

Prostate Cancer Trends 1973-1995, SEER Program National Cancer Institute

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FOREWORD

This report assembles under one cover the most detailed information available on the demographic and clinical features of prostate cancer. These population-based data will be extremely important in furthering our understanding of this cancer, which has the distinction of being the most frequently diagnosed cancer in men and their second leading cause of cancer death. Prostate cancer has been the source of enormous public and professional interest over the last few years. The recent introduction of PSA screening and changes in disease management have led to changes in incidence trends and treatment, and these are extensively chronicled in this publication. Where there has been great controversy about the role of screening for prostate cancer, this report provides much of the data that were lacking previously.

Cancer of the prostate exhibits large variations by race and ethnicity. It is well known that African American men have the highest incidence and mortality rates of all men not only in the United States, but indeed in the entire world. For the first time in one volume, this report offers extensive racial and ethnic comparisons related to demographic details and clinical features. These are the kind of data that will help scientists and clinicians gain insights needed to unravel the differences behind the variation in rates.

Finally, I would like to thank the staff members of the National Cancer Institute and their colleagues across the United States and at Information Management Services, Inc., who have been involved with the Surveillance, Epidemiology and End Results (SEER) Program. It is through their diligence that these data have been collected, analyzed, and interpreted. This report highlights how important the SEER Program has become as a national resource. We look forward to the extensive use of this information and the contributions we are confident it will engender in the understanding of prostate cancer.

Barbara K. Rimer, Dr. P.H.
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Highlights of Prostate Cancer Trends, 1973-1995

The SEER Program of the National Cancer Institute is pleased to release this monograph on prostate cancer in the United States from 1973 through 1995. This monograph resulted from the work of the 11 SEER registries, the SEER staff, and the editors. Since prostate cancer is the number one incident cancer and the number two cause of cancer deaths among U.S. men, the data in this monograph are important for researchers, clinicians, policy makers and citizens in understanding this disease. A few of the highlights from the monograph are listed below:

Monograph Data (Page 1)

- Data are from the SEER program which has registries covering 14% of the U.S. population.
- 272,689 cases with histologically confirmed adenocarcinoma of the prostate newly diagnosed between 1973 and 1995 are included.
- Mortality data are both from the SEER areas and the entire U.S. population.
- Data for the 23-year period are presented for whites and blacks. Data for Asians, Native Americans, and Hispanics are only available for 1990-1995 and are presented in a separate section.

Incidence (Page 7)

- Black men have about a 60% higher incidence rate than white men.
- Incidence rates modestly increased from 1973-1986, rapidly increased from 1987-1992, and declined from 1993-1995.
- Incidence rates increased 108% for white men from 1986-1992 and 102% for black men from 1986-1993; these increases in rates are believed to be related to use of the prostate-specific antigen (PSA) blood test as a new screening tool.
- The increase from 1986-1992 occurred in all age groups; the median age at diagnosis decreased by one year for whites and for blacks between 1980-1985 and 1990-1995.
- The increase from 1986-1992 occurred for both localized and regional stages of disease and mostly in moderately differentiated tumors.
- Incidence of distant stage prostate cancer peaked in 1985 and by 1995 declined by 56%.

Mortality (Page 7)

- Black men have about a 2-fold higher mortality rate than white men.
- Death rates from prostate cancer have gradually increased over the last 20 years, but peaked in 1991 and 1993 for white and black men, respectively.
- The median age of death increased between 1980-1985 and 1990-1995 by one year in both whites and blacks.

- Though death rates have slightly decreased in recent years, a decline in the absolute number of deaths was first noted in 1995. In white men under age 75, the age-adjusted mortality rate declined by 15% between 1990 and 1995.

Grade and Stage (Page 17)

- Between 1973-1995, about 60% of prostate cancers were diagnosed at a localized stage and about 40% were graded as moderately differentiated. The percent of moderately differentiated cancers differed little by race, but decreased slightly with advancing age.
- Stage and grade are correlated; as the grade becomes less differentiated the stage is likely to be more advanced.
- The rapid increase in prostate cancer incidence from 1986-1992 was confined to moderately differentiated cancers for all ages and for whites and blacks.

Treatment (Page 29)

- Only treatment data for 1983-1995 are included, as these are the only years with consistent coding. The monograph focuses on treatment patterns in localized and regional stage cancers.
- The increased incidence (1986-1992) was accompanied by increases in more aggressive therapy (radical prostatectomy or radiation therapy) for localized and regional cancers.
- Recent treatment patterns for local/regional cancers vary by age: radical prostatectomy is more frequent among men under age 70, radiation therapy in those age 70-79, and conservative therapy (no treatment or hormonal therapy) in those over age 79.
- Treatment for distant stage cancers has not changed over time with about 65% of patients receiving hormonal therapy.

Survival (Page 41)

- Based on cases diagnosed in 1990 and followed through 1995, 93% of all men diagnosed with prostate cancer will survive five years or longer.
- Relative survival rates have increased since 1973 for both black and white men, but the difference between blacks and whites has increased over time (survival has not improved as rapidly in black men).
- Consistent improvements in relative survival have occurred over time (1973 to 1993) for localized and regional stage cancers, with relative five-year survival now exceeding 99%.
- Relative survival has increased over time for all grades of cancer.
- Relative survival for younger men (age <50) is lower than for older men.
- Five-year relative survival for distant stage disease is 34% and has not improved over time.

Race/Ethnicity (Page 47)

- The lowest incidence rates are found in Native Americans and all other groups have lower rates than whites and blacks. The incidence rates peaked in 1992 for all groups except blacks, where it peaked in 1993.
- National mortality rates are not available for Asians and Native Americans; mortality rates are available for white-Hispanics, and their rates have not decreased as they have for blacks and white non-Hispanics.
- Stage distribution is similar across races, except the proportion with distant stage disease is higher for Hawaiians, Filipinos, and Native Americans.
- Filipino men have slightly more poorly differentiated cancers than the other groups. The proportion of tumors that are well or moderately differentiated is similar across all groups.
- Of patients with localized or regional stage prostate cancer, Native Americans have the poorest relative survival of all racial/ethnic groups. Blacks and white-Hispanics have the lowest five-year relative survival rates among patients with distant stage disease.

Prostate cancer is a major public health problem, which over a lifetime will affect an estimated one in five American men. The American Cancer Society predicts that in 1998 alone, 184,500 men will be diagnosed with prostate cancer and 39,200 will die from the disease. Despite its distinction as the most frequently diagnosed noncutaneous cancer and the second leading cause of cancer deaths in

men, little is known about the causes of prostate cancer. Incidence rates increase more sharply with age for prostate cancer than for any other cancer type. Prostate cancer incidence rates are higher among men with a family history of the disease, and are higher in blacks compared to whites or Asian Americans. International incidence rates vary more than 65-fold from low-risk to high-risk populations (Figure 1.1), although this variation is at least partially explained by differences in prostate cancer screening and early detection programs across countries. Migrant studies of prostate cancer show that men who move from low-incidence to higher-incidence countries experience a shift in risk toward that of men from the higher risk areas, implicating environmental determinants in the development of this disease.

Epidemiologic studies have suggested several factors that may play a role in prostate cancer. In most instances, the evidence is fragmentary or inconsistent (e.g., certain occupational exposures, sexually transmitted infectious agents, sexual activity level, history of benign prostatic hyperplasia, vasectomy, androgenic hormones, weight or obesity, cigarette smoking, alcohol consumption, and vitamin D, vitamin E, and selenium intake). The evidence for dietary fat and red meat intake is somewhat stronger and more consistent, but as yet is inconclusive. Age, race, and a family history of prostate cancer are the only

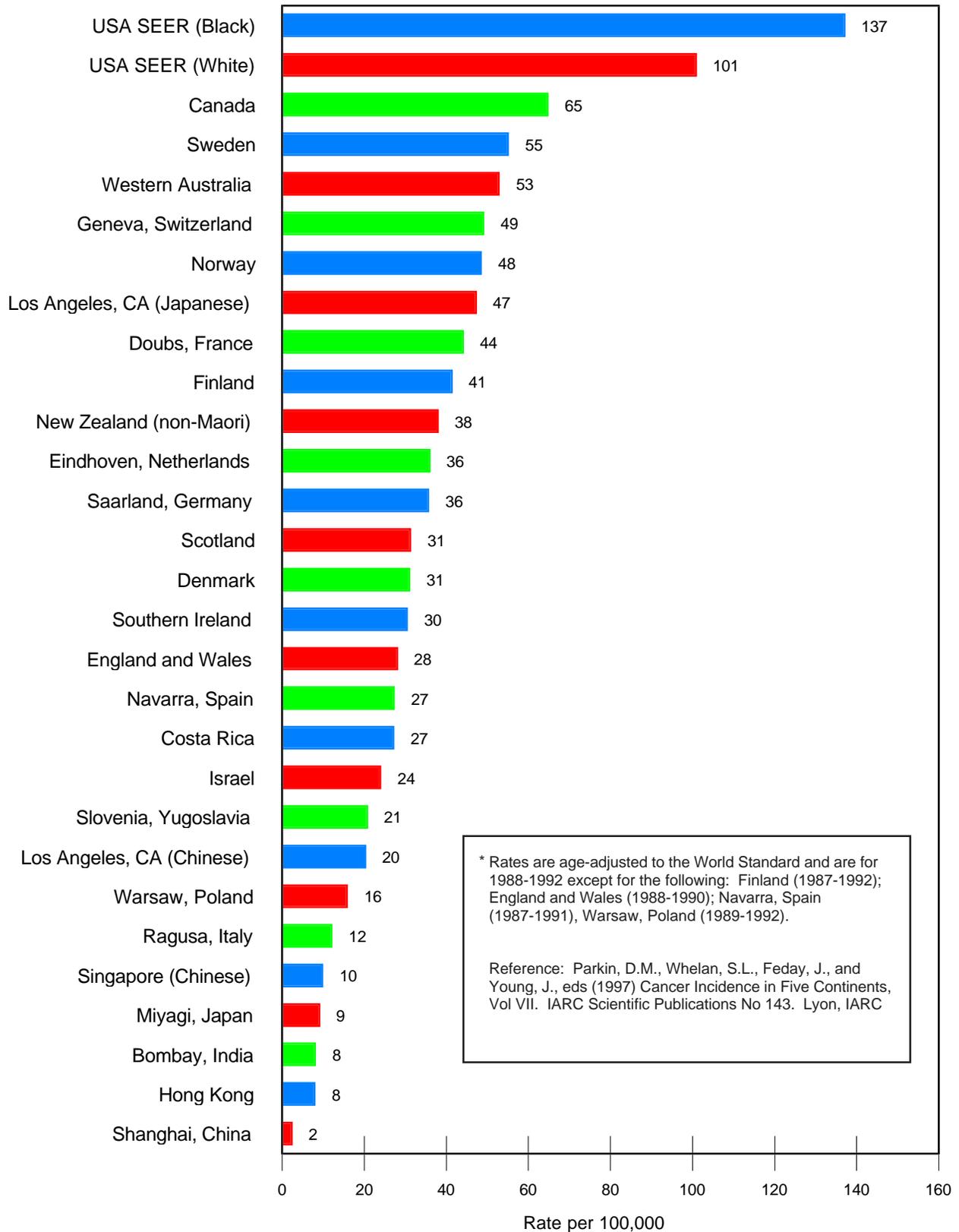
well established risk factors for prostate cancer. Further research is clearly needed on the underlying causes of this cancer.

Over the past decade, there have been dramatic changes in the descriptive epidemiology of prostate cancer. Following the introduction in 1986 of the serum prostate-specific antigen (PSA) test to monitor progression and recurrence of prostate cancer, the incidence of this disease began to rise steeply to a peak in 1992, and subsequently declined each year from 1993 through 1995. This pattern is most pronounced for localized and regional stage disease. An evaluation of histologic grade indicates that most of the increase in incidence has been in moderately differentiated, not well differentiated, tumors. By comparison, the age-adjusted incidence of distant stage prostate cancer peaked in 1985 and declined in subsequent years. Concurrent with the shift toward earlier stage disease, there has been a shift toward earlier ages at diagnosis among both blacks and whites. The mean age at diagnosis is about two years younger among black men compared to their white counterparts.

The widespread use of PSA screening and early detection programs are thought to explain most of the changing patterns in prostate cancer incidence, although the benefit of screening on the

Figure 1.1

Prostate Cancer International Incidence Rates*



mortality from this disease remains undetermined. The overall age-adjusted mortality rate peaked in 1991, and a 6.7% decline was observed by 1995. The magnitude of this decline is about 1.8 deaths per 100,000 men per year.

The purpose of this monograph is to provide a descriptive review of temporal trends (1973-1995) in the epidemiological and clinical characteristics of prostate cancer patients ascertained through the population-based cancer registries that participate in the Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute. Age-adjusted and age-specific incidence rates (1973-1995) are shown by race for blacks and whites. Recent data (1990-1995) for racial minorities and Hispanic populations are described separately. Incidence trends are examined by age, histologic grade, stage of disease at diagnosis and first course of treatment. Relative survival following the diagnosis of prostate cancer is also examined. Mortality data are provided by the National Center for Health Statistics and the rates are based on prostate cancer deaths between 1973 and 1995 for the SEER areas and for the entire United States population.

The SEER Program

The Surveillance, Epidemiology and End Results (SEER) Program was established in 1973 as part of the National Cancer Institute. The SEER Program has a mandate to collect cancer incidence, treatment, and survival data, which can be used to monitor the impact of cancer in the United States population. There are currently eleven SEER geographic areas that maintain population-based cancer reporting systems, including the states of Connecticut, Hawaii, Iowa, New Mexico, and Utah, and the metropolitan areas of Atlanta, Georgia,

Detroit, Michigan, Los Angeles, San Francisco-Oakland, and San Jose-Monterey, California and Seattle-Puget Sound, Washington. These regions cover about 14% of the total United States population and were selected to provide information from diverse population subgroups such as various racial and ethnic groups as well as urban and rural residents. Data used for this report are primarily from the nine standard SEER geographic areas for the period 1973-1995. Data from two more recently added registries, San Jose-Monterey and Los Angeles, California, were available only for the period 1988-1995 and are included in some analyses as indicated.

Cancer Trends

The primary measures associated with assessing the impact of cancer in the general population are the number of new cases per year per 100,000 persons (incidence rate), the number of deaths per year per 100,000 persons (mortality rate), and a determination of the proportion of patients alive at some point subsequent to the diagnosis of their cancer (relative survival rate). All three measures are included in this report. The incidence and mortality rates are age-adjusted to the 1970 United States standard population, unless otherwise specified. Age-adjustment minimizes the effect of differences in age distributions when comparing rates between two or more populations or between two or more time periods in the same population. This report includes incidence, mortality and relative survival data from 1973 through 1995.

Eligible Cancer Cases

All newly diagnosed prostate cancer cases (ICD-O-1 site code 185.9 and ICD-O-2 C61.9) who were residents of the defined geographic regions covered by the SEER

registries were abstracted and entered into the SEER database. (An internal SEER audit of hospital reporting from 1991 indicated that the incidence data for all cancer sites were 98 to 99 percent complete.) Data items collected include: demographic information, primary site, tumor histology, tumor behavior (in situ, invasive), tumor grade or differentiation, diagnostic confirmation, extent of disease at diagnosis, and first course of cancer-directed therapy. All incident prostate cancer cases remain under lifetime surveillance for survival.

For the purposes of this monograph, only newly diagnosed invasive cases of adenocarcinoma (histology codes 8010, 8140-8570) of the prostate (n=284,925) were considered eligible for inclusion, representing 98.7 % of the 288,539 available cases diagnosed during 1973-1995. In addition, cases that were not microscopically confirmed (n=8,731) and those that were diagnosed only

by autopsy or on a death certificate (n=3,505) were excluded, leaving 272,689 patients for analysis. The distributions of these incident cases by age and race are shown in Figure 1.2 and Table 1.1. Overall, 83.8% of cases are white and 10.3% are black. Across all races shown in Table 1.1, 4.2% of cases are of Hispanic origin.

Mortality Data

A public use tape containing information on all deaths occurring in the United States by calendar year is obtained annually from the National Center for Health Statistics (NCHS). Information on each death includes age at death, sex, geographic area of residence, underlying and contributing causes of death. Only the underlying cause of death was used in the calculation of mortality rates. Numbers and mortality rates for the total U.S. and for the SEER geographic areas were obtained from these tapes.

Figure 1.2
Prostate Cancer Cases
Distribution by Age
SEER Program*, 1973-1995

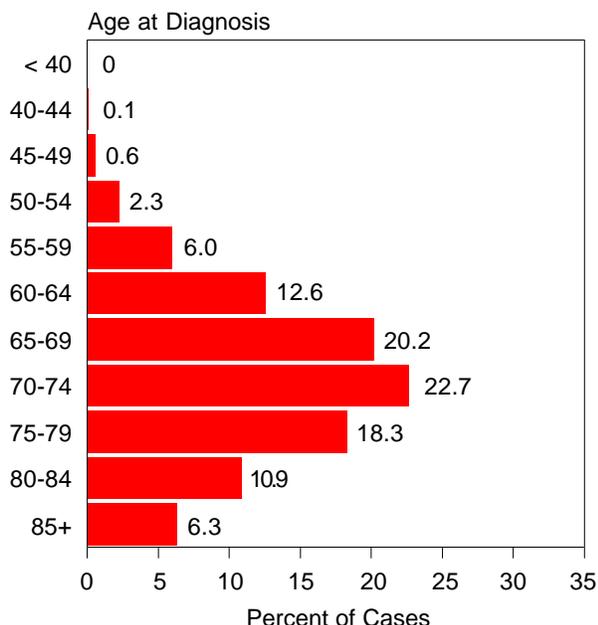


Table 1.1
Prostate Cancer Cases
Distribution by Race
SEER Program*, 1973-1995

Race	Number	Percent
White	228,602	83.8
Black	28,172	10.3
Asians	9,721	3.6
Japanese	3,489	1.3
Filipino	3,014	1.1
Chinese	1,880	0.7
Hawaiian	594	0.2
Korean	158	0.1
Other Asian	586	0.2
Native American	466	0.2
Other race	390	0.1
Unknown	5,338	2.0
Total	272,689	100.0

* Data from San Jose-Monterey and Los Angeles used only for 1988-1995.

Population Data

Population estimates were obtained from the U.S. Bureau of the Census. Estimates of the populations of U.S. counties were obtained by five-year age group (0-4, 5-9, ..., 85 and over), sex, and race (white, black, other) for each year as of July 1.

Explanation of Terms

Several measures for assessing the impact of prostate cancer in the general population are used in this report. The following definitions are presented to clarify their meaning.

The cancer **incidence rate** is the number of new cancers of the prostate diagnosed in a specified population during a defined time period such as a year, expressed as the number of cancers per 100,000 men. Except for five-year age-specific rates, all incidence rates are age-adjusted to the 1970 U.S. standard population.

The prostate cancer **mortality rate** is the number of deaths with prostate cancer given as the underlying cause of death occurring in a specified population during a defined time period such as a year, expressed as the number of deaths due to prostate cancer per 100,000 men. Except for age-specific rates, all mortality rates are age-adjusted to the 1970 U.S. standard population.

An **age-adjusted rate** is a weighted average of the age-specific cancer incidence (or mortality) rates, where the weights are the proportions of persons in the corresponding age groups of a standard population. Age-adjustment allows direct comparison of cancer incidence or mortality rates between two or more years in the same population or between two or more

populations with different age structures. For this report, the 1970 United States standard million population is used in computing all age-adjusted rates.

The **observed survival rate** is obtained using standard life table procedures and represents the proportion of prostate cancer patients surviving for a specified length of time after diagnosis.

The **relative survival rate** is the ratio of the observed survival rate to the expected survival rate for a patient cohort. The expected rate is based on mortality rates for the total population taking into account, as appropriate, the age, sex, race, and calendar year of diagnosis of the patients. It is assumed that the presence of cancer is the only factor which distinguishes the cancer patient cohort from the general population, with the relative survival rate indicating the probability that patients will escape death due to causes associated with their diagnosed cancer.

Stage of disease at diagnosis of prostate cancer is defined as follows:
Localized - an invasive neoplasm confined entirely to the prostate. **Regional** - a neoplasm that has directly extended beyond the limits of the prostate capsule into surrounding organs or tissue; into regional lymph nodes, or both. **Distant** - a neoplasm that has spread to parts of the body remote from the primary prostate tumor, i.e., metastatic. **Unstaged** - information is not sufficient to assign a stage. For prostate cancer, SEER records the best available information on stage of disease as it appears in the medical record within two months of diagnosis. No distinction is made between clinical or pathological stage. Surgically treated cases undergoing radical prostatectomy may be reclassified from clinically localized to regional stage disease

based on the more accurate information obtained from the operative or pathology report. Since this does not occur with other therapies (i.e., radiation or hormonal treatments), it presents a problem of selective upstaging. To evaluate how this problem may affect trends by stage of disease, cases undergoing radical prostatectomy with stage coded as regional disease were re-coded as clinically localized disease for some analyses.

The **histologic grade** or degree of differentiation of malignant prostatic tumors is coded as well differentiated (corresponding to Gleason score 2-4), moderately differentiated (Gleason 5-7), poorly differentiated or undifferentiated (Gleason 8-10), or unknown grade.

Treatment is the first course of cancer-directed treatment that is administered or planned within four months of the initial course of therapy as recorded in the medical records. The primary source of treatment information is the hospital medical record. Only treatment data for 1983-1995 are included since these are the only years during which a consistent coding scheme was used for site-specific surgery. Treatment data were classified according to the following hierarchy: radical prostatectomy (alone or with radiation, hormone therapy, or chemotherapy), radiation therapy (alone or with hormone therapy or chemotherapy), hormone therapy (alone or with chemotherapy), other treatments, and no treatment.

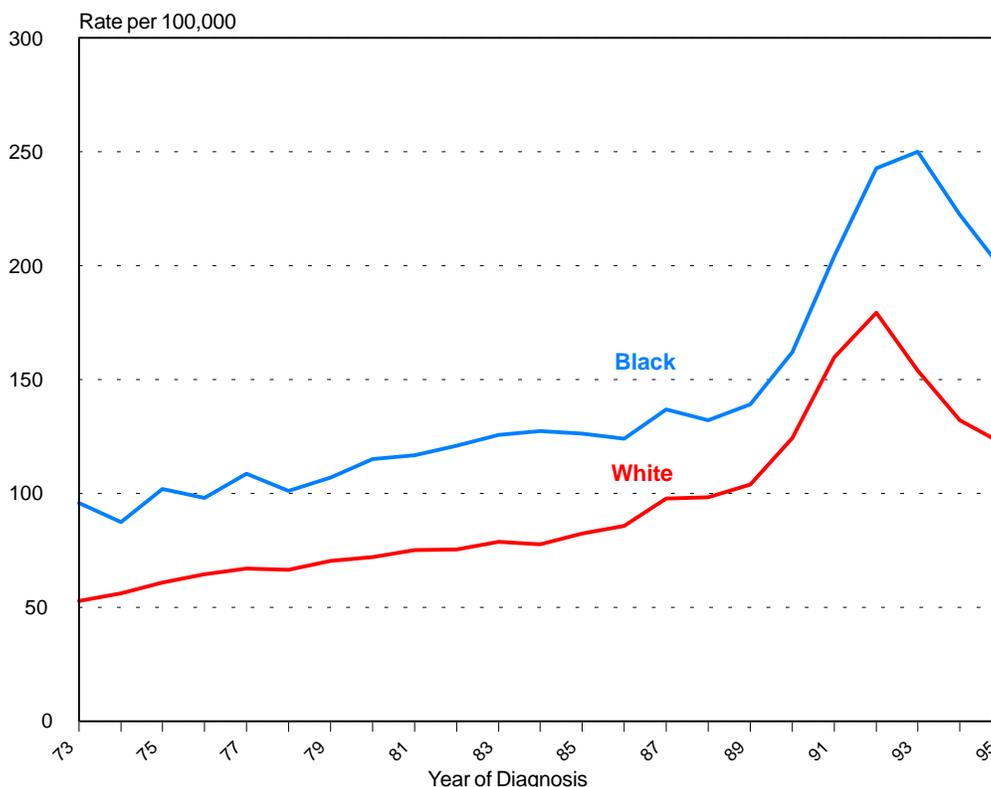
**INCIDENCE
AND
MORTALITY**

Substantial changes in prostate cancer incidence have occurred since the introduction of the prostate-specific antigen (PSA) blood test. This test was first approved by the Food and Drug Administration in 1986 as a method to monitor prostate cancer progression. The potential of the PSA test as a cancer screening tool was quickly recognized, leading to its widespread use in early detection programs.

Prostate cancer incidence rates increased gradually in black and white men from 1973 through the late 1980s, when rates began to rise sharply (Figure 2.1). Between 1986 and 1992, when the rate peaked in whites, the overall age-adjusted incidence rate increased by 108%, from 86 to 179 per 100,000 men per year. The overall rate in blacks peaked in 1993, representing a 102% increase from 1986 to 1993 (from 124 to 250 per 100,000).

Following these peak incident years, a decline in incidence was observed in both racial groups. As shown in Figure 2.2, these patterns are apparent in both white and black men under age 65 years, those aged 65-74, and men aged 75 years and older at diagnosis. The increase was most pronounced in younger men (age < 65), whereas the recent decline was primarily observed in men aged 75 years and older.

Figure 2.1
Prostate Cancer
SEER Incidence Rates, 1973-1995



Note: Rates are age-adjusted to the 1970 U.S. standard. Rates from 1973-1987 are based on data from the 9 standard SEER registries. Data from San Jose and Los Angeles are included in the rate calculations for 1988-1995.

Reasons for these changing patterns are not entirely clear. Although the recent peak in prostate cancer incidence is likely due to PSA-based screening, the modest increase prior to the PSA era may reflect, in part, changes in the prevalence of risk factors in the population.

There has also been a shift in the age-specific incidence of prostate cancer toward younger ages at diagnosis (Figure 2.3). Age curves comparing the period prior to PSA availability (1980-1985) with the PSA era (1990-1995) indicate a decrease in mean age at diagnosis of 1.7 years in whites and 1.3 years in blacks. Based on data from the most recent six-year period, black men have a younger mean (1.9 years younger) and median (2 years younger) age at diagnosis compared to whites.

Prostate cancer mortality increased over the past two decades in both white and black men (Figure 2.4), based on data for both the entire U.S. population and for the SEER geographic regions. Among white men in the U.S., the age-adjusted mortality rate increased from 20.3 per 100,000 in 1973 to a peak of 24.7 per 100,000 in 1991. Subsequently, the mortality rate declined to 22.9 per 100,000 in 1995, representing about a 7.3% decrease from 1991 to 1995.

Among blacks, the prostate cancer mortality rate based on U.S. data was 39.5 per 100,000 in 1973 and rose to a peak of 56.2 per 100,000 men in 1993. A 4.8% decline in overall mortality was noted in 1995 (53.5 per 100,000).

Mortality rates based on SEER data are consistent with those for the whole U.S. population. These data provide evidence that the SEER data are representative of the entire U.S. population with respect to trends in prostate cancer mortality rates, although

SEER rates fluctuate more due to smaller numbers of deaths recorded in the SEER areas compared to the nation.

The overall mortality trends vary by age in whites and blacks (Figure 2.5). In whites under age 75, mortality rates peaked in 1990 at 2.7 (aged less than 65) and 111.5 (aged 65-74) per 100,000 men and then declined to 2.3 and 95.2, respectively, in 1995. This represents about a 15% decrease in mortality for white men under age 75. The mortality rate in older (aged 75+) whites peaked in 1993 at 420.0 per 100,000. In blacks under age 65, the mortality rate peaked in 1992 at 7.8 per 100,000 and then dropped to 6.9 in 1995. Mortality in middle-aged (65-74 years) blacks peaked in 1994 at 281.7 per 100,000. In older (aged 75+) blacks, there was a steady rise in the mortality rate from 1974 to its peak in 1993 at 874.9 per 100,000. This represents a 69% increase in the mortality rate for older black men over the 20-year period.

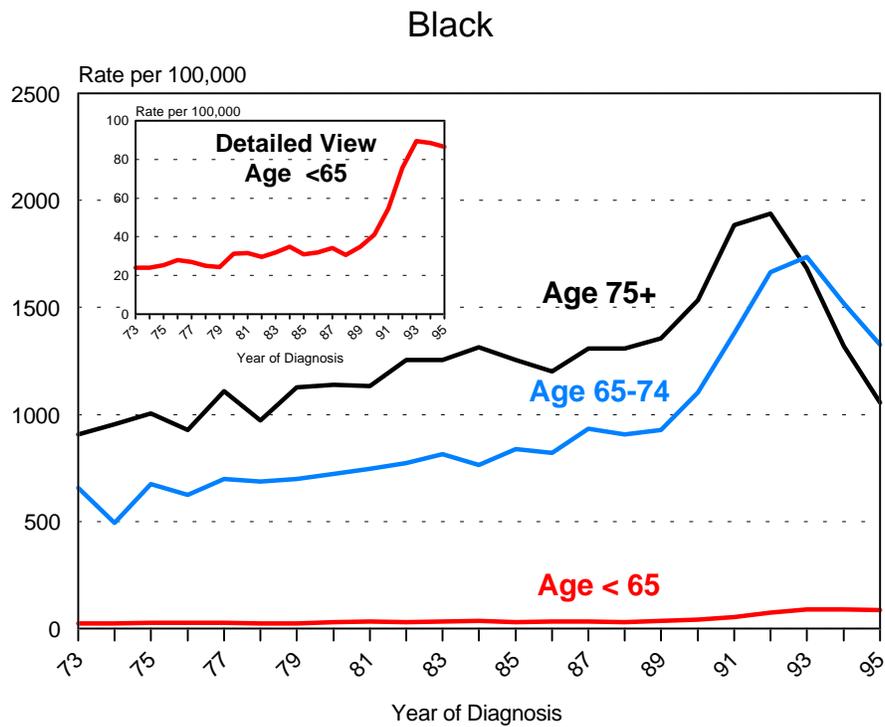
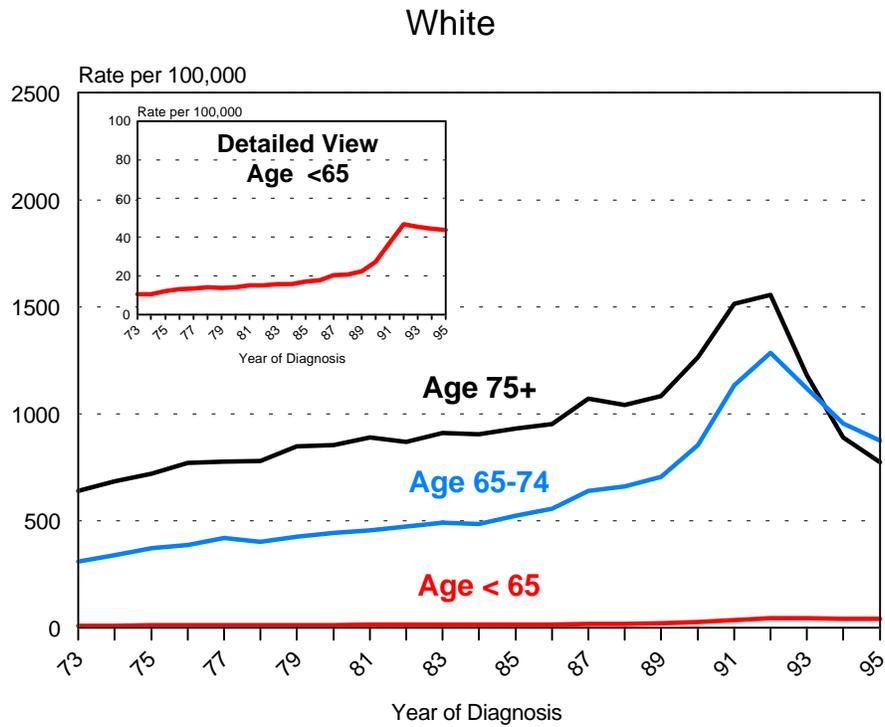
The age-specific mortality curves for two time periods, 1980-1985 and 1990-1995, indicate that both the mean and median ages at death from prostate cancer have increased by 1.4 years and 1 year, respectively, in both races (Figure 2.6). During the most recent time period, the median age at death from prostate cancer was 78 years in whites and 76 years in blacks.

Despite the recent decline in mortality rates (Figure 2.4), the actual number of men dying of prostate cancer declined for the first time in 1995 (Figure 2.7). Figure 2.7 also shows the estimated number of newly diagnosed prostate cancer cases in the U.S. population for 1990-1995, assuming that the annual age-specific incidence rates observed in the SEER regions are representative of the U.S.

population as a whole. The recent decrease in the age-adjusted incidence rate of prostate cancer is reflected in the declining number of cases estimated to have been diagnosed each year from 1993 through 1995 compared to 1992.

Figure 2.2

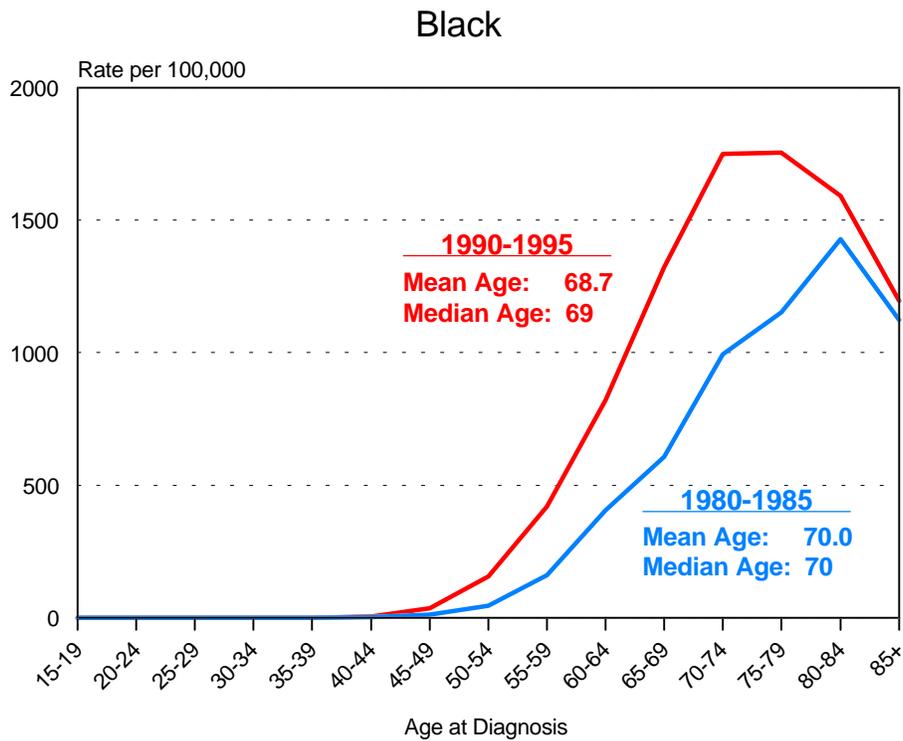
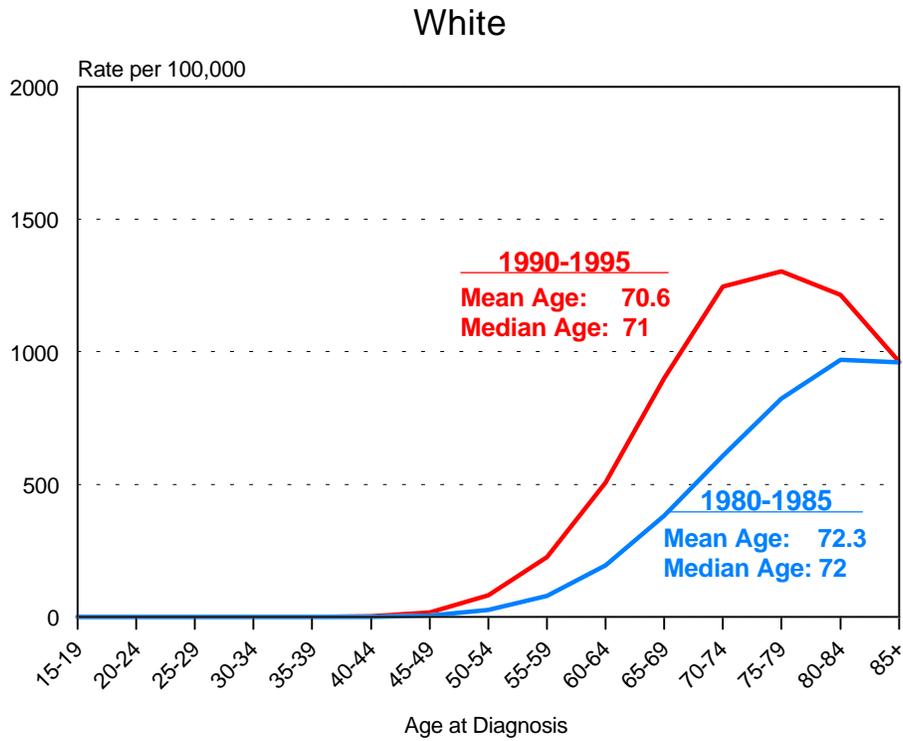
Prostate Cancer SEER Incidence Rates by Age at Diagnosis, 1973-1995



Note: Rates are age-adjusted to the 1970 U.S. standard. Rates from 1973-1987 are based on data from the 9 standard SEER registries. Data from San Jose and Los Angeles are included in the rate calculations for 1988-1995.

Figure 2.3

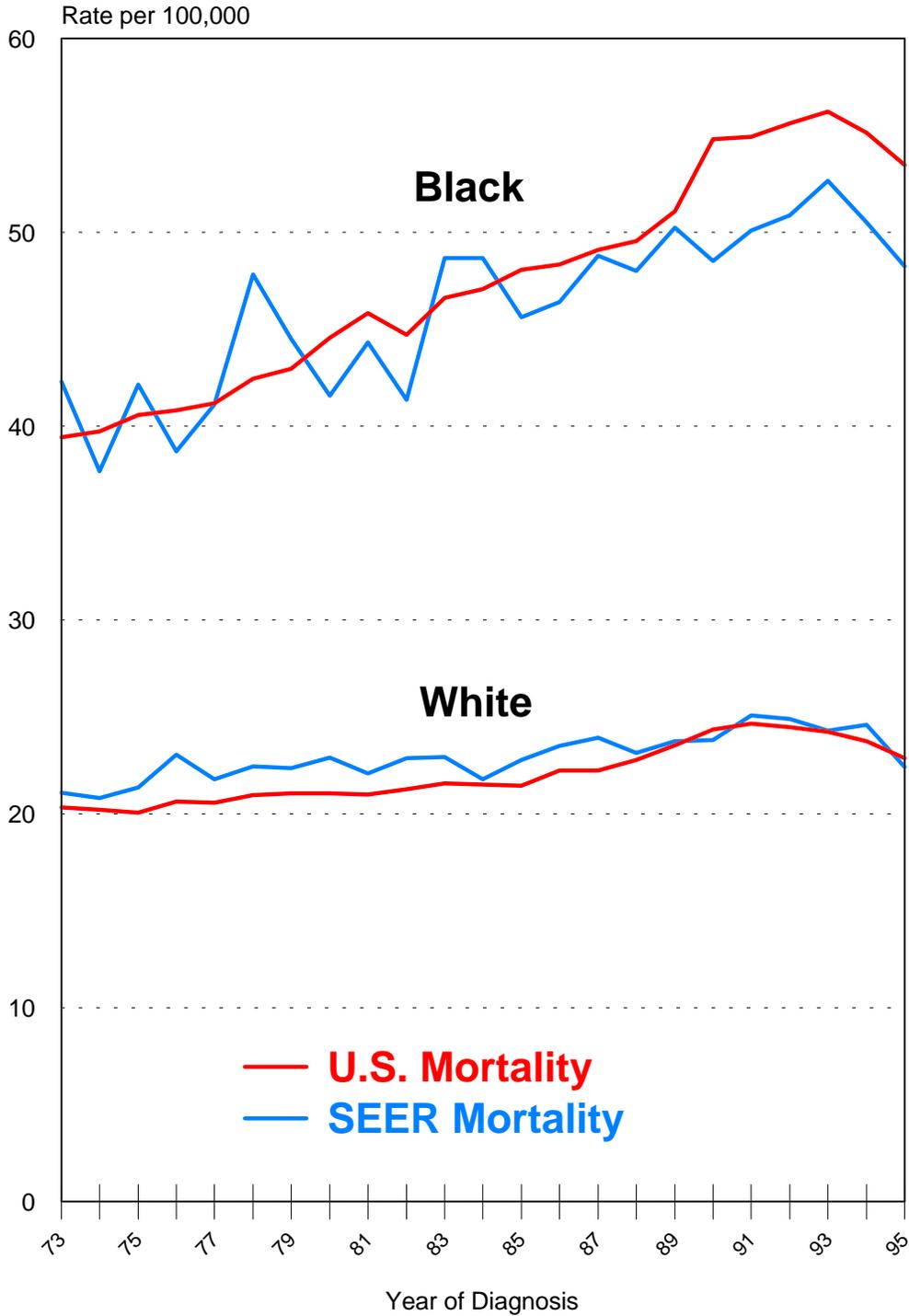
Prostate Cancer SEER Incidence Rates by Age at Diagnosis for Two Time Periods



Note: Based on data from the 9 standard SEER registries.

Figure 2.4

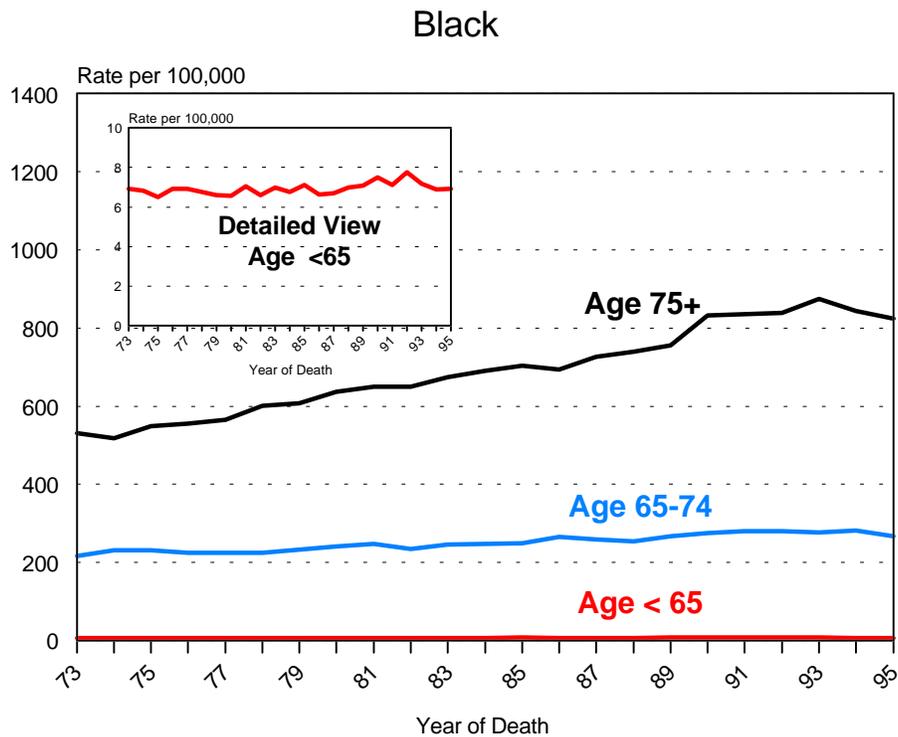
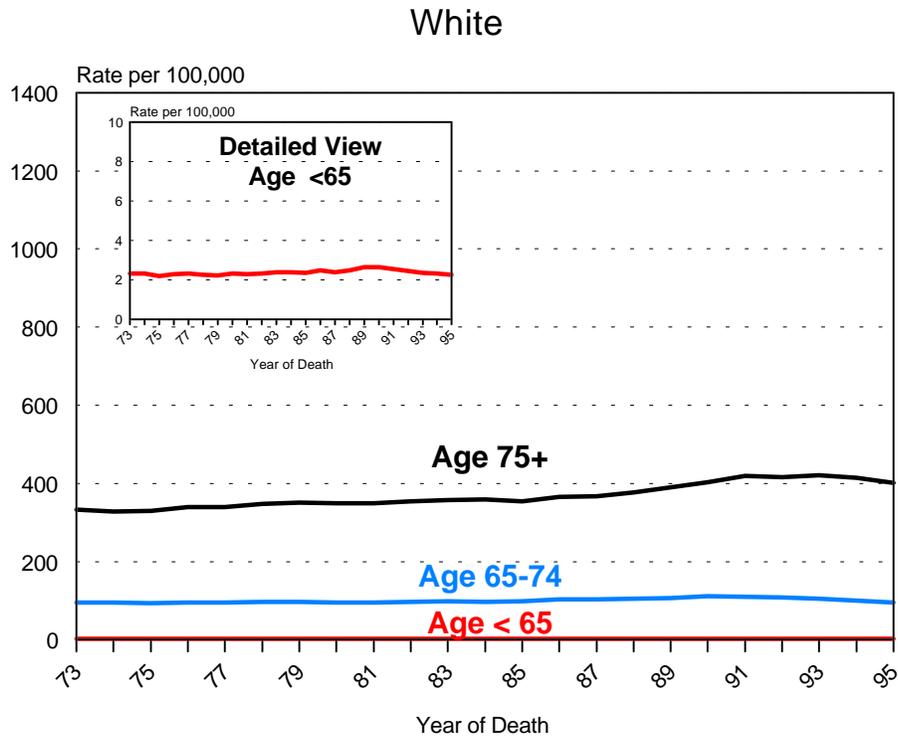
Prostate Cancer Mortality Rates, 1973-1995



Note: Rates are age-adjusted to the 1970 U.S. standard. SEER rates are based on data from the 9 standard registries for 1973-1987, data from San Jose and Los Angeles are included in the 1988-1995 rates.

Figure 2.5

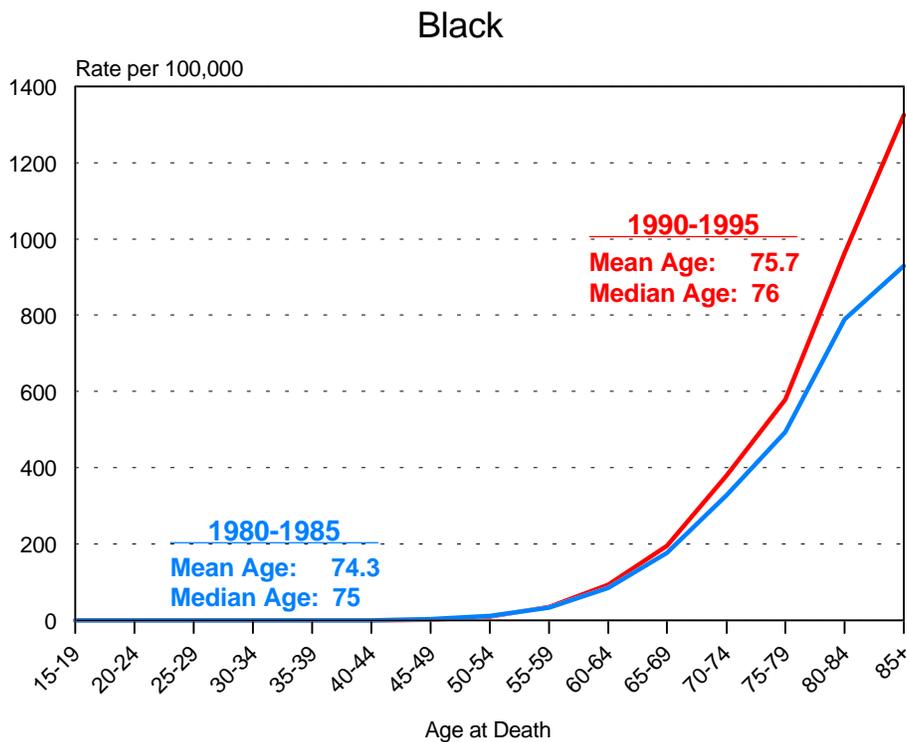
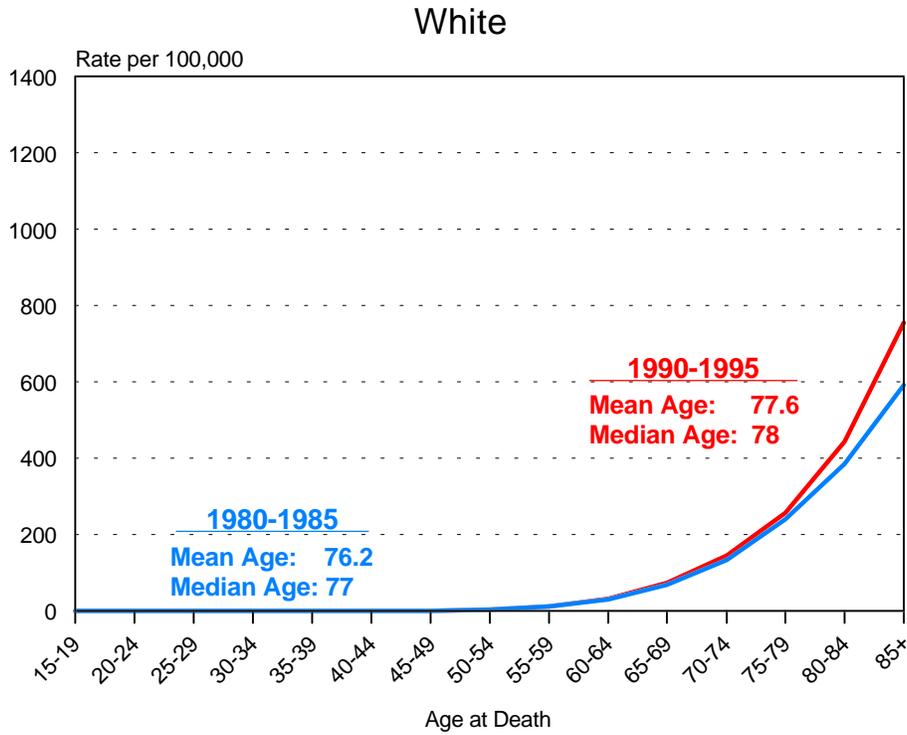
Prostate Cancer U.S. Mortality Rates by Age at Death, 1973-1995



Note: Rates are age-adjusted to the 1970 U.S. standard.

Figure 2.6

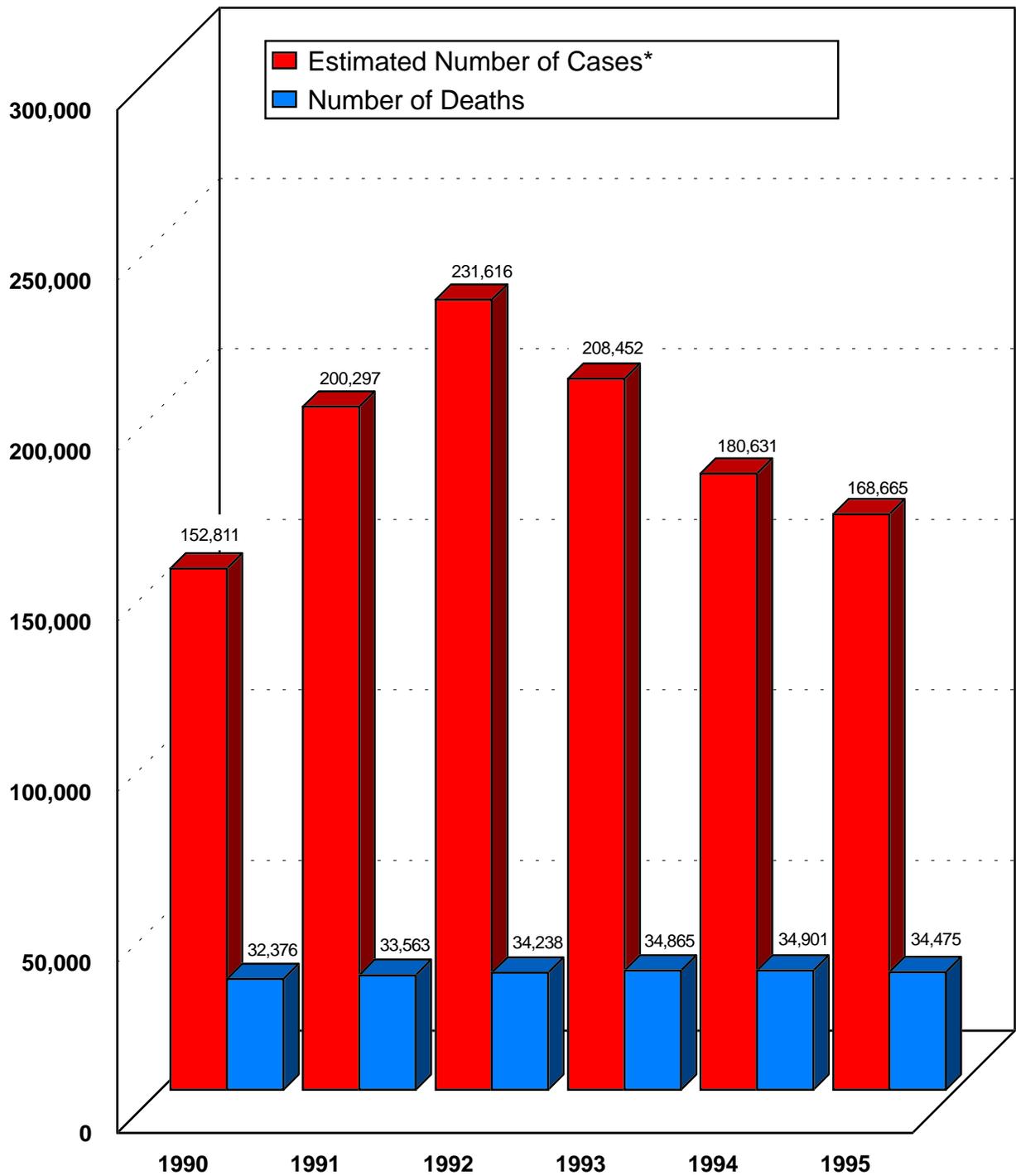
Prostate Cancer U.S. Mortality Rates by Age at Death for Two Time Periods



Note: Rates are age-adjusted to the 1970 U.S. standard.

Figure 2.7

Prostate Cancer Incidence and Mortality in the United States, 1990-1995



*Estimates obtained by multiplying the age-specific incidence rates for the 11 SEER registries by the U.S. population for each year.

HISTOLOGIC GRADE AND STAGE

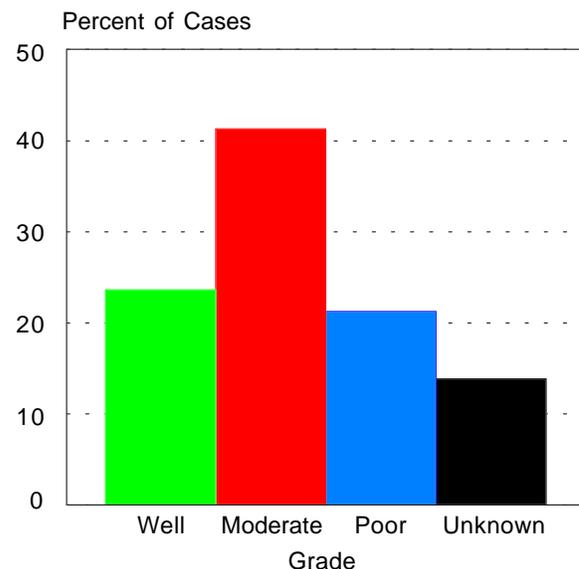
Histologic grade and clinical or pathological stage are used as descriptors of biological potential in prostate cancer. These measures are associated with likelihood of survival and with choice of treatment.

Grade is determined by a pathologist examining a sample of the tumor under a microscope. Normal tissue is composed of cells arranged in highly organized structures unique to each organ. Cancers show varying degrees of loss of this highly organized structure. Before the 1980s, the degree of this loss of organization in prostate cancer was described by pathologists as the histologic grade. Grade has three categories, based on the degree of tissue organization: well differentiated, moderately differentiated, and poorly differentiated. Tumors that are not classified by pathologists are listed as having unknown grade. A new method for describing the grade of prostate cancers, the Gleason score, was implemented in the 1980s. In this method, pathologists assign a score from 2 to 10 based on the patterns of tissue architecture. In order to compare tumor grades from earlier and later time periods, SEER has equated Gleason scores with the three grade categories as follows: tumors with Gleason scores of 2-4 are classified as well differentiated, scores of 5-7 as moderately differentiated, and scores of 8-10 as poorly differentiated (or undifferentiated).

Describing the variations and trends of histologic grades is useful for understanding the biology of prostate cancer and the import of the recent epidemic increase in prostate cancer incidence rates following the introduction of the prostate-specific antigen (PSA) test. Grade and stage of disease trends presented in this chapter are based on data from the 9 standard SEER registries.

Most prostate cancers diagnosed during the 1973-1995 time period were moderately differentiated (Figure 3.1). The overall distribution of grade varied by age and race. Elderly men had a lower proportion of moderately differentiated tumors and a higher proportion of poorly differentiated and unknown grade tumors (Figure 3.2). An assessment of grade distribution by race reveals that blacks have a slightly higher proportion of poorly differentiated and unknown grade tumors (Figure 3.3). Blacks have higher age-adjusted incidence rates than whites for each differentiation category (Figure 3.4).

Figure 3.1
Prostate Cancer Cases
Distribution by Grade
SEER Program, 1973-1995

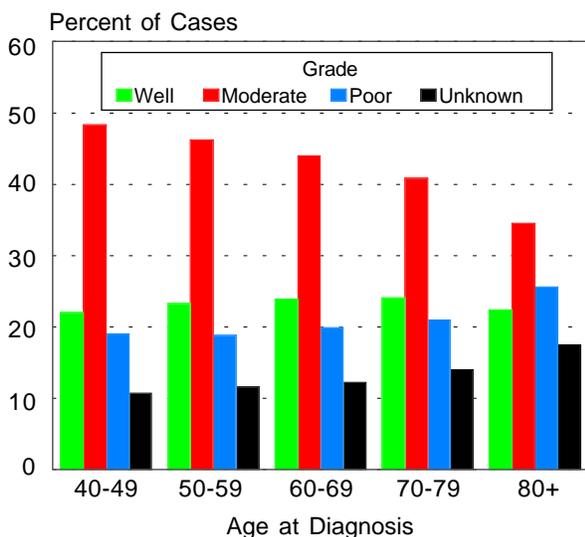


Note: Based on data from the 9 standard SEER registries.

Although most men were diagnosed at a localized stage of disease, the distribution of stage was markedly different among men with different grade tumors (Figure 3.5). More than 80% of men with well differentiated tumors were diagnosed with localized disease. In contrast, only 42% of men with poorly or undifferentiated tumors had localized disease. As the degree of differentiation decreased, the proportion of tumors diagnosed at a regional or distant stage increased.

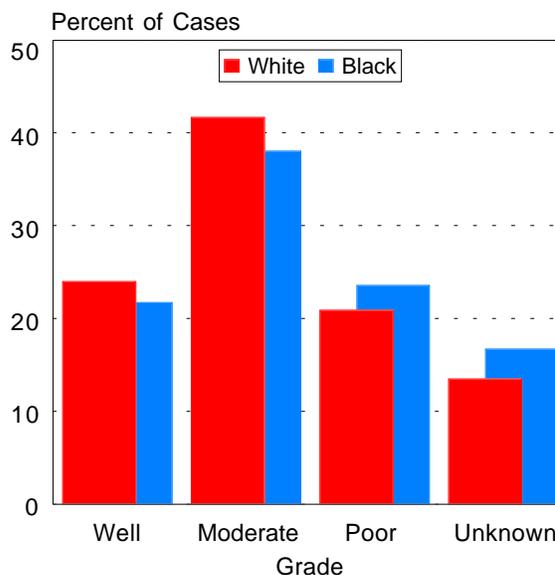
The rise in incidence rates for prostate cancer following the introduction of PSA for screening consisted primarily of an increase in the rate of moderately differentiated cancers (Figure 3.6). The incidence of well differentiated and poorly differentiated cancers also increased, but the changes were smaller in magnitude. These trends in grade-specific rates were associated with an increase in the proportion of prostate cancers that were moderately differentiated and a decrease in the proportions that were well differentiated, poorly differentiated and of unknown grade (Figure 3.6). The same pattern of temporal trends in

Figure 3.2
Prostate Cancer Cases
Distribution by Grade and Age
SEER Program, 1973-1995



Note: Based on data from the 9 standard SEER registries.

Figure 3.3
Prostate Cancer Cases
Distribution by Race and Grade
SEER Program, 1973-1995

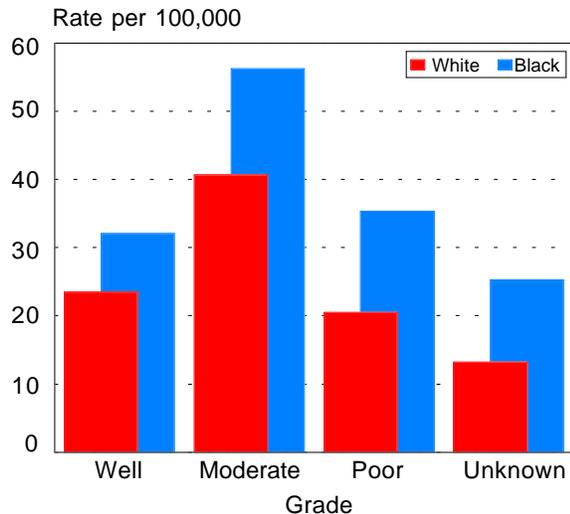


Note: Based on data from the 9 standard SEER registries.

grade-specific rates and proportions was apparent for men less than 65 years of age and men 65 years of age or older (Figure 3.7). The largest increase in incidence rates for both black and white men was in moderately differentiated cancers (Figure 3.8). During recent years, blacks had a larger increase than whites in the incidence of poorly differentiated tumors.

Surgical procedures may also have had some effect upon the temporal trends in tumor grade. The diagnosis and surgical treatment of prostate cancer have changed dramatically since 1983 (Figure 3.9). The incidence rates of prostate cancer treated by radical prostatectomy or diagnosed only by biopsy have increased in whites and blacks. At the same time, the rates of prostate cancer diagnosed or treated by transurethral resection of the prostate (TURP) have decreased in both races. Because these procedures provide different types and amounts of tissue for pathologists to review, these trends may have affected the patterns of prostate cancer by

Figure 3.4
Prostate Cancer Cases
Incidence Rates by Race and Grade
SEER Program, 1973-1995



Note: Rates are age-adjusted to the 1970 U.S. standard population and are based on data from the 9 standard SEER registries.

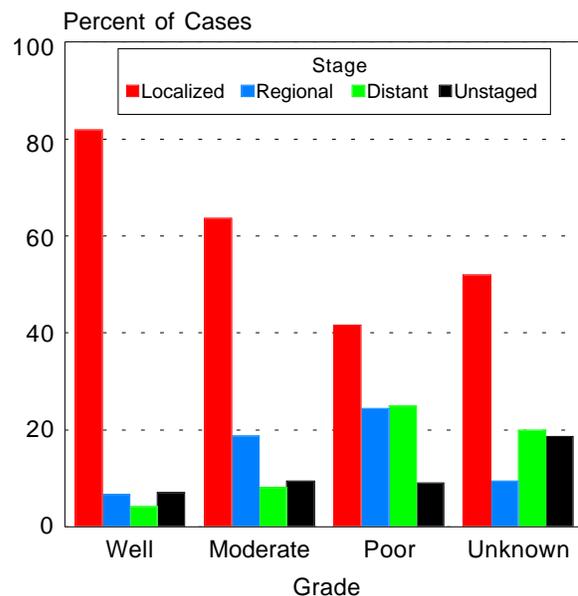
grade. As shown in Figure 3.10, the rates for moderate grade tumors increased in each surgical procedure group (except TURP), suggesting that trends in surgery contribute to, but do not entirely account for, the changes in incidence rates by grade.

The trends in incidence by SEER stage at diagnosis (historic stage) demonstrate that during the PSA screening years, the rate of distant disease fell by 56% (from 14.9 in 1985 to 6.6 per 100,000 in 1995), but there was a steep increase in the rate of localized stage disease (Figure 3.11, Historic Stage). Smaller increases in rates of regional and unstaged disease were observed during 1986-1992. Trends in localized, regional, and unknown stage however, require cautious interpretation. First, the rate of unknown stage disease has been rising in recent years, which may be due to changes in the SEER coding scheme or to a decline in the use of bone scans as clinicians depend more on pre-treatment PSA levels for clinical staging. Second, men undergoing radical prostatectomy are staged on the basis of

the surgical pathology report, while non-surgical cases are staged using clinical parameters only. As a result, men with clinically localized prostate cancer who undergo radical prostatectomy may be upstaged to regional disease. One approach to evaluating the effect of this upstaging on trends was to recode radical prostatectomy cases with regional stage disease to clinically localized disease (Figure 3.11, Clinical Stage). (This recoding of the SEER data can only be done for 1983 and later, based on implementation of a more detailed treatment coding scheme in 1983.) As shown, the 1988-1992 increase in regional stage disease (Figure 3.11, Historic Stage) may primarily be explained by the upstaging of prostatectomy cases with clinically localized disease (Figure 3.11, Clinical Stage).

Another approach in dealing with the above problem of interpreting stage data is to examine prostatectomy versus non-prostatectomy cases separately (Figure 3.12). During recent years, the incidence of regional

Figure 3.5
Prostate Cancer Cases
Distribution by Stage and Grade
SEER Program, 1973-1995



Note: Based on data from the 9 standard SEER registries.

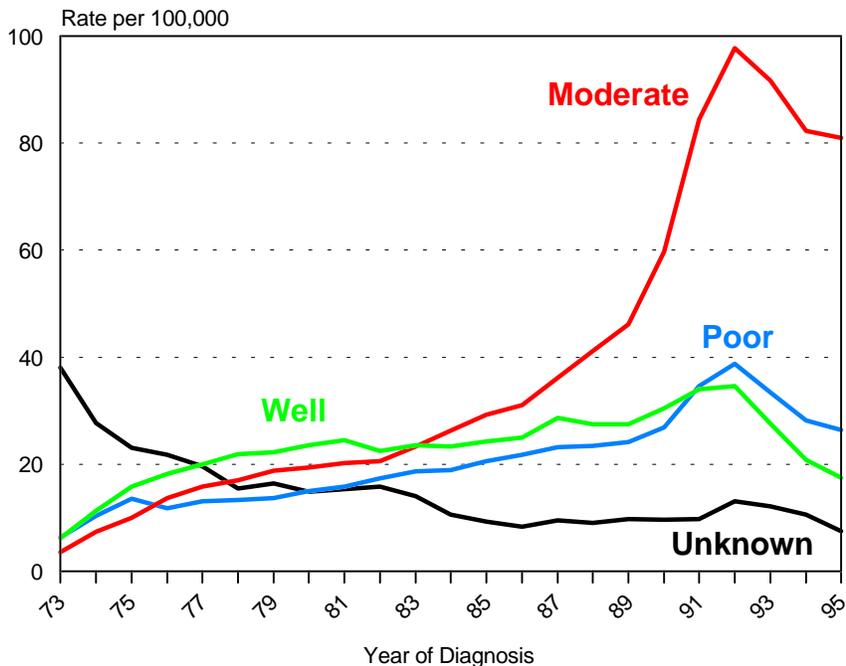
stage disease increased more steeply in radical prostatectomy cases. About 40% of prostatectomy cases are classified as having regional disease compared to only 10% of non-prostatectomy cases.

These trends in prostate cancer stage and grade indicate that the recent epidemic of prostate cancer has been accompanied by a shift toward earlier stage disease at diagnosis, but no shift toward low grade cancer. Rather, there has been a substantial increase in moderately differentiated tumors during the PSA screening years.

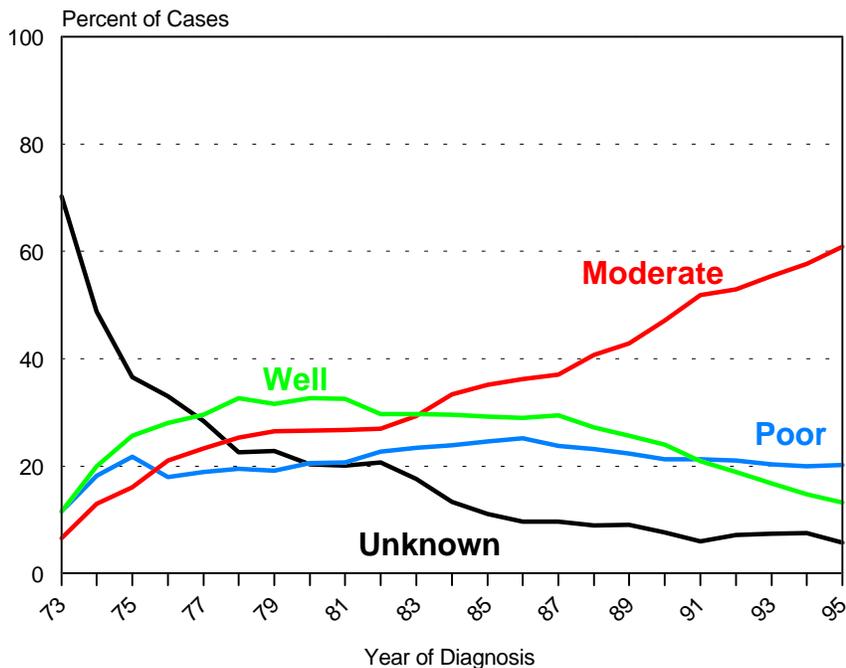
Figure 3.6

Prostate Cancer SEER Program, 1973-1995

Incidence Rates by Grade



Distribution of Cases by Grade

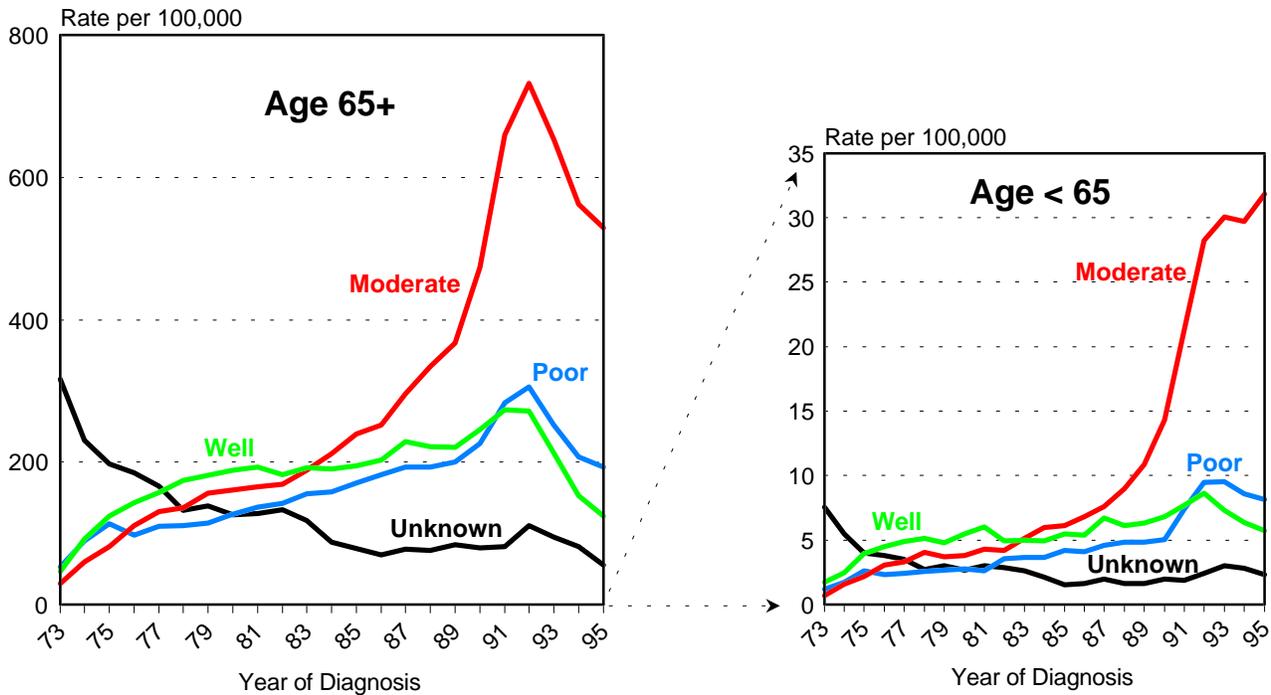


Note: Based on data from the 9 standard SEER registries. Rates are age-adjusted to the 1970 U.S. standard.

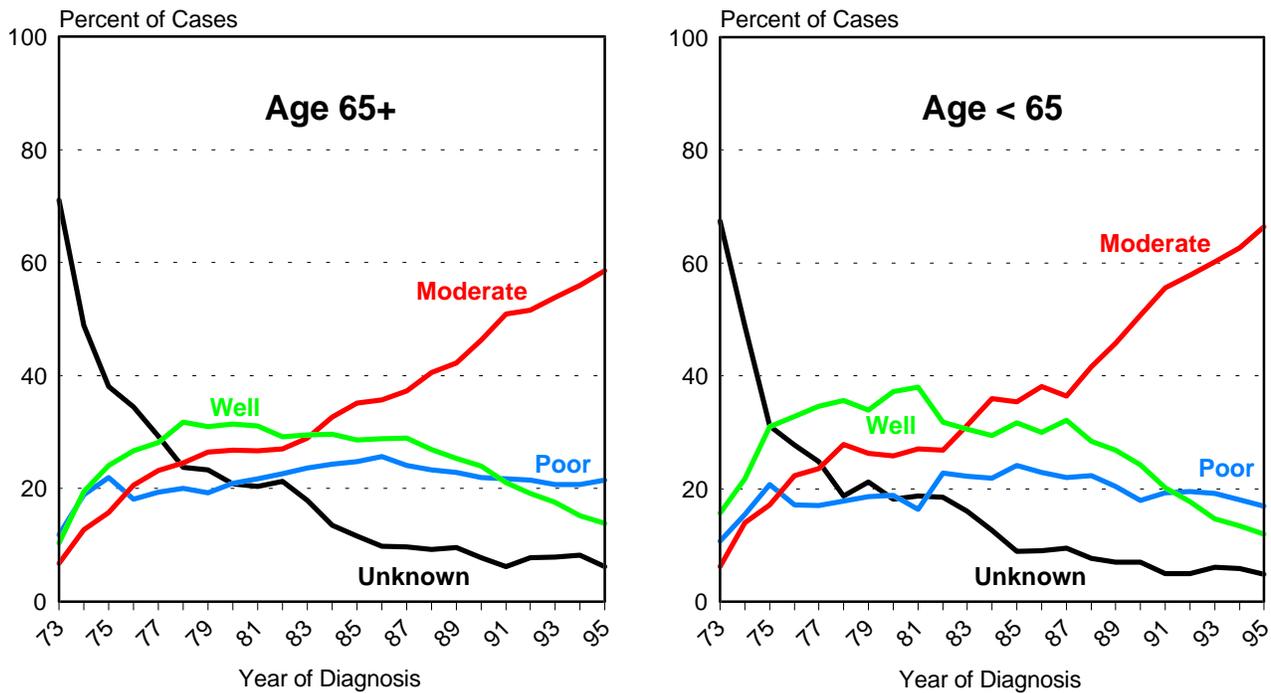
Figure 3.7

Prostate Cancer SEER Program, 1973-1995

Incidence Rates by Age and Grade



Distribution of Cases by Age and Grade

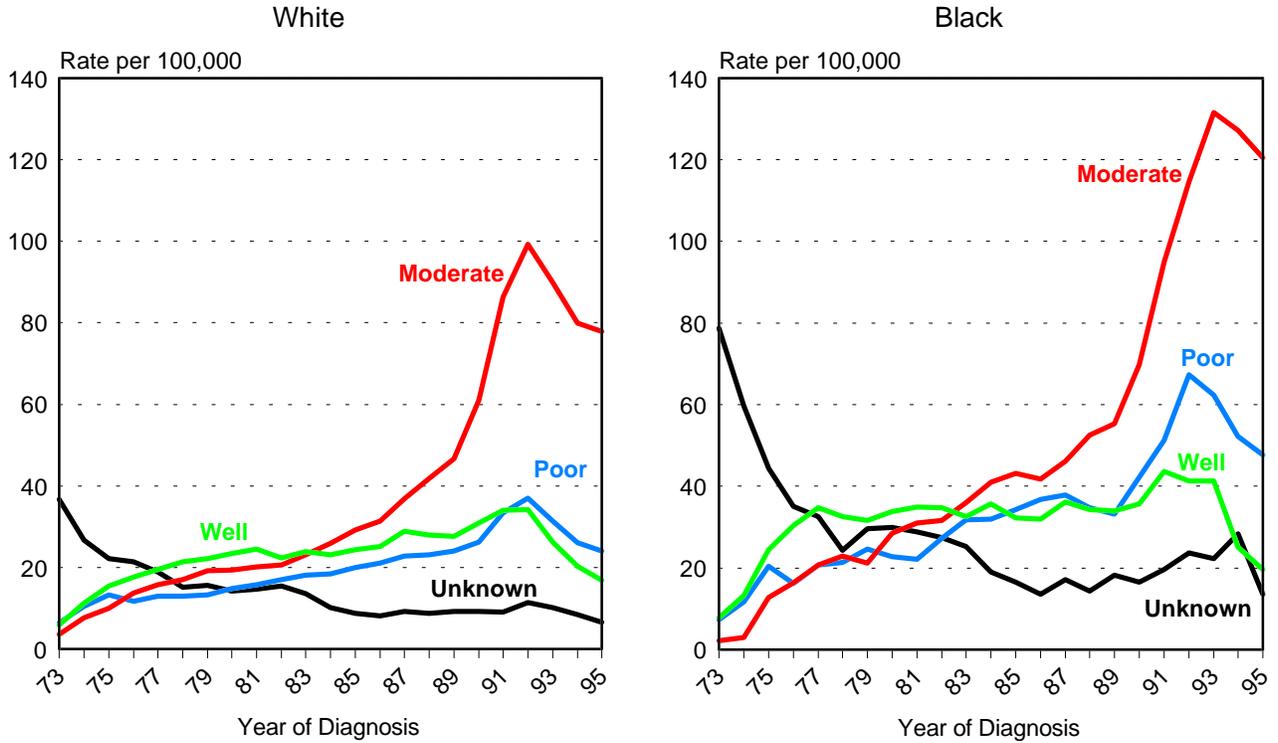


Note: Based on data from the 9 standard SEER registries. Rates are age-adjusted to the 1970 U.S. standard.

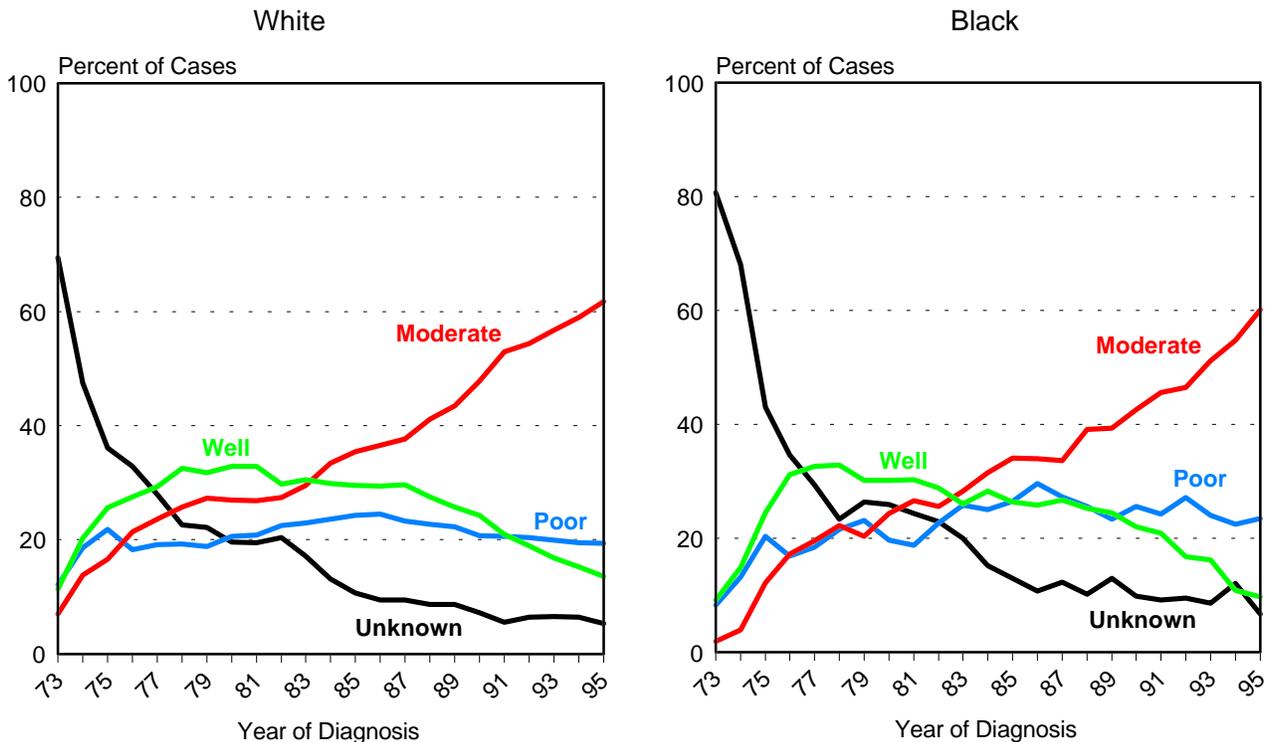
Figure 3.8

Prostate Cancer SEER Program, 1973-1995

Incidence Rates by Race and Grade



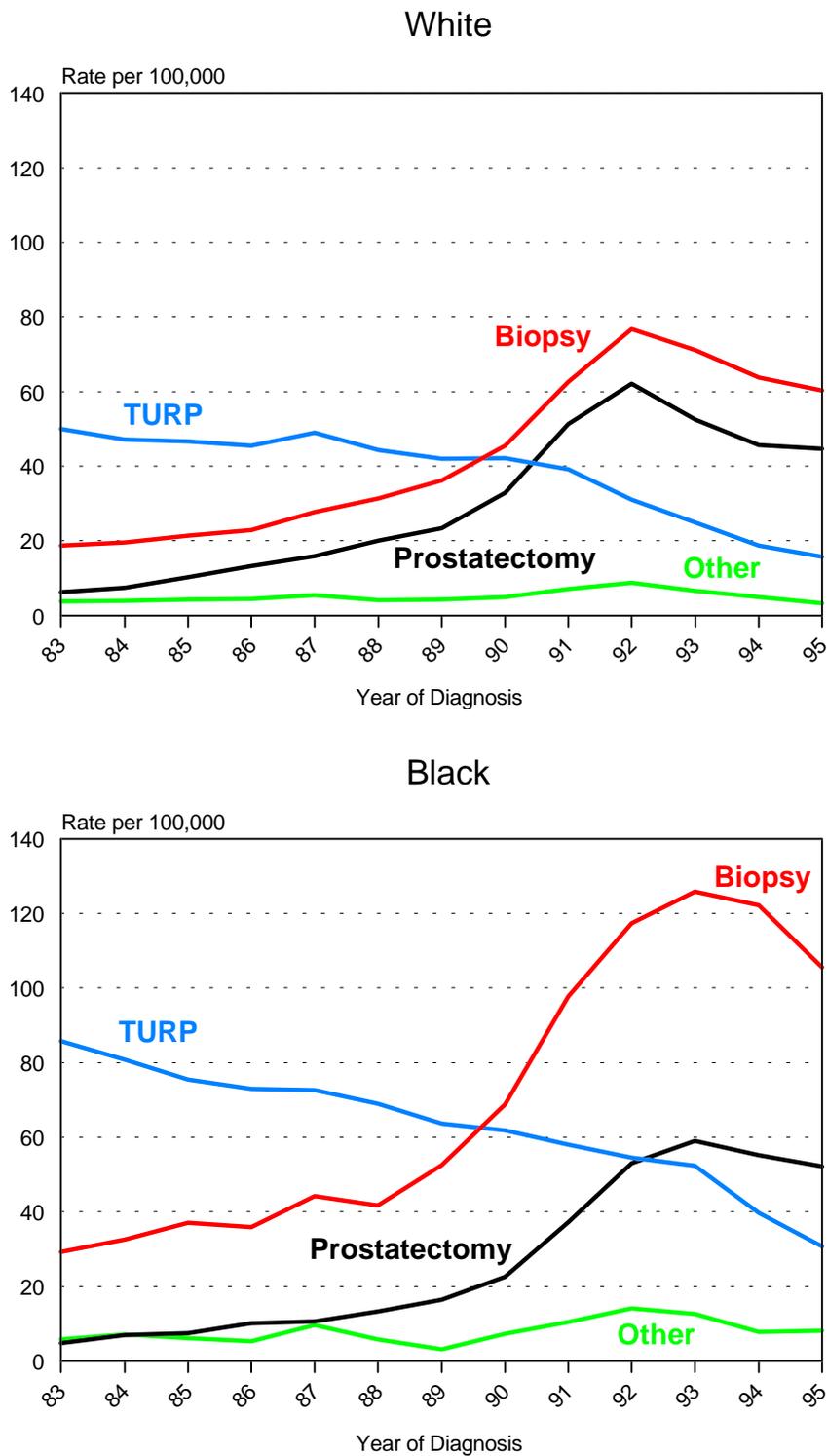
Distribution of Cases by Race and Grade



Note: Based on data from the 9 standard SEER registries. Rates are age-adjusted to the 1970 U.S. standard.

Figure 3.9

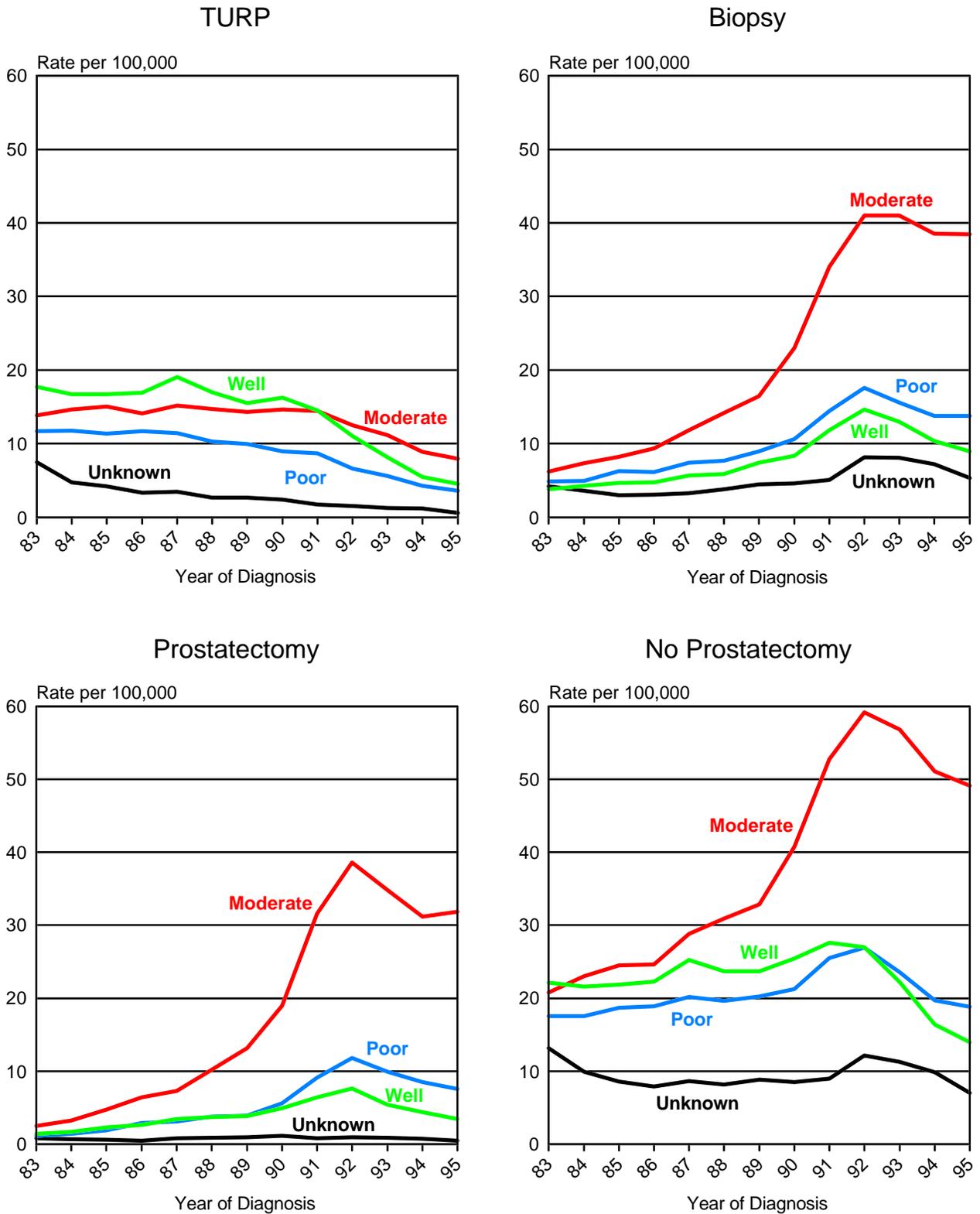
Prostate Cancer SEER Incidence Rates by Race and Surgical Procedure, 1983-1995



Note: Rates are age-adjusted to the 1970 U.S. standard and are based on data from the 9 standard SEER registries.

Figure 3.10

Prostate Cancer SEER Incidence Rates by Surgical Procedure and Grade, 1983-1995

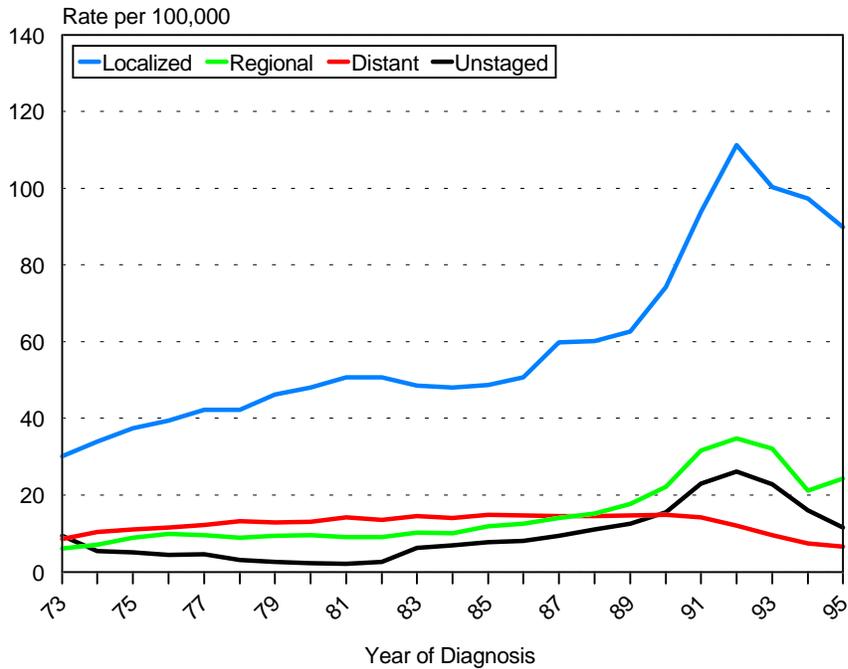


Note: Rates are age-adjusted to the 1970 U.S. standard and are based on data from the 9 standard SEER registries.

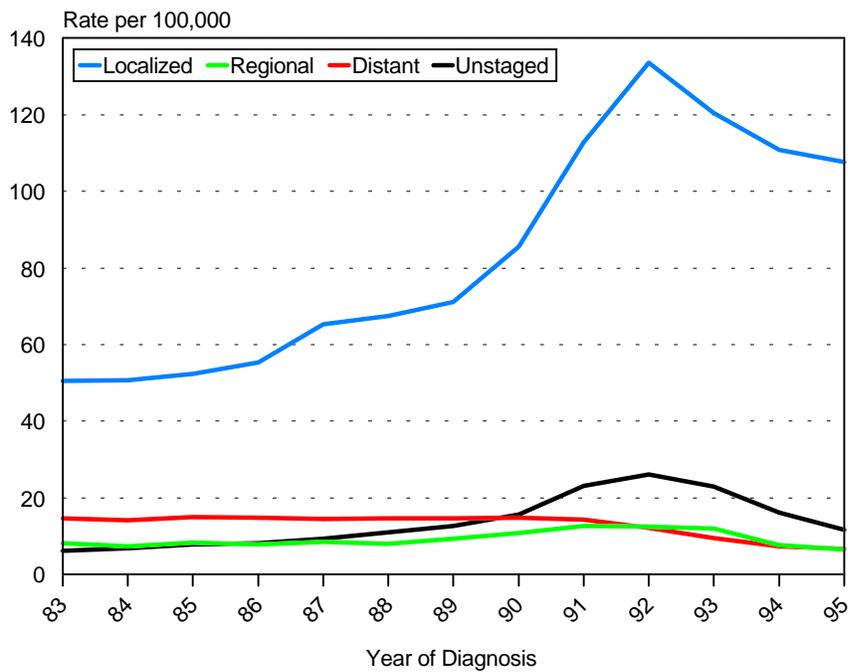
Figure 3.11

Prostate Cancer SEER Incidence Rates by Stage

Historic Stage (1973-1995)



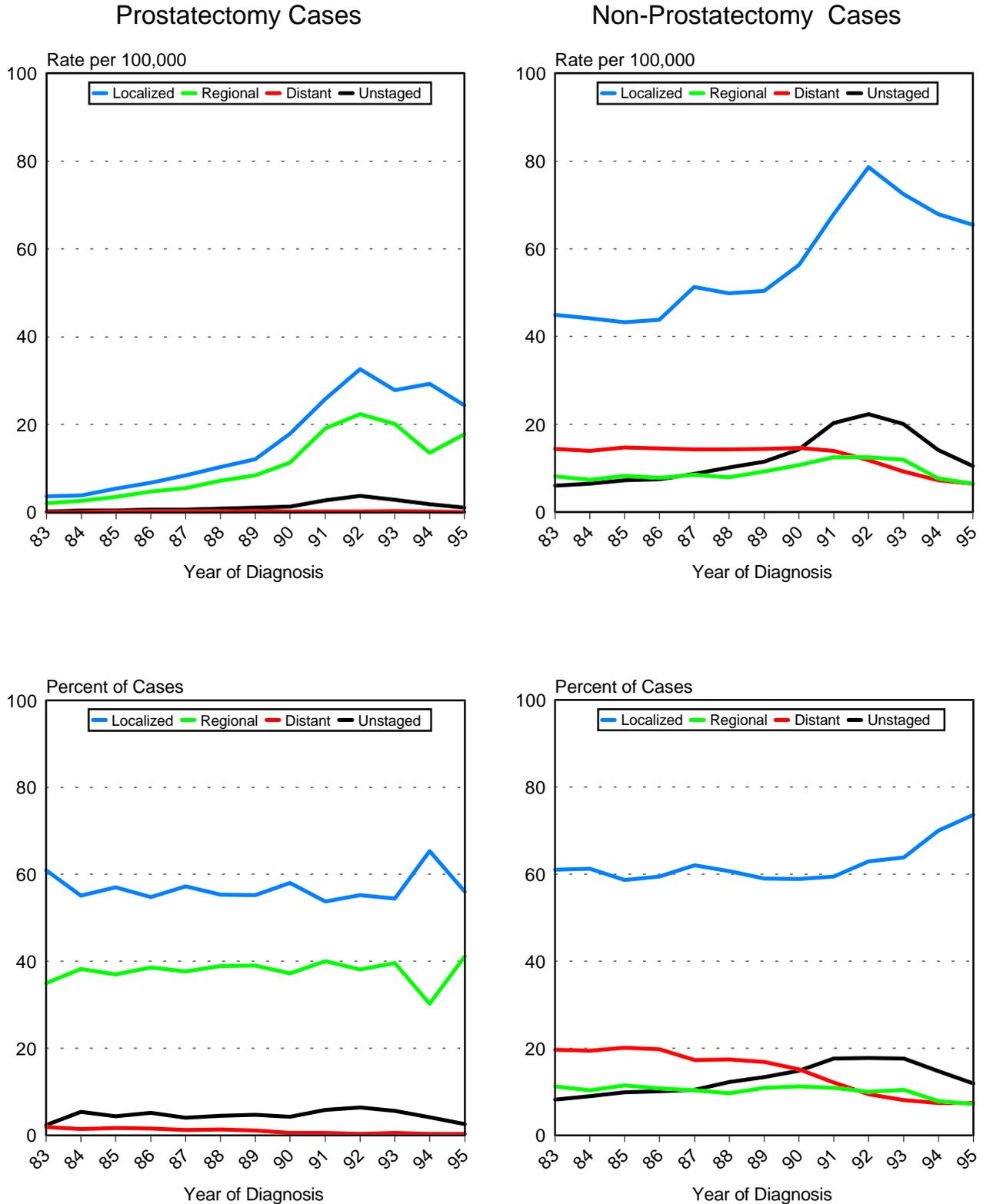
Clinical Stage* (1983-1995)



Note: Rates are age-adjusted to the 1970 U.S. standard and are based on data from the 9 standard SEER registries.
*Prostatectomy cases with regional stage disease recoded to localized stage.

Figure 3.12

Prostate Cancer SEER Incidence by Treatment and Stage, 1983-1995



Note: Based on data from the 9 standard SEER registries. Rates are age-adjusted to the 1970 U.S. standard.

The optimal treatment of prostate cancer continues to be a topic of heated debate and persisting uncertainty. Resolution of this debate has been difficult due to qualities inherent in both the disease and the affected individuals, as well as a lack of data from randomized clinical trials evaluating treatment modalities. The natural history of prostate cancer is prolonged relative to other cancers.

Few untreated men with localized prostate cancer succumb to the disease within 5 years of diagnosis, and only a minority succumb within 10 years. Nevertheless, prostate cancer is the second leading cause of cancer death in men. Prostate cancer tends, however, to occur in elderly men where competing causes of death have significant impact. The SEER data presented in this chapter provide population-based information regarding treatment patterns and the impact of PSA on treatment. Data are presented separately for localized plus regional stages of disease and distant disease.

Localized and Regional Disease

Figure 4.1 displays the incidence trends in patients with localized or regional stage disease by type of treatment for 1983-1995. Concurrent with rising incidence rates (Figure 2.1), substantial increases in age-adjusted rates were noted for men having radical prostatectomy or radiation therapy, with lesser increases for those receiving no treatment or hormone therapy. Incidence rates for men undergoing radical prostatectomy increased rapidly from 1989 to 1992. Similar but less dramatic increases in rates were observed in the radiation therapy group. Concurrent with falling incidence rates subsequent to 1992 (Figure 2.1), the rates in all treatment subgroups fell (Figure 4.1).

Change in treatment patterns over time can be assessed by examining the percent of cases by treatment type in each year. Figure 4.1 indicates that the proportion of cases treated by radical prostatectomy increased while those receiving no treatment decreased from 1983 to 1995. The fractions having radiation therapy and hormone therapy have remained relatively stable. In 1983, the distribution of treatments for localized and regional cases was radical prostatectomy in 10%, radiation therapy in 27%, hormone therapy in 13%, and no treatment in 50%, (Figure 4.1). By 1992, the rank order of treatment type for cases with localized and regional disease changed, with 37% undergoing radical prostatectomy, 32% undergoing radiation therapy, 8% having hormone therapy, and 23% having no treatment. Since 1992, the proportion of cases having no treatment has risen while the proportions undergoing radical prostatectomy or radiation therapy have fallen slightly. Since 1991, radical prostatectomy has been the most common treatment for localized and regional stages of disease.

SEER coding rules dictate that the grade from surgical pathology reports be coded as the grade for radical prostatectomy cases. As a result, the diagnostic biopsy grade is not available for prostatectomy

cases. For other treatment modalities, the diagnostic biopsy or TURP grade is coded. Therefore, grade comparisons between treatment groups are subject to a potential bias, with upgrading following prostatectomy due to a larger tissue volume being available for pathologic review. Nonetheless, examination of grade reveals that the proportion of cases with moderate tumor differentiation has increased for every treatment category and is the predominant tumor grade in the PSA era (Figure 4.2). Even after rates began falling in 1992 and 1993, the proportion of cases with moderately differentiated tumors continued to increase (Figure 4.2). It is also interesting to note that the historic predominance of well differentiated TURP specimens has been replaced with moderately differentiated tumors in 1992-1995 (Figure 4.3).

Figure 4.4 displays the age-specific incidence rates by treatment for time periods before the PSA era (1983-1985) and during the PSA era (1993-1995). The peak age-specific rate shifted slightly to a younger age in the no treatment category from 1983-1985 to 1993-1995, but did not shift for other treatment categories. Between these two time periods, age-specific rates rose most dramatically for radical prostatectomy, increasing about 8-fold in men aged <60 years, and 6-fold in men aged 60-69 years. Rates in the radiation therapy group rose modestly (from 1.2- to 2.7-fold) for all age categories. In the no treatment and hormone therapy groups, rates remained relatively stable.

The percentage of men treated with radical prostatectomy, radiation therapy, hormone therapy and no treatment changes as a function of age, as physicians and patients attempt to reconcile cancer treatment decisions and the risk of death from prostate cancer with the risk of death

from competing causes. The most recent data (1993-1995) in Figure 4.5 demonstrate an inverse relationship of age to radical prostatectomy, a direct relationship of age to no treatment and hormone therapy, and an increase in radiation therapy with age up to age 75 and then a decline. Comparison of the treatment curves for 1983-1985 and 1993-1995 reveals that a higher proportion of younger men (aged <70 years) are undergoing radical prostatectomy during recent years. There was a 2.4-fold increase in the proportion of 70-74 year old cases receiving radical prostatectomy between 1983-1985 and 1993-1995.

Racial differences in incidence rates by treatment are displayed for localized and regional stages in Figure 4.6. In 1983, blacks had substantially higher rates of no treatment compared to whites, but both groups had similar rates of radical prostatectomy, radiation therapy, and hormone therapy.

Treatment patterns, as measured by the percent of cases receiving each type of treatment, are different in whites and blacks with localized and regional stages of prostate cancer (Figure 4.7). In 1983, 57% of blacks and 49% of whites received no treatment. However, this difference in choice of no treatment has narrowed. By 1995, 27% of blacks and whites had no treatment. As the percent of black cases having no treatment decreased, the percent undergoing radical prostatectomy or radiation therapy increased. In contrast, as the percent having no treatment decreased in whites, the percent undergoing radiation therapy remained quite stable. In whites, the proportion of cases having radical prostatectomy increased. In 1983, 6% of blacks and 11% of whites received radical prostatectomy, and 22% of blacks and 27% of whites received radiation therapy. In 1995, 31% of blacks and 37% of whites received radical prostatectomy, and

33% of blacks and 28% of whites received radiation therapy. The proportion of cases receiving hormone therapy declined slightly in both whites and blacks from 1983 to 1995.

Distant Disease

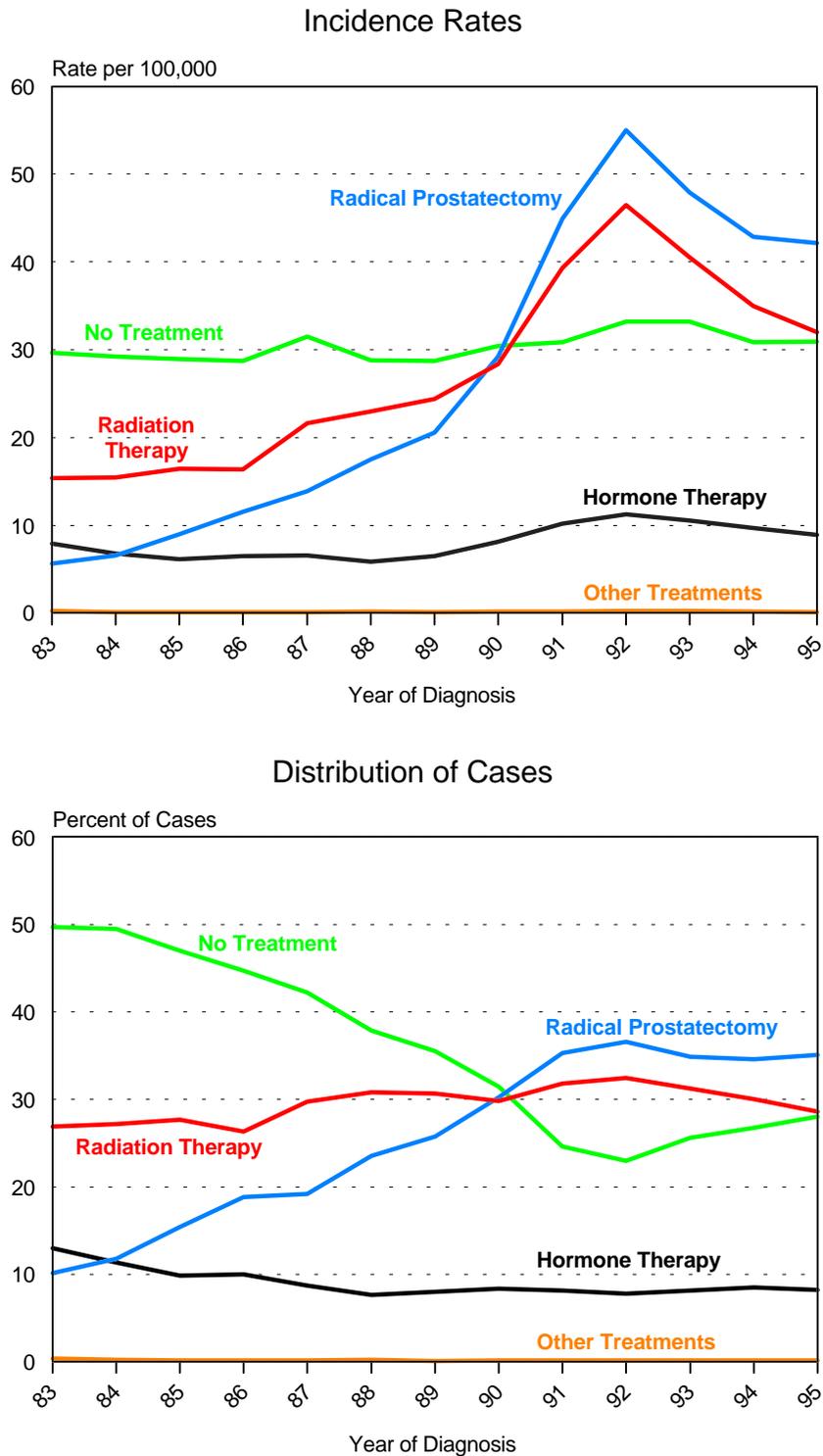
Figure 4.8 demonstrates that treatment patterns as measured by the percent of cases receiving hormone therapy, no treatment and radiation therapy have been fairly stable over time for white and black patients with distant stage disease. These data indicate that while the rate of distant disease has been falling (see Figure 3.11), the treatment for men with advanced stage prostate cancer has not changed.

Summary

Substantial changes have occurred in the treatment of prostate cancer from 1983 (prior to widespread use of PSA) to 1995 (PSA widely used). SEER data demonstrate a substantial shift toward more aggressive therapy for clinically localized prostate cancer, most notably toward radical prostatectomy. In the interval from 1983-1995, significant shifts in grade toward moderate differentiation have taken place regardless of the type of treatment received. Rates of aggressive therapy have increased in both black and white men. However, there are racial differences in treatment patterns. For localized and regional stages of disease, white men are more likely than black men to receive radical prostatectomy while black men are more likely to receive radiation therapy. Treatment patterns are strongly influenced by age with younger men tending to have radical prostatectomy, middle aged men tending to have radiation therapy and older men tending to have conservative approaches (no treatment or hormone therapy). The distribution of treatments for advanced stage disease has remained stable.

Figure 4.1

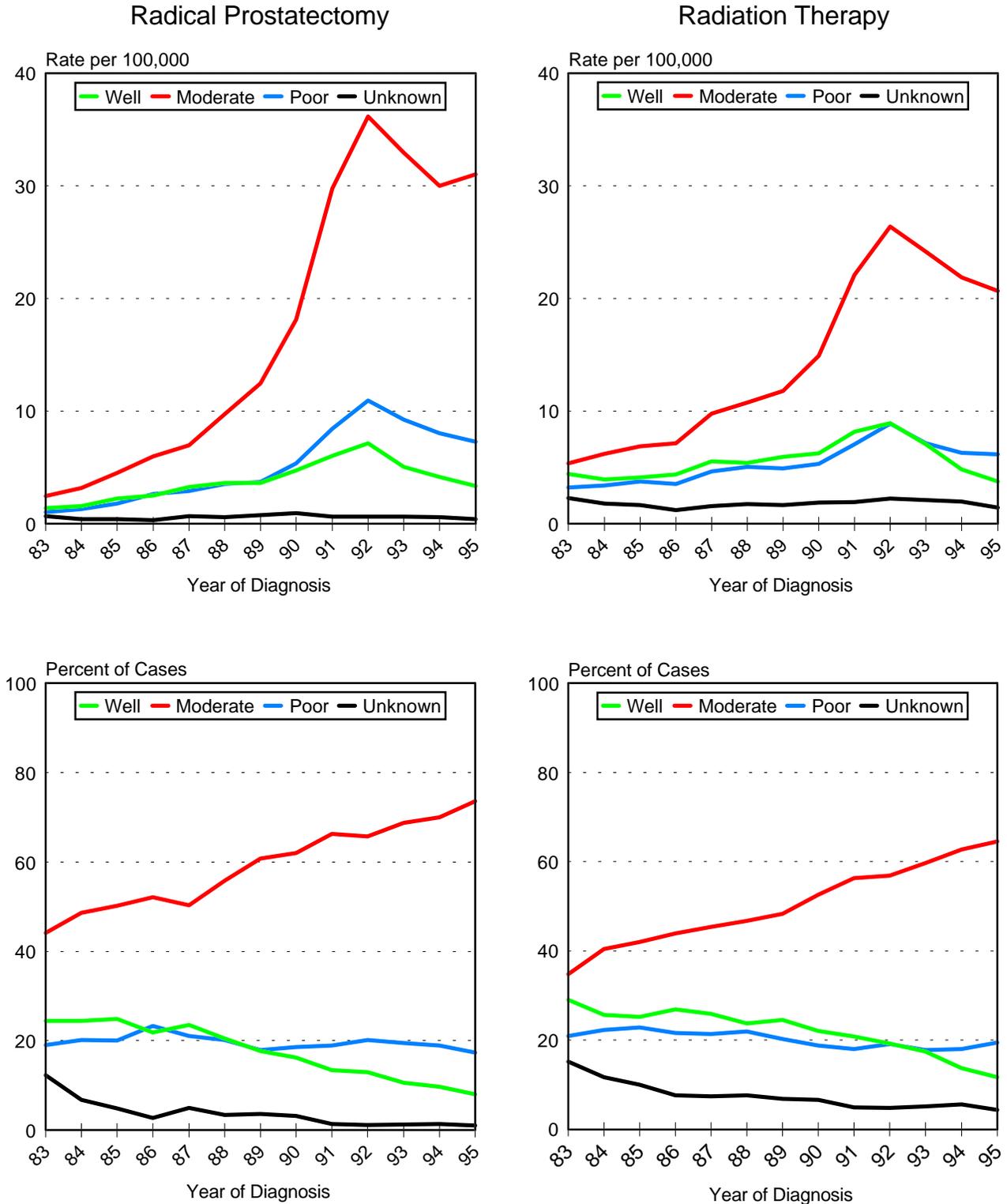
Prostate Cancer SEER Incidence by Treatment, 1983-1995 Localized and Regional Stages



Note: Based on data from the 9 standard SEER registries. Rates are age-adjusted to the 1970 U.S. standard.

Figure 4.2

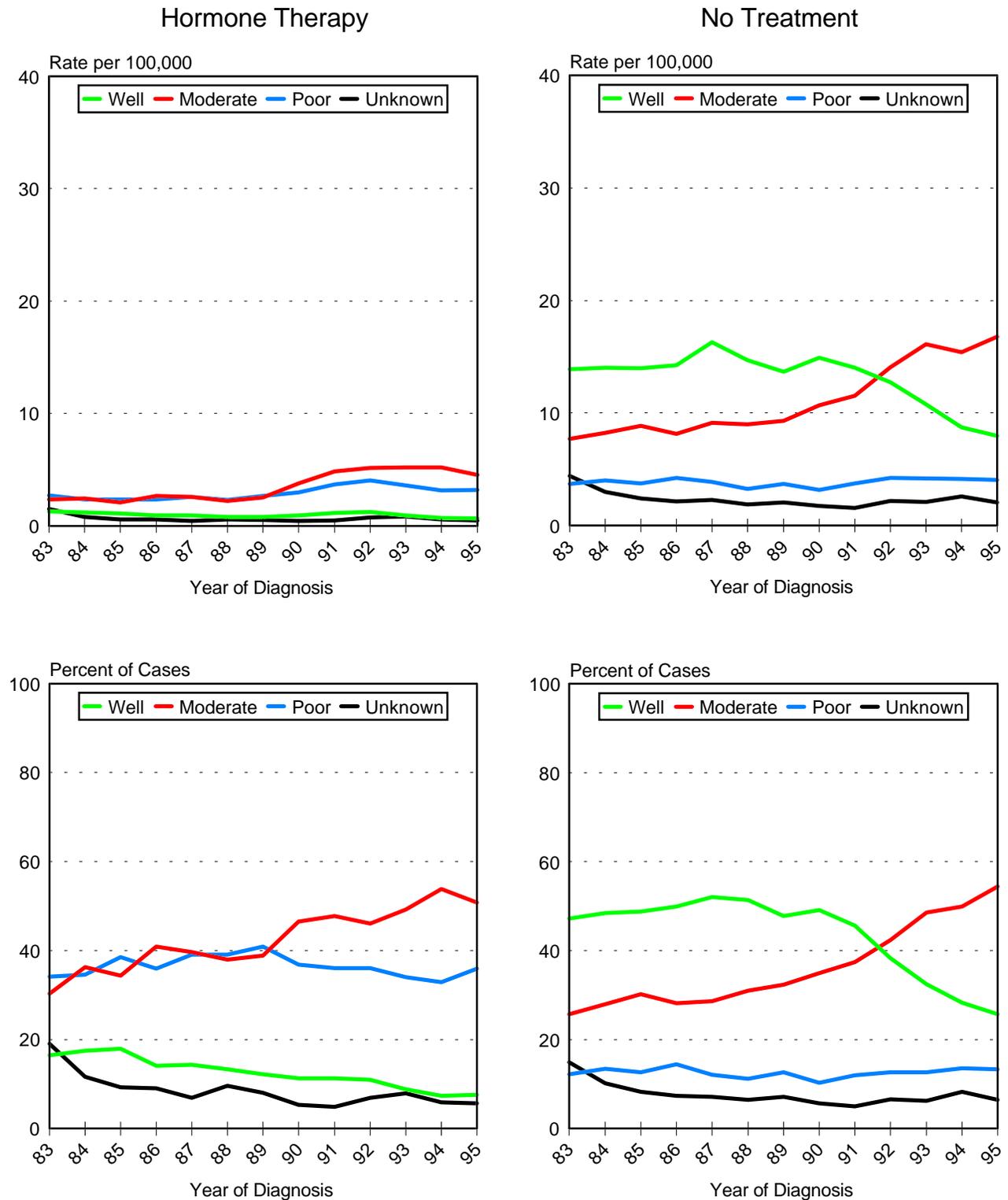
Prostate Cancer SEER Incidence by Grade and Treatment, 1983-1995 Localized and Regional Stages



Note: Based on data from the 9 standard SEER registries. Rates are age-adjusted to the 1970 U.S. standard.

Figure 4.2 (continued)

Prostate Cancer
SEER Incidence by Grade and Treatment, 1983-1995
Localized and Regional Stages

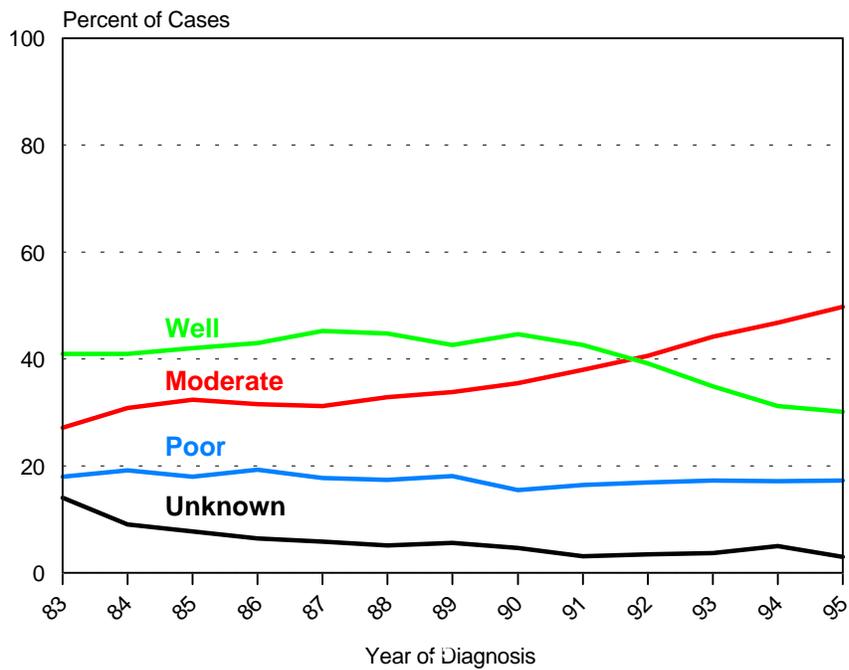
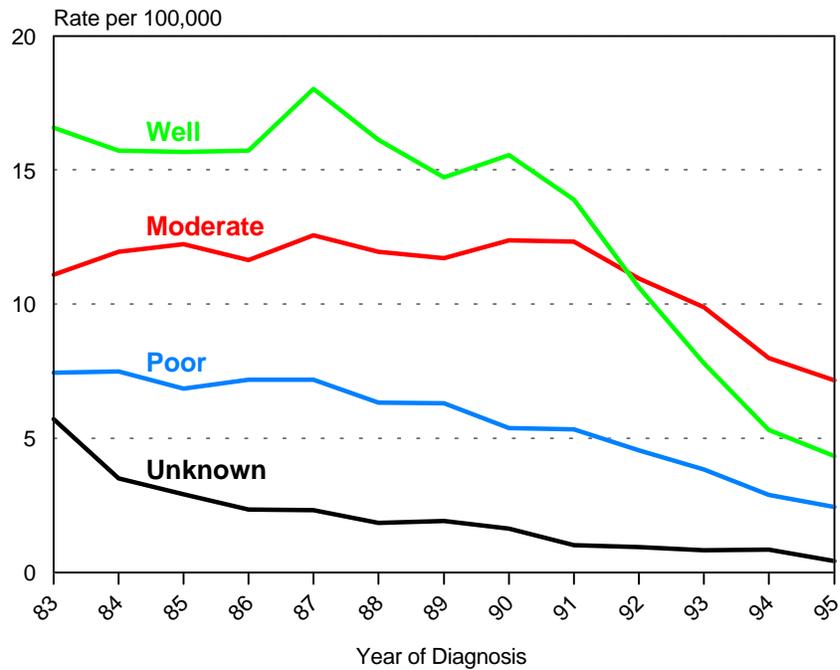


Note: Based on data from the 9 standard SEER registries. Rates are age-adjusted to the 1970 U.S. standard.

Figure 4.3

Prostate Cancer SEER Incidence by Grade, 1983-1995 Localized and Regional Stages

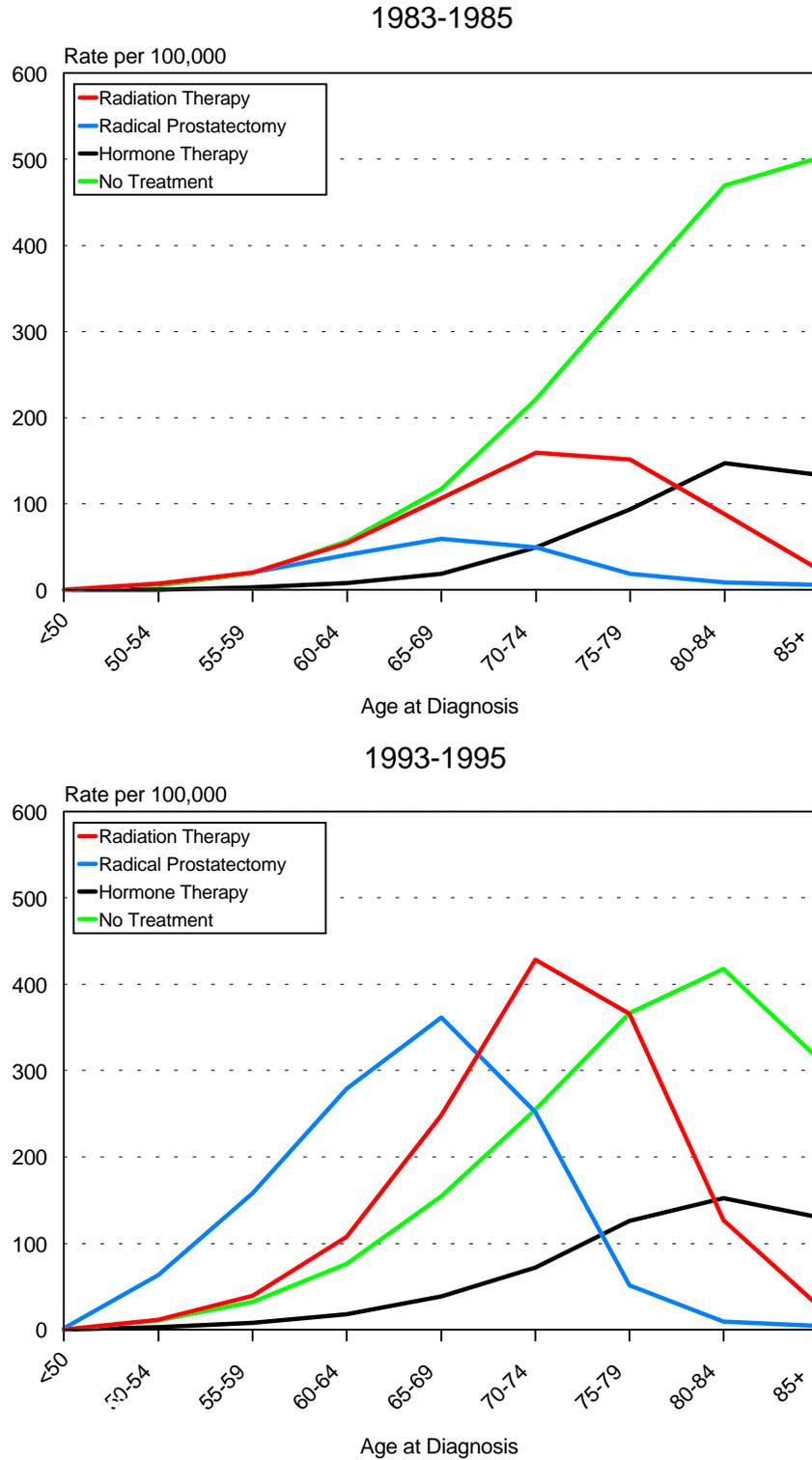
TURP Cases



Note: Based on data from the 9 standard SEER registries. Rates are age-adjusted to the 1970 U.S. standard.

Figure 4.4

Prostate Cancer SEER Incidence by Age and Treatment Localized and Regional Stages

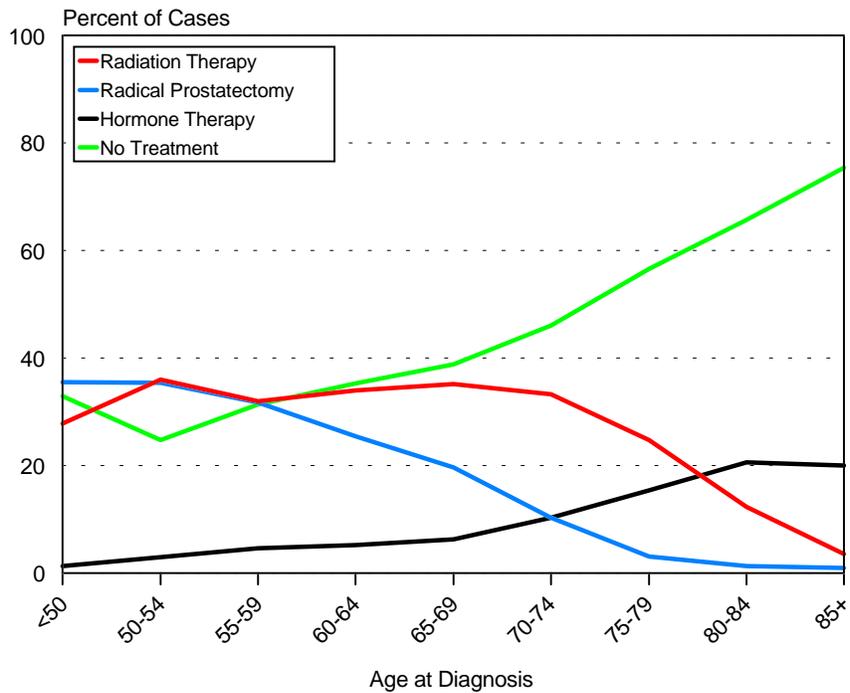


Note: Rates are age-adjusted to the 1970 U.S. standard and are based on data from the 9 standard SEER registries.

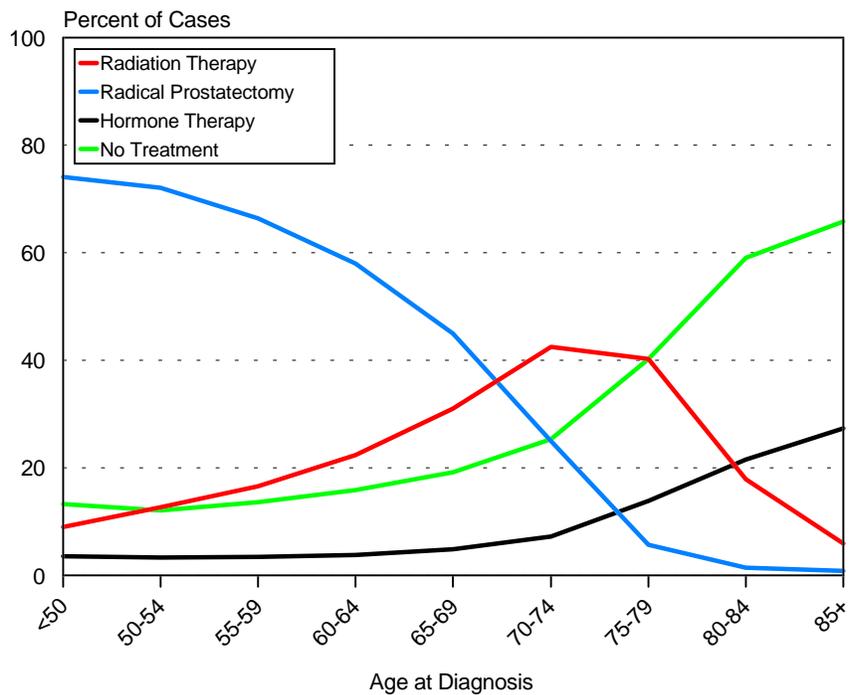
Figure 4.5

Prostate Cancer Distribution of SEER Cases by Age and Treatment Localized and Regional Stages

1983-1985



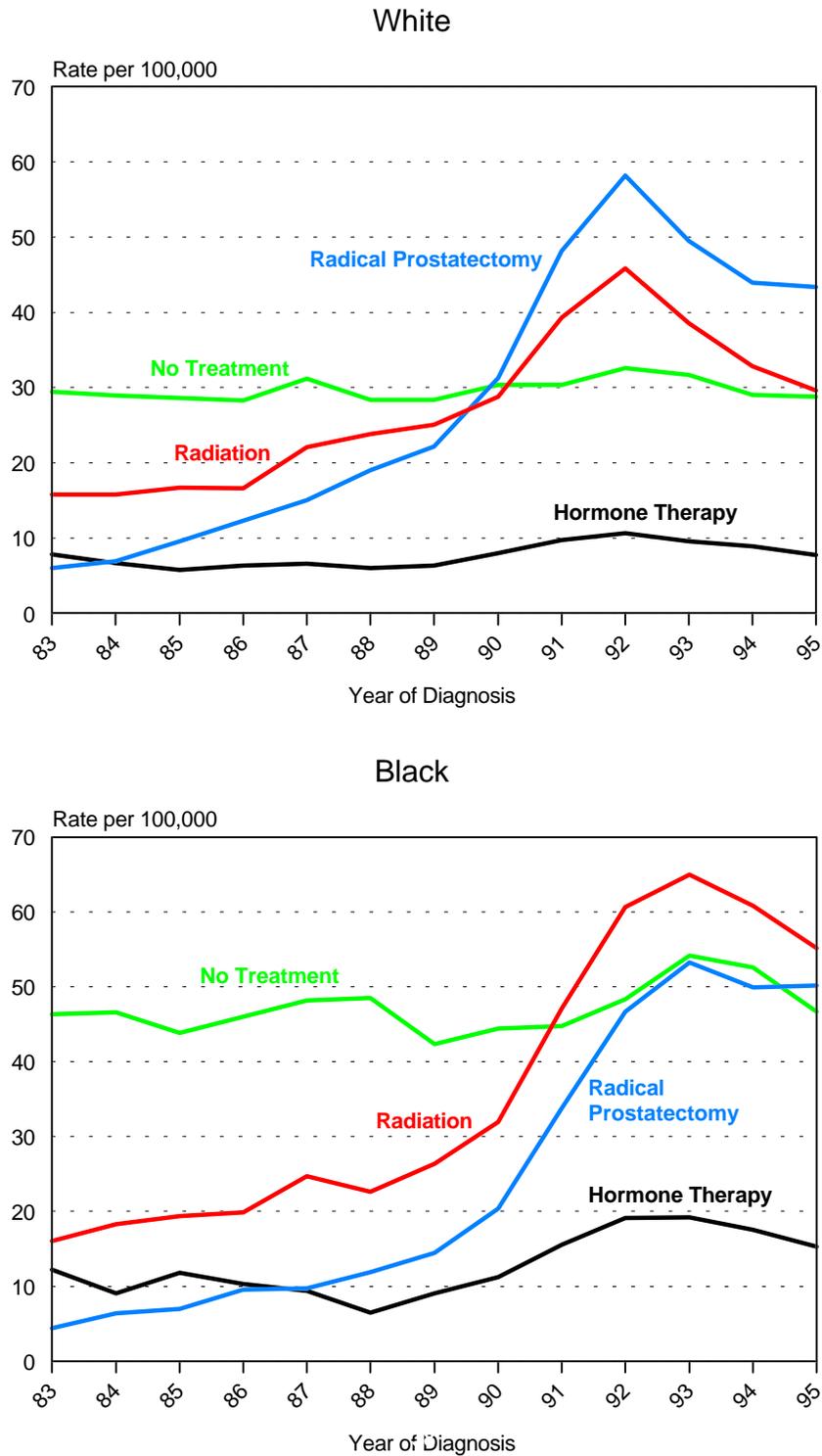
1993-1995



Note: Based on data from the 9 standard SEER registries.

Figure 4.6

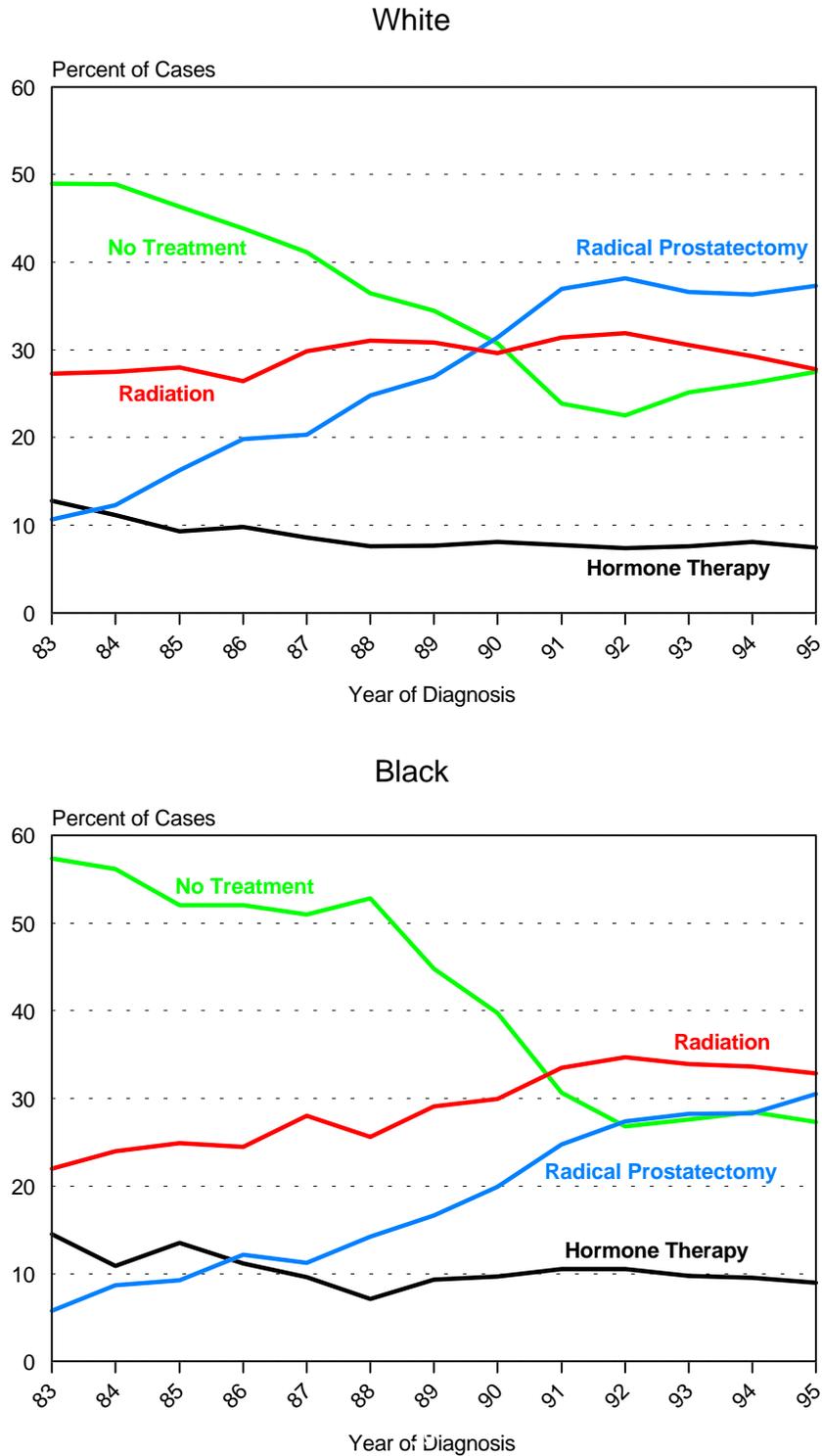
Prostate Cancer SEER Incidence Rates by Race and Treatment, 1983-1995 Localized and Regional Stages



Note: Rates are age-adjusted to the 1970 U.S. standard population and are based on data from the 9 standard SEER registries.

Figure 4.7

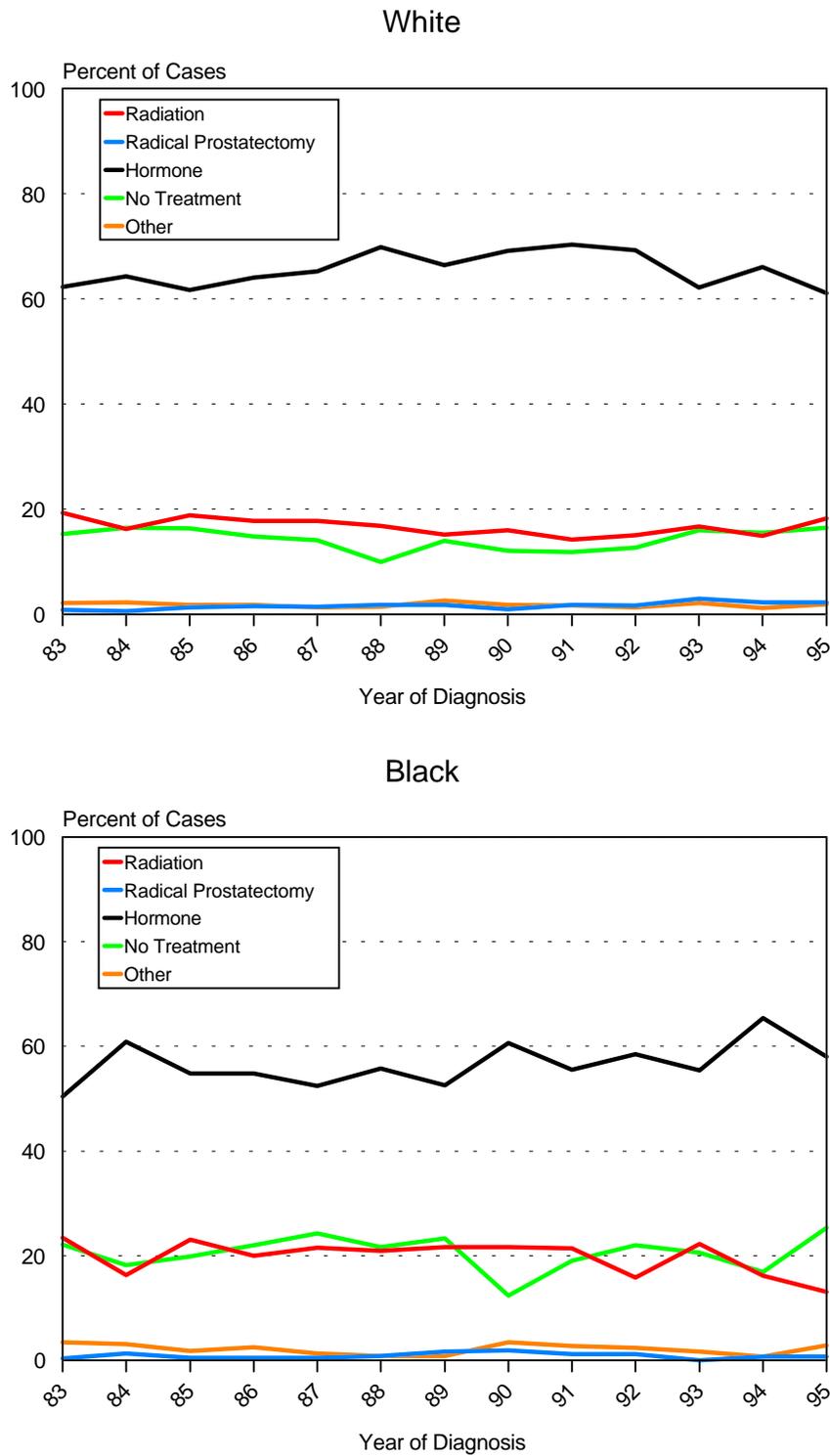
Prostate Cancer Distribution of Cases by Race and Treatment, 1983-1995 Localized and Regional Stages



Note: Based on data from the 9 standard SEER registries.

Figure 4.8

Prostate Cancer Distribution of Cases by Race and Treatment, 1983-1995 Distant Stage



Note: Based on data from the 9 standard SEER registries.

SURVIVAL

One of the primary measures employed in assessing the impact of prostate cancer in men is the survival rate, a measure of the proportion of patients still living at some time point subsequent to the diagnosis of their cancer.

The fact that one of the treatment options for some men is no treatment or “watchful waiting” (a delay in active treatment) suggests that the expected number of years of life remaining without treatment is equal to or greater than that with treatment. Given that a man may survive for many years after a diagnosis of prostate cancer, information on survival probabilities can play an important role in planning treatment strategies. In addition, differences in survival between defined subgroups of patients allow clinicians and policy makers to better target interventions.

One way to describe the survival experience of a cohort of patients over an extended period of time is the five-year survival rate. This value is simply the cumulative proportion of patients surviving at the end of the fifth year after initial diagnosis. Since a large proportion of prostate cancer patients survive for many years, however, it is desirable to evaluate the survival experience of patients beyond the five-year point. SEER survival data are currently available for up to 22 years following initial diagnosis.

Changes in cancer survival data are often subject to factors other than improvements in treatment. In the case of prostate cancer, transurethral resection of the prostate (TURP) and prostate-specific antigen (PSA) testing each have the potential to increase the survival time of individual

patients by allowing diagnosis at points in time which may be years prior to when the cancer would have become detectable by physical examination. This may result in lead time bias, meaning that men who are identified by PSA testing appear to survive longer than men who are identified by other methods. In such a situation, PSA screening would appear to help men survive longer, when in reality there would be no real difference in the time to death between screened and unscreened men.

Another potential problem with screening and survival analysis relates to length time bias. PSA screening is more likely to identify slower growing tumors, which may exist for longer time intervals prior to the development of clinical symptoms compared to fast growing tumors. Thus, men who are identified by PSA testing survive longer because they may have slower growing tumors. These issues must be considered in the interpretation of survival trends.

Relative survival (adjusted for other causes of death) is primarily presented in this section. Only the overall 5- and 10-year observed survival rates are included.

The five-year observed survival of men with prostate cancer has increased steadily from a low of 45.1% for men newly diagnosed in 1973 to 66.9% for men newly

diagnosed in 1990 (Figure 5.1). The average annual increase was 1.3. The ten-year observed survival rate has also increased over time, but at a slightly slower pace. The ten-year observed survival has increased by about 0.9 per year from 21.8% for men newly diagnosed in 1973 to 32.2% for men newly diagnosed in 1985.

The five-year relative survival has also increased steadily from a low of 64.0% for men newly diagnosed in 1973 to 92.9% for men newly diagnosed in 1990 (Figure 5.1). The average annual increase was 1.6. Similar to the five-year relative survival rate, the ten-year relative survival rate has increased by about 1.7 per year, from 46.8% for men newly diagnosed in 1973 to 68.5% for men newly diagnosed in 1985.

While the relative survival rate of both black men and white men has increased over time, black men continue to have a lower five-year relative survival than white men (Figure 5.2). For men diagnosed from 1973 to 1977, whites experienced a five-year relative survival that averaged 8.5% higher than that of blacks. This difference has expanded over time, with average differences of 10.2%, 14.1%, and 14.6% in the time periods 1978-1982, 1983-1987, and 1988-1993, respectively.

Stratifying the SEER data by age and stage of disease at diagnosis does not completely explain these differences. Within each age group, white men have a better five-year relative survival rate than black men. Also, within each stage of prostate cancer at diagnosis, white men have a better five-year relative survival rate than black men.

Age-specific relative survival patterns support the concept that prostate cancer may be more severe or advanced in younger men

(Figure 5.2). Men 40-49 years of age at diagnosis from 1988-1993 had a five-year relative survival of 84.1%, which is the lowest of all age groups. During this most recent time period, the five-year relative survival was 90.1%, 94.7%, 96.8%, and 89.2% for men 50-59, 60-69, 70-79, and 80+ years of age at diagnosis, respectively.

The relative survival experience of men with prostate cancer depends in large part on the stage of disease at diagnosis. The relative survival rates of men diagnosed with prostate cancer at either a localized or regional stage are now (1988-1993) over 99%, but the relative survival of men with distant stage disease remains poor (Figure 5.3). The relative survival rate for men with localized stage prostate cancer has increased in a linear pattern throughout the period of observation (Figure 5.3). Survival rates for men with distant stage disease have remained essentially unchanged from 1973-1993.

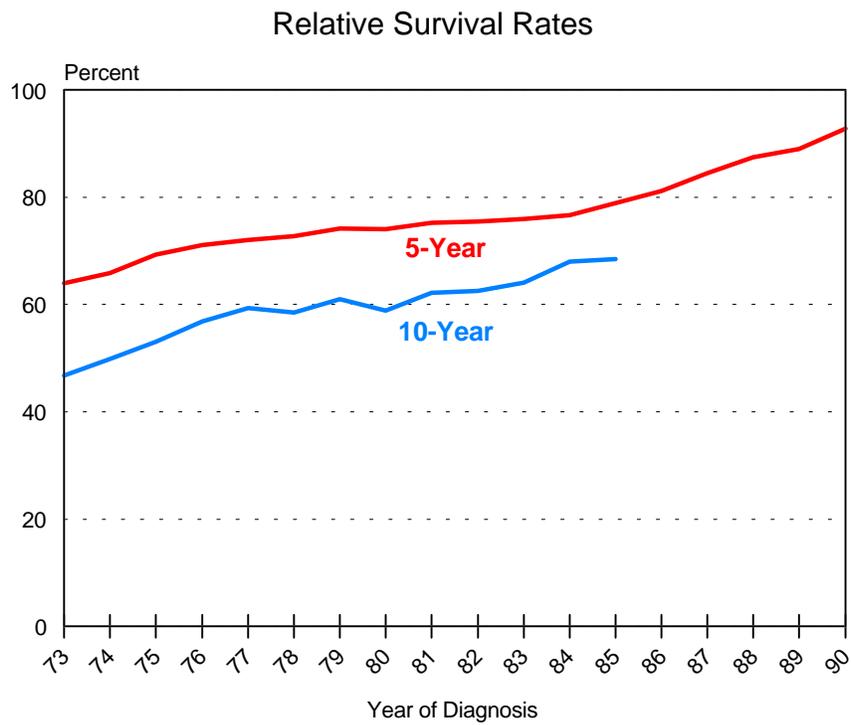
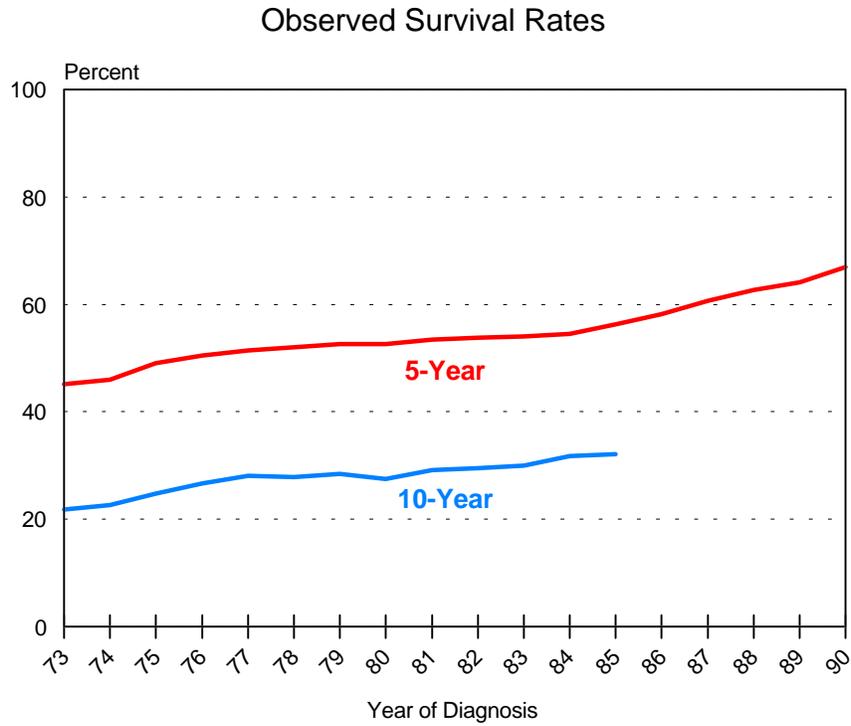
There is a marked variation in relative survival by grade, with men having well differentiated tumors experiencing the highest relative survival and those with poorly differentiated tumors having the worst relative survival (Figure 5.3). Men newly diagnosed with well differentiated prostate cancer from 1988 to 1993 had a five-year relative survival of 100%. During this same time frame, men with moderately differentiated and poorly differentiated prostate cancer had five-year relative survival rates of 99.6% and 73.5%, respectively. Controlling for stage of disease did not appreciably alter these findings.

These survival data suggest that almost two out of every three men diagnosed with prostate cancer today may be expected to survive for at least five years. Consistent improvements in survival have occurred over the last two decades. Given the lower

survival of men diagnosed with distant stage prostate cancer, effective means to detect prostate cancer at an earlier stage may prove useful. However, final confirmation of the usefulness of such efforts must be based on a clear reduction in prostate cancer mortality.

Figure 5.1

Prostate Cancer SEER 5-Year and 10-Year Survival Rates, 1973-1990

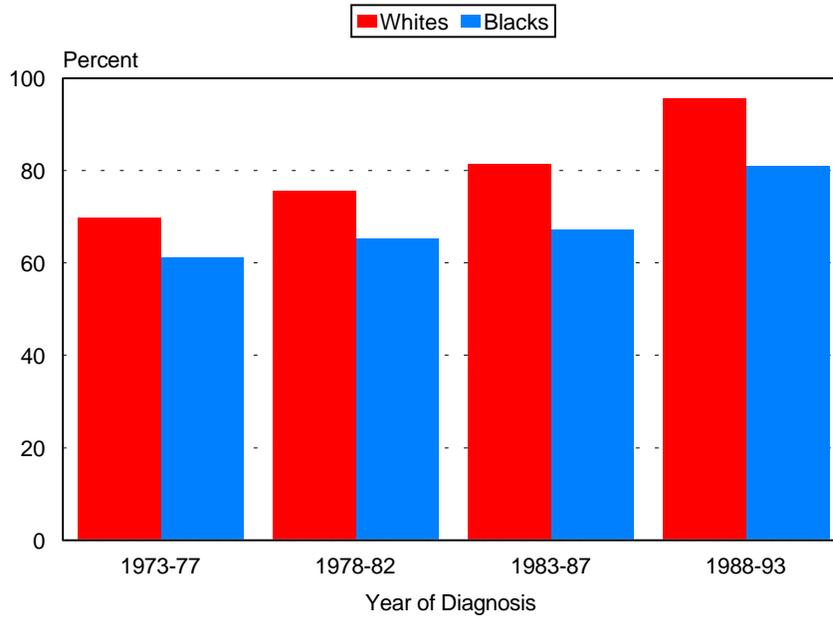


Note: Rates are based on data from the 9 standard SEER registries.

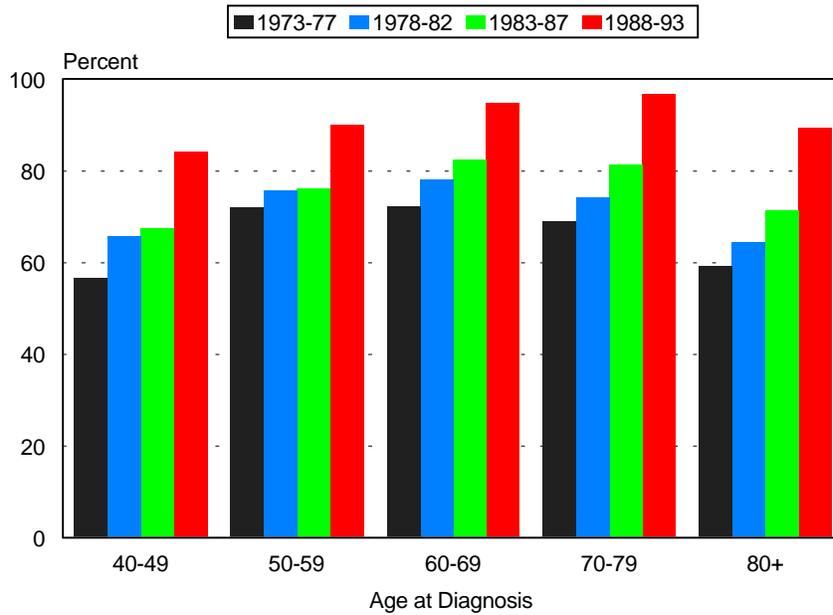
Figure 5.2

Prostate Cancer SEER 5-Year Relative Survival Rates

By Race



By Age at Diagnosis

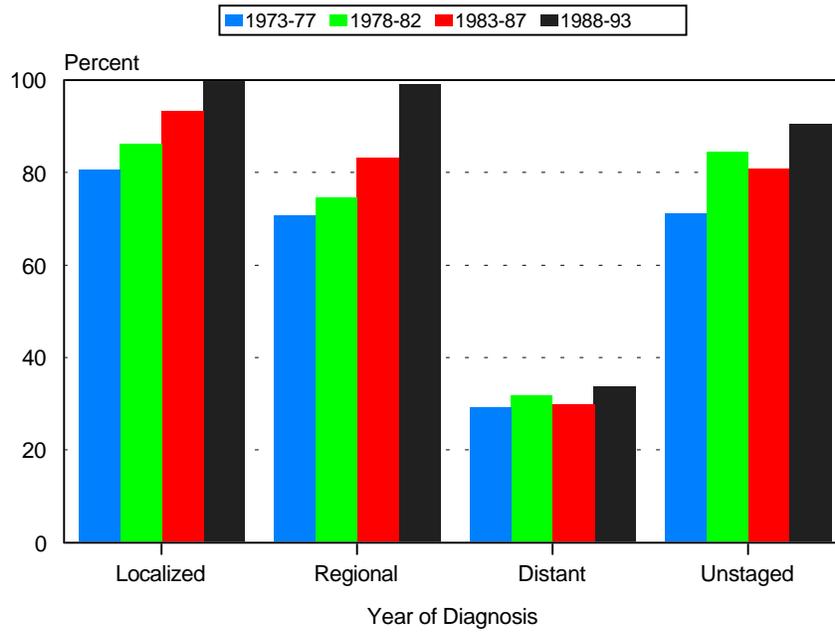


Note: Rates are based on data from the 9 standard SEER registries.

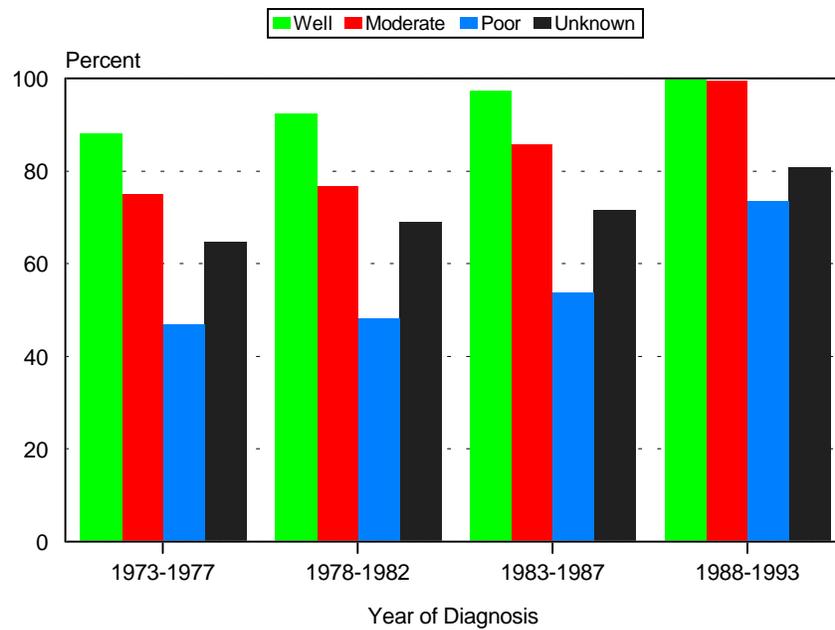
Figure 5.3

Prostate Cancer SEER 5-Year Relative Survival Rates

By Stage



By Grade



Note: Rates are based on data from the 9 standard SEER registries.

Problems arise when analyzing cancer incidence, mortality and survival for racial or ethnic groups other than whites and blacks due to the small numbers of cases. Detailed racial and ethnic information has been collected by the SEER program since its inception and coverage of a myriad of racial and ethnic groups within the U.S. has been one of the program goals (Table 6.1). This level of detail is,

however, lacking in the U.S. mortality data and intercensal population estimates. With the exception of Chinese, Japanese, and Filipinos, detailed information for other Asian populations is not available from U.S. mortality data. Hispanic ethnicity has been available in U.S. mortality data for all 50 states only since 1990. Denominator counts for detailed racial/ethnic groups are available only at the 1990 census, making it possible to compute incidence and mortality rates for short time periods

around the census, but not long-term trends. Changes in the definition of Hispanic status over time, both by SEER and by the Bureau of the Census, also complicate the computation of rates and trends. Finally, the lack of life-table data for several specific groups, for example Koreans and Vietnamese, makes it impossible to calculate relative survival. Despite these limitations, several racial/ethnic comparisons can be examined and are presented in this section.

Table 6.1

Number of Persons in the U.S. Population and SEER Areas, 1990s Census Data¹

RACE	TOTAL U.S.	TOTAL SEER	SEER % of U.S.
All Races	248,709,873	34,639,485	13.9
Black	29,986,060	3,673,998	12.3
Chinese	1,645,472	708,454	43.1
Filipino	1,406,770	692,445	49.2
Hawaiians	211,014	163,698	77.6
Hispanic ²	22,354,059	5,575,822	24.9
Japanese	847,562	507,983	59.9
Native American	1,959,234	532,973	27.2
White	199,686,070	24,951,371	12.5

¹ The source of the population numbers in this table is the Bureau of the Census 1990 STF2C data tape. These population numbers may not be identical to those used in the calculation of rates appearing in other publications.

² The "Hispanic" classification is a further description of persons already included in the other racial/ethnic categories and thus constitutes a double count.

SEER incidence and U.S. mortality rates for prostate cancer have been previously calculated for the time period 1988-1992 as part of the *Racial/Ethnic Patterns of Cancer in the United States 1988-1992* monograph. Results from this publication indicate that incidence and mortality rates are 34% and 123% higher, respectively, for blacks compared to whites. The incidence and mortality rates observed in Asians, Hawaiians and Native Americans are significantly lower than either the white or black rates (Table 6.2). Rates for whites are subdivided into Hispanic and non-Hispanic components. Rates for white Hispanics are about one-third lower than rates for white non-Hispanics.

Table 6.2
Prostate Cancer
SEER Incidence and U.S. Mortality
1988-1992

	Incidence	Mortality
Black	180.6	53.7
Chinese	46.0	6.6
Filipino	69.8	13.5
Hawaiian	57.2	19.9
Japanese	88.0	11.7
Native American*	52.5	16.2
White (Total)	134.7	24.1
White Hispanic	92.8	15.9
White Non-Hispanic	137.9	24.4
Rates are per 100,00 and are age-adjusted to the 1970 U.S. standard. Source: <i>Racial/Ethnic Patterns of Cancer in the United States, 1988-1992</i> ; NIH Pub. No. 96-4104.		
*Based only on data from New Mexico		

Beginning with the 1990 Decennial Census, yearly estimates have been available for Asian/Pacific Islander, Native American and Hispanic (total, white Hispanic, non-

white Hispanic) populations, allowing for the calculation of recent time trends in incidence rates for these groups and mortality rates for Hispanics. Incidence rates are highest for blacks and lowest for Native Americans (Figure 6.1). Incidence rates peaked in 1992 for all groups except blacks, whose rate peaked in 1993. Incidence declined from 1993 through 1995 in all groups. Rates for Native Americans remain the lowest of the five groups.

Mortality rates are higher for white non-Hispanics compared to white Hispanics (Figure 6.1). The rate for white non-Hispanics began to decline in 1992, but for white Hispanics the rate first decreased slightly in 1995.

The distributions by stage (Figure 6.2) and grade (Figure 6.3) are relatively consistent among racial and ethnic groups. In all groups, between 59-64% of prostate cancers are diagnosed at a localized stage. Around 20% of the cases have regional and 6-13% distant disease at diagnosis. Hawaiians, Native Americans, and blacks have the highest proportions of men diagnosed with distant stage disease.

Across all racial/ethnic groups, the highest proportion (46-56%) of prostate cancers is moderately differentiated. About 15-20% of the tumors are well differentiated and 21-29% poorly differentiated. Filipino and Hawaiian men have the highest proportions of poorly differentiated tumors.

Five-year relative survival rates vary by stage across racial/ethnic groups (Figure 6.4). For localized and regional stage prostate cancers, Native Americans have the lowest relative survival rates followed by Filipino men. Blacks, white Hispanics, Native Americans and Filipinos diagnosed with distant disease had lower rates than

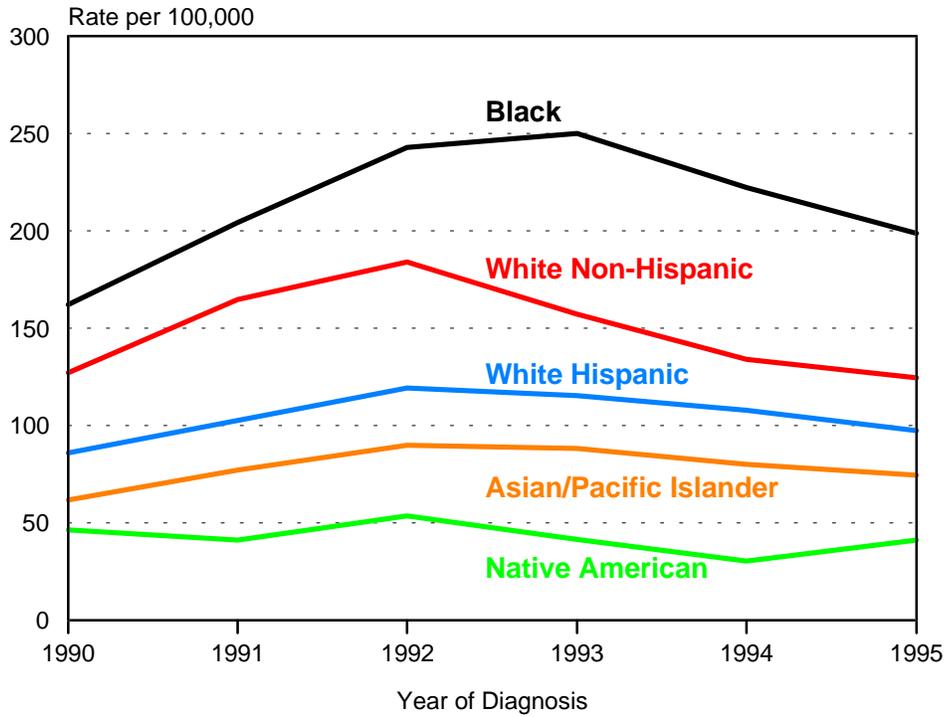
other groups. Over all stages, survival is higher for white non-Hispanics compared to white Hispanics.

The distributions of treatment for localized and regional stage disease (Figure 6.5) and distant disease (Figure 6.6) varied by racial/ethnic groups. The proportion of men undergoing radical prostatectomy for localized and regional stages was higher in white non-Hispanic, white Hispanic, and Chinese populations compared to other racial/ethnic groups. Japanese, Hawaiians and blacks had higher proportions of men receiving radiation therapy than other racial/ethnic groups. The highest proportion of men receiving no treatment was observed in Native Americans. The majority of men with distant stage disease receive hormone therapy, regardless of race or ethnic subgroup.

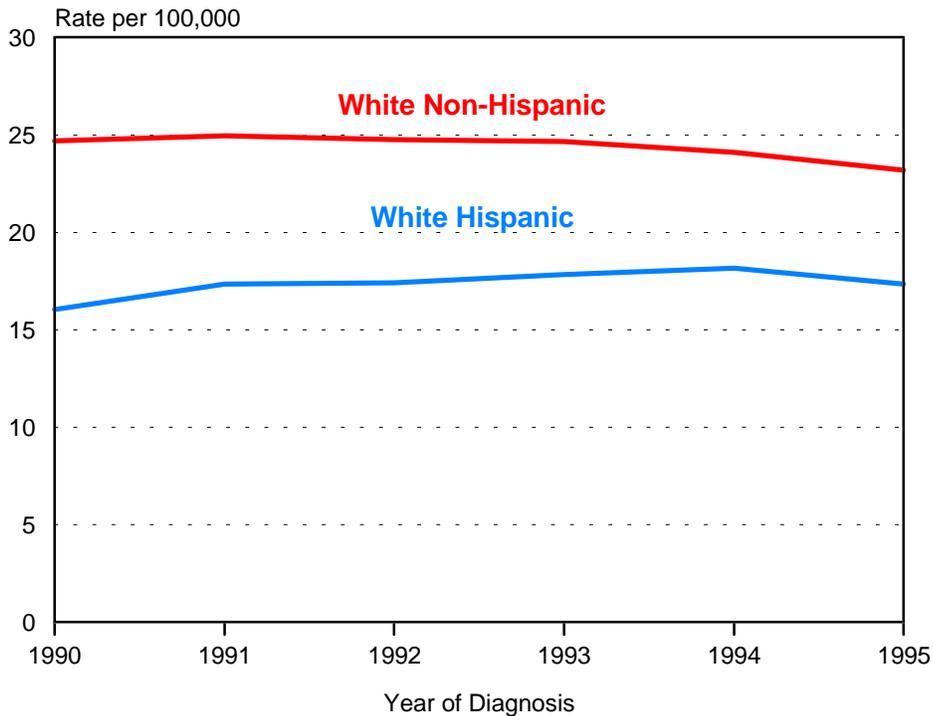
FIGURE 6.1

**Prostate Cancer
Incidence and Mortality Rates by Race/Ethnicity, 1990-1995**

SEER Incidence Rates



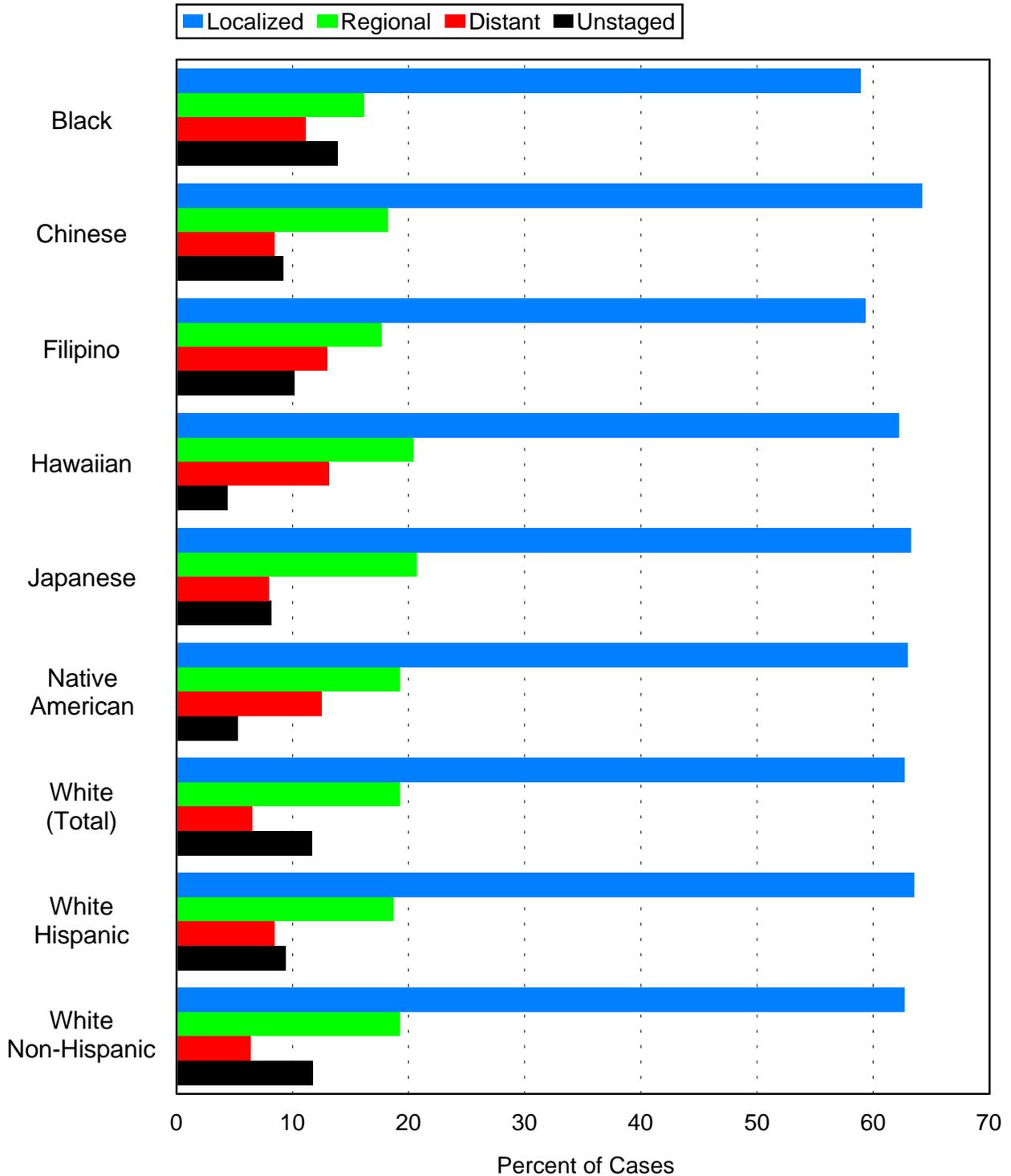
U.S. Mortality Rates



Note: Rates are age-adjusted to the 1970 U.S. standard; incidence rates are based on data from 11 SEER registries. Mortality rates do not include data from Connecticut, Louisiana, New Hampshire, or Oklahoma.

FIGURE 6.2

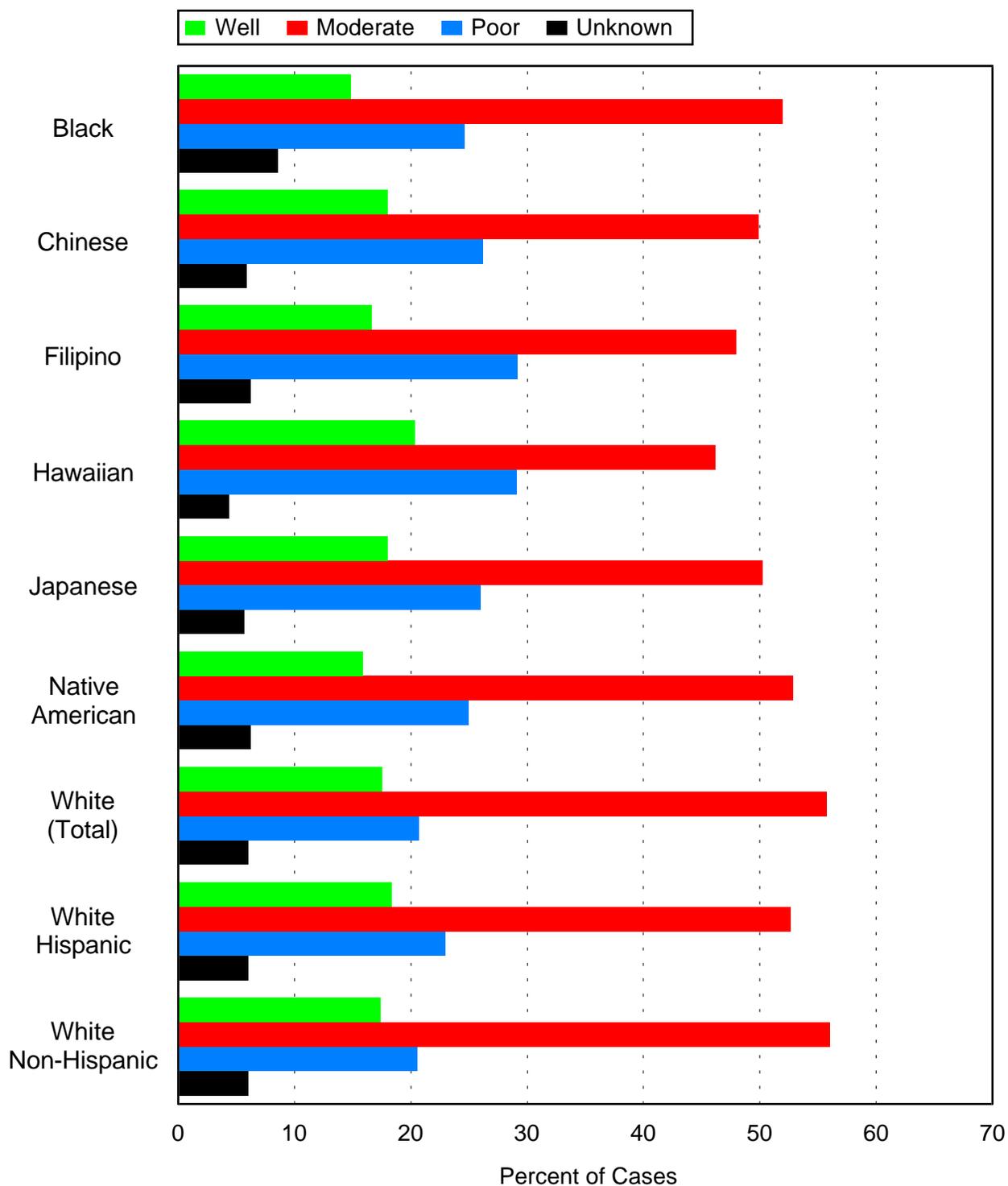
**Prostate Cancer
Distribution of SEER Cases by Race/Ethnicity and Stage, 1990-1995**



Note: Based on data from the 11 SEER registries. Los Angeles data used only for 1992-1995.

FIGURE 6.3

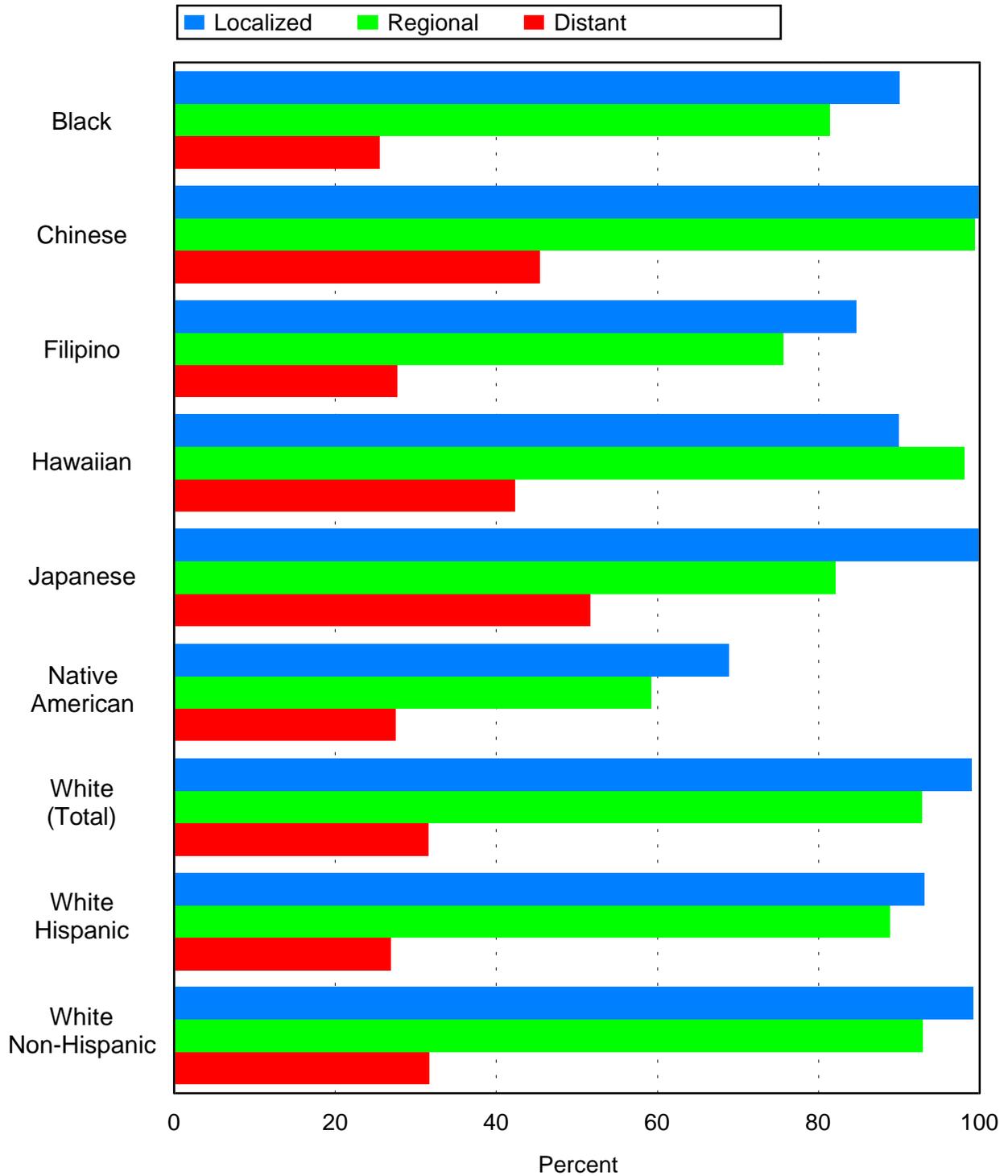
**Prostate Cancer
Distribution of SEER Cases by Race/Ethnicity and Grade, 1990-1995**



Note: Based on data from the 11 SEER registries. Los Angeles data used only for 1992-1995.

FIGURE 6.4

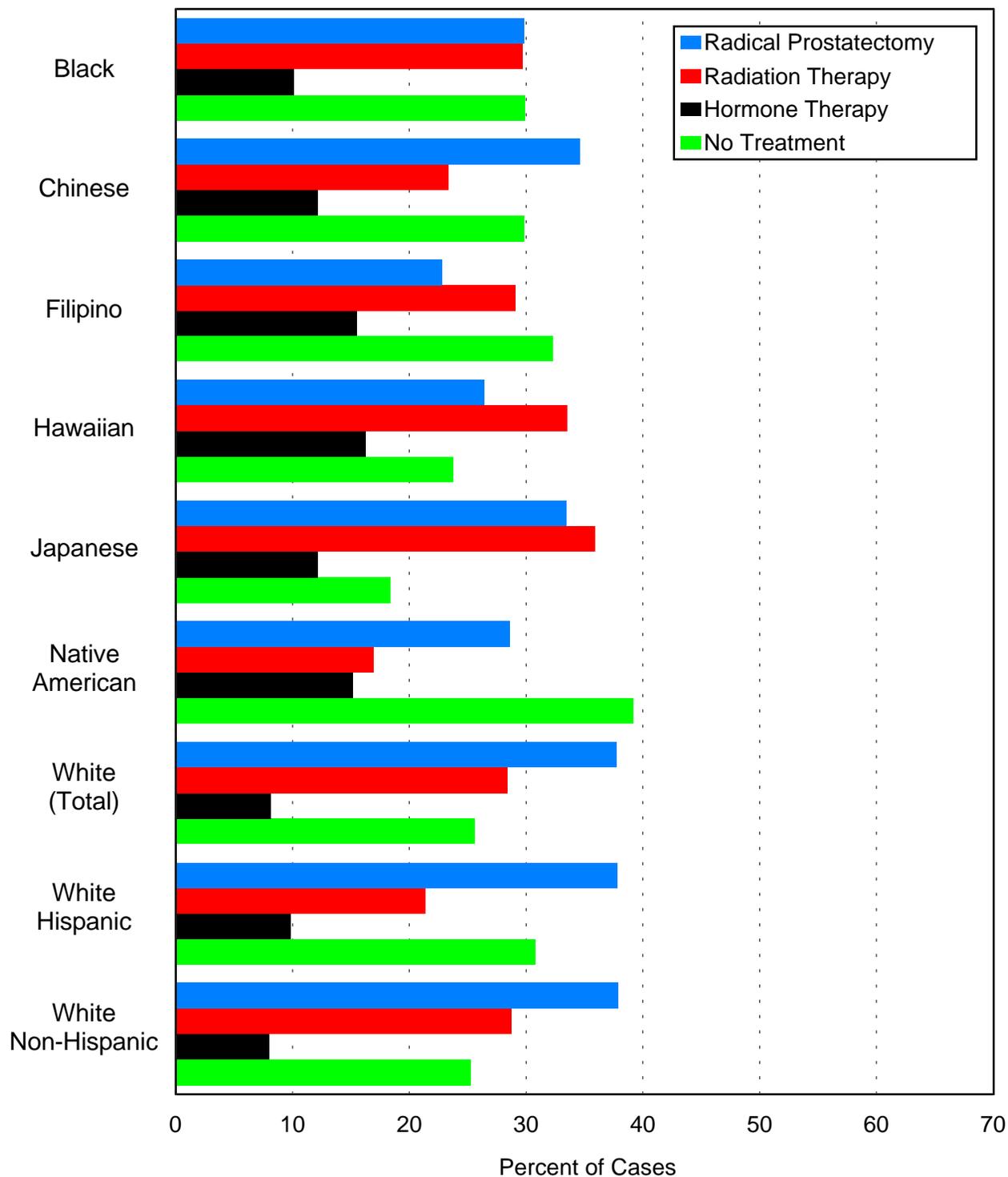
**Prostate Cancer
5-Year Relative Survival by Race/Ethnicity and Stage, 1983-1993**



Note: Based on data from the 11 SEER registries.

FIGURE 6.5

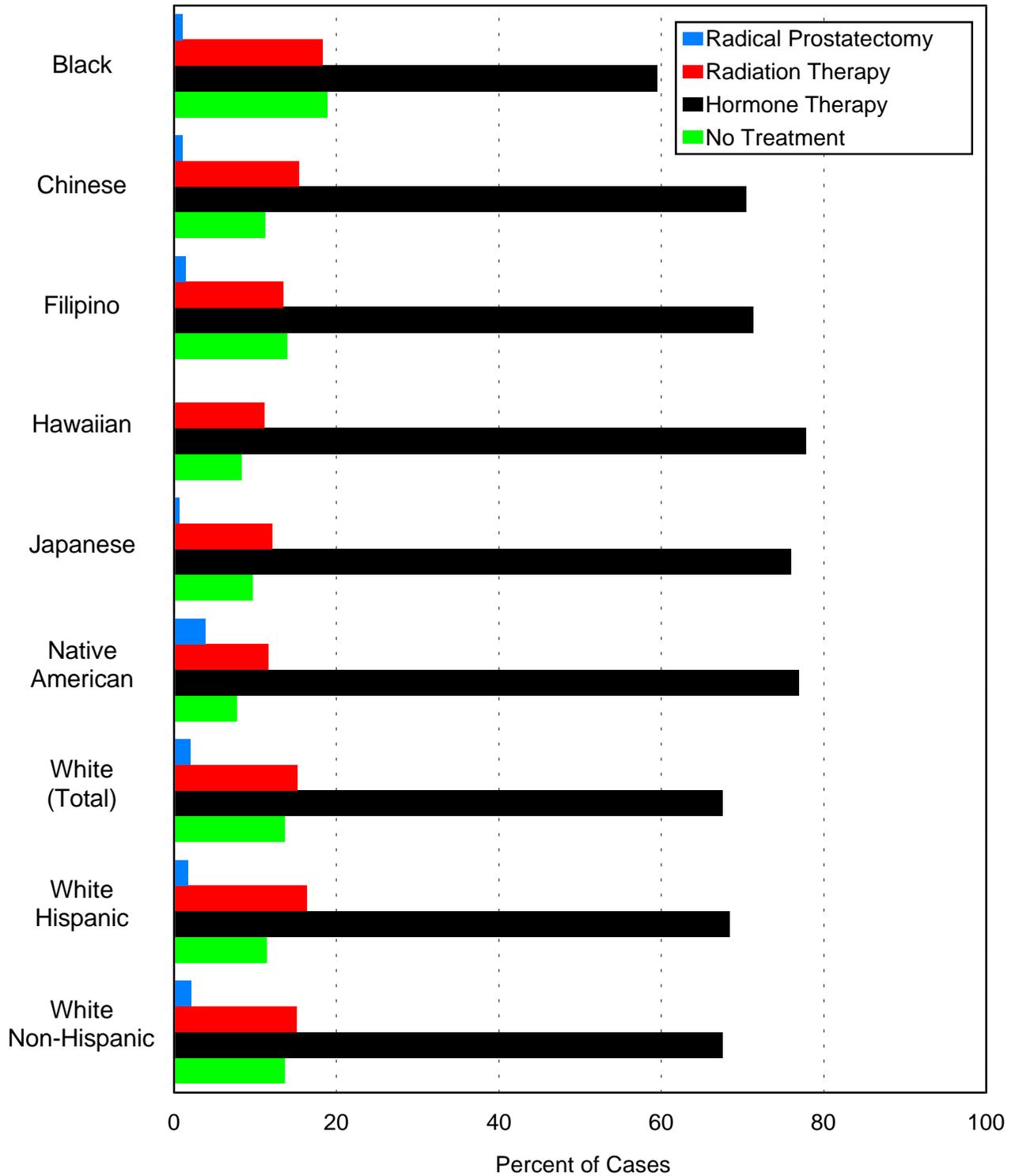
Prostate Cancer
Distribution of SEER Cases by Race/Ethnicity and Treatment, 1990-1995
Localized and Regional Stages



Note: Based on data from the 11 SEER registries. Los Angeles data used only for 1992-1995.

FIGURE 6.6

Prostate Cancer
Distribution of SEER Cases by Race/Ethnicity and Treatment, 1990-1995
Distant Stages



Note: Based on data from the 11 SEER registries. Los Angeles data used only for 1992-1995.

SUMMARY

This volume offers one of the most comprehensive population-based evaluations ever published on demographic and clinical features of prostate cancer cases. The results provide insights into the likely directions for prostate cancer research over the next decade, related to etiology and prevention, early detection and therapy.

Prostate cancer is the most frequently diagnosed cancer in the United States, yet our understanding of risk factors and the causes of prostate cancer continues to lag far behind that of other major cancers. The strong racial-ethnic variation in incidence and mortality offers one of the most interesting leads to the etiology of this disease. Although the dramatic trends in prostate cancer incidence rates observed by SEER between 1987 and 1995 due to the increased utilization of PSA testing have made international comparisons of prostate cancer incidence more difficult, blacks, as they have for decades, continue to have the highest prostate cancer rates in the world. Non-Hispanic whites in the United States also have relatively high rates in comparison to other populations around the world, even though their age-adjusted incidence rate in recent years remains approximately 40% less than that of blacks. Hispanic whites have substantially lower rates than non-Hispanic whites and Asian-Americans and Native Americans have even lower incidence rates. Nonetheless, Asian-Americans have prostate cancer rates which are increased over those of Asians in their native lands. This extraordinary racial-ethnic variation in incidence is most likely due to a combination of genetic and environmental influences and etiologic research is currently focused on identifying the precise genetic and environmental factors predisposing to prostate cancer development.

Although many environmental factors are being explored as prostate cancer risk factors, one focus of environmental research in the near future will be on diet. Dietary fat consumption is now reasonably well established as a contributor to prostate cancer development. However, little is known about the details of this relationship in terms of which subcomponents of fat are most associated with risk, during what periods of life high fat consumption conveys the greatest risk, or through what biological mechanisms fat operates to influence prostate carcinogenesis.

Other dietary hypotheses are being pursued with equal vigor. Dietary fiber, such as that found in certain grains and fruits, is of current interest. Certain male hormones which influence prostate growth are secreted from the liver into the small intestine and then reabsorbed. Fiber binds these hormones, leading to excretion rather than reabsorption and thereby reducing exposure to the prostate.

Micronutrients, especially certain vitamins and minerals, have long been of interest as cancer chemopreventive agents. Prominent among these have been vitamins which serve as antioxidants. These agents inactivate chemical moieties known as free radicals that can damage DNA, inducing mutations or other genetic changes, which

are critical to the carcinogenic process. Lycopene is one of a family of carotenoid antioxidant micronutrients which is being studied as a possible cancer prevention agent. Lycopene is found primarily in tomato or tomato products and is one of the more potent carotenoid antioxidants. For unknown reasons, it is concentrated by the prostate. Prospective epidemiologic studies have provided highly suggestive evidence that lycopene reduces prostate cancer risk. A recent clinical trial of skin cancer chemoprevention unexpectedly found a reduced risk of prostate cancer with selenium supplementation, which will likely become a target of future investigations.

Finally, phytoestrogens, i.e., plant estrogens such as isoflavonoids found in soy products, have been suggested as possible preventive nutrients for prostate cancer, because they can weakly bind androgen hormone receptors in the prostate and interfere with prostate growth. As Asian populations are traditionally heavy consumers of phytoestrogen-rich foods, this hypothesis may help explain the low prostate cancer rates in these populations.

Genetic studies related to prostate cancer etiology likely will focus in the near future around two major themes. Prostate cancer is a familial disease; first degree relatives of men with prostate cancer have a two- to three-fold excess risk of developing the disease. When thinking about prostate cancer occurring in families, it is important to distinguish the terms hereditary and familial. Hereditary prostate cancer is more specific and describes a distribution of cancer cases within a family that is consistent with inheritance of a single gene. This type of genetic susceptibility is characterized by an early age at onset and multiple affected men within the family. Several of these types of susceptibility genes have already been

identified and cloned for other cancers such as breast cancer, and there is strong evidence that multiple such genes also exist for prostate cancer. The putative locus of one such gene was recently narrowed to a small area of chromosome 1q. A major focus of genetic studies of prostate cancer in the near future will be the identification, cloning and characterization of this and other such susceptibility genes. However, these genes, while important, are not responsible for the majority of prostate cancer (although nearly half of prostate cancers diagnosed among men under age 55 may be due to these genes, current estimates suggest that approximately 9% of all prostate cancers are due to these genes). Prostate cancer that occurs more commonly in relatives of an affected individual than in the general population is given the more general term familial. Much familial and non-familial prostate cancer is likely to be multifactorial, involving more than one gene in combination with environmental exposures, as well as probably complex interactions between genes and environmental factors. A series of candidate genes that will likely contribute to prostate cancer risk in more subtle ways than the single inherited genetic traits that are necessary and sufficient to cause cancer have already been proposed. Lifelong exposure to the effects of these genes is needed to increase prostate cancer risk. Individually these genes lead to low relative increments in cancer risk but, in combination, are likely to be responsible for a large percentage of prostate cancer cases. Among the genes in this category already proposed to influence prostate cancer risk are a series of genes whose products influence androgen secretion and metabolism, the vitamin D receptor gene as vitamin D influences proliferation and differentiation of prostate cells, genes involved in metabolism and transport of fatty acids, and genes involved in the metabolic activation or detoxification of environmental

carcinogens. All of these proposed candidate genes are polymorphic, i.e., there exist small sequence variations in the structure of these genes among individuals and populations. Moreover, for some genes these polymorphisms have been shown to influence the gene product (i.e., they are functional polymorphisms) and, for some, there are substantial variations in the frequency of the polymorphic alleles among the racial-ethnic groups showing the greatest variation in prostate cancer incidence.

As discussed at length in the sections above, the rapid increase in incidence of prostate cancer during the late 1980's and early 1990's is thought to be due largely, if not entirely, to increased utilization of prostate specific antigen (PSA) testing. PSA is a prostate-specific protease that is produced by prostatic epithelial cells and is being extensively evaluated in serum as a screening method for detecting occult prostate cancer (i.e., asymptomatic prostate cancer confined to the prostate in otherwise healthy individuals). The increased incidence of prostate cancer that has occurred in the past decade has not been confined only to an increase in localized disease, however, as one might anticipate if PSA screening was solely responsible. In fact, there has been an increase in regional disease (i.e., disease that has extended through the prostatic capsule and beyond). However, this increase in regional disease is likely an indirect consequence of PSA screening. A common therapy for men with PSA-detected cancer is radical prostatectomy. Staging is often upgraded as a result of the detailed histologic examination of the prostate which occurs following surgical removal.

Strong evidence is presented in this monograph that PSA detected prostate cancer is largely moderate grade (Gleason score 5-7). As moderate grade prostate

cancer detected clinically carries with it substantial mortality from prostate cancer, PSA appears to be detecting largely clinically meaningful disease. These encouraging data regarding the possible value of PSA screening further magnify the importance of the ongoing national trial to determine the efficacy of PSA in reducing prostate cancer mortality (the ultimate measure of the efficacy of any cancer screening tool). In the meantime, PSA has already become widely utilized in clinical practice, in large part because it is a non-invasive and relatively inexpensive test. The sensitivity of PSA testing for prostate cancer (i.e., the proportion of men with prostate cancer who test positive) in one large study was 67% although others have reported higher values. One study reported the specificity (i.e., the proportion of men without prostate cancer who are negative by screening) of PSA screening to be as high as 97%, but most other studies have reported much lower values. Future research in early detection strategies for prostate cancer, in addition to determining whether PSA screening is efficacious in reducing prostate cancer mortality, is likely to focus on strategies which maximize both sensitivity and specificity of PSA screening. Using PSA biochemical subfractions, incorporating age- and race-specific cutpoints of positivity, and adjusting serum PSA concentrations by prostatic volume (PSA density) are among the methods which will be undergoing further evaluation. As prostate cancer outcome is highly dependent on detection prior to distant spread, identification of a suitable screening test for prostate cancer is a critical public health issue.

It is clear from this report that prostate cancer mortality has declined slightly in recent years, with apparent gains in increasing short- and long-term survival from prostate cancer diagnosed at a localized

or regional stage. Noteworthy is the continued absence of improvement in survival from distant stage prostate cancer. The situation in black men is particularly urgent, as survival is worse among black men at every stage at diagnosis and the survival gap with whites continues to widen. Radical prostatectomy or external beam radiation therapy are both widely used as definitive therapy for localized prostate cancer, although some cancer specialists question whether any treatment is required for very early prostate cancer, especially among the elderly. Hormonal therapy (by androgen blockade or by other methods of reducing androgen exposure to prostate cancer cells) has been the mainstay of initial treatment for advanced prostate cancer for over 50 years. Despite early responsiveness to hormonal manipulation, prostate cancer eventually becomes androgen refractory, through genetic changes that are just now being understood. Translational research, aimed at understanding the basic biology and molecular genetics of prostate cancer so that targeted therapies can be developed and implemented, holds the key to more effective therapeutic management of advanced prostate cancer in the future.