The American Cancer Society's

PRINCIPLES OF ONCOLOGY

Prevention to Survivorship

Edited by
The American Cancer Society

WILEY Blackwell

The American Cancer Society's Principles of Oncology
Prevention to Survivorship

The American Cancer Society is a global grassroots force of nearly 2 million volunteers dedicated to saving lives, celebrating lives, and leading the fight for a world without cancer. From breakthrough research, to free lodging near treatment, a 24/7/365 live helpline, free rides to treatment, and convening powerful activists to create awareness and impact, the Society is the only organization attacking cancer from every angle. For more information go to www.cancer.org.

The American Cancer Society's

Principles of Oncology

Prevention to Survivorship

Edited by The American Cancer Society

Atlanta, Georgia, USA

WILEY Blackwell

Registered Office(s)
John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, USA
John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

Editorial Office
9600 Garsington Road, Oxford, OX4 2DQ, UK

For details of our global editorial offices, customer services, and more information about Wiley products visit us at www.wiley.com.

Wiley also publishes its books in a variety of electronic formats and by print-on-demand. Some content that appears in standard print versions of this book may not be available in other formats.

Library of Congress Cataloging-in-Publication Data

Names: American Cancer Society, editor.
Title: The American Cancer Society's principles of oncology : prevention to survivorship / edited by the American Cancer Society.
Other titles: Principles of oncology
Description: Hoboken, NJ : Wiley, 2018. | Includes bibliographical references and index. |
Identifiers: LCCN 2017040597 (print) | LCCN 2017041494 (ebook) | ISBN 9781119468875 (pdf) | ISBN 9781119468882 (epub) | ISBN 9781119468844 (cloth)
Subjects: | MESH: Neoplasms–prevention & control | Neoplasms–therapy | Survivors | Early Medical Intervention–standards | United States | Practice Guideline
Classification: LCC RC268 (ebook) | LCC RC268 (print) | NLM QZ 250 | DDC 616.99/4052–dc23
LC record available at https://lccn.loc.gov/2017040597

Cover design by Wiley
Cover image: © Tendo/Shutterstock

Set in 9.5/11.5 pt Warnock by SPi Global, Pondicherry, India

10 9 8 7 6 5 4 3 2 1

Contents

Editorial Board

Reviewers

American Cancer Society Content Staff

List of Contributors

Catherine M. Alfano, PhD
Vice President
Survivorship
Cancer Control
American Cancer Society
Atlanta, Georgia, USA

Joseph E. Bauer, PhD
Strategic Director
Statistics and Evaluation Center
American Cancer Society
Atlanta, Georgia, USA

Shrujal S. Baxi, MD, MPH
Medical Oncologist
Department of Medicine
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Victoria Blinder, MD, MSc
Medical Oncologist
Department of Medicine
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Otis W. Brawley, MD
Chief Medical Officer
American Cancer Society
Atlanta, Georgia, USA

Paul Brittain, MD
Second Year Fellow
University of Colorado Anschutz Medical Campus
Aurora, Colorado, USA

Eduardo Bruera, MD
Department Chair
Department of Palliative Care and Rehabilitation Medicine
University of Texas MD Anderson Cancer Center
Houston, Texas, USA

Jeanne Carter, PhD
Head, Female Sexual Medicine and Women's Health Program
Gynecology Service
Department of Surgery
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Bradley C. Carthon, MD, PhD
Assistant Professor, Hematology and Medical Oncology
Medical Director, Inpatient Medical Oncology
Winship Cancer Institute
Emory University School of Medicine
Atlanta, Georgia, USA

Alejandro Chaoul, PhD
Assistant Professor
Palliative, Rehabilitation and Integrative Medicine
University of Texas MD Anderson Cancer Center
Houston, Texas, USA

Lorenzo Cohen, PhD
Professor
Palliative, Rehabilitation, and Integrative Medicine
University of Texas MD Anderson Cancer Center
Houston, Texas, USA

Dexter L. Cooper, MPH
Research Assistant II
Morehouse School of Medicine
Atlanta, Georgia, USA

Kerry S. Courneya, PhD
Professor
Faculty of Physical Education and Recreation
University of Alberta
Edmonton, Alberta, Canada

Diwakar Davar, MD
Assistant Professor of Medicine
Division of Hematology-Oncology
University of Pittsburgh Medical Center
Pittsburgh, Pennsylvania, USA

S. Lindsey Davis, MD
Assistant Professor of Medical Oncology
University of Colorado Anschutz Medical Campus
Aurora, Colorado, USA

Wendy Demark-Wahnefried, PhD, RD
Professor of Nutrition Sciences
Associate Director for Cancer Prevention and Control
University of Alabama at Birmingham
Birmingham, Alabama, USA

Rony Dev, DO
Associate Professor
Department of Palliative Care and Rehabilitation Medicine
University of Texas MD Anderson Cancer Center
Houston, Texas, USA

Curtiland Deville, Jr., MD
Assistant Professor of Radiation Oncology and Molecular Radiation Sciences
Department of Radiation Oncology and Molecular Radiation Sciences
Johns Hopkins University School of Medicine
Baltimore, Maryland, USA

Maura N. Dickler, MD
Medical Oncologist
Gynecology Service, Department of Surgery
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Colleen Doyle, MS, RD
Managing Director
Nutrition and Physical Activity
Cancer Control
American Cancer Society
Atlanta, Georgia, USA

Deborah L. Driscoll, BA
Program Manager
Statistics and Evaluation Center
American Cancer Society
Atlanta, Georgia, USA

S. Gail Eckhardt, MD
Professor and Co-Division Head of Medical Oncology
University of Colorado Anschutz Medical Campus
Aurora, Colorado, USA

Stacey Fedewa, PhD, MPH
Strategic Director
Risk Factors and Screening Surveillance
Intramural Research
American Cancer Society
Atlanta, Georgia, USA

Darren R. Feldman, MD
Medical Oncologist
Department of Medicine
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Ted Gansler, MD, MPH, MBA
Strategic Director
Pathology Research
American Cancer Society
Atlanta, Georgia, USA

Heidi Ganzer, MS, RD, CSO, LD
Nutrition Therapy Director
Minnesota Oncology
St. Paul, Minnesota, USA

Susan M. Gapstur, PhD, MPH
Vice President
Epidemiology Research Program
American Cancer Society
Atlanta, Georgia, USA

M. Kay Garcia, DrPH, MSN, RN, LAc
Associate Professor
Oncology/Integrative Medicine Program
University of Texas MD Anderson Cancer Center
Houston, Texas, USA

Emily Glogowski, MS, MSc, LCGC
Genomics Consultant
GeneDx
Gaithersburg, Massachusetts, USA

Thomas J. Glynn, PhD
Consulting Professor
School of Medicine
Stanford University
Palo Alto, California, USA

Shari B. Goldfarb, MD
Medical Oncologist
Department of Surgery
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Frederick L. Greene, MD, FACS
Clinical Professor of Surgery
UNC School of Medicine
Chapel Hill, North Carolina, USA

Olwen M. Hahn, MD
Associate Professor of Hematology-Oncology
The University of Chicago
Chicago, Illinois, USA

R. Donald Harvey, PharmD, BCOP, FCCP, FHOPA
Associate Professor
Hematology, Medical Oncology, and Pharmacology
Winship Cancer Institute
Emory University School of Medicine
Atlanta, Georgia, USA

William J. Hogan, MB, BCh
Internist
Division of Hematology
Mayo Clinic
Rochester, Minnesota, USA

Andreas M. Hötker, MD
Clinical Research Fellow
Department of Radiology
Memorial Sloan-Kettering Cancer Center
New York, New York, USA

Hedvig Hricak, MD, PhD
Professor of Radiology
Department of Radiology
Memorial Sloan-Kettering Cancer Center
New York, New York, USA

Arti Hurria, MD
Professor
Department of Medical Oncology and Therapeutics Research
City of Hope Comprehensive Cancer Center
Duarte, California, USA

Richard D. Hurt, MD
Emeritus Medical Director
Nicotine Dependence Center
Primary Care Internal Medicine
Rochester, Minnesota, USA

Eric J. Jacobs, PhD, MS
Strategic Director
Pharmacoepidemiology
Epidemiology Research Program
American Cancer Society
Atlanta, Georgia, USA

Adrienne Jaeger, BA, RN
Advanced Nursing Program
Yale School of Nursing
Yale University
New Haven, Connecticut, USA

Ahmedin Jemal, DVM, PhD
Vice President
Surveillance and Health Services Research
American Cancer Society
Atlanta, Georgia, USA

Christopher G. Kanakry, MD
Assistant Clinical Investigator
National Cancer Institute
Experimental Transplantation and Immunology Branch
Bethesda, Maryland, USA

Elizabeth Kessler, MD
Assistant Professor of Medical Oncology
University of Colorado Anschutz Medical Campus
Aurora, Colorado, USA

Fadlo R. Khuri, MD
Professor, Hematology and Medical Oncology
Adjunct Professor of Medicine, Pharmacology and Otolaryngology
Winship Cancer Institute
Emory University School of Medicine
Atlanta, Georgia, USA

John M. Kirkwood, MD
Usher Professor of Medicine Dermatology and Translational Science Division of Hematology-Oncology
University of Pittsburgh Medical Center
Pittsburgh, Pennsylvania, USA

Lauren A. Kosinski, MD
Managing Partner
The Seed House
Chestertown, Maryland, USA

Elizabeth Kvale, MD
Associate Professor of Medicine
Department of Medicine
University of Alabama at Birmingham
Birmingham, Alabama, USA

Richard Lee, MD
Associate Professor of Medicine
Case Western Reserve University
Cleveland, Ohio, USA

Stephen Leong, MD
Associate Professor of Medical Oncology
University of Colorado Anschutz Medical Campus
Aurora, Colorado, USA

Mark A. Lewis, MD
Hematology/Oncology
Intermountain Healthcare,
Salt Lake City, Utah, USA

Benjamin D. Li, MD, FACS
Cancer Center Director
MetroHealth System
Cleveland, Ohio, USA

Christopher H. Lieu, MD
Assistant Professor, Division of Medical Oncology
Director, Colorectal Medical Oncology
University of Colorado Anschutz Medical Campus
Aurora, Colarado, USA

Jennifer A. Ligibel, MD
Director
Leonard P. Zakim Center for Integrative Therapies Senior Physician
Associate Professor of Medicine
Dana-Farber Cancer Institute,
Boston, Massachusetts, USA

Gabriel Lopez, MD
Medical Director, Integrative Medicine Program
Assistant Professor, Palliative, Rehabilitation and Integrative Medicine
University of Texas MD Anderson Cancer Center
Houston, Texas, USA

Leo Luznik, MD
Associate Professor of Oncology
Johns Hopkins Hospital
Sidney Kimmel Comprehensive Cancer Center
Bethesda, Maryland, USA

Matthew Matasar, MD, MS
Hematologic Oncologist
Department of Medicine
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Marji L. McCullough, ScD, RD
Strategic Director
Nutritional Epidemiology
Intramural Research
American Cancer Society
Atlanta, Georgia, USA

Jeffrey A. Meyerhardt, MD, MPH
Clinical Director
Gastrointestinal Cancer Center
Associate Professor of Medicine
Dana-Farber Cancer Institute
Boston, Massachusetts, USA

Maura Miccò, MD
Clinical Research Fellow
Department of Radiology
Memorial Sloan-Kettering Cancer Center
New York, New York, USA

Kimberly D. Miller, MPH
Epidemiologist
Surveillance and Health Services Research
American Cancer Society
Atlanta, Georgia, USA

Timothy J. Moynihan, MD
Oncologist
Department of Medical Oncology
Mayo Clinic
Rochester, Minnesota, USA

John P. Mulhall, MD
Director
Male Sexual and Reproductive Medicine Program
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Christian J. Nelson, PhD
Psychologist
Gynecology Service, Department of Surgery
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Danielle Novetsky Friedman, MD
Pediatrician
Department of Pediatrics
Memorial Sloan Kettering Cancer Center;
Weill Cornell Medical College
New York, New York, USA

Kevin C. Oeffinger
Professor
Division of Medical Oncology
Department of Medicine
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Kenneth Offit, MD, MPH
Chief
Clinical Genetics Service
Department of Medicine
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Sumanta K. Pal, MD
Assistant Clinical Professor
Department of Medical Oncology and Therapeutics Research
City of Hope Comprehensive Cancer Center
Duarte, California, USA

David M. Panicek, MD, FACR
Vice Chair for Clinical Affairs
Department of Radiology
Memorial Sloan-Kettering Cancer Center
New York, New York, USA

Alpa V. Patel, PhD
Strategic Director
CPS-3
Intramural Research
American Cancer Society
Atlanta, Georgia, USA

John D. Pfeifer, MD, PhD
Professor of Pathology and Immunology
Department of Pathology and Immunology
Washington University Medical Center
St. Louis, Missouri, USA

William C. Phelps, PhD
Vice President
Extramural Research
American Cancer Society
Atlanta, Georgia, USA

Ramesh Rengan, MD, PhD
Medical Director
SCCA Proton Therapy Center
Department of Radiation Oncology
University of Washington
Seattle, Washington, USA

Laura Q. Rogers, MD, MPH, FACP, FACSM
Professor of Nutrition Sciences
University of Alabama at Birmingham
Birmingham, Alabama, USA

Andrew J. Roth, MD
Psychiatrist
Department of Psychiatry and Behavioral Sciences
Memorial Sloan-Kettering Cancer Center;
Weill Cornell Medical Center
New York, New York, USA

Talya Salz, PhD
Assistant Attending Outcomes Research Scientist
Department of Epidemiology and Biostatistics
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Charles Saxe, PhD
Director
Extramural Grants
American Cancer Society
Atlanta, Georgia, USA

Richard L. Schilsky, MD, FACP, FASCO
Senior Vice President and Chief Medical Officer
American Society of Clinical Oncology
Alexandria, Virginia, USA

Arvind M. Shinde, MD, MBA, MPH
Attending Physician
Hematology and Oncology
Samuel Oschin Comprehensive Cancer Institute
Cedars-Sinai
Los Angeles, California, USA

Kasmintan A. Schrader, MBBS, FRCPC, PhD
Assistant Professor
Department of Medical Genetics
University of British Columbia
Vancouver, British Columbia, Canada

Armin Shahrokni
Internist and Hematologic Oncologist
Department of Medicine
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Gaurav Shukla, MD, PhD
Resident Physician
Department of Radiation Oncology
Thomas Jefferson University
Philadelphia, Pennsylvania, USA

M. Andrew Sicard, MD
Surgeon
Department of Surgery
Surgical Associates of Opelousas
Opelousas, Louisiana, USA

Rebecca L. Siegel, MPH
Strategic Director
Surveillance Information Services
Intramural Research
American Cancer Society
Atlanta, Georgia, USA

Edgar P. Simard, PhD, MPH
Adjunct Assistant Professor
Epidemiology Department
Rollins School of Public Health
Emory University
Atlanta, Georgia, USA

Gopal K. Singh, PhD, MS, MSc
Senior Health Equity Advisor
Office of Health Equity
US Department of Health and Human Services
Health Resources and Services Administration
Office of Health Equity
Rockville, Maryland, USA

Robert A. Smith, PhD
Vice President
Cancer Screening
Cancer Control
American Cancer Society
Atlanta, Georgia, USA

Tenbroeck Smith, MA
Strategic Director
Behavioral Research Center
American Cancer Society
Atlanta, Georgia, USA

Yukio Sonoda, MD
Surgeon
Ovarian Cancer Surgery
Gynecology Service
Department of Surgery
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Kevin D. Stein, PhD
Adjunct Associate Professor
Department of Behavioral Sciences and Health Education,
Emory University Rollins School of Public Health
Atlanta, Georgia, USA

Nicole L. Stout, DPT, CLT-LANA
Cancer Rehabilitation Project Lead
Office of Strategic Research
Department of Rehabilitation Medicine
National Institutes of Health Clinical Center
Bethesda, Maryland, USA

Kelly L. Stratton, MD
Assistant Professor
Department of Urology
Stephenson Cancer Center
Oklahoma City, Oklahoma, USA

Ahmad A. Tarhini, MD, PhD
Associate Professor of Medicine
Division of Hematology-Oncology
University of Pittsburgh Medical Center
Pittsburgh, Pennsylvania, USA

Charles R. Thomas, Jr., MD
Professor and Chair
Department of Radiation Medicine
Oregon Health and Science University
Portland, Oregon, USA

Cynthia A. Thomson, PhD, RD
Professor, Mel and Enid Zuckerman College of Public Health
Director, Canyon Ranch Center for Prevention and Health Promotion
University of Arizona Cancer Center
Tucson, Arizona, USA

Emily Tonorezos, MD, MPH
Internist
Department of Medicine
Memorial Sloan Kettering Cancer Center
New York, New York, USA

Lindsey A. Torre, MSPH
Senior Epidemiologist
Surveillance and Health Services Research
American Cancer Society
Atlanta, Georgia, USA

Andrew C. Walls, MD
Instructor in Dermatology
Brigham and Women's Hospital
Harvard Medical School
Boston, Massachusetts, USA

Elizabeth Ward, PhD
Senior Vice President
Intramural Research
American Cancer Society
Atlanta, Georgia, USA

Martin A. Weinstock, MD, PhD
Professor of Dermatology
Brown University School of Public Health
Providence, Rhode Island, USA

Richard C. Wender, MD
Chief Cancer Control Officer
American Cancer Society
Atlanta, Georgia, USA

J. Lee Westmaas, PhD
Strategic Director
Tobacco Control Research
American Cancer Society
Atlanta, Georgia, USA

Andreas G. Wibmer, MD
Clinical Research Fellow
Department of Medical Physics
Memorial Sloan-Kettering Cancer Center
New York, New York, USA

Mark R. Wick, MD
Professor of Pathology
Associate Director of Surgical Pathology
Department of Pathology
University of Virginia Health System
Charlottesville, Virginia, USA

Joshua F. Zeidner, MD
Assistant Professor of Medicine
Division of Hematology/Oncology
University of North Carolina
Lineberger Comprehensive Cancer Center
Chapel Hill, North Carolina, USA

Amelia B. Zelnak, MD, MSc
Medical Oncologist
Atlanta Cancer Care
Northside Hospital Cancer Institute
Atlanta, Georgia, USA

Introduction

The American Cancer Society (ACS) published its first textbook in 1963 with the objective of introducing students and practicing clinicians to the rapidly emerging field of oncology. Since then, eleven editions of this book have been published under a variety of titles. These books have steadily grown in size, reflecting the accumulation of cancer-related knowledge. Due to the growing body of cancer information available, we have divided the content into two books to cover the information we considered most essential.

In this first book, *The American Cancer Society's Principles of Oncology: Prevention to Survivorship,* we review the epidemiological and biological principles relevant to cancer prevention and cancer screening; introduce the principles and methods of cancer diagnosis and modalities of cancer treatment; and review follow-up and survivorship concepts and recommendations, symptom management, and other quality-of-life-related topics.

The last edition of the ACS textbook was published in 2001, and our hiatus was based in part on uncertainty regarding the value of textbooks in the era of ubiquitous access to online information. Our return to this project was motivated by a constant stream of requests from physicians, nurses, public health professionals, cancer registrars, and others, as well as a decisive survey of academic oncologists involved in teaching medical students and residents. Recognizing the distinction between chunks of reference material available online and textbooks that present a coherent and coordinated body of knowledge, this textbook and its companion (*The American Cancer Society's Oncology in Practice: Clinical Management*) are written for those who are new to this field or to a particular aspect of multidisciplinary cancer control, and for experienced practitioners who have not recently updated their general knowledge of cancer or some aspect thereof.

These books are comprised of the contributions of the distinguished chapter authors who took time from their busy clinical and/or research schedules to organize and summarize their knowledge on a particular aspect of cancer control. We sincerely thank them for their time and expertise.

In addition to the authors, I would like to thank our editorial board of prominent experts who selected chapter authors and reviewed/edited chapter manuscripts; the additional reviewers (listed in the frontmatter) who added their expertise to the editorial process; our dedicated colleagues at Wiley Blackwell who patiently navigated us through production; and the American Cancer Society staff who helped organize and coordinate this project. And of course, this book and everything else done by the American Cancer Society depends on the support of our volunteers and donors, and is inspired by our constituents.

Ted Gansler, MD, MBA, MPH

Section 1

Cancer Causes, Prevention, and Early Detection

1

Descriptive Epidemiology

Rebecca L. Siegel, Kimberly D. Miller, and Ahmedin Jemal

Surveillance and Health Services Research, American Cancer Society, Atlanta, Georgia, USA

Introduction

Cancer was the eighth leading cause of death in the United States (US) in 1900 [1], but has been the second leading cause of death, after heart disease, during the last half of the twentieth century, accounting for approximately one in every four deaths [2]. Despite its prevalence throughout history, the recording of cancer incidence at the population level has only been available in the US since the mid-1970s.

Cancer Surveillance in the US

Cancer surveillance is the systematic collection and analysis of data about cancer diagnoses, including information about the patient (e.g., date of birth, sex, race), the tumor (e.g., site of origin, stage, histology), and the initial course of treatment. Cancer registration is useful to the public health in many important ways. These data are used to measure cancer occurrence in the population, including incidence, mortality, survival, and patterns of care; to plan and evaluate cancer control programs; to prioritize the allocation of healthcare resources; and to advance population-based epidemiologic and health services research. Population-based cancer statistics can also be used to corroborate medical hypotheses. For example, the rapid rise and fall of endometrial cancer incidence rates that mirrored the rise and fall in the use of unopposed estrogen as menopausal hormone therapy affirmed the association between estrogen and endometrial cancer risk [3,4]. Likewise, the dramatic 7% decline in breast cancer incidence from 2002 to 2003 reflects the abrupt decrease in menopausal hormone use after the Women's Health Initiative study reported its association with increased breast cancer risk [5,6].

The coverage and quality of cancer surveillance data have improved greatly over time. The current system of cancer registration in the US involves hospital registries, which furnish data for the evaluation of care within the hospital, and population-based registries, which are usually associated with state health departments or related institutions. Hospital registries also serve as the primary data source for central state registries. The cancer registrar carries the major responsibility for data collection and other day-to-day registry operations [7]. As patients are increasingly being diagnosed and treated in outpatient settings, case finding by cancer registrars at central registries has expanded to other medical facilities, including physician offices, pathology laboratories, and freestanding treatment centers.

Registry operations and the quality of the data collected by the registrar are guided by standards established by the Commission on Cancer (CoC) of the American College of Surgeons, the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI), the National Program of Cancer Registries (NPCR) of the Centers for Disease Control and Prevention (CDC), the American Joint Committee on Cancer (AJCC), and the North American Association of Central Cancer Registries (NAACCR).

Surveillance, Epidemiology, and End Results Program

The NCI's SEER Program was established as a result of the National Cancer Act of 1971, which mandated the collection, analysis, and dissemination of data to aid in the prevention, treatment, and diagnosis of cancer in the US [8]. Case ascertainment began on January 1, 1973. The original catchment area, known as SEER 9, covered 9% of the US population and included registries in five states (Connecticut, Iowa, New Mexico, Utah, and Hawaii) and four metropolitan areas (Detroit, Michigan; San Francisco–Oakland, California; Atlanta, Georgia; and Seattle–Puget Sound, Washington). The SEER 9 data are the only source for long-term, population-based cancer incidence and survival trends in the US. The SEER program expanded over

The American Cancer Society's Principles of Oncology: Prevention to Survivorship, First Edition. Edited by The American Cancer Society.

time to include 18 registries covering 28% of the population, including 26% of African Americans, 38% of Hispanics, 44% of American Indians and Alaska Natives, 50% of Asians, and 67% of Hawaiian/Pacific Islanders [9]. Since its inception, quality control has been an integral component of the SEER program, which is considered the gold standard for cancer registration around the world. Cancer incidence and survival data from SEER and cancer mortality data from the National Center for Health Statistics are published annually in the *SEER Cancer Statistics Review*.

National Program of Cancer Registries

In 1992, Congress enacted the Cancer Registries Amendment Act to establish the NPCR at the CDC [10]. At the time this legislation was passed, 10 states had no cancer registry and most states with registries lacked the resources necessary to achieve minimum reporting standards. Today, NPCR supports central cancer registries in 45 states, the District of Columbia, Puerto Rico, and the US Pacific Island Jurisdictions [11]. Together, the SEER Program and NPCR collect and disseminate data that approaches 100% coverage of the US population.

North American Association of Central Cancer Registries

The NAACCR was established in 1987 as an umbrella organization to provide support to cancer registries and tumor registrars in the US and Canada. The organization works collaboratively with government agencies, professional associations, and private and nonprofit organizations toward the compatibility of cancer registry data. The NAACCR sets reporting standards, certifies central registries based on data quality criteria, and aggregates and distributes surveillance data for epidemiologic research. Registry-specific and combined national cancer incidence rates for the US have been published annually in *Cancer Incidence in North America* (*CINA*) for the past 26 years.

National Cancer Data Base

In contrast to population-based SEER and NPCR registries, the National Cancer Data Base (NCDB) is a hospital-based registry jointly sponsored by the American Cancer Society and the American College of Surgeons. The NCDB includes approximately 70% of all cancer diagnoses in the US from more than 1,400 hospitals accredited by the American College of Surgeons' CoC [12]. The database was established in 1989 and now contains more than 26 million records. One of the primary purposes of the NCDB is to provide information back to CoC treatment facilities about their quality of care. Additionally, the NCDB is a rich data source for cancer epidemiologists who study outcomes because it contains standardized data on patient demographics and insurance status; cancer type, histology, and staging; and first course of treatment. However, these data are somewhat limited for research purposes because they are not representative of the general population and because cancer cases that tend to be diagnosed and treated in nonhospital settings (e.g., melanoma and prostate cancer) are less likely to be captured.

National Center for Health Statistics

The National Center for Health Statistics (NCHS) is an agency within the CDC that serves as the principal repository for vital and health statistics in the US. State legislation requires that death certificates be completed for all deaths, and federal legislation requires national collection and reporting of deaths. Causes of death and other patient information are reported by certifying physicians on standard death certificates filed in the states and then processed and consolidated by the NCHS. For cancer mortality statistics, the underlying cause of death is classified according to the procedures specified by the World Health Organization's International Classification of Diseases (ICD) codes, which are periodically updated and currently in the 10th revision.

Measuring the Cancer Burden

The key measures for describing the occurrence of cancer are prevalence, incidence, mortality, and survival. Incidence and mortality data are also used by American Cancer Society researchers to estimate the number of new cancer cases and cancer deaths that will occur in the US in the current year [13,14]. These estimates are useful because cancer incidence and death data lag 2–4 years behind the current year due to the time required for collection, compilation, quality control, and dissemination. While these model-based projections are not informative for tracking temporal trends, they provide an estimate of the contemporary cancer burden and are widely cited by researchers, cancer control advocates, and public health planners.

Prevalence

Cancer prevalence refers to the number of individuals living in a population with a previous cancer diagnosis. It is a mixture of new and pre-existing cases, and thus is a function of incidence and survival. Population prevalence may be estimated for diagnoses within a specified time period (limited-duration) or for all diagnoses (complete). The complete prevalence estimate is often referred to as the number of cancer survivors.

Incidence

Cancer incidence is the number of newly diagnosed cases during a specified time period in a defined population. It is usually expressed as an annual rate per 100,000 population such that the numerator is the number of new cancer cases and the denominator is the size of the population at risk. For example, the denominator for cancers that only occur in one sex is the sex-specific population. Sometimes the appropriate denominator is not straightforward. For example, the population at risk for uterine cancer is not the entire female population, but the fraction of women (approximately 80%) who have not had a hysterectomy (surgical removal of the uterus). Routine reporting of uterine cancer incidence rates typically fail to account for hysterectomy and thus substantially underestimate the burden of this disease [15].

Cancer registry data are corrected and updated over time due to delays or errors in case reporting. To account for the effect of

reporting delays on registry data, NCI and NAACCR provide delay-adjusted rates. Delay-adjustment has the largest effect on data in the most recent time period for cancers that are frequently diagnosed in outpatient settings, such as melanoma, leukemia, and prostate cancer [16]. For example, leukemia incidence rates in the most recent reporting year are 14% higher after delay-adjustment [8]. Cancer incidence rates presented in this chapter were adjusted for delays in reporting whenever possible.

Mortality

Cancer mortality refers to the number of individuals who die from cancer during a specified time period in a defined population. Like incidence, it is typically expressed as an annual rate per 100,000 population such that the numerator is the number of cancer deaths in a given year and the denominator is the population size. The cancer death rate represents the risk of death among the entire population as opposed to the risk specifically among cancer patients. Therefore, it is a function of both incidence and survival.

Cancer death rates are calculated based on information obtained from death certificates, including age at death, sex, place of residence, and underlying cause of death. On the US Standard Certificate of Death, the underlying cause of death is the disease or injury that initiated the chain of events leading to death, as opposed to the final disease condition. For example, the death of a patient who died from sepsis as a result of lung cancer would be coded as lung cancer. The accuracy of death certificate data depends on the cause of death (e.g., rapidly fatal diseases are recorded more accurately) and the physician who records the death (e.g., attending physician versus the coroner).

Age Standardization

The risk of cancer diagnosis or death increases exponentially with age. For this reason, cancer-related vital statistics are conventionally reported as either age-specific or age-standardized rates. Age-standardized rates have been weighted to a common population age distribution to eliminate the effect of age on cancer rates and allow valid comparison between populations with different age structures. For example, without age-standardization, the risk of cancer appears much higher in Florida (572 per 100,000) than in Alaska (370 per 100,000) because Florida has a much older population. However, after age adjustment, the incidence rates in these states are quite similar (438 versus 432 per 100,000, respectively). Current cancer incidence and death rates for the US are generally weighted to the 2000 US standard population [17] unless they are being compared to international rates, when the world standard population is used.

Survival

The cancer survival rate is the percentage of patients who are alive at a specified time following cancer diagnosis, usually 5 years. There are several different methods of calculating survival. Observed survival represents overall survival and includes death from cancer as well as other causes. Relative survival is the ratio of the proportion of survivors in a cohort of cancer patients to the proportion of expected survivors in a comparable group of cancer-free individuals [18]. For example, a relative survival rate of 100% indicates that the likelihood of survival after a cancer diagnosis is the same as survival in the general population. Cancer-specific survival is the probability of surviving cancer in the absence of other causes of death [19]. Relative and cancer-specific survival are measures of net survival because they estimate cancer survival in the absence of death from other causes.

Relative survival is the measure most often presented in cancer surveillance reports because it is useful for tracking trends and comparing survival between populations. It is typically expressed as a 5-year rate, although it may be presented for 10 or even 15 years postdiagnosis for less fatal cancers.

Although survival rates are useful for monitoring progress in the early detection and treatment of cancer, they have several limitations and should be interpreted with caution. First, they do not reflect the most recent advances in treatment because they are based on the experiences of patients who were diagnosed several years ago due to both the lag time in data reporting (typically 2–4 years) and the necessity for sufficient follow-up time. Second, survival statistics are not useful for predicting individual prognosis because factors that strongly influence survival, such as treatment protocols, comorbidities, and biological and behavioral differences in tumor and patient characteristics, cannot be controlled. Third, survival rates for cancers with early detection practices (e.g., prostate, breast) are subject to lead time bias, as discussed in Chapter 11 [20]. This bias, for example, is reflected in the 5-year relative survival rate for prostate cancer in the US, which increased from 68% in the mid-1970s to nearly 100% since around 2000 [8,21].

Lifetime, Relative, and Attributable Risk

Epidemiologists use the word *risk* in several ways. Lifetime risk refers to the probability that an individual will be diagnosed with or die from cancer over the course of a lifetime. For example, in the US, the lifetime risk of developing lung cancer is approximately one in 14 for men and one in 17 for women [8]. Risk can also be assessed for particular age groups; for instance, one in 29 women who are cancer-free at age 59 will develop breast cancer by age 69 [2].

Relative risk in cancer studies measures the strength of the relationship between a specific risk factor and cancer by comparing risk among persons with a specific trait or exposure to risk among persons without the trait or exposure. For example, the relative risk of lung cancer death among smokers is 26 for women and 25 for men [22]; in other words, smoking increases the risk of dying from lung cancer about 25-fold. Most relative risks are not this large, however.

Attributable risk, or attributable fraction, refers to the contribution of a particular exposure or trait to the cancer burden. In other words, it is the difference in the disease burden between exposed and unexposed populations who are similar in other respects. For example, an analysis of smoking-attributable mortality (SAM) found that 83% of lung cancer deaths in men in 2011 were attributable to smoking [23].

Cancer Occurrence Patterns in the US

Prevalence

The NCI estimates that there were 15.5 million Americans with a history of cancer alive on January 1, 2016, a number that will grow to about 20 million by 2026 [24]. The number of survivors is growing rapidly because of advances in the early detection and treatment of cancer, which have lengthened survival times, as well as the growth and aging of the population. Almost half of cancer survivors are 70 years of age or older. The most common diagnoses among male survivors are prostate or colorectal cancer, while among women they are breast or uterine corpus cancers.

Incidence

In the US, the lifetime risk of developing cancer is slightly less than one in two for men and a little more than one in three for women [8]. An estimated 1,688,780 persons received a new cancer diagnosis in 2017 [2]. Historically, the occurrence of cancer has increased over time; however, from about 2000 to 2013, incidence rates decreased in men and were stable in women (Figure 1.1). The four most common cancer types – prostate, female breast, lung and bronchus, and colorectal – account for about half of all new cancer cases and thus strongly influence overall trends (Figure 1.2).

Cancer incidence trends reflect changes in behavior and medical practice. For example, much of the rise in male cancer incidence rates between 1975 and 1992 was due to increased detection of clinically asymptomatic prostate cancer, first via transurethral resection of the prostate (TURP) [25] and later via prostate-specific antigen (PSA) testing [26]. In less than two decades, prostate cancer incidence rates more than doubled, from 94 cases per 100,000 men in 1975 to 237 cases per 100,000 men in 1992 [8]; rates subsequently fell rapidly as the proportion of men undergoing a first PSA test diminished [27] (Figure 1.3).

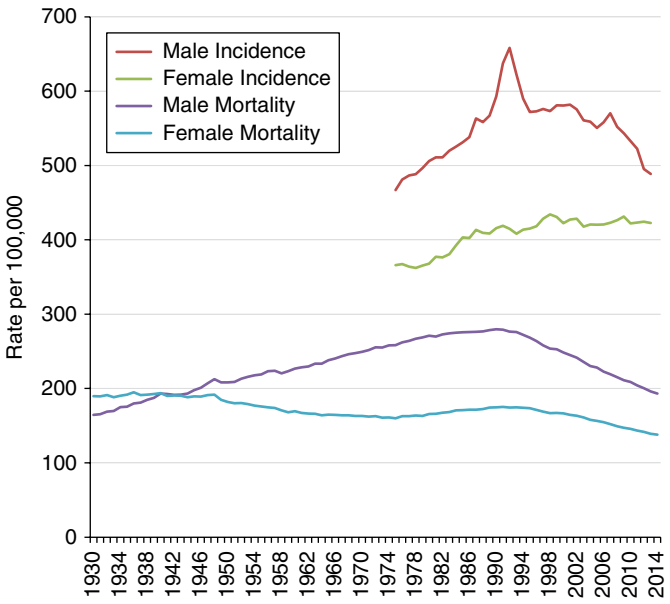

Figure 1.1 Long-term trends in age-adjusted cancer incidence and death rates, 1930–2014. *Source:* Incidence – Surveillance, Epidemiology, and End Results Program (SEER) 9 registries (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta), November 2015 submission, National Cancer Institute. Rates were adjusted for delays in reporting. Mortality – US Mortality Volumes 1930–1959; US Mortality Data 1960–2014, National Center for Health Statistics, Centers for Disease Control and Prevention.

Cancer incidence trends have also been strongly influenced by tobacco use. Most (80%) lung cancers in the US are due to smoking [23]. As a result of the smoking epidemic, lung cancer among men catapulted from a rare disease to the most commonly diagnosed cancer during the first half of the twentieth century [28,29]. Lung cancer rates and trends vary by sex because of historic differences in smoking patterns between men and women; smoking prevalence peaked at 65% around 1950 among men and at 38% around 1960 among women [30]. The lag period between peak population smoking prevalence and peak lung cancer rates is 30–40 years. Circa 1930, lung cancer rates began a long period of increase that peaked in the 1980s in men and around 2005 in women (Figures 1.3 and 1.4) [8]. During the most recent 5 years of data (2009–2013), lung cancer incidence rates declined annually by 2.9% in men and 1.4% in women.

Breast cancer is the most commonly diagnosed cancer among women (Figure 1.2). Breast cancer incidence rates increased rapidly from 1980 to 1987 because of increased diagnosis of asymptomatic tumors due to the widespread dissemination of mammography screening (Figure 1.4) [31]. Breast cancer rates have also been influenced over time by changes in reproductive patterns (e.g., later age at first birth, fewer births) that often accompany economic growth and are associated with an increased risk of breast cancer. Incidence rates gradually increased by 0.4% per year from 2004 to 2013, driven by trends in non-White women [8].

Cancers located in the colon or rectum are the third most commonly diagnosed cancers in both men and women (Figure 1.2). Colorectal cancer is one of only two cancer types (cervical cancer is the other) that can be prevented with screening. Screening prevents colorectal cancer by detecting and allowing for the removal of adenomatous polyps, from which most malignancies in the colorectum develop [32,33]. Colorectal cancer incidence rates have been decreasing since the mid-1980s, with similar patterns for men and women [8]. It has been estimated that half of this decline is due to changes in risk factors and half is due to colorectal cancer screening [34]. However, the recent acceleration in the pace of decline has been attributed primarily to increased colonoscopy uptake [34,35].

Survival and Mortality

Advances in cancer screening strategies and targeted therapies have greatly improved cancer outcomes. Over the past 70 years, the 5-year relative survival rate for cancer has more than doubled, from 24% in men and 33% in women for diagnoses between 1935 and 1940 [28] to 67% in both sexes for diagnoses between 2006 and 2012 [8]. Still, one in four men and one in five women will die from cancer [36], the equivalent of approximately 600,920 people in 2017 [2]. The median age of death from cancer is 72 years [8].

Estimated New Cases*

	Males			Females		
Prostate	161,360	19%		Breast	252,710	30%
Lung & bronchus	116,990	14%		Lung & bronchus	105,510	12%
Colon & rectum	71,420	9%		Colon & rectum	64,010	8%
Urinary bladder	60,490	7%		Uterine corpus	61,380	7%
Melanoma of the skin	52,170	6%		Thyroid	42,470	5%
Kidney & renal pelvis	40,610	5%		Melanoma of the skin	34,940	4%
Non-Hodgkin lymphoma	40,080	5%		Non-Hodgkin lymphoma	32,160	4%
Leukemia	36,290	4%		Leukemia	25,840	3%
Oral cavity & pharynx	35,720	4%		Pancreas	25,700	3%
Liver & intrahepatic bile duct	29,200	3%		Kidney & renal pelvis	23,380	3%
All Sites	**836,150**	**100%**		**All Sites**	**852,630**	**100%**

Estimated Deaths

	Males			Females		
Lung & bronchus	84,590	27%		Lung & bronchus	71,280	25%
Colon & rectum	27,150	9%		Breast	40,610	14%
Prostate	26,730	8%		Colon & rectum	23,110	8%
Pancreas	22,300	7%		Pancreas	20,790	7%
Liver & intrahepatic bile duct	19,610	6%		Ovary	14,080	5%
Leukemia	14,300	4%		Uterine corpus	10,920	4%
Esophagus	12,720	4%		Leukemia	10,200	4%
Urinary bladder	12,240	4%		Liver & intrahepatic bile duct	9,310	3%
Non-Hodgkin lymphoma	11,450	4%		Non-Hodgkin lymphoma	8,690	3%
Brain & other nervous system	9,620	3%		Brain & other nervous system	7,080	3%
All Sites	**318,420**	**100%**		**All Sites**	**282,500**	**100%**

Figure 1.2 Leading new cancer cases and deaths in the US in 2017. Ranking is based on modeled projections and may differ from the most recent observed data. *Estimates are rounded to the nearest 10 and cases exclude basal cell and squamous cell skin cancers and *in situ* carcinoma except urinary bladder. *Source:* Siegel *et al.*[2]. Reproduced with permission of John Wiley & Sons.

Notable improvements in 5-year relative survival rates over the past three decades have occurred among both Whites and Blacks (Table 1.1). Advances in treatment have resulted in particularly dramatic improvement in survival for most types of leukemia. For example, in large part due to the discovery of the targeted drug imatinib, the 5-year relative survival rate for chronic myeloid leukemia increased from 31% for cases diagnosed between 1990 and 1992 to 66% for diagnoses between 2006 and 2012 [8,37]. Survival rates for some cancers, such as lung and pancreas, have been slow to improve.

Currently cancer death rates among men are about 40% higher than those among women, although historically rates were higher among women (Figure 1.1). Cancer death rates among men increased 70% from 1930 to 1990, but have since declined by 31%. Cancer death rates among women have been less variable, declining by 21% since 1991.

Lung cancer is the leading cause of cancer death among both men and women, accounting for more than one-quarter of all cancer deaths in the US (Figure 1.2). Lung cancer death rates among men increased 21-fold from 1930 to 1990 as a result of the smoking epidemic, although they have since decreased by 43% (Figure 1.5). Similarly, lung cancer death rates among women increased 16-fold before beginning to drop in 2003 (Figure 1.6) [8]. Due to few early symptoms, the majority (57%) of lung cancer cases are diagnosed at a distant stage, for which the 5-year relative survival rate is 4%. For the 16% of cases diagnosed at a localized stage, survival increases to 55%.

Breast cancer is the second leading cause of cancer death among women, accounting for 14% of all female cancer deaths (Figure 1.2). Breast cancer death rates fluctuated little from 1930 to 1989, but have since decreased by 38% [8] (Figure 1.6). Approximately half of this decline has been attributed to

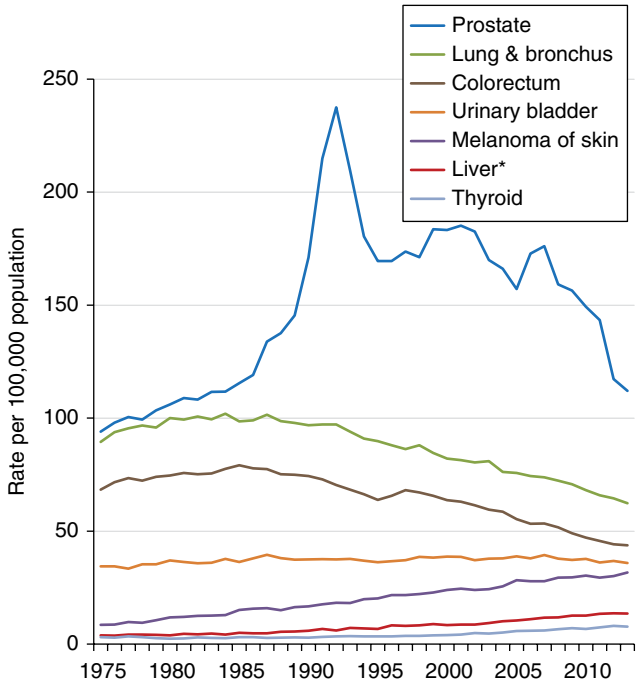

Figure 1.3 Long-term trends in age-adjusted cancer incidence rates among men, 1975–2013. *Source:* Surveillance, Epidemiology, and End Results Program (SEER) 9 registries (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta), November 2015 submission. Rates were adjusted for delays in reporting. *Includes intrahepatic bile duct.

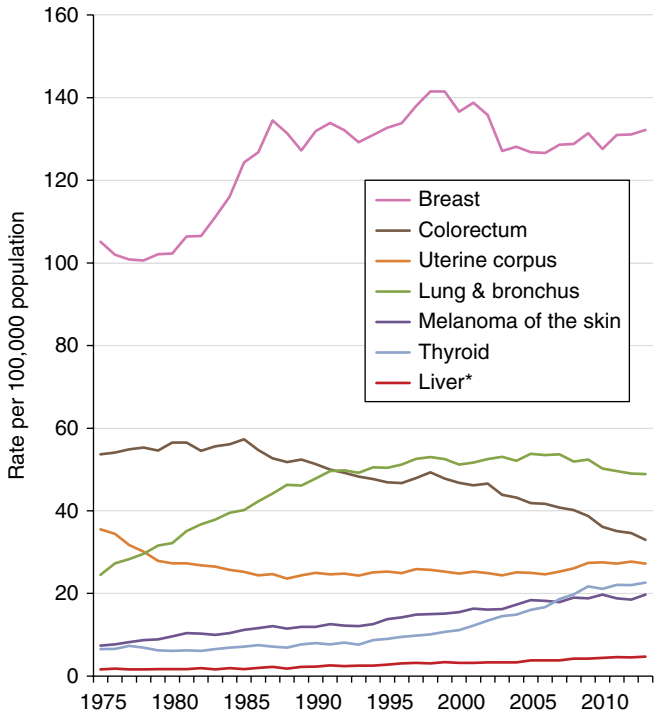

Figure 1.4 Long-term trends in age-adjusted cancer incidence rates among women, 1975–2013. *Source:* Surveillance, Epidemiology, and End Results Program (SEER) 9 registries (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta), November 2015 submission. Rates were adjusted for delays in reporting. *Includes intrahepatic bile duct.

mammography screening and half to improvements in adjuvant treatment [38]. Most breast cancers (61%) are diagnosed at a localized stage, for which the 5-year relative survival rate is 99%; survival drops to 85% or 26% for women whose cancer has reached a regional or distant stage, respectively, by the time of diagnosis [8].

Prostate cancer accounts for about 8% of male cancer deaths (Figure 1.2). Prostate cancer death rates increased during the first half of the twentieth century, were relatively stable for several decades, then rose and fell concurrently with the distinct peak in incidence rates associated with widespread uptake of PSA testing (Figure 1.5). This rapid rise and fall in mortality rates is thought to be a result of attribution bias: deaths due to other causes mistakenly attributed to prostate cancer on death certificates because of a prevalent prostate cancer diagnosis [39]. However, the continued decrease since the mid-1990s is likely to be real and due to advances in both primary and salvage treatments, as well as early detection, although results from randomized clinical trials evaluating the efficacy of PSA testing have been equivocal [40,41]. Prostate cancer death rates decreased by 3.4% per year from 2010 to 2014 [8]. Ninety-two percent of prostate cancer patients are diagnosed at a localized or regional stage, for which the 5-year relative survival rate approaches 100%.

Colorectal cancer accounts for 8–9% of all cancer deaths in men and women (Figure 1.2). Colorectal cancer death rates have been declining since around 1950 among women and since the mid-1980s among men (Figures 1.5 and 1.6). Mortality declines from 1975 to 2000 have been attributed to screening (53%), changes in risk factors (35%), and improvements in treatment (12%) [34]. From 2010 to 2014, death rates declined by 2.5% per year among men and 2.8% per year among women [8]. Although several different screening tests effectively diagnose colorectal cancer early, less than half (39%) of patients are diagnosed with local stage disease, for which 5-year relative survival is 90% [8]. One in five colorectal cancer patients is still diagnosed with distant stage disease, for which the 5-year survival rate is just 14%; for those diagnosed with regional stage disease, 5-year survival is 71%.

Demographic and Geographic Patterns

The occurrence of cancer is strongly influenced by demographic characteristics, including age, sex, race, socioeconomic status, and place of residence. One of the strongest risk factors for cancer is increasing age. This is primarily because 10 or more years usually pass between exposure to external factors and detectable cancer. Between 2009 and 2013, slightly more than half (53%) of new cancer cases and 69% of cancer deaths occurred among individuals who were age 65 years or older [8]. Sex also influences cancer risk; the lifetime probability of developing cancer is slightly higher for men than for women – 41% versus 38% between 2011 and 2013. Reasons for this disparity are not completely understood, but are likely related to differences in risk factor behaviors, hormone exposure, and healthcare utilization [42].

Race and ethnicity substantially modify cancer risk (Table 1.2 and Table 1.3). Of the five major racial and ethnic groups in the US (non-Hispanic White, non-Hispanic Black, Asian/Pacific Islander, American Indian/Alaska Native, and Hispanic), Black

Table 1.1 Trends in 5-year relative survival rates[1] (%) by race, US, 1975–2012.

	All races			White			Black		
	1975–77	1987–89	2006–12	1975–77	1987–89	2006–2012	1975–77	1987–89	2006–12
All sites	49	55	69	50	57	70	39	43	63
Brain and other nervous system	22	29	35	22	28	33	25	32	44
Breast (female)	75	84	91	76	85	92	62	71	82
Colon and rectum	50	60	66	50	60	67	45	52	59
Esophagus	5	9	21	6	11	22	4	7	13
Hodgkin lymphoma	72	79	89	72	80	89	70	72	86
Kidney and renal pelvis	50	57	75	50	57	75	49	55	75
Larynx	66	66	62	67	67	64	58	56	52
Leukemia	34	43	63	35	44	64	33	35	58
Liver and intrahepatic bile duct	3	5	18	3	6	18	2	3	13
Lung and bronchus	12	13	19	12	13	19	11	11	16
Melanoma of the skin	82	88	93	82	88	93	57[2]	79[2]	69
Myeloma	25	27	50	24	27	50	29	30	52
Non-Hodgkin lymphoma	47	51	73	47	51	74	49	46	65
Oral cavity and pharynx	53	54	67	54	56	69	36	34	47
Ovary	36	38	46	35	38	46	42	34	38
Pancreas	3	4	9	3	3	9	2	6	8
Prostate	68	83	99	69	84	>99	61	71	97
Stomach	15	20	31	14	18	30	16	19	30
Testis	83	95	97	83	95	97	73[2,3]	88	90
Thyroid	92	94	98	92	94	99	90	92	97
Urinary bladder	72	79	79	73	80	79	50	63	66
Uterine cervix	69	70	69	70	73	71	65	57	58
Uterine corpus	87	82	83	88	84	86	60	57	66

Source: Howlader *et al.* [8].
[1] Rates are adjusted for normal life expectancy and are based on cases diagnosed in the SEER 9 areas from 1975 to 1977, 1987 to 1989, and 2006 to 2012, all followed through 2013.
[2] The standard error is between 5 and 10 percentage points.
[3] Survival rate is for cases diagnosed from 1978 to 1980.

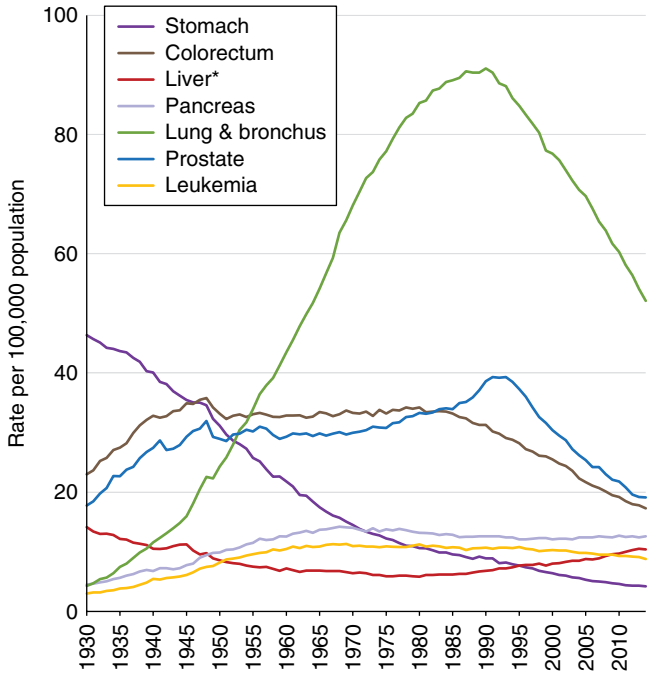

Figure 1.5 Long-term trends in age-adjusted male cancer death rates by site, 1930–2014. *Source:* US Mortality Volumes 1930–1959; US Mortality Data 1960–2014, National Center for Health Statistics, Centers for Disease Control and Prevention. *Includes intrahepatic bile duct.

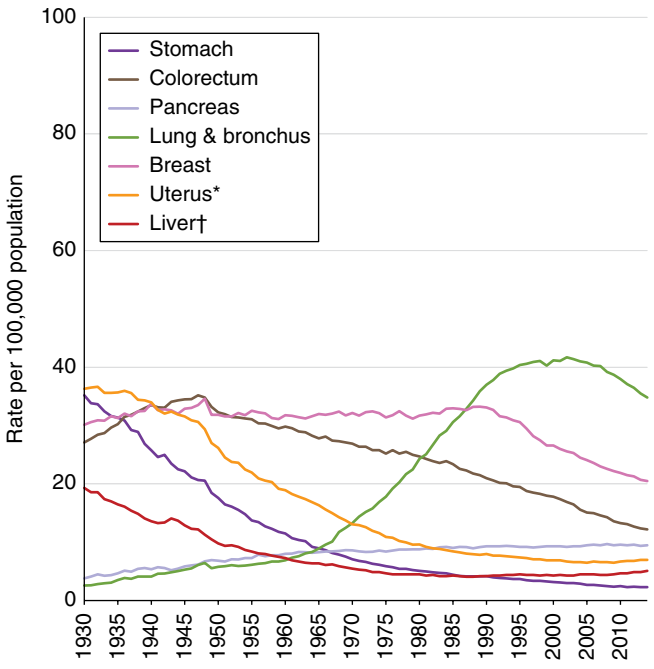

Figure 1.6 Long-term trends in age-adjusted female cancer death rates by site, 1930–2014. *Source:* US Mortality Volumes 1930–1959; US Mortality Data 1960–2014, National Center for Health Statistics, Centers for Disease Control and Prevention. *Uterus refers to uterine corpus and uterine cervix combined. †Includes intrahepatic bile duct.

men have the highest overall rates of cancer incidence and death and Black females have the lowest survival rates [8]. Racial inequalities in the cancer burden primarily reflect obstacles to receiving healthcare services related to cancer prevention, early detection, and high-quality treatment, as opposed to biological differences [43].

While Americans of Asian, Hispanic, or American Indian descent generally have lower rates than non-Hispanic Whites or Blacks for the most common cancers, they have a higher burden of cancers related to infectious agents, such as cancers of the liver (hepatitis B and C viruses), stomach (*Helicobacter pylori*), and cervix (human papillomavirus) [2]. Factors that contribute to this disparity include a higher prevalence of cancer-related infections in immigrant countries of origin for Hispanics and Asian/Pacific Islanders [44] and lower rates of screening for cervical cancer [41]. In addition, some groups of American Indians and Alaska Natives have substantially higher rates of lung and kidney cancers, which is thought to reflect the higher prevalence of risk factors for these cancers, such as smoking, obesity, hypertension, and end-stage renal disease [45]. It is important to note that because cancer surveillance data in the US are reported for very broadly defined racial and ethnic categories, important differences in the cancer burden within groups is masked. For example, the age-adjusted cancer death rate among Cuban men is approximately 15% higher than that among Mexican men [46]. In addition, race misclassification among American Indians and Alaska Natives continues to be a challenge in accurately measuring the cancer burden in this population.

Poverty is the driving factor for the majority of health inequalities in the US. Members of minority populations are substantially more likely than Whites to be economically disadvantaged; in 2015, 24% of Blacks and 21% of Hispanics lived in poverty compared to 9% of non-Hispanic Whites [47]. Importantly, however, persons of lower socioeconomic status have disproportionately higher cancer death rates than those who are more affluent, regardless of race or ethnicity. One study estimated that eliminating socioeconomic disparities would prevent twice as many premature cancer deaths as eliminating racial disparities [48].

Cancer rates also vary geographically. For example, male lung cancer incidence rates from 2009 to 2013 ranged from 34 (cases per 100,000 men) in Utah to 118 in Kentucky [2]. Lung cancer shows the largest geographic variation of any cancer type because it is driven by historical smoking prevalence, which varies dramatically by state [49]. In 2015, smoking prevalence ranged from 9% in Utah to 26% in Kentucky and West Virginia [50]. State smoking prevalence is influenced by differences in state and local tobacco control activities, tobacco industry marketing, and social norms about tobacco use.

Conclusion

Cancer is a major public health problem in the US, as well as many other parts of the world. Cancer surveillance is essential for monitoring the cancer burden; identifying high-risk populations; quantifying progress in prevention, early detection, and

Table 1.2 Incidence rates by site, race, and ethnicity, US, 2009–2013.[1]

	All races combined	Non-Hispanic White	Non-Hispanic Black	Asian/Pacific Islander	American Indian/ Alaska Native[2]	Hispanic
All sites						
Male	512.1	519.3	577.3	310.2	426.7	398.1
Female	418.5	436.0	408.5	287.1	387.3	329.6
Breast (female)	123.3	128.3	125.1	89.3	98.1	91.7
Colorectum						
Male	46.9	46.1	58.3	37.8	51.4	42.8
Female	35.6	35.2	42.7	27.8	41.2	29.8
Kidney and renal pelvis						
Male	21.7	21.9	24.4	10.8	29.9	20.7
Female	11.3	11.3	13.0	4.8	17.6	11.9
Liver and intrahepatic bile duct						
Male	11.8	9.7	16.9	20.4	18.5	19.4
Female	4.0	3.3	5.0	7.6	8.9	7.5
Lung and bronchus						
Male	75.0	77.7	90.8	46.6	71.3	42.2
Female	53.5	58.2	51.0	28.3	56.2	25.6
Prostate	123.2	114.8	198.4	63.5	85.1	104.9
Stomach						
Male	9.2	7.8	14.7	14.4	11.2	13.1
Female	4.6	3.5	7.9	8.4	6.5	7.8
Uterine cervix	7.6	7.0	9.8	6.1	9.7	9.9

Source: Siegel *et al.* [2]. Reproduced with permission of John Wiley & Sons.
Hispanic origin is not mutually exclusive from Asian/Pacific Islander or American Indian/Alaska Native.
[1] Rates are per 100,000 population and age adjusted to the 2000 US standard population.
[2] Data based on Indian Health Service Contract Health Service Delivery Areas and exclude data from Kansas.

Table 1.3 Death rates by site, race, and ethnicity, US, 2010–2014.[1]

	All races combined	Non-Hispanic White	Non-Hispanic Black	Asian/Pacific Islander	American Indian/ Alaska Native[2]	Hispanic
All sites						
Male	200.4	204.0	253.4	122.7	183.6	142.5
Female	141.5	145.5	165.9	88.8	129.1	97.7
Breast (female)	21.2	21.1	30.0	11.3	14.1	14.4
Colorectum						
Male	17.7	17.3	25.9	12.4	19.5	15.0
Female	12.4	12.3	16.9	8.8	14.0	9.2
Kidney and renal pelvis						
Male	5.6	5.8	5.7	2.7	8.9	4.9
Female	2.4	2.5	2.5	1.1	4.2	2.3
Liver and intrahepatic bile duct						
Male	9.2	8.0	13.3	14.3	14.9	13.1
Female	3.7	3.3	4.6	6.1	6.8	5.8
Lung and bronchus						
Male	55.9	58.3	69.8	31.7	46.2	27.3
Female	36.3	39.8	35.5	18.0	30.8	13.4
Prostate	20.0	18.7	42.8	8.8	19.4	16.5
Stomach						
Male	4.4	3.4	8.7	7.1	7.5	6.9
Female	2.3	1.7	4.2	4.3	3.8	4.1
Uterine cervix	2.3	2.1	3.9	1.7	2.8	2.6

Source: Siegel *et al.* [2]. Reproduced with permission of John Wiley & Sons.
Hispanic origin is not mutually exclusive from Asian/Pacific Islander or American Indian/Alaska Native.
[1] Rates are per 100,000 population and age adjusted to the 2000 US standard population.
[2] Data based on Indian Health Service Contract Health Service Delivery Areas.

treatment strategies; and informing cancer control programs. Descriptive cancer epidemiology research has also greatly contributed to the current understanding of cancer. The foundation of cancer surveillance is population-based cancer registration. The expansion in population coverage of high-quality cancer data collection in the US, from 9% in the mid-1970s to almost 100% today, is a major public health milestone. This achievement has the potential to further reduce the cancer burden by facilitating widespread, targeted interventions at the community level, where health inequalities arise.

References

1 Linder FE, Grove RD. *Vital Statistics Rates in the United States 1900–1940*. Washington: United States Government Printing Office, 1947.
2 Siegel R, Miller KD, Jemal A. Cancer Statistics, 2017. *CA Cancer J Clin* 2017;67:7–30.
3 Weiss NS, Szekely DR, Austin DF. Increasing incidence of endometrial cancer in the United States. *N Engl J Med* 1976;294:1259–62.
4 Ziel HK, Finkle WD. Increased risk of endometrial carcinoma among users of conjugated estrogens. *N Engl J Med* 1975;293:1167–70.
5 Coombs NJ, Cronin KA, Taylor RJ, Freedman AN, Boyages J. The impact of changes in hormone therapy on breast cancer incidence in the US population. *Cancer Causes Control* 2010;21:83–90.
6 Ravdin PM, Cronin KA, Howlader N, *et al.* The decrease in breast-cancer incidence in 2003 in the United States. *N Engl J Med* 2007;356:1670–74.
7 Hutchison C, Menck H, Burch M, Gottschalk R. *Cancer Registry Management: Principals and Practice, 2nd edn*. National Cancer Registrar's Association, Inc., 2004.
8 Howlader N, Noone AM, Krapcho M, *et al. SEER Cancer Statistics Review, 1975–2013*. Bethesda: National Cancer Institute, 2016.
9 National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Available from: seer.cancer.gov (accessed 11 May 2017).
10 Centers for Disease Control and Prevention. State cancer registries: status of authorizing legislation and enabling regulations–United States, October 1993. MMWR 1994;43:71,74–5.
11 Centers for Disease Control and Prevention. National Program of Cancer Registries. Available from: cdc.gov/cancer/npcr/about.htm (accessed 11 May 2017).
12 Bilimoria KY, Stewart AK, Winchester DP, Ko CY. The National Cancer Data Base: a powerful initiative to improve cancer care in the United States. *Ann Surg Oncol* 2008;15:683–90.
13 Chen HS, Portier K, Ghosh K, *et al.* Predicting US- and state-level cancer counts for the current calendar year: Part I: evaluation of temporal projection methods for mortality. *Cancer* 2012;118:1091–9.
14 Zhu L, Pickle LW, Ghosh K, *et al.* Predicting US- and state-level cancer counts for the current calendar year: Part II: evaluation of spatiotemporal projection methods for incidence. *Cancer* 2012;118:1100–9.
15 Siegel RL, Devesa SS, Cokkinides V, Ma J, Jemal A. State-level uterine corpus cancer incidence rates corrected for hysterectomy prevalence, 2004 to 2008. *Cancer Epidemiol Biomarkers Prev* 2013;22:25–31.
16 Clegg LX, Feuer EJ, Midthune DN, Fay MP, Hankey BF. Impact of reporting delay and reporting error on cancer incidence rates and trends. *J Natl Cancer Inst* 2002;94:1537–45.
17 Day JG. *Population Projections of the United States by Age, Sex, Race, and Hispanic Origin: 1995 to 2050*. US Government Printing Office, Washington, DC: US Bureau of the Census, 1996.
18 Ederer F, Axtell LM, Cutler SJ. The Relative Survival Rate: A Statistical Methodology. *National Cancer Institute Monograph* 6; 101–21, 1961.
19 Marubini E, Valsecchi MG. *Analysing Survival Data from Clinical Trials and Observational Studies*. New York: John Wiley & Sons, Inc., 1995.
20 Hutchison GB, Shapiro S. Lead time gained by diagnostic screening for breast cancer. *J Natl Cancer Inst* 1968;41:665–81.
21 Brawley OW. Trends in prostate cancer in the United States. *J Natl Cancer Inst Monogr* 2012;2012:152–6.
22 Thun MJ, Carter BD, Feskanich D, *et al.* 50-year trends in smoking-related mortality in the United States. *N Engl J Med* 2013;368:351–64.
23 Siegel RL, Jacobs EJ, Newton CC, *et al.* Deaths due to cigarette smoking for 12 smoking-related cancers in the United States. *JAMA Intern Med* 2015;175(9):1574–6.
24 Miller KD, Siegel RL, Lin CC, *et al.* Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin* 2016;66:271–89.
25 Potosky AL, Kessler L, Gridley G, Brown CC, Horm JW. Rise in prostatic cancer incidence associated with increased use of transurethral resection. *J Natl Cancer Inst* 1990;82:1624–8.
26 Potosky AL, Miller BA, Albertsen PC, Kramer BS. The role of increasing detection in the rising incidence of prostate cancer. *JAMA* 1995;273:548–52.
27 Legler JM, Feuer EJ, Potosky AL, Merrill RM, Kramer BS. The role of prostate-specific antigen (PSA) testing patterns in the recent prostate cancer incidence decline in the United States. *Cancer Causes Control* 1998;9:519–27.
28 Griswold MH, Wilder CS, Cutler SJ, Pollack ES. *Cancer in Connecticut 1935–1951*. Hartford, Connecticut: Connecticut State Department of Health, 1955.
29 Proctor RN. Tobacco and the global lung cancer epidemic. *Nat Rev Cancer* 2001;1:82–6.
30 Weiss W. Cigarette smoking and lung cancer trends. A light at the end of the tunnel? *Chest* 1997;111:1414–6.
31 DeSantis CE, Fedewa SA, Goding Sauer A, *et al.* Breast Cancer Statistics, 2015. *CA Cancer J Clin* 2015;66:31–42.
32 Stryker SJ, Wolff BG, Culp CE, *et al.* Natural history of untreated colonic polyps. *Gastroenterology* 1987;93:1009–13.
33 Winawer SJ, Zauber AG, Ho MN, *et al.* Prevention of colorectal cancer by colonoscopic polypectomy. *The National Polyp Study Workgroup. N Engl J Med* 1993;329:1977–81.

34 Edwards BK, Ward E, Kohler BA, *et al.* Annual report to the nation on the status of cancer, 1975–2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. *Cancer* 2010;116:544–73.

35 Cress RD, Morris C, Ellison GL, Goodman MT. Secular changes in colorectal cancer incidence by subsite, stage at diagnosis, and race/ethnicity, 1992–2001. *Cancer* 2006;107:1142–52.

36 DevCan: Probability of Developing or Dying of Cancer, Version 6.7.4 Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Insititute, 2015.

37 O'Brien S, Berman E, Borghaei H, *et al.* NCCN clinical practice guidelines in oncology: chronic myelogenous leukemia. *J Natl Compr Canc Netw* 2009;7:984–1023.

38 Berry DA, Cronin KA, Plevritis SK, *et al.* Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med* 2005;353:1784–92.

39 Feuer EJ, Merrill RM, Hankey BF. Cancer surveillance series: interpreting trends in prostate cancer--part II: cause of death misclassification and the recent rise and fall in prostate cancer mortality. *J Natl Cancer Inst* 1999;91:1025–32.

40 Etzioni R, Gulati R, Tsodikov A, *et al.* The prostate cancer conundrum revisited: treatment changes and prostate cancer mortality declines. *Cancer* 2012;118:5955–63.

41 Fedewa SA, Sauer AG, Siegel RL, Jemal A. Prevalence of major risk factors and use of screening tests for cancer in the United States. *Cancer Epidemiol Biomarkers Prev* 2015;24:637–52.

42 Cook MB, Dawsey SM, Freedman ND, *et al.* Sex disparities in cancer incidence by period and age. *Cancer Epidemiol Biomarkers Prev* 2009;18:1174–82.

43 Bach PB, Schrag D, Brawley OW, *et al.* Survival of blacks and whites after a cancer diagnosis. *JAMA* 2002;287:2106–13.

44 Torre LA, Bray F, Siegel RL, *et al.* Global cancer statistics, 2012. *CA Cancer J Clin* 2015;65:87–108.

45 Espey DK, Wu XC, Swan J, *et al.* Annual report to the nation on the status of cancer, 1975–2004, featuring cancer in American Indians and Alaska Natives. *Cancer* 2007;110:2119–52.

46 Siegel RL, Fedewa SA, Miller KD, *et al.* Cancer statistics for Hispanics/Latinos, 2015. *CA Cancer J Clin* 2015;65:457–80.

47 Proctor BD, Semega JL, Kollar MA. US Census Bureau Current Population Reports, P60-252. Income and Poverty in the United States: 2015. Washington, D.C.: U.S. Census Bureau, 2016.

48 Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer J Clin* 2011;61:212–36.

49 Jemal A, Thun MJ, Ries LA, *et al.* Annual report to the nation on the status of cancer, 1975–2005, featuring trends in lung cancer, tobacco use, and tobacco control. *J Natl Cancer Inst* 2008;100:1672–94.

50 Behavioral Risk Factor Surveillance System (BRFSS), Centers for Disease Control and Prevention, 2015. Public Use Data File, 2016.

2

Fundamentals of Cancer Epidemiology

Susan M. Gapstur and Eric J. Jacobs

Epidemiology Research Program, American Cancer Society, Atlanta, Georgia, USA

"An ounce of prevention is worth a pound of cure"
Benjamin Franklin

Introduction

Epidemiology (from Greek "epi" = upon and "demos" = people) is the study of the factors that influence health and disease occurrence and distribution in populations, and is the scientific foundation of public health and preventive medicine.

Several early observations were critical in launching the field of cancer epidemiology. For example, in 1713, Bernardino Ramazzini, an Italian physician, reported the virtual absence of cervical cancer and relatively high incidence of breast cancer in nuns, and hypothesized that these findings were related to their celibate lifestyle. These observations were an important first step towards understanding the role of sexually transmitted infections and hormones in cancer etiology. In 1761, John Hill, a London physician, wrote the book *Cautions Against the Immoderate Use of Snuff* in which he linked tobacco (snuff) to cancer risk. These observations led to epidemiologic research in the 1950s and early 1960s that established smoking as a cause of lung cancer, which was recognized in the 1964 United States (US) Surgeon General's report on *Smoking and Health*. In 1775, Percivall Pott, an English surgeon, described cancer of the scrotum in chimney sweeps, establishing a link between an occupational exposure and cancer. This research led to many studies identifying other carcinogenic occupational exposures that informed the development of policies to establish limits on those exposures [1].

Critically important methodological developments subsequently contributed to advancements in cancer epidemiology. William Farr and Marc d'Espine created a nomenclature system for grouping diseases in the mid-nineteenth century. This nomenclature formed the basis for the International Classification of Disease, which is used to code cause of death. In the early part of the twentieth century, the first population-based cancer registries were established for the collection of information on newly diagnosed cancer cases. In the US, cancer registries now exist in all 50 states and Puerto Rico, and play a critical role in identifying cancer cases for epidemiologic studies. Over the past century, new laboratory and computer technologies, study designs and statistical methods for data analyses have enhanced the contribution of cancer epidemiology to cancer surveillance and to the identification of host, lifestyle, and environmental factors that increase or reduce risk of cancer.

A comprehensive review of epidemiologic methods is beyond the scope of this chapter, and can be found in many epidemiology textbooks. Instead, this chapter is intended to provide the reader with a fundamental understanding of key terminology, different types of study design, measures of associations, threats to validity, approaches to combining results from several studies, and criteria for judging causal relationships. Understanding these concepts is important because evidence from well-designed epidemiologic research guides clinical and public health practice, regulations, policies, and guidelines.

Exposures and Disease Occurrence

In epidemiologic investigations, the term "exposure" is used broadly to describe a factor that may be associated with higher or lower risk of disease. Exposures may relate to an agent (sometimes broadly referred to as "environmental" factor), person, place, or time. More specifically, exposures can include sociodemographic factors (e.g., age, sex, race, ethnicity, education, income), behavioral or lifestyle factors (e.g., tobacco smoking, alcohol consumption, poor diet or nutrition, physical inactivity, sun exposure), medical factors (e.g., high body mass index, diabetes mellitus status, reproductive characteristics), biomarkers (e.g., circulating markers, urinary markers), genetic and epigenetic factors (e.g., white blood cell telomere length, germline genetic variants), and classical environmental factors including aspects of the chemical, physical, and biological

The American Cancer Society's Principles of Oncology: Prevention to Survivorship, First Edition. Edited by The American Cancer Society.

Table 2.1 Basic measures of cancer occurrence or burden used in epidemiology.

Measure	Definition
Case counts	Number of cancer cases or deaths (usually new cases or deaths in a year)
Prevalence	Proportion of the population with cancer at one point in time
Incidence rate	Number of new cancer cases per 100,000 persons per year
Mortality rate	Number of new cancer deaths per 100,000 persons per year
Survival rate	Proportion of cancer patients surviving for a given period of time (usually 5 years in cancer)

environment such as exposure to ozone or infectious organisms. Detailed information on cancer-specific risk factors, including genetic and medical factors, reproductive factors, infectious agents, occupational and environmental contaminants, and lifestyle factors such as tobacco, nutrition, physical activity, and sun exposure are described in other chapters of this textbook.

Several different measures describe the burden of cancer as defined in Table 2.1. Understanding the differences between these measures is essential for medical and public health professionals.

Case counts are the number of individuals with a specific type of cancer (e.g., invasive breast cancer or multiple myeloma) at one point in time, or who develop or die of cancer over a given period. They are used in the numerator for computing prevalence, incidence, mortality, and survival statistics. Case counts are generally identified through hospital, state and national registries, or death certificates. The prevalence of a cancer (also called point prevalence) is the number of people with that cancer (regardless of when it was diagnosed) divided by the total number of people in the population at a particular point in time. While prevalence is sometimes referred to as a prevalence rate, this is incorrect because, by definition, it does not specify any unit of time over which the cases occurred. By themselves, case counts and prevalence estimates are most useful for planning and allocation of resources and less useful for epidemiologic investigations of disease causation.

Measures frequently used in cancer surveillance and etiology research include incidence rates, mortality rates, and survival rates. An incidence rate is the number of new cases of a disease (e.g., cancer) in a population during a specified time period, divided by the total number of person-years in that population. Similarly, the mortality rate is the number of deaths from a disease (e.g., cancer) in a population during a specified time period, divided by the total number of person-years in that population. These measures can provide quite different information. For example, among women aged 55 and older in the US, the incidence rate and prevalence of breast cancer is higher than the incidence rate and prevalence of lung cancer. However, because of the low survival rate among women with lung cancer, the lung cancer mortality rate is considerably higher than that for breast cancer.

Study Designs

Epidemiologic studies are often classified as either descriptive or analytic. Descriptive epidemiologic studies typically report patterns of disease occurrence or health-related factors (e.g., the prevalence of smoking) by demographic characteristics, place, and/or time. Such studies can provide early clues about etiology and generate hypotheses, but are not designed to test specific hypotheses about exposure–disease associations.

Descriptive studies often use routinely collected data including cancer registry or surveillance data, national surveys, census information, employment records, or clinical records. Cancer surveillance data, often gathered by cancer registries, are used to compute annual cancer incidence rates, mortality rates, prevalence, and survival. Such surveillance data are useful for describing cancer occurrence for specific geographic regions, over time and among demographic groups such as those based on age, race/ethnicity, and gender. In addition, cross-sectional surveys are used to describe the prevalence of a health condition or risk factor in a population at specific points in time. For example, using data from the National Health and Nutrition Examination Survey, researchers described the prevalence of obesity in the US for different categories of sex, age, and race/ethnicity, and over time [2]. Case reports or case series can be considered descriptive studies, as they may include detailed information about a specific patient or group of patients with suggestive patterns of exposure. However, because case reports or case series lack a comparison group of people without the condition of interest, they are not suitable for making sound inferences about disease causation. Overall, the information generated from descriptive studies is important for identifying high-risk populations, for monitoring progress in cancer prevention, early detection and treatment, and for informing analytic studies of exposure–disease relationships.

Analytic epidemiologic studies, unlike descriptive studies, are specifically designed to test hypotheses about exposure–disease associations. There are two broad groups of epidemiologic study designs – experimental and observational. In an experimental study (discussed in more detail later in this section) the investigator increases or decreases exposure to the factor(s) of interest, usually based on random assignment, though not always. In contrast, in an observational analytic epidemiologic study, the investigator does not control the exposure of research study participants, but rather observes, records, and analyzes information as it exists.

There are several different types of observational study designs, including *ecologic studies, cross-sectional studies, case-control studies*, and *cohort studies*. Because these study designs have different strengths and limitations, it is useful to be able to distinguish them. The type of study design used will depend on factors including the characteristics of the cancer to be studied, the nature of the exposure (e.g., occupational, diet, medical) or intervention (e.g., screening tool), and the type and availability of pre-existing data.

Ecologic studies compare a group level measure of an exposure with a group level measure of an outcome. For example, an early ecologic study of diet and breast cancer showed a strong positive correlation between per capita fat intake and breast

cancer mortality rates across 39 countries [3]. However, countries with high fat intake may differ substantially in many ways from countries with low fat intake. It is possible that other breast cancer risk factors correlated with per capita fat intake, such as body mass index, explained the observed correlation with breast cancer mortality. Because only country level information on fat intake was available, it was difficult to determine if this association also existed at the level of the individual. This potential difference in detecting an association at the group vs the individual level is known as the "ecologic fallacy". Ecologic studies are typically less able to statistically adjust for correlated risk factors than studies with detailed information collected from individuals. Therefore, studies that rely on individual level data are often preferable to ecological studies.

Cross-sectional studies can be used to examine exposure–disease relationships at one point in time based on individual level data, and often rely on data that already exist or data that can be collected relatively quickly and cost-effectively. Cross-sectional studies can be informative about exposure–disease relationships when the exposure does not change as a result of the disease and the disease is unlikely to be fatal. For example, a cross-sectional study would be reasonable for examining an association between germ-line genetic mutations, which do not change as a result of the outcome, and the prevalence of colorectal polyps, which for most people does not lead to premature death. However, if the exposure changes as a result of the disease or if the disease has a poor survival, then the estimate of association between an exposure and a disease might not be valid. For example, in a cross-sectional study examining the association between heavy alcohol drinking and the prevalence of pancreatic cancer, individuals with pancreatic cancer might have reduced their alcohol consumption because they were not feeling well, potentially underestimating the true association between alcohol consumption and risk of pancreatic cancer. Moreover, as pancreatic cancer is usually rapidly fatal, individuals alive with pancreatic cancer at any point in time will tend to be those with less rapidly fatal forms of the disease, and therefore are unlikely to be representative of pancreatic cancer cases in general.

Case-control studies and *cohort* studies are the two most commonly used study designs in analytic epidemiology. In a case-control study of cancer, newly diagnosed cancer cases in a defined population and time period are identified and enrolled, and their exposure history is compared to that of a random sample of "control" individuals from the same source population as the cases, without the cancer of interest. In a case-control study, exposure information collected from cases and controls must refer to the time period prior to disease so that temporal relationships between an exposure and a disease can be reasonably inferred. An example of a case-control study is the Western Australia Bowel Health Study [4]. In that study, colorectal cancer cases diagnosed between 2005 and 2007 were identified through the Western Australia state cancer registry, and randomly selected controls were identified from the Western Australia state voter registration rolls from the same time period (voter registration is compulsory in Australia). Both cases and controls then completed a questionnaire asking about colorectal cancer risk factors, such as physical activity.

Case-control studies are a valuable research design, and are particularly well-suited for studying rare diseases, including many cancers, which can be difficult to study in cohort studies. Compared to cohort studies, they require fewer participants and can often provide results more quickly. However, they generally examine only a single type of cancer outcome. Several different biases can arise in case-control studies and should be kept in mind. For example, recall bias can occur in a case-control study if cases report their prior exposure differently than controls. Evidence of recall bias is well-illustrated in studies of induced abortion and breast cancer. Early case-control studies were suggestive of a positive association between induced abortion and risk of breast cancer. However, the stigma of induced abortion can create the appearance of associations between abortion and breast cancer risk where there is none. That is, cases (women with breast cancer) are more likely to report their reproductive history accurately, including that they had an induced abortion, than controls (women without breast cancer). This "recall bias" in case-control studies led to a positive estimate of the association between induced abortion and breast cancer risk that was not subsequently replicated in prospective cohort studies, leading a number of groups with expertise on this topic, including the American College of Obstetricians and Gynecologists, to determine that induced abortion is not associated with an increased risk [5].

In *cohort* studies, information about exposures is collected from a group of generally healthy individuals, or individuals without the disease of interest, and then this group is followed over time to determine who develops disease. Cohort studies can be either prospective or retrospective. In *a prospective cohort study*, exposure information is collected at the start of the study and then cases of disease are identified as they occur over time, usually over many years or even decades. Prospective cohort study populations can be defined and selected on the basis of different factors. For example, some prospective cohorts are defined by geographic area (e.g., the Iowa Women's Health Study, a population-based cohort of postmenopausal women [6]), or by occupation (e.g., the Nurses' Health Study) [7]. The study population for other cohorts can be more broadly defined, such as the American Cancer Society's (ACS) Cancer Prevention Study-II, which includes men and women recruited by ACS volunteers nationwide [8]. In a *retrospective cohort study*, previously recorded information on exposure and disease occurrence over time in a defined group of people is assembled and analyzed. Retrospective cohort study designs are commonly used to investigate occupational exposure–disease relationships.

Cohort studies have both notable advantages and disadvantages. Compared to case-control studies, there is little potential for bias from "differential" recall of exposure, because recall is unlikely to differ systematically between those who go on to develop cancer and those who do not. In addition, unlike in case-control studies, absolute incidence and mortality rates can be calculated within the cohort, and many different disease outcomes can be studied. However, prospective cohort studies can be costly due to the high cost of following a large number of participants over time, and many years may be needed to obtain results, particularly for rare cancers. Despite these disadvantages, a well-conducted prospective cohort study – particularly one in

which follow-up exposure information is updated and loss of study participants is minimized – can provide strong evidence for or against causal associations between risk factors and disease outcomes, including cancer.

Participants in cohort studies are usually not representative of the general population. Although this does not threaten the internal validity of associations observed within a cohort, the generalizability of associations observed in cohorts to other populations should be considered. However, experience has shown that biologic associations between exposure and disease are usually generalizable. For example, while participants in the British Doctors Study from the 1950s were in no way representative of the British general population, the association between cigarette smoking and risk of lung cancer observed in the British Doctors Study has subsequently been observed in a wide variety of other study populations [9].

Experimental (or intervention) studies are conducted among individuals or among groups to evaluate the efficacy or effectiveness of treatments, procedures, behavioral or lifestyle changes, programs, or services on a specific outcome or outcomes. Unlike an observational study in which the investigator does not intervene to change the participants' exposure, in an experimental study participants are assigned to different groups in an attempt to modify exposure to a specific factor. In a "single-blinded" experimental study, study subjects do not know which exposure groups (i.e., treatment vs placebo or standard of care) they have been assigned to whereas in a "double-blinded" study neither the study subject nor the investigator knows who is assigned to which exposure group. Therefore, in a single-blinded study, potential bias introduced by the perceptions of study subjects is minimized, whereas in a double-blinded study potential bias from both the perceptions of the study subjects and the investigators is minimized.

In most experimental studies (though not all) assignment of individuals or groups to the exposure is done randomly. Studies in which the exposure is randomly assigned are usually referred to as randomized trials or randomized clinical trials. Random assignment assures that the exposure groups are, on average, comparable on all other factors – both known and unknown – except the exposure (often a treatment or intervention), making it unlikely that differences in outcomes between exposure groups can be explained by other factors. When feasible, randomized trials are considered to provide the most reliable evidence that an exposure causes or prevents a disease.

Despite the important advantages of randomized trials, they cannot be used to answer all research questions. Randomized trials are usually costly and, particularly for cancer outcomes, can take many years. In addition, it is unethical to assign participants to a potentially hazardous exposure from which they would be unlikely to benefit, such as a potent pesticide.

Measures of Association

Data collected in epidemiologic studies are used to quantitatively estimate associations between an exposure and a disease outcome. In cancer epidemiology, a common measure of association is the *rate ratio* (RR), sometimes referred to as the *risk ratio*. The rate ratio is the incidence rate of disease in individuals with a particular exposure divided by the incidence rate in individuals without this exposure. For example, consider a hypothetical cohort study of men aged 55 years and older. If the observed incidence rate of bladder cancer among current cigarette smokers in this study was 400 per 100,000 person-years, and the observed incidence rate of bladder cancer among never smokers was 100 per 100,000 person-years, then the rate ratio for current smoking would be 4.0.

Table 2.2 Hypothetical data from 1 year of follow-up in a cohort study of 400,000 men.

	Developed bladder cancer?		
	Yes	No	Total number of men
Current smokers (exposed)	400	99,600	100,000
Never smokers (not exposed)	300	299,700	300,000

A closely related measure is the *relative risk*, which is the proportion of study participants in the exposed group who develop the disease during a defined time period divided by the same proportion among study participants in the unexposed group. For example, consider the hypothetical data shown in Table 2.2 from a cohort study that included only men aged 55 years and older who were current cigarette smokers or never smokers, and followed them for 1 year. The relative risk is 400/100,000 divided by 300/300,000, or 4.0. The relative risk is technically a different measure than the rate ratio because it is based on counts while the rate ratio is based on rates that include person-years in the denominator. However, the relative risk will be virtually identical to the rate ratio when the disease outcome is relatively uncommon (as is true in most studies of cancer) and/or when the time period under observation is relatively short.

Odds ratios from case-control studies of incident cancer outcomes can nearly always be interpreted the same way as a relative risk. For example, it would be accurate to say that in this study current smoking compared to never smoking was associated with fourfold higher risk of developing bladder cancer. More comprehensive explanations of the derivation and use of these and other measures of associations can be found in standard epidemiology textbooks.

As described later in this section, the size of rate ratios, relative risks and odds ratios is one of several criteria used when assessing whether an association is causal. Once an association is established as causal, however, measures of *absolute risk* are more relevant than measures of relative risk, both clinically and for public health.

Absolute risk due to an exposure is often measured by the *attributable risk*, sometimes referred to as the *risk difference*, or *rate difference*. Attributable risk is defined as the difference in incidence or mortality rates between the exposed and unexposed, and represents the excess rate of disease in the exposed group that can be attributed to the exposure.

Table 2.3 illustrates relative risks and attributable risks using results from a large ACS study comparing men who were

Table 2.3 Relative risk and attributable risk of cancer mortality by pipe smoking.

	Rate per 100,000 person-years in pipe smokers	Rate per 100,000 person-years in never smokers	Relative risk	Attributable risk per 100,000 person years
Pancreatic cancer	45.9	29.1	1.6	16.8
Esophageal cancer	14.4	6.0	2.5	8.4

exclusive pipe smokers with those who had never smoked [10]. The relative risk associated with pipe smoking was greater for esophageal cancer mortality (2.5) than for pancreatic cancer mortality (1.6). However, because deaths from esophageal cancer were less common than deaths from pancreatic cancer, the attributable risk was greater for pancreatic cancer mortality than for esophageal cancer mortality. These results therefore suggested that a man's pipe smoking is more likely to cause him to die from pancreatic cancer than from esophageal cancer.

Another measure of absolute risk is the *population attributable risk*, which provides an estimate of the health impact of an exposure on a population taking into account how common the exposure is. The population attributable risk is defined as the difference between the incidence or mortality rate in the overall population (both exposed and unexposed) and that in just the exposed portion of the population. For example, if the incidence rate of pancreatic cancer in the entire population of women in the US aged 55 years and older was 50 per 100,000 person-years, and the incidence rate among women of this age in the US who had never smoked was 40 per 100,000 person-years, then the population attributable risk for smoking would be 10 per 100,000 person-years. The population attributable risk depends on both the strength of the exposure–disease association (i.e., the relative risk) and how common the exposure is. A common exposure with a relatively low relative risk may have a larger population attributable risk than a rare exposure with a high relative risk.

Threats to Validity

Before an association can be considered potentially causal it is important to consider the possibility that it is a chance finding (random error), or a result of systematic error caused by information bias, selection bias, and/or confounding. These systematic errors can result from limitations in the study design, data collection, or statistical analysis.

The role of chance, or random error, needs to be considered in the interpretation of epidemiologic results. Most epidemiologic investigations test hypotheses about whether an exposure increases or decreases the risk of disease based on data collected from a sample of a larger underlying population. Statistical hypothesis testing begins with stating the null hypothesis, which, for example, is that the risk of disease in the exposed group is the same as that in the unexposed group. Then statistical techniques are used to ask, if the null hypothesis is true, what is the probability of detecting an association as large as or larger than the one observed? This probability is known as the *P*-value. In biomedical research, an association with a *P*-value of 0.05 or smaller is often described as "statistically significant", and interpreted as being less likely to be due to chance. For any given true association, the size of the *P*-value is closely related to the sample size (a.k.a., power) of the study. The larger the sample size, the lower the *P*-value is likely to be, and the more likely the association will be found to be statistically significant. Conversely, studies with small sample sizes are less likely to find an association to be statistically significant.

Even very low *P*-values cannot be used to infer causality because other information also is necessary to draw such conclusions. Indeed, an observed association that is "statistically significant" may still be due purely to chance. The plausibility of an association needs to be taken into account when assessing how likely it is to be due to chance. For example, a statistically significant association between astrological sign and cancer risk may be more likely to be a chance finding than a similar association between cigarette smoking and cancer risk.

As mentioned previously, when interpreting results of a study it is important to rule out systematic errors. Information bias is a type of systematic error that occurs when the exposure and/or outcome data are assessed inaccurately. Information bias is a particular concern when exposure assessment differs between those with disease (or who go on to develop disease) and those without disease. One type of information bias is recall bias, which was described above for the association between induced abortion and risk of breast cancer in the section on case-control studies. In that scenario, cases recalled and reported their history of induced abortion more accurately than controls resulting in an increased risk that was not replicated in cohort studies where all participants report their history before breast cancer occurs.

Selection bias is a second type of systematic error, which can occur when the participation rates of potential study subjects differ based on both exposure and disease status. Using the same example of induced abortion and breast cancer risk, selection bias would occur if cases that agreed to participate represented all cases in the population but women with a history of induced abortion were less likely to agree to participate as controls. Information and selection bias can be minimized by using a carefully developed study protocol, properly training data collection staff, and maintaining high study response rates and data quality.

Confounding is a third type of systematic error which can occur when another exposure (i.e., the confounder) is related to both the main exposure of interest and the disease outcome. Confounding is well-illustrated by a study of the relationship between coffee drinking and risk of oral/pharyngeal cancer. In many populations, heavy coffee drinkers are more likely to smoke cigarettes and drink alcohol than people who do not drink coffee. In addition, cigarette smoking and alcohol consumption increase risk of oral/pharyngeal cancer. Without

proper consideration of smoking and drinking, heavy coffee consumption will be associated with increased risk of oral/pharyngeal cancer even if coffee has no effect on oral/pharyngeal cancer (or possibly even if it was beneficial). Therefore, examination of the relationship between coffee consumption and risk of oral/pharyngeal cancer requires approaches to deal with confounding by cigarette smoking and alcohol drinking.

Several approaches can be used to deal with confounding in observational epidemiologic studies. One approach is to adjust for smoking and drinking history using commonly available statistical methods during the study analysis. Indeed, in a recent analysis of data from a large prospective cohort study of men and women, before adjustment for smoking history, the relative risk for consumption of more than four cups/day of coffee compared to no coffee consumption in relation to fatal oral/pharyngeal cancer was 1.52; however, after statistical adjustment for smoking history, alcohol consumption and other potential confounding factors, the relative risk was 0.58 [11]. An alternative approach for minimizing or eliminating the effects of known confounding factors is to exclude participants who have been or are exposed to the known confounding factors, effectively eliminating the confounding factor. In addition, in case-control studies, the investigator may consider selecting cases and controls who are matched on one or more known confounders, although such matching must be accounted for in the statistical analysis and will make it impossible to examine the association of the matching factor with risk of the disease outcome. Although these approaches can be quite effective, particularly when confounders are known and well-measured, no observational study can entirely rule out confounding, as not all confounding factors may be known.

Summarizing or Combining Data from Multiple Studies

Summarizing evidence from epidemiologic studies on specific exposure–disease relationships can be useful when findings from different studies are inconsistent, or when individual studies are limited in size, particularly if the strength of association is weak. Approaches for summarizing epidemiologic evidence include traditional narrative reviews, meta-analyses, and pooled analyses. Traditional narrative reviews provide a qualitative assessment of the state of the evidence from multiple individual observational and/or experimental studies. Epidemiologic meta-analyses typically combine published relative risks or odds ratios from multiple individual studies to calculate a summary estimate of the relative risk. The contribution of each study to the summary risk estimate is weighted according to its size, so that larger studies have more influence. In contrast, in pooled analyses, data on individual study participants from several studies are combined into a single data set, which is then used to calculate an overall risk. If well-conducted, all of these approaches can be useful for better understanding the association between an exposure and risk of cancer.

Narrative reviews, meta-analyses, and pooled analyses have all become increasingly available and it is important to understand their strengths and limitations. A strength of narrative reviews and meta-analyses is that they can be done quickly as they make use of already published results. However, published studies often vary widely in study design and quality. It is critical that narrative reviews, meta-analyses and pooled analyses consider and discuss differences between studies as well as the potential limitations of the individual studies they include. Both meta-analyses and pooled analyses provide more precise measures of exposure–disease relationships by combining results from individual studies. However, different studies are likely to have used different questions or other methods to assess exposure. Therefore, one concern in both meta-analyses and pooled analyses is that the level of detail included in a summary estimate for given exposure may sometimes be reduced to that of the study with the minimum amount of information.

Both reviews and meta-analyses can be affected by publication bias, which occurs when studies with null findings are less likely to be published than those with statistically significant results. Therefore, reviews or meta-analyses may overestimate the true strength of an association. Methods for detecting publication bias have been developed and can be incorporated into meta-analyses and reviews [12, 13]. Publication bias, however, may be less likely to occur in pooled analyses, because even when a study has not been published due to imprecise or null findings, investigators are often willing to contribute data to a pooled analysis. Through efforts such as the National Cancer Institute's Cohort Consortium [14], there is a growing body of research using pooled analyses to examine uncommon exposures (for example low frequency genetic variants) and/or rare cancers (e.g., male breast cancer).

"Proof" of Causality

The strongest evidence for a causal association between an exposure and a disease comes from randomized trials that compare incidence or mortality rates between individuals who were randomized to receive an exposure and those who were not. However, as noted above, it is unethical to conduct experiments exposing humans to agents that cause or are suspected to cause diseases such as cancer. Therefore, it is often necessary to assess evidence carefully for causality from the body of observational epidemiologic studies.

Guiding principles about the total body of epidemiologic evidence that constitutes "proof" of a causal relationship have been proposed to help inform public health and clinical policies, guidelines and recommendations. In the 1964 Surgeon General's Report on Smoking and Health, the Advisory Committee of the US Public Health Service described five principles that were considered in determining that the associations between smoking and several diseases found in observational epidemiologic studies were causal [15]. These principles were subsequently expanded by Sir Austin Bradford Hill and are described in Table 2.4 [16]. Importantly, no single principle is sufficient to infer that an exposure is causally related to a disease.

Organizations such as the World Health Organization's International Agency for Research on Cancer (IARC) apply

Table 2.4 Criteria for assessing causality between an exposure and cancer incidence and/or mortality.

(1)	Strength	A large (strong) relative risk or odds ratio is more likely to support a causal relationship than a small (weak) one. However, a small relative risk or odds ratio does not exclude the possibility of a causal relationship.
(2)	Consistency	The association is replicated in several studies of the same or different design, conducted by different investigators, under different circumstances and in different populations.
(3)	Specificity	The exposure is specific in causing tumors at one site or of one morphological/histological type. However, evidence of causality can be supported if the exposure causes cancer at multiple sites that share common carcinogenic pathways.
(4)	Temporality	There is evidence that the exposure preceded the onset of disease.
(5)	Gradient	The strength of association increases as dose or intensity of the exposure increases, or the association decreases as exposure decreases or is removed. However, the absence of a biologic gradient does not preclude a causal relationship.
(6)	Plausibility	A causal relationship is supported if there is evidence that the association is biologically plausible.
(7)	Coherence	The epidemiologic evidence is consistent with evidence from other types of research, and does not conflict with other types of research evidence or what is known about the exposure and the disease.
(8)	Experiment	Experimental evidence that removal of the exposure (e.g., in an occupational setting) reduces risk, or evidence from a clinical trial showing that administration of a treatment or preventive agent (e.g., selective estrogen receptor modulator prevention of breast cancer in high-risk women). This type of evidence is not always available.
(9)	Analogy	A similar exposure (e.g., chemical classes, hormonal factors) to the one of interest shows evidence of a causal relationship.

Source: adapted from Hill (1965) [16].

these and other criteria to support inferences about causal relationships between an exposure and cancer risk. Indeed, since the 1970s IARC has convened expert working groups to review the strength of scientific evidence on the carcinogenic effects of chemical, occupational, physical, biological, and lifestyle factors in order to identify the causes of human cancer. The information reviewed by the working groups and their conclusions are published in the *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans* [17]. There are four primary areas of scientific evidence that are summarized and evaluated by the working groups: (1) exposure data based on production, use, occurrence and exposure levels in the environment, workplace and human body tissue/fluids; (2) human evidence based on epidemiological studies, including dose-response and other quantitative data if available; (3) evidence-based research in experimental animals; and (4) mechanistic and other relevant data including toxicokinetics and other mechanism(s) of carcinogenesis. The overall evaluation of the carcinogenicity of an agent to humans is based on the strength of the evidence derived from the entire body of research, and ultimately, the working group classifies an agent into one of five groups: Group 1, The agent is carcinogenic to humans; Group 2A, The agent is probably carcinogenic to humans; Group 2B, The agent is possibly carcinogenic to humans; Group 3, The agent is not classifiable as to its carcinogenicity to humans; and Group 4, The agent is probably not carcinogenic to humans. A more detailed description of these classifications can be found in Chapter 8 of this textbook. Overall, these IARC reviews contributes to the scientific evidence on which international and national health agencies set policies to reduce human exposure to occupational and environmental carcinogens, and to promote healthy lifestyles.

Summary

Epidemiology has evolved considerably over the past century and has made critical contributions to what we know about the role of occupational, environmental, lifestyle, medical and host factors in cancer etiology. New advancements in molecular and genetic technologies continue to emerge, and epidemiologists are working in transdisciplinary teams with laboratory and clinical scientists to apply these methods to identify individuals at high risk of developing cancer. These results will be helpful for informing who might benefit from enhanced screening or chemoprevention recommendations (such as anti-estrogen use for prevention of breast cancer). Regardless, rigorous epidemiologic methodology and careful assessment of causality remain the foundation on which public health policies and guidelines are established.

References

1 Greenwald P, Dunn BK. Landmarks in the history of cancer epidemiology. *Cancer Res* 2009;69(6):2151–62.

2 Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999–2010. *JAMA* 2012;307(5):491–7.

3 Carroll KK. Experimental evidence of dietary factors and hormone-dependent cancers. *Cancer Res* 1975;35(11):3374–83.

4 Boyle T, Fritschi L, Heyworth J, Bull F. Long-term sedentary work and the risk of subsite-specific colorectal cancer. *Am J Epidemiol* 2011;173(10):1183–91.

5 Committee on Gynecologic Practice. ACOG Committee Opinion No. 434: induced abortion and breast cancer risk. *Obstet Gynecol* 2009;113(6):1417–8.

6 Folsom AR, Kushi LH, Anderson KE, *et al*. Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. *Arch Intern Med* 2000;160(14):2117–28.

7 Belanger CF, Hennekens CH, Rosner B, Speizer FE. The nurses' health study. *Am J Nurs* 1978;78(6):1039–40.

8 Calle EE, Rodriguez C, Jacobs EJ, *et al*. The American Cancer Society Cancer Prevention Study II Nutrition Cohort: rationale, study design, and baseline characteristics. *Cancer* 2002;94(2):500–11.

9 Doll R, Hill AB. The mortality of doctors in relation to their smoking habits; a preliminary report. *Br Med J* 1954;1(4877):1451–5.

10 Henley SJ, Thun MJ, Chao A, Calle EE. Association between exclusive pipe smoking and mortality from cancer and other diseases. *J Natl Cancer Inst* 2004;96(11):853–61.

11 Hildebrand JS, Patel AV, McCullough ML, *et al*. Coffee, tea, and fatal oral/pharyngeal cancer in a large prospective US cohort. *Am J Epidemiol* 2013;177(1):50–8.

12 Ioannidis JP, Trikalinos TA. The appropriateness of asymmetry tests for publication bias in meta-analyses: a large survey. *CMAJ* 2007;176(8):1091–6.

13 Ferguson CJ, Brannick MT. Publication bias in psychological science: prevalence, methods for identifying and controlling, and implications for the use of meta-analyses. *Psychol Methods* 2012;17(1):120–8.

14 National Cancer Institute Cohort Consortium. Available from: http://epi.grants.cancer.gov/Consortia/cohort.html (accessed 11 May 2017).

15 US Department of Health EaW, Public Health Service. *Smoking and Health: Report of the Advisory Comittee to the Surgeon General of the Publc Health Service*. United States Public Health Service, Office of the Surgeon General, Washington, D.C., 1964.

16 Hill AB. The environment and disease: association or causation? *Proc Roy Soc Med* 1965;58:295–300.

17 IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Available from: http://monographs.iarc.fr (accessed May 11 2017).

3

Socioeconomic Inequalities in Cancer Incidence and Mortality

Gopal K. Singh[1] *and Ahmedin Jemal*[2]

[1] *US Department of Health and Human Services, Health Resources and Services Administration, Office of Health Equity, Rockville, Maryland, USA*
[2] *Surveillance and Health Services Research, American Cancer Society, Atlanta, Georgia, USA*

Introduction

Monitoring health inequalities according to socioeconomic status (SES) and other key demographic factors such as race/ethnicity and rural/urban residence has long been an important focus of epidemiologic and public health research in the United States (US) [1–3]. Reduction of health inequalities by these characteristics has been an integral part of the national health policy initiative in the US for the past four decades [1, 2]. Previous research has shown the dynamic nature of socioeconomic disparities in cancer rates as the association between SES and incidence and mortality from major cancers has changed markedly during the past five decades [4–6]. Temporal patterns have changed largely as a result of differential rates of decline or increase in mortality among those in various SES or deprivation groups and changing socioeconomic patterns in major cancer risk factors such as smoking, diet, obesity, and physical inactivity [3–6].

Association between cancer mortality or incidence and SES, whether measured at the individual- or area-level, varies for specific cancers [3–15]. Area-based association is determined using cancer and socioeconomic data aggregated to a community or geographic area of residence such as counties or census tracts. Contemporary data indicate that higher SES is associated with lower rates of lung, stomach, liver, cervical, esophageal, and oropharyngeal cancer and higher rates of breast cancer and melanoma [3–17]. The major behavioral determinants of cancer, such as smoking, diet, alcohol use, obesity, physical inactivity, reproductive behavior, occupational and environmental exposures, and cancer screening are themselves substantially influenced by individual- and area-level socioeconomic factors [2, 3, 6, 14, 17–19].

Analyzing socioeconomic patterns in cancer mortality and incidence is important because it allows us to quantify cancer-related health disparities between the least and most advantaged socioeconomic groups and to identify areas or population groups that are at greatest risk of cancer diagnosis and mortality and who may therefore benefit from focused social and medical interventions [3, 6]. Such an analysis is also useful for tracking progress toward reducing health disparities in cancer as recent estimates of cancer disparities can be compared with those that prevailed in the previous decades [3, 6]. Comparison of cancer rates and trends across population groups or areas may provide important insights into the impact of cancer control interventions, such as smoking cessation, cancer screening, physical activity campaigns, and cancer treatment [3–6, 9].

Reliable individual-level SES data for all ages, particularly for ages 65 and older, are lacking on US death certificates, which provide the basis for computing cancer mortality rates for various demographic groups and geographic areas [3–6, 9, 20]. Individual-level data on education, income, and occupation are not available for cancer patients in the SEER database, which has been the primary source of data on cancer incidence, stage at diagnosis, treatment, and survival patterns in the US for the past four decades [6, 9, 15, 21]. Given such data limitations, population-based studies of socioeconomic disparities in cancer rates in the US have generally utilized area-based socioeconomic data linked to both individual- and aggregate-level cancer data [3–6, 9, 13, 16, 17]. Recent linkages of the census and Current Population Survey records with the National Death Index and cancer patient medical records have led to the development of the National Longitudinal Mortality Study (NLMS) and the SEER-NLMS Record Linkage Study [10, 15, 22, 23]. These longitudinal, cohort databases allow the estimation and analysis of cancer incidence, mortality, disease stage, and survival patterns according to individual-level socioeconomic characteristics [10, 15, 22, 23].

In this chapter, we examine temporal area–socioeconomic disparities in US all-cancer, lung, colorectal, prostate, breast, and cervical cancer mortality, and present area–socioeconomic patterns in cancer incidence using the SEER database. Using the linked NLMS data, we also present socioeconomic inequalities in mortality and incidence from all cancers combined and lung, colorectal, prostate, breast, cervical, stomach, liver, and esophageal cancers. Lung cancer is the leading cause of cancer mortality, and colorectal, prostate, and breast cancers are among the most commonly diagnosed cancers; these sites, along with stomach, liver, esophageal, and cervical cancer, contribute greatly to the overall cancer burden in the US [3, 20, 21, 24, 25].

The American Cancer Society's Principles of Oncology: Prevention to Survivorship, First Edition. Edited by The American Cancer Society.

Taken together, these cancers account for more than half of all cancer deaths and new cancer cases in the US [21, 24, 25]. Additionally, breast, cervical, colorectal, and prostate cancers are the cancer sites for which established screening tests have been introduced into the general population [3, 6, 25].

Data Sources and Methodology

Socioeconomic disparities in cancer mortality and incidence are examined by using three national data sources: the national mortality database, the NLMS, and the SEER cancer registry database [2, 3, 10, 20–22]. Since the vital-statistics-based national mortality database lacks reliable socioeconomic data for all ages, socioeconomic patterns in mortality were derived by linking census-based county-level socioeconomic data with the national mortality statistics [3–6, 9, 16]. A composite socioeconomic deprivation index, developed for various census time periods, was used to define the socioeconomic standing of all 3,141 counties in the US and census tracts in the 11 SEER cancer registries. Indicators of education, occupation, wealth, income distribution, unemployment rate, poverty rate, and housing quality were used to construct the deprivation index [3–5, 26]. Higher index scores denote higher levels of SES and lower levels of deprivation. Index scores were categorized into five area groups, ranging from being the most deprived (first quintile) to the least disadvantaged (fifth quintile) county or neighborhood groups [3–6, 26]. Details of the US deprivation index are provided elsewhere [3–5, 26].

Cancer mortality and incidence rates for each county, area deprivation, or individual-level socioeconomic group were age-adjusted by the direct method using the age-composition of the 2000 US population as the standard [6, 15, 20, 21]. Log-linear models were used to estimate annual rates of change in SES-specific mortality trends from 1950 to 2013 [16, 17]. Socioeconomic disparities in mortality and incidence, estimated separately for men and women, were described by rate ratios (relative risks) and rate differences (absolute inequalities), which were tested for statistical significance at the 0.05 level. When using the NLMS data, cohort-based incidence and mortality rates were computed using the person-years approach [15, 22].

Socioeconomic Disparities in Cancer Mortality Based on Aggregate County-Level Data

Figure 3.1 shows changing socioeconomic patterns in US all-cancer mortality rates over time. Between 1950 and 2007, there was a gradual change from higher cancer mortality in high-SES areas to higher mortality in low-SES areas. The correlation between area-level SES and all-cancer mortality rates changed

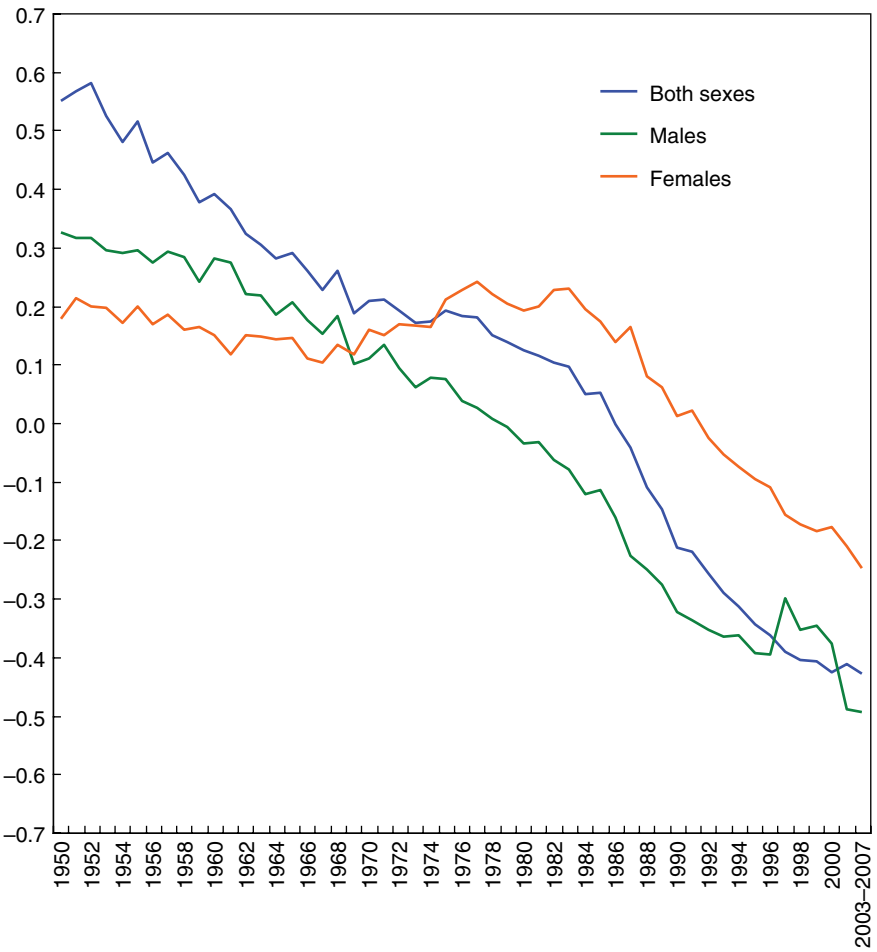

Figure 3.1 Weighted correlations between area socioeconomic index and county-level age-adjusted cancer mortality rates, US, 1950–2007.

from +0.55 in 1950 to −0.43 in 2007. The relationship between SES and all-cancer mortality rates reversed earlier for males than females. Between 1950 and 2007, the correlation changed from +0.33 to −0.50 for males and from +0.18 to −0.25 for females. Currently, there is a consistent, inverse SES gradient in all-cancer mortality rates. From 2009 to 2013, those in the most-deprived groups had a 19% higher mortality rate than those in the least-deprived group. Socioeconomic gradients and absolute inequalities are steeper for men than for women. Compared to their counterparts in the least-deprived group, men had 25% higher mortality and women 11% higher mortality in the most-deprived group (data not shown).

Socioeconomic trends in lung cancer mortality differed for men and women. From 1950 to 1974, men in more affluent areas had higher lung cancer mortality than those in more deprived areas. Socioeconomic differentials reversed and started to widen by the early 1980s for men and by 2002 for women (Figure 3.2). From 2009 to 2013, socioeconomic

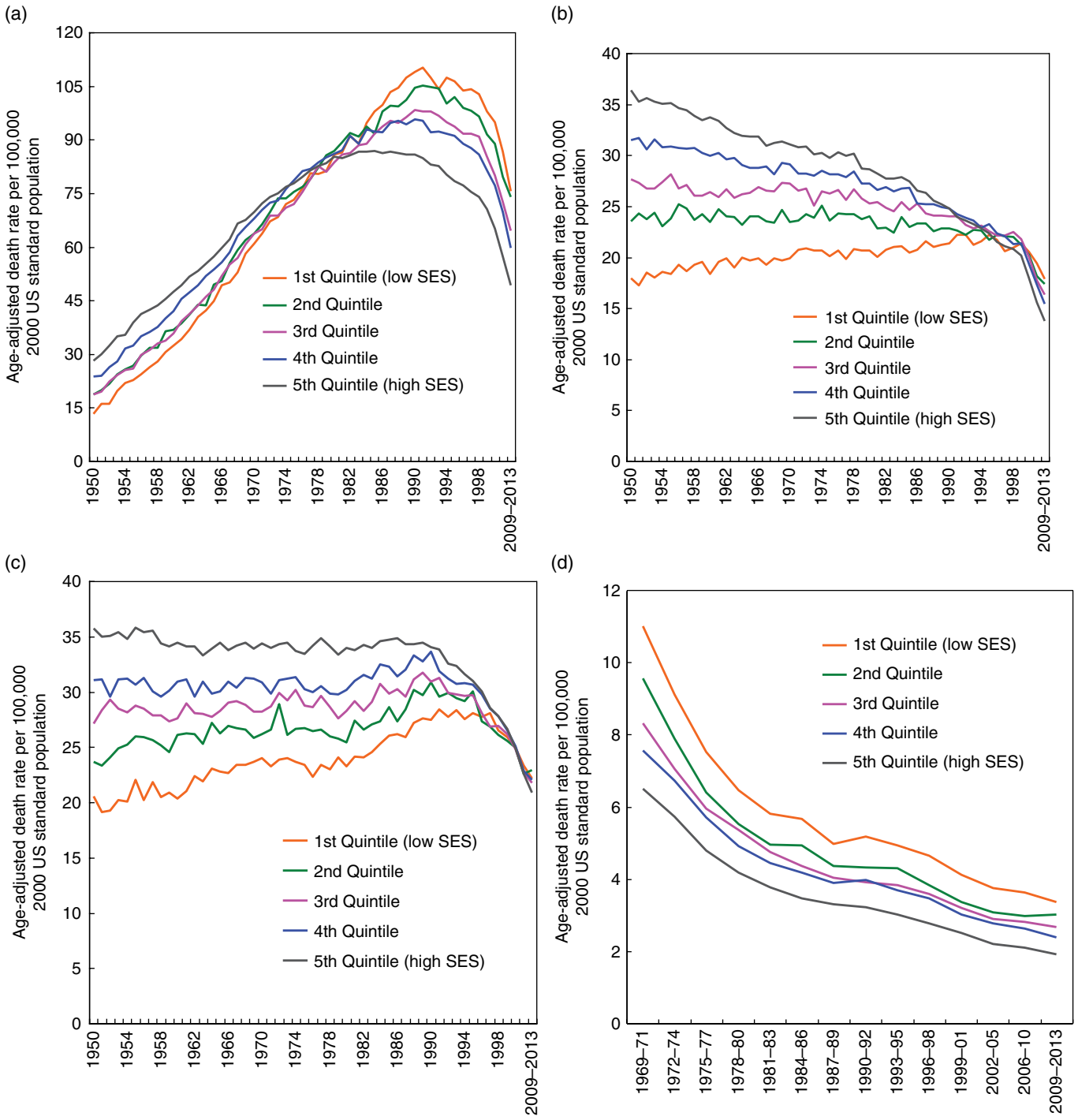

Figure 3.2 Trends in (a) lung, (b) colorectal, (c) female breast, and (d) cervical cancer mortality rates by area socioeconomic deprivation index, US, 1950–2013.

inequalities in lung cancer mortality were larger and more consistent for men than for women. Men and women in the most-deprived group had 54% and 16% higher lung cancer mortality rates than their most affluent counterparts, respectively.

From 1950 to 1990, lung cancer mortality among men increased at 5.1% per year in the most-deprived group, significantly faster than the annual rate of increase of 2.8% for men in the most-affluent group. Moreover, from 1991 to 2013, lung cancer mortality fell at a more rapid pace for men in the more affluent groups (2.53% annually in the most-affluent group vs 1.61% in the most-deprived group). From 1950 to 2013, there were marked increases in lung cancer mortality among women in all deprivation groups, although the annual rate of increase in mortality was somewhat higher in the more deprived groups.

Socioeconomic trends in US colorectal cancer mortality changed dramatically between 1950 and 2013, with the positive SES gradients in mortality narrowing over time and then reversing at the turn of the twenty-first century (Figure 3.2). From 2009 to 2013, there was an inverse SES gradient, with those in the two most-deprived groups having 30% and 27% higher rates of colorectal cancer mortality than their most-affluent counterparts, respectively. From 1950 to 2013, colorectal cancer mortality increased at 0.25% per year in the most-deprived group, whereas it fell consistently in the higher SES groups; the annual rates of decline in mortality in the two most-affluent groups were 1.24% and 0.87%, respectively. Socioeconomic trends in colorectal cancer mortality were generally similar for men and women.

Prostate cancer mortality did not vary appreciably over time by area deprivation. However, during the past two decades, an inverse socioeconomic gradient in prostate cancer mortality was found, with mortality rates falling similarly in all deprivation groups between 1995 and 2013. From 2009 to 2013, men in the most-deprived group had 19% higher prostate cancer mortality than men in the most-affluent group.

Socioeconomic differences in breast cancer mortality have narrowed over time and appear to have reversed during the past decade, as higher deprivation levels are now associated with higher breast cancer mortality rates. The reversal of the trend has occurred as breast cancer mortality rates have declined over time for more affluent women and have increased or remained stable for women in more deprived groups. From 1950 to 2013, the breast cancer mortality rate increased by 0.54% annually for women in the most-deprived group, while it decreased by 0.48% per year for women in the most-affluent group. From 2009 to 2013, women in the most-deprived group had 6% higher mortality than their most-affluent counterparts. In 1950, women in the most-deprived group had 42% lower mortality than women in the most-affluent group (Figure 3.2).

Cervical cancer mortality rates in the US have declined consistently for the past six decades, and rates of mortality decline among women in all deprivation groups have been similar. However, despite the decline, substantial inverse socioeconomic gradients in cervical cancer mortality have persisted. From 2009 to 2013, women in the two most-deprived groups had 76% and 58% higher cervical cancer mortality rates, respectively, than their most-advantaged counterparts, a pattern of inequality that also characterized the trends from 1969 to 2010 (Figure 3.2).

Socioeconomic Disparities in Cancer Mortality Based on Individual-level Data

All-cancer mortality rates among men varied consistently by individual-level education and income levels. Men with less than a high school education had 70% higher cancer mortality than those with a college degree, whereas men below the poverty level had 43% higher cancer mortality than men with incomes ≥600% of the poverty level (Table 3.1). Although higher cancer mortality was associated with lower education and income levels in women, the gradients were less marked in women than in men. Socioeconomic inequalities in lung cancer mortality, especially among men, were very marked, with men with less than a high school education having 2.4 times higher lung cancer mortality, and those below the poverty level having 1.8 times higher mortality than their more educated and affluent counterparts. Education and income were also inversely related to female lung cancer mortality, with education having a stronger impact than income.

Both education and income were significantly associated with colorectal cancer mortality; men with less than a high school education had 53% higher mortality risk than those with a college degree. Both prostate and breast cancer mortality rates did not vary by education and income levels. There were steep education and income gradients in cervical cancer mortality, with women with less than a high school education and below the poverty level having 2.5 and 4.4 times higher cervical cancer mortality than women with the highest education and income levels, respectively. Rates of stomach, liver, and esophageal cancer mortality also varied substantially and inversely by education and income levels (Table 3.1). More recent follow-up data from the NLMS need to be analyzed to determine if the magnitude of SES disparities in major cancers has increased.

Socioeconomic Disparities in Site-Specific Cancer Incidence

The patterns of socioeconomic disparities in cancer incidence are generally similar to those in cancer mortality [6, 9]. According to the analysis of the 1988–1992 SEER data, higher neighborhood SES was associated with higher cancer incidence rates for the total population and for women in particular (data not shown) [6]. The male lung cancer incidence rate was 61% higher in the most-deprived than the least-deprived neighborhoods. Lung cancer incidence in women did not vary by neighborhood deprivation. Prostate cancer incidence rates increased with increasing neighborhood SES; men in the most-affluent neighborhoods had a 36% higher prostate cancer incidence rate than men in the most-deprived neighborhoods. Higher neighborhood SES levels were associated with higher breast cancer incidence rates. Women in the most-affluent neighborhoods had 47% higher breast cancer incidence rates than their most-disadvantaged counterparts. Cervical cancer incidence increased consistently with increasing deprivation levels. Women in the most-deprived neighborhoods had a 2.7 higher risk of cervical cancer than women in the most-affluent neighborhoods. Higher

Table 3.1 Age-adjusted all-cancer and site-specific cancer mortality rates per 100,000 population and relative risk (RR) of mortality among those aged ≥25 years by educational attainment and poverty status.

	Age-adjusted mortality			Age-adjusted mortality			Age-adjusted mortality		
	Rate	SE	RR	Rate	SE	RR	Rate	SE	RR
	All cancers combined, male			**All cancers combined, female**			**Lung cancer, male**		
Educational attainment (years)									
<12	418.15	4.14	1.57*	251.18	3.05	1.23*	153.05	2.53	2.36*
12	351.49	4.44	1.32*	228.32	2.59	1.12*	111.67	2.38	1.72*
13–15	334.57	6.92	1.26*	218.20	4.30	1.07	95.40	3.53	1.47*
16+	265.88	5.34	1.00	204.40	4.66	1.00	64.94	2.56	1.00*
Poverty status (ratio of family income to poverty threshold)									
<100%	425.92	8.01	1.43*	264.01	4.60	1.26*	151.81	4.82	1.83*
100–150%	418.24	7.99	1.40*	245.02	5.06	1.17*	146.93	4.83	1.77*
150–200%	396.53	7.47	1.33*	235.06	4.93	1.12*	138.87	4.44	1.67*
200–400%	360.04	3.99	1.21*	225.60	2.74	1.08*	115.51	2.20	1.39*
400–600%	320.14	5.35	1.07	216.11	3.90	1.03	99.99	2.86	1.20*
Above 600%	298.19	6.15	1.00	208.97	4.60	1.00	83.04	3.06	1.00
	Lung cancer, female			**Colorectal cancer, male**			**Colorectal cancer, female**		
Educational attainment (years)									
<12	58.82	1.51	1.83*	40.81	1.25	1.53*	29.21	0.95	1.16
12	52.84	1.22	1.65*	40.11	1.52	1.51*	25.91	0.89	1.03
13–15	46.06	1.98	1.44*	37.27	2.33	1.40*	24.45	1.46	0.97
16+	32.08	1.87	1.00	26.65	1.70	1.00	25.12	1.67	1.00
Poverty status (ratio of family income to poverty threshold)									
<100%	58.97	2.24	1.28*	39.54	2.41	1.24*	29.59	1.44	1.29*
100–150%	54.19	2.43	1.17*	41.59	2.47	1.31*	29.30	1.62	1.28*
150–200%	49.28	2.26	1.07	41.12	2.39	1.29*	28.20	1.63	1.23
200–400%	48.83	1.27	1.06	39.08	1.33	1.23*	25.75	0.93	1.12
400–600%	48.70	1.80	1.05	37.16	1.88	1.17	26.05	1.39	1.13
Above 600%	46.18	2.13	1.00	31.77	2.05	1.00	22.96	1.56	1.00
	Prostate cancer			**Breast cancer, female**			**Cervical cancer**		
Educational attainment (years)									
<12	49.50	1.29	1.03	39.76	1.30	0.89	6.76	0.58	2.49*
12	43.49	1.74	0.91	41.58	1.11	0.93	3.87	0.34	1.42
13–15	48.18	2.92	1.00	42.24	1.86	0.94	2.76	0.46	1.01
>16	47.97	2.49	1.00	44.88	2.12	1.00	2.72	0.53	1.00
Poverty status (ratio of family income to poverty threshold)									
<100%	45.36	2.51	0.95	44.84	1.98	1.13	8.34	0.90	4.39*
100–150%	49.93	2.52	1.04	41.39	2.22	1.04	6.29	0.88	3.31*
150–200%	47.62	2.53	0.99	42.70	2.17	1.08	4.99	0.79	2.63*
200–400%	49.60	1.58	1.03	41.78	1.19	1.05	3.88	0.36	2.04*
400–600%	43.90	2.22	0.92	38.86	1.64	0.98	2.61	0.42	1.37
Above 600%	47.95	2.78	1.00	39.69	1.98	1.00	1.90	0.45	1.00

(*Continued*)

Table 3.1 (Continued)

	Age-adjusted mortality			Age-adjusted mortality			Age-adjusted mortality		
	Rate	SE	RR	Rate	SE	RR	Rate	SE	RR
	Stomach cancer, male			**Stomach cancer, female**			**Liver and IBD cancer, male**		
Educational attainment (years)									
<12	14.50	0.76	1.92*	7.38	0.51	1.74*	8.47	0.60	1.34*
12	9.15	0.70	1.21	4.85	0.38	1.14	6.60	0.61	1.05
13–15	8.98	1.12	1.19	3.80	0.57	0.89	7.98	1.04	1.27
16+	7.56	0.92	1.00	4.25	0.68	1.00	6.30	0.76	1.00
Poverty status (ratio of family income to poverty threshold)									
<100%	14.00	1.44	1.65*	6.47	0.69	1.20*	10.47	1.27	1.43*
100–150%	13.89	1.41	1.64*	6.64	0.81	1.24*	8.43	1.16	1.15
150–200%	11.94	1.30	1.41*	6.03	0.79	1.12*	7.46	1.05	1.02
200–400%	11.61	0.71	1.37*	5.39	0.42	1.00*	6.74	0.53	0.92
400–600%	7.69	0.82	0.91	4.18	0.57	0.78	6.29	0.72	0.86
Above 600%	8.46	1.03	1.00	5.37	0.75	1.00	7.34	0.90	1.00
	Liver and IBD cancer, female			**Esophageal cancer, male**			**Esophageal cancer, female**		
Educational attainment (years)									
<12	4.20	0.40	1.84*	10.22	0.67	1.89*	3.02	0.34	1.24
12	3.13	0.30	1.37	10.13	0.71	1.88*	2.25	0.26	0.93
13–15	3.08	0.52	1.35	8.01	0.98	1.48*	2.76	0.49	1.14
16+	2.28	0.50	1.00	5.40	0.67	1.00	2.43	0.52	1.00
Poverty status (ratio of family income to poverty threshold)									
<100%	4.52	0.59	1.91*	13.77	1.48	1.90*	3.39	0.55	1.22
100–150%	5.25	0.74	2.22*	9.59	1.27	1.32	2.67	0.50	0.96
150–200%	3.44	0.58	1.45	10.72	1.24	1.48	3.32	0.60	1.19
200–400%	2.77	0.31	1.17	8.85	0.61	1.22	2.12	0.26	0.76
400–600%	2.83	0.45	1.19	7.42	0.75	1.02	2.19	0.40	0.78
Above 600%	2.37	0.49	1.00	7.24	0.87	1.00	2.79	0.54	1.00

Source: 1979–1998 National Longitudinal Mortality Study.
Mortality rates are age-adjusted to the 2000 US standard population.
* $P < 0.05$.

deprivation levels were associated with higher rates of stomach, liver, and esophageal cancer incidence. Compared to their most-affluent counterparts, those in the most-deprived neighborhoods had 64%, 90%, and 93% higher rates of stomach, liver, and esophageal cancer incidence, respectively.

The linked SEER-NLMS data show slightly different individual-level SES patterns in cancer incidence than the area-level patterns [15]. This is partly due to the different time periods covered in the two databases. Overall cancer incidence rates were 12–13% higher among the poor and those with less than a high school education compared to their most-educated or affluent counterpart [15]. Men and women with less than a high school education had 3.0 and 2.0 times higher lung cancer incidence rates, respectively than those with a college degree [15]. Those below the poverty level had 52–72% higher lung cancer incidence rates than their counterparts with incomes at ≥600% of the poverty level [15]. Individuals with the lowest education and income levels had higher colorectal cancer incidence rates than their most-advantaged counterpart [15]. Higher education and income levels were associated with higher prostate and breast cancer incidence rates; men and women with less than a high school education had 21% and 26% lower prostate and breast cancer incidence rates, respectively, than their counterparts with a college degree [15]. Consistent with the neighborhood pattern, women with less than a high education had 3.2 times higher cervical cancer incidence than those with a college degree [15].

Summary and Conclusions

In this chapter, we have examined socioeconomic disparities in mortality and incidence from all cancers combined and from major cancers using both aggregate community- and individual-level data. Analysis of long-term trends and contemporary SES inequalities in cancer adds to the voluminous literature on

Table 3.2 Prevalence (%) of current smoking, obesity, and cancer screening by education and income/poverty level in the United States.

	Current smoking (male)	Current smoking (female)	Obesity (male)	Obesity (female)	Mammogram within the past 2 years[1]	Pap test within the past 3 years[1]	Ever had a Colonoscopy[1]
Educational attainment (years)							
Total	17.9	14.4	31.6	30.8	73.2	82.7	65.3
<High school	27.2	20.1	31.7	37.1	63.1	74.1	50.6
High school graduate	25.7	20.1	36.0	34.8	68.7	76.2	62.6
Some college/associate degree	19.7	17.0	37.0	35.2	73.7	82.4	66.4
College graduate +	7.2	5.7	23.8	21.8	80.2	89.0	73.4
Poverty status (ratio of family income to poverty threshold)							
<100%	34.1	26.4	31.7	40.4	64.1	76.8	48.0
100–200%	26.2	19.5	31.5	38.2	64.3	77.9	55.4
200–300%	19.8	15.9	33.9	33.1	69.1	80.5	64.4
300–400%	18.9	12.3	33.8	32.3	74.3	83.3	69.8
400–500%	13.3	9.4	31.7	26.7	78.0	87.4	70.7
Above 500%	9.7	7.8	30.0	21.6	81.0	88.2	73.7

Source: The 2014–2015 National Health Interview Survey.
Note: ages were ≥ 40 years for mammography, 25–64 years for Pap test, ≥50 years for colonoscopy, and ≥25 years for obesity and smoking.
[1] 2015 National Health Interview Survey, Cancer Control Supplement.

SES and cancer disparities. Socioeconomic patterns in US cancer mortality have reversed over time, and the continued widening of the inverse socioeconomic gradients in all-cancer, lung, and colorectal cancer mortality appears to be consistent with those observed for all-cause and cardiovascular disease mortality in the US [2, 3, 26].

Socioeconomic inequalities in cancer incidence and mortality in the US are particularly marked in lung, cervical, stomach, and liver cancer [3–6, 9, 10, 15]. Substantial socioeconomic disparities exist not only in cancer incidence and mortality but also in stage at cancer diagnosis and survival [3, 6, 9, 15, 23]. Such inequalities have been shown to exist for Whites, Blacks, and other major racial/ethnic groups such as Hispanics, Asians/Pacific Islanders, and American Indians/Alaska Natives [3, 6, 9].

Socioeconomic disparities in incidence and mortality from various cancers may reflect differences in smoking prevalence, dietary fat intake, obesity, physical inactivity, reproductive factors (e.g., delayed childbearing, childlessness, and breastfeeding), alcohol use, human papillomavirus (HPV) infection, cancer screening, and healthcare factors [3, 5, 6, 11, 14, 19, 27]. Higher smoking rates are more prevalent among men and women in lower SES groups and in more deprived areas (Table 3.2) [2, 5, 16, 19, 28]. Smoking rates have fallen more rapidly for those in higher SES groups, which largely explains temporal SES trends in all-cancer and lung cancer mortality rates [2, 4–6]. Dietary factors such as fat intake, red meat consumption, and high calorie intake have been mentioned as risk factors for colorectal, prostate, and breast cancer and inequalities in both incidence and mortality may in part reflect differences in these factors [3, 5, 6, 14]. Studies have found higher consumption of lower-quality diets and energy-dense foods and lower intakes of fruits and vegetables among lower SES groups but higher total calorie and fat intake among higher SES groups [2, 3, 18]. The higher prostate and breast cancer incidence rates in the more advantaged groups may partly reflect their higher utilization of screening.

Disparities in healthcare factors play a prominent role in producing socioeconomic disparities in mortality from colorectal, prostate, breast, and cervical cancer. Low-SES individuals and residents of more deprived neighborhoods have substantially higher rates of late-stage diagnoses of lung, colorectal, prostate, breast, and cervical cancer and significantly lower rates of cancer survival than their counterparts from more affluent neighborhoods or SES backgrounds [6, 9, 15, 23, 29–35]. Lack of health insurance, limited access to care, and lower rates of regular pap smear, mammography, and colorectal cancer screening among lower SES individuals (as shown in Table 3.2) and among residents of more disadvantaged areas may account for their higher rates of late-stage cancer diagnoses [2, 3, 6, 31–33]. However, lower cancer survival rates among the disadvantaged may not only reflect their higher rates of late-stage cancer diagnoses, but also less favorable cancer treatment or medical care [3, 6, 33].

Research suggests that SES and area deprivation levels do not fully account for racial/ethnic disparities in cancer incidence, mortality, and outcomes in the US [3, 6, 9, 10, 13]. For example, within each deprivation group, Blacks have higher all-cancer mortality rates than Whites. Indeed, the overall cancer mortality and incidence rates for Blacks in the most-affluent group are similar to or exceed those for Whites in the most-deprived group [3, 6]. Within each SES or deprivation group, black women have approximately two times higher cervical cancer mortality and 50% higher breast cancer mortality than white women [3, 6]. Black men in each deprivation group have at least two times higher prostate cancer mortality rates than their

white counterparts [3, 6]. Such marked racial inequalities may exist partly because Blacks are socially and materially worse off than Whites across different socioeconomic strata [2, 3]. Moreover, they are more likely to be disadvantaged than Whites in health-risk behaviors, healthcare access and use, and cancer treatment and survival within each deprivation group [2, 3, 6].

Detection of cancer at an early, localized stage may be considered a marker for access to healthcare and preventive health services, including cancer screening [6, 25]. Studies have shown significant black–white and socioeconomic disparities in stage at cancer diagnosis [6, 9]. Within each SES or deprivation group, Blacks have a higher likelihood than Whites of being diagnosed with advanced-stage colorectal, prostate, breast, and cervical cancers [6, 9]. Additionally, even after controlling for stage at diagnosis, Blacks, in each deprivation group, have significantly lower survival rates from colorectal, prostate, breast, and cervical cancer than Whites [6, 9, 36–38].

Comparison with International Patterns

Although studies of cancer inequalities vary widely in their use of socioeconomic measures and coverage of time periods, socioeconomic disparities in US cancer mortality and incidence are generally consistent with patterns observed for the other industrialized countries [3, 11, 14]. Consistent with the US pattern, all-cancer mortality rates in England from 2004 to 2006 increased consistently by area deprivation levels [39]. In several European populations, cancer mortality rates are significantly higher among both males and females in lower education groups [11]. Consistent with the US pattern, lung cancer mortality rates for both men and women in Canada increased in relation to deprivation levels [40]. Higher lung cancer mortality rates are found among men in lower SES groups in many European countries [11, 41]. Inverse socioeconomic gradients in US colorectal cancer mortality rates are compatible with occupational and educational patterns in mortality observed among several European countries [11, 42]. Marked socioeconomic disparities in US cervical cancer mortality reported here are generally consistent with those shown for other industrialized countries. An approximately twofold higher cervical cancer mortality was found among women in low- rather than high-SES groups in a study that compared inequalities in various low/middle income countries, North America, and Europe, although the magnitude of socioeconomic inequalities was greater in North America than in Europe [39, 43, 44].

Caution should be exercised when comparing area-based SES effects with individual-level effects. Area socioeconomic measures are qualitatively different from individual-level SES and should be viewed as community, neighborhood, or social structural influences. Although area-based socioeconomic patterns in cancer mortality and incidence reported here are generally consistent with those at the individual level, the area-level effects are smaller in magnitude than individual-level SES effects [3, 6–10, 15]. This may partly be due to the compositional heterogeneity of the counties examined, which are socioeconomically more heterogeneous than census tracts [3–6]. Unfortunately, the national mortality database does not include census-tract geocodes because of confidentiality concerns [3, 20].

Cancer is the leading cause of mortality in the US for those aged <85 years and is the most prominent cause of death in terms of years of potential life lost [2, 3, 20]. The extent of socioeconomic disparities in cancer mortality and incidence reported here contributes greatly to overall health inequalities in the US. With large socioeconomic inequalities in smoking, obesity, and physical inactivity among young people continuing to persist, inequalities in US cancer mortality and incidence are not expected to diminish in the foreseeable future [2, 3]. Efforts to reduce cancer disparities, especially those in lung cancer, therefore might include tobacco control policies at the national and local levels that place greater smoking restrictions or legislate against smoking in public places, ban tobacco marketing, reduce tobacco availability, increase financial and other barriers to smoking, and provide targeted smoking cessation programs for those with low SES or in disadvantaged areas [3, 6]. Healthcare inequalities in the US have also risen in both absolute and relative terms and socioeconomic disparities in stage at diagnosis and survival from major cancers have persisted [3, 6]. These trends would also imply continuation of socioeconomic inequalities in cancer mortality and incidence. Health policies therefore should also enhance access to cancer screening programs among socioeconomically disadvantaged populations or those in rural and medically underserved areas. Lastly, social policy measures aimed at improving the broader social determinants, such as general living conditions and the social and physical environments, are needed to tackle health inequalities, including those in cancer mortality and incidence [3, 6].

The views expressed are the authors' and not necessarily those of the Health Resources and Services Administration or the US Department of Health and Human Services.

References

1 US Department of Health and Human Services. Healthy People 2020. Available from: http://www.healthypeople.gov/2020/default.aspx (accessed 11 May 2017).

2 National Center for Health Statistics. *Health, United States, 2011 with Special Feature on Socioeconomic Status and Health*. Hyattsville, MD: US Department of Health and Human Services, 2012.

3 Singh GK, Williams SD, Siahpush M, Mulhollen A. Socioeconomic, rural-urban, and racial inequalities in US cancer mortality: part I – all cancers and lung cancer and Part II–colorectal, prostate, breast, and cervical cancers. *J Cancer Epidemiol* 2012:1–27.

4 Singh GK, Miller BA, Hankey BF, Feuer EJ, Pickle LW. Changing area socioeconomic patterns in U.S. cancer mortality, 1950–1998: part I - all cancers among men. *J Natl Cancer Ins 2002*; 94(12):904–15.

5 Singh GK, Miller BA, Hankey BF. Changing area socioeconomic patterns in U.S. cancer mortality, 1950–1998: part II - lung and colorectal cancers. *J Natl Cancer Inst* 2002;94(12):916–25.