 5. Gritz ER, Cororve Fingeret M, Vidrine DJ, Lazev AB, Mehta NV, Reece GP. Successes and failures of the teachable moment: smoking cessation in cancer patients. Cancer. 2006;106(1):17-27. doi: 10.1002/cncr.21598.
- 6. McBride CM, Ostroff JS. Teachable moments for promoting smoking cessation: the context of cancer care and survivorship. Cancer Control. 2003;10(4):325-33. doi: 10.1177/107327480301000407.
- Fiore MC, D'Angelo H, Baker TB. Effective cessation treatment for patients with cancer who smoke—the fourth pillar of cancer care. JAMA Netw Open. 2019;2(9):e1912264. doi: 10.1001/jamanetworkopen.2019.12264.
- 8. Croyle RT, Morgan GD, Fiore MC. Addressing a core gap in cancer care—the NCI Moonshot program to help oncology patients stop smoking. N Engl J Med. 2019;380(6):512-5. doi: 10.1056/NEJMp1813913.
- 9. D'Angelo H, Rolland B, Adsit RT, Baker TB, Rosenblum M, Pauk D, et al. Tobacco treatment program implementation at NCI Cancer Centers: progress of the NCI Cancer Moonshot-funded Cancer Center Cessation Initiative. Cancer Prev Res (Phila). 2019;12(11):735-40. doi: 10.1158/1940-6207.Capr-19-0182.
- 10. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: smoking cessation (version 1.2022) [Internet]. Plymouth Meeting, PA: NCCN; 2022 [cited 2022 June 5]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/smoking.pdf.
- 11. Toll BA, Brandon TH, Gritz ER, Warren GW, Herbst RS. Assessing tobacco use by cancer patients and facilitating cessation: an American Association for Cancer Research policy statement. Clin Cancer Res. 2013;19(8):1941-8. doi: 10.1158/1078-0432.Ccr-13-0666.
- Hanna N, Mulshine J, Wollins DS, Tyne C, Dresler C. Tobacco cessation and control a decade later: American Society of Clinical Oncology policy statement update. J Clin Oncol. 2013;31(25):3147-57. doi: 10.1200/jco.2013.48.8932.
- 13. Bialous SA, Sarna L. ISNCC tobacco position statement. Cancer Nurs. 2016:39(1):80-1. doi: 10.1097/ncc.00000000000309.
- 14. International Society of Nurses in Cancer Care (ISNCC) [Internet]. Pittsburgh: ISNCC; c2014 [cited 2022 June 5]. ISNCC tobacco position statement; [about 5 screens]. Available from: <u>https://www.ons.org/make-difference/ons-center-advocacy-and-health-policy/position-statements/isncc-tobacco-position</u>.
- 15. Jassem J [Internet]. Denver: IASLC; c2019 [cited 2022 June 5]. Declaration from IASLC: tobacco cessation after cancer diagnosis; [about 2 screens]. Available from: <u>https://www.iaslc.org/iaslc-news/press-release/declaration-iaslc-tobacco-cessation-after-cancer-diagnosis</u>.
- 16. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. Am J Public Health. 1999;89(9):1322-7. doi: 10.2105/ajph.89.9.1322.
- 17. Glasgow RE, Estabrooks PE. Pragmatic applications of RE-AIM for health care initiatives in community and clinical settings. Prev Chronic Dis. 2018;15:e02. doi: 10.5888/pcd15.170271.
- 18. D'Angelo H, Ramsey AT, Rolland B, Chen LS, Bernstein SL, Fucito LM, et al. Pragmatic application of the RE-AIM framework to evaluate the implementation of tobacco cessation programs within NCI-Designated Cancer Centers. Front Public Health. 2020;8:221. doi: 10.3389/fpubh.2020.00221.
- 19. Fiore MC, Jaen CR, Baker TB, Bailey WC, Benowitz NL, Curry SJ, et al. Treating tobacco use and dependence: 2008 update. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service; 2008. Available from: https://www.ncbi.nlm.nih.gov/books/NBK63952/.
- 20. Salloum RG, Lee J, Lee JH, Boeckmann M, Xing C, Warren GW. Smoking-cessation methods and outcomes among cancer survivors. Am J Prev Med. 2020;59(4):615-7. doi: 10.1016/j.amepre.2020.03.016.

- 21. Babb S, Malarcher A, Schauer G, Asman K, Jamal A. Quitting smoking among adults—United States, 2000–2015. MMWR Morb Mortal Wkly Rep. 2017;65(52):1457-64. doi: 10.15585/mmwr.mm6552a1.
- 22. Boyle RG, Solberg LI, Fiore MC. Use of electronic health records to support smoking cessation. Cochrane Database Syst Rev. 2014;(12):CD008743. doi: 10.1002/14651858.CD008743.pub3.
- 23. Vidrine JI, Shete S, Cao Y, Greisinger A, Harmonson P, Sharp B., et al. Ask-advise-connect: a new approach to smoking treatment delivery in health care settings. JAMA Intern Med. 2013;173(6):458-64. doi: 10.1001/jamainternmed.2013.3751.
- 24. Carlini BH, McDaniel AM, Weaver MT, Kauffman RM, Cerutti B, Stratton RM, et al. Reaching out, inviting back: using interactive voice response (IVR) technology to recycle relapsed smokers back to quitline treatment—a randomized controlled trial. BMC Public Health. 2012;12:507. doi: 10.1186/1471-2458-12-507.
- 25. Carlini BH, Miles L, Doyle S, Celestino P, Koutsky J. Using diverse communication strategies to re-engage relapsed tobacco quitline users in treatment, New York State, 2014. Prev Chronic Dis. 2015;12:150191. doi: 10.5888/pcd12.150191.
- 26. Haas JS, Linder JA, Park ER, Gonzalez I, Rigotti NA, Klinger EV, et al. Proactive tobacco cessation outreach to smokers of low socioeconomic status: a randomized clinical trial. JAMA Intern Med. 2015;175(2):218-26. doi: 10.1001/jamainternmed.2014.6674.
- 27. Nahhas GJ, Wilson D, Talbot V, Cartmell KB, Warren GW, Toll BA., et al. Feasibility of implementing a hospital-based "opt-out" tobacco-cessation service. Nicotine Tob Res. 2017;19(8):937-43. doi: 10.1093/ntr/ntw312.
- 28. Rigotti NA, Chang Y, Rosenfeld LC, Japuntich SJ, Park ER, Tindle HA, et al. Interactive voice response calls to promote smoking cessation after hospital discharge: pooled analysis of two randomized clinical trials. J Gen Intern Med. 2017;32(9):1005-13. doi: 10.1007/s11606-017-4085-z.
- 29. Richter KP, Ellerbeck EF. It's time to change the default for tobacco treatment. Addiction. 2015;110(3):381-6. doi: 10.1111/add.12734.
- 30. Kotsen C, Dilip D, Carter-Harris L, O'Brien M, Whitlock CW, de Leon-Sanchez S, et al. Rapid scaling up of telehealth treatment for tobacco-dependent cancer patients during the COVID-19 outbreak in New York City. Telemed J E Health. 2021;27(1):20-9. doi: 10.1089/tmj.2020.0194.
- Henry J, Pylypchuk Y, Searcy T, Patel V. (2016). Adoption of electronic health record systems among U.S. non-federal acute care hospitals: 2008–2015. ONC Data Brief No. 35. Washington: Office of the National Coordinator for Health Information Technology; 2016 May.
- 32. Adsit RT, Fox BM, Tsiolis T, Ogland C, Simerson M, Vind LM, et al. Using the electronic health record to connect primary care patients to evidence-based telephonic tobacco quitline services: a closed-loop demonstration project. Transl Behav Med. 2014;4(3):324-32. doi: 10.1007/s13142-014-0259-y.
- 33. Baker TB, Berg KM, Adsit RT, Skora AD, Swedlund MP, Zehner ME, et al. Closed-loop electronic referral from primary care clinics to a state tobacco cessation quitline: effects using real-world implementation training. Am J Prev Med. 2021;60(3 Suppl 2):S113-22. doi: 10.1016/j.amepre.2019.12.026.
- 34. Fiore MC, Adsit RT, Zehner M, McCarthy DE, Lundsten S, Hartlaub P, et al. An electronic health record– based interoperable eReferral system to enhance smoking quitline treatment in primary care. J Am Med Inform Assoc. 2019;26(8-9):778-86. doi: 10.1093/jamia/ocz044.
- 35. Ramsey AT, Baker TB, Stoneking F, Smock N, Chen J, Pham G, et al. Increased reach and effectiveness with a low-burden point-of-care tobacco treatment program in cancer clinics. J Natl Compr Canc Netw. 2022;20(5):488-495.e4. doi: 10.6004/jnccn.2021.7333.
- 36. Lindholm C, Adsit RT, Bain P, Reber PM, Brein T, Redmond L, et al. A demonstration project for using the electronic health record to identify and treat tobacco users. WMJ. 2010;109(6):335-40.
- 37. McCarthy DE, Adsit RT, Zehner ME, Mahr TA, Skora AD, Kim N, et al. Closed-loop electronic referral to SmokefreeTXT for smoking cessation support: a demonstration project in outpatient care. Transl Behav Med. 2020;10(6):1472-80. doi: 10.1093/tbm/ibz072.
- 38. Bernstein SL, Rosner J, DeWitt M, Tetrault J, Hsiao AL, Dziura J, et al. Design and implementation of decision support for tobacco dependence treatment in an inpatient electronic medical record: a randomized trial. Transl Behav Med. 2017;7(2):185-95. doi: 10.1007/s13142-017-0470-8.
- Karn S, Fernandez A, Grossberg LA, Robertson T, Sharp B, Huang P, et al. Systematically improving tobacco cessation patient services through electronic medical record integration. Health Promot Pract. 2016;17(4):482-9. doi: 10.1177/1524839916643910.
- 40. Cupertino AP, Richter KP, Cox LS, Garrett S, Ramirez R, Mujica F, et al. Feasibility of a Spanish/English computerized decision aid to facilitate smoking cessation efforts in underserved communities. J Health Care Poor Underserved. 2010;21(2):504-17. doi: 10.1353/hpu.0.0307.

- 41. Duncan MS, Freiberg MS, Greevy RA Jr, Kundu S, Vasan RS, Tindle HA. Association of smoking cessation with subsequent risk of cardiovascular disease. JAMA. 2019;322(7):642-50. doi: 10.1001/jama.2019.10298.
- 42. Tindle HA, Duncan MS, Greevy RA, Vasan RS, Kundu S, Massion PP, et al. Lifetime smoking history and risk of lung cancer: results from the Framingham Heart Study. J Natl Cancer Inst. 2018;110(11):1201-7. doi: 10.1093/jnci/djy041.
- 43. Karam-Hage M, Cinciripini PM, Gritz ER. Tobacco use and cessation for cancer survivors: an overview for clinicians. CA Cancer J Clin. 2014;64(4):272-90. doi: 10.3322/caac.21231.
- 44. Wilson DK, Lorig K, Klein WM, Riley W, Sweeney AM, Christensen A. Efficacy and cost-effectiveness of behavioral interventions in nonclinical settings for improving health outcomes. Health Psychol. 2019;38(8):689-700. doi: 10.1037/hea0000773.
- 45. Anderson CM, Zhu SH. Tobacco quitlines: looking back and looking ahead. Tob Control. 2007;16 Suppl 1:i81-6. doi: 10.1136/tc.2007.020701.
- 46. Cummins S, Bailey L, Campbell S, Koon-Kirby C, Zhu SH. Tobacco cessation quitlines in North America: a descriptive study. Tob Control. 2007;16 Suppl 1:i9-15. doi: 10.1136/tc.2007.020370.
- 47. North American Quitline Consortium (NAQC). Results from the 2018 NAQC annual survey of quitlines [Internet]. Rudie M, editor. Phoenix, AZ: The Consortium; 2018 [cited 2022 June 5]. Available from: http://www.naquitline.org/page/2018Survey.
- 48. North American Quitline Consortium (NAQC). Results from the 2019 NAQC annual survey of quitlines [Internet]. Stein CC, editor. Phoenix, AZ: The Consortium; 2019 [cited 2022 June 5]. Available from: https://www.naquitline.org/page/2019survey.
- 49. Centers for Disease Control and Prevention (CDC) [Internet]. Atlanta: Office on Smoking and Health; c2019 [cited 2022 June 5]. 1-800-QUIT-NOW: 15 years of helping people quit; [about 9 screens]. Available from: <u>https://www.cdc.gov/tobacco/features/quitlines/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Ftobacco%2Ffeatures%2Fquitlines%2F15th-anniversary%2Findex.html</u>.
- 50. Fiore MC, Baker TB. Ten million calls and counting: progress and promise of tobacco quitlines in the U.S. Am J Prev Med. 2021;60(3 Suppl 2):S103-6. doi: 10.1016/j.amepre.2020.06.021.
- 51. Matkin W, Ordonez-Mena JM, Hartmann-Boyce J. Telephone counselling for smoking cessation. Cochrane Database Syst Rev. 2019;(5):CD002850. doi: 10.1002/14651858.CD002850.pub4.
- 52. Zhu SH, Anderson CM, Tedeschi GJ, Rosbrook B, Johnson CE, Byrd M, et al. Evidence of real-world effectiveness of a telephone quitline for smokers. N Engl J Med. 2002;347(14):1087-93. doi: 10.1056/NEJMsa020660.
- 53. Cummings KM, Fix B, Celestino P, Carlin-Menter S, O'Connor R, Hyland A. Reach, efficacy, and costeffectiveness of free nicotine medication giveaway programs. J Public Health Manag Pract. 2006;12(1):37-43. doi: 10.1097/00124784-200601000-00009.
- 54. Hollis JF, McAfee TA, Fellows JL, Zbikowski SM, Stark M, Riedlinger K. The effectiveness and cost effectiveness of telephone counselling and the nicotine patch in a state tobacco quitline. Tob Control. 2007;16 Suppl 1:i53-9. doi: 10.1136/tc.2006.019794.
- 55. Tinkelman D, Wilson SM, Willett J, Sweeney CT. Offering free NRT through a tobacco quitline: impact on utilisation and quit rates. Tob Control. 2007;16 Suppl 1:i42-6. doi: 10.1136/tc.2007.019919.
- 56. North American Quitline Consortium (NAQC). Guide for implementing eReferral using certified EHRs [Internet]. Phoenix, AZ: The Consortium; 2015 [cited 2022 June 5]. Available from: https://cdn.ymaws.com/sites/naquitline.site-ym.com/resource/resmgr/eRef/GuideforImpeRefFeb2016.pdf.
- 57. Jenssen BP, Muthu N, Kelly MK, Baca H, Shults J, Grundmeier RW, et al. Parent eReferral to tobacco quitline: a pragmatic randomized trial in pediatric primary care. Am J Prev Med. 2019;57(1):32-40. doi: 10.1016/j.amepre.2019.03.005.
- 58. Bernstein SL, Weiss J, DeWitt M, Tetrault JM, Hsiao AL, Dziura J, et al. A randomized trial of decision support for tobacco dependence treatment in an inpatient electronic medical record: clinical results. Implementation Sci. 2019;14(1):8. doi: 10.1186/s13012-019-0856-8.
- 59. Hood-Medland EA, Stewart SL, Nguyen H, Avdalovic M, MacDonald S, Zhu SH, et al. Health system implementation of a tobacco quitline eReferral. Appl Clin Inform. 2019;10(4);735-42. doi: 10.1055/s-0039-1697593.
- 60. Tindle HA, Daigh R, Reddy VK, Bailey LA, Ochs JA, Maness MH, et al. eReferral between hospitals and quitlines: an emerging tobacco control strategy. Am J Prev Med. 2016;51(4):522-6. doi: 10.1016/j.amepre.2016.05.024.
- 61. Notier AE, Hager P, Brown KS, Petersen L, Bedard L, Warren GW. Using a quitline to deliver opt-out smoking cessation for cancer patients. JCO Oncol Pract. 2020;16(6):e549-56. doi: 10.1200/jop.19.00296.

- 62. Prutzman YM, Wiseman KP, Grady MA, Budenz A, Grenen EG, Vercammen LK, et al. Using digital technologies to reach tobacco users who want to quit: evidence from the National Cancer Institute's Smokefree.gov Initiative. Am J Prev Med. 2021;60(3 Suppl 2):S172-84. doi: 10.1016/j.amepre.2020.08.008.
- 63. Reid RD, Mullen KA, Slovinec DME, Aitken DA, Papadakis S, Haley PM, et al. Smoking cessation for hospitalized smokers: an evaluation of the "Ottawa Model." Nicotine Tob Res. 2010;12(1):11-8. doi: 10.1093/ntr/ntp165.
- 64. Rigotti NA, Regan S, Levy DE, Japuntich S, Chang Y, Park ER, et al. Sustained care intervention and postdischarge smoking cessation among hospitalized adults: a randomized clinical trial. JAMA. 2014;312(7):719-28. doi: 10.1001/jama.2014.9237.
- 65. Rigotti NA, Tindle HA, Regan S, Levy DE, Chang Y, Carpenter KM, et al. A post-discharge smokingcessation intervention for hospital patients: Helping Hand 2 randomized clinical trial. Am J Prev Med. 2016;51(4):597-608. doi: 10.1016/j.amepre.2016.04.005.
- 66. Cartmell KB, Dismuke CE, Dooley M, Mueller M, Nahhas GJ, Warren GW, et al. Effect of an evidence-based inpatient tobacco dependence treatment service on 1-year postdischarge health care costs. Med Care. 2018;56(10):883-9. doi: 10.1097/mlr.00000000000979.
- 67. Cartmell KB, Dooley M, Mueller M, Nahhas GJ, Dismuke CE, Warren GW, et al. Effect of an evidence-based inpatient tobacco dependence treatment service on 30-, 90-, and 180-day hospital readmission rates. Med Care. 2018;56(4):358-63. doi: 10.1097/mlr.00000000000884.
- 68. Fu SS, van Ryn M, Sherman SE, Burgess DJ, Noorbaloochi S, Clothier B, et al. Proactive tobacco treatment and population-level cessation: a pragmatic randomized clinical trial. JAMA Intern Med. 2014;174(5):671-7. doi: 10.1001/jamainternmed.2014.177.
- 69. Fu SS, van Ryn M, Nelson D, Burgess DJ, Thomas JL, Saul J, et al. Proactive tobacco treatment offering free nicotine replacement therapy and telephone counselling for socioeconomically disadvantaged smokers: a randomised clinical trial. Thorax. 2016;71(5):446-53. doi: 10.1136/thoraxjnl-2015-207904.
- Joseph AM, Arikian NJ, An LC, Nugent SM, Sloan RJ, Pieper CF, et al. Results of a randomized controlled trial of intervention to implement smoking guidelines in Veterans Affairs medical centers: increased use of medications without cessation benefit. Med Care. 2004;42(11):1100-10. doi: 10.1097/00005650-200411000-00009.
- 71. Greenberg MR, Greco NM, Batchelor TJ, Miller AHF, Doherty T, Aziz AS, et al. Physician-directed smoking cessation using patient "opt-out" approach in the emergency department: A pilot program. J Am Coll Emerg Physicians Open. 2020;1(5):782-89. doi: 10.1002/emp2.12176.
- 72. Rigotti NA, Clair C, Munafo MR, Stead LF. Interventions for smoking cessation in hospitalised patients. Cochrane Database Syst Rev. 2012;(5):CD001837. doi: 10.1002/14651858.CD001837.pub3.
- 73. Ylioja T, Reddy V, Ambrosino R, Davis EM, Douaihy A, Slovenkay K, et al. Using bioinformatics to treat hospitalized smokers: successes and challenges of a tobacco treatment service. Jt Comm J Qual Patient Saf. 2017;43(12):621-32. doi: 10.1016/j.jcjq.2017.06.010.
- 74. Danan ER, Joseph AM, Sherman SE, Burgess DJ, Noorbaloochi S, Clothier B, et al. Does motivation matter? Analysis of a randomized trial of proactive outreach to VA smokers. J Gen Intern Med. 2016;31(8):878-87. doi: 10.1007/s11606-016-3687-1.
- Faseru B, Yeh HW, Ellerbeck EF, Befort C, Richter KP. Prevalence and predictors of tobacco treatment in an academic medical center. Jt Comm J Qual Patient Saf. 2009;35(11):551-7. doi: 10.1016/s1553-7250(09)35075-8.
- 76. Ohde JW, Master Z, Tilburt JC, Warner DO. Presumed consent with opt-out: an ethical consent approach to automatically refer patients with cancer to tobacco treatment services. J Clin Oncol. 2021;39(8):876-80. doi: 10.1200/jco.20.03180.
- 77. Johnson EJ, Goldstein D. Do defaults save lives? Science. 2003;302(5649):1338-9. doi: 10.1126/science.1091721.
- 78. Sunstein, CR. Nudging: a very short guide. J Consum Policy. 2014;37:583-8. doi: 10.1007/s10603-014-9273-1.
- 79. Nolan MB, Ridgeway JL, Ghosh K, Martin D, Warner DO. Design, implementation, and evaluation of an intervention to improve referral to smoking cessation services in breast cancer patients. Support Care Cancer. 2019;27(6):2153-8. doi: 10.1007/s00520-018-4486-5.
- 80. Warren GW, Marshall JR, Cummings KM, Zevon MA, Reed R, Hysert P, et al. Automated tobacco assessment and cessation support for cancer patients. Cancer. 2014;120(4):562-9. doi: 10.1002/cncr.28440.
- Taylor KL, Fallon S, Subramaniam D, Davis K, To C, Lobo T, et al. Implementation of the Smoking Treatment and Recovery (STAR) program: healthy cancer survivorship through integrated tobacco control. J Cancer Surviv. 2020;14(1):53-8. doi: 10.1007/s11764-019-00826-1.

- Gali K, Pike B, Kendra MS, Tran C, Fielding-Singh P, Jimenez K, et al. Integration of tobacco treatment services into cancer care at Stanford. Int J Environ Res Public Health. 2020;17(6):2101. doi: 10.3390/ijerph17062101.
- Himelfarb-Blyth S, Vanderwater C, Hartwick J. Implementing a 3As and 'opt-out' tobacco cessation framework in an outpatient oncology setting. Curr Oncol. 2021;28(2):1197-203. doi: 10.3390/curroncol28020115.
- 84. Jose T, Ohde JW, Hays JT, Burke MV, Warner DO. Design and pilot implementation of an electronic health record–based system to automatically refer cancer patients to tobacco use treatment. Int J Environ Res Public Health. 2020;17(11):4054. doi: 10.3390/ijerph17114054.
- 85. Cancer Center Cessation Initiative Telehealth Working Group. Telehealth delivery of tobacco cessation treatment in cancer care: an ongoing innovation accelerated by the COVID-19 pandemic. J Natl Compr Canc Netw. 2021;19(Suppl_1):S21-24. doi: 10.6004/jnccn.2021.7092.
- 86. Park ER, Perez GK, Regan S, Muzikansky A, Levy DE, Temel JS, et al. 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. JAMA. 2020;324(14):1406-18. doi: 10.1001/jama.2020.14581.
- 87. Cinciripini PM, Karam-Hage M, Kypriotakis G, Robinson JD, Rabius V, Beneventi D, et al. Association of a comprehensive smoking cessation program with smoking abstinence among patients with cancer. JAMA Netw Open. 2019;2(9):e1912251. doi: 10.1001/jamanetworkopen.2019.12251.
- Karam-Hage M, Oughli HA, Rabius V, Beneventi D, Wippold RC, Blalock JA, et al. Tobacco cessation treatment pathways for patients with cancer: 10 years in the making. J Natl Compr Canc Netw. 2016;14(11):1469-77. doi: 10.6004/jnccn.2016.0153.
- 89. Gaglio B, Shoup JA, Glasgow RE. The RE-AIM framework: a systematic review of use over time. Am J Public Health. 2013;103(6):e38-46. doi: 10.2105/ajph.2013.301299.
- American Society of Clinical Oncology. American Society of Clinician Oncology policy statement update: tobacco control—reducing cancer incidence and saving lives. J Clin Oncol. 2003;21(14):2777-86. doi: 10.1200/JCO.2003.04.154
- 91. Shields PG. New NCCN guidelines: smoking cessation for patients with cancer. J Natl Compr Canc Netw. 2015;13(5 Suppl):643-5. doi: 10.6004/jnccn.2015.0191.
- 92. Goldstein AO, Ripley-Moffitt CE, Pathman DE, Patsakham KM. Tobacco use treatment at the U.S. National Cancer Institute's designated Cancer Centers. Nicotine Tob Res. 2013;15(1):52-8. doi: 10.1093/ntr/nts083.
- 93. Price SN, Studts JL, Hamann HA. Tobacco use assessment and treatment in cancer patients: a scoping review of oncology care clinician adherence to clinical practice guidelines in the U.S. Oncologist. 2019;24(2):229-38. doi: 10.1634/theoncologist.2018-0246.
- 94. Warren GW, Marshall JR, Cummings KM, Toll BA, Gritz ER, Hutson A, et al. Practice patterns and perceptions of thoracic oncology providers on tobacco use and cessation in cancer patients. J Thorac Oncol. 2013;8(5):543-8. doi: 10.1097/JTO.0b013e318288dc96.
- 95. Warren GW, Marshall JR, Cummings KM, Toll BA, Gritz ER, Hutson A, et al. Addressing tobacco use in patients with cancer: a survey of American Society of Clinical Oncology members. J Oncol Pract. 2013;9(5):258-62. doi: 10.1200/jop.2013.001025.
- 96. Bjurlin MA, Goble SM, Hollowell CM. Smoking cessation assistance for patients with bladder cancer: a national survey of American urologists. J Urol. 2010;184(5):1901-6. doi: 10.1016/j.juro.2010.06.140.
- 97. Cooley ME, Poghosyan H, Sprunck-Harrild K, Winickoff JP, Edge SB, Emmons KM. Tobacco treatment implementation within 28 Commission on Cancer accredited programs in the Northeast region of the USA: a pilot study. Transl Behav Med. 2018;8(5):706-13. doi: 10.1093/tbm/ibx024.
- Corrigan JM. Crossing the quality chasm. In: Reid PP, Compton WD, Grossman JH, Fanjiang G, editors. Building a better delivery system: a new engineering/health care partnership. Washington: National Academies Press; 2005. p. 95-7.
- 99. Institute of Medicine. To err is human: building a safer health system. Washington: The National Academies Press; 2000.
- 100. Fiore MC, Goplerud E, Schroeder SA. The Joint Commission's new tobacco-cessation measures will hospitals do the right thing? N Engl J Med. 2012;366. doi: 10.1056/NEJMp1115176.
- 101. Centers for Medicare and Medicaid Services (CMS) [Internet]. Baltimore: The Centers; 2021 [cited 4 February 2022]. Centers for Medicare and Medicaid Services Measures Inventory Tool; [about 2 screens]. Available from:

https://cmit.cms.gov/CMIT_public/ViewMeasureComparison?measureId=1482,5792&sortByDifferences=true.

- 102. American Lung Association. Tobacco cessation and quality measures: an overview [Internet]. Chicago: The Association; 2019 [cited 2020 May 8]. Available from: <u>https://resources.chronicdisease.org/dir/wp-content/uploads/2020/04/TCCP</u> tools ala tob cess qual measures.pdf.
- 103. American Lung Association. Quality measures and tobacco cessation [Internet]. Chicago: The Association; 2020 [cited 2020 May 8]. Available from: <u>https://www.lung.org/getmedia/956552a2-99cc-4b38-</u> bd50-ba8bcc3d60ee/quality-measures-and-tobacco.pdf.pdf.
- 104. Carrillo S, Nazir N, Howser E, Shenkman L, Laxson M, Scheuermann TS, et al. Impact of the 2015 CMS inpatient psychiatric facility quality reporting rule on tobacco treatment. Nicotine Tob Res. 2017;19(8):976-82. doi: 10.1093/ntr/ntw386.
- 105. Scharf D, Fabian T, Fichter-DeSando C, Douaihy A. Nicotine replacement prescribing trends in a large psychiatric hospital, before and after implementation of a hospital-wide smoking ban. Nicotine Tob Res. 2011;13(6):466-73. doi: 10.1093/ntr/ntr026.
- 106. Sarna LP, Fiore MC, Schroeder SA. Tobacco dependence treatment is critical to excellence in health care. JAMA Intern Med. 2020;180(11):1413-4. doi: 10.1001/jamainternmed.2020.3972.
- 107. Joint Commission. 2022 ORYX® performance measure reporting requirements: hospital accreditation program (HAP) and critical access hospital accreditation (CAH) program [Internet]. Oakbrook Terrace, IL: The Commission; 2021 [cited 2022 June 5]. Available from: <u>https://www.jointcommission.org/-/media/tjc/documents/measurement/oryx/2022-oryx-reporting-requirements--october-19-2021.pdf</u>.
- 108. Kline RM, Bazell C, Smith E, Schumacher H, Rajkumar R, Conway PH. Centers for Medicare and Medicaid Services: using an episode-based payment model to improve oncology care. J Oncol Pract. 2015;11(2):114-6. doi: 10.1200/jop.2014.002337.
- 109. Centers for Medicare and Medicaid Services (CMS) [Internet]. Baltimore: The Centers; c2020 [cited 29 May 2020]. Shared Savings Program: about the program; [about 4 screens]. Available from: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/sharedsavingsprogram/about.
- 110. Centers for Medicare and Medicaid Services [Internet]. Baltimore: The Centers; n.d. [cited 2022 June 5]. Adult and child health care quality measures; [about 2 screens]. Available from: https://www.medicaid.gov/medicaid/quality-of-care/performance-measurement/adult-and-child-health-care-quality-measures/index.html
- 111. National Quality Forum. Preventive Care and Screening: Tobacco Use: Screening and Cessation Intervention. 2020. Available from: <u>https://www.qualityforum.org/QPS/0028.</u>
- 112. National Quality Forum. Tobacco Use and Help with Quitting Among Adolescents. 2020. Available from: https://www.qualityforum.org/QPS/2803
- 113. National Quality Forum. Medical Assistance With Smoking and Tobacco Use Cessation. 2021. Available from: https://www.qualityforum.org/QPS/0027
- 114. Blumenthal D. Launching HITECH. N Engl J Med. 2010;362(5):382-5. doi: 10.1056/NEJMp0912825.
- 115. Blumenthal D, Tavenner M. The "meaningful use" regulation for electronic health records. N Engl J Med. 2010;363(6):501-4. doi: 10.1056/NEJMp1006114.
- 116. McAfee T, Babb S, McNabb S, Fiore MC. Helping smokers quit—opportunities created by the Affordable Care Act. N Engl J Med. 2015;372(1):5-7. doi: 10.1056/NEJMp1411437.
- 117. U.S. Preventive Services Task Force. Screening for lung cancer: US Preventive Services Task Force recommendation statement. JAMA. 2021;325(10):962-70. doi: 10.1001/jama.2021.1117.
- 118. DiGiulio A, Jump Z, Babb S, Schecter A, Williams KAS, Yembra D, et al. State Medicaid coverage for tobacco cessation treatments and barriers to accessing treatments—United States, 2008–2018. MMWR Morb Mortal Wkly Rep. 2020;69:155-60. doi: 10.15585/mmwr.mm6906a2.
- 119. Fraze TK, Lewis VA, Tierney E, Colla CH. Quality of care improves for patients with diabetes in Medicare Shared Savings accountable care organizations: organizational characteristics associated with performance. Popul Health Manag. 2018;21(5):401-8.
- 120. Maclean JC, Pesko MF, Hill SC. The effect of insurance expansions on smoking cessation medication prescriptions: evidence from ACA Medicaid expansions: working paper 23450 [Internet]. Cambridge, MA: National Bureau of Economic Research; 2017 May [cited 2022 June 5]. Available from: <u>https://www.nber.org/papers/w23450</u>.
- 121. Koma JW, Donohue JM, Barry CL, Huskamp HA, Jarlenski M. Medicaid coverage expansions and cigarette smoking cessation among low-income adults. Med Care. 2017;55(12):1023-9. doi: 10.1097/mlr.0000000000821.
- 122. Cohen RA, Cha AE, Martinez ME, Terlizzi EP [Internet]. Health insurance coverage: early release of estimates from the National Health Interview Survey, 2019. Hyattsville, MD: National Center for Health Statistics; 2020

Sep [cited 13 Sep 2021]. Available from: <u>https://www.cdc.gov/nchs/data/nhis/earlyrelease/insur202009-508.pdf</u>.

- 123. Nolan MB, Warner DO. Perioperative tobacco use treatments: putting them into practice. BMJ. 2017;358:j3340. doi: 10.1136/bmj.j3340.
- 124. Simmons VN, Litvin EB, Unrod M, Brandon TH. Oncology healthcare providers' implementation of the 5A's model of brief intervention for smoking cessation: patients' perceptions. Patient Educ Couns. 2012;86(3):414-9. doi: 10.1016/j.pec.2011.06.016.
- 125. Ramsey AT, Chiu A, Baker T, Smock N, Chen J, Lester T, et al. 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. Transl Behav Med. 2020;10(6):1504-14. doi: 10.1093/tbm/ibz107.
- 126. Vinci C, Haslam A, Lam CY, Kumar S, Wetter DW. The use of ambulatory assessment in smoking cessation. Addict Behav. 2018;83:18-24. doi:10.1016/j.addbeh.2018.01.018.
- 127. Evans WK, Truscott R, Cameron E, Peter A, Reid R, Selby P, et al. Lessons learned implementing a provincewide smoking cessation initiative in Ontario's cancer centres. Curr Oncol. 2017;24(3):e185-90. doi: 10.3747/co.23.3506.
- 128. Evans WK, Truscott R, Cameron E, Rana S, Isaranuwatchai W, Haque M, et al. Implementing smoking cessation within cancer treatment centres and potential economic impacts. Transl Lung Cancer Res. 2019;8 Suppl 1:S11-20. doi: 10.21037/tlcr.2019.05.09.
- 129. Tong EK, Wolf T, Cooke DT, Fairman N, Chen MS Jr. 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. Int J Environ Res Public Health. 2020;17(9):3241. doi: 10.3390/ijerph17093241.
- 130. Salloum RG, D'Angelo H, Theis RP, Rolland B, Hohl S, Pauk D, et al. Mixed-methods economic evaluation of the implementation of tobacco treatment programs in National Cancer Institute-designated cancer centers. Implement Sci Commun. 2021;2(1):41. doi: 10.1186/s43058-021-00144-7.
- 131. Barua RS, Rigotti NA, Benowitz NL, Cummings KM, Jazayeri MA, Morris PB, et al. 2018 ACC expert consensus decision pathway on tobacco cessation treatment: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol. 2018;72(25):3332-65. doi: 10.1016/j.jacc.2018.10.027.
- 132. Hollis JF, Bills R, Whitlock E, Stevens VJ, Mullooly J, Lichtenstein E. Implementing tobacco interventions in the real world of managed care. Tob Control. 2000;9 Suppl 1:i18-24. doi: 10.1136/tc.9.suppl_1.i18.
- 133. Heisey-Grove D, King JA. Physician and practice-level drivers and disparities around meaningful use progress. Health Serv Res. 2017;52(1):244-67. doi: 10.1111/1475-6773.12481.
- 134. Morgan GD, Fiore MC. Chapter 6—prevention, information technology, and cancer. In: Hesse BW, Ahern DK, Beckjord E, editors. Oncology informatics. Boston: Academic Press; 2016. p. 103-22.
- 135. Morales NA, Romano MA, Cummings KM, Marshall JR, Hyland AJ, Hutson A, et al. Accuracy of selfreported tobacco use in newly diagnosed cancer patients. Cancer Causes Control. 2013;24(6):1223-30. doi: 10.1007/s10552-013-0202-4.
- 136. Warren GW, Arnold SM, Valentino JP, Gal TJ, Hyland AJ, Singh AK, et al. Accuracy of self-reported tobacco assessments in a head and neck cancer treatment population. Radiother Oncol. 2012;103(1):45-8. doi: 10.1016/j.radonc.2011.11.003.
- 137. Cataldo JK, Slaughter R, Jahan TM, Pongquan VL, Hwang WJ. Measuring stigma in people with lung cancer: psychometric testing of the Cataldo Lung Cancer Stigma Scale. Oncol Nurs Forum. 2011;38(1):E46-54. doi: 10.1188/11.Onf.E46-e54.
- 138. Riley KE, Ulrich MR, Hamann HA, Ostroff JS. Decreasing smoking but increasing stigma? Anti-tobacco campaigns, public health, and cancer care. AMA J Ethics. 2017;19(5):475-85. doi: 10.1001/journalofethics.2017.19.5.msoc1-1705.
- 139. Simmons VN, Litvin EB, Patel RD, Jacobsen PB, McCaffrey JC, Bepler G, et al. Patient-provider communication and perspectives on smoking cessation and relapse in the oncology setting. Patient Educ Couns. 2009;77(3):398-403. doi: 10.1016/j.pec.2009.09.024.
- 140. Alberg AJ, Worley ML, Tooze JA, Hatcher JL, Carpenter MJ, Day TA, et al. The validity of self-reported recent smoking in head and neck cancer surgical patients. Otolaryngol Head Neck Surg. 2015;153(6):990-5. doi: 10.1177/0194599815594385.
- 141. Klesges RC, Krukowski RA, Klosky JL, Liu W, Srivastava DK, Boyett JM, et al. Efficacy of a tobacco quitline among adult cancer survivors. Prev Med. 2015;73:22-7. doi: 10.1016/j.ypmed.2014.12.019.

- 142. Thong AE, Petruzella S, Orlow I, Zabor EC, Ehdaie B, Ostroff JS, et al. Accuracy of self-reported smoking exposure among bladder cancer patients undergoing surveillance at a tertiary referral center. Eur Urol Focus. 2016;2(4):441-4. doi: 10.1016/j.euf.2015.12.002.
- 143. Land SR, Toll BA, Moinpour CM, Mitchell SA, Ostroff JS, Hatsukami DK, et al. Research priorities, measures, and recommendations for assessment of tobacco use in clinical cancer research. Clin Cancer Res. 2016;22(8):1907-13. doi: 10.1158/1078-0432.Ccr-16-0104.
- 144. Land SR, Warren GW, Crafts JL, Hatsukami DK, Ostroff JS, Willis GB, et al. Cognitive testing of tobacco use items for administration to patients with cancer and cancer survivors in clinical research. Cancer. 2016;122(11):1728-34. doi: 10.1002/cncr.29964.
- 145. Benowitz NL, Bernert JT, Foulds J, Hecht SS, Jacob P, Jarvis MJ, et al. Biochemical verification of tobacco use and abstinence: 2019 update. Nicotine Tob Res. 2020;22(7):1086-97. doi: 10.1093/ntr/ntz132.
- 146. Burde H. The HITECH Act: an overview. Virtual Mentor. 2011;13(3):172-5. doi: 10.1001/virtualmentor.2011.13.3.hlaw1-1103.
- 147. Bae J, Ford EW, Kharrazi HH, Huerta TR. Electronic medical record reminders and smoking cessation activities in primary care. Addict Behav. 2018;77:203-9. doi: 10.1016/j.addbeh.2017.10.009.
- 148. Fortmann SP, Bailey SR, Brooks NB, Hitsman B, Rittner SS, Gillespie SE, et al. Trends in smoking documentation rates in safety net clinics. Health Serv Res. 2020;55(2):170-7. doi: 10.1111/1475-6773.13259.
- 149. Warren GW, Sobus S, Gritz ER. The biological and clinical effects of smoking by patients with cancer and strategies to implement evidence-based tobacco cessation support. Lancet Oncol. 2014;15(12):e568-80. doi: 10.1016/s1470-2045(14)70266-9.
- 150. Jenssen BP, Leone F, Evers-Casey S, Beidas R, Schnoll R. Building systems to address tobacco use in oncology: early benefits and opportunities from the Cancer Center Cessation Initiative. J Natl Compr Canc Netw. 2019;17(6):638-43. doi: 10.6004/jnccn.2019.7312.
- 151. Burris JL, Studts JL, DeRosa AP, Ostroff JS. Systematic review of tobacco use after lung or head/neck cancer diagnosis: results and recommendations for future research. Cancer Epidemiol Biomarkers Prev. 2015;24(10):1450-61. doi: 10.1158/1055-9965.Epi-15-0257.
- 152. Kumar PC, Cleland CM, Gourevitch MN, Rotrosen J, Strauss S, Russell L, et al. Accuracy of the Audio Computer Assisted Self Interview version of the Alcohol, Smoking and Substance Involvement Screening Test (ACASI ASSIST) for identifying unhealthy substance use and substance use disorders in primary care patients. Drug Alcohol Depend. 2016;165:38-44. doi: 10.1016/j.drugalcdep.2016.05.030.
- 153. Jamal A, Dube SR, Babb SD, Malarcher AM; Centers for Disease Control and Prevention (CDC). Tobacco use screening and cessation assistance during physician office visits among persons aged 11-21 years—National Ambulatory Medical Care Survey, United States, 2004-2010. MMWR Suppl. 2014;63(2):71-9.
- 154. Morgan G, Schnoll RA, Alfano CM, Evans SE, Goldstein A, Ostroff J, et al. National Cancer Institute conference on treating tobacco dependence at cancer centers. J Oncol Pract. 2011;7(3):178-82. doi: 10.1200/JOP.2010.000175.
- 155. Burcu M, Steinberger EK, Sorkin JD. Health care access and smoking cessation among cancer survivors: implications for the Affordable Care Act and survivorship care. J Cancer Surviv. 2016;10(1):1-10. doi: 10.1007/s11764-015-0446-y.
- 156. Coups EJ, Ostroff JS. A population-based estimate of the prevalence of behavioral risk factors among adult cancer survivors and noncancer controls. Prev Med. 2005;40(6):702-11. doi: 10.1016/j.ypmed.2004.09.011.
- 157. Gallaway MS, Glover-Kudon R, Momin B, Puckett M, Buchanan Lunsford N, Ragan KR, et al. Smoking cessation attitudes and practices among cancer survivors—United States, 2015. J Cancer Surviv. 2019;13(1):66-74. doi: 10.1007/s11764-018-0728-2.
- 158. Mayer DK, Carlson J. Smoking patterns in cancer survivors. Nicotine Tob Res. 2010;13(1):34-40. doi: 10.1093/ntr/ntq199.
- 159. Ramaswamy AT, Toll BA, Chagpar AB, Judson BL. Smoking, cessation, and cessation counseling in patients with cancer: a population-based analysis. Cancer. 2016;122(8):1247-53. doi: 10.1002/cncr.29851.
- 160. Shoemaker ML, White MC, Hawkins NA, Hayes NS. Prevalence of smoking and obesity among U.S. cancer survivors: estimates from the National Health Interview Survey, 2008-2012. Oncol Nurs Forum. 2016;43(4):436-41. doi: 10.1188/16.ONF.43-04AP.
- 161. Tseng TS, Lin HY, Moody-Thomas S, Martin M, Chen T. Who tended to continue smoking after cancer diagnosis: the National Health and Nutrition Examination Survey 1999-2008. BMC Public Health. 2012;12:784. doi: 10.1186/1471-2458-12-784.

- 162. Westmaas JL, Alcaraz KI, Berg CJ, Stein KD. Prevalence and correlates of smoking and cessation-related behavior among survivors of ten cancers: findings from a nationwide survey nine years after diagnosis. Cancer Epidemiol Biomarkers Prev. 2014;23(9):1783-92. doi: 10.1158/1055-9965.Epi-14-0046.
- 163. Swoboda CM, Walker DM, Huerta TR. Likelihood of smoking among cancer survivors: an updated Health Information National Trends Survey analysis. Nicotine Tob Res. 2019;21(12):1636-43. doi: 10.1093/ntr/ntz007.
- 164. Park ER, Japuntich SJ, Rigotti NA, Traeger L, He Y, Wallace RB, et al. A snapshot of smokers after lung and colorectal cancer diagnosis. Cancer. 2012;118(12):3153-64. doi: 10.1002/cncr.26545.
- 165. Cooley ME, Sarna L, Kotlerman J, Lukanich JM, Jaklitsch M, Green SB, et al. Smoking cessation is challenging even for patients recovering from lung cancer surgery with curative intent. Lung Cancer. 2009;66(2):218-25. doi: 10.1016/j.lungcan.2009.01.021.
- 166. Walker MS, Vidrine DJ, Gritz ER, Larsen RJ, Yan Y, Govindan R, et al. Smoking relapse during the first year after treatment for early-stage non–small-cell lung cancer. Cancer Epidemiol Biomarkers Prev. 2006;15(12):2370. doi: 10.1158/1055-9965.EPI-06-0509.
- 167. Allison PJ. Factors associated with smoking and alcohol consumption following treatment for head and neck cancer. Oral Oncol. 2001;37(6):513-20. doi: 10.1016/s1368-8375(01)00015-x.
- 168. Cornelius ME, Loretan CG, Wang TW, Jamal A, Homa DM. Tobacco product use among adults United States, 2020. MMWR Morb Mortal Wkly Rep. 2022;71(11):397-405. doi: 10.15585/mmwr.mm7111a1.
- 169. Finney Rutten LJ, Augustson EM, Moser RP, Beckjord EB, Hesse BW. Smoking knowledge and behavior in the United States: sociodemographic, smoking status, and geographic patterns. Nicotine Tob Res. 2008;10(10):1559-70. doi: 10.1080/14622200802325873.
- 170. Truth Initiative. Tobacco nation: an ongoing crisis [Internet]. Washington: Truth Initiative; 2019. [cited 2022 June 5]. Available from: <u>https://truthinitiative.org/sites/default/files/media/files/2019/06/Tobacco-Nation-An-Ongoing-Crisis.pdf</u>.
- 171. D'Angelo H, Webb Hooper M, Burris JL, Rolland B, Adsit RT, Pauk D, et al. Achieving equity in the reach of smoking cessation services within the NCI Cancer Moonshot-funded Cancer Center Cessation Initiative. Health Equity. 2021;5(1):424-30. doi: 10.1089/heq.2020.0157.
- 172. Guzzo TJ, Hockenberry MS, Mucksavage P, Bivalacqua TJ, Schoenberg MP. Smoking knowledge assessment and cessation trends in patients with bladder cancer presenting to a tertiary referral center. Urology. 2012;79(1):166-71. doi: 10.1016/j.urology.2011.06.055.
- 173. Hoover DS, Spears CA, Vidrine DJ, Walker JL, Shih YT, Wetter DW. Smoking cessation treatment needs of low SES cervical cancer survivors. Am J Health Behav. 2019;43(3):606-20. doi: 10.5993/ajhb.43.3.14.
- 174. Puleo GE, Borger TN, Montgomery D, Rivera-Rivera JN, Burris JL. A qualitative study of smoking-related causal attributions and risk perceptions in cervical cancer survivors. Psychooncology. 2020;29(3):500-6. doi: 10.1002/pon.5291.
- 175. Westhoff E, Maria de Oliveira-Neumayer J, Aben KK, Vrieling A, Kiemeney LA. Low awareness of risk factors among bladder cancer survivors: new evidence and a literature overview. Eur J Cancer. 2016;60:136-45. doi: 10.1016/j.ejca.2016.03.071.
- 176. Finney Rutten LJ, Blake KD, Hesse BW, Augustson EM, Evans S. Illness representations of lung cancer, lung cancer worry, and perceptions of risk by smoking status. J Cancer Educ. 2011;26(4):747-53. doi: 10.1007/s13187-011-0247-6.
- 177. Weinstein ND, Marcus SE, Moser RP. Smokers' unrealistic optimism about their risk. Tob Control. 2005;14(1):55-9. doi: 10.1136/tc.2004.008375.
- 178. Borrelli B, Hayes RB, Dunsiger S, Fava JL. Risk perception and smoking behavior in medically ill smokers: a prospective study. Addiction. 2010;105(6):1100-8. doi: 10.1111/j.1360-0443.2010.02900.x.
- 179. Dillard AJ, McCaul KD, Klein WM. Unrealistic optimism in smokers: implications for smoking myth endorsement and self-protective motivation. J Health Commun. 2006;11 Suppl 1:93-102. doi: 10.1080/10810730600637343.
- 180. Oakes W, Chapman S, Borland R, Balmford J, Trotter L. "Bulletproof skeptics in life's jungle": which selfexempting beliefs about smoking most predict lack of progression towards quitting? Prev Med. 2004;39(4):776-82. doi: 10.1016/j.ypmed.2004.03.001.
- 181. Shepperd JA, Waters E Weinstein ND, Klein WM. A primer on unrealistic optimism. Curr Dir Psychol Sci. 2015;24(3):232-7. doi: 10.1177/0963721414568341.
- 182. Hay JL, Ostroff J, Burkhalter J, Li Y, Quiles Z, Moadel A. Changes in cancer-related risk perception and smoking across time in newly-diagnosed cancer patients. J Behav Med. 2007;30(2):131-42. doi: 10.1007/s10865-007-9094-7.

- 183. Giuliani M, Brual J, Eng L, Liu G, Papadakos T, Giannopoulos E, et al. Investigating the smoking cessation informational needs of Cancer Patients and Informal Caregivers. J Cancer Educ. 2020;35(5):954-64. doi: 10.1007/s13187-019-01547-w.
- 184. Bassett JC, Gore JL, Kwan L, Ritch CR, Barocas DA, Penson DF, et al. Knowledge of the harms of tobacco use among patients with bladder cancer. 2014;120(24):3914-22. doi: 10.1002/cncr.28915.
- 185. Kathuria H, Koppelman E, Borrelli B, Slatore CG, Clark JA, Lasser KE, et al. Patient-physician discussions on lung cancer screening: a missed teachable moment to promote smoking cessation. Nicotine Tob Res. 2020;22(3):431-9. doi: 10.1093/ntr/nty254.
- 186. Cox LS, Patten CA, Ebbert JO, Drews AA, Croghan GA, Clark MM, et al. Tobacco use outcomes among patients with lung cancer treated for nicotine dependence. J Clin Oncol. 2002;20(16):3461-9. doi: 10.1200/jco.2002.10.085.
- 187. Gritz ER, Carr CR, Rapkin D, Abemayor E, Chang LJ, Wong WK, et al. Predictors of long-term smoking cessation in head and neck cancer patients. Cancer Epidemiol Biomarkers Prev. 1993;2(3):261-70.
- 188. Schnoll RA, Malstrom M, James C, Rothman RL, Miller SM, Ridge JA, et al. Correlates of tobacco use among smokers and recent quitters diagnosed with cancer. Patient Educ Couns. 2002;46(2):137-45. doi: 10.1016/s0738-3991(01)00157-4.
- Barrett JR, Cherney-Stafford L, Alagoz E, Piper ME, Cook J, Campbell-Flohr S, et al. Smoking and gastrointestinal cancer patients-is smoking cessation an attainable goal? J Surg Oncol. 2019;120(8):1335-40. doi: 10.1002/jso.25749.
- Solberg LI, Enstad CJ, Boyle RG, Nelson WW. Physician-patient interaction for smoking cessation medications: a dance of mutual accommodation? J Am Board Fam Med. 2006;19(3):251-7. doi: 10.3122/jabfm.19.3.251.
- 191. Berg CJ, Carpenter MJ, Jardin B, Ostroff JS. Harm reduction and cessation efforts and interest in cessation resources among survivors of smoking-related cancers. J Cancer Surviv. 2013;7(1):44-54. doi: 10.1007/s11764-012-0243-9.
- 192. Berg CJ, Thomas AN, Mertens AC, Schauer GL, Pinsker EA, Ahluwalia JS, et al. Correlates of continued smoking versus cessation among survivors of smoking-related cancers. Psychooncology. 2013;22(4):799-806. doi: 10.1002/pon.3077.
- 193. Bronson DL, Flynn BS, Solomon LJ, Vacek P, Secker-Walker RH. Smoking cessation counseling during periodic health examinations. Arch Intern Med. 1989;149(7):1653-6.doi: 10.1001/archinte.1989.00390070159027.
- 194. Li VC, Coates TJ, Ewart CK, Kim YJ. The effectiveness of smoking cessation advice given during routine medical care: physicians can make a difference. Am J Prev Med. 1987;3(2):81-6.
- 195. Blalock JA, Lam C, Minnix JA, Karam-Hage M, Gritz ER, Robinson JD, et al. The effect of mood, anxiety, and alcohol use disorders on smoking cessation in cancer patients. J Cogn Psychother. 2011;25(1):82-96. doi: 10.1891/0889-8391.25.1.82.
- 196. Boyes AW, Girgis A, D'Este C, Zucca AC. Flourishing or floundering? Prevalence and correlates of anxiety and depression among a population-based sample of adult cancer survivors 6 months after diagnosis. J Affect Disord. 2011;135(1-3):184-92. doi: 10.1016/j.jad.2011.07.016.
- 197. Hopenhayn C, Christian WJ, Christian A, Studts J, Mullet T. Factors associated with smoking abstinence after diagnosis of early stage lung cancer. Lung Cancer. 2013;80(1):55-61. doi: 10.1016/j.lungcan.2012.12.013.
- 198. Martinez E, Tatum KL, Weber DM, Kuzla N, Pendley A, Campbell K, et al. Issues related to implementing a smoking cessation clinical trial for cancer patients. Cancer Causes Control. 2009;20(1):97-104. doi: 10.1007/s10552-008-9222-x.
- 199. Schnoll RA, Martinez E, Langer C, Miyamoto C, Leone F. Predictors of smoking cessation among cancer patients enrolled in a smoking cessation program. Acta Oncol. 2011;50(5):678-84. doi: 10.3109/0284186X.2011.572915.
- 200. Simmons VN, Litvin EB, Jacobsen PB, Patel RD, McCaffrey JC, Oliver JA, et-al. Predictors of smoking relapse in patients with thoracic cancer or head and neck cancer. Cancer. 2013;119(7):1420-7. doi: 10.1002/cncr.27880.
- 201. Chang EH, Braith A, Hitsman B, Schnoll RA. Treating nicotine dependence and preventing smoking relapse in cancer patients. Expert Rev Qual Life Cancer Care. 2017;2(1):23-39. doi: 10.1080/23809000.2017.1271981.
- 202. Vander Ark W, DiNardo LJ, Oliver DS. Factors affecting smoking cessation in patients with head and neck cancer. Laryngoscope. 1997;107(7):888-92. doi: 10.1097/00005537-199707000-00010.

- 203. Wells M, Aitchison P, Harris F, Ozakinci G, Radley A, Bauld L, et al. Barriers and facilitators to smoking cessation in a cancer context: a qualitative study of patient, family and professional views. BMC Cancer. 2017;17(1):348. doi: 10.1186/s12885-017-3344-z.
- 204. Warner ET, Park ER, Luberto CM, Rabin J, Perez GK, Ostroff JS. Internalized stigma among cancer patients enrolled in a smoking cessation trial: The role of cancer type and associations with psychological distress. Psychooncology. 2022;31(5):753-60. doi:10.1002/pon.5859.
- 205. Charlesworth L, Hutton D, Hussain H. Therapeutic radiographers' perceptions of the barriers and enablers to effective smoking cessation support. Radiography (Lond). 2019;25(2):121-8. doi: 10.1016/j.radi.2018.12.002.
- 206. Coovadia S, D'Alimonte L, Bristow B, Curle E, Gibson L, Di Prospero L. Catalyst for change: measuring the effectiveness of training of all health care professionals to provide brief intervention for smoking cessation to cancer patients. J Med Imaging Radiat Sci. 2019. doi: 10.1016/j.jmir.2019.10.002.
- 207. Day FL, Sherwood E, Chen TY, Barbouttis M, Varlow M, Martin J, et al. Oncologist provision of smoking cessation support: a national survey of Australian medical and radiation oncologists. Asia Pac J Clin Oncol. 2018;14(6):431-8. doi: 10.1111/ajco.12876.
- 208. Ostroff JS, Copeland A, Borderud SP, Li Y, Shelley DR, Henschke CI. Readiness of lung cancer screening sites to deliver smoking cessation treatment: current practices, organizational priority, and perceived barriers. Nicotine Tob Res. 2016;18(5):1067-75. doi: 10.1093/ntr/ntv177.
- 209. Rodgers-Melnick SN, Webb Hooper M. Implementation of tobacco cessation services at a comprehensive cancer center: a qualitative study of oncology providers' perceptions and practices. Support Care Cancer. 2021;29(5):2465-74. doi: 10.1007/s00520-020-05749-7.
- Warren GW, Dibaj S, Hutson A, Cummings KM, Dresler C, Marshall JR. Identifying targeted strategies to improve smoking cessation support for cancer patients. J Thorac Oncol. 2015;10(11):1532-7. doi: 10.1097/jto.00000000000659.
- 211. Weaver KE, Danhauer SC, Tooze JA, Blackstock AW, Spangler J, Thomas L, et al. Smoking cessation counseling beliefs and behaviors of outpatient oncology providers. Oncologist. 2012;17(3):455-62. doi: 10.1634/theoncologist.2011-0350.
- 212. Sheffer CE, Brackman SL, Anders M, Barone C, Steinberg MB. Tobacco intervention practices of primary care physicians treating lower socioeconomic status patients. Am J Med Sci. 2012;343(5):388-96. doi: 10.1097/MAJ.0b013e3182302749.
- 213. Duffy SA, Louzon SA, Gritz ER. Why do cancer patients smoke and what can providers do about it? Community Oncol. 2012;9(11):344-52. doi: 10.1016/j.cmonc.2012.10.003.
- 214. Ostroff JS, Bolutayo GKL, O'Brien M, deLeon-Sanchez ST, Whitlock CW, Kotsen CS, et al. Training oncology care providers in the assessment and treatment of tobacco use and dependence. Cancer. 2021;127(16):3010-8. doi: 10.1002/cncr.33545.
- 215. Agency for Healthcare Research and Quality [Internet]. Rockville: The Agency; c2013 [cited 2022 June 5]. Practice Facilitation Handbook: Module 10. Academic Detailing as a Quality Improvement Tool; [about 9 screens]. Available from: <u>https://www.ahrq.gov/ncepcr/tools/pf-handbook/mod10.html</u>.
- 216. Sheffer MA, Baker TB, Fraser DL, Adsit RT, McAfee TA, Fiore MC. Fax referrals, academic detailing, and tobacco quitline use: a randomized trial. Am J Prev Med. 2012;42(1):21-8. doi: 10.1016/j.amepre.2011.08.028.
- 217. Sarna LP, Bialous SA, Kralikova E, Kmetova A, Felbrova V, Kulovana S, et al. Impact of a smoking cessation educational program on nurses' interventions. J Nurs Scholarsh. 2014;46(5):314-21. doi: 10.1111/jnu.12086.
- 218. Council for Tobacco Treatment Training Programs [Internet]. Madison, WI: The Council; c2020 [cited 2022 June 5]. Council for Tobacco Treatment Training Programs: accreditation for tobacco treatment specialist training programs; [about 2 screens]. Available from: <u>https://ctttp.org</u>.
- 219. Sheffer CE, Payne T, Ostroff J, Jolicoeur D, Steinberg M, Czabafy S, et al. Increasing the quality and availability of evidence-based treatment for tobacco dependence through unified certification of tobacco treatment specialists. J Smok Cessat. 2016;11(4):229-35. doi: 10.1017/jsc.2014.30.
- 220. Sheffer CE, Al-Zalabani A, Aubrey A, Bader R, Beltrez C, Bennett S, et al. The emerging global tobacco treatment workforce: characteristics of tobacco treatment specialists trained in council-accredited training programs from 2017 to 2019. Int J Environ Res Public Health. 2021;18(5):2416. doi: 10.3390/ijerph18052416.
- 221. Kotz D, Brown J, West R. Prospective cohort study of the effectiveness of smoking cessation treatments used in the "real world." Mayo Clin Proc. 2014;89(10):1360-7. doi: 10.1016/j.mayocp.2014.07.004.
- 222. McDermott MS, Beard E, Brose LS, West R, McEwen A. Factors associated with differences in quit rates between "specialist" and "community" stop-smoking practitioners in the English stop-smoking services. Nicotine Tob Res. 2013;15(7):1239-47. doi: 10.1093/ntr/nts262.

- 223. Ostroff JS, Burkhalter JE, Cinciripini PM, Li Y, Shiyko MP, Lam CY, et al. Randomized trial of a presurgical scheduled reduced smoking intervention for patients newly diagnosed with cancer. Health Psychol. 2014;33(7):737-47. doi: 10.1037/a0033186.
- 224. Song F, Maskrey V, Blyth A, Brown TJ, Barton GR, Aveyard P, et al. Differences in longer-term smoking abstinence after treatment by specialist or nonspecialist advisors: secondary analysis of data from a relapse prevention trial. Nicotine Tob Res. 2016;18(5):1061-6. doi: 10.1093/ntr/ntv148.
- 225. West R, Coyle K, Owen L, Coyle D, Pokhrel S. Estimates of effectiveness and reach for 'return on investment' modelling of smoking cessation interventions using data from England. Addiction. 2018;113 Suppl 1:19-31. doi: 10.1111/add.14006.
- 226. Kumiko S, Tomotaka S, Masakazu N, Akira O, Keiji W, Nobuyuki H, et al. Smoking prevalence and beliefs on smoking cessation among members of the Japanese Cancer Association in 2006 and 2010. Cancer Sci. 2012;103(8):1595-9. doi: 10.1111/j.1349-7006.2012.02322.x.
- 227. Conlon MS, Santi SA, Meigs ML, Davidson SM, Saunders D. Cigarette-smoking characteristics and interest in cessation in patients with head-and-neck cancer. Curr Oncol. 2020;27(5):e478-85. doi: 10.3747/co.27.6019.
- 228. Meadows-Taylor M, Ward KD, Chen W, Faris NR, Fehnel C, Ray MA, et al. Interest in cessation treatment among people who smoke in a community-based multidisciplinary thoracic oncology program. JTO Clin Res Rep. 2021;2(6):100182. doi: 10.1016/j.jtocrr.2021.100182.
- 229. McDonnell KK, Hollen PJ, Heath J, Andrews JO. Recruiting family dyads facing thoracic cancer surgery: challenges and lessons learned from a smoking cessation intervention. Eur J Oncol Nurs. 2016;20:199-206. doi: 10.1016/j.ejon.2015.08.006.
- 230. Bernstein SL, Boudreaux ED. Emergency department-based tobacco interventions improve patient satisfaction. J Emerg Med. 2010;38(4):e35-40. doi: 10.1016/j.jemermed.2008.03.034.
- 231. Conroy MB, Majchrzak NE, Regan S, Silverman CB, Schneider LI, Rigotti NA. The association between patient-reported receipt of tobacco intervention at a primary care visit and smokers' satisfaction with their health care. Nicotine Tob Res. 2005;7 Suppl 1:S29-34. doi: 10.1080/14622200500078063.
- 232. Schulte DM, Duster M, Warrack S, Valentine S, Jorenby D, Shirley D, et al. Feasibility and patient satisfaction with smoking cessation interventions for prevention of healthcare-associated infections in inpatients. Subst Abuse Treat Prev Policy. 2016;11:15. doi: 10.1186/s13011-016-0059-0.
- 233. Solberg LI, Boyle RG, Davidson G, Magnan SJ, Carlson CL. Patient satisfaction and discussion of smoking cessation during clinical visits. Mayo Clin Proc. 2001:76(2)138-43. doi: 10.1016/s0025-6196(11)63119-4.
- 234. Curry S, Keller P, Orleans C, Fiore MC. The role of health care systems in increased tobacco cessation. Annu Rev Public Health. 2008;29:411-28. doi: 10.1146/annurev.publhealth.29.020907.090934.
- 235. Balogh EP, Dresler C, Fleury ME, Gritz ER, Kean TJ, Myers ML, et al. Reducing tobacco-related cancer incidence and mortality: summary of an Institute of Medicine workshop. Oncologist. 2014;19(1):21-31. doi: 10.1634/theoncologist.2013-0230.
- 236. Hutton D, Gee I, McGee CE, Mellor R. No ifs, no butts: compliance with smoking cessation in secondary care guidance (NICE PH48) by providers of cancer therapies (radiotherapy and chemotherapy) in the UK. Int J Environ Res Public Health, 2016;13(12):1244. doi: 10.3390/ijerph13121244.
- 237. Ramsey AT, Baker TB, Pham G, et al. Low burden strategies are needed to reduce smoking in rural healthcare settings: A lesson from cancer clinics. Int J Environ Res Public Health. 2020;17(5):1728. Published 2020 Mar 6. doi:10.3390/ijerph17051728.
- 238. Demark-Wahnefried W, Aziz NM, Rowland JH, Pinto BM. Riding the crest of the teachable moment: promoting long-term health after the diagnosis of cancer. J Clin Oncol. 2005;23(24):5814-30. doi: 10.1200/JCO.2005.01.230.
- 239. Deppen SA, Grogan EL, Aldrich MC, Massion PP. Lung cancer screening and smoking cessation: a teachable moment? J Natl Cancer Inst. 2014;106(6):dju122. doi: 10.1093/jnci/dju122.
- 240. Poghosyan H, Kennedy SL, Cooley ME. The impact of computed tomography screening for lung cancer on smoking behaviors: a teachable moment? Cancer Nurs. 2012;35(6):446-75. doi: 10.1097/NCC.0b013e3182406297.
- 241. Taylor KL, Hagerman CJ, Luta G, Bellini PG, Stanton C, Abrams DB, et al. Preliminary evaluation of a telephone-based smoking cessation intervention in the lung cancer screening setting: a randomized clinical trial. Lung Cancer. 2017;108:242-6. doi: 10.1016/j.lungcan.2017.01.020.
- 242. Wilson JM, Jungner G. Principles and practice of screening for disease; public health papers no. 34. [Internet]. Geneva: World Health Organization; 1968 [cited 2022 June 5]. Available from: https://apps.who.int/iris/bitstream/handle/10665/37650/WHO_PHP_34.pdf.

- 243. Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365(5):395-409. doi: 10.1056/NEJMoa1102873.
- 244. Henschke CI, Naidich DP, Yankelevitz DF, McGuinness G, McCauley DI, Smith JP, et al. Early lung cancer action project: initial findings on repeat screenings. Cancer. 2001;92(1):153-9. doi: 10.1002/1097-0142(20010701)92:1<153::aid-cncr1303>3.0.co;2-s.
- 245. Ostroff JS, Buckshee N, Mancuso CA, Yankelevitz DF, Henschke CI. Smoking cessation following CT screening for early detection of lung cancer. Prev Med. 2001;33(6):613-21. doi: 10.1006/pmed.2001.0935.
- 246. Taylor KL, Cox LS, Zincke N, Mehta L, McGuire C, Gelmann E. Lung cancer screening as a teachable moment for smoking cessation. Lung Cancer. 2007;56(1):125-34. doi: 10.1016/j.lungcan.2006.11.015.
- 247. Moyer VA. Screening for lung cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2014;160(5):330-8. doi: 10.7326/m13-2771.
- 248. Centers for Medicare and Medicaid Services (CMS) [Internet]. Baltimore: The Centers; c2015 [cited 2022 June 5]. NCA—decision memo for screening for lung cancer with low dose computed tomography (LDCT) (CAG-00439N); [about 148 screens]. Available from: <u>https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=274</u>.
- 249. Clark MM, Cox LS, Jett JR, Patten CA, Schroeder DR, Nirelli LM, et al. Effectiveness of smoking cessation self-help materials in a lung cancer screening population. Lung Cancer. 2004;44(1):13-21. doi: 10.1016/j.lungcan.2003.10.001.
- 250. Cox LS, Clark MM, Jett JR, Patten CA, Schroeder DR, Nirelli LM, et al. Change in smoking status after spiral chest computed tomography scan screening. Cancer. 2003;98(11):2495-501. doi: 10.1002/cncr.11813.
- 251. Ferketich AK, Otterson GA, King M, Hall N, Browning KK, Wewers ME. A pilot test of a combined tobacco dependence treatment and lung cancer screening program. Lung Cancer. 2012;76(2):211-15. doi: 10.1016/j.lungcan.2011.10.011.
- 252. Marshall HM, Courtney DA, Passmore LH, McCaul EM, Yang IA, Bowman RV, et al. Brief tailored smoking cessation counseling in a lung cancer screening population is feasible: a pilot randomized controlled trial. Nicotine Tob Res. 2016;18(7):1665-9. doi: 10.1093/ntr/ntw010.
- 253. Munshi V, McMahon P. Importance of smoking cessation in a lung cancer screening program. Curr Surg Rep. 2013;1(4):10.1007/s40137-013-0030-1. doi: 10.1007/s40137-013-0030-1.
- 254. Slatore CG, Baumann C, Pappas M, Humphrey LL. Smoking behaviors among patients receiving computed tomography for lung cancer screening: systematic review in support of the U.S. Preventive Services Task Force. Ann Am Thorac Soc. 2014;11(4):619-27. doi: 10.1513/AnnalsATS.201312-460OC.
- 255. Styn MA, Land SR, Perkins KA, Wilson DO, Romkes M, Weissfeld JL. Smoking behavior 1 year after computed tomography screening for lung cancer: effect of physician referral for abnormal CT findings. Cancer Epidemiol Biomarkers Prev. 2009;18(12):3484-9. doi: 10.1158/1055-9965.Epi-09-0895.
- 256. Tammemagi MC, Berg CD, Riley TL, Cunningham CR, Taylor KL. Impact of lung cancer screening results on smoking cessation. J Natl Cancer Inst. 2014;106(6):dju084. doi: 10.1093/jnci/dju084.
- 257. Townsend CO, Clark MM, Jett JR, Patten CA, Schroeder DR, Nirelli LM, et al. Relation between smoking cessation and receiving results from three annual spiral chest computed tomography scans for lung carcinoma screening. Cancer. 2005;103(10):2154-62. doi: 10.1002/cncr.21045.
- Tremblay A, Taghizadeh N, Huang J, Kasowski D, MacEachern P, Burrowes P, et al. A randomized controlled study of integrated smoking cessation in a lung cancer screening program. J Thorac Oncol. 2019;14(9):1528-37. doi: 10.1016/j.jtho.2019.04.024.
- 259. van der Aalst CM, de Koning HJ, van den Bergh KA, Willemsen MC, van Klaveren RJ. The effectiveness of a computer-tailored smoking cessation intervention for participants in lung cancer screening: a randomised controlled trial. Lung Cancer. 2012;76(2):204-10. doi: 10.1016/j.lungcan.2011.10.006.
- 260. Lawson PJ, Flocke SA. Teachable moments for health behavior change: a concept analysis. Patient Educ Couns. 2009;76(1):25-30. doi: 10.1016/j.pec.2008.11.002.
- 261. Park ER, Gareen IF, Japuntich S, Lennes I, Hyland K, DeMello S, et al. Primary care provider–delivered smoking cessation interventions and smoking cessation among participants in the National Lung Screening Trial. JAMA Intern Med. 2015;175(9):1509-16. doi: 10.1001/jamainternmed.2015.2391.
- 262. Filippo L, Principe R, Cesario A, Apolone G, Carleo F, Ialongo P, et al. Smoking cessation intervention within the framework of a lung cancer screening program: preliminary results and clinical perspectives from the "Cosmos-II" trial. Lung. 2015;193(1):147-9. doi: 10.1007/s00408-014-9661-y.

- 263. Pozzi P, Munarini E, Bravi F, Rossi M, La Vecchia C, Boffi R, et al. A combined smoking cessation intervention within a lung cancer screening trial: a pilot observational study. Tumori. 2015;101(3):306-11. doi: 10.5301/tj.5000282.
- 264. National Cancer Institute [Internet]. Washington: National Cancer Institute; 2020 [cited 2022 June 5]. Smoking cessation at lung examination: The SCALE collaboration; [about 5 screens]. Available from: https://cancercontrol.cancer.gov/brp/tcrb/scale-collaboration.
- 265. Joseph AM, Rothman AJ, Almirall D, Begnaud A, Chiles C, Cinciripini PM, et al. Lung cancer screening and smoking cessation clinical trials: SCALE (Smoking Cessation within the Context of Lung Cancer Screening) collaboration. Am J Respir Crit Care Med. 2018;197(2):172-82. doi: 10.1164/rccm.201705-0909CI.
- 266. Ritzwoller DP, Meza R, Carroll NM, Blum-Barnett E, Burnett-Hartman AN, Greenlee RT, et al. Evaluation of population-level changes associated with the 2021 US Preventive Services Task Force lung cancer screening recommendations in community-based health care systems. JAMA Netw Open. 2021;4(10):e2128176. doi: 10.1001/jamanetworkopen.2021.28176.
- 267. Centers for Medicare and Medicaid Services (CMS) [Internet]. Baltimore: The Centers; c2022 [cited 9 May 2022]. NCA—decision memo for screening for lung cancer with low dose computed tomography (LDCT) (CAG-00439R); [about 99 screens]. Available from: https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=Y&ncaid=304&.
- 268. Meza R, Cao P, Jeon J, Taylor KL, Mandelblatt JS, Feuer EJ, et al. Impact of joint lung cancer screening and cessation interventions under the new recommendations of the U.S. Preventive Services Task Force. J Thorac Oncol. 2022;17(1):160-6. doi: 10.1016/j.jtho.2021.09.011.
- 269. Tremblay A. Reply and commentary to "smoking cessation interventions in the setting of low-dose computed tomography: are they effective?". J Thorac Oncol. 2020;15(4):e61-2. doi: 10.1016/j.jtho.2020.02.004.
- 270. Fucito LM, Czabafy S, Hendricks PS, Kotsen C, Richardson D, Toll BA. Pairing smoking-cessation services with lung cancer screening: a clinical guideline from the Association for the Treatment of Tobacco Use and Dependence and the Society for Research on Nicotine and Tobacco. Cancer. 2016;122(8):1150-9. doi: 10.1002/cncr.29926.
- 271. Westmaas JL, Newton CC, Stevens VL, Flanders WD, Gapstur SM, Jacobs EJ. Does a recent cancer diagnosis predict smoking cessation? An analysis from a large prospective US cohort. J Clin Oncol. 2015;33(15):1647-52. doi: 10.1200/JCO.2014.58.3088.
- 272. Shi Y, Warner DO. Surgery as a teachable moment for smoking cessation. Anesthesiology. 2010;112(1):102-7. doi: 10.1097/ALN.0b013e3181c61cf9.
- 273. Nayan S, Gupta MK, Strychowsky JE, Sommer DD. Smoking cessation interventions and cessation rates in the oncology population: an updated systematic review and meta-analysis. Otolaryngol Head Neck Surg. 2013;149(2):200-11. doi: 10.1177/0194599813490886.
- 274. Dresler CM, Bailey M, Roper CR, Patterson GA, Cooper JD. Smoking cessation and lung cancer resection. Chest. 1996;110(5):1199-202. doi: 10.1378/chest.110.5.1199.
- 275. Wong J, An D, Urman RD, Warner, DO, Tonnesen H, Raveendran R, et al. Society for Perioperative Assessment and Quality Improvement (SPAQI) consensus statement on perioperative smoking cessation. Anesth Analg. 2020;131(3):955-68. doi: 10.1213/ane.000000000004508.
- 276. Derksen JW, Warren GW, Jordan K, Rauh S, Vera Garcia R, O'Mahony D, et al. European practice patterns and barriers to smoking cessation after a cancer diagnosis in the setting of curative versus palliative cancer treatment. Eur J Cancer. 2020;138:99-108. doi: 10.1016/j.ejca.2020.07.020.
- 277. Leventakos K, Schwecke AJ, Deering E, Cathcart-Rake E, Sanh AC, Jatoi A. The need to prioritize and reprioritize palliative care options: smoking cessation as a case-in-point. Curr Treat Options Oncol. 2019;20(4):33. doi: 10.1007/s11864-019-0632-7.
- 278. Gibson TM, Liu W, Armstrong GT, Srivastava DK, Hudson MM, Leisenring WM, et al. Longitudinal smoking patterns in survivors of childhood cancer: an update from the Childhood Cancer Survivor Study. Cancer. 2015;121(22):4035-43. doi: 10.1002/cncr.29609.
- 279. Emmons KM, Puleo E, Mertens A, Gritz ER, Diller L, Li FP. Long-term smoking cessation outcomes among childhood cancer survivors in the Partnership for Health study. J Clin Oncol. 2009;27(1):52-60. doi: 10.1200/JCO.2007.13.0880.
- 280. Klesges RC, Krukowski RA, Klosky JL, Liu W, Srivastava DK, Boyett JM, et al. Efficacy of a tobacco quitline among adult survivors of childhood cancer. Nicotine Tob Res. 2015;17(6):710-8. doi: 10.1093/ntr/ntu216.

- 281. Huang IC, Klosky JL, Young C, Murphy S, Srivastava DK, Hudson MM, et al. Accuracy of self-reported smoking status in adult survivors of childhood cancer: A report from St. Jude Lifetime Cohort Study. J Clin Oncol. 2017;35(15_suppl):10570. doi 10.1200/JCO.2017.35.15_suppl.10570.
- 282. de Moor JS, Elder K, Emmons KM. Smoking prevention and cessation interventions for cancer survivors. Semin Oncol Nurs. 2008;24(3):180-92. doi: 10.1016/j.soncn.2008.05.006.
- 283. National Cancer Institute [Internet]. Washington: National Cancer Institute; 2021 [cited 2022 June 9]. Annual report to the nation 2021: Special topic: Patient economic burden of cancer care; [about 7 screens]. Available from: https://seer.cancer.gov/report_to_nation/special.html.
- 284. Xu X, Shrestha SS, Trivers KF, Neff L, Armour BS, King BA. U.S. healthcare spending attributable to cigarette smoking in 2014. Prev Med. 2021;150:106529. doi: 10.1016/j.ypmed.2021.106529.
- 285. National Cancer Institute and World Health Organization. The economics of tobacco and tobacco control. National Cancer Institute Tobacco Control Monograph 21. NIH Publication No. 16-CA-8029A [Internet]. Bethesda, MD: U.S. Department of Health and Human Services, National Institute of Health, National Cancer Institute; 2016 [cited 2022 June 5]. Co-published by the World Health Organization (CH). Available from: https://cancercontrol.cancer.gov/sites/default/files/2020-08/m21_complete.pdf.
- 286. Warren GW, Cartmell KB, Garrett-Mayer E, Salloum RG, Cummings KM. Attributable failure of first-line cancer treatment and incremental costs associated with smoking by patients with cancer. JAMA Netw Open. 2019;2(4):e191703. doi: 10.1001/jamanetworkopen.2019.1703.
- 287. Isaranuwatchai W, de Oliveira C, Mittmann N, Evans WK, Peter A, Truscott R, et al. Impact of smoking on health system costs among cancer patients in a retrospective cohort study in Ontario, Canada. BMJ Open. 2019;9(6):e026022. doi: 10.1136/bmjopen-2018-026022.
- 288. Kaul S, Avila JC, Jupiter D, Rodriguez AM, Kirchhoff AC, Kuo YF. Modifiable health-related factors (smoking, physical activity and body mass index) and health care use and costs among adult cancer survivors. J Cancer Res Clin Oncol. 2017;143(12):2469-80. doi: 10.1007/s00432-017-2494-3.
- 289. Murphy CC, Incalcaterra JR, Albright HW, Correa AM, Swisher SG, Hofstetter WL. Pretreatment patient comorbidity and tobacco use increase cost and risk of postoperative complications after esophagectomy at a high-volume cancer center. J Oncol Pract. 2013;9(5):233-9. doi: 10.1200/jop.2013.001047.
- 290. Sari AA, Rezaei S, Arab M, Majdzadeh R, Matin BK, Zandian H. Effects of smoking on cost of hospitalization and length of stay among patients with lung cancer in Iran: a hospital-based study. Asian Pac J Cancer Prev. 2016;17(9):4421-6.
- 291. Ambrosio A, Jeffery DD, Hopkins L, Burke HB. Cost and healthcare utilization among non-elderly head and neck cancer patients in the military health system, a single-payer universal health care model. Mil Med. 2019;184(5-6):e400-7. doi: 10.1093/milmed/usy192.
- 292. Jeffery DD, Ambrosio A, Hopkins L, Burke HB. Mental health comorbidities and cost/utilization outcomes in head and neck cancer patients. J Psychosoc Oncol. 2019;37(3):301-18. doi: 10.1080/07347332.2018.1519626.
- 293. Rezaei S, Akbari SA, Arab M, Majdzadeh R, Mohammad PA. Economic burden of smoking: a systematic review of direct and indirect costs. Med J Islam Repub Iran. 2016;30:397.
- 294. Slatore CG, Au DH, Hollingworth W. Cost-effectiveness of a smoking cessation program implemented at the time of surgery for lung cancer. J Thorac Oncol. 2009;4(4):499-504. doi: 10.1097/JTO.0b013e318195e23a.
- 295. Djalalov S, Masucci L, Isaranuwatchai W, Evans W, Peter A, Truscott R, et al. Economic evaluation of smoking cessation in Ontario's regional cancer programs. Cancer Med. 2018;7(9):4765-72. doi: 10.1002/cam4.1495.
- 296. Emmons KM, Puleo E, Park E, Gritz ER, Butterfield RM, Weeks JC, et al. Peer-delivered smoking counseling for childhood cancer survivors increases rate of cessation: the Partnership for Health study. J Clin Oncol. 2005;23(27):6516-23. doi: 10.1200/jco.2005.07.048.
- 297. Villanti AC, Jiang Y, Abrams DB, Pyenson BS. A cost-utility analysis of lung cancer screening and the additional benefits of incorporating smoking cessation interventions. PLoS One. 2013;8(8):e71379. doi: 10.1371/journal.pone.0071379.
- 298. Goffin JR, Flanagan WM, Miller AB, Fitzgerald NR, Memon S, Wolfson MC, et al. Biennial lung cancer screening in Canada with smoking cessation-outcomes and cost-effectiveness. Lung Cancer. 2016;101:98-103. doi: 10.1016/j.lungcan.2016.09.013.
- 299. Evans WK, Gauvreau CL, Flanagan WM, Memon S, Yong JH, Goffin JR, et al. Clinical impact and costeffectiveness of integrating smoking cessation into lung cancer screening: a microsimulation model. CMAJ Open. 2020;8(3):E585-92. doi: 10.9778/cmajo.20190134.

- 300. Cadham CJ, Cao P, Jayasekera J, Taylor KL, Levy DT, Jeon J, et al. Cost-effectiveness of smoking cessation interventions in the lung cancer screening setting: a simulation study. J Natl Cancer Inst. 2021;113(8):1065-73. doi: 10.1093/jnci/djab002.
- 301. McMahon PM, Kong CY, Bouzan C, Weinstein MC, Cipriano LE, Tramontano AC, et al. Cost-effectiveness of computed tomography screening for lung cancer in the United States. J Thorac Oncol. 2011;6(11):1841-8. doi: 10.1097/JTO.0b013e31822e59b3.
- 302. Boyle RG, Solberg LI, Fiore MC. Electronic medical records to increase the clinical treatment of tobacco dependence: a systematic review. Am J Prev Med. 2010;39(6):S77-82.
- 303. Hartmann-Boyce J, Livingstone-Banks J, Ordonez-Mena JM, Fanshawe TR, Lindson N, Freeman SC, et al. Behavioural interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database Syst Rev. 2021;(1):CD013229. doi: 10.1002/14651858.CD013229.pub2.
- 304. Joint Commission [Internet]. Oakbrook Terrace, IL: The Commission; c2020 [cited 2022 June 5]. Specifications manual for Joint Commission National Quality Measures (v2021A): Tobacco Treatment Measures (TOB); [about 4 screens]. Available from: https://manual.jointcommission.org/releases/TJC2021A/TobaccoTreatmentMeasures.html.
- 305. National Cancer Institute. C-TUQ user manual: cancer patient tobacco use questionnaire [Internet]. Washington: National Cancer Institute; 2017 [cited 2022 June 5]. Available from: https://cancercontrol.cancer.gov/sites/default/files/2021-02/C-TUQ_User_Manual.pdf.
- 306. Tual S, Piau JP, Jarvis MJ, Dautzenberg B, Annesi-Maesano I. Impact of tobacco control policies on exhaled carbon monoxide in non-smokers. J Epidemiol Community Health. 2010;64(6):554-6. doi: 10.1136/jech.2008.086256.
- 307. Benowitz NL, Dains KM, Dempsey D, Herrera B, Yu L, Jacob P 3rd. Urine nicotine metabolite concentrations in relation to plasma cotinine during low-level nicotine exposure. Nicotine Tob Res. 2009;11(8):954-60. doi: 10.1093/ntr/ntp092.
- 308. Jarvis MJ, Fidler J, Mindell J, Feyerabend C, West R. Assessing smoking status in children, adolescents and adults: cotinine cut-points revisited. Addiction. 2008;103(9):1553-61. doi: 10.1111/j.1360-0443.2008.02297.x.
- 309. Benowitz NL, Jain S, Dempsey DA, Nardone N, Helen GS, Jacob P 3rd. Urine cotinine screening detects nearly ubiquitous tobacco smoke exposure in urban adolescents. Nicotine Tob Res. 2017;19(9):1048-54. doi: 10.1093/ntr/ntw390.
- Achilihu H, Feng J, Wang L, Bernert JT. Tobacco use classification by inexpensive urinary cotinine immunoassay test strips. J Anal Toxicol. 2019;43(2):149-53. doi: 10.1093/jat/bky075.

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 (<u>https://cancercontrol.cancer.gov/c3i</u>) and the University of Wisconsin-Madison C3I website (<u>https://c3i.wiscweb.wisc.edu/publications/</u>).

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

Year Published	Title	Authors	Site	Publication Information
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 to bacco 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.2019.1226 4		
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.2019.1225 1		

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 \geq 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 This page left blank intentionally.

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

Introduction	226
The Socioecological Model	227
Combinatorial Effects on Vulnerabilities	228
Stigma in Medically Underserved and Vulnerable Populations	228
Prevalence and Trends in Smoking: Relevance to Medically Underserved and	
Vulnerable Populations With Cancer	229
Heterogeneity Among Medically Underserved and Vulnerable Populations	232
Cancer Burden	232
Factors Associated With Cancer Burden	234
Summary: Cancer Burden	234
Smoking Cessation Treatment for Medically Underserved and Vulnerable Populations in the	3
Clinical Cancer Care Context	234
Smoking Among Socioeconomically Disadvantaged Populations With Cancer	234
Epidemiology	234
Smoking Cessation	235
Barriers to Smoking Cessation	235
Summary: Smoking Among Socioeconomically Disadvantaged Populations With	
Cancer	236
Smoking Among Racial and Ethnic Minority Populations With Cancer	236
Epidemiology	236
Smoking Cessation	238
Barriers to Smoking Cessation.	240
Summary: Smoking Among Racial and Ethnic Minority Populations With Cancer	242
Smoking Among Rural Populations With Cancer	242
Epidemiology	242
Smoking Cessation	242
Barriers to Smoking Cessation	243
Summary: Smoking Among Rural Populations with Cancer	244
Smoking Among Sexual and Gender Minority (SGM) Populations with Cancer	244
Enidemiology	244
Smoking Cessation	245
Barriers to Smoking Cessation	246
Summary: Smoking Among SGM Populations With Cancer	247
Smoking Among People With Co-Occurring Substance Use Disorders and Cancer	247
Fnidemiology	248
Smoking Cessation	252
Barriers to Smoking Cessation	253
Summary: Smoking Among People With Co-Occurring Substance Use Disorders	233
and Cancer	254
Smoking Among Individuals With Serious Mental Illness (SMI) and Cancer	255
Enidemiology	255
Smoking Cessation	255
Barriers to Smoking Cessation	255
Summary: Smoking Among Individuals With SMI and Cancer	257
Summary. Smoking Among marviduals with Sivil and Cancel	290

Effectiveness of Smoking Cessation Treatment	.260
Summary	.261
Conclusions	.261
References	.263

Figures and Tables

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

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 life⁶ 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 5.1Prevalence 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	i	i				i	i	i	i	i				i	
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	1	I	1	1		1	1	1	1	1	1	1	1	1	
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			1	1							1	1	1		
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)	ſ	1	1	1		ſ	1	1	1	1	1	1	1	1	
<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 attainme	ent ^b	I				I	I	I	I	I				I	
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
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	1						1			1	1	1	1	1	
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

Table 5.1 (continued)

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.

^aAll 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. ^bAdditional categories were added to education in 1999. Educational attainment data are provided for individuals aged 25 years or older. GED = general educational development certificate. ^cResponse options provided on the NHIS were "straight, that is, not gay" for men, and "straight, that is, not gay or lesbian" for women.

Source: National Health Interview Survey, 1994–2019: Agaku et al. 2014³⁶²; Centers for Disease Control and Prevention (CDC) 1996,³⁶³ 2000,³⁶⁴ 2004,³⁶⁵ 2007,³⁶⁶ 2012³⁶⁷; Cornelius et al. 2020,³⁶⁸ 2022⁴¹; Creamer et al. 2019³⁶⁹; Jamal et al. 2014,³⁷⁰ 2015,³⁷¹ 2016,³⁷² 2018³⁷³; 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 cessation¹³⁷ 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 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 use⁸⁷ 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 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 quitting¹⁶³ or making a quit attempt¹⁰⁴ 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 smoking¹⁸⁰ 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 evidencebased 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 medications¹⁹⁴ 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 webbased 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 inperson 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 populations¹⁷⁶ 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 (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 (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



^aCigarette 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.

Substance use disorder (SUD)ª	Cancer (unweighted <i>N</i> = 1,571)	No cancer (unweighted <i>N</i> = 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 disorderc	0.2%	0.5%	.01
Other use disorder ^d	0.4%	0.7%	.11
Past-month cigarette smoking	5.0%	24.0%	<.001

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

Note: Percentages are weighted and unadjusted for demographic characteristics. Percentages may not sum to 100% due to rounding. ^aNontobacco 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. ^cIncludes prescription stimulant and cocaine use disorder. ^dIncludes 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 colleagues²⁶⁹ 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 Australia²⁷⁵ 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 conseling 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.

References

- 1. Henley SJ, Thomas CC, Sharapova SR, Momin B, Massetti GM, Winn DM, et al. Vital signs: disparities in tobacco-related cancer incidence and mortality—United States, 2004–2013. MMWR Morb Mortal Wkly Rep. 2016;65:1212-8. doi: 10.15585/mmwr.mm6544a3.
- 2. Simmons VN, Pineiro B, Hooper MW, Gray JE, Brandon TH. Tobacco-related health disparities across the cancer care continuum. Cancer Control. 2016 Oct;23(4):434-41. doi: 10.1177/107327481602300415.
- 3. McLeroy KR, Bibeau D, Steckler A, Glanz K. An ecological perspective on health promotion programs. Health Educ Q. 1988;15(4):351-77. doi: 10.1177/109019818801500401.
- 4. Bronfenbrenner U. Toward an experimental ecology of human development. American psychologist. 1977;32(7):513-31. doi: 10.1037/0003-066X.32.7.513.
- National Cancer Institute (NCI). A socioecological approach to addressing tobacco-related health disparities. National Cancer Institute Tobacco Control Monograph 22. NIH Publication No. 17-CA-8035A. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute; 2017.
- 6. Hamann HA, Ver Hoeve ES, Carter-Harris L, Studts JL, Ostroff JS. Multilevel opportunities to address lung cancer stigma across the cancer control continuum. J Thorac Oncol. 2018 Aug 1;13(8):1062-75. doi: 10.1016/j.jtho.2018.05.014.
- Sorensen G, Barbeau E, Hunt MK, Emmons K. Reducing social disparities in tobacco use: a social-contextual model for reducing tobacco use among blue-collar workers. Am J Public Health. 2004;94(2):230-9. doi: 10.2105/ajph.94.2.230.
- 8. Vidrine J, Reitzel LR, Wetter DW. The role of tobacco in cancer health disparities. Curr Oncol Rep. 2009;11(6):475-81. doi: 10.1007/s11912-009-0064-9.
- Kcomt L, Evans-Polce RJ, Engstrom CW, West BT, McCabe SE. Discrimination, sexual orientation discrimination, and severity of tobacco use disorder in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions-III. Nicotine Tob Res. 2021;23(6):920-30. doi: 10.1093/ntr/ntaa197.
- 10. Sheffer CE, Williams JM, Erwin DO, Smith PH, Carl E, Ostroff JS. Tobacco-related disparities viewed through the lens of intersectionality. Nicotine Tob Res. 2022;24(2):285-8. doi: 10.1093/ntr/ntab193.
- 11. Todorova IL, Tucker KL, Jimenez MP, Lincoln AK, Arevalo S, Falcon LM. Determinants of self-rate health and the role of acculturation: implications for health inequalities. Ethn Health. 2013;18(6). doi: 10.1080/13557858.2013.771147. Epub 2013 Feb 21.
- 12. Tsigos C, Chrousos GP. Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and stress. J Psychosom Res. 2002;52(4):865-71. doi: 10.1016/s0022-3999(02)00429-4.
- 13. Kobayashi LC, Smith SG. Cancer fatalism, literacy, and cancer information seeking in the American public. Health Educ Behav. 2016;43(4):461-70. doi: 10.1177/1090198115604616.
- 14. Powe BD, Finnie R. Cancer fatalism: the state of the science. Cancer Nurs. 2003 Dec;26(6):454-65; quiz 466-7. doi: 10.1097/00002820-200312000-00005.
- 15. Perlick DA, Rosenheck RA, Clarkin JF, Sirey JA, Salahi J, Struening EL, et al. Stigma as a barrier to recovery: adverse effects of perceived stigma on social adaptation of persons diagnosed with bipolar affective disorder. Psychiatr Serv. 2001;52(12):1627-32. doi: 10.1176/appi.ps.52.12.1627.
- Riley KE, Ulrich MR, Hamann HA, Ostroff JS. Decreasing smoking but increasing stigma? anti-tobacco campaigns, public health, and cancer care. AMA J Ethics. 2017;19(5):475-85. doi: 10.1001/journalofethics.2017.19.5.msoc1-1705.
- 17. Simmons VN, Litvin EB, Patel RD, Jacobsen PB, McCaffrey JC, Bepler G, et al. Patient-provider communication and perspectives on smoking cessation and relapse in the oncology setting. Patient Educ Couns. 2009;77(3):398-403. doi: 10.1016/j.pec.2009.09.024.
- Abramson CM, Hashemi M, Sanchez-Jankowski M. Perceived discrimination in U.S. healthcare: charting the effects of key social characteristics within and across racial groups. Prev Med Rep. 2015 Jul 21;2:615-21. doi: 10.1016/j.pmedr.2015.07.006.
- Ayhan CH, Bilgin H, Uluman OT, Sukut O, Yilmaz S, Buzlu S. A systematic review of the discrimination against sexual and gender minority in health care settings. Int J Health Serv. 2020;50(1):44-61. doi: 10.1177/0020731419885093. Epub 2019 Nov 4.
- 20. Nong P, Raj M, Creary M, Kardia SL, Platt JE. Patient-reported experiences of discrimination in the US health care system. JAMA Netw Open. 2020;3(12):e2029650. doi: 10.1001/jamanetworkopen.2020.29650.

- 21. Gamarel KE, Mereish EH, Manning D, Iwamoto M, Operario D, Nemoto T. Minority stress, smoking patterns, and cessation attempts: findings from a community-sample of transgender women in the San Francisco Bay Area. Nicotine Tob Res. 2016;18(3):306-13. doi: 10.1093/ntr/ntv066.
- 22. Huebner DM, McGarrity LA, Perry NS, Spivey LA, Smith TW. Cardiovascular and cortisol responses to experimentally-induced minority stress. Health Psychol. 2021;40(5):316-25. doi: 10.1037/hea0001067.
- Kcomt L, Gorey KM, Barrett BJ, McCabe SE. Healthcare avoidance due to anticipated discrimination among transgender people: a call to create trans-affirmative environments. SSM Popul Health. 2020 May 28;11:100608. doi: 10.1016/j.ssmph.2020.100608.
- 24. Moagi MM, van Der Wath AE, Jiyane PM, Rikhotso RS. Mental health challenges of lesbian, gay, bisexual and transgender people: an integrated literature review. Health SA. 2021;26:1487. doi: 10.4102/hsag.v26i0.1487.
- 25. Scandurra C, Mezza F, Maldonato NM, Bottone M, Bochicchio V, Valerio P, et al. Health of non-binary and genderqueer people: a systematic review. Front Psychol. 2019 Jun 25;10:1453. doi: 10.3389/fpsyg.2019.01453.
- Drope J, Liber AC, Cahn Z, Stoklosa M, Kennedy R, Douglas CE, et al. Who's still smoking? Disparities in adult cigarette smoking prevalence in the United States. CA Cancer J Clin. 2018 Mar;68(2):106-15. doi: 10.3322/caac.21444. Epub 2018 Jan 31.
- 27. Hamann HA, Ostroff JS, Marks EG, Gerber DE, Schiller JH, Lee SJ. Stigma among patients with lung cancer: a patient-reported measurement model. Psychooncology. 2014;23(1):81-92. doi: 10.1002/pon.3371. Epub 2013 Oct 3.
- 28. Hammett P, Fu SS, Nelson D, Clothier B, Saul JE, Widome R, et al. A proactive smoking cessation intervention for socioeconomically disadvantaged smokers: the role of smoking-related stigma. Nicotine Tob Res. 2018 Feb 7;20(3):286-94. doi: 10.1093/ntr/ntx085.
- 29. Stuber J, Galea S. Who conceals their smoking status from their health care provider? Nicotine Tob Res. 2009 Mar 1;11(3):303-7. doi: 10.1093/ntr/ntn024. Epub 2009 Feb 20.
- Evans-Polce RJ, Castaldelli-Maia JM, Schomerus G, Evans-Lacko SE. The downside of tobacco control? Smoking and self-stigma: a systematic review. Soc Sci Med. 2015;145:26-34. doi: 10.1016/j.socscimed.2015.09.026.
- 31. Helweg-Larsen M, Sorgen LJ, Pisinger C. Does it help smokers if we stigmatize them? A test of the stigma-induced identity threat model among U.S. and Danish smokers. Soc Cogn. 2019;37(3):294-313. doi: 10.1521/soco.2019.37.3.294.
- 32. Conron KJ, Goldberg SK. Fact sheet: adult LGBT population in the United States [Internet]. Los Angeles: UCLA, The Williams Institute; 2020 Jul. [cited 2022 June 9]. Available from: https://williamsinstitute.law.ucla.edu/wp-content/uploads/LGBT-Adult-US-Pop-Jul-2020.pdf.
- 33. Gates GJ. How many people are lesbian, gay, bisexual, and transgender? [Internet]. Los Angeles: UCLA, The Williams Institute; 2011 Apr. [cited 2022 June 9]. Available from: <u>https://williamsinstitute.law.ucla.edu/wp-content/uploads/Gates-How-Many-People-LGBT-Apr-2011.pdf</u>.
- 34. Ratcliffe M, Burd C, Holder K, Fields A. Defining rural at the U.S. Census Bureau. Washington: U.S. Census Bureau; 2016 Dec. 8 p. Report No.: ACSGEO-1.
- 35. Doogan NJ, Roberts ME, Wewers ME, Stanton CA, Keith DR, Gaalema DE, et al. A growing geographic disparity: rural and urban cigarette smoking trends in the United States. Prev Med. 2017;104:79-85. doi: 10.1016/j.ypmed.2017.03.011.
- 36. Tseng TS, Lin HY, Martin MY, Chen T, Partridge EE. Disparities in smoking and cessation status among cancer survivors and non-cancer individuals: a population-based study from National Health and Nutrition Examination Survey. J Cancer Surviv. 2010;4(4):313-21. doi: 10.1007/s11764-010-0127-9.
- 37. Westmaas JL, Alcaraz KI, Berg CJ, Stein KD. Prevalence and correlates of smoking and cessation-related behavior among survivors of ten cancers: findings from a nationwide survey nine years after diagnosis. Cancer Epidemiol Biomarkers Prev. 2014;23(9):1783-92. doi: 10.1158/1055-9965.Epi-14-0046.
- 38. U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. National Survey on Drug Use and Health 2020 (NSDUH-2020-DS0001). Retrieved from: <u>https://www.samhsa.gov/data/sites/default/files/reports/rpt35323/NSDUHDetailedTabs2020/NSDUHDetabs2020/NSDUHDetabs2020/NSDUHDet</u>
- Lipari RN, Van Horn SL. Smoking and mental illness among adults in the United States: the CBHSQ report. Rockville, MD: Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality; 2017.

- 40. Centers for Disease Control and Prevention (CDC). Vital signs: current cigarette smoking among adults aged >/=18 years with mental illness—United States, 2009–2011. MMWR Morb Mortal Wkly Rep. 2013;62:81-7.
- 41. Cornelius ME, Loretan CG, Wang TW, Jamal A, Homa DM. Tobacco product use among adults—United States, 2020. MMWR Morb Mortal Wkly Rep. 2022;71(11):397-405. doi: 10.15585/mmwr.mm7111a1.
- 42. U.S. Department of Health and Human Services (USDHHS). Tobacco use among U.S. racial/ethnic minority groups—African Americans, American Indians and Alaska Natives, Asian American and Pacific Islanders, and Hispanics: a report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 1998.
- 43. Emory K, Kim Y, Buchting F, Vera L, Huang J, Emery SL. Intragroup variance in lesbian, gay, and bisexual tobacco use behaviors: evidence that subgroups matter, notably bisexual women. Nicotine Tob Res. 2016;18(6):1494-501. doi: 10.1093/ntr/ntv208.
- 44. Quinn GP, Sanchez JA, Sutton SK, Vadaparampil ST, Nguyen GT, Green BL, et al. Cancer and lesbian, gay, bisexual, transgender/transsexual, and queer/questioning (LGBTQ) populations. CA Cancer J Clin. 2015;65(5):384-400. doi: 10.3322/caac.21288.
- 45. Wheldon CW, Wiseman KP. Tobacco use among transgender and gender non-conforming adults in the United States. Tob Use Insights. 2019 May 23;12:1179173X19849419. doi: 10.1177/1179173X19849419.
- 46. Ngo B, Lee SJ. Complicating the image of model minority success: a review of Southeast Asian American education. Rev Educ Res. 2007;77(4):415-53. doi: 10.3102/0034654307309918.
- 47. National Heart, Lung, and Blood Institute (NHLBI). Addressing cardiovascular health in Asian American and Pacific Islanders: a background report [Internet]. Bethesda, MD: NHLBI; 2000 [cited 2022 Feb 18]. Available from: https://www.nhlbi.nih.gov/files/docs/resources/heart/aapibkgd.pdf.
- Ramakrishnan K, Ahmad FZ. Income and poverty. In: Ramakrishnan K, Ahmad F, editors. State of Asian Americans and Pacific Islanders series [Internet]. Washington: Center for American Progress; 2014 [cited 2022 June 9]. Available from: <u>https://americanprogress.org/wp-content/uploads/2014/09/AAPIReportcomp.pdf?_ga=2.98870295.862929155.1654752182-1982429079.1654752182.</u>
- 49. Srinivasan S, Moser RP, Willis G, Riley W, Alexander M, Berrigan D, et al. Small is essential: importance of subpopulation research in cancer control. Am J Public Health. 2015;105 Suppl 3:S371-3. doi: 10.2105/AJPH.2014.302267.
- 50. Singh GK, Jemal A. Socioeconomic and racial/ethnic disparities in cancer mortality, incidence, and survival in the United States, 1950-2014: over six decades of changing patterns and widening inequalities. J Environ Public Health. 2017;2017:2819372. doi: 10.1155/2017/2819372. Epub 2017 Mar 20.
- 51. Clegg LX, Reichman ME, Miller BA, Hankey BF, Singh GK, Lin YD, et al. Impact of socioeconomic status on cancer incidence and stage at diagnosis: selected findings from the surveillance, epidemiology, and end results: National Longitudinal Mortality Study. Cancer Causes Control. 2009;20(4):417-35. doi: 10.1007/s10552-008-9256-0. Epub 2008 Nov 12.
- 52. Lewis DR, Clegg LX, Johnson NJ. Lung disease mortality in the United States: the National Longitudinal Mortality Study. Int J Tuberc Lung Dis. 2009;13(8):1008-14.
- Lawrence WR, McGee-Avila JK, Vo JB, Luo Q, Chen Y, Inoue-Choi M, et al. Trends in cancer mortality among Black individuals in the US from 1999 to 2019. JAMA Oncol. 2022:e221472. doi: 10.1001/jamaoncol.2022.1472.
- 54. DeSantis CE, Miller KD, Goding Sauer A, Jemal A, Siegel RL. Cancer statistics for African Americans, 2019. CA Cancer J Clin. 2019;69(3):211-33. doi: 10.3322/caac.21555.
- 55. Ryan BM. Lung cancer health disparities. Carcinogenesis. 2018;39(6):741-51. doi: 10.1093/carcin/bgy047.
- 56. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin. 2017;67(1):7-30. doi: 10.3322/caac.21387.
- 57. Surveillance, Epidemiology, and End Results Program (SEER) [Internet]. SEER*Explorer: an interactive website for SEER cancer statistics [Internet]. Washington: National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program. [cited 2022 June 9]. Available from: https://seer.cancer.gov/explorer/.
- 58. Zahnd WE, James AS, Jenkins WD, Izadi SR, Fogleman AJ, Steward DE, et al. Rural–urban differences in cancer incidence and trends in the United States. Cancer Epidemiol Biomarkers Prev. 2018;27(11):1265-74. doi: 10.1158/1055-9965.EPI-17-0430.
- 59. Henley SJ, Anderson RN, Thomas CC, Massetti GM, Peaker B, Richardson LC. Invasive cancer incidence, 2004–2013, and deaths, 2006–2015, in nonmetropolitan and metropolitan counties—United States. MMWR Surveill Summ. 2017;66(14):1-13. doi: 10.15585/mmwr.ss6614a1.

- 60. O'Neil ME, Henley SJ, Rohan EA, Ellington TD, Gallaway MS. Lung cancer incidence in nonmetropolitan and metropolitan counties—United States, 2007-2016. MMWR Morb Mortal Wkly Rep. 2019;68(44):993-8. doi: 10.15585/mmwr.mm6844a1.
- 61. Gonzales G, Zinone R. Cancer diagnoses among lesbian, gay, and bisexual adults: results from the 2013–2016 National Health Interview Survey. Cancer Causes Control. 2018;29(9):845-54. doi: 10.1007/s10552-018-1060-x.
- 62. Turati F, Garavello W, Tramacere I, Pelucchi C, Galeone C, Bagnardi V, et al. A meta-analysis of alcohol drinking and oral and pharyngeal cancers: results from subgroup analyses. Alcohol. 2013;48(1):107-18. doi: 10.1093/alcalc/ags100. Epub 2012 Sep 4.
- 63. Hashibe M, Brennan P, Chuang SC, Boccia S, Castellsague X, Chen C, et al. Interaction between tobacco and alcohol use and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. Cancer Epidemiol Biomarkers Prev. 2009;18(2):541-50. doi: 10.1158/1055-9965.EPI-08-0347. Epub 2009 Feb 3.
- 64. Knight JA, Fan J, Malone KE, John EM, Lynch CF, Langballe R, et al. Alcohol consumption and cigarette smoking in combination: a predictor of contralateral breast cancer risk in the WECARE study. Int J Cancer. 2017;141(5):916-24. doi: 10.1002/ijc.30791.
- 65. Tabuchi T, Ozaki K, Ioka A, Miyashiro I. Joint and independent effect of alcohol and tobacco use on the risk of subsequent cancer incidence among cancer survivors: a cohort study using cancer registries. Int J Cancer. 2015;137(9):2114-23. doi: 10.1002/ijc.29575.
- 66. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, et al. Light alcohol drinking and cancer: a meta-analysis. Ann Oncol. 2013;24(2):301-8. doi: 10.1093/annonc/mds337. Epub 2012 Aug 21.
- 67. Chen WY, Rosner B, Hankinson SE, Colditz GA, Willett WC. Moderate alcohol consumption during adult life, drinking patterns, and breast cancer risk. JAMA 2011; 306(17):1884-90.
- LoConte NK, Brewster AM, Kaur JS, Merrill JK, Alberg AJ. Alcohol and cancer: a statement of the American Society of Clinical Oncology. J Clin Oncol. 2018;36(1):83-93. doi: 10.1200/JCO.2017.76.1155. Epub 2017 Nov 7.
- 69. McGinty EE, Zhang Y, Guallar E, Ford DE, Steinwachs D, Dixon LB, et al. Cancer incidence in a sample of Maryland residents with serious mental illness. Psychiatr Serv. 2012;63(7):714-7. doi: 10.1176/appi.ps.201100169.
- American Cancer Society (ACS). Cancer facts & figures 2021 [Internet]. Atlanta: ACS; 2021 [cited 2022 June 9]. Available from <u>https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annualcancer-facts-and-figures/2021/cancer-facts-and-figures-2021.pdf.</u>
- 71. Onega T, Duell EJ, Shi X, Wang D, Demidenko E, Goodman D. Geographic access to cancer care in the U.S. Cancer. 2008;112(4):909-18. doi: 10.1002/cncr.23229.
- 72. Warren Andersen S, Blot WJ, Lipworth L, Steinwandel M, Murff HJ, Zheng W. Association of race and socioeconomic status with colorectal cancer screening, colorectal cancer risk, and mortality in southern US adults. JAMA Netw Open. 2019;2(12):e1917995. doi: 10.1001/jamanetworkopen.2019.17995.
- 73. Turrini G, Branham DK, Chen L, Conmy AB, Chappel AR, De Lew N, et al. Access to affordable care in rural America: current trends and key challenges [Internet]. Washington: U.S. Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation, Office of Health Policy; 2021 [cited 2022 June 9]. Research Report No.: HP-2021-16. Available from: <u>https://aspe.hhs.gov/sites/default/files/2021-07/rural-health-rr.pdf</u>.
- 74. Yabroff KR, Han X, Zhao J, Nogueira L, Jemal A. Rural cancer disparities in the United States: a multilevel framework to improve access to care and patient outcomes. JCO Oncol Pract. 2020;16(7):409-13. doi: 10.1200/OP.20.00352.
- 75. Boehmer U, Cooley TP, Clark MA. Cancer and men who have sex with men: a systematic review. Lancet Oncol. 2012;13(12):e545-53. doi: 10.1016/S1470-2045(12)70347-9.
- Saunders CL, Meads C, Abel GA, Lyratzopoulos G. Associations between sexual orientation and overall and site-specific diagnosis of cancer: evidence from two national patient surveys in England. J Clin Oncol. 2017;35(32):3654-61. doi: 10.1200/JCO.2017.72.5465.
- Alexander LA, Trinidad DR, Sakuma KK, Pokhrel P, Herzog TA, Clanton MS, et al. Why we must continue to investigate menthol's role in the African American smoking paradox. Nicotine Tob Res. 2016;18 Suppl 1:S91-101. doi: 10.1093/ntr/ntv209.
- 78. Gardiner PS. The African Americanization of menthol cigarette use in the United States. Nicotine Tob Res. 2004;6 Suppl 1:S55-65. doi: 10.1080/14622200310001649478.
- 79. Shopland DR. Tobacco use and its contribution to early cancer mortality with a special emphasis on cigarette smoking. Environ Health Perspect. 1995;103 Suppl 8:131-42. doi: 10.1289/ehp.95103s8131.
- 80. Gonzales G, Przedworski J, Henning-Smith C. Comparison of health and health risk factors between lesbian, gay, and bisexual adults and heterosexual adults in the United States: results from the National Health Interview Survey. JAMA Intern Med. 2016;176(9):1344-51. doi: 10.1001/jamainternmed.2016.3432.
- Dickerson F, Origoni A, Schroeder J, Schweinfurth LAB, Stallings C, Savage CLG, et al. Mortality in schizophrenia and bipolar disorder: clinical and serological predictors. Schizophr Res. 2016;170(1):177-83. doi: 10.1016/j.schres.2015.11.010.
- 82. Tam J, Warner K, Meza R. Smoking and the reduced life expectancy of individuals with serious mental illness. Am J Prev Med. 2016;51(6):958-66. doi: 10.1016/j.amepre.2016.06.007
- de Leon J, Diaz FJ. A meta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviors. Schizophr Res. 2005 Jul 15;76(2-3):135-57. doi: 10.1016/j.schres.2005.02.010.
- Siahpush M, Singh GK, Jones PR, Timsina LR. Racial/ethnic and socioeconomic variations in duration of smoking: results from 2003, 2006 and 2007 Tobacco Use Supplement of the Current Population Survey. J Public Health (Oxf). 2010;32(2):210-8. doi: 10.1093/pubmed/fdp104.
- 85. U.S. Department of Health and Human Services (USDHHS). Smoking cessation: a report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2020.
- Asfar T, Dietz NA, Arheart KL, Tannenbaum SL, McClure LA, Fleming LE, et al. Smoking behavior among adult childhood cancer survivors: what are we missing? J Cancer Surviv. 2016;10(1):131-41. doi: 10.1007/s11764-015-0459-6. Epub 2015 Jun 2.
- 87. Burcu M, Steinberger EK, Sorkin JD. Health care access and smoking cessation among cancer survivors: implications for the Affordable Care Act and survivorship care. J Cancer Surviv. 2016;10(1):1-10. doi: 10.1007/s11764-015-0446-y. Epub 2015 Apr 11.
- Gallaway MS, Glover-Kudon R, Momin B, Puckett M, Lunsford NB, Ragan KR, et al. Smoking cessation attitudes and practices among cancer survivors—United States, 2015. J Cancer Surviv. 2019;13(1):66-74. doi: 10.1007/s11764-018-0728-2.
- Mann AJ, Malcolm JC. Associations between sociodemographic characteristics and tobacco usage in adult cancer survivors: evidence from a population-based study. Epidemiol Biostat Public Health. 2019;16(3):e13117-1-9. doi: 10.2427/13117.
- 90. Poghosyan H, Darwish SA, Kim SS, Cooley ME. The association between social support and smoking status in cancer survivors with frequent and infrequent mental distress: results from 10 US states, 2010. J Cancer Surviv. 2016;10(6):1078-88. doi: 10.1007/s11764-016-0551-6.
- 91. Sterba KR, Garrett-Mayer E, Carpenter MJ, Tooze JA, Hatcher JL, Sullivan C, et al. Smoking status and symptom burden in surgical head and neck cancer patients. Laryngoscope. 2017;127(1):127-33. doi: 10.1002/lary.26159. Epub 2016 Jul 9.
- 92. Park JJ, Park HA. Prevalence of cigarette smoking among adult cancer survivors in Korea. Yonsei Med J. 2015;56(2):556-62. doi: 10.3349/ymj.2015.56.2.556.
- 93. Park ER, Japuntich SJ, Rigotti NA, Traeger L, He Y, Wallace RB, et al. A snapshot of smokers after lung and colorectal cancer diagnosis. Cancer. 2012;118(12):3153-64. doi: 10.1002/cncr.26545. Epub 2012 Jan 23.
- Talluri R, Fokom Domgue J, Gritz ER, Shete S. Assessment of trends in cigarette smoking cessation after cancer diagnosis among US adults, 2000 to 2017. JAMA Netw Open. 2020 Aug 3;3(8):e2012164. doi: 10.1001/jamanetworkopen.2020.12164.
- 95. Scott GM, Best C, Fung K, Gupta M, Sommer D, Szeto C, et al. Impact of marginalization on tobacco use in individuals diagnosed with head and neck cancer. J Otolaryngol Head Neck Surg. 2019;48(1):54. doi: 10.1186/s40463-019-0380-5.
- Underwood JM, Townsend JS, Tai E, White A, Davis SP, Fairley TL. Persistent cigarette smoking and other tobacco use after a tobacco-related cancer diagnosis. J Cancer Surviv. 2012;6(3):333-44. doi: 10.1007/s11764-012-0230-1.
- Walker MS, Larsen RJ, Zona DM, Govindan R, Fisher EB. Smoking urges and relapse among lung cancer patients: findings from a preliminary retrospective study. Prev Med. 2004;39(3):449-57. doi: 10.1016/j.ypmed.2004.04.035.
- Bolt DM, Piper ME, McCarthy DE, Japuntich SJ, Fiore MC, Smith SS, et al. The Wisconsin Predicting Patients' Relapse questionnaire. Nicotine Tob Res. 2009;11(5):481-92. doi: 10.1093/ntr/ntp030. Epub 2009 Apr 16.

- Businelle MS, Kendzor DE, Reitzel LR, Costello TJ, Cofta-Woerpel C, Li Y, et al. Mechanisms linking socioeconomic status to smoking cessation: a structural equation modeling approach. Health Psychol. 2010;29(3):262-73. doi: 10.1037/a0019285.
- 100. El-Khoury LF, Bolze C, Melchior M. Factors associated with successful vs. unsuccessful smoking cessation: data from a nationally representative study. Addict Behav. 2018;80:110-5. doi: 10.1016/j.addbeh.2018.01.016.
- 101. Kalkhoran S, Berkowitz SA, Rigotti NA, Baggett TP. Financial strain, quit attempts, and smoking abstinence among U.S. adult smokers. Am J Prev Med. 2018 Jul:55(1):80-8. doi: 10.1016/j.amepre.2018.01.036.
- 102. Kendzor DE, Businelle MS, Costello TJ, Castro Y, Reitzel LR, Cofta-Woerpel LM, et al. Financial strain and smoking cessation among racially/ethnically diverse smokers. Am J Public Health. 2010;100(4):702-6. doi: 10.2105/AJPH.2009.172676.
- 103. Koo HY, Lee K, Park SM, Chang J, Kim K, Choi S, et al. Prevalence and predictors of sustained smoking after a cancer diagnosis in Korean men. Cancer Res Treat. 2020 Jan;52(1):139-48. doi: 10.4143/crt.2018.609. Epub 2019 Jun 25.
- 104. Poghosyan H, Scarpino SV. Food insecure cancer survivors continue to smoke after their diagnosis despite not having enough to eat: implications for policy and clinical interventions. Cancer Causes Control. 2019;30(3):241-8. doi: 10.1007/s10552-019-01137-7.
- 105. Reitzel LR, Mazas CA, Cofta-Woerpel L, Li Y, Cao Y, Businelle MS, et al. Subjective social status affects smoking abstinence during acute withdrawal through affective mediators. Addiction. 2010;105(5):928-36. doi: 10.1111/j.1360-0443.2009.02875.x.
- 106. U.S. Department of Health and Human Services (USDHHS). The health consequences of smoking—50 years of progress: a report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014. Printed with corrections: 2014 Jan.
- 107. Wetter DW, Cofta-Gunn L, Fouladi RT, Irvin JE, Daza P, Mazas C, et al. Understanding the associations among education, employment characteristics, and smoking. Addict Behav. 2005;30(5):905-14. doi: 10.1016/j.addbeh.2004.09.006.
- 108. Winters BR, Wen L, Holt SK, Dash A, Gore JL, Schade GR, et al. Does the diagnosis of bladder cancer lead to higher rates of smoking cessation? Findings from the Medicare Health Outcomes Survey. J Urol. 2019;202(2):241-6. doi: 10.1097/JU.00000000000206.
- 109. Browning KK, Ferketich AK, Salsberry PJ, Wewers ME. Socioeconomic disparity in provider-delivered assistance to quit smoking. Nicotine Tob Res. 2008;10(1):55-61. doi: 10.1080/14622200701704905.
- 110. DeNavas-Walt C, Proctor BD, Lee CH. Income, poverty, and health insurance coverage in the United States: 2005. U.S. Census Bureau, current population reports. Washington: U.S. Census Bureau; 2006.
- 111. Fox JB, Shaw FE. Relationship of income and health care coverage to receipt of recommended clinical preventive services by adults—United States, 2011-2012. MMWR Morb Mortal Wkly Rep. 2014;63(31):666-70.
- 112. Jamal A, Dube SR, Malarcher AM, Shaw L, Engstrom MC; Centers for Disease Control and Prevention (CDC). Tobacco use screening and counseling during physician office visits among adults—National Ambulatory Medical Care Survey and National Health Interview Survey, United States, 2005-2009. MMWR Suppl. 2012;61(2):38-45.
- 113. Ku L, Brantley E, Bysshe T, Steinmetz E, Bruen BK. How Medicaid and other public policies affect use of tobacco cessation therapy, United States, 2010-2014. Prev Chronic Dis. 2016;13:e150. doi: 10.5888/pcd13.160234.
- 114. Singleterry J, Jump Z, DiGiulio A, Babb S, Sneegas K, MacNeil A, et al. State Medicaid coverage for tobacco cessation treatments and barriers to coverage—United States, 2014–2015. MMWR Morb Mortal Wkly Rep. 2015;64(42):1194-9. doi: 10.15585/mmwr.mm6442a3.
- 115. Voelker R. Decades of work to reduce disparities in health care produce limited success. JAMA. 2008;299(12):1411-3. doi: 10.1001/jama.299.12.1411.
- 116. Voelker R. Preventive care linked with income, health insurance status. JAMA. 2014;312(12):1186.
- 117. Hiscock R, Bauld L, Amos A, Fidler JA, Munafo M. Socioeconomic status and smoking: a review. Ann N Y Acad Sci. 2012 Feb;1248:107-23. doi: 10.1111/j.1749-6632.2011.06202.x. Epub 2011 Nov 17.
- 118. Twyman L, Bonevski B, Paul C, Bryant J. Perceived barriers to smoking cessation in selected vulnerable groups: a systematic review of the qualitative and quantitative literature. BMJ Open. 2014;4(12):e006414. doi: 10.1136/bmjopen-2014-006414.

- 119. Kong AY, Myers AE, Isgett LF, Ribisl KM. Neighborhood racial, ethnic, and income disparities in accessibility to multiple tobacco retailers: Mecklenburg County, North Carolina, 2015. Prev Med Rep. 2019;17:101031. doi: 10.1016/j.pmedr.2019.101031.
- 120. Lee JG, Henriksen L, Rose SW, Moreland-Russell S, Ribisl KM. A systematic review of neighborhood disparities in point-of-sale tobacco marketing. Am J Public Health. 2015;105(9):e8-e18. doi: 10.2105/AJPH.2015.302777.
- 121. Yu D, Peterson NA, Sheffer MA, Reid RJ, Schneider JE. Tobacco outlet density and demographics: analysing the relationships with a spatial regression approach. Public Health. 2010;124(7):412-6. doi: 10.1016/j.puhe.2010.03.024. Epub 2010 Jun 11.
- 122. Christiansen BA, Reeder KM, Hill M, Baker TB, Fiore MC. Barriers to effective tobacco-dependence treatment for the very poor. J Stud Alcohol Drugs. 2012;73(6):874-84. doi: 10.15288/jsad.2012.73.874.
- 123. Dotinga A, Schrijvers CT, Voorham AJ, Mackenbach JP. Correlates of stages of change of smoking among inhabitants of deprived neighbourhoods. Eur J Public Health. 2005;15(2):152-9. doi: 10.1093/eurpub/cki112.
- 124. Christiansen BA, Reeder KM, Fiore MC, Baker TB. Changing low income smokers' beliefs about tobacco dependence treatment. Subst Use Misuse. 2014;49(7):852-63. doi: 10.3109/10826084.2014.880724. Epub 2014 Feb 6.
- 125. Christiansen BA, Reeder KM, TerBeek EG, Fiore MC, Baker TB. Motivating low socioeconomic status smokers to accept evidence-based smoking cessation treatment: a brief intervention for the community agency setting. Nicotine Tob Res. 2015;17(8):1002-11. doi: 10.1093/ntr/ntu345.
- 126. McMenamin SB, Halpin HA, Bellows NM. Knowledge of Medicaid coverage and effectiveness of smoking treatments. Am J Prev Med. 2006;31(5):369-74. doi: 10.1016/j.amepre.2006.07.015.
- 127. Wilkinson AV, Vasudevan V, Honn SE, Spitz MR, Chamberlain RM. Sociodemographic characteristics, health beliefs, and the accuracy of cancer knowledge. J Cancer Educ. 2009;24(1):58-64. doi: 10.1080/08858190802664834.
- 128. Hoover DS, Spears CA, Vidrine DJ, Walker JL, Shih YC, Wetter DW. Smoking cessation treatment needs of low SES cervical cancer survivors. Am J Health Behav. 2019;43(3):606-20. doi: 10.5993/AJHB.43.3.14.
- 129. Sood A, Andoh J, Rajoli N, Hopkins-Price P, Verhulst SJ. Characteristics of smokers calling a national reactive telephone helpline. Am J Health Promot. 2008;22(3):176-9. doi: 10.4278/ajhp.22.3.176.
- 130. Davis KC, Alexander RL Jr, Shafer P, Mann N, Malarcher A, Zhang L. The dose-response relationship between tobacco education advertising and calls to quitlines in the United States, March-June, 2012. Prev Chronic Dis. 2015;12:e191. doi: 10.5888/pcd12.150157.
- 131. Fiore MC, Baker TB. Ten million calls and counting: progress and promise of tobacco quitlines in the U.S. Am J Prev Med. 2021;60(3 Suppl 2):S103-6. doi: 10.1016/j.amepre.2020.06.021.
- 132. Sheffer M, Redmond L, Kobinksky K, Keller P, McAfee T, Fiore M. Creating a perfect storm to increase consumer demand for Wisconsin's tobacco quitline. Am J Prev Med. 2010;38(3S0):S343-6. doi: 10.1016/j.amepre.2009.11.014.
- 133. Kaplan RC, Bangdiwala SI, Barnhart JM, Castaneda SF, Gellman MD, Lee DJ, et al. Smoking among U.S. Hispanic/Latino adults: the Hispanic community health study/study of Latinos. Am J Prev Med. 2014;46(5):496-506. doi: 10.1016/j.amepre.2014.01.014.
- 134. American Lung Association (ALA) [Internet]. Chicago: ALA; c2022 [cited 2022 June 9]. Tobacco use in racial and ethnic populations; 2020; [about 7 screens]. Available from: <u>https://www.lung.org/quit-smoking/smoking-facts/impact-of-tobacco-use/tobacco-use-racial-and-ethnic</u>.
- 135. Villarroel MA, Blackwell DL, Jen A. Tables of summary health statistics for U.S. adults: 2018 National Health Interview Survey [Internet]. Washington: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics; 2019. [cited 2022 June 9]. Available from: <u>https://ftp.cdc.gov/pub/Health_Statistics/NCHS/NHIS/SHS/2018_SHS_Table_A-12.pdf</u>.
- 136. Wang TW, Walton K, Reyes-Guzman C, Cullen KA, Jamal A. State-specific prevalence of tobacco product use among US women, tobacco use supplement to the current population survey, 2018-2019. Prev Chronic Dis. 2021;18:e36. doi: 10.5888/pcd18.200547.
- 137. Holford TR, Levy DT, Meza R. Comparison of smoking history patterns among African American and White cohorts in the United States born 1890 to 1990. Nicotine Tob. Res. 2016;18 Suppl 1:S16–29. doi: 10.1093/ntr/ntv274.
- 138. Perez-Stable EJ, Herrera B, Jacob P 3rd, Benowitz NL. Nicotine metabolism and intake in black and white smokers. JAMA. 1998;280(2):152-6. doi: 10.1001/jama.280.2.152.

- Haiman CA, Stram DO, Wilkens LR, Pike MC, Kolonel LN, Henderson BE, et al. Ethnic and racial differences in the smoking-related risk of lung cancer. N Engl J Med. 2006;354(4):333-42. doi: 10.1056/NEJMoa033250.
- 140. Reyes-Guzman CM, Pfeiffer RM, Lubin J, Freedman ND, Cleary SD, Levine PH, et al. Determinants of light and intermittent smoking in the United States: results from three pooled national health surveys. Cancer Epidemiol Biomarkers Prev. 2017;26(2):228-39. doi: 10.1158/1055-9965.EPI-16-0028. Epub 2016 Oct 19.
- 141. Trinidad DR, Perez-Stable EJ, Emery SL, White MM, Grana RA, Messer KS. Intermittent and light daily smoking across racial/ethnic groups in the United States. Nicotine Tob Res. 2009;11(2):203-10. doi: 10.1093/ntr/ntn018.
- 142. Tsai J, Homa DM, Gentzke AS, Mahoney M, Sharapova SR, Sosnoff CS, et al. Exposure to secondhand smoke among nonsmokers—United States, 1988-2014. MMWR Morb Mortal Wkly Rep. 2018;67(48):1342-6. doi: 10.15585/mmwr.mm6748a3.
- 143. Brody DJ, Faust E, Tsai J. Secondhand smoke exposure among nonsmoking adults: United States, 2015–2018 [Internet]. Hyattsville, MD: National Center for Health Statistics; 2021 Feb. [cited 2022 June 9]. NCHS Data Brief No. 396. Available from: <u>https://www.cdc.gov/nchs/data/databriefs/db396-H.pdf</u>.
- 144. Centers for Disease Control and Prevention (CDC) [Internet]. Atlanta: CDC; c2022 [cited 2022 June 9]; Menthol and cigarettes; [about 9 screens]. Available from: https://www.cdc.gov/tobacco/basic_information/tobacco_industry/menthol-cigarettes/index.html.
- 145. Villanti AC, Mowery PD, Delnevo CD, Niaura RS, Abrams DB, Giovino GA. Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004-2014. Tob Control. 2016;25(Suppl 2):ii14-ii20. doi: 10.1136/tobaccocontrol-2016-053329.
- 146. Weinberger AH, Giovenco DP, Zhu J, Lee J, Kashan RS, Goodwin RD. Racial/ethnic differences in daily, nondaily, and menthol cigarette use and smoking quit ratios in the United States: 2002 to 2016. Prev Med. 2019;125:32-9. doi: 10.1016/j.ypmed.2019.04.009.
- 147. U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. National Survey on Drug Use and Health 2019. Retrieved from: Available from <u>https://pdas.samhsa.gov/#/survey/NSDUH-2019-</u> <u>DS0001?column=NEWRACE2&control=CATAGE_RECODE&filter=CIG30MEN%21%3D91%2C93%2C94</u> %2C97%2C98%26CATAGE_RECODE%3DRecoded_New_Category_youth%2CRecoded_New_Category_a dult&recodes=CATAGE_RECODE%7C1%3DRecoded_New_Category_youth%262%3DRecoded_New_Cate gory_adult%263%3DRecoded_New_Category_adult%264%3DRecoded_New_Category_adult&results_receiv ed=true&row=CIG30MEN&run_chisq=false&weight=ANALWT_C. Accessed 2022 May 31.
- 148. Delnevo CD, Gundersen DA, Hrywna M, Echeverria SE, Steinberg MB. Smoking-cessation prevalence among U.S. smokers of menthol versus non-menthol cigarettes. Am J Prev Med. 2011;41(4):357-65. doi: 10.1016/j.amepre.2011.06.039.
- 149. Gundersen DA, Delnevo CD, Wackowski O. Exploring the relationship between race/ethnicity, menthol smoking, and cessation, in a nationally representative sample of adults. Prev Med. 2009;49(6):553-7. doi: 10.1016/j.ypmed.2009.10.003.
- 150. Levy DT, Blackman K, Tauras J, Chaloupka FJ, Villanti AC, Niaura RS, et al. Quit attempts and quit rates among menthol and nonmenthol smokers in the United States. Am J Public Health. 2011;101(7):1241-7. doi: 10.2105/AJPH.2011.300178.
- 151. Mills SD, Hao Y, Ribisl KM, Wiesen CA, Hassmiller Lich K. The relationship between menthol cigarette use, smoking cessation, and relapse: findings from waves 1 to 4 of the Population Assessment of Tobacco and Health Study. Nicotine Tob Res. 2021;23(6):966-75. doi: 10.1093/ntr/ntaa212.
- 152. Stahre M, Okuyemi KS, Joseph AM, Fu SS. Racial/ethnic differences in menthol cigarette smoking, population quit ratios and utilization of evidence-based tobacco cessation treatments. Addiction. 2010;105:75-83. doi: 10.1111/j.1360-0443.2010.03200.x.
- 153. Smith PH, Assefa B, Kainth S, Salas-Ramirez KY, Mckee SA, Giovino GA. Use of mentholated cigarettes and likelihood of smoking cessation in the United States: a meta-analysis. Nicotine Tob Res. 2020;22(3):307-16. doi: 10.1093/ntr/ntz067.
- 154. Trinidad DR, Pérez-Stable EJ, Messer K, White MM, Pierce JP. Menthol cigarettes and smoking cessation among racial/ethnic groups in the United States. Addiction. 2010;105 Suppl 1(0 1):84-94. doi: 10.1111/j.1360-0443.2010.03187.x.
- 155. Leas EC, Benmarhnia T, Strong DR, Pierce JP. Effects of menthol use and transitions in use on short-term and long-term cessation from cigarettes among US. Tob Control. 2021;tobaccocontrol-2021-056596. doi: 10.1136/tobaccocontrol-2021-056596. Epub 2021 Jul 6.

- 156. Azagba S, Shan L, Manzione L. Cigarette, e-cigarette, alcohol, and marijuana use by cancer diagnosis status: a longitudinal analysis. Subst Abuse. 2020;14:1178221820980470. doi: 10.1177/1178221820980470.
- 157. Swoboda CM, Walker DM, Huerta TR. Likelihood of smoking among cancer survivors: an updated Health Information National Trends Survey analysis. Nicotine Tob Res. 2019;21(12):1636-43. doi: 10.1093/ntr/ntz007.
- 158. Mayer DK, Carlson J. Smoking patterns in cancer survivors. Nicotine Tob Res. 2011;13(1):34-40. doi: 10.1093/ntr/ntq199.
- 159. Salloum RG, Huo J, Lee JH, Lee J, Dallery J, George T, et al. Tobacco and e-cigarette use among cancer survivors in the United States. PLoS One. 2019;14(12):e0226110. doi: 10.1371/journal.pone.0226110.
- 160. Blair CK, McDougall JA, Chiu VK, Wiggins CL, Rajput A, Harding EM, et al. Correlates of poor adherence to a healthy lifestyle among a diverse group of colorectal cancer survivors. Cancer Causes Control. 2019;30(12):1327-39. doi: 10.1007/s10552-019-01241-8. Epub 2019 Oct 26.
- 161. Ruiz ME, Sender L, Torno L, Fortier MA. The associations of age and ethnicity on substance use behaviors of adolescent and young adult childhood cancer survivors. Psychooncology. 2016;25(10):1229-36. doi: 10.1002/pon.4225. Epub 2016 Sep 7.
- 162. Babb S, Malarcher A, Schauer G, Asman K, Jamal A. Quitting smoking among adults—United States, 2000-2015. MMWR Morb Mortal Wkly Rep. 2017;65(52):1457-64. doi: 10.15585/mmwr.mm6552a1.
- 163. Gritz ER, Talluri R, Fokom Domgue J, Tami-Maury I, Shete S. Smoking behaviors in survivors of smoking-related and non–smoking-related cancers. JAMA Netw Open. 2020;3(7):e209072. doi: 10.1001/jamanetworkopen.2020.9072.
- 164. Tseng TS, Lin HY, Moody-Thomas S, Martin M, Chen T. Who tended to continue smoking after cancer diagnosis: the National Health and Nutrition Examination Survey 1999-2008. BMC Public Health. 2012;12:784. doi: 10.1186/1471-2458-12-784.
- 165. Kulak JA, Cornelius ME, Fong GT, Giovino GA. Differences in quit attempts and cigarette smoking abstinence between whites and African Americans in the United States: literature review and results from the international tobacco control US survey. Nicotine Tob Res. 2016;18(Suppl 1):S79-87. doi: 10.1093/ntr/ntv228.
- 166. Nollen NL, Mayo MS, Cox LS, Benowitz NL, Tyndale RF, Ellerbeck EF, et al. Factors that explain differences in abstinence between Black and White smokers: a prospective intervention study. J Natl Cancer Inst. 2019;111(10):1078-87. doi: 10.1093/jnci/djz001.
- 167. Burgess DJ, van Ryn M, Noorbaloochi S, Clothier B, Taylor BC, Sherman S, et al. Smoking cessation among African American and White smokers in the Veterans Affairs health care system. Am J Public Health. 2014;104 Suppl 4:S580-7. doi: 10.2105/AJPH.2014.302023.
- 168. Cropsey KL, Weaver MF, Eldridge GD, Villalobos GC, Best AM, Stitzer ML. Differential success rates in racial groups: results of a clinical trial of smoking cessation among female prisoners. Nicotine Tob Res. 2009;11(6):690-7. doi: 10.1093/ntr/ntp051. Epub 2009 Apr 22.
- Gariti P, Lynch K, Alterman A, Kampman K, Xie H, Varillo K. Comparing smoking treatment programs for lighter smokers with and without a history of heavier smoking. J Subst Abuse Treat. 2009;37(3):247-55. doi: 10.1016/j.jsat.2009.01.006.
- 170. Lando H, Hennrikus D, McCarty M, Vessey J. Predictors of quitting in hospitalized smokers. Nicotine Tob Res. 2003;5(2):215-22. doi: 10.1080/0955300031000083436.
- 171. Nollen NL, Ahluwalia JS, Cox LS, Okuyemi K, Lawrence D, Samuels L, et al. Assessment of racial differences in pharmacotherapy efficacy for smoking cessation: secondary analysis of the EAGLES randomized clinical trial JAMA Network Open. 2021;4(1):e2032053. doi: 10.1001/jamanetworkopen.2020.32053.
- 172. West R, Evins AE, Benowitz NL, Russ C, McRae T, Lawrence D, et al. Factors associated with the efficacy of smoking cessation treatments and predictors of smoking abstinence in EAGLES. Addiction. 2018;113(8):1507-16. doi: 10.1111/add.14208.
- 173. Daza P, Cofta-Woerpel L, Mazas C, Fouladi RT, Cinciripini PM, Gritz ER, et al. Racial and ethnic differences in predictors of smoking cessation. Subst Use Misuse. 2006;41(3):317-39. doi: 10.1080/10826080500410884.
- 174. Fu SS, Burgess DJ, Hatsukami DK, Noorbaloochi S, Clothier BA, Nugent S, et al. Race and nicotine replacement treatment outcomes among low-income smokers. Am J Prev Med. 2008;35 Suppl 6:S442-8. doi: 10.1016/j.amepre.2008.09.009.
- 175. Hooper MW, Rogers BG, Okuyemi K. Smoking cessation among racial/ethnic minorities, 2010–2014. Curr Addict Rep. 2015;2(1):24-32. doi: 10.5993/AJHB.43.3.14.

- 176. Fiore MC, Jaen CR, Baker TB, Bailey WC, Benowitz NL, Curry SJ, et al. Treating tobacco use and dependence: 2008 update. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service; 2008. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK63952/</u>.
- 177. Matthews AK, Sanchez-Johnsen L, King AC. Development of a culturally targeted smoking cessation intervention for African American smokers. J Community Health. 2009;34(6):480-92. doi: 10.1007/s10900-009-9181-5.
- 178. Webb Hooper M, Antoni MH, Okuyemi K, Dietz NA, Resnicow K. Randomized controlled trial of group-based culturally specific cognitive behavioral therapy among African American smokers. Nicotine Tob Res. 2017;19(3):333-41. doi: 10.1093/ntr/ntw181.
- 179. Paradies Y, Ben J, Denson N, Elias A, Priest N, Pieterse A, et al. Racism as a determinant of health: a systematic review and meta-analysis. PLoS One. 2015;10(9):e0138511. doi: 10.1371/journal.pone.0138511.
- Fedele DA, Tooley E, Busch A, McQuaid EL, Hammond SK, Borrelli B. Comparison of secondhand smoke exposure in minority and nonminority children with asthma. Health Psychol. 2016;35(2):115-22. doi: 10.1037/hea0000220.
- 181. Lee JG, Sun DL, Schleicher NM, Ribisl KM, Luke DA, Henriksen L. Inequalities in tobacco outlet density by race, ethnicity and socioeconomic status, 2012, USA: results from the ASPiRE study. J Epidemiol Community Health. 2017;71(5):487-92. doi: 10.1136/jech-2016-208475. Epub 2017 Mar 1.
- 182. Widome R, Brock B, Noble P, Forster JL. The relationship of neighborhood demographic characteristics to point-of-sale tobacco advertising and marketing. Ethn Health. 2013;18(2):136-151. doi: 10.1080/13557858.2012.701273.
- 183. Mills SD, Kong AY, Reimold AE, Baggett CD, Wiesen CA, Golden SD. Sociodemographic disparities in tobacco retailer density in the United States, 2000–2017. Nicotine Tob Res. 2022;ntac020. doi: 10.1093/ntr/ntac020.
- 184. Howard DH, Sentell T, Gazmararian JA. Impact of health literacy on socioeconomic and racial differences in health in an elderly population. J Gen Intern Med. 2006;21(8):857-61. doi: 10.1111/j.1525-1497.2006.00530.x.
- 185. Institute of Medicine (IOM) (US) Committee on Understanding and Eliminating Racial and Ethnic Disparities in Health Care, Smedley BD, Stith AY, Nelson AR, editors. Unequal treatment: confronting racial and ethnic disparities in health care. Washington: National Academies Press (US); 2003.
- 186. Liu SY, Lu L, Pringle D, Mahler M, Niu C, Charow R, et al. Impact of immigration status on health behaviors and perceptions in cancer survivors. Cancer Med. 2019;8(5):2623-35. doi: 10.1002/cam4.2079.
- 187. Hooks-Anderson DR, Salas J, Secrest S, Skiold-Hanlin S, Scherrer JF. Association between race and receipt of counselling or medication for smoking cessation in primary care. Fam Pract. 2018;35(2):160-5. doi: 10.1093/fampra/cmx099.
- 188. Houston TK, Scarinci IC, Person SD, Greene PG. Patient smoking cessation advice by health care providers: the role of ethnicity, socioeconomic status, and health. Am J Public Health. 2005;95(6):1056-61. doi: 10.2105/AJPH.2004.039909.
- 189. Cokkinides VE, Halpern MT, Barbeau EM, Ward E, Thun MJ. Racial and ethnic disparities in smoking-cessation interventions. Am J Prev Med. 2008;34(5):404-12. doi: 10.1016/j.amepre.2008.02.003.
- Danesh D, Paskett ED, Ferketich AK. Disparities in receipt of advice to quit smoking from health care providers: 2010 National Health Interview Survey. Prev Chronic Dis 2014;11:140053. doi: 10.5888/pcd11.140053.
- 191. Landrine H, Corral I, Campbell K. Racial disparities in healthcare provider advice to quit smoking. Prev Med Rep. 2018;10:172-5. doi: 10.1016/j.pmedr.2018.03.003.
- 192. Sonnenfeld N, Schappert SM, Lin SX. Racial and ethnic differences in delivery of tobacco-cessation services. Am J Prev Med. 2009;36(1):21-8. doi: 10.1016/j.amepre.2008.09.028.
- 193. Trinidad DR, Perez-Stable EJ, White MM, Emery SL, Messer KS. A nationwide analysis of US racial/ethnic disparities in smoking behaviors, smoking cessation, and cessation-related factors. Am J Public Health. 2011;101(4):699-706. doi: 10.2105/AJPH.2010.191668.
- 194. Webb Hooper M, Payne M, Parkinson KA. Tobacco cessation pharmacotherapy use among racial/ethnic minorities in the United States: considerations for primary care. Fam Med Community Health. 2017;5(3):193-203. doi: 10.15212/FMCH.2017.0138.
- 195. Cohen RA, Cha AE, Martinez ME, Terlizzi EP. Health insurance coverage: early release of estimates from the National Health Interview Survey, 2019 [Internet]. Washington: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics; 2020 [cited 2022 June 9]. Available from: <u>https://www.cdc.gov/nchs/data/nhis/earlyrelease/insur202009-508.pdf</u>.

- 196. D'Angelo H, Webb Hooper M, Burris JL, Rolland B, Adsit R, Pauk D, et al. Achieving equity in the reach of smoking cessation services within the NCI Cancer Moonshot-funded Cancer Center Cessation Initiative. Health Equity. 2021;5(1):424-30. doi: 10.1089/heq.2020.0157.
- 197. Baker TB, Berg KM, Adsit RT, Skora AD, Swedlund MP, Zehner ME, et al. Closed loop eReferral from primary care clinics to a state tobacco cessation quitline; an implementation and maintenance evaluation. Am J Prev Med. 2021;60(3 Suppl 2):S113-S122.
- 198. Malburg CM, Fucinari J, Ruterbusch JJ, Ledgerwood DM, Beebe-Dimmer JL, Schwartz AG, et al. Continued smoking in African American cancer survivors: the Detroit Research on Cancer Survivors Cohort. Cancer Med. 2020;9(20):7763-71. doi: 10.1002/cam4.3368.
- 199. King AC, Cao D, Southard CC, Matthews AK. Racial differences in eligibility and enrollment in a smoking cessation clinical trial. Health Psychol. 2011;30(1):40-8.
- 200. Nazha B, Mishra M, Pentz R, Owonikoko TK. Enrollment of racial minorities in clinical trials: old problem assumes new urgency in the age of immunotherapy. Am Soc Clin Oncol Educ Book. 2019;39:3-10. doi: 10.1200/EDBK_100021.
- 201. Park ER, Weiss ES, Moy B. Recruiting and enrolling minority patients to cancer clinical trials. Community Oncol. 2007;4(4):254-7.
- 202. Webb Hooper M, Mitchell C, Marshall VJ, Cheatham C, Austin K, Sanders K, et al. Understanding multilevel factors related to urban community trust in healthcare and research. Int J Environ Res Public Health. 2019;16(18):3280. doi: 10.3390/ijerph16183280.
- 203. Matthews KA, Croft JB, Liu Y, Lu H, Kanny D, Wheaton AG, et al. Health-related behaviors by urban-rural county classification—United States, 2013. MMWR Surveill Summ. 2017;66(5):1-8. doi: 10.15585/mmwr.ss6605a1.
- 204. Roberts ME, Doogan NJ, Stanton CA, Quisenberry AJ, Villanti AC, Gaalema DE, et al. Rural versus urban use of traditional and emerging tobacco products in the United States, 2013-2014. Am J Public Health. 2017;107(10):1554-9. doi: 10.2105/AJPH.2017.303967. Epub 2017 Aug 17.
- 205. Weaver KE, Palmer N, Lu L, Case LD, Geiger AM. Rural-urban differences in health behaviors and implications for health status among US cancer survivors. Cancer Causes Control. 2013;24(8):1481-90. doi: 10.1007/s10552-013-0225-x.
- 206. Schootman M, Homan S, Weaver KE, Jeffe DB, Yun S. The health and welfare of rural and urban cancer survivors in Missouri. Prev Chronic Dis. 2013;10:E152. doi: 10.5888/pcd10.130052.
- 207. Healthy People 2020 [Internet]. Washington, DC: U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion; 2019 [cited 2022 June 9]. Healthy people 2020: tobacco use TU-1.1, reduce cigarette smoking by adults. Available from: <u>https://www.healthypeople.gov/2020/topics-objectives/topic/Tobacco-Use/objectives#5287</u>.
- 208. Healthy People 2020 [Internet]. Washington, DC: U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion; 2019 [cited 2022 June 9]. Healthy people 2020: tobacco use TU-4.1, increase smoking cessation attempts by adult smokers. 2019. Available from: https://www.healthypeople.gov/2020/topics-objectives/topic/Tobacco-Use/objectives#5359.
- 209. Coughlin SS, Vernon M, Majeed B, Clary C, Moore J, Islam KM, et al. Tobacco cessation, rural residence, and lung cancer. J Environ Health Sci. 2020;6(1):1-4. Epub 2020 Feb 17.
- 210. Carlson LE, Lounsberry JJ, Maciejewski O, Wright K, Collacutt V, Taenzer P. Telehealth-delivered group smoking cessation for rural and urban participants: feasibility and cessation rates. Addict Behav. 2012;37(1):108-14. doi: 10.1016/j.addbeh.2011.09.011. Epub 2011 Sep 16.
- 211. Vander Weg MW, Cunningham CL, Howren MB, Cai X. Tobacco use and exposure in rural areas: findings from the Behavioral Risk Factor Surveillance System. Addict Behav. 2011;36(3):231-6. doi: 10.1016/j.addbeh.2010.11.005. Epub 2010 Nov 10.
- 212. American Lung Association (ALA). Cutting tobacco's rural roots: tobacco use in rural communities [Internet]. Chicago: ALA; 2012 [cited 2022 June 9]. Available from https://healthforward.org/wp-content/uploads/2015/07/cutting-tobaccos-rural-roots.pdf.
- 213. Association of American Medical Colleges (AAMC). The complexities of physician supply and demand: projections from 2019 to 2034 [Internet]. Washington: AAMC; 2021 [cited 2022 June 9]. Available from: https://www.aamc.org/media/54681/download?attachment.
- 214. Kirkwood MK, Bruinooge SS, Goldstein MA, Bajorin DF, Kosty MP. Enhancing the American Society of Clinical Oncology workforce information system with geographic distribution of oncologists and comparison of data sources for the number of practicing oncologists. J Oncol Pract. 2014;10(1):32-8. doi: 10.1037/a0021649.

- 215. Ward MM, Ullrich F, Matthews K, Rushton G, Tracy R, Bajorin DF, et al. Access to chemotherapy services by availability of local and visiting oncologists. J Oncol Pract. 2014;10(1):26-31. doi: 10.1200/JOP.2013.001217.
- 216. Ballas LK, Elkin EB, Schrag D, Minsky BD, Bach PB. Radiation therapy facilities in the United States. Int J Radiat Oncol Biol Phys. 2006;66:1204-11. doi: 10.1016/j.ijrobp.2006.06.035.
- 217. Chung K, Burke SC. Characteristics of hospice patients utilizing hospice inpatient/residential facilities. Am J Hosp Palliat Care. 2013;30(7):640-7. doi: 10.1177/1049909112469717. Epub 2012.
- 218. Meilleur A, Subramanian SV, Plascak JJ, Fisher JL, Paskett ED, Lamont EB. Rural residence and cancer outcomes in the United States: issues and challenges. Cancer Epidemiol Biomarkers Prev. 2013;22(10):1657-67. doi: 10.1158/1055-9965.EPI-13-0404.
- 219. Pew Research Center. Internet/broadband fact sheet [Internet]. Washington: The Center; 2021 [cited 2022 June 9]. Available from: <u>https://www.pewresearch.org/internet/fact-sheet/internet-broadband</u>.
- 220. Anderson M. About a quarter of rural Americans say access to high-speed internet is a major problem [Internet]. Washington: Pew Research Center; 2018 [cited 2022 June 9]. Available from: <u>https://www.pewresearch.org/fact-tank/2018/09/10/about-a-quarter-of-rural-americans-say-access-to-high-speed-internet-is-a-major-problem/</u>.
- 221. Meit M, Knudson A, Gilbert T, Tzy-Chyi A, Tanenbaum E, Ormson E, et al. The 2014 update of the ruralurban chartbook [Internet]. Grand Forks, ND: Rural Health Reform Policy Research Center; 2014 [cited 2022 June 9]. Available from: <u>https://ruralhealth.und.edu/projects/health-reform-policy-research-center/pdf/2014rural-urban-chartbook-update.pdf</u>.
- 222. Lee JG, Griffin GK, Melvin CL. Tobacco use among sexual minorities in the USA, 1987 to May 2007: a systematic review. Tob Control. 2009;18(4):275-82. doi: 10.1136/tc.2008.028241.
- 223. Fallin A, Goodin A, Lee YO, Bennett K. Smoking characteristics among lesbian, gay, and bisexual adults. Prev Med. 2015;74:123-30. doi: 10.1016/j.ypmed.2014.11.026.
- 224. Boehmer U, Miao X, Ozonoff A. Health behaviors of cancer survivors of different sexual orientations. Cancer Causes Control. 2012;23(9):1489-96. doi: 10.1007/s10552-012-0023-x. Epub 2012 Jul 3.
- 225. Kamen C, Blosnich JR, Lytle M, Janelsins MC, Peppone LJ, Mustian KM. Cigarette smoking disparities among sexual minority cancer survivors. Prev Med Rep. 2015;2:283-6. doi: 10.1016/j.pmedr.2015.04.004.
- 226. Baskerville NB, Dash D, Shuh A, Wong K, Abramowicz A, Yessis J, et al. Tobacco use cessation interventions for lesbian, gay, bisexual, transgender and queer youth and young adults: a scoping review. Prev Med Rep. 2017;6:53-62. doi: 10.1016/j.pmedr.2017.02.004.
- 227. Berger I, Mooney-Somers J. Smoking cessation programs for lesbian, gay, bisexual, transgender, and intersex people: a content-based systematic review. Nicotine Tob Res. 2017;19(12):1408-17. doi: 10.1093/ntr/ntw216.
- 228. Lee JG, Matthews AK, McCullen CA, Melvin CL. Promotion of tobacco use cessation for lesbian, gay, bisexual, and transgender people: a systematic review. Am J Prev Med. 2014;47:823-31. doi: 10.1016/j.amepre.2014.07.051.
- 229. Eliason MJ, Dibble SL, Gordon R, Soliz GB. The last drag: an evaluation of an LGBT-specific smoking intervention. J Homosex. 2012;59(6):864-78. doi: 10.1080/00918369.2012.694770.
- 230. Matthews AK, Li CC, Kuhns LM, Tasker TB, Cesario JA. Results from a community-based smoking cessation treatment program for LGBT smokers. J Environ Public Health. 2013; 2013:984508. doi: 10.1155/2013/984508.
- 231. Vogel EA, Thrul J, Humfleet GL, Delucchi KL, Ramo DE. Smoking cessation intervention trial outcomes for sexual and gender minority young adults. Health Psychol. 2019;38(1):12-20. doi: 10.1037/hea0000698.
- 232. Vogel EA, Ramo DE, Meacham MC, Prochaska JJ, Delucchi KL, Humfleet GL. The Put It Out Project (POP) Facebook intervention for young sexual and gender minority smokers: outcomes of a pilot, randomized, controlled trial. Nicotine Tob Res. 2020;22(9):1614-21. doi: 10.1093/ntr/ntz184.
- 233. Covey LS, Weissman J, LoDuca C, Duan N. A comparison of abstinence outcomes among gay/bisexual and heterosexual male smokers in an intensive, non-tailored smoking cessation study. Nicotine Tob Res. 2009;11(11):1374-7. doi: 10.1093/ntr/ntp137. Epub 2009 Sep 24.
- 234. Grady ES, Humfleet GL, Delucchi KL, Reus VI, Munoz RF, Hall SM. Smoking cessation outcomes among sexual and gender minority and nonminority smokers in extended smoking treatments. Nicotine Tob Res. 2014;16(9):1207-15. doi: 10.1093/ntr/ntu050. Epub 2014 Apr 11.
- 235. Matthews AK, Steffen AD, Kuhns LM, Ruiz RA, Ross NA, Burke LA, et al. Evaluation of a randomized clinical trial comparing the effectiveness of a culturally targeted and nontargeted smoking cessation intervention for lesbian, gay, bisexual, and transgender smokers. Nicotine Tob Res. 2019;21(11):1506-16. doi: 10.1093/ntr/nty184.

- 236. Heffner JL, Mull KE, Watson NL, McClure JB, Bricker JB. Long-term smoking cessation outcomes for sexual minority vs. non-minority smokers in a large randomized controlled trial of two web-based interventions. Nicotine Tob Res. 2020;22(9):1596-604. doi: 10.1093/ntr/ntz112.
- 237. Kcomt L. Profound health-care discrimination experienced by transgender people: rapid systematic review. Soc Work Health Care. 2019;58(2):201-19. doi: 10.1080/00981389.2018.1532941.
- 238. Langston ME, Fuzzell L, Lewis-Thames MW, Khan S, Moore JX. Disparities in health information-seeking behaviors and fatalistic views of cancer by sexual orientation identity: a nationally representative study of adults in the United States. LGBT Health. 2019;6(4):192-201. doi: 10.1089/lgbt.2018.0112.
- 239. Gonzales G, Henning-Smith C. Health disparities by sexual orientation: results and implications from the Behavioral Risk Factor Surveillance System. J Community Health. 2017;42(6):1163-72. doi: 10.1007/s10900-017-0366-z.
- 240. Burns EK, Deaton EA, Levinson AH. Rates and reasons: disparities in low intentions to use a state smoking cessation quitline. Am J Health Promot. 2011;25 Suppl 5:S59-65. doi: 10.4278/ajhp.100611-QUAN-183.
- 241. Patterson JG, Jabson Tree JM, Kamen C. Cultural competency and microaggressions in the provision of care to LGBT patients in rural and Appalachian Tennessee. Patient Educ Couns. 2019;102(11):2081-90. doi: 10.1016/j.pec.2019.06.003.
- 242. Shetty G, Sanchez JA, Lancaster JM, Wilson LE, Quinn GP, Schabath MB. Oncology healthcare providers' knowledge, attitudes, and practice behaviors regarding LGBT health. Patient Educ Couns. 2016;99(10):1676-84. doi: 10.1016/j.pec.2016.05.004.
- 243. Sutter ME, Simmons VN, Sutton SK, Vadaparampil ST, Sanchez JA, Bowman-Curci M, et al. Oncologists' experiences caring for LGBTQ patients with cancer: qualitative analysis of items on a national survey. Patient Educ Coun. 2021;104(4):871-6.
- 244. Schabath MB, Blackburn CA, Sutter ME, Kanetsky PA, Vadaparampil ST, Simmons VN, et al. National survey of oncologists at National Cancer Institute–designated comprehensive cancer centers: attitudes, knowledge, and practice behaviors about LGBTQ patients with cancer. J Clin Oncol. 2019;37(7):547.
- 245. Margolies L, Brown CG. Increasing cultural competence with LGBTQ patients. Nursing. 2019;49(6):34-40. doi: 10.1097/01.NURSE.0000558088.77604.24.
- 246. Wheldon CW, Schabath MB, Hudson J, Bowman Curci M, Kanetsky PA, Vadaparampil ST, et al. Culturally competent care for sexual and gender minority patients at National Cancer Institute–Designated Comprehensive Cancer Centers. LGBT Health. 2018;5(3):203-11. doi: 10.1089/lgbt.2017.0217.
- 247. Knudsen HK. Implementation of smoking cessation treatment in substance use disorder treatment settings: a review. Am J Drug Alcohol Abuse. 2017;43(2):215-25. doi: 10.1080/00952990.2016.1183019.
- 248. Moussas GI, Papadopoulou AG. Substance abuse and cancer. Psychiatriki. 2017;28(3):234-41. doi: 10.22365/jpsych.2017.283.234.
- 249. Grant BF, Hasin DS, Chou SP, Stinson FS, Dawson DA. Nicotine dependence and psychiatric disorders in the United States: results from the national epidemiologic survey on alcohol and related conditions. Arch Gen Psychiatry. 2004;61(11):1107-15. doi: 10.1001/archpsyc.61.11.1107.
- 250. Hayford KE, Patten CA, Rummans TA, Schroeder DR, Offord KP, Croghan IT, et al. Efficacy of bupropion for smoking cessation in smokers with a former history of major depression or alcoholism. Br J Psychiatry. 1999;174(2):173-8. doi: 10.1192/bjp.174.2.173.
- 251. Hays JT, Schroeder DR, Offord KP, Croghan IT, Patten CA, Hurt RD, et al. Response to nicotine dependence treatment in smokers with current and past alcohol problems. Ann Behav Med. 1999;21(3):244-50. doi: 10.1007/BF02884841.
- 252. Novy P, Hughes JR, Callas P. A comparison of recovering alcoholic and non-alcoholic smokers. Drug Alcohol Depend. 2001;65(1):17-23. doi: 10.1016/s0376-8716(01)00141-7.
- 253. Richter KP, Ahluwalia HK, Mosier MC, Nazir N, Ahluwalia JS. A population-based study of cigarette smoking among illicit drug users in the United States. Addiction. 2002;97(7):861-9. doi: 10.1046/j.1360-0443.2002.00162.x.
- 254. Richter KP, Gibson CA, Ahluwalia JS, Schmelzle KH. Tobacco use and quit attempts among methadone maintenance clients. Am J Pub Health. 2001;91(2):296-9. doi: 10.2105/ajph.91.2.296.
- 255. Yusufov M, Braun IM, Pirl WF. A systematic review of substance use and substance use disorders in patients with cancer. Gen Hosp Psychiatry. 2019;60:128-36. doi: 10.1016/j.genhosppsych.2019.04.016.
- 256. Streck JM, Parker MA, Weinberger AH, Rigotti NA, Park ER. Association of cigarette use and substance use disorders among US adults with and without a recent diagnosis of cancer. Curr Oncol. 2020;28(1):86-93. doi: 10.3390/curroncol28010011.

- 257. Abdel-Rahman O. Patterns of cigarette smoking and alcohol drinking among Canadian adults with cancer in a contemporary national cohort. J Cancer Surviv. 2021. doi: 10.1007/s11764-021-00992-1. Epub ahead of print.
- 258. Substance Abuse and Mental Health Data Archive. Washington: U.S. Department of Health and Human Services. c2022 [cited 2022 June 9]. Available from: <u>https://pdas.samhsa.gov/</u>
- 259. Dev R, Haider A. Alcohol, tobacco, and substance use and association with opioid use disorder in patients with non-malignant and cancer pain: a review. Curr Anesthesiol Rep. 2020;10:388-95. doi: 10.1007/s40140-020-00415-4.
- 260. Dev R, Kim YJ, Reddy A, Hui D, Tanco K, Liu D, et al. Association between tobacco use, pain expression, and coping strategies among patients with advanced cancer. Cancer. 2019;125(1):153-60. doi: 10.1002/cncr.31783.
- 261. Dev R, Parsons HA, Palla S, Palmer JL, Del Fabbro E, Bruera E. Undocumented alcoholism and its correlation with tobacco and illegal drug use in advanced cancer patients. Cancer. 2011;117(19):4551-6. doi: 10.1002/cncr.26082.
- 262. Kim YJ, Dev R, Reddy A, Hui D, Tanco K, Park M, et al. Association between tobacco use, symptom expression, and alcohol and illicit drug use in advanced cancer patients. J Pain Symptom Manage. 2016;51(4):762-8. doi: 10.1016/j.jpainsymman.2015.11.012.
- 263. Zayed S, Lin C, Boldt RG, Sathya J, Venkatesan V, Read N, et al. Risk of chronic opioid use after radiation for head and neck cancer: a systematic review and meta-analysis. Adv Radiat Oncol. 2021;6(2):100583. doi: 10.1016/j.adro.2020.09.023.
- 264. Novy DM, Lam C, Gritz ER, Hernandez M, Driver LC, Koyyalagunta D. Distinguishing features of cancer patients who smoke: pain, symptom burden, and risk for opioid misuse. J Pain. 2012;13(11):1058-67. doi: 10.1016/j.jpain.2012.07.012.
- 265. Kim DH, Park JY, Karm MH, Bae HY, Lee JY, Soo Ahn H, et al. Smoking may increase postoperative opioid consumption in patients who underwent distal gastrectomy with gastroduodenostomy for early stomach cancer. Clin J Pain. 2017;33(10):905-11. doi: 10.1097/AJP.00000000000472.
- 266. Ditre JW, Gonzalez BD, Simmons VN, Faul LA, Brandon TH, Jacobsen PB. Associations between pain and current smoking status among cancer patients. Pain. 2011;152(1):60-5. doi: 10.1016/j.pain.2010.09.001.
- 267. National Institute on Drug Abuse (NIDA) [Internet]. Washington: U.S. Department of Health and Human Services, National Institutes of Health, National Institute on Drug Abuse; revised 2020 Apr [cited 2022 Feb 18]. Common comorbidities with substance use disorders research report; [about 4 screens]. Available from: <u>https://www.drugabuse.gov/publications/research-reports/common-comorbidities-substance-use-disorders/part-</u>2-co-occurring-substance-use-disorder-physical-comorbidities.
- 268. Rajabi A, Dehghani M, Shojaei A, Farjam M, Motevalian SA. Association between tobacco smoking and opioid use: a meta-analysis. Addict Behav. 2019;92:225-35. doi: 10.1016/j.addbeh.2018.11.043.
- 269. Sanford NN, Sher DJ, Xu X, Ahn C, D'Amico AV, Aizer AA, et al. Alcohol use among patients with cancer and survivors in the United States, 2000-2017. J Natl Compr Canc Netw. 2020;18(1):69-79. doi: 10.6004/jnccn.2019.7341.
- 270. Kai K, Koga H, Aishima S, Kawaguchi A, Yamaji K, Ide T, et al. Impact of smoking habit on surgical outcomes in non-B non-C patients with curative resection for hepatocellular carcinoma. World J Gastroenterol. 2017;23(8):1397-405. doi: 10.3748/wjg.v23.i8.1397.
- 271. Weinberger AH, Funk AP, Goodwin RD. A review of epidemiologic research on smoking behavior among persons with alcohol and illicit substance use disorders. Prev. Med. 2016:92:148-59. doi: 10.1016/j.ypmed.2016.05.011. Epub 2016 May 16.
- 272. Blalock JA, Lam C, Minnix JA, Karam-Hage M, Gritz ER, Robinson JD, et al. The effect of mood, anxiety, and alcohol use disorders on smoking cessation in cancer patients. J Cogn Psychother. 2011;25(1):82-96. doi: 10.1891/0889-8391.25.1.82.
- 273. Vander Ark W, DiNardo LJ, Oliver DS. Factors affecting smoking cessation in patients with head and neck cancer. Laryngoscope. 1997;107(7):888-92. doi: 10.1097/00005537-199707000-00010.
- 274. Chan Y, Irish JC, Wood SJ, Sommer DD, Brown DH, Gullane PJ, et al. Smoking cessation in patients diagnosed with head and neck cancer. J Otolaryngol. 2004;33(2):75-81. doi: 10.2310/7070.2004.00075.
- 275. Smith J, Woolley T, Brown A, Vangaveti V, Chilkuri M. Smoking cessation in head and neck cancer patients: factors influencing successes and failures. J Med Imaging Radiat Oncol. 2021;65(2):233-41. doi: 10.1111/1754-9485.13158.
- 276. Kim H, Kim MH, Park YS, Shin JY, Song YM. Factors that predict persistent smoking of cancer survivors. J Korean Med Sci. 2015;30(7):853-9. doi: 10.3346/jkms.2015.30.7.853. Epub 2015 Jun 10.

- 277. Augustson EM, Wanke KL, Rogers S, Bergen AW, Chatterjee N, Synder K, et al. Predictors of sustained smoking cessation: a prospective analysis of chronic smokers from the alpha-tocopherol beta-carotene cancer prevention study. Am J Public Health. 2008;98:549-55. doi: 10.2105/AJPH.2005.084137. Epub 2007 Jun 28.
- 278. Dollar KM, Homish GG, Kozlowski LT, Leonard KE. Spousal and alcohol-related predictors of smoking cessation: a longitudinal study in a community sample of married couples. Am J Public Health. 2009;99:231-3. doi: 10.2105/AJPH.2008.140459. Epub 2008 Dec 4.
- 279. Kahler CW, Spillane NS, Metrik J. Alcohol use and initial smoking lapses among heavy drinkers in smoking cessation treatment. Nicotine Tob Res. 2010;12(7):781-5. doi: 10.1093/ntr/ntq083.
- 280. Lynch KL, Twesten JE, Stern A, Augustson EM. Level of alcohol consumption and successful smoking cessation. Nicotine Tob Res. 2019;21(8):1058-64. doi: 10.1093/ntr/nty142.
- 281. Osler M, Prescott E, Godtfredsen N, Hein HO, Schnohr P. Gender and determinants of smoking cessation: a longitudinal study. Prev Med. 1999;29:57-62. doi: 10.1006/pmed.1999.0510.
- 282. Leeman RF, Huffman CJ, O'Malley SS. Alcohol history and smoking cessation in nicotine replacement therapy, bupropion sustained release and varenicline trials: a review. Alcohol. 2007;42(3):196-206. doi: 10.1093/alcalc/agm022.
- 283. Prochaska JJ, Delucchi K, Hall SM. A meta-analysis of smoking cessation interventions with individuals in substance abuse treatment or recovery. J Consult Clin Psychol. 2004;72(6):1144-56. doi: 10.1037/0022-006X.72.6.1144.
- 284. Apollonio D, Philipps R, Bero L. Interventions for tobacco use cessation in people in treatment for or recovery from substance use disorders. Cochrane Database Syst Rev. 2016;(11):CD010274. doi: 10.1002/14651858.CD010274.pub2.
- 285. Burling TA, Burling AS, Latini D. A controlled smoking cessation trial for substance-dependent inpatients. J Consult Clin Psychol. 2001;69:295-304. doi: 10.1037//0022-006x.69.2.295.
- 286. McKelvey K, Thrul J, Ramo D. Impact of quitting smoking and smoking cessation treatment on substance use outcomes: an updated and narrative review. Addict Behav. 2017;65:161-70. doi: 10.1016/j.addbeh.2016.10.012.
- 287. Thurgood SL, McNeill A, Clark-Carter D, Brose LS. A systematic review of smoking cessation interventions for adults in substance abuse treatment or recovery. Nicotine Tob Res. 2016;18(5):993-1001. doi: 10.1093/ntr/ntv127.
- 288. Streck JM, Hyland KA, Regan S, Muzikansky A, Rigotti NA, Ponzani CJ, et al. Examining the effects of problematic alcohol use on cigarette abstinence in recently diagnosed cancer patients enrolled in a cessation trial: a secondary analysis. Addict Behav. 2021;115:106794. doi: 10.1016/j.addbeh.2020.106794.
- 289. Prochaska JJ, Das S, Young-Wolff KC. Smoking, mental illness, and public health. Annu Rev Public Health. 2017;38:165-85. doi: 10.1146/annurev-publhealth-031816-044618. Epub 2016 Dec 16.
- 290. Schroeder SA, Morris CD. Confronting a neglected epidemic: tobacco cessation for persons with mental illnesses and substance abuse problems. Annu Rev Public Health. 2010;31:297-314. doi: 10.1146/annurev.publhealth.012809.103701.
- 291. Schulte MT, Hser YI. Substance use and associated health conditions throughout the lifespan. Public Health Rev. 2013;35(2). doi: 10.1007/BF03391702.
- 292. Clarke JG, Stein MD, McGarry KA, Gogineni A. Interest in smoking cessation among injection drug users. Am J Addict. 10, 2001;10(2):159-66. doi: 10.1080/105504901750227804.
- 293. Ellingstad TP, Sobell LC, Sobell MB, Cleland PA, Agrawal S. Alcohol abusers who want to quit smoking: implications for clinical treatment. Drug Alcohol Depend. 1999;54(3):259-65. doi: 10.1016/s0376-8716(98)00180-x.
- 294. Knudsen HK, Studts JL. The implementation of tobacco-related brief interventions in substance abuse treatment: a national study of counselors. J Subst Abuse Treat. 2010;38(3):212-9. doi: 10.1016/j.jsat.2009.12.002.
- 295. Marynak K, VanFrank B, Tetlow S, Mahoney M, Phillips E, Jamal Mbbs A, et al. Tobacco cessation interventions and smoke-free policies in mental health and substance abuse treatment facilities—United States, 2016. MMWR Morb Mortal Wkly Rep. 2018;67(18):519-23. doi: 10.15585/mmwr.mm6718a3.
- 296. Cather C, Pachas GN, Cieslak KM, Evins AE. Achieving smoking cessation in individuals with schizophrenia: special considerations. CNS Drugs. 2017;31(6):471-81. doi: 10.1007/s40263-017-0438-8.
- 297. Lawrence D, Hancock K, Kisely S. Cancer and mental illness. In: Sartorius N, Holt R, Maj M, editors. Comorbidity of mental and physical disorders. Key issues in mental health [Internet]. Switzerland: Karger; 2015. [cited 2022 June 9] Available from: <u>https://www.karger.com/Article/FullText/365541</u>.

- 298. Ng HS, Roder D, Koczwara B, Vitry A. Comorbidity, physical and mental health among cancer patients and survivors: an Australian population-based study. Asia-Pac. J. Clin. Oncol. 2018;14:e181-92. doi: 10.1111/ajco.12677.
- 299. Gfroerer J, Dube SR, King BA, Garrett BE, Babb S, McAfee T. Vital signs: current cigarette smoking among adults aged≥ 18 years with mental illness—United States, 2009–2011. MMWR Morb Mortal Wkly Rep. 2013;62(5):81-7.
- 300. Heffner JL, Strawn JR, DelBello MP, Strakowski SM, Anthenelli RM. The co-occurrence of cigarette smoking and bipolar disorder: phenomenology and treatment considerations. Bipolar Disord. 2011;13(5-6):439-53. doi: 10.1111/j.1399-5618.2011.00943.x.
- 301. McClave AK, McKnight-Eily LR, Davis SP, Dube SR. Smoking characteristics of adults with selected lifetime mental illnesses: results from the 2007 National Health Interview Survey. Am J Public Health. 2010;100(12):2464-72. doi: 10.2105/AJPH.2009.188136.
- 302. Ziedonis D, Hitsman B, Beckham JC, Zvolensky M, Adler LE, Audrain-McGovern J, et al. Tobacco use and cessation in psychiatric disorders: National Institute of Mental Health report. Nicotine Tob Res. 2008;10(12):1691-715. doi: 10.1080/14622200802443569.
- 303. Kelly C, McCreadie R. Cigarette smoking and schizophrenia. Adv Psychiatr Treat. 2000:6(5):327-31. doi: 10.1192/apt.6.5.327.
- 304. Hitsman B, Spring B, Wolf W, Pingitore R, Crayton JW, Hedeker D. Effects of acute tryptophan depletion on negative symptoms and smoking topography in nicotine-dependent schizophrenics and nonpsychiatric controls. Neuropsychopharmacology. 2005;30(3):640-8. doi: 10.1038/sj.npp.1300651.
- 305. Olincy A, Young DA, Freedman R. Increased levels of the nicotine metabolite cotinine in schizophrenic smokers compared to other smokers. Biol Psychiatry. 1997;42(1):1-5. doi: 10.1016/S0006-3223(96)00302-2.
- 306. Strand JE, Nyback H. Tobacco use in schizophrenia: a study of cotinine concentrations in the saliva of patients and controls. Eur Psychiatry. 2005;20(1):50-4. doi: 10.1016/j.eurpsy.2004.09.005.
- 307. Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: a population-based prevalence study. JAMA. 2000;284(20):2606-10. doi: 10.1001/jama.284.20.2606.
- 308. Agrawal A, Sartor C, Pergadia ML, Huizink AC, Lynskey MT. Correlates of smoking cessation in a nationally representative sample of U.S. adults. Addict Behav. 2008;33(9):1223-6. doi: 10.1016/j.addbeh.2008.04.003. Epub 2008 Apr 8.
- 309. Griesler PC, Hu MC, Schaffran C, Kandel DB. Comorbid psychiatric disorders and nicotine dependence in adolescence. Addiction. 2011;106(5):1010-20. doi: 10.1111/j.1360-0443.2011.03403.x.
- 310. Hickman NJ 3rd, Delucchi KL, Prochaska JJ. A population-based examination of cigarette smoking and mental illness in Black Americans. Nicotine Tob Res. 2010;12(11):1125-32. doi: 10.1093/ntr/ntq160.
- 311. Snell M, Harless D, Shin S, Cunningham P, Barnes A. A longitudinal assessment of nicotine dependence, mental health, and attempts to quit smoking: evidence from waves 1-4 of the Population Assessment of Tobacco and Health (PATH) study. Addict Behav. 2021;115:106787. doi: 10.1016/j.addbeh.2020.106787.
- 312. Alghzawi H, Trinkoff A, Zhu S, Storr C. Remission from nicotine dependence among people with severe mental illness who received help/services for tobacco/nicotine use. Int J Methods Psychiatr Res. 2020;29(4):1-11. doi: 10.1002/mpr.1845. Epub 2020 Sep 18.
- 313. Rajalu BM, Jayarajan D, Muliyala KP, Sharma P, Gandhi S, Chand PK, et al. Non-pharmacological interventions for smoking in persons with schizophrenia spectrum disorders a systematic review. Asian J Psychiatr. 2021;56:102530. doi: 10.1016/j.ajp.2020.102530. Epub 2021 Jan 14.
- 314. Siskind DJ, Wu BT, Wong TT, Firth J, Kisely S. Pharmacological interventions for smoking cessation among people with schizophrenia spectrum disorders: a systematic review, meta-analysis, and network meta-analysis. Lancet Psychiatry. 2020;7(9):762-74. doi: 10.1016/S2215-0366(20)30261-3.
- 315. Kalkhoran S, Thorndike AN, Rigotti NA, Fung V, Baggett TP. Cigarette smoking and quitting-related factors among US adult health center patients with serious mental illness. J Gen Intern Med. 2019;34:986-91. doi: 10.1007/s11606-019-04857-3.
- 316. Secades-Villa R, González-Roz A, García-Pérez Á, Becoña E. Psychological, pharmacological, and combined smoking cessation interventions for smokers with current depression: A systematic review and meta-analysis. PLoS One. 2017;12(12):e0188849. doi: 10.1371/journal.pone.0188849.
- 317. Tidey JW, Miller ME. Smoking cessation and reduction in people with chronic mental illness. BMJ. 2015;351:h4065. doi: 10.1136/bmj.h4065.
- 318. Brunette MF, Pratt SI, Bartels SJ, Scherer EA, Sigmon SC, Ferron JC, et al. Randomized trial of interventions for smoking cessation among Medicaid beneficiaries with mental illness. Psychiatr Serv. 2018;69(3):274-80. doi: 10.1176/appi.ps.201700245. Epub 2017 Nov 15.

- 319. Hall SM, Tsoh JY, Prochaska JJ, Eisendrath S, Rossi JS, Redding CA, et al. Treatment for cigarette smoking among depressed mental health outpatients: a randomized clinical trial. Am J Public Health. 2006;96(10):1808-14. doi: 10.2105/AJPH.2005.080382.
- 320. Munoz RF, Marin BV, Posner SF, Perez-Stable EJ. Mood management mail intervention increases abstinence rates for Spanish-speaking Latino smokers. Am J Community Psychol. 1997;25(3):325-43. doi: 10.1023/a:1024676626955.
- 321. Thorsteinsson HS, Gillin JC, Patten CA, Golshan S, Sutton LD, Drummond S, et al. The effects of transdermal nicotine therapy for smoking cessation on depressive symptoms in patients with major depression. Neuropsychopharmacology. 2001;24(4):350-8. doi: 10.1016/S0893-133X(00)00217-7.
- 322. Addington J, el-Guebaly N, Campbell W, Hodgins DC, Addington D. Smoking cessation treatment for patients with schizophrenia. Am J Psychiatry. 1998;155(7):974-6. doi: 10.1176/ajp.155.7.974.
- 323. Anthenelli RM, Benowitz NL, West R, St Aubin L, McRae T, Lawrence D, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. Lancet. 2016; 387(10037):2507-20. doi: 10.1016/S0140-6736(16)30272-0. Epub 2016 Apr 22.
- 324. Weiner E, Buchholz A, Coffay A, Liu F, McMahon RP, Buchanan RW, et al. Varenicline for smoking cessation in people with schizophrenia: a double blind randomized pilot study. Schizophr Res. 2011;129(1):94-5. doi: 10.1016/j.schres.2011.02.003.
- 325. Williams JM, Anthenelli RM, Morris CD, Treadow J, Thompson JR, Yunis C, et al. A randomized, doubleblind, placebo-controlled study evaluating the safety and efficacy of varenicline for smoking cessation in patients with schizophrenia or schizoaffective disorder. J Clin Psychiatry. 2012;73(5):654-60. doi: 10.4088/JCP.11m07522.
- 326. Ziedonis D, George TP. Schizophrenia and nicotine use: Report of a pilot smoking cessation program and review of neurobiological and clinical issues. Schizophr Bull. 1997;23(2):247-54. doi: 10.1093/schbul/23.2.247.
- 327. Cahill K, Lindson-Hawley N, Thomas KH, Fanshawe TR, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database Syst Rev. 2016;2016(5):CD006103. doi: 10.1002/14651858.CD006103.pub7.
- 328. Patnode CD, Henderson JT, Melnikow J, Coppola EL, Durbin S, Thomas R. Interventions for tobacco cessation in adults, including pregnant women: an evidence update for the U.S. Preventive Services Task Force. Rockville, MD: Agency for Healthcare Research and Quality (US); 2021 Jan.
- 329. Evins AE, Cather C, Pratt SA, Pachas GN, Hoeppner SS, Goff DC, et al. Maintenance treatment with varenicline for smoking cessation in patients with schizophrenia and bipolar disorder: a randomized clinical trial. JAMA. 2014; 311(2):145-54. doi: 10.1001/jama.2013.285113.
- 330. Evins AE, Benowitz NL, West R, Russ C, McRae T, Lawrence D, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with psychotic, anxiety, and mood disorders in the EAGLES trial. J Clin Psychopharmacol. 2019;39(2):108-16. doi: 10.1097/JCP.00000000001015.
- 331. Tsoi DT, Porwal M, Webster AC. Interventions for smoking cessation and reduction in individuals with schizophrenia. Cochrane Database Syst Rev. 2013;(2):CD007253. doi: 10.1002/14651858.CD007253.pub3.
- 332. Food and Drug Administration (FDA) [Internet]. Washington: FDA; 2018 [cited 2022 June 9]. FDA drug safety communication: FDA revises description of mental health side effects of the stop-smoking medicines Chantix (varenicline) and Zyban (bupropion) to reflect clinical trial findings; [about 4 screens]. Available from: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-revises-description-mental-health-side-effects-stop-smoking.
- 333. Buchanan RW, Kreyenbuhl J, Kelly DL, Noel JM, Boggs DL, Fischer BA, et al. The 2009 schizophrenia PORT psychopharmacological treatment recommendations and summary statements. Schizophr Bull. 2010;36(1):71-93. doi: 10.1093/schbul/sbp116. Epub 2009 Dec 2.
- 334. Evins AE, Cather C, Culhane MA, Birnbaum A, Horowitz J, Hsieh E, et al. A 12-week double-blind, placebocontrolled study of bupropion SR added to high-dose dual nicotine replacement therapy for smoking cessation or reduction in schizophrenia. J Clin Psychopharmacol. 2007; 27(4):380-6. doi: 10.1097/01.jcp.0b013e3180ca86fa.
- 335. Evins AE, Cather C, Deckersbach T, Freudenreich O, Culhane MA, Olm-Shipman CM, et al. A double-blind placebo-controlled trial of bupropion sustained-release for smoking cessation in schizophrenia. J Clin Psychopharmacol. 2005;25(3):218-25. doi: 10.1097/01.jcp.0000162802.54076.18.

- 336. George TP, Vessicchio JC, Termine A, Bregartner TA, Feingold A, Rounsaville BJ, et al. A placebo controlled trial of bupropion for smoking cessation in schizophrenia. Biol Psychiatry. 2002;52(1):53-61. doi: 10.1016/s0006-3223(02)01339-2.
- 337. Roberts E, Evins AE, McNeill A, Robson D. Efficacy and tolerability of pharmacotherapy for smoking cessation in adults with serious mental illness: a systematic review and network meta-analysis. Addiction. 2016;111(4):599-612. doi: 10.1111/add.13236. Epub 2016 Jan 19.
- 338. Gilbody S, Peckham E, Bailey D, Arundel C, Heron P, Crosland S, et al. Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial. Lancet Psychiatry. 2019;6(5):379-90. doi: 10.1016/S2215-0366(19)30047-1.
- 339. Carr RM, Christiansen B, Jehn L, Matitz D. Meeting the challenge of tobacco use within the Medicaid population. WMJ. 2001;100(3):59-66.
- 340. Kerr S, Woods C, Knussen C, Watson H, Hunter R. Breaking the habit: a qualitative exploration of barriers and facilitators to smoking cessation in people with enduring mental health problems. BMC Public Health. 2013;13:221. doi: 10.1186/1471-2458-13-221.
- 341. Lawn SJ, Pols RG, Barber JG. Smoking and quitting: a qualitative study with community-living psychiatric clients. Soc Sci Med. 2002;54(1):9-104. doi: 10.1016/s0277-9536(01)00008-9.
- 342. Lum A, Skelton E, Wynne O, Bonevski B. A systematic review of psychosocial barriers and facilitators to smoking cessation in people living with schizophrenia. Front Psychiatry. 2018;9:565. doi: 10.3389/fpsyt.2018.00565.
- 343. Trainor K, Leavey G. Barriers and facilitators to smoking cessation among people with severe mental illness: a critical appraisal of qualitative studies. Nicotine Tob Res. 2017;19(1):14-23. doi: 10.1093/ntr/ntw183.
- 344. Shankar A, McMunn A, Banks J, Steptoe A. Loneliness, social isolation, and behavioral and biological health indicators in older adults. Health Psychology. 2011;30(4):377-85. doi: 10.1037/a0022826.
- 345. Philip KEJ, Bu F, Polkey MI, Brown J, Steptoe A, Hopkinson NS, et al. Relationship of smoking with current and future social isolation and loneliness: 12-year follow-up of older adults in England. Lancet Reg Health Eur. 2022;14:100302. doi: 10.1016/j.lanepe.2021.100302.
- 346. Acton GS, Prochaska JJ, Kaplan AS, Small T, Hall SM. Depression and stages of change for smoking in psychiatric outpatients. Addict Behav. 2001;26(5):621-31. doi: 10.1016/s0306-4603(01)00178-2.
- 347. Forchuk C, Norman R, Malla A, Martin ML, McLean T, Cheng S, et al. Schizophrenia and the motivation for smoking. Perspect Psychiatr Care. 2002;38(2):41-9. doi: 10.1111/j.1744-6163.2002.tb00656.x.
- 348. Steinberg ML, Ziedonis DM, Krejci JA, Brandon TH. Motivational interviewing with personalized feedback: a brief intervention for motivating smokers with schizophrenia to seek treatment for tobacco dependence. J Consult Clin Psychol. 2004;72(4),723-8. doi: 10.1037/0022-006X.72.4.723.
- 349. Ziedonis D, Williams JM, Smelson D. Serious mental illness and tobacco addiction: a model program to address this common but neglected issue. Am J Med Sci. 2003;326(4):223-30.
- 350. Steinberg ML, Williams JM, Stahl NF, Budsock PD, Cooperman NA. An adaptation of motivational interviewing increases quit attempts in smokers with serious mental illness. Nicotine Tob Res. 2016;18(3):243-50. doi: 10.1093/ntr/ntv043.
- 351. Weinstein LC, Stefancic A, Cunningham AT, Hurley KE, Cabassa LJ, Wender RC. Cancer screening, prevention, and treatment in people with mental illness. CA Cancer J Clin. 2016;66(2):134-51. doi: 10.3322/caac.21334.
- 352. Mitchell AJ, Vancampfort D, De Hert M, Stubbs B. Do people with mental illness receive adequate smoking cessation advice? A systematic review and meta-analysis. Gen Hosp Psychiatry. 2015;37(1):14-23. doi: 10.1016/j.genhosppsych.2014.11.006.
- 353. Stead LF, Buitrago D, Preciado N, Sanchez G, Hartmann-Boyce J, Lancaster T. Physician advice for smoking cessation. Cochrane Database Syst Rev. 2013;(5):CD000165. doi: 10.1002/14651858.CD000165.pub4.
- 354. Association of American Medical Colleges (AAMC). Physician behavior and practice patterns related to smoking cessation. Washington: The Association; 2007.
- 355. Taylor GM, Itani T, Thomas KH, Rai D, Jones T, Windmeijer F, et al. Prescribing prevalence, effectiveness, and mental health safety of smoking cessation medicines in patients with mental disorders. Nicotine Tob Res. 2020;22(1):48-57. doi: 10.1093/ntr/ntz072.
- 356. Thorndike AN, Stafford RS, Rigotti NA. US physicians' treatment of smoking in outpatients with psychiatric diagnoses. Nicotine Tob Res. 2001;3(1):85-91. doi: 10.1080/14622200020032132.
- 357. Srivastava B, Ramsey AT, McIntosh LD, Bailey TC, Fisher SL, Fox L, et al. Tobacco use prevalence and smoking cessation pharmacotherapy prescription patterns among hospitalized patients by medical specialty. Nicotine Tob Res. 2018;21(5):631-7. doi: 10.1093/ntr/nty031.

- 358. Kisely S, Crowe E, Lawrence D. Cancer-related mortality in people with mental illness. JAMA Psychiatry. 2013;70(2):209-17. doi: 10.1001/jamapsychiatry.2013.278.
- 359. U.S. Preventive Services Task Force (USPSTF), Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, et al. Interventions for tobacco smoking cessation in adults, including pregnant persons: US Preventive Services Task Force recommendation statement. JAMA. 2021;325(3):265-79. doi: 10.1001/jama.2020.25019.
- 360. Kock L, Brown J, Hiscock R, Tattan-Birch H, Smith C, Shahab L. Individual-level behavioural smoking cessation interventions tailored for disadvantaged socioeconomic position: a systematic review and meta-regression. Lancet Public Health. 2019;4(12):e628-44. doi: 10.1016/S2468-2667(19)30220-8.
- 361. Baker TB, Piper ME, Stein JH, Smith SS, Bolt DM, Fraser DL, et al. Effects of nicotine patch vs varenicline vs combination nicotine replacement therapy on smoking cessation at 26 weeks: a randomized clinical trial. JAMA. 2016;315(4):371-9. doi: 10.1001/jama.2015.19284.
- 362. Agaku IT, King BA, Dube SR. Current cigarette smoking among adults—United States, 2005-2012. MMWR Morb Mortal Wkly Rep. 2014;63(2):31-4.
- 363. Centers for Disease Control and Prevention (CDC). Cigarette smoking among adults—United States, 1994. MMWR Morb Mortal Wkly Rep. 1996;45(27):588-90.
- 364. Centers for Disease Control and Prevention (CDC). Cigarette smoking among adults—United States, 1998. MMWR Morb Mortal Wkly Rep. 2000;49(39):881-4.
- 365. Centers for Disease Control and Prevention (CDC). Cigarette smoking among adults—United States, 2002. MMWR Morb Mortal Wkly Rep. 2004;53(20):427-31.
- 366. Centers for Disease Control and Prevention (CDC). Cigarette smoking among adults—United States, 2006. MMWR Morb Mortal Wkly Rep. 2007;56(44):1157-61.
- 367. Centers for Disease Control and Prevention (CDC). Current cigarette smoking among adults—United States, 2011. MMWR Morb Mortal Wkly Rep. 2012;61(44):889-94.
- 368. Cornelius ME, Wang TW, Jamal A, Loretan CG, Neff LJ. Tobacco product use among adults—United States, 2019. MMWR Morb Mortal Wkly Rep. 2020;69(46):1736-42. doi: 10.15585/mmwr.mm6946a4.
- 369. Creamer MR, Wang TW, Babb S, Cullen KA, Day H, Willis G, et al. Tobacco product use and cessation indicators among adults—United States, 2018. MMWR Morb Mortal Wkly Rep. 2019;68(5):1013-9. doi: 10.15585/mmwr.mm6845a2.
- 370. Jamal A, Agaku IT, O'Connor E, King BA, Kenemer JB, Neff L. Current cigarette smoking among adults— United States 2005-2013. MMWR Morb Mortal Wkly Rep. 2014;63(47):1108-12.
- 371. Jamal A, Homa DM, O'Connor E, Babb SD, Carraballo RS, Singh T, et al. Current cigarette smoking among adults—United States, 2005-2014. MMWR Morb Mortal Wkly Rep. 2015;64(44):1233-40.
- 372. Jamal A, King BA, Neff LJ, Whitmill J, Babb SD, Graffunder CM. Current cigarette smoking among adults— United States, 2005-2015. MMWR Morb Mortal Wkly Rep. 2016;65(44):1205-11.
- 373. Jamal A, Phillips E, Gentzke AS, Homa DM, Babb SD, King BA, et al. Current cigarette smoking among adults—United States, 2016. MMWR Morb Mortal Wkly Rep. 2018;67(2):53-59. doi: 10.15585/mmwr.mm6702a1.
- 374. Wang TW, Asman K, Gentzke AS, Cullen KA, Holder-Hayes E, Reyes-Guzman C, et al. Tobacco product use among adults—United States, 2017. MMWR Morb Mortal Wkly Rep. 2018;67(44):1225-32. doi: 10.15585/mmwr.mm6744a2.
- 375. National Institute on Drug Abuse (NIDA) [Internet]. Washington: U.S. Department of Health and Human Services, National Institutes of Health, National Institute on Drug Abuse; 2019 [cited 2022 June 9]. Marijuana drug facts; [about 11 screens]. Available from: https://www.drugabuse.gov/publications/drugfacts/marijuana#ref.
- 376. Substance Abuse and Mental Health Services Administration (SAMHSA). Key substance use and mental health indicators in the United States: results from the 2020 National Survey on Drug Use and Health [Internet]. Rockville, MD: Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality; 2021 [cited 2022 June 9]. Available from: https://www.samhsa.gov/data/sites/default/files/reports/rpt35325/NSDUHFFRPDFWHTMLFiles2020/2020NS DUHFFR1PDFW102121.pdf.
- 377. Conway KP, Green VR, Kasza KA, Silveira ML, Borek N, Kimmel HL, et al. Co-occurrence of tobacco product use, substance use, and mental health problems among adults: Findings from Wave 1 (2013-2014) of the Population Assessment of Tobacco and Health (PATH) Study. Drug Alcohol Depend. 2017;177:104-11. doi: 10.1016/j.drugalcdep.2017.03.032. Epub 2017 May 30.

- 378. Strong DR, Myers MG, Pulvers K, Noble M, Brikmanis K, Doran N. Marijuana use among US tobacco users: findings from Wave 1 of the Population Assessment of Tobacco Health (PATH) Study. Drug Alcohol Depend. 2018;186:16-22. doi: 10.1016/j.drugalcdep.2017.12.044.
- 379. Reboussin BA, Wagoner KG, Cornacchione Ross J, Suerken CK, Sutfin EL. Tobacco and marijuana co-use in a cohort of young adults: patterns, correlates and reasons for co-use. Drug Alcohol Depend. 2021;227:109000. doi: 10.1016/j.drugalcdep.2021.109000. Epub 2021 Aug 28.
- 380. Vogel EA, Rubinstein ML, Prochaska JJ, Ramo DE. Associations between marijuana use and tobacco cessation outcomes in young adults. J Subst Abuse Treat. 2018;94:69-73. doi: 10.1016/j.jsat.2018.08.010. Epub 2018 Aug 28.
- 381. Weinberger AH, Delnevo CD, Wyka K, Gbedemah M, Lee J, Copeland J, et al. Cannabis use is associated with increased risk of cigarette smoking initiation, persistence, and relapse among adults in the United States. Nicotine Tob Res. 2020;22(8):1404-8. doi: 10.1093/ntr/ntz085.
- 382. Weinberger AH, Dierker L, Zhu J, Levin J, Goodwin RD. Cigarette dependence is more prevalent and increasing among US adolescents and adults who use cannabis, 2002-2019. Tob Control. 2021;tobaccocontrol-2021-056723. doi: 10.1136/tobaccocontrol-2021-056723. Epub 2021 Nov 23.
- 383. National Conference of State Legislatures (NCSL) [Internet]. Denver: State Legislatures Magazine [cited 2022 June 9]. Deep dive marijuana; [about 3 screens]. Available from: <u>https://www.ncsl.org/bookstore/state-legislatures-magazine/marijuana-deep-dive.aspx</u>.
- 384. Do EK, Ksinan AJ, Kim SJ, Del Fabbro EG, Fuemmeler BF. Cannabis use among cancer survivors in the United States: analysis of a nationally representative sample. Cancer. 2021;127(21):4040-9. doi: 10.1002/cncr.33794.
- 385. National Academies of Sciences, Engineering, and Medicine (NASEM); Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on the Health Effects of Marijuana: An Evidence Review and Research Agenda. The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. Washington: National Academies Press; 2017.
- 386. National Cancer Institute [Internet]. Bethesda, MD: National Cancer Institute; 2022 [cited 2022 June 9]. Cannabis and cannabinoids (PDQ®)–health professional version; [about 38 screens]. Available from: <u>https://www.cancer.gov/about-cancer/treatment/cam/hp/cannabis-pdq</u>.
- 387. Gentzke AS, Wang TW, Jamal A, et al. Tobacco product use among middle and high school students—United States, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(50):1881-8. doi: 10.15585/mmwr.mm6950a1.
- 388. Lipari RN, Van Horn SL. Trends in smokeless tobacco use and initiation: 2002 to 2014: the CBHSQ Report. Rockville, MD: Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality; 2017.
- 389. National Cancer Institute (NCI) and Centers for Disease Control and Prevention (CDC). Smokeless tobacco and public health: a global perspective. Bethesda, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Institutes of Health, National Cancer Institute; 2014. NIH Publication No. 14-7983.
- 390. Cogliano V, Straif K, Baan R, Grosse Y, Secretan B, El Ghissassi F, et al. Smokeless tobacco and tobaccorelated nitrosamines. Lancet Oncol. 2004;5(12):708. doi: 10.1016/s1470-2045(04)01633-x.
- 391. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Smokeless tobacco and some tobacco-specific N-nitrosamines. IARC Monogr Eval Carcinog Risks Hum. 2007;89:1-592.
- 392. Rostron BL, Chang CM, van Bemmel DM, Xia Y, Blount BC. Nicotine and toxicant exposure among U.S. smokeless tobacco users: results from 1999 to 2012 National Health and Nutrition Examination Survey data. Cancer Epidemiol Biomarkers Prev. 2015;24(12):1829-37. doi: 10.1158/1055-9965.EPI-15-0376.
- 393. Chang JT, Levy DT, Meza R. Trends and factors related to smokeless tobacco use in the United States. Nicotine Tob Res. 2016;18(8):1740-8. doi: 10.1093/ntr/ntw090. doi: 10.1093/ntr/ntw090. Epub 2016 Mar 19.
- 394. Renner CC, Lanier AP, Lindgren B, Jensen J, Patten CA, Parascandola M, et al. Tobacco use among southwestern Alaska Native people. Nicotine Tob Res. 2013;15(2):401-6. doi: 10.1093/ntr/nts137. Epub 2012 Sep 4.
- 395. Noonan D, Duffy SA. Factors associated with smokeless tobacco use and dual use among blue collar workers. Public Health Nurs. 2014;31(1):19-27. doi: 10.1111/phn.12095.
- 396. Cheng YC, Rostron BL, Day HR, Stanton CA, Hull LC, Persoskie A, et al. Patterns of use of smokeless tobacco in US adults, 2013–2014. Am J Public Health. 2017;107(9):1508-14. doi: 10.2105/AJPH.2017.303921. Epub 2017 Jul 20.
- 397. Tomar SL, Alpert HR, Connolly GN. Patterns of dual use of cigarettes and smokeless tobacco among US males: findings from national surveys. Tob Control. 2010;19(2):104-9. doi: 10.1136/tc.2009.031070.

- 398. Kypriotakis G, Robinson JD, Green CE, Cinciripini PM. Patterns of tobacco product use and correlates among adults in the Population Assessment of Tobacco and Health (PATH) Study: a latent class analysis. Nicotine Tob Res. 2018;20 Suppl 1:S81-7. doi: 10.1093/ntr/nty025.
- 399. Ebbert JO, Elrashidi MY, Stead LF. Interventions for smokeless tobacco use cessation. Cochrane Database Syst Rev. 2015;2015(10):CD004306. doi: 10.1002/14651858.CD004306.pub5.
- 400. Schwartz J, Fadahunsi O, Hingorani R, Mainali NR, Oluwasanjo A, Aryal MR, et al. Use of varenicline in smokeless tobacco cessation: a systematic review and meta-analysis. Nicotine Tob Res. 2016;18(1):10-6. doi: 10.1093/ntr/ntv010. Epub 2015 Feb 2.
- 401. Sankaranarayanan R, Ramadas K, Thara S, Muwonge R, Thomas G, Anju G, et al. Long term effect of visual screening on oral cancer incidence and mortality in a randomized trial in Kerala, India. Oral Oncol. 2013;49(4):314-21. doi: 10.1016/j.oraloncology.2012.11.004. Epub 2012 Dec 21.
- 402. Siddiqi K, Husain S, Vidyasagaran A, Readshaw A, Mishu MP, Sheikh A. Global burden of disease due to smokeless tobacco consumption in adults: an updated analysis of data from 127 countries. BMC Med. 2020;18:222. doi: 10.1186/s12916-020-01677-9.

This page left blank intentionally.

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

Chapter 6 Monograph Conclusions and Future Research Directions

Chapter Contents

Introduction	287
Major Conclusions	287
Chapter Summaries and Conclusions	289
Chapter 1: Introduction and Overview	289
Chapter 2: Smoking in Patients With Cancer: Biological Factors	289
Conclusions	289
Chapter 3: Treating Tobacco Use and Dependence in Cancer Populations	289
Conclusions	289
Chapter 4: Implementing Smoking Cessation Treatment Programs in Cancer Care	
Settings: Challenges, Strategies, Innovations, and Models of Care	290
Conclusions	291
Chapter 5: Addressing Smoking in Medically Underserved and Vulnerable Cancer	
Populations	292
Conclusions	292
Future Research Directions	292
Clarifying the Effects of Continued Smoking and Smoking Cessation Treatment on	
Cancer Outcomes	294
Assessing the Economic Effects of Continued Smoking and Cessation After a Cancer	
Diagnosis	294
Achieving Better Tobacco Use Assessment in Cancer Care	295
Addressing Barriers to the Implementation of Effective Treatment of Tobacco Use in	
Cancer Care	295
Understanding the Effects of New Tobacco Products and Other Drug Use in Patients	
With Cancer	297
Optimizing Smoking Cessation Treatment for Medically Underserved and Vulnerable	
Populations With Cancer	297
NCI Initiatives to Support Implementation of Smoking Cessation Treatment in Cancer Care	and
Screening Settings	299
Cancer Center Cessation Initiative (C3I)	299
Smoking Cessation at Lung Examination (SCALE) Collaboration	
Conclusion	
References	

Figures and Tables

Table 6.1	Summary of Research I	Needs	293
-----------	-----------------------	-------	-----

Chapter 6 Monograph Conclusions and Future Research Directions

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 MoonshotSM-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 payfor-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.

Торіс	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 6.1Summary of Research Needs

Table 6.1 (continued)

Торіс	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 MoonshotSM, 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 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 recommendations⁴ 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.

References

- Land SR, Toll BA, Moinpour CM, Mitchell SA, Ostroff JS, Hatsukami DK, et al. Research priorities, measures, and recommendations for assessment of tobacco use in clinical cancer research. Clin Cancer Res 2016; 22(8): 1907-13.
- U.S. Department of Health and Human Services (USDHHS). Smoking cessation: a report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2020.
- 3. Croyle RT, Morgan GD, Fiore MC. Addressing a core gap in cancer care—the NCI Moonshot program to help oncology patients stop smoking. N Engl J Med. 2019;380(6):512-15. doi: 10.1056/NEJMp1813913.
- U.S. Preventive Services Task Force, Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, et al. Screening for lung cancer: U.S. Preventive Services Task Force recommendation statement. JAMA. 2021;325(10):962-70. doi: 10.1001/jama.2021.1117.
- National Cancer Institute [Internet]. Bethesda (MD): NCI; 2022 [cited 2022 Feb 15]. Smoking cessation at lung examination: the SCALE Collaboration; [about 5 screens]. Available from: <u>https://cancercontrol.cancer.gov/brp/tcrb/scale-collaboration</u>.
