2. Cancer Incidence and Mortality

Contents

LIST OF TABLES

LIST OF FIGURES

2

Cancer Incidence and Mortality

INTRODUCTION

In 1979, cancer killed more than 400,000 Americans (254) and 765,000 new serious cancers' were diagnosed (6) (see table 3). Over 3 million Americans alive today have had a diagnosed cancer. Cancer accounts for about *20* percent of total U.S. mortality, second only to heart diseases, which are responsible for about 38 percent of deaths. Moreover, cancer is the number one killer of adult Americans, ages 25 to 44 (see table 4).

Of equal or greater importance than knowing the number of cancers and cancer deaths is the matter of whether age-specific cancer *rates* are increasing, decreasing, or remaining constant. Are people of a given age at greater risk of developing cancer today than were people of that age in the past? This question of changing rates bears on whether aspects of the modern environment, largely introduced within the last two to four decades, might be causing today's cancers. If so, preventive efforts should start by identifying these elements in the environment and modifying them. If most of the now common cancers have been common for a long time, it might suggest that the causes of cancer have not changed greatly. In that case, prevention might require changes in long-established aspects of the American lifestyle.

When seeking means to prevent cancer, special attention must be given to increases in cancers at particular sites. This attention is warranted because the increase indicates that the cause (or causes) might have been introduced recently and can presumably be identified and eliminated. However, to concentrate on a search for new agents to the exclusion of other causes may ignore the possibility of preventing pres-

'Not including nonmelanoma skin cancers, estimated at 400,000 per year.

Table 3.—Estimated New Cancer Cases and Deaths by Sex for Major Sites, 1981

					Females				Males			
	Total cases		Total deaths		Cases		Deaths		Cases		Deaths	
Site	Number	Percent of total	Number	Percent of total	Number	Percent of total	Number	Percent of total	Number	Percent of total	Number	Percent of total
Lung	122,000	15.0	105,000	25.0	34,000	8.3	28,000	14.5	88,000	21.8	77,000	33.8
Colon-rectum	120,000	14.7	54,900	13.1	62,000	15.0	28,700	14.9	58,000	14.4	26,200	11.5
Breast	110,900	13.6	37,100	8.8	110,000	26.7	36,800	19.1	900	0.2	300	0.1
Prostate	70,000	8.6	22,700	5.4	—	—	—	—	70,000	17.4	22,700	10.0
Uterus	54,000	6.6	10,300	2.5	54,000	13.1	10,300	5.4	—	—	—	—
Urinary	54,600	6.7	18,700	4.5	16,600	4.0	6,500	3.4	38,000	9.4	12,200	5.4
Oral (Buccal cavity and pharynx)	26,600	3.3	9,150	2.2	8,200	2.0	2,850	1.5	18,400	4.6	6,300	2.8
Pancreas	24,200	3.0	22,000	5.2	11,500	2.8	10,500		12,700	3.2	11,500	5.1
Leukemia	23,400	2.9	15,900	3.8	10,400	2.5	7,000	:: ;	13,000	3.2	8,900	3.9
Ovary	18,000	2.2	11,400	2.7	18,000	4.4	11,400	5.9	—	—	—	—
Skin	14,300	1.8	6,700	1.6	7,300	1.8	2,700	1.4	7,000	1.7	4,000	1.8
All others	177,000	21.7	106,150	25.3	80,000	19.4	47,750	24.8	97,000	24.1	58,400	25.7
Total	815,000		420,000		412,000		192,500		403,000		227,500	

[a] Invasive cancer only.
[b] Melanoma only.

NOTE: Estimates of new cancer cases and deaths are offered as a rough guide and should not be regarded as definitive

SOURCE: American Cancer Society, 1980.

Table 4.—Ranked Causes of Death by Life Stages, United States, 1977 (based on age-specific death rates)

Cause of death	Total population (all ages)	Age group: Infants (under 1)	Children (1-14)	Adolescents/ young adults (15-24)	Adults (25-44)	Adults (45-64)	Older adults (over 65)
Chronic diseases							
Cancer	2	—	3	5	1	2	2
Heart disease	1	—		6	2	1	1
Stroke	3	—	8[b]	9	8	3	3
Arteriosclerosis	9'	—	—	—	—	—	5
Bronchitis, emphysema and asthma	—	—	—	—	—	10	**8**
Diabetes mellitus	7	—	—	10	10	**8**	**6**
Cirrhosis of the liver	8	—	—	—	7	4	9
Infectious diseases							
Influenza and pneumonia	5	2	6	8	9	9	4
Meningitis	—	—	8[b]	—	—	—	—
Septicemia	—	3	—	—	—	—	—
Trauma							
Accidents:							
Motor vehicle	6	—	2	1	3	7	10
All other		4	1	2	4	5	7
Suicide	9[a]	—	10	**3**	**5**	**6**	**–**
Homicide	—	—	5	4	6	–	–
Developmental problems	—	1	*4*	*7*	—	—	—

[a] Rates for arteriosclerosis and suicide are at about the same level in the total Population.
[b] Rates for meningitis and stroke are at about the same level among children aged 1 to 14.

SOURCE Public Health Service (299)

ent-day cancers which are due to factors prevalent in the Western World since the last century or before.

Apart from whether or not cancer rates are changing, many variables contribute to the greater prominence accorded the disease today as compared to even a few decades ago. A major factor in its emergence is the sharp decrease in deaths from infectious diseases such as tuberculosis, dysentery, and diphtheria over the past 150 years. Before the mid-19th century, these diseases killed far more people than did chronic diseases. General improvements in living conditions, public sanitation, and nutrition began to reduce the rates of infectious diseases, and the decline was hastened by advances in biology and medicine early in the 20th century.

As the decades passed, these improvements have shifted the age structure of the population upward. As a result, there is a larger proportion of people over 65, and cancer risks have always been 10 or 100 times greater among them than among younger people. This increases the actual number of cases and deaths (crude incidence and crude mortality) but not necessarily the age-standardized cancer rates.

Second, cancer has become *relatively* more common as a cause of death because of the prevention or cure of other diseases. This phenomenon is illustrated by the mortality data for females in 1935 and 1975 (see table 5). Nonrespiratory cancer death rates decreased substantially, but the death rates from all other causes decreased even more. Therefore, the *percentage* of female deaths attributable to nonrespiratory cancer was greater in 1975 than ***40*** years earlier, even though female cancer risks had declined during that period.

Third, many cancers, which might previously have gone unnoticed, are now diagnosed both during medical treatment and in subsequent death certification. This change is especially pronounced among the elderly who today receive more medical attention than in premedicare years.

Table 5.–Death Rates per 1,000 Females, 1935 and 1975

Year	All causes except cancer	All nonrespiratory cancers	Respiratory tract cancers	All causes
1935 (1933-37)	11 .92[a] (87.6 °/o)[b]	1.65 (12.1°/0)	0.03 (0.2°/0)	13.60 (lOC°/o)
1975 (1973-77)	4.96 (78.80/o)	1.17 (18.670)	0.16 (2.50/o)	6.29 (lOOO/o)

[a]All ages, age-standardized to the U.S. 1970 census population.
[b]Percentage of rate for all causes

SOURCE: Doll and Peto (93).

Finally, cancer is discussed more openly in the media and among friends and relatives of cancer patients; public figures no longer try to conceal their diseases. Previously, such matters were often hushed up and the diagnosis perhaps withheld even from the victim. The jump in the reported incidence of breast cancer in 1974 and 1975 is attributed to the publicity surrounding Happy Rockefeller's and Betty Ford's breast cancer surgery. Greater public awareness led to more women being examined and the detection of more cancers, but the reported increase in those years is not considered to reflect a real increase in incidence.

Cancer has a major impact on the Nation's economy, both from the personal costs of treatment and lost income, and from public expenditures for screening programs, public education, and cancer research. In 1977, the most recent year for which information is available, direct costs for all cancers, including hospital care and physicians' services, amounted to about 7 percent of these costs for all illness (168). Indirect costs, based on a lost earnings approach (discounted at 6 percent), amounted to approximately 19 percent of total indirect costs (preliminary estimate; 168). The costs of cancer are not exclusively economic, though these are enormous. Social costs have taken on increasing prominence in recent years, and include more than the obvious pain and suffering of the victim. Relatives and friends of victims and care givers may suffer direct consequences of the victim's morbidity and mortality. Social isolation, economic dependence, lost personal and business opportunities, and many undesirable alterations in lifestyle are inevitable. Serious emotional and psychological problems requiring professional attention are not uncommon among victims and their family members, often producing irreversible changes in family structure and relationships.

A common measure of disease impact is the number of years of life lost due to premature mortality. This index takes into account both the number of deaths and the age at which people die. Therefore, the death of a younger person will contribute more person-years lost than will the death of a person who is closer to having lived to full life expectancy. Cancer accounted for approximately 19 percent of all deaths in 1975, and about 16 percent of all years of life lost (308), indicating that the average age of those who die from cancer is greater than the average age of those who die from the aggregate of all other causes of death.

Cancer Biology

The 200 or so human cancers are diseases in which some cells replicate out of control of normal growth processes. Such cells produce millions of similar self-replicating descendent cells. The cancerous state is reached when parts of this cell mass cross the boundaries of their "normal territory" and invade neighboring tissue directly, or travel to distant sites through the circulatory system. This event is called metastasis. The ability to invade or to metastasize characterizes these tumors as malignant, or cancerous, in contrast to benign tumors which remain confined to the tissues in which they arise, The possibility of complete surgical removal and cure is very high for benign tumors, with some notable exceptions, but declines precipitously with metastasis.

Over the past several years, a preponderance of evidence has accumulated supporting the view that cancers may arise from single cells, a conclusion reached after long debate. This evidence means that changes occurring in only 1 of the 10 trillion cells in the body can initiate a tumor. However, not all cells are at equal risk, which is obvious from the orders of magnitude differences in the occurrence of cancer at different sites (see table 3).

Certain characteristics of cells have been identified as contributing to the observed differences. The rates of cell growth and division in adults vary from organ to organ, from constant and fairly rapid multiplication, to none at all. Some common cancer sites, particularly the gastrointestinal tract, skin, and bone marrow, are those at which regular cell division occurs throughout life. The cells of other organs, for example those of the liver, and cells of the thyroid and other glands seldom multiply but retain that capability to repair tissue damage. They are important, but somewhat less common, cancer sites. At the other extreme, nerve cells have no capacity for multiplication at maturity, and cancers of these cells are not found in adults. This distinction is not a rigid one, but the rate of cell division contributes in some way, at least in many sites, to the total probability y of cancer development.

Another determinant of the frequency of cancer at different sites seems to be the degree of exposure of the cells to outside influences. More than half of all cancers arise in external epithelial cells which are in direct contact with the outside environment. The sites affected are mainly the skin and the linings of the gastrointestinal tract, lung, and cervix. This observation supports the view that most cancers are caused by the environment and are not simply inevitable consequences of the aging process. (For a general discussion of cancer biology, see Cairns (42).)

Cancer causation is thought to involve several steps. The simplest multistage process consists of two parts: initiation and promotion. Initiation is seen as occurring in response to an external stimulus and produces a cell that is "latently premalignant" (302). The initiation event may be a mutational change in the cell's genetic material, but the change is unexpressed, i.e., it causes no detectable change in the cell's growth pattern. "Initiated cells can remain as such for at least a large segment of the animal's life without being removed, destroyed, or otherwise harmed in any measurable way" (116)1,

In laboratory experiments, exposure of an initiated cell to another substance, a promoter, converts the cell to an "irreversible malignancy" (302). Promoters convert only initiated cells to tumor cells and have no lasting effect on noninitiated cells. (A review and discussion of current research about initiation and promotion can be found in 240.)

Many different agents may be initiators or promoters or both, and depending on an individual's exposures, years may elapse between initiation and promotion. The introduction of a potent initiator into society this year might cause no detectable increase in cancer for several years because of the rarity of the required subsequent promotion stage. Alternatively, a potent promoter that interacts with previously initiated cells might result in an increase being seen in a shorter time.

Classification of Neoplasms

There are three main classes of malignant neoplasms. Cancers of the epithelia, including the external epithelia and the internal epithelia which line various glands, are called *carcinomas.* These afflictions account for over 90 percent of all cancers, excluding the common, but not usually fatal, nonmelanoma skin cancers. The remaining cancers are either *sarcomas* (cancers of supportive tissues, e.g., bone, muscle, tendon, cartilage), or leukemias and lymphomas (cancers of circulating cells).

Cancers in these broad categories are conventionally recognized and recorded by the site at which they occur and by the cell type of the malignancy, and are regarded, for the most part, as separate disease entities. As knowledge of causation of specific cancers has improved, and definite associations elucidated between exposures and the development of cancers, it has become clear that sites are selectively affected by particular exposures and behaviors, and the

classification system has some validity for considering preventive strategies.

Reducing Cancer's Impact

There are three approaches to reduce cancer's impact: prevention, the ultimate goal; earlier detection; and improved treatment. The general consensus that most cancers are caused by extrinsic forces has led to the view that many cancers are preventable. Estimates of theoretically preventable cancers have reached as high as 90 percent of the total, though the practical limits undoubtedly will be lower.

Once identified, exposures to carcinogens may be reduced either through voluntary or regulatory methods. There has been one notable success among efforts to influence personal behavior—reduction in cigarette smoking among adults. The decrease is most notable among adult males, and can confidently be attributed to the publicity and attention given to adverse health effects of tobacco. Between 1965 and 1979, the proportion of adult male smokers dropped from 51 to 37 percent. The decline among women over the same period was much smaller, from 33 to 28 percent (287).

It is generally believed that American eating habits are healthier than they were early in this century and that some of the changes, though not specifically identified, may have spurred the decrease in stomach cancer rates. Future cancer-reducing changes in dietary habits may result from research into mechanisms by which dietary components cause or prevent cancers, or from epidemiologic observations of associations between dietary components and cancers.

About two dozen laws provide for the regulation of carcinogenic agents to protect public health. Through them, exposures to some 100 chemicals are controlled. (Ch. 6 describes laws and regulation.)

Early detection of cancers may improve overall survival rates when efficacious treatment is available. Localized cancers detected before they metastasize can be excised completely, leaving the patient with an excellent chance for survival. Between the early 1950's and the late 1960's, the proportion of prostate cancers diagnosed as "localized" increased from 48 to 63 percent. Over that period, the 5-year relative survival for prostatic cancer climbed from 43 to 57 percent. The overall relative survival rate is the ratio of the observed survival rate of the treated group to the expected survival rate for persons of the same age, sex, and race in the general population. Three elements may contribute to the apparent improvement. Part may be artifactual and result from detecting less serious tumors in the late 1960's, that, had they occurred in the early 1950's, would not have come to clinical attention. Some of the improvement probably resulted from better treatment. However, a major component of the gain resulted from detection of tumors at earlier stages when they could be more successfully treated (247).

Surgery, radiation therapy, and chemotherapy are the mainstays of cancer treatment. Vincent DeVita, Director of the National Cancer Institute (NCI), asserted that "approximately 41 percent of patients with the more serious forms of cancer are curable using therapies now available . . . . By cure we mean that a patient remains free of disease and has the same life expectancy as a person who never had cancer" (85), Attaining a 41-percent cure rate is dependent, however, on every patient receiving optimal treatment.

Advances have occurred in all three areas: Surgical techniques have been refined, radiotherapy is more widely available, and aggressive chemotherapy is developing and appears to hold the greatest potential. To date, the number of people actually helped by chemotherapy is modest, but dramatic advances have been made against many of the leukemias and lymphomas. Chemotherapy, used along with surgery and radiotherapy, has proven successful for a significant, but small, fraction of patients with some cancers. These represent promising medical advances, but because most people who receive the drugs, which are often accompanied by undesirable side effects, experience no gain in life expectancy, a backlash against chemotherapy has developed (86).

CANCER RATES

The examination of cancer rates focuses on each body site individually, since some are increasing, some decreasing, and some remaining more or less stable. Trends for the aggregate of all cancers obscure these individual trends.

The trend that dominates all others is the increase in lung cancer, largely a result of the widespread adoption of cigarette smoking earlier in this century. Male lung cancer rates have been rising steadily for at least half a century. Female lung cancer rates started to rise about 25 years ago and are now increasing rapidly. All other changes are small in comparison with the large increases in smoking-related cancers, although the decreases in cancer of the stomach and uterus are also important.

Currently, there is a general tendency for the rates of change at each cancer site to be slightly more favorable for people under 65 than for those over 65: If the site-specific rate for all ages is increasing, it is increasing at a slower pace among the younger group. If the rate is decreasing, the decrease is more pronounced in those under 65. Two clear exceptions stand out. First, skin cancer in males is increasing much more rapidly among people under 65 than among those over 65. Second, mortality rates of brain tumors appear to be moving in opposite directions. Despite falling death rates in middle age, there are large increases in old age, perhaps because diagnosis has improved for older people.

If attention is restricted to those younger than 65, for almost all types of cancer except those strongly affected by smoking (cancers of the respiratory and upper digestive tracts), the most recent trends in mortality are downward. The chief exceptions are pancreatic cancer in women, and melanoma in whites of both sexes.

Incidence and mortality rates differ because not all people who contract cancer die of it. Rates are calculated by relating the number of cases or deaths to the "population at risk" of either contracting cancer or dying from the disease. "Crude rates" are the total number of cases or deaths divided by the total population. These rates are affected by changes in the age structure of the population, that is, the fact that there are more older people in the population today, and hence more people contracting and dying of cancer means that the crude rates will increase. All of the overall comparisons in this report are based on rates "age-standardized" to the composition of the population determined in the 1970 census. Changes in these rates occur because of changes in the risk of cancer among people of a given age; increases or decreases in the proportion of old people in the population do not affect age-standardized rates. When a figure or comparison refers to a specific age class, the rates are based on the cases or deaths as a proportion of the total number of people in that class.

The remainder of this chapter deals with the data used in computing cancer rates and in analyzing trends, and some of the problems associated with those processes. A discussion of cancer at body sites of major importance follows.

Population Estimates

To evaluate changes in either incidence or mortality over time, it is necessary to know the population at risk, i.e., the number of people in the United States who might contract or die from the disease. Ideally, one would like this information cross-classified by such characteristics as age, race, and sex. More detailed information, such as the socioeconomic characteristics of the population, is also desirable.

The principal source of population data is the Census of Population, which is carried out once every 10 years. For each year after the census, all years ending with 1 through 9, "postcensal estimates" are prepared, using statistical techniques which use the data from the last census and possibly earlier censuses, along with vital statistics data, immigration data, and other data relating to population change. When the next decennial enumeration is completed, these estimates are replaced by "intercensal estimates;" prepared by interpolation between the two) censuses. However, the intercensal estimates are

not available until several years after the latest census is completed. Thus, there may be large discontinuities between the later postcensal population estimates and the actual census count—the adjusted estimate for the number of males age 85 or older between 1959 (postcensal estimate based on the 1950 census) and 1960 (census enumeration) shows a 50-percent increase. These discrepancies are not present when *intercensal* estimates for 1959 are compared to 1960 figures.

The censuses have been characterized by underenumerations which vary from census to census. The undercounts are thought to be small, near zero, for some demographic groups, such as white females 40 to 45 years old (in 1970), but are considerably greater for other groups, such as black males 25 to 45 years old, for whom the estimated undercounts are on the order of 10 percent or more (see fig. 1) (349). A number of studies have shown that serious undercount of the population exists for the very elderly, those age 85 years and over (350).

Mortality Data

Information on deaths has been collected through the national vital registration system since the beginning of this century and is the most reliable basis for calculating U.S. cancer rates. Since 1933, data have been collected continuously for the entire United States. National vital statistics functions are centered in the Division of Vital Statistics of the National Center for Health Statistics (NCHS). U.S. mortality statistics are based on information obtained directly from copies of original death certificates received from the registration offices and from data provided to NCHS through the Cooperative Health Statistics System. A number of States *now* provide their data—medical and demographic—entirely on computer tapes.

NCHS is not a repository of original certificates. Those are available only from the States. U.S. mortality statistics for all years except 1972 are based on information for all deaths. In 1972, they were based on a 50-percent sample, because of unusual budgetary and personnel constraints.

The mortality figures used in this report are based on vital statistics information from NCHS, which (except for the most recent years) have been published in the annual volumes of *Vital Statistics of the United States, Volume II, Mortality.* The data refer to the aggregate population of the 50 States and the District of Columbia.

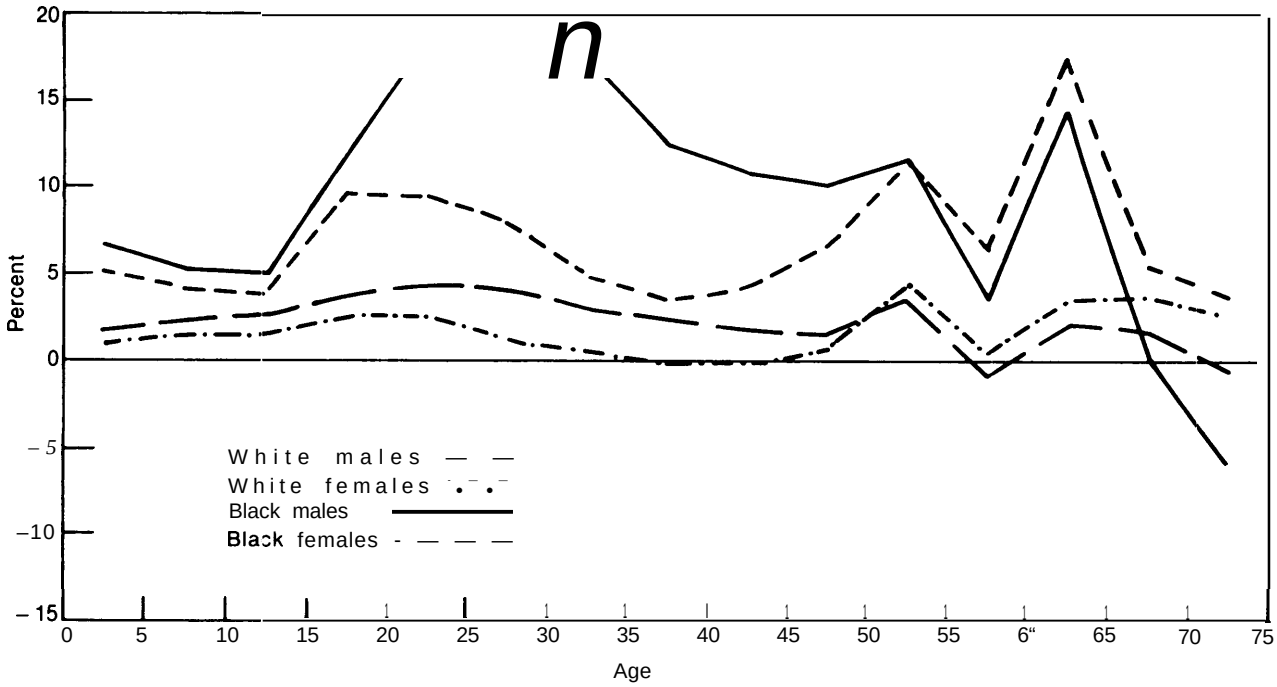
Incidence Data

While mortality data are extremely useful for studying cancer, incidence data are necessary to advance the state of knowledge about when and where cancers occur, irrespective of outcome. Population-based cancer registries are attempts to identify all incident cases in a defined population. In practical terms, registries cover discrete political or geographic areas. There are a number of countrywide cancer registries (e. g., Canada, Norway, and Sweden). These registries have generally taken advantage of preexisting, centralized data-collection mechanisms. There is no nationwide cancer registry in the United States. By law, cancer is a reportable disease in about 30 States and the District of Columbia (58), but most States have not put in place the mechanisms necessary to handle reported data. The most prominent efforts by States are Connecticut's statewide registry, operating since 1935, and the New York State registry, in operation since ***1940 (New*** York City was not included until 1973).

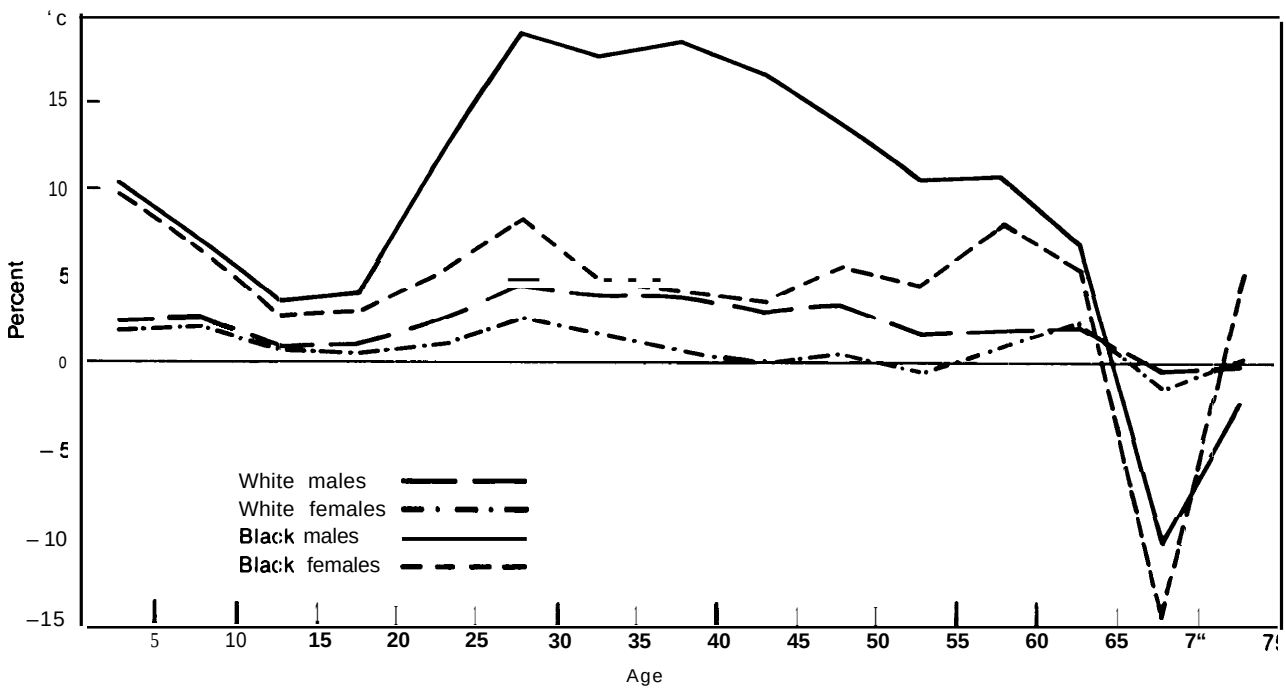
The first major cancer incidence surveys in the United States were the Ten Cities Surveys of 1937 and 1947', (now referred to as the First and Second National Cancer Surveys, FNCS and SNCS, respectively; see table 6), and the Iowa study of 1950. Metropolitan areas were chosen for FNCS and SNCS to assure a high percentage of correctly diagnosed cases. The areas surveyed were selected to provide reliable data and included about 10 percent of the U.S. population. The sample population was representative of the geographic distribution of Northern, Southern, and Western cities with populations greater than 100,000, but was not entirely demographically representative of the U.S. population.

Figure 1.—Comparison by Race and Sex of Percent Net Census Undercounts, by Age, 1960 and 1970

Percent Net Undercounts, by Age, Race, and Sex, 1960



Percent Net Undercounts, by Age, Race, and Sex, 1970



Note: Estimates for 1970 are based on adjusted census data, A negative sign denotes a net census overcount.

SOURCE: U.S. Bureau of the Census (349)

Table 6.—Areas Covered by the Three National Cancer Surveys and the Surveillance, Epidemiology, and End Results Program of NCI

Area	FNCS (1937-39)	SNCS (1947-48)	TNCS (1969-71)	SEER 1973-present	SEER + 1-3 NCS[a]	SEER + TNCS[b]
Atlanta	Cherokee, Clayton, Cobb, DeKalb, Douglas, Fayette, Forsythe, Fulton, Gwinnett	Cherokee, Clayton, Cobb, DeKalb, Douglas, Fayette, Forsythe, Fulton, Gwinnett	Clayton, Cobb, DeKalb, Fulton, Gwinnett	X	X	X
Birmingham	Jefferson	Jefferson	Jefferson, Shelby, Walker			
Dallas	Dallas	Dallas	Collin, Dallas, Denton, Ellis, Kaufman, Rockwell			
Denver	Denver	Adams, Arapahoe, Denver, Jefferson	Adams, Arapahoe, Denver, Jefferson, Boulder			
Detroit	Wayne	Wayne	Macomb, Oakland, Wayne	X	X	X
Pittsburgh	Allegheny	Allegheny	Allegheny, Beaver, Washington, Westmoreland			
San Francisco-Oakland	Alameda, San Francisco	Alameda, San Francisco	Alameda, Contra Costa, Marin, San Francisco, San Mateo	X	X	X
Chicago	Cook	Cook				
New Orleans	Orleans	Orleans		X[c]		
Philadelphia	Philadelphia	Philadelphia				
Fort Worth	Tarrant		Johnson, Tarrant			
Colorado			Entire State			
Iowa			Entire State	X		X
Minneapolis-St. Paul			Anoka, Dakota, Hennepin, Ramsey, Washington			
Seattle - Puget Sound Area (13 counties)				X		
Connecticut (entire State)				x		
Hawaii (entire State)				x		
Utah (entire State)				x		
Puerto Rico				x		
New Mexico (entire State)				X		

Abbreviations: FNCS — First National Cancer Survey.
SNCS — Second National Cancer Survey.
TNCS — Third National Cancer Survey.
SEER — Surveillance, Epidemiology and End Results.
NCS — National Cancer Survey.

[a] "X" Indicates area was covered by all 3 NCSs and SEER.
[b] "X" indicates area was covered by TNCS and SEER.
[c] New Orleans is being dropped from the SEER program in 1981.

SOURCE Devesa and Silverman (84) and Off Ice of Technology Assessment

Several changes took place in the next major effort, the Third National Cancer Survey (TNCS) of 1969 through 1971 (84). The reporting period was 3 years instead of 1. The timeframe was used to improve data for rare cancers and for smaller population groups. Working under contract to NCI, local, nonprofit medical organizations (e.g., schools of public health, medical schools, health department offices) conducted the project at each site. Ten percent of the cancer patients were included in a more intensive survey to determine methods of treatment used, duration of hospitalization, cost of medical care, and economic impact on the family. There was considerable geographical overlap between FNCS, SNCS, and TNCS. Seven of the original 10 cities were included in TNCS, although coverage was expanded from only central city areas to their Standard Metropolitan Statistical Areas. The entire state of Iowa was added. The Commonwealth of Puerto Rico cancer registry also supplied data (see table 6).

The first nationally coordinated, continuous-registration system, the Surveillance, Epidemiology, and End Results (SEER) program, was

begun in 1973 by NCI. NCI derives the SEER program mandate from the National Cancer Act of 1971 which directs that the Director of NCI:

> Collect, analyze, and disseminate all data useful in the prevention, diagnosis, and treatment of cancer . . . . (sec. 407(b)(4)).

In SEER areas, attempts are made to ascertain every primary cancer, excluding nonmelanoma skin cancer. All information pertaining to a case is consolidated into one record, to facilitate followup and to correlate survival data with treatment, age, and other variables.

Eight geographical locations, four in common with TNCS were chosen originally, and three were added subsequently (see table 6). Recently, one area, New Orleans, was dropped from the program. Approximately 10 percent of the U.S. population resides in SEER areas. A SEER report for the first 4 years of operation compared the demographic characteristics of the population with the total U.S. population (248):

> . . . the participants . . . are fairly representative with respect to age. Blacks are somewhat underrepresented while other nonwhite populations (Chinese, Japanese, Hawaiians, and American Indians) are somewhat overrepresented. Rural populations (especially rural blacks) are also underrepresented.

The SEER program has considered adding registration areas toward the goal of improving the reliability of data for all segments of society. Exact proportional representation is not, however, the ideal situation, since for small demographic groups overrepresentation may be necessary to produce reliable data.

As of September 1980, data were available from the first 6 years of SEER operation. NCI plans to publish complete incidence and mortality data every 5 years, and to make available data for interim years. A small amount of treatment and survival data have been published as the "Cancer Patient Survival" reports (247,251) following the earlier "End Results in Cancer" series. As more years of followup data are accumulated, NCI survival analyses will increasingly draw on SEER program information.

Error and Bias in Mortality and Incidence Data

There are various sources of error and bias in both mortality and incidence data. Reasoned interpretation of trends depends on understanding the forces, other than true changes in incidence and mortality, which impact on certified mortality (cause of death as reported on death certificates) and registered incidence. The important impacts are outlined below:

1. *Improper* diagnosis. -Individuals may contract cancer and die but the correct diagnosis may never be made, affecting both incidence and mortality rates. It is possible, for reasons of inadequate medical care or simple oversight, for lung cancer to be diagnosed as pneumonia; brain cancer as stroke or senility, and leukemias or lymphomas as infectious diseases. Conversely, cancer may be reported as the cause of death for people dying of other causes. For instance, in a 1970 autopsy series in Atlanta, Engel et al. (99) found that 86 percent of cancers found at autopsy were listed as the underlying cause of death on the death certificate. A missed diagnosis of cancer in a dying patient is presumably more likely to occur among old than among young cancer patients, if only because the old are less likely to be hospitalized. These errors are likely to have become less numerous over the past few decades, particularly in older people after the introduction of medicare in 1966.

2. *Improvements in ascertainment. —It* is likely that fewer cancers are missed today than in the past, affecting both incidence and mortality rates, probably to a greater degree in the older age groups. In addition, incidence rates may be influenced by a progressive improvement in the readiness of physicians to collaborate with a cancer registry. Data from the Connecticut cancer registry suggest that since its inception in 1935, the completeness of coverage may have improved so as to in-

troduce substantial upward biases into the rates. Better ascertainment of incident cases is also seen in comparing SNCS to TNCS. The proportions of cases that were ascertained by death certificate only, and for which no clinical record was ever found, were 11.8 and 2.2 percent, respectively (84). This suggests that the earlier survey may have underestimated total incidence rates. Overall, there is a tendency for better recording of cases over time, which causes an apparent increase in incidence.

3. Primary *site not specified.* —The site of the primary cancer in patients with metastatic disease may never be determined. Six to eight percent of American cancer death certificates are for cancer of an unspecified primary site (255). This percentage is a little lower among whites than among nonwhites, and among middle-aged than among older people, but it has not materially changed for decades, and may not seriously bias the assessment of trends in cancers at specified sites. However, the more than 20,000 cancer deaths per year now classified as unspecified represent an uncomfortably large amount of missing information.
4. Incorrect primary site or cell type. — Misdiagnosis of the primary site or cell type of fatal cancer is probably the most important bias affecting cancer death certification rates. Patients with cancer of one primary site (e. g., lung) may be misdiagnosed as having a cancer originating from another site (e.g., pancreas or brain), if the cancer has either extended itself to other nearby organs, or metastasized to distant organs. Boyd et al. (93), concluded that at ages over 65 most bone tumor deaths were in fact misdiagnosed secondaries from other sites. This may also have been true in the past for liver cancer, since bone and liver are not sites where cancers commonly arise but, along with brain and lung, are sites to which cancers commonly spread. Likewise, cancers of one particular cell type may be misdiagnosed as cancers of another cell type. This problem can sometimes be circumvented by grouping together particular types of cancers which are often misdiagnosed as each other, e.g., all benign and malignant brain tumors or all colon and rectal cancers. Colon and rectum cancers, which together account for 18 percent of cancer deaths, are often lumped together to improve the reliability of the statistic. However, they are different diseases and their individual characteristics are obliterated by this procedure.
5. *Incomplete transfer of information to death certificates.* —Even if the cancer is correctly diagnosed while the patient is alive, the correct information may never reach the death certificates. Percy, Stanek, and Gloeckler (291) tabulated correspondence between the primary site of cancer, as diagnosed in the hospital, and the primary site as it eventually appeared on the death certificate for 48,826 patients in TNCS. Many discrepancies emerged. Cancers of the colon were overreported while cancers of the rectum were underreported on death certificates as compared to hospital records. In addition, in over 50 percent of all cases where a more specific cancer site (cecum, ascending colon and appendix, transverse colon, etc.) appears in hospital records, it was recorded differently—most often as “colon, not otherwise specified’’—on the death certificate. Cancers of specific uterine sites (cervix and corpus) suffer from the same problem. Cancers of the buccal cavity are underreported on death certificates, while bone cancer is overreported, and other sites are misreported to varying degrees.
6. *Inclusion of prevalent cases.* —This bias is limited to incidence data. In a study which runs for a relatively short period, “prevalent” cases, which were actually diagnosed before the start of the study period, *may* inadvertently be included. This was more likely a problem in FNCS and SNCS, somewhat less so in TNCS, and less still in the ongoing SEER program.
7. *Changes in the definitions for some cancers.* —The definition of what constitutes a

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cancer changes with increasing knowledge. For instance, all salivary gland tumors, whether malignant or of mixed cellularity, were classified as cancer up to 1967, but the mixed tumors were dropped thereafter. Likewise, all brain tumors were counted in SNCS, while only those specified as malignant were included in TNCS, causing a substantial artifactual decrease in brain tumor incidence between the two surveys (84).

8. *Increased access to medical care and changes in diagnosis.* —An even more serious bias stems not from classification changes but from the more vigorous search for lumps, and improvements in diagnostic procedures which affect mainly incidence rates. By old age the human body may contain various lumps which, if examined histologically, would be classified as cancer, yet many are biologically benign and cause no reductions in lifespan. For instance, by age 70, 2.5 percent of males in the areas covered by TNCS were diagnosed as having prostatic cancer, while at autopsy *25* percent of males aged 70 or over who died of unrelated causes were found to have cancerous prostates (33). Similarly, among women undergoing mastectomy for cancer of one breast, and in whom cancer is not clinically evident in the opposite breast, biopsy and histological examination of the opposite breast finds 15 to 20 percent of them cancerous (93). Normally only 0.5 percent of these women will develop clinical evidence of cancer in the opposite breast. The scope for biased trends in incidence which are due to either more complete registration or the identification of cancer which would not cause a serious disease is probably large but unknowable with current procedures.

INCIDENCE AND MORTALITY TREND ANALYSIS

The magnitude and rate of change in incidence and mortality at any particular cancer site are seldom equal. Highly fatal cancers are the exception. In fact, comparable incidence and mortality rates are seen for pancreatic and lung cancers which have the poorest survival rates of the leading cancer sites. The same does not hold true for cancers of the endometrium, breast, or bladder, for which survival rates are much higher and improved over the recent past.

Major problems confront analysis of existing U.S. cancer incidence data, while such problems are less severe for mortality data. Incidence data representative of the U.S. population were collected at only three points in time over a period of more than 30 years before 1973. During that time there were changes in survey methods, definitions of disease, diagnostic patterns, classification of disease, and in the rules for assigning cause of death, as well as improvements in access to medical care. All of these factors may have affected registered incidence. The more recent SEER data, while collected according to the same basic procedures since the program's inception, may reflect different degrees of ascertainment in startup years as compared with subsequent years. More importantly, the program has been operating for too short a time for trends which are real but small in magnitude to emerge. Comparing SEER data with information from one or more of the earlier surveys raises questions about whether data from such different sources can be analyzed together with sufficient validity. Despite these drawbacks, data from the national cancer surveys and SEER have been analyzed for trends, and provide some useful indicators, though authors of the analyses acknowledge inherent problems.

Devesa and Silverman (84) analyzed incidence data from the national cancer surveys when TNCS was completed, along with mortality data for corresponding years. They reported that between the two survey points, 1947 and 1970, the "overall age-adjusted incidence rate for all sites combined decreased 3.9 percent." This summary figure is the result of ups and

downs in race-sex-site groups, including an overall striking decrease for women and an overall increase for men. Lung cancer was by far the most active site, increasing more than 350 percent between FNCS, when it ranked eighth in incidence as a primary site, and TNCS, when it took first place. Uterine cancer, which had the highest incidence rate in FNCS, had decreased 40 percent. Even more dramatic was the overall *72* percent decrease in stomach cancer by the time of TNCS. Incidence trends for the most frequent sites and for all sites combined, as reported by Devesa and Silverman are displayed in figures 2 and 3.

Devesa and Silverman believe that some of the apparent changes may be artifactual, notably part of the dramatic increase in cancers of the lung and prostate in nonwhite males. In addition, the lower rates for nonwhites in the earlier periods may reflect underdiagnosis. However, they conclude (84):

> Changes are likely to have occurred in the prevalence of carcinogenic agents either in the general or personal environment, since the shifts in trends, especially when considered by race and sex, are greater than those that could be explained by the problems discussed earlier.

Doll and Peto (93) conclude that the most reliable estimates of trends in cancer incidence are probably those derived by direct comparison of SNCS and TNCS, though even in this comparison substantial artifacts are possible. Figures 4 and 5 display the age-standardized male and female incidence data from SNCS and TNCS, respectively. Figures 6 and 7 display age-standardized mortality for the period 1955 through 1975. The important changes are increases in lung cancers and melanomas, a decrease in stomach cancers for both sexes, increasing rates of prostate, bladder, and kidney cancers in males, and a sharp decrease in cervical cancer in women.

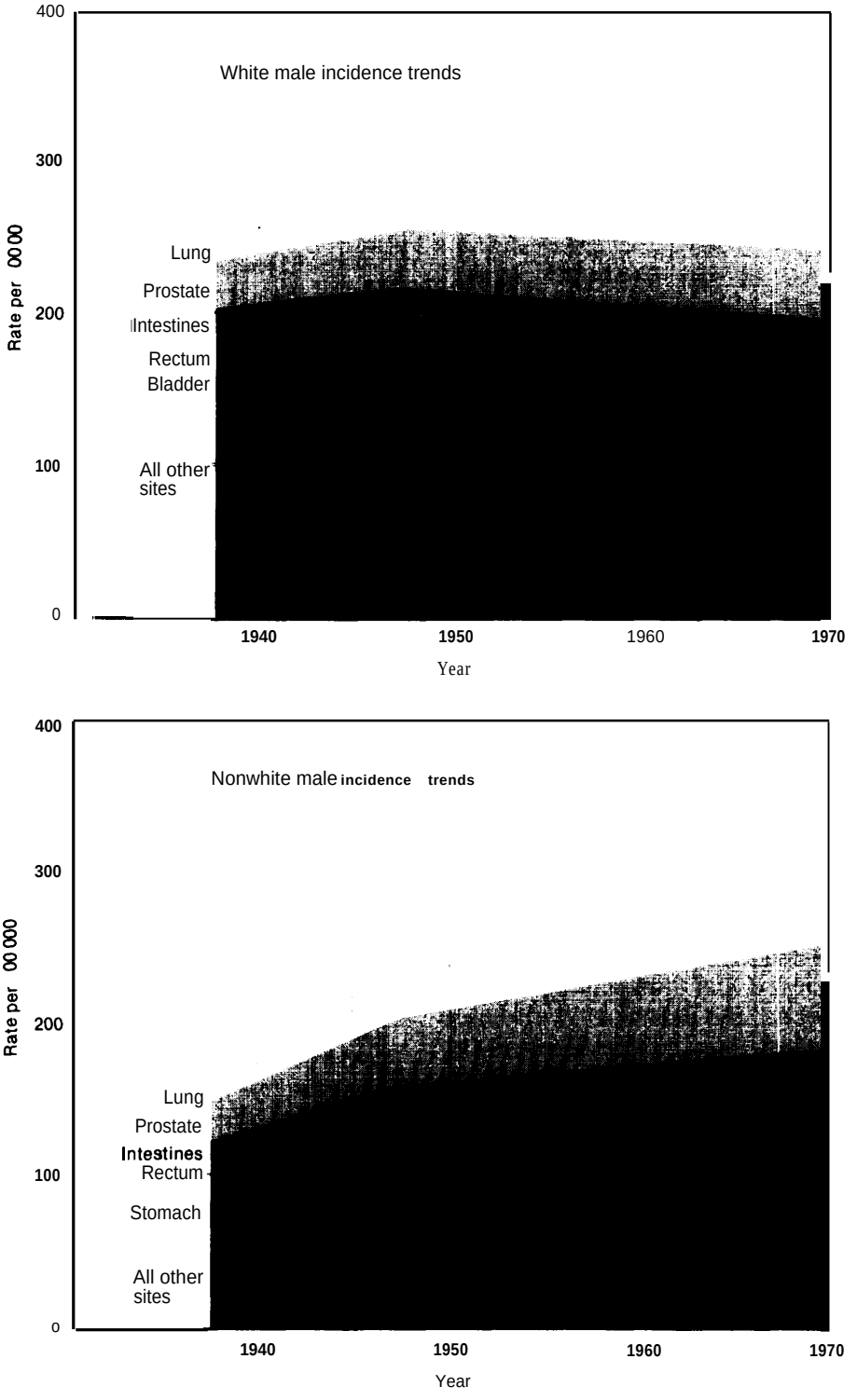
Pollack and Horm (296) presented the first analysis of cancer incidence rates from SEER data. The paper, according to the authors, had three objectives:

1. to assess the comparability of the cancer incidence rates across the total SEER program over the period 1973-76;
2. to assess the validity of use of TNCS incidence rates for 1969-71 and SEER rates for 1973-76 to analyze incidence trends over the period 1969-76; and
3. to present trends in cancer incidence and mortality for 1969-76, where data are sufficiently comparable, for some of the major forms of cancer and to summarize these trends by use of a convenient set of measures.

For whites, rates for all SEER areas combined, for individual cancer sites and all cancer sites combined were found to be "reasonably comparable. " However, rates for blacks over the 4-year period are not comparable, and therefore analysis of incidence data was carried out for whites only; mortality data were analyzed for whites and blacks. The authors concluded, regarding the second stated purpose, that "the use of incidence rates for TNCS areas for 1969-71 and for SEER areas for 1973-76 appears to provide a good approximation to trends over that total time period for the white population" (296). Pollack (295) reached the same conclusion after comparing Connecticut tumor registry data, the data from the three national cancer surveys and the SEER program.

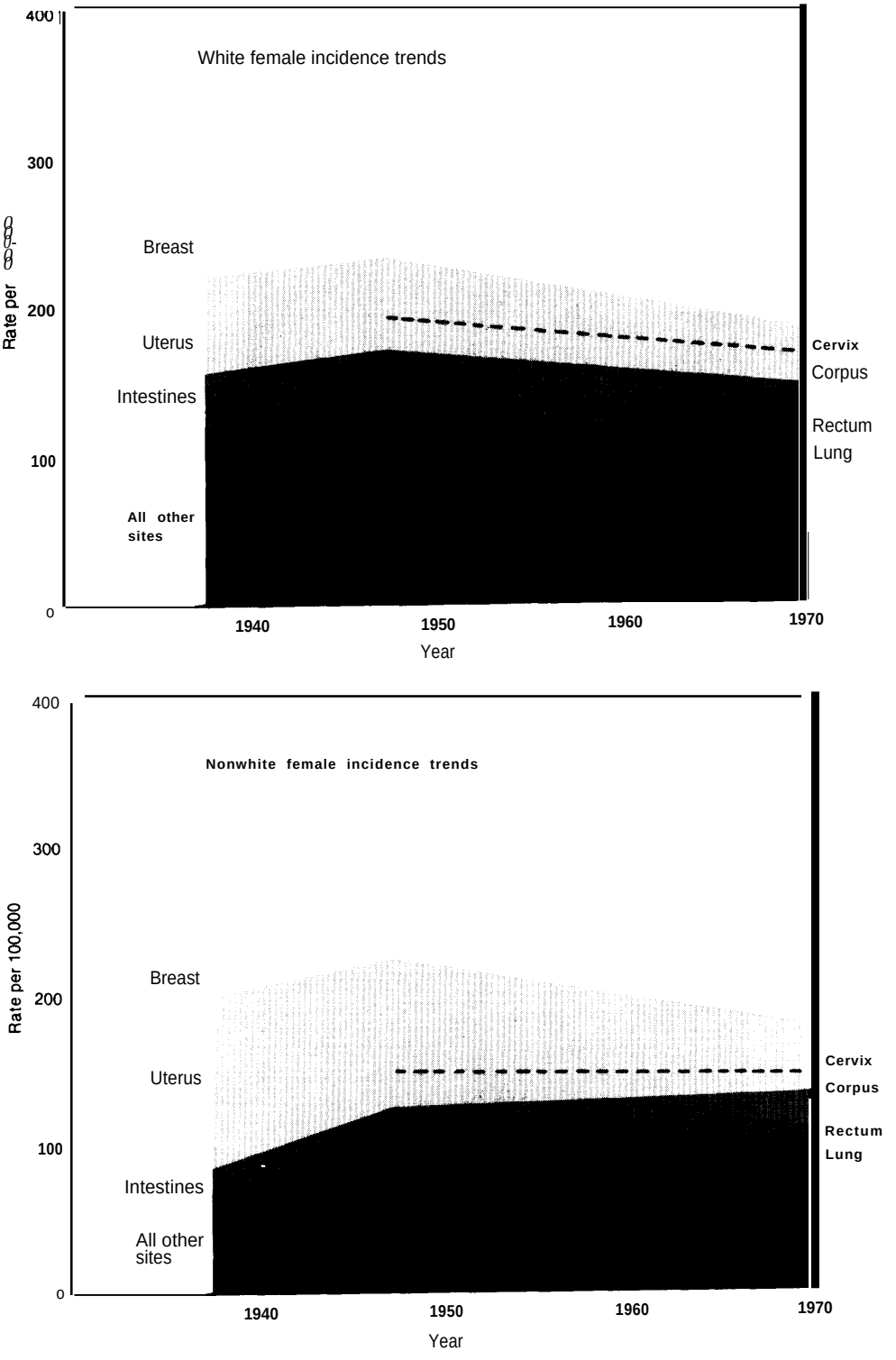
The authors (296) calculated the average annual percent change in incidence at each site and all sites combined for each sex (see table 7). However, they caution that "it can be misleading to focus on the picture for *all* sites" because these overall figures are affected by many dynamic rates for different sites. For all sites combined, the incidence rate increased an average of 1.3 percent/yr for white males, and 2.0 percent/yr for white females. Mortality rates for all sites combined increased an average of 0.9 and 0.2 percent/yr for white males and white females, respectively. Mortality rates for blacks increased an average of 2.1 and 0.6 percent/yr for males and females, respectively.

Figure 2.—Age-Adjusted Cancer Incidence Trends Among Males for All Sites Combined Showing the Most Frequent Sites



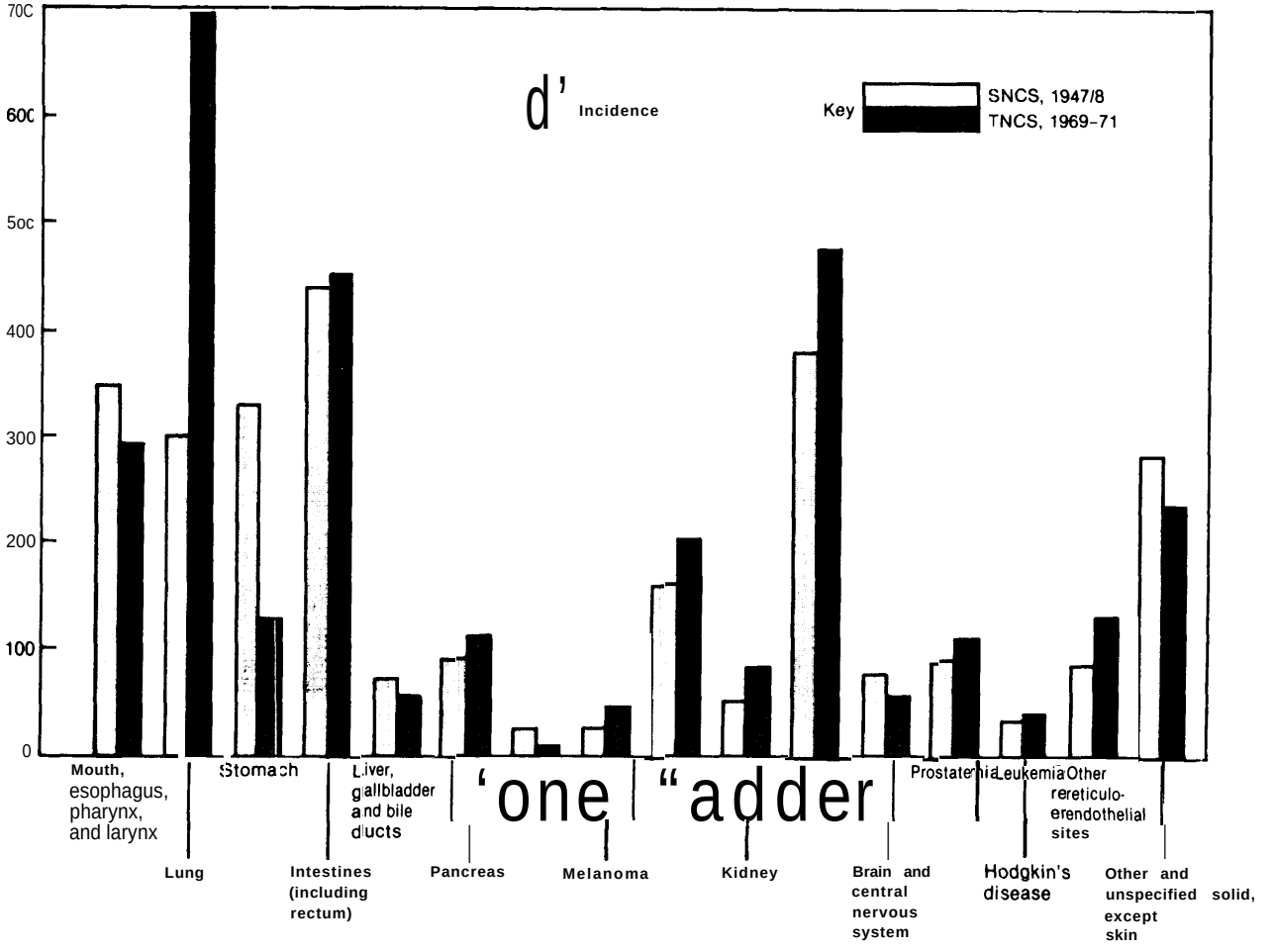
SOURCE From Devesa and Silverman (84)

Figure 3.—Age-Adjusted Cancer Incidence Trends Among Females for All Sites Combined Showing the Most Frequent Sites



SOURCE From Devesa and Silverman (84)

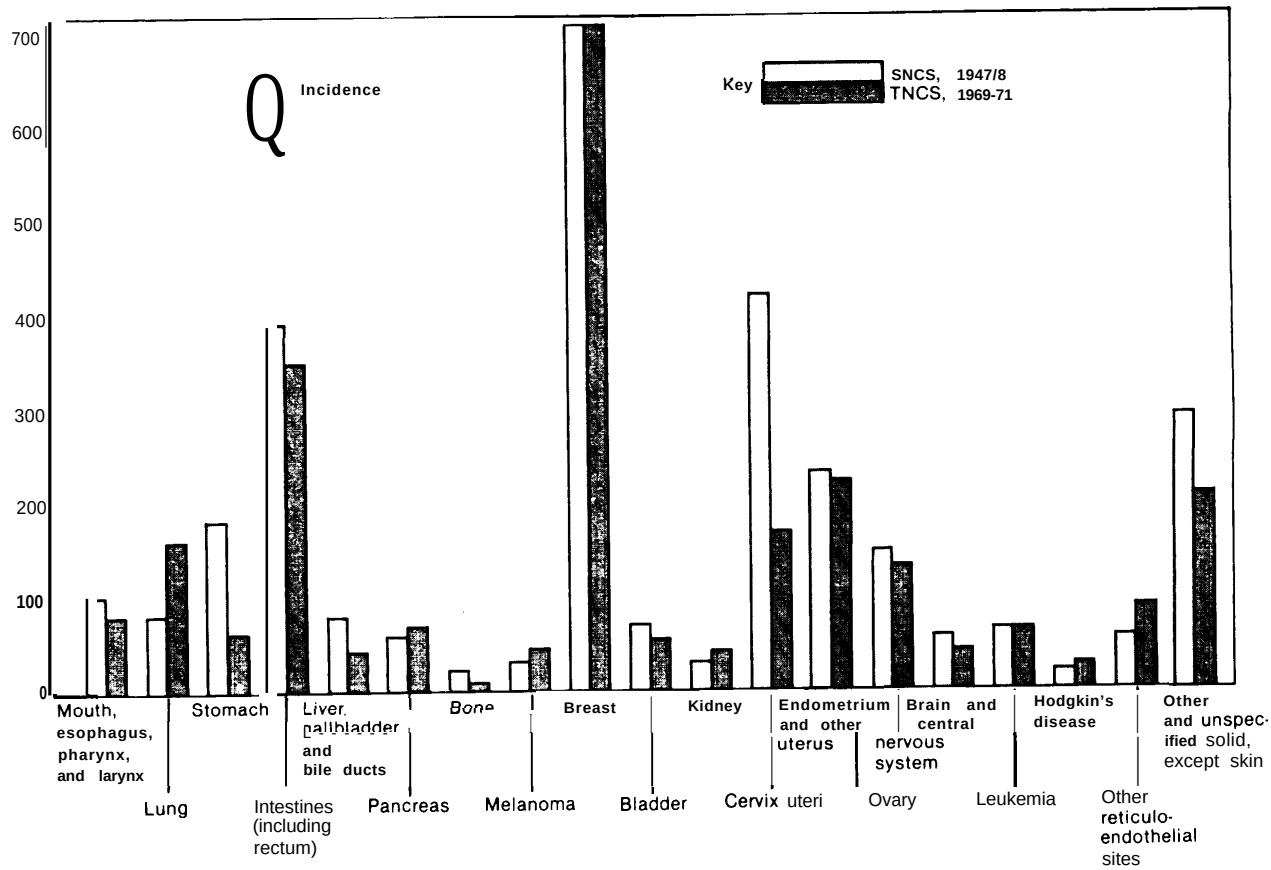
Figure 4.—Site-Specific Cancer Incidence Rates per Million Males, All Ages[a]



a *Age.standardized* to 1950 U.S. Census population, assuming 90 percent of the population is white.

SOURCE: Doll and Peto (93).

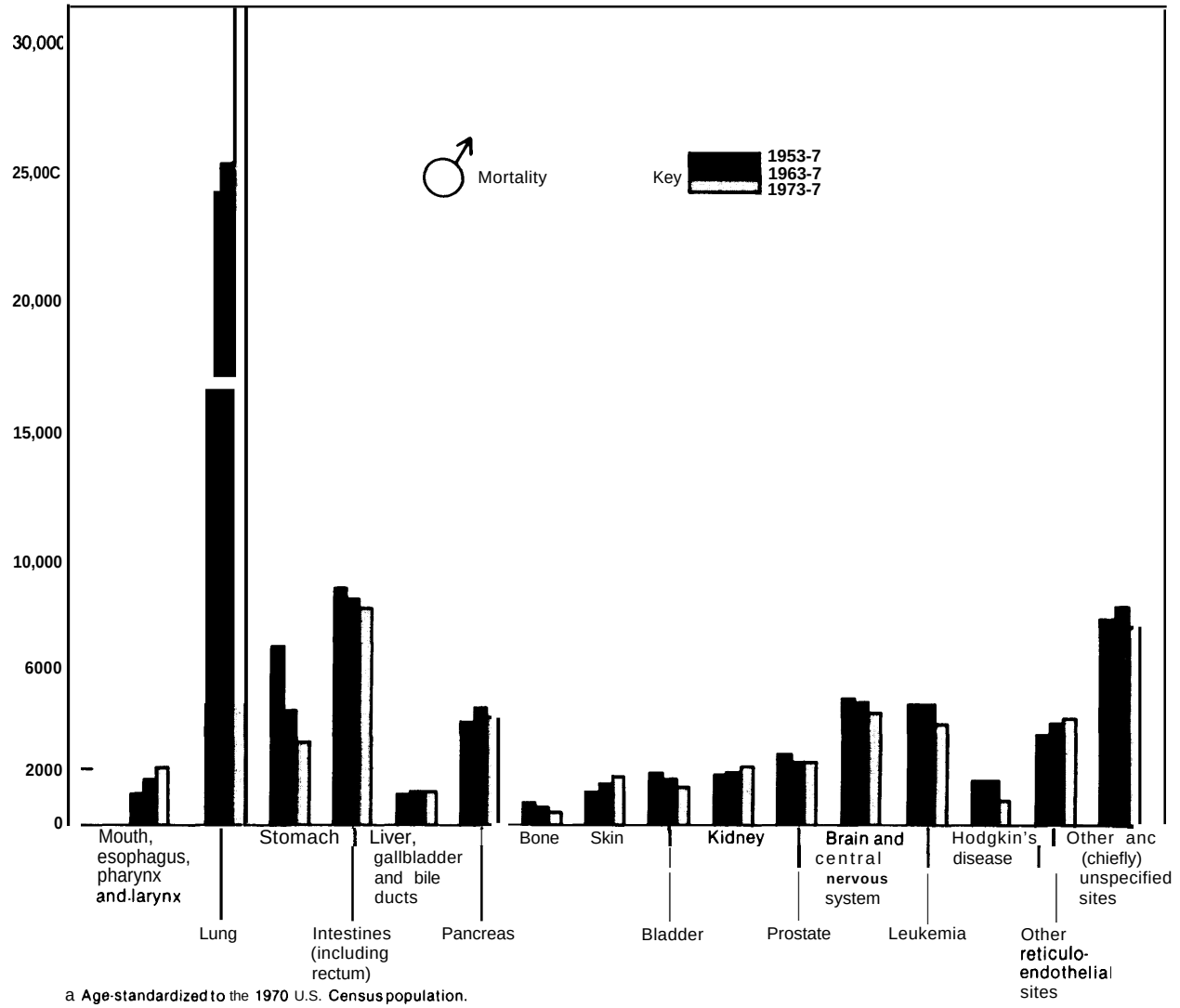
Figure 5.—Site-Specific Cancer Incidence Rates per Million Females, All Ages[a]



a Age-standardized to 1950 U.S Census population, assuming 90 percent of the population is white

SOURCE Doll and Peto (93)

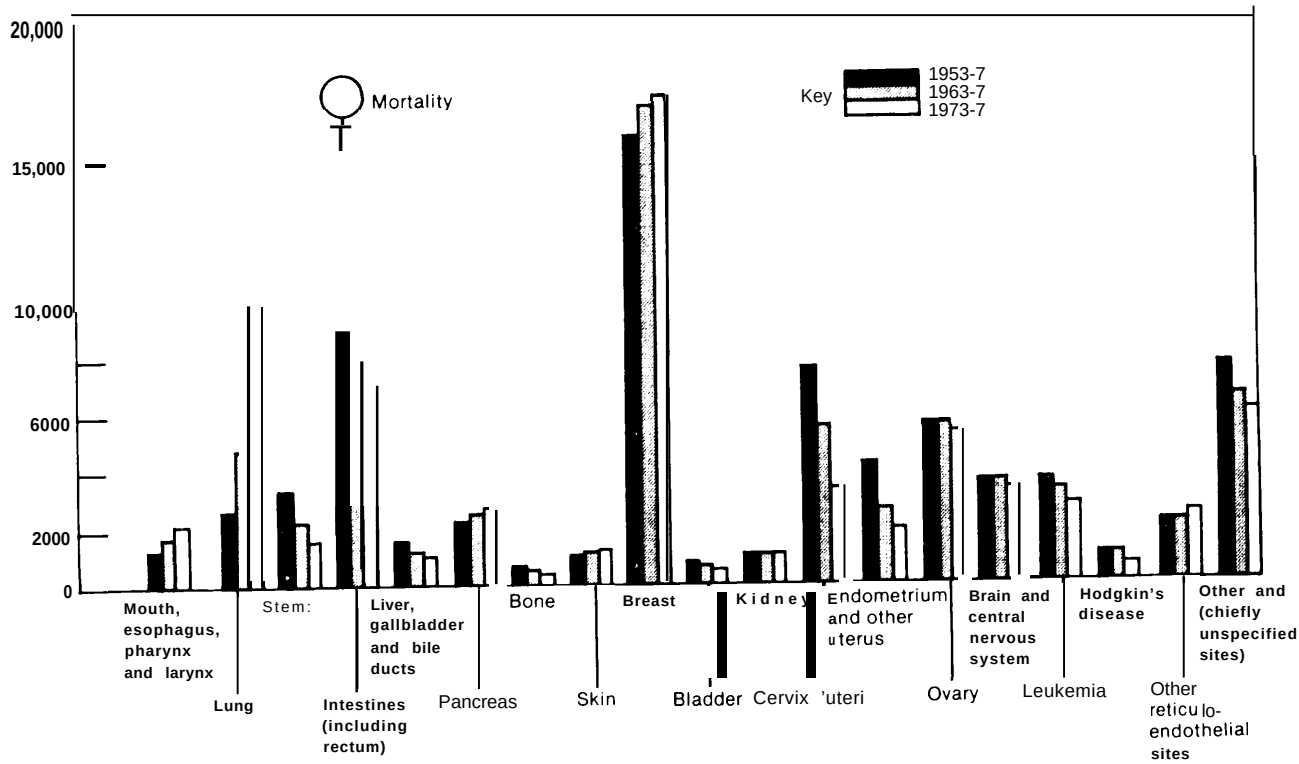
Figure 6.--Site-Specific Cancer Mortality Rates per Million Males at Ages[a] O-64 Years: 1953-57; 1963=67; and 1973-77



a Age-standardized to the 1970 U.S. Census population.

SOURCE: Doll and Peto (33)

Figure 7.—Site-Specific Cancer Mortality Rates per Million Females at Ages[a] O-64 Years: 1953-57; 1963”67; and 1973”77



a Age-standardized to the 1970 U S Census population

SOURCE Doll and Peto (93)

Table 7.—Age.Adjusted[a] Cancer Incidence Rates per 100,000 Population for Selected Sites by Sex and Year, and Average Annual Percent Change, TNCS Areas 1969-71 and SEER Areas 1973-76: Whites

Site	Sex	Incidence rate/100,000 population							Average annual percent change	95 "/0 confidence interval	
		1969	1970	1971	1973	1974	1975	1976			
Ail sites	M	346.6	343.7	337.2	355.5	365.3	365.8	**374.0**	1.3	**0.74**	1.86
	F	271.5	268.6	270.9	287.3	305.2	301.8	**301.2**	2.0	**1.28**	2.72
Stomach	M	15.4	14.1	13.4	13.8	13.1	12.7	**12.6**	– 2.3	**– 3.34**	– 1.26
	F	7.1	7.0	6.3	6.1	5.9	5.4	**5.6**	– 3.7	**– 4.70**	– 2.70
Colon excluding rectum.	M	34.5	33.2	32.4	34.2	37.3	35.5	**36.9**	1,5	**0.29**	2.71
	F	30.6	28.9	28.6	29.7	30.1	30.6	**31.4**	0.7	**– 0.22**	1.62
Rectum	M	17.5	17.8	18.1	18.8	19.3	18.3	**19.4**	1.3	**0.60**	.2.00
	F	11.1	10.6	10.6	11.3	11.2	12.0	**11.4**	1.2	**0.18**	.2.22
Pancreas	M	12.1	12.1	12.3	12.7	11.2	12.5	**11.5**	– 0.5	**– 1.96**	0.96
	F	7.5	7.3	7.0	7.5	8.0	7.2	**8.0**	0.9	**– 0.61**	2.41
Lung.	M	70.6	71.5	70.0	72.3	74.5	76.4	**77.8**		**0.87**	1.93
	F	13.3	14.4	15.5	17.7	20.0	21.8	**23.7**	8.6	**8.06**	!3.14
Melanoma	M	4.4	4.7	4.7	5.8	6.3	6.4	**6.8**	6.8	**5.75**	"7.85
	F	4.1	4.2	4.8	5.1	5.5	6.0	**6.1**	6.2	**5.32**	7.08
Breast[b]		73.9	76.1	75.1	81.0	92.5	86.2	**83.5**	1.8	**1.17**	2,43
Cervix.	F	16.0	14.5	14.3	12.6	11.5	10.7	**10.6**	– 5.9	**– 6.67**	– !i.13
Corpus–uterus NOS[c]		22.6	22.7	24.6	29.0	31.1	32.4	**31.2**	5.9	**4.48**	7.32
Ovary	F	14.9	14.2	13.6	14.2	14.9	14.2	**13.6**	– 0.4	**– 1.61**	().81
Prostate gland	M	59.0	57.4	56.7	61.0	62.1	64.8	**68.6**	2.3	**1.27**	3.33
Bladder	M	23.8	23.3	23.4	25.5	27.1	25.8	**26.4**	2.3	**1.31**	3.29
	F	6.3	5.9	6.3	6.1	6.9	6.9	**7.3**	2.5	**1.01**	3.99
Kidney	M	9.0	8.7	8.2	9.4	9.1	9.0	**9.6**	1.2	**– 0.20**	2.60
	F	4.3	4.0	3.8	4.4	4.1	4.0	**4.8**	1.3	**– 1.09**	3.69
Leukemia.	M	13.2	13.6	12.2	13.2	13.4	12.5	**13.1**	– 0.2	**– 1.51**	1.11
	F	8.0	7.6	7.2	7.8	7.5	7.3	**7.1**	– I o	**– 2.14**	0.14

[a] 1970 U.S. population was used as standard.
[b] 1974 and 1975 were not included in the computation of trend for breast cancer.
[c] Not otherwise specified.

SOURCE: Pollack and Horm, 1980.

Schneiderman (320) also reported incidence trends from TNCS/SEER data, and his estimates of site-specific and overall change are similar to those of Pollack and Horm. The Toxic Substances Strategy Committee (TSSC) (345) stated that "even after correcting for age, both mortality (death) rates and incidence (new cases) of cancer are increasing, " based on Schneiderman's analysis. However, TSSC was cautious about drawing firm conclusions about the magnitude of any increase because of the problems and uncertainties inherent in the data and the comparison of data sets.

Doll and Peto (93) consider the TNCS/SEER comparison "completely unreliable. " These authors compared incidence from the SNCS/TNCS/SEER series with registered incidence from Connecticut and upstate New York. They also looked at U.S. mortality for the concurrent period, and found that the TNCS/SEER portion yielded "fantastic and irregular variations in incidence . . . ten times greater than could plausibly be attributed to chance, and a hundred times greater than the corresponding annual changes in mortality over the past few decades. " Morgan (242) and Rothman (314) also have challenged the validity of analyzing incidence trends using a TNCS/SEER comparison. Further, they do not feel there is adequate evidence t. support claims that incidence is rising. Resolving the differences of opinion concerning trends is not possible at this time.

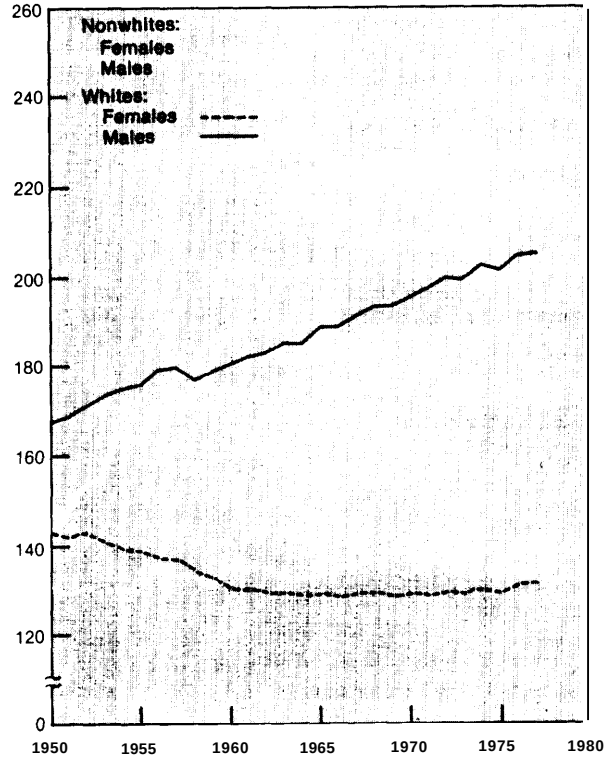
TRENDS IN SITE-SPECIFIC CANCER RATES

After allowing for all the biases and difficulties in interpretation, it is refreshing that some conclusions can be drawn about trends in cancer rates at specific body sites. As discussed earlier in this chapter, mortality rates in this country are more reliable than the available incidence rates, thus this discussion of site-specific trends relies more heavily on mortality than incidence rates.

Although it is uncertain how far back cancer death certification rates can be considered reliable, **1950** is a sensible starting point for discussing modern trends, In 1950, there were new rules for coding death certificates and a new census. The classification of cancers had just begun to be based on a reasonably modern International Classification of Diseases (the sixth ICD). For example, Hodgkins' disease was classified as a neoplasm rather than an infectious disease, the lymphomas were listed separately, and the important distinction between cancer of the cervix and other uterine cancers had recently begun. Moreover, by **1950,** fairly modern standards of diagnostic radiology already existed, and nontoxic anesthesia and the chemotherapy of infectious diseases had just developed, allowing for successful operations against cancer (93).

Trends in mortality rates from all malignancies are depicted in figure 8, Mortality rates and rate of charge differ between whites and nonwhites and between males and females. Consideration of such overall rates are not so informative as consideration of rates at particular sites, which follows. The discussions draw on data presented in tables 8 and 9 which display cancer mortality rates for people under 65 and over 65, respectively and figures 9 through 17 which present age-standardized cancer mortality trends for the years 1950-78.

Figure 8.—Mortality Rates for All Malignancies (ICD 8: 140-209) per 100,000, Age-Standardized to U.S. 1970 Population;: 1950-77



SOURCE" Office of Technology Assessment

Respiratory cancer sites, dominated by lung cancer, shows the most dramatic increases (see fig. 9). Male respiratory cancer rates appear to have been rising for at least half a century. Female respiratory cancer death certification rates started to rise 25 years ago and are now increasing rapidly. Before 1950, almost the whole of the apparent increase in female lung cancer and some of the apparent increase in male lung cancer may be artifactual, due to increasingly accurate detection during the period 1933 to

Table 8.—U.S. Age-Standardized Cancer Death Rates for Males and Females Under 65 1953-78

Site	Sex	Average annual rates/100 million aged under 65[a] 1953-57	1958-62	1963-67	1968-72	1973-77	Only 1978
Mouth, pharynx,	M	**5,936**	**6,485**	**6,858**	**7,059**	**7,123**	7,200
larynx, or esophagus	F	**1,213**	**1,478**	**1,700**	2,000	2,143	2,111
Remaining respiratory:							
Trachea, bronchus,	M				28,799	30,911	32,080
or lung[c]	F				7,133	9,803	11,598
Pleura, nasal sinuses,	M				475	447	408
and all other	F				215	192	178
Both	M	**18,275**	**21,290**	**25,390**	29,274	31,358	32,488
	F	**2,714**	**3,378**	**4,734**	7,348	9,995	11 ,776
Stomach	M	**6,808**	**5,539**	**4,478**	3,753	3,270	2,983
	F	**3,293**	**2,717**	**2,216**	1,815	1,551	1,403
Intestines (chiefly large	M	**8,954**	**8,739**	**8,624**	8,521	8,298	8,276
intestine, i.e., colon and rectum[d])	F	**9,014**	**8,576**	**7,977**	7,486	7,130	6,807
Liver[e]	M				807	795	*789*
	F				354	347	383
Gallbladder and	M				535	488	487
ducts[f]	F				712	644	625
Both	M	**1,203**	**1,396**	**1,362**	1,342	1,283	1,277
	F	**1,520**	**1,425**	**1,219**	1,066	991	1,008
Pancreas	M	**3,984**	**4,336**	**4,536**	4,464	4,267	4,148
	F	**2,210**	**2,363**	**2,459**	2,482	2,598	2,618
Remaining digestive (chiefly	M	**465**	**427**	**404**	351	283	256
peritoneum*	F	**414**	**370**	**330**	265	212	193
Bone	M	**936**	**795**	**747**	680	600	575
	F	**656**	**552**	**483**	444	380	360
Connective and soft tissue	M	**355**	**419**	**492**	516	464	473
sarcomas	F	**276**	**338**	**373**	421	414	426
Skin (chiefly melanoma[b])	M	**1,325**	**1,410**	**1,659**	1,547	1,828	1,996
	F	**916**	**935**	**1,040**	1,022	1,086	1,161
Breast	M	**138**	**127**	**121**	130	123	110
	F	**15,880**	**16,158**	**17,053**	17,358	17,260	17,229
Bladder[i]	M	**2,066**	**1,919**	**1,810**	1,658	1,538	1,386
	F	**760**	**676**	**655**	547	500	455
Kidney[i]	M	**2,012**	**2,051**	**2,134**	2,206	2,236	2,300
	F	**1,008**	**1,006**	**991**	1,018	1,016	1,011
Cervix uteri	F	**7,550**	**6,651**	**5,673**	4,423	3,365	2,911
Endometrium[j]	F	**4,218**	**3,282**	**2,650**	2,193	1,966	1,815
Ovary	F	**5,692**	**5,736**	**5,680**	5,621	5,304	5,042
Prostate	M	**2,785**	**2,602**	**2,549**	2,555	2,612	2,590
Other genital:							
Malignant	M	**854**	**852**	**837**	811	729	540
Malignant	F	**356**	**326**	**291**	274	246	224
Benign and unspecified	F	**835**	**444**	**302**	173	95	53
Brain or nerves, malignant,	M	**4,908**	**4,822**	**4,831**	4,693	4,475	4,293
or benign[k]	F	**3,675**	**3,663**	**3,653**	3,520	3,364	3,246
Eye	M	**127**	**120**	**102**	92	77	70
	F	**116**	**106**	**100**	82	66	58
Thyroid	M	**236**	**207**	**186**	182	153	146
	F	**340**	**304**	**255**	210	177	181
Leukemia	M	**4,754**	**4,843**	**4,705**	4,344	4,036	3,845
	F	**3,562**	**3,477**	**3,338**	3,049	2,753	2,622

Table 8.– U.S. Age-Standardized Cancer Death Rates for Males and Females Under 65,1953-78 (Continued)

Site	Sex	Average annual rates/100 million aged under 65[a]					
		1953-57	1958-62	1963-67	1968-72	1973-77	Only 1978
Hodgkin's disease	M	1,775	1,770	1,770	1,573	1,065	830
	F	992	999	1,025	918	620	486
All other lymphomas[l]	M	3,603	3,862	4,070	4,429	4,254	4,267
	F	2,260	2,543	2,720	2,884	2,875	2,876
Remainder (chiefly[m] deaths where the anatomic site or origin of the cancerous cells was not recorded)	M	5,935	5,775	6,490	5,805	6,029	6,304
	F	5,244	4,800	4,868	4,669	4,734	4,613

a There are currently about 100 million people of each sex aged under 65, so the cited rates are roughly similar to the actual numbers of such deaths.
b These are the cancers which are strongly affected both by alcohol and by all forms of tobacco.
c Lung (including trachea and bronchus) cancer rates are affected more strongly by cigarette than by pipe smoking, and the Increases in respiratory cancer among people aged under 65 during the past quarter century can be chiefly ascribed to prior widespread adoption of cigarette smoking.
d Cancer of the Intestines may arisein the small intestine,in the ascending, transverse, descending or sigmoid colon, or in the rectum, U S. mortality data do not seem to be sufficiently precise to allow unbiased examination of the trends in *any* of these separate parts, not even merely "colon" and "rectum".
e Liverspecified as primary,including the bile ducts Inside the liver.
f Gallbladder, including the bile ducts outside the liver
g Mesentery, peritoneum and unspecified digestive sites (the latter comprising the minority in 1948, when separate totals were last published).
h In middle age there are now so few deaths from nonmelanoma skin cancers that the data for "total skin" represent the melanoma death rates reasonably accurately, but in old age the continuing decrease in the death rates from nonmelanoma skin cancers still dilutes the progressive increasein melanoma death rates.
i "Other urinary organs" (ureter and urethra, where cancers are rare) were included with "bladder" up to 1967, and were then transferred to "kidney" from 1968 onwards
j Endometrium,including all cancers of unspecified parts of the uterus
k The distinction between "mall ignan" and "benig" is less clear-cut for brain tumors than for most other neoplasms, and so the most meaningful analysis Seem s to be of all fatal tumors of the central nervous system, Irrespective of histology. However, even here, large biases are possible, for in old age symptoms due to brain tumors may be misdiagnosed as due to senility or vascular disease Such errors are, of course, less likely in middle age, which may account for the marked upward trend in brain tumor death *certification* rates in old age being entirely absent in middle age.
l There is considerable diagnostic uncertainty between lymphosarcoma, reticulum cell sarcoma and various other lymphomas, so we have not attempted to examine them separately Myeloma is also included since data on myeloma were published separately only from 1968
m In years when any d istinction between them can be made from the U.S Government publications, the "unspecified site" death certificates greatly outnumber the "specified sites" among those remaining cancers, although the distinction between them seems surprisingly erratic (e g., comparing 1957 with 1958)

SOURCE Doll and Peto (93)

1950, but some of the pre-1950 male increase and virtually all of the more recent increases in both sexes are real and largely or wholly caused by the delayed effects of the adoption of the habit of cigarette smoking decades ago.

The long delay between cause and full effect arises because the exact age at which smoking began during the late teens or early twenties is a surprisingly important determinant of lung cancer risks in middle or old age. The dependence of lung cancer risks in old age on cigarette smoking habits in early adult life means that lung cancer rates among people in their sixties during the 1970's are strongly influenced by the smoking habits of teenagers and people in their early twenties back about 1930 (93).

An encouraging sign is the decrease in lung cancer mortality rates among white men in all age groups under age 50 (fig. 10). This decrease is associated with both decreased smoking rates among men and decreased tar yield of new cigarettes. Smoking rates among women rose at least throughout the 1960's. (Trends during the 1970's are not clear.) As a result, all age-specific female rates are still rising, except those at ages 30 through 39, which apparently have stopped rising. These increasing rates suggest that by the turn of the century, lung cancer rates among middle-aged women may no longer be rising, but rates among older women will probably continue increasing because of higher smoking rates during their early adult lives (93).

Mouth, pharynx, larynx, and esophagus (figure 11) are the sites at which cancers can be caused by alcohol and by tobacco, including the pipe tobacco which men have used since the last century. The combination of both alcohol and tobacco exposure seems to cause an increase in the risk of these cancers which greatly exceeds the sum of the two separate risks. Mortality rates at these sites have remained relatively constant since 1950 for whites, but nonwhite males

Table 9.—U.S. Age-Standardized Cancer Death Rates for Males and Females Over 65,1953-78

Site	Sex	Average annual rates/10 million aged 65 or over[a] 1953-57	1958-62	1963-67	1968-72	1973-77	Only 1978
Mouth, pharynx, larynx, or esophagus	M	8,027	7,580	7,214	7,324	7,478	7,487
	F	1,786	1,654	1,551	1,643	1,787	1,933
Remaining respiratory:							
Trachea, bronchus or lung[c]	M	—	—		31,539	37,424	40,888
	F	—	—	—	4,692	6,550	8,296
Pleura, nasal sinuses, and all other	M	—		—	483	492	468
	F	—		—	205	195	203
Both	M	14,277	19,016	24,823	32,022	37,916	41,:356
	F	2,937	2,981	3,442	4,897	6,745	8,499
Stomach	M	14,368	11,827	9,552	7,708	6,519	5,892
	F	7,547	5,930	4,635	3,667	3,047	2,870
Intestines (chiefly large intestine, i.e. colon and rectum[d]):	M	17,916	17,749	17,761	17,958	18,265	18,839
	F	15,502	14,672	14,024	13,497	13,256	13,437
Liver[e]	M	—		—	926	957	1,067
	F	—	—	—	364	376	395
Gallbladder and ducts	M	—	—	—	1,267	1,193	1,192
	F	—	—	—	1,749	1,479	1,459
Both	M	1,921	2,106	2,208	2,193	2,150	2,259
	F	2,651	2,561	2,357	2,113	1,855	1,854
Pancreas	M	5,816	6,426	6,899	7,090	7,169	7,247
	F	3,842	4,074	4,226	4,390	4,463	4,637
Remaining digestive (chiefly peritoneum	M	729	668	628	500	483	417
	F	649	610	540	431	365	317
Bone	M	837	617	521	502	465	436
	F	468	359	308	286	261	244
Connective and soft tissue sarcomas	M	228	273	323	357	353	355
	F	156	184	209	243	244	273
Skin (chiefly melanoma[b])	M	1,867	1,739	1,679	1,448	1,527	1,608
	F	1,118	961	863	780	789	840
Breast	M	201	166	175	192	188	181
	F	11,356	10,633	10,351	10,603	11,087	11 ,070
Bladder[i]	M	5,416	5,496	5,501	5,626	5,781	5,732
	F	2,258	2,042	1,876	1,673	1,615	1,623
Kidney[j]	M	1,735	1,969	2,166	2,488	2,543	2,670
	F	1,047	1,066	1,105	1,160	1,222	1,252
Cervix uteri	F	3,127	2,884	2,513	2,021	1,642	1,403
Endometrium[j]	F	4,068	3,512	3,175	2,861	2,662	2,593
Ovary	F	3,195	3,344	3,460	3,680	3,743	3,796
Prostate	M	19,300	18,584	18,488	18,591	19,465	20,392
Other genital:							
Malignant	M	435	359	320	295	252	224
Malignant	F	645	604	545	514	495	470
Benign and unspecified	F	240	147	115	72	51	39
Brain or nerves, malignant or benign[k]	M	935	1,068	1,375	1,731	2,163	2,581
	F	596	692	857	1,187	1,522	1,862
Eye	M	131	123	106	112	99	102
	F	106	91	79	79	70	64
Thyroid	M	276	251	234	232	210	217
	F	524	450	417	372	338	310
Leukemia	M	3,924	4,512	4,855	5,015	5,053	5,142
	F	2,273	2,474	2,612	2,704	2,609	2,627

Table 9.—U.S. Age-Standardized Cancer Death Rates for Males and Females Over 65,1953-78 (Continued)

Site	Sex	Average annual rates/10 million aged 65 or over[a]					
		1953-57	1958-62	1963-67	1968-72	1973-77	Only 1978
Hodgkin's disease	M	626	600	626	592	468	384
	F	388	374	397	385	296	261
All other lymphomas[l]	M	2,701	3,303	3,900	5,126	5,787	6,266
	F	1,849	2,227	2,634	3,470	3,894	4,184
Remainder (chiefly[m] deaths where the anatomic site or origin of the cancerous cells was not recorded)	M	8,637	7,945	8,650	8,198	9,248	9,666
	F	7,324	6,341	6,294	6,038	6,354	6,502

a There are currently about 10 million Americans of each sex aged 65 or over, so the cited values are roughly similar in magnitude to the actual numbers of such deaths.
b These are the cancers which are strongly affected both by alcohol and by all forms of tobacco.
c Lung (including trachea and bronchus) cancer rates are affected more strongly by cigarette than by pipe smoking, and the Increases in respiratory cancer among People aged under 65 during the past quarter century can be chiefly ascribed to prior widespread adoption of cigarette smoking.
d Cancer of the intestines may arise in the small Intestine, in the ascending, transverse, descending or sigmoid colon, or in the rectum. U.S. mortality data do not seem to be sufficiently precise to allow unbiased examination of the trends in *any* of these separate parts, not even merely "colon" and "rectum".
e Liver specified as primary, including the bile ducts inside the liver.
f Gallbladder, including the bile ducts outside the liver.
g Mesentery, peritoneum and unspecified digestive sites (the latter comprising the minority in 1948, when separate totals were last published).
h In middle age there are now so few deaths from nonmelanoma skin cancers that the data for "total skin" represent the melanoma death rates reasonably accurately, but in old age the continuing decrease in the death rates from nonmelanoma skin cancers still dilutes the progressive increase in melanoma death rates.
i "Other urinary organs" (ureter and urethra, where cancers are rare) were included with "bladder" up to 1967, and were then transferred to "kidney" from 1968 onwards.
j Endometrium, Including all cancers of unspecified parts of the uterus.
k The distinction between "mall ignant" and "benign" is less clear-cut for brain tumors than for most other neoplasms, and so the most meaningful analysis seems to be of all fatal tumors of the central nervous system, irrespective of histology. However, even here, large biases are possible, for in old age symptoms due to brain tumors may be misdiagnosed as due to senility or vascular disease. Such errors are, of course, less likely in middle age, which may account for the marked upward trend in brain tumor death *certification* rates in old age being entirely absent in middle age.
l There is considerable diagnostic uncertainty between lymphosarcoma, reticulum cell sarcoma and various other lymphomas, so we have not attempted to examine them separately Myeloma is also included since data on myeloma were published separately only from 1968
m In years when any distinction between them can be made from the U S. Government publications, the "unspecified site" death certificates greatly outnumber the "specified sites" among those remaining cancers, although the distinction between them seems surprisingly erratic (e.g., comparing 1957 with 1958).

SOURCE: Doll and Peto (93)

experienced a large increase and nonwhite females a smaller, but notable, increase.

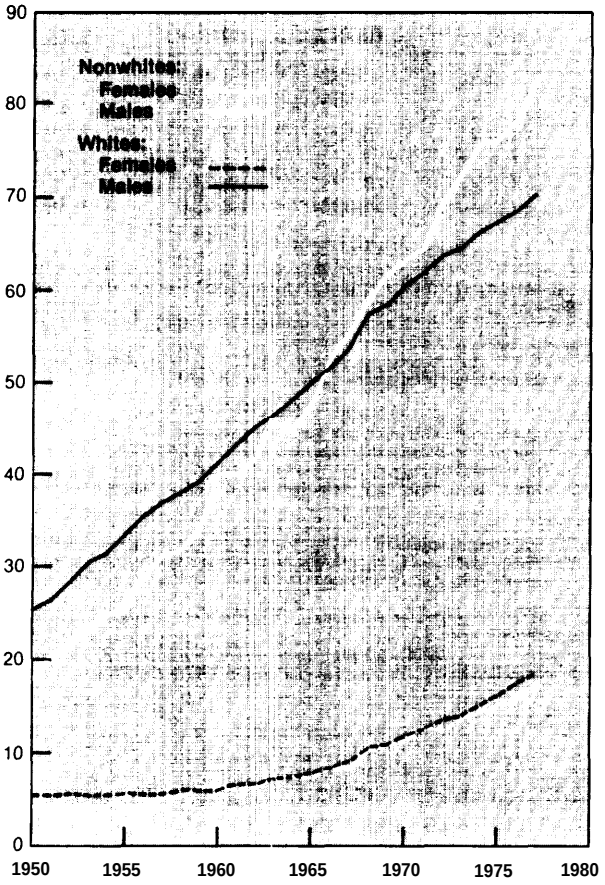
Stomach cancer (fig. 12) is now decreasing throughout the developed world. The enormously encouraging feature of the U.S. stomach cancer trends is that they are continuing downwards throughout middle age, which strongly suggests that as those people and subsequent cohorts age, they will have lower rates in old age than do older people today. The United States, which used to have very high stomach cancer rates, now has incidence rates which are among the lowest recorded in any country in the world.

No single explanation adequately explains the decrease, but several factors have been suggested as contributors: modern techniques of food preparation and storage, increased consumption of green vegetables, fruits, and antioxidant (as food preservatives), and increased milk intake (237). These associations are difficult to study epidemiologically because individuals may alter their diet throughout life and it is difficult to reconstruct past consumption patterns.

Intestinal cancer (fig. 13) may either be of a specified or of an unspecified part of the intestine. In 1958, about two-thirds of male intestinal cancer deaths were certified as being of some specific intestinal site (small intestine, ascending colon, transverse colon, descending colon, sigmoid colon, or rectum), and one-third were of an unspecified intestinal site, while by 1977 the converse was true. Overall there was little change in total male intestinal cancer mortality during this period. Clearly, although the male death certification rates for each specific intestinal site have been approximately halved, these decreases cannot be accepted as real, since the "unspecified site" rates have doubled.

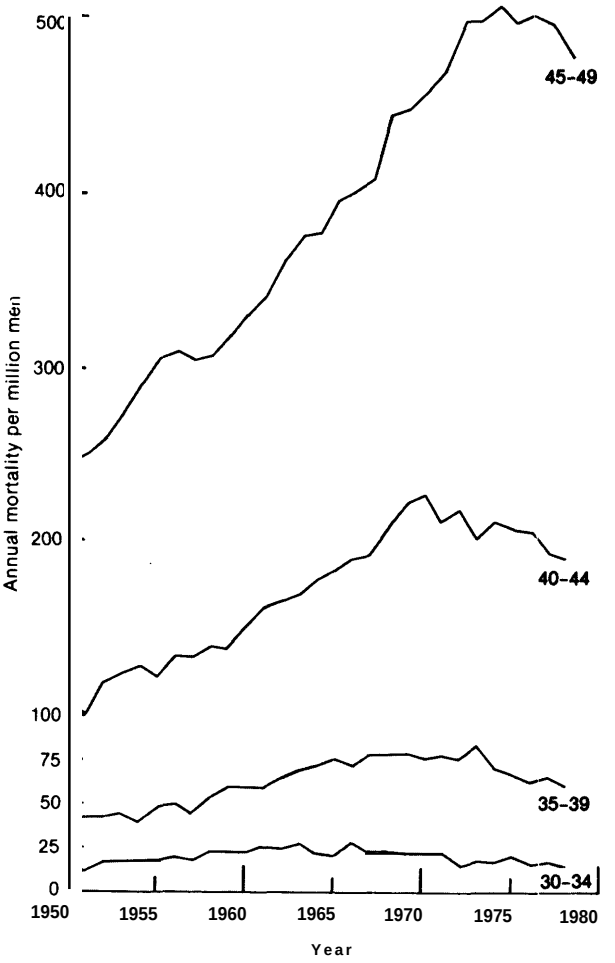
Moreover, it has been traditional to compile separate data for the "rectum," the last foot or

Figure 9.–Respiratory Cancer (ICD 8: 160-163) Mortality Rates per 100,000, Age-Standardized to U.S. 1970 Population: 1950-77



SOURCE Office of Technology Assessment

Figure 10.—Trends Since 1950 in U.S. Male 'Lung Cancer Mortality at Young Ages

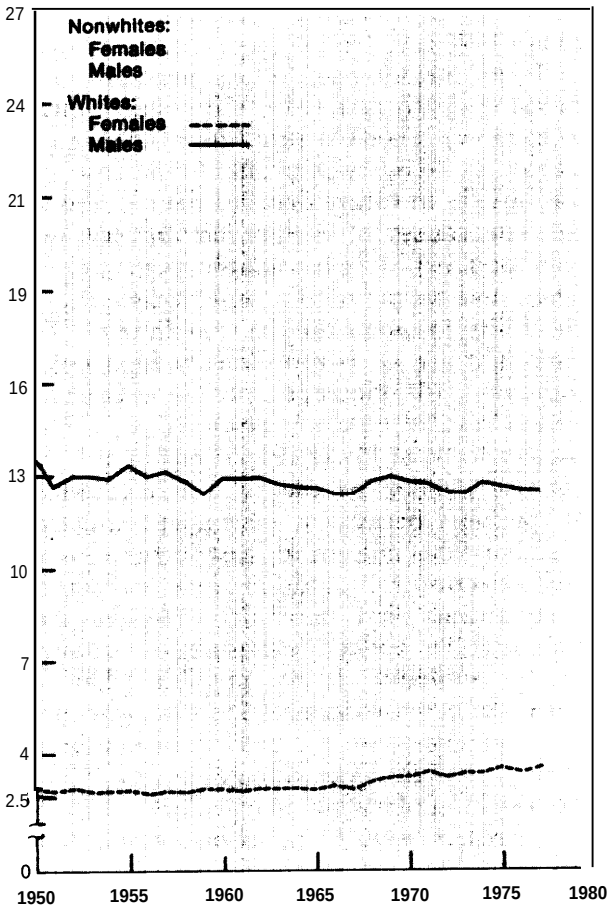


SOURCE: Doll and Peto (93).

so of the large intestine, and to describe the remainder, including unspecified intestinal sites, as "colon." Inspection of the data gives the misleading impression that rectal cancer rates are decreasing and colon cancer rates are increasing, while in fact the decreases in the death certification rates for rectum are if anything slightly less extreme than for other specified parts of the intestines. In view of the fact that half of all fatal cancers diagnosed in hospital as "rectum" in TNCS, were eventually certified as "colon," the most plausible interpretation of the data is that there have been no material trends in either colon or rectal cancer mortality during the past 25 years among males, although both the incidence and mortality data do suggest a slight decrease in onset rates below 65 years of age (93). Similar difficulties of classification affect data for females, and when all intestinal sites are combined, total female intestinal cancer death rates appear to be decreasing steadily since 1950.

Liver cancer currently accounts for 0.8 percent of cancer deaths among Americans under 65 and no statistically significant trends in liver cancer mortality are evident during the past decade. Incidence trends show a decrease in liver cancer, which is probably artifactual and due to improving differential diagnosis between primary liver cancer and cancers which have metastasized from other sites to the liver. This

Figure 11 .—Combined Mouth, Pharynx, Larynx, and Esophagus Cancer(ICD8:140-150~ 161) Mortality Rates per 100,000, Age-Standardized to U.S. 1970 Population: 1950-77

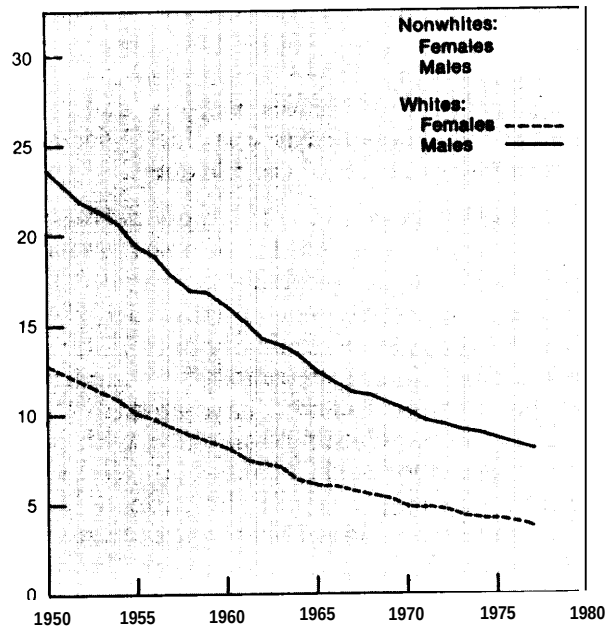


SOURCE Off Ice of Technology Assessment

decrease may be somewhat surprising in that the liver is intimately exposed to much of what is ingested, and it is composed of cells which are capable of rapid proliferation when necessary. Moreover, many of the chemicals that have thus far been found to be carcinogenic in animal feeding experiments cause liver cancer in animals.

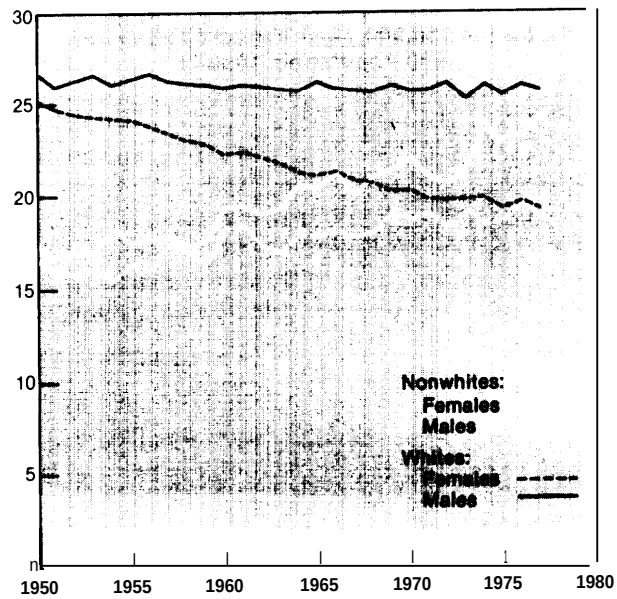
Gallbladder and bile duct cancers are unfortunately not reported separately either in mortality data or in the data from SNCS, though they are in TNCS. Cancers at these sites have different causes, however. Gallstones are a risk factor for gallbladder but not bile duct cancer. According to TNCS data, females develop

Figure 12.—Stomach Cancer (ICD 8: 151) Mortality Rates per 100,000, Age-Standardized to U.S. 1970 Population: 1950-77



SOURCE Off Ice of Technology Assessment

Figure 13.—Combined Small Intestine, Colon, and Rectum Cancer (ICD 8: 152-154) Mortality Rates per 100,000, Age-Standardized to U.S. 1970 Population: 1950-77



SOURCE Office of Technology Assessment

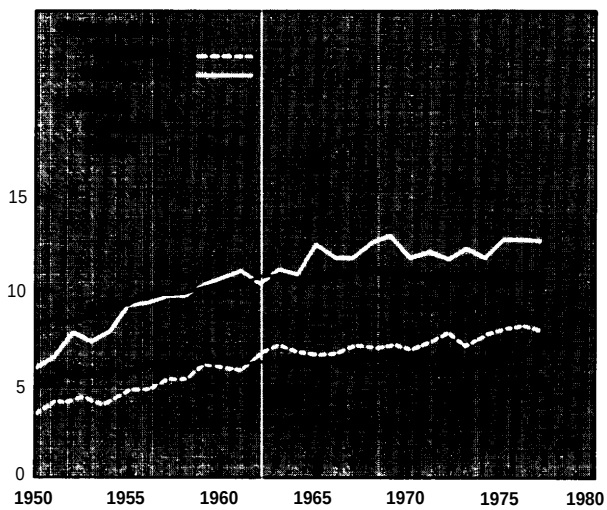
cancer of the gallbladder more frequently than cancer of the bile ducts, while for males the ratio is the inverse.

Decreases have occurred and are continuing to occur in the aggregate of the two cancers, and these decreases are larger among females than among males. The figures suggest that it is cancer of the gallbladder that is chiefly decreasing, rather than cancer of the bile ducts.

Pancreatic cancer (fig. 14) is now decreasing in males at ages under 65, the decreases in early middle age being particularly rapid. This decrease is especially encouraging because it comes after decades of gradually but steadily increasing rates. Pancreatic cancer is so uniformly fatal that treatment cannot have affected these trends. If the correlation of smoking with pancreatic cancer represents a cause-and-effect relationship, one might expect the ratio of rates among smokers to nonsmokers to be increasing, as has been the case in recent years for lung cancer. If the association is causal, then among middle-aged nonsmokers the trend in pancreatic cancer mortality must be even more steeply downwards than these national data suggest.

Bone cancer death certification (and incidence) have shown apparent decreases, which may be due largely to the progressive elimination of misdiagnosed secondaries (93). However, it is now impossible to determine whether or not actual decreases have occurred.

Figure 14.—Pancreas Cancer (ICD 8: 157) Mortality Rates per 100,000, Age-Standardized to U.S. 1970 Population: 1950.77

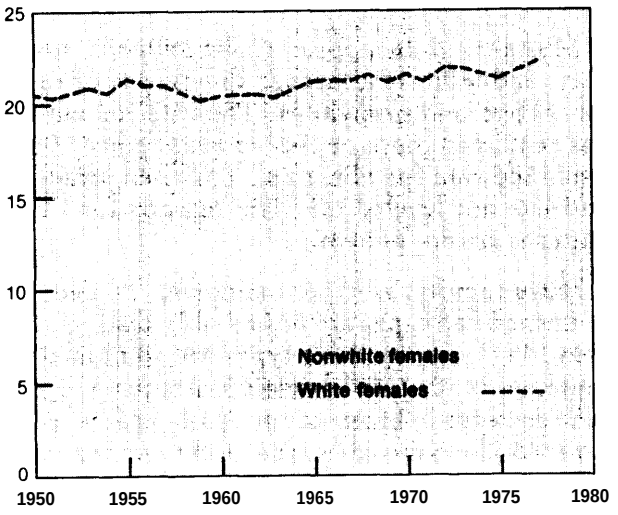


SOURCE. Off Ice of Technology Assessment

Skin cancer mortality increases from 1950 through 1978 are a result of an increasing death rate from melanomas, offset partially by a decreasing death rate from other skin tumors. The increases are most rapid in middle age, so the rates in old age will probably increase even more rapidly in future decades than is now the case. The causes of melanoma are not well-understood; exposure to sunlight seems to be involved, and people with a genetic deficiency in their ability to repair the damage done to DNA by sunlight are at extraordinarily high risk of melanoma ***(310).*** However, people whose work involves regular outdoor exposure seem paradoxically to be at lower risk of melanoma than otherwise similar people who work indoors (93), perhaps because a permanent suntan is protective. This may be at least in part a result of self-selection for outdoor work, or perhaps the conditions that maximize risk are those which involve sudden exposure of untanned skin to sunlight. It is possible that the worldwide increases in melanoma are due merely to some change in the pattern of human exposure to sunlight, e.g., changes in clothing and increases in sunbathing, particularly since the chief increases seem to be in melanoma of the trunk and legs rather than face (93). Alternatively since melanocytes are subject to hormonal influences, it could be that other causes are also important.

Breast cancer (fig. 15) incidence and mortality at ages under 65 show no substantial changes, but that overall rate conceals smaller fluctuations in mortality in particular age groups. Based on the accepted association of age at first childbirth and breast cancer risk (219), Blot (27) has argued that the reproductive patterns of different cohorts of American women can account for some or all of the small fluctuations in breast cancer death rates in particular cohorts of women. Women who were young during the Great Depression of the 1930's somewhat delayed having their children, and their breast cancer mortality now is slightly increased.

Figure 15.— Breast Cancer (ICD 8: 174) Mortality Rates per 100,000, Age-Standardized to U.S. 1970 Population: 1950-77



SOURCE Off Ice of Technology Assessment

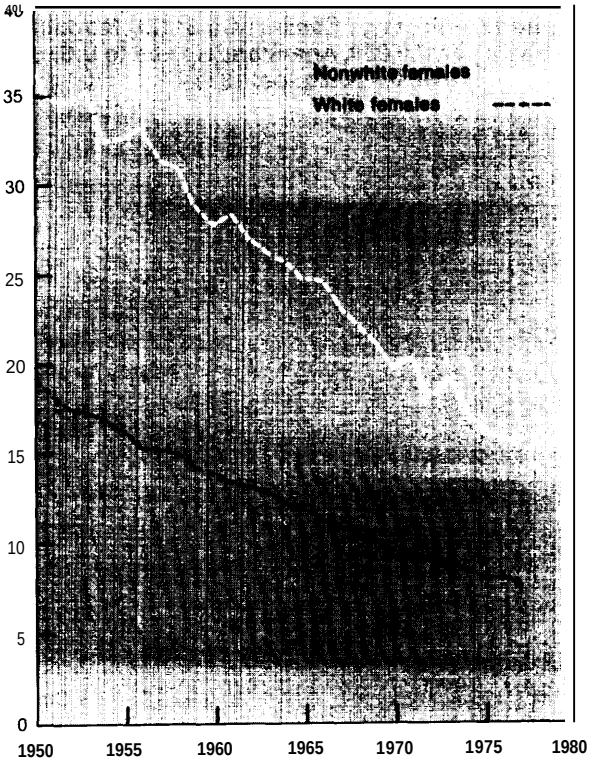
Women bearing children in the postwar baby boom had their babies at earlier ages and have now, in early middle age, substantially decreased breast cancer rates because of their early pregnancies.

Bladder cancer death rates in both sexes are decreasing steadily. The trend is encouraging, since bladder cancer can be caused by occupational exposure to various carcinogens. However, the discrepancy between rising incidence and falling mortality is more marked for bladder than for any other type of cancer except thyroid cancer (see p. 60). These diverging trends may be partly accounted for by improved treatment, but another reason is a shift in the classification of the two types of bladder tumors: papillomas and carcinomas. Lesions that are today considered carcinomas and included in incidence statistics, would formerly have been labeled papillomas, and not counted as such (93).

Kidney cancer death rates have been slowly but continually increasing for 25 years in males under age 65. Rates for females have just recently begun to rise. The mortality increases are accompanied by slight increases in incidence in both sexes. Mutagens have been detected in the urine of male smokers (369), and epidemiologic studies suggest about a 40 percent excess of kidney cancer among smokers (see ch. 3, "Tobacco"). Additional evidence is needed to confirm or refute an association of kidney *cancer* and smoking. If confirmed, all or most of the upward trend in mortality from kidney cancer could be attributed to tobacco.

Uterine cancer (fig. 16) mortality has decreased dramatically throughout the past 50 years, the combined effect of large decreases in cervical cancer mortality and smaller decreases in mortality from endometrial cancer. The downward trend in cervical cancer began long before screening for cancer of the cervix became widespread, and is the chief reason for the large, steady decrease in female nonrespiratory death rates over the past 40 years. The causes of this substantial improvement are not fully understood, although effects of improved personal

Figure 16.—Uterus Cancer (ICD 8: 180-182) Mortality Rates per 100,000, Age-Standardized to U.S. 1970 Population: 1950-77



SOURCE Off Ice of Technology Assessment

hygiene may be relevant. It is not known what effect cervical cancer screening programs have had on cervical cancer mortality. Also, many cervical deaths between 1933 and 1978 were certified merely as being due to "cancer of the uterus" (with the exact site not otherwise specified). If these deaths could be transferred from endometrium, where they now are, to cervix, the downward trend in cervical cancer would presumably be much steeper and that from cancer of the endometrium much shallower, which is supported by the trends in incidence. Finally, an increasing percentage of American women in middle and old age, when cancer is most common, have already undergone hysterectomy for various reasons, thereby removing both uterine cervix and endometrium (and, sometimes, both ovaries) from risk. A better statistic for these cancers might be the death rate per uterus or per ovary and not per woman.

Prostate cancer (fig. 17) becomes increasingly common with age, more so than for most other cancers. Incidence rates for prostate cancer probably are not reliable, being influenced by poorer census data for older age groups, and most importantly, the more thorough search for lumps, which would not have come to clinical attention in earlier years.

Figure 17.—Prostate Cancer(ICD 8: 185) Mortality Rates per 100,000, Age-Standardized to U.S. 1970 Population: 1950.77

SOURCE. Off Ice of Technology Assessment.

Mortality data appear to be reliable, however, and indicate a marked divergence of rates for whites and nonwhites. The rate for whites has remained more or less constant since '1950, while the rate for nonwhites has risen steadily, and has not leveled off. The reasons for these patterns are not known.

Brain tumors, whether malignant, benign, or of unspecified types are not reliably distinguishable, therefore the three types are combined to examine trends. Under age 65, a l-percent per year decrease in brain tumor death rates is seen. Over 65, the opposite is true, and there is a very rapid increase in brain cancer death rates, possibly due to a steady improvement of diagnostic standards.

Thyroid cancer is not common, accounting for less than 1 percent of all cancer deaths. "Thyroid cancer death rates have fallen steadily from 1950 to the present, while a large increase in incidence occurred through at least 1970. The discrepancy between incidence and mortality can be at least partly explained by the many cases, mostly nonfatal, induced by medical radiation of the thyroid, head, and neck. These X-ray practices have largely been discontinued. The decrease in mortality may be a result of improved treatment, as well as possible real decreases in the incidence of serious cases.

Hodgkin's disease and certain forms of *leukemia* are much more treatable now than a decade or two ago. This fact alone accounts for the observed substantial downward trends in mortality, especially among younger people. The availability of successful treatments may also have encouraged more thorough efforts at correct diagnosis. Reliable estimation of trends in the various completely different types of leukemia is, unfortunately, not possible from the available data. The lack of any net trend in either direction in leukemia mortality among older people may represent a balance between increasingly thorough diagnosis among elderly patients who are dying of leukemia and slightly

better treatment of the disease. The incidence data suggest that some decreases in real onset rates for leukemia are in progress, at least among females (93).

Myelomatosis death rates have been rising steadily from 1968 through 1978, more so for older than for middle-aged people, for unknown reasons. The apparent increase may be real, but may be largely or wholly due merely to be improved case-finding, for improved case-finding must have occurred during 1968-78 and might be expected to have its greatest effect among the old.

Unspecified sites account for 6 to 8 percent of all cancers at ages below 65. The exact percentage varies irregularly from 1950. Rather surprisingly, given better diagnostic criteria in recent years, slight increases in cancer at unspecified sites have been seen during the past decade,

SUMMARY

The ability to analyze cancer incidence and mortality depends on the available data. Qualifications are attached to the reliability of both kinds of data, more to incidence data because they have been collected over smaller geographical regions for shorter periods of time, but certain conclusions can be drawn.

Respiratory cancer incidence and mortality have increased dramatically in both sexes, but the last few years have seen a decline in 1ung cancer rates among young men, The increases and the more encouraging decreases are associated with changes in smoking habits. The decrease in cancer death rates for females during the last 50 years is partly explained by dramatic decreases in deaths from cancer of the uterine cervix. Stomach cancer mortality has decreased substantially in both sexes.

When cancer mortality from all nonrespiratory sites are considered together, a decrease is seen in females since 1950 (due to decreased cervical and stomach cancers). Male death rates have remained about level over the same period. While stomach cancer death rates have decreased in men increases at other sites have balanced those decreases.

A controversy is swirling around the interpretation of incidence rates. Data collected in TNCS (1969-71) and NCI's SEER program (1973-78) show that overall cancer incidence increased more than 1 percent per year over that decade. The large changes, major increases in lung cancer and decreases in cervical and stomach cancers, are the same as those observed in mortality trends. However, increases seen at other sites are not universally accepted as reflecting actual change, because of differences in methodology between TNCS and SEER. Continuation of the SEER program may provide data to better answer questions about cancer incidence.