SEER Survival Monograph

Cancer Survival Among Adults: U.S. SEER Program, 1988-2001

Patient and Tumor Characteristics

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Suggested Citation:

Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner M-J (editors). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program, NIH Pub. No. 07-6215, Bethesda, MD, 2007 .

Additional information and this monograph in PDF format with any errata are available on the SEER web site:

http://www.seer.cancer.gov

Acknowledgements:

The editors and authors would like to thank Kathleen Cronin, Eric Feuer, Leyda Su Ham, Nadia Howlader, Lan Huang, Carol Kosary, Denise Lewis, Angela Mariotto, Barry Miller, Antoinette Percy-Laurry, Marsha Reichman, and David Stinchcomb for reviewing this monograph. We are grateful to Peter McCarron, Trish Murphy, Hong Vo, and Philip Zimmerman who provided publication assistance. We also thank the SEER-funded organizations for providing high quality cancer survival data for this monograph.

Dedicated to
Dr. Charles Smart

a dedicated pioneer in the field of cancer registration and surveillance
whose vision helped establish the blueprint for cancer control
through an understanding of cancer incidence and survival
while caring about the patients behind the numbers.

Lynn & John

Charles R. Smart was a surgeon, innovator and a man to which faith and family mattered foremost. He served in the Army in World War II and graduated from Temple University School of Medicine. He worked as surgeon at UCLA Medical Center and became Chief of Surgery at Latter Day Saints Hospital (Salt Lake City) in 1975. He served as Director for the Cancer Division of the American College of Surgeons. He founded the Utah Cancer Registry, one of the earliest central cancer registries in the United States. In 1985, he became chief of the Early Detection Branch of National Cancer Institute. He was a founding member of the North American Association of Central Cancer Registries (NAACCR). He "fathered" cancer registry computer software, and published the first national data set standard. He received the 1996 David Rockefeller Spirit of Service Award for his volunteer work establishing registries in Ecuador and Hungary.

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Chapter 1
Introduction

Lynn A. Gloeckler Ries, Marie-Josephe D. Horner, and John L. Young, Jr.

INTRODUCTION

The Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI) has devoted this monograph to examining cancer survival by patient and tumor characteristics for cancers diagnosed during the period 1988-2001. The analyses focus on cancer survival in adults aged 20 years and older, with the exceptions of acute lymphoblastic leukemia (all ages), placenta (ages 15+), and Hodgkin lymphoma (ages 15+). This chapter describes the sources of the data and the methods used. It also provides a summary of the results. Each subsequent chapter focuses on a distinct anatomical site and associated histologies.

DATA SOURCES

Surveillance, Epidemiology, and End Results (SEER) Program

The Surveillance, Epidemiology, and End Results (SEER) Program was established in 1973 as part of the National Cancer Institute (NCI). A sequel to two earlier NCI initiatives (the End Results Program and the Third National Cancer Survey), the SEER Program has evolved in response to the mandate of the National Cancer Act of 1971, which requires the collection, analysis, and dissemination of data relevant to the prevention, diagnosis, and treatment of cancer. The SEER Program (http://seer.cancer.gov) collects cancer incidence, treatment, and survival data which are used to monitor the burden of cancer on the population of the United States. The NCI contracts with medically-oriented nonprofit institutions, such as universities and state health departments, to obtain data on all in situ and invasive cancers diagnosed in residents of the SEER geographic areas, except for basal cell and squamous cell carcinomas of the skin and in situ cervical cancer.

The analyses in this monograph are based on data from 12 geographic areas representing approximately 14% of the United States population: the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Atlanta, San Francisco, San Jose, Los Angeles, and Seattle; and ten counties in rural Georgia. Cases were diagnosed during the period 1988-2001 and followed through 2002. All registries contributed data for diagnosis years 1988-2001, except Los Angeles, which contributed data for 1992-2001.

Table 1.1: All Cancers: Number of Cases and Exclusions, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
2,246,603	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
1,925,529	321,074	Select first primary only
1,901,067	24,462	Exclude death certificate only or at autopsy
1,874,432	26,635	Exclude unknown race
1,870,229	4,203	Active follow-up and exclude alive with no survival time
1,846,162	24,067	Exclude children (000-019)
1,736,210	109,952	Exclude in situ cancers for all except breast & bladder cancer
1,660,376	75,834	Exclude no or unknown microscopic confirmation
1,629,964	30,412	Exclude sarcomas

A total of 1,629,955 primary cancers were used in analyses. Survival rates are calculated on demographic and tumor information. Cases of second or later primaries, cases identified by death certificate or autopsy only, cases of unknown race, and those alive with no follow-up were excluded from the analysis (Table 1.1).

The SEER data are available for analyses by researchers. See www.seer.cancer.gov for further information.

SEER*Stat Software

The SEER*Stat statistical software, a convenient, intuitive mechanism for the analysis of SEER and other cancer-related databases, was used for analyses. It is a powerful PC tool to view individual cancer records and to produce statistics for studying the impact of cancer on a population. It is available at the following website: http://seer.cancer.gov/seerstat/

Tumor Information

The SEER program collects the month and year of diagnosis, primary tumor site, behavior, histology, extent of disease at diagnosis, and, starting in 1990, breast cancer receptor status. The International Classification of Diseases for Oncology, 2nd edition (ICD-O-2) (1) was the standard reference for classifying primary site, histology, behavior and grade. The ICD-O-2 tumor site and morphology codes allow for precise coding of tumor location (including sub-location within an organ) and histology. For 2001 cases, the third edition of ICD-O (ICD-O-3) was used and all prior histology data were converted to ICD-O-3 (2).

The histologic grade of malignant tumors is also collected: *grade I* is well differentiated; *grade II* is moderately differentiated; *grade III* is poorly differentiated, and *grade IV* is undifferentiated or anaplastic (1, 2). For leukemias and lymphomas, the grade code can reflect T-cell, B-cell, and N-K cell phenotype.

Extent of Disease

SEER has collected extent of disease (EOD) information on all cancers since the inception of the program. Extent of disease information since 1988, consists of five data items: tumor size where applicable, extension (within the primary site or contiguous or metastatic), highest involved lymph node chain, number of regional lymph nodes found positive (with certain exceptions), and number of regional nodes examined (with certain exceptions). The extension and lymph node fields are specific to the site of the primary tumor. The detail and amount of information collected for EOD have varied over time.

Stage

Stage of disease is determined from EOD information. In this monograph several different staging systems were used depending on the extent of disease information available. The American Joint Committee on Cancer's (AJCC) Staging Manual for the third edition (3), the fifth edition (4), and sixth edition (5) TNM: *tumor size/extent* (T), *node involvement* (N), and *distant metastases* (M) and then combines TNM into stages. Sometimes additional information is needed such as grade.

Since 1988, the tumor extension information in EOD is collected utilizing only one variable (except for prostate since 1995) and is based on the best information available on the furthest extension of the tumor. For some AJCC schemas, there is both a clinical T and a pathologic T. Therefore, in the conversion from EOD to AJCC, the T information is based on a combination of clinical and pathologic information. If there are distant metastases, the SEER EOD conversion will be TX M1, i.e. the T information is not recorded. Similarly, if distant nodes are involved, the information on regional nodes is not recorded in SEER. For many primary sites AJCC tumor extension classifications can range from T0 to T4 with subcategories, node involvement classifications can range from N0 to N3 with subcategories, and metastasis classifications can range from M0 to M1. The AJCC T, N, and M are then combined into stage ranging from Stage 0 through Stage IV. There are some primary sites for which there is no TNM and/or no AJCC stage. For all cancer sites except bladder and breast, in situ lesions were excluded from the analyses. For most cancer sites, this means that Stage 0 is excluded, but for breast and colon/rectum, Stage 0 includes more than in situ alone. For colon/rectum, Stage 0 also includes cases confined to the lamina propria with no nodes and for breast, Paget disease with no underlying tumor.

To perform the analyses in this monograph covering data from 1988-2001, it was necessary to achieve consistency of the stage variable over time. Changes to EOD were made in 1988 to be compatible with the AJCC third edition. In 1998, some of the EOD schemas were changed to be compatible with the fifth edition of AJCC so that SEER EOD information could be easily converted into the TNM staging classifications based on the fifth edition of the AJCC Manual for Staging of Cancer. Therefore, depending

on the cancer site and the changes between the third and fifth editions of AJCC, some chapters present data according to the AJCC third, AJCC fifth, or a different stage definitions (see below). Except for lymphomas, the AJCC staging criteria were applied to all histologies for each primary site. In some chapters, a *SEER modified AJCC* stage was used. The main difference between the SEER modified and AJCC versions, is that NX was combined with N0 in the conversion of TNM to AJCC stage.

SEER has also used a more simplistic stage with five levels: *In situ* tumors are those that have not yet broken through the adjacent basement membrane. For most cancer sites treated in this monograph, in situ tumors are excluded from the analysis; the urinary bladder and the female breast are exceptions. The term *localized* describes tumors, regardless of size, that are confined to the organ of origin. *Regional* tumors are those that have metastasized to the regional lymph nodes or have extended directly from the organ of origin. *Distant* describes a tumor whose metastases have traveled to other parts of the body. (Leukemia and myeloma are considered distant at diagnosis.) When information is not sufficient to assign a stage, a cancer is said to be *Unstaged or Unknown*. Most of the chapters which use stages of localized, regional, and distant are based on the SEER Summary Stage (1977) (6). Based on the same principles as Summary Stage 1977, SEER has used more historical definitions that are more consistent over time for historical trends back to 1973. In a few places the SEER historic stage is used. The SEER Summary Staging Manual 2000 lists the definitions for SEER Summary Stage 2000 and in the footnotes for each site describes how the SEER Summary Stage 1977 and the SEER historic stage differ from it (7).

SURVIVAL METHODS

The *observed survival rate,* obtained using the actuarial (life table) method, is the proportion of cancer patients surviving for a specified time interval after diagnosis. The *expected survival rate* for a hypothetical cohort of persons of the same sex, age, and race as the patient cohort is the proportion, based on the 1990 life table, of the given cohort that will survive to the end of the given time interval. For some sites, median survival times are presented. The median survival time is based on the observed survival rate and is defined as the point at which 50% have died and 50% are alive.

Most of the survival analyses in this monograph is based on the *relative survival rate* (8), except in Chapter 31 on race and ethnicity, where the *cause-specific survival rate* (9) is used.

Relative survival is a *net survival* measure representing cancer survival in the absence of other causes of death. Relative survival is defined as the ratio expressed as a percent, of the proportion of *observed* survivors in a co-

Table 1.2: Ten Most Common Cancer Sites: 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates by Site, Ages 20+, 12 SEER Areas, 1988-2001

Site	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
			Percent	Percent	Percent	Percent	Percent	Percent
All sites (except male and female breast in situ)	1,584,884	100.0	79.5	72.3	68.7	64.4	60.6	58.6
Prostate	275,280	17.4	100.0	99.5	98.9	97.6	94.5	91.7
Breast (female, in situ)	44,875	2.8	100.0	100.0	100.0	100.0	100.0	100.0
Breast (female, invasive)	257,888	16.3	97.8	94.8	91.9	87.1	81.9	79.2
Lung	201,067	12.7	42.6	25.9	20.0	15.5	12.4	11.0
Colon/Rectum	182,589	11.5	83.3	75.1	69.9	63.6	59.2	57.7
Melanoma	55,039	3.5	97.1	94.4	92.4	90.0	88.2	87.9
Urinary Bladder	67,528	4.3	91.5	87.1	84.8	81.9	78.9	77.4
Non-Hodgkin Lymphoma	65,932	4.2	74.2	66.3	62.1	56.3	49.9	47.0
Uterine Corpus	48,642	3.1	93.5	89.5	87.0	84.7	83.1	82.6
Leukemia (all ages)	42,678	2.7	67.0	58.0	53.4	47.2	40.7	38.1
Kidney and Renal Pelvis	32,583	2.1	80.8	73.8	70.4	65.5	60.9	57.9

hort of cancer patients (the observed survival rate defined above) to the proportion of expected survivors (the expected survival rate defined above). Thus, a relative survival of 100% means that a cancer patient cohort is just as likely to survive the given interval as a cohort in the general population of the same sex, age, and race. It does not mean that everyone will survive their cancer. For example, in a group of screening found cancers, many of the people seek medical care on a more routine basis than the general population and may have better non-cancer survival than the general population. In this case the expected life table is too low which makes the relative rate too high. On the other hand, lung cancer patients who smoke may be at excess risk of dying of other smoking related causes than the general population and the calculated expected rate would be too high which means that the relative survival rate may be lower than it would be if life tables based on smoking could be used.

While many times 5-year relative survival rates are presented, a five year rate may be less informative than a survival rate over a shorter time frame for a site or group with poor survival or over a longer time frame for a site or characteristic with good survival. Up to 10-year survival rates are shown for many sites.

The conditional survival rate, while difficult to explain, may be the most clinically informative of the survival rates. Instead of evaluating survival from diagnosis, for example a 5-year relative survival rate from diagnosis, the conditional survival rate can start anytime after diagnosis, i.e., it is conditioned on the cohort surviving to that point of time and then a survival rate is calculated for the patients who have survived to that point. For this monograph, 5-year relative survival rates are presented for some sites conditioned on specific times after diagnosis. For some sites where survival is very poor, the eight year survival rate may obscure that for the small group of patients who have already survived 3 years, their probability of surviving the next 5 years may be quite high.

For certain racial and ethnic groups, the life tables that are typically used for calculating expected survival do not accurately represent the experience of that specific racial/ethnic population. Since the calculation of relative survival rates needs accurate life tables, the relative survival rates are not shown for race/ethnic groups other than white or black in the individual site chapters. In order to present information for race/ethnic groups other than white patients or black patients, a cause-specific (c-s) survival rate was used. Since survival calculated under different methods can not be compared to one another, the survival rates for more specific racial/ethnic groups were put in a special chapter on race-and-ethnicity, Chapter 31. The c-s rate is dependent on knowledge not only of the date of death but also accurate information on the cause of death. The c-s rate is similar to the observed survival rate except that only patients who died of their cancer are considered as deaths and patients who died of other causes are 'censored' at the time of death. This method avoids problems of finding appropriate expected survival rates which are needed for the relative survival rate, but is dependent on which cause of deaths are considered due to the cancer. The cause-specific rate, however, is dependent on accurate cause of death (COD) information. When the population used in calculating the expected survival is similar to the population of cancer patients except for the latter's cancer experience, the relative survival rate and the cause-specific survival rate will

Table 1.3: Ten Most Common Cancer Sites: Five-Year Relative Survival Rates by Sex and Race, Ages 20+, 12 SEER Areas, 1988-2001

Site	Total	Male	Female	White Male	White Female	Black Male	Black Female
All sites (except male and female Breast in situ)	64.4	63.6	65.3	65.3	66.5	55.8	52.9
Prostate	97.6	97.6	n/a	98.4	n/a	93.5	n/a
Breast (female, in situ)	100.0	n/a	100.0	n/a	100.0	n/a	100.0
Breast (female, invasive)	87.1	n/a	87.1	n/a	88.3	n/a	74.5
Lung	15.5	13.6	18.0	13.9	18.4	10.9	15.0
Colon/Rectum	63.6	63.7	63.5	64.6	64.4	55.3	54.9
Melanoma	90.0	88.2	92.1	88.4	92.4	70.1	76.3
Urinary Bladder	81.9	84.0	75.9	84.8	77.3	69.3	55.4
Non-Hodgkin Lymphoma	56.3	52.5	60.9	53.4	61.5	43.4	54.8
Uterine Corpus	84.7	n/a	84.7	n/a	86.4	n/a	61.8
Leukemia (ages 0-19 and 20+)	47.2	48.0	46.2	49.6	47.6	37.2	37.9
Kidney and Renal Pelvis	65.5	65.2	66.0	65.9	66.2	61.4	64.8

Table 1.4: Number of Cases by Leading Cancer Site and Stage at Diagnosis, 5-Year Relative Survival Rates, Ages 20+, 12 SEER Areas, 1988-2001

	Relative Survival						
Site	Localized	5-year percent (localized)	Regional	5-year percent (regional)	Distant	5-year percent (distant)	Unstaged
Prostate	@	@	236,377	100.0	17,953	35.8	20,950
Breast (female, invasive)	160,105	97.4	78,299	79.2	14,359	24.4	5,125
Lung	32,709	50.5	75,551	15.8	78,510	1.9	14,297
Colon/Rectum	70,343	90.6	69,942	66.2	34,756	9.4	7,548
Melanoma	44,969	97.2	5,869	61.1	1,931	14.6	2,270
Urinary Bladder	50,331	93.9	12,686	48.5	2,166	5.8	2,345
Non-Hodgkin Lymphoma	19,971	69.4	9,098	61.1	30,468	44.3	6,395
Uterine Corpus	35,646	95.7	7,237	66.2	3,993	26.0	1,766
Kidney and Renal Pelvis	17,591	90.4	7,316	60.2	6,598	8.2	1,078

@ Local combined with Regional for Prostate

be nearly equal. That is, the relative survival rate closely indicates the probability that a patient will not die due to cancer-related causes within the given time interval. When the population used for the expected survival is dissimilar to the population of cancer patients, the relative survival may differ from the cause-specific survival rate by tumor and patient characteristics. Comparisons of survival rates should be based on the same survival method for calculating rates.

RESULTS

Relative survival up to 10 years after diagnosis of invasive cancer is shown in Table 1.2 for patients diagnosed in the 12 SEER catchment areas during 1988-2001. Survival rates vary substantially according to the cancer site. Among the most frequently diagnosed cancers, the sites with the highest 10-year relative survival rates are prostate, female breast in situ, uterine corpus, and melanoma, which have 10-year relative survival rates of 83% (uterine corpus) to 100% (female breast in situ). Lung cancer has the least favorable survival across the 10-year period following diagnosis (11%).

Survival by sex and race is presented in Table 1.3 for select cancer sites. For all cancers combined, excluding male and female breast in situ, there is only a small difference by sex in terms of 5-year relative survival rates. However, a survival advantage by sex varies by cancer site as well as within race groups. For example, five-year survival for non-Hodgkin lymphoma among white women is 62% compared to 53% in white males. Among black women the non-Hodgkin lymphoma 5-year survival rate (55%) is twelve percentage points higher than in black men (43%). Among white males, the 5-year relative survival rate for urinary bladder is 85% compared to 77% in white females. Blacks seem to fare worse with this disease, where the 5-year survival rate is 69% among black males and 55% among black females.

Survival by summary stage is presented in Table 1.4 for select cancers. The differences in 5-year survival by stage are notable. The earlier the stage at diagnosis, the more favorable is the 5-year survival. For screenable cancer sites, survival ranges from 91% at localized stage to 9% at distant stage for colorectal cancer, and 97% at localized stage to 24% at distant stage for female invasive breast cancer. Other cancer sites are as extreme in terms of survival by stage of diagnosis (urinary bladder, melanoma).

DISCUSSION

Many times in population-based statistics the emphasis is on incidence and mortality statistics. While these are important in measuring cancer, they are not as relevant to the medical community concerned about prognosis. The focus of this monograph is to present descriptive analyses of cancer survival by patient and tumor characteristics.

Since the emphasis is on the influence of patient and tumor characteristics on survival and not on how survival rates have changed over time, a discussion of biases in survival trends is not presented here. See the introduction of the SEER Cancer Statistics Review for a discussion of survival biases (10). In comparing any two groups, one should consider whether any differences in survival may be due to the two groups being different by some other characteristic than the comparison. For example, in a cohort of patients over 85 years of age, due to co-morbid conditions some may not have had as extensive staging work-up as a younger age group.

The analyses presented in this monograph did not test for statistical significance of observed differences between population groups, therefore neither confidence intervals nor p- values are provided. Any comparisons of survival rates between age, sex, race groups, or tumor characteristics are based on point estimates, and thus, issues related to small case numbers need to be considered when making or interpreting comparisons. The numbers of cases are given in most cases so that one has a general idea about the variability of the point estimates. Survival rates were not calculated for fewer than 25 cases.

An attempt was made to include all cancer sites. A chapter on rare cancers contains information on cancers not included in the site-specific chapters.

REFERENCES

1. Percy C, Van Holten V, Muir C, editors. International classification of diseases for oncology, 2nd ed. Geneva: World Health Organization; 1990.
2. Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, Whelan S. International Classification of Diseases for Oncology--Third Edition. Geneva: World Health Organization, 2000.
3. Beahrs, OH, Henson DE, Hutter RVP, Myers MH (eds). AJCC Cancer Staging Manual, Third edition. American Joint Committee on Cancer. Philadelphia: Lippincott, 1988.
4. Fleming ID, Cooper JS, Henson DE, Hutter RVP, Kennedy BJ, Murphy, GP, O'Sullivan, B, Sobin LH and Yarbro, JW (eds) AJCC Cancer Staging Manual, Fifth Edition, Lippincott-Raven, Philadelphia, 1998.
5. Greene FL, Page DL, Fleming ID, Fritz AG, Balch CM, Haller DG, Morrow M (eds). AJCC Cancer Staging Manual, Sixth edition. American Joint Committee on Cancer. New York: Springer 2002.
6. Shambaugh, EM, Weiss, MA. Axtell, LM (eds), The 1977 Summary Staging Guide for the Cancer Surveillance, Epidemiology and End Results Reporting Program. National Cancer Institute, SEER Program, Bethesda, MD, April 1977.
7. Young JL Jr, Roffers SD, Ries LAG, Fritz AG, Hurlbut AA (eds). SEER Summary Staging Manual – 2000; Codes and Coding Instructions, National Cancer Institute, NIH Pub. No. 01-4969, Bethesda, MD, 2001.
8. Ederer F, Axtell LM, Cutler SJ. The relative survival rate: a statistical methodology. J Natl Cancer Inst Monogr 1961;6:101 121.
9. Clegg LX, Li FP, Hankey BF, Chu K, Edwards BK. Cancer survival among US whites and minorities: a SEER (Surveillance, Epidemiology, and End Results) Program population-based study. Arch Intern Med 2002;162:1985-1993.
10. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Eisner MP, Horner MJ, Howlader N, Hayat M, Hankey BF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site, 2006.

Chapter 2
Cancers of the Head and Neck

Jay F. Piccirillo, Irene Costas, and Marsha E. Reichman

INTRODUCTION

This chapter provides survival analyses for 40,811 histologically confirmed adult cases of cancers of the head and neck obtained from the Surveillance, Epidemiology, and End Results (SEER) Program of the NCI. These cases included cancers of the lip, oral cavity, oropharynx, hypopharynx, tonsil, salivary glands, nasopharynx, nose, paranasal sinus, and middle ear. The tumors in this chapter all originate from the lining of the upper aerodigestive tract. The cell type of origin for the vast majority of patients is squamous cell. However, this is not the case for cancers of the paranasal sinus and salivary gland cancers, which are primarily of mixed cell types. Head and neck cancers can be divided into several groups. Epidemiologists often treat cancers of the tongue, gum, floor, and other parts of the mouth and of the pharynx as a single group referred to as oral cancer. However, some differences exist among these cancers in terms of epidemiology. Cancers of the lip have very different epidemiologic characteristics from the oral cancers and are generally considered separately. Cancers of the nose and paranasal sinuses have a low risk in the general population and have been associated with occupational and chemical exposures. The most frequently occurring cancers in the head and neck group (1) were tongue (21%), gum and other mouth sites (15%), tonsil (11%), and salivary gland (10%).

Tobacco and alcohol are major risk factors for many of these tumors (2). Prolonged exposure to sunlight, as occurs with farmers and others with outdoor occupations, is a clear contributor to carcinomas of the lip. In India and other parts of Asia, betel nut (arecoline) use and habitual reverse smoking in which the lighted end of the cigarette is held within the oral cavity are other etiologic agents (1).

MATERIALS AND METHODS

The NCI SEER Program contracts individually with central cancer registries, based in organizations such as universities and state health departments, to obtain data on all cancers diagnosed in residents of the registry's catchment area. SEER collects data on all invasive and in situ cancers except basal cell and squamous cell carcinomas of the skin and in situ carcinomas of the uterine cervix.

SEER cancer registries are selected on the basis of two criteria: the registry's ability to operate and maintain a population-based cancer reporting system and the epidemiologic significance of their population subgroups. While some cancer registries have remained in the SEER Program since it began, others have left; additional registries have joined at a later date or left for a period of time and rejoined the Program later. This analysis is based on data from 12 geographic areas, which collectively represent approximately 14% of the total US population and include

Table 2.1: Cancer of the Head and Neck: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
53,251	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
43,661	9,590	Select first primary only
43,413	248	Exclude death certificate only or at autopsy
43,047	366	Exclude unknown race
42,966	81	Exclude alive with no survival time
42,598	368	Exclude children (Ages 0-19)
41,501	1,097	Exclude in situ cancers for all except breast & bladder cancer
41,090	411	Exclude no or unknown microscopic confirmation
40,811	279	Exclude sarcomas

the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii, and the metropolitan areas of Detroit, Atlanta, San Francisco, Seattle, San Jose, and Los Angeles, plus 10 counties in rural Georgia. Los Angeles contributed data for diagnosis years 1992 to 2001, while other areas for diagnosis years from 1988 to 2001.

Survival analyses performed here are based on relative survival rates, defined as observed survival divided by expected survival. Relative survival the effect of the cancer in the cohort, while observed survival takes into account deaths due to all causes. When 5-year relative survival is 100%, a patient has the same chance to live 5 years as a demographically similar cancer-free person.

This chapter used SEER modified American Joint Committee on Cancer (AJCC) staging, 5th edition (3) to classify cancers of the head and neck, with the exception of cancers of the nose, nasal cavity, and middle ear which used SEER historic staging. SEER historic staging categories include in situ, localized, regional, distant and unstaged. Epidemiologists classify an invasive neoplasm confined entirely to the organ of origin as *localized*. They define a neoplasm that has extended either beyond the organ or into regional lymph nodes as *regional*. *Distant* stage describes a neoplasm that has spread to parts of the body remote from the primary tumor. *Unstaged* denotes cancers that lack sufficient information to assign stage.

As shown in Table 2.1, this study excluded the following types of cancer cases: head and neck cancer not the first primary cancer, autopsy or death certificate only (no determination of diagnosis date makes survival impossible to calculate), patients of unknown race, patients alive with no survival time, patients less than 20 years of age, in situ cases, cases without microscopic confirmation, and sarcomas.

RESULTS

Table 2.2 shows the site distribution and ICD-O code (4) of the 40,811 adult cancers in this study. As mentioned previously, the majority of cancers are from the tongue (21%), gum and other mouth sites (15%), tonsil (11%), and salivary gland (10%).

Table 2.3 displays the site-specific demographic characteristics of the patients. Head and neck cancers tend to be diagnosed at older ages. Nasopharynx shows a younger age at diagnosis than other cancers described here, with 40% of cases diagnosed at ages younger than 50. Cancer of the lip is diagnosed more frequently at older ages than cancers at other head and neck sites described here, with approximately 70% of cases diagnosed at age 60 or older. While cancers at all sites are diagnosed more frequently among males, the percentages for males and females are closest for gum and other mouth cancers (54% male) and for salivary gland cancers (56% male). The distribution by sex is most extreme for cancers of the lip (81% male) and hypopharynx (78% male). The racial distribution tends to reflect the general population from these geographic regions (whites 81%, blacks 11%, and other 9%) with the exception of cancer of the lip, found overwhelmingly in whites (98%), and "other cancers of the oral cavity and pharynx," cancers of the hypopharynx, and cancers of the oropharynx and tonsil, where the percentage of black patients was somewhat elevated (17%, 16%, and 15%, respectively). Although not shown in these data, a significantly larger proportion of patients with nasopharyngeal cancer are of Asian/Pacific Islander, specifically Chinese, origin. These racial differences in nasopharyngeal cancer incidence have been previously noted (5,6). Population data on Asian/Pacific Islanders are available for this data set from 1990 forward. Over this period the makeup of the population is white 79%, black 10%, Asian/Pacific Islanders 10% and American

Table 2.2: Cancers of the Head and Neck: Number and Distribution of Cases by Primary Site, Ages 20+, 12 SEER Areas, 1988-2001

Primary Site	ICD-O	Cases	Percent
Lip	C00.0-C00.9	3,982	9.8
Tongue	C01.9-C02.9	8,637	21.2
Gum & Other Mouth	C03.0-C03.9, C05.0-C06.9	5,946	14.6
Floor of Mouth	C04.0-C04.9	3,286	8.1
Salivary Gland	C07.9-C08.9	4,058	9.9
Oropharynx	C10.0-C10.9	1,081	2.6
Tonsil	C09.0-C09.9	4,420	10.8
Nasopharynx	C11.0-C11.9	2,819	6.9
Hypopharynx	C12.9-C13.9	3,273	8.0
Other Oral Cavity & Pharynx	C14.0, C14.2-C14.8	1,010	2.5
Nose and Middle Ear	C30.0-C30.1	1,091	2.7
Paranasal Sinus	C31.0-C31.9	1,208	3.0
Total		40,811	100.0

Indian/Alaskan Natives 1%. Thus the very high percentage of other (49%) for nasopharyngeal cancer is likely to reflect primarily Asian/Pacific Islanders (7).

Figure 2.1 shows relative survival curves for cancers of various head and neck sites. Table 2.4 provides corresponding numeric data. Patients with lip cancer had the best prognosis, with 5-year relative survival approximately 94%. Cancer of the salivary gland also shows a 5-year relative survival rate (74%) higher than most other head and neck cancers. On the other hand, cancers of the hypopharynx (5-year relative survival rate 30%) and "other cancers of the oral cavity and pharynx" (5-year relative survival rate 30%) have the worst prognoses in terms of relative survival rates. Figure 2.1 and Table 2.4 display a rapidly decreasing slope in relative survival until sometime between 18 and 36 months followed by a leveling off for many head and neck cancer sites. Thus, the usually quoted 5-year relative survival figures may be less significant for patient prognosis than a 2- or 3-year relative survival figure.

Figure 2.2 provides a more detailed look at relative survival curves for several sites that have 5-year relative survival approximately 50 to 60%. Among this group, cancers of the tonsil and oropharynx have the worst relative survival, the only site in this group dipping slightly below 50% at 5

Table 2.3: Cancer of the Head and Neck: Number and Distribution of Cases by Primary Site, Age (20+), Sex and Race, 12 SEER Areas, 1988-2001

Primary Site	Lip		Tongue		Floor of Mouth		Gum & Other Mouth		Oropharynx & Tonsil	
Characteristics	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Age (years)										
20-29	45	1.1	106	1.2	5	0.2	86	1.4	12	0.2
30-39	200	5.0	425	4.9	55	1.7	203	3.4	164	3.0
40-49	363	9.1	1,309	15.2	425	12.9	616	10.4	1,060	19.3
50-59	602	15.1	2,134	24.7	872	26.5	1,176	19.8	1,599	29.1
60-69	1,013	25.4	2,191	25.4	1,048	31.9	1,519	25.5	1,488	27.0
70-79	1,064	26.7	1,721	19.9	660	20.1	1,437	24.2	924	16.8
80+	695	17.5	751	8.7	221	6.7	909	15.3	254	4.6
Sex										
Male	3,232	81.2	5,764	66.7	2,261	68.8	3,188	53.6	4,111	74.7
Female	750	18.8	2,873	33.3	1,025	31.2	2,758	46.4	1,390	25.3
Race										
White	3,892	97.7	7,123	82.5	2,741	83.4	4,891	82.3	4,457	81.0
Black	40	1.0	904	10.5	429	13.1	691	11.6	803	14.6
Other	50	1.3	610	7.1	116	3.5	364	6.1	241	4.4

Table 2.3 (continued)

Primary Site	Hypopharynx		Salivary Gland		Nasopharynx		Nose, Paranasal Sinus & Middle Ear		Other Oral Cavity & Pharynx	
Characteristics	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Age (years)										
20-29	<5		180	4.4	127	4.5	53	2.3	<5	
30-39	25	0.8	351	8.6	341	12.1	136	5.9	11	1.1
40-49	320	9.8	576	14.2	661	23.4	287	12.5	90	8.9
50-59	819	25.0	667	16.4	648	23.0	417	18.1	233	23.1
60-69	1,117	34.1	883	21.8	603	21.4	561	24.4	336	33.3
70-79	774	23.6	840	20.7	335	11.9	519	22.6	257	25.4
80+	217	6.6	561	13.8	104	3.7	326	14.2	81	8.0
Sex										
Male	2,560	78.2	2,281	56.2	1,961	69.6	1,329	57.8	701	69.4
Female	713	21.8	1,777	43.8	858	30.4	970	42.2	309	30.6
Race										
White	2,508	76.6	3,412	84.1	1,203	42.7	1,842	80.1	805	79.7
Black	536	16.4	318	7.8	226	8.0	223	9.7	176	17.4
Other	229	7.0	328	8.1	1,390	49.3	234	10.2	29	2.9

years. Cancers of the gum and other mouth have the best relative survival, almost 60% at 5 years.

Overall, the 5-year relative survival rate for all patients with head and neck cancers was 57% (Table 2.4). The 5-year relative survival rate for head and neck cancers for whites was 60% and for blacks was 40%. The 5-year relative survival rate for males was 45%, for females 55%. Table 2.5 examines relative survival by site, race, and sex. As a function of race and sex, 5-year relative survival rates tended to be higher for white males and females than black males and females. However, differences in survival rates according to race and sex must be interpreted in light of differences in types of tumors and stage of presentation. In addition, the distribution of other important prognostic factors like comorbidities are not even across race and sex categories and will impact the interpretation of these results (8, 13).

In general, a strong correlation existed between stage at diagnosis and relative survival, with cancers that tend to be diagnosed at more localized stages having higher relative survival. In accord with this, as Table 2.6 shows, cancers of the lip have the highest percentage of cases diagnosed at stage I (83%), which had the highest relative survival at one (100%), three (99%) and five (96%) years after diagnosis. Other cancers in the head and neck group have a much lower percentage of cases diagnosed at stage I. Following lip cancer, cancers of the floor of the mouth, gum and other mouth cancers, and cancers of the salivary gland have between 36% and 40% of cases diagnosed at stage I. Diagnosis of hypopharyngeal cancers occurred at stage I less than 10% of the time, and these cancers have among the lowest relative survival rates of head and neck cancers. Table 2.6 also provides some insight into the unstaged group of cancers in terms of relative survival as compared to cancers diagnosed at various stages.

Table 2.7 shows 1-, 2- 3-, 5-, 8-, and 10-year relative survival rates by grade for each of the head and neck cancer sites. In most cases, at each time point survival increases with increasing level of differentiation. Exceptions occur for hypopharynx, nasopharynx, oropharynx/tonsil, and "other oral cavity and pharynx" cancers. For some of the head and neck sites, the survival of the unknown group of cancers is between that of grade II and grade III-IV, although for four sites (nasopharynx, other oral cavity and pharynx, hypopharynx, oropharynx/tonsil) it is worse than grade III-IV. For salivary cancer, 39% of cancers do not have a grade assigned. The percentage is also high for lip and for nose, nasal cavity, and middle ear. For these three sites the unknown group as a whole shows survival better than that associated with diagnosis at stages III-IV, and in the case of nose, nasal cavity, and middle ear better than that associated with diagnoses at grade II. In general, relative survival decreases more rapidly with time for grades II and for III-IV than for grade I.

Table 2.8 shows 1-, 2-, 3-, 5-, 8-, and 10-year relative survival by size of tumor for each of the head and neck cancer sites. In general, relative survival decreases at each time point with increasing tumor size. This is less clear cut for cancers of the oropharynx and tonsil and those of the nasopharynx. Cancers at the following sites had 40% or more with unknown tumor size: lip; oropharynx and tonsil; hypopharynx; nasopharynx; nose, nasal cavity, and middle ear; and other oral cavity and pharynx. As is observed for grade, survival decreases more rapidly with time for increasing tumor size.

Figure 2.1: Cancer of the Head and Neck: Relative Survival Rate (%) by Primary Site, Ages 20+, 12 SEER Areas, 1988-2001

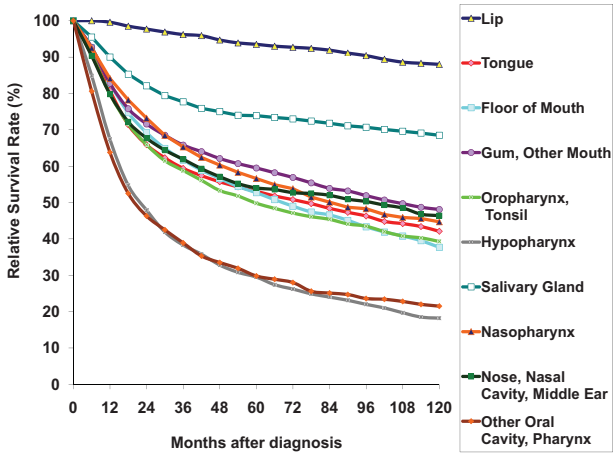
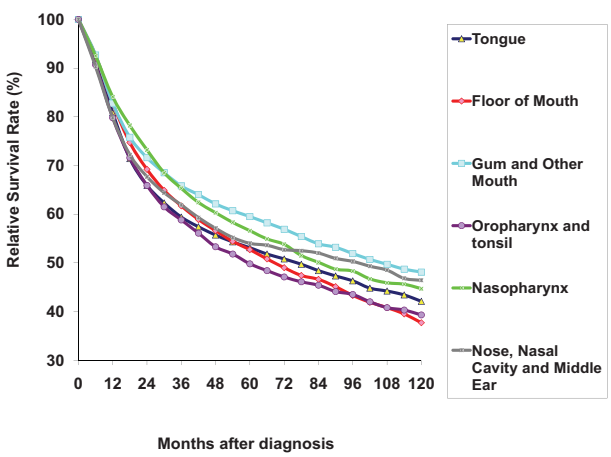


Figure 2.2: Cancer of the Head and Neck: Relative Survival Rate (%) by Primary Site, Ages 20+, 12 SEER Areas, 1988-2001



A discussion of patient relative survival characteristics for individual head and neck sites follows.

Lip

The median survival for cancer of the lip is greater than 120 months (Table 2.6). This is also the case for patients with cancers diagnosed at stage I. Patients diagnosed with cancers at stage II had a median survival of 99 months, stage III had a median survival of 50 months, and those with stage IV diagnoses a median survival time of 37 months (Table 2.6). Figure 2.3 shows relative survival for lip cancer by stage at diagnosis. Even for lip cancers diagnosed at stage IV, relative survival is nearly 50% at 5 years. Only 4% of lip cancers are diagnosed at stages III or IV, while 6% are diagnosed at stage II. The vast majority of lip cancers, 83%, are diagnosed at stage I. Lip cancers of unknown stage show survival patterns only slightly worse than those for all stages combined, indicating a lack of substantial bias.

Tongue

Median survival for tongue cancer is 48 months (Table 2.6). This varies from 95 months for patients diagnosed with stage I cancer to 22 months for those diagnosed with stage IV cancer. Figure 2.4 shows survival of tongue cancers by stage of diagnosis. Five year relative survival rates for tongue cancers diagnosed at stage I is 71%, stage II is 59%, stage III 47%, and stage IV 37%. Approximately 34% of tongue cancers are diagnosed at stage I. This figure has not changed appreciably in three decades, nor has the 5-year relative survival rate. The survival curve for unstaged cancers lies between those diagnosed at stages III and IV.

Tongue cancers are divided into those of the anterior and of the basal portions of the tongue. Cancers of the anterior tongue represent 56% of tongue cancers. Table 2.9 provides data on the stage at diagnosis for cancers of the basal and anterior tongue. Cancers of the anterior tongue

Table 2.4: Cancer of the Head and Neck: Number and Distribution of Cases, and 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Primary Site, Ages 20+, 12 SEER Areas, 1988-2001

Primary Site	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total Head & Neck	40,811	100.0	82.5	70.3	64.0	57.1	50.5	46.6
Lip	3,982	9.8	99.6	97.7	96.2	93.5	90.4	88.0
Tongue	8,637	21.2	80.8	65.9	59.4	53.1	46.3	42.1
Gum & Other Mouth	5,946	14.6	82.8	71.6	65.8	59.5	51.9	48.1
Floor of Mouth	3,286	8.1	82.8	69.2	61.7	52.7	43.3	37.7
Oropharynx & Tonsil	5,501	13.5	79.8	65.9	58.8	49.8	43.5	39.3
Hypopharynx	3,273	8.0	67.4	47.9	38.3	29.5	22.0	18.2
Salivary Gland	4,058	9.9	90.0	82.1	77.7	73.9	70.7	68.5
Nasopharynx	2,819	6.9	84.1	73.2	65.3	56.6	48.3	44.7
Nose, Nasal Cavity & Middle Ear	2,299	5.6	79.8	67.7	61.9	54.0	50.3	46.4
Other Oral Cavity & Pharynx	1,010	2.5	63.8	46.3	38.9	29.8	23.6	21.5

Figure 2.3: Cancer of the Lip: Relative Survival Rate (%) by Stage, Ages 20+, 12 SEER Areas, 1988-2001

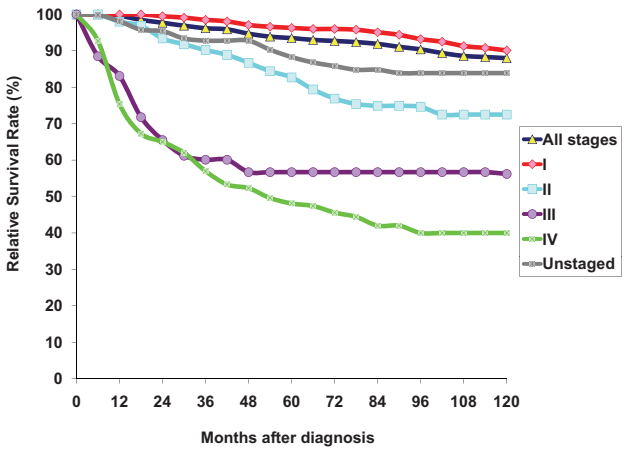
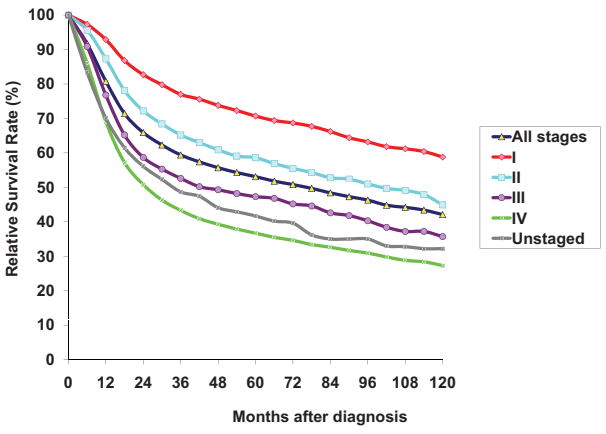


Figure 2.4: Cancer of the Tongue: Relative Survival Rate (%) by Stage, Ages 20+,12 SEER Areas, 1988-2001



are much more likely to be diagnosed at an earlier stage than cancers of the basal tongue. While 48% of cancers of the anterior tongue are diagnosed at stage I, only 16% of cancers of the base of tongue are diagnosed at stage I. By comparison, 19% of cancers of the anterior tongue are diagnosed at stage IV, while 46% of cancers of the base of tongue are diagnosed at stage IV. A similar percentage of anterior and basal tongue cancers are unstaged: 7% and 6%, respectively. Table 2.10 shows 1-, 2-, 3-, 5-, 8-, and 10-year relative survival rates for cancers of the basal and anterior tongue by stage at diagnosis. For all stages combined, cancers of the anterior tongue have a higher relative survival rate at each time point, with a growing differential as time increases. Although cancers of the anterior tongue have better survival rates when diagnosed at stage I, this does not appear to be the case for cancers diagnosed at stages II, III, or IV. This suggests that the overall differences in survival between cancers of the anterior and basal tongue may be due primarily to the larger percentage of cases of cancer of the anterior tongue diagnosed at stage I.

Floor of Mouth

Median survival for all cancers of the floor of the mouth is 50 months (Table 2.6). This varies from 94 months for those diagnosed with stage I to 19 months for those diagnosed with stage IV cancers. Five-year relative survival rates decrease from 73% for patients with cancers diagnosed at stage I to 30% for patients with cancers diagnosed at stage IV. Figure 2.5 shows relative survival curves for cancer of the floor of the mouth by SEER modified AJCC stage. Unstaged cancers have relative survival rates somewhat between stages III and IV, lower than those for all cancers combined.

Gum and Other Mouth

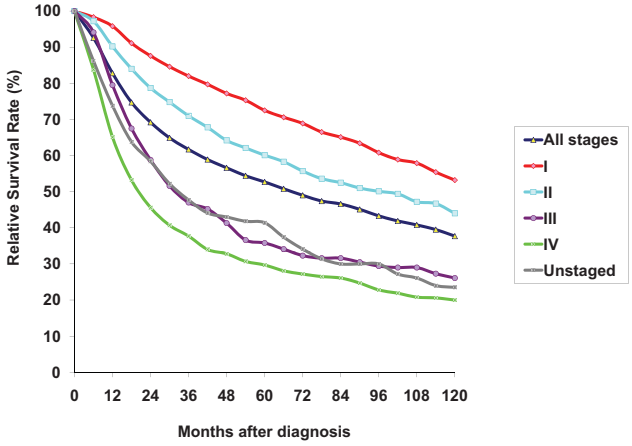
Median survival for all patients with cancers of the "gum and other mouth" category is 59 months. This decreases from 113 months for patients diagnosed with stage I disease to 22 months for patients diagnosed with stage IV disease (Table 2.6). Similarly, five-year relative survival rates

Table 2.5: Cancer of the Head and Neck: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Site, Race, and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Site/Race/Sex	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Lip	3,982	100.0	99.6	97.7	96.2	93.5	90.4	88.0
White Female	708	17.8	99.7	96.7	96.4	93.1	90.0	89.9
White Male	3,184	80.0	99.9	98.2	96.4	93.9	90.6	87.7
Black Female	22	0.6	~	~	~	~	~	~
Black Male	18	0.5	~	~	~	~	~	~
Tongue	8,637	100.0	80.8	65.9	59.4	53.1	46.3	42.1
White Female	2,382	27.6	82.4	68.8	63.0	57.9	49.2	44.5
White Male	4,741	54.9	82.2	67.4	61.0	54.0	48.3	44.5
Black Female	230	2.7	71.2	54.0	46.1	37.8	28.8	27.8
Black Male	674	7.8	66.6	47.1	37.2	30.6	22.7	14.2
Floor of Mouth	3,286	100.0	82.8	69.2	61.7	52.7	43.3	37.7
White Female	882	26.8	83.2	72.4	66.8	59.3	50.2	43.2
White Male	1,859	56.6	84.5	71.7	63.5	53.1	42.9	37.3
Black Female	104	3.2	78.5	57.5	55.1	51.5	35.6	35.6
Black Male	325	9.9	72.6	49.9	39.7	32.0	27.1	23.3
Gum & Other Mouth	5,946	100.0	82.8	71.6	65.8	59.5	51.9	48.1
White Female	2,331	39.2	83.9	75.5	71.0	66.4	61.5	58.1
White Male	2,560	43.1	83.4	71.1	64.5	57.3	47.4	41.9
Black Female	263	4.4	78.8	68.8	65.1	60.2	49.9	47.5
Black Male	428	7.2	74.8	56.8	47.7	38.1	29.8	27.6
Oropharynx & Tonsil	5,501	100.0	79.8	65.9	58.8	49.8	43.5	39.3
White Female	1,151	20.9	81.0	68.2	60.5	51.0	44.4	37.3
White Male	3,306	60.1	81.7	68.4	61.8	53.4	47.0	43.2
Black Female	175	3.2	72.6	52.6	44.9	34.0	29.5	26.9
Black Male	628	11.4	68.3	48.7	38.4	27.8	21.1	18.9

decrease from 81% for those diagnosed with stage I disease to 40% for those diagnosed with stage IV disease. Figure 2.6 shows relative survival curves by stage at diagnosis for those with "gum and other mouth" cancers. For all stages combined, the 1-, 3-, and 5-year relative survival rates are 83%, 66%, and 60%, respectively.

Figure 2.5: Cancer of the Floor of Mouth: Relative Survival Rate (%) by Stage, Ages 20+, 12 SEER Areas, 1988-2001



Oropharynx and Tonsil

Table 2.6 presents survival of cancers of the oropharynx and tonsil stratified by stage at diagnosis. The overall 1-, 3-, and 5-year relative survival rates are 80%, 59%, and

Figure 2.6: Cancer of Gum and Other Mouth: Relative Survival Rate (%) by Stage, Ages 20+, 12 SEER Areas, 1988-2001

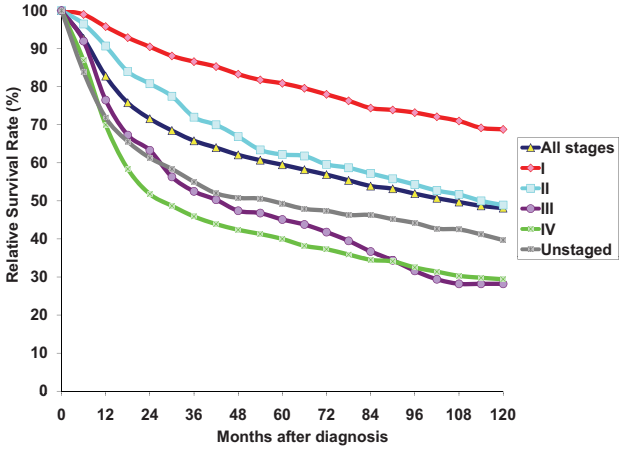


Table 2.5 (continued)

Site/Race/Sex	Cases	Percent	Relative Survival Rate (%) 1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Hypopharynx	3,273	100.0	67.4	47.9	38.3	29.5	22.0	18.2
White Female	591	18.1	70.8	50.5	42.2	33.3	24.2	20.3
White Male	1,917	58.6	68.3	49.9	39.9	30.6	23.1	19.2
Black Female	97	3.0	56.5	33.2	26.6	19.7	15.6	12.6
Black Male	439	13.4	58.8	38.4	27.9	19.9	14.7	11.9
Salivary Gland	4,058	100.0	90.0	82.1	77.7	73.9	70.7	68.5
White Female	1,455	35.9	92.2	85.8	82.5	79.3	75.5	74.2
White Male	1,957	48.2	88.3	78.5	73.9	68.9	65.4	62.3
Black Female	159	3.9	91.5	86.4	80.5	77.4	76.4	76.0
Black Male	159	3.9	82.5	73.2	65.3	64.1	63.6	61.3
Nasopharynx	2,819	100.0	84.1	73.2	65.3	56.6	48.3	44.7
White Female	379	13.4	72.4	59.1	51.2	45.7	39.6	34.0
White Male	824	29.2	78.6	66.5	58.9	49.8	43.2	41.1
Black Female	68	2.4	83.6	68.8	53.9	42.9	35.0	35.0
Black Male	158	5.6	80.3	63.6	55.4	45.8	32.2	31.7
Nose, Nasal Cavity and Middle Ear	2,299	100.0	79.8	67.7	61.9	54.0	50.3	46.4
White Female	774	33.7	79.4	68.0	62.9	56.3	53.7	47.1
White Male	1,068	46.5	81.2	70.1	63.9	56.5	50.8	48.6
Black Female	104	4.5	66.4	47.1	45.0	35.7	31.6	23.3
Black Male	119	5.2	73.9	56.8	49.0	37.2	36.0	36.0
Other Oral Cavity and Pharynx	1,010	100.0	63.8	46.3	38.9	29.8	23.6	21.5
White Female	260	25.7	64.5	49.1	40.6	30.4	26.7	25.8
White Male	545	54.0	67.3	49.0	41.9	32.5	25.1	21.6
Black Female	47	4.7	47.8	23.5	16.7	14.8	7.9	7.9
Black Male	129	12.8	50.4	33.8	26.2	19.3	15.2	12.0

~Statistic not displayed due to less than 25 cases.

50%, respectively. The majority of tumors were diagnosed at stage IV (43%). Approximately equal numbers were diagnosed at stage III (23%) and stage I (19%), with 9% diagnosed at stage II. The median survival for patients diagnosed at stages I to III was between 55 and 63 months, while for those diagnosed with stage IV disease the median survival was 32 months (Table 2.6). Figure 2.7 shows survival curves for cancers of the oropharynx and tonsil by SEER modified AJCC stage at diagnosis.

Hypopharynx

Figure 2.8 illustrates the survival of cancer of the hypopharynx by SEER modified AJCC stage at diagnosis. The majority of patients were diagnosed at stage IV (56%), while 17% were diagnosed at stage III, 12% at stage II and 10% at stage I (Table 2.6). Overall 1-, 3-, and 5-year relative survival, as reported in Table 2.6 was 67%, 38%, and 30%, respectively. Five-year relative survival by stages varies from 49% for stage I to 23% for stage IV. The median survival for stage I tumors was 42 months, 25 months at stage II, 25 months at stage III, and 17 months at stage IV. The survival pattern for unstaged cancers was similar to that for stage IV.

Salivary Gland

For cancer of the salivary gland, the overall 1-, 3-, and 5-year relative survival rates were 90%, 78%, and 74%, respectively (Table 2.6). Table 2.11 and Figure 2.9 show the relative survival rates for salivary gland cancers by cell type. Patients with mucoepidermoid well differentiated carcinomas and acinar cell carcinomas had the best prognosis,

Table 2.6: Cancer of the Head and Neck: Number and Distribution of Cases, Median Survival Time (Months) and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (5th Edition) and Site, Ages 20+, 12 SEER Areas, 1988-2001

Site/AJCC Stage	Cases	Percent	Median Survival (Months)	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Lip	3,982	100.0	> 120	99.6	97.7	96.2	93.5	90.4	88.0
Stage I	3,314	83.2	> 120	100.0	99.5	98.5	96.3	93.2	90.1
Stage II	221	5.5	98.6	98.0	93.4	90.2	82.7	74.6	72.5
Stage III	58	1.5	44.9	83.1	65.5	60.1	56.7	56.7	56.2
Stage IV	87	2.2	37.2	75.4	65.0	57.0	48.1	40.0	40.0
Unstaged	302	7.6	> 120	98.1	95.4	92.8	88.3	83.9	83.9
Tongue	8,637	100.0	47.6	80.8	65.9	59.4	53.1	46.3	42.1
Stage I	2,927	33.9	95.4	92.9	82.7	77.0	70.7	63.2	58.8
Stage II	1,081	12.5	58.4	87.3	72.2	65.2	58.6	51.0	44.9
Stage III	1,416	16.4	32.7	76.8	58.7	52.6	47.3	40.3	35.7
Stage IV	2,647	30.6	22.1	69.1	50.8	43.3	36.7	30.9	27.3
Unstaged	566	6.6	26.6	70.1	56.1	48.7	41.7	35.0	32.2
Floor of Mouth	3,286	100.0	49.7	82.8	69.2	61.7	52.7	43.3	37.7
Stage I	1,324	40.3	93.6	95.8	87.6	82.0	72.5	60.8	53.2
Stage II	435	13.2	63.7	90.2	78.7	71.0	60.1	50.1	44.0
Stage III	326	9.9	29.2	79.5	58.8	47.0	35.8	29.4	26.1
Stage IV	982	29.9	18.9	65.1	45.6	37.7	29.7	22.8	20.0
Unstaged	219	6.7	28.8	73.8	58.4	47.7	41.4	30.0	23.5
Gum & Other Mouth	5,946	100.0	59.2	82.8	71.6	65.8	59.5	51.9	48.1
Stage I	2,244	37.7	112.7	95.8	90.5	86.6	80.9	73.2	68.8
Stage II	712	12.0	66.4	90.7	80.8	72.0	62.2	54.3	48.9
Stage III	394	6.6	30.9	76.5	63.3	52.5	45.1	31.6	28.2
Stage IV	2,075	34.9	22.1	70.0	51.8	45.9	40.0	32.5	29.4
Unstaged	521	8.8	33.1	71.9	61.3	55.0	49.3	44.2	39.7
Oropharynx & Tonsil	5,501	100.0	45.4	79.8	65.9	58.8	49.8	43.5	39.3
Stage I	1,035	18.8	55.2	84.7	73.0	66.6	56.0	48.4	41.9
Stage II	506	9.2	62.9	91.0	77.1	70.8	58.3	51.0	46.1
Stage III	1,236	22.5	58.9	83.7	70.5	64.1	55.4	48.6	43.5
Stage IV	2,350	42.7	32.0	74.1	58.6	50.9	43.4	38.8	36.5
Unstaged	374	6.8	33.1	75.1	61.8	52.2	43.8	35.4	31.6

while patients with squamous call and adenocarcinoma had the worst prognosis.

Nasopharynx

As shown in Table 2.6, the 1-, 3-, and 5-year relative survival rates for cancer of the nasopharynx were 84%, 65%, and 57%, respectively. Figure 2.10 presents the survival of cancer of the nasopharynx by stage. Among patients diagnosed with cancer of the nasopharynx, 15% were diagnosed at stage I, 6.7% at stage II, 22% at stage III, and 45% at stage IV. The median survival for patients presenting at stage I was over 120 months. This decreased to 47 months for patients presenting at stage IV. Relative survival at 5 years varied from 78% for stage I to 47% for stage IV. Unstaged cases show a survival curve similar to that for all stages.

Figure 2.7: Cancer of the Oropharynx and Tonsil: Relative Survival Rate (%) by Stage, Ages 20+ 12 SEER Areas, 1988-2001

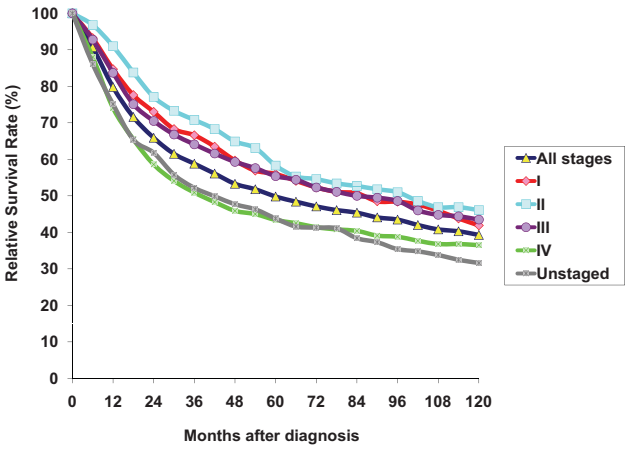


Table 2.6 (continued)

Site/AJCC Stage	Cases	Percent	Median Survival (Months)	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Hypopharynx	3,273	100.0	19.7	67.4	47.9	38.3	29.5	22.0	18.2
Stage I	315	9.6	41.5	80.6	67.0	58.5	48.7	32.4	26.7
Stage II	389	11.9	25.3	73.6	55.4	47.0	38.6	31.7	24.9
Stage III	568	17.4	24.9	72.0	55.6	42.7	34.1	24.5	18.8
Stage IV	1,819	55.6	16.5	63.1	41.3	32.2	23.2	17.8	15.0
Unstaged	182	5.6	14.8	59.3	42.2	32.3	26.3	18.4	16.8
Salivary Gland	4,058	100.0	112.2	90.0	82.1	77.7	73.9	70.7	68.5
Stage I	1,457	35.9	> 120	99.4	98.0	96.2	95.7	92.4	91.6
Stage II	630	15.5	106.8	92.0	84.1	81.2	76.7	73.9	67.4
Stage III	188	4.6	98.8	92.1	84.6	80.8	72.6	68.5	57.5
Stage IV	1,032	25.4	27.7	77.1	58.1	47.7	37.2	30.0	27.5
Unstaged	751	18.5	109.3	86.4	80.6	77.5	74.1	73.6	73.6
Nasopharynx	2,819	100.0	67.8	84.1	73.2	65.3	56.6	48.3	44.7
Stage I	424	15.0	> 120	93.5	86.8	81.3	78.4	68.2	62.6
Stage II	189	6.7	76.4	89.8	78.9	71.7	63.7	51.6	51.6
Stage III	615	21.8	72.8	86.5	74.7	67.7	59.5	49.8	46.2
Stage IV	1,276	45.3	46.8	78.2	65.9	57.3	46.7	40.9	37.1
Unstaged	315	11.2	72.3	86.9	77.9	67.9	57.8	47.1	44.6
Nose, Nasal Cavity and Middle Ear	2,299	100.0	47.9	79.8	67.7	61.9	54.0	50.3	46.4
Localized	594	25.8	> 120	95.1	90.2	88.2	82.5	79.8	77.4
Regional	1,181	51.4	37.0	77.7	63.6	55.8	47.3	43.0	37.7
Distant	325	14.1	15.5	59.5	41.9	34.9	25.3	24.8	21.7
Unstaged	199	8.7	47.7	79.4	67.6	63.4	55.5	49.7	45.3
Other Oral Cavity and Pharynx	1,010	100.0	18.1	63.8	46.3	38.9	29.8	23.6	21.5
Stage I	169	16.7	26.7	73.9	55.8	48.6	40.8	36.1	36.1
Stage II	70	6.9	43.2	74.8	69.4	58.7	46.2	33.3	28.2
Stage III	148	14.7	18.0	69.4	43.4	36.8	23.2	21.9	21.0
Stage IV	478	47.3	14.4	56.4	39.0	31.7	22.3	17.8	13.4
Unstaged	145	14.4	20.1	65.2	50.9	43.8	39.3	26.0	23.3

Table 2.7: Cancer of the Head and Neck: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Primary Site and Grade, Ages 20+, 12 SEER Areas, 1988-2001

Site/Grade	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Lip	3,982	100.0	99.6	97.7	96.2	93.5	90.4	88.0
Grade I	1,531	38.4	100.0	99.2	98.1	96.2	94.0	90.3
Grade II	971	24.4	99.1	97.2	95.1	91.3	85.8	84.0
Grades III-IV	186	4.7	93.6	88.1	79.8	73.5	65.3	62.2
Unknown	1,294	32.5	99.2	97.4	96.7	94.2	91.6	88.6
Tongue	8,637	100.0	80.8	65.9	59.4	53.1	46.3	42.1
Grade I	1,428	16.5	86.9	76.4	71.0	65.8	59.1	53.9
Grade II	3,506	40.6	80.7	64.3	57.1	49.8	42.9	38.7
Grades III-IV	2,314	26.8	78.1	61.5	54.3	48.0	41.7	37.9
Unknown	1,389	16.1	79.0	66.8	61.8	56.9	49.4	45.4
Floor of Mouth	3,286	100.0	82.8	69.2	61.7	52.7	43.3	37.7
Grade I	568	17.3	89.5	78.9	72.5	63.4	53.0	45.1
Grade II	1,586	48.3	83.2	68.9	60.5	51.4	41.1	35.4
Grades III-IV	563	17.1	73.4	56.9	49.3	40.1	33.7	30.1
Unknown	569	17.3	84.6	72.5	66.5	58.0	48.4	43.1
Gum & Other Mouth	5,946	100.0	82.8	71.6	65.8	59.5	51.9	48.1
Grade I	1,258	21.2	86.9	79.0	73.8	69.6	63.9	57.4
Grade II	2,557	43.0	83.3	71.3	65.7	59.5	51.2	47.0
Grades III-IV	880	14.8	74.1	56.7	47.9	38.9	31.7	29.1
Unknown	1,251	21.0	84.0	75.3	70.8	64.4	56.0	54.1
Oropharynx & Tonsil	5,501	100.0	79.8	65.9	58.8	49.8	43.5	39.3
Grade I	341	6.2	78.2	65.5	59.7	50.3	39.2	32.8
Grade II	2,132	38.8	78.8	64.9	57.2	47.0	40.7	37.4
Grades III-IV	2,208	40.1	83.5	70.1	63.5	55.2	50.2	46.1
Unknown	820	14.9	73.4	57.4	49.4	42.1	35.1	29.4
Hypopharynx	3,273	100.0	67.4	47.9	38.3	29.5	22.0	18.2
Grade I	173	5.3	66.5	44.6	36.2	25.9	23.2	19.6
Grade II	1,326	40.5	68.3	49.3	40.0	31.0	20.8	17.5
Grades III-IV	1,297	39.6	67.9	48.1	37.7	29.2	23.5	18.7
Unknown	477	14.6	63.6	44.9	35.6	26.6	19.2	16.7
Salivary Gland	4,058	100.0	90.0	82.1	77.7	73.9	70.7	68.5
Grade I	357	8.8	97.4	96.3	94.8	94.6	93.6	93.6
Grade II	897	22.1	95.6	90.7	87.6	86.1	85.9	84.2
Grades III-IV	1,239	30.5	80.8	64.7	57.3	47.8	40.3	34.6
Unknown	1,565	38.6	92.2	87.2	83.3	80.3	76.5	74.9
Nasopharynx	2,819	100.0	84.1	73.2	65.3	56.6	48.3	44.7
Grade I	59	2.1	50.5	46.1	41.4	38.3	31.3	31.3
Grade II	269	9.5	70.7	54.5	48.6	39.6	30.1	25.1
Grades III-IV	1,874	66.5	86.7	76.3	68.0	59.1	51.1	47.7
Unknown	617	21.9	85.0	74.2	66.3	57.5	48.3	44.5
Nose, Nasal Cavity and Middle Ear	2,299	100.0	79.8	67.7	61.9	54.0	50.3	46.4
Grade I	261	11.4	87.0	77.7	74.8	67.2	64.0	60.7
Grade II	475	20.7	80.7	67.7	63.4	56.8	54.3	51.7
Grades III-IV	770	33.5	74.0	60.8	51.8	42.0	38.1	33.3
Unknown	793	34.5	82.4	71.1	66.6	59.8	55.5	50.6
Other Oral Cavity and Pharynx	1,010	100.0	63.8	46.3	38.9	29.8	23.6	21.5
Grade I	65	6.4	63.4	45.7	38.2	30.5	28.4	27.1
Grade II	392	38.8	65.2	43.0	33.9	24.9	20.3	16.6
Grades III-IV	323	32.0	60.9	46.2	41.2	32.2	26.0	24.1
Unknown	230	22.8	65.7	52.7	44.6	34.5	24.1	22.6

Paranasal Sinus

Table 2.12 and Figure 2.11 show the relative survival rates for paranasal sinus cancers according to cell type. Patients with adenoid cystic carcinomas had the best 5-year relative survival (61%), while patients with epithelial neoplasms had the worst 5-year relative survival (32%).

Nose, Paranasal Sinus, and Middle Ear

Figure 2.12 shows the survival of patients with nose, nasal cavity, or middle ear cancer according to SEER historic stage. The overall 1-, 3-, and 5-year relative survival rates, as presented in Table 2.6, were 80%, 62%, and 54%, respectively. Among patients diagnosed with cancer of the nose, nasal cavity, or middle ear, 26% had localized tumors, 51% regional, and 14% distant. The median survival for patients with localized disease at presentation was greater than 120 months; for regional disease it was 37 months, and for distant disease, 16 months. Five-year relative survival by stage varied from 83% for local to 25% for distant disease.

Table 2.8: Cancer of the Head and Neck: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Primary Site and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

Primary Site/Grade	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Lip	3,982	100.0	99.6	97.7	96.2	93.5	90.4	88.0
<1 cm	879	22.1	100.0	100.0	99.6	97.3	95.3	92.0
1.0-1.9 cm	901	22.6	100.0	97.1	94.1	91.1	86.5	82.2
2.0-2.9 cm	267	6.7	98.5	92.5	89.9	82.6	80.9	80.8
3.0-3.9 cm	99	2.5	93.8	84.4	82.5	76.0	65.2	60.0
4.0+ cm	87	2.2	79.8	67.1	63.0	63.0	62.7	60.1
Unknown	1,749	43.9	100.0	99.2	98.9	96.3	93.4	91.1
Tongue	8,637	100.0	80.8	65.9	59.4	53.1	46.3	42.1
<1 cm	498	5.8	99.8	92.2	87.6	81.5	74.4	70.0
1.0-1.9 cm	1,329	15.4	94.2	82.8	77.2	71.6	62.4	58.2
2.0-2.9 cm	1,434	16.6	88.2	71.2	64.4	55.8	47.1	41.4
3.0-3.9 cm	1,084	12.6	80.2	63.5	56.1	49.2	42.8	40.1
4.0+ cm	1,459	16.9	67.2	48.2	40.8	34.9	29.0	22.6
Unknown	2,833	32.8	74.5	60.6	54.1	48.6	42.9	39.7
Floor of Mouth	3,286	100.0	82.8	69.2	61.7	52.7	43.3	37.7
<1 cm	214	6.5	97.2	92.6	90.4	81.8	70.4	59.2
1.0-1.9 cm	555	16.9	94.1	86.3	79.6	70.0	57.0	51.8
2.0-2.9 cm	593	18.0	91.6	75.5	66.4	54.8	44.0	38.2
3.0-3.9 cm	404	12.3	83.8	63.9	53.4	42.9	34.4	30.9
4.0+ cm	546	16.6	63.3	46.7	39.2	32.7	25.7	20.4
Unknown	974	29.6	78.5	65.2	58.2	50.2	42.1	36.5
Gum & Other Mouth	5,946	100.0	82.8	71.6	65.8	59.5	51.9	48.1
<1 cm	311	5.2	98.1	93.9	91.3	84.5	78.2	72.3
1.0-1.9 cm	895	15.1	96.2	89.9	85.4	79.8	74.9	70.9
2.0-2.9 cm	982	16.5	87.9	77.3	70.8	64.0	55.0	51.7
3.0-3.9 cm	709	11.9	81.3	65.8	57.9	49.9	40.5	35.6
4.0+ cm	907	15.3	67.8	50.5	43.2	36.7	28.2	23.2
Unknown	2,142	36.0	79.5	68.6	63.5	57.8	49.9	46.9
Oropharynx & Tonsil	5,501	100.0	79.8	65.9	58.8	49.8	43.5	39.3
<1 cm	110	2.0	93.1	84.4	81.1	62.9	62.0	54.1
1.0-1.9 cm	398	7.2	93.9	87.5	83.8	72.0	68.9	64.1
2.0-2.9 cm	728	13.2	89.3	77.4	69.1	58.4	51.4	48.1
3.0-3.9 cm	713	13.0	88.2	73.7	68.5	58.1	50.9	42.8
4.0+ cm	1,075	19.5	73.6	56.3	49.3	42.4	34.4	30.9
Unknown	2,477	45.0	74.5	60.1	51.9	43.8	37.8	34.2

Figure 2.8: Cancer of the Hypopharynx: Relative Survival Rate (%) by Stage, Ages 20+, 12 SEER Areas, 1988-2001

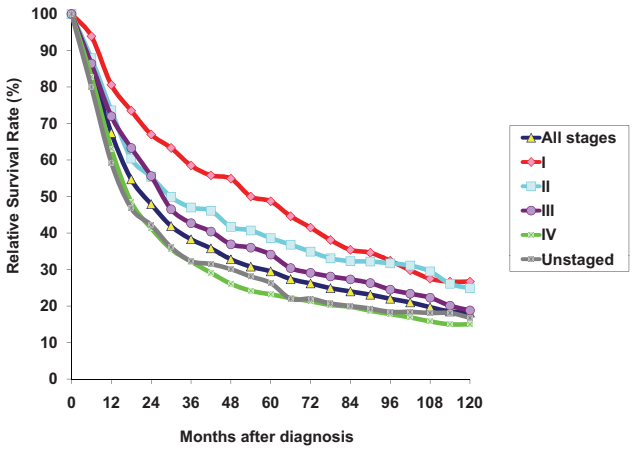


Figure 2.9: Cancer of the Salivary Gland: Relative Survival Rate (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

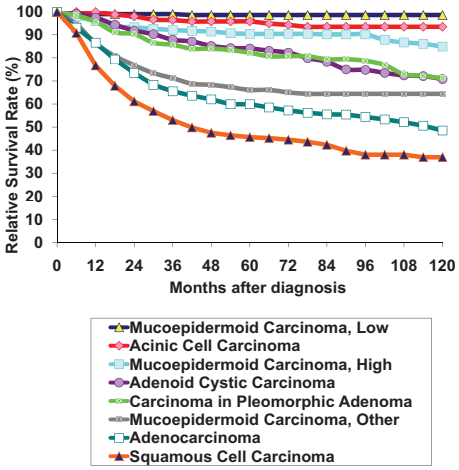


Table 2.8 (continued): Cancer of the Head and Neck: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Site and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

Site/Grade	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Hypopharynx	3,273	100.0	67.4	47.9	38.3	29.5	22.0	18.2
<1 cm	45	1.4	86.1	73.3	65.9	50.3	45.8	30.3
1.0-1.9 cm	198	6.0	83.4	67.5	57.6	46.2	38.7	24.6
2.0-2.9 cm	416	12.7	81.5	67.1	55.6	42.6	29.1	24.8
3.0-3.9 cm	409	12.5	78.2	53.5	44.5	35.4	30.4	27.2
4.0+ cm	666	20.3	63.7	42.7	32.5	22.0	17.2	12.3
Unknown	1,539	47.0	59.6	40.2	30.9	24.6	16.3	14.7
Salivary Gland	4,058	100.0	90.0	82.1	77.7	73.9	70.7	68.5
<1 cm	152	3.7	100.0	100.0	99.2	99.2	97.1	88.9
1.0-1.9 cm	830	20.5	98.6	96.6	95.0	92.5	88.5	85.3
2.0-2.9 cm	884	21.8	96.0	90.0	84.1	80.6	78.0	76.1
3.0-3.9 cm	526	13.0	92.8	82.9	75.9	71.0	63.7	62.8
4.0+ cm	728	17.9	77.3	61.3	56.1	49.4	44.3	38.9
Unknown	938	23.1	82.9	73.6	69.1	63.9	63.3	63.3
Nasopharynx	2,819	100.0	84.1	73.2	65.3	56.6	48.3	44.7
<1 cm	35	1.2	89.6	84.2	81.7	72.3	64.6	43.5
1.0-1.9 cm	95	3.4	95.0	86.9	80.2	74.1	69.8	45.4
2.0-2.9 cm	201	7.1	90.1	84.8	81.7	77.7	65.9	62.7
3.0-3.9 cm	161	5.7	88.6	76.4	70.3	58.2	53.6	49.4
4.0+ cm	379	13.4	84.8	73.0	61.1	51.3	44.5	43.8
Unknown	1,948	69.1	82.3	70.8	62.9	54.1	45.1	42.4
Nose, Nasal Cavity and Middle Ear	2,299	100.0	79.8	67.7	61.9	54.0	50.3	46.4
<1 cm	55	2.4	97.1	89.9	89.4	89.4	81.5	74.5
1.0-1.9 cm	125	5.4	91.7	87.3	84.5	82.1	81.5	77.0
2.0-2.9 cm	183	8.0	88.2	75.6	72.3	57.1	53.9	53.9
3.0-3.9 cm	136	5.9	84.1	75.4	67.5	62.2	55.7	55.7
4.0+ cm	384	16.7	77.4	59.8	51.6	43.3	36.8	27.2
Unknown	1,416	61.6	77.2	65.4	59.5	51.5	48.0	44.0
Other Oral Cavity and Pharynx	1,010	100.0	63.8	46.3	38.9	29.8	23.6	21.5
<1 cm	11	1.1	~	~	~	~	~	~
1.0-1.9 cm	44	4.4	78.8	61.6	57.4	40.7	38.6	36.1
2.0-2.9 cm	84	8.3	83.3	66.2	65.0	39.5	34.5	34.5
3.0-3.9 cm	100	9.9	78.0	63.8	47.3	36.9	25.8	23.5
4.0+ cm	208	20.6	59.8	43.3	34.9	27.0	21.1	13.6
Unknown	563	55.7	58.0	39.7	33.0	26.5	20.3	18.7

~ Statistic not displayed due to less than 25 cases.

Table 2.9: Cancer of the Base and Anterior of Tongue: Number and Distribution of Cases by AJCC Stage at Diagnosis (5th Edition, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Base of Tongue		Anterior of Tongue	
	Cases	Percent	Cases	Percent
Total	3,796	100.0	4,841	100.0
Stage I	605	15.9	2,322	48.0
Stage II	346	9.1	735	15.2
Stage III	859	22.6	557	11.5
Stage IV	1,745	46.0	902	18.6
Unstaged	241	6.3	325	6.7

Table 2.10: Cancer of the Base and Anterior Tongue: 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

Stage at Diagnosis	Relative Survival Rate (%)											
	Base of Tongue						Anterior Tongue					
	1-Year	2-Year	3-Year	5-Year	8-Year	10-Year	1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	77.8	62.3	55.3	47.5	40.9	36.8	83.1	68.8	62.6	57.5	50.6	46.2
Stage I	84.3	69.6	62.2	51.5	40.6	35.7	95.2	86.1	80.9	75.9	69.4	65.1
Stage II	89.4	75.1	68.9	60.2	54.7	51.8	86.3	70.8	63.5	57.5	48.7	40.8
Stage III	79.7	64.1	58.0	52.7	46.9	41.4	72.3	50.2	44.0	38.8	30.5	26.8
Stage IV	72.8	56.6	49.3	41.9	36.1	32.5	61.8	39.5	31.7	26.5	20.9	17.3
Unstaged	74.4	59.6	52.0	41.4	35.5	33.1	66.8	53.4	46.2	42.0	34.5	31.1

Table 2.11: Cancer of the Salivary Gland: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology	ICD-O-3 Code	Cases	Percent	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total		4,058	100.0	90.0	82.1	77.7	73.9	70.7	68.5
Squamous Cell Carcinoma	8050-8089	695	17.1	76.7	61.1	53.0	45.6	38.0	36.9
Adenocarcinoma	8140-8147,8190, 8255,8260- 8263, 8290,8310,8480,8481, 8560,8570-8574	616	15.2	86.6	73.5	65.5	59.9	54.4	48.5
Adenoid Cystic Carcinoma	8200	546	13.5	97.5	91.9	87.9	84.1	74.8	70.8
Mucoepidermoid Carcinoma, Poorly Differentiated	8430-8439	537	13.2	95.9	93.3	92.1	90.4	90.2	84.9
Acinic (Acinar) Cell Carcinoma	8550-8559	505	12.4	99.9	98.0	96.4	95.8	93.5	93.5
Mucoepidermoid Carcinoma (Other)	8430-8439	273	6.7	86.3	76.8	71.2	66.1	64.4	64.4
Carcinoma in Pleomorphic Adenoma (Malignant Mixed Tumor)	8940-8949	213	5.2	95.7	90.3	85.7	82.2	78.7	71.1
Mucoepidermoid Carcinoma, Well Differentiated	8430-8439	132	3.3	99.0	99.0	99.0	98.6	98.6	98.6
Other	All Others	541	13.3	~	~	~	~	~	~

~ Survival statistics not reported due to heterogeneous composition of remaining cell types

Table 2.12: Cancer of the Paranasal Sinus: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year (Yr) Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology	ICD-O-3 Code	Cases	Percent	Relative Survival Rate (%)					
				1-Yr	2-Yr	3-Yr	5-Yr	8-Yr	10-Yr
Total		1,208	100.0	72.0	57.6	50.3	42.0	38.1	34.7
Squamous Cell Carcinoma	8050-8052,8070-8078, 8082-8084	649	53.7	66.4	51.1	42.7	36.3	33.3	30.6
Epithelial Neoplasms	8010-8049	134	11.1	69.6	55.3	47.0	32.1	25.5	25.5
Adenoid Cystic Carcinoma (Cylindroma)	8200	124	10.3	91.1	80.0	76.0	61.1	51.0	45.2
Adenocarcinoma	8140-8147,8255,826082 63,8290,8310,8480-8481, 8560,8570-8574	108	8.9	81.7	68.7	63.2	51.0	50.6	45.8
Other	All Others	193	16.0	74.5	59.2	53.1	48.4	43.9	38.0

Figure 2.10: Cancer of the Nasopharynx: Relative Survival Rate (%) by Stage, Ages 20+, 12 SEER Areas, 1988-2001

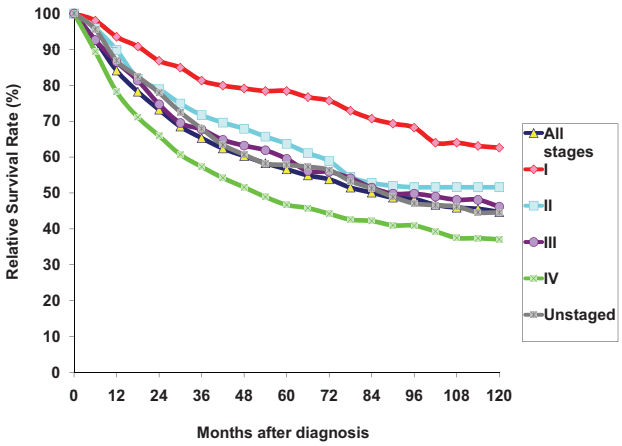


Figure 2.11: Cancer of the Paranasal Sinus: Relative Survival Rate (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

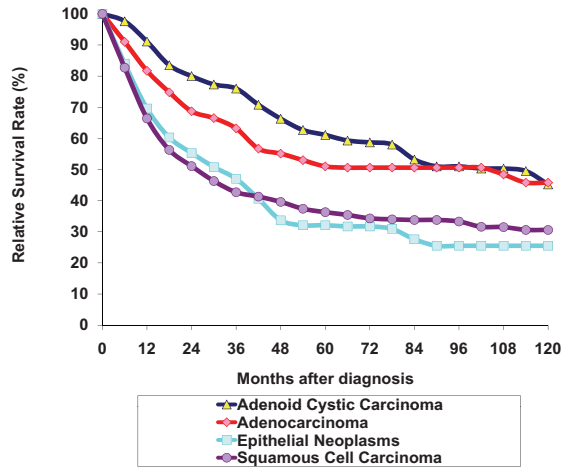
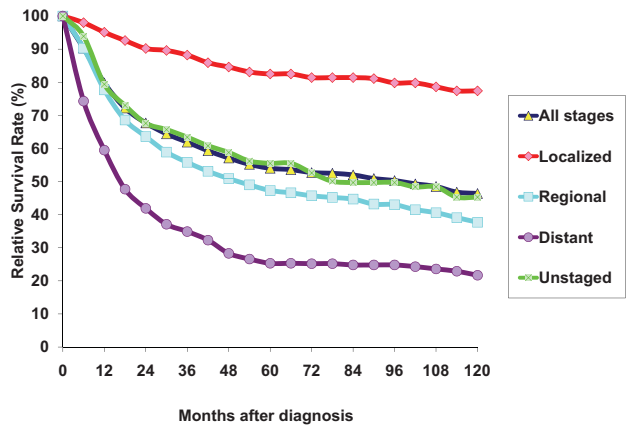


Figure 2.12: Cancer of the Nose, Paranasal Sinus, and Middle Ear: Relative Survival Rate (%) by SEER Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001



DISCUSSION

Head and neck cancers consist of a heterogeneous collection of anatomic sites and cell types. The majority of head and neck cancers are in the oral cavity. In men, cancers of the oral cavity and pharynx account for 3% of all new cancer cases and are the 8th most common cancer site (5).

While 5-year relative survival is most frequently quoted, the survival curves shown here indicate that survival may level off for some head and neck sites before the 5-year time point. Relative survival at 2 or 3 years may convey as much if not more meaning for patient prognosis.

A major limitation of the data is the lack of additional host-based prognostic factors. Several researchers have identified comorbidities (9-16) and performance status (15) as important prognostic factors for patients with head and neck cancers. Since SEER does not routinely collect this information, it is not available for inclusion in this monograph.

REFERENCES

1. Mayne ST, Morse DE, Winn DM. Cancers of the oral cavity and pharynx. In: Schottenfeld D, Fraumeni FJ, eds. Cancer epidemiology and prevention, 3rd edition. Oxford Univ Press, 2006.
2. Alvi A, Myers EN, Johnson JT: Cancer of the Oral Cavity, in myers EN, Suen JY, eds: Cancer of the Head and Neck. Philadelphia, W.B. Saunders Company; 1996: 321-361.
3. Fleming ID, Cooper JS, Henson DE, Hutter RVP, Kennedy BJ, Murphy GP, O'Sullivan B, Sobin LH, Yarbro, JW (eds). AJCC Cancer Staging Manual, Fifth edition, American Joint Committee on Cancer. Philadelphia: Lippincott-Raven, 1997.
4. International Classification of Diseases for Oncology, Geneva. World Health Organization, 2000.
5. American Cancer Society. Cancer Facts and Figures 2006. Atlanta: American Cancer Society; 2006.
6. Jemal A, Thomas A, Murray T, Thun MJ: Cancer Statistics, 2002. CA.A Cancer Journal for Clinicians 2002; 52: 23-47.
7. Marks JE, Phillips JL, Menck HR: The National Cancer Data Base report on the relationship of race and national origin to the histology of nasopharyngeal carcinoma. Cancer 1998; Aug 1; 83: 582-588.
8. Dominitz JA, Samas GP, Landsman P, Provenzale D: Race, treatment, and survival among colorectal carcinoma patients in an equal-access medical system. Cancer 1998; 82: 2312-2320.
9. Piccirillo JF: Purposes, problems, and proposals for progress in cancer staging. Arch Otolaryngol Head Neck Surg. 1995 Feb;121(2):145-9.
10. Singh B, Bhaya M, Zimbler M, et al: Impact of comorbidity on outcome of young patients with head and neck squamous cell carcinoma. Head and Neck surgery 1998; 20: 1-7.
11. Ribeiro KC, Kowalsik LP, Latorre MR: Impact of comorbidity, symptoms and patient's characteristics on the prognosis of oral carcinoma. Arch. Otolaryngol. Head Neck surg. 2000; 126: 1079-1085.

12. Piccirillo JF: Impact of comorbidity and symptoms on the prognosis of patients with oral carcinoma. Arch Otolaryngol Head Neck Surg 2000; 126: 1086-1087.
13. Piccirillo JF: Importance of comorbidity in head and neck cancer. Laryngoscope 2000; 110: 5923-602.
14. Hall SF, Groome PA, Rothwell D: The impact of comorbidity on the survival of patients with squamous cell carcinoma of the head and neck. Head & Neck 2000; 22: 317-322.
15. Reid BC, Alberg AJ, Klassen AC, et al: Comorbidity and survival of elderly head and neck carcinoma patients. Cancer 2001; 92:2109-2116.
16. Baatenburg de Jong RJ, Hermans J, Molenaar J, Briaire JJ, le Cessie S: Prediction of survival in patients with head and neck cancer. Head & Neck 2001; 23: 718-724.

Chapter 3
Cancers of the Esophagus, Stomach, and Small Intestine

Charles Key and Angela L.W. Meisner

INTRODUCTION

Cancers of the esophagus, stomach, and small intestine together account for a approximately 3% of the malignant neoplasms diagnosed in the United States each year. Approximately 43,000 people were diagnosed with one of these cancers in 2006 (1). About one-third will be cancer of the esophagus (14,550), one-half will be cancer of the stomach (22,280) and the remainder will be cancer of the small intestine (6,170) (1). However, because as a group they have relatively poor survival rates, these upper gastrointestinal cancers are responsible for about 4.7% of the annual U.S. cancer deaths, 26,270 estimated deaths in 2006 (1).

In the 14 year period 1988-2001, the SEER Program recorded 19,410 cancers of the esophagus, 39,623 stomach cancers and 6,879 malignant neoplasms of the small intestine (including 2,202 carcinoids).

The tables and text in this chapter address some of the *patient* characteristics (sex, race, and age) and *tumor* characteristics (tumor stage, grade, size, subsite location, and histology) that may be associated with differences in patients' prognosis and outcome.

The text primarily cites 5-year relative survival rates as the primary outcome measure because of its wide general use. However, for cancers associated with poor survival, readers may find the tabulations of 1-, 2-, and 3-year relative survival rates to be more informative.

MATERIALS AND METHODS

The NCI contracts with medically-oriented, nonprofit institutions located in specific geographic areas to obtain data on all cancers diagnosed in residents of the SEER geographic areas. SEER collects data on all invasive and in situ cancers except basal cell and squamous cell carcinomas of the skin (of non-genital anatomic sites) and in situ carcinomas of the uterine cervix. SEER actively follows all previously diagnosed patients on an annual basis to obtain vital status allowing the calculation of observed and relative survival rates.

This analysis is based on data from 12 SEER geographic areas which collectively cover about 14% of the total US

Table 3.1: Cancers of the Esophagus, Stomach, and Small Intestine: Number of Cases and Exclusions, 12 SEER Areas, 1988-2001

Esophagus		Stomach		Small Intestine		
Number Selected/ Remaining	Number Excluded	Number Selected/ Remaining	Number Excluded	Number Selected/ Remaining	Number Excluded	Reason for Exclusion/Selection
19,410	0	39,623	0	6,879	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
15,934	3,476	33,871	5,752	5,210	1,669	Select first primary only
15,702	232	33,356	515	5,101	109	Exclude death certificate only or at autopsy
15,668	34	33,269	87	5,084	17	Exclude unknown race
15,650	18	33,198	71	5,073	11	Exclude alive with no survival time
15,644	6	33,170	28	5,061	12	Exclude children (000-019)
15,446	198	32,839	331	5,023	38	Exclude in situ cancers
14,999	447	31,996	843	4,945	78	Exclude no or unknown microscopic confirmation
14,959	40	31,045	951	4,264	681	Exclude sarcomas (including stromal 8930-8939)
14,932	27	30,382	663	2,062	2,202	Exclude Carcinoids

Table 3.2: Cancer of the Esophagus (Excluding carcinoids): Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates by Sex, Race, Age, Historic Stage, Grade, Primary Site and Tumor Size, 12 SEER Areas, 1988-2001

Characteristics	Cases	Percent	Median Survival (Months)	Relative Survival					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
				Percent	Percent	Percent	Percent	Percent	Percent
All Cases	14,932	100.0	9.2	42.1	24.3	18.2	13.6	10.9	9.8
Sex									
Male	11,168	74.8	9.2	42.4	24.3	18.2	13.5	11.0	9.8
Female	3,764	25.2	9.0	41.1	24.3	18.5	13.7	10.6	9.6
Race									
White	11,561	77.4	9.5	43.7	25.9	19.5	14.6	11.8	10.5
Black	2,412	16.2	8.0	35.8	17.5	13.0	9.4	6.9	6.6
Other	959	6.4	8.6	~	~	~	~	~	~
Age									
20-49	1,272	8.5	11.1	46.9	27.4	21.9	18.0	15.7	14.7
50-64	4,948	33.1	10.8	47.0	27.5	20.4	14.8	11.6	9.9
65+	8,712	58.3	8.0	38.4	21.8	16.2	11.9	9.2	8.4
Historic Stage									
Localized	3,828	25.6	17.0	62.7	44.5	36.1	28.5	23.2	21.1
Regional	4,260	28.5	11.0	48.1	26.0	18.8	13.0	9.5	8.4
Distant	4,037	27.0	5.1	19.5	6.3	3.6	2.3	1.6	1.5
Unstaged	2,807	18.8	8.0	37.4	20.0	14.4	10.8	9.7	9.3
Grade									
Well	722	4.8	12.5	53.6	36.2	30.5	25.9	22.2	18.9
Moderate	4,861	32.6	10.0	45.0	26.4	19.5	13.9	10.5	9.8
Poor	6,341	42.5	8.5	38.9	20.4	15.0	11.1	8.7	7.9
Undifferentiated	405	2.7	7.1	36.5	20.4	13.8	8.0	6.1	6.1
Unknown	2,603	17.4	9.0	42.1	27.2	21.3	16.4	13.9	12.2
Primary Site									
Cervical	431	2.9	10.0	44.6	27.8	19.6	14.9	10.8	7.8
Thoracic	463	3.1	8.8	39.3	22.8	17.6	14.7	12.3	9.8
Abdominal	179	1.2	9.1	42.8	27.6	22.3	15.3	13.9	13.9
Upper third	963	6.4	8.3	38.6	21.7	15.9	10.9	8.0	8.0
Middle third	3,467	23.2	9.1	41.0	22.3	16.3	11.6	7.9	6.7
Lower third	7,400	49.6	9.9	44.8	26.4	20.1	15.2	12.9	11.8
Overlapping lesion	807	5.4	7.1	36.6	20.0	13.1	8.8	6.1	5.9
Esophagus, NOS	1,222	8.2	7.0	34.6	20.6	16.6	13.2	11.4	10.1
Tumor Size									
≤ 2 cm	903	6.0	19.0	64.5	48.2	39.9	32.7	26.1	23.6
2.1-5 cm	3,556	23.8	11.3	49.7	28.5	21.2	15.8	12.3	10.4
5.1-10 cm	3,003	20.1	8.5	37.6	19.5	13.6	10.2	7.6	7.2
>10 cm	449	3.0	7.5	35.3	18.9	13.3	7.6	5.8	5.2
Unknown	7,021	47.0	7.9	37.7	21.5	16.3	11.8	9.8	9.0

~ Not calculated.

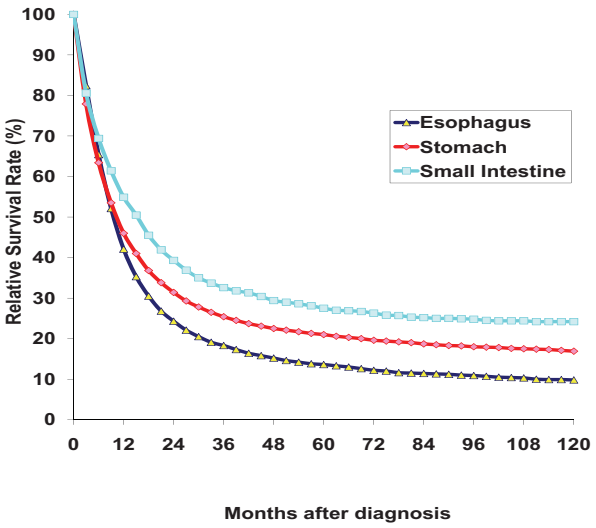
population. The areas are the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Michigan; Atlanta, Georgia; San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; and 10 counties in rural Georgia. Los Angeles contributed data for diagnosis years 1992 to 2001, all other areas for 1988-2001.

The following cases were excluded from this survival analysis: patients for whom the upper gastrointestinal cancer was not the first primary, cases diagnosed at autopsy or by death certificate only, persons of unknown race, patients alive with no recorded survival time, patients less than 20 years old, and cases without microscopic confirmation. Gastrointestinal sarcomas and lymphomas are excluded here, but appear in the Sarcoma and Lymphoma chapters of this monograph. Remaining cases (including carcinoids) available for analysis are as follows: 14,959 esophageal cancers; 31,045 stomach cancers; 4,264 small intestine cancers (Table 3.1). Because the 5-year relative survival for carcinoids of the stomach and small intestine exceeds 70%, they are shown separately in the relative survival tables.

Survival analysis is based on relative survival rates calculated by the life-table (actuarial) method. Relative survival, defined as observed survival in the cohort divided by expected survival in the cohort, adjusts for the expected mortality that the cohort would experience from other causes of death. Expected survival is based on decennial life tables for the United States in 1990.

The staging definitions utilized in this chapter are SEER historic stage: *localized* – confined to the primary site; *regional* – spread to regional lymph nodes or by direct extension beyond the primary; *distant* – metastatic spread.

Figure 3.1: Relative Survival Rates (%) by Primary Site (Esophagus, Stomach, Small Intestine) and Months after Diagnosis, Ages 20+, 12 SEER Areas, 1988-2001



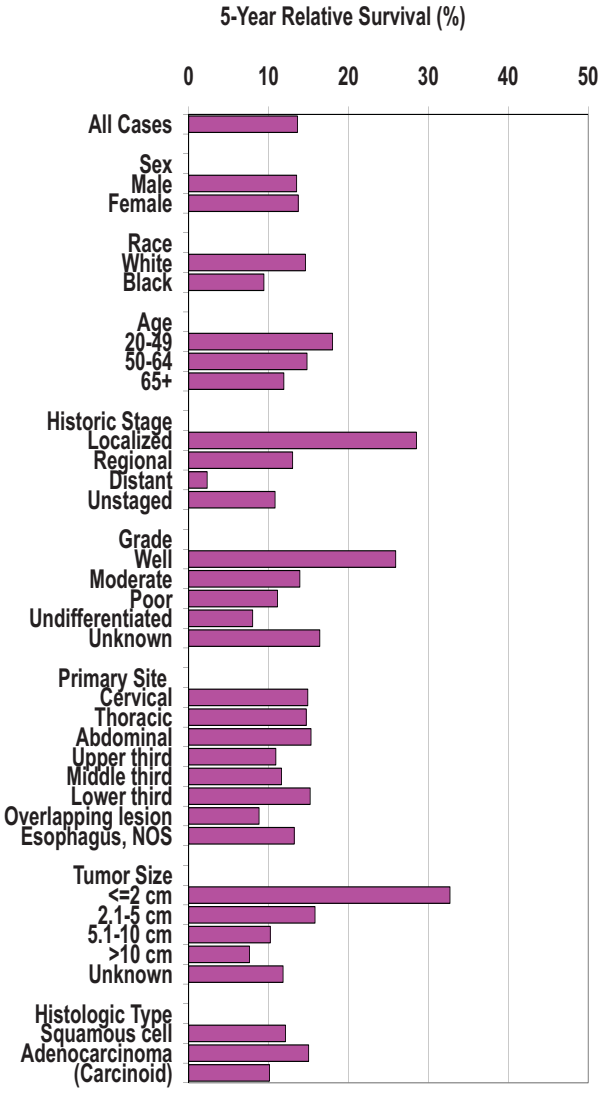
RESULTS

The relative survival curves for esophagus, stomach, and small intestine cancer are shown in Figure 3.1.

Esophagus

Overall short median survival time (9.2 months) and low 5-year relative survival rates (14%) serve as baseline measures for the following esophageal cancer tables and text. Five-year relative survival rates are presented graphically in Figure 3.2.

Figure 3.2: Cancer of the Esophagus: 5-Year Relative Survival Rates by Sex, Race, Age, Stage, Grade, Primary Site, Tumor Size and Histology, Ages 20+, 12 SEER Areas, 1988-2001



Sex, Race, and Age

Among 14,932 esophageal cancers cases eligible for this analysis, males outnumbered females by a factor of 3 to 1. However, the observed sex-specific median survival times (9.2 and 9.0 months) and 5-year relative survival rates (14%) were virtually identical. Survival experience of white patients was slightly better than the experience of black patients. Fifty-eight percent of the patients were 65 years and older and their survival experience was worse than that of patients in the younger age groups (Table 3.2).

Tumor Stage, Grade, and Size

Localized tumor stage, well differentiated tumor grade and small tumor size (2 cm or less) were associated with 5-year relative survival rates of 26% to 33%, whereas for distant stage, undifferentiated grade and large tumor size (more than 10 cm) rates were 2% to 8% (Table 3.2).

Esophageal Subsite and Histology

Squamous cell carcinoma is the predominant histologic type of esophageal carcinoma worldwide, but in recent decades there has been a striking increase of adenocarcinoma, especially in U.S. white males. Squamous cell carcinomas moderately outnumber adenocarcinomas in total, but adenocarcinomas predominate in the lower third of the esophagus. Relative 5-year survival was 12% for patients with squamous cell carcinoma and only slightly better (15%) for adenocarcinoma patients (Table 3.3). Patients whose cancers were coded to locations in the lower third of the esophagus or abdominal esophagus had relative 5-year survival of about 15%.

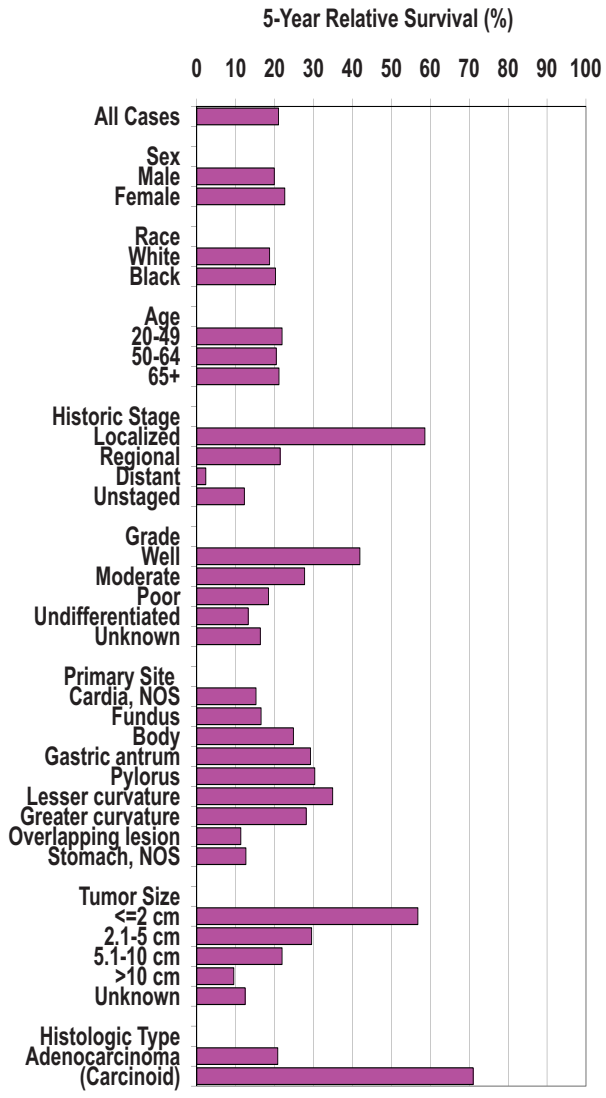
Carcinoid tumors are not very common in the esophagus when compared to other parts of the upper gastrointestinal tract. In this series, the ones that did occur had much poorer relative 5-year survival (10%) than those in the stomach (71%) or small intestine (77%). Five-year relative survival rates by tumor and patient characteristics are presented graphically in Figure 3.2.

Table 3.3: Cancer of the Esophagus: Distribution, Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology (ICD-O code)	Cases	Percent	Median Survival (Months)	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases excluding carcinoids	14,932	100.0	9.2	42.1	24.3	18.2	13.6	10.9	9.8
Carcinoma excluding carcinoids 8010-8231, 8247-8572	14,839	99.4	9.2	42.1	24.2	18.2	13.5	10.8	9.8
Squamous-cell carcinoma 8050-8076	7,465	50.0	8.9	40.2	22.4	16.6	12.1	9.4	8.3
Adenocarcinoma 8140-8141,8191-8231, 8260-8263,8310,8430, 8480-8490,8560, 8570-8572	6,514	43.6	10.0	45.4	26.9	20.1	15.0	12.4	11.3
Other specified carcinomas	178	1.2	8.8	40.5	22.8	17.3	9.8	5.2	5.2
Unspecified carcinoma 8010-8034	682	4.6	6.0	31.1	19.7	16.9	14.3	14.3	13.4
Unspecified Cancer 8000-8004	75	0.5	8.8	40.7	34.7	34.7	34.3	25.9	21.5
Other specified cancer	18	0.1	~	~	~	~	~	~	~
Carcinoids 8240-8246	27	0.2	12.5	53.6	24.1	10.1	10.1	10.1	10.1

~ Statistic not displayed due to less than 25 cases.

Figure 3.3: Cancer of the Stomach: 5-Year Relative Survival Rates by Sex, Race, Age, Stage, Grade, Primary Site, Tumor Size and Histology, Ages 20+, 12 SEER Areas, 1988-2001



Stomach

Short median survival time (10 months) and low 5-year relative survival rates (21%) are the overall baseline measures for the stomach cancer tables and text. Five-year relative survival rates by tumor and patient characteristics are presented graphically in Figure 3.3.

Sex, Race, and Age

There were a total of 30,382 stomach cancer cases available for this analysis with male cancers exceeding female by about 1.7 to 1. Female patients experienced a slight relative survival advantage at each follow-up interval between 1 year and 10 years, but median survival time for both sexes was less than 10 months from initial diagnosis. Survival for black patients was similar to that for white patients. While relative survival rates are not shown for other races, it should be noted that most of the "Other" races are Asian/Pacific Islanders, whose incidence rate of stomach cancer is high; their median survival time (13.5 months) is higher than for blacks or whites. Almost 2/3 of the eligible stomach cancer patients in this analysis were 65 years old or older. During the first year after diagnosis, persons 65 years of age and older had lower relative survival (44%) than those 20-49 years of age (52%) and 50-64 years (49%). However, at intervals between 2 and 10 years the survival rates were remarkably similar (Table 3.4).

Tumor Stage, Grade, and Size

About 20% had cancers that had not spread beyond the stomach and their 5-year relative survival was 59%. About 1/3 of the patients exhibited extension of tumor to adjacent structures or metastasis to regional lymph nodes and their 5-year relative survival dropped to 21%. Another 1/3 of the cases had recognized tumor spread to distant organs or lymph nodes at the time of diagnosis and they experienced only 2% relative survival at 5 years. Tumors measuring 2 cm or less were associated with far better 5-year relative survival rate (57%) than tumors measuring 2.1-5.0 cm (30%) or 5.1-10 cm (22%) or greater than 10 cm (10%). Tumors assigned a histologic grade of "well differentiated" were associated with better 5-year relative survival rate (42%) than the less differentiated grades, but they accounted for only about 4% of the cases (Table 3.4).

Table 3.4: Cancer of the Stomach (Excluding Carcinoids): Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates by Sex, Race, Age (20+), Historic Stage, Grade, Primary Site and Tumor Size, 12 SEER Areas, 1988-2001

Characteristics	Cases	Percent	Median Survival (Months)	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases	30,382	100.0	9.6	46.0	31.4	25.4	21.0	18.0	16.9
Sex									
Male	19,034	62.6	9.7	45.9	30.9	24.8	19.9	16.8	15.5
Female	11,348	37.4	9.5	46.0	32.1	26.4	22.6	20.0	19.0
Race									
White	21,276	70.0	9.0	44.0	29.2	23.2	18.7	15.7	14.4
Black	3,519	11.6	8.8	44.1	30.4	24.8	20.2	16.8	15.8
Other	5,587	18.4	13.5	~	~	~	~	~	~
Age									
20-49	3,270	10.8	13.0	52.2	33.5	26.6	21.9	18.3	17.5
50-64	7,179	23.6	11.5	49.3	32.8	25.8	20.4	17.3	16.7
65+	19,933	65.6	8.4	43.6	30.4	25.1	21.1	18.5	17.0
Historic Stage									
Localized	6,085	20.0	45.5	78.5	69.1	63.7	58.6	54.0	51.8
Regional	10,272	33.8	15.3	59.7	38.4	28.8	21.4	17.2	15.9
Distant	10,401	34.2	4.3	17.7	6.3	3.7	2.3	1.7	1.6
Unstaged	3,624	11.9	6.2	33.8	20.3	15.1	12.2	10.5	10.2
Grade									
Well	1,232	4.1	22.6	65.2	53.8	47.2	41.9	37.3	36.3
Moderate	7,014	23.1	13.2	54.8	39.7	33.0	27.7	23.6	21.5
Poor	16,687	54.9	9.0	43.9	28.5	22.6	18.4	16.0	15.0
Undifferentiated	894	2.9	7.6	38.6	24.9	18.7	13.2	10.4	10.4
Unknown	4,555	15.0	6.6	36.2	24.2	19.8	16.3	14.0	13.3
Primary Site									
Cardia, NOS	7,760	25.5	10.0	45.2	27.4	20.3	15.2	12.0	11.2
Fundus	1,241	4.1	7.3	38.5	24.9	20.2	16.5	12.8	12.0
Body	2,240	7.4	9.1	45.6	33.1	28.0	24.8	22.2	21.8
Gastric antrum	6,282	20.7	12.9	54.3	40.2	34.1	29.2	25.6	24.8
Pylorus	964	3.2	14.6	58.4	42.3	34.7	30.3	25.4	21.5
Lesser curvature, NOS	2,996	9.9	16.8	60.4	46.1	39.9	34.9	31.8	29.9
Greater curvature, NOS	1,306	4.3	11.7	51.4	39.5	33.2	28.1	23.9	22.8
Overlapping lesion	2,967	9.8	6.8	34.9	20.0	14.8	11.3	10.0	8.9
Stomach, NOS	4,626	15.2	5.6	31.8	20.3	16.0	12.6	10.5	9.5
Tumor Size									
≤ 2 cm	2,056	6.8	46.4	77.6	68.9	62.7	56.8	50.0	48.0
2.1-5 cm	6,986	23.0	17.1	61.8	44.3	36.2	29.5	26.0	23.9
5.1-10 cm	5,842	19.2	12.6	53.4	35.4	27.5	21.9	17.6	15.8
>10 cm	2,584	8.5	7.5	36.4	18.9	13.0	9.5	7.9	7.4
Unknown	12,914	42.5	5.6	30.8	18.9	15.1	12.4	10.7	10.3

- Not calculated.

Table 3.5: Cancer of the Stomach: Distribution, Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology (ICD-O code)	Cases	Percent	Median Survival (Months)	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases excluding carcinoids	30,382	100.0	9.6	46.0	31.4	25.4	21.0	18.0	16.9
Carcinoma excluding carcinoids 8010-8231,8247-8572	30,156	99.3	9.6	46.0	31.3	25.3	20.8	17.9	16.8
Squamous-cell carcinoma 8050-8076	256	0.8	7.4	34.2	23.4	18.4	15.2	14.3	14.3
Adenocarcinoma 8140-8141,8191-8231, 8260-8263,8310,8430, 8480-8490,8560, 8570-8572	25,322	83.3	9.5	45.4	30.7	24.8	20.4	17.3	16.2
Other specified carcinomas	3,635	12.0	13.5	54.7	39.4	32.2	26.8	23.9	22.2
Unspecified carcinoma 8010-8034	943	3.1	4.5	28.9	18.5	14.8	11.8	11.2	10.5
Unspecified Cancer 8000-8004	212	0.7	9.1	47.8	41.9	38.5	37.9	36.5	30.9
Other specified cancer	14	0.0	~	~	~	~	~	~	~
Carcinoids 8240-8247	663	2.1	103.8	84.5	77.5	74.4	71.0	67.4	66.0

~ Statistic not displayed due to less than 25 cases.

Stomach Subsite and Histology

Cancers arising in proximal regions (cardia, fundus) of the stomach are associated with lower relative survival than those arising in the greater and lesser curvatures, antrum, and pylorus. Adenocarcinomas (of many subtypes) account for a large majority of stomach cancer histologic diagnoses (Table 3.5). In addition, there are about 3,400 patients with primary gastric lymphomas and about 950 patients with soft tissue tumors (sarcomas, stromal tumors) of the stomach discussed elsewhere in this monograph.

In this analysis, the 663 eligible patients with carcinoid tumors of the stomach had a median survival time of 104 months, 5-year relative survival of 71%, and 10-year relative survival of 66%.

Small Intestine

Short median survival time (14.0 months) and 5-year relative survival (27%) are the overall baseline outcome measures for cancers (mostly adenocarcinomas) of the small intestine that are included in this analysis. The small intestine is remarkable for the relative rarity of malignant neoplasms occurring in such a large (surface area) organ. Five-year relative survival rates are presented graphically in Figure 3.4.

Sex, Race, and Age

Of 2,062 small intestine cancers included in this analysis, a little more than half (52.6%) occurred in males. This contrasts with the much stronger male predominance observed for cancers of the esophagus and stomach. Males exhibit slightly better relative survival at years 1 and 2 after diagnosis; relative survival is virtually equal at years 3 and 5; and there is a slight female advantage at years 8 and 10. Beginning at year 3, white patients maintain a consistent survival advantage over patients who are black. A larger percent of small intestine cancer patients (17.0%) are in the youngest age group than for the other upper gastrointestinal cancers (esophagus 8.5%, stomach 10.8%) and a smaller percent in the oldest age group. The younger patients have an early survival advantage that diminishes by 10 years after diagnosis (Table 3.6).

Tumor Stage, Grade, and Size

About 21% of the cancers were confined to the small intestine at the time of diagnosis and they were associated with more favorable 5-year relative survival (57%), compared to those with regional (34%) or distant spread (3%). Tumor grades of well and moderate differentiation were associated with similar survival outcomes (35% and 35%, respectively) in contrast to poor differentiation (21%). Smaller tumors (2 cm or less) have moderately better outcomes than larger tumors, but the gradient associated with increasing tumor size is less striking than the gradient for cancers of the esophagus and stomach.

The 2,202 patients with small intestine carcinoid tumors in this series experienced a median survival time of 97.6 months and 5- and 10-year relative survival rates of 77% and 62%, respectively (Table 3.7).

Carcinoid tumors outnumber carcinomas in this series by a factor of 1.11 (2,202/1,985). Additionally, about 681 sarcomas and 1,367 primary lymphomas of the small intestine are excluded from this analysis, but are discussed in other chapters of this monograph.

Figure 3.4: Cancer of the Small Intestine: 5-Year Relative Survival Rates by Sex, Race, Age, Stage, Grade, Primary Site, Tumor Size and Histology, Age 20+, 12 SEER Areas, 1988-2001

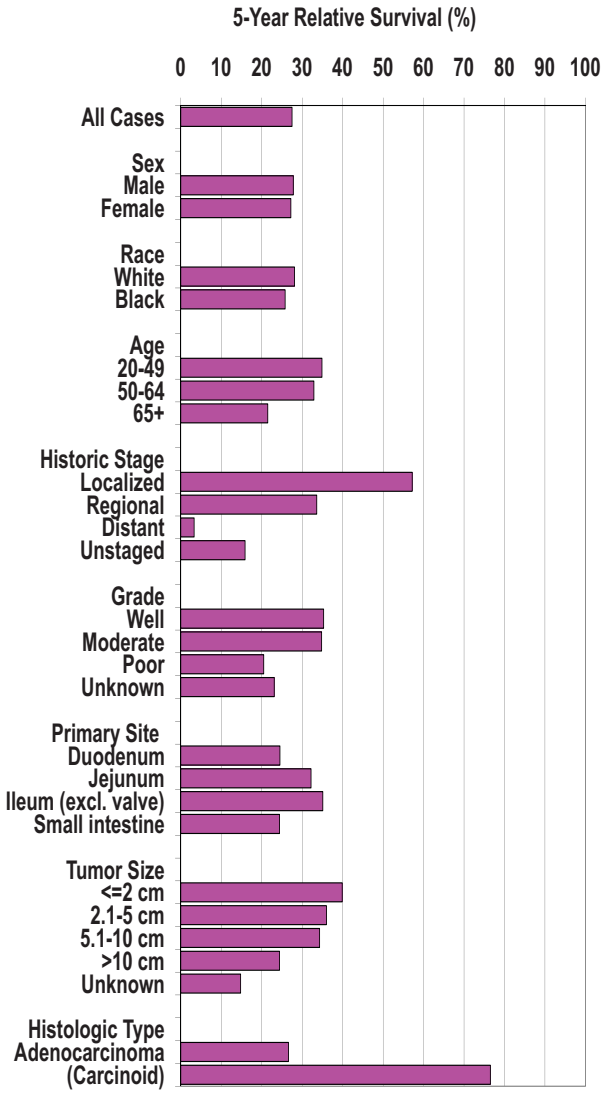


Table 3.6: Cancer of the Small Intestine (Excluding Carcinoids): Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates by Sex, Race, Age, Historic Stage, Grade, Primary Site and Tumor Size, 12 SEER Areas, 1988-2001

Characteristics	Cases	Percent	Median Survival (Months)	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases	2,062	100.0	14.0	55.1	39.3	32.6	27.5	24.8	24.3
Sex									
Male	1,084	52.6	14.4	56.7	40.1	32.7	27.8	23.8	23.8
Female	978	47.4	13.3	53.3	38.3	32.7	27.2	25.4	24.8
Race									
White	1,561	75.7	13.7	54.8	39.7	33.5	28.1	25.9	25.6
Black	348	16.9	15.8	57.6	40.7	31.3	25.8	21.0	19.5
Other	153	7.4	12.2	~	~	~	~	~	~
Age									
20-49	350	17.0	22.2	67.5	48.0	41.4	34.9	31.5	28.7
50-64	546	26.5	18.6	61.6	46.5	38.7	32.9	29.5	28.4
65+	1,166	56.5	10.0	48.0	32.7	26.4	21.5	18.4	18.0
Historic Stage									
Localized	438	21.2	49.8	79.7	70.1	62.5	57.2	54.5	54.0
Regional	784	38.0	22.2	69.7	51.0	41.4	33.6	28.5	27.9
Distant	660	32.0	5.1	25.7	9.6	5.6	3.3	2.6	2.6
Unstaged	180	8.7	6.8	39.2	22.1	20.4	15.9	13.7	12.0
Grade									
Well	178	8.6	19.4	66.3	47.3	40.3	35.3	34.2	34.2
Moderate	790	38.3	20.9	65.8	50.0	41.3	34.8	29.6	27.9
Poor	658	31.9	9.3	45.4	30.3	24.5	20.5	18.7	18.2
Undifferentiated	45	2.2	3.1	16.1	4.8	4.8	!	!	!
Unknown	391	19.0	10.7		33.0	28.6	23.1	21.6	21.4
Primary Site									
Duodenum	1,140	55.3	10.8	49.4	34.1	28.0	24.5	22.0	21.7
Jejunum	394	19.1	21.2	68.1	49.3	39.6	32.2	26.6	26.2
Ileum (excl. valve)	255	12.4	18.6	60.9	48.9	43.4	35.1	32.2	30.1
Meckels diverticulum	8	0.4	~	~	~	~	~	~	~
Overlapping lesion	20	1.0	~	~	~	~	~	~	~
Small intestine, NOS	245	11.9	13.1	53.7	36.2	29.6	24.4	21.5	21.5
Tumor Size									
<2 cm	165	8.0	24.0	76.4	53.4	47.3	39.9	37.7	35.7
2.1-5 cm	641	31.1	21.7	67.3	51.2	42.8	36.0	29.8	29.8
5.1-10 cm	370	17.9	19.2	64.8	48.7	41.4	34.3	31.0	28.2
>10 cm	67	3.2	11.6	50.0	36.7	29.4	24.4	24.4	24.4
Unknown	819	39.7	7.0	37.0	22.8	17.6	14.8	13.8	13.4

! Not enough intervals to produce rate.
~ Statistic not displayed due to less than 25 cases.

Table 3.7: Cancer of the Small Intestine: Distribution, Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Histology, ages 20+, 12 SEER Areas, 1988-2001

Histology (ICD-O code)	Cases	Percent	Median Survival (Months)	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases excluding carcinoids	2,062	100.0	14.0	55.1	39.3	32.6	27.5	24.8	24.3
Carcinoma excluding carcinoids 8010-8572	1,985	96.3	13.4	54.3	38.4	31.6	26.5	24.1	23.7
Squamous-cell carcinoma 8050-8076	7	0.3	~	~	~	~	~	~	~
Adenocarcinoma 8140-8141,8191-8231, 8260-8263,8310,8430, 8480-8490,8560, 8570-8572	1,852	89.8	13.9	55.1	38.7	31.7	26.6	24.1	23.6
Other specified carcinomas	40	1.9	41.3	69.7	62.5	56.4	41.3	41.3	41.3
Unspecified carcinoma 8010-8034	86	4.2	5.4	33.8	24.4	20.5	19.5	14.7	14.7
Unspecified Cancer 8000-8004	66	3.2	52.4	73.1	63.4	61.5	54.8	43.1	22.7
Other specified cancer	11	0.5	~	~	~	~	~	~	~
Carcinoids	2,202	51.6	97.6	89.9	87.5	84.8	76.5	67.1	61.5

~ Statistic not displayed due to less than 25 cases.

DISCUSSION

Survival rates for these three sites were generally poor. Overall the 5-year relative survival rates were 14% for esophageal, 21% for stomach, and 28% for small intestine cancers. Even though survival rates were higher for localized disease, well differentiated tumors, and small sized tumors, the survival rates were still lower than those for many primary sites such as breast, prostate, and colon/rectum. Carcinoids of the stomach and small intestine had the highest 5-year survival rates, 71% and 77%, respectively.

REFERENCE

1. American Cancer Society. Cancer Facts and Figures 2006. Atlanta: American Cancer Society, 2006.

Chapter 4
Cancers of the Colon and Rectum

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INTRODUCTION

Cancers of the colon and rectum are the third most common cancer among both men and women in the United States and the second leading cause of cancer death (1). Fifty-three percent of colorectal cancers occur in either the lower (sigmoid) colon or the rectum and should be easy to detect at an early stage.

MATERIALS AND METHODS

The NCI contracts with medically-oriented, nonprofit institutions located in specific geographic areas to obtain data on all cancers diagnosed in residents of the SEER geographic areas. SEER collects data on all invasive and in situ cancers except basal cell and squamous cell carcinomas of the skin (of non-genital anatomic sites) and in situ carcinomas of the uterine cervix. SEER actively follows all previously diagnosed patients on an annual basis to obtain vital status allowing the calculation of observed and relative survival rates.

This analysis is based on data from 12 SEER geographic areas which collectively cover about 14% of the total US population. The areas are the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Michigan; Atlanta, Georgia; San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; and 10 counties in rural Georgia. Los Angeles contributed data for diagnosis years 1992 to 2001, all other areas for 1988-2001.

In situ diagnoses have been excluded, except as noted in the staging section. Cases diagnosed in children and adolescents aged 0-19 have also been excluded. Some patients have more than one diagnosis of cancer, but only the first diagnosis of cancer has been included. Death certificate only cases, autopsy only cases, and all other cases with no survival time have been excluded. Further, cases with no microscopic confirmation have been excluded. Finally, sarcomas arising in the colon and rectum have also been excluded from this analysis as they have been included in Chapter 11 of this monograph. Table 4.1 shows the numbers of cases excluded by category.

Survival analysis is based on relative survival rates calculated by the life-table (actuarial) method. Relative survival, defined as observed survival in the cohort divided by expected survival in the cohort, adjusts for the expected mortality that the cohort would experience from other causes of death. Expected survival is based on decennial life tables for the United States in 1990.

Table 4.1: Cancers of the Colon and Rectum: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
247,671	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
201,637	46,034	Select first primary only
199,425	2,212	Exclude death certificate only or at autopsy
198,521	904	Exclude unknown race
198,331	190	Exclude alive with no survival time
198,242	89	Exclude children (Ages 0-19)
187,201	11,041	Exclude in situ cancers
182,752	4,449	Exclude no or unknown microscopic confirmation
182,589	163	Exclude sarcomas

Table 4.2: Cancers of the Colon and Rectum: Distribution by Subsite, Sex, Race and 5th Edition AJCC Stage Group, Ages 20+, 12 SEER Areas, 1988-2001

		Sex		Race			AJCC Stage (%)				
Primary Site/Subsite	Total	Male	Female	White	Black	Other	0/I	II	III	IV	Unknown
Colon and rectum	182,589	92,880	89,709	150,522	16,830	15,237	26.3	28.5	23.3	17.4	4.4
Colon	129,445	62,825	66,620	106,695	12,732	10,018	22.8	31.1	23.9	18.5	3.6
Cecum	30,203	13,186	17,017	25,528	3,166	1,509	17.3	31.9	27.9	20.4	2.5
Appendix	1,455	726	729	1,210	146	99	18.4	36.7	11.3	31.1	2.5
Ascending	19,236	8,682	10,554	15,966	1,961	1,309	19.9	35.0	26.0	16.0	3.0
Hepatic flexure	6,998	3,361	3,637	5,782	655	561	17.0	37.9	24.9	16.7	3.5
Transverse	11,142	5,012	6,130	9,231	1,073	838	16.1	38.3	24.9	18.1	2.5
Splenic flexure	5,045	2,725	2,320	4,012	689	344	14.5	36.8	26.4	19.7	2.5
Descending	8,194	4,248	3,946	6,380	994	820	25.4	33.4	21.8	16.4	3.0
Sigmoid	43,016	22,767	20,249	35,220	3,520	4,276	32.8	26.3	21.6	16.4	2.9
Overlapping	1,129	584	545	911	135	83	11.5	32.7	26.4	25.6	3.8
Colon, NOS	3,027	1,534	1,493	2,455	393	179	6.5	6.9	4.8	45.2	36.7
Rectum and rectosigmoid	53,144	30,055	23,089	43,827	4,098	5,219	34.8	22.0	21.9	14.8	6.5
Rectosigmoid	17,984	9,967	8,017	14,897	1,403	1,684	27.1	26.1	25.7	17.5	3.6
Rectum	35,160	20,088	15,072	28,930	2,695	3,535	38.7	20.0	19.9	13.4	7.9

RESULTS

Table 4.2 shows the case distribution by subsite and by sex, race, and 5th edition American Joint Committee on Cancer (AJCC) Stage (2) for the 182,589 cases included in this analysis. There were slightly more females included in the colon category while males predominated the rectum and rectosigmoid category. Blacks comprised 9.2% of the cases while races other than white or black accounted for 8.3% of the cases. With the exceptions of cases arising in the colon "not otherwise specified" or cases overlapping two colon subsites, more than 50% of the cases were diagnosed at an early stage (I or II). For the unknown colon subsite, the percentage of cases with unknown stage was large which contributed to the percentage of early stage being low. The percentage of stage I cases was greatest for the sigmoid colon, the rectum, and the rectosigmoid junction.

Table 4.3 shows the 1-, 3-, 5-, and 10-year relative survival rates by subsite of the colon and rectum and by sex. With the exception of a cancer which overlapped two subsites or a lesion which arose in an unidentified subsite of the colon, 5-year survival rates differed little by subsite or between the colon (64%) and the rectum (63%). The other two subsites (overlapping and NOS) had much poorer survival. There was essentially no difference by subsite or overall in survival of men and women, both 64%.

Table 4.4 shows the relative survival by subsite for whites and blacks. As has been noted, with the exception of overlapping or unspecified subsites, there was little variation by subsite within race. However, whites had a clear survival advantage (65% overall after 5 years) over blacks (55%).

Relative survival rates for the four age groups 20-49, 50-64, 65-74, and 75+ are shown in Table 4.5. Interestingly, roughly one-third of the cases occurred in each of the age groups 20-64, 65-74, and 75+. Overall, there was a slight increase in the 5-year relative rate with increasing age before age 75, however, these differences are small (63%-65%). Again, with the exception of the overlapping and unspecified subsites, there was very little difference in survival rates across subsites for cases within the same age group.

Table 4.6 shows relative survival rates by subsite for the three time periods 1988-1991, 1992-1996 and 1997-2001. It should be noted that there was a higher percentage of cases included in the later two time periods due to the inclusion of the Los Angeles County data beginning in 1992. Surprisingly, there was no change in the survival rates for first two time periods, 63% vs. 63% overall at 5 years with a slight increase to 65% in the last time period.

The distribution by stage categories as defined in the 5th Edition of the AJCC Staging Handbook (2) and subsite is shown in Table 4.7. While in situ lesions were excluded from this analysis, the AJCC considers invasion of the lamina propria to be equivalent to in situ or non-invasive disease. Thus while cancers which meet these criteria are

Table 4.3: Cancers of the Colon and Rectum: 1-, 3- ,5- and 10-Year (Yr) Relative Survival Rates (%) by Subsite and Sex, Ages 20+, 12 SEER Areas, 1988-2001

	Relative Survival Rate (%)											
	Total				Male				Female			
Primary Site/Subsite	1-Yr	3-Yr	5-Yr	10-Yr	1-Yr	3-Yr	5-Yr	10-Yr	1-Yr	3-Yr	5-Yr	10-Yr
Colon and rectum	83.3	69.9	63.6	57.7	84.2	70.6	63.7	57.8	82.4	69.1	63.5	57.5
Colon	82.0	69.3	64.0	58.9	83.0	70.4	64.7	60.0	81.1	68.3	63.4	57.9
Cecum	79.8	65.7	61.2	56.7	80.9	66.2	60.7	56.6	78.9	65.4	61.6	56.7
Appendix	85.0	68.2	59.3	50.4	84.3	68.4	59.1	49.2	85.6	68.1	59.2	51.3
Ascending	81.7	70.3	66.0	60.7	82.8	70.6	66.0	60.6	80.8	70.0	66.0	60.8
Hepatic flexure	78.6	66.6	62.1	55.0	78.7	66.1	61.1	55.0	78.4	67.0	62.9	54.8
Transverse	79.7	67.2	62.4	56.6	80.9	69.2	63.6	58.6	78.7	65.6	61.4	54.9
Splenic flexure	80.1	64.9	59.6	53.3	81.0	66.3	60.3	54.6	79.1	63.3	58.7	51.4
Descending	84.8	72.4	65.5	58.3	85.9	74.0	66.8	60.1	83.6	70.8	64.1	56.5
Sigmoid	86.9	74.8	68.7	64.0	87.4	75.8	69.7	65.5	86.4	73.6	67.7	62.5
Overlapping	74.3	60.1	54.7	50.9	74.6	58.2	52.9	43.9	73.9	62.2	55.9	55.9
Colon, NOS	50.1	34.6	29.2	23.4	52.5	38.3	33.7	28.4	47.7	30.9	24.5	17.9
Rectum and rectosigmoid	86.5	71.3	62.7	55.0	86.7	71.1	61.9	53.8	86.1	71.5	63.7	56.5
Rectosigmoid	86.3	71.4	62.8	55.6	86.4	71.0	61.6	53.2	86.2	72.0	64.3	58.1
Rectum	86.5	71.2	62.6	54.7	86.9	71.2	62.1	54.1	86.1	71.3	63.3	55.5

Table 4.4: Cancers of the Colon and Rectum: 1-, 3- ,5- and 10-Year Relative Survival Rates (%) by Subsite and Race, Ages 20+, 12 SEER Areas, 1988-2001

	Relative Survival Rate (%)							
	White				Black			
Primary Site/Subsite	1-Year	3-Year	5-Year	10-Year	1-Year	3-Year	5-Year	10-Year
Colon and rectum	83.5	70.5	64.5	58.7	78.9	62.5	55.1	48.7
Colon	82.2	70.0	65.0	60.1	77.7	61.7	55.2	49.3
Cecum	80.1	66.5	62.2	57.6	76.6	59.1	52.7	49.0
Appendix	84.2	67.9	59.9	52.0	89.9	69.7	55.5	43.9
Ascending	82.0	71.0	67.0	62.5	76.7	63.1	56.4	47.6
Hepatic flexure	78.3	67.3	63.2	56.0	79.5	62.1	55.1	49.5
Transverse	79.4	67.6	62.7	57.0	76.9	58.9	52.9	46.7
Splenic flexure	80.6	66.1	61.2	55.9	75.5	57.5	51.2	39.6
Descending	85.1	73.1	66.5	58.9	80.0	67.1	59.1	52.8
Sigmoid	87.2	75.6	69.8	65.3	82.1	66.7	60.5	54.4
Overlapping	75.2	61.7	56.6	52.7	64.7	50.7	43.1	38.8
Colon, NOS	49.8	34.6	29.3	23.5	48.5	31.1	25.5	17.4
Rectum and rectosigmoid	86.5	71.7	63.2	55.7	82.6	64.7	54.7	47.0
Rectosigmoid	86.6	72.1	63.5	56.5	80.2	62.7	52.8	42.8
Rectum	86.5	71.5	63.1	55.2	83.9	65.8	55.7	49.2

considered to be malignant neoplasms, with respect to AJCC stage they are classified as Stage 0. Thus, in the tables containing information by AJCC stage category, Stage 0 is limited only to those patients whose tumor had extended to the lamina propria. For stage 0/I with the exception of patients whose cancer overlapped two subsites and rectal cancers, all other colorectal subsites had 5-year relative survival rates of 90% or higher. For stage II cancers, with the exception of colon not otherwise specified, there was a distinct survival advantage (83% overall) for colon versus rectum and rectosigmoid (70% overall). Among persons with Stage III disease there were no notable differences among the colon or rectal subsites with the exception of the appendix and the unspecified colon, both of which had much poorer relative survival rates at five years. For stage IV cancers, 5-year survival rates were less than 8% for all subsites with the

Table 4.5: Cancers of the Colon and Rectum: 1-, 3- ,5- and 10-Year Relative Survival Rates (%) by Subsite and Age Group (Ages 20+), 12 SEER Areas, 1988-2001

Subsite/Age Group (Years)	Total	Percent	Relative Survival Rate (%)			
			1-Year	3 -Year	5-Year	10-Year
Colon and rectum	182,589	100.0				
20-49	15,670	8.6	87.6	70.0	62.8	56.7
50-64	44,949	24.6	87.4	72.2	64.9	59.0
65-74	54,379	29.8	85.0	71.7	65.0	59.3
75+	67,591	37.0	77.9	66.2	61.3	55.1
Colon	129,445	100.0				
20-49	9,834	7.6	85.9	68.4	61.7	56.4
50-64	29,344	22.7	85.7	70.5	64.3	59.4
65-74	38,563	29.8	84.0	71.2	65.4	60.6
75+	51,704	39.9	77.5	66.9	63.1	57.5
Cecum	30,203	100.0				
20-49	1,808	6.0	84.8	66.0	60.3	55.0
50-64	5,722	18.9	81.5	63.3	57.7	53.4
65-74	8,654	28.7	81.0	66.5	61.4	58.2
75+	14,019	46.4	77.5	66.4	63.4	59.3
Appendix	1,455	100.0				
20-49	487	33.5	93.2	74.6	68.1	61.1
50-64	442	30.4	85.0	67.5	56.4	46.5
65-74	284	19.5	82.6	65.6	56.1	40.1
75+	242	16.6	69.9	57.0	44.7	37.4
Ascending	19,236	100.0				
20-49	1,125	5.8	83.1	66.6	61.7	56.5
50-64	3,744	19.5	83.7	67.3	61.8	57.8
65-74	5,662	29.4	84.2	72.3	67.4	61.7
75+	8,705	45.3	78.8	70.9	68.1	64.1
Hepatic flexure	6,998	100.0				
20-49	476	6.8	80.1	65.8	62.6	58.4
50-64	1,317	18.8	80.9	66.9	62.9	57.8
65-74	2,029	29.0	81.1	67.7	61.4	53.9
75+	3,176	45.4	75.5	65.6	61.8	51.0
Transverse	11,142	100.0				
20-49	838	7.5	82.5	65.0	58.4	53.5
50-64	2,319	20.8	82.4	66.7	61.6	56.2
65-74	3,243	29.1	83.0	69.9	64.1	58.7
75+	4,742	42.6	75.3	65.8	62.3	54.0
Splenic flexure	5,045	100.0				
20-49	482	9.6	87.8	67.6	60.2	55.0
50-64	1,176	23.3	84.7	66.4	59.6	53.9
65-74	1,518	30.1	82.1	68.4	62.8	56.5
75+	1,869	37.0	73.2	59.4	55.8	45.3

Table 4.5 (continued): Cancers of the Colon and Rectum: 1-, 3- ,5- and 10-Year Relative Survival Rates (%) by Subsite and Age Group (Ages 20+), 12 SEER Areas, 1988-2001

Subsite/Age Group (Years)	Total	Percent	Relative Survival Rate (%)			
			1-Year	3 -Year	5-Year	10-Year
Descending	8,194	100.0				
20-49	742	9.1	87.3	71.4	62.3	57.0
50-64	2,139	26.1	88.7	74.5	67.4	60.2
65-74	2,506	30.6	87.1	75.1	67.8	61.1
75+	2,807	34.3	78.6	68.1	62.1	52.2
Sigmoid	43,016	100.0				
20-49	3,463	8.1	89.4	72.0	64.2	58.9
50-64	11,577	26.9	90.9	78.2	71.5	66.7
65-74	13,558	31.5	90.9	78.2	71.5	66.7
75+	14,418	33.5	81.5	70.1	65.1	60.3
Overlapping	1,129	100.0				
20-49	122	10.8	74.7	53.5	47.9	47.9
50-64	263	23.3	75.7	58.8	49.8	40.4
65-74	285	25.2	76.6	62.0	58.0	55.4
75+	459	40.7	71.7	61.8	57.5	55.1
Colon, NOS	3,027	100.0				
20-49	291	9.6	67.5	48.5	42.2	33.4
50-64	645	21.3	56.0	36.7	31.8	26.6
65-74	824	27.2	52.8	36.4	28.1	22.0
75+	1,267	41.9	40.6	27.9	23.7	16.2
Rectum & rectosigmoid	53,144	100.0				
20-49	5,836	11.0	90.3	72.9	64.7	57.0
50-64	15,605	29.4	90.7	75.3	65.9	58.2
65-74	15,816	29.8	87.5	72.8	64.2	56.2
75+	15,887	29.9	79.4	64.0	55.6	47.7
Rectosigmoid	17,984	100.0				
20-49	1,663	9.2	89.6	70.1	61.5	52.8
50-64	5,211	29.0	89.9	74.5	65.0	57.9
65-74	5,654	31.4	87.6	72.7	64.5	57.5
75+	5,456	30.3	80.1	66.9	58.4	50.2
Rectum	35,160	100.0				
20-49	4,173	11.9	90.6	74.0	66.0	58.7
50-64	10,394	29.6	91.1	75.7	66.3	58.3
65-74	10,162	28.9	87.4	72.9	63.9	55.2
75+	10,431	29.7	79.1	62.5	54.1	46.1

Table 4.6: Cancers of the Colon and Rectum: 1-, 3- , and 5-Year Relative Survival Rates (%) by Subsite and Sex, Ages 20+, 12 SEER Areas, 1988-2001

	Relative Survival Rate (%)								
	Diagnosis Year 1988-1991			Diagnosis Year 1992-1996			Diagnosis Year 1997-2001		
Primary Site/Subsite	1-Year	3 -Year	5-Year	1-Year	3 -Year	5-Year	1-Year	3 -Year	5-Year
Colon and rectum	83.0	69.0	62.6	82.9	69.1	62.9	83.9	71.3	65.2
Colon	81.8	68.8	63.6	81.8	68.6	63.3	82.4	70.2	65.0
Cecum	79.2	64.9	60.6	78.9	64.4	60.0	81.0	67.7	62.3
Appendix	82.0	67.7	61.0	86.5	67.4	57.8	85.0	68.9	59.2
Ascending	80.3	69.5	65.1	81.9	69.8	65.4	82.3	70.9	66.8
Hepatic flexure	78.2	66.4	60.0	78.2	66.4	62.6	79.1	66.6	62.9
Transverse	79.3	65.2	61.2	79.0	66.6	61.6	80.6	69.1	63.2
Splenic flexure	78.8	63.7	58.6	79.6	63.6	58.6	81.5	67.0	60.9
Descending	85.4	73.9	66.6	84.6	72.3	64.6	84.6	71.2	66.9
Sigmoid	86.5	73.8	67.9	86.9	74.3	68.0	87.2	76.1	70.7
Overlapping	72.8	60.4	56.1	75.0	60.1	53.9	74.2	60.0	54.8
Colon, NOS	56.1	40.2	35.4	50.9	36.2	31.2	45.7	29.4	20.2
Rectum & rectosigmoid	86.0	69.3	60.2	85.8	70.1	62.0	87.4	73.9	65.5
Rectosigmoid	86.0	69.8	60.8	85.6	70.6	62.3	87.3	73.8	65.3
Rectum	85.9	69.1	59.9	85.8	69.9	61.8	87.5	74.0	65.6

Table 4.7: Cancers of the Colon and Rectum: 1-, 5-, and 10-Year Relative Survival Rates (%) by Subsite and AJCC Stage (5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage											
	Stage 0,I			Stage II			Stage III			Stage IV		
Primary Site/Subsite	1-Yr	5-Yr	10-Yr	1-Yr	5-Yr	10-Yr	1-Yr	5-Yr	10-Yr	1-Yr	5-Yr	10-Yr
Colon and rectum	96.9	92.7	89.0	93.0	79.7	71.8	88.6	58.3	50.5	43.6	6.9	4.8
Colon	96.7	94.8	92.6	93.2	82.7	75.9	87.2	59.1	52.7	41.8	7.0	5.0
Cecum	95.5	94.4	91.4	94.0	85.8	81.0	85.4	56.9	51.7	39.1	6.8	5.1
Appendix	97.4	89.9	83.2	92.6	73.9	63.9	89.2	48.3	37.0	65.9	25.4	16.2
Ascending	95.4	93.0	89.0	94.3	87.5	80.8	84.6	58.8	54.2	36.6	5.9	3.4
Hepatic flexure	94.6	93.2	89.7	91.3	81.0	72.4	83.5	54.8	46.0	31.5	5.5	4.0
Transverse	95.0	89.9	86.3	92.0	83.3	76.4	83.8	56.3	49.2	37.6	7.4	6.2
Splenic flexure	94.2	89.9	87.4	91.3	78.6	70.7	86.9	59.7	49.7	42.7	6.6	5.9
Descending	96.5	92.4	84.9	93.0	81.5	72.8	89.1	58.4	50.2	48.7	7.1	5.3
Sigmoid	98.0	96.8	95.1	93.4	79.4	72.1	91.9	63.3	55.8	51.0	7.5	4.9
Overlapping	93.2	81.6	80.0	94.0	84.9	79.2	85.5	57.0	49.0	31.1	4.9	4.4
Colon, NOS	94.9	90.2	82.5	78.1	57.9	49.7	67.0	40.7	28.9	19.8	2.1	0.8
Rectum and rectosigmoid	97.3	89.5	84.0	92.5	69.7	59.2	92.2	56.4	44.9	49.0	6.9	4.2
Rectosigmoid	97.8	93.4	89.9	93.4	74.3	64.7	92.4	59.4	47.8	52.0	7.6	4.8
Rectum	97.1	88.1	81.6	91.9	66.7	55.2	92.0	54.4	43.0	47.0	6.4	3.7

Table 4.8: Cancers of the Colon and Rectum: 1-, 3- ,5- and 10-Year Relative Survival Rates (%) for AJCC (5th Edition) Stage 0/I Cancers by Extension, Ages 20+, 12 SEER Areas, 1988-2001

Extension- Invasive tumor confined to:	Relative Survival Rate (%)							
	Colon				Rectum and rectosigmoid			
	1-Year	3-Year	5-Year	10-Year	1-Year	3-Year	5-Year	10-Year
Mucosa, NOS	96.6	94.5	93.6	92.9	97.4	92.4	90.0	88.6
Lamina propria*	96.5	95.6	94.2	91.9	98.3	95.3	93.0	89.5
Muscularis mucosae	96.6	95.0	94.1	93.9	98.1	94.9	92.6	85.7
Head of polyp	98.4	98.4	98.2	96.3	99.3	99.3	99.2	86.0
Stalk of polyp	98.8	98.4	96.5	93.8	98.3	95.8	92.6	90.9
Polyp, NOS	96.5	94.9	93.5	91.7	98.5	95.8	92.7	85.8
Submucosa	97.5	97.4	96.2	94.3	98.6	96.7	93.4	89.3
Muscularis propria invaded	97.0	97.0	96.2	92.1	97.9	95.0	89.4	81.3

* Considered Stage 0

Table 4.9: Cancers of the Colon and Rectum: 1-, 3- ,5- and 10-Year Relative Survival Rates (%) for AJCC Stage II (5th Edition) Cancers by Extension, Ages 20+, 12 SEER Areas, 1988-2001

Extension	Relative Survival Rate (%)			
	Stage II Colon Cancers			
	1-Year	3-Year	5-Year	10-Year
Invasion through muscularis propria or muscularis, NOS	95.5	92.5	89.3	81.6
Fat, NOS	93.3	90.8	~	~
Extension to adjacent (connective) tissue	95.0	89.0	84.2	77.5
Invasion of/through serosa	93.4	87.8	82.8	76.6
Invasion of/through serosa with extension to fat, NOS or adjacent tissue	88.5	78.4	71.4	66.7
Greater omentum, spleen, pelvic wall, small intestine	74.9	60.0	55.9	49.8
Abdominal wall, retroperitoneum	72.4	52.1	44.9	39.0
Ureter, kidney	67.1	37.0	26.2	18.0
Uterus, ovary, fallopian tube	75.2	52.8	44.2	38.6
Urinary bladder, adrenal gland, diaphragm, other segments of colon via serosa	76.7	59.6	49.3	43.2
Further contiguous direct extension	60.9	38.5	29.7	26.3
	Stage II - Rectum/Rectosigmoid Cancers			
	1-Year	3-Year	5-Year	10-Year
Invasion through muscularis propria or muscularis, NOS	96.1	89.2	79.4	67.6
Fat, NOS	98.5	90.3	~	~
Extension to adjacent (connective) tissue	94.1	82.5	71.6	61.5
Invasion of/through serosa	92.5	81.5	69.2	60.2
Invasion of/through serosa with extension to fat, NOS or adjacent tissue	92.9	78.2	61.1	48.9
Greater omentum, spleen, pelvic wall, small intestine	77.0	49.3	38.3	28.4
Uterus, ovary, fallopian tube	71.9	41.1	30.7	18.4
Further contiguous direct extension	71.2	35.6	29.4	21.4

~ Statistic not displayed due to less than 25 cases.

Table 4.10: Cancers of the Colon and Rectum: 1-, 3- ,5- and 10-Year Relative Survival Rates (%) by Subsite and Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology (ICD-O code)	Relative Survival Rate (%)							
	Colon				Rectum and Rectosigmoid			
	1-Year	3-Year	5-Year	10-Year	1-Year	3-Year	5-Year	10-Year
Unspecified (8000-8004)	56.2	35.1	31.2	25.6	65.5	52.3	43.6	32.9
Carcinoma, NOS (8010)	57.1	42.8	38.6	30.5	60.6	43.0	32.7	24.8
Undifferentiated carcinoma (8012-8032,8230-8231,8510)	46.7	35.9	33.2	28.4	26.9	10.7	10.7	10.7
Small cell carcinoma (8041-8044)	29.3	18.6	18.6	15.6	49.2	19.1	16.6	~
Other and unspecified carcinoma (8050-8130,8141-8201,8310-8460,8550,8570)	70.5	57.9	48.7	39.2	81.8	62.4	56.3	45.7
Adenocarcinoma, NOS (8140)	80.5	66.2	60.3	54.8	84.9	67.6	57.8	49.2
Adenocarcinoma in adenomatous polyp (8210-8211)	95.9	93.5	91.8	91.0	96.7	90.9	86.6	79.8
Adenocarcinoma in adenomatous polyposis coli (8220-8221)	91.4	81.1	74.0	55.5	78.5	71.1	63.3	63.3
Carcinoid (8240-8246)	80.9	72.8	69.6	65.1	97.0	95.9	94.1	91.8
Papillary adenocarcinoma, NOS (8260)	84.4	76.2	70.0	65.3	89.2	79.2	67.8	59.6
Adenocarcinoma in villous adenoma (8261)	91.1	84.3	80.1	75.0	91.6	82.7	76.0	70.0
Villous adenocarcinoma (8262)	89.5	83.0	81.8	71.2	90.7	78.5	70.6	60.2
Adenocarcinoma in tubulovillous adenoma (8263)	93.7	89.3	86.8	84.1	95.3	89.2	84.8	82.3
Mucinous adenocarcinoma (8470-8480)	81.9	67.3	61.5	54.4	84.1	63.0	52.8	41.6
Mucin producing adenocarcinoma (8481)	78.0	63.0	58.3	51.9	81.1	57.8	47.4	40.9
Signet ring cell carcinoma (8490)	61.5	37.3	28.2	21.3	60.1	33.0	23.9	18.0
Adenosquamous carcinoma (8560)	42.5	27.7	26.7	24.2	66.0	36.5	33.4	30.0
Melanoma (8720-8772)	~	~	~	~	79.9	30.0	22.8	22.8
Other (8930-9100)	66.8	42.5	25.9	~	88.6	78.6	78.6	~

~ Statistic not displayed due to less than 25 cases.

Figure 4.1: Cancer of the Colon: Relative Survival Rates (%) for the Five Most Common Histologic Types by Months Since Diagnosis, Age 20+, 12 SEER Areas, 1988-2001

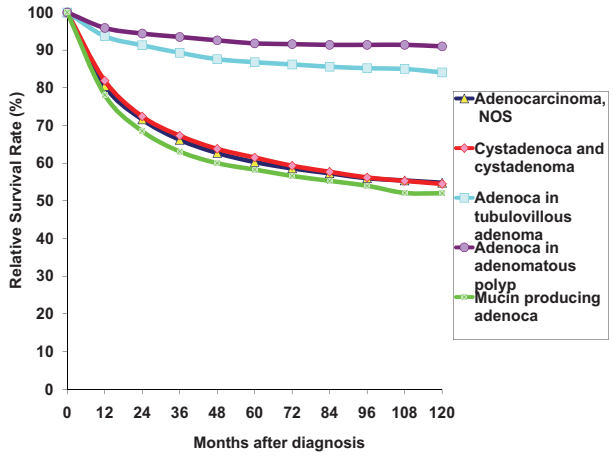
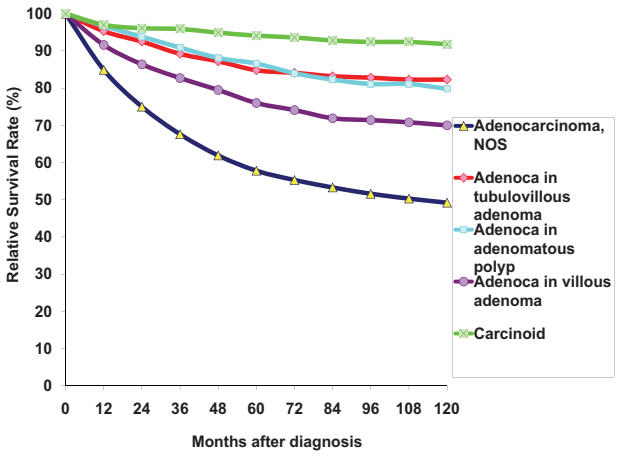


Figure 4.2: Cancer of the Rectum: Relative Survival Rates (%) for the Five Most Common Histologic Types by Months Since Diagnosis, Age 20+, 12 SEER Areas, 1988-2001



exception of cases with appendix cancer whose 5-year relative rate was 25%.

Stage 0/I cancers are those cancers which are clearly confined to the colon, i.e. cancers which have not extended through the wall of the colon or of the rectum. These cancers can be further subdivided into the depth of penetration into the wall based on SEER Extent of Disease (EOD) extension codes. Table 4.8 shows survival rates for Stage 0/I cancers by depth of extension for colon and for rectal cancers separately. For cancers arising in the colon, all categories experienced five-year survival rates of 94% or better, and for cancers of the rectum and rectosigmoid junction, all had survival of 89% or better after five-years. The highest relative survival occurred among those patients whose disease was limited to the head of a polyp, 98% for colon and 99% for rectum. Interestingly, patients whose tumor had extended to the lamina propria (AJCC Stage 0) had no better survival than patients included in Stage 1.

Stage II tumors are tumors which have extended deeper into the wall of the colon or directly extended through the colon wall into adjacent structures but are node negative and have no discontinuous metastases. Table 4.9 shows survival rates by SEER extension codes. Clearly, once the tumor has penetrated the serosa, survival becomes much poorer, with the poorest survival occurring among patients whose tumor has extended to the ureter or kidney.

Table 4.10 shows survival rates for colon and rectal cancers separately by histology. As might be expected, cancers of the rectum arising in a polyp or an adenoma and carcinoid tumors had the best 5-year relative survival 85-90%. The poorest survival rates, i.e. less than 30% survival at 5-years, were experienced by patients with small cell carcinoma, signet ring carcinoma, and adenosquamous carcinoma of the colon. Among patients with rectal cancer, undifferentiated carcinoma, small cell carcinoma, signet ring cell carcinoma, and melanoma histologic groups all had survival rates under 30% at 5-years. Persons with adenocarcinoma not otherwise specified which represented the majority of the cases (69%) had a five-year relative rate of 58-60%.

Ten-year survival curves for the five most common histologies for colon cancers are shown in Figure 4.1 and for rectal cancers in Figure 4.2. For colon cancer patients the best survival was experienced by patients whose cancer arose in either an adenomatous polyp or in a tubulovillous adenoma while the poorest survival was experienced by those with mucin-producing adenocarcinomas. By contrast, for rectal cancers persons with malignant carcinoid tumors had the highest survival while those with non-specific adenocarcinomas had the lowest relative survival.

DISCUSSION

The lack of substantial variation in survival rates by subsites of the colon and rectum is interesting. This is best explained by the fact that each subsite had a similar stage distribution at diagnosis with 50-60% in each group being diagnosed early, Stage 0/I or II. The poorer survival among patients whose subsite could not be determined is probably explained by the fact that many of these patients had multifocal colon cancer, i.e. simultaneous lesions arising in multiple polyposis; or else occurred in patients whose disease was so extensive within the colon at the time of diagnosis that the point of origin could not be determined.

There was no difference in survival between males and females, but the disparity among race groups was once again noted with whites having higher survival rates than blacks for each subsite.

Since most analyses based on stage 0 would include both in situ and confined to the lamina propria, it is interesting that when only the confined to the lamina propria group are shown, the patients had no better survival than those whose cancer arose in a polyp or extended to the submucosa. Further, one component of stage II had poor survival, node negative patients whose tumors had extended from the colon to the kidney and/or ureter.

REFERENCES

1. American Cancer Society, Facts and Figures, 2006, American Cancer Society, Atlanta, Georgia.
2. Fleming ID, Cooper JS, Henson DE, Hutter RVP, Kennedy BJ, Murphy, GP, O'Sullivan, B, Sobin LH and Yarbro, JW (eds) AJCC Cancer Staging Manual, Fifth Edition, Lippincott-Raven, Philadelphia, 1998.

Chapter 5
Cancer of the Anus

Margaret M. Madeleine and Laura M. Newcomer

INTRODUCTION

Anal cancer includes tumors of the anus, anal canal, and anorectum. The anal canal extends from the rectum to the perianal skin and it is lined by a mucous membrane that covers the interior anal sphincter (1, 2). It is a rare disease, with an annual age-adjusted incidence rate of 1.5 per 100,000 people in the U.S. (3). Approximately 4,660 new cases and 660 deaths from anal cancer are expected in the U.S. annually (4). Although both sexes have seen an increase in incidence in recent years, this rise has been more pronounced in men.

Oncogenic human papillomavirus (HPV) types, the same HPV types found to cause cervical cancer, have been detected in the majority of anal tumors (5). Epidemiologic studies suggest that in addition to infection with HPV, smoking is a major risk factor for anal cancer in men and women; also, men who have sex with men are at a particularly increased risk of anal cancer (6-8).

Small tumors of the anal margin not including the anal sphincter are usually treated by wide local incision; however, tumors of the anal canal that involve the anal sphincter or that are too large for excision are treated by radiation or combination chemotherapy and radiation (9). In this report we use U.S. SEER registry data to explore the impact of demographic and tumor characteristics on anal cancer survival.

MATERIALS AND METHODS

Between 1988 and 2001, 6,411 patients with primary invasive anal cancer were diagnosed in the SEER catchment area. The following cases were excluded from the analysis: patients for whom anal cancer was not the first primary cancer, cases identified through autopsy or death certificate only, those with unknown race, cases without active follow-up or alive with no survival time, patients less than 20 years old, cases without microscopic confirmation, and tumors identified as in situ lesions, sarcomas, or carcinoids. After these exclusions, 4,296 adult cases remained for analysis (Table 5.1).

This relative survival analysis focused on demographic descriptors of the patients and tumor characteristics. The demographics of interest included age at diagnosis (20-49, 50-64, 65+), sex, race (white, black), and geographic location. Key tumor characteristics, specifically histology, grade, size, site, and stage, are described in detail below.

Anal cancer histology was identified by using ICD-O-2/ICD-O-3 histology codes as follows: squamous cell cancer

Table 5.1 Cancer of the Anus: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001.

Number Selected/Remaining	Number Excluded	Reason for Exclusion/selection
6,411	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
5,243	1,168	Select first primary only
5,232	11	Exclude death certificate only or at autopsy
5,162	70	Exclude unknown race
5,148	14	Exclude alive with no survival time and children (Ages 0-19)
4,329	819	Exclude in situ cancers
4,302	27	Exclude no or unknown microscopic confirmation
4,296	6	Exclude sarcomas

(coded as 8010-8089), cloacogenic or basaloid tumors (8123-8124), adenocarcinomas (8140-8263 and 8480-8481), melanomas (8720), and other for the remainder of the histologic types. Due to a small number of cases, melanoma of the anus was combined with other for black patients.

The amount of microscopically determined cell differentiation at diagnosis is described as grade 1 or well-differentiated tumors, grade 2 or moderately well-differentiated tumors, grade 3 or poorly differentiated tumors, and grade 4 or undifferentiated or anaplastic tumors. Information on grade was available for 69% of the tumors.

Tumor size is based on the length in the greatest dimension and was categorized as ≤ 2 cm, 2-5 cm, and >5 cm. When the site of the anal cancer was specified, it was described as occurring in the anal canal, as an overlapping lesion of the rectum, anus, and anal canal, or as in the cloacogenic zone. Cancers of the perianal skin are classified with skin cancers and are not included in this analysis.

The stage of disease is compiled from information on the size the tumor, extent of invasion, and lymph node involvement according to guidelines of the American Joint Committee on Cancer and the International Union Against Cancer, 5th edition (1, 2). Localized stage is defined as an invasive neoplasm confined entirely to the anal site. Regional stage is defined as a neoplasm that has extended either beyond the anal site or into regional lymph nodes. Distant stage is defined as a neoplasm that has spread to parts of the body remote from the primary tumor. Unstaged cancers lack sufficient information to assign stage. Staging for localized, regional, and distant was available for 87% of the anal cancer tumors.

RESULTS

Demographic characteristics: Effect of age, gender, race, and geographic location

Table 5.2 shows the distribution of cases by race, sex and age, and the specific 5-year relative survival rates by these characteristics. The overall relative survival for men with anal cancer was 58% compared with 69% for women. Among women, the percent surviving decreased with increasing age: 76% for women 20-49 years old, 72% for women 50-64 years old, and 64% for women over 64 years old. In contrast, the worst prognosis for men was for the youngest age group, with better prognosis for middle-aged men. It should be noted that the case distribution among black men is younger, with 49% of black males falling in the 20-49 age group, compared to 28% of white males.

Relative survival was also markedly different by race, with 66% of white patients surviving at 5 years post di-

Table 5.2: Cancer of the Anus: Number and Distribution of Cases and 5-Year Relative Survival Rates (%) by Race, Age (20+) and Sex,12 SEER Areas, 1988-2001.

	Sex								
	Total			Male			Female		
Race/Age Group (Years)	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent
All Races	4,296	100.0	64.0	1,824	100.0	57.9	2,472	100.0	68.5
20-49	1,031	24.0	63.8	569	31.2	54.0	462	18.7	75.7
50-64	1,294	30.1	67.6	617	33.8	63.3	677	27.4	71.5
65+	1,971	45.9	61.7	638	35.0	56.2	1,333	53.9	64.1
White	3,636	100.0	65.7	1,486	100.0	60.2	2,150	100.0	69.5
20-49	800	22.0	66.7	418	28.1	56.4	382	17.8	78.0
50-64	1,090	30.0	68.8	515	34.7	65.7	575	26.7	71.5
65+	1,746	48.0	63.2	553	37.2	57.8	1,193	55.5	65.5
Black	471	100.0	52.5	248	100.0	47.0	223	100.0	58.5
20-49	183	38.9	52.6	122	49.2	46.3	61	27.4	65.3
50-64	156	33.1	57.8	77	31.0	49.3	79	35.4	65.2
65+	132	28.0	44.0	49	19.8	43.1	83	37.2	43.7

Table 5.3: Cancer of the Anus: Number and Distribution of Cases and 5-Year Relative Survival Rates (%) by Race, Histology and Sex, Ages 20+, 12 SEER Areas, 1988-2001.

Race/Histology (ICD-O code)	Sex								
	Total			Male			Female		
	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent
All Races	4,296	100.0	64.0	1,824	100.0	57.9	2,472	100.0	68.5
Squamous Cell (8010-8089)	2,594	60.4	67.0	1,129	61.9	60.3	1,465	59.3	72.3
Cloacogenic or Basaloid (8123-8124)	771	17.9	70.2	229	12.6	62.4	542	21.9	73.2
Adenocarcinoma (8140-8263,8480-8481)	757	17.6	53.4	387	21.2	52.9	370	15.0	54.2
Melanoma (8720)	75	1.7	26.9	23	1.3	~	52	2.1	22.0
Other	99	2.3	37.3	56	3.1	29.3	43	1.7	45.9
White	3,636	100.0	65.7	1,486	100.0	60.2	2,150	100.0	69.5
Squamous Cell (8010-8089)	2,226	61.2	68.1	946	63.7	62.1	1,280	59.5	72.6
Cloacogenic or Basaloid (8123-8124)	689	18.9	71.5	199	13.4	64.4	490	22.8	74.2
Adenocarcinoma (8140-8263,8480-8481)	580	16.0	55.6	280	18.8	54.9	300	14.0	56.4
Melanoma (8720)	64	1.8	27.4	19	1.3	~	45	2.1	20.2
Other	77	2.1	40.9	42	2.8	32.5	35	1.6	48.7
Black	471	100.0	52.5	248	100.0	47.0	223	100.0	58.5
Squamous Cell (8010-8089)	296	62.8	57.3	155	62.5	50.3	141	63.2	65.2
Cloacogenic or Basaloid (8123-8124)	57	12.1	53.8	24	9.7	~	33	14.8	57.7
Adenocarcinoma (8140-8263,8480-8481)	104	22.1	40.8	60	24.2	43.4	44	19.7	35.5
Other	14	2.9	~	9	3.6	~	5	2.2	~

~Statistic not displayed due to less than 25 cases.

agnosis compared to 53% for black patients. Black patients had worse survival than white patients in every age group; markedly worse survival was reported for black men and women in the oldest age group.

Geographic differences as represented by the 12 contributing tumor registries were not assessable due to small numbers of patients by registry.

Tumor characteristics: effect of primary site, histology, size, stage, and differentiation

Tumors of the anus, anal canal, cloacogenic zone, and overlapping lesions of the rectum and anus are reported separately. The distribution of cases by site of diagnosis was 38.8% anus, 29.5% anal canal, 7.8% cloacogenic zone, and 23.9% overlapping lesions. Overall, 5-year relative survival did not differ substantially by site, ranging from a high of 68% for anal canal tumors to a low of 56% for overlapping lesions.

The largest proportion of invasive anal cancer cases had squamous cell histology (60.4%), followed by cloacogenic (or basaloid) tumors (17.9%), adenocarcinomas (17.6%), melanomas (1.7%), and other histologies (2.3%). The distribution of histologic types varies with sex, with more adenocarcinomas among males and more cloacogenic cancers among females. The 5-year relative survival by histology was 67% for squamous cell cancers, 70% for cloacogenic cancers, 53% for adenocarcinomas, 27% for melanoma, and 37% for other histologies. Survival rates were higher for females than for males especially for squamous cell carcinomas and cloacogenic carcinomas (Table 5.3).

Figure 5.1: Cancer of the Anus: 5-Year Relative Survival Rate (%) by Tumor Size and Subsite, Ages 20+, 12 SEER Areas, 1988-2001

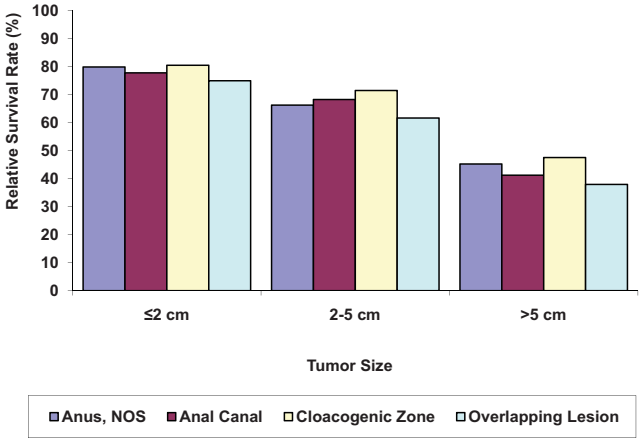


Figure 5.2: Cancer of the Anus: 5-Year Relative Survival Rate (%) by Grade and Sex, Ages 20+, 12 SEER Areas, 1988-2001

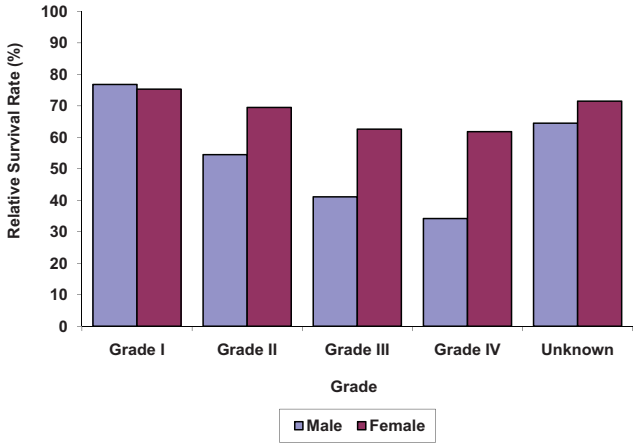


Figure 5.3: Cancer of the Anus: 5-Year Relative Survival (%) by Grade and Race, Ages 20+, 12 SEER Areas, 1988-2001

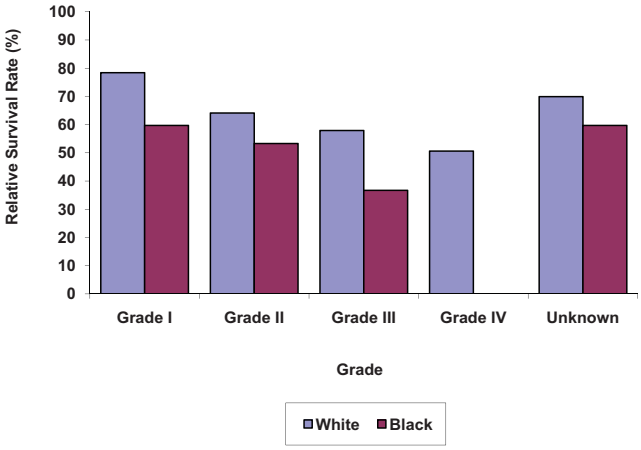
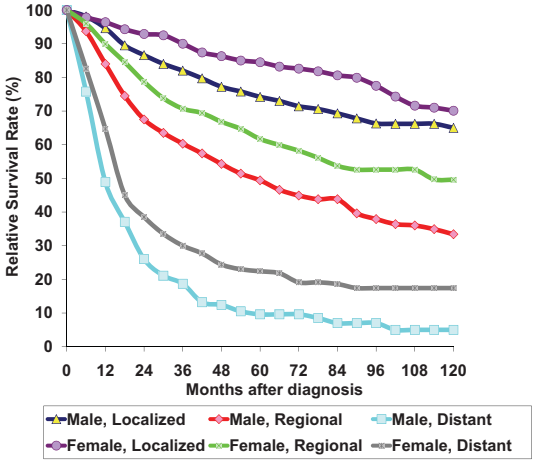


Figure 5.4: Cancer of the Anus: Relative Survival Rate (%) by Sex and Stage, Ages 20+, 12 SEER Areas, 1988-2001



For anus, NOS, the relative survival rate at 5 years post diagnosis decreased with increasing size: 80% for ≤ 2 cm, 66% for 2-5 cm, and 45% for >5 cm for all races and both genders. Figure 5.1 shows relative survival by site and size of tumor, with less than 50% survival for tumors larger than 5 cm for each site.

The amount of cell differentiation or grade of disease at diagnosis was unknown for 31% of the tumors, but tumors with unknown grade had a relatively high survival rate (69%). For tumors with a known grade, the 5-year relative survival ranged from 77% for well-differentiated grade I lesions, 62% for moderately differentiated grade II lesions to a low of 55% for poorly differentiated, undifferentiated or anaplastic grade III and IV lesions. Men had slightly better prognosis for well-differentiated tumors only, and women had better prognosis for the other grades especially for grade III/IV (Figure 5.2, Table 5.4).

The 5-year relative survival by grade also differed strongly by race, with consistently lower survival for every grade of tumors for black as compared to white patients (Figure 5.3). There were fewer than 25 black patients with grade IV tumors and therefore, the survival rate was not calculated for this group.

Table 5.4: Cancer of the Anus: Number and Distribution of Cases and 5-Year Relative Survival Rates (%) by Race, Grade and Sex, Ages 20+, 12 SEER Areas, 1988-2001

	Sex								
	Total			Male			Female		
Race/Grade	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent
Total	4,296	100.0	64.0	1,824	100.0	57.9	2,472	100.0	68.5
Well differentiated (I)	459	10.7	76.5	257	14.1	76.8	202	8.2	75.3
Moderately differentiated (2)	1,355	31.5	62.4	634	34.8	54.5	721	29.2	69.5
Poorly/undifferentiated (3/4)	1,159	27.0	55.1	396	21.7	40.7	763	30.9	62.5
Unknown	1,323	30.8	68.7	537	29.4	64.5	786	31.8	71.5
White	3,636	100.0	65.7	1,486	100.0	60.2	2,150	100.0	69.5
Well differentiated (I)	388	10.7	78.4	217	14.6	77.3	171	8.0	78.8
Moderately differentiated (2)	1,124	30.9	64.1	506	34.1	56.8	618	28.7	70.1
Poorly/undifferentiated (3/4)	998	27.4	57.4	326	21.9	45.4	672	31.3	63.2
Unknown	1,126	31.0	69.9	437	29.4	65.8	689	32.0	72.5
Black	471	100.0	52.5	248	100.0	47.0	223	100.0	58.5
Well differentiated (I)	48	10.2	59.7	31	12.5	62.5	17	7.6	~
Moderately differentiated (2)	171	36.3	53.3	93	37.5	45.6	78	35.0	62.0
Poorly/undifferentiated (3/4)	115	24.4	37.7	52	21.0	20.2	63	28.3	51.8
Unknown	137	29.1	59.7	72	29.0	60.8	65	29.1	58.7

~Statistic not displayed due to less than 25 cases.

Stage of disease was the most important single predictor of survival. Overall, local disease had an 80% 5-year relative survival rate, regional disease had 57% survival rate, and distant disease had only a 17% survival rate. About 13% of the tumors were unstaged, and their survival rate was 55% (Table 5.5).

Stage was an important prognostic factor for men and women of all races, with women having better survival at every stage of disease (Figure 5.4). Among patients with distant disease, 5-year relative survival was only 10% for men compared to 22% for women. Stage and sex together predict outcome at 5 years that is similar to the outcome at 10 years post-diagnosis (data not shown).

DISCUSSION

The major prognostic factors are stage, sex (females have better prognosis at every stage of disease), and race. Blacks have worse prognosis than whites overall, and black men have the worst prognosis at all tumor stages. There were also differences in prognosis predicted by two components of stage: tumor size and differentiation. Primary tumors 2 centimeters or less in size have a better prognosis than larger tumors, and well-differentiated tumors are more favorable than poorly differentiated tumors.

The worse prognosis for men less than 50 years old was seen consistently across races, stage of disease, anal cancer sites, grades, and tumor size. It may be that this worse survival is due to the toll of HIV/AIDS on young men. Although anal cancer is not an AIDS-defining illness, there is an increased risk for anal dysplasia and cancer among men who have sex with men that is increased more strongly among HIV positive men who have sex with men (10). This increased risk has led to higher cytologic surveillance of this group, which may have affected the survival trends for anal cancer.

Table 5.5: Cancer of the Anus: Number and Distribution of Cases and 5-Year Relative Survival Rates (%) by Race, Historic Stage and Sex, Ages 20+, 12 SEER Areas, 1988-2001

	Sex								
	Total			Male			Female		
Race/Historic Stage	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent
All Races	4,296	100.0	64.0	1,824	100.0	57.9	2,472	100.0	68.5
Localized	2,031	47.3	79.9	899	49.3	74.2	1,132	45.8	84.5
Regional	1,342	31.2	56.6	550	30.2	49.4	792	32.0	61.7
Distant	384	8.9	16.8	173	9.5	9.6	211	8.5	22.4
Unstaged	539	12.5	54.7	202	11.1	47.6	337	13.6	58.7
White	3,636	100.0	65.7	1,486	100.0	60.2	2,150	100.0	69.5
Localized	1,735	47.7	81.3	748	50.3	75.6	987	45.9	85.6
Regional	1,130	31.1	58.4	436	29.3	51.7	694	32.3	62.8
Distant	296	8.1	17.4	128	8.6	9.5	168	7.8	23.0
Unstaged	475	13.1	54.7	174	11.7	50.1	301	14.0	57.1
Black	471	100.0	52.5	248	100.0	47.0	223	100.0	58.5
Localized	198	42.0	66.9	108	43.5	63.3	90	40.4	70.3
Regional	150	31.8	51.9	81	32.7	46.7	69	30.9	58.3
Distant	73	15.5	17.2	37	14.9	11.9	36	16.1	21.9
Unstaged	50	10.6	45.1	22	8.9	~	28	12.6	66.9

~Statistic not displayed due to less than 25 cases.

REFERENCES

1. Anal canal. In: American Joint Committee on Cancer: AJCC Cancer Staging Manual. Philadelphia, Pa: Lippincott-Raven Publishers, 5th ed., 1997, pp 91-95.
2. Anal canal. In: Sobin LH, Wittekind C, eds.: TNM: Classification of Malignant Tumours. New York, NY: Wiley-Liss, Inc., 5th ed., 1997, pp 70-73.
3. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Eisner MP, Horner MJ, Howlader N, Hayat M, Hankey BF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site, 2006.
4. Cancer Facts and Figures 2006, American Cancer Society, Inc., 2006.
5. Carter JJ, Madeleine MM, Shera K, Schwartz SM, Cushing-Haugen KL, Wipf GC, Daling JR, McDougall JK, Galloway DA. Human papillomavirus 16 and 18 L1 serology compared across anogenital cancer sites. Cancer Res. 2001:61;1934-1940.
6. Daling J, Weiss N, Hislop G, et al. Sexual practices, sexually transmitted diseases and the incidence of anal cancer. N Engl J Med 1987;317:973-977.
7. Daling J, Sherman K, Hislop G, et al. Smoking and the risk of anogenital cancer. Am J Epidemiol 1992;135:180-189.
8. Palefsky J, Holly E, Gonzales J, Berline J, Ahn DK, Greenspan J. Detection of human papillomavirus DNA in anal intraepithelial neoplasia and anal cancer. Cancer Res 1991;51:1014-1019.
9. Ryan DP, Compton CC, Mayer RJ: Carcinoma of the anal canal. N Engl J Med 342 (11): 792-800, 2000.
10. Palefsky JM, Holly EA, Hogeboom CJ, Raltson ML, DaCosta MM, Botts R, Berry JM, Jay N, Darragh TM. Virologic, immunologic, and clinical parameters in the incidence and progression of anal squamous intraepithelial lesions in HIV-positive and HIV-Negative Homosexual Men. J AIDS Human Retrovirology 1998:17:314-319.

Chapter 6
Cancers of the Liver and Biliary Tract

Charles Key and Angela L.W. Meisner

INTRODUCTION

In the 14 year period, 1988-2001, the SEER Program recorded 22,065 cancers of the liver and intrahepatic bile ducts, 5,723 gallbladder cancers, 2,474 cancers of the ampulla of Vater and 3,908 other biliary cancers (mostly cancers of the extrahepatic bile duct).

The tables and text in this chapter address some of the patient characteristics (Sex, Race and Age) and tumor characteristics (Tumor Stage, Grade, Size, Subsite Location and Histology) that may be associated with differences in patients' prognosis and outcome.

The text primarily cites 5-year relative survival as the primary outcome measure because of its wide general use. However, for cancers associated with poor survival, readers may find the tabulations of 1-, 2-, and 3-year relative survivals to be more informative.

MATERIALS AND METHODS

The NCI contracts with medically-oriented, nonprofit institutions located in specific geographic areas to obtain data on all cancers diagnosed in residents of the SEER geographic areas. SEER collects data on all invasive and in situ cancers except basal cell and squamous cell carcinomas of the skin (of non-genital anatomic sites) and in situ carcinomas of the uterine cervix. SEER actively follows all previously diagnosed patients on an annual basis to obtain vital status allowing the calculation of observed and relative survival rates.

This analysis is based on data from 12 SEER geographic areas which collectively cover about 14% of the total US population. The areas are the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Michigan; Atlanta, Georgia; San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; and 10 counties in rural Georgia. Los Angeles contributed data for diagnosis years 1992 to 2001, all other areas for 1988-2001.

Table 6.1: Liver and Biliary Tract Cancer: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

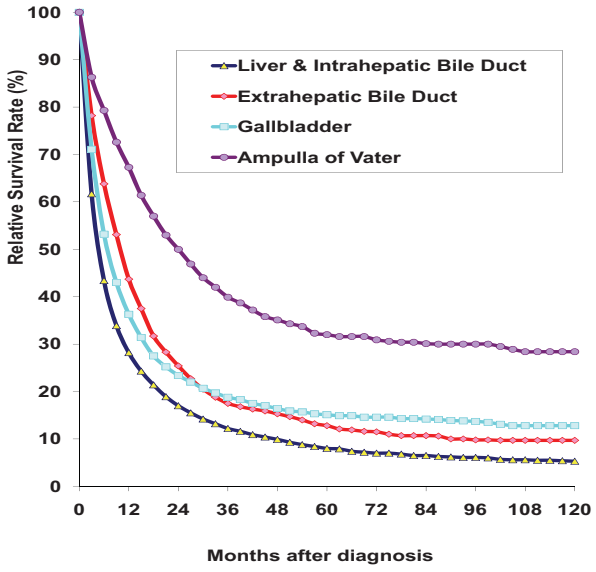
Liver & Intrahepatic Bile Duct		Gallbladder		Other Biliary		Ampulla of Vater		
Number Selected/ Remaining	Number Excluded	Number Selected/ Remaining	Number Excluded	Number Selected/ Remaining	Number Excluded	Number Selected/ Remaining	Number Excluded	Reason for Exclusion/selection
22,065	0	5,723	0	3,908	0	2,474	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
19,717	2,348	5,041	682	3,344	564	2,050	424	Select first primary only
18,747	970	4,962	79	3,271	73	2,039	11	Exclude death certificate only or at autopsy
18,657	90	4,945	17	3,266	5	2,032	7	Exclude unknown race and alive with no survival time
18,364	293	4,755	190	3,239	27	1,995	37	Exclude children (000-019) and in situ cancers
13,622	4,742	4,458	297	2,660	579	1,873	122	Exclude no or unknown microscopic confirmation
13,409	213	4,392	66	2,640	20	1,832	41	Exclude sarcomas (including stromal 8930-8939) and carcinoids

The following cases were excluded from this survival analysis: patients for whom liver or biliary tract cancer was not the first primary, cases diagnosed at autopsy or by death certificate only, persons of unknown race, alive with no recorded survival time, patients less than 20 years old, and cases without microscopic confirmation. Since some of the exclusions had very small cell sizes, some of the reasons for exclusion were combined. Sarcomas, lymphomas and carcinoids are excluded here from this analysis which focuses primarily on the cancers of epithelial origin (carcinomas). Remaining cases available for analysis are as follows: 13,409 liver & intrahepatic bile duct cancers; 4,392 gallbladder cancers; 2,640 other biliary (mostly extrahepatic bile duct) cancers, and 1,832 cancers of the ampulla of Vater (Table 6.1). Carcinoids are shown separately in the relative survival tables by histologic type but they are not included in the total cases.

Survival analysis is based on relative survival rates calculated by the life-table (actuarial) method. Relative survival, defined as observed survival in the cohort divided by expected survival in the cohort, adjusts for the expected mortality that the cohort would experience from other causes of death. Expected survival is based on decennial life tables for the United States in 1990.

The staging definitions utilized in this chapter are SEER historic stage: localized – confined to the primary site; regional – spread to regional lymph nodes or by direct extension beyond the primary; distant – metastatic spread.

Figure 6.1: Relative Survival Rates (%) by Primary Site (Liver & Intrahepatic Bile Duct, Extrahepatic Bile Duct, Gallbladder, Ampulla of Vater) and Months after Diagnosis, Ages 20+, 12 SEER Areas. 1988-2001



RESULTS

Cancers of the liver & intrahepatic bile duct, gallbladder and extrahepatic bile duct all have low survival rates. The survival rates decrease rapidly during the first 3 years after diagnosis and then the rates plateau after about 5-years (Figure 6.1). The survival rates for ampulla of Vater are much higher than the other 3 cancers.

Cancers of the Liver and Intrahepatic Ducts

Sex, Race and Age

Among 13,409 adult cases of liver or intrahepatic bile duct cancer, almost twice as many cases occurred in males (69%) over females (31%). However, relative survival rates are consistently at least one percentage point higher for females

Figure 6.2: Cancer of the Liver and Intrahepatic Bile Duct: 5-Year Relative Survival Rates by Sex, Race, Age, Historic Stage, Grade, Primary Site, Tumor Size, and Histology, Ages 20+, 12 SEER Areas, 1988-2001

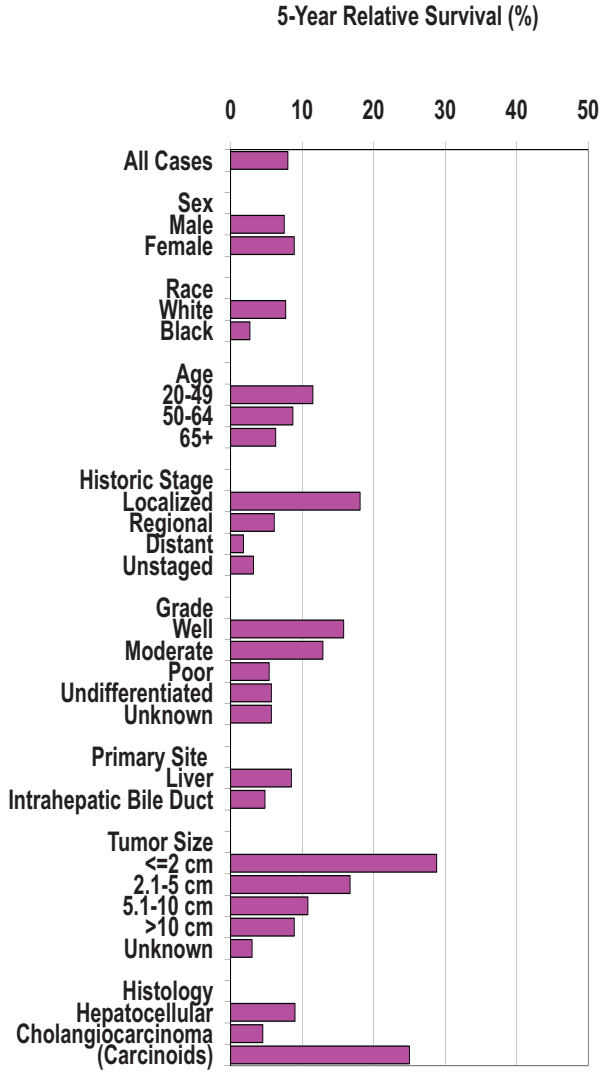


Table 6.2: Cancer of the Liver and Intrahepatic Bile Duct (excluding carcinoids): Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates by Sex, Race, Age, Historic Stage, Grade, Primary Site and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

Characteristics	Cases	Percent	Median Survival (Months)	Relative Survival Rates (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases	13,409	100.0	4.6	28.2	17.0	12.2	8.0	6.1	5.3
Sex									
Male	9,224	68.8	4.3	27.2	16.3	11.7	7.5	5.9	4.7
Female	4,185	31.2	5.3	30.5	18.7	13.3	8.9	6.5	6.3
Race									
White	8,619	64.3	4.3	26.8	16.2	11.6	7.7	5.9	5.3
Black	1,497	11.2	3.5	22.1	11.4	7.6	2.7	1.5	1.5
Other	3,293	24.6	6.0	-	-	-	-	-	-
Age									
20-49	2,030	15.1	5.5	32.3	20.7	15.6	11.5	9.0	8.3
50-64	4,235	31.6	5.0	30.8	19.0	14.3	8.7	6.5	5.3
65+	7,144	53.3	4.1	25.4	14.7	9.9	6.3	4.6	4.0
Historic Stage									
Localized	4,021	30.0	9.8	46.9	33.0	25.4	18.1	14.4	12.5
Regional	3,487	26.0	4.8	27.5	14.1	9.8	6.1	4.2	3.3
Distant	3,299	24.6	2.8	12.3	5.4	3.2	1.8	1.1	1.1
Unstaged	2,602	19.4	3.7	20.5	11.3	6.9	3.2	2.2	2.0
Grade									
Well	1,717	12.8	10.3	47.5	32.0	24.3	15.8	13.1	10.7
Moderate	1,860	13.9	7.0	38.0	24.9	19.2	12.9	9.0	7.5
Poor	1,904	14.2	3.4	20.7	11.2	7.3	5.4	3.0	2.7
Undifferentiated	273	2.0	2.7	18.2	9.9	6.6	5.7	5.7	3.4
Unknown	7,655	57.1	4.0	23.7	13.5	9.3	5.7	4.4	4.0
Primary Site									
Liver	11,598	86.5	4.4	28.2	17.5	12.9	8.5	6.5	5.6
Intrahepatic Bile Duct	1,811	13.5	5.6	27.9	14.5	8.5	4.8	3.4	3.2
Tumor Size									
<=2 cm	489	3.6	18.8	59.0	47.0	39.4	28.8	23.8	17.3
2.1-5 cm	2,077	15.5	10.2	47.5	33.3	24.7	16.7	13.0	10.9
5.1-10 cm	2,386	17.8	6.4	36.2	21.2	15.5	10.8	7.9	6.4
>10 cm	1,236	9.2	5.4	30.1	16.7	11.8	8.9	7.3	6.8
Unknown	7,221	53.9	3.2	17.5	9.1	5.9	3.0	2.0	1.8

! Not enough intervals to produce rate.
- Not calculated.

(31% at 1 year, 19% at 2 years, 13% at 3 years, 9% at 5 years, 7% at 8 years and 6% at 10 years) than males (27%, 16%, 12%, 8%, 6% and 5% for 1-,2-,3-,5-,8-, and 10-year relative survival rates, respectively).

Other races had a higher median survival with 6 months, followed by whites with 4 months and then blacks with 3 months. Younger age had better relative survival rates, with a 5 year relative survival rate of 12% amongst 20-49 year olds, compared to 6% amongst those patients 65 and over (Table 6.2, Figure 6.2)).

Tumor Stage, Grade and Size

Localized tumor stage, well differentiated tumor grade and moderate differentiated tumor grade were associated with 5-year relative survival rates greater than 10%. Tumor size less or equal to 2 cm had a 5-year relative survival rate of 29%. Tumor size was unknown for more than half of the

cases and the 5-year relative survival rates was only 3% (Table 6.2, Figure 6.2)

Liver Subsite and Histology

Histologic classification separates hepatocellular carcinomas (liver cell origin) from adenocarcinomas arising from ductal or glandular structures (grouped here as cholangiocarcinomas, probably arising from intrahepatic bile ducts).

The histologic designation seems preferable to the subsite designation for distinguishing between these two major liver cancer types because many adenocarcinomas (cholangiocarcinomas) are included under the liver site code. Hepatocellular carcinomas were four times more common and 5-year relative survival rates were double that of cholangiocarcinomas (9% vs. 5% respectively), although median survival time for both is less than 5 months (Table 6.3).

The 77 cases of primary carcinoid tumors arising in the liver had a median survival time of about 12 months and 25% relative survival at 5 years.

Cancers of the Gallbladder

Sex, Race and Age

Cases of cancer of the gallbladder were three times more common in females than males, with survival about equal. More than 70% of patients were diagnosed at 65 years of age or older. Their median survival time (5.5 months) was about half of that characterized in the younger age groups (10 and 9 months for ages 20-49 and 50-64 years, respectively). At five years, the relative survival for ages 50-64 years (15%) was more comparable to the older (14%) rather than the younger age group (22%; Table 6.4) Five year relative survival rates were similar for whites and blacks (14 and 13%; Table 6.4).

Tumor Stage, Grade and Size

The 5-year relative survival rate was over 40% for cases with localized tumor stage. Well differentiated tumors and tumors ≤ 2 cm had 5-year relative survival rates greater than 30%, whilst distant stage, poor differentiation, and tumors > 10 cm had 5-year relative survival rate between 0-7% (Table 6.4, Figure 6.3).

Table 6.3: Cancer of the Liver and Intrahepatic Bile Duct: Histologic Distribution and Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Histology, Ages 20+,12 SEER Areas, 1988-2001

Histology	Cases	Percent	Median Survival (Months)	Relative Survival Rates (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases excluding carcinoids	13,409	100.0	4.6	28.2	17.0	12.2	8.0	6.1	5.3
Carcinomas excluding carcinoids 8010-8572	13,290	99.1	4.6	28.3	17.1	12.3	8.0	6.1	5.3
Hepatocellular carcinoma 8170-8171	9,981	74.4	4.6	29.3	18.3	13.5	9.0	7.0	6.0
Cholangiocarcinoma 8050,8140-8141, 8160-8161,8260, 8440,8480-8500, 8550,8560,8570-8572	2,463	18.4	4.6	24.6	12.9	7.9	4.5	2.9	2.6
Other specified carcinoma	453	3.4	7.4	38.4	23.1	15.4	9.8	6.9	6.9
Unspecified carcinoma 8010-8034	393	2.9	2.8	15.2	6.5	4.3	2.4	1.3	!
Hepatoblastoma 8970	<5	0.0	~	~	~	~	~	~	~
Unspecified cancer 8000-8004	112	0.8	2.6	16.9	8.2	8.2	5.9	4.4	!
Other specified cancer 9064,9364,9500	<5	0.0	~	~	~	~	~	~	~
Carcinoids 8240-8246	77	-	12.8	55.0	40.9	35.5	25.0	7.3	!

! Not enough intervals to produce rate.
- Not calculated.
~ Statistic not displayed due to less than 25 cases.

Gallbladder Histology

The histologic type was almost all adenocarcinomas (91%). The relative survival rate was similar between squamous cell carcinomas and adenocarcinomas (Table 6.5).

Other Biliary Cancers

Sex, Race and Age

Slightly more cases occurred in males (52%) than females and they had better 5-year relative survival rates (14% vs. 10%). Whites had better 5-year relative survival rates of 13% compared with blacks (8%) and there was an age gradient with patients between 20-49 years old having 5-year survival rates three times of those 65 and older, 24% and 8%, respectively (Table 6.6, Figure 6.4).

Tumor Stage, Grade, and Size

Five-year survival was over 20% for localized tumors, well differentiated tumors, and tumors ≤2 cm. Tumor grade was very prognostic. For example, the gradient of relative survival at 2 years ranged from 40% for well differentiated tumors down to 10% for undifferentiated tumors. The tumor size was unknown for most of these cancers, but there was a survival differential for those with known tumor size from 30% at 5 years for small tumors and only 11% for 5.1-10 cm tumors (Table 6.6, Figure 6.4).

Table 6.4: Cancer of the Gallbladder (excluding carcinoids): Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates by Sex, Race, Age, Historic Stage, Grade, and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

Characteristics	Cases	Percent	Median Survival (Months)	Relative Survival Rates (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases	4,392	100.0	6.5	36.3	23.4	18.9	15.1	13.7	12.8
Sex									
Male	1,131	25.8	6.2	35.5	23.2	18.0	14.9	12.8	12.0
Female	3,261	74.2	6.6	36.6	23.5	19.2	15.1	13.9	13.0
Race									
White	3,511	79.9	6.4	35.9	22.9	18.5	14.3	13.1	12.2
Black	329	7.5	5.5	32.0	19.1	14.6	13.1	11.7	9.7
Other	552	12.6	8.4	-	-	-	-	-	-
Age									
20-49	287	6.5	10.4	46.8	30.9	27.1	22.3	18.8	17.8
50-64	954	21.7	9.1	41.3	25.2	19.1	15.0	12.7	12.7
65+	3,151	71.7	5.5	33.8	22.1	17.9	14.2	13.4	12.0
Historic Stage									
Localized	943	21.5	24.8	71.3	55.7	48.7	41.7	39.5	36.8
Regional	1,752	39.9	8.4	41.4	24.5	18.3	13.6	11.4	10.8
Distant	1,578	35.9	3.2	10.4	2.8	2.0	1.2	0.9	0.9
Unstaged	119	2.7	6.0	30.6	26.3	17.8	13.1	10.9	10.6
Grade									
Well	492	11.2	21.0	62.8	50.5	41.8	33.7	31.5	30.0
Moderate	1,288	29.3	9.9	46.3	31.4	24.6	19.7	17.2	16.5
Poor	1,526	34.7	4.9	25.6	12.0	9.4	6.9	5.4	5.3
Undifferentiated	120	2.7	3.6	24.1	13.7	11.7	7.9	7.9	3.2
Unknown	966	22.0	4.7	28.1	18.3	15.4	12.8	12.8	11.3
Tumor Size									
<=2 cm	449	10.2	18.3	62.5	46.6	40.1	34.7	31.9	29.5
2.1-5 cm	627	14.3	10.3	48.1	29.2	24.2	19.0	16.2	14.5
5.1-10 cm	271	6.2	4.8	26.4	12.6	11.4	10.7	10.7	10.7
>10 cm	40	0.9	3.8	18.0	2.7	2.7	0.0	!	!
Unknown	3,005	68.4	5.5	31.1	20.0	15.5	12.0	10.9	10.2

! Not enough intervals to produce rate.
- Not calculated.

Other Biliary Subsite and Histology

Most of the cancers described under 'Other biliary' were in the extrahepatic bile duct (86%). Almost all of the cases were carcinomas and of these the majority were adenocarcinoma (Table 6.7). There were very few carcinoids in other biliary (Table 6.7).

Cancers of the Ampulla of Vater

Cancers of the Ampulla of Vater showed better survival than the other cancers in this chapter (Figure 6.1). But these cancers are less common, only 8% of the liver and biliary tract cancers. Five-year relative survival rates by tumor and patient characteristics are summarized in Figure 6.5.

Sex, Race, and Age

There were slightly more males (55%) than females (45%) and males had slightly better survival rates after 2 years after diagnosis (Table 6.8). Survival rates are higher for white patients than black patients but the survival advantage narrowed over time since diagnosis. At 2 years after diagnosis, 51% of white patients survived compared to only 38% for blacks, but at 10-years after diagnosis, the rates were 29 and 26%, respectively.

Tumor Stage, Grade and Size

There were survival gradients for stage, grade, and size. Five-year relative survival was over 50% for localized tumors and well differentiated tumors. Survival rates were

Figure 6.3: Cancer of the Gallbladder: 5-Year Relative Survival Rates by Sex, Race, Age, Historic Stage, Grade, Tumor Size, and Histology, Ages 20+, 12 SEER Areas, 1988-2001

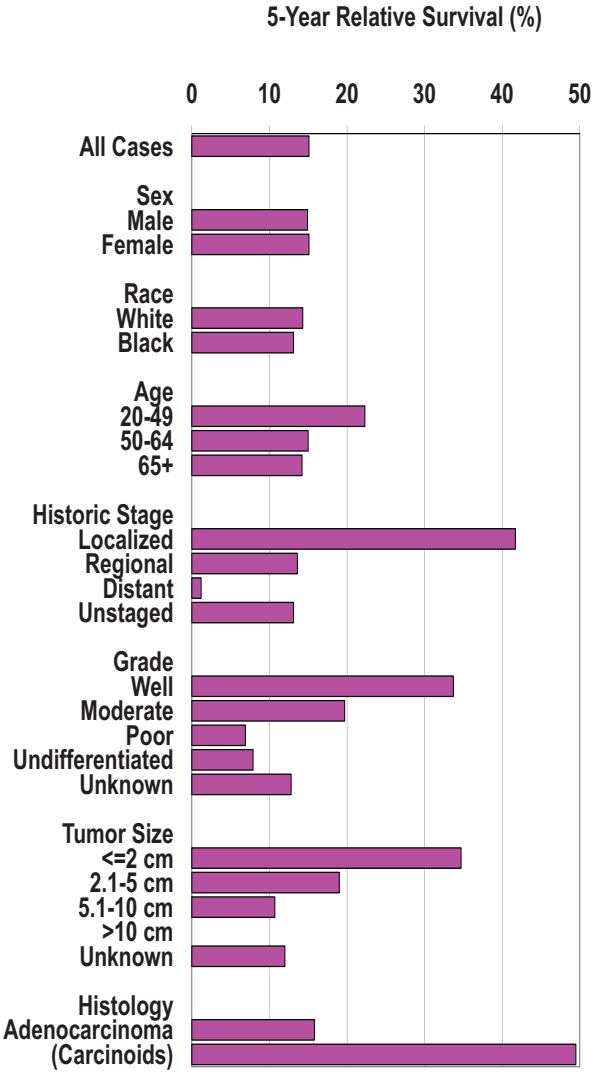


Figure 6.4: Cancer of Other Biliary Sites: 5-Year Relative Survival Rates by Sex, Race, Age, Historic Stage, Grade, Primary Site, Tumor Size, and Histology, Ages 20+, 12 SEER Areas, 1988-2001

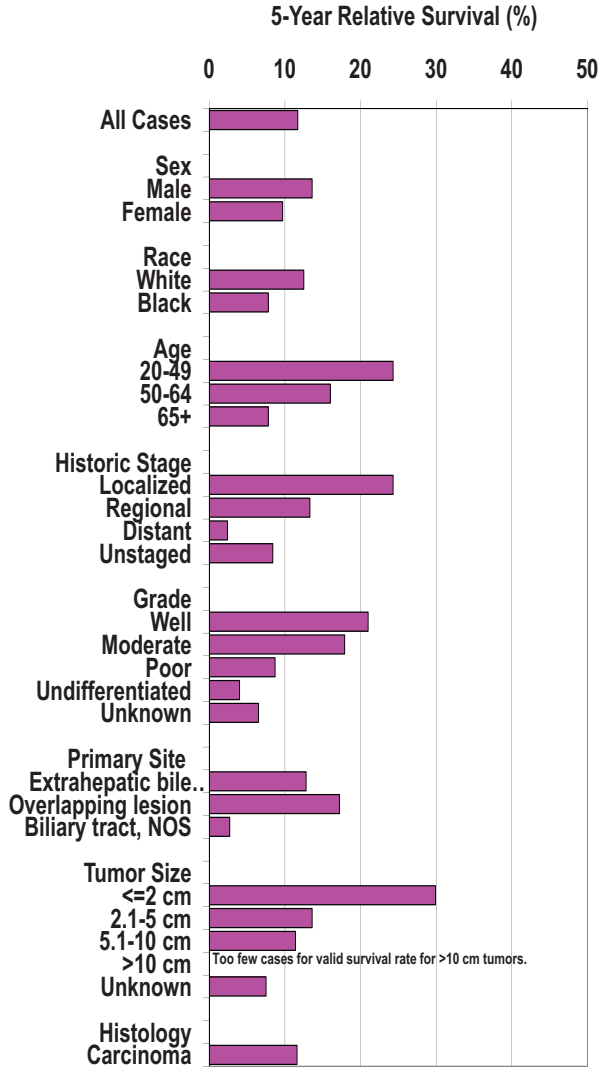


Table 6.5: Cancer of the Gallbladder: Distribution and Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology/ ICD-O code	Cases	Percent	Median Survival (Months)	Relative Survival Rates (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases excluding carcinoids	4,392	100.0	6.5	36.3	23.4	18.9	15.1	13.7	12.8
Carcinoma excluding carcinoids 8010-8231,8247-8572	4,369	99.5	6.5	36.4	23.4	18.9	15.1	13.7	12.8
Squamous-cell carcinoma 8050-8076	78	1.8	4.6	22.0	16.6	16.6	16.5	15.6	11.4
Adenocarcinoma 8140-8141,8191-8231, 8260-8263,8310,8430, 8480-8490,8560, 8570-8572	4,000	91.1	6.9	37.7	24.5	19.7	15.8	14.2	13.2
Other specified carcinomas	81	1.8	8.4	40.5	9.6	5.9	5.9	!	!
Unspecified carcinoma 8010-8034	210	4.8	3.0	14.9	9.7	7.1	4.9	4.9	4.9
Unspecified Cancer 8000-8004	18	0.4	~	~	~	~	~	~	~
Other specified cancer 8720,8940	5	0.1	~	~	~	~	~	~	~
Carcinoids 8240-8246	46	-	21.4	62.9	49.9	49.9	49.5	49.5	49.5

! Not enough intervals to produce rate.
- Not calculated.
~ Statistic not displayed due to less than 25 cases.

very poor for those with distant disease with the 3-year survival rate of less than 1%. However, less than 10% of the patients had distant spread at the time of diagnosis (Table 6.8).

Histology

Nearly all of the tumors were carcinomas and most of those were adenocarcinomas. There were few carcinoids but the survival rates for those with carcinoids was much higher even after only 1-year, 76%, compared to those with carcinomas (67%) (Table 6.9).

DISCUSSION

Overall survival rates were similar for liver, gallbladder, and other biliary cancers. Survival rates were higher for cancer of the ampulla of Vater, behaving more like those of the small intestine (1).

REFERENCES

1. Key C and Meisner A. Cancers of the Esophagus, Stomach, and Small Intestine. *In* Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner, M-J (editors). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program. NIH Pub. No. 07-6215, 2007.

Table 6.6: Other Biliary Cancer (excluding ampulla & carcinoids): Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates by Sex, Race, Age, Historic Stage, Grade, Primary Site and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

Characteristics	Cases	Percent	Median Survival (Months)	Relative Survival Rates (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases	2,640	100.0	8.4	40.6	23.3	16.0	11.7	8.9	8.6
Sex									
Male	1,376	52.1	9.4	44.2	25.3	17.1	13.6	10.7	10.7
Female	1,264	47.9	7.3	36.7	21.2	14.9	9.7	7.0	6.3
Race									
White	2,082	78.9	8.3	40.2	23.5	16.5	12.5	10.1	10.0
Black	177	6.7	6.4	38.1	20.6	12.7	7.8	3.5	!
Other	381	14.4	9.1	-	-	-	-	-	-
Age									
20-49	217	8.2	15.1	53.8	34.4	28.2	24.3	16.8	16.8
50-64	632	23.9	12.3	51.2	31.3	23.0	16.0	12.3	11.9
65+	1,791	67.8	6.6	35.0	18.7	11.5	7.8	5.3	4.7
Historic Stage									
Localized	445	16.9	15.2	58.2	41.3	33.2	24.3	19.5	19.5
Regional	1,100	41.7	12.0	51.6	29.1	19.3	13.3	9.7	8.8
Distant	645	24.4	3.4	14.3	4.9	2.5	2.4	1.1	1.1
Unstaged	450	17.0	6.8	33.7	17.3	9.8	8.4	6.1	6.1
Grade									
Well	315	11.9	16.2	59.1	40.2	32.4	21.0	14.9	12.8
Moderate	675	25.6	12.7	53.8	32.7	22.9	17.9	12.5	12.5
Poor	509	19.3	7.8	37.5	20.8	13.3	8.7	5.3	4.3
Undifferentiated	43	1.6	5.4	33.9	10.1	7.7	4.0	4.0	!
Unknown	1,098	41.6	5.3	28.6	14.0	8.1	6.5	6.1	6.1
Primary Site									
Extrahepatic bile duct	2,270	86.0	9.4	43.7	25.4	17.5	12.8	9.8	9.7
Overlapping lesion	42	1.6	8.3	45.3	30.6	22.8	17.2	14.1	7.6
Biliary tract, NOS	328	12.4	3.1	18.5	7.7	4.6	2.7	1.3	1.3
Tumor Size									
<=2 cm	373	14.1	20.1	67.6	48.6	37.3	29.9	26.2	25.1
2.1-5 cm	356	13.5	11.1	47.4	25.6	17.1	13.6	8.9	7.9
5.1-10 cm	58	2.2	8.5	41.0	11.4	11.4	11.4	4.5	4.5
>10 cm	9	0.3	~	~	~	~	~	~	~
Unknown	1,844	69.8	6.4	33.7	18.0	11.5	7.5	5.2	5.1

! Not enough intervals to produce rate.
- Not calculated.
~ Statistic not displayed due to less than 25 cases.

Table 6.7: Other Biliary Cancer (excluding Ampulla): Distribution and Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology/ICD-O Code	Cases	Percent	Median Survival (Months)	Relative Survival Rates (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases excluding carcinoids	2,640	100.0	8.4	40.6	23.3	16.0	11.7	8.9	8.6
Carcinoma excluding carcinoids: 8010-8572	2,596	98.3	8.4	40.6	23.2	16.0	11.6	8.7	8.4
Squamous-cell carcinoma 8050-8076	23	0.9	~	~	~	~	~	~	~
Adenocarcinoma 8140-8141,8191-8231, 8260-8263,8310,8430, 8480-8490,8560, 8570-8572	2,039	77.2	8.5	41.0	23.4	16.7	11.8	9.0	8.6
Other specified carcinomas	401	15.2	9.2	42.5	24.7	14.0	11.6	7.4	7.4
Unspecified carcinoma 8010-8034	133	5.0	4.9	30.4	14.3	6.7	4.0	4.0	4.0
Unspecified Cancer: 8000-8004	44	1.7	6.3	38.3	32.0	18.8	18.8	18.8	!
Carcinoids: 8340-8246	16	-	~	~	~	~	~	~	~

! Not enough intervals to produce rate.
- Not calculated.
~ Statistic not displayed due to less than 25 cases.

Table 6.8: Cancer of the Ampulla of Vater (excluding Carcinoids): Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates by Sex, Race, Age, Historic Stage, Grade, Primary Site, and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

Characteristics	Cases	Percent	Median Survival (Months)	Relative Survival Rates (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases	1,832	100.0	20.3	67.3	50.0	39.9	32.0	30.0	28.4
Sex									
Male	1,002	54.7	20.8	67.1	50.6	41.7	33.6	32.2	29.6
Female	830	45.3	19.7	67.5	49.2	37.7	29.9	27.1	26.8
Race									
White	1,458	79.6	20.6	67.1	51.0	40.6	32.3	30.6	29.1
Black	107	5.8	14.3	58.7	37.7	32.3	29.7	25.7	25.5
Other	267	14.6	22.4	-	-	-	-	-	-
Age									
20-49	171	9.3	34.6	81.2	61.5	49.4	41.0	36.4	31.5
50-64	445	24.3	34.5	79.5	60.2	50.7	36.1	31.2	28.2
65+	1,216	66.4	15.3	60.5	44.0	33.7	28.4	27.4	27.0
Historic Stage									
Localized	396	21.6	34.3	76.2	64.7	57.1	51.7	49.7	47.7
Regional	1,068	58.3	24.9	74.5	55.2	43.0	32.7	30.5	28.3
Distant	165	9.0	5.5	26.4	5.5	0.8	!	!	!
Unstaged	203	11.1	8.6	44.2	27.1	17.7	8.6	4.0	!
Grade									
Well	289	15.8	43.2	78.4	67.1	60.1	52.2	42.8	38.4
Moderate	748	40.8	24.1	72.6	54.5	42.3	35.5	34.9	32.1
Poor	425	23.2	16.8	63.1	42.5	31.0	19.9	19.6	19.3
Undifferentiated	24	1.3	~	~	~	~	~	~	~
Unknown	346	18.9	12.2	53.4	36.2	29.7	22.6	20.7	20.7
Tumor Size									
<=2 cm	570	31.1	35.9	82.4	65.5	54.8	43.2	41.2	38.8
2.1-5 cm	477	26.0	24.0	71.2	53.3	41.1	34.0	31.2	29.5
5.1-10 cm	47	2.6	19.5	70.0	45.2	31.3	24.0	14.6	!
>10 cm	<5	-	~	~	~	~	~	~	~
Unknown	735	40.1	11.9	52.7	35.5	27.2	20.9	18.4	17.9

! Not enough intervals to produce rate.
- Not calculated.
~ Statistic not displayed due to less than 25 cases.

Table 6.9: Cancer of the Ampulla of Vater: Distribution and Median Survival Time and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology/ ICD-O Code	Cases	Percent	Median Survival (Months)	Relative Survival Rates (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases excluding carcinoids	1,832	100.0	20.3	67.3	50.0	39.9	32.0	30.0	28.4
Carcinoma excluding carcinoids: 8010-8231,8247-8572	1,823	99.5	20.4	67.4	50.0	39.9	32.0	30.1	28.7
Squamous-cell carcinoma 8050-8076	9	0.5	~	~	~	~	~	~	~
Adenocarcinoma 8140-8141,8191-8231, 8260-8263,8310,8430, 8480-8490,8560, 8570-8572	1,686	92.0	21.3	68.3	51.1	40.7	33.0	31.2	29.6
Other specified carcinomas	49	2.7	19.1	70.0	41.5	33.0	12.0	!	!
Unspecified carcinoma: 8010-8034	79	4.3	10.5	46.6	31.9	27.5	17.0	16.1	16.1
Unspecified Cancer: 8000-8004	9	0.5	~	~	~	~	~	~	~
Carcinoids: 8240-8246	35	-	98.2	76.0	71.3	65.3	59.0	59.0	59.0

! Not enough intervals to produce rate.
- Not calculated.
~ Statistic not displayed due to less than 25 cases.

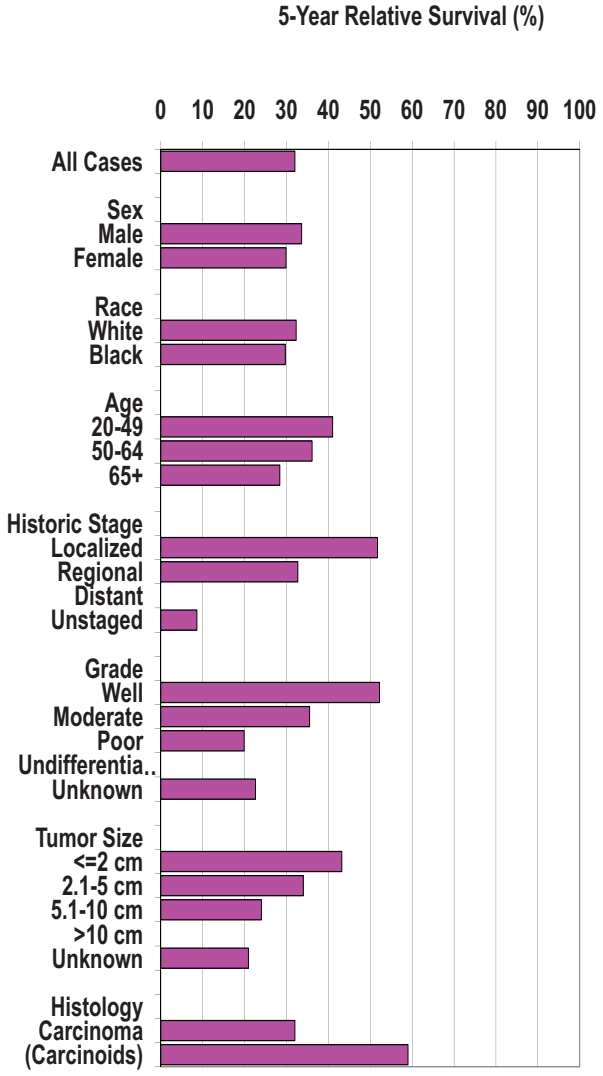


Figure 6.5 (at right): Cancer of the Ampulla of Vater: 5-Year Relative Survival Rates by Sex, Race, Age, Historic Stage, Grade, Tumor Size, and Histology, Ages 20+, 12 SEER Areas, 1988-2001

Chapter 7
Cancer of the Pancreas

Charles Key

INTRODUCTION

Cancer of the pancreas is one of the most rapidly fatal of all cancers, and most cases are first recognized at a far advanced clinical stage. The American Cancer Society estimates that there will be 33,730 new cases of pancreatic cancer in 2006 and 32,300 deaths. Only cancers of the lung, colon, and breast cause more deaths than pancreatic cancer each year. (1) Currently there are few definitive recommendations for prevention and early detection. Cigarette smoking is probably the most consistently identified causal risk factor. Treatment is often limited to supportive care, palliation and pain control.

The lifetime risk of being diagnosed with pancreatic cancer is 1.29% for white males and 1.18% for black males. For white and black females the lifetime risks are 1.25% and 1.46% respectively (2). Because survival rates are low and survival times are short, the lifetime risks of dying from pancreatic cancer are only slightly lower than the risks of being diagnosed.

The pancreas is a complex organ, with exocrine components (acinar glands and ducts) that produce and deliver digestive enzymes and fluids to the small intestine. Endocrine components (islets of Langerhans) secrete hormones (including insulin) into the blood stream. Both components can give rise to malignant neoplasms, but the vast majority of all pancreatic cancers are exocrine adenocarcinomas arising from cells of the pancreatic ducts. Acinar cells comprise at least 80% of the cells of the pancreas (3), however, acinar cell carcinomas were less than 1% of the total pancreatic cancers in this series.

Endocrine carcinomas of the pancreas represent about 3% of all pancreatic cancers. They tend to occur at younger ages and have a better prognosis.

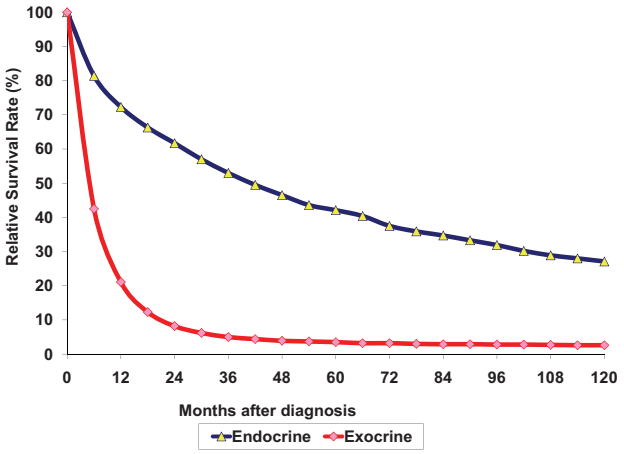
MATERIALS AND METHODS

Between 1988 and 2001, 46,968 cases of cancer of the pancreas were diagnosed within the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). Please see the introductory chapter of this monograph for a full explanation of materials and methods. Table 7.1 shows the number of cases excluded, by reason, leaving 29,729 microscopically confirmed cases of cancer of the pancreas diagnosed between 1988 and 2001 in patients 20 years of age and older. The largest number of exclusions was for no microscopic confirmation. The AJCC Cancer Staging Manual (sixth edition) (4) coding scheme excludes endocrine and carcinoid tumors. Subsites were defined according to the International Classification of Diseases for Oncology, 2nd edition (ICD-O-2) (5).

Table 7.1: Cancer of the Pancreas: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/selection
46,968	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
40,241	6,727	Select first primary only
38,681	1,560	Exclude death certificate only or at autopsy
38,625	56	Exclude unknown race
38,586	39	Exclude alive with no survival time
38,553	33	Exclude children (Ages 0-19)
38,500	53	Exclude in situ cancers
29,765	8,735	Exclude no or unknown microscopic confirmation
29,729	36	Exclude sarcomas

Figure 7.1: Cancer of the Pancreas: Relative Survival Rates (%) by Histologic Subtype, Ages 20+, 12 SEER Areas, 1988-2001



The analysis described herein addresses demographic factors, histologic classification, extent of disease, and stage classification as they affect survival of patients with pancreatic cancer.

RESULTS

Cancers of the pancreas rank at or near the bottom of the list of all cancers in relation to patient survival following diagnosis. For the pancreatic cancers that arose from the exocrine pancreas, the 5-year relative survival rate was 4%. Cancers arising from endocrine elements of the pancreas were much less common and the 5-year survival rate was 42% (Figure 7.1.).

Sixty-month (5-year) relative survival rates were 5% for the histologically confirmed cancers analyzed in this report and were similar to the survival for those that weren't microscopically confirmed.

Anatomic Subsite

Table 7.2 outlines invasive cancers of the pancreas by subsite within the pancreas. More than half of the cancers were located in the head of the pancreas and 8.5% and 10.1% were in the body and tail respectively. Very few (0.2%) were in the Islets of Langerhans and pancreatic duct (0.6%). The remaining, nearly 30% of the cancers, were not assigned to a specific pancreatic region. Cancers of the head of the pancreas had a modest survival advantage over the body of pancreas at 12 months after diagnosis, but the advantage disappeared after 5 years after diagnosis.

Race and Sex

Overall survival rates were 23% at one year following diagnosis, and declined to 7%, 5%, and 4% at 3, 5, 10 years, respectively (Table 7.3). Twelve-month survival rates were poorer among blacks compared to whites, but at 36, 60 and 120 months following diagnosis, survival was fairly uniform across categories of race and sex.

Age Group

More than three fourths of cancers of the pancreas were diagnosed in patients over 60 years of age, whereas less than 2% of cases were diagnosed in adults less than 40 years of age. (Table 7.4) Survival rates were lowest for patients over age 60 and were higher for the younger patients who tend to have relatively greater proportions of the less lethal endocrine and neuroendocrine tumors. All age groups experienced dramatic overall decreases in survival as time since diagnosis increased.

Table 7.2: Cancer of the Pancreas: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Primary Site, Ages 20+, 12 SEER Areas, 1988-2001

Primary Site	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	29,729	100.0	22.8	10.0	6.7	4.8	3.9	3.6
Head of Pancreas	15,440	51.9	27.2	11.6	7.3	5.1	4.1	3.7
Body of Pancreas	2,525	8.5	19.0	7.8	5.7	4.8	4.2	3.7
Tail of Pancreas	2,995	10.1	19.0	11.3	8.9	7.2	6.4	6.0
Pancreatic Duct	189	0.6	49.7	28.2	19.8	15.4	8.2	8.2
Islets of Langerhans	50	0.2	79.2	68.0	54.9	47.8	22.1	22.1
Other Specified Parts of Pancreas	111	0.4	25.9	12.5	9.4	9.4	!	!
Overlapping Lesion of Pancreas	2,277	7.7	17.5	6.4	4.4	3.2	2.3	2.2
Pancreas, NOS*	6,142	20.7	15.7	6.7	4.4	2.9	2.2	1.8

! Not enough intervals to produce rates.
* NOS: Not Otherwise Specified

Table 7.3: Cancer of the Pancreas: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Race/Sex	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Races	29,729	100.0	22.8	10.0	6.7	4.8	3.9	3.6
Male	15,015	50.5	22.1	9.7	6.5	4.6	3.6	3.1
Female	14,714	49.5	23.4	10.4	6.9	5.1	4.3	4.0
White	23,937	80.5	23.2	10.1	6.7	4.9	3.9	3.5
Male	12,169	40.9	22.8	9.8	6.7	4.8	3.7	3.2
Female	11,768	39.6	23.5	10.3	6.7	4.9	4.1	3.8
Black	3,471	11.7	19.2	8.7	5.5	3.7	3.4	3.3
Male	1,665	5.6	17.3	7.5	4.9	2.9	2.6	2.1
Female	1,806	6.1	21.0	9.8	6.0	4.3	4.1	4.1

Histologic Classification

Cancers of the pancreas are aggregated into histologic categories and listed in decreasing order of frequency in Table 7.5 by the endocrine vs. exocrine pancreas. About 97% were carcinomas of the exocrine pancreas with overall survival rates of 21%, 5%, 4%, and 3% at 1, 3, 5, 10 years, respectively. The exocrine carcinomas with the best prognosis were cystadenocarcinomas and acinar cell carcinomas, but together these histologic categories accounted for less than 2% of the cases. Most of the exocrine tumors were adenocarcinomas not otherwise specified with a 5-year relative survival rate of only 2%.

One-year relative survival rates were higher for islet cell carcinomas, neuroendocrine carcinomas and carcinoid tumors; however, these histologic types only comprised 1.7%, 1.4% and 0.2% of all cancers of the pancreas.

Histology and Age

The most frequent histologic types of cancers of the pancreas are tabulated by age group in Table 7.6; the histologic types are listed in descending order according to their relative percentages. Above age 80, almost all of the cancers arose from the exocrine pancreas, whereas at 20-29 years of age the percentage was only 59%.

Extent of Disease

Tables 7.7 through 7.9 present survival by extent of disease (EOD) by the following classifications defined in the SEER Extent of Disease Codes and Coding Instructions: tumor size, extension, and lymph node involvement (6). As expected, survival rates declined as extent of disease increased.

For the majority of tumors of the pancreas, tumor size was unknown or not stated (53%) (Table 7.7). Survival was best for cancers that were 2.0 cm or less at the time of diagnosis, but above 2 cm, the relation of tumor size to outcome was inconsistent (data not shown). Distant

Table 7.4: Cancer of the Pancreas: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Age (20+), SEER 1988-2001

Age (Years)	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total (20+)	29,729	100.0	22.8	10.0	6.7	4.8	3.9	3.6
20-29	69	0.2	71.1	55.8	49.2	43.6	41.6	35.2
30-39	472	1.6	44.8	29.4	25.3	19.5	17.3	15.8
40-49	2,010	6.8	31.8	17.1	12.7	9.8	7.0	6.0
50-59	4,792	16.1	28.5	12.9	9.0	6.5	4.9	4.2
60-69	8,430	28.4	23.6	10.1	6.2	4.0	3.1	2.7
70-79	9,650	32.5	19.8	7.7	4.7	3.1	2.3	2.1
80+	4,306	14.5	12.9	4.7	2.6	1.8	1.6	1.2

Table 7.5: Cancer of the Pancreas: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, 10-Year Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology	ICD-O Code	Cases	Percent	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	8000-9970	29,729	100.0	22.8	10.0	6.7	4.8	3.9	3.6
Cancers of the Endocrine Pancreas	8150-8155, 8240-8246	975	3.3	72.3	61.7	53.0	42.1	31.9	27.1
Islet Cell Carcinoma	8150-8155	494	1.7	80.7	70.0	59.3	47.7	37.8	32.5
Neuroendocrine Carcinoma	8246	411	1.4	61.5	50.3	43.7	32.2	20.9	18.4
Carcinoid Tumor	8240-8245	70	0.2	76.3	68.7	61.8	55.1	43.2	25.8
Cancers of the Exocrine Pancreas	8000-8149, 8156-8239, 8247-9970	28,754	96.7	21.1	8.2	5.0	3.5	2.8	2.6
Adenocarcinoma, NOS*	8140-8149	20,829	70.1	19.2	6.5	3.6	2.3	1.7	1.5
Carcinoma, NOS*	8010-8011	2,404	8.1	17.5	6.9	4.2	3.1	2.3	2.1
Mucin-Producing Adenocarcinoma	8480-8481	1,814	6.1	21.5	9.6	6.7	4.6	3.5	2.5
Infiltrating Duct Carcinoma	8500-8503	1,820	6.1	40.1	18.8	11.5	7.1	6.1	5.9
Malignant Neoplasm, NOS*	8000-8004	512	1.7	19.5	10.5	8.6	6.5	5.5	5.1
Cystadenocarcinoma	8440-8479	243	0.8	64.7	52.7	48.4	47.3	44.6	43.0
Carcinoma, Undifferentiated	8020-8039, 8230-8231	200	0.7	12.5	8.0	6.9	5.1	5.1	5.1
Adenosquamous Carcinoma	8560-8570	186	0.6	16.7	6.9	4.0	3.3	2.6	1.5
Papillary Adenocarcinoma	8050-8260	138	0.5	35.0	19.8	15.8	13.8	13.8	10.6
Signet Ring Cell Carcinoma	8490	155	0.5	17.5	9.7	3.3	2.3	!	!
Large Cell Carcinoma	8012	121	0.4	7.7	1.8	!	!	!	!
Small Cell Carcinoma	8040-8045	98	0.3	24.5	9.4	5.6	2.9	1.7	1.7
Squamous Cell Carcinoma	8051-8082	75	0.3	15.1	7.9	6.4	6.4	6.4	6.4
Acinar Cell Carcinoma	8550	76	0.3	61.4	44.5	33.7	28.3	26.6	24.4
Other Histologies		83	0.3	39.9	24.9	21.9	13.6	11.5	11.5

* NOS: Not Otherwise Specified
! Not enough intervals to produce rate.

metastasis at the time of diagnosis was documented in nearly half of the histologically confirmed cases (Table 7.8). Additionally, for the majority of cancers of the pancreas, lymph node involvement was unknown or not stated (Table 7.9).

AJCC Stage Classification (6th Edition)

Survival by AJCC stage classifications (6th Edition) (4) for carcinomas of the exocrine pancreas is presented in Table 7.10. The majority of cancers of the pancreas were diagnosed at Stage IV (49.5%) or the stage of disease was unknown (18.8%); whereas very few cancers of the pancreas were diagnosed in early stages: Stage IA and Stage IB comprise only 0.7% and 2.7% of diagnoses, respectively.

Figure 7.2 illustrates relative survival rate curves for AJCC Stages IA – IV (6th Edition). The unstaged cases, which represent about one-fifth of the total, most closely match the Stage III group. Table 7.11 shows the components of stage based on SEER Extent of Disease (EOD) codes for Tumor Size, Extension, and Lymph Node Involvement.

DISCUSSION

Survival rates for cancers of the pancreas are very poor. The relative survival rate for all cases was only 23% at one year with dramatic decreases shown at 3 years (7%), 5 years (5%) and 10 years (4%). The majority of cancers of the pancreas were adenocarcinomas of the exocrine pancreas that occurred in patients 60 years of age and older. Malignant endocrine tumors arising from the islets of Langerhans, neuroendocrine carcinomas and carcinoid tumors had relatively better survival rates (48%, 32%, and 55%, respectively at 5 years).

Most cancers of the pancreas were diagnosed in late stages of disease. Frequently, information was incomplete re-

Table 7.6: Cancer of the Pancreas: Histologic Type Distribution by Age (20+), 12 SEER Areas, 1988-2001

Histology	Age (Years)								
	Total (20+)		20-29	30-39	40-49	50-59	60-69	70-79	80+
	Cases	Percent	Cases	Cases	Cases	Cases	Cases	Cases	Cases
Total	29,729	100.0	69	472	2,010	4,792	8,430	9,650	4,306
Cancers of the Endocrine Pancreas	975	3.3	28	92	171	213	226	195	50
Islet Cell Carcinoma	494	1.7	14	54	93	110	119	93	11
Neuroendocrine Carcinoma	411	1.4	13	29	68	91	93	87	30
Carcinoid Tumor	70	0.2	<5	9	10	12	14	15	9
Cancers of the Exocrine Pancreas	28,754	96.7	41	380	1,839	4,579	8,204	9,455	4,256
Adenocarcinoma, NOS*	20,829	70.1	19	246	1,275	3,329	6,075	6,860	3,025
Carcinoma, NOS*	2,404	8.1	<5	34	142	334	573	826	493
Mucin-Producing Adenocarcinoma	1,814	6.1	<5	24	147	299	548	577	217
Infiltrating Duct Carcinoma	1,820	6.1	<5	22	122	345	545	607	177
Malignant Neoplasm, NOS*	512	1.7	5	9	27	52	108	170	141
Cystadenocarcinoma	243	0.8	<5	15	31	38	53	72	32
Carcinoma, Undifferentiated	200	0.7	<5	6	17	40	49	62	25
Adenosquamous Carcinoma	186	0.6	0	<5	17	30	45	65	26
Papillary Adenocarcinoma	138	0.5	5	6	9	16	32	42	28
Signet Ring Cell Carcinoma	155	0.5	0	<5	14	30	41	46	22
Large Cell Carcinoma	121	0.4	0	<5	13	21	32	36	16
Small Cell Carcinoma	98	0.3	<5	<5	7	12	26	30	20
Squamous Cell Carcinoma	75	0.3	0	<5	<5	6	29	25	10
Acinar Cell Carcinoma	76	0.3	0	5	8	11	23	16	13
Other Histologies	83	0.3	<5	<5	6	16	25	21	11

* NOS: Not Otherwise Specified

garding tumor size and lymph node involvement, but evidence of distant metastasis permitted the cases to be classified as Stage IV.

Pancreatic cancers present huge challenges for future research across the entire cancer continuum (cause and prevention; screening and early detection; imaging and diagnosis; investigational therapeutics; standard treatment and management; quality of life; pain management and other end of life issues).

REFERENCES

1. American Cancer Society. Cancer facts & figures 2006, The American Cancer Society, Atlanta, (GA), 2006.
2. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Eisner MP, Horner MJ, Howlader N, Hayat M, Hankey BF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site, 2006.
3. Solicia E, Capella C, Kloppel G. Tumors of the pancreas. In: Atlas of tumor pathology, 3rd series, fascicle 20. Washington (DC): Armed Forces Institute of Pathology, 1995.
4. Greene FL, Page DL, Fleming ID, Fritz AG, Balch CM, Haller DG, Morrow M (eds). AJCC Cancer Staging Manual, Sixth edition. American Joint Committee on Cancer. New York: Springer 2002.
5. International Classification of Diseases for Oncology, 2nd ed. Geneva: World Health Organization, 1990.
6. SEER extent of disease – codes and coding instructions, 2nd ed, Cancer Statistics Branch, Surveillance Program, Division of Cancer Prevention and Control, National Cancer Institute, National Institutes of Health, NIH Publication 92-2313, June 1992.

Table 7.7: Cancer of the Pancreas: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

Tumor Size	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	29,729	100.0	22.8	10.0	6.7	4.8	3.9	3.6
0 - 2 cm	1,404	4.7	45.7	26.1	20.0	14.9	12.7	12.0
> 2 cm	12,696	42.7	26.7	12.6	8.6	6.4	5.2	4.7
Unknown	15,629	52.6	17.5	6.5	4.0	2.7	2.1	1.9

Table 7.8: Cancer of the Pancreas: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Extension, Ages 20+, 12 SEER Areas, 1988-2001

Extension (Code)	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	29,729	100.0	22.8	10.0	6.7	4.8	3.9	3.6
Confined to Pancreas (10-30)	3,011	10.1	44.8	26.8	20.2	17.7	16.5	16.3
Limited Extension (40-52)	4,769	16.0	41.5	19.0	12.6	8.5	6.8	6.0
Further Extension (54-80)	4,234	14.2	28.0	9.4	5.0	3.2	2.2	1.9
Metastasis (85)	14,468	48.7	9.9	3.9	2.6	1.7	0.9	0.6
Unknown (99)	3,247	10.9	25.4	9.7	6.0	3.9	3.5	3.1

Table 7.9: Cancer of the Pancreas: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Lymph Node Involvement, Ages 20+, 12 SEER Areas, 1988-2001

Nodal Status (Code)	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	29,729	100.0	22.8	10.0	6.7	4.8	3.9	3.6
No Positive Nodes (0)	6,720	22.6	35.9	18.7	13.5	11.1	9.7	8.9
Positive Regional Nodes (1)	5,747	19.3	31.5	14.1	9.1	6.1	4.4	4.3
Positive Distant Nodes (7)	929	3.1	14.0	3.8	1.2	1.2	0.8	0.8
Positive Nodes, NOS (8)	158	0.5	17.6	7.7	4.3	4.3	3.7	2.7
Unknown (9)	16,175	54.4	14.7	5.3	3.3	2.0	1.5	1.2

Figure 7.2: Carcinomas of the Exocrine Pancreas: Relative Survival Rates (%) by AJCC Stage, 6th Edition, Ages 20+, 12 SEER Areas, 1988-2001

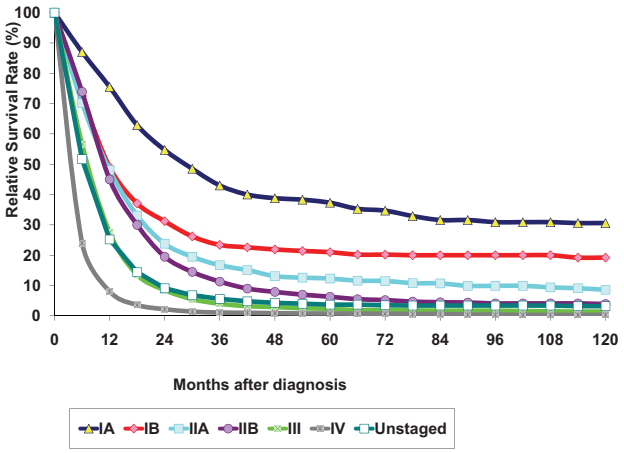


Table 7.10: Carcinomas of the Exocrine Pancreas: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (6th Edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	28,754	100.0	21.1	8.2	5.0	3.5	2.8	2.6
IA (T1, N0, M0)	201	0.7	75.5	54.7	43.0	37.3	30.9	30.6
IB (T2, N0, M0)	788	2.7	49.1	31.2	23.4	21.0	20.0	19.2
IIA (T3, N0, M0)	1,617	5.6	48.1	23.8	16.7	12.3	9.9	8.6
IIB (T1-3, N1, M0)	2,472	8.6	45.0	19.5	11.3	6.3	4.1	3.9
III (T4, any N, M0)	4,043	14.1	27.5	8.5	4.0	2.3	1.7	1.4
IV (any T, any N, M1)	14,230	49.5	8.1	2.2	1.1	0.8	0.4	0.3
Unstaged/Unknown	5,403	18.8	25.2	9.1	5.6	3.7	3.4	3.2

Table 7.11: Carcinomas of the Exocrine Pancreas: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by TNM Values, Ages 20+, 12 SEER Areas, 1988-2001

T Values	N Values											
	Total		No Positive Nodes (N0)		Positive Regional Nodes (N1)		Positive Distant Nodes (M1)		Positive Nodes, NOS (NX)		Unknown (NX)	
	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)
Total	28,754	3.5	6,465	8.8	5,515	3.8	898	0.7	157	3.6	15,719	1.3
Confined to Pancreas (Ext. 10-30)	2,842	13.4	1,428	20.9	712	6.1	34	!	<5	~	664	5.6
0 - 2 cm (T1)	315	27.4	201	37.3	74	14.8	0	~	0	~	40	4.2
> 2 cm (T2)	1,542	14.0	788	21.0	423	6.7	17	~	<5	~	311	6.0
Unknown Size (TX)	985	7.7	439	12.7	215	1.9	17	~	<5	~	313	5.0
Limited Extension (Ext. 40-52 - T3)	4,682	7.2	1,617	12.3	1,760	6.4	80	!	18	~	1,207	1.3
Further Extension (Ext. 54-80 - T4)	4,136	2.2	1,337	3.1	1,005	2.3	93	!	23	~	1,678	1.5
Metastasis (Ext. 85 - M1)	13,926	0.8	1,895	1.3	1,790	1.2	594	0.6	98	1.1	9,549	0.6
Unknown (Ext. 99 - TX/MX)	3,168	2.6	188	3.1	248	3.0	97	!	14	~	2,621	2.6

~ Statistic not displayed due to less than 25 cases.
! Not enough intervals to produce rate.

Chapter 8
Cancer of the Larynx

Jay F. Piccirillo and Irene Costas

INTRODUCTION

The larynx, positioned in the neck slightly below the point where the pharynx divides into separate respiratory and digestive tracts, is critical to breathing, swallowing, and speaking. The glottis is the portion of the larynx where the vocal cords are located. The area above the vocal cords is referred to as the supraglottis and that below the vocal cords as the subglottis.

This chapter provides survival analyses for 14,950 histologically confirmed adult cases of cancer of the larynx. Cases were obtained from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). Cancer of the larynx is second only to oral cavity cancer as the most common cancer of the upper aerodigestive tract (1). Tobacco and alcohol use are widely recognized as the key causative factors for many of these tumors (2). The cell type of origin for the vast majority of these tumors is squamous cell (3).

MATERIAL AND METHODS

The NCI contracts with medically oriented nonprofit institutions, such as universities and state health departments, to obtain data on all cancers diagnosed in residents of the SEER geographic areas. SEER collects data on all invasive and in situ cancers except basal cell and squamous cell carcinomas of the skin and in situ carcinoma of the uterine cervix.

SEER selects participating institutions on the basis of two criteria: their ability to operate and maintain a population-based cancer reporting system and the epidemiologic significance of their population subgroups. At times, registries will withdraw; at times, registries will be added. This analysis is based on data from 12 geographic areas, that collectively contain about 14% of the total US population. The areas are the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Atlanta, San Francisco, Seattle, San Jose, and Los Angeles; and 10 counties in rural Georgia. Los Angeles contributed data for diagnosis years 1992 to 2001, the others for 1988 to 2001.

To ensure maximal ascertainment of cancer cases, each registry abstracts the records of all cancer patients in hospitals, laboratories, and all other health service units that provide diagnostic services. Data collected by SEER registries on each patient include patient demographics, primary tumor site, tumor morphology, diagnostic methods, extent of disease, and first course of cancer-directed therapy. A separate record is coded for each primary cancer. All patients are followed from diagnosis to death, allowing detailed survival analysis.

Table 8.1: Cancer of the Larynx: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
19,807	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
16,660	3,147	Select first primary only
16,516	144	Exclude death certificate only or at autopsy
16,445	71	Exclude unknown race
16,433	12	Exclude alive with no survival time
16,428	5	Exclude children (Ages 0-19)
15,145	1,283	Exclude in situ cancers for all except breast & bladder cancer
15,007	138	Exclude no or unknown microscopic confirmation
14,950	57	Exclude sarcomas

Table 8.2: Cancer of the Larynx: Number and Distribution of Cases by Age (20+), Sex, Race, Primary Site, Historic Stage and Grade, 12 SEER Areas, 1988-2001

Characteristics	Cases	Percent
Total	14,950	
Age 20+ (Years)	14,950	
20-29	29	0.2
30-39	228	1.5
40-49	1,360	9.1
50-59	3,485	23.3
60-69	5,128	34.3
70-79	3,623	24.2
80+	1,097	7.3
Sex		
Male	11,975	80.1
Female	2,975	19.9
Race		
White	12,190	81.5
Black	2,148	14.4
Other	612	4.1
Primary Site		
Glottis (ICD-O C32.0)	8,160	54.6
Supraglottis (ICD-O C32.1)	4,920	32.9
Subglottis (ICD-O C32.2)	211	1.4
Laryngeal Cartilage (ICD-O C32.3)	80	0.5
Overlapping Lesion (ICD-O C32.8)	650	4.3
Larynx, NOS (ICD-O C32.9)	929	6.2
SEER Historic Stage		
Localized	7,472	50.0
Regional	6,373	42.6
Distant	538	3.6
Unstaged	567	3.8
Grade (Differentiation)		
Well differentiated; Grade I	2,501	16.7
Moderately differentiated; Grade II	6,775	45.3
Poorly differentiated; Grade III	2,916	19.5
Undifferentiated; anaplastic; Grade IV	140	0.9
Unknown	2,618	17.5

SEER has collected extent of disease (EOD) information on all cancers since the inception of the program. The detail and amount of information collected, however, have varied over time.

Relative Survival

The survival analysis is based largely on relative survival rates calculated by the life-table method. The relative rate is used to estimate the effect of cancer on the survival of the cohort. Relative survival, defined as observed survival divided by expected survival, adjusts for the expected mortality that the cohort would experience from other causes of death. When relative survival is 100%, a patient has the same chance to live 5 more years as a cancer-free person of the same age and sex.

Stage Classification

SEER historic stage is used in this chapter to classify the extent of cancer within and beyond the larynx. Categories include in situ, localized, regional, distant, and unstaged. The cases with a SEER stage of in situ are excluded from this study, as seen in Table 8.1. An invasive neoplasm confined entirely to the organ is classified as localized. A neoplasm that has extended either beyond the organ or into regional lymph nodes is defined as regional. Distant stage is defined as a neoplasm that has spread to parts of the body remote from the primary tumor. Cancers that lack sufficient information to assign stage are defined as unstaged.

Exclusions

As shown in Table 8.1, patients were excluded from this study for any of the following reasons: larynx cancer was not the first primary, cases identified through autopsy or death certificate only, persons of unknown race, cases without active follow-up, patients less than 20 years old, in situ cases, cases without microscopic confirmation, and sarcomas.

RESULTS

The demographic characteristics of the patient and morphologic characteristics of the tumors are displayed in Table 8.2. About 66% of the people in this sample are aged 60 years or older. The majority of patients are white and male. The majority of tumors were based in the glottis while approximately one-third of the tumors were supraglottic. At the time of diagnosis, one-half of the tumors were localized.

Table 8.3: Cancer of the Larynx: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Race/Sex	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total*	14,338	100.0	87.8	78.3	72.5	65.0	57.3	52.8
White Male	9,761	68.1	89.3	80.6	75.1	68.2	61.0	56.6
White Female	2,429	16.9	85.8	76.0	70.4	62.1	54.2	48.6
Black Male	1,686	11.8	83.3	70.5	62.9	54.5	45.2	41.2
Black Female	462	3.2	81.4	69.8	63.2	51.2	41.5	38.9

* Relative survival not computed for Other Race

Race and Sex

The 1-, 3-, 5-, 8- and 10-year relative survival rates by race and gender are shown in Table 8.3 and Figure 8.1. The 5-year relative survival rate for whites was 65% and for blacks was 53%. The 5-year relative survival rate was 61% for males and 57% for females. White males had the best 5-year relative survival at 68%, followed by white females, black males, and black females. The median observed survival for both white males and white females was 79 months, while for black males it was 48 months and for black females 50 months.

Stage at Diagnosis.

In Table 8.4 and Figure 8.2 survival is stratified by SEER historic stage at diagnosis. Localized tumors account for 50% of larynx tumors followed by regional (42.6%), unstaged (3.8%) and distant (3.6%). Five-year relative survival rate varies by stage from 83% for localized to 19% for distant. The median observed survival for patients with localized disease was 115 months, regional disease was 43 months, and distant disease was 11 months.

Grade at Diagnosis

Table 8.5 presents the 1-, 3-, 5-, 8- and 10-year relative survival rates by grade at diagnosis for all cancers of the larynx. At each time interval shown there is a clear survival gradient as tumor grade goes from well differentiated to undifferentiated.

Table 8.6 presents 5-year relative survival rates by race, sex, and stage. For patients with localized disease, white males had the best survival at 85%, followed by white females 78%, black males 75%, and black females 68%. For patients with regional disease white males and females had a 5-year relative survival of about 50%, while that of black males and females was approximately 42%.

Site at Diagnosis

Relative survival for patients with tumors of the glottis, supraglottis, and subglottis is shown in Figure 8.3. The median observed survival for patients with glottic cancer at presentation was 111 months, for supraglottic tumors was 43 months, and for subglottic tumors was 30 months.

Figure 8.1: Cancer of the Larynx: Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

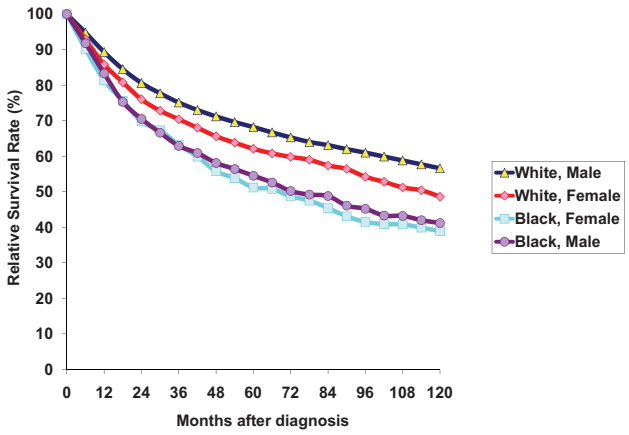


Figure 8.2: Cancer of the Larynx: Relative Survival Rates (%) by Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001

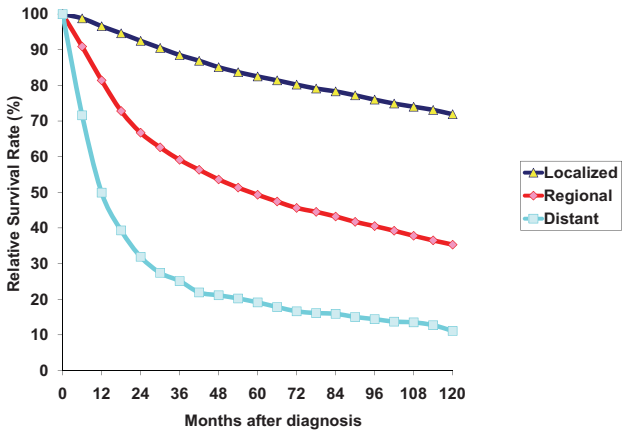


Table 8.4: Cancer of the Larynx: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates by Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001

Historic Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	14,950	100.0	87.9	78.4	72.7	65.2	57.6	53.1
Localized	7,472	50.0	96.6	92.5	88.5	82.5	76.0	71.9
Regional	6,373	42.6	81.4	66.7	59.1	49.3	40.5	35.3
Distant	538	3.6	49.9	31.9	25.1	19.1	14.4	11.1
Unstaged	567	3.8	81.7	69.5	63.5	58.2	47.6	46.2

Table 8.5: Cancer of the Larynx: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates by Grade, Ages 20+, 12 SEER Areas, 1988-2001

Grade	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	14,950	100.0	87.9	78.4	72.7	65.2	57.6	53.1
Well differentiated; Grade I	2,501	16.7	94.0	89.2	85.4	79.3	71.0	66.0
Moderately differentiated; Grade II	6,775	45.3	89.3	79.4	73.2	66.3	58.9	54.1
Poorly differentiated; Grade III	2,916	19.5	80.2	65.7	57.4	47.6	39.3	34.6
Undifferentiated; anaplastic; Grade IV	140	0.9	75.1	56.5	53.0	37.6	31.4	22.7
Unknown	2,618	17.5	87.4	80.9	77.3	70.1	62.9	60.1

Table 8.6: Cancer of the Larynx: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by Historic Stage, Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Historic Stage/Race	Total	Sex			
		Male		Female	
	Cases	Cases	5-Year RSR(%)	Cases	5-Year RSR(%)
Local:					
White	6,321	5,186	85.0	1,135	77.6
Black	854	672	75.1	182	67.5
Regional:					
White	4,988	3,874	50.6	1,114	50.0
Black	1,107	870	42.2	237	42.1
Distant:					
White	411	333	19.5	78	15.5
Black	106	84	20.1	22	~

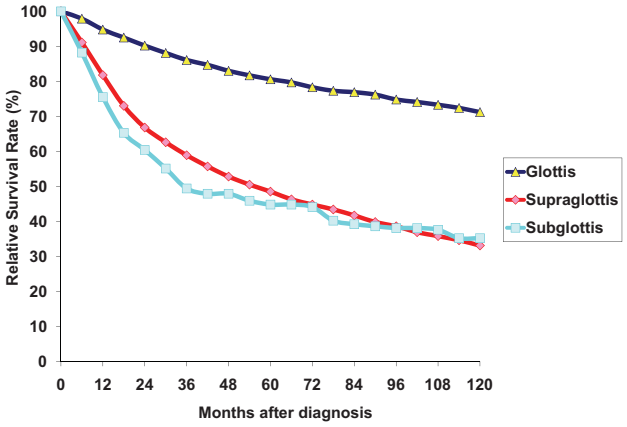
~ Statistic not displayed due to less than 25 cases.

Table 8.7 presents 5–year relative survival rates as a function of site, sex, and race. For glottic tumors, white males fared best with 82% survival. For supraglottic tumors, white females had the best 5-year relative survival (53%).

In Table 8.8 and Figure 8.4 the survival of patients with glottic cancer as a function of morphologic stage at diagnosis is shown. Localized tumors accounted for 67.3% of glottic tumors followed by regional (28.7%), unstaged (2.9%) and distant (1.2%). At each time point shown relative survival varies by stage with the highest relative survival for localized disease and the lowest for distant disease at diagnosis. The median observed survival for patients with localized disease at presentation was greater than 120 months, while patients with regional tumors had a median survival of 63 months, and those with distant disease 18 months.

In Table 8.9 and Figure 8.5 the survival of patients with supraglottic cancer as a function of morphologic stage at diagnosis is shown. Localized tumors account for 30.4% of glottic tumors, regional for 61.1%, distant for 5.5% and unstaged for 3.0%. At each time point shown relative survival decreases from diagnosis at localized to distant stage. The median observed survival for patients with localized disease at presentation was 73 months, regional disease was 36 months, and for distant disease was 11 months.

Figure 8.3: Cancer of the Larynx: Relative Survival Rates (%) by Subsite, Ages 20+, 12 SEER Areas, 1988-2001



DISCUSSION

Cancer of the larynx is closely related to tobacco and alcohol use. It remains primarily a disease of white men, although the number of women with this disease is increasing. For example, DeRienzo, Greenberg, and Fraire (4) found that the male-to-female ratio was 5.6 to 1 for the years of 1959-1973 and 4.5 to 1 for 1974-1988. In the population reported here, the male-to-female ratio in 1988-1998 decreased to 4 to 1. Small differences in relative survival by race were observed in this data. However, other researchers (5) have shown that these racial disparities disappear after controlling for other prognostic factors, including: treatment delay, type of therapy, and quality of care.

The vast majority (>95%) of tumors are of squamous cell origin. The overall prognosis is good and sub-site survival rates are much better for patients with glottic cancer than supraglottic or subglottic. This difference in survival may be due to the fact that the larynx is anatomically and clinically divided into these three distinct subsites. Anatomically, the glottis has much fewer lymphatic channels and vascular support than either the supraglottis or subglottis. Clinically, patients with glottic cancer will develop symptoms, such as hoarseness, earlier in the course of their disease than patients with tumors of the supraglottis or subglottis. The paucity of lymphatic and vascular supply and the development of symptoms earlier in the course of glottic cancer may explain why patients with glottic tumors generally present with local, rather than regional, disease. For all sub-sites, survival was strongly related to morphologic extent of disease at the time of diagnosis. Survival was also related to the degree of differentiation; as the degree of differentiation decreased survival worsened.

It would be informative to be able to include in analyses of larynx cancer survival host factors like comorbidity (6, 7) and performance status (8); socioeconomic factors like income and education; and tumor biology factors like p53 and epidermal growth factor receptor. However, many of these variables are not routinely found in medical records and are not generally part of the SEER analytic files.

Table 8.7: Cancer of the Larynx: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by Race, Primary Site and Sex, Ages 20+, 12 SEER Areas, 1988-2001

	Total	Male		Female	
Primary Site/Race	Cases	Cases	5-Year RSR(%)	Cases	5-Year RSR(%)
Glottis					
White	6,849	5,887	82.2	962	78.0
Black	956	830	72.8	126	69.9
Supraglottis					
White	3,956	2,765	48.5	1,191	52.7
Black	798	533	36.9	265	45.7
Subglottis					
White	163	118	46.5	45	37.7
Black	35	25	30.3	10	~

~ Statistic not displayed due to less than 25 cases.

Table 8.8: Cancer of the Glottis: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001

Historic Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	8,160	100.0	94.8	90.2	86.1	80.6	74.8	71.2
Localized	5,489	67.3	98.9	96.5	93.5	89.5	84.8	82.0
Regional	2,338	28.7	87.0	77.5	70.9	61.3	52.9	46.8
Distant	95	1.2	60.0	40.5	37.0	34.3	25.3	22.2
Unstaged	238	2.9	91.7	85.4	80.9	77.0	68.1	67.9

Table 8.9: Cancer of the Supraglottis: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001

Historic Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	4,920	100.0	81.8	66.8	58.9	48.5	38.6	33.1
Localized	1,494	30.4	90.8	81.9	75.4	64.1	52.0	44.5
Regional	3,008	61.1	80.6	62.7	54.1	43.8	34.5	29.7
Distant	270	5.5	49.6	31.7	22.4	15.4	12.0	9.8
Unstaged	148	3.0	76.3	59.4	54.9	45.8	35.9	30.6

Figure 8.4: Cancer of the Glottis: Relative Survival Rates (%) by Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001

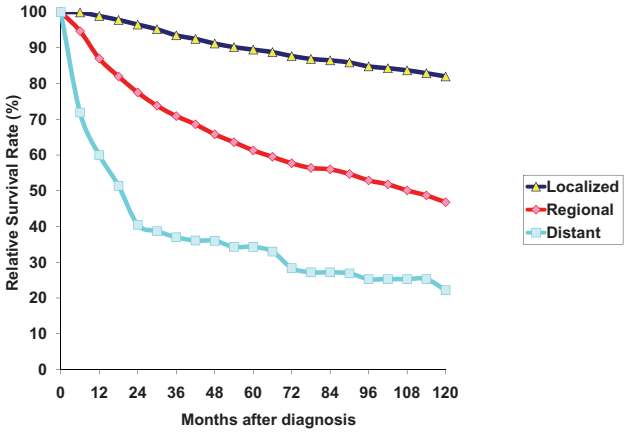
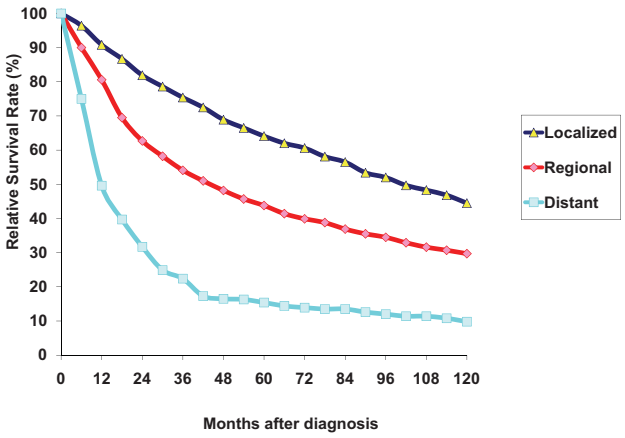


Figure 8.5: Cancer of the Supraglottis: Relative Survival Rates (%) by Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001



REFERENCES

1. Jemal A, Thomas A, Murray T, Thun MJ. Cancer Statistics, 2002. CA A Cancer Journal for Clinicians 2002; 52(1):23-47.
2. Shaha A, Strong EW. Cancer of the Head and Neck. In: Murphy GP, Lawrence W, Lenhard REJr, editors. Clinical Oncology. Atlanta, GA: American Cancer Society, 1995: 355-377.
3. Sinard RJ, Netterville JL, Garrett CG, Ossoff RH. Cancer of the Larynx. In: Myers EN, Suen JY, editors. Cancer of the Head and Neck. Philadelphia: W.B.Saunders Company, 1996: 381-421.
4. DeRienzo DP, Greenberg SD, Fraire AE. Carcinoma of the larynx. Changing incidence in women. Archives of Otolaryngology -- Head & Neck Surgery 1991; 117(6):681-684.
5. Roach M, Alexander M, Coleman JL. The prognostic significance of race and survival from laryngeal carcinoma. Journal of the National Medical Association 1992; 84:668-674.
6. Piccirillo JF, Wells CK, Sasaki CT, Feinstein AR. New clinical severity staging system for cancer of the larynx. Five-year survival rates. Annals of Otology, Rhinology & Laryngology 1994; 103(2):83-92.
7. Piccirillo JF. Inclusion of comorbidity in a staging system for head and neck cancer. Oncology 1995; 9:831-836.
8. Stell PM. Prognosis in laryngeal carcinoma: host factors. Clin Otolaryngol 1990; 15(2):111-119.

Chapter 9
Cancer of the Lung

Lynn A. Gloeckler Ries and Milton P. Eisner

INTRODUCTION

This study provides survival analyses for 201,067 histologically confirmed adult cases of lung cancer diagnosed from 1988 through 2001. Cases were obtained from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). The SEER Program -- a sequel to two earlier NCI initiatives, the End Results Program and the Third National Cancer Survey -- has evolved in response to the National Cancer Act of 1971, which requires the collection, analysis, and dissemination of data relevant to the prevention, diagnosis, and treatment of cancer. This chapter focuses on the influence of extent of disease, histologic grade, and demographic factors on lung cancer survival.

MATERIALS AND METHODS

The NCI contracts with medically oriented nonprofit institutions -- such as universities and state health departments -- to obtain data on all cancers diagnosed in residents of the SEER geographic areas. SEER collects data on all invasive and in situ cancers except basal cell and squamous cell carcinomas of the skin and in situ carcinoma of the uterine cervix.

SEER selects participating institutions on the basis of two criteria: their ability to operate and maintain a population-based cancer reporting system and the epidemiologic significance of their population subgroups. At times, registries will withdraw; at times, registries will be added. This analysis is based on data from 12 geographic areas, which collectively contain about 14% of the total US population. The areas are the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Atlanta, San Francisco, Seattle, San Jose, and Los Angeles; and 10 counties in rural Georgia. Los Angeles contributed data for diagnosis years 1992 to 2001, the others for 1988 to 2001.

To ensure maximal ascertainment of cancer cases, each registry abstracts the records of all cancer patients in hospitals, laboratories, and all other health service units that provide diagnostic services. Data collected by SEER registries on each patient include patient demographics, primary tumor site, tumor morphology, diagnostic methods, extent of disease, and first course of cancer-directed therapy. A separate record is coded for each primary cancer. All patients are followed from diagnosis to death, allowing detailed survival analysis.

SEER has collected extent of disease (EOD) information on all cancers since the inception of the program. The detail and amount of information collected, however, have varied over time. In 1988, there were revisions to the lung cancer EOD scheme allowing the SEER EOD information to be collapsed into the TNM classification described in the third edition of the American Joint Committee on Cancer (AJCC) Manual for Staging of Cancer (1). The AJCC TNM classification for lung cancer is the same as that of the International Union Against Cancer.

Relative Survival

The survival analysis is based on relative survival rates calculated by the life-table method. The relative rate is used to estimate the effect of cancer on the survival of the cohort. Relative survival, defined as observed survival divided by expected survival, adjusts for the expected mortality that the cohort would experience from other causes of death. When relative survival is 100%, a patient has the same chance to live 5 more years as a cancer-free person of the same age and sex. For lung cancer, the relative rate may underestimate survival slightly, since the expected mortality tables are based on the entire US population, whose expected survival is greater than the smoking population's expected survival.

Exclusions

The following were excluded from the analysis: patients for whom lung cancer was not the first primary; cases identified through autopsy or death certificate only; persons of unknown race; cases without active follow-up; patients

Table 9.1: Cancer of the Lung: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
273,521	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
225,617	47,904	Select first primary only
220,264	5,353	Exclude death certificate only or at autopsy
219,919	345	Exclude unknown race
219,768	151	Active follow-up and exclude alive with no survival time
219,713	55	Exclude children (Ages 0-19)
219,577	136	Exclude in situ cancers for all except breast & bladder cancer
201,502	18,075	Exclude no or unknown microscopic confirmation
201,067	435	Exclude sarcomas

less than 20 years old; in situ cases; cases without microscopic confirmation; and sarcomas. Table 9.1 details the exclusions. There were 201,067 cases for analysis.

RESULTS

Overall, the relative survival rate was poor; only 15% survived 5 years. In most of the following tables, each prognostic factor is presented both individually and in relation to a second factor.

Race and Sex

Overall, the 5-year relative survival rate for whites was 16% and for blacks was 12%. The overall 5-year relative survival rates were 14% for males and 18% for females (Table 9.2).

Geographic Location

Five-year relative survival rates in the 12 SEER areas represented in this study ranged from 13% in New Mexico and Rural Georgia to 17% in Connecticut (Table 9.3).

Stage of Disease

Lung cancer was seldom found (only 13.4%) when it was still confined to the lung. Rather, over 60% of the patients had stage III or IV disease at diagnosis. Twenty-one percent of the cases did not have enough diagnostic information to be staged. The stage distributions for males and females were similar (Table 9.4).

Stage of disease was a strong predictor of survival, as was expected. The 5-year relative survival rates ranged from a high of 57% for stage I to a low of 2% for stage IV (Table 9.4). Table 9.4 shows the survival rates for males and females by stage. Females had higher survival rates at all stages.

Sex, Stage, and Histology

Table 9.5 shows that the histologic type distributions of lung cancers in males and females are somewhat different. Adenocarcinomas comprise 41% of female cases but only 33% of male cases, while squamous cell carcinomas comprise 15% of female cases but 24% of male cases. The other types are roughly equal in males and in females.

Based on 5-year relative survival rates for both sexes combined, patients with adenocarcinoma survived longer than those with squamous cell, large cell, or small cell carcinoma for all stages combined and for stage I (Table 9.5). For stage II, however, patients with squamous cell carcinoma had a slightly better survival rate than those with adenocarcinoma.

For males, relative survival rates were similar for adenocarcinoma and squamous cell carcinoma for all stages, but for stage I adenocarcinoma had higher survival and for stage II squamous cell carcinoma had higher survival (Figure 9.1). For females, relative survival rates were higher for adenocarcinomas for stage I and II (Figure 9.2). Survival rates were more influenced by stage than by histology. For non-small cell carcinoma and small cell carcinoma, survival curves by stage are shown in figure 9.3 and 9.4, respectively. Survival rates are lower for

Table 9.2: Cancer of the Lung: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by Race and Sex, Ages 20+, 12 SEER Areas,1988-2001

	Male and Female		Male		Female	
Race	Cases	5-Year RSR %	Cases	5-Year RSR %	Cases	5-Year RSR %
All Races	201,067	15.5	117,472	13.6	83,595	18.0
White	165,487	15.9	94,728	13.9	70,759	18.4
Black	22,219	12.5	14,120	10.9	8,099	15.0
Other	13,361	~	8,624	~	4,737	~

~ Rate not shown.

Table 9.3: Cancer of the Lung: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by SEER Area, Ages 20+, 12 SEER Areas, 1988-2001

SEER Geographic Area	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	201,067	100.0	42.6	25.9	20.0	15.5	12.4	11.0
Atlanta and Rural Georgia	13,754	6.8	42.6	26.4	20.5	15.9	13.1	11.4
Atlanta (Metropolitan) - 1988+	12,956	6.4	42.9	26.7	20.8	16.1	13.3	11.6
Rural Georgia - 1988+	798	0.4	38.0	21.5	16.2	13.0	10.2	8.8
California								
Los Angeles - 1992+	30,677	15.3	41.3	25.1	19.4	14.8	11.8	10.1
Greater Bay Area	33,987	16.9	42.1	25.6	19.5	15.2	12.2	10.8
San Francisco-Oakland SMSA - 1988+	23,746	11.8	41.8	25.0	19.0	14.7	11.6	10.3
San Jose-Monterey - 1988+	10,241	5.1	42.7	26.9	20.8	16.5	13.7	11.9
Connecticut - 1988+	26,207	13.0	45.0	28.1	21.9	17.2	14.0	12.3
Detroit (Metropolitan) - 1988+	33,074	16.4	43.1	26.3	20.6	15.8	12.7	11.3
Hawaii - 1988+	6,480	3.2	44.3	26.8	20.6	16.1	13.1	12.3
Iowa - 1988+	21,548	10.7	41.9	24.5	18.6	14.0	10.7	9.3
New Mexico - 1988+	7,159	3.6	38.4	22.3	17.3	13.0	10.4	9.3
Seattle (Puget Sound) - 1988+	23,799	11.8	43.7	26.6	20.9	16.3	12.6	11.6
Utah - 1988+	4,382	2.2	38.4	22.6	17.7	13.9	11.9	11.1

small cell carcinoma, but even within small cell carcinoma, survival rates vary by stage (Figure 9.4).

Sex, Stage, and Age

Table 9.6 presents the survival statistics by sex, stage, and age at diagnosis. Females had better relative survival rates than males. The largest differences were for stage I cancers and very young or older patients. Females under 45 with stage I disease had a 72% 5-year relative survival rate; in contrast, the rate was 41% for females 85 and over. In general, younger patients survived better than older patients for stage I and II disease. Survival rates were poor for stage IV at all ages.

Laterality

Tumors were more frequently diagnosed in the right lung than the left lung. But, survival rates were nearly identical for patients whose tumors arose in the right lung as compared to the left lung (Table 9.7). 'Other' category includes not a paired site, only one side - side unspecified, bilateral - single primary, and paired site (but no information concerning laterality).

Subsite

Over 40% of the lung cancers originated in the upper lobe no matter at which stage they were diagnosed. For stage I, 61.6% of the cancers originated in the upper lobe and 28.9% in the lower lobe. For stage II, 53.9% of the cancers originated in the upper lobe and 34.1% in the lower lobe. For stages III, IV, and unknown, the origin

Table 9.4: Cancer of the Lung: Number of Cases, Stage Distribution, and 5-Year Relative Survival Rates (%) by AJCC Stage (3rd edition) and Sex, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage (3rd edition)	Male and Female			Male			Female		
	Cases	Percent	5-Year Relative Survival Percent	Cases	Percent	5-Year Relative Survival Percent	Cases	Percent	5-Year Relative Survival Percent
All Stages	201,067	100.0	15.5	117,472	100.0	13.6	83,595	100.0	18.0
I	26,879	13.4	56.9	14,598	12.4	53.5	12,281	14.7	60.8
II	5,635	2.8	33.7	3,402	2.9	32.4	2,233	2.7	35.7
III	50,254	25.0	9.4	29,863	25.4	9.0	20,391	24.4	10.1
IV	75,057	37.3	1.8	44,783	38.1	1.6	30,274	36.2	2.2
Unknown	43,242	21.5	18.0	24,826	21.1	15.0	18,416	22.0	21.9

of the cancer was not specified 16.8%, 24.7%, and 17.9%, respectively. Overall, the 5-year relative survival rates were lower for patients whose tumor originated in the main stem bronchus (a category that includes the carina and hilum) than for those whose tumor originated in the upper, middle, or lower lobe (Table 9.8). If the lobe was not specified, the 5-year relative survival rate was 5%. For tumors that crossed lobe boundaries, survival rates were intermediate. For patients diagnosed at stage I, those whose tumor had originated in the upper lobe had a survival rate (60%) more than double that of those whose tumors originated in the main bronchus, carina, or hilum (23%) (Table 9.9).

Extent of Disease

Only cases with no lymph nodes involved (approximately one-fourth of the cases) were used to investigate the influence of extent of disease on survival (Table 9.10). Five-year

Figure 9.1: Male Lung Cancer: 5-Year Relative Survival Rates (%) by Histology and AJCC Stage, Ages 20+, 12 SEER Areas, 1988-2001

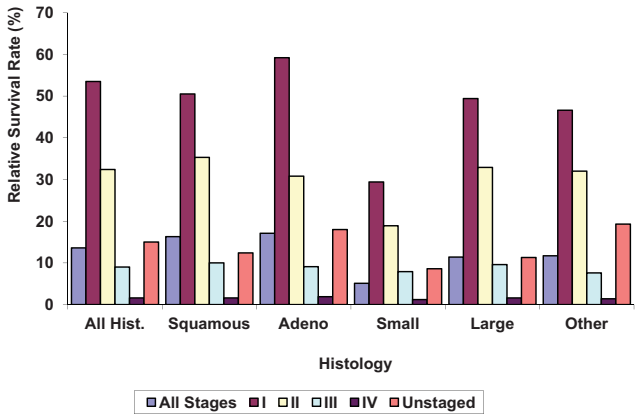


Figure 9.2: Female Lung Cancer: 5-Year Relative Survival Rates (%) by Histology and AJCC Stage, Ages 20+, 12 SEER Areas, 1988-2001

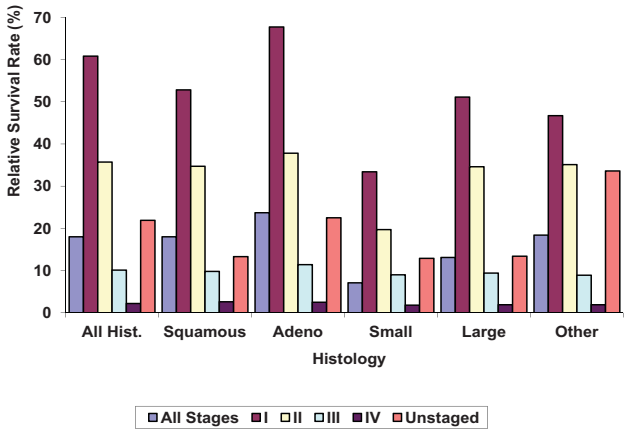


Table 9.5: Cancer of the Lung: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by Sex, Histology and AJCC Stage (3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage (3rd edition)											
	Total		I		II		III		IV		Unknown	
Sex/Histology	Cases	5-Year RSR %	Cases	5-Year RSR %	Cases	5-Year RSR %	Cases	5-Year RSR %	Cases	5-Year RSR %	Cases	5-Year RSR %
Male and Female	201,067	15.5	26,879	56.9	5,635	33.7	50,254	9.4	75,057	1.8	43,242	18.0
Squamous cell	41,212	16.8	7,196	51.3	1,698	35.1	12,061	9.9	10,263	1.9	9,994	12.7
Adenocarcinoma	73,535	20.3	14,432	63.8	2,802	34.4	17,587	10.2	27,593	2.2	11,121	20.2
Small Cell	33,008	6.0	953	31.4	270	19.3	8,213	8.4	16,962	1.5	6,610	10.7
Large Cell	14,945	12.1	1,705	50.2	365	33.7	3,931	9.5	6,014	1.7	2,930	12.2
Others	38,367	14.5	2,593	46.6	500	33.1	8,462	8.1	14,225	1.6	12,587	26.0
Male	117,472	13.6	14,598	53.5	3,402	32.4	29,863	9.0	44,783	1.6	24,826	15.0
Squamous cell	28,463	16.3	4,734	50.5	1,281	35.3	8,516	10.0	7,116	1.6	6,816	12.4
Adenocarcinoma	39,303	17.1	6,865	59.2	1,406	30.8	9,562	9.1	15,584	1.9	5,886	18.0
Small Cell	17,827	5.1	488	29.4	134	18.9	4,166	7.9	9,579	1.2	3,460	8.6
Large Cell	9,033	11.4	965	49.4	239	32.9	2,361	9.6	3,753	1.6	1,715	11.3
Others	22,846	11.7	1,546	46.6	342	32.0	5,258	7.6	8,751	1.4	6,949	19.3
Female	83,595	18.0	12,281	60.8	2,233	35.7	20,391	10.1	30,274	2.2	18,416	21.9
Squamous cell	12,749	18.0	2,462	52.8	417	34.7	3,545	9.8	3,147	2.6	3,178	13.3
Adenocarcinoma	34,232	23.7	7,567	67.7	1,396	37.8	8,025	11.4	12,009	2.5	5,235	22.5
Small Cell	15,181	7.1	465	33.4	136	19.7	4,047	9.0	7,383	1.8	3,150	12.9
Large Cell	5,912	13.1	740	51.1	126	34.6	1,570	9.4	2,261	1.9	1,215	13.4
Others	15,521	18.4	1,047	46.7	158	35.1	3,204	8.9	5,474	1.9	5,638	33.6

relative survival ranged from a high of 60% for cases in which the cancer was confined to one lung down to 4% for those with metastases. For nearly every category, women fared better than men. For those patients whose tumor was confined to one lung, women had a 64% 5-year relative survival rate compared to 56% for men.

Grade

Nearly 40% of the cases did not have histologic grade. But for stage I, only 18% were not graded. For all stages combined, survival was four times higher for grade 1 compared to grade 4. Within stages, the survival differences by grade were not as pronounced (Table 9.11). For stage I, grade 1 cases had better survival (73%) than grade 4 cases (48%). Stage I adenocarcinomas had a similar range (Table 9.12). For adenocarcinomas, grade III and IV had similar survival and for stage IV, the survival was less than 4% no matter which grade (Table 9.12).

DISCUSSION

While lung cancer survival rates overall are generally poor, lung cancer survival rates vary by patient and tumor charac-

Table 9.6: Cancer of the Lung: Number of Cases and 5-Year Relative Survival Rates (%) by Sex, Age (20+), and AJCC Stage (3rd edition) at Diagnosis, 12 SEER Areas, 1988-2001

Sex/Age (Years)	AJCC Stage (3rd edition)											
	Total		I		II		III		IV		Unknown	
	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent
Male and Female	201,067	15.5	26,879	56.9	5,635	33.7	50,254	9.4	75,057	1.8	43,242	18.0
20-44	6,148	21.6	497	69.7	132	52.5	1,450	14.8	2,734	2.4	1,335	46.7
45-49	7,995	17.5	759	64.9	234	42.5	1,934	13.6	3,681	2.3	1,387	32.4
50-54	13,789	17.6	1,549	66.5	470	42.3	3,361	13.2	6,029	2.5	2,380	24.9
55-59	20,684	17.0	2,620	62.1	626	36.8	5,048	12.2	8,733	2.2	3,657	22.4
60-64	29,038	16.4	3,829	61.2	910	36.8	7,090	11.2	11,677	1.7	5,532	19.1
65-69	36,469	16.2	5,443	57.6	1,102	32.3	8,872	9.7	13,518	1.8	7,534	16.9
70-74	36,666	14.8	5,512	53.9	1,130	27.2	9,166	7.6	12,745	1.7	8,113	14.7
75-79	28,228	12.3	4,074	48.9	713	26.0	7,101	5.6	9,391	1.0	6,949	11.5
80-84	15,235	10.2	1,963	42.6	251	24.6	4,114	3.7	4,637	1.5	4,270	10.2
85+	6,815	6.6	633	33.9	67	16.9	2,118	2.1	1,912	0.7	2,085	7.6
Male	117,472	13.6	14,598	53.5	3,402	32.4	29,863	9.0	44,783	1.6	24,826	15.0
20-44	3,378	18.4	240	67.1	73	47.6	836	14.7	1,565	2.4	664	39.5
45-49	4,603	14.8	359	66.1	133	41.1	1,167	11.8	2,185	1.5	759	27.8
50-54	8,124	14.9	787	61.0	284	43.9	2,053	12.7	3,648	1.9	1,352	19.2
55-59	12,245	14.7	1,397	58.5	373	36.3	3,137	11.5	5,250	2.1	2,088	17.3
60-64	17,738	14.6	2,169	58.1	545	34.4	4,405	10.2	7,275	1.3	3,344	16.8
65-69	21,847	14.4	3,061	54.3	699	32.0	5,336	9.1	8,260	1.5	4,491	14.3
70-74	21,536	13.0	3,028	50.5	679	25.1	5,467	7.2	7,670	1.6	4,692	12.2
75-79	16,043	10.9	2,209	45.4	441	21.2	4,130	5.2	5,343	0.8	3,920	10.1
80-84	8,384	8.1	1,007	35.4	138	25.3	2,243	3.4	2,594	1.4	2,402	7.5
85+	3,574	4.9	341	26.4	37	14.4	1,089	1.0	993	0.4	1,114	5.4
Female	83,595	18.0	12,281	60.8	2,233	35.7	20,391	10.1	30,274	2.2	18,416	21.9
20-44	2,770	25.5	257	71.9	59	58.5	614	14.9	1,169	2.5	671	53.6
45-49	3,392	21.1	400	63.8	101	44.5	767	16.3	1,496	3.4	628	37.8
50-54	5,665	21.4	762	72.2	186	39.5	1,308	13.9	2,381	3.2	1,028	32.1
55-59	8,439	20.3	1,223	66.1	253	37.7	1,911	13.4	3,483	2.4	1,569	29.1
60-64	11,300	19.3	1,660	65.2	365	40.1	2,685	12.6	4,402	2.3	2,188	22.3
65-69	14,622	18.6	2,382	61.7	403	32.6	3,536	10.6	5,258	2.1	3,043	20.6
70-74	15,130	17.1	2,484	57.9	451	30.0	3,699	8.1	5,075	1.8	3,421	17.8
75-79	12,185	13.9	1,865	52.5	272	32.7	2,971	5.9	4,048	1.3	3,029	13.1
80-84	6,851	12.4	956	48.9	113	23.5	1,871	4.1	2,043	1.3	1,868	13.1
85+	3,241	8.1	292	40.6	30	17.2	1,029	2.8	919	1.1	971	9.6

Table 9.7: Cancer of the Lung: Number of Cases and 5-Year Relative Survival Rates (%) by AJCC Stage (3rd edition) and Laterality, Ages 20+, 12 SEER Areas, 1988-2001

	Laterality							
	Total		Right		Left		Other	
AJCC Stage	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent
All Stages	201,067	15.5	109,776	16.2	79,276	16.2	12,015	4.0
I	26,879	56.9	15,554	57.5	11,311	56.1	14	~
II	5,635	33.7	2,994	32.2	2,637	35.5	<5	~
III	50,254	9.4	28,596	9.5	20,287	9.6	1,371	5.2
IV	75,057	1.8	38,949	1.7	28,041	1.9	8,067	2.0
Unstaged/Unknown	43,242	18.0	23,683	18.9	17,000	18.1	2,559	9.4

~ Statistic not displayed due to less than 25 cases.

Table 9.8: Cancer of the Lung: Number of Cases and 5-Year Relative Survival Rates (%) by Subsite and Sex, Ages 20+, 12 SEER Areas, 1988-2001

	Male and Female		Male		Female	
Subsite	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent
All Subsites	201,067	15.5	117,472	13.6	83,595	18.0
Main bronchus	11,384	7.0	6,620	6.4	4,764	7.8
Upper lobe	97,916	19.0	57,830	16.9	40,086	21.8
Middle lobe	8,496	19.7	4,632	16.5	3,864	23.2
Lower lobe	44,106	17.8	25,390	15.2	18,716	21.0
Overlapping	3,940	14.7	2,346	14.2	1,594	15.3
NOS	35,225	4.7	20,654	3.7	14,571	5.9

Table 9.9: Cancer of the Lung: Number of Cases and 5-Year Relative Survival Rates (%) by Subsite and AJCC Stage (3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage (3rd edition)											
	Total		I		II		III		IV		Unknown	
Subsite	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent	Cases	5-Year Relative Survival Percent
All Subsites	201,067	15.5	26,879	56.9	5,635	33.7	50,254	9.4	75,057	1.8	43,242	18.0
Main bronchus	11,384	7.0	303	23.1	149	27.4	4,130	8.0	4,597	1.1	2,205	13.9
Upper lobe	97,916	19.0	16,567	59.9	3,036	38.3	24,834	11.6	32,845	2.2	20,634	18.7
Middle lobe	8,496	19.7	1,351	55.4	248	30.1	1,877	8.7	2,898	1.5	2,122	29.7
Lower lobe	44,106	17.8	7,763	53.5	1,921	28.1	9,756	8.5	14,813	1.7	9,853	20.9
Overlapping	3,940	14.7	478	50.0	183	33.5	1,219	9.8	1,353	1.3	707	19.9
NOS	35,225	4.7	417	34.9	98	20.7	8,438	4.7	18,551	1.5	7,721	10.4

Figure 9.3: Non-small-cell Lung Cancer: Relative Survival Rates (%) by AJCC Stage, Ages 20+, 12 SEER Areas, 1988-2001

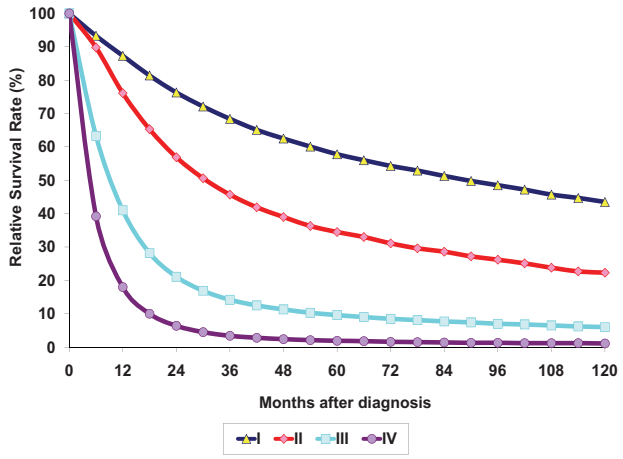


Figure 9.4: Small-cell Lung Cancer: Relative Survival Rates (%) by AJCC Stage, Ages 20+, 12 SEER Areas, 1988-2001

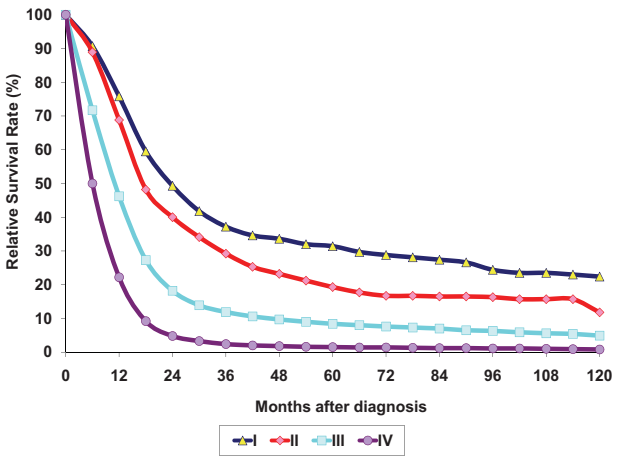


Table 9.10: Cancer of the Lung without lymph node involvement: Number and Distribution of Cases and 5-Year Relative Survival Rates (%) by Extension and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Extension	Male and Female			Male			Female		
	Cases	Percent	5-Year RSR	Cases	Percent	5-Year RSR	Cases	Percent	5-Year RSR
All Cases without Lymph Node Involvement	49,758	100.0	41.5	27,861	100.0	37.3	21,897	100.0	46.5
10-One lung	22,200	44.6	59.7	11,683	41.9	55.7	10,517	48.0	64.0
20-Involving MSB, away from carina	1,206	2.4	56.0	715	2.6	49.1	491	2.2	65.3
30-Localized, NOS	3,261	6.6	38.7	1,860	6.7	36.0	1,401	6.4	42.1
40-Atelectasis/obs. pneumonitis < entire lung, w/o pleural effusion	6,459	13.0	51.6	3,629	13.0	47.3	2,830	12.9	56.7
50-Involving MSB, close to carina	344	0.7	24.8	223	0.8	25.2	121	0.6	23.8
60-Atelectasis/obstructive pneumonitis of entire lung	1,765	3.5	27.1	1,143	4.1	25.2	622	2.8	30.4
65-Multiple masses - same lobe	293	0.6	+	137	0.5	+	156	0.7	+
70-Carina/trachea	1,837	3.7	17.5	1,207	4.3	17.2	630	2.9	17.9
71-Heart	135	0.3	13.6	94	0.3	11.9	41	0.2	16.8
72-Malignant pleural effusion	2,569	5.2	9.4	1,500	5.4	8.4	1,069	4.9	10.7
73-Adjacent rib	632	1.3	16.2	405	1.5	16.1	227	1.0	16.3
75-Sternum/vertebrae	304	0.6	14.7	193	0.7	14.3	111	0.5	15.2
77-Separate lobes (same lung)	255	0.5	!	120	0.4	!	135	0.6	!
78-Contralateral	494	1.0	11.2	258	0.9	7.8	236	1.1	14.4
80-Further extension	68	0.1	10.9	43	0.2	3.0	25	0.1	23.9
85-Metastasis	6,994	14.1	4.3	4,097	14.7	3.7	2,897	13.2	4.9
99-Unknown	885	1.8	16.2	519	1.9	14.7	366	1.7	18.1

Bases on 49,758 cases with no lymph node involvement. Extensions with fewer than 50 cases excluded.

\+ The statistic could not be calculated.

! Not enough intervals to produce rate.

Table 9.11: Cancer of the Lung: Number of Cases and 5-Year Relative Survival Rates (%) by Grade and AJCC Stage (3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage (3rd edition)											
	Total		I		II		III		IV		Unknown	
Grade	Cases	5-Year RSR Percent	Cases	5-Year RSR Percent	Cases	5-Year RSR Percent	Cases	5-Year RSR Percent	Cases	5-Year RSR Percent	Cases	5-Year RSR Percent
All Grades	201,067	15.5	26,879	56.9	5,635	33.7	50,254	9.4	75,057	1.8	43,242	18.0
1	6,831	41.4	2,645	73.3	237	39.3	1,143	15.9	1,187	3.6	1,619	33.9
2	25,993	29.8	8,000	63.0	1,685	37.7	6,086	12.8	5,319	2.8	4,903	22.2
3	61,072	15.8	9,364	54.3	2,467	33.7	16,349	11.4	22,116	1.9	10,776	14.1
4	27,991	9.4	1,940	47.8	533	30.6	7,270	9.5	12,632	1.6	5,616	11.9
Unknown	79,180	10.4	4,930	46.4	713	24.7	19,406	6.1	33,803	1.6	20,328	19.7

Table 9.12: Adenocarcinoma of the Lung: Number of Cases and 5-Year Relative Survival Rates (%) by Grade and AJCC Stage (3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage (3rd edition)											
	Total		I		II		III		IV		Unknown	
Grade	Cases	5-Year RSR Percent	Cases	5-Year RSR Percent	Cases	5-Year RSR Percent	Cases	5-Year RSR Percent	Cases	5-Year RSR Percent	Cases	5-Year RSR Percent
Total	73,535	20.3	14,432	63.8	2,802	34.4	17,587	10.2	27,593	2.2	11,121	20.2
1	4,915	46.5	2,248	76.2	174	36.8	625	19.9	906	3.9	962	34.7
2	13,284	35.7	4,915	67.5	992	37.0	2,446	15.9	3,080	3.1	1,851	29.1
3	26,197	17.6	4,567	56.3	1,226	33.4	6,762	12.3	10,053	2.0	3,589	16.9
4	1,470	16.2	218	50.5	84	35.8	413	11.1	545	3.4	210	16.0
Unknown	27,669	10.8	2,484	60.3	326	28.4	7,341	5.1	13,009	1.8	4,509	16.3

teristics. For lung cancer, stage had the most prognosis, but other factors such as grade, age, sex, and histologic type also played a role. Many of these results expand on similar analyses performed on earlier SEER data (2).

While females have somewhat better survival than males, it does not appear to be due to more cases with a favorable extent of disease; the differential also exists within most of the detailed EOD categories.

Lung cancer is a major disease in the US for both males and females; survival of lung cancer is worse than survival of most other types of cancer. While overall survival was poor, the 5-year relative survival rate for stage I patients was 57%.

Females had better survival than males for most lung cancer histologic types, even though females had a higher proportion of small cell carcinoma (18% in women and 15% in men in our data set), which has a much worse prognosis than the other tumor types (Table 9.5).

Although the prognosis for lung cancer is dismal for most patients, there are some groups that are exceptional. For instance, females under age 45 with stage I lung cancer had a 5-year relative survival rate of 72%.

Since relative survival rates are higher for younger persons than for older, some of the female-male survival differential may be due to a greater proportion of younger patients in the female group. However, even within age groups, females tended to survive better than males.

TNM stage was a good predictor of survival even when analyzed by various demographic and tumor factors. There were, however, wide ranges of survival possible within a particular stage, especially for stage I. For instance, as mentioned above, young females with stage I lung cancer had a 5-year relative survival rate of 72%; for females aged 85 and over, the corresponding rate was only 41%.

REFERENCES

1. Beahrs, OH, Henson DE, Hutter RVP, Myers MH (eds). AJCC Cancer Staging Manual, Third edition. American Joint Committee on Cancer. Philadelphia: Lippincott, 1988.
2. Ries LAG. Influence of extent of disease, histology, and demographic factors on lung cancer survival in the SEER population-based data. Semin Surg Oncol 1994;10:21-30.

Chapter 10
Cancers of the Bone and Joint

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INTRODUCTION

Cancer of the bone and joint is a rare form of cancer. The most recent annual incidence rate among the SEER sites in the United States is 0.9 cases per 100,000 between 2000 and 2003 (1). In the U.S., incidence trends have mostly fluctuated, however there has been a slight decrease in incidence since 1994 (1). Bone and joint cancer mortality in the U.S. has decreased since 1969, with a large decrease reported in the late 1970's. U.S. mortality was reported at 0.4 deaths per 100,000 in 2006 (1). Survival statistics indicate better survival and quality of life, as surgery for these malignancies can incorporate limb sparing options. The 5-year survival rate for bone and joint cancer was 54% for patients diagnosed between 1975 and 1977 and 68% for patients diagnosed between 1996 and 2002.

MATERIALS AND METHODS

Between 1988 and 2001, there were 4,062 cases of bone and joint cancer diagnosed and reported to the SEER program (Table 10.1). Table 10.1 shows the exclusion of bone and joint cases from the initial number with the reason given for the exclusion. Cases from the Los Angeles registry were contributed for the years 1992 through 2001. Nearly 1,093 cases (27%) of the original cases were in children aged 0 to 19 years old, and were excluded from further analysis. More than half of the remaining cases were available for analysis (N=2,273), as they represent histologically confirmed, first primary adult cases of bone and joint cancer reported to the SEER program between 1988 and 2001.

Histologic Classification

Bone cancers have three major histologic types: osteosarcomas, chondrosarcomas, and Ewing sarcoma (2). These three types arise in the growing ends of long bones, cartilage, and the axial skeleton, respectively. In addition, there are numerous other histologic types that arise due to the precise location of the tumor and whether the tumor involves a combination of other tissue types including bone, joint and even muscle tissues (2). Of the major histologic types of bone and joint cancer, most in our analysis were chondrosarcomas (n=944), followed by osteosarcomas (n=625), and Ewing sarcoma (n=187; Table 10.2). Histologic classification for the current analysis was achieved using the ICD-O-2/ICD-O-3 morphology codes into the following categories of ICD-O M-9260, 9364, and 9473 for Ewing sarcoma; ICD-O M-9180-9185, 9192, 9193 for osteosarcoma; and ICD-O M-9220, 9221, 9231, 9240, 9242, and 9243 for chondrosarcoma. Twenty-

Table 10.1: Cancer of the Bone and Joint: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/selection
4,062	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
3,665	397	Select first primary only
3,633	32	Exclude death certificate only or at autopsy
3,600	33	Exclude unknown race
3,590	10	Exclude alive with no survival time
2,497	1,093	Exclude children (Ages 0-19)
2,497	0	Exclude in situ cancers for all except breast & bladder cancer
2,427	70	Exclude no or unknown microscopic confirmation
2,273	154	Exclude selected histologies*

* The following histologies were excluded from the present analysis due to small case numbers (n<30): Neoplasm, malignant (8000/3), Tumor cells, malignant (8801/3); Malignant tumor, small cell type (8002/3); Malignant tumor, giant cell type (8003/3); Squamous cell carcinoma (8070/3); Squamous cell carcinoma, keratinizing, not otherwise specified (8071/3); Paraganglioma, malignant (8680/3); Sarcoma, not otherwise specified (8800/3); Spindle cell sarcoma (8801/3); Giant cell sarcoma (8802/3); Small cell sarcoma (8803/3); Liposarcoma, not otherwise specified (8850/3); Leiomyosarcoma, not otherwise specified (8890/3); Rhabdoid sarcoma (8963/3); Mesenchymoma, malignant (8990/3); Synovial sarcoma, not otherwise specified (9040/3); Synovial sarcoma, spindle cell (9041/3); Ependymoma, not otherwise specified (9391/3); Meningioma, not otherwise specified (9530/3); Neurofibrosarcoma (9540/3); Neurilemmoma, malignant (9560/3).

two additional categories were included in the 'other' histology category.

Stage

Bone and joint cancers are staged according to SEER historical stage as localized, regional, distant, or unstaged. The staging categories are derived from the 10-digit Extent of Disease (EOD) codes. Codes are assigned based on the clinical, operative, and pathologic diagnosis of cancer. Bone and joint cancer stages are designated according to localized defined as confined to the primary site, regional defined as spreading directly beyond the primary site or involving regional lymph nodes, distant defined as metastatic. Unstaged tumors are also included.

Other Tumor Characteristics

Bone and joint cancers are also categorized according to grade (well, moderate or poorly differentiated, undifferentiated, and unknown), primary site (limbs or other site), and tumor size (0 to 8 centimeters, greater than 8 centimeters, or unknown size).

Age and Race

To investigate median and relative survival among bone and joint cancer cases, age was categorized as 20-39, 40-59, and 60 or more years of age. Two age categories, 40-59 and 60+ were combined for the analysis of Ewing sarcoma. Race-specific survival was calculated for whites, blacks, and other race, except for Ewing sarcoma where a separate analysis of race was not performed.

RESULTS

Table 10.2 shows the histology frequency distributions for adult bone and joint cancer. Of the 2,273 cases included in the analysis, 187 (8.2%) were classified as Ewing sarcoma, 625 (27.5%) were osteosarcoma, and 944 (41.5%) were chondrosarcoma. The remainder were classified in 'other' histologies, where chordoma was the most frequent type (219 cases; 9.6%), followed by malignant fibrous histiocytoma (72 cases; 3.2%). Within Ewing sarcoma, the majority (92.5%) was Ewing sarcoma, not otherwise specified (NOS). Within osteosarcoma, the majority were osteosarcoma, NOS (59.8%) followed by chondroblastic osteosarcoma (13.9%) and parosteal osteosarcoma (10.1%). Chondrosarcoma, NOS contributed to the majority of chondrosarcoma (89.8%) followed by myxoid chondrosarcoma (7.3%).

Demographic and Tumor Characteristics

Table 10.3 shows the demographic and tumor characteristics for bone and joint cancer at the time of diagnosis. For each of the histologic categories, a majority were diagnosed in males (69% for Ewing sarcoma, 54.1% for osteosarcoma, and 53.6% for chondrosarcoma). Bone and joint cancer of 'other' histologic types were also more frequent in males (57.6%). Bone and joint cancers were mostly diagnosed among whites, which is a reflection of the racial distribution within the SEER population.

Interestingly, the distribution of bone cancer histologies varied by race. Among whites, the most common histologies were chondrosarcoma (42.9% of cases), followed by osteosarcoma (25.1%), 'other' histologies (21.9%), and Ewing sarcoma (9.2%). In contrast, osteosarcoma represented 40.0% of black cases, followed by chondrosarcoma at 31.5%. Ewing sarcoma was rare, representing less than 5.0% of black cases.

Ewing sarcoma and osteosarcoma were mostly diagnosed in the 20-39 year age group (82.9% and 51.8% respectively), while chondrosarcoma was mostly diagnosed in the 40-59 year age group (38.6%). Bone and joint cancer in the 'other' histologic group was mostly diagnosed in the 60+ year age group (36.2%).

Historic stage frequencies indicate that cases were diagnosed in the regional stage most often for Ewing sarcoma (39.0%), osteosarcoma (41.3%), and in 'other' histologic types (39.8%). Chondrosarcoma was most often diagnosed in the localized stage (50.7%).

Chondrosarcomas were more often moderately differentiated at the time of diagnosis (39.8%), while osteosarcoma was mostly undifferentiated at diagnosis (35.7%). Ewing sarcoma and 'other' histologic types had a majority of unknown grade. Osteosarcoma and chondrosarcoma tended to be diagnosed in the limbs (63.5% and 54.3% respectively), while Ewing sarcoma was more frequently diagnosed in locations other than the limbs. When information about tumor size at diagnosis was available, most were in the 0 to 8 centimeter range (23.5% for Ewing sarcoma, 37.1% for osteosarcoma, 41.9% for chondrosarcoma, and 32.3% for 'other' histologic type).

Overall Survival

Table 10.4 shows the median survival time and the 1-, 2-, 3-, 5-, 8-, and 10-year relative survival rates by histologic type for 12 SEER registries from 1988 through 2001. For the 2,273 cases in the analysis, the median survival (in months) indicates that chondrosarcoma had

the longest median survival at more than 120 months, followed by bone and joint cancer of 'other' histology with a median survival of over 106 months, osteosarcoma with a median survival of 84.5 months and Ewing sarcoma with a median survival of 59 months. Relative survival indicated that those with bone and joint cancer had relative survival percentages of 88 percent at 1 year. Ewing sarcoma and osteosarcoma tended to have relative survival rates that were below the relative survival for chondrosarcoma (Table 10.4 and Figure 10.1). Bone and joint cancer with 'other' histologies had relative survival rates that were lower than chondrosarcoma.

Sex

Median survival for Ewing sarcoma was greater in females at more than 120 months compared with males at 53.8 months (Table 10.5). Relative survival among females with Ewing sarcoma was also greater than among males at the 3-, 5-, 8- and 10- year intervals. Females also had a higher median survival for osteosarcoma (93.7 months) compared to males (83.3 months; Table 10.6). Relative survival for 1- and 2- year interval was higher among males, and similar at 3-, 5-, and 8-years after diagnosis. Relative survival rates at 10-years were higher among females. Median survival was the same for males and females for chondrosarcoma at more than 120 months. The relative survival percentages for chondrosarcoma for females started slightly higher than for males at one year post-diagnosis. Females continued to have more favorable relative survival percentages through 10-years after diagnosis. Median survival for 'other' types of bone sarcoma was higher among females at greater than 120 months and 96.9 months for males (Table 10.8). For 'other' types, relative survival rates were higher for females after 5-years.

Table 10.2: Cancer of the Bone and Joint: Histology Distribution, Age 20+, 12 SEER Areas, 1988-2001

Histology Group	Histology/ICD-O Code	Cases	Percent of Category	Percent of Total
Total		2,273		100.0
Ewing Sarcoma		187	100.0	8.2
	Ewing sarcoma, NOS* (9260)	173	92.5	7.6
	Other (9364, 9473)	14	7.5	0.6
Osteosarcoma		625	100.0	27.5
	Osteosarcoma, NOS* (9180)	374	59.8	16.5
	Chondroblastic osteosarcoma (9181)	87	13.9	3.8
	Fibroblastic osteosarcoma (9182)	56	9.0	2.5
	Telangiectatic osteosarcoma (9183)	15	2.4	0.7
	Osteosarcoma in Paget's disease of bone (9184)	21	3.4	0.9
	Parosteal osteosarcoma (9192)	63	10.1	2.8
	Other (9185, 9193)	9	1.4	0.4
Chondrosarcoma		944	100.0	41.5
	Chondrosarcoma, NOS* (9220)	848	89.8	37.3
	Juxtacortical chondrosarcoma (9221)	7	0.7	0.3
	Myxoid chondrosarcoma (9231)	69	7.3	3.0
	Mesenchymal chondrosarcoma (9240)	14	1.5	0.6
	Other (9242, 9243)	6	0.6	0.3
Other Histologies		517	100.0	22.7
	Fibrosarcoma, NOS* (8810)	21	4.1	0.9
	Fibrous histiocytoma, malignant (8830)	72	13.9	3.2
	Hemangiosarcoma (9120)	26	5.0	1.1
	Hemangioendothelioma, malignant (9130)	13	2.5	0.6
	Epithelioid hemangioendothelioma, malignant (9133)	8	1.5	0.4
	Chondroblastoma, malignant (9230)	8	1.5	0.4
	Giant cell tumor of bone, malignant (9250)	52	10.1	2.3
	Adamantinoma of long bones (9261)	18	3.5	0.8
	Odontogenic tumor, malignant (9270)	29	5.6	1.3
	Ameloblastoma, malignant (9310)	36	7.0	1.6
	Chordoma (9370)	219	42.4	9.6
	Other (8072, 8805, 8811, 8823, 8851, 8910, 9043, 9150, 9321, 9330, 9371)	15	2.9	0.7

* NOS: Not Otherwise Specified

Age

The different types of cancer have very different survival time depending on the age of the patient. As seen in Table 10.5, younger Ewing sarcoma patients between 20 and 39 years old had better short term survival but not long-term survival. Relative survival rate tended to be lower in the 60+ age group for osteosarcoma, chondrosarcoma and 'other' bone sarcomas (Tables 10.6, 10.7, 10.8).

Race

Race information is not shown for Ewing sarcoma since there were few cases among non-white patients. Median survival for osteosarcoma varied by race, with whites having a higher median survival (82.6 months) than blacks (65.7 months, Table 10.6). For chondrosarcoma, blacks and whites shared a median survival greater than 120 months. Only slight survival differences were seen at the 10-year mark between whites (78%) and blacks (83%; Table 10.7). Median survival for 'other' bone cancer histologies was slightly higher in blacks (>120 months) than in whites (104.6 months; Table 10.8).

Historic Stage

Median survival was highest for each of the bone and joint cancers that had localized historic stage (Tables 10.6, 10.7, 10.8; median survival greater than 120 months). Tumors that were identified as regional historic stage also had long median survival times of greater than 120 months for Ewing sarcoma and chondrosarcoma. Osteosarcoma and 'other' bone sarcoma both had median survival of more than 90 months for regional historic stage, 93.6 months and 91.7 months, respectively. Tumors classified as distant historic stage had lower median survival times of 21.9 months for Ewing sarcoma, 9.9 months for osteosarcoma, 17 months

Table 10.3: Cancer of the Bone and Joint: Distributions by Sex, Race, Age (20+), Historic Stage, Grade, Primary Site, Tumor Size, and Histology, Ages 20+,12 SEER Areas, 1988-2001

	Histology							
	Ewing Sarcoma		Osteosarcoma		Chondrosarcoma		Other	
Characteristics	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
All Cases	187	100.0	625	100.0	944	100.0	517	100.0
Sex								
Male	129	69.0	338	54.1	506	53.6	298	57.6
Female	58	31.0	287	45.9	438	46.4	219	42.4
Race								
White	178	95.2	504	80.6	832	88.1	425	82.2
Black	<6	<5.0	76	12.2	60	6.4	51	9.9
Other	<6	<5.0	45	7.2	52	5.5	41	7.9
Age at Diagnosis (years)								
20-39	155	82.9	324	51.8	293	31.0	167	32.3
40-59	26	13.9	153	24.5	364	38.6	163	31.5
60+	6	3.2	148	23.7	287	30.4	187	36.2
Historic Stage								
Localized	34	18.2	200	32.0	479	50.7	176	34.0
Regional	73	39.0	258	41.3	343	36.3	206	39.8
Distant	58	31.0	108	17.3	61	6.5	79	15.3
Unstaged	22	11.8	59	9.4	61	6.5	56	10.8
Grade								
Well	0	0.0	46	7.4	354	37.5	21	4.1
Moderate	0	0.0	61	9.8	376	39.8	36	7.0
Poor	18	9.6	105	16.8	57	6.0	36	7.0
Undifferentiated	41	21.9	223	35.7	55	5.8	43	8.3
Unknown	128	68.4	190	30.4	102	10.8	381	73.7
Primary Site								
Limbs	71	38.0	397	63.5	513	54.3	163	31.5
Other	116	62.0	228	36.5	431	45.7	354	68.5
Tumor Size								
<= 8 cm	44	23.5	232	37.1	396	41.9	167	32.3
> 8 cm	42	22.5	126	20.2	192	20.3	68	13.2
Unknown	101	54.0	267	42.7	356	37.7	282	54.5

for chondrosarcoma, and 16.5 months for 'other' bone sarcoma.

Grade

Grade classification was not shown for Ewing sarcoma cases. In general, median survival was highest in the well and moderately differentiated cases for osteosarcoma and chondrosarcoma (median survival was greater than 120 months in these groups). A majority of cases of osteosarcoma had poor, undifferentiated, or unknown grade, and had median survival of 78.2 months, 46.6 months, and 43.4 months, respectively (Table 10.6). In contrast, approximately 23% of all chondrosarcoma cases had poor, undifferentiated, and unknown grade (Table 10.7). These cases had median survival times of 60.9 months, 15.4 months, and more than 120 months, respectively. Most of the 'other' bone sarcoma cases had unknown grade (74%; Table 10.8). Relative survival rates for osteosarcoma exceeded 85% at each of the 1-year, 2-year, 3-year, 5-year, 8-, and 10-year intervals for cases with well and moderate grades. Poor, undifferentiated, and unknown grade osteosarcoma relative survival ranged from 82% for 1-year relative survival for cases with poor or undifferentiated grade to 38% for undifferentiated cases at 10-years after diagnosis.

Relative survival rates for well or moderately differentiated chondrosarcoma exceeded 75% for the 1-year, 2-year, 3-year, 5-year, 8-, and 10-year relative survival intervals. Chondrosarcomas with unknown differentiation had relative survival percentages that remained above 71%. Poor and undifferentiated chondrosarcoma had lower relative survival percentages that ranged from 77 percent (1-year relative survival for poor grade) to 30 percent (8- and 10-year relative survival for undifferentiated). Most of the 'other' bone sarcomas had unknown differentiation and the 10 year relative survival rate was 62%.

Table 10.4: Cancer of the Bone and Joint: Number and Distribution of Cases, Median Survival Time (Months) and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology	Cases	Percent	Median Survival (Months)	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	2,273	100.0	>120	88.0	79.9	75.7	70.2	65.5	63.6
Ewing Sarcoma	187	8.2	59.0	83.2	68.9	60.3	48.4	44.6	44.6
Osteosarcoma	625	27.5	84.5	82.2	67.9	65.0	59.2	54.5	51.8
Chondrosarcoma	944	41.5	>120	93.0	88.9	85.4	81.6	79.1	78.5
Other Histologies	517	22.7	106.6	87.6	82.0	76.9	70.7	61.6	58.3

Table 10.5: Ewing Sarcoma: Number and Distribution of Cases, Median Survival Time (Months) and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Sex, Age (20+), Historic Stage, Primary Site and Tumor Size, 12 SEER Areas, 1988-2001

Characteristics	Cases	Percent	Median Survival (Months)	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases	187	100.0	59.0	83.2	68.9	60.3	48.4	44.6	44.6
Sex									
Male	129	69.0	53.8	83.3	69.3	59.2	45.7	41.5	41.5
Female	58	31.0	>120	82.8	68.1	62.4	53.6	50.9	50.9
Age (years)									
20-39	155	82.9	59.5	84.5	69.4	60.4	48.9	44.5	44.5
40+	32	17.1	39.8	76.7	66.4	59.7	46.7	46.7	46.7
Historic Stage									
Localized	34	18.2	>120	98.4	79.0	72.4	60.4	60.4	60.4
Regional	73	39.0	>120	90.6	81.8	73.5	66.6	61.3	61.3
Distant	58	31.0	21.9	63.9	47.8	41.9	24.7	24.7	24.7
Unstaged	22	11.8	~	~	~	~	~	~	~
Primary Site									
Limbs	71	38.0	53.6	88.1	72.0	62.0	45.7	39.5	39.5
Other	116	62.0	59.4	80.1	67.1	59.2	49.9	47.1	47.1
Tumor Size									
<= 8 cm	44	23.5	>120	91.0	88.4	82.7	68.7	63.5	63.5
> 8 cm	42	22.5	34.7	69.1	52.0	49.3	36.2	32.6	32.6
Unknown	101	54.0	47.0	85.7	68.1	55.9	45.5	42.2	42.2

~ Statistic not displayed due to less than 25 cases.

Primary Site

Primary site classification was available for each of the subtypes of bone and joint cancer. Bone and joint cancer with the primary site reported in the limbs had median survival that exceeded 120 months for osteosarcoma, chondrosarcoma, and 'other' bone sarcoma. Median survival for Ewing sarcoma in the limbs was 53.6 months. Median survival for 'other' primary site varied at 59.4 months, 24.0 months, greater than 120 months, and 89.4 months for Ewing sarcoma, osteosarcoma, chondrosarcoma, and 'other' bone sarcoma, respectively. At 10 years after diagnosis, relative survival was highest for chondrosarcoma of the limbs (83%) and lowest for osteosarcoma of sites other than limbs (35%). Relative survival rates for Ewing sarcoma exceeded 80% for limbs primary site and 'other' primary site at the 1-year mark, then declined for both primary sites to 40% and 47% for limbs and 'other' primary site respectively at the 10-year mark. Relative survival for osteosarcoma ranged from 89% at 1 year to 61% at 10 years for limbs as the primary site, and 71% at 1-year for 35% at 10 years for 'other' primary site.

Tumor Size

Each of the bone and joint cancer subtypes of tumor size 0 to 8 centimeters had a median survival that exceeded 120 months, with the exception of 'other' bone sarcoma which had a median survival of 116.3 months. Median survival for bone and joint cancers that were greater than 8 centimeters varied with subtype, as Ewing sarcoma had a median survival of 34.7 months, osteosarcoma had a median survival of 31.3 months, chondrosarcoma had a median survival of more than 120 months, and 'other' bone sarcoma had a median survival of 56.8 months.

Table 10.6: Osteosarcoma: Number and Distribution of Cases, Median Survival Time (Months) and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Sex, Race, Age (20+), Historic Stage, Grade, Primary Site and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

Characteristics	Cases	Percent	Median Survival (Months)	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases	625	100.0	84.5	82.2	67.9	65.0	59.2	54.5	51.8
Sex									
Male	338	54.1	83.3	83.4	68.4	64.6	59.9	54.3	50.6
Female	287	45.9	93.7	81.0	67.4	65.4	58.3	54.5	53.1
Race									
White	504	80.6	82.6	81.2	67.0	63.8	58.4	54.0	52.0
Black	76	12.2	65.7	85.0	68.7	67.7	61.1	47.4	47.4
Other	45	7.2	>120	89.1	77.7	72.5	63.9	63.9	52.3
Age (years)									
20-39	324	51.8	>120	92.4	80.8	77.4	70.3	63.4	58.8
40-59	153	24.5	103.3	84.7	67.7	64.1	60.2	53.4	47.8
60+	148	23.7	14.2	56.4	37.8	35.1	27.9	25.6	25.6
Historic Stage									
Localized	200	32.0	>120	96.3	88.0	84.7	81.2	79.6	76.4
Regional	258	41.3	93.6	86.5	70.9	67.6	60.2	54.4	50.8
Distant	108	17.3	9.9	48.8	24.8	22.4	14.9	3.7	!
Unstaged	59	9.4	38.9	76.4	63.8	61.1	51.8	46.1	42.9
Grade									
Well	46	7.4	>120	100.0	100.0	100.0	96.2	96.2	86.7
Moderate	61	9.8	>120	97.1	90.7	90.7	87.3	85.3	85.3
Poor	105	16.8	78.2	81.7	67.9	65.1	56.6	51.7	51.7
Undifferentiated	223	35.7	46.6	81.1	61.9	56.6	50.5	39.3	37.7
Unknown	190	30.4	43.4	74.6	59.2	56.7	51.1	47.9	44.4
Primary Site									
Limbs	397	63.5	>120	88.9	77.1	74.6	67.6	62.5	60.7
Other	228	36.5	24.0	70.5	51.8	48.0	43.8	39.7	34.5
Tumor Size									
<= 8 cm	232	37.1	> 120	92.1	81.8	79.5	73.1	65.6	62.7
> 8 cm	126	20.2	31.3	73.3	54.6	51.4	45.9	43.8	41.4
Unknown	267	42.7	56.5	77.9	62.0	58.5	52.8	48.8	46.2

! Not enough intervals to produce rate.

Tumors of unknown size had median survival times of 47 months and 56.5 months for Ewing sarcoma and osteosarcoma respectively, while median survival for both chondrosarcoma and 'other' bone sarcoma of unknown tumor size was greater than 120 months. Relative survival rates were highest for tumor sizes of 0 to 8 centimeters (all were greater than 59% at 10-years after diagnosis).

DISCUSSION

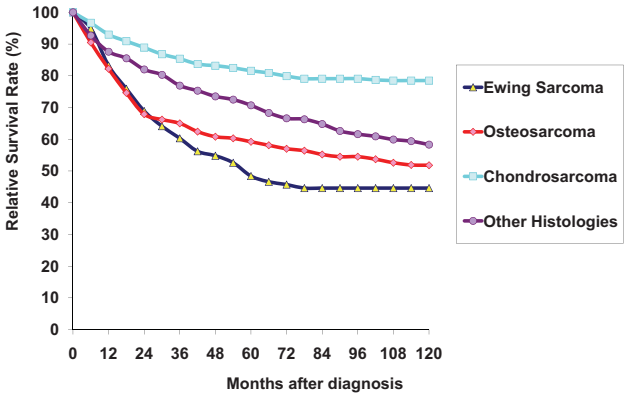
A review by Miller et al. (2) discussed various environmental factors, including exposure to ionizing radiation, chemicals, viruses, trauma, and metal implants as potential risk factors for bone and joint cancer. Host factors of importance for bone and joint cancer include pre-existing bone defects and familial aggregation of these cancers along with reports of multiple neoplasms. This review noted that in various populations, there has been no improvement in survival among patients of all ages in the U.S. or among children in Europe over the past 15 years. [Note: cell types differ for Ewing sarcoma and osteosarcoma, perhaps indicating different origins. Chondrosarcoma is epidemiologically dissimilar to osteosarcoma.]

A case-control study of 88 bone cancer cases aged 8 to 25 years and 3 matched control groups from Austria evaluated a variety of exposures to previous illness, bone injury or disease, nutrition, social and emotional factors and risk of bone cancer (3). Previous viral illnesses including chickenpox and mumps significantly increased the risk for bone cancer. Exposure to repeated polio vaccinations also were associated with elevated risk. Difficulties at school were associated with in an increased risk for bone cancer in both univariate and multivariate analyses. In a separate analy-

Table 10.7: Chondrosarcoma: Number and Distribution of Cases, Median Survival Time (Months) and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Sex, Race, Age (20+), Historic Stage, Grade, Primary Site and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

Characteristics	Cases	Percent	Median Survival (Months)	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases	944	100.0	>120	93.0	88.9	85.4	81.6	79.1	78.5
Sex									
Male	506	53.6	>120	92.5	87.6	83.5	77.8	74.3	73.7
Female	438	46.4	>120	93.6	90.5	87.6	86.0	84.1	84.0
Race									
White	832	88.1	>120	92.8	89.0	85.8	81.9	78.7	77.7
Black	60	6.4	>120	96.0	89.8	86.5	83.0	83.0	83.0
Other	52	5.5	>120	92.7	86.7	74.8	72.8	72.8	72.8
Age (years)									
20-39	293	31.0	>120	95.7	91.9	89.3	87.8	83.5	83.0
40-59	364	38.6	>120	96.6	91.2	88.7	86.4	83.5	81.6
60+	287	30.4	80.8	85.5	82.6	76.7	68.5	67.2	67.2
Historic Stage									
Localized	479	50.7	>120	98.9	98.3	94.9	93.8	92.0	91.8
Regional	343	36.3	>120	90.4	83.5	79.3	71.8	67.2	64.7
Distant	61	6.5	17.0	62.8	44.5	40.9	34.3	34.3	34.3
Unstaged	61	6.5	>120	91.3	89.2	85.6	82.6	77.0	77.0
Grade									
Well	354	37.5	>120	98.6	98.2	97.0	95.1	92.3	92.2
Moderate	376	39.8	>120	95.9	91.3	87.5	80.2	75.9	75.9
Poor	57	6.0	60.9	77.1	69.3	63.8	58.6	52.7	50.7
Undifferentiated	55	5.8	15.4	65.0	40.7	30.1	30.1	29.9	29.9
Unknown	102	10.8	>120	86.4	82.4	76.7	74.3	71.8	71.2
Primary Site									
Limbs	513	54.3	>120	94.8	92.1	88.3	86.2	84.2	83.0
Other	431	45.7	>120	90.9	85.1	81.7	76.2	72.5	72.4
Tumor Size									
<= 8 cm	396	41.9	> 120	97.2	95.2	92.1	87.6	84.3	82.4
> 8 cm	192	20.3	> 120	91.8	83.7	79.0	74.7	74.1	74.1
Unknown	356	37.7	> 120	89.0	84.7	81.2	78.6	74.5	74.5

Figure 10.1: Cancer of the Bone & Joint: Relative Survival Rates (%) by Histology, Ages 20+,12 SEER Areas, 1988-2001



sis of osteosarcoma cases, having more than one lifetime residence was associated with increased risk, along with difficulties at school (3).

REFERENCES

1. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Eisner MP, Horner MJ, Howlader N, Hayat M, Hankey BF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site, 2006.
2. Miller RW, Boice JD, Jr., Curtis RE. Bone cancer. In: Cancer Epidemiology and Prevention, 3rd edition. Schottenfeld D, and Fraumeni JF, Jr., Eds. New York: Oxford University Press, 1996, pp. 946-958.
3. Frentzel-Beyme R, Becher H, Salzer-Kuntschik M, Kotz R, Salzer M. Factors affecting the incident juvenile bone tumors in an Austrian case-control study. Cancer Detection and Prevention 2004; 28: 159-169.

Table 10.8: Other Bone Sarcoma: Number and Distribution of Cases, Median Survival Time (Months) and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Sex, Age (20+), Historic Stage, Grade, Primary Site and Tumor Size, 12 SEER areas 1988-2001

Characteristics	Cases	Percent	Median Survival (Months)	Relative Survival Rate (%)					
				1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Cases	517	100.0	106.6	87.6	82.0	76.9	70.7	61.6	58.3
Sex									
Male	298	57.6	96.9	86.7	83.4	77.0	69.3	59.5	55.7
Female	219	42.4	>120	88.5	79.8	76.7	71.9	64.5	61.6
Race									
White	425	82.2	104.6	86.3	81.9	77.3	71.4	61.1	57.3
Black	51	9.9	>120	94.8	83.6	79.8	76.1	74.3	74.3
Other	41	7.9	68.1	90.6	80.6	69.5	56.5	44.9	37.0
Age (years)									
20-39	167	32.3	>120	95.9	91.6	86.2	81.7	81.0	77.0
40-59	163	31.5	>120	90.0	86.0	82.1	76.6	62.2	58.8
60+	187	36.2	44.7	77.6	69.1	63.0	52.7	35.0	28.1
Historic Stage									
Localized	176	34.0	>120	94.1	88.7	85.3	79.5	75.4	75.4
Regional	206	39.8	91.7	94.2	87.8	81.6	71.9	57.7	52.3
Distant	79	15.3	16.5	54.3	46.3	41.1	41.1	26.6	24.3
Unstaged	56	10.8	>120	88.8	88.7	83.1	78.3	73.7	66.4
Grade									
Well	21	4.1	~	~	~	~	~	~	~
Moderate	36	7.0	>120	95.6	88.6	86.2	78.1	78.1	74.5
Poor	36	7.0	33.6	78.7	59.0	51.5	43.8	30.3	!
Undifferentiated	43	8.3	12.5	52.4	45.5	41.4	30.9	23.1	23.1
Unknown	381	73.7	>120	91.2	87.2	82.2	76.6	66.1	62.2
Primary Site									
Limbs	163	31.5	>120	84.9	76.9	73.6	72.6	69.4	69.4
Other	354	68.5	89.4	88.7	84.2	78.2	69.3	56.0	51.1
Tumor Size									
<= 8 cm	167	32.3	116.3	89.6	85.4	77.5	75.5	65.6	59.6
> 8 cm	68	13.2	56.8	87.9	74.1	71.1	51.6	38.8	33.6
Unknown	282	54.5	> 120	86.1	81.7	77.5	71.9	63.8	61.1

~ Statistic not displayed due to less than 25 cases.
! Not enough intervals to produce rate.

Chapter 11
Sarcomas

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INTRODUCTION

Sarcomas are tumors of diverse cell types which are mostly of mesodermal origin. They primarily arise in the soft tissues of the body including the retroperitoneum and peritoneum, pleura, heart, mediastinum and spleen but can also arise in the structural cells or parenchyma of specialized organs such as the stomach and kidney. The classification of tumors according to both the anatomic site in which they arose and the morphology of the tumor itself using the International Classification of Disease for Oncology (1) allows these tumors to be analyzed together as a group. Consequently, authors of other chapters in this monograph may have elected to exclude the sarcomas from their analyses knowing that they would be included here.

MATERIALS AND METHODS

The NCI contracts with medically-oriented, nonprofit institutions located in specific geographic areas to obtain data on all cancers diagnosed in residents of the SEER geographic areas. SEER collects data on all invasive and in situ cancers except basal cell and squamous cell carcinomas of the skin (of non-genital anatomic sites) and in situ carcinomas of the uterine cervix. SEER actively follows all previously diagnosed patients on an annual basis to obtain vital status allowing the calculation of observed and relative survival rates.

This analysis is based on data from 12 geographic areas which collectively cover about 14% of the total US population. The areas are the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Michigan; Atlanta, Georgia; San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; and 10 counties in rural Georgia. Los Angeles contributed data for diagnosis years 1992 to 2001, all other areas for 1988-2001.

Cases diagnosed in children and adolescents aged 0-19 have been excluded. Some patients have more than one diagnosis of cancer, but only the first diagnosis of cancer has been included. Death certificate only cases, autopsy only cases, and all other cases with no survival time have been excluded. Further, cases with no microscopic confirmation have been excluded. Finally, sarcomas arising in bone (osteosarcomas) have also been excluded from this analysis but are included in the bone chapter (2). Table 11.1 shows the numbers of cases excluded by category.

Survival analysis is based on relative survival rates calculated by the life-table (actuarial) method. Relative survival, defined as observed survival in the cohort divided by expected survival in the cohort, adjusts for the expected mortality that the cohort would experience from other causes of death. Expected survival is based on unabridged life tables for the United States in 1990. Although the American Joint Committee on Cancer's Staging Manual

Table 11.1: Sarcomas: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number selected/ remaining	Number excluded	Reason for exclusion/selection
41,408	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
37,314	4,094	Select first primary only
36,979	335	Exclude death certificate only or at autopsy
36,425	554	Exclude unknown race
36,337	88	Active follow-up and exclude alive with no survival time
33,820	2,517	Exclude children (000-019)
33,820	0	Exclude in situ cancers
30,183	3,637	Exclude no or unknown microscopic confirmation
28,758	1,425	Exclude cancer of the bone (C40.0-C41.9)

Table 11.2: Sarcomas: Number and Distributions by Sex, Race, SEER Summary Stage 1977 and Histology Group, Ages 20+, 12 SEER Areas, 1988-2001

	Sex			Race		Stage Percent			
Histology Group	Total	Male	Female	White	Black	Localized	Regional	Distant	Unstaged
Total	28,758	18,226	10,532	23,195	3,588	37.5	12.6	10.5	39.4
Perivascular sarcomas	174	95	79	130	31	28.2	28.2	28.2	15.5
Liposarcomas	2,368	1,413	955	1,986	190	65.9	21.3	5.7	7.1
Dermatofibrosarcomas	2,142	996	1,146	1,612	366	84.8	5.2	0.5	9.5
Other fibrosarcomas	511	250	261	391	71	57.1	23.9	9.2	9.8
Fibrohistiocytic sarcoma	3,063	1,823	1,240	2,626	218	61.2	21.1	9.9	7.8
Leiomyosarcomas	4,486	1,625	2,861	3,516	544	51.0	18.6	21.9	8.5
Rhabdosarcomas	299	178	121	223	49	27.8	28.8	29.8	13.7
Kaposi sarcoma	9,513	9,208	305	7,849	1,374	0.0	0.0	0.0	100.0
Vascular sarcomas excluding Kaposi	614	332	282	513	44	41.5	18.9	24.1	15.5
Chondro-oseous sarcomas	93	42	51	76	11	45.2	32.3	15.1	7.5
Sarcomas of uncertain differentiation	5,495	2,264	3,231	4,273	690	45.9	20.3	22.5	11.3

does contain a staging scheme for sarcomas, the scheme only applies to those sarcomas arising in soft tissues. Since this analysis is based on all sarcomas including those arising in any anatomic site except bone, the staging definitions utilized in this chapter are those of the 1977 Summary Staging Guide (3) whose staging categories are generally equivalent across the spectrum of anatomic sites. For simplicity, all categories of regional disease in the summary staging scheme have been added together into a single group. Finally, the sarcomas have been categorized into 11 subgroups roughly following the recommended classification of the World Health Organization (4) as shown below based on ICD-O-3 codes:

Perivascular Sarcomas 8680-8713
Liposarcomas 8850-8858
Dermatofibrosarcomas 8832-8833
Other fibrosarcomas 8810-8811,8813-8814,8825
Fibrohistiocytic sarcoma 8830
Leiomyosarcomas 8890-8891,8894,8896
Rhabdosarcomas 8900-8902,8910,8912,8920
Kaposi sarcoma 9140
Vascular sarcomas excluding Kaposi 9120,9133,9161
Chondro-oseous sarcomas 9180-9185,9192-9193,9221, 9230,9240,9243,9250
Sarcomas of uncertain differentiation 8800-8806,8823,8930-8936,8963,8990-8991,9040-9044,9231,9260-9261, 9364,9370-9371,9560-9561,9571,9580-9581.

RESULTS

Table 11.2 shows the distribution by sex, race, and summary stage for eleven categories of sarcomas. The largest category by far is Kaposi sarcoma (33%) with the smallest being the chondro-oseous (extraosseous) sarcomas (0.3%). Sarcomas occur more commonly among males, especially Kaposi of which only 3% of the cases occurred among females. Since there was no specific summary staging scheme for Kaposi, 100% of these cases were classified as "unstaged." Almost 30% of perivascular sarcomas and rhabdosarcomas were already staged as distant at the time of diagnosis.

Table 11.3 presents 5-year relative survival rates by anatomic site, histology and sex. Patients with sarcomas arising in soft tissues had much better survival than did patients whose tumors arose in other non-parenchymous sites (pleura, mediastinum, heart, retroperitoneum, peritoneum, and spleen) or in other organs, 68% vs. 43% and 44%, respectively. For Kaposi sarcoma, survival for those tumors arising in the soft tissue vs. other sites (primarily skin) was more than double – 53% vs. 25%. The best survival, regardless of site was among patients with dermatofibrosarcoma, 99.9%.

The 1-, 3-, 5- and 10-year relative survival rates for each subgroup are shown for males and for females in Table 11.4. The relative survival rates for dermatofibrosarcomas were almost 100% across all years being 98% at 10 years for males and 99.9% for females.

The poorest 10-year relative survival rate among males was experienced by patients with Kaposi sarcoma, 18%, followed closely by patients with other vascular sarcomas, 24%. Among females, the poorest relative survival at both 5 and 10 years was among those with a diagnosis of rhabdosarcoma.

A comparison of 1-,3-,5-, and 10-year relative survival rates for whites and for blacks is shown in Table 11.5. Overall, whites had higher survival rates at each interval compared to blacks, but the advantage diminished with time since diagnosis with the advantage being small at 10 years, 44% for whites compared to 41% for blacks. For the category of "other fibrosarcomas", blacks had much

Table 11.3: Sarcomas: 5-Year Relative Survival Rates (5) by Histology Group, Site, and Sex, Ages 20 +, 12 SEER Areas, 1988-2001

	Site											
	Total			Soft Tissue			Other Non-parenchymous			All Other		
Histology Group	All	Male	Female	All	Male	Female	All	Male	Female	All	Male	Female
Total	50.3	42.6	64.0	68.0	68.1	67.9	42.6	39.8	45.3	43.9	34.7	64.4
Perivascular sarcomas	63.3	62.0	64.9	~	~	~	69.6	~	~	61.8	60.1	63.5
Liposarcomas	82.8	82.4	83.1	85.9	84.8	87.1	65.1	60.0	70.2	94.4	97.0	81.9
Dermatofibrosarcomas	99.9	99.6	100.0	98.4	96.6	99.3	!	!	!	99.9	99.7	100.0
Other fibrosarcomas	72.4	68.5	75.5	79.8	79.0	80.3	38.6	~	~	61.1	40.4	70.7
Fibrohistiocytic sarcoma	67.0	67.9	65.7	67.6	67.6	67.6	25.4	26.4	24.2	77.7	79.5	72.9
Leiomyosarcomas	51.9	55.7	49.9	62.0	67.4	57.0	36.4	32.7	38.6	50.3	52.8	49.4
Rhabdosarcomas	35.0	35.9	33.9	40.4	40.1	39.7	~	~	~	31.0	32.6	29.4
Kaposi sarcoma	24.7	23.9	54.9	52.6	45.9	~	~	~	!	24.5	23.8	53.4
Vascular sarcomas excluding Kaposi	36.3	32.1	40.9	37.9	42.0	33.4	12.9	12.3	~	40.0	30.9	48.6
Chondro-oseous sarcomas	54.7	46.8	59.4	53.6	~	54.4	~	~	~	60.8	~	~
Sarcomas of uncertain differentiation	55.6	49.1	59.9	57.4	56.0	58.9	35.4	34.0	36.0	57.8	43.9	63.0

~ Statistic not displayed due to less than 25 cases.
! Not enough intervals to produce rate

Table 11.4: Sarcomas: 1-, 3- ,5- and 10-Year (Yr) Relative Survival Rates (%) by Histology Group and Sex, Ages 20+, 12 SEER Areas, 1988-2001

	Relative Survival Rate (%)											
	Total				Male				Female			
Histology Group	1-Yr	3-Yr	5-Yr	10-Yr	1-Yr	3-Yr	5-Yr	10-Yr	1-Yr	3-Yr	5-Yr	10-Yr
Total	77.7	56.8	50.3	43.9	74.8	49.8	42.6	35.7	82.8	69.2	64.0	58.6
Perivascular sarcomas	90.2	75.1	63.3	47.5	88.5	71.1	62.0	38.4	92.2	80.0	64.9	58.8
Liposarcomas	93.4	85.8	82.8	74.4	93.9	85.8	82.4	76.4	92.8	85.9	83.1	71.0
Dermatofibrosarcomas	100.0	99.9	99.9	99.3	100.0	99.6	99.6	98.2	100.0	100.0	100.0	99.9
Other fibrosarcomas	87.2	77.8	72.4	65.4	86.3	76.8	68.5	63.1	88.1	78.6	75.5	66.5
Fibrohistiocytic sarcoma	85.0	71.2	67.0	64.0	85.4	72.5	67.9	63.5	84.3	69.4	65.7	63.2
Leiomyosarcomas	80.6	60.8	51.9	43.1	81.9	63.0	55.7	47.5	79.9	59.5	49.9	40.8
Rhabdosarcomas	65.6	42.6	35.0	30.5	70.4	43.9	35.9	32.3	58.5	40.5	33.9	27.2
Kaposi sarcoma	66.9	32.9	24.7	18.8	66.4	31.9	23.9	18.2	80.9	65.4	54.9	47.2
Vascular sarcomas excluding Kaposi	60.2	40.6	36.3	29.5	55.9	35.8	32.1	23.7	65.3	46.2	40.9	35.5
Chondro-osseous sarcomas	83.3	65.7	54.7	48.0	78.1	62.3	46.8	44.0	87.5	68.1	59.4	50.9
Sarcomas of uncertain differentiation	76.0	60.4	55.6	50.5	73.8	55.2	49.1	40.7	77.6	63.8	59.9	56.0

better survival than did whites with the 10-year relative survival rate being 79% for blacks compared to only 61% for whites. For rhabdosarcomas, the opposite was true with whites having much higher survival at each interval with the 10-year rate being 35% for whites compared to only 19% for blacks. The 10-year rate for patients with Kaposi sarcoma was almost equal among the two groups – 19% for whites and 18% for blacks.

Table 11.6 presents 5- and 10-year survival rates by summary stage. Patients with distant disease had uniformly poor survival (11% overall) at 10-years while survival for patients diagnosed at a localized stage was 78%. Among patients with localized disease, those with rhabdosarcoma had the poorest survival with rates of 59% at 5 years and 53% at 10 years.

DISCUSSION

In order to have sufficient numbers of cases for analyses the classification of sarcomas suggested by the World Health Organization (4) was utilized. Even so, several of the categories contained very few cases. Whenever possible, major subgroups were examined separately, namely, dermatofibrosarcomas from the fibrosarcoma group and Kaposi sarcoma from the vascular sarcoma group. In other categories, some interesting differences may have been obscured by the grouping of categories. For example, among the rhabdosarcomas, there were enough cases of alveolar rhabdosarcoma to examine separately.

Mack (5) has described in detail the heterogeneity of sarcomas and the various ways of classifying them over

Table 11.5: Sarcomas: 1-, 3- ,5- and 10-Year Relative Survival Rates (%) by Histology Group and Race, Ages 20+, 12 SEER Areas, 1988-2001

Histology Group	Relative Survival Rate (%)							
	White				Black			
	1-Year	3-Year	5-Year	10-Year	1-Year	3-Year	5-Year	10-Year
Total	78.5	57.1	50.4	43.9	71.5	51.4	46.4	40.8
Perivascular Sarcomas	88.9	74.7	62.8	47.2	94.3	75.0	66.6	49.0
Liposarcomas	93.1	85.1	82.5	73.4	94.8	88.2	83.3	79.7
Dermatofibrosarcomas	100.0	99.8	99.8	99.8	100.0	100.0	100.0	97.7
Other fibrosarcomas	85.5	75.4	69.4	61.3	98.3	90.9	87.2	79.4
Fibrohistiocytic sarcoma	85.6	73.1	69.0	65.6	78.5	55.1	53.7	52.4
Leiomyosarcomas	81.8	62.0	53.2	44.4	73.2	52.1	45.6	37.9
Rhabdosarcomas	68.1	46.1	39.1	35.0	51.5	21.4	21.4	18.6
Kaposi sarcoma	68.5	33.2	24.6	18.9	58.5	31.2	24.9	17.9
Vascular sarcomas excluding Kaposi	61.0	42.2	37.4	29.0	58.5	43.3	39.5	37.0
Chondro-osseous sarcomas	84.6	66.8	56.5	49.4	~	~	~	~
Sarcomas of uncertain differentiation	76.5	61.5	56.7	51.6	70.3	51.5	47.4	41.3

~ Statistic not displayed due to less than 25 cases.

Table 11.6: Sarcomas: 5- & 10-Year (Yr) Relative Survival Rates (%) by Histology Group and SEER Summary Stage, 12 SEER Areas, 1988-2001

Histology Group	Stage									
	Total		Local		Regional		Distant		Unstaged	
	Relative Survival		Relative Survival		Relative Survival		Relative Survival		Relative Survival	
	5-Yr	10-Yr	5-Yr	10-Yr	5-Yr	10-Yr	5-Yr	10-Yr	5-Yr	10-Yr
	%	%	%	%	%	%	%	%	%	%
Total	50.3	43.9	83.1	78.1	54.0	46.1	16.2	11.1	28.8	22.2
Perivascular Sarcomas	63.3	47.5	82.1	59.3	82.6	73.5	43.0	21.0	37.3	21.0
Liposarcomas	82.8	74.4	90.9	81.5	74.4	65.4	30.8	15.4	70.1	66.9
Dermatofibrosarcomas	99.9	99.3	99.9	99.3	100.0	100.0	~	~	99.4	97.3
Other fibrosarcomas	72.4	65.4	88.3	83.0	54.3	44.4	24.2	19.5	67.3	56.0
Fibrohistiocytic sarcoma	67.0	64.0	81.4	79.1	55.2	49.8	11.8	9.3	53.8	43.7
Leiomyosarcomas	51.9	43.1	71.8	61.4	44.4	35.3	13.6	8.9	45.4	32.4
Rhabdosarcomas	35.0	30.5	58.6	52.6	40.2	34.5	6.3	6.3	34.8	27.1
Kaposi sarcoma	24.7	18.8	!	!	!	!	!	!	24.7	18.8
Vascular sarcomas excluding Kaposi	36.3	29.5	57.6	52.2	31.7	24.2	12.9	7.3	25.4	15.5
Chondro-osseous sarcomas	54.7	48.0	62.3	53.5	65.5	57.1	~	~	~	~
Sarcomas of uncertain differentiation	55.6	50.5	80.3	76.0	48.5	39.5	17.1	13.4	41.0	31.8

~ Statistic not displayed due to less than 25 cases.
! Not enough intervals to produce rate

time. He has also described the genetic determinants as well as the environmental agents believed to play a role in the etiology of sarcomas. It is not unreasonable that these factors might influence survival as well, particularly among patients with certain chromosomal abnormalities.

REFERENCES

1. Percy C, Van Holten V, and Muir C (eds). International Classification of Diseases for Oncology – Second Edition, World Health Organization, Geneva, 1990
2. Lewis DR and Ries LAG. Cancers of the Bone and Joint. In: Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner, M-J (editors). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program. NIH Pub. No. 07-6215, 2007.
3. Shambaugh EM and Weiss MA (eds). The 1977 Summary Staging Guide, National Cancer Institute, Bethesda, MD 1977.
4. Christopher DM, Fletcher KU and Fredrik M (eds), World Health Organization Classification of Tumors: Pathology and Genetics of Tumours of Soft Tissue and Bone, World Health Organization, Geneva, 2002
5. Mack TM, Sarcomas and Other Malignancies of Soft Tissue, Retroperitoneum, Peritoneum, Pleura, Heart, Mediastinum, and Spleen, Supplement to Cancer, 75:211-244, 1995.

Chapter 12
Melanoma

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INTRODUCTION

In general, it is considered that mortality from melanoma is in most cases preventable, because the disease is characterized by an easily recognizable lesion (unusual moles or nevi), and early intervention appears to guarantee an excellent prognosis with limited recurrence (1). While the incidence of melanoma has been rising in most countries and populations worldwide since the 1960s (2), there is some evidence that at least part of this increase can be attributed to wider reaching screening programs that attempt to capitalize on the benefit of early detection (3). Were this true we would expect to see improvements in survival through time; indeed, this has been observed in the white populations of Sweden (4, 5) and Switzerland (6), particularly among females, who overall have better chances of survival from melanoma than males (6), but among whom one might first expect to see improvements in survival due to self-screening and general health awareness.

The documentation of improved melanoma survival over time has been limited to these two populations, whose rates of melanoma are not very high by world standards – the highest rates in the world are found in Australia, New Zealand, and in the Southwest of the United States, particularly Los Angeles (7). Among these populations, whose high rates of melanoma are attributed to excessive childhood sun exposure, little is known about the factors related to survival. In the Swedish and Swiss populations, females have uniformly better survival rates than males, survival is substantially better with thinner lesions (which presumably represent tumors diagnosed at an earlier stage of development, and therefore are more amenable to intervention), but no differences are observed in survival among the major histologic types of melanoma. The majority of melanomas can be regarded as having either an invasive, infiltrating histologic type (nodular melanomas, NM) or a less invasive, thinner form which is more likely to spread radially across the skin's surface rather than vertically into the dermis (superficial spreading melanoma, SSM). Given the relationship between lesion thickness and melanoma prognosis, SSM ought to have better survival than NM. While there is conflicting evidence on whether or not these two main types of lesion are biologically distinct (8), data from Sweden indicate an increase in the incidence of SSM that might signify a role of earlier detection in the overall increase in melanoma incidence in most developed countries worldwide (5, 9). A third form of melanoma, Hutchinson's melanotic freckle, represents a distinct histologic entity whose prognosis is unclear, because in most data sets they are too rare to draw firm conclusions.

Finally, there are substantial differences in the incidence of melanomas at differing anatomical locations of the body, which in part support (and in fact were responsible for the development of) the hypothesis that sunlight ex-

Table 12.1: Melanoma: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/selection
103,334	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
85,854	17,480	Select first primary only
85,733	121	Exclude death certificate only or at autopsy
81,246	4,487	Exclude unknown race
80,633	613	Exclude alive with no survival time
79,954	679	Exclude children (Ages 0-19)
55,173	24,781	Exclude in situ cancers for all except breast & bladder cancer
55,039	134	Exclude no or unknown microscopic confirmation

Table 12.2: Melanoma: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Race/Sex	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
White	54,197	100.0	97.2	94.6	92.6	90.2	88.4	88.1
Male	29,785	55.0	96.6	93.5	91.0	88.4	86.5	86.3
Female	24,412	45.0	97.8	95.9	94.4	92.4	90.4	90.0
Black	305	100.0	88.6	82.9	79.7	73.4	70.3	70.3
Male	155	50.8	85.2	78.4	75.0	70.1	69.6	69.6
Female	150	49.2	92.1	87.4	84.4	76.3	69.8	69.8

posure plays a role in melanoma – in males, melanomas are more common on the trunk and ears or head than in females, who have melanomas more frequently on their lower legs and their arms (10). These findings coincide roughly with the differences in sun protection afforded males and females by virtue of their clothing choices and hairstyles. Whether or not these site-specific differences are reflected in differing survival is of interest given the increased likelihood that lesions will be recognized earlier on sun-exposed skin surfaces. Swiss data show that survival is greater at every anatomic location for females than males, but that observation is based on very few data points (6).

MATERIALS AND METHODS

Case selection

Cases were selected from those reported to the NCI SEER Program with a diagnosis occurring between 1988 and 2001 (except for those cases obtained from the Los Angeles Cancer Surveillance Program which included the years 1992-2001 only). Cases were followed for vital status until 2003. Further descriptions of the NCI SEER Program, data selection and relative survival analysis can be found in Chapter 1: "Materials and Methods". We used the first primary diagnosis of melanoma only, and excluded those cases whose report was obtained solely from a death certificate or from report at autopsy, or those with no microscopic confirmation of diagnosis. In order to complete race-specific analyses, we excluded those with an unknown race, and in order to obtain complete data on survival time, we excluded those cases for whom active follow-up continued, but for whom there was no available survival time (that is, follow-up date was the same as diagnosis date, and no further follow-up data had been obtained). All cases under the age of 20 years were excluded both because melanoma is extremely rare in this age group, and because separate monographs have been published for childhood and adolescent/young adult cancers.

We conducted age- and sex-specific analyses, using 10-year age groups to ensure sufficient sample sizes in each age/sex group, as previous reports indicated a more favorable survival among both the young, and among females (11). Despite the comparative rarity of melanoma among blacks, we had sufficient data to consider sex-specific survival rates among both blacks and whites (but not age-specific rates for blacks). In all subsequent analyses (anatomic site, tumor thickness and histology, as detailed below) we

Table 12.3: Melanoma (Among Whites): Age Distribution (20+) by Sex, 12 SEER Areas, 1988-2001

Sex	Male		Female	
Age Group (Years)	Cases	Percent	Cases	Percent
Total	29,785	100.0	24,412	100.0
20-29	1,179	4.0	2,079	8.5
30-39	3,445	11.6	4,570	18.7
40-49	5,766	19.4	5,251	21.5
50-59	6,067	20.4	4,035	16.5
60-69	6,142	20.6	3,473	14.2
70-79	4,980	16.7	3,030	12.4
80+	2,206	7.4	1,974	8.1

Figure 12.1: Melanoma (Among Whites): Relative Survival Rates (%) for Males by Age (20+), 12 SEER Areas, 1988-2001

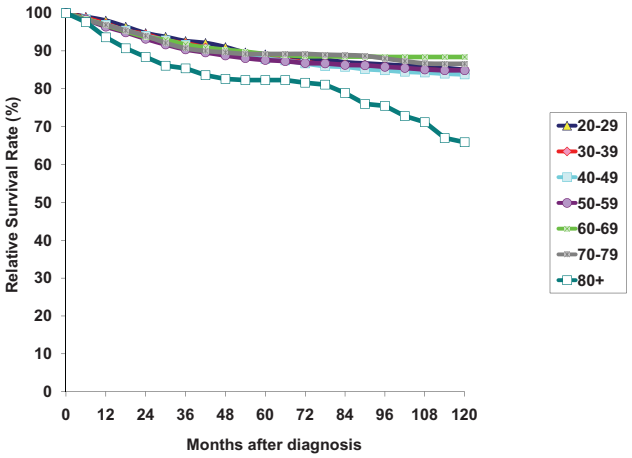
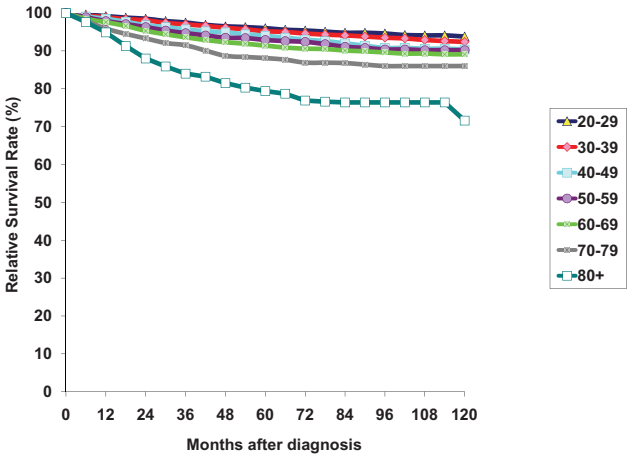


Figure 12.2: Melanoma (Among Whites): Relative Survival Rates (%) for Females by Age (20+), 12 SEER Areas, 1988-2001



focus on whites only, as data for blacks were too sparse. In all these subsequent analyses we separate analyses for males and females.

Anatomic site classification

Few data sources provide the opportunity to investigate melanoma survival by anatomic site of the lesion, yet there is substantial evidence that risk of developing melanoma is related to anatomic site, and it is fair to assume that, because melanoma can be prevented by the early recognition of lesions, those occurring on more exposed body sites would have the most favorable prognosis and a higher rate of survival. We classified the site of melanomas according to ICDO-2 site coding: C44.0 (lip); C44.1 (eyelid); C44.2 (ear); C44.3 (face excluding eyelid); C44.4 (scalp and neck excluding ear); C44.5 (trunk); C44.6 (upper limb and shoulder); C44.7 (lower limb and hip); C44.8 (overlapping site); C44.9 (site not specified).

Tumor thickness classification

Likewise, one of the strongest predictors of melanoma prognosis from case series and the few survival studies with sufficient data to investigate the same is the thickness of the tumor at diagnosis, with tumors of the greatest depth having the worst prognosis and survival. Thickness of melanomas is recorded as the depth in millimeters of the lesion, and we categorized the thicknesses in the same groups as found in Levi et al (1998), for comparative purposes – these thickness groupings (<0.75mm, 0.75-1.49mm, 1.50-2.49mm, 2.50-3.99mm, >3.99mm and unknown) also represent the levels most commonly used to describe the changing incidence of melanoma, as they are considered representative of the severity of disease: those <0.75mm rarely recur after removal, those 0.75-1.49mm have a greater chance of recurrence but a small chance of mortality, and those >3.99mm have an almost universal prognosis of multiple recurrence and short survival time in clinical series.

Histologic type classification

We categorized melanomas on the basis of ICDO-2 histology code: superficial spreading melanoma (SMM): 8743; nodular melanoma (NM): 8721; acral lentiginous melanoma (ALM): 8744; Hutchinson's melanotic freckle (HMF): 8742. The remainder of histologic types comprised those recorded simply as 'malignant melanoma' (MM): 8720, and those recorded as 'other or not specified' (8722-8741, 8745-8790).

RESULTS

Case selection

Between 1988 and 2001, 103,334 melanomas cases were diagnosed and reported to SEER. We removed from analysis 17,480 cases which were not first primaries, a further 5,355 cases because they were obtained from death certificate only, had no microscopic confirmation of diagnosis, had an unknown race, or no follow-up data (see Table 12.1 for details); 679 cases aged between 0 and 19 years; and finally, 24,781 cases reported as in situ cancers. There were 55,039 adult cases remaining for analysis.

Table 12.4: Melanoma (Among Whites): Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Sex and Anatomic Site, Ages 20+, 12 SEER Areas, 1988-2001

Sex/Anatomic Site	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Male	29,785	100.0	96.6	93.5	91.0	88.4	86.5	86.3
Lip	56	0.2	91.3	85.0	81.7	71.9	69.1	69.1
Eyelid	81	0.3	100.0	99.2	99.2	91.1	82.2	81.5
Ear	1,336	4.5	99.0	96.8	95.3	94.5	91.2	90.8
Face	2,825	9.5	99.3	96.3	93.5	90.4	89.4	89.4
Scalp & Neck	2,347	7.9	97.4	92.0	86.9	82.2	77.4	76.2
Trunk	12,340	41.4	98.4	96.0	93.8	91.4	89.4	88.9
Upper Limb/Shoulder	6,378	21.4	99.2	97.0	95.5	93.5	93.5	93.5
Lower Limb/Hip	2,852	9.6	98.8	95.9	93.1	89.7	86.5	85.6
Overlapping	41	0.1	98.7	94.9	90.8	90.2	77.2	70.4
NOS	1,529	5.1	59.3	48.0	43.6	39.8	37.3	36.2
Female	24,412	100.0	97.8	95.9	94.4	92.4	90.4	90.0
Lip	37	0.2	96.4	87.2	81.8	81.8	81.8	81.8
Eyelid	79	0.3	100.0	95.2	93.3	89.5	84.4	78.5
Ear	185	0.8	99.0	98.5	97.6	93.5	83.3	80.8
Face	1,916	7.8	99.1	97.2	95.6	93.6	90.8	90.8
Scalp & Neck	918	3.8	98.0	93.5	89.8	83.4	79.5	78.6
Trunk	6,240	25.6	98.4	96.8	95.2	93.0	90.6	90.3
Upper Limb/Shoulder	6,266	25.7	99.1	98.0	96.8	95.6	94.4	93.3
Lower Limb/Hip	7,930	32.5	99.2	97.5	96.4	94.8	93.1	92.5
Overlapping	20	0.1	~	~	~	~	~	~
NOS	821	3.4	65.9	55.8	51.9	46.6	45.2	44.1

~ Statistic not displayed due to less than 25 cases.

Table 12.5: Melanoma (Among Whites): Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Sex and Tumor Thickness, Ages 20+, SEER 1988-2001

Sex/Tumor Thickness	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Male	29,785	100.0	96.6	93.5	91.0	88.4	86.5	86.3
< 0.75 mm	12,948	43.5	100.0	100.0	100.0	100.0	100.0	100.0
0.75 - 1.49 mm	5,545	18.6	100.0	98.7	97.2	94.8	92.6	92.0
1.50 - 2.49 mm	2,729	9.2	99.0	95.0	89.5	81.6	75.4	74.4
2.50 - 3.99 mm	1,558	5.2	96.4	87.5	79.2	67.4	58.9	58.2
4.00+ mm	1,633	5.5	90.0	73.9	62.8	54.0	46.9	45.9
Unknown	5,372	18.0	84.8	78.3	75.0	71.8	69.2	68.2
Female	24,412	100.0	97.8	95.9	94.4	92.4	90.4	90.0
< 0.75 mm	12,201	50.0	100.0	100.0	100.0	99.7	99.2	99.2
0.75 - 1.49 mm	4,458	18.3	99.9	99.0	97.8	95.6	93.3	92.0
1.50 - 2.49 mm	1,867	7.6	98.3	94.5	91.0	86.0	80.0	77.8
2.50 - 3.99 mm	1,002	4.1	97.1	90.3	83.6	75.8	70.1	68.0
4.00+ mm	965	4.0	93.1	79.9	70.5	61.3	51.2	49.9
Unknown	3,919	16.1	89.2	84.7	82.7	79.7	77.8	77.2

Figure 12.3: Melanoma (Among Whites): Relative Survival Rates (%) For Males by Tumor Thickness, Ages 20+, 12 SEER Areas, 1988-2001

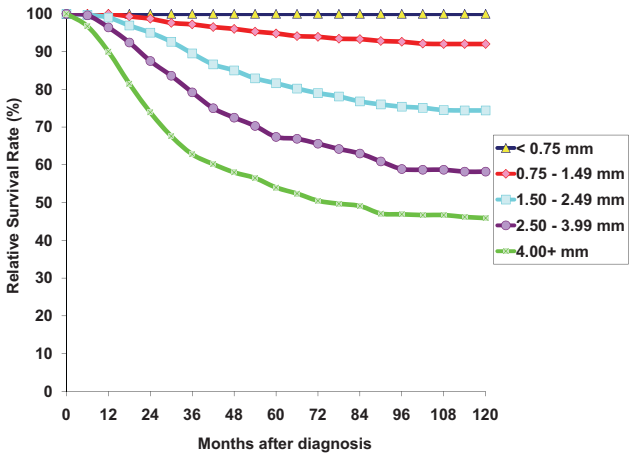
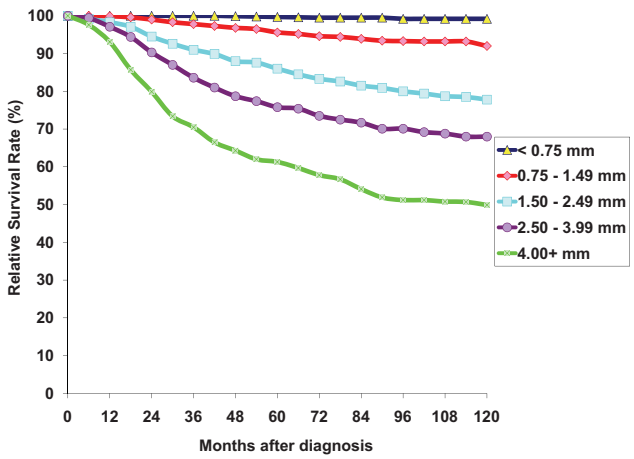


Figure 12.4: Melanoma (Among Whites): Relative Survival Rates (%) for Females by Tumor Thickness, Ages 20+, 12 SEER Areas, 1988-2001



Age, sex and race

Even though melanoma is rare among the black population, it is clear that black patients have a far poorer prognosis of melanoma than white patients (Table 12.2). This was true both overall, and separately for males and females. While white females experienced increasingly better survival rates than white males from 12 months all the way to 10 years beyond diagnosis, the same was not true for black females – black females experienced substantially better survival than black males up to 5 years, but 8- and 10-year survival rates were similar in black males and females.

Age-specific data were too sparse among blacks for meaningful analysis, but among whites (Table 12.3), the age distribution was younger for females (Table 12.3) and the relative survival rates were substantially worse among the older (particularly among those aged 80 years and over) than the younger (Figures 12.1 and 12.2). Older men had the poorest survival. For the younger age groups, there appeared to be more of a survival differential for females by age than males (Figures 12.1 (males) and 12.2 (females)).

Table 12.6: Melanoma (Among Whites): Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Sex and Histology, Ages 20+, 12 SEER Areas, 1988-2001

Sex/Histology (ICD-O code)	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Male	29,785	100.0	96.6	93.5	91.0	88.4	86.5	86.3
Superficial Spreading (8743)	11,510	38.6	100.0	99.0	98.0	96.6	95.3	95.2
Nodular (8721)	2,671	9.0	93.7	84.4	77.0	68.4	63.0	61.6
Acral Lentiginous (8744)	242	0.8	98.8	91.9	87.8	75.7	67.9	61.5
Other and Not Specified	1,185	4.0	94.9	88.7	83.7	80.5	79.5	78.2
Malignant Melanoma, NOS (8720)	12,019	40.4	93.2	89.2	86.2	83.4	81.1	80.8
Hutchinson's Melanotic Freckle (8742)	2,158	7.2	100.0	100.0	100.0	100.0	100.0	100.0
Female	24,412	100.0	97.8	95.9	94.4	92.4	90.4	90.0
Superficial Spreading (8743)	10,780	44.2	100.0	99.7	99.0	98.0	96.8	96.6
Nodular (8721)	1,739	7.1	95.2	87.6	82.0	74.6	68.8	67.4
Acral Lentiginous (8744)	302	1.2	99.4	96.1	93.5	89.1	79.1	79.1
Other and Not Specified	794	3.3	94.5	90.2	84.9	83.3	81.4	77.7
Malignant Melanoma, NOS (8720)	9,591	39.3	95.5	92.8	91.3	88.9	86.9	85.9
Hutchinson's Melanotic Freckle (8742)	1,206	4.9	100.0	100.0	100.0	99.4	96.1	95.5

Figure 12.5: Melanoma (Among Whites): Relative Survival Rates (%) for Males by Histology, Ages 20+, 12 SEER Areas, 1988-2001

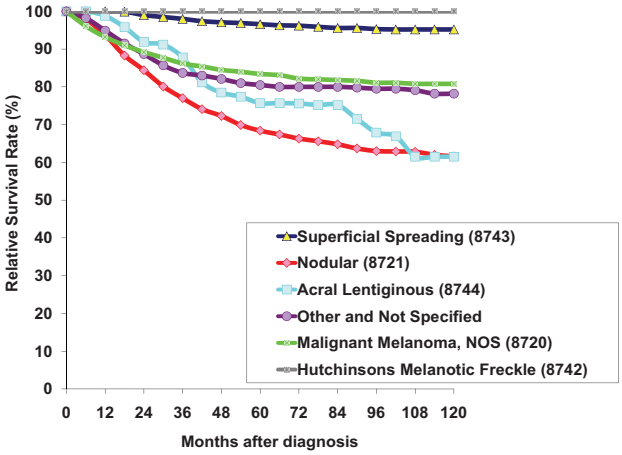
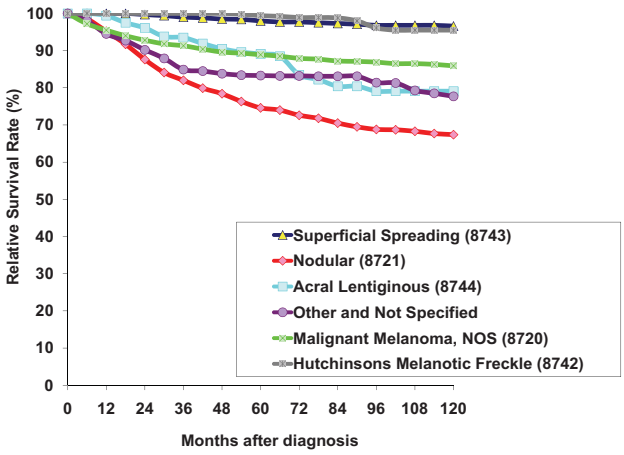


Figure 12.6: Melanoma (Among Whites): Relative Survival Rates (%) for Females by Histology, Ages 20+, 12 SEER Areas, 1988-2001



Anatomic site

While the majority of melanomas occurred on the trunk and upper limbs, there were sufficient cases at all recorded anatomic sites to determine that the site-specific distribution and survival of melanoma differs substantially between males and females (Table 12.4). For males over 40% of the melanomas were on the trunk contrasted to 26% for females. For females, 32% were on the lower limb/hip contrasted to less than 10% for males. Overall the worst site-specific survival rate occurred for melanomas with an unspecified site, and among those of the scalp and neck. Melanomas occurring on the limbs and at overlapping sites had relatively better survival. Notable sex-specific differences in relative survival rates were seen for melanomas occurring on the ear, where males experienced better survival to 10 years than females, and the lower limbs, where females experienced better survival than males (relative to other sites).

Thickness of tumor

While a large proportion (18.0% for males and 16.1% for females) of cases had no reported thickness data (Table 12.5), survival clearly worsened with increasing tumor thickness (Figure 12.3 and Figure 12.4). Thin lesions (less than 0.75 mm) experienced almost negligible mortality even at ten years, but thick lesions (4 mm and over) had a relative survival rate 46% for males and 50% for females by 10 years, and there was a clear 'dose-response' relation between thickness and survival, making lesion thickness easily the most predictive aspect of melanoma survival. This was true for both males and females, although males experienced worse survival for each thickness level. Survival for people with tumors of an unknown thickness paralleled survival experienced by the median lesion thickness (data not shown), indicating that the group with an unknown thickness did not differ substantially from the group with reported lesion thickness.

Histologic type

For both males and females, the majority of tumors were evenly divided between superficial spreading melanomas (SSM) and malignant melanomas with no further specified histology (MM), with small percentages of the other histologic types (Table 12.6). Survival rates for SSM were only slightly better in females than in males, whereas nodular (NM) tumors had a worse prognosis in males (Figures 12.5 and 12.6). Ten year relative survival rates under 65% were seen for males with NM or acral lentiginous melanomas. Ten year rates more than 95% were seen for superficial spreading and Hutchinson's melanotic freckle (Figures 12.5 and 12.6).

Geographic location

Substantial differences appeared to exist between sex-specific survival rates across registries in the SEER program (Table 12.7). Hawaii experienced the highest overall survival for both males and females, and also appeared to have one of the smallest differences in survival between the sexes of any registry (Table 12.7). While relative survival rates were lower 5 years after diagnosis in Rural Georgia, this observation was based on very small numbers. Iowa had lower melanoma survival rates for males than most of the other registries, and the largest difference in survival rates between males and females.

Table 12.7: Melanoma (Among Whites): Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by SEER Geographic Area and Sex (Ages 20+), 12 SEER Areas, 1988-2001

Sex/SEER Geographic Area	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	54,197	100.0	97.2	94.6	92.6	90.2	88.4	88.1
Atlanta and Rural Georgia	4,394	8.1	97.8	96.2	94.6	92.6	91.0	90.3
Atlanta (Metropolitan) - 1988+	4,282	7.9	97.9	96.2	94.7	92.8	91.3	90.6
Rural Georgia - 1988+	112	0.2	95.9	93.9	89.3	84.0	79.4	76.5
California								
Los Angeles - 1992+	7,496	13.8	96.5	93.0	90.5	87.6	84.9	84.0
Greater Bay Area	9,483	17.5	97.5	94.9	92.7	90.2	87.5	86.6
San Francisco-Oakland SMSA - 1988+	6,147	11.3	97.6	95.1	92.9	90.3	88.2	87.5
San Jose-Monterey - 1988+	3,336	6.2	97.3	94.6	92.4	90.0	86.1	85.0
Connecticut - 1988+	7,263	13.4	97.6	94.8	92.6	90.4	89.6	89.6
Detroit (Metropolitan) - 1988+	5,644	10.4	97.3	95.0	93.1	91.0	89.2	88.8
Hawaii - 1988+	1,381	2.5	98.2	96.2	95.2	94.8	94.5	94.5
Iowa - 1988+	4,871	9.0	95.7	92.2	89.7	87.0	83.5	83.3
New Mexico - 1988+	2,599	4.8	96.4	93.4	92.0	89.1	88.4	86.3
Seattle (Puget Sound) - 1988+	7,755	14.3	97.9	96.1	94.3	92.4	90.9	90.7
Utah - 1988+	3,311	6.1	96.3	94.0	92.0	89.3	87.3	86.4
Male	29,785	100.0	96.6	93.5	91.0	88.4	86.5	86.3
Atlanta and Rural Georgia	2,407	8.1	97.3	95.0	93.2	90.1	88.1	87.8
Atlanta (Metropolitan) - 1988+	2,351	7.9	97.3	95.1	93.2	90.3	88.1	87.9
Rural Georgia - 1988+	56	0.2	98.6	93.0	91.6	82.5	82.2	75.7
California								
Los Angeles - 1992+	4,252	14.3	96.4	92.2	89.1	86.0	83.2	81.9
Greater Bay Area	5,345	17.9	96.9	93.7	90.9	87.6	85.7	84.6
San Francisco-Oakland SMSA - 1988+	3,473	11.7	96.9	93.9	91.3	87.8	85.9	84.8
San Jose-Monterey - 1988+	1,872	6.3	97.0	93.4	90.0	87.4	84.9	84.5
Connecticut - 1988+	3,984	13.4	97.4	94.3	91.6	89.9	89.4	89.4
Detroit (Metropolitan) - 1988+	3,138	10.5	96.9	94.2	92.1	89.5	87.5	87.4
Hawaii - 1988+	853	2.9	97.7	95.5	94.5	94.2	93.6	93.6
Iowa - 1988+	2,516	8.4	94.9	90.6	87.5	83.7	79.6	79.2
New Mexico - 1988+	1,456	4.9	95.6	91.2	89.7	86.5	86.0	84.6
Seattle (Puget Sound) - 1988+	4,035	13.5	97.0	94.9	92.5	90.7	88.3	87.5
Utah - 1988+	1,799	6.0	95.5	93.0	90.3	87.3	85.5	83.9
Female	24,412	100.0	97.8	95.9	94.4	92.4	90.4	90.0
Atlanta and Rural Georgia	1,987	8.1	98.4	97.5	96.2	95.5	93.9	92.9
Atlanta (Metropolitan) - 1988+	1,931	7.9	98.6	97.6	96.4	95.8	94.5	93.4
Rural Georgia - 1988+	56	0.2	93.1	93.1	85.6	84.5	74.2	74.2
California								
Los Angeles - 1992+	3,244	13.3	96.7	94.0	92.2	89.5	86.7	85.7
Greater Bay Area	4,138	17.0	98.2	96.5	95.1	93.4	89.6	88.9
San Francisco-Oakland SMSA - 1988+	2,674	11.0	98.4	96.7	95.0	93.5	90.9	90.7
San Jose-Monterey - 1988+	1,464	6.0	97.8	96.1	95.4	93.2	87.1	85.5
Connecticut - 1988+	3,279	13.4	97.9	95.4	93.8	90.9	89.6	89.6
Detroit (Metropolitan) - 1988+	2,506	10.3	97.8	96.0	94.4	92.7	91.2	90.2
Hawaii - 1988+	528	2.2	98.8	97.2	96.3	95.0	95.0	95.0
Iowa - 1988+	2,355	9.6	96.5	93.9	91.8	90.3	87.2	86.8
New Mexico - 1988+	1,143	4.7	97.3	95.9	94.7	92.1	89.9	87.9
Seattle (Puget Sound) - 1988+	3,720	15.2	98.9	97.4	96.2	94.1	93.4	93.3
Utah - 1988+	1,512	6.2	97.2	95.3	94.0	91.5	89.2	88.9

DISCUSSION

Clearly the factor most predictive of melanoma survival is thickness of the tumor at diagnosis, which reinforces the notion that there is much that can be achieved in preventing melanoma mortality, by early detection. However, we noted that the often observed survival differential that favors females over males also occurs within strata of tumor thickness. In addition, the melanomas among females were not as thick as those for males.

Melanoma among blacks, while rare, is a more lethal disease than it is among whites, and therefore deserves special attention and particularly more research into why blacks have lower survival rates. The only reports of melanoma survival among blacks come from case series (12) largely because melanoma among blacks is rare. We have identified sufficient cases of melanoma among blacks to be able to compare their survival to that of whites, and notice that blacks have far poorer melanoma survival than whites. This could be attributable to access to care, or could reflect the relative lack of knowledge of the risk of melanoma/skin cancer in black populations. Black populations may not be as carefully or regularly screened, and consequently may not benefit from improved survival due to early detection of lesions. One hint in future investigation of poor survival among blacks may come from the unusual observation that after 5 years there is no longer a survival difference between males and females, although the statistical significance of this finding needs to be established.

The only previous data presented on anatomical site-specific survival found as we have that survival varies with site in a manner similar to the incidence of melanoma (6). This observation is consistent with a 'visible skin' hypothesis (i.e. sun exposure is greater on visible skin areas, and visible skin is an easy place to detect lesions early), and argues again for a substantial role of early detection in improved survival. Overlapping lesions presumably have more favorable survival because they have spread outwards rather than downwards, and are therefore less invasive. We hypothesize that lesions of an unspecified anatomic site experience poor survival because they are discovered at an advanced stage when it is unclear where they started.

Similarly, the most vertically invasive histologic type (NM) has one of the poorest survival. However, the magnitude of the difference in survival between SSM and NM is substantial, and may provide further evidence that the two histologic types are quite separate disease processes. We present sufficient data on other forms of melanoma, Hutchinson's melanotic freckle and acral lentiginous melanoma to estimate their survival relative to the more common NM and SSM, which had not been presented elsewhere, to our knowledge, due to the comparative rarity of their presentation.

Substantial geographic variation in melanoma survival exists, which probably reflects access to care (it does not reflect racial or sex differences in survival), socioeconomic status (which is certainly related to melanoma incidence but which we were unable to measure), availability of screening, or awareness of melanoma as a problem. We do not find much evidence that the areas most likely to have active skin screening programs in place, such as Los Angeles, have substantially better survival than the median.

REFERENCES

1. MacKie, R.M., et al., Cutaneous malignant melanoma in Scotland: incidence, survival, and mortality, 1979-94. The Scottish Melanoma Group. Bmj., 1997. 315(7116): p. 1117-21.
2. Armstrong, B.K. and A. Kricker, Cutaneous melanoma. Cancer Surveys., 1994. 19-20: p. 219-40.
3. Koh, H.K., et al., Evaluation of the American Academy of Dermatology's National Skin Cancer Early Detection and Screening Program. Journal of the American Academy of Dermatology, 1996. 34(6): p. 971-8.
4. Stenbeck, M., M. Rosen, and L.E. Holm, Cancer survival in Sweden during three decades, 1961-1991. Acta Oncologica., 1995. 34(7): p. 881-91.
5. Masback, A., et al., Cutaneous malignant melanoma in southern Sweden 1965, 1975, and 1985. Prognostic factors and histologic correlations. Cancer., 1997. 79(2): p. 275-83.
6. Levi, F., et al., Prognostic factors for cutaneous malignant melanoma in Vaud, Switzerland. International Journal of Cancer., 1998. 78(3): p. 315-9.
7. Parkin, D., et al., Cancer Incidence in Five Continents, Volume VI. Vol. 120. 1992, Lyon: IARC Scientific Publications.
8. Langholz, B., et al., Skin characteristics and risk of superficial spreading and nodular melanoma (United States). Cancer Causes & Control, 2000. 11(8): p. 741-50.
9. Thorn, M., et al., Trends in tumour characteristics and survival of malignant melanoma 1960-84: a population-based study in Sweden. British Journal of Cancer., 1994. 70(4): p. 743-8.
10. Bulliard, J.L., B. Cox, and J.M. Elwood, Comparison of the site distribution of melanoma in New Zealand and Canada. International Journal of Cancer, 1997. 72(2): p. 231-5.
11. Gordon, L.G., et al., Poor prognosis for malignant melanoma in Northern Ireland: a multivariate analysis. British Journal of Cancer., 1991. 63(2): p. 283-6.
12. Crowley, N.J., et al., Malignant melanoma in black Americans. A trend toward improved survival. Archives of Surgery., 1991. 126(11): p. 1359-64; discussion 1365.

Chapter 13
Cancer of the Female Breast

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INTRODUCTION

This study presents survival analyses for female breast cancer based on 302,763 adult cases from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). This chapter focuses on the influence of extent of disease (extension of tumor, size, nodal involvement, number of nodes involved), histology, histologic grade, receptor status, and demographic factors on female breast cancer survival.

MATERIALS AND METHODS

The NCI contracts with medically oriented nonprofit institutions -- such as universities and state health departments -- to obtain data on all cancers diagnosed in residents of the SEER geographic areas except basal cell and squamous cell carcinomas of the skin and in situ cervical cancer.

SEER selects areas on the basis of their ability to operate and maintain a population-based cancer reporting system and the epidemiologic significance of their population subgroups. The analysis in this article is from 12 geographic areas representing approximately 14% of the United States population. The geographic areas include the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Atlanta, San Francisco, San Jose, Los Angeles, and Seattle; Alaska Natives; and ten counties in rural Georgia. All registries contributed data for diagnosis years 1988-2001 except Los Angeles, which contributed data for 1992-2001.

Each registry is responsible for abstracting the records of all cancer patients who reside in the given area. To ensure maximal ascertainment of cancer cases, registries seek records from hospitals, laboratories, and all other health service units that provide diagnostic services. Data collected on each patient include patient demographics, primary tumor site, morphology, diagnostic methods, extent of disease, and first course of cancer-directed therapy. A separate record is coded for each primary cancer. With the exception of cases of in situ carcinoma of the uterine cervix, all patients are followed from diagnosis to death, allowing for detailed survival analysis.

SEER has collected extent-of-disease (EOD) information on all cancers since the inception of the program. The detail and amount of information collected, however, have varied over time. In 1988, there were some minor revi-

Table 13.1: Cancer of the Female Breast: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/selection
365,042	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
309,467	55,575	Select first primary only
307,746	1,721	Exclude death certificate only or at autopsy
305,757	1,989	Exclude unknown race
305,483	274	Active follow-up and exclude alive with no survival time
305,455	28	Exclude children (Ages 0-19)
303,045	2,410	Exclude no or unknown microscopic confirmation
302,763	282	Exclude sarcomas

sions to the breast cancer EOD scheme so that SEER EOD information could be easily converted into the TNM staging classifications based on the third edition of the American Joint Committee on Cancer (AJCC) Manual for Staging of Cancer (1). (The AJCC TNM schemes are the same as those published by the International Union Against Cancer.)

The term localized refers to tumors that are confined to breast tissue only. Regional refers to tumors that have metastasized to the regional lymph nodes or have extended directly from the breast to the pectoral fascia, subcutaneous tissue, chest wall, ribs, or skin (peau d'orange, satellite nodules, etc.). Distant refers to distant metastases or further direct extension.

Analysis

The survival analysis was based on 5-year relative survival rates calculated by the life-table method. The relative survival rate was used to estimate the effect of cancer on the survival of the cohort. Relative survival is observed survival divided by survival that would be expected in the absence of cancer; thus, relative survival adjusts for the normal mortality that the cohort would experience from other causes of death. When relative survival is 100%, a patient cohort has the same chance to live 5 more years as a cancer-free cohort based on the same age, race, and sex.

Exclusions

The following were excluded from the analysis: male breast cancers, cases in which the breast cancer was not the first primary, cases identified through autopsy and death certificate only, cases with unknown race, cases with unknown survival time, cases where the age at diagnosis was less than 20, cases with no microscopic confirmation, and sarcomas. After exclusions, 302,763 adult female breast cancers diagnosed from 1988 to 2001 were available for analysis (Table 13.1). Of these 44,875 (14.8%) were in situ and 257,888 (85.2%) were malignant. Note that 45,033 cases were Stage 0 which includes in situ plus Paget disease of the nipple with no underlying tumor.

RESULTS

This analysis is based on prognostic factors for breast cancer, with an emphasis on extent of disease at diagnosis especially the role of tumor size, extension of the primary tumor, and lymph node status. Survival rates were also calculated by demographic characteristics such as age and race (white, black). In most tables, each prognostic factor is presented both individually and in relation to a second factor.

Stage

As expected, survival rates varied by stage (Table 13.2). For patients of all ages, patients diagnosed in stages 0 and I had a 100% 5-year relative survival rate. The five-year relative survival rate for stage II was 86%; for stage III,

Table 13.2: Cancer of the Female Breast: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by Age (20+) and AJCC Stage (3rd edition), 12 SEER Areas, 1988-2001

Age (Years)	AJCC Stage													
	Total		0		I		II		III		IV		Unknown	
	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
Total	302,763	89.3	45,033	100.0	108,346	100.0	91,989	86.2	16,928	57.2	11,222	19.9	29,245	83.4
20-34	6,802	77.8	563	98.7	1,565	94.5	3,042	77.6	649	50.5	291	17.5	692	74.4
35-39	12,827	83.5	1,665	99.7	3,343	95.1	5,231	82.1	1,021	55.8	384	19.4	1,183	79.4
40-44	24,914	88.0	4,615	99.9	7,127	97.0	8,790	86.3	1,667	59.4	683	25.8	2,032	83.0
45-49	33,784	89.5	6,382	100.0	10,400	97.6	11,427	87.8	2,132	62.6	968	25.4	2,475	85.2
50-54	34,868	89.5	6,462	100.0	12,023	98.3	10,857	86.7	1,943	59.2	1,147	20.5	2,436	85.4
55-59	32,701	89.6	5,496	100.0	12,029	99.0	9,920	87.5	1,636	57.5	1,234	19.5	2,386	84.6
60-64	32,680	90.1	4,930	100.0	12,949	100.0	9,306	86.7	1,587	57.3	1,308	18.9	2,600	86.3
65-69	34,435	91.0	4,986	100.0	14,194	100.0	9,404	87.8	1,542	57.6	1,374	20.3	2,935	84.6
70-74	32,686	91.8	4,363	100.0	13,731	100.0	8,697	87.2	1,408	57.8	1,299	17.7	3,188	86.9
75-79	27,134	91.4	3,141	100.0	11,101	100.0	7,295	86.2	1,335	54.8	1,147	15.6	3,115	82.4
80-84	17,475	90.7	1,683	100.0	6,461	100.0	4,684	87.0	999	52.5	792	20.7	2,856	77.6
85+	12,457	86.6	747	100.0	3,423	100.0	3,336	83.9	1,009	41.5	595	14.8	3,347	78.9

Table 13.3: Cancer of the Female Breast: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by Race and AJCC Stage (3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage													
	Total		0		I		II		III		IV		Unknown	
Race	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
All Races	302,763	89.3	45,033	100.0	108,346	100.0	91,989	86.2	16,928	57.2	11,222	19.9	29,245	83.4
White	254,919	90.4	37,397	100.0	94,023	100.0	76,296	87.1	13,467	60.0	8,970	21.2	24,766	84.8
Black	25,467	78.4	3,782	100.0	6,448	97.5	8,564	78.5	2,270	40.1	1,532	12.6	2,871	71.7

"Total" category includes 22,377 cases that are neither white nor black.

57%. For stage IV, the relative survival rate was poor: 20%. The 5-year relative survival rate for unknown stage was just below that for stage II.

Stage at diagnosis and age at diagnosis

For all stages combined, the survival rates increased by age group from 78% for 20-34 to 92% for 70-74 and then decreased to 87% for 85 years and over. For stage I, relative survival increased with age, approaching 100% for those aged 60 and older. For Stage III, survival rates ranged from 41 to 63% with the youngest and oldest age groups experiencing the worst survival rates. Stage IV cases had the worst survival for each age group (Table 13.2).

Stage and race

The overall 5-year relative survival rates were 90% for whites and 78% for blacks (Table 13.3). The fact that black women had a less favorable stage distribution than white women does not fully explain the survival differential, since even within each stage grouping except Stage 0, blacks had poorer survival. "All Races" category includes 22,397 cases that are races other than white or black.

Stage and Grade (Adenocarcinoma)

For adenocarcinomas, 5-year relative survival rates decreased by stage at diagnosis as expected (Table 13.4). Patients diagnosed with stage I cancer had a 5-year relative survival rate of 100%; those diagnosed with stage IV had a rate of 21%. Histologic grade was also a predictor of outcome except for grades 3 and 4; survival was highest for grade 1 and lowest for grade 3 or 4 and intermediary for grade 2. Survival ranged from 100% for grade 1 stage I down to 14% for grade 4 stage IV. In stages II-IV, histologic grade played an important prognostic role.

Stage and Histology

Table 13.5 contains a similar breakdown by stage and histology. The highest relative survival rates were for tubular and adenoid cystic adenocarcinomas (100%) and the lowest was for inflammatory carcinoma (34%). Even within stage IV disease, there were wide variations in survival by histology from 11% for inflammatory to 34% mucinous adenocarcinoma or papillary adenocarcinoma.

Size and Stage

The effect of tumor diameter (size) on survival is shown for all stages in Table 13.6. Size is categorized by 5-mm groups. The size groupings were chosen so that the middle size in each group was 0.5, 1.0, 1.5, 2.0, 2.5,…, 9.5 cm, respectively; the sizes most frequently cited in the hospital medical record. Five-year relative survival rates ranged from 100% for <8 mm tumors to 34% for diffuse tumors.

Due to the interrelationship of tumor size and extent of disease, results are given by size category for different extension groups: tumors localized to the breast, those regional by nodes, those regional by extension (peau d'orange, pectoral fascia, chest wall, extensive skin involvement, etc.), those with distant metastasis, and those with unknown extension.

Within each extension category, tumor size played an important prognostic role (Table 13.6). Patients with small tumors and either regional nodal involvement or direct extension of the tumor survived as well or better than those with large tumors confined to the breast. It should be noted, however, that there was a relationship between size and extension of the tumor. Tumors confined to the breast were smaller in general than tumors with distant metastases. For example, 59.5% of the localized tumors measured 17 mm or less compared to less than 7% for those with distant metastases. For those with distant disease 39% had tumors that measured over 57 mm or were diffuse (Table 13.7).

Table 13.4: Adenocarcinoma of the Female Breast (Non Stage 0): Number of Cases and 5-Year Relative Survival Rates (%) by Histologic Grade and AJCC Stage (3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage											
	Total		I		II		III		IV		Unknown	
Grade	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
Total	251,828	87.6	107,595	100.0	90,994	86.3	16,576	57.5	10,270	20.5	26,393	84.9
1	32,620	100.0	21,588	100.0	7,173	98.7	599	79.4	325	31.1	2,935	97.6
2	80,761	93.2	38,784	100.0	29,435	91.4	3,956	69.3	2,110	26.9	6,476	89.3
3	74,165	77.6	22,096	96.8	34,322	79.6	8,028	50.9	3,947	17.1	5,772	71.7
4	5,946	78.6	1,888	98.2	2,545	80.2	667	53.8	329	13.8	517	72.3
Unknown	58,336	87.1	23,239	100.0	17,519	87.5	3,326	57.2	3,559	20.2	10,693	86.6

Excludes 45,033 stage 0 cases and 5,902 non-adenocarcinomas not in stage 0.

Adenocarcinoma defined as histologies 8050,8140-8147,8160-8162,8180,8190-8191,8200-8202,8204,8210-8215,8220-8221,8250-8255,8260-8264,8270-8272,8280-8281,8290,8300,8310-8325,8330-8337,8340-8347,8350,8360-8361,8370-8375,8380-8384,8390-8392,8400-8410,8413,8420,8430,8440-8444,8450-8454,8460-8463,8470-8473,8480-8482,8490,8500-8506,8510,8520-8525,8530,8540-8543,8550,8560,8570-8574,8576,8940-8941.

Extension of tumor and nodal involvement

The SEER data allow for the extension categories presented in Tables 13.6 and 13.7 to be evaluated in greater detail. The localized extension category is limited to those tumors confined to breast tissue. Regional by direct extension cases can be further divided into those involving subcutaneous tissue, those involving the pectoral fascia, those involving the chest wall, ribs, and muscles versus those with extensive skin involvement (skin edema, peau d'orange, ulceration of the skin of breast, satellite nodules in skin, etc.). The AJCC (5th edition) T-categories of T1-T3a include tumors confined to breast tissue, those involving subcutaneous tissue and those involving the pectoral fascia and the specific T-category is assigned based on the size of tumor. Table

Table 13.5: Cancer of the Female Breast (Non Stage 0): Number of Cases and 5-Year Relative Survival Rates (%) by Histology and AJCC Stage (3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage											
	Total		I		II		III		IV		Unknown	
Histology	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
Total	257,730	87.1	108,346	100.0	91,989	86.2	16,928	57.2	11,222	19.9	29,245	83.4
Adeno, NOS	5,559	62.2	1,137	99.0	1,341	81.4	453	49.4	1,460	15.3	1,168	64.9
Tubular adeno	3,771	100.0	2,939	100.0	286	95.8	13	~	8	~	525	99.7
Infiltrating duct	183,122	87.5	79,900	100.0	68,437	85.1	10,597	57.5	6,493	20.3	17,695	83.6
Scirrhous adeno	456	81.7	172	94.3	188	83.9	16	~	30	13.5	50	71.7
Mucinous adeno	6,476	98.3	3,643	100.0	1,665	94.8	176	75.0	120	33.8	872	95.7
Comedo	5,020	89.9	2,218	99.3	1,653	82.7	223	51.3	82	19.4	844	96.0
Lobular	20,140	91.6	7,640	100.0	7,594	93.0	1,600	72.6	921	30.5	2,385	87.9
Infiltrating duct & lobular	16,060	92.9	6,801	100.0	6,564	91.4	1,013	69.8	375	29.0	1,307	89.5
Inflammatory carcinoma	2,668	34.1	<5	~	25	49.5	2,003	40.9	570	11.2	67	21.6
Paget	1,937	82.6	498	95.8	524	77.7	193	46.3	66	14.3	656	93.0
Papillary adeno	1,646	94.5	741	100.0	463	92.3	67	85.7	43	34.2	332	92.6
Adenoid cystic/ cribriform	712	100.0	409	100.0	177	95.3	14	~	6	~	106	96.3
Other adeno	4,261	89.1	1,494	98.7	2,077	88.8	208	57.7	96	21.2	386	84.6
Medullary	3,122	89.5	1,037	98.2	1,703	88.8	131	63.2	33	29.6	218	75.1
Other Non-adeno	5,785	64.8	699	99.2	945	80.1	348	42.4	952	13.8	2,841	70.1

Excludes 45,033 stage 0 cases.

~ Statistic not displayed due to less than 25 cases.
NOS: Not Otherwise Specified; adeno: adenocarcinoma

Table 13.6: Malignant Cancer of the Female Breast: Number of Cases and 5-Year Relative Survival Rates (%) by Tumor Size (mm) and Extension, Ages 20+, 12 SEER Areas, 1988-2001

	Extension											
	Total		Localized		Regional by Nodes		Regional by Extension		Distant		Unknown	
Tumor Size (mm)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
All sizes	257,888	87.1	160,105	97.4	64,224	82.3	14,075	64.7	14,359	24.4	5,125	62.9
Micro focus	4,439	98.9	4,016	100.0	332	88.2	59	74.9	20	~	12	~
Mammography only	944	97.9	842	99.9	77	81.1	13	~	<5	~	8	~
3-7	21,231	100.0	19,261	100.0	1,635	94.8	166	88.9	102	30.3	67	93.8
8-12	47,548	99.8	39,561	100.0	6,879	94.3	624	87.3	349	34.7	135	84.3
13-17	43,576	95.8	31,659	98.9	10,202	91.0	1,046	86.9	509	29.2	160	80.2
18-22	37,530	90.3	23,347	95.2	11,728	86.4	1,497	78.2	766	32.6	192	60.2
23-27	22,163	85.9	11,985	92.1	8,177	83.1	1,284	75.1	622	29.6	95	65.5
28-32	17,160	78.9	8,220	89.4	6,605	75.8	1,355	67.3	822	23.5	158	52.2
33-37	7,791	76.0	3,318	87.2	3,321	73.0	763	64.4	353	26.5	36	49.3
38-42	8,346	71.5	3,212	83.3	3,394	72.7	973	61.2	664	24.7	103	47.4
43-47	3,397	69.7	1,168	84.0	1,492	69.5	493	54.4	223	27.5	21	~
48-52	5,303	65.9	1,615	83.4	2,160	68.1	829	55.9	621	24.1	78	57.9
53-57	1,638	67.6	481	87.2	701	67.5	320	54.6	131	25.2	5	~
58-62	3,221	60.7	788	82.8	1,249	64.9	656	54.8	468	20.2	60	55.5
63-67	875	60.9	214	86.2	373	58.4	187	50.3	96	32.4	5	~
68-72	1,953	57.5	431	86.0	703	64.5	432	47.3	349	19.6	38	48.6
73-77	484	61.4	108	88.9	197	65.8	113	46.0	63	23.2	<5	~
78-82	1,675	51.8	308	83.4	519	63.5	429	49.7	385	13.7	34	32.2
83-87	272	62.6	56	82.4	90	71.9	72	60.1	53	25.9	<5	~
88-92	760	55.5	141	81.9	237	71.2	205	48.5	167	20.6	10	~
93-97	164	51.1	33	90.3	43	51.2	55	51.6	33	3.9	0	~
>97	2,510	45.2	378	79.1	516	64.8	760	48.4	806	15.1	50	26.4
Diffuse	3,686	34.1	67	79.3	109	63.4	311	45.7	3,174	30.7	25	37.5
Unknown	21,222	72.7	8,896	96.9	3,485	79.2	1,433	55.6	3,579	18.2	3,829	63.0

Excludes 44,875 in situ cases.
Unknown size category includes Paget disease of the nipple with no demonstrable tumor.
~ Statistic not displayed due to less than 25 cases.

13.8 shows that patients with tumors confined to the breast survived better at 5 years than patients whose tumor had invaded the subcutaneous tissue or the pectoral fascia (93% vs. 72% to 69%). Invasion of the subcutaneous tissue and involvement of the pectoral fascia had similar 5-year survival rates. Within stage IIIB (AJCC/UICC staging classification, 5th edition) and with regional by direct extension (LRD staging classification), extensive skin involvement had a less favorable outcome than involvement of the chest wall, ribs, etc. For each extension category, involvement of the lymph nodes still remained a predictor of survival. Even for cases with distant metastases, 5-year survival ranged from 32% when regional lymph nodes are negative to only 12% when distant lymph nodes were involved.

Size of tumor and nodal involvement

In data from 1988-2001, the size of the tumor has first been taken from the pathology report and then from radiology reports if there was no path or no size information on path. If there was no size given on either report, the clinical size was used. Figure 13.1 shows the relationship of tumor size to the percentage of women who have lymph node involvement. The curve shown on the graph shows the logistic regression fit. The size of the primary tumor

Table 13.7: Malignant Cancer of the Female Breast: Tumor Size (mm) Distribution by Extension, Ages 20+, 12 SEER Areas, 1988-2001

	Extension											
	Total		Localized		Regional by Nodes		Regional by Extension		Distant		Unknown	
Tumor Size (mm)	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%
All sizes	257,888	100.0	160,105	100.0	64,224	100.0	14,075	100.0	14,359	100.0	5,125	100.0
Micro focus	4,439	1.7	4,016	2.5	332	0.5	59	0.4	20	0.1	12	0.2
Mammography only	944	0.4	842	0.5	77	0.1	13	0.1	<5	0.0	8	0.2
3-7	21,231	8.2	19,261	12.0	1,635	2.5	166	1.2	102	0.7	67	1.3
8-12	47,548	18.4	39,561	24.7	6,879	10.7	624	4.4	349	2.4	135	2.6
13-17	43,576	16.9	31,659	19.8	10,202	15.9	1,046	7.4	509	3.5	160	3.1
18-22	37,530	14.6	23,347	14.6	11,728	18.3	1,497	10.6	766	5.3	192	3.7
23-27	22,163	8.6	11,985	7.5	8,177	12.7	1,284	9.1	622	4.3	95	1.9
28-32	17,160	6.7	8,220	5.1	6,605	10.3	1,355	9.6	822	5.7	158	3.1
33-37	7,791	3.0	3,318	2.1	3,321	5.2	763	5.4	353	2.5	36	0.7
38-42	8,346	3.2	3,212	2.0	3,394	5.3	973	6.9	664	4.6	103	2.0
43-47	3,397	1.3	1,168	0.7	1,492	2.3	493	3.5	223	1.6	21	0.4
48-52	5,303	2.1	1,615	1.0	2,160	3.4	829	5.9	621	4.3	78	1.5
53-57	1,638	0.6	481	0.3	701	1.1	320	2.3	131	0.9	5	0.1
58-62	3,221	1.2	788	0.5	1,249	1.9	656	4.7	468	3.3	60	1.2
63-67	875	0.3	214	0.1	373	0.6	187	1.3	96	0.7	5	0.1
68-72	1,953	0.8	431	0.3	703	1.1	432	3.1	349	2.4	38	0.7
73-77	484	0.2	108	0.1	197	0.3	113	0.8	63	0.4	<5	0.1
78-82	1,675	0.6	308	0.2	519	0.8	429	3.0	385	2.7	34	0.7
83-87	272	0.1	56	0.0	90	0.1	72	0.5	53	0.4	<5	0.0
88-92	760	0.3	141	0.1	237	0.4	205	1.5	167	1.2	10	0.2
93-97	164	0.1	33	0.0	43	0.1	55	0.4	33	0.2	0	0.0
>97	2,510	1.0	378	0.2	516	0.8	760	5.4	806	5.6	50	1.0
Diffuse	3,686	1.4	67	0.0	109	0.2	311	2.2	3,174	22.1	25	0.5
Unknown	21,222	8.2	8,896	5.6	3,485	5.4	1,433	10.2	3,579	24.9	3,829	74.7

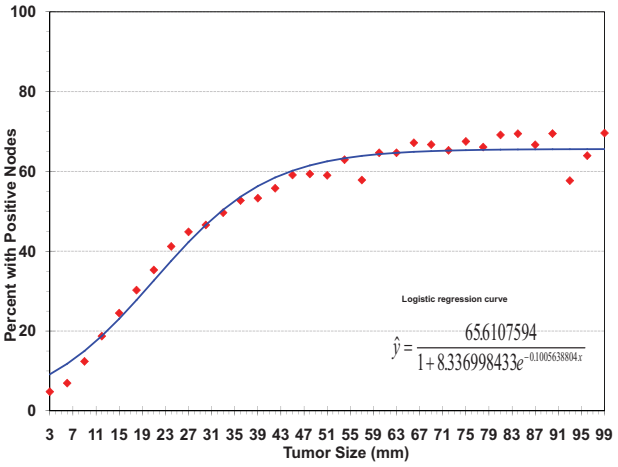
Excludes 44,875 in situ cases.
Unknown size category includes Paget disease of the nipple with no demonstrable tumor.

correlated with the percentage of women who had lymph node involvement in that the larger the tumor the higher the percentage of cases with lymph node involvement. While few women with very small tumors had lymph node involvement, over 60% of women with tumors over 54 mm had regional lymph nodes involved at the time of diagnosis. Five-year relative survival rates were high for women with small tumors and positive lymph nodes; they were lower for women with large tumors and positive lymph nodes. Survival rates decreased as size of tumor increased even when nodal involvement is divided into no positive lymph nodes, 1-3 lymph nodes positive, and 4 or more lymph nodes positive (Figure 13.2, Table 13.9). There were few cases with 4 or more nodes involved that had small tumors; therefore, the survival rate is not shown for the smallest size categories. This is consistent with the data from Table 13.7, which show that only a small proportion of women with regional lymph nodes involved had tumors less than 8 mm in diameter.

Receptor Status

Information on estrogen receptor (ER) and progesterone receptor (PR) status has been collected since 1990. Table 13.10 shows the 3-year relative survival rates by estrogen receptor status (ER) and progesterone receptor status (PR). ER positive tumors had better relative survival rates than

Figure 13.1: Cancer of the Female Breast: Existence of Positive Nodes by Tumor Size, 12 SEER Areas, 1988-2001



ER negative for each PR group. Women with ER+ and PR+ had a 97% 3-year relative survival rate compared with only 83% for women with PR- and ER-.

Table 13.11 shows the 3-year relative survival rates by ER status, historic stage, and age. Within each stage, ER status is an important prognostic variable. Even within distant stage, the 5 year relative survival rate was 28% for ER negative but much higher, 50% for ER positive women. Younger women have a higher percentage of cases that are ER negative than older women. This contributes towards the younger women having poorer survival than older women.

Laterality and Tumor Location

Table 13.12 shows the relationship between relative survival rates with respect to left or right breast and location within the breast. Laterality, left or right side, did not have any noticeable effect on survival. It should be noted that left or right designates the side where the tumor originated. The location of the tumor within the breast did not seem to be of prognostic value except when it was not specified.

DISCUSSION

While breast cancer survival rates overall are generally good, they vary by patient and tumor characteristics. Although stage has a large impact on survival, other factors such as tumor size, histology, ER status, PR status, grade, age, race, and number of positive nodes also played a role in prognosis. Some of these results expand on an earlier analysis performed on earlier SEER data (2).

Breast cancer is the number one cancer among U.S. women and it is expected that 212,920 women will be diagnosed with breast cancer in 2006 (3). Although breast cancer is a major disease in the US for women, its survival rates are better overall than those for many other types of cancer (4). The 5-year relative survival rate for localized invasive disease (all tumor sizes combined) was 97%. For patients diagnosed in stage I (tumor size < 20 mm), the 5-year relative survival rate was 100%. Some groups, however, especially young women, had a less favorable outcome. For women diagnosed in stage I, those 20-34 years of age had a 94% 5-year relative survival rate, compared to 100% for those over age 60. Differences by age are even greater for stage II patients.

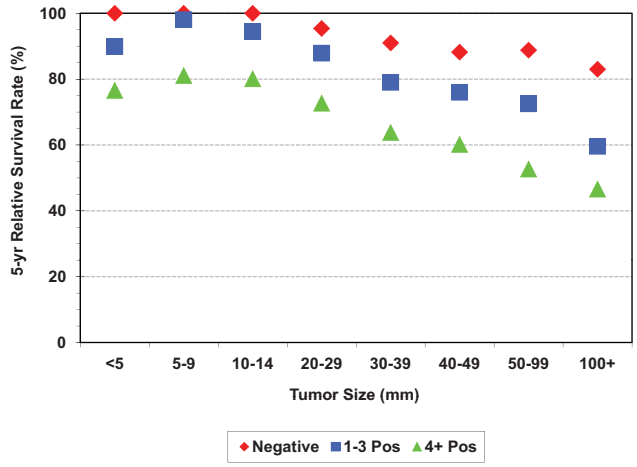
Table 13.8: Malignant Cancer of the Female Breast: Number of Cases and 5-Year Relative Survival Rates (%) by Tumor Extension and Lymph Node Status, Ages 20+, 12 SEER Areas, or 13 1988-2001

	Nodes Involved											
	Total		Negative Regional		Positive Regional		Fixed Regional		Distant		Unknown	
Extension	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
Total	257,888	87.1	154,918	97.2	73,153	77.5	5,009	55.2	1,719	22.9	23,089	61.4
Confined to breast	223,777	93.0	149,125	98.2	60,249	83.3	3,088	68.2	335	48.0	10,980	86.7
Subcutaneous tissue	7,481	71.7	2,320	87.7	4,036	68.5	317	51.5	47	26.5	761	51.2
Pectoral fascia	1,916	69.2	724	84.7	899	62.0	95	49.4	16	~	182	61.5
Chest wall, ribs, muscles	897	62.2	289	79.8	371	56.6	63	30.7	12	~	162	56.6
Extensive skin involvement	3,994	47.3	777	66.7	1,946	48.8	411	35.1	138	14.8	722	37.0
Inflammatory	3,173	39.9	343	60.5	1,603	41.6	269	34.7	131	19.3	827	34.0
Distant metastasis	10,500	18.7	1,038	32.3	3,247	21.2	681	17.0	902	12.3	4,632	15.5
Unknown	6,150	62.7	302	77.4	802	67.4	85	49.9	138	35.2	4,823	62.0

Excludes 44,875 in situ cases.

~Statistic not displayed due to less than 25 cases.

Figure 13.2: Cancer of the Female Breast: 5-Year Relative Survival Rate (%) by Tumor Size & Number of Nodes, Ages 20+, 12 SEER Areas, 1988-2001



Relative survival, like the name implies, is relative to the general population. When relative survival is 100%, the correct interpretation is that the cohort of patients has the same chance to live 5 more years as cancer-free persons of the same age and sex. This does not mean that no woman will die of breast cancer but rather that they may be under better medical surveillance than the general population and that their excess risk of breast cancer deaths is offset by their lower excess risk of dying from other non-cancer causes.

Even though relative survival rates increased with age at diagnosis until age 70, then decreased for the oldest age groups (Table 13.2), the survival differences by age were not due to differences in the stage distribution. Except for older patients having a higher proportion of unstaged disease, the stage distribution was similar for all age groups. Also, understaging of disease probably occurred with greater frequency among older patients, since many older patients did not have axillary node dissections. Since the relative survival rate adjusts for other causes of death, the differences in survival rates by age should not be attributed to the older patients dying from causes other than cancer at a higher rate than the younger cohorts. While for most other cancer sites, relative survival rates decreased with increasing age, this was not true of breast cancer except for the oldest age group.

There was a correlation between tumor size and percentage of women with positive lymph nodes (Figure 13.1). The survival rates generally decreased as the tumor size and the number of lymph nodes involved increased (Figure 13.2).

These data show that the evaluation of regional and distant lymph nodes should not be ignored when a patient has distant metastases. For patients with distant metastases, involvement of lymph nodes still plays an important prognostic role (Table 13.8). Those with no lymph node involvement have a 5-year relative survival rate of 32%; in contrast, the corresponding rate was 12% for those with distant lymph nodes involved.

While this analysis shows the value of the TNM system of staging, both tumor size and extent of disease influence the survival rates. Figure 13.3 shows the survival curves by the T, N, and M components of AJCC stage, 5th edition. Even though T1 (< 20 mm) N0 M0 has a distinct survival curve from T2 (20-50 mm) N0 M0, which in turn has a distinct survival curve from T3 (> 50 mm) N0 M0, other size groupings would also have produced distinct survival curves. The size groupings in any staging scheme are artificial and a matter of convenience. As shown (Table 13.6), survival rates vary by small changes in the tumor size. This points out that there was significant variation in survival within each TNM size category. Similarly, this chapter also points out that within extension (of tumor) groupings in TNM or within N1, there are survival variations when these groups are further subdivided by how far the tumor has extended (Table 13.8) or by the number of lymph nodes involved (Table 13.9), respectively.

Based on a large cohort, the probability of lymph node involvement directly correlates with the size of the primary tumor. Further, there is a survival relationship among tumor size, extension of tumor, and number of lymph nodes involved.

Figure 13.3: Cancer of the Female Breast: Relative Survival Rates (%) of Breast Cancer by Combinations of T, N, and M, Ages 20+, 12 SEER Areas, 1988-2001

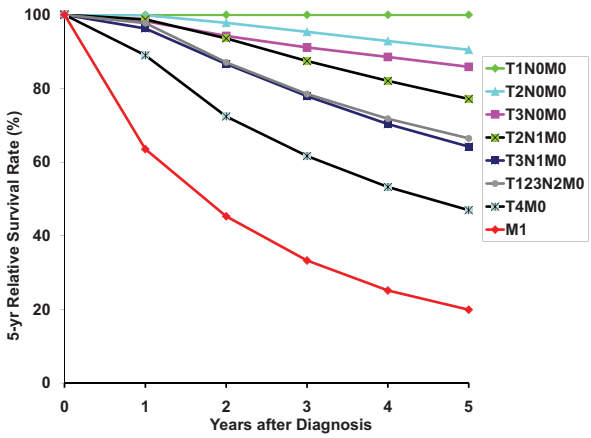


Table 13.9: Cancer of the Female Breast : Number of Cases and 5-Year Relative Survival Rates (%) by Tumor Size (mm) and Regional Lymph Nodes Involved, Ages 20+, 12 SEER Areas, 1988-2001

	Nodes Involved									
	Total		0 Nodes		1-3 Nodes		4+ Nodes		Unknown Number	
Tumor Size (mm)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)
Total	302,763	89.3	148,192	98.8	43,418	86.8	26,923	65.5	84,230	81.2
1-4	21,530	100.0	9,721	100.0	563	89.9	197	76.6	11,049	100.0
5-9	37,075	100.0	23,816	100.0	2,261	98.1	541	81.1	10,457	100.0
10-19	93,875	97.2	58,654	100.0	14,035	94.5	4,475	80.1	16,711	91.8
20-29	54,610	88.0	27,139	95.4	12,194	87.9	6,440	72.7	8,837	75.7
30-39	23,880	78.1	9,497	91.0	5,704	79.0	4,412	63.8	4,267	61.3
40-49	11,786	72.1	3,866	88.2	2,692	76.0	2,753	60.2	2,475	54.2
50-99	17,015	63.2	4,120	88.8	3,135	72.5	5,054	52.7	4,706	45.7
100+	2,580	46.8	382	83.0	290	59.6	670	46.6	1,238	32.6
Diffuse	3,734	35.1	218	84.0	350	51.1	907	39.6	2,259	27.0
Unknown	36,678	84.9	10,779	100.0	2,194	81.8	1,474	63.1	22,231	78.4

Unknown size category includes Paget disease of the nipple with no demonstrable tumor.

REFERENCES

1. Beahrs, OH, Henson DE, Hutter RVP, Myers MH (eds). AJCC Cancer Staging Manual, Third edition. American Joint Committee on Cancer. Philadelphia: Lippincott, 1988.
2. Ries LAG, Henson DE, Harras A. Survival from breast cancer according to tumor size and nodal status. Surg Oncol Clin N Am 1994;3:35-53.
3. American Cancer Society. Cancer Facts and Figures 2006. Atlanta: American Cancer Society, 2006.
4. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Eisner MP, Horner MJ, Howlader N, Hayat M, Hankey BF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site, 2006.

Table 13.10: Malignant Cancer of the Female Breast: Number of Cases and 3-Year Relative Survival Rates (%) by Progesterone Receptor (PR) and Estrogen Receptor (ER) Status, Ages 20+, 12 SEER Areas, 1990-2001

	ER Status							
	Total		Positive		Negative		Other/Unknown	
PR Status	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)
Total (1990+)	230,922	92.1	140,857	96.4	43,030	83.6	47,035	87.2
Positive	118,718	96.6	112,352	97.1	5,618	88.5	748	90.7
Negative	59,375	86.5	22,623	92.7	36,204	82.9	548	83.1
Other/Unknown	52,829	88.2	5,882	96.8	1,208	83.2	45,739	87.2

Table 13.11: Female Malignant Breast Cancer: 3-Year Relative Survival Rates (%) by Age (20+), SEER Historic Stage and ER Status, 12 SEER Areas, 1990-2001

Age/Historic Stage	ER Status									
	Total		Positive		Negative		Borderline		Other/Unknown	
	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)	Cases	3-Year Relative Survival Rate (%)
All Ages (1990+)	230,922	92.1	140,857	96.4	43,030	83.6	1,502	86.5	45,533	87.2
Localized	144,309	99.2	91,097	100.0	24,698	95.2	877	94.5	27,637	98.2
Regional	69,408	88.3	43,208	93.7	14,978	76.3	540	79.8	10,682	84.4
Distant	12,814	38.6	5,700	50.0	3,001	27.6	72	40.1	4,041	30.8
Unstaged	4,391	73.0	852	81.2	353	57.4	13	~	3,173	72.6
Ages 20-49 (1990+)	58,630	90.5	31,200	95.4	16,020	83.8	574	88.2	10,836	86.6
Localized	32,123	97.2	17,271	98.9	8,624	94.5	318	94.0	5,910	96.4
Regional	22,424	87.7	12,624	93.9	6,274	77.4	225	85.4	3,301	84.3
Distant	3,068	44.0	1,157	59.7	1,001	33.6	27	42.6	883	35.5
Unstaged	1,015	77.9	148	87.6	121	59.6	<5	~	742	79.0
Ages 50-64 (1990+)	75,173	92.3	46,305	96.2	14,540	84.5	479	87.7	13,849	88.2
Localized	46,733	98.8	29,446	100.0	8,471	95.3	279	95.5	8,537	98.2
Regional	23,080	89.7	14,724	94.4	4,952	78.0	173	81.0	3,231	87.1
Distant	4,275	39.7	1,913	51.6	1,013	26.9	21	~	1,328	32.4
Unstaged	1,085	76.4	222	76.8	104	62.5	6	~	753	78.0
Ages 65+ (1990+)	97,119	93.0	63,352	97.2	12,470	82.4	449	82.8	20,848	87.0
Localized	65,453	100.0	44,380	100.0	7,603	95.9	280	94.0	13,190	99.1
Regional	23,904	87.5	15,860	92.8	3,752	71.7	142	68.0	4,150	82.3
Distant	5,471	34.2	2,630	43.9	987	21.5	24	~	1,830	26.9
Unstaged	2,291	68.5	482	81.2	128	50.2	<5	~	1,678	66.4

~Statistic not displayed due to less than 25 cases.

Table 13.12: Cancer of the Female Breast: Number of Cases and 5-Year Relative Survival Rates (%) by Subsite and Laterality, Ages 20+, 12 SEER Areas, 1988-2001

Subsite	Laterality					
	Total		Right		Left	
	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)
Total (With Distinct Laterality)	301,375	89.5	147,546	89.6	153,829	89.4
Nipple	3,089	90.1	1,507	90.1	1,582	90.2
Central	18,567	88.9	8,996	88.6	9,571	89.1
Upper Inner	26,847	93.0	12,875	93.3	13,972	92.7
Lower Inner	15,494	92.3	7,242	92.5	8,252	92.0
Upper Outer	106,575	91.9	53,103	91.8	53,472	91.9
Lower Outer	18,788	91.2	8,909	91.6	9,879	90.8
Axillary Tail	2,159	86.9	1,076	86.3	1,083	87.4
Overlapping	58,813	88.9	29,039	89.1	29,774	88.6
Other/unknown	51,043	82.4	24,799	82.6	26,244	82.2

Excludes 1,388 cases classified as only one (unknown) side, bilateral, or paired site/no information.

Chapter 14
Cancer of the Cervix Uteri

Carol L. Kosary

INTRODUCTION

Despite the existence of effective screening through the use of Pap smears since the 1950's, there were 9,710 estimated cases of invasive cervical cancer and 3,700 deaths in 2006 (1). This makes cervical cancer the 14th leading cancer in women and the 15th leading cancer death in 2006 (1). The cervical uterine cancer incidence rates for white women are lower than those for black women (2). The incidence rates for both blacks and whites have been decreasing for many years (2). The three most common histologic types are squamous, adenocarcinoma, and adenosquamous. Five-year survival of cancers of the cervix uteri have increased slightly over time (2).

MATERIALS AND METHODS

The NCI contracts with medically-oriented, nonprofit institutions located in specific geographic areas to obtain data on all cancers diagnosed in residents of the SEER geographic areas. SEER collects data on all invasive and in situ cancers except basal cell and squamous cell carcinomas of the skin (of non-genital anatomic sites) and in situ carcinomas of the uterine cervix. SEER actively follows all previously diagnosed patients on an annual basis to obtain vital status allowing the calculation of observed and relative survival rates.

This analysis is based on data from 12 SEER geographic areas which collectively cover about 14% of the total US population. The areas are the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Michigan; Atlanta, Georgia; San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; and 10 counties in rural Georgia. Los Angeles contributed data for diagnosis years 1992 to 2001, all other areas for 1988-2001.

Between 1988-2001, there were 95,353 cases of cancer of the cervix uteri diagnosed in SEER. The following were excluded from the analysis: patients for whom cervical cancer was not the first primary, cases identified through autopsy or death certificate only, persons of unknown race, alive with no survival time, patients less than 20 years old, in situ cases, cases without microscopic confirmation, sarcomas and carcinoids. After these exclusions, 21,431 cases remained for analysis (Table 14.1).

Table 14.1: Cancer of the Cervix Uteri: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/selection
95,353	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
91,957	3,396	Select first primary only
91,824	133	Exclude death certificate only or at autopsy
83,929	7,895	Exclude unknown race
36,272	47,657	Exclude alive with no survival time
35,764	508	Exclude children (Ages 0-19)
21,789	13,975	Exclude in situ cancers
21,622	167	Exclude no or unknown microscopic confirmation
21,533	89	Exclude sarcomas
21,467	66	Exclude carcinoids
21,431	36	Exclude stromal sarcomas

Staging

Uterine cervical cancer staging by the Federation Internationale de Gynecologie et d'Obstetrique (FIGO) and the American Joint Committee on Cancer (AJCC) third edition are in the AJCC 3rd edition (3):

Stage I is carcinoma strictly confined to the cervix; extension to the uterine corpus should be disregarded

Stage IA: Invasive cancer identified only microscopically. Invasion is limited to measured stromal invasion with a maximum depth of 5 mm and no wider than 7 mm.

Stage IB: Clinical lesions confined to the cervix or preclinical lesions greater than stage IA.

Stage II is carcinoma that extends beyond the cervix but has not extended onto the pelvic wall. The carcinoma involves the vagina, but not as far as the lower third.

Stage IIA: No obvious parametrial involvement. Involvement of up to the upper two thirds of the vagina.

Stage IIB: Obvious parametrial involvement, but not onto the pelvic sidewall.

Stage III is carcinoma that has extended onto the pelvic sidewall. On rectal examination, there is no cancer-free space between the tumor and the pelvic sidewall. The tumor involves the lower third of the vagina. All cases with a hydronephrosis or nonfunctioning kidney should be included, unless they are known to be due to other causes.

Stage IIIA: No extension onto the pelvic sidewall but involvement of the lower third of the vagina.

Stage IIIB: Extension onto the pelvic sidewall or hydronephrosis or nonfunctioning kidney

Stage IV is carcinoma that has extended beyond the true pelvis or has clinically involved the mucosa of the bladder and/or rectum.

Stage IVA: Spread of the tumor onto adjacent pelvic organs.

Stage IVB: Spread to distant organs

Since the emphasis is on extension, a SEER modified version of stage was used in which positive lymph nodes went to N1 and Stage IIIB but unknown lymph node involvement was ignored, i.e. treated like N0.

RESULTS

Age and Race

Of the 21,431 adult cases, 56.9% were diagnosed under age 50 (Table 14.2). Almost 50% were between the ages of 30-49 years. The age distribution for white women

Table 14.2: Cancer of the Cervix Uteri: Age Distribution by Race, 12 SEER Areas, 1988-2001

	Total		White		Black		Other	
Age Group (Years)	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	21,431	100.0	16,196	100.0	2,798	100.0	2,437	100.0
20-29	1,586	7.4	1,332	8.2	183	6.5	71	2.9
30-39	5,060	23.6	4,074	25.2	576	20.6	410	16.8
40-49	5,542	25.9	4,162	25.7	721	25.8	659	27.0
50-59	3,487	16.3	2,527	15.6	465	16.6	495	20.3
60-69	2,873	13.4	2,045	12.6	400	14.3	428	17.6
70-79	1,876	8.8	1,326	8.2	284	10.2	266	10.9
80+	1,007	4.7	730	4.5	169	6.0	108	4.4

Table 14.3: Cancer of the Cervix Uteri: Number of Cases, 5-Year Survival Rates (%) and Median Survival Time (Months) by Race and Age (20+), 12 SEER Areas, 1988-2001

		Median Survival Time (Months)	5-Year Survival Rate (%)		
Race and Age Group	Cases		Observed	Expected	Relative
All Races, 20+	21,431	> 120	67.6	94.5	71.5
White, 20+	16,196	> 120	69.0	94.9	72.8
Black, 20+	2,798	99.8	56.8	91.6	61.9
All Races, 20-49	12,188	> 120	78.5	99.1	79.2
White, 20-49	9,568	> 120	80.5	99.3	81.1
Black, 20-49	1,480	> 120	65.5	98.2	66.7
All Races, 50-69	6,360	116.0	61.2	94.9	64.5
White, 50-69	4,572	113.7	61.2	95.1	64.3
Black, 50-69	865	69.8	52.7	91.7	57.4
All Races, 70+	2,883	29.8	36.5	74.3	49.0
White, 70+	2,056	27.8	34.5	73.9	46.8
Black, 70+	453	27.6	36.3	70.0	51.2

Table 14.4: Cancer of the Cervix: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by SEER Geographic Area, Ages 20+, 12 SEER Areas, 1988-2001

SEER Geographic Area	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	21,431	100.0	89.2	80.6	76.1	71.5	68.7	67.2
Atlanta and Rural Georgia	1,707	8.0	89.8	82.2	77.2	73.5	72.4	70.8
Atlanta (Metropolitan) - 1988+	1,598	7.5	90.4	83.0	78.2	74.3	73.0	71.7
Rural Georgia - 1988+	109	0.5	81.1	69.9	63.1	61.3	61.3	58.3
California								
Los Angeles - 1992+	5,091	23.8	89.4	79.6	74.1	68.6	66.1	62.0
Greater Bay Area	3,613	16.9	89.9	80.9	77.0	71.6	68.3	66.8
San Francisco-Oakland SMSA - 1988+	2,294	10.7	88.9	80.1	76.4	71.6	67.9	65.8
San Jose-Monterey - 1988+	1,319	6.2	91.6	82.2	78.0	71.5	68.8	68.4
Connecticut - 1988+	1,926	9.0	87.1	79.0	75.3	71.3	68.1	67.7
Detroit (Metropolitan) - 1988+	2,688	12.5	86.1	76.7	71.7	66.6	62.5	59.8
Hawaii - 1988+	762	3.6	89.5	82.7	78.6	72.4	70.4	69.9
Iowa - 1988+	1,732	8.1	91.1	83.2	79.2	74.8	71.2	70.1
New Mexico - 1988+	1,083	5.1	89.7	81.9	76.9	73.0	70.5	69.0
Seattle (Puget Sound) - 1988+	1,967	9.2	90.7	83.3	79.4	76.6	74.7	73.9
Utah - 1988+	862	4.0	89.0	83.5	79.3	76.8	73.7	73.1

Table 14.5: Cancer of the Cervix Uteri: Number and Distribution of Cases and 5-Year Relative Survival by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology	ICD-O Code	Cases	Percent	5-Year Relative Survival Rate(%)
Total	8000-9989	21,431	100.0	71.5
Squamous	8050-8130	15,579	72.7	71.5
Keratinizing	8071	1,959	9.1	65.8
Non-keratinizing	8072	2,399	11.2	68.2
Microinvasive	8076	2,156	10.1	98.3
All Other Squamous	8050-8070,8073-8075,8077-8130	9,065	42.3	66.9
Adenocarcinoma	8140-8147,8160-8162,8180-8221,8250-8506,8520-8550,8570-8573,8940-8941	3,656	17.1	75.0
Adenosquamous	8560	1,034	4.8	64.5
Other Specified Carcinomas	8030-8045,8150-8155,8170-8171,8230-8248,8510-8512,8561-8562,8580-8671	149	0.7	32.9
Small Cell Carcinomas	8041	140	0.7	34.7
All Other Specified Carcinomas	8030-8040,8042-8045,8150-8155,8170-8171,8230-8248,8510-8512,8561-8562,8580-8671	9	0.0	~
Carcinoma, NOS*	8010-8022	875	4.1	73.5
Other Specified Types	8720-8790,8935,8950-8982,9000-9030,9060-9110,9350-9364,9380-9512,9530-9539	56	0.3	49.0
Unspecified	8000-8004	82	0.4	70.3

~ Statistic not displayed due to less than 25 cases.
* NOS: Not Otherwise Specified

was slightly younger than that for black women or women of other races.

For all women, survival declines with age. In women ages 20-49, the 5-year relative survival rate is 79% compared to 65% in women 50-69 and 49.0% in women aged 70 and older. Survival is also lower for black women compared to white women in all age groups presented with the exception of ages over 70 (Table 14.3).

Geographic Location

There is some evidence of geographic variation in survival. Five-year relative survival rates in the 12 SEER areas represented in this study ranged from 77% in Utah and Seattle to 61% in Rural Georgia (Table 14.4).

Histology

Distribution by histology is presented in Table 14.5. Tumors classified as squamous comprise 72.7% of all cancers of the cervix uteri. Among squamous histologies 12.6% were keratinizing, 15.4% non-keratinizing, and 13.8% microinvasive. Tumors classified as adenocarcinoma comprised 17.1% of the total with adenosquamous making up slightly less than 5%. Survival rates were highest for microinvasive squamous cell carcinoma, 98%, but survival rates were similar for keratinizing and non-keratinizing squamous cell carcinoma, 66 and 68%, respectively (Table 14.5).

SQUAMOUS

Stage

Table 14.6 and Figure 14.1 show the contrast in survival rates across stage at diagnosis over time since diagnosis for squamous cell carcinoma. In stages II-IV, the steepest declines in survival are observed within 2-3 years of diagnosis. Survival continues to decline throughout the 10 years observed in these stages.

Age and Stage

Of the 15,579 cases of squamous, enough information to establish stage at diagnosis was available for 14,819 (95%). Across all age groups, 54.5% were diagnosed in Stage I. The percent diagnosed in stage I declines with age, from 64.9% in ages 20-49, 44.2% in ages 50-69, and 34.5% in ages 70+. At the same time the percent diagnosed in stage IV increases from 5.9% in ages 20-49 to 14.4% in ages 70+ (Table 14.7).

A survival differential across age exists for all stages except stage II, particularly for women aged 70+ compared to women ages 20-69. (Table 14.6, Figure 14.2).

Table 14.6: Squamous Carcinoma of the Cervix Uteri: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	15,579	100.0	89.9	81.0	76.2	71.5	68.5	66.7
Stage I	8,492	54.5	98.6	95.8	93.8	91.3	88.7	86.9
IA	3,776	24.2	99.7	99.1	98.6	98.1	96.8	95.5
IB	3,293	21.1	98.5	94.6	92.0	88.2	85.3	83.1
I NOS*	1,423	9.1	95.8	89.8	85.4	80.3	75.9	73.2
Stage II	2,439	15.7	92.2	79.3	70.5	60.7	54.8	52.9
IIA	726	4.7	91.8	81.8	75.1	67.2	62.6	60.9
IIB	1,713	11.0	92.4	78.3	68.5	57.9	51.4	49.6
Stage III	2,526	16.2	80.5	62.6	53.9	46.8	43.4	41.2
IIIA	290	1.9	73.7	53.1	43.3	38.6	33.9	29.6
IIIB	2,236	14.4	81.4	63.8	55.2	47.7	44.4	42.4
Stage IV	1,362	8.7	51.6	30.2	22.0	15.8	13.5	12.0
IVA	296	1.9	56.0	32.8	23.5	19.9	17.5	13.6
IVB	1,064	6.8	50.4	29.6	21.7	14.6	12.2	11.7
IV NOS*	<5	0.0	~	~	~	~	~	~
Unknown/Unstaged	760	4.9	84.6	70.9	64.5	56.5	52.2	45.9

~ Statistic not displayed due to less than 25 cases.
* NOS: Not Otherwise Specified

Table 14.7: Squamous Carcinoma of the Cervix Uteri: Number, Distribution of Cases, and 5-Year Relative Survival Rates by AJCC Stage (SEER modified 3rd edition) and Age (20+), 12 SEER Areas, 1988-2001

	Age (Years)											
	Total			20-49			50-69			70+		
AJCC Stage	Cases	Percent	5-Year Relative Survival Rate(%)	Cases	Percent	5-Year Relative Survival Rate(%)	Cases	Percent	5-Year Relative Survival Rate(%)	Cases	Percent	5-Year Relative Survival Rate(%)
Total	15,579	100.0	71.5	8,730	100.0	78.3	4,792	100.0	64.9	2,057	100.0	53.4
Stage I	8,492	54.5	91.3	5,666	64.9	93.0	2,117	44.2	88.3	709	34.5	85.0
IA	3,776	24.2	98.1	2,810	32.2	98.3	749	15.6	96.9	217	10.5	98.4
IB	3,293	21.1	88.2	2,112	24.2	89.4	904	18.9	86.4	277	13.5	83.8
I NOS*	1,423	9.1	80.3	744	8.5	83.6	464	9.7	78.6	215	10.5	70.0
Stage II	2,439	15.7	60.7	1,002	11.5	61.2	980	20.5	63.4	457	22.2	52.6
IIA	726	4.7	67.2	252	2.9	70.7	293	6.1	68.4	181	8.8	58.9
IIB	1,713	11.0	57.9	750	8.6	57.9	687	14.3	61.1	276	13.4	48.5
Stage III	2,526	16.2	46.8	1,221	14.0	50.9	893	18.6	46.0	412	20.0	32.5
IIIA	290	1.9	38.6	77	0.9	44.1	113	2.4	44.4	100	4.9	25.6
IIIB	2,236	14.4	47.7	1,144	13.1	51.4	780	16.3	46.2	312	15.2	34.7
Stage IV	1,362	8.7	15.8	515	5.9	20.9	550	11.5	12.8	297	14.4	10.2
IVA	296	1.9	19.9	96	1.1	28.6	117	2.4	16.2	83	4.0	13.6
IVB	1,064	6.8	14.6	419	4.8	19.1	433	9.0	11.7	212	10.3	8.8
IV NOS*	<5	0.0	~	0	0.0	~	0	0.0	~	<5	0.1	~
Unknown/ Unstaged	760	4.9	56.5	326	3.7	66.3	252	5.3	50.5	182	8.8	43.4

* NOS: Not Otherwise Specified

Figure 14.1: Squamous Cell Carcinoma of the Cervix Uteri: Relative Survival Rate (%) by AJCC Stage, Ages 20+, 12 SEER Areas, 1988-2001

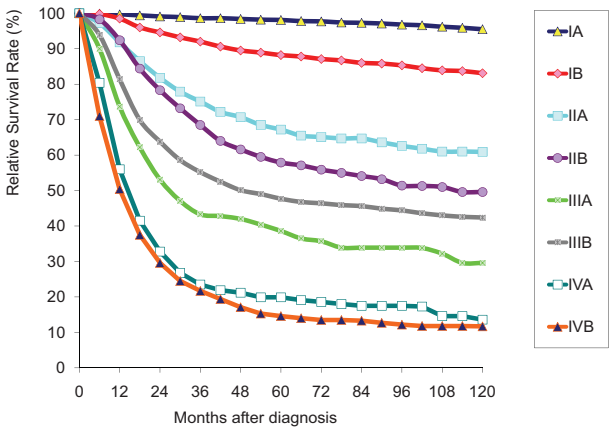
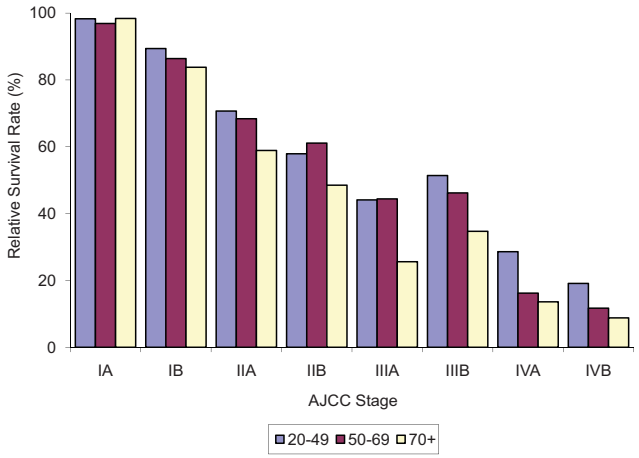


Figure 14.2: Squamous Cell Carcinoma of the Cervix Uteri: 5-Year Relative Survival Rate (%) by AJCC Stage and Age (20+), 12 SEER Areas, 1988-2001



Subtype and Stage

Microinvasive cases show a positive survival advantage compared to the other subtypes in stage I. Little difference exists between the other three subtypes in stages I-IV (Table 14.8).

Stage and Grade

Table 14.9 shows survival rates by AJCC Stage and histologic grade. With the exception of cases diagnosed in stages I and II, no consistent relationship is observed between stage and grade (Table 14.9 & Figure 14.3).

Tumor Size (Stage I and II)

In stages IB-IIB, survival is higher for those tumors less than 3 cm in size when compared to those 3 cm or greater (Table 14.10, Figure 14.4). A very small difference by tumor size was seen for stage IA.

Figure 14.3: Squamous Cell Carcinoma of the Cervix Uteri: 5-Year Relative Survival Rate (%) by AJCC Stage and Grade, Ages 20+, 12 SEER Areas, 1988-2001

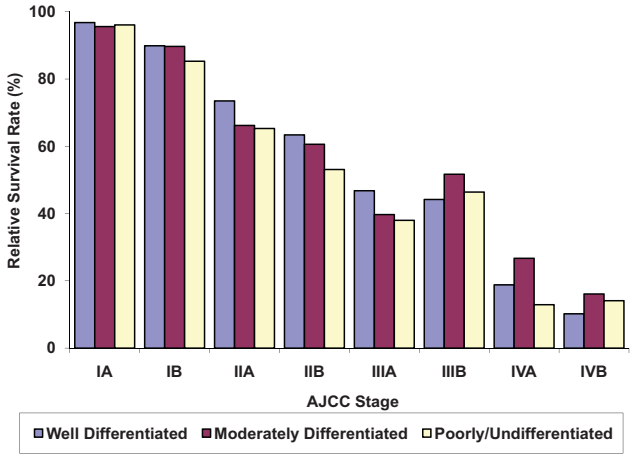


Figure 14.4: Stage I & II Squamous Cell Carcinoma of the Cervix Uteri: 5-Year Relative Survival Rate (%) by AJCC Stage and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

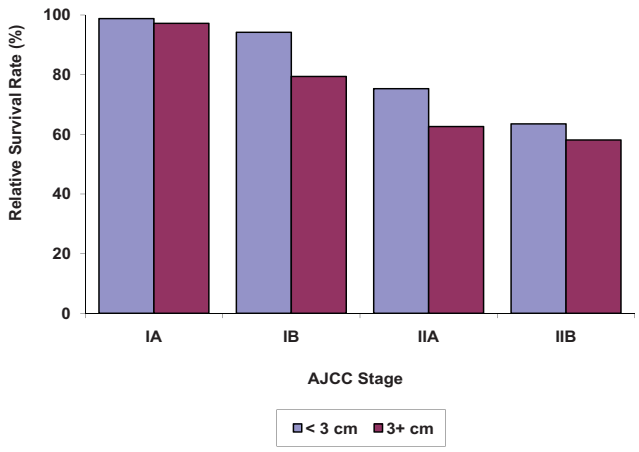


Table 14.8: Squamous Carcinoma of the Cervix Uteri: Number of Cases and 5-Year Relative Survival Rates (%) by Histology and AJCC Stage (SEER modified 3rd edition), Ages 20+,SEER 1988-2001

	AJCC Stage											
	Total		I		II		III		IV		Unknown/ Unstaged	
Histology	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)
Total Squamous	15,579	71.5	8,492	91.3	2,439	60.7	2,526	46.8	1,362	15.8	760	56.5
Keratinizing	1,959	65.8	890	88.5	366	61.5	416	46.3	203	18.1	84	46.1
Non-keratinizing	2,399	68.2	1,165	88.5	422	63.8	493	47.4	222	19.4	97	51.8
Microinvasive	2,156	98.3	2,100	98.8	15	~	13	~	7	~	21	~
All Other Squamous	9,065	66.9	4,337	88.8	1,636	59.6	1,604	46.5	930	14.3	558	57.2

~ Statistic not displayed due to less than 25 cases.

Table 14.9: Squamous Carcinoma of the Cervix Uteri: Number of Cases and 5-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition) and Grade, Ages 20+, 12 SEER Areas, 1988-2001

	Grade									
	Total		Well Differentiated		Moderately Differentiated		Poorly/ Undifferentiated		Unknown	
AJCC Stage	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)
Total	15,579	71.5	720	76.9	3,930	68.6	4,542	59.7	6,387	80.7
Stage I	8,492	91.3	437	93.2	1,892	88.3	1,852	84.5	4,311	95.1
IA	3,776	98.1	238	96.8	442	95.6	249	96.1	2,847	98.7
IB	3,293	88.2	136	89.9	1,075	89.7	1,205	85.3	877	90.0
I NOS*	1,423	80.3	63	86.1	375	76.3	398	75.1	587	85.3
Stage II	2,439	60.7	113	66.2	717	62.2	890	56.7	719	63.1
IIA	726	67.2	31	73.5	213	66.2	264	65.3	218	69.2
IIB	1,713	57.9	82	63.4	504	60.6	626	53.1	501	60.3
Stage III	2,526	46.8	96	44.6	823	50.3	1,002	45.7	605	44.1
IIIA	290	38.6	12	~	103	39.7	96	38.0	79	36.4
IIIB	2,236	47.7	84	44.2	720	51.7	906	46.4	526	45.1
Stage IV	1,362	15.8	40	11.9	337	18.9	609	13.9	376	16.2
IVA	296	19.9	11	~	85	26.7	124	12.9	76	23.0
IVB	1,064	14.6	29	10.2	250	16.1	485	14.1	300	14.3
IV NOS*	<5	~	0	~	2	~	0	~	0	~
Unknown/Unstaged	760	56.5	34	61.1	161	53.2	189	41.6	376	64.9

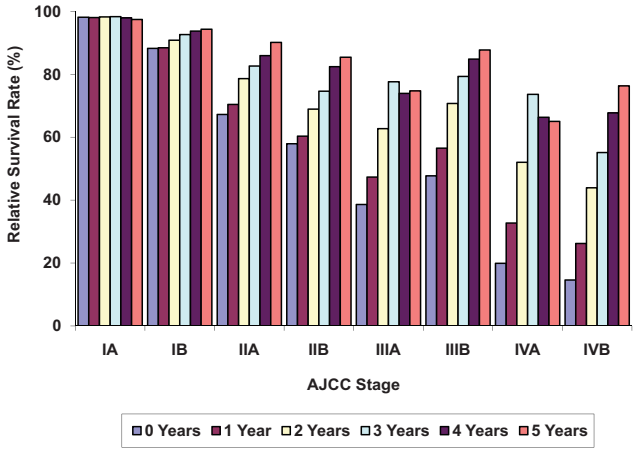
~ Statistic not displayed due to less than 25 cases.
* NOS: Not Otherwise Specified

Table 14.10: Squamous Carcinoma of the Cervix Uteri (Stage I and II): Number of Cases and 5-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition) and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

	Tumor Size									
	Total		No/Microscopic Mass		< 3 cm		3+ cm		Unknown	
AJCC Stage	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)
Total I & II	10,931	84.6	923	98.3	1,754	93.2	2,114	69.6	6,140	85.4
Stage I	8,492	91.3	914	98.5	1,608	95.4	1,067	79.2	4,903	91.3
IA	3,776	98.1	847	99.1	545	98.8	54	97.2	2,330	97.5
IB	3,293	88.2	38	84.3	953	94.2	825	79.4	1,477	89.5
I NOS*	1,423	80.3	29	94.6	110	87.3	188	73.3	1,096	80.2
Stage II	2,439	60.7	9	~	146	69.9	1,047	59.3	1,237	60.6
IIA	726	67.2	5	~	77	75.3	268	62.6	376	68.7
IIB	1,713	57.9	<5	~	69	63.5	779	58.1	861	57.0

~ Statistic not displayed due to less than 25 cases.
* NOS: Not Otherwise Specified

Figure 14.5: Squamous Cell Carcinoma of the Cervix Uteri: 5-Year Relative Survival Rate (%), Conditioned on Years Since Diagnosis, by AJCC Stage, Ages 20+, 12 SEER Areas, 1988-2001



Conditional Survival

Five-year relative survival rates, conditioned on years since diagnosis, are presented in Table 14.11 and Figure 14.5. For stages IB-IV, the probability of surviving through the next 5 years generally increases as time since diagnosis increases. This is most marked for the 5-year relative survival rates starting from one to three years after diagnosis for the stage IVA & IVB cases. For stage IVA, five years survival rate from time of diagnosis is 20%. For those individuals who survive 1 year post diagnosis, the 5-year survival rate increases to 33%. This increases to 72% for those individuals who survived 3years. For stage IVB, five year survival rate from time of diagnosis is 15%. For those individuals who survive 1 year post diagnosis, 5-year survival rate increases to 26%. This increases to 67% for those individuals who survived 4 years.

ADENOCARCINOMA

Stage

Of the 3,656 cases of adenocarcinoma, enough information to establish stage at diagnosis was available for 3,446 (94%). 65.1% of the cases were diagnosed in Stage I, with the remaining cases distributed almost evenly among stages II-IV (Table 14.12).

A five year survival difference between stage IA and IB is observed, with 5 year relative survival rate at 99% for stage IA and 90% for IB. Five-year survival decreases to 54% in stage II cases (Table 14.12). The stage distribution is slightly better for adenocarcinoma compared to squamous. For example, 65.1% of adenocarcinomas are staged as stage I in comparison to only 54.5% of squamous. Survival for adenocarcinoma, however, exhibits few differences by stage

Table 14.11: Squamous Carcinoma of the Cervix Uteri: 5-Year Relative Survival Rates (%) , Conditioned on Years Since Diagnosis by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	5-Year Relative Survival Rate (%)					
	Years Since Diagnosis					
AJCC Stage	0	1	2	3	4	5
Total	71.5	77.7	85.1	88.9	91.3	92.2
Stage I	91.3	91.7	93.5	94.5	95.0	95.1
IA	98.1	98.0	98.2	98.3	97.9	97.4
IB	88.2	88.4	90.8	92.6	93.7	94.2
I NOS	80.3	82.4	86.6	88.3	89.9	90.8
Stage II	60.7	63.3	71.9	77.2	83.5	86.6
IIA	67.2	70.4	78.4	82.5	85.4	89.5
IIB	57.9	60.3	68.8	74.6	82.4	85.1
Stage III	46.8	55.6	70.0	79.1	83.8	86.5
IIIA	38.6	47.3	62.0	76.7	73.9	73.5
IIIB	47.7	56.5	70.7	79.3	84.8	87.6
Stage IV	15.8	27.7	45.9	59.5	66.8	72.4
IVA	19.9	32.6	51.8	72.1	66.3	65.0
IVB	14.6	26.1	43.8	54.9	67.2	76.1
IV NOS	~	~	~	~	~	~
Unknown/Unstaged	56.5	63.0	73.4	79.0	82.1	79.5

* NOS: Not Otherwise Specified
~ Statistic not displayed due to less than 25 cases.

when compared to squamous of the cervix uteri (Tables 14.6 and 14.12).

Figure 14.6 show the contrast in the relative survival rates between stage at diagnosis and years since diagnosis. In stages II-IV, the steepest declines in survival are observed within 2-3 years of diagnosis. Survival continues to decline throughout the 10 years observed in these stages.

Stage and Grade

The 3,656 cases of adenocarcinoma are shown by histologic grade (Table 14.13 & Figure 14.7). Within stage, 5-year relative survival declines as grade increases from well differentiated to poorly/anaplastic. Within stage I, the 5-year survival rates vary from 97% for well differentiated tumors to 77% for poorly/undifferentiated tumors. Squamous cell carcinoma showed less variation by grade within stage.

Conditional Survival

Five year relative survival rates, conditioned on years since diagnosis, are presented in Table 14.14 and Figure 14.8. For stages IB-IV, the probability of surviving through the next 5 years increases as time since diagnosis increases. This is most marked for the stage IV cases. The 5-year survival rate from time of diagnosis was 14%. For those individuals who survive 1 year post diagnosis, survival over the next 5-years increased to 26%. This increased to 57% for the group of individuals who survived 4 years after diagnosis.

Figure 14.6: Adenocarcinoma of the Cervix Uteri: Relative Survival Rate (%) by AJCC Stage, Ages 20+, 12 SEER Areas, 1988-2001

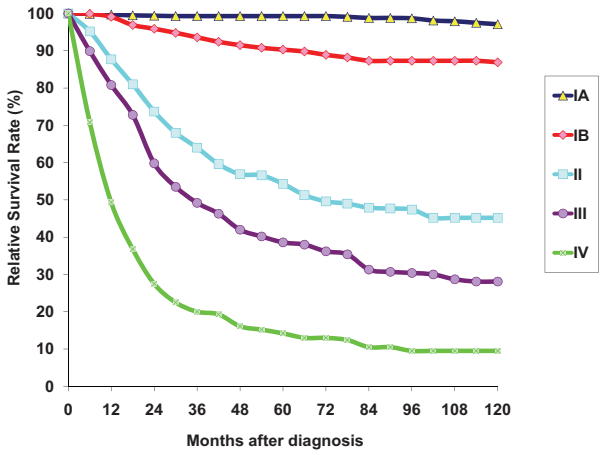


Figure 14.7: Adenocarcinoma of the Cervix Uteri: 5-Year Relative Survival Rate (%) by AJCC Stage and Grade, Ages 20+, 12 SEER Areas, 1988-2001

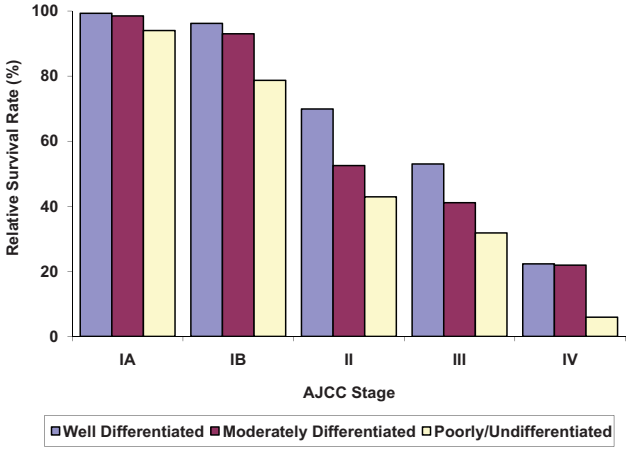


Table 14.12: Adenocarcinoma of the Cervix Uteri: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	3,656	100.0	90.3	82.8	78.6	75.0	72.3	71.2
Stage I	2,379	65.1	98.6	95.8	94.0	91.9	90.3	89.0
IA	630	17.2	99.7	99.4	99.3	99.3	98.7	97.1
IB	1,150	31.5	99.1	95.9	93.6	90.3	87.3	86.9
I NOS*	599	16.4	96.6	91.9	89.2	86.9	86.7	84.8
Stage II	356	9.7	87.7	73.7	64.0	54.3	47.4	45.2
Stage III	353	9.7	80.8	59.8	49.2	38.6	30.4	28.1
Stage IV	358	9.8	49.3	27.5	20.0	14.2	9.5	9.5
Unknown/Unstaged	210	5.7	85.7	78.8	71.1	67.0	63.0	57.9

* NOS: Not Otherwise Specified

Table 14.13: Adenocarcinoma of the Cervix Uteri: 5-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition) and Grade, Ages 20+, 12 SEER Areas, 1988-2001

	Grade									
	Total		Well Differentiated		Moderately Differentiated		Poorly/ Undifferentiated		Unknown	
AJCC Stage	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)
Total	3,656	75.0	877	89.7	1,100	75.9	779	49.2	900	80.6
Stage I	2,379	91.9	711	96.9	707	92.8	345	77.0	616	93.1
IA	630	99.3	198	99.3	143	98.5	48	94.0	241	99.5
IB	1,150	90.3	351	96.2	396	93.0	217	78.7	186	86.6
I NOS*	599	86.9	162	94.1	168	86.1	80	62.2	189	90.5
Stage II	356	54.3	58	69.9	140	52.5	86	42.9	72	55.6
Stage III	353	38.6	51	53.0	111	41.1	141	31.8	50	34.3
Stage IV	358	14.2	32	22.3	92	21.9	174	5.9	60	20.9
Unknown/Unstaged	210	67.0	25	70.7	50	58.7	33	53.7	102	73.1

* NOS: Not Otherwise Specified

Table 14.14: Adenocarcinoma of the Cervix Uteri: 5-Year Relative Survival Rates (%), Conditioned on Years Since Diagnosis by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	5-Year Relative Survival Rate(%)					
	Years Since Diagnosis					
AJCC Stage	0	1	2	3	4	5
Total	75.0	80.6	86.1	90.2	92.5	92.9
Stage I	91.9	92.2	94.0	95.7	96.6	96.4
IA	99.3	99.5	99.3	99.1	97.8	97.2
IB	90.3	89.8	91.0	93.2	95.5	96.0
I NOS*	86.9	89.0	93.3	96.1	96.9	96.3
Stage II	54.3	55.5	63.4	72.0	77.4	81.0
Stage III	38.6	43.9	50.3	58.9	64.0	68.6
Stage IV	14.2	25.8	36.5	45.8	57.2	65.5
Unknown/Unstaged	67.0	73.0	79.2	84.9	85.4	82.5

* NOS: Not Otherwise Specified

Table 14.15: Adenosquamous Cancer of the Cervix Uteri: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

			Relative Survival Rate (%)					
AJCC Stage	Cases	Percent	1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	1,034	100.0	85.3	76.1	70.6	64.5	61.0	60.1
Stage I	550	53.2	97.2	92.2	88.9	84.1	80.3	80.1
IA	110	10.6	99.2	98.7	98.7	97.0	92.4	92.4
IB	310	30.0	97.5	92.1	85.6	81.1	77.4	75.5
I NOS*	130	12.6	94.7	86.8	86.8	79.7	76.9	76.9
Stage II	127	12.3	89.2	74.0	66.3	60.2	51.0	43.5
Stage III	168	16.2	77.0	65.0	55.3	43.3	40.8	40.8
Stage IV	140	13.5	47.9	31.6	20.4	15.6	15.6	15.6
Unknown/Unstaged	49	4.7	75.7	61.7	59.7	54.3	46.0	41.3

* NOS: Not Otherwise Specified

ADENOSQUAMOUS

Stage

Of the 1,034 cases of adenosquamous, enough information to establish stage at diagnosis was available for 985 (95%). 53% of the cases were diagnosed in Stage I, with the remaining cases distributed almost evenly stages II-IV (Table 14.15).

A five year survival difference between stage IA and IB was observed, with 5 year relative survival rate at 97% for stage IA and 81% for IB. Survival decreased to 60% in stage II cases (Table 14.15). Survival for adenosquamous may be slightly lower in stages IA and IB compared to squamous and adenocarcinoma, however, survival in stages II-IV is similar for all three histologies.

Figure 14.9 and Table 14.15 show the contrast in survival across stage at diagnosis over time since diagnosis. In stages IB-IV, the steepest declines in survival are observed within 2-4 years of diagnosis. Survival continues to decline throughout the 10 years observed only for stage II. The survival rates for the other stages appear to plateau.

Conditional Survival

Five year relative survival rates, conditioned on years since diagnosis, are presented in Table 14.16 and Figure 14.10. For stages IB-IV, the probability of surviving through the next 5 years increases as time since diagnosis increases. This is most marked for the stage IV cases. Five years survival from time of diagnosis was 16%. For those individuals who survived 1 year post diagnosis, 5-year survival rate increased to 32%. This increased to 100% for those individuals who survived 5 years.

DISCUSSION

Five-year relative survival rates declined with age at diagnosis, with women 70 years or older having less than 50% survival. Black women tended to fare worse than white women in all age groups, except those 70 years or older. By histology, squamous carcinomas represented approximately three-quarters of all cases. The proportion of squamous cases diagnosed at stage IV increased with age. There is an age differential in survival rates across all stages of squamous tumors, except stage II, with older women faring slightly worse than younger women. There is little difference in survival between adenocarcinoma histologies and squamous histologies by stage. For all stages combined, women with adenocarcinoma had a slightly better survival rate since there was a higher proportion of stage I among the women with adenocarcinoma compared to squamous. Women with

Figure 14.8: Adenocarcinoma of the Cervix Uteri: 5-Year Relative Survival Rate (%), Conditioned on Years Since Diagnosis by AJCC Stage, Ages 20+, 12 SEER Areas, 1988-2001

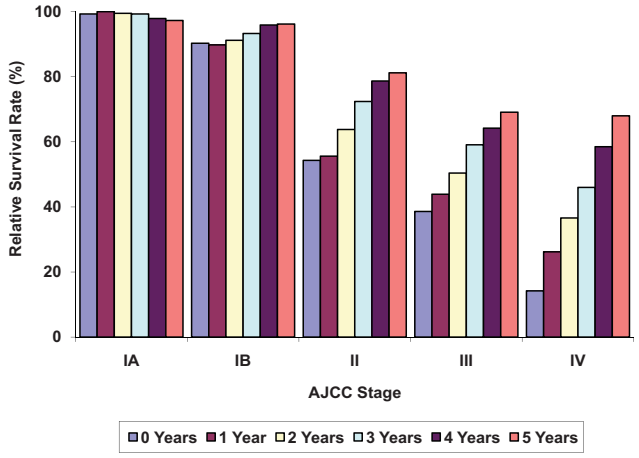


Figure 14.9: Adenosquamous Carcinoma of the Cervix Uteri: Relative Survival Rate (%) by AJCC Stage, Ages 20+, 12 SEER Areas, 1988-2001

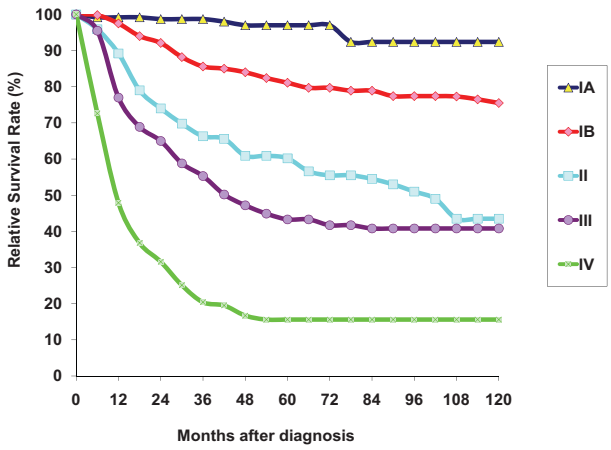


Figure 14.10: Adenosquamous Carcinoma of the Cervix Uteri: 5-Year Relative Survival Rate (%), Conditioned on Years Since Diagnosis by AJCC Stage, Ages 20+, 12 SEER Areas, 1988-2001

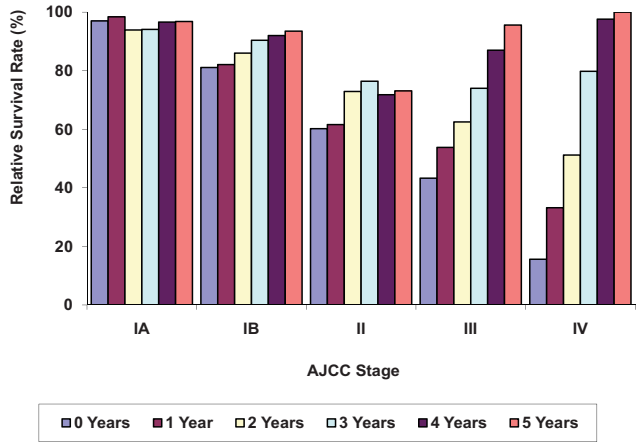


Table 14.16: Adenosquamous Cancer of the Cervix Uteri: 5-Year Relative Survival Rates (%), Conditioned on Years Since Diagnosis by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	5-Year Relative Survival Rate (%)					
	Years Since Diagnosis					
AJCC Stage	0	1	2	3	4	5
Total	64.5	73.3	81.1	85.7	89.9	92.5
Stage I	84.1	85.4	88.5	90.1	93.1	95.4
IA	97.0	97.5	93.7	93.4	95.4	95.0
IB	81.1	81.8	85.6	90.1	92.0	93.3
I NOS*	79.7	82.3	90.1	87.2	93.1	95.8
Stage II	60.2	61.5	72.9	76.2	71.8	71.7
Stage III	43.3	53.8	62.3	73.3	85.8	93.6
Stage IV	15.6	32.4	49.2	76.1	93.6	100.0
Unknown/Unstaged	54.3	64.2	79.6	76.6	72.7	76.0

* NOS: Not Otherwise Specified

adenosquamous histologies have a slightly lower survival in stage I tumors compared to adenocarcinoma and squamous histologies, but all three histologies were similar for stages II-IV. Advanced tumor grade for adenocarcinomas, was associated with poorer survival within stage.

REFERENCES

1. American Cancer Society. Cancer Facts and Figures 2006. Atlanta: American Cancer Society, 2006.
2. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Eisner MP, Horner MJ, Howlader N, Hayat M, Hankey BF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site, 2006.
3. Beahrs, OH, Henson DE, Hutter RVP, Myers MH (eds). AJCC Cancer Staging Manual, Third edition. American Joint Committee on Cancer. Philadelphia: Lippincott, 1988.

Chapter 15
Cancer of the Corpus Uteri

Carol L. Kosary

INTRODUCTION

Cancer of the endometrium, the lining of the uterus, is the most common gynecologic malignancy. It is the 4th leading cancer in women (behind breast, lung and colorectal) and accounts for approximately 6% of all cancers in women (1). Uterine sarcomas are rare, comprising less than 8% of all uterine malignancies. These tumors arise primarily from two distinct tissues: 1) leiomyosarcoma from myometrial muscle and 2) mesodermal (Mullerian) and stromal sarcomas from endometrial epithelium.

MATERIALS AND METHODS

The NCI contracts with medically-oriented, nonprofit institutions located in specific geographic areas to obtain data on all cancers diagnosed in residents of the SEER geographic areas. SEER collects data on all invasive and in situ cancers except basal cell and squamous cell carcinomas of the skin (of non-genital anatomic sites) and in situ carcinomas of the uterine cervix. SEER actively follows all previously diagnosed patients on an annual basis to obtain vital status allowing the calculation of observed and relative survival rates.

This analysis is based on data from 12 SEER geographic areas which collectively cover about 14% of the total US population. The areas are the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Michigan; Atlanta, Georgia; San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; and 10 counties in rural Georgia. Los Angeles contributed data for diagnosis years 1992 to 2001, all other areas for 1988-2001.

Between 1988-2001, there were 57,769 cases of cancer of the corpus uteri diagnosed in SEER. Note: cancer of the corpus uteri does not include uterus, not otherwise specified (NOS). The following were excluded from the analysis: patients for whom cancer of the corpus uteri was not the first primary, cases identified through autopsy or death certificate only, persons of unknown race, alive cases with no survival time, patients less than 20 years old, cases of in situ cancers, cases without microscopic confirmation, and carcinoids. Unlike other chapters, sarcomas were included. After these exclusions, 48,642 adult cases remained for analysis (see Table 15.1).

Table 15.1: Cancer of the Corpus Uteri: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/selection
57,769	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
50,570	7,199	Select first primary only
50,453	117	Exclude death certificate only or at autopsy
50,144	309	Exclude unknown race
50,083	61	Exclude alive with no survival time
50,073	10	Exclude children (Ages 0-19)
48,877	1,196	Exclude in situ cancers
48,661	216	Exclude no or unknown microscopic confirmation
48,642	19	Exclude carcinoids

RESULTS

Age and Race

Of the 48,642 cases, 63.5% of adults with cancer of the corpus uteri were diagnosed after age 60 years and older (Table 15.2). Over 50% were between the ages of 60-79 years. Eighty-seven percent were white. Little difference exists in age distribution for white and black women, but the age distribution for women of other races was younger.

For all women, relative survival declines with age. In women 20-49 year of age, the 5-year relative survival rate is 90% compared to 87% in women 50-69 and 79% in women aged 70 and older. Survival is also lower for black women compared to white women in all age groups presented (Table 15.3). The largest survival difference was for age group 70+ where the 5-year relative survival rate was 49% for black females compared to 81% for white females.

Geographic Location

There is little variation in survival by geographic area. Five-year relative survival rates in the 12 SEER areas presented in this study ranged from 89% in Seattle to 81% in Detroit (Table 15.4).

Histology

Distribution by histology is presented in Table 15.5. Tumors classified as adenocarcinoma comprise over 90% of all cancers of the corpus uteri. Of these, the most common subclassification was adenocarcinoma, NOS, which accounted for slightly more than 53% of all adenocarcinomas registered. Endometrioid adenocarcinoma was the next most common adenocarcinoma, at 30% followed by papillary serous (3.5%), adenosquamous (2.9%), papillary (2.3%), squamous metaplasia (2.6%), mucinous (1.9%), and clear cell (1.6%).

Sarcomas and Other Specified Types comprise 7.7% of the total. Of these 34% are Mullerian, 25% leiomyosarcoma, 19% carcinosarcoma and 16% endometrial stromal sarcoma.

The 5-year relative survival rates vary greatly by histology from over 90% for adenocarcinoma, NOS, mucinous/mucin producing adenocarcinoma, and endometrioid adenocarcinoma to less than 50% for papillary serous adenocarcinoma, leiomyosarcoma, and Mullerian mixed tumor.

Staging

Uterine corpus cancer staging by the Federation Internationale de Gynecologie et d'Obstetrique (FIGO) and the American Joint Committee on Cancer (AJCC) are in the AJCC *Manual for Staging of Cancer*, 3rd edition (2):

Stage I tumor confined to the corpus uteri.

Stage IA: tumor limited to endometrium

Stage IB: tumor invades less than one half of the myometrium

Stage IC: tumor invades one half or more of the myometrium

Stage II tumor invades the cervix, but has not extended outside the uterus.

Stage III tumor extends outside of the uterus but is confined to the true pelvis.

Stage IV tumor involves the bladder or bowel mucosa or has metastasized to distant sites (including abdominal lymph nodes other than para-aortic, and/or inguinal lymph nodes; excludes metastasis to vagina, pelvic serosa, or adnexa).

Since the emphasis is on extension, a SEER modified version of stage was used in which positive lymph nodes went to N1 and Stage III but unknown lymph node involvement was ignored, i.e. treated like N0.

ADENOCARCINOMA

Stage

Table 15.6 and Figure 15.1 show the contrast across stage over time since diagnosis. In stages II-IV, the steepest declines in survival are observed within 1-3 years of diagnosis. Survival continues to decline throughout the 10 years observed for stage III.

Age and Stage

Of the 44,059 cases of adenocarcinoma, enough information to establish stage at diagnosis was available for 42,589 (96.7%). Across all age groups, 70% or more of all cancers were diagnosed in Stage I. The percent of tumors limited to the endometrium or invading less than half of the myometrium (Stages IA and IB) declines from 64% in women age 20-49 to 46% in women 70 and over. Stage IV disease rises from 5% in women age 20-49 to 9% in women 70 and over. (Table 15.7).

Across all age groups, a slight survival advantage is seen in Stage IA and IB disease compared to Stage IC. For all women, this translates to 99% 5-year survival for Stages IA & IB versus 92% for stage IC. Median survival time is over 10 years for all ages within Stage I, with the exception of women aged 70 and older diagnosed with Stage IC, where median survival time was found to be

Table 15.2: Cancer of the Corpus Uteri: Age (20+) and Race Distributions, 12 SEER Areas, 1988-2001

	Total		White		Black		Other	
Age Group (Years)	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	48,642	100.0	42,220	100.0	3,065	100.0	3,357	100.0
20-29	218	0.4	154	0.4	25	0.8	39	1.2
30-39	1,542	3.2	1,145	2.7	146	4.8	251	7.5
40-49	5,254	10.8	4,198	9.9	309	10.1	747	22.3
50-59	10,740	22.1	9,226	21.9	576	18.8	938	27.9
60-69	13,816	28.4	12,032	28.5	1,016	33.1	768	22.9
70-79	11,972	24.6	10,792	25.6	700	22.8	480	14.3
80+	5,100	10.5	4,673	11.1	293	9.6	134	4.0

Table 15.3: Cancer of the Corpus Uteri: Number of Cases, Median Survival Time (Months) and 5-Year Survival Rates (%) by Race and Age (20+), 12 SEER Areas, 1988-2001

		Median Survival Time	5-Year Survival Rates (%)		
Race/Age	Cases	(Months)	Observed	Expected	Relative
All Races, 20+	48,642	> 120	75.1	88.6	84.7
White, 20+	42,220	> 120	76.3	88.2	86.4
Black, 20+	3,065	72.1	53.2	86.1	61.8
All Races, 20-49	7,014	> 120	88.7	98.9	89.7
White, 20-49	5,497	> 120	90.0	98.9	91.0
Black, 20-49	480	> 120	76.5	97.8	78.1
All Races, 50-69	24,556	> 120	82.1	94.3	87.0
White, 50-69	21,258	> 120	83.9	94.4	88.9
Black, 50-69	1,592	99.8	57.4	90.6	63.4
All Races, 70+	17,072	89.0	59.8	76.1	78.6
White, 70+	15,465	92.2	61.3	76.0	80.6
Black, 70+	993	28.4	35.6	73.3	48.6

Table 15.4: Cancer of the Corpus Uteri: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by SEER Geographic Area, Ages 20+, 12 SEER Areas, 1988-2001

			Relative Survival Rate (%)					
SEER Geographic Area	Cases	Percent	1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	48,642	100.0	93.5	89.5	87.0	84.7	83.1	82.6
Atlanta and Rural Georgia	2,646	5.4	93.1	88.3	85.4	82.9	80.1	79.6
Atlanta (Metropolitan) - 1988+	2,508	5.2	93.0	88.1	85.5	82.9	80.3	79.8
Rural Georgia - 1988+	138	0.3	95.0	91.1	84.1	81.5	76.8	72.1
California								
Los Angeles - 1992+	7,978	16.4	92.1	87.2	84.6	81.7	80.4	79.0
Greater Bay Area	8,591	17.7	93.8	89.7	87.6	85.6	83.8	83.6
San Francisco-Oakland SMSA - 1988+	5,882	12.1	93.8	89.6	87.5	85.9	83.6	83.2
San Jose-Monterey - 1988+	2,709	5.6	93.8	90.1	87.7	85.0	84.3	84.0
Connecticut - 1988+	6,198	12.7	94.6	90.8	88.7	86.5	85.2	84.2
Detroit (Metropolitan) - 1988+	6,451	13.3	91.8	86.7	83.6	81.0	79.2	78.4
Hawaii - 1988+	1,585	3.3	93.9	89.7	87.4	84.1	81.5	81.0
Iowa - 1988+	5,266	10.8	93.8	90.2	87.7	85.7	84.6	84.1
New Mexico - 1988+	1,837	3.8	94.4	91.0	87.8	85.4	82.8	82.6
Seattle (Puget Sound) - 1988+	5,860	12.0	95.4	92.6	90.6	89.2	88.1	88.1
Utah - 1988+	2,230	4.6	94.0	90.4	88.0	85.1	83.2	82.1

Table 15.5: Cancer of the Corpus Uteri: Number and Distribution of Cases and 5-Year Relative Survival Rate (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology	ICD-O Code	Cases	Percent	5-Year RSR (%)
All Values	8000-9989	48,642	100.0	84.7
Epidermoid	8051-8130	132	0.3	61.1
Adenocarcinoma	8050,8140-8147,8160-8162,8180-8221,8250-8506,8520-8550,8560,8570-8573,8940-8941	44,059	90.6	87.9
Adenocarcinoma, NOS*	8140	23,489	48.3	90.8
Papillary	80508260	1,035	2.1	70.3
Clear Cell	8310	704	1.4	64.8
With Squamous Metaplasia	8570	1,151	2.4	93.8
Mucinous & Mucin Producing	8480-8481	824	1.7	95.0
Adenosquamous	8560	1,256	2.6	74.0
Endometrioid	8380	13,258	27.3	91.2
Papillary Serous	8460	1,555	3.2	44.7
All Other Adenocarcinoma	8141-8147,8160-8162,8180-8221,8250-8259,8261-8309,8311-8379,8381-8459,8461-8479,8482-8506,8520-8550,8571-8573,8940-8941	787	1.6	68.5
Other Specified Carcinomas	8030-8045,8150-8155,8170-8171,8230-8248,8510-8512,8561-8562,8580-8671	24	0.0	~
Carcinoma, NOS*	8010-8022	608	1.2	58.4
Sarcomas and Other Specified Types	8680-8713,8720-8790,8800-8920,8930-8933,8950-8982,8990-8991,9000-9030,9040-9055,9060-9110,9120-9134,9141-9340,9350-9364,9380-9512,9530-9581	3,742	7.7	53.3
Leiomyosarcoma	8890-8897	939	1.9	48.2
Carcinosarcoma	8933,8980-8981	706	1.5	53.7
Endometrial Stromal	8930	610	1.3	74.6
Mullerian	8950-8951	1,264	2.6	45.3
All Other	8680-8713,8720-8790,8800-8889,8898-8920,8931-8932,8935,8952-8979,8982,8990-8991,9000-9030,9040-9055,9060-9110,9120-9134,9141-9340,9350-9364,9380-9512,-9530-9581	230	0.5	53.9
Unspecified	8000-8004	70	0.1	55.1

~ Statistic not displayed due to less than 25 cases.
* NOS: Not Otherwise Specified

Table 15.6: Adenocarcinoma of the Corpus Uteri: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate(%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	44,059	100.0	95.2	92.1	89.9	87.9	86.4	86.0
Stage I	33,179	75.3	99.7	99.1	98.3	97.4	96.3	95.7
IA	9,528	21.6	99.9	99.8	99.5	99.3	99.0	99.0
IB	15,084	34.2	100.0	100.0	99.7	99.2	98.3	97.5
IC	4,142	9.4	99.1	97.2	95.0	91.9	88.4	86.2
I NOS*	4,425	10.0	97.8	95.8	93.8	92.1	90.5	90.2
Stage II	3,475	7.9	94.8	89.7	85.1	80.2	77.2	76.5
Stage III	2,651	6.0	87.5	75.8	68.2	59.6	53.4	50.5
Stage IV	3,284	7.5	61.5	44.4	35.8	28.6	25.3	25.3
Unknown/Unstaged	1,470	3.3	83.5	72.5	66.8	63.5	60.3	59.6

* NOS: Not Otherwise Specified

Table 15.7: Adenocarcinoma of the Corpus Uteri: Distribution by AJCC Stage (SEER modified 3rd edition) and Age (20+), 12 SEER Areas, 1988-2001

	Age (Years)							
	Total		20-49		50-69		70+	
AJCC Stage	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	44,059	100.0	5,931	100.0	22,606	100.0	15,522	100.0
Stage I	33,179	75.3	4,604	77.6	17,679	78.2	10,896	70.2
IA	9,528	21.6	2,040	34.4	5,224	23.1	2,264	14.6
IB	15,084	34.2	1,723	29.1	8,500	37.6	4,861	31.3
IC	4,142	9.4	193	3.3	1,789	7.9	2,160	13.9
I NOS*	4,425	10.0	648	10.9	2,166	9.6	1,611	10.4
Stage II	3,475	7.9	481	8.1	1,592	7.0	1,402	9.0
Stage III	2,651	6.0	352	5.9	1,250	5.5	1,049	6.8
Stage IV	3,284	7.5	317	5.3	1,539	6.8	1,428	9.2
Unknown/Unstaged	1,470	3.3	177	3.0	546	2.4	747	4.8

*NOS: Not Otherwise Specified

Table 15.8: Adenocarcinoma of the Corpus Uteri: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by AJCC Stage (SEER modified 3rd edition) and Age (20+), 12 SEER Areas, 1988-2001

	Total			20-49			50-69			70+		
AJCC Stage	Cases	5-Year RSR (%)	Median Survival Time (Months)	Cases	5-Year RSR (%)	Median Survival Time (Months)	Cases	5-Year RSR (%)	Median Survival Time (Months)	Cases	5-Year RSR (%)	Median Survival Time (Months)
Total	44,059	87.9	> 120	5,931	93.2	> 120	22,606	89.7	> 120	15,522	82.5	96.5
Stage I	33,179	97.4	> 120	4,604	98.2	> 120	17,679	97.2	> 120	10,896	97.8	> 120
IA	9,528	99.3	> 120	2,040	98.9	> 120	5,224	99.4	> 120	2,264	99.3	> 120
IB	15,084	99.2	> 120	1,723	98.1	> 120	8,500	98.2	> 120	4,861	100.0	> 120
IC	4,142	91.9	> 120	193	94.8	> 120	1,789	90.4	> 120	2,160	93.3	107.4
I NOS	4,425	92.1	> 120	648	97.4	> 120	2,166	93.8	> 120	1,611	86.6	102.4
Stage II	3,475	80.2	> 120	481	91.1	> 120	1,592	84.1	> 120	1,402	70.3	64.7
Stage III	2,651	59.6	66.6	352	76.0	> 120	1,250	65.3	102.3	1,049	45.5	32.9
Stage IV	3,284	28.6	17.8	317	46.0	42.4	1,539	31.9	21.2	1,428	19.3	12.6
Unknown/ Unstaged	1,470	63.5	62.8	177	83.3	> 120	546	77.3	> 120	747	42.2	23.3

Figure 15.1: Adenocarcinoma of the Corpus Uteri: Relative Survival Rate (%) by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

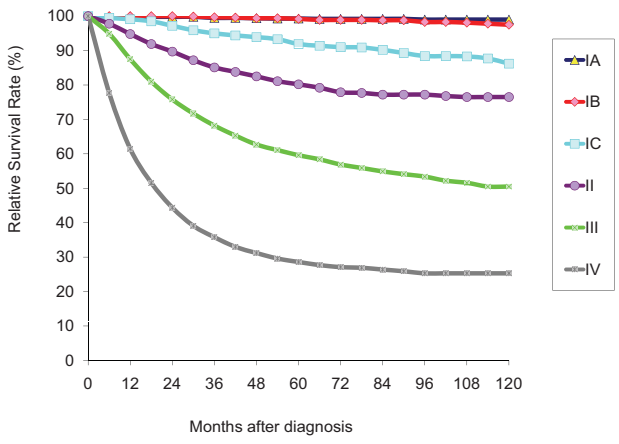
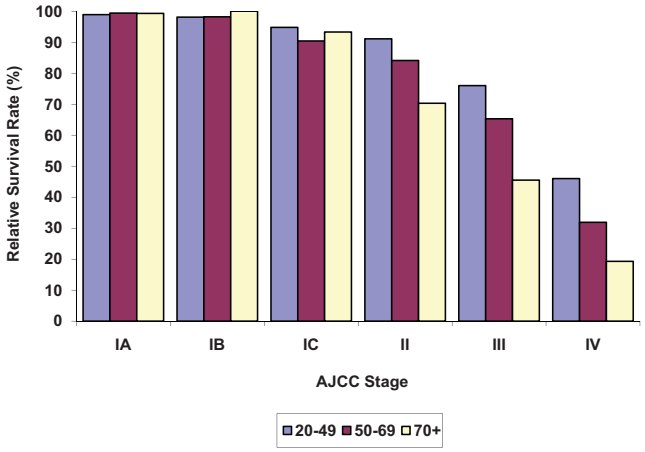


Figure 15.2: Adenocarcinoma of the Corpus Uteri: 5-Year Relative Survival Rate (%) by AJCC Stage (SEER modified 3rd edition) and Age Group (20+), 12 SEER Areas, 1988-2001



107 months. A survival differential across age exists for Stages II-IV. Women ages 20-49 diagnosed with Stage II disease experience a 5-year relative survival rate of 91%. This falls to 84% for women age 50-69 and 70% for women ages 70 and older. For Stage III, survival is 76% in women 20-49, 65% in those 50-69 and 45% for those aged 70 and over. For Stage IV, survival is 46% in women under 50, 32% in those 50-69 and 19% for those aged 70 and over (Table 15.8, Figure 15.2).

Subtype and Stage

Survival by subtype and stage is presented in Table 15.9 and Figure 15.3. A survival disadvantage is seen in tumors of the papillary serous subtype across all stages. These tumors are histologically similar to those found in the ovary. Similar but smaller differentials are observed for clear cell and papillary subtypes. Adenosquamous may have a slight survival disadvantage in Stage I. This may be due to more of these tumors being diagnosed in Stage IC and fewer in Stage IA (Table 15.10). Tumors exhibiting squamous metaplasia exhibit higher survival, particularly in stages III

Figure 15.3: Adenocarcinoma of the Corpus Uteri: 5-Year Relative Survival Rate (%) by Histology and AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

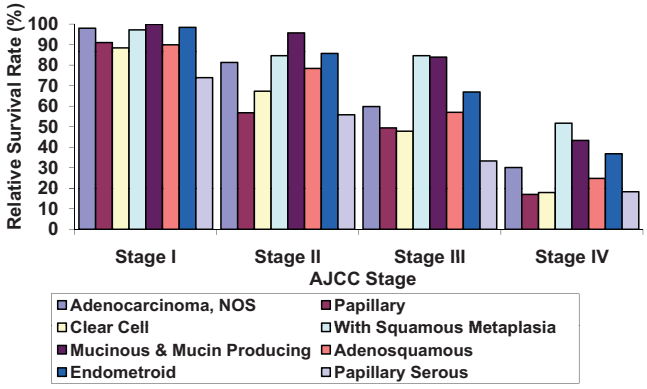


Figure 15.4: Adenocarcinoma of the Corpus Uteri: 5-Year Relative Survival Rate (%) by Grade and AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

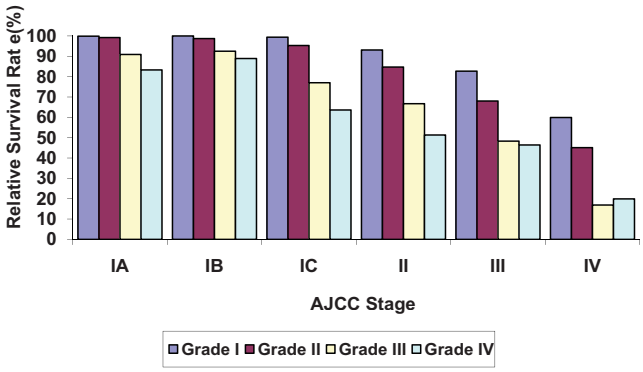


Table 15.9: Adenocarcinoma of the Corpus Uteri: Number of Cases and 5-Year Relative Survival Rates (%) by Histology and AJCC Stage (SEER modified 3rd edition) , Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage											
	Total		I		II		III		IV		Unknown/ Unstaged	
Histology	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
Total	44,059	87.9	33,179	97.4	3,475	80.2	2,651	59.6	3,284	28.6	1,470	63.5
Adenocarcinoma, NOS*	23,489	90.8	18,775	98.0	1,602	81.3	965	59.8	1,272	30.1	875	66.6
Papillary	1,035	70.3	634	91.0	107	56.8	80	49.4	162	17.0	52	23.4
Clear Cell	704	64.8	338	88.4	90	67.3	94	47.8	139	17.9	43	54.1
With Squamous Metaplasia	1,151	93.8	952	97.2	82	84.6	47	84.6	46	51.7	24	~
Mucinous & Mucin Producing	824	95.0	621	99.9	53	95.7	63	83.9	60	43.3	27	73.1
Adenosquamous	1,256	74.0	730	89.9	161	78.4	136	57.0	191	24.8	38	55.1
Endometrioid	13,258	91.2	10,149	98.4	1,149	85.7	904	66.9	727	36.8	329	65.4
Papillary Serous	1,555	44.7	531	73.9	163	55.8	258	33.3	542	18.3	61	34.4
All Other Adenocarcinoma	787	68.5	449	92.5	68	46.7	104	42.5	145	14.5	21	~

~ Statistic not displayed due to less than 25 cases.
* NOS: Not Otherwise Specified

Table 15.10: Stage I Adenocarcinoma of the Corpus Uteri: Distribution by Histology and Detailed AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage									
	Total Stage I		IA		IB		IC		I NOS	
Histology	Cases	Row Percent	Cases	Row Percent	Cases	Row Percent	Cases	Row Percent	Cases	Row Percent
Total	33,179	100.0	9,528	28.7	15,084	45.5	4,142	12.5	4,425	13.3
Adenocarcinoma, NOS*	18,775	100.0	5,327	28.4	8,352	44.5	2,239	11.9	2,857	15.2
Papillary	634	100.0	180	28.4	249	39.3	77	12.1	128	20.2
Clear Cell	338	100.0	107	31.7	140	41.4	42	12.4	49	14.5
With Squamous Metaplasia	952	100.0	277	29.1	461	48.4	101	10.6	113	11.9
Mucinous & Mucin Producing	621	100.0	199	32.0	268	43.2	73	11.8	81	13.0
Adenosquamous	730	100.0	125	17.1	345	47.3	153	21.0	107	14.7
Endometrioid	10,149	100.0	2,944	29.0	4,888	48.2	1,353	13.3	964	9.5
Papillary Serous	531	100.0	193	36.3	211	39.7	69	13.0	58	10.9
All Other Adenocarcinoma	449	100.0	176	39.2	170	37.9	35	7.8	68	15.1

* NOS: Not Otherwise Specified

and IV. Clear cell and papillary types show lower survival in stages II-IV.

Stage and Grade

Five-year relative survival rates for adenocarcinoma are shown by tumor grade in Table 15.11 and Figure 15.4. Within stage, 5-year relative survival rates declined as grade increases with the exception of poorly differentiated and anaplastic Stage IV tumors.

Conditional Survival

Five year relative survival rates, conditioned on years since diagnosis, are presented in Table 15.12 and Figure 15.5. For stages IC-IV, the probability of surviving the next 5 years increases as time since diagnosis increases. This is most marked for the stage IV cases. Five year survival from time of diagnosis is 29%. For those individuals who survive 1 year post diagnosis, 5-year survival increases to 43%. This increases to 86% for those individuals who survived 5 years.

Table 15.11: Adenocarcinoma of the Corpus Uteri: Number of Cases and 5-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition) and Grade, Ages 20+, 12 SEER Areas, 1988-2001

	Grade											
	Total		Well Differentiated		Moderately Differentiated		Poorly Differentiated		Anaplastic		Unknown	
AJCC Stage	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
Total	44,059	87.9	17,429	99.2	15,002	90.8	7,544	64.9	1,294	54.8	2,790	72.9
Stage I	33,179	97.4	15,472	100.0	11,492	97.2	4,061	86.6	557	79.7	1,597	93.0
IA	9,528	99.3	5,517	99.9	2,599	99.2	741	90.9	114	83.3	557	95.3
IB	15,084	99.2	6,631	100.0	5,741	98.7	1,895	92.5	261	88.9	556	95.7
IC	4,142	91.9	1,161	99.4	1,813	95.3	899	77.0	124	63.6	145	88.0
I NOS*	4,425	92.1	2,163	98.4	1,339	89.9	526	75.3	58	60.9	339	85.2
Stage II	3,475	80.2	847	93.1	1,399	84.7	835	66.7	150	51.3	244	68.3
Stage III	2,651	59.6	370	82.7	898	68.0	970	48.3	210	46.4	203	45.0
Stage IV	3,284	28.6	269	59.9	801	45.1	1,426	16.9	323	19.9	465	21.1
Unknown/Unstaged	1,470	63.5	471	79.4	412	63.1	252	36.3	54	38.3	281	62.8

* NOS: Not Otherwise Specified

SARCOMA AND OTHER SPECIFIED TYPES

Subtype and Stage

Of the 3,742 cases of sarcoma and other specified types, enough information to establish stage at diagnosis was available for 3,580 (96%). Fifty six percent were diagnosed in Stage I, while 22% were Stage IV (Table 15.13).

Survival by stage for sarcomas overall is presented in Figure 15.6. Survival by subtype and stage is presented in Table 15.14. Despite some data sparseness in Stage II, it is observed that endometrial stromal tumors experience a better survival across stage than do either tumors categorized as leiomyosarcoma, carcinosarcoma, or Mullerian, which had similar survival rates.

Stage and Grade

Despite data sparseness in well differentiated, within stage, 5-year relative survival declines as grade increases (Table 15.15).

Conditional Survival

Five year relative survival, conditioned on years since diagnosis, is presented in Table 15.16 and Figure 15.7 for sarcomas and other specific types. For all stages, the probability of surviving the next 5 years increased as time since

Figure 15.5: Adenocarcinoma of the Corpus Uteri: 5-Year Relative Survival Rate (%), Conditioned on Years Since Diagnosis, by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

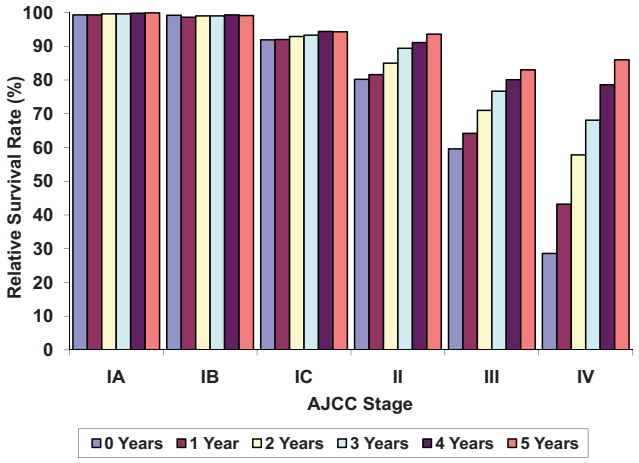


Figure 15.6: Sarcoma and Other Specified Types of Cancer of the Corpus Uteri: Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

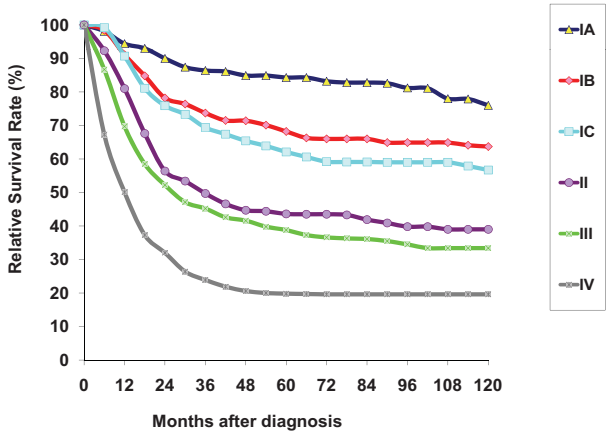


Table 15.12: Adenocarcinoma of the Corpus Uteri: 5-Year Relative Survival Rates (%), Conditioned on Years Since Diagnosis, by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	5-Year Relative Survival Rate (%)					
	Years Since Diagnosis					
AJCC Stage	0	1	2	3	4	5
Total	87.9	91.2	93.9	95.5	96.9	97.4
Stage I	97.4	97.3	97.9	98.1	98.7	98.7
IA	99.3	99.3	99.6	99.6	99.8	99.9
IB	99.2	98.6	99.0	99.0	99.3	99.1
IC	91.9	92.0	92.9	93.3	94.4	94.3
I NOS*	92.1	93.2	94.6	95.7	97.1	97.2
Stage II	80.2	81.6	85.0	89.4	91.1	93.6
Stage III	59.6	64.2	71.0	76.7	80.1	83.0
Stage IV	28.6	43.2	57.8	68.1	78.6	86.0
Unknown/Unstaged	63.5	71.5	79.4	84.2	86.0	87.5

* NOS: Not Otherwise Specified

Table 15.13: Sarcoma & Other Specified Types of Corpus Uterine Cancer: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
			Percent	Percent	Percent	Percent	Percent	Percent
Total	3,742	100.0	78.4	64.4	58.4	53.3	50.0	49.1
Stage I	2,081	55.6	92.2	81.4	76.3	70.8	66.2	64.5
IA	397	10.6	94.4	90.0	86.4	84.3	81.2	76.0
IB	558	14.9	91.1	78.2	73.7	68.2	64.9	63.7
IC	280	7.5	90.7	75.9	69.4	62.1	59.0	56.7
I NOS	846	22.6	92.4	81.3	75.4	68.7	61.7	61.0
Stage II	277	7.4	81.0	56.4	49.7	43.6	39.8	39.0
Stage III	394	10.5	69.7	52.2	45.2	38.8	34.5	33.4
Stage IV	828	22.1	50.1	32.0	23.9	19.8	19.6	19.6
Unknown/Unstaged	162	4.3	62.0	49.2	44.8	39.7	35.9	34.6

* NOS: Not Otherwise Specified

Table 15.14: Sarcoma & Other Specified Types of Corpus Uterine Cancer: Number of Cases and 5-Year Relative Survival Rates (%) by Histology and AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

Histology	AJCC Stage											
	Total		I		II		III		IV		Unknown/ Unstaged	
	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)
Total	3,742	53.3	2,081	70.8	277	43.6	394	38.8	828	19.8	162	39.7
Leiomyosarcoma	939	48.2	623	60.0	28	35.1	64	27.7	185	14.9	39	51.6
Carcinosarcoma	706	53.7	401	73.7	62	43.3	97	26.2	122	13.6	24	~
Endometrial Stromal	610	74.6	372	89.8	27	40.0	85	64.3	106	37.0	20	~
Mullerian	1,264	45.3	570	66.7	147	45.7	132	34.8	353	18.2	62	19.4
All Other	223	53.6	115	74.3	13	~	16	~	62	21.4	17	~

~ Statistic not displayed due to less than 25 cases.

Table 15.15: Sarcoma & Other Specified Types of Corpus Uterine Cancer: Number of Cases and 5-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition) and Grade, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Grade									
	Total		Well Differentiated		Moderately Differentiated		Poorly/ Undifferentiated		Unknown	
	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)
Total	3,742	53.3	218	86.1	593	79.2	1,351	35.8	1,580	52.8
Stage I	2,081	70.8	167	92.6	435	84.8	603	54.8	876	69.8
IA	397	84.3	37	96.2	80	88.8	60	71.6	220	82.8
IB	558	68.2	32	88.0	93	84.0	215	58.6	218	66.7
IC	280	62.1	10	~	48	84.6	118	47.6	104	63.3
I NOS*	846	68.7	88	90.4	214	83.1	210	49.9	334	64.4
Stage II	277	43.6	8	~	26	78.6	124	36.0	119	39.2
Stage III	394	38.8	14	~	59	68.6	177	28.2	144	35.8
Stage IV	828	19.8	20	~	58	47.9	407	13.2	343	20.7
Unknown/Unstaged	162	39.7	9	~	15	~	40	9.1	98	44.3

~ Statistic not displayed due to less than 25 cases.

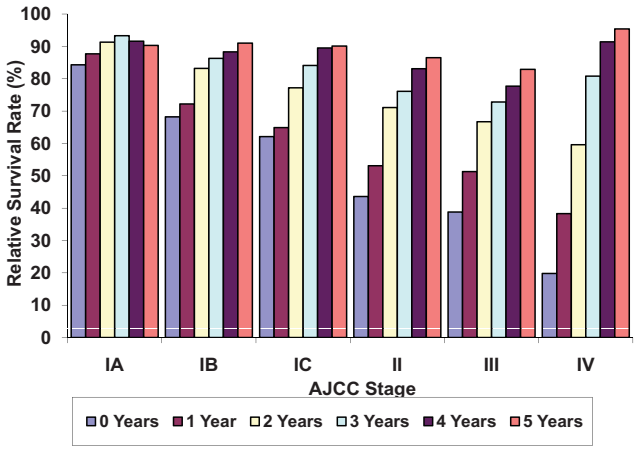
* NOS: Not Otherwise Specified

Table 15.16: Sarcoma & Other Specified Types of Corpus Uterine Cancer: 5-Year Relative Survival Rates (%), Conditioned on Years Since Diagnosis, by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	5-Year Relative Survival Rate(%)					
	Years Since Diagnosis					
AJCC Stage	0	1	2	3	4	5
Total	53.3	64.8	77.8	83.2	87.2	89.5
Stage I	70.8	73.8	82.6	85.6	88.2	90.0
IA	84.3	87.7	91.3	93.3	91.6	90.3
IB	68.2	72.2	83.2	86.3	88.3	91.0
IC	62.1	64.9	77.2	84.1	89.5	90.1
I NOS*	68.7	70.6	78.4	81.1	84.9	88.2
Stage II	43.6	53.1	71.1	76.1	83.1	86.5
Stage III	38.8	51.3	66.7	72.8	77.7	82.9
Stage IV	19.8	38.3	59.6	80.8	91.4	95.4
Unknown/Unstaged	39.7	56.5	67.1	69.9	73.7	74.5

* NOS: Not Otherwise Specified

Figure 15.7: Sarcoma and Other Specified Types of Cancer of the Corpus Uteri: 5-Year Relative Survival Rate (%), Conditioned on Years Since Diagnosis, by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001



diagnosis increased. This is most marked for the stage IV cases. Five year survival from time of diagnosis was 20%. For those individuals who survived 1 year post diagnosis, 5-year survival increased to 38%. This increased to 91% for those individuals who survived 4 years.

DISCUSSION

Survival is lower for blacks compared to whites regardless of age, and is most pronounced in women over 70 years of age. The majority of corpus uteri tumors are adenocarcinomas. Of these, more than 70% are diagnosed in stage I and have a median survival greater than 10 years for women of all age groups, except in women over 70 years of age with stage IC where the median survival is slightly less than 10 years. There exists a differential in survival by age and across stage of disease II-IV. The poorer survival in older women is compounded by advanced stage. In later stages, particularly stages III and IV, survival declines rapidly over time since diagnosis.

Overall, all histologies in stage I had a favorable 5-year survival. The papillary serous histology had the worst survival across all stages, while papillary metaplasia had the highest survival in stages II-IV. In the group of sarcoma histologies, endometrial stromal sarcomas had a better survival across stage than other sarcomas.

Across all stages, survival declined with advanced stage of disease, with the exception of poorly differentiated and anaplastic tumors where there is little difference in survival for adenocarcinomas.

REFERENCES

1. American Cancer Society. Cancer Facts and Figures 2006. Atlanta: American Cancer Society, 2006.
2. Beahrs, OH, Henson DE, Hutter RVP, Myers MH (eds). AJCC Cancer Staging Manual, Third edition. American Joint Committee on Cancer. Philadelphia: Lippincott, 1988.

Chapter 16
Cancer of the Ovary

Carol L. Kosary

INTRODUCTION

Epithelial carcinoma of the ovary is one of the most common gynecologic malignancies. It is also the fifth most frequent cause of cancer death in women (behind lung, breast, colorectal, and pancreas). A little over 15% of epithelial ovarian tumors are of low malignant potential. These "borderline" tumors were classified as malignant in the International Classification of Diseases for Oncology second edition (ICD-O-2) (1) and were classified as non-malignant with the 2001 implementation of the third edition, ICD-O-3 (2), and they are different from the frank malignant invasive carcinomas. Uncommon tumors include germ cell tumors of the ovary, seen most often in younger women.

MATERIALS AND METHODS

The NCI contracts with medically-oriented, nonprofit institutions located in specific geographic areas to obtain data on all cancers diagnosed in residents of the SEER geographic areas. SEER collects data on all invasive and in situ cancers except basal cell and squamous cell carcinomas of the skin (of non-genital anatomic sites) and in situ carcinomas of the uterine cervix. SEER actively follows all previously diagnosed patients on an annual basis to obtain vital status allowing the calculation of observed and relative survival rates.

This analysis is based on data from 12 SEER geographic areas which collectively cover about 14% of the total US population. The areas are the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Michigan; Atlanta, Georgia; San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; and 10 counties in rural Georgia. Los Angeles contributed data for diagnosis years 1992 to 2001, all other areas for 1988-2001.

Between 1988-2001, there were 40,250 cases of cancer of the ovary reported to SEER. The following were excluded from the analysis: patients for whom ovarian cancer was not the first primary, cases identified through autopsy or death certificate only, persons of unknown race, patients who were alive with no survival time, patients less than 20 years old, cases without microscopic confirmation, in situ tumors, sarcomas including stromal, mesenchymoma, and embryonal sarcomas, and carcinoids. After these exclusions, 32,019 cases remained for analysis (Table 16.1).

Table 16.1: Cancer of the Ovary: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
40,250	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
35,047	5,203	Select first primary only
34,607	440	Exclude death certificate only or at autopsy
34,468	139	Exclude unknown race
34,401	67	Exclude alive with no survival time
33,880	521	Exclude children (ages 0-19)
33,804	76	Exclude in situ cancers
32,374	1,430	Exclude no or unknown microscopic confirmation
32,160	214	Exclude sarcomas
32,040	120	Exclude carcinoids
32,019	21	Exclude stromal, mesenchymoma, and embryonal sarcomas

Staging

Ovarian cancer staging by the Federation Internationale de Gynecologie et d'Obstetrique (FIGO) and the American Joint Committee on Cancer (AJCC) are in the AJCC *Manual for Staging of Cancer*, 3rd edition (3):

Stage I ovarian cancer is growth limited to the ovaries.

Stage IA: growth limited to one ovary; no ascites. No tumor on the external surface; capsule intact.

Stage IB: growth limited to both ovaries; no ascites. No tumor on the external surfaces; capsules intact.

Stage IC: tumor either stage IA or IB, but with tumor on the surface of one or both ovaries; or with capsule ruptured; or with ascites present containing malignant cells or with positive peritoneal washings.

Stage II ovarian cancer is growth involving one or both ovaries with pelvic extension.

Stage IIA: extension and/or metastases to the uterus and/or tubes.

Stage IIB: extension to other pelvic tissues.

Stage IIC: tumor either stage IIA or stage IIB, but with tumor on the surface of one or both ovaries; or with capsule(s) ruptured; or with ascites present containing malignant cells or with positive peritoneal washings.

Stage III ovarian cancer is tumor involving one or both ovaries with peritoneal implants outside the pelvis and/or positive retroperitoneal or inguinal nodes. Superficial liver metastasis equals stage III. Tumor is limited to the true pelvis but with histologically verified malignant extension to small bowel or omentum.

Stage IIIA: tumor grossly limited to the true pelvis with negative nodes but with histologically confirmed microscopic seeding of abdominal peritoneal surfaces.

Stage IIIB: tumor of one or both ovaries with histologically confirmed implants of abdominal peritoneal surfaces, none exceeding 2 centimeters in diameter. Nodes negative.

Stage IIIC: abdominal implants greater than 2 centimeters in diameter and/or positive retroperitoneal or inguinal nodes.

Stage IV ovarian cancer is growth involving one or both ovaries with distant metastasis. If pleural effusion is present, there must be positive cytologic test results to allot a case to stage IV. Parenchymal liver metastasis equals stage IV.

Since the emphasis is on extension, SEER modified version of stage was used in which positive lymph nodes were N1 and Stage IIIC but unknown lymph node involvement was ignored, i.e. treated like N0.

RESULTS

Age and Race

Of the 32,019 eligible adult cases, approximately half occurred before age 60 (Table 16.2). Eighty-six percent of eligible patients were white. White women were slightly older than black women with ovarian cancer.

For all women, relative survival declines with age. In adult women under age 50, 5-year relative survival is 76.6% compared to 50.2% in women 50-69 and 31.6% in women aged 70 and older. Survival is lower for black women compared to white women in all age groups presented, especially ages 50-69 (Table 16.3).

Geographic Location

There was little variation in survival by geographic area. Five-year relative survival rates in the 12 SEER areas represented in this study ranged from 57.0% in Los Angeles to 48.4% in Rural Georgia (Table 16.4).

Histology

Distribution by histology is presented in Table 16.5. Tumors classified as adenocarcinoma comprise almost 90% of all cancers of the ovary. Of these, the most common subclassification was papillary serous cystadenocarcinoma, which accounted for slightly more than one fourth of all cancers and 29% of all adenocarcinomas registered. "Borderline" adenocarcinoma was the next most common, at 15.9%, which is slightly underestimated since it wasn't collected prior to 1991 or after 2000. Adenocarcinoma, Not Otherwise Specified (12.6%), endometrioid (9.8%), serous cystadenocarcinoma (5.8%), papillary (5.5%), mucinous cystadenocarcinoma (4.2%), clear cell (4.0%), mucinous adenocarcinoma (3.4%) and cystadenocarcinoma (1.3%) were also observed.

Table 16.2: Cancer of the Ovary: Age Distribution by Race, Ages 20+, 12 SEER Areas, 1988-2001

	Total		White		Black		Other	
Age Group (Years)	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	32,019	100.0	27,595	100.0	2,035	100.0	2,389	100.0
20-29	1,292	4.0	1,009	3.7	122	6.0	161	6.7
30-39	2,736	8.5	2,243	8.1	196	9.6	297	12.4
40-49	5,081	15.9	4,231	15.3	345	17.0	505	21.1
50-59	6,226	19.4	5,299	19.2	376	18.5	551	23.1
60-69	6,954	21.7	6,036	21.9	466	22.9	452	18.9
70-79	6,525	20.4	5,837	21.2	370	18.2	318	13.3
80+	3,205	10.0	2,940	10.7	160	7.9	105	4.4

Table 16.3: Cancer of the Ovary: Number of Cases, Median Survival Time (Months) and 5-year Survival Rates (%) by Race and Age (20+), 12 SEER Areas, 1988-2001

Race/Age (years)	Cases	Median Survival Time (Months)	5-Year Survival Rate (%)		
			Observed	Expected	Relative
All Races, 20+	32,019	54.5	48.4	89.9	53.8
White, 20+	27,595	53.7	48.0	89.6	53.6
Black, 20+	2,035	38.0	43.1	88.6	48.5
All Races, 20-49	9,109	> 120	75.8	99.1	76.6
White, 20-49	7,483	> 120	76.7	99.1	77.4
Black, 20-49	663	> 120	71.4	98.1	72.7
All Races, 50-69	13,180	53.2	47.5	94.5	50.2
White, 50-69	11,335	54.1	47.9	94.6	50.6
Black, 50-69	842	30.7	35.1	91.1	38.6
All Races, 70+	9,730	18.7	23.8	75.2	31.6
White, 70+	8,777	18.8	23.5	74.9	31.3
Black, 70+	530	13.5	20.6	72.8	27.7

Table 16.4: Cancer of the Ovary: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by SEER Geographic Area, Ages 20+, 12 SEER Areas, 1988-2001

SEER Geographic Area	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	32,019	100.0	80.3	69.3	61.8	53.8	49.4	48.5
Atlanta and Rural Georgia	2,007	6.3	80.0	71.1	65.1	56.5	51.9	50.8
Atlanta (Metropolitan) - 1988+	1,911	6.0	80.3	71.7	65.7	56.9	52.1	50.9
Rural Georgia - 1988+	96	0.3	74.5	59.8	52.5	48.4	46.3	46.3
California								
Los Angeles - 1992+	5,593	17.5	81.9	72.0	65.4	57.0	52.9	51.9
Greater Bay Area	5,723	17.9	80.1	69.7	61.3	52.9	48.0	46.6
San Francisco-Oakland SMSA - 1988+	3,814	11.9	79.0	68.2	59.4	51.5	47.8	46.6
San Jose-Monterey - 1988+	1,909	6.0	82.2	72.8	65.2	55.5	48.5	46.5
Connecticut - 1988+	3,580	11.2	80.7	68.2	60.2	51.7	46.0	45.3
Detroit (Metropolitan) - 1988+	4,092	12.8	77.2	66.6	58.1	51.1	46.8	45.3
Hawaii - 1988+	943	2.9	82.8	72.7	65.9	56.5	51.4	50.0
Iowa - 1988+	3,278	10.2	77.7	65.4	59.2	52.1	49.0	48.7
New Mexico - 1988+	1,341	4.2	78.7	67.6	59.0	50.2	46.8	45.2
Seattle (Puget Sound) - 1988+	4,012	12.5	83.0	70.8	63.6	55.6	51.2	51.0
Utah - 1988+	1,450	4.5	80.1	68.9	60.8	53.8	51.5	49.6

Table 16.5: Cancer of the Ovary: Number and Distribution of Cases and 5-Year Relative Survival Rate (RSR) (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology	ICD-O Code	Cases	Percent	5-Year RSR (%)
Total	8000-9989	32,019	100.0	53.8
Epidermoid	8051-8130	174	0.5	51.3
Adenocarcinoma	8050,8140-8147,8160-8162,8180-8221,8250-8506,8520-8550,8560,8570-8575,8940-8941,9110	28,728	89.7	54.4
Adenocarcinoma NOS*	8140	4,021	12.6	18.3
Papillary	8050,8260	1,750	5.5	21.0
Clear Cell	8310,9110	1,291	4.0	61.5
Endometrioid	8380-8381,8570	3,133	9.8	70.9
Serous Cystadenocarcinoma	8441	1,863	5.8	44.2
Cystadenocarcinoma	8440,8450	427	1.3	50.7
Papillary Serous Cystadenocarcinoma	8460-8461	8,458	26.4	39.6
Mucinous Cystadenocarcinoma	8470-8471	1,346	4.2	77.7
Mucinous Adenocarcinoma	8480-8481	1,089	3.4	49.1
"Borderline"	8442,8451,8462,8472-8473	5,094	15.9	98.2
All Other Adenocarcinomas	8141-8147,8160-8162,8180-8221,8250-8259,8261-8309,8311-8379,8382-8439,8443-8449,8452-8459,8463-8469,8474-8479,8482-8506,8520-8550,8560,8571-8575,8940-8941	256	0.8	44.2
Other Specified Carcinomas	8030-8046,8150-8155,8170-8171,8230-8231,8247-8248,8510-8512,8561-8562,8580-8671	460	1.4	76.5
Stromal Cell	8620-8631,8650	353	1.1	87.8
All Other Specified Carcinomas	8030-8046,8150-8155,8170-8171,8230-8231,8247-8248,8510-8512,8561-8562,8580-8619,8632-8649,8651-8671	107	0.3	37.3
Carcinoma NOS	8010-8022	1,299	4.1	26.8
Other Specified Types	8240-8246,8720-8790,8935,8950-8982,9000-9030,9060-9104,9350-9364,9380-9512,9530-9539	1,153	3.6	61.4
Mullerian	8950-8951,8980	547	1.7	29.8
Brenner	9000	69	0.2	67.9
Germ Cell	9060-9090,9102	486	1.5	91.0
Dysgerminoma	9060	153	0.5	96.8
Teratoma	9080-9085,9102	248	0.8	89.1
All Other Germ Cells	9061-9079,9086-9090	85	0.3	85.1
All Other Specified Types	8240-8246,8720-8790,8935,8952-8979,8981-8982,9001-9030,9091-9101,9103-9104,9350-9364,9380-9512,9530-9539	51	0.2	71.7
Unspecified	8000-8004	205	0.6	23.0

* NOS: Not Otherwise Specified

Germ cell was observed in 1.5% of all cases. Of these 31% were dysgerminoma and 51% teratoma. Tumors classified as Mullerian comprised 1.7% of all cases.

Five-year relative survival rates varied by histologic type. The highest rates were seen for "borderline" tumors, 98%, but "borderline" tumors were only considered reportable and malignant for 1991-2000. The germ cell tumors also had survival rates over 85%. Survival rates under 25% were seen for unspecified malignant tumors, adenocarcinomas NOS, and papillary adenocarcinomas (Table 16.5).

ADENOCARCINOMA (NON-BORDERLINE)

The histologies used for adenocarcinoma are in Table 16.5 in the category "Adenocarcinoma" (28,728 cases) excluding the "Borderline" cases (5,094). There were a total of 23,634 adenocarcinomas excluding borderline.

Table 16.6: Adenocarcinoma of the Ovary (excluding Borderline Tumors): Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) for Cases (Ages 20+) by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	23,634	100.0	77.5	64.0	54.4	43.9	37.8	36.4
I	5,215	22.1	96.8	94.3	92.1	89.3	85.6	84.1
IA	3,108	13.2	98.9	97.3	96.1	94.0	91.1	88.9
IB	337	1.4	98.0	94.5	93.2	91.1	82.4	78.7
IC	1,548	6.5	92.4	88.1	84.5	79.8	76.0	76.0
I NOS*	222	0.9	94.8	92.8	88.2	84.7	77.0	73.7
II	1,833	7.8	87.1	78.9	73.2	65.5	58.4	55.7
IIA	485	2.1	96.4	89.5	84.7	76.4	69.0	66.8
IIB	587	2.5	88.3	80.6	73.6	66.9	63.2	57.4
IIC	699	3.0	80.4	70.7	65.1	57.0	47.0	45.9
II NOS*	62	0.3	78.0	71.0	68.8	58.9	50.2	38.8
III	8,346	35.3	78.8	62.0	48.9	33.5	24.4	22.2
IIIA	469	2.0	86.4	71.6	61.8	45.3	34.1	31.4
IIIB	660	2.8	81.5	66.8	54.0	38.6	27.2	26.1
IIIC	4,596	19.4	82.2	65.5	51.2	35.2	25.3	22.6
III NOS*	2,621	11.1	70.5	52.8	40.8	26.9	20.0	17.9
IV	7,499	31.7	61.7	42.5	30.1	17.9	11.6	10.4
Unknown/Unstaged	741	3.1	61.8	49.3	41.5	29.5	24.2	20.2

* NOS = Not Otherwise Specified

Stage

Table 16.6 and Figure 16.1 show the contrast between stage at diagnosis and months/years since diagnosis. In stages II-IV, the steepest declines in survival are observed within 3-5 years of diagnosis. Survival continues to decline throughout the 10 years observed in these stages.

Age and Stage

Of the 23,634 cases of non-borderline adenocarcinoma, enough information to establish stage at diagnosis was available for 22,893 (97%). Across all age groups, 31.7% of all cancers were diagnosed in Stage IV. Stage IV disease occurs in 19.4% among women ages 20-49 to 38.5% in women over age 70, while Stage I declines from 39.6% to 13.1% in these same age groups (Table 16.7).

For all ages combined, little difference is seen between survival in stages IA & IB (Table 16.8, Figure 16.2). No survival differential with increased age is present. Stages IA & IB both involve tumor confined to the ovary, with an intact capsule. However, a difference does exist between Stages IA & IB and Stage IC with stage IC having much poorer survival than IA or IB.

Stage IC also involves tumor limited to the ovary, however, capsule rupture, external invasion or ascites also exist. For stages IC and higher, a survival differential by age is observed, with declining survival with increasing age (Table 16.8 & Figure 16.2).

Figure 16.1: Adenocarcinoma of the Ovary (excluding Borderline Tumors): Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

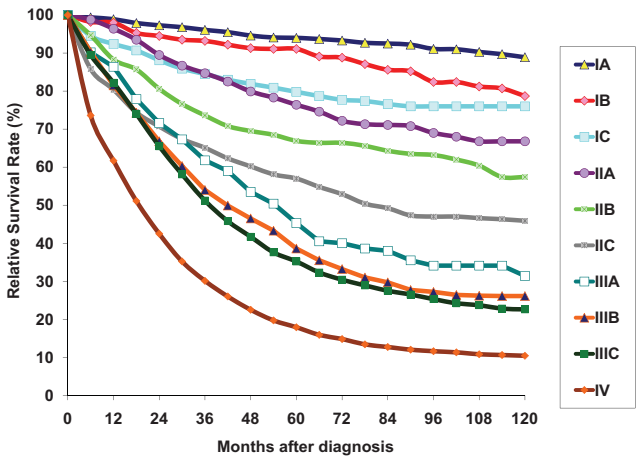


Table 16.7: Adenocarcinoma of the Ovary (excluding Borderline Tumors): Number and Distribution of Cases by AJCC Stage (SEER modified 3rd edition) and Age (20+), 12 SEER Areas, 1988-2001

	Age (Years)							
	Total		20-49		50-69		70+	
AJCC Stage	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	23,634	100.0	5,090	100.0	10,576	100.0	7,968	100.0
I	5,215	22.1	2,016	39.6	2,156	20.4	1,043	13.1
IA	3,108	13.2	1,300	25.5	1,223	11.6	585	7.3
IB	337	1.4	118	2.3	156	1.5	63	0.8
IC	1,548	6.5	506	9.9	695	6.6	347	4.4
I NOS*	222	0.9	92	1.8	82	0.8	48	0.6
II	1,833	7.8	446	8.8	815	7.7	572	7.2
IIA	485	2.1	144	2.8	222	2.1	119	1.5
IIB	587	2.5	135	2.7	257	2.4	195	2.4
IIC	699	3.0	153	3.0	313	3.0	233	2.9
II NOS*	62	0.3	14	0.3	23	0.2	25	0.3
III	8,346	35.3	1,540	30.3	3,896	36.8	2,910	36.5
IIIA	469	2.0	103	2.0	216	2.0	150	1.9
IIIB	660	2.8	146	2.9	319	3.0	195	2.4
IIIC	4,596	19.4	901	17.7	2,301	21.8	1,394	17.5
III NOS*	2,621	11.1	390	7.7	1,060	10.0	1,171	14.7
IV	7,499	31.7	988	19.4	3,445	32.6	3,066	38.5
Unknown/ Unstaged	741	3.1	100	2.0	264	2.5	377	4.7

* NOS: Not Otherwise Specified

Histology and Stage

Tumors of the papillary subtype and adenocarcinoma NOS are associated with poor survival. Mucinous cystadenocarcinoma has the highest five-year survival rate (77.7%) for all stages combined, due to a high percentage of cases diagnosed in Stage I. Tumors of the endometrioid type have better prognosis in each stage (Table 16.9 & Figure 16.3).

Figure 16.2: Adenocarcinoma of the Ovary (excluding Borderline Tumors): 5-Year Relative Survival Rate (%) by AJCC Stage (SEER modified 3rd edition) and Age Group (20+), 12 SEER Areas, 1988-2001

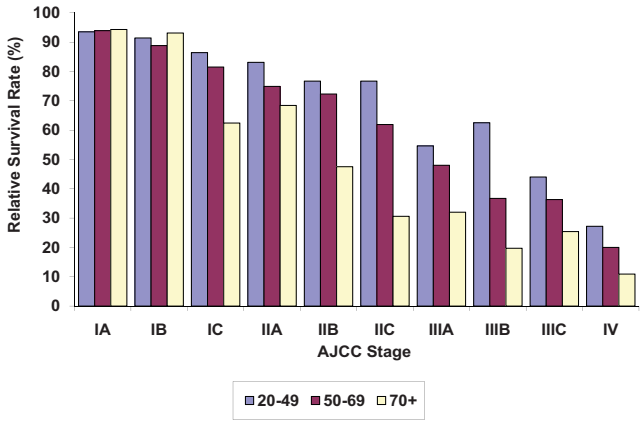


Figure 16.3: Adenocarcinoma of the Ovary (excluding Borderline Tumors): 5-Year Relative Survival Rate (%) by Histology and AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

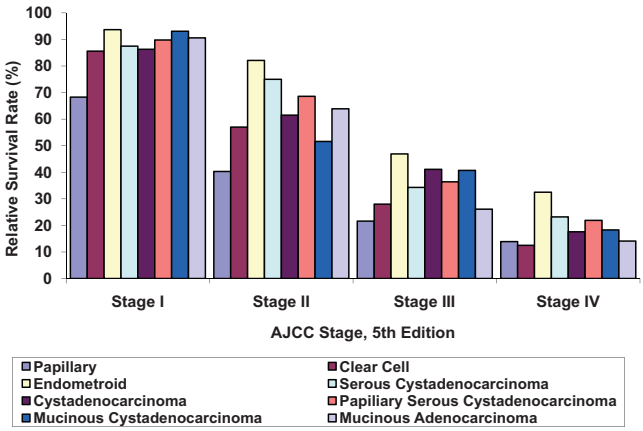


Table 16.8: Adenocarcinoma of the Ovary (excluding Borderline Tumors): Number of Cases and 5-Year Relative Survival Rates (RSR) (%) for Patients with by AJCC Stage (SEER modified 3rd edition) and Age (20+), 12 SEER Areas, 1988-2001

	Total		20-49		50-69		70+	
AJCC Stage	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
Total	23,634	43.9	5,090	63.3	10,576	44.0	7,968	27.5
I	5,215	89.3	2,016	91.2	2,156	89.2	1,043	83.8
IA	3,108	94.0	1,300	93.5	1,223	93.9	585	94.3
IB	337	91.1	118	91.4	156	88.8	63	93.1
IC	1,548	79.8	506	86.4	695	81.5	347	62.4
I NOS	222	84.7	92	85.1	82	82.9	48	85.6
II	1,833	65.5	446	78.7	815	68.9	572	45.5
IIA	485	76.4	144	83.1	222	74.9	119	68.4
IIB	587	66.9	135	76.7	257	72.3	195	47.5
IIC	699	57.0	153	76.7	313	61.9	233	30.6
II NOS	62	58.9	14	~	23	~	25	39.3
III	8,346	33.5	1,540	45.9	3,896	35.3	2,910	21.8
IIIA	469	45.3	103	54.6	216	48.0	150	32.0
IIIB	660	38.6	146	62.5	319	36.7	195	19.7
IIIC	4,596	35.2	901	44.0	2,301	36.3	1,394	25.4
III NOS	2,621	26.9	390	42.1	1,060	30.1	1,171	16.3
IV	7,499	17.9	988	27.2	3,445	20.0	3,066	10.9
Unknown/Unstaged	741	29.5	100	56.0	264	33.5	377	16.1

* NOS: Not Otherwise Specified

~ Statistic not displayed due to less than 25 cases.

Table 16.9: Adenocarcinoma of the Ovary (excluding Borderline Tumors): Number of Cases and 5-Year Relative Survival Rates (%) by Histology and AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage											
	Total		I		II		III		IV		Unknown/ Unstaged	
Histology	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)
Total Adenocarcinoma	23,634	43.9	5,215	89.3	1,833	65.5	8,346	33.5	7,499	17.9	741	29.5
Adenocarcinoma NOS*	4,021	18.3	276	61.7	233	35.2	1,189	21.2	2,021	8.9	302	14.5
Papillary	1,750	21.0	84	68.3	83	40.3	649	21.6	845	13.9	89	20.3
Clear Cell	1,291	61.5	708	85.6	145	57.0	271	28.0	151	12.5	16	~
Endometrioid	3,133	70.9	1,404	93.7	454	82.1	743	46.9	483	32.5	49	56.3
Serous Cystadenocarcinoma	1,863	44.2	331	87.5	147	75.0	786	34.3	567	23.2	32	24.9
Cystadenocarcinoma	427	50.7	131	86.3	33	61.5	137	41.1	111	17.6	15	~
Papillary Serous Cystadenocarcinoma	8,458	39.6	885	89.8	570	68.6	3,999	36.4	2,829	21.9	175	41.0
Mucinous Cystadenocarcinoma	1,346	77.7	953	93.1	68	51.6	175	40.7	126	18.3	24	~
Mucinous Adenocarcinoma	1,089	49.1	378	90.6	74	63.9	299	26.1	301	14.1	37	30.1
All Other Adenocarcinomas	256	44.2	65	87.7	26	60.1	98	27.5	65	12.6	<5	~

* NOS: Not Otherwise Specified

~ Statistic not displayed due to less than 25 cases.

Table 16.10: Adenocarcinoma of the Ovary (excluding Borderline Tumors): Number of Cases and 5-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition) and Grade, Ages 20+, 12 SEER Areas, 1988-2001

	Grade									
	Total		Well Differentiated		Moderately Differentiated		Poorly/ Undifferentiated		Unknown	
AJCC Stage	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)
Total	23,634	43.9	2,071	82.6	4,505	54.9	10,511	35.3	6,547	36.3
I	5,215	89.3	1,277	95.1	1,451	92.6	1,051	82.6	1,436	85.1
IA	3,108	94.0	896	95.9	872	94.9	494	88.8	846	93.3
IB	337	91.1	75	90.7	84	91.9	101	90.4	77	89.5
IC	1,548	79.8	253	92.3	439	88.2	409	74.3	447	68.2
I NOS^	222	84.7	53	95.3	56	88.1	47	71.8	66	80.3
II	1,833	65.5	179	85.8	421	73.9	781	62.8	452	52.8
IIA	485	76.4	54	94.4	131	80.5	201	70.8	99	69.9
IIB	587	66.9	61	75.4	148	73.4	261	65.3	117	55.2
IIC	699	57.0	62	87.2	131	66.1	288	56.2	218	42.0
II NOS^	62	58.9	<5	~	11	~	31	45.2	18	~
III	8,346	33.5	370	62.3	1,473	36.4	4,720	33.0	1,783	25.2
IIIA	469	45.3	51	79.1	100	52.4	202	40.5	116	30.0
IIIB	660	38.6	40	62.7	142	36.5	360	40.5	118	25.2
IIIC	4,596	35.2	173	63.4	777	35.1	2,851	34.8	795	30.1
III NOS^	2,621	26.9	106	51.6	454	34.6	1,307	26.2	754	19.3
IV	7,499	17.9	212	37.7	1,083	21.0	3,769	19.6	2,435	11.6
Unknown/ Unstaged	741	29.5	33	79.4	77	41.8	190	25.6	441	24.4

~ Statistic not displayed due to less than 25 cases.
^ NOS: Not Otherwise Specified

Stage and Grade

Of the 23,634 cases of non-borderline adenocarcinoma, 17,087 (72%) had information on tumor grade (Table 16.10 & Figure 16.4). Within stage, 5-year relative survival generally declines as grade increases with the exception of stage IB tumors, where little difference is seen by grade (possibly due to the small number of cases).

Figure 16.4: Adenocarcinoma of the Ovary (excluding Borderline Tumors): 5-Year Relative Survival Rate (%) by Grade and AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

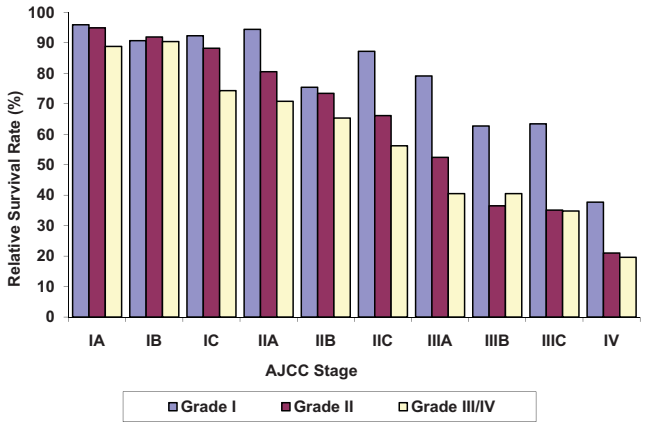


Table 16.11: Adenocarcinoma of the Ovary (excluding Borderline Tumors): 5-Year Relative Survival Rates (%), Conditioned on Years Since Diagnosis by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Surviving the Next 5 Years					
	From Diagnosis	After 1 Year	After 2 Years	After 3 Years	After 4 Years	After 5 years
Total	43.9	51.5	59.3	66.8	73.6	79.2
I	89.3	90.5	91.8	92.6	94.1	94.1
IA	94.0	94.3	95.1	95.0	95.8	95.1
IB	91.1	90.5	90.8	88.7	89.1	86.5
IC	79.8	82.8	85.5	88.6	91.5	94.3
I NOS	84.7	85.5	84.0	87.2	88.9	87.4
II	65.5	70.5	74.4	77.4	79.6	82.4
IIA	76.4	74.7	78.6	80.7	82.6	86.7
IIB	66.9	73.5	77.8	83.1	84.0	83.4
IIC	57.0	63.5	67.0	69.3	73.5	76.2
II NOS	58.9	73.8	80.5	70.9	62.4	62.9
III	33.5	36.1	41.9	48.2	54.9	63.2
IIIA	45.3	45.6	51.5	53.2	61.9	66.5
IIIB	38.6	40.0	43.4	49.0	54.7	65.2
IIIC	35.2	36.5	41.2	48.2	55.2	62.2
III NOS	26.9	32.1	40.0	46.5	52.1	62.3
IV	17.9	23.0	28.6	36.6	45.2	54.5
Unknown/ Unstaged	29.5	40.8	49.0	53.4	60.1	62.2

Conditional Survival

Five year relative survival, conditioned on years since diagnosis, is presented in Table 16.11 and Figure 16.5. Except for stages IA and IB, the probability of surviving for 5 years increases as time since diagnosis increases. This is most marked for the stage IV cases. For stage IV, five year survival from time of diagnosis is 18%. For those individuals who survived 1 year post diagnosis, 5-year survival increased to 23%. This increased to 55% for those individuals who survived 5 years after they had already survived 5 years.

Figure 16.5: Adenocarcinoma of the Ovary (excluding Borderline Tumors): 5-Year Relative Survival Rate (%), Conditioned on Years Since Diagnosis, by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

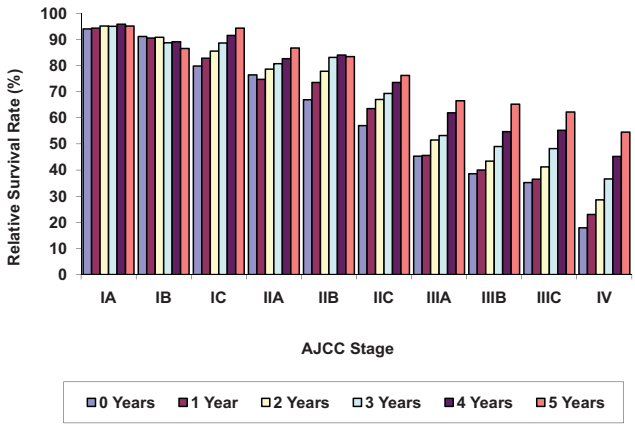


Table 16.12: Borderline Tumors of the Ovary: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2000

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total (1988-2000 only)	5,092	100.0	99.3	99.1	98.8	98.2	97.2	96.1
I	4,176	82.0	99.6	99.5	99.3	99.1	98.8	98.0
IA	3,131	61.5	99.8	99.7	99.6	99.5	99.4	99.1
IB	329	6.5	99.7	99.2	99.2	97.9	94.0	90.8
IC	520	10.2	98.7	98.6	97.9	97.4	95.8	95.7
I NOS^	196	3.8	98.5	98.5	98.1	97.9	95.4	94.2
II	290	5.7	99.2	99.1	98.2	98.2	95.4	93.6
IIA	92	1.8	100.0	99.8	97.8	96.6	94.9	90.3
IIB	94	1.8	98.5	98.5	98.1	97.5	92.5	92.5
IIC	98	1.9	98.4	98.0	98.0	98.0	97.1	95.2
II NOS^	6	0.1	~	~	~	~	~	~
III	449	8.8	99.1	98.9	98.4	95.7	90.2	88.1
IIIA	112	2.2	98.9	98.6	98.6	97.1	91.0	88.5
IIIB	50	1.0	100.0	100.0	100.0	97.3	91.4	91.4
IIIC	139	2.7	97.7	97.1	96.9	96.6	89.8	85.3
III NOS^	148	2.9	99.5	99.5	97.5	93.2	88.6	86.9
IV	114	2.2	90.1	84.7	82.7	76.9	74.7	70.0
Unknown/Unstaged	63	1.2	97.7	93.5	92.4	91.0	84.7	84.7

~ Statistic not displayed due to less than 25 cases.

^ NOS: Not Otherwise Specified

ADENOCARCINOMA ("BORDERLINE")

Stage

"Borderline" adenocarcinoma is of low malignant potential. These tumors are no longer reportable as malignant with the implementation of ICD-O-3, but were reportable during the years 1988-2000. Eighty-two percent of these tumors were diagnosed in stage I (Table 16.12) compared to 22% in the non-borderline adenocarcinomas (Table 16.7). Survival is quite high across all stages with five-year relative survival in the high 90% range in stages IA-IIIC, and 77% at stage IV (Table 16.12).

Table 16.13: Germ Cell Cancer of the Ovary: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Age (20+), 12 SEER Areas, 1988-2001

Age (Years)	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	486	100.0	94.6	92.7	91.6	91.0	90.3	90.3
20-29	241	49.6	98.0	97.6	96.7	96.2	95.6	95.6
30-39	161	33.1	96.3	92.4	92.4	91.8	91.8	91.8
40-49	46	9.5	87.1	84.9	82.7	82.7	82.7	82.7
50-69	29	6.0	75.1	67.8	63.8	53.1	46.9	46.9
70+	9	1.9	~	~	~	~	~	~

~ Statistic not displayed due to less than 25 cases.

GERM CELL

Stage

Germ cell tumors are seen in younger women. Of the 486 reported in 12 SEER areas, between 1988-2001, almost 83% were diagnosed in women under the age of 40 (Table 16.13). For germ cell tumors, survival decreased as age increased (Table 16.13).

For germ cell tumors, 67.1% were diagnosed in stage I (Table 16.14). Table 16.14 and Figure 16.6 show stage at diagnosis for germ cell by years since diagnosis. After two years from diagnosis, stage III survival is slightly better than stage II survival. Survival rates level off for each stage but at different times. In stages I and IV, survival begins to level later than for stages II and III: 8 years for stage I, 2 years for stage II, 3 years for stage III, and 5 years for stage IV.

Figure 16.6: Germ Cell Cancer of the Ovary: Relative Survival Rate (%) by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

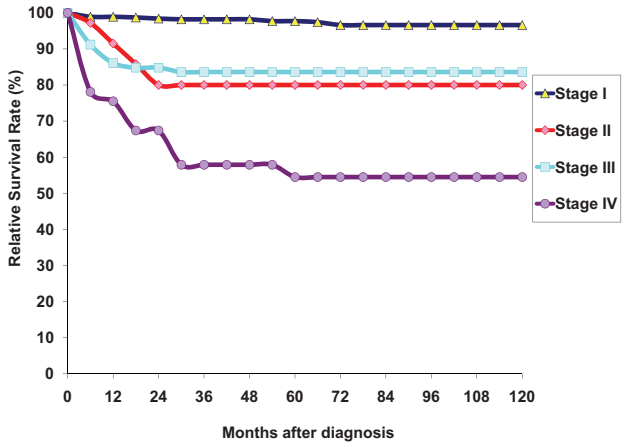


Table 16.14: Germ Cell Cancer of the Ovary: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	486	100.0	94.6	92.7	91.6	91.0	90.3	90.3
Stage I	326	67.1	98.9	98.4	98.2	97.7	96.6	96.6
Stage II	35	7.2	91.5	80.0	80.0	80.0	80.0	80.0
Stage III	79	16.3	86.1	84.8	83.6	83.6	83.6	83.6
Stage IV	36	7.4	75.5	67.4	57.9	54.5	54.5	54.5
Unknown/Unstaged	10	2.1	~	~	~	~	~	~

~ Statistic not displayed due to less than 25 cases.

Table 16.15: Germ Cell Cancer of the Ovary: By AJCC Stage (SEER modified 3rd edition): Surviving the Next Five Years From Diagnosis, 1, 2, 3, 4 and 5 Years After Diagnosis, Ages 20+, 12 SEER Areas, 1988-2001

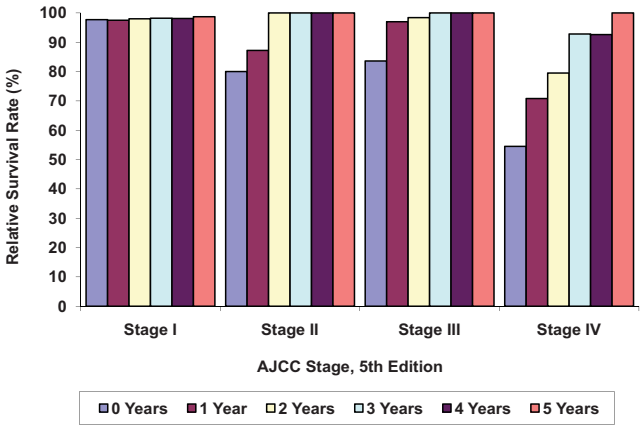
AJCC Stage	Surviving the Next 5 Years					
	From Diagnosis	After 1 Year	After 2 Years	After 3 Years	After 4 Years	After 5 Years
Total	91.0	95.0	97.2	98.2	98.1	99.1
Stage I	97.7	97.5	98.0	98.2	98.1	98.7
Stage II	80.0	87.2	100.0	100.0	100.0	100.0
Stage III	83.6	97.0	98.4	100.0	100.0	100.0
Stage IV	54.5	70.8	79.5	92.8	92.6	100.0
Unknown/Unstaged	~	~	~	~	~	~

~ Statistic not displayed due to less than 25 cases.

Conditional Survival

Five year relative survival, conditioned on years since diagnosis, is presented in Table 16.15 and Figure 16.7. For stages II-IV, the probability of surviving the next five years after diagnosis increases as time since diagnosis increases. This is most marked for the stage IV cases. For stage IV, five year survival from time of diagnosis is 55%. For stage IV, for those individuals who survive 1 year post diagnosis, 5-year survival increases to 71%. This increases to 94% for those individuals who survive 4 years and approximately 100% for those who have already survived 5 years. Five-year relative survival reaches approximately 100% for stage II patients who have already survived two years; for stage III patients who have already survived 3 years; and is over 98% for stage I patients who have already survived 2 years.

Figure 16.7: Germ Cell Cancer of the Ovary: 5-Year Relative Survival Rate (%), Conditioned on Years Since Diagnosis, By AJCC Stage (SEER modified 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001



DISCUSSION

Survival rates were presented for three groups of ovarian cancer: non-borderline adenocarcinoma, borderline adenocarcinoma, and germ cell tumors. Women with cancer of the ovary have poorer survival than women with other gynecologic cancers. While overall 5-year relative survival is under 50% for adenocarcinoma of the ovary, the 5-year relative survival rates were better for stage I (89%), younger women (63%) and well-differentiated tumors (83%). For borderline tumors, survival rates were very high. Even the 10-year relative survival rate was over 95%. For germ cell tumors, a larger percentage (67.1%) were found as stage I at diagnosis which yielded a high overall 5-year relative survival rate, 91%.

REFERENCES

1. Percy, C., Van Holten, V., and Muir, C. International Classification of Diseases for Oncology--second edition. Geneva: World Health Organization, 1990.
2. Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, Whelan S. International Classification of Diseases for Oncology--Third Edition. Geneva: World Health Organization, 2000.
3. Beahrs, OH, Henson DE, Hutter RVP, Myers MH (eds). AJCC Cancer Staging Manual, Third edition. American Joint Committee on Cancer. Philadelphia: Lippincott, 1988.

Chapter 17
Cancer of the Placenta

Carol L. Kosary

INTRODUCTION

Cancers of the placenta are rare tumors arising from the products of conception in the uterus. The most common antecedent pregnancy is that of a hydatidiform mole, usually a genetic disorder of pregnancy in which only placental-like tissue is present. Cancer of the placenta most commonly follows a molar pregnancy. It can, however, also follow a normal pregnancy, ectopic pregnancy, or abortion.

MATERIALS AND METHODS

Between 1988-2001, there were 249 cases of cancer of the placenta diagnosed in SEER. The following were excluded from the analysis: patients for whom placental cancer was not the first primary, cases identified through autopsy or death certificate only, persons of unknown race, cases without active follow-up or alive with no survival time, patients less than 15 years old, sarcomas and carcinoids. After these exclusions, 244 cases remained for analysis (Table 17.1).

RESULTS

Age

85% of all cases were diagnosed in women under age 40 and 10% were in women ages 15-19. No cases were seen in women age 70 and older and few cases in women age 50 and over (Table 17.2).

Histology

The majority of these cases were categorized as chorio-carcinoma (over 90%) (Table 17.3).

Staging

The Federation Internationale de Gynecologie et d'Obstetrique (FIGO) and the American Joint Committee

Table 17.1: Cancer of the Placenta: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/selection
249	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
249	0	Select first primary only
244	5	Exclude death certificate only or at autopsy, unknown race, and children (<15)

Table 17.2: Cancer of the Placenta: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, 10-Year Relative Survival by Age (15+), 12 SEER Areas, 1988-2001

Age Group (Years)	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total (15+)	244	100.0	95.9	93.1	92.1	91.7	89.8	89.0
15-19	25	10.2	100.0	95.5	95.5	95.5	95.5	95.5
20-29	107	43.9	99.1	96.2	96.2	95.1	91.7	89.1
30-39	75	30.7	94.7	92.1	90.6	90.6	90.6	90.6
40-49	29	11.9	86.3	82.9	78.9	78.9	73.0	73.0
50-69	8	3.3	~	~	~	~	~	~
70+	0	0.0	~	~	~	~	~	~

~ Statistic not displayed due to less than 25 cases.

Table 17.3: Cancer of the Placenta: Number and Distribution of Cases and 5-Year Relative Survival Rates (%) by Histology, Ages 15+, 12 SEER Areas, 1988-2001

Histology	ICD-O Code	Cases	Percent	5-Year Relative Survival Rate(%)
Total	8000-9989	244	100.0	91.7
Epidermoid	8051-8130	0	0.0	~
Adenocarcinoma	8140-8147,8160-8162,8180-8221,8250-8506,8520-8550,8560,8570-8573,8940-8941	0	0.0	~
Other Specified Carcinomas	8030-8045,8150-8155,8170-8171,8230-8248,8510-8512,8561-8562,8580-8671	0	0.0	~
Carcinoma, NOS	8010-8022	0	0.0	~
Other Specified Types	8720-8790,8931-8932,8950-8979,8982,9000-9030,9060-9110,9350-9364,9380-9512,9530-9539	242	99.2	91.7
Choriocarcinoma	9100-9101	221	90.6	91.3
All Other Specified Types	8720-8790,8931-8932,8950-8979,8982,9000-9030,9060-9099,9102-9110,9350-9364,9380-9512,9530-9539	21	8.6	~
Unspecified	8000-8004	<5	~	~

~ Statistic not displayed due to less than 25 cases.

Table 17.4: Cancer of the Placenta: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified, 3th Edition), Ages 15+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	244	100.0	95.9	93.1	92.1	91.7	89.8	89.0
I	65	26.6	100.0	98.5	98.5	98.5	98.5	98.5
II	<5	~	~	~	~	~	~	~
III	<8	~	~	~	~	~	~	~
IV	135	55.3	92.6	88.9	87.2	86.3	85.1	83.2
Unknown/Unstaged	34	13.9	100.0	100.0	100.0	100.0	96.4	96.4

~ Statistic not displayed due to less than 25 cases.

on Cancer (AJCC) have designated staging for cancers of the placenta. Cancer of the placenta was staged using SEER modified AJCC staging, 3rd edition. This was combined with staging for the corpus uteri:

Stage I tumor is confined to the uterus.

Stage II tumor invades the cervix, but has not extended outside the uterus.

Stage III tumor extends outside of the uterus but is confined to the true pelvis.

Stage IV tumor involves the bladder or bowel mucosa or has metastasized to distant sites (including abdominal lymph nodes other than para-aortic, and/or inguinal lymph nodes; excludes metastasis to vagina, pelvic serosa, or adnexa).

Survival by Stage

Over half of the cases were diagnosed at stage IV (55.3%), which is indicative of tumor metastasis to distant sites. Almost 27% of cases were stage I. Stage II and III were rarely observed (Table 17.4).

Cancer of the placenta is highly curable even at advanced stages. The 5-year relative survival for stage IV cases is 86% and stage I survival is 99%.

DISCUSSION

Ten percent of cases of cancer of the placenta occur in women under the age of 20, while 85% occur in women under 40. Choriocarcinoma is the predominant histologic type. Over half of the patients were diagnosed at stage IV. Despite late staging, placental cancer is a highly curable disease.

REFERENCE

1. Beahrs, OH, Henson DE, Hutter RVP, Myers MH (eds). AJCC Cancer Staging Manual, Third edition. American Joint Committee on Cancer. Philadelphia: Lippincott, 1988.

Chapter 18
Cancer of the Vulva

Carol L. Kosary

INTRODUCTION

Cancers of the vulva are relatively rare; they account for slightly less than 5% of all cancers of the female genital organs. Approximately 3,740 women are diagnosed with cancer of the vulva in the United States each year (1).

MATERIALS AND METHODS

Between 1988 and 2001, there were 13,949 cases of cancer of the vulva diagnosed in SEER. The following were excluded from the analysis: patients for whom vulvar cancer was not the first primary, cases identified through autopsy or death certificate only, persons of unknown race, cases without active follow-up or alive with no survival time, patients less than 20 years old, cases without microscopic confirmation, sarcomas, and carcinoids. There were 6,280 in situ cancers of the vulva excluded from analyses. After these exclusions, 4,098 cases remained for analysis (Table 18.1).

RESULTS

Age and Race

Of the 4,098 adult patients, 18.3% were diagnosed in adults under age 50 (Table 18.2). Over 52% of all cases were diagnosed in women age 70 and over. Almost 89% of the patients were white. The percentage of adult black women diagnosed before the age of 50 is twice that of white women (35% vs. 17%). A slight difference is observed in the percent of black women diagnosed between the ages of 50 and 59 compared to white women (16% vs. 12%). Thirty-two percent of the black women were diagnosed at age 70 or older, compared to 55% of white women.

For all women, survival declined with age (Table 18.3). In 5-year relative survival rates, only minor differences between white and black women (Table 18.3) were observed. The largest survival differential was seen for ages 70+, where white women had a 5-year relative survival rate of 67%, compared to 60% for black females.

Geographic Location

Five-year relative survival rates in the 12 SEER areas included in this chapter ranged from 84.7% in Hawaii to 71.5% in Los Angeles (Table 18.4).

Histology

Distribution by histology is presented in Table 18.5. Tumors classified as squamous comprise 82.7% of all invasive cancers of the vulva with 50.6% Not Otherwise Specified (NOS), 14.2% keratinizing, 9.8% basal cell, and

Table 18.1: Cancer of the Vulva: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/selection
13,949	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
11,226	2,723	Select first primary only
11,199	27	Exclude death certificate only or at autopsy
10,671	528	Exclude unknown race
10,619	52	Exclude alive with no survival time
10,486	133	Exclude children (Ages 0-19)
4,206	6,280	Exclude in situ cancers
4,169	37	Exclude no or unknown microscopic confirmation
4,098	71	Exclude sarcomas and carcinoids

Table 18.2: Cancer of the Vulva: Age (20+) and Race Distributions, 12 SEER Areas, 1988-2001

	Total		White		Black		Other	
Age Group (Years)	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total (20+)	4,098	100.0	3,637	100.0	296	100.0	165	100.0
20-29	51	1.2	40	1.1	7	2.4	4	2.4
30-39	215	5.2	177	4.9	29	9.8	9	5.5
40-49	486	11.9	400	11.0	69	23.3	17	10.3
50-59	508	12.4	443	12.2	46	15.5	19	11.5
60-69	675	16.5	590	16.2	49	16.6	36	21.8
70-79	1,104	26.9	1,002	27.6	53	17.9	49	29.7
80+	1,059	25.8	985	27.1	43	14.5	31	18.8

8.1% other specified epidermoid types. Tumors classified as adenocarcinoma comprised 8.5% of the total, while melanoma comprised 5.9%. These three histology groups are the ones analyzed here.

Staging

The Federation Internationale de Gynecologie et d'Obstetrique (FIGO) and the American Joint Committee on Cancer (AJCC) have designated staging for cancers of the vulva excluding melanoma. Lack of specificity in the SEER data prevents a detailed breakdown of Stages IA-B and IVA-B for all years. SEER modified AJCC staging, 5th edition, was used for analyses in this chapter. The 5th edition AJCC staging (2) states:

Stage I vulvar cancer is defined as lesions 2 cm or less confined to the vulva or perineum. There are no lymph node metastases

Stage II vulvar cancer is defined as tumor either confined to the vulva and/or perineum or more than 2 cm in the greatest dimension with no nodal metastases.

Stage III vulvar cancer is defined as tumor of any size arising on the vulva and/or perineum with either adjacent spread to the lower urethra, the vagina, or the anus, or unilateral regional lymph node metastases.

Stage IV vulvar cancer is defined as tumor invading any of the following: upper urethra, bladder mucosa, rectal mucosa, pelvic bone and/or bilateral regional nodal metastases or any distant metastasis including pelvic lymph nodes.

Vulvar melanoma used the SEER modified AJCC 5th edition staging for melanoma.

Squamous

Survival by Age and Stage

Of the 3,390 patients with squamous cell carcinoma, enough information to establish stage at diagnosis was available for 3,171 (94%). The percent diagnosed in stage I declines with age, from 56% in ages 20-69 to 38% in ages 70+. Stages II and III show increases with age. Percent of stage IV cases is almost equal across age groups (Table 18.6).

Table 18.3: Cancer of the Vulva: Number and Distribution of Cases, Median Survival Time (Months) and 5-year Survival Rates (%) by Race and Age (20+), 12 SEER Areas, 1988-2001

		Median Survival Time (Months)	5-Year Survival Rate (%)		
Race/Age (Years)	Cases		Observed	Expected	Relative
All Races, 20+	4,098	104.2	62.3	81.6	76.4
White, 20+	3,637	99.7	61.5	81.0	76.0
Black, 20+	296	107.7	65.0	86.0	75.3
All Races, 20-69	1,935	> 120	81.6	96.0	85.0
White, 20-69	1,650	> 120	81.8	96.1	85.1
Black, 20-69	200	> 120	77.5	94.6	81.6
All Races, 70+	2,163	51.6	46.0	68.8	66.8
White, 70+	1,987	50.7	45.5	68.4	66.5
Black, 70+	96	42.8	41.1	68.0	59.9

Table 18.4: Cancer of the Vulva: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by SEER Geographic Area, Ages 20+, 12 SEER Areas, 1988-2001

			Relative Survival Rate (%)					
SEER Geographic Area	Cases	Percent	1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	4,098	100.0	89.5	82.9	79.8	76.4	73.0	69.7
Atlanta and Rural Georgia	286	7.0	91.6	84.2	82.5	78.3	72.1	68.1
Atlanta (Metropolitan) - 1988+	265	6.5	91.1	83.7	81.8	77.9	70.6	66.0
Rural Georgia - 1988+	21	0.5	~	~	~	~	~	~
California								
Los Angeles - 1992+	596	14.5	84.9	78.6	75.5	71.5	65.4	61.5
Greater Bay Area	624	15.2	91.7	85.9	80.8	78.4	73.7	69.9
San Francisco-Oakland SMSA - 1988+	408	10.0	90.9	85.0	80.2	76.7	72.2	66.0
San Jose-Monterey - 1988+	216	5.3	93.1	87.6	82.1	80.6	76.2	76.2
Connecticut - 1988+	616	15.0	87.3	78.5	74.8	73.3	70.3	70.3
Detroit (Metropolitan) - 1988+	592	14.4	88.5	80.3	76.1	72.3	69.2	63.6
Hawaii - 1988+	95	2.3	93.6	93.0	88.0	84.7	80.9	65.9
Iowa - 1988+	519	12.7	92.3	85.3	84.3	80.5	77.2	72.2
New Mexico - 1988+	162	4.0	91.5	86.3	84.4	74.1	69.6	69.6
Seattle (Puget Sound) - 1988+	461	11.2	90.2	85.9	83.6	78.6	77.8	75.1
Utah - 1988+	147	3.6	91.3	84.1	81.3	81.3	80.5	72.1

~ Statistic not displayed due to less than 25 cases.

Table 18.5: Cancer of the Vulva: Number and Distribution of Cases and 5-Year Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology	ICD-O Code	Cases	Percent	5-Year Relative Survival Rate (%)
Total	8000-9970	4,098	100.0	76.4
Squamous	8050-8130	3,390	82.7	75.9
Squamous, NOS	8070	2,073	50.6	73.7
Squamous, Keratinizing	8071	582	14.2	60.2
Basal Cell	8090-8110	403	9.8	99.4
Other Epidermoid	8050-8069,8072-8089,8111-8130	332	8.1	84.8
Adenocarcinoma	8140-8147,8160-8162,8180-8221,8250-8506,8520-8550,8560,8570-8573,8940-8941	347	8.5	91.9
Paget, Extramammary	8542	238	5.8	99.0
All Other Adenocarcinoma	8140-8147,8160-8162,8180-8221,8250-8506,8520-8541,8543-8550,8560,8570-8573,8940-8941	109	2.7	68.2
Other Specified Carcinomas	8030-8045,8150-8155,8170-8171,8230-8248,8510-8512,8561-8562,8580-8671	<5	~	~
Carcinoma, NOS	8010-8022	105	2.6	77.1
Other Specified Types	8720-8790,8931-8932,8950-8979,8982,9000-9030,9060-9110,9350-9364,9380-9512,9530-9539	244	6.0	58.9
Melanoma	8720-8790	240	5.9	58.9
All Other Specified Types	8931-8932,8950-8979,8982,9000-9030,9060-9110,9350-9364,9380-9512,9530-9539	<5	~	~
Unspecified	8000-8004	11	0.3	~

~ Statistic not displayed due to less than 25 cases.

A survival differential across age exists for Stages II-IV and unknown stage with women aged 70 and older exhibiting lower survival compared to women aged 20-69. No difference by age is observed in stage I (Table 18.7, Figure 18.1).

Survival by Stage

Table 18.8 and Figure 18.2 show the survival by stage and time since diagnosis for squamous cell carcinoma. In stages III-IV, the steepest declines in survival are observed within the first and second years since diagnosis. Survival continues to decline throughout the 10 years observed in these stages.

Survival by Histology and Stage

Basal cell carcinoma shows a positive survival advantage compared to the other squamous histologic subtypes in stage I and II. Keratinizing has the least favorable survival for these stages. Little difference exists between the other two squamous subtypes in stages I-IV (Table 18.9).

Figure 18.1: Squamous Cell Carcinoma of the Vulva: 5-Year Relative Survival Rate (%) by Age (20+) and AJCC Stage (SEER modified, 5th Edition), 12 SEER Areas, 1988-2001

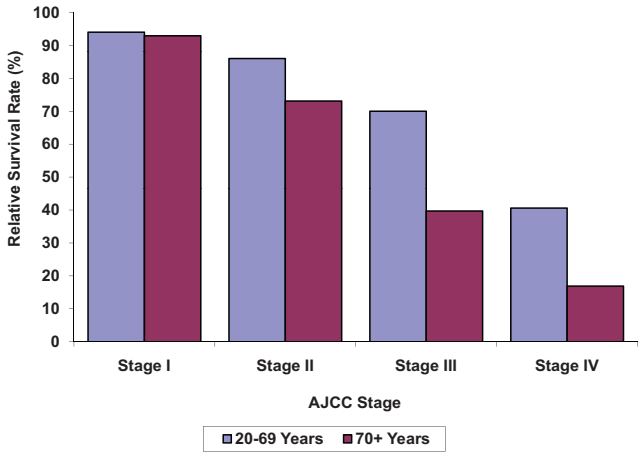


Table 18.6: Squamous Cell Carcinoma of the Vulva: Number and Distribution of Cases by AJCC Stage (SEER modified, 5th Edition) and Age (20+), 12 SEER Areas, 1988-2001

	Age (Years)					
	Total 20+		20-69		70+	
AJCC Stage	Cases	Percent	Cases	Percent	Cases	Percent
Total	3,390	100.0	1,566	100.0	1,824	100.0
Stage I	1,567	46.2	882	56.3	685	37.6
Stage II	650	19.2	253	16.2	397	21.8
Stage III	744	21.9	275	17.6	469	25.7
Stage IV	210	6.2	90	5.7	120	6.6
Unknown/Unstaged	219	6.5	66	4.2	153	8.4

Table 18.7: Squamous Cell Carcinoma of the Vulva: Number of Cases and 5-Year Relative Survival Rates (%) by AJCC Stage (SEER modified, 5th Edition) and Age (20+), 12 SEER Areas, 1988-2001

	Age (Years)					
	Total 20+		20-69		70+	
AJCC Stage	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)
Total	3,390	75.9	1,566	84.8	1,824	66.4
Stage I	1,567	93.3	882	94.0	685	92.9
Stage II	650	78.7	253	86.0	397	73.1
Stage III	744	52.7	275	70.0	469	39.7
Stage IV	210	28.7	90	40.6	120	16.9
Unknown/Unstaged	219	57.0	66	74.5	153	44.5

Survival by Stage and Grade

Five-year relative survival rates are shown by stage and grade for the 3,390 patients with squamous cell carcinoma in Table 18.10 & Figure 18.3. Within stage, 5-year relative survival declines as grade increases from well differentiated to poorly differentiated/undifferentiated/anaplastic. In stages II and IV, little difference is seen between well- and moderately-differentiated tumors. In Stage III, little difference is seen between moderately differentiated and poorly differentiated/undifferentiated/anaplastic tumors.

Survival by Tumor Size and Nodal Status for Stage III

In stage III tumors, both lymph node status and tumor size are prognostic, with both larger tumors (those greater than 2 cm) and positive regional lymph nodes predicting poorer survival (Table 18.11 and Figure 18.4).

Conditional Survival

Five-year relative survival rates, conditioned on years since diagnosis, are presented in Table 18.12 and Figure 18.5 for squamous cell carcinoma of the vulva. For stage III, the probability of surviving the next 5 years increases

Figure 18.2: Squamous Cell Carcinoma of the Vulva: Relative Survival Rates (%) by AJCC Stage (SEER modified, 5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

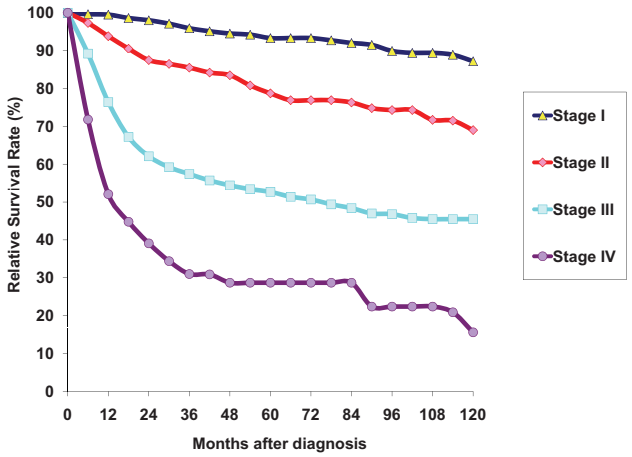


Table 18.8: Squamous Cell Carcinoma of the Vulva: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified, 5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	3,390	100.0	89.1	82.6	79.6	75.9	72.1	69.4
Stage I	1,567	46.2	99.5	98.0	95.9	93.3	89.9	87.2
Stage II	650	19.2	93.8	87.5	85.5	78.7	74.3	69.0
Stage III	744	21.9	76.4	62.1	57.4	52.7	46.8	45.5
Stage IV	210	6.2	52.1	39.1	31.0	28.7	22.4	15.6
Unstaged	219	6.5	77.5	65.9	61.8	57.0	51.4	51.1

Table 18.9: Squamous Cell Carcinoma of the Vulva: Number of Cases and 5-Year Relative Survival Rates (RSR) by Histology and AJCC Stage (SEER modified, 5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

Histology	AJCC Stage											
	Total		I		II		III		IV		Unknown/ Unstaged	
	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)	Cases	5-Year RSR (%)
Total	3,390	75.9	1,567	93.3	650	78.7	744	52.7	210	28.7	219	(%)
Squamous, NOS*	2,073	73.7	900	91.5	376	77.8	510	54.7	142	27.6	145	49.1
Squamous, Keratinizing	582	60.2	186	82.7	145	64.4	187	43.7	45	23.9	19	~
Basal Cell	403	99.4	292	100.0	61	97.7	5	~	<5	~	43	85.2
Other Epidermoid	332	84.8	189	94.7	68	88.3	42	57.5	21	~	12	~

~ Statistic not displayed due to less than 25 cases.
* NOS: Not Otherwise Specified

Table 18.10: Squamous Cell Carcinoma of the Vulva: Number of Cases and 5-Year Relative Survival Rates (%) by AJCC Stage (SEER modified, 5th Edition) and Grade, Ages 20+, 12 SEER Areas, 1988-2001

	Grade									
	Total		Well Differentiated		Moderately Differentiated		Poorly/ Undifferentiated		Unknown	
AJCC Stage	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)
Total	3,390	75.9	746	83.6	1,045	66.0	494	49.2	1,105	90.9
Stage I	1,567	93.3	403	95.5	337	86.9	107	77.4	720	96.4
Stage II	650	78.7	167	79.8	242	75.8	87	51.1	154	94.5
Stage III	744	52.7	110	64.6	332	46.6	202	43.4	100	76.2
Stage IV	210	28.7	29	33.7	85	32.0	65	18.5	31	31.3
Unknown/Unstaged	219	57.0	37	41.1	49	50.2	33	43.6	100	68.9

as time since diagnosis increases. For stage IV cases, the 5-year relative survival rate from time of diagnosis is 29%, but for those individuals who survive one year post-diagnosis, 5-year survival increases to 54%. This increases to 71% for those individuals who survive 4 years. However, 5-year survival decreases to 46% for those who have already survived five years after diagnosis. Stage I, which has a 93% 5-year survival rate from diagnosis, exhibits little gain in 5-year survival several years after diagnosis.

Adenocarcinoma

Survival by Stage

Survival by stage at diagnosis is shown for the 347 cases of adenocarcinoma. The most common stage at diagnosis was stage I, with nearly half of the cases. Over 70% were diagnosed in stages I-II (Table 18.13). Very few adult women were diagnosed with stage IV (5%).

Both stages I and II show 5-year relative survival rates of 92% or higher. Five-year relative survival falls to 74.1% at stage III. There are not enough cases to calculate survival at stage IV, (Table 18.13)

Melanoma

Survival by Stage

Melanoma of the vulva has been staged using the melanoma staging scheme (2). Of the 240 cases of melanoma, enough information to analyze stage at diagnosis was available for 223 (93%). The most common stage at diagnosis was stage I with 40% of the cases. Twenty-nine percent of the adult women were diagnosed with stage III and 19% were diagnosed with stage II (Table 18.14).

The Stage I five-year survival rate is 83%. Survival falls to 64% at stage II and 35% at stage III (Table 18.14).

Figure 18.3: Squamous Cell Carcinoma of the Vulva: 5-Year Relative Survival Rate (%) by AJCC Stage (SEER modified, 5th Edition) and Grade, Ages 20+, 12 SEER Areas, 1988-2001

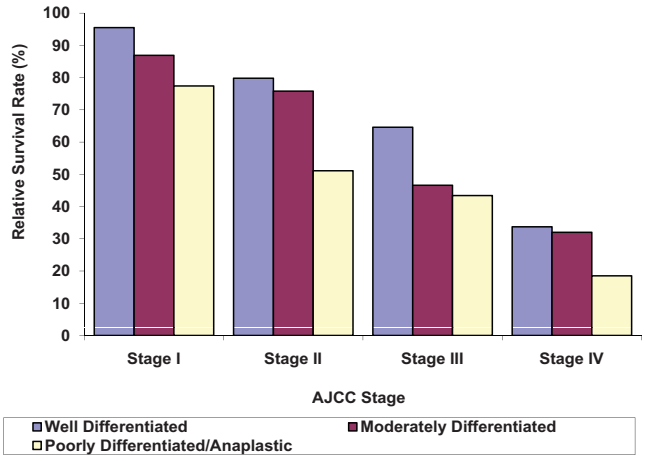


Figure 18.4: Stage III Squamous Cell Carcinoma of the Vulva: 5-Year Relative Survival Rate (%) by Nodal Status and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

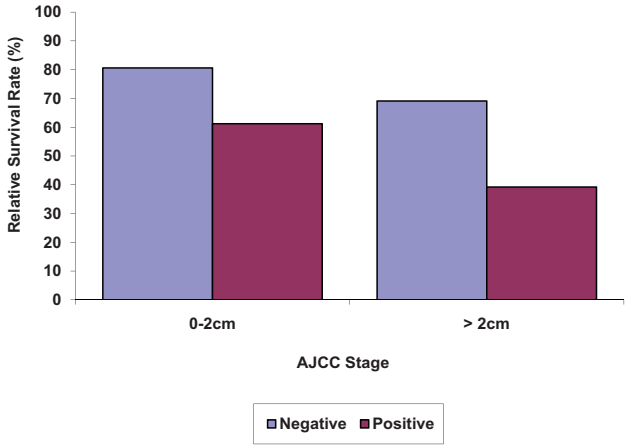


Table 18.11: Stage III Squamous Cell Carcinoma of the Vulva: Number of Cases and 5-Year Relative Survival Rates (%) by Nodal Status and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

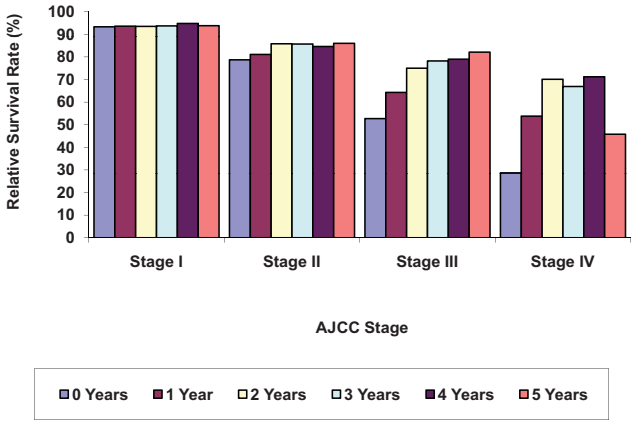
	Tumor Size							
	Total		<= 2cm		> 2cm		Unknown	
Nodal Status	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)
Total	744	52.7	111	67.4	488	48.1	145	54.8
Negative	179	71.9	23	~	114	69.1	42	71.1
Positive	476	43.1	76	61.2	337	39.2	63	39.2
Unknown	89	59.6	12	~	37	52.7	40	57.2

~ Statistic not displayed due to less than 25 cases.

Table 18.12: Squamous Cell Carcinoma of the Vulva: 5-Year Relative Survival Rates (%) , Conditioned on Years Since Diagnosis, by AJCC Stage (SEER modified, 5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

	5-Year Relative Survival Rate (%)					
	Years Since Diagnosis					
AJCC Stage	0	1	2	3	4	5
Total	75.9	83.2	87.4	88.5	89.4	89.3
Stage I	93.3	93.6	93.5	93.7	94.8	93.8
Stage II	78.7	81.1	85.8	85.7	84.6	86.0
Stage III	52.7	64.3	75.0	78.2	79.0	82.1
Stage IV	28.7	53.8	70.1	66.9	71.2	45.8
Unstaged	57.0	68.6	75.1	77.3	78.8	82.9

Figure 18.5: Squamous Cell Carcinoma of the Vulva: 5-Year Relative Survival Rate (%), Conditioned on Years Since Diagnosis, by AJCC Stage (SEER modified, 5th Edition), Ages 20+, 12 SEER Areas, 1988-2001



DISCUSSION

A larger proportion of black women than of white women are diagnosed with vulvar cancer at younger ages. The proportion of adult black women diagnosed before the age of 50 (35%) is nearly double that of whites (17%). Overall, there are no major differences in survival between blacks and whites for cancer of the vulva. For older women, 70 years and over, however, white women have better survival. By stage, there is little difference in survival by age groups (20-69 years compared to 70+ years) for women with stage I (2). In contrast, women over 70 years of age have increasingly worse survival across stages II to IV, compared to women 20-69 years of age with the same stage.

Early stage of disease is associated with the most favorable survival. Among adenocarcinomas, stages I and II have the most favorable survival among this histologic category. Among squamous histologies, representing 83% of all cancers of the vulva, basal cell has a distinct survival advantage in stage I and II over other squamous cell carcinomas. Survival declines with advanced stage of disease.

Table 18.13: Adenocarcinoma of the Vulva: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified, 5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	347	100.0	96.2	95.1	93.1	91.9	89.9	82.5
Stage I	172	49.6	100.0	100.0	100.0	100.0	97.5	88.5
Stage II	75	21.6	98.6	98.6	94.1	92.2	86.7	72.0
Stage III	51	14.7	97.6	86.5	83.3	74.1	74.1	70.9
Stage IV	18	5.2	~	~	~	~	~	~
Unstaged	31	8.9	91.0	91.0	90.9	84.8	84.8	84.8

~ Statistic not displayed due to less than 25 cases.

Table 18.14: Melanoma of the Vulva: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified, 5th Edition - Melanoma Staging Used), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	240	100.0	89.1	72.3	63.5	58.9	53.0	46.6
I	96	40.0	99.4	91.8	84.5	83.0	76.5	71.3
II	45	18.8	96.2	76.9	76.4	64.3	64.3	57.4
III	69	28.8	81.1	55.7	39.7	35.1	27.0	21.5
IV	13	5.4	~	~	~	~	~	~
Unknown/Unstaged	17	7.1	~	~	~	~	~	~

~ Statistic not displayed due to less than 25 cases.

REFERENCES

1. American Cancer Society, Cancer Facts and Figures 2006, American Cancer Society, #500806, 2006.
2. Fleming ID, Cooper JS, Henson DE, Hutter RVP, Kennedy BJ, Murphy GP, O'Sullivan B, Sobin LH, Yarbro, JW (eds). AJCC Cancer Staging Manual, Fifth edition, American Joint Committee on Cancer. Philadelphia: Lippincott-Raven, 1997.

Chapter 19
Cancer of the Vagina

Carol L. Kosary

INTRODUCTION

Cancers of the vagina are extremely rare, accounting for approximately 1% of all cancers of the female genital organs. Nearly 50% of cancers of the vagina cases are diagnosed in women age 70 and over. The most common histologic types of vaginal cancer are squamous cell carcinoma and adenocarcinoma. The 5-year relative survival rate for squamous cell carcinoma is 54%. The 5-year relative survival rate for patients with adenocarcinoma is nearly 60%.

MATERIALS AND METHODS

Exclusions

Between 1988 and 2001, there were 3,471 cases of cancer of the vagina diagnosed in SEER. The following were excluded from the analysis: patients for whom vaginal cancer was not the first primary, cases identified through autopsy or death certificate only, persons of unknown race, cases without active follow-up or alive with no survival time, patients less than 20 years old, cases without microscopic confirmation, sarcomas and carcinoids. After these exclusions, 1,041 adult cases remained for analysis (Table 19.1).

AJCC Staging

The Federation Internationale de Gynecologie et d'Obstetrique (FIGO) and the American Joint Committee on Cancer (AJCC) have designated staging for cancers of the vagina. SEER modified AJCC staging, 3rd edition, was used for analyses in this chapter. The 3th Edition AJCC staging (1) states:

Stage I vaginal cancer is defined as tumor confined to vagina with no lymph node metastases.

Stage II vaginal cancer is defined as tumor which invades paravaginal tissues but not to pelvic wall with no lymph node metastases.

Stage III vaginal cancer is defined as tumor extending to pelvic wall, or either tumor confined to the vagina or tumor with lymph note metastases invading paravaginal tissues.

Stage IV vaginal cancer is defined as either tumor invasion of the mucosa of the bladder or rectum or extension beyond the true pelvis.

Table 19.1: Cancer of the Vagina: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
3,471	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
2,249	1,222	Select first primary only
2,241	8	Exclude death certificate only or at autopsy
2,140	101	Exclude unknown race
2,131	9	Exclude alive with no survival time
2,082	49	Exclude children (Ages 0-19)
1,104	978	Exclude in situ cancers
1,082	22	Exclude no or unknown microscopic confirmation
1,041	41	Exclude sarcomas, stromal sarcomas, and carcinoids

Table 19.2: Cancer of the Vagina: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Age (20+), 12 SEER Areas, 1988-2001

Age (Years)	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total 20+	1,041	100.0	75.5	62.1	56.4	49.4	43.6	40.7
20-29	10	1.0	~	~	~	~	~	~
30-39	43	4.1	81.3	69.1	66.5	63.0	63.0	51.9
40-49	108	10.4	84.5	68.4	60.2	54.2	51.1	51.1
50-59	157	15.1	82.5	70.9	66.1	57.0	50.4	49.0
60-69	210	20.2	83.8	70.6	62.3	51.8	42.4	41.8
70-79	261	25.1	74.7	61.3	53.1	45.4	36.8	29.3
80+	252	24.2	57.4	42.3	38.6	34.1	28.1	22.7

~ Statistic not displayed due to less than 25 cases.

Table 19.3: Cancer of the Vagina: Number of Cases, Median Survival Time (Months) and 5-Year Survival Rates (%) by Race and Age (20+), 12 SEER Areas, 1988-2001

Race and Age Group (Years)	Cases	Median Survival Time (Months)	5-Year Survival Rate (%)		
			Observed	Expected	Relative
All Races, 20+	1,041	36.8	40.5	82.1	49.4
White, 20+	834	38.3	41.2	81.9	50.3
Black, 20+	135	24.0	34.9	79.9	43.5
All Races, 20-69	528	69.2	52.9	95.5	55.4
White, 20-69	424	72.2	54.0	95.7	56.4
Black, 20-69	67	45.1	44.0	93.4	46.7
All Races, 70+	513	19.5	28.2	68.4	41.3
White, 70+	410	19.9	28.3	67.6	41.7
Black, 70+	68	14.5	26.4	66.6	39.1

RESULTS

Age

Nearly half of eligible adult cases were diagnosed in women ages 70 and over. Only 15% of all adult cases were diagnosed in women 20-49 years of age (Table 19.2).

Eight-year and 10-year relative survival rates following diagnosis of vaginal cancer were found to decline with age at diagnosis (Table 19.2).

Race and Age

Survival rates were lower for black females. The largest survival difference was for age groups 20-69 where the 5-year relative survival rate was 47% for black females compared to 56% for white females 20-69 years of age (Table 19.3).

Geographic Location

Five-year relative survival rates in the 12 SEER areas included in this study ranged from 56% in San Francisco-Oakland to 34% in Hawaii. However, small numbers of cases within most registries makes survival rates by geographic area difficult to compare (Table 19.4).

Histology

Approximately 68% of the vaginal cancer cases are squamous, with an additional 17% adenocarcinoma, 9% melanoma, and the remainder consisting of various other histologies. Patients with melanoma of the vagina had the lowest 5-year relative survival rates, 13% (Table 19.5).

Survival by Age and Stage

Little difference in stage distribution is seen for women under 70 compared to those over the age of 70, with 62%

Table 19.4: Cancer of the Vagina: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by SEER Geographic Area, Ages 20+, 12 SEER Areas, 1988-2001

SEER Geographic Area	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	1,041	100.0	75.5	62.1	56.4	49.4	43.6	40.7
Atlanta and Rural Georgia	90	8.6	77.2	59.1	57.0	47.3	42.0	36.9
Atlanta (Metropolitan) - 1988+	86	8.3	77.3	59.7	57.5	47.7	42.5	37.4
Rural Georgia - 1988+	4	0.4	~	~	~	~	~	~
California								
Los Angeles - 1992+	186	17.9	78.0	63.7	56.6	52.7	46.5	22.5
Greater Bay Area	178	17.1	82.0	67.7	63.1	55.1	46.3	43.8
San Francisco-Oakland SMSA - 1988+	107	10.3	78.6	66.8	63.6	56.0	45.1	41.6
San Jose-Monterey - 1988+	71	6.8	87.0	69.1	62.0	52.9	45.2	45.2
Connecticut - 1988+	129	12.4	72.3	64.0	57.9	47.0	32.3	32.3
Detroit (Metropolitan) - 1988+	161	15.5	73.3	58.5	51.1	41.2	38.3	38.3
Hawaii - 1988+	29	2.8	63.3	48.9	37.4	33.8	!	!
Iowa - 1988+	83	8.0	73.5	61.5	53.0	47.0	44.5	43.4
New Mexico - 1988+	47	4.5	74.4	53.3	48.8	43.0	39.5	37.3
Seattle (Puget Sound) - 1988+	104	10.0	68.8	60.9	56.8	54.1	53.0	43.5
Utah - 1988+	34	3.3	81.2	67.4	57.9	47.7	39.0	39.0

~ Statistic not displayed due to less than 25 cases.
! Not enough intervals to produce rate.

Table 19.5: Cancer of the Vagina: Number and Distribution of Cases and 5-Year Relative Survival by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology	ICD-O Code	Cases	Percent	5-Year Relative Survival Rate(%)
Total	8000-9989	1,041	100.0	49.4
Squamous	8050-8130	705	67.7	53.6
Squamous, NOS*	8070	530	50.9	52.4
All Other Squamous	8050-8069,8071-8130	175	16.8	56.8
Adenocarcinoma	8140-8147,8160-8162,8180-8221,8250-8506,8520-8550,8560,8570-8573,8940-8941	172	16.5	59.0
Clear Cell	8310	20	1.9	~
All Other Adenocarcinoma	8140-8147,8160-8162,8180-8221,8250-8309,8311-8506,8520-8550,8560,8570-8573,8940-8941	152	14.6	58.5
Other Specified Carcinomas	8030-8045,8150-8155,8170-8171,8230-8248,8510-8512,8561-8562,8580-8671	13	1.2	~
Carcinoma, NOS*	8010-8022	40	3.8	32.9
Other Specified Types	8720-8790,8935,8950-8979,8982,9000-9030,9060-9110,9350-9364,9380-9512,9530-9539	106	10.2	16.9
Melanoma	8720-8790	92	8.8	13.3
All Other Specified Types	8935,8950-8979,8982,9000-9030,9060-9110,9350-9364,9380-9512,9530-9539	14	1.3	~
Unspecified	8000-8004	5	0.5	~

~ Statistic not displayed due to less than 25 cases.
* NOS : Not Otherwise Specified

Table 19.6: Cancer of the Vagina: Number and Distribution of Cases by AJCC Stage (SEER modified, 3rd edition) and Age (20+), 12 SEER Areas, 1988-2001

	Age (Years)					
	Total 20+		20-69		70+	
AJCC Stage	Cases	Percent	Cases	Percent	Cases	Percent
Total	1,041	100.0	528	100.0	513	100.0
I	368	35.4	204	38.6	164	32.0
II	236	22.7	124	23.5	112	21.8
III	120	11.5	66	12.5	54	10.5
IV	164	15.8	70	13.3	94	18.3
Unknown/Unstaged	153	14.7	64	12.1	89	17.3

Table 19.7: Cancer of the Vagina: Number of Cases and 5-Year Relative Survival Rates (%) by AJCC Stage (SEER modified, 3rd edition) and Age (20+), 12 SEER Areas, 1988-2001

	Age (Years)					
	Total 20+		20-69		70+	
AJCC Stage	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)
Total	1,041	49.4	528	55.4	513	41.3
I	368	68.4	204	72.9	164	61.9
II	236	54.3	124	61.7	112	43.3
III	120	35.5	66	33.0	54	37.0
IV	164	20.3	70	23.6	94	17.4
Unknown/Unstaged	153	31.7	64	43.5	89	20.0

~ Statistic not displayed due to less than 25 cases.

and 54% of cases diagnosed in stages I-II, respectively (Table 19.6).

Somewhat lower survival is seen in stages I, II, IV, and unknown for women ages 70 and above compared to younger women. Small numbers, however, make comparisons difficult (Table 19.7 & Figure 19.1).

Survival by Stage

Table 19.8 and Figure 19.2 show the contrast across stage over time since diagnosis. In stages II-IV, the steepest declines in survival are observed within 2 years of diagnosis. Survival continues to decline throughout the 10years observed in stages I-III, but somewhat stabilizes 5 years after diagnosis in stage IV.

Survival by Stage and Grade

Stages I and II had more well/moderately differentiated tumors and stages III and IV had more poorly/undifferentiated tumors. Grade is found to impact survival in cases diagnosed in stage I, II, and IV (Table 19.9 & Figure 19.3).

Conditional Survival

Five-year relative survival rates, conditioned on years since diagnosis, are presented in Table 19.10 and Figure 19.4. For stages I-IV, the probability of surviving the next 5 years increases as time since diagnosis increases. This is most marked for the stage IV cases. The 5-year relative survival rate from time of diagnosis is 20%. For those individuals who survive 1 year post-diagnosis, 5-year survival increases to 37%. This increases to 91% for those individuals who survive 5 years, albeit few cases survive the first five years to be able to survive the next five years.

DISCUSSION

Cancer of the vagina is a very rare cancer. The comparisons of survival rates between subgroups presented in this

Table 19.8: Cancer of the Vagina: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates by Stage (SEER modified AJCC, 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	1,041	100.0	75.5	62.1	56.4	49.4	43.6	40.7
I	368	35.4	91.0	82.8	76.6	68.4	60.4	55.2
II	236	22.7	83.2	67.1	62.8	54.3	45.2	42.8
III	120	11.5	69.9	54.6	44.7	35.5	27.6	24.8
IV	164	15.8	47.5	31.2	25.5	20.3	18.7	18.4
Unknown/Unstaged	153	14.7	59.5	41.5	35.6	31.7	28.6	28.6

~ Statistic not displayed due to less than 25 cases.

Table 19.9: Cancer of the Vagina: Number of Cases and 5-Year Relative Survival Rates (%) by Stage (SEER modified AJCC, 3rd edition) and Grade, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Grade							
	Total		Well/Moderately Differentiated		Poorly/ Undifferentiated		Unknown	
	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)	Cases	5-Year Relative Survival Rate(%)
Total	1,041	49.4	338	58.7	349	42.5	354	46.6
I	368	68.4	131	76.6	95	60.0	142	65.4
II	236	54.3	97	60.3	81	54.7	58	41.5
III	120	35.5	41	36.3	54	33.0	25	34.6
IV	164	20.3	37	30.0	66	18.7	61	15.7
Unknown/Unstaged	153	31.7	32	30.0	53	24.0	68	37.8

Figure 19.1: Cancer of the Vagina: 5-Year Relative Survival Rate (%) by Age (20+) and Stage (SEER modified AJCC, 3rd edition), 12 SEER Areas, 1988-2001

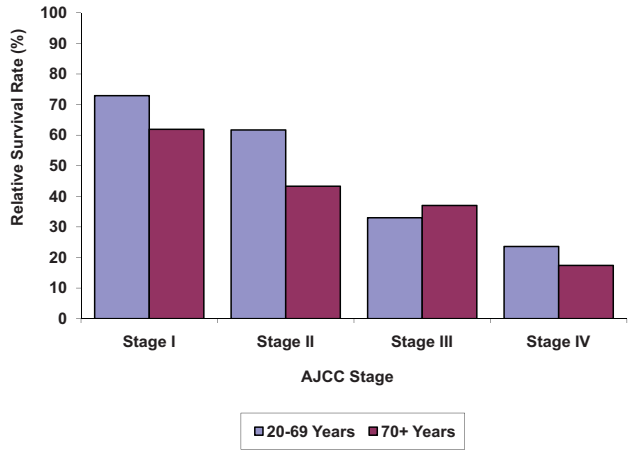


Figure 19.2: Cancer of the Vagina: Relative Survival Rates (%) by Stage (SEER modified AJCC, 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

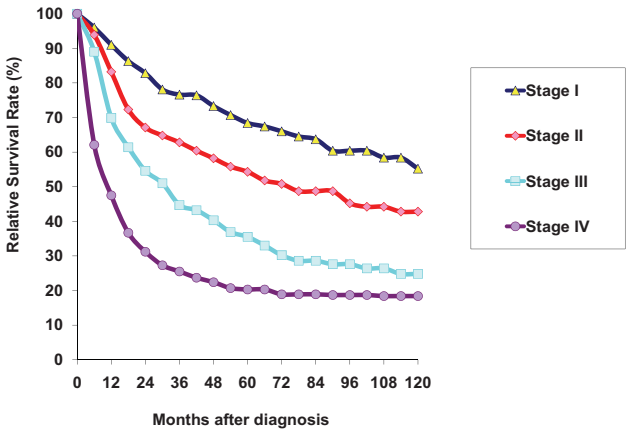


Table 19.10: Cancer of the Vagina: 5-Year Relative Survival Rates (%), Conditioned on Years Since Diagnosis, by AJCC Stage (SEER modified, 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	5-Year Relative Survival Rate (%)					
	Years Since Diagnosis					
	0	1	2	3	4	5
Total	49.4	59.5	69.7	73.8	77.0	79.6
I	68.4	71.5	75.4	77.0	78.8	79.9
II	54.3	60.2	70.1	69.5	73.5	75.1
III	35.5	42.4	51.1	58.9	63.9	70.2
IV	20.3	36.9	57.7	69.7	82.2	91.1
Unknown/Unstaged	31.7	44.9	61.8	73.7	74.9	79.2

Figure 19.3: Cancer of the Vagina: 5-Year Relative Survival Rate (%) by AJCC Stage (SEER modified, 3rd edition) and Grade, Ages 20+, 12 SEER Areas, 1988-2001

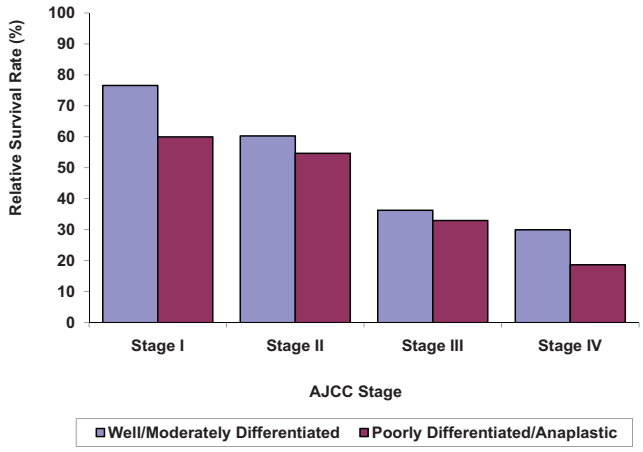
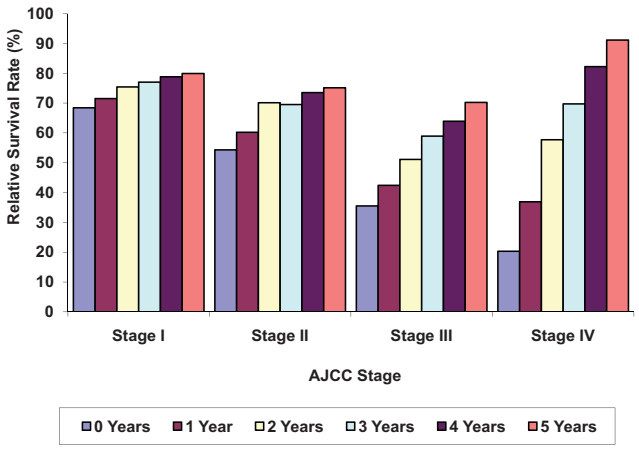


Figure 19.4: Cancer of the Vagina: 5-Year Relative Survival Rate (%), Conditioned on Years Since Diagnosis, by AJCC Stage (SEER modified, 3rd edition), Ages 20+, 12 SEER Areas, 1988-2001



chapter are for descriptive purposes only. As confidence intervals were not included here, interpretation of differences between groups should be made with caution, especially given the rarity of this cancer.

In terms of histologic distribution, approximately two-thirds of these cancers are squamous, 17% are adenocarcinoma, and less than 10% are melanoma. Melanomas have the lowest 5-year survival rate. Black women exhibit a lower survival rate than white women, especially in the age group of 20-69 years.

Over half of cancers of the vagina are diagnosed in stage I and II. Lower survival is seen in women 70 years or older with stages I and II. The steepest decline in relative survival for all stages is during the first 2 to 3 years after diagnosis. The negative impact of advanced tumor grade is seen primarily for stage I, II, and IV survival rates.

REFERENCES

1. Beahrs, OH, Henson DE, Hutter RVP, Myers MH (eds). AJCC Cancer Staging Manual, Third edition. American Joint Committee on Cancer. Philadelphia: Lippincott, 1988.

Chapter 20
Cancer of the Fallopian Tube

Carol L. Kosary

INTRODUCTION

Cancer of the fallopian tube is very rare, accounting for fewer than 1% of all cancers of the female genital organs. In this cancer, tumor develops from cells inside the fallopian tubes. It is much more common for a tumor to metastasize to the fallopian tube from either the ovary or endometrium than for a primary cancer to develop inside the fallopian tube. Even major medical centers may see no more than a handful of cases of fallopian tube cancer over several years. The majority of the cases are diagnosed in women age 50 and older.

MATERIALS AND METHODS

Between 1988 and 2001, there were 1,033 cases of cancer of the fallopian tube diagnosed in SEER. The following were excluded from the analysis: patients for whom fallopian tube cancer was not the first primary, cases identified through autopsy or death certificate only, persons of unknown race, cases without active follow-up or alive with no survival time, patients less than 20 years old, cases without microscopic confirmation, in situ cancers, sarcomas, and carcinoids. After these exclusions, 769 adult cases remained for analysis (Table 20.1).

RESULTS

Age

Among adults, 84% of the cases were diagnosed in women aged 50 and older, with 33% diagnosed in women aged 70 and older (Table 20.2).

Only slight differences are observed in 5-year survival rate by age for ages 50+ (Table 20.2). The 40-49 age group had better survival than the other age groups (Table 20.3). When broader age groups are used, there is a slight decrease in survival as age increases. While the survival rates for black females are based on few cases, the 5-year relative survival rate (73%) was higher than for white females (65%) (Table 20.3).

Geographic Location

Five-year relative survival rates in the 12 SEER areas represented in this study ranged from 76% in San Francisco-Oakland to 50% in San Jose-Monterey, both part of the Greater Bay area (Table 20.4).

Histology

Eighty-seven percent of the cases were categorized as adenocarcinoma (Table 20.5). There is not a substantial difference in survival by histology.

Table 20.1: Cancer of the Fallopian Tube: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
1,033	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
816	217	Select first primary only
810	6	Exclude death certificate only or at autopsy
802	8	Exclude unknown race; children (<20); no microscopic confirmation, carcinoids
802	0	Exclude alive with no survival time
788	14	Exclude in situ cancers
769	19	Exclude sarcomas

Table 20.2: Cancer of the Fallopian Tube: Number and Distribution fo Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Age (20+), 12 SEER Areas, 1988-2001

Age (Years)	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total 20+	769	100.0	93.4	85.1	76.7	64.7	56.7	54.8
20-29	6	0.8	~	~	~	~	~	~
30-39	17	2.2	~	~	~	~	~	~
40-49	98	12.7	99.1	91.6	90.5	73.9	66.6	63.4
50-59	171	22.2	98.2	91.9	78.8	61.8	59.0	52.0
60-69	221	28.7	93.1	80.4	71.7	64.6	56.3	56.3
70-79	192	25.0	86.9	79.8	71.6	58.8	42.6	36.6
80+	64	8.3	88.1	81.2	73.1	61.2	56.3	56.3

Table 20.3: Cancer of the Fallopian Tube: Number of Cases, Median Survival Time (Months) and 5-Year Survival Rates (%) by Race and Age (20+), 12 SEER Areas, 1988-2001

Race/Age (Years)	Cases	Median Survival Time (Months)	5-Year Survival Rate (%)		
			Observed	Expected	Relative
All Races, 20+	769	78.2	58.0	89.7	64.7
White, 20+	677	76.0	58.0	89.5	64.8
Black, 20+	49	> 120	66.4	88.2	72.7
All Races, 20-59	292	> 120	66.7	97.6	68.3
White, 20-59	248	> 120	65.9	97.7	67.5
Black, 20-59	21	~	~	~	~
All Races, 60-69	221	84.9	59.5	92.2	64.6
White, 60-69	189	102.5	60.2	92.5	65.1
Black, 60-69	21	~	~	~	~
All Races, 70+	256	53.7	47.1	78.6	60.0
White, 70+	240	58.2	48.4	78.6	61.5
Black, 70+	7	~	~	~	~

~ Statistic not displayed due to less than 25 cases.

Staging

The Federation Internationale de Gynecologie et d'Obstetrique (FIGO) and the American Joint Committee on Cancer (AJCC) have designated staging for cancers of the Fallopian Tube. The fifth edition of AJCC staging comprises (1):

Stage I: Tumor limited to one or both tubes, with or without ascites

Stage II: Tumor involves one or both tubes with pelvic extension and/or metastasis to the uterus or ovary or extension to other pelvic tissues.

Stage III: Tumor involves one or both tubes with peritoneal implants outside the pelvis and/or regional nodes.

Stage IV: Distant metastasis outside the peritoneal cavity.

Survival by Stage

Women diagnosed at age 60 or older are more likely to be diagnosed in stages III or IV (57%) than are women diagnosed under the age of 60 (42%) (Table 20.6).

Sparse numbers make it difficult to examine survival by stage and age. Five-year survival rates (%) are observed to decline with increased stage at diagnosis from 93% for stage I versus 40% for stage IV (Table 20.7 and Figure 20.1). Within stage, survival generally declines as years since diagnosis increases.

Conditional Survival

Five year relative survival rates, conditioned on years since diagnosis, are presented in Table 20.8 and Figure 20.2. For stages II-IV, increases in the 5-year survival rate are observed between diagnosis and 5 years past diagnosis. That is, the probability of surviving through the next 5 years generally increases as time since diagnosis increases. For women who have already survived five years, the survival rate for the next five years shows

Table 20.4: Cancer of the Fallopian Tube: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by SEER Geographic Area, Ages 20+, 12 SEER Areas, 1988-2001

SEER Geographic Area	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	769	100.0	93.4	85.1	76.7	64.7	56.7	54.8
Atlanta and Rural Georgia	50	6.5	91.8	82.0	72.8	62.7	60.8	55.2
California								
Los Angeles - 1992+	131	17.0	90.9	86.1	83.5	73.0	68.5	68.5
Greater Bay Area	140	18.2	97.3	89.6	83.3	69.5	57.5	57.5
San Francisco-Oakland SMSA - 1988+	99	12.9	99.2	92.7	85.9	76.0	64.2	64.1
San Jose-Monterey - 1988+	41	5.3	91.3	81.9	76.6	49.8	39.1	39.1
Connecticut - 1988+	119	15.5	94.5	84.7	72.4	58.4	49.7	44.6
Detroit (Metropolitan) - 1988+	73	9.5	89.4	81.7	69.8	65.4	52.2	44.5
Hawaii - 1988+	15	2.0	~	~	~	~	~	~
Iowa - 1988+	68	8.8	87.3	76.7	72.1	51.2	40.1	34.0
New Mexico - 1988+	45	5.9	96.5	91.0	79.6	67.0	61.8	60.3
Seattle (Puget Sound) - 1988+	108	14.0	94.2	84.3	73.6	64.6	56.0	56.0
Utah - 1988+	20	2.6	~	~	~	~	~	~

~ Statistic not displayed due to less than 25 cases.

Table 20.5: Cancer of the Fallopian Tube: Number and Distribution of Cases and 5-Year Relative Survival Rates (RSR) (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology	ICD-O Code	Cases	Percent	5-Year RSR (%)
Total	8000-9989	769	100.0	64.7
Squamous	8050-8130	15	2.0	~
Adenocarcinoma	8140-8147,8160-8162,8180-8221,8250-8506,8520-8550,8570-8573,8940-8941	672	87.4	64.3
Other Specified Carcinomas	8030-8045,8150-8155,8170-8171,8230-8248,8510-8512,8560-8562,8580-8671	8	1.0	~
Carcinoma, NOS	8010-8022	44	5.7	72.3
Other Specified Types	8720-8790,8931-8932,8950-8979,8982,9000-9030,9060-9110,9350-9364,9380-9512,9530-9539	27	3.5	67.7
Choriocarcinoma	9100-9101	<6	~	~
All Other Specified Types	8720-8790,8931-8932,8950-8982,9000-9030,9060-9099,9102-9110,9350-9364,9380-9512,9530-9539	22	2.9	~
Unspecified	8000-8004	<6	~	~

~ Statistic not displayed due to less than 25 cases.
* NOS: Not Otherwise Specified

Table 20.6: Cancer of the Fallopian Tube: Number and Distribution of Cases by AJCC Stage (5th Edition) and Age (20+), 12 SEER Areas, 1988-2001

AJCC Stage	Age (Years)					
	Total 20+		20-59		60+	
	Cases	Percent	Cases	Percent	Cases	Percent
Total	769	100.0	292	100.0	477	100.0
I	204	26.5	107	36.6	97	20.3
II	102	13.3	43	14.7	59	12.4
III	81	10.5	30	10.3	51	10.7
IV	259	33.7	69	23.6	190	39.8
Unstaged	123	16.0	43	14.7	80	16.8

Table 20.7: Cancer of the Fallopian Tube: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (5th Editon), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	769	100.0	93.4	85.1	76.7	64.7	56.7	54.8
I	204	26.5	99.3	98.3	96.6	92.9	87.0	85.7
II	102	13.3	98.6	96.7	92.1	74.1	64.6	64.6
III	81	10.5	90.3	83.4	72.8	66.4	57.8	54.0
IV	259	33.7	86.3	68.5	54.8	40.2	32.7	29.8
Unstaged	123	16.0	94.2	88.6	79.1	62.4	47.8	44.3

Table 20.8: Cancer of the Fallopian Tube: 5-Year Relative Survival Rates (%), Conditioned on Years Since Diagnosis, by AJCC Stage (5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	5-Year Relative Survival Rate (%) Years Since Diagnosis					
	0	1	2	3	4	5
Total	64.7	63.5	66.6	73.5	77.5	84.2
I	92.9	89.1	88.2	90.1	93.1	93.0
II	74.1	65.5	66.2	69.6	77.2	86.0
III	66.4	70.9	70.2	81.6	77.3	79.9
IV	40.2	42.2	49.6	58.7	59.1	73.8
Unstaged	62.4	56.1	54.5	59.7	66.9	71.1

much less variation by stage (93% for stage I to 74% for stage IV) than for females at diagnosis whose 5-year relative survival rates ranged from 93% (stage I) to 40% (stage IV).

DISCUSSION

Cancer of the fallopian tube is a very rare cancer. Women 40-49 have better survival than older women. Only small differences in survival between blacks and whites are observed with black females having the better survival. These differences are based on few cases for black females. Stages III and IV are more common in women 60 years and older compared to women less than 60.

REFERENCE

1. Fleming ID, Cooper JS, Henson DE, Hutter RVP, Kennedy BJ, Murphy GP, O'Sullivan B, Sobin LH, Yarbro, JW (eds). AJCC Cancer Staging Manual, Fifth edition, American Joint Committee on Cancer. Philadelphia: Lippincott-Raven, 1997.

Figure 20.1: Cancer of the Fallopian Tube: Relative Survival Rates (%) by AJCC Stage (5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

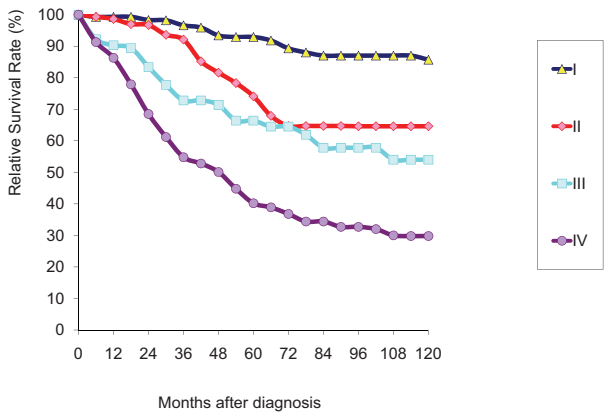
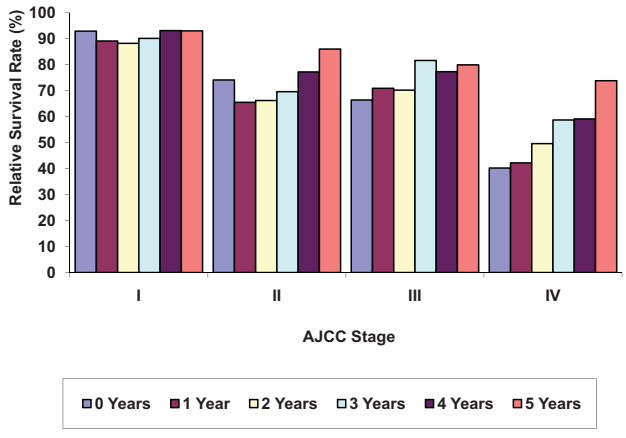


Figure 20.2: Cancer of the Fallopian Tube: 5-Year Relative Survival Rate (%), Conditioned on Years Since Diagnosis, by AJCC Stage (5th Edition), Ages 20+, 12 SEER Areas, 1988-2001



Chapter 21
Cancer of the Testis

Mary L. Biggs and Stephen M. Schwartz

INTRODUCTION

Testicular cancer is a relatively rare cancer, with an estimated 8,250 new cases diagnosed in U.S. men in 2006 (1). Despite the fact that it accounts for only 1% of all malignancies in males, it is the most common malignancy in men aged 20-34, and in the U.S. and most western countries the incidence has more than doubled since the 1940s (2,3). Survival of patients with testicular, particularly those with metastatic disease, has improved significantly since the early 1970's as the result of the development and wide-spread use of cisplatin-containing combination chemotherapy. The 5-year survival rate for testicular cancer patients, including all stages, was 72% in 1970-1973, and 91% for patients diagnosed in 1983-1985 (4). For men diagnosed with testicular cancer during 1992-1998, the 5-yr survival rate was 95% (4), and today, testicular cancer is considered one of the most curable solid neoplasms (5).

MATERIALS AND METHODS

There were 12,978 adult cases of testicular cancer (other than testicular lymphomas) diagnosed from 1988 through 2001 and reported to the SEER program. A detailed description of the source of these data is given in the introductory chapter of this monograph. Table 21.1 shows the numbers of cases excluded from the present analysis, by reason. This chapter describes survival analysis of the remaining 11,606 histologically confirmed, first primary cases of adult testicular cancer diagnosed from 1988 through 2001 and reported to the SEER Program.

Histologic Classification

Germ cell carcinomas comprise the overwhelming majority (98.9%) of adult testicular carcinomas (6). Because non-germ cell testis tumors are uncommon and comprise a heterogeneous group, the focus of the analysis was on germ cell carcinomas. Within the germ cell neoplasms, tumors can be classified, based on pathologic and clinical features, into two broad histologic groups: seminomas and non-seminomas. Seminomas tend to grow more slowly and are very sensitive to radiation therapy, compared to non-seminomas which are more clinically aggressive and do not respond well to radiotherapy (7). Approximately 61% of testicular germ cell carcinomas are pure seminomas with the remainder comprised of non-seminomas (teratomas, embryonal carcinomas, choriocarcinomas, yolk sac tumors), and mixtures of two or more types (8). Germ cell carcinomas were classified using ICD-O-2/ICD-O-3 morphology codes into broad categories of seminoma (ICD 9060-9064) and non-seminoma (ICD 9070-9101), or more narrowly into specific histologic groups: seminoma (ICD 9060-9064), embryonal carcinoma (ICD 9070), yolk sac tumor (ICD 9071), teratoma (ICD 9080, 9082-9084), mixed

Table 21.1: Cancer of the Testis: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
12,978	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
12,528	450	Select first primary only
12,511	17	Exclude death certificate only or at autopsy
12,394	117	Exclude unknown race
12,366	28	Exclude alive with no survival time
11,707	659	Exclude children (Ages 0-19)
11,699	8	Exclude in situ cancers
11,651	48	Exclude no or unknown microscopic confirmation
11,606	45	Exclude sarcomas

germ cell tumor (ICD 9081, 9085, 9101), and choriocarcinoma (ICD 9100).

Stage

Testicular cancers are staged within the SEER data using the categories in situ, localized, regional, distant, and unstaged. Staging information on the cancer is also contained within the 10-digit Extent of Disease (EOD) code, which is based on clinical, operative, and pathologic diagnoses of the cancer. The EOD code encodes tumor size, extension of the tumor into surrounding tissues, and lymph node involvement. We used EOD coding to stage tumors according to the American Joint Committee on Cancer (AJCC) classification system, 5th Edition (9). The SEER modified AJCC stages (5th edition) for testicular cancer are as follows: Stage I (no spread to lymph nodes or distant organs), Stage II (the cancer has spread to regional lymph nodes but not to lymph nodes in other parts of the body or to distant organs), and Stage III (the cancer has spread to non regional lymph nodes and/or to distant organs). We were not able to further subclassify stages (ie., A, B, C) because substaging relies on serum tumor marker data which was not collected by the SEER program prior to 1998.

Tumor Size

Information on tumor size is contained within the 10-digit Extent of Disease (EOD) code. We examined the influence of tumor size (< 5 cm vs. 5+ cm) on relative survival among patients diagnosed with Stage I testicular cancer.

Age & Race

To investigate the impact of age at diagnosis on relative survival, testicular cancer cases were grouped into the following age groups: 20-29, 30-39, 40-49, 50-59, 60-69, 70+. To examine race-specific survival, patients were classified into 3 groups: black, white and all (includes blacks, whites, and all other races).

RESULTS

Table 21.2 shows the frequency of testicular cancer cases classified by histology and age at diagnosis. Seminomas comprised the largest histologic group (61.1%). Germ cell tumors of mixed histologic types comprised the next largest group (23.2%). Non-germ cell and unspecified tumors comprised 1% of eligible tumors. More than 72% of the testicular cancer cases were diagnosed between the ages of 20-39. For men diagnosed with seminomas, the peak frequency occurred in the 30-39 year age group, while for men diagnosed with non-seminomas it was among 20-29 year olds.

Three-quarters of all men with testicular carcinomas were diagnosed in Stage I (Table 21.3). However, the proportion of tumors diagnosed at early and late stages varied with the histologic type of the tumor. The largest proportion of testis tumors diagnosed in Stage I were seminomas (85.8%). Choriocarcinomas had the smallest proportion of Stage I tumors (20.7%) and the largest proportion of Stage III tumors (74.1%).

Overall Survival

Overall, survival among men diagnosed with testicular cancer was very high. Relative survival rate was 98% at 1 year following diagnosis, 97% at 2 years, 96% at 5 year, and 95% at 10 years after diagnosis (Table 21.4).

Histology

The relative survival rate varied with the histologic type of the tumor (Figure 21.1). The highest survival rate was observed for men diagnosed with pure seminomas; 10-year relative survival was 98. The 10-year relative survival

Table 21.2: Cancer of the Testis: Number and Distribution of Cases by Histology and Age (20+), 12 SEER Areas, 1988-2001

	Age (Years)							
	Total		20-29	30-39	40-49	50-59	60-69	70+
Histology	Cases	Percent	Cases	Cases	Cases	Cases	Cases	Cases
Total	11,606	100.0	3,663	4,746	2,329	581	196	91
Germ Cell	11,480	98.9	3,639	4,710	2,307	563	183	78
Seminomas	7,086	61.1	1,471	3,137	1,802	455	153	68
Non-seminomas	4,394	37.9	2,168	1,573	505	108	30	10
Embryonal	1,315	11.3	624	479	164	36	8	<5
Yolk Sac	126	1.1	56	46	17	<5	<5	<5
Teratoma	203	1.7	117	62	21	<5	0	<5
Mixed Germ Cell	2,692	23.2	1,344	968	294	65	17	<5
Choriocarcinoma	58	0.5	27	18	9	<5	<5	0
Non-Germ Cell and Unspecified	126	1.1	24	36	22	18	13	13

Table 21.3: Cancer of the Testis: Number and Distribution of Cases by Histology and AJCC Stage (SEER modified 5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

	AJCC Stage									
	Total		I		II		III		Unknown/ Unstaged	
Histology	Cases	Percent	Cases	Row Percent	Cases	Row Percent	Cases	Row Percent	Cases	Row Percent
Total	11,606	100.0	8,847	76.2	1,343	11.6	1,214	10.5	202	1.7
Germ Cell	11,480	100.0	8,781	76.5	1,340	11.7	1,175	10.2	184	1.6
Seminomas	7,086	100.0	6,077	85.8	507	7.2	393	5.5	109	1.5
Non-seminomas	4,394	100.0	2,704	61.5	833	19.0	782	17.8	75	1.7
Embryonal	1,315	100.0	728	55.4	339	25.8	226	17.2	22	1.7
Yolk Sac	126	100.0	72	57.1	18	14.3	34	27.0	<5	1.6
Teratoma	203	100.0	145	71.4	27	13.3	24	11.8	7	3.4
Mixed Germ Cell	2,692	100.0	1,747	64.9	449	16.7	455	16.9	41	1.5
Choriocarcinoma	58	100.0	12	20.7	0	0.0	43	74.1	<5	5.2
Non-Germ Cell and Unspecified	126	100.0	66	52.4	<5	2.4	39	31.0	18	14.3

rate for non-seminomas was lower, 91% (Table 21.4), but varied by histologic type from 46% for choriocarcinoma to 92% for embryonal tumors and mixed germ cell tumors (Figure 21.1).

Stage and histology

Testicular cancer relative survival decreased with increasing stage at diagnosis. Ten-year relative survival rates were over 95% for both Stage I and Stage II. When comparing tumors diagnosed at the same stage, survival rates for seminomas and non-seminomas were similar, with the exception of tumors diagnosed at Stage III (Table 21.4). Among men diagnosed with advanced disease, those diagnosed with seminomas had substantially better 2-, 3-, 5-, 8-, and 10- year survival rates than men diagnosed with non-seminomas.

Tumor size

Relative survival of patients diagnosed with Stage I testicular cancer was higher for those with tumors smaller than 5 cm compared to patients diagnosed with tumors that were 5 cm or larger (Table 21.5). Size accounted for more of a survival difference for non-seminomas than seminomas, but 10-year survival rates were over 92% even for non-seminomas 5 cm and over.

Age at Diagnosis

Among men diagnosed with seminomas, those aged 20-49 had similar, though slightly higher, survival to those over 50 years (Fig. 21.2). Among men with non-seminomas, the difference in survival between the two age groups was more pronounced: 2-year survival rate was 95% in the younger age group versus 84% in the older one; 5-year survival rate was 93% in the 20-49 age group versus 79% in those over 50 years of age. The distribution of stage at diagnosis of testicular tumors was similar among men aged 20-49 and those aged 50+ (results not shown).

Race

For seminomas, survival was slightly less among black men than among white men (Fig. 21.3). The disparity was more marked among men diagnosed with non-seminomas; 5-year relative survival rate was 93% among white men diagnosed with non-seminomas compared to 75% among black men. The distribution of specific histologic types did not vary appreciably by race (results not shown).

Race and Stage

Black men were more likely to be diagnosed with higher stage germ cell carcinomas compared to white men (Table 21.6). For any given stage, the relative survival rate among black men was poorer than survival rate among white men (Table 21.7). The racial disparity was most pronounced among patients diagnosed in Stage III; 5-year relative survival rate among white men was 75% compared to 58% among black men. Black men had larger tumors, on average, than white men diagnosed at the same stage (results not shown).

DISCUSSION

Overall, the survival rates for patients diagnosed with testicular cancer during 1988-2001 was excellent, with 95% surviving 10 years. Improvements in treatment, the most dramatic resulting from the introduction of cisplatin-containing combination chemotherapy in the 1970's, have

Table 21.4: Germ Cell Carcinoma of the Testis: Number of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 5th Edition) and Histology, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage/Histology	Cases	Relative Survival Rate (%)					
		1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	11,480	98.2	96.8	96.2	96.0	95.4	95.3
Seminomas	7,086	99.0	98.4	98.1	98.0	97.7	97.7
Non-seminomas	4,394	96.8	94.2	93.2	92.6	91.8	91.3
Stage I	8,781	99.8	99.4	99.0	99.0	98.6	98.5
Seminomas	6,077	100.0	99.7	99.5	99.5	99.4	99.4
Non-seminomas	2,704	99.5	98.5	97.8	97.5	96.8	96.5
Stage II	1,340	98.5	97.0	96.5	96.1	95.5	95.2
Seminomas	507	98.4	96.8	96.3	95.9	95.1	95.1
Non-seminomas	833	98.5	97.1	96.6	96.0	95.7	94.9
Stage III	1,175	85.8	78.1	75.3	74.0	71.5	71.1
Seminomas	393	85.9	81.9	79.3	78.5	75.2	74.7
Non-seminomas	782	85.7	76.2	73.3	71.7	69.7	68.7
Unknown/Unstaged	184	97.4	94.9	93.9	93.1	93.1	93.1
Seminomas	109	96.5	94.0	93.2	93.2	93.2	93.2
Non-seminomas	75	98.7	96.2	95.0	92.2	92.2	92.2

Table 21.5: Stage I Germ Cell Carcinoma of the Testis: Number of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Histology and Tumor Size, Ages 20+, 12 SEER Areas, 1988-2001

Histology/Tumor Size	Cases	Relative Survival Rate (%)					
		1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Germ Cell	8,781	99.8	99.4	99.0	99.0	98.6	98.5
< 5 cm	5,166	100.0	99.8	99.8	99.8	99.8	99.8
5+ cm	2,321	99.6	98.8	97.9	97.6	96.8	96.4
Unknown	1,294	99.3	98.4	97.3	97.0	96.0	95.5
Seminomas	6,077	100.0	99.7	99.5	99.5	99.4	99.4
< 5 cm	3,497	100.0	100.0	100.0	100.0	100.0	100.0
5+ cm	1,671	99.8	99.3	98.6	98.4	97.9	97.8
Unknown	909	99.4	98.9	98.3	98.1	96.9	96.6
Non-seminomas	2,704	99.5	98.5	97.8	97.5	96.8	96.5
< 5 cm	1,669	99.7	99.2	99.1	99.1	98.9	98.9
5+ cm	650	99.1	97.6	96.0	95.3	93.0	92.4
Unknown	385	98.8	97.3	95.0	94.0	93.7	92.5

Figure 21.1: Cancer of the Testis: Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

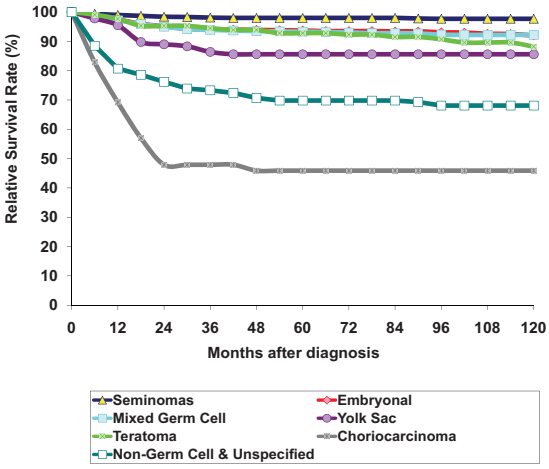


Figure 21.2: Cancer of the Testis: Relative Survival Rates (%) Histology and Age Group (20+), 12 SEER Areas, 1988-2001

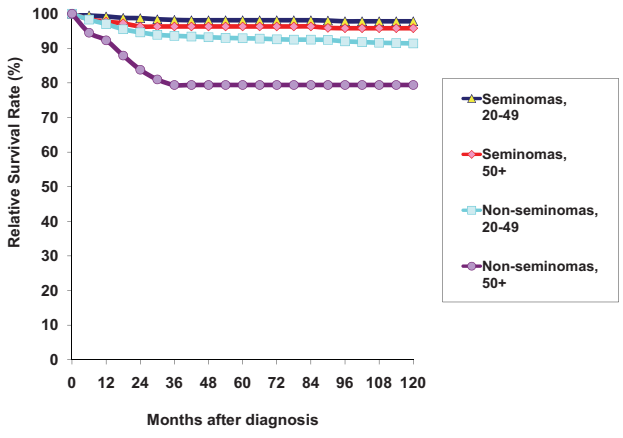


Table 21.6: Germ Cell Carcinoma of the Testis: Number and Distribution of Cases by AJCC Stage (SEER modified 5th Edition) and Race, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Race					
	Total		White		Black	
	Cases	Percent	Cases	Percent	Cases	Percent
Total	11,480	100.0	10,711	100.0	250	100.0
Stage I	8,781	76.5	8,208	76.6	181	72.4
Stage II	1,340	11.7	1,253	11.7	30	12.0
Stage III	1,175	10.2	1,073	10.0	36	14.4
Unknown/ Unstaged	184	1.6	177	1.7	3	1.2

led to improved survival and declining mortality over the past 30 years (5).

Survival of patients with testicular cancer varied by the histologic type of the tumor, and differences in stage at diagnosis are likely to have contributed to this variation. Patients diagnosed with pure seminomas (predominantly diagnosed in Stage I) had the best survival; 10-year survival was 98%. Compared to those with seminomas, patients diagnosed with non-seminomas tended to be diagnosed with a more advanced stage of disease and had poorer survival, reflecting the more clinically aggressive nature of non-seminomas. Patients diagnosed with choriocarcinomas (largely diagnosed in Stage III) had the poorest survival.

Among non-seminoma testicular cancer patients diagnosed at Stage I, tumor size was related to survival. Patients diagnosed with tumors smaller than 5 cm experienced better relative survival than those diagnosed with tumors that were 5 cm or larger. For Stage I non-seminomas, the five-year survival among those with smaller tumors (< 5 cm) was 99% compared to 95% for patients diagnosed with larger tumors (5+ cm).

The age at diagnosis of testicular cancer had an impact on survival, particularly among men diagnosed with non-seminomas. Men diagnosed with non-seminomas between the ages of 20 and 49 had a 5-year survival of 93%, compared to 79% for those aged 50 and above. Stage at diagnosis was similar between younger and older men and could not account for the difference in survival observed.

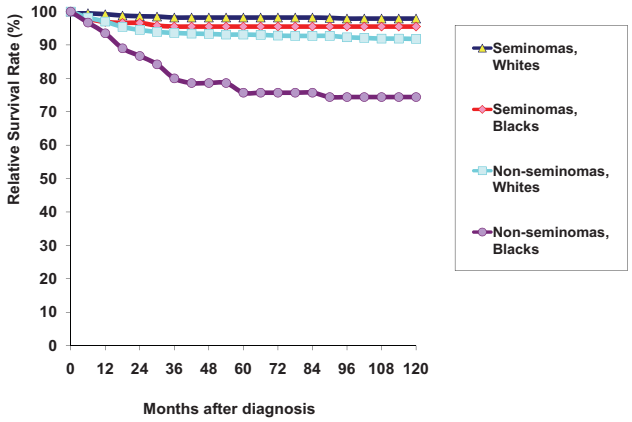
Testicular cancer survival also depended on the race of the patient, with black men experiencing poorer survival than white men. The differences in race-specific survival were partially explained by disease stage at diagnosis; compared to whites, a higher proportion of black men were diagnosed with advanced-stage disease. However, even when comparing men diagnosed at the same stage, survival was worse among black men compared to white men. The disparity in survival was particularly apparent among patients diagnosed with Stage III cancer; 5-year survival among men diagnosed with Stage III testicular cancer was 75% in white men compared to 58% in black men. The survival differential may be related to the larger average tumor size in black men, reflecting more advanced disease not captured in the 3-category staging classification that we used. Using these data, we were unable to explore the possible reasons for black men presenting with more advanced disease, nor whether this fully accounted for the survival differential between black and white testicular cancer patients.

Table 21.7: Germ Cell Carcinoma of the Testis: Number of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 5th Edition) and Race, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage/Race		Relative Survival Rate (%)					
	Cases	1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Germ Cell	11,480	98.2	96.8	96.2	96.0	95.4	95.3
White	10,711	98.4	97.0	96.4	96.2	95.7	95.6
Black	250	95.8	93.5	90.2	89.7	89.7	89.7
Stage I	8,781	99.8	99.4	99.0	99.0	98.6	98.5
White	8,208	99.8	99.4	99.1	99.0	98.7	98.6
Black	181	99.3	99.1	95.6	95.6	95.6	95.6
Stage II	1,340	98.5	97.0	96.5	96.1	95.5	95.2
White	1,253	98.8	97.4	96.9	96.6	96.1	95.6
Black	30	97.1	93.8	90.3	86.1	86.1	86.1
Stage III	1,175	85.8	78.1	75.3	74.0	71.5	71.1
White	1,073	86.5	79.0	76.1	74.9	72.8	72.2
Black	36	75.5	63.7	60.6	57.5	54.2	54.2
Unknown/Unstaged	184	97.4	94.9	93.9	93.1	93.1	93.1
White	177	97.3	94.7	93.6	92.7	92.7	92.7
Black	3	~	~	~	~	~	~

~ Statistic not displayed due to less than 25 cases.

Figure 21.3: Cancer of the Testis: Relative Survival Rates (%) by Histology and Race, Ages 20+, 12 SEER Areas, 1988-2001



While survival of patients with testicular cancer is quite favorable in the 10 years following diagnosis, recent reports describe the occurrence of adverse health effects in long-term survivors more than 10 years after diagnosis. These include an increased risk of secondary malignant neoplasms (10) and cardiovascular events (11), some of which have been attributed to the radiation and chemotherapy treatments received by patients. Circulating levels of cisplatin may be detectable up to 20 years following treatment (12), for example. Given the early age of diagnosis and long life expectancy of most testicular cancer patients, consideration of these late effects is particularly important. Concern over long-term health effects, as well as more immediate quality-of-life issues (for instance, preservation of fertility) has led to the adoption of more conservative treatment regimens to minimize treatment-related morbidity. While in the past, patients with Stage I testis tumors routinely received additional treatment following orchiectomy, surgery followed by active surveillance alone is now a standard treatment option (13). Five-year survival rates for patients placed under active surveillance after orchiectomy as treatment for clinical Stage I seminomas appear to be comparable to those of patients treated with adjuvant radiation therapy (14-16). Similarly, 5-year survival does not appear to differ between patients undergoing retroperitoneal lymph node dissection (RPLND) and those entering a surveillance protocol after orchiectomy as treatment for clinical Stage I nonseminomatous testicular cancer (16,17).

In summary, testicular carcinoma remains one of the most highly curable malignant neoplasms. Additional research is needed to understand the reasons for the differences in the stage distribution of tumors according to race and the poorer survival of black patients and older patients, so that approaches to eliminating survival differences can be developed.

REFERENCES

1. American Cancer Society. Cancer Facts & Figures 2006. 2006.
2. Brown LM, Pottern LM, Hoover RN, Devesa SS, Aselton P, Flannery JT. Testicular cancer in the United States: trends in incidence and mortality. Int J Epidemiol 1986; 15:164-70.
3. Bergstrom R, Adami HO, Mohner M, Zatonski W, Storm H, Ekbom A, et al. Increase in testicular cancer incidence in six European countries: a birth cohort phenomenon. J Natl Cancer Inst 1996; 88:727-33.
4. Ries LAG, Kosary CL, Hankey BF, Miller BA, Clegg L, Edwards BK, eds. SEER Cancer Statistics Review, 1973-1999. Bethesda, MD: National Cancer Institute, 2002.
5. Einhorn LH. Curing metastatic testicular cancer. Proc Natl Acad Sci U S A 2002; 99:4592-5.
6. Schottenfeld D. Testicular cancer. In: Schottenfeld D, Fraumeni JF Jr., eds. Cancer Epidemiology and Prevention. New York: Oxford University Press, 1996: 1207-19.
7. Cotran RS, Kumar V, Collins T. Robbins Pathologic Basis of Disease. Philadelphia, PA: W.B. Saunders Company, 1999: 1023.
8. Bosl GJ, Motzer RJ. Testicular germ-cell cancer [published erratum appears in N Engl J Med 1997 Nov 6;337(19):1403]. N Engl J Med 1997; 337:242-53.
9. Fleming ID, Cooper JS, Henson DE, Hutter RVP, Kennedy BJ, Murphy GP, et al. Eds. AJCC Cancer Staging Manual. 5th edition. Philadelphia: Lippincott-Raven, 1997.
10. Travis LB, Curtis RE, Storm H, Hall P, Holowaty E, Van Leeuwen FE, et al. Risk of second malignant neoplasms among long-term survivors of testicular cancer. J Natl Cancer Inst 1997; 89:1429-39.
11. Meinardi MT, Gietema JA, van der Graaf WT, van Veldhuisen DJ, Runne MA, Sluiter WJ, et al. Cardiovascular morbidity in long-term survivors of metastatic testicular cancer. J Clin Oncol 2000; 18:1725-32.
12. Gietema JA, Meinadi MT, Messerschmidt J, Gelevert T, Alt F, Uges DRA, et al. Citrlating plasma platinum more than 10 years after cisplatin treatment for testicular cancer. Lancet 2000; 355:1075-6.
13. National Cancer Institute. Physician Data Query(PDQ). (TM). Available at: http://www.nci.nih.gov/cancerinfo/pdq/. Updated August 14, 2002.
14. Warde P, Gospodarowicz MK, Banerjee D, Panzarella T, Sugar L, Catton CN, et al. Prognostic factors for relapse in stage I testicular seminoma treated with surveillance. J Urol 1997; 157:1705-9; discussion 1709-10.
15. Gospodarwicz MK, Sturgeon JF, Jewett MA. Early stage and advanced seminoma: role of radiation therapy, surgery, and chemotherapy. Semin Oncol 1998; 25:160-73.
16. Francis R, Bower M, Brunstrom G, Holden L, Newlands ES, Rustin GJ, et al. Surveillance for stage I testicular germ cell tumours: results and cost benefit analysis of management options. Eur J Cancer 2000; 36:1925-32.
17. Spermon JR, Roeleveld TA, van der Poel HG, Hulsbergen-van de Kaa CA, Ten Bokkel Huinink WW, van de Vijver M, et al. Comparison of surveillance and retroperitoneal lymph node dissection in Stage I nonseminomatous germ cell tumors. Urology 2002; 59:923-9.

Chapter 22
Cancer of the Prostate

Ann Hamilton and Lynn A. Gloeckler Ries

INTRODUCTION

This study provides survival analyses for 275,280 histologically confirmed adult cases of prostate cancer diagnosed from 1988 through 2001. Cases were obtained from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). The SEER Program -- a sequel to two earlier NCI initiatives, the End Results Program and the Third National Cancer Survey -- has evolved in response to the National Cancer Act of 1971, which requires the collection, analysis, and dissemination of data relevant to the prevention, diagnosis, and treatment of cancer. This study analyzes the influence of clinical extent of disease, histologic grade, age at diagnosis, race/ethnicity, SEER registry, and type of therapy on prostate cancer survival.

MATERIALS AND METHODS

The NCI contracts with medically oriented nonprofit institutions -- such as universities and state health departments -- to obtain data on all cancers diagnosed in residents of the SEER geographic areas. SEER collects data on all invasive and in situ cancers except basal cell and squamous cell carcinomas of the skin and in situ carcinoma of the uterine cervix.

SEER selects participating institutions on the basis of two criteria: their ability to operate and maintain a population-based cancer reporting system and the epidemiologic significance of their population subgroups. At times, registries will withdraw; at times, registries will be added. This analysis is based on data from 12 SEER geographic areas, which collectively contain about 14% of the total US population. The areas are the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Atlanta, San Francisco, Seattle, San Jose, and Los Angeles; and 10 counties in rural Georgia. Los Angeles contributed data for diagnosis years 1992 to 2001, the others for 1988 to 2001

To ensure maximal ascertainment of cancer cases, each registry abstracts the records of all cancer patients in hospitals, laboratories, and all other health service units that provide diagnostic services. Data collected by SEER registries on each patient include patient demographics, primary tumor site, tumor morphology, diagnostic methods, extent of disease, and first course of cancer-directed therapy. A separate record is coded for each primary cancer. All patients are followed from diagnosis to death, allowing detailed survival analysis.

SEER has collected site-specific extent of disease (EOD) information on all cancers since the inception of the program in 1973. Major changes to EOD were made in 1988 to be compatible with the American Joint Committee on Cancer (AJCC) *Manual for Staging of Cancer*, third edition (1). For prostate cancer, this meant that the extension information was based mainly on results from transurethral resection of the prostate (TURP) and clinical information. In 1994, the prostate EOD schema underwent a major rewrite to attempt to capture both clinical and pathologic assessment of the extension of the tumor to be compatible with the AJCC 4th edition (2). The 4th edition introduced "T1c, tumor identified by a needle biopsy (e.g., because of elevated PSA)" (2). Since the 1994 EOD extension codes were so complicated, it was decided to split the extension information into two fields: one a clinical assessment and the other a pathologic assessment based only on prostatectomy results beginning with cases diagnosed in 1995. In 1998, the AJCC published the 5th edition of the AJCC staging manual (3). Even though there were changes between the 4th and 5th editions, the SEER EOD schemas had enough detail to be converted to either the 4th or 5th edition for cases diagnosed 1995 and forward. The prostate EOD codes can be translated to other staging schemes (AUS, AJCC) and a mapping for extension codes of the EOD is presented in Table 22.1. Therefore, for staging data comparable to AJCC 5th edition, the analyses was limited to only 1995-2001 but for tables/figures which did not contain AJCC 5th edition stage,

Table 22.1: SEER Prostate EOD codes for Clinical Stage, by Year of Diagnosis

SEER Description of Extent of Disease	Approximate correspondence to		SEER EOD Codes used for cases diagnosed during:		
	AUS	AJCC T category, 5th ed.	1988-93	1994	1995-2001
Local Disease					
Clinically inapparent tumor not palpable by imaging; incidentally found microscopic carcinoma in one or both lobes					
Number of foci or % of involved tumor not specified	A, NOS	T1x	10	10	10
≤ 3 microscopic foci	A1 focal		11	11	11
> 3 microscopic foci	A1 diffuse		12	12	12
Incidental histologic finding in 5% or less of tissue resected		T1a	--	13	13
Incidental histologic finding in more than 5% of tissue resected.		T1b	--	14	14
Tumor identified by needle bx, e.g. for elevated PSA		T1c	--	15	15
Clinically/radiographically apparent					
Involvement of one lobe, NOS	B	T2a	20	20,23	20
½ or less of one lobe involved	B	T2a		21,24	21
More than ½ of one lobe involved, not both lobes	B	T2b		22,26	22
More than one lobe involved	B2	T2b , T2c (6th edition)	25	25,28	23
Clinically apparent tumor confined to prostate, NOS	B,NOS	T2,NOS		27,29	24
Localized, Unknown if apparent or inapparent					
Localized, NOS confined to prostate (not stated if clinically apparent or inapparent)	A,B	T1,T2	30	30,31	30
Into capsule/apex, but still localized					
Into prostatic apex/ arising in apex				48,49	31,33
Extension into apex/arising elsewhere					34
Invasion into (but not beyond) prostatic capsule			40	40,41	32
Regional Disease					
Extension to periprostatic tissue, extracapsular extension (beyond prostatic capsule) NOS, Through capsule, NOS	C1	T3, NOS	50	50	41
Unilateral extracapsular extension		T3a	50	51	42
Bilateral extracapsular extension		T3b	50	52	43
Extraprostatic urethra			50	53	44
Extension to seminal vesicles	C2	T3c	55	55	45
Periprostatic extension , NOS			56	56	49
Extension to or fixation to adjacent structures other than seminal vesicles		T4, NOS	60	60	50
Extension to bladder neck		T4a		61	51
Extension to rectum, external sphincter of rectum		T4a		62	52
Distant Disease					
Extension to levator muscles, skeletal muscle		T4b		65	53
Extension to or fixation to pelvic wall or bone		T4b		70	60
Extension to of fixation to other skeletal muscle					61
Further extension to bone, soft tissue, or other organs	D2			80	70
Metastasis, NOS	D2		85	85	85
Unknown if extension or metastasis			99	99	90

Table 22.2: Cancer of the Prostate: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
318,776	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
290,881	27,895	Select first primary only
288,213	2,668	Exclude death certificate only or at autopsy
282,703	5,510	Exclude unknown race
282,412	291	Exclude alive with no survival time
282,392	20	Exclude children (Ages 0-19)
282,219	173	Exclude in situ cancers for all except breast & bladder cancer
275,327	6,892	Exclude no or unknown microscopic confirmation
275,280	47	Exclude sarcomas

the analyses used 1988-2001 data. For 1988-2001, the EOD data were converted to a more simplistic staging system of localized (confined to the prostate); regional (extension beyond the prostate by direct extension and/or involvement of regional nodes), and distant disease (metastasis). A comparison of the three sets of EOD codes and stage is shown in Table 22.1.

Relative Survival

The survival analysis is based on relative survival rates calculated by the life-table method. The relative rate is used to estimate the effect of cancer on the survival of the cohort. Relative survival, defined as observed survival divided by expected survival, adjusts for the expected mortality that the cohort would experience from other causes of death. When the 5-year relative survival is 100%, for example, a patient has the same chance to live 5 more years as a cancer-free person of the same race, age and sex.

Exclusions

The following cases were excluded from the analysis (as shown in Table 22.2): patients for whom prostate cancer was not the first primary, cases identified through autopsy or death certificate only, persons of unknown race, cases without active follow-up, patients less than 20 years old, in situ cases, cases without microscopic confirmation, and sarcomas. After the exclusions, there were 275,280 prostate cases for analysis.

RESULTS

Characteristics of Cases

During the 14-year period (1988-2001) during which these cases were diagnosed, 42% were aged 65-74 at diagnosis compared to 29% 20-64 and 29% aged 75 or over (Table 22.3). Blacks had a higher proportion of cases in the youngest age group compared to whites. Eighty-eight percent of all cases were diagnosed with localized disease, 3% had regional disease, 4% had distant disease, and another 4% had unknown stage of disease. Blacks had a higher proportion with distant disease and unknown stage than did whites (Table 22.4). The majority of all cases (60%), had tumors that were graded as moderately differentiated (Gleason Score 5-7) (Table 22.3).

Relative Survival by Stage of Disease

Stage of disease at diagnosis is a critical determinant of relative survival among prostate cancer cases. Among all cases, there is 100% relative survival rate at 1, 2, 3, 4, and 5 years after diagnosis (Table 22.4). Blacks fared slightly worse than whites after 3 years from diagnosis. The distribution of cases by stage at diagnosis, will affect the overall group's relative survival rate and blacks had a higher proportion of distant disease cases than whites (Table 22.3), which may contribute to their slightly lower survival. For localized disease, white males and black males had 100% survival through the first 5-years after diagnosis. A 100% relative survival rate does not mean that no men will die from prostate cancer but rather that they do not have excess mortality compared to comparably aged men of the same race. For regional disease, there is a 6 percentage point difference between whites (90%) and blacks (84%) at 5 years. Among those with distant disease, both groups did poorly, approximately 35% survived 5-years (Table 22.4). Figure 22.1 shows the continuous relative survival curve by stage of disease by race over the years after diagnosis.

Relative survival by stage of disease is shown by age at diagnosis in Table 22.5. Men diagnosed under 65 years of age tended to have worse survival for distant disease, than did those diagnosed between 65 and 74 years of age.

Table 22.3: Cancer of the Prostate: Number and Distribution of Cases by Age (20+), Clinical Stage, Grade, and Geographic Area by Race, 12 SEER Areas, 1988-2001

Characteristics	Total		Race			
			White		Black	
	Cases	Percent	Cases	Percent	Cases	Percent
Total	275,280	100.0	227,239	100.0	33,010	100.0
Age (Years)						
20-64	79,778	29.0	64,029	28.2	12,728	38.6
65-74	116,555	42.3	96,869	42.6	13,157	39.9
75+	78,947	28.7	66,341	29.2	7,125	21.6
Clinical Stage of Disease (1995-2001)						
All Stages 1995-2001	150,949	100.0	122,047	100.0	19,686	100.0
All Localized Disease	133,163	88.2	108,522	88.9	16,802	85.3
Clinically inapparent, detected by PSA (T1c)	44,371	29.4	35,781	29.3	6,008	30.5
Other clinically inapparent	8,733	5.8	7,299	6.0	946	4.8
Clinically apparent but confined to prostate	39,884	26.4	32,813	26.9	4,534	23.0
Localized but unknown if apparent or inapparent	17,187	11.4	14,753	12.1	1,939	9.8
Into capsule/apex, but still localized	22,988	15.2	17,876	14.6	3,375	17.1
Regional Disease	5,076	3.4	4,021	3.3	645	3.3
Distant Disease	6,660	4.4	4,864	4.0	1,162	5.9
Unknown Stage	6,050	4.0	4,640	3.8	1,077	5.5
Grade						
Well differentiated; Grade I	34,012	12.4	28,932	12.7	3,276	9.9
Moderately differentiated; Grade II	166,041	60.3	138,415	60.9	19,679	59.6
Poorly differentiated; Grade III	57,270	20.8	45,481	20.0	7,368	22.3
Undifferentiated; anaplastic; Grade IV	1,675	0.6	1,403	0.6	200	0.6
Unknown Grade	16,282	5.9	13,008	5.7	2,487	7.5
Geographic Area						
Atlanta and Rural Georgia	17,681	6.4	12,179	5.4	5,352	16.2
Atlanta (Metropolitan)	16,855	6.1	11,703	5.2	5,004	15.2
Rural Georgia	826	0.3	476	0.2	348	1.1
California						
Los Angeles	45,893	16.7	34,930	15.4	7,624	23.1
Greater Bay Area	44,628	16.2	36,158	15.9	4,418	13.4
San Francisco-Oakland SMSA	30,417	11.0	23,517	10.3	3,984	12.1
San Jose-Monterey	14,211	5.2	12,641	5.6	434	1.3
Connecticut	30,029	10.9	27,542	12.1	2,294	6.9
Detroit (Metropolitan)	42,550	15.5	30,917	13.6	11,401	34.5
Hawaii	8,469	3.1	2,690	1.2	94	0.3
Iowa	25,919	9.4	25,527	11.2	357	1.1
New Mexico	13,002	4.7	12,436	5.5	241	0.7
Seattle (Puget Sound)	32,812	11.9	30,764	13.5	1,151	3.5
Utah	14,297	5.2	14,096	6.2	78	0.2

Total includes other races in addition to White and Black; Based on year of diagnosis and EOD code as shown in Table 22.1

Table 22.4: Cancer of the Prostate: Number and Distribution of Cases and 1-, 2-, 3-, 4-, & 5-Year Relative Survival Rates (%) by Clinical Stage and Race, Ages 20+, 12 SEER Areas, 1995-2001

Race/Stage	Cases	Percent	Relative Survival Rate (%)				
			1-Year	2-Year	3-Year	4-Year	5-Year
All Races	150,949	100.0	100.0	100.0	100.0	100.0	100.0
All Localized Disease	133,163	88.2	100.0	100.0	100.0	100.0	100.0
Clinically inapparent, detected by PSA (T1c)	44,371	29.4	100.0	100.0	100.0	100.0	100.0
Other clinically inapparent	8,733	5.8	99.9	99.9	99.7	98.2	97.9
Clinically apparent by confined to prostate	39,884	26.4	100.0	100.0	100.0	100.0	100.0
Local but unknown if apparent or inapparent	17,187	11.4	100.0	100.0	100.0	100.0	100.0
Into capsule/apex, but still localized	22,988	15.2	100.0	100.0	100.0	100.0	100.0
Regional Disease	5,076	3.4	99.8	96.9	94.4	91.7	88.7
Distant Disease	6,660	4.4	81.7	61.5	50.1	42.5	36.5
Unknown	6,050	4.0	97.5	94.3	91.9	90.0	87.1
White	122,047	100.0	100.0	100.0	100.0	100.0	100.0
All Localized Disease	108,522	88.9	100.0	100.0	100.0	100.0	100.0
Clinically inapparent, detected by PSA (T1c)	35,781	29.3	100.0	100.0	100.0	100.0	100.0
Other clinically inapparent	7,299	6.0	100.0	100.0	99.8	98.4	98.0
Clinically apparent by confined to prostate	32,813	26.9	100.0	100.0	100.0	100.0	100.0
Local but unknown if apparent or inapparent	14,753	12.1	100.0	100.0	100.0	100.0	100.0
Into capsule/apex, but still localized	17,876	14.6	100.0	100.0	100.0	100.0	100.0
Regional Disease	4,021	3.3	99.9	97.0	94.8	92.3	89.6
Distant Disease	4,864	4.0	81.2	61.1	49.6	42.2	35.5
Unknown	4,640	3.8	97.7	95.1	93.0	91.5	88.4
Black	19,686	100.0	100.0	99.3	99.1	98.5	98.1
All Localized Disease	16,802	85.3	100.0	100.0	100.0	100.0	100.0
Clinically inapparent, detected by PSA (T1c)	6,008	30.5	100.0	100.0	100.0	100.0	100.0
Other clinically inapparent	946	4.8	99.4	99.4	99.2	96.6	96.6
Clinically apparent by confined to prostate	4,534	23.0	100.0	100.0	100.0	100.0	100.0
Local but unknown if apparent or inapparent	1,939	9.8	100.0	100.0	100.0	100.0	100.0
Into capsule/apex, but still localized	3,375	17.1	100.0	100.0	100.0	100.0	100.0
Regional Disease	645	3.3	98.6	95.7	90.3	88.3	83.8
Distant Disease	1,162	5.9	80.5	58.9	46.7	38.4	35.1
Unknown	1,077	5.5	97.0	91.8	88.1	84.6	81.3

Relative Survival by Geographic Area

The SEER Registries contributing over 15% of the cases each included Detroit and Los Angeles (which included cases from 1992-2001), followed by Seattle, San Francisco-Oakland SMSA, Connecticut, and Iowa contributing between 10-12% each, and then by Atlanta, Utah, San Jose-Monterey, and New Mexico with 5-6% each. In addition, 3% of the cases were from Hawaii and 0.3% from rural Georgia. The black cases were largely from 4 registries including Detroit, Los Angeles, Atlanta, and San Francisco-Oakland SMSA (Table 22.6). Table 22.6 shows relative survival by stage of disease by SEER Registry. Survival differences by geographic area were minimal within each stage group (Table 22.6).

Relative Survival by Tumor Grade

In addition to stage at diagnosis, tumor grade plays an important role in prostate cancer survival. Tumor grade reflects the cell differentiation and/or Gleason score. Grade I is well differentiated and/or Gleason scores of 2-4; grade II is moderately differentiated and/or Gleason scores of 5-7; grade III is poorly differentiated and/or Gleason scores of 8-10; and grade IV is undifferentiated or anaplastic. Figure 22.2 shows the relative survival

Table 22.5: Cancer of the Prostate: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Clinical Stage and Age (20+), 12 SEER Areas, 1988-2001

Stage/Age (Years)	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Localized Disease	214,858	100.0	100.0	100.0	100.0	100.0	100.0	99.5
20-64	66,381	30.9	100.0	100.0	100.0	100.0	100.0	100.0
65-74	92,156	42.9	100.0	100.0	100.0	100.0	100.0	100.0
75+	56,321	26.2	100.0	100.0	100.0	100.0	100.0	98.2
Regional Disease	21,448	100.0	100.0	99.6	98.4	96.0	93.5	92.1
20-64	6,107	28.5	100.0	98.8	97.3	93.5	89.1	86.8
65-74	10,304	48.0	100.0	100.0	100.0	99.0	97.2	96.9
75+	5,037	23.5	99.5	97.3	94.9	91.7	88.4	85.8
Distant Disease	17,374	100.0	82.8	62.5	49.9	35.4	23.4	19.0
20-64	3,623	20.9	85.4	62.0	47.7	31.9	20.4	16.6
65-74	6,318	36.4	85.5	64.8	51.6	36.6	25.1	20.9
75+	7,433	42.8	79.1	60.6	49.5	36.8	24.7	20.4
Unknown	21,600	100.0	99.0	97.0	94.8	90.5	83.7	79.7
20-64	3,667	17.0	98.8	96.1	93.5	89.5	84.8	81.4
65-74	7,777	36.0	98.8	97.0	94.9	91.8	85.9	83.1
75+	10,156	47.0	99.2	97.4	95.4	90.0	81.3	76.0

by tumor grade for up to 10 years after diagnosis. There was 100% relative survival rate at 10 years for grade I (with Gleason scores of 2-4). Those with grade II tumors (Gleason scores 5-7) did well through 10 years with a 10 year survival rate of 99%. (Note: the Grade II survival curve is on top of the Grade I curve in Figure 22.2). The largest declines in survival with increasing time after diagnosis are seen for those with poorly differentiated, undifferentiated, or unknown tumor grade. By 10 years after diagnosis, relative survival was 73% for those with unknown tumor grade, 69% for those with grade IV (Gleason scores of 8-10) and 50% for those with undifferentiated or anaplastic tumors.

Figure 22.1: Cancer of the Prostate: Relative Survival Rates (%) by Clinical Stage and Race, Ages 20+, 12 SEER Areas, 1988-2001

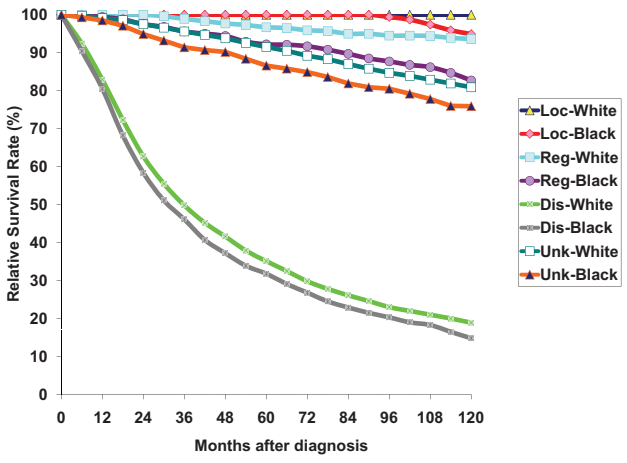


Figure 22.2: Cancer of the Prostate: Relative Survival Rates (%) by Grade, Ages 20+, 12 SEER Areas, 1988-2001

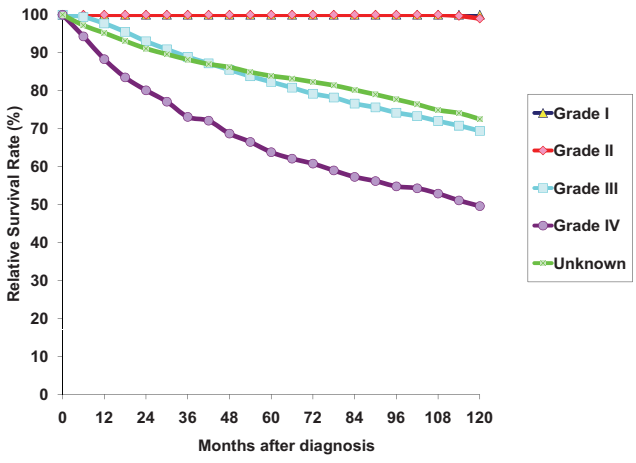


Table 22.6: Cancer of the Prostate: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Clinical Stage and SEER Geographic Area, Ages 20+, 12 SEER Areas, 1988-2001

Stage/Geographic Area	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Stages	275,280	100.0	100.0	99.5	98.9	97.6	94.5	91.7
Atlanta and Rural Georgia	17,681	6.4	99.7	99.0	98.1	96.5	93.1	90.2
Atlanta (Metropolitan)	16,855	6.1	99.9	99.1	98.4	97.0	94.0	91.1
Rural Georgia	826	0.3	97.0	95.9	91.8	86.4	72.9	68.6
California								
Los Angeles	45,893	16.7	100.0	100.0	100.0	99.6	97.1	95.1
Greater Bay Area	44,628	16.2	100.0	99.4	98.8	97.3	94.1	91.4
San Francisco-Oakland SMSA	30,417	11.0	100.0	99.1	98.4	96.9	93.7	90.5
San Jose-Monterey	14,211	5.2	100.0	100.0	99.6	98.2	95.0	93.2
Connecticut	30,029	10.9	99.9	98.9	97.7	96.2	92.3	87.4
Detroit (Metropolitan)	42,550	15.5	99.7	99.0	98.3	96.5	93.1	90.3
Hawaii	8,469	3.1	99.4	98.1	96.7	94.8	89.9	85.4
Iowa	25,919	9.4	99.9	99.0	97.9	95.6	92.0	88.7
New Mexico	13,002	4.7	99.9	99.3	98.3	97.3	94.2	91.9
Seattle (Puget Sound)	32,812	11.9	100.0	100.0	100.0	100.0	97.8	96.4
Utah	14,297	5.2	100.0	100.0	100.0	99.4	98.9	97.7
Localized Disease	214,858	100.0	100.0	100.0	100.0	100.0	100.0	99.5
Atlanta and Rural Georgia	13,057	6.1	100.0	100.0	100.0	100.0	100.0	98.2
Atlanta (Metropolitan)	12,509	5.8	100.0	100.0	100.0	100.0	100.0	98.9
Rural Georgia	548	0.3	99.8	99.8	98.9	95.4	84.6	79.7
California								
Los Angeles	36,067	16.8	100.0	100.0	100.0	100.0	100.0	100.0
Greater Bay Area	33,957	15.8	100.0	100.0	100.0	100.0	100.0	100.0
San Francisco-Oakland SMSA	23,141	10.8	100.0	100.0	100.0	100.0	100.0	100.0
San Jose-Monterey	10,816	5.0	100.0	100.0	100.0	100.0	100.0	100.0
Connecticut	24,213	11.3	100.0	100.0	100.0	100.0	99.4	94.2
Detroit (Metropolitan)	33,968	15.8	100.0	100.0	100.0	100.0	99.8	97.1
Hawaii	6,599	3.1	100.0	100.0	100.0	100.0	98.0	93.9
Iowa	19,204	8.9	100.0	100.0	100.0	100.0	100.0	97.2
New Mexico	11,004	5.1	100.0	100.0	100.0	100.0	99.8	96.9
Seattle (Puget Sound)	25,691	12.0	100.0	100.0	100.0	100.0	100.0	100.0
Utah	11,098	5.2	100.0	100.0	100.0	100.0	100.0	100.0

Note: table continued on next page

Relative survival rates for blacks were lower than for whites for each tumor grade category, except for grade I where the differences were on the order of only 0.2% (Figure 22.3). (Note: The survival curves for grade I and II for whites and grade I for blacks were so similar that only the line for grade II for whites is visible in Figure 22.3).

Relative Survival by Stage of Disease and Tumor Grade

With both stage at diagnosis and tumor grade affecting relative survival, Figures 22.4-22.7 show relative survival rates for each of the four stages of disease (localized, regional, distant, and unknown) separately by tumor grade. For both localized and regional disease (Figures 22.4 and 22.5) there is little difference in relative survival rates between those with well differentiated (grade I) and moderately differentiated tumors (grade II). (Note: For Figures 22.4 and 22.5, the survival curve for grade I is hidden by the survival curve for grade II). Those with poorly differentiated (grade III) and undifferentiated/anaplastic (grade IV) tumors showed marked declines in relative survival over time, with the latter group declining to 72% for those with localized disease and to 51% in those with regional disease

Table 22.6 (continued): Cancer of the Prostate: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Clinical Stage and SEER Geographic Area, Ages 20+, 12 SEER Areas, 1988-2001

Stage/Geographic Area	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Regional Disease	21,448	100.0	100.0	99.6	98.4	96.0	93.5	92.1
Atlanta and Rural Georgia	1,052	4.9	99.9	99.6	96.5	94.5	93.3	88.5
Atlanta (Metropolitan)	1,004	4.7	99.7	99.4	96.5	94.4	93.1	88.5
Rural Georgia	48	0.2	100.0	100.0	96.3	93.9	87.9	81.6
California								
Los Angeles	3,316	15.5	100.0	99.8	99.3	98.8	97.1	97.1
Greater Bay Area	4,537	21.2	100.0	99.8	99.2	96.6	94.3	92.3
San Francisco-Oakland SMSA	3,182	14.8	100.0	99.8	99.0	96.8	93.6	90.5
San Jose-Monterey	1,355	6.3	100.0	99.9	99.7	96.0	94.8	94.8
Connecticut	1,587	7.4	99.4	97.3	96.2	92.7	89.8	86.5
Detroit (Metropolitan)	2,307	10.8	99.4	97.8	94.4	91.5	88.8	87.6
Hawaii	753	3.5	99.9	98.6	96.8	92.6	85.7	83.3
Iowa	2,516	11.7	100.0	99.9	98.7	95.9	93.4	91.7
New Mexico	918	4.3	100.0	100.0	98.9	96.0	94.7	94.6
Seattle (Puget Sound)	3,244	15.1	100.0	100.0	100.0	97.0	92.9	91.6
Utah	1,218	5.7	99.8	99.8	99.8	99.3	98.0	96.6
Distant Disease	17,374	100.0	82.8	62.5	49.9	35.4	23.4	19.0
Atlanta and Rural Georgia	993	5.7	79.3	58.6	47.3	32.6	22.5	16.9
Atlanta (Metropolitan)	914	5.3	80.1	59.2	47.7	33.7	23.4	18.2
Rural Georgia	79	0.5	70.1	51.5	42.6	19.9	11.0	3.4
California								
Los Angeles	2,619	15.1	82.7	63.2	52.6	38.6	25.6	20.0
Greater Bay Area	3,314	19.1	84.5	63.4	49.2	36.0	23.5	19.4
San Francisco-Oakland SMSA	2,345	13.5	84.1	63.2	48.8	35.7	23.2	18.2
San Jose-Monterey	969	5.6	85.4	63.9	50.1	36.4	24.4	22.4
Connecticut	1,930	11.1	81.1	60.4	46.5	32.0	20.3	16.8
Detroit (Metropolitan)	2,489	14.3	76.1	56.0	45.7	32.2	21.6	17.6
Hawaii	796	4.6	87.7	71.2	60.5	45.8	35.3	28.5
Iowa	2,106	12.1	86.2	65.7	51.3	34.5	22.4	18.3
New Mexico	721	4.1	81.0	60.3	47.6	31.6	16.6	11.8
Seattle (Puget Sound)	1,620	9.3	86.9	65.5	51.1	35.7	21.8	17.6
Utah	786	4.5	85.9	66.1	53.2	39.3	29.4	24.6

at 10 years after diagnosis. For those with distant disease (Figure 22.6), even those with grade I tumors had only a 45% relative survival rate by 10 years after diagnosis while those with grade IV tumors experienced a relative survival rate of 3% at 10 years. Cases with unknown stage (Figure 22.7) displayed a pattern that appeared to be intermediate between those with regional disease and distant disease. For unknown stage (Figure 22.7), those with grade I tumors did well, with a relative survival of 100% by 10 years, but those with grade II experienced a decline to 89% by 10 years, unlike cases with comparable tumor grade who had regional disease. For unknown stage, the survival rates for grade III and grade IV were similar. While men with grade III regional disease had a relative survival rate of 51% at 10 years, the comparable figure was 58% for those with unknown stage. The difference in relative survival for the grade IV was the most extreme between those diagnosed with localized disease and those with distant disease. Among the former, the relative survival was 72% at 10 years compared to 3% among the latter. Thus, the importance of diagnosing aggressive tumors at an early stage is critical.

Figure 22.3: Cancer of the Prostate: Relative Survival Rates (%) by Grade and Race, Ages 20+, 12 SEER Areas, 1988-2001

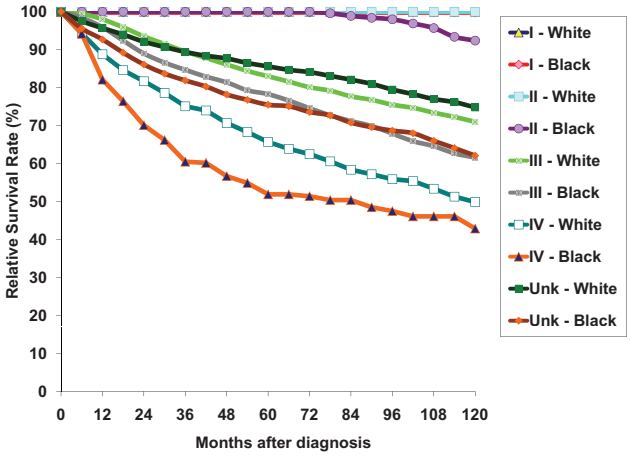
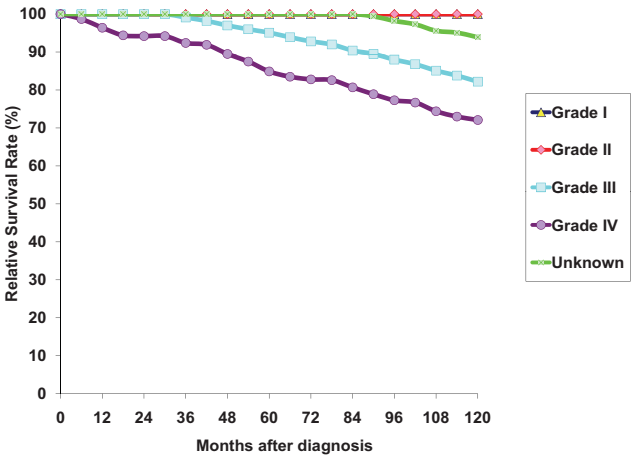


Figure 22.4: Localized Cancer of the Prostate: Relative Survival Rates (%) by Grade, Ages 20+, 12 SEER Areas, 1988-2001



Relative Survival by Year of Diagnosis

During this time period there have been major changes in the treatment and diagnosis of prostate cancer, including the use of anti-androgens in the late 1980's, the advent of PSA testing and screening beginning in 1986, and the increasing use of surgery to treat the disease (4). Figure 22.8 shows the dramatic improvement in survival that occurred from 1988-89 to 1990-91 and then again from 1990-91 to 1992-93. Since that time survival has remained relatively constant at a very high level. (Note: the survival rates are so similar after 1996, that it is hard to distinguish the curves in Figures 22.8 and 22.9). Similar trends are seen for whites (Figure 22.9) and blacks (Figure 22.10), although improvement for blacks has continued to be seen from 1992-93, 1994-95 and in 1996-97. This continuation of the survival increase for black men has had the result of putting their survival on par with those of white men. This is in contrast to the large survival gap that existed in 1988-89 when the 10-year relative survival rate for white men was 81% compared to only 62% for black men.

DISCUSSION

Overall, relative survival for prostate cancer has continued to improve over time (5). In 1986, for example, 5- and 10-year relative survival rates were 78% and 68%, respectively, whereas they hover near 100% at 5 years since 1994. Prognosis is excellent for those with early stage disease and especially for those with well differentiated (grade I) tumors.

Many of the survival rates were 100% or close to 100%. The survival is being measured relative to the general population matched on race and age. These high rates do not mean that the men don't have any deaths due to prostate

Figure 22.5: Regional Cancer of the Prostate: Relative Survival Rates (%) by Grade, Ages 20+, 12 SEER Areas, 1988-2001

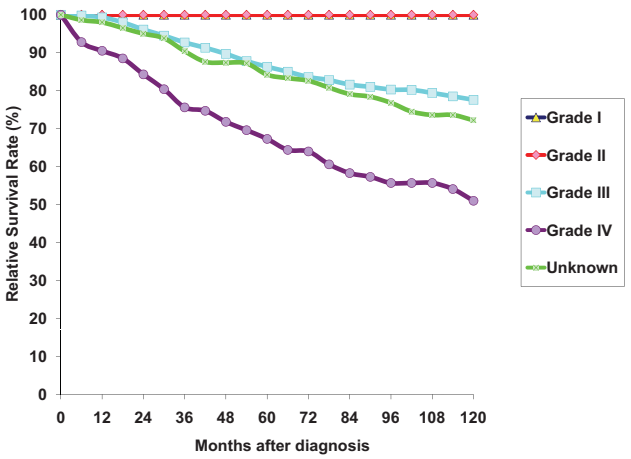


Figure 22.6: Distant Cancer of the Prostate: Relative Survival Rates (%) by Grade, Ages 20+, 12 SEER Areas, 1988-2001

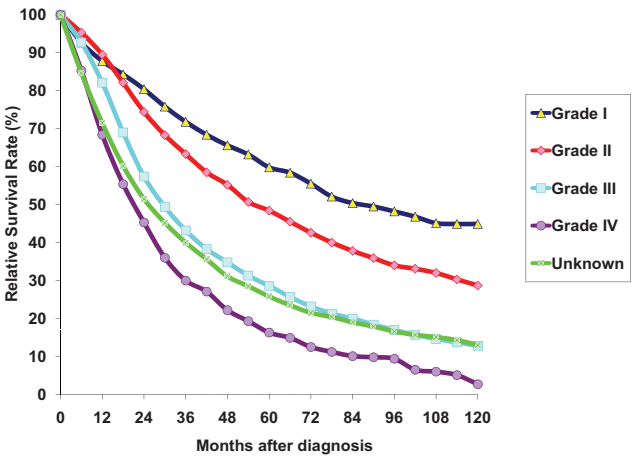
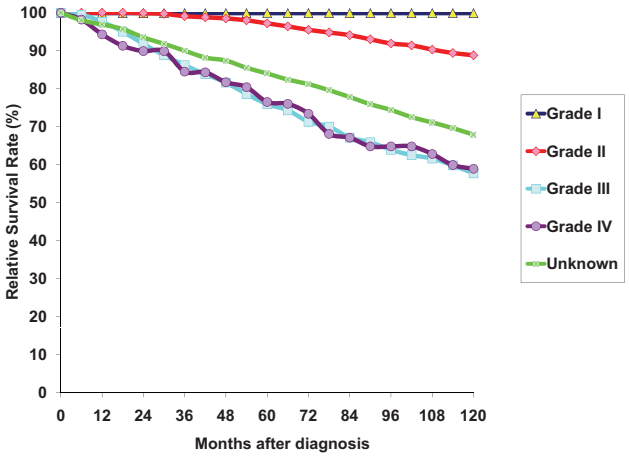


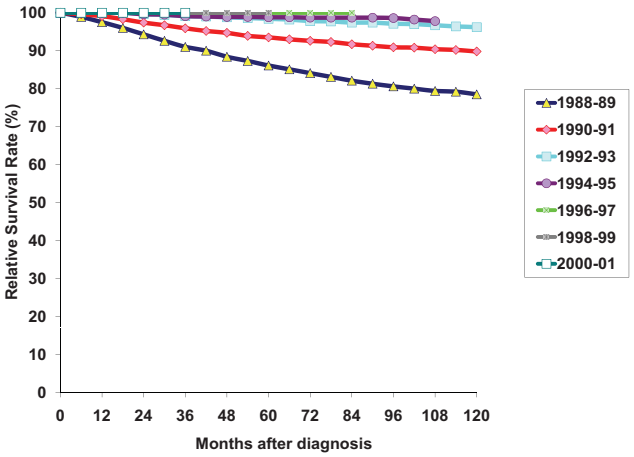
Figure 22.7: Cancer of the Prostate with Unknown Stage: Relative Survival Rates (%) by Grade, Ages 20+, 12 SEER Areas, 1988-2001



cancer but rather when their cancer and non-cancer deaths are taken together, their survival profile was similar to the general population. They may be under more medical surveillance than the general population and therefore, have a better overall survival from non-cancer causes than the general population which offsets the excess prostate cancer mortality.

Survival for those diagnosed with distant disease and with poorly and undifferentiated tumors is poor, pointing to the benefit of earlier diagnosis. Even within stage, grade was an important prognostic factor. Relative survival is poorer for blacks than whites, even within stage and tumor grade categories. Since survival has continued to improve among blacks and there have only been slight additional incremental improvements in relative survival among whites, the survival gap between white men and black men has lessened considerably.

Figure 22.8: Cancer of the Prostate: Relative Survival Rates (%) for All Races by Year of Diagnosis, Ages 20+, 12 SEER Areas, 1988-2001



REFERENCE

1. Beahrs, OH, Henson DE, Hutter RVP, Myers MH (eds). AJCC Cancer Staging Manual, Third edition. American Joint Committee on Cancer. Philadelphia: Lippincott, 1988.
2. Beahrs, OH, Henson DE, Hutter RVP, Kennedy BJ (eds). AJCC Cancer Staging Manual, Fourth edition. American Joint Committee on Cancer. Philadelphia: Lippincott, 1992.
3. Fleming ID, Cooper JS, Henson DE, Hutter RVP, Kennedy BJ, Murphy GP, O'Sullivan B, Sobin LH, Yarbro, JW (eds). AJCC Cancer Staging Manual, Fifth edition, American Joint Committee on Cancer. Philadelphia: Lippincott-Raven, 1998.
4. Hankey, BF, Feuer, EJ, Clegg, LX, Hayes, RB, Legler, JM, Prorok, PC, Ries, LA, Merrill, RM, and Kaplan, RS. Cancer surveillance series: Interpreting trends in prostate cancer Part I: Evidence of the effects of screening in recent prostate cancer incidence, mortality, and survival rates. JNCI 91:1017-24, 1999.
5. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Eisner MP, Horner MJ, Howlader N, Hayat M, Hankey BF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data 1975-2003, National Cancer Institute. Bethesda, MD.

Figure 22.9: Cancer of the Prostate: Relative Survival Rates (%) for Whites by Year of Diagnosis, Ages 20+, 12 SEER Areas, 1988-2001

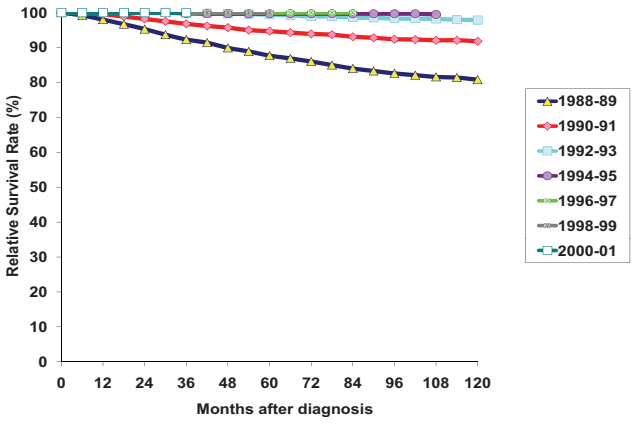
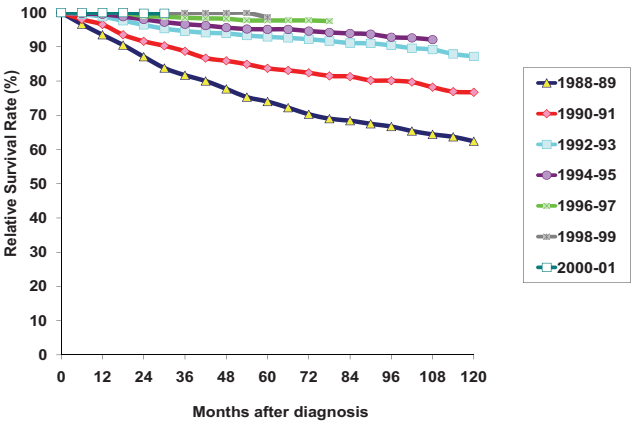


Figure 22.10: Cancer of the Prostate: Relative Survival Rates (%) for Blacks by Year of Diagnosis, Ages 20+, 12 SEER Areas, 1988-2001



Chapter 23
Cancer of the Urinary Bladder

Charles F. Lynch, Jessica A. Davila, and Charles E. Platz

INTRODUCTION

Cancer of the urinary bladder most commonly originates in the urothelium, the epithelium that lines the bladder. During 2006, this is reported as the 4th most common incident cancer among males (estimated 44,690 new cases) and the 9th most common incident cancer among females (estimated 16,730 new cases) (1).

Racial and sex variation in the incidence and mortality for urinary bladder cancer has been observed previously using SEER data (2-4). Bladder cancer incidence is significantly higher in males than females, and in whites compared with blacks. However, the incidence in white females has been steadily increasing, while no significant changes have occurred in white males, black males, or black females (3).

In addition, average annual mortality rates for urinary bladder cancer are higher in white males compared with black males, white females, and black females (3,4). Secular trends in mortality rates have been decreasing for black males, black females, and white males and have been flat for white females (3).

Five-year relative survival rates are generally higher for males than females, regardless of stage of disease. Blacks diagnosed with bladder cancer have consistently lower survival than whites (5). Extent of disease at time of diagnosis has been found to be significantly greater for blacks than whites and helps to explain the lower survival that persists among blacks (6).

There are three major histologic types of urinary bladder cancer: transitional cell carcinoma, squamous cell carcinoma, and adenocarcinoma. Overwhelmingly, the most common type is transitional cell carcinoma. There are two common histologic subtypes of early, noninvasive transitional cell carcinoma, papillary and nonpapillary (flat), terms that describe both the gross and histologic appearances of these cancers (7). Nonpapillary (flat) carcinoma in situ lesions are by definition high-grade. Papillary lesions, which are also "in situ" though not specifically designated as such, can be low-grade or high-grade. High grade lesions are comprised of cells with large, irregular hyperchromatic nuclei that are present over the entire thickness of the epithelium, while low grade lesions are comprised of cells with nuclei that more closely resemble the nuclei seen in normal urothelial cells. High grade lesions are typically associated with more aggressive tumor behavior.

MATERIALS AND METHODS

The materials and methods are those provided in the introductory chapter with one noteworthy exception, the inclusion of in situ cancers. Since the 1985 Annual Cancer Statistics Review, the SEER Program has combined in situ and invasive bladder cancers when reporting incidence and survival rates, because of a perceived difficulty in identifying the presence or absence of superficial or early invasion in pathology reports (8). In great part this occurred because urologists and pathologists understood the term papillary transitional carcinoma to mean a noninvasive process unless invasion was specifically stated, in contrast to the conventional terminology understood for most sites (9). Incidence trends for this group of tumors were based on information obtained primarily from the hospital medical record, and were not subjected to secondary pathology review, and varied significantly from one SEER area to another (9). This practice of combining in situ and invasive bladder cancers has persisted to the present. Nevertheless, we will separate them in this report by including stage 0 cases (which include both Ta and Tis non-invasive cases) in the tables and discussion.

The number of persons with cancers of the urinary bladder from this population for the period from 1988 to 2001 is provided in Table 23.1, accompanied by the numbers and reasons for those excluded for this survival analysis.

Staging is based on American Joint Committee on Cancer Staging, Fifth Edition (10).

RESULTS

All Bladder Cancers

Distribution and survival by age, sex, and race

Of the 67,528 adult bladder cancers, 79.3% were diagnosed at 60 years of age or older (Table 23.2). The greatest frequency occurred in the 70-79 age group, and 59.4% were between the ages of 60-79 years. Most were male and the overwhelming majority (> 90%) were white.

Overall, males had greater relative survival rates compared with females, while whites had greater relative survival rates than blacks. White males had the greatest 5-year relative survival rate (85%), followed in order by white females (77%), black males (69%), and black females (55%). The median survival times were 103 months for white males and 102 for white females compared with 67 months for black males and 40 months for black females (Table 23.3, Figure 23.1).

White males and females diagnosed between the ages of 20 and 49 years had the greatest observed and relative survival percentages compared with blacks (Table 23.3). The median survival time was greater than 10 years for white males and females and black males and females.

For persons over age 50, white males had the greatest observed and relative 5-year survival rate, while black females had the lowest. As anticipated, differences between observed and relative survival percentages were greatest in the 50+ age group.

Survival by histology

Of the 67,528 cases, over 95% were diagnosed with transitional cell carcinoma (Table 23.4). Among transitional cell carcinomas, papillary neoplasms accounted for a much higher percentage (73.4%) than nonpapillary neoplasms (26.6%). The second most common histologic type was squamous cell carcinoma, diagnosed in only 1.4%. Adenocarcinoma accounted for only 1.2%. Small cell carcinoma and related neuroendocrine tumor histologic types were very rarely diagnosed, together accounting for only 0.2% of observed histologies. In the "other" histology category, malignant neoplasm (ICD-O M-8000) (112 cases), carcinoma, not otherwise specified (NOS) (ICD-O M-8010) (705 cases), and undifferentiated carcinoma (ICD-O M-8020) (39) accounted for 85% of all the 1,004 "other" cancers (Table 23.4).

Figure 23.1: Cancer of the Urinary Bladder: Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

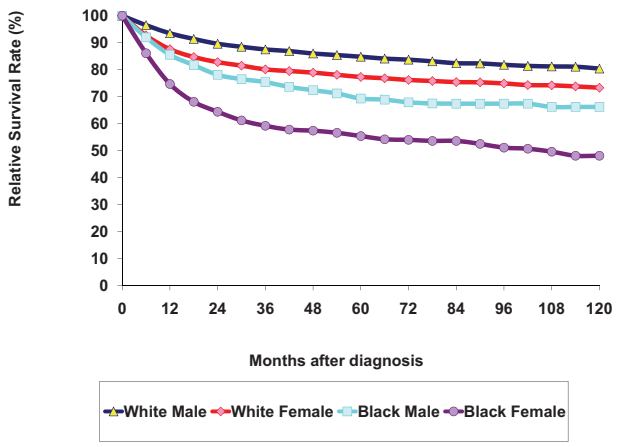


Table 23.1: Cancer of the Urinary Bladder: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
86,187	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
69,302	16,885	Select first primary only
68,934	368	Exclude death certificate only or at autopsy
68,475	459	Exclude unknown race
68,409	66	Exclude alive with no survival time
68,344	65	Exclude children (Ages 0-19)
67,746	598	Exclude no or unknown microscopic confirmation
67,581	165	Exclude sarcomas
67,528	53	Exclude carcinoids

Table 23.2: Cancer of the Urinary Bladder: Number and Distribution of Cases by Age (20+), Race, and Sex, 12 SEER Areas, 1988-2001

	Total		Race/Sex							
			White				Black			
			Male		Female		Male		Female	
Age Group (Years)	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	67,528	100.0	46,342	100.0	15,296	100.0	1,960	100.0	1,085	100.0
20-39	1,318	2.0	846	1.8	322	2.1	60	3.1	21	1.9
40-49	3,661	5.4	2,550	5.5	723	4.7	179	9.1	52	4.8
50-59	9,059	13.4	6,388	13.8	1,840	12.0	352	18.0	118	10.9
60-69	17,864	26.5	12,840	27.7	3,519	23.0	530	27.0	255	23.5
70-79	22,198	32.9	15,466	33.4	4,853	31.7	560	28.6	357	32.9
80+	13,428	19.9	8,252	17.8	4,039	26.4	279	14.2	282	26.0

Table 23.3: Cancer of the Urinary Bladder: Number of Cases, Median Survival Time (Months) and 5-Year Survival Rates (%) by Race, Sex, and Age Group, Ages 20+, 12 SEER Areas, 1988-2001

Race, Sex, and Age Group (Years)	Cases	Median Survival Time (Months)	5-Year Survival Rate (%)		
			Obs	Exp	Rel
White Females, 20-49	1,045	> 120	88.9	99.0	89.8
White Males, 20-49	3,396	> 120	89.4	97.9	91.2
Black Females, 20-49	73	> 120	58.5	97.7	59.7
Black Males, 20-49	239	> 120	72.9	95.1	76.6
White Females, 50+	14,251	93.0	60.3	79.1	76.2
White Males, 50+	42,946	94.8	63.1	75.0	84.2
Black Females, 50+	1,012	36.9	42.1	76.5	55.0
Black Males, 50+	1,721	58.0	49.5	72.6	68.0
White Females, 20+	15,296	101.7	62.2	80.4	77.3
White Males, 20+	46,342	102.8	65.1	76.7	84.8
Black Females, 20+	1,085	39.5	43.2	77.9	55.4
Black Males, 20+	1,960	66.7	52.4	75.3	69.3

Table 23.4: Cancer of the Urinary Bladder: Number and Distribution of Cases by Histology, Ages 20+, 12 SEER Areas, 1988-2001

ICD-O-3 Histology	Cases	Pct
Total	67,528	100.0
Papillary transitional cell carcinoma	47,399	70.2
Papillary carcinoma, NOS (8050)	610	0.9
Papillary trans. cell carcinoma (8130)	46,779	69.3
Other Pap. Trans. (8121,8131)	10	0.0
Nonpapillary transitional cell carcinoma	17,211	25.5
Transitional cell carcinoma, NOS (8120)	17,167	25.4
Trans. cell carcinoma, spindle cell (8122)	44	0.1
Squamous cell carcinoma	918	1.4
Squamous cell carcinoma, NOS (8070)	697	1.0
Sq. cell carcinoma, keratinizing, NOS (8071)	193	0.3
Other Sq. Cell (8051-8052,8072,8074,8076)	28	0.0
Adenocarcinoma	838	1.2
Adenocarcinoma, NOS (8140)	480	0.7
Mucinous adenocarcinoma (8480)	89	0.1
Mucin-producing adenocarcinoma (8481)	80	0.1
Signet ring cell carcinoma (8490)	94	0.1
Other Adeno (8141,8144,8255,8260,8310, 8320,8323,8440,8470,8472,8570)	95	0.1
Small cell carcinoma and related neuroendocrine tumors (8041-8042)	158	0.2
Other	1,004	1.5
Neoplasm, malignant (8000)	112	0.2
Carcinoma, NOS (8010)	705	1.0
Carcinoma, undifferentiated type, NOS (8020)	39	0.1
Other (8001-8002,8004,8012,8021-8022, 8030,8032-8033,8044,8046,8082-8083, 8230,8262,8560,8700,8720,8933,8935,8940, 8950-8951,9064,9100,9364)	148	0.2

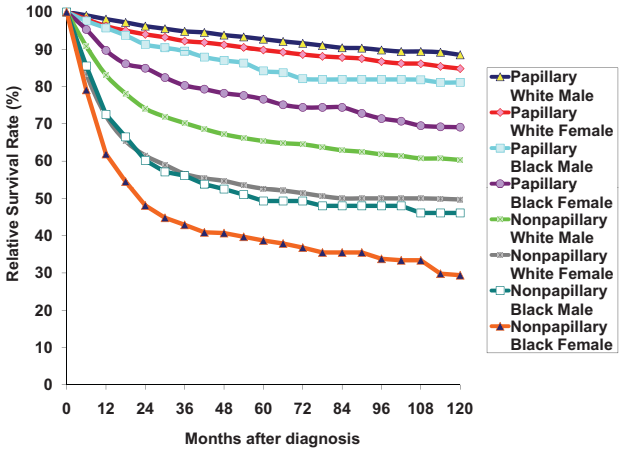
Table 23.5: Cancer of the Urinary Bladder: Number and Distribution of Cases, Median Survival Time (Months) and 5-Year Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology	Cases	Percent	Median Survival Time (Months)	5-Year Survival Rate (%)		
				Observed	Expected	Relative
Total	67,528	100.0	101.1	63.7	77.8	81.9
Papillary transitional cell carcinoma	47,399	70.2	> 120	71.8	78.5	91.5
Nonpapillary transitional cell carcinoma	17,211	25.5	50.3	46.6	76.1	61.2
Squamous cell carcinoma	918	1.4	9.5	23.7	76.7	30.9
Adenocarcinoma	838	1.2	31.3	34.5	79.7	43.3
Small cell carcinoma and related neuroendocrine tumors	158	0.2	13.3	21.8	77.9	26.2

Table 23.6: Cancer of the Urinary Bladder: Number and Distribution of Cases, Median Survival Time (Months) and 5-Year Survival Rates (%) by AJCC Stage (5th Edition), 12 SEER Areas, 1988-2001

AJCC Stage (5th Edition)	Cases	Percent	Median Survival Time (Months)	5-Year Relative Survival Rate (%)		
				Obs	Exp	Rel
Total	67,528	100.0	101.1	63.7	77.8	81.9
Stage 0	29,638	43.9	> 120	78.0	79.3	98.4
Stage I	8,611	12.8	108.3	68.1	77.7	87.7
Stage II	4,541	6.7	54.6	47.7	76.2	62.6
Stage III	2,496	3.7	28.3	35.8	78.7	45.5
Stage IV	3,775	5.6	9.7	11.8	79.9	14.8
Unknown	18,467	27.3	80.6	57.4	75.3	76.3

Figure 23.2: Transitional Cell Carcinoma of the Urinary Bladder: Relative Survival Rates (%) by Histology, Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001



Five-year observed and relative survival rates and median survival time were greatest for papillary transitional cell carcinoma compared with other histologic types (Table 23.5). Squamous cell carcinoma had the lowest median survival time, of 9.5 months.

Survival by stage

Observed and relative 5-year survival rates decreased through the progression of urinary bladder cancer to later stages (Table 23.6). Median survival times were greater than 10 years for stage 0 but less than 5 years for all other stages except stage I. Patients with unknown stage of disease had observed and relative 5-year survival rates and a median survival time that was higher than all other stages, except stages 0 and I. This finding suggests that a substantial proportion of patients with unknown stage had in situ (stage 0) or superficially invasive (stage I) disease.

Transitional Cell Carcinoma

Survival by histology, age, sex, and race

Of those diagnosed with transitional cell carcinoma, the male to female ratio for whites was 3.2:1 and for blacks was 2.3:1. Seventy-eight percent of the cases occurred after 60 years and older (Table 23.7). Persons in the 60-79 age groups alone accounted for 59% of all these cancers. The greatest percent of 60-79 year olds occurred in white males (69.3%). The 20-59 age group accounted for 22.1% of all papillary transitional cell carcinomas, but only 17.1% of the nonpapillary transitional cell carcinomas. Black males and females accounted for 6.0% of all nonpapillary transitional cell carcinomas, but only 3.6% of papillary transitional cell carcinomas.

Table 23.7: Transitional Cell Carcinoma of the Urinary Bladder: Number and Distribution of Cases by Histology, Age (20+), Race and Sex, 12 SEER Areas, 1988-2001

Histology	Age Group (Years)	Total		Race/Sex							
				White				Black			
				Male		Female		Male		Female	
		Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Papillary	Total	47,399	100.0	33,465	100.0	10,427	100.0	1,188	100.0	527	100.0
	20-39	1,071	2.3	711	2.1	262	2.5	39	3.3	11	2.1
	40-49	2,754	5.8	2,001	6.0	533	5.1	103	8.7	19	3.6
	50-59	6,648	14.0	4,753	14.2	1,363	13.1	217	18.3	65	12.3
	60-69	12,708	26.8	9,355	28.0	2,461	23.6	321	27.0	122	23.1
	70-79	15,466	32.6	11,043	33.0	3,285	31.5	347	29.2	178	33.8
	80+	8,752	18.5	5,602	16.7	2,523	24.2	161	13.6	132	25.0
Nonpapillary	Total	17,211	100.0	11,320	100.0	3,940	100.0	604	100.0	423	100.0
	20-39	177	1.0	100	0.9	45	1.1	13	2.2	6	1.4
	40-49	715	4.2	460	4.1	134	3.4	52	8.6	23	5.4
	50-59	2,055	11.9	1,434	12.7	389	9.9	102	16.9	36	8.5
	60-69	4,456	25.9	3,086	27.3	863	21.9	166	27.5	95	22.5
	70-79	5,851	34.0	3,929	34.7	1,291	32.8	173	28.6	153	36.2
	80+	3,957	23.0	2,311	20.4	1,218	30.9	98	16.2	110	26.0

For papillary transitional cell carcinoma, relative survival rates for both males and females were higher for white than black adults (Figure 23.2). Between the ages of 20 and 49 years, white males and females had the highest five-year relative survival rates (Table 23.8). In this age range, median survival times were greater than 10 years for males and females and both races. For persons 50 and older, white males had the highest 5-year relative survival rate of 92%, while black females had the lowest percentage (76%). The median survival times were higher for whites than blacks in both sexes.

For nonpapillary transitional cell carcinoma, relative survival rates were highest for white males, followed by white females and black males with black females having the lowest rates (Figure 23.2). Between the ages of 20 and 49 years, whites had the highest five-year relative survival rates (Table 23.8). Black females in this age group had a very low median survival time of 33 months, but this should be interpreted with caution since there were only 29 cases. For persons 50 and older, white males had the highest 5-year relative survival rate of 65%, while black females had the lowest rate (38%). For ages 20+, the median survival times were higher for whites than blacks in both sexes and were three times as long in white males than black females.

Survival rates in adults were substantially higher in both races and sexes for papillary transitional cell carcinoma compared with nonpapillary transitional cell carcinoma. This was especially true for the 50+ age group.

Survival by histology, stage, and grade

For papillary transitional cell carcinoma in each race and sex group, the greatest number of cases was diagnosed at stage 0 and accounted for 57% among white females, 56% among white males, 46% among black males, and 44% among black females (Table 23.9). The percentage of stage IV papillary transitional cell carcinomas was highest among black females (5.1%) followed by black males (2.4%), white females (2.1%), and white males (1.5%). Blacks and whites with stage 0 disease had median survival times greater than 10 years. However, for stage I disease, the median survival time for black males and females was lower than for whites. For stages II, III, and IV, median survival times were higher among males compared with females in each race group (Table 23.9).

Relative survival curves for papillary transitional cell carcinoma by stage and sex were generally higher in whites than blacks. This was particularly so for stage III and stage IV (Figures 23.3 (males) and 23.4 (females)). In Figure 23.4, the survival curve for stage III black females is not shown due to insufficient case numbers.

For nonpapillary transitional cell carcinoma in each race and sex group, the greatest number of cases was diagnosed

Table 23.8: Transitional Cell Carcinoma of the Urinary Bladder: Number of Cases, Median Survival Time (Months) and 5-Year Survival Rates (%) by Histology, Race, Sex, and Age (20+), 12 SEER Areas, 1988-2001

Histology	Race, Sex, and Age Group (Years)	Cases	Median Survival Time (Months)	5-Year Survival Rate (%)		
				Observed	Expected	Relative
Papillary	All	47,399	> 120	71.8	78.5	91.5
	White Females, 20-49	795	> 120	97.0	99.0	98.0
	White Males, 20-49	2,712	> 120	94.7	98.0	96.7
	Black Females, 20-49	30	> 120	88.7	97.9	90.2
	Black Males, 20-49	142	> 120	85.7	95.1	89.4
	White Females, 50+	9,632	> 120	71.2	80.0	89.0
	White Males, 50+	30,753	111.7	69.7	75.5	92.3
	Black Females, 50+	497	85.2	58.5	77.1	75.5
	Black Males, 50+	1,046	87.0	61.0	72.9	83.4
	White Females, 20+	10,427	> 120	73.2	81.5	89.8
	White Males, 20+	33,465	> 120	71.7	77.3	92.7
	Black Females, 20+	527	88.6	60.2	78.3	76.6
	Black Males, 20+	1,188	102.4	63.9	75.6	84.2
Nonpapillary	All	17,211	50.3	46.6	76.1	61.2
	White Females, 20-49	179	> 120	69.7	98.9	70.4
	White Males, 20-49	560	> 120	72.5	97.8	74.1
	Black Females, 20-49	29	32.9	43.3	97.5	44.2
	Black Males, 20-49	65	> 120	55.9	95.0	58.5
	White Females, 50+	3,761	32.6	39.8	77.2	51.5
	White Males, 50+	10,760	54.3	47.9	73.8	64.9
	Black Females, 50+	394	17.8	29.1	76.2	38.2
	Black Males, 50+	539	27.0	34.6	71.7	47.7
	White Females, 20+	3,940	34.7	41.1	78.2	52.6
	White Males, 20+	11,320	57.2	49.1	75.0	65.4
	Black Females, 20+	423	19.0	30.1	77.6	38.7
	Black Males, 20+	604	29.2	37.0	74.2	49.3

Table 23.9: Papillary Transitional Cell Carcinoma of the Urinary Bladder: Number and Distribution of Cases and Median Survival Time (Months) by AJCC Stage (5th Edition), Race, and Sex, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage (5th Edition)	Race/Sex											
	White						Black					
	Male			Female			Male			Female		
	Cases	Percent	Median Survival Time (Months)	Cases	Percent	Median Survival Time (Months)	Cases	Percent	Median Survival Time (Months)	Cases	Percent	Median Survival Time (Months)
Total	33,465	100.0	> 120	10,427	100.0	> 120	1,188	100.0	102.4	527	100.0	88.6
Stage 0	18,628	55.7	> 120	5,997	57.5	> 120	551	46.4	> 120	233	44.2	> 120
Stage I	4,655	13.9	112.8	1,322	12.7	110.4	186	15.7	90.3	79	15.0	94.6
Stage II	1,174	3.5	65.2	371	3.6	58.9	60	5.1	67.6	40	7.6	33.3
Stage III	502	1.5	34.5	93	0.9	22.3	36	3.0	14.8	10	1.9	~
Stage IV	514	1.5	14.0	223	2.1	10.6	28	2.4	14.0	27	5.1	9.2
Unknown	7,992	23.9	105.1	2,421	23.2	114.1	327	27.5	81.5	138	26.2	78.5

~ Statistic not displayed due to less than 25 cases.

as unstaged. Among those with known stage, the greatest number was stage IV for white females, black males, and black females and stage 0 for white males (Table 23.10). Stage I accounted for approximately 10% of all cancers in each race and sex group (Table 23.10). The percentage of stage IV nonpapillary transitional cell carcinomas was highest among black females (21.7%) compared with black males (16.7%), white females (16.3%) or white males (11.5%). Median survival times were higher among males compared with females in each race group, except for stage 0 in whites where they were both >10 years and stage IV for blacks (Table 23.10).

Relative survival curves for nonpapillary transitional cell carcinoma by stage and sex were also higher for whites than blacks in each sex (Figures 23.5 (males) and 23.6 (females)). Among males at each stage, white males had better survival than black males (Figure 23.5). The rates for black females were lower than those for white females except for stage IV after 7 years (Figure 23.6). Note, that the rates for blacks are based on small numbers of cases and therefore, have more variability.

Among males at each stage, the papillary subtype had better relative survival rate than the nonpapillary subtype in each race; however, in females this was less apparent for stage II disease and higher.

When histologic subtypes of transitional cell carcinoma were stratified by tumor grade, 5-year relative survival

Figure 23.3: Male Papillary Transitional Cell Carcinoma of the Urinary Bladder: Relative Survival Rates (%) by AJCC Stage (5th Edition) and Race, Ages 20+, 12 SEER Areas, 1988-2001

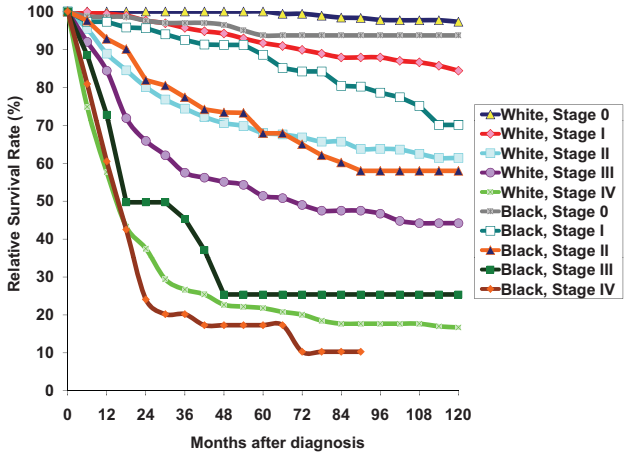


Figure 23.4: Female Papillary Transitional Cell Carcinoma of the Urinary Bladder: Relative Survival Rates (%) by AJCC Stage (5th Edition) and Race, Ages 20+, 12 SEER Areas, 1988-2001

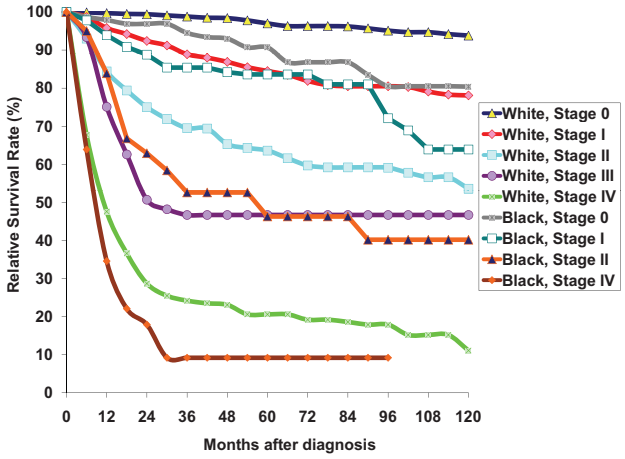


Table 23.10: Nonpapillary Transitional Cell Carcinoma of the Urinary Bladder: Number and Distribution of Cases and Median Survival Time (Months) by AJCC Stage (5th edition), Race, and Sex, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage (5th Edition)	Race/Sex											
	White						Black					
	Male			Female			Male			Female		
	Cases	Percent	Median Survival Time (Months)	Cases	Percent	Median Survival Time (Months)	Cases	Percent	Median Survival Time (Months)	Cases	Percent	Median Survival Time (Months)
Total	11,320	100.0	57.2	3,940	100.0	34.7	604	100.0	29.2	423	100.0	19.0
Stage 0	2,138	18.9	> 120	540	13.7	> 120	74	12.3	> 120	34	8.0	76.3
Stage I	1,303	11.5	93.1	385	9.8	85.6	54	8.9	96.9	45	10.6	57.0
Stage II	1,606	14.2	53.3	620	15.7	40.0	80	13.2	32.8	66	15.6	23.5
Stage III	988	8.7	28.2	319	8.1	23.4	53	8.8	18.9	37	8.7	11.1
Stage IV	1,303	11.5	10.6	642	16.3	8.6	101	16.7	7.4	92	21.7	8.0
Unknown	3,982	35.2	54.1	1,434	36.4	28.5	242	40.1	35.6	149	35.2	20.1

rates were higher for papillary carcinomas than nonpapillary at each stage and grade (Table 23.11). In general for each histologic subtype within each stage, survival decreased as tumor grade increased except grade IV where survival was similar to grade III and sometimes slightly higher by stage.

When early stage transitional cell carcinomas were separated into papillary and nonpapillary histologic subtypes by tumor grade, 5-year relative survival rates were lower among the high-grade nonpapillary carcinomas for each race and sex group (Table 23.12). Although these high-grade nonpapillary carcinomas comprised a small proportion of very early transitional cell carcinomas in whites, they comprised a higher percentage for black males and black females which contributed to the lower survival rates seen in Figures 23.3 through 23.6 for blacks compared with whites at early stages.

Survival curves for early stage transitional cell carcinoma showed all stage 0 and stage I and low grade, papillary, lesions with 10-year relative survival rates above 85%. In contrast, high grade, nonpapillary, stage I lesions had a 10-year relative survival rate of only 67% (Figure 23.7).

Figure 23.5: Male Nonpapillary Transitional Cell Carcinoma of the Urinary Bladder: Relative Survival Rates (%) by AJCC Stage (5th Edition) and Race, Ages 20+, 12 SEER Areas, 1988-2001

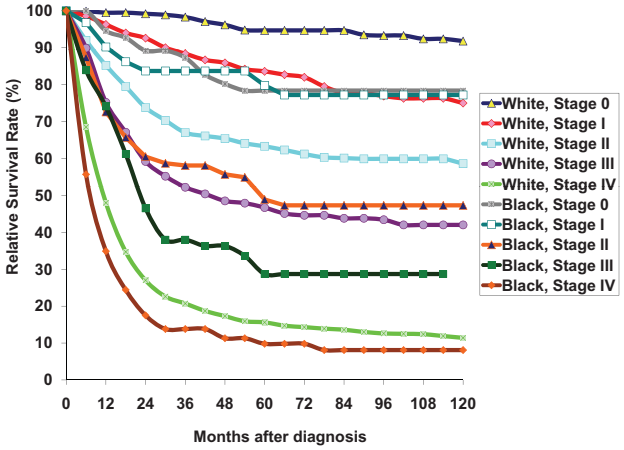
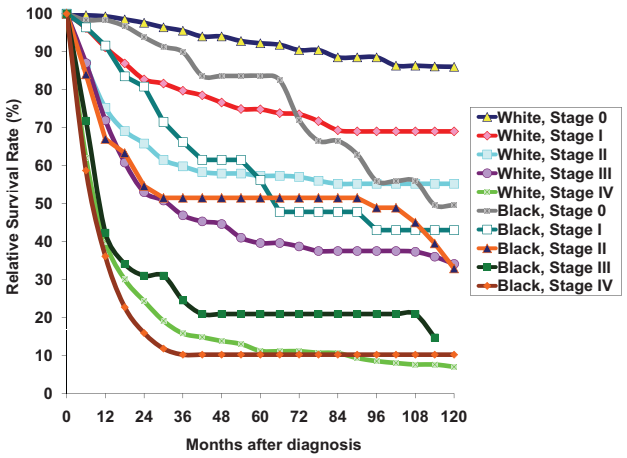


Figure 23.6: Female Nonpapillary Transitional Cell Carcinoma of the Urinary Bladder: Relative Survival Rates (%) by AJCC Stage (5th Edition) and Race, Ages 20+, 12 SEER Areas, 1988-2001



Squamous Cell Carcinoma

Survival by age, sex, and race

Over 80% of the squamous cell carcinomas were diagnosed in persons at least 60 years of age or older (Table 23.13). The male to female ratio for all races was 1.1:1 for whites and 1.0:1 for blacks. White females had the highest proportion of 80+ year olds (32.1%).

Relative survival curves were similar for males and females (Figure 23.8). A significant decline in survival was observed within the first 12 months after diagnosis.

Survival by stage

The stage distribution for squamous cell carcinoma was similar for males and females (Table 23.14). For stage 0/I disease, males had a much higher median survival time than females. For females, stage 0/I had low median survival time but it was based on a small number of cases. Overall, median survival times were relatively low for squamous cell stages II-IV compared with other histologies.

Figure 23.7: Early Stage Transitional Cell Carcinoma of the Urinary Bladder: Relative Survival Rates (%) by AJCC Stage 0 and I, Histology, and Grade, Ages 20+, 12 SEER Areas, 1988-2001

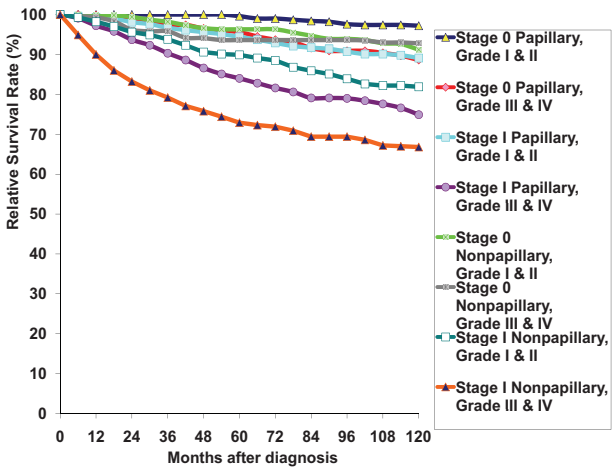


Table 23.11: Transitional Cell Carcinoma of the Urinary Bladder: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) of White and Blacks by Histology, AJCC Stage (5th Edition) and Tumor Grade, Ages 20+, 12 SEER Areas, 1988-2001

Histology	AJCC Stage (5th Edition)	Tumor Grade											
		Total		I		II		III		IV		Unknown	
		Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)
Papillary	Total	45,607	91.6	9,553	99.3	21,410	95.5	10,329	79.0	2,437	71.6	1,878	93.5
	Stage 0	25,409	99.1	7,036	100.0	13,500	98.7	3,249	95.9	535	91.5	1,089	98.7
	Stage I	6,242	90.0	757	96.2	2,737	92.2	2,101	84.7	464	84.0	183	94.9
	Stage II	1,645	66.5	25	81.2	318	72.1	916	63.2	357	67.5	29	61.0
	Stage III	641	49.1	10	~	122	57.6	348	43.1	149	49.2	12	~
	Stage IV	792	21.1	13	~	116	24.0	452	19.6	193	22.8	18	~
	Unknown	10,878	86.9	1,712	95.2	4,617	92.7	3,263	76.0	739	70.2	547	85.9
Nonpapillary	Total	16,287	60.9	970	95.1	2,589	83.4	7,245	49.6	3,367	48.0	2,116	74.8
	Stage 0	2,786	93.9	526	97.5	820	94.5	344	92.3	131	90.6	965	90.1
	Stage I	1,787	80.9	129	91.9	485	87.4	766	74.8	295	75.8	112	82.6
	Stage II	2,372	61.1	11	~	161	68.0	1,404	59.7	744	61.7	52	68.0
	Stage III	1,397	43.8	7	~	78	45.4	840	40.9	433	50.1	39	35.2
	Stage IV	2,138	13.7	7	~	89	16.3	1,218	12.7	698	16.4	126	7.3
	Unknown	5,807	60.8	290	92.2	956	83.3	2,673	51.9	1,066	45.4	822	67.9

~ Statistic not displayed due to less than 25 cases.

Table 23.12: Stage 0 & I Transitional Cell Carcinoma of the Urinary Bladder (with Known Grade): Number of Cases and 5-Year Relative Survival Rates (%) by Race, Sex, Histology, and Grade, Ages 20+, 12 SEER Areas, 1988-2001

Race/Sex	Histology								
	Papillary				Nonpapillary			
	Grade				Grade			
	Low-Grade (I & II)		High-Grade (III & IV)		Low-Grade (I & II)		High-Grade (III & IV)	
	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)
Total (White & Black)	24,030	98.6	6,349	91.1	1,960	93.9	1,536	81.2
White Male	17,472	99.5	4,870	93.3	1,452	94.2	1,153	83.7
White Female	5,774	96.9	1,256	83.7	440	92.9	300	74.3
Black Male	555	92.8	155	88.8	43	87.5	47	76.4
Black Female	229	92.4	68	74.8	25	72.8	36	56.9

Table 23.13: Squamous Cell Carcinoma of the Urinary Bladder: Number and Distribution of Cases by Age (20+), Race, and Sex, 12 SEER Areas, 1988-2001

Age Group (Years)	Total		Race/Sex							
			White				Black			
			Male		Female		Male		Female	
	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	918	100.0	398	100.0	377	100.0	56	100.0	55	100.0
20-59	176	19.2	83	20.9	55	14.6	17	30.4	11	20.0
60-69	220	24.0	92	23.1	85	22.5	14	25.0	19	34.5
70-79	278	30.3	127	31.9	116	30.8	16	28.6	10	18.2
80+	244	26.6	96	24.1	121	32.1	9	16.1	15	27.3

Survival curves for males were higher than females for stages 0/I and II squamous cell carcinoma (Figure 23.9). In contrast, for stages III and IV, females had higher survival for most years.

Adenocarcinoma

Survival by age, sex, and race

Overall, less than 30% of all cases were diagnosed when younger than 60 years (Table 23.15). Black males and females had a younger age distribution than white males and females. The male to female ratio for whites was 1.9 and for blacks was 1.5.

Overall, males had a slightly higher 5-year relative survival rate (48%) compared with females (36%) diagnosed with adenocarcinoma (Figure 23.10).

Survival by stage

Later stage (III and IV) adenocarcinoma was more frequent in females compared with males (Table 23.16), which contributed to an all stage median survival time that was higher in males compared with females. The survival curves, however, were not consistently higher for males compared to females within stage (Figure 23.11).

DISCUSSION

For the 67,528 cases presented herein, the greatest number of bladder cancers was diagnosed between the ages of 60 and 79 years of age. Among adults, the 5-year relative survival rate was greatest for white males (85%) followed by white females (77%), black males (69%), and black females (55%). Transitional cell carcinoma was the most common histologic type, accounting for over 95% of all bladder cancers. Within this type, papillary transitional cell carcinoma was the most common subtype, accounting for 70.2% of all bladder cancers and nonpapillary transitional cell carcinoma accounting for an additional 25.5% of the bladder cases. The next most frequent histologic type was squamous cell carcinoma, which comprised 1.4% of all urinary bladder cancers, followed by adenocarcinoma, which accounted for 1.2%. Papillary transitional cell carcinoma had the highest median survival time (> 10 years) followed by nonpapillary transitional cell carcinoma, adenocarcinoma, and squamous cell carcinoma. The male to female ratio was greatest for transitional cell carcinoma and least for squamous cell carcinoma. For papillary transitional cell carcinoma, most were diagnosed at stages 0 and I. When early stage transitional cell carcinomas were stratified by histologic subtype and tumor grade, high-grade nonpapillary lesions had the poorest survival.

We know there is inherent misclassification in the SEER data involving separation of in situ/noninvasive and superficially invasive carcinomas as well as papillary and nonpapillary lesions (9). Because of this, it is likely the differences we have reported here are somewhat inaccurate. For example, the number of low grade nonpapillary transitional cell carcinomas probably includes misclassifications since the usual histologic criteria for nonpapillary carcinoma in situ are flat, noninvasive, high grade lesions. In fact the low grade stage 0 nonpapillary transitional cell carcinomas likely consist of low grade stage 0 papillary carcinomas in which the papillary component was not clearly defined in the pathology report. In addition, the percentage of stage 0 may be under-reported since additional terms to determine non-invasion based on the study (9) were not added to the extent of disease coding systems until 1991. The pathology community recognizes the need to more consistently specify grade, level of invasion, and histologic type (7,11) and this continues to be a challenge (12). Registry abstractors need to record findings from the pathology report correctly and coders need to classify this information accurately. This can be accomplished in part by recognizing that, in contrast to many other tumor sites, the absence of a statement of invasion is taken to indicate a noninvasive process by pathologists and urologists, and should be done so by abstractors and coders as well. As these deficiencies are addressed, SEER data will be able to delineate survival differences better within the common subtypes of transitional cell carcinoma.

The median survival times presented are based on the observed survival rate. Any characteristic that implies better survival in the general population such as young age will influence the median survival time. If the relative survival rates were similar between males and females and they

Table 23.14: Squamous Cell Carcinoma of the Urinary Bladder: Number and Distribution of Cases and Median Survival Time (Months) by AJCC Stage (5th Edition) and Sex, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage (5th Edition)	Male			Female		
	Cases	%	Median Survival Time (Months)	Cases	%	Median Survival Time (Months)
Total	470	100.0	10.0	448	100.0	9.1
Stage 0/I	29	6.2	> 120	35	7.8	24.4
Stage II	87	18.5	46.4	72	16.1	30.4
Stage III	86	18.3	16.9	73	16.3	23.6
Stage IV	130	27.7	4.8	129	28.8	5.3
Unknown	138	29.4	7.3	139	31.0	6.6

Figure 23.8: Squamous Cell Carcinoma of the Urinary Bladder: Relative Survival Rates (%) by Sex, Ages 20+, 12 SEER Areas, 1988-2001

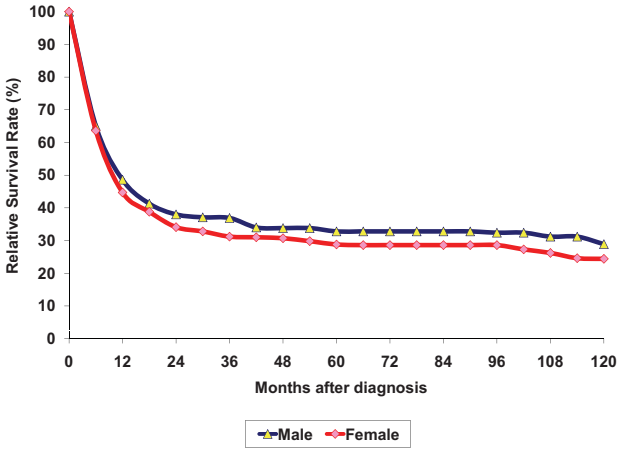


Figure 23.9: Squamous Cell Carcinoma of the Urinary Bladder: Relative Survival Rates (%) by Sex and AJCC Stage (5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

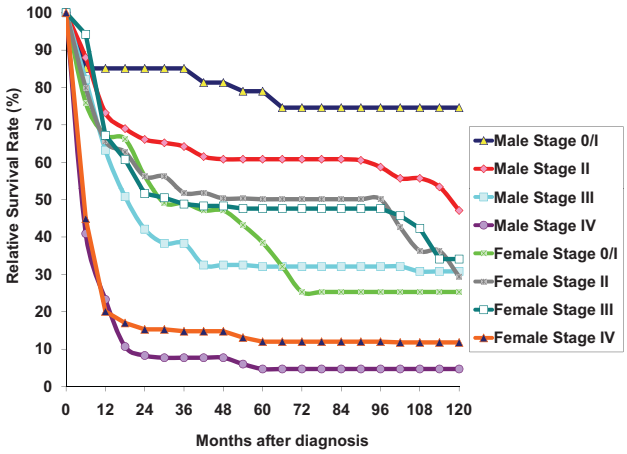


Figure 23.10: Adenocarcinoma of the Urinary Bladder: Relative Survival Rates (%) by Sex, Ages 20+, 12 SEER Areas, 1988-2001

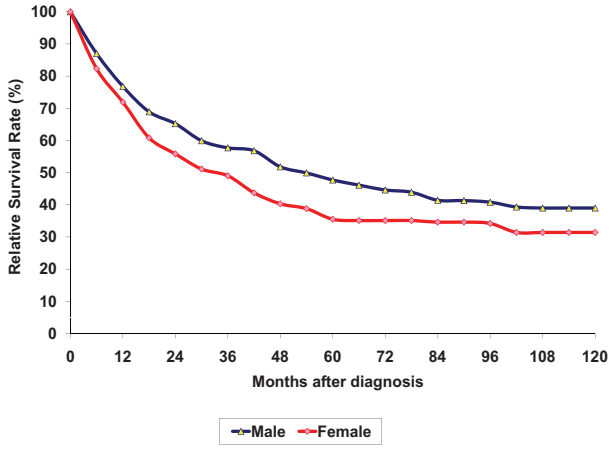


Figure 23.11: Adenocarcinoma of the Urinary Bladder: Relative Survival Rates (%) by Sex and AJCC Stage (5th Edition), 12 SEER Areas, 1988-2001

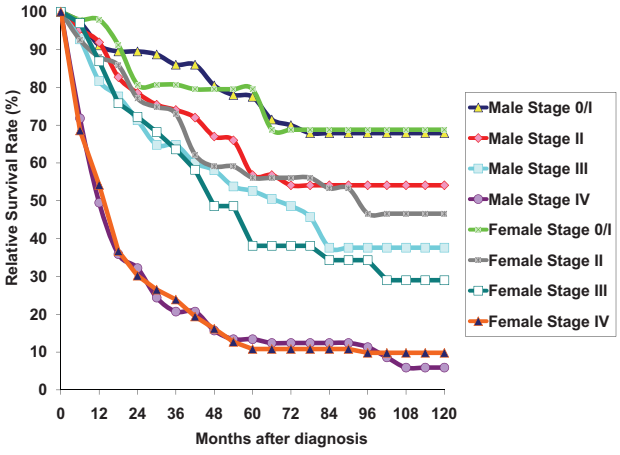


Table 23.15: Adenocarcinoma of the Urinary Bladder: Number and Distribution of Cases by Age (20+), Race, and Sex, 12 SEER Areas, 1988-2001

			Race/Sex							
			White				Black			
	Total		Male		Female		Male		Female	
Age Group (Years)	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	838	100.0	454	100.0	242	100.0	60	100.0	41	100.0
20-59	244	29.1	120	26.4	61	25.2	29	48.3	15	36.6
60-69	203	24.2	122	26.9	47	19.4	16	26.7	10	24.4
70+	391	46.7	212	46.7	134	55.4	15	25.0	16	39.0

Table 23.16: Adenocarcinoma of the Urinary Bladder: Number and Distribution of Cases and Median Survival Time (Months) by AJCC Stage (5th Edition) and Sex, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage (5th Edition)	Male			Female		
	Cases	%	Median Survival Time (Months)	Cases	%	Median Survival Time (Months)
Total	540	100.0	36.1	298	100.0	24.9
Stage 0/I	78	14.4	75.4	30	10.1	> 120
Stage II	77	14.3	57.3	34	11.4	56.4
Stage III	63	11.7	48.4	53	17.8	43.2
Stage IV	132	24.4	11.6	80	26.8	12.7
Unknown	190	35.2	43.4	101	33.9	18.4

had approximately the same age distribution, the median survival times may be longer for the females since women have longer life expectancy than men.

Squamous cell carcinomas and adenocarcinomas were rare. Overall survival rates among males for adenocarcinoma were 3 times higher than for squamous cell carcinoma, while among females it was 2.5 times higher. The survival advantage typically associated with early stage disease was less apparent for squamous cell carcinoma.

REFERENCES

1. American Cancer Society. Cancer facts & figures 2006, The American Cancer Society, Atlanta, (GA), 2006.
2. Miller BA, Kolonel LN, Bernstein L, Young, Jr. JL, Swanson GM, West D, Key CR, Liff JM, Glover CS, Alexander GA, et al. (eds). Racial/Ethnic Patterns of Cancer in the United States 1988-1992, National Cancer Institute. NIH Pub. No. 96-4104. Bethesda, MD, 1996.Lynch CF, Cohen MB. Urinary System. Cancer 1995;75:316-329.
3. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Eisner MP, Horner MJ, Howlader N, Hayat M, Hankey BF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site, 2006.
4. Mungen NA, Aben KK, Schoenberg MP, Visser O, Coebergh JW, Witjes JA, Kiemeney LA. Gender differences in stage-adjusted bladder cancer survival. Urology 2000; 55(6):876-880.
5. Underwood W, Dunn RL, Williams C, Lee CT. Gender and geographic influence on the racial disparity in bladder cancer mortality in the US. J Am Coll Surg 2006; 2002 (2):284-290.
6. Prout GR Jr, Wesley MN, Greenberg RS, Chen VW, Brown CC, Miller AW, Weinstein RS, Robboy SJ, Haynes MA, Blacklow RS, Edwards BK. Bladder cancer: Race differences in extent of disease at diagnosis. Cancer 2000; 89(6)1349-1358.
7. Epstein JI, Amin MB, Reuter VR, Mostofi FK, and the Bladder Consensus Conference Committee. The World Health Organization/International Society of Urologic Pathology consensus classification of urothelial (transitional cell) neoplasms of the urinary bladder. Am J Surg Pathol 1998;22(12):1435-1448.
8. Hankey BF, Edwards BK, Ries LA, Percy CL, Shambaugh E. Problems in cancer surveillance: delineating in situ and invasive bladder cancer. J Natl Cancer Inst 1991;83:384-385.
9. Lynch CF, Platz CE, Jones MP, Gazzaniga JM. Cancer registry problems in classifying invasive bladder cancer. J Natl Cancer Inst 1991;83:433-437.
10. Fleming ID, Cooper JS, Henson DE, Hutter RVP, Kennedy BJ, Murphy GP, O'Sullivan B, Sobin LH, Yarbro, JW (eds). AJCC Cancer Staging Manual, Fifth edition, American Joint Committee on Cancer. Philadelphia: Lippincott-Raven, 1997.
11. Murphy WM. The term 'superficial bladder cancer' should be abandoned. Eur Urol 2000;38:597-599.
12. Maruniak NA, Takezawa K, Murphy WM. Accurate pathological staging of urothelial neoplasms requires better cystoscopic sampling. J Urol 2002;167(6):2404-2407.

Chapter 24
Cancers of the Kidney and Renal Pelvis

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INTRODUCTION

Cancers of the kidney arise primarily from cells that compose the renal tubules and are most often designated as renal cell carcinomas or clear cell adenocarcinomas (1). Cancers of the renal pelvis and calyces arise in the transitional epithelium that lines these structures and are most often designated as nonpapillary or papillary transitional cell carcinomas. Over 80% of these cancers arise in the renal parenchyma, while less than 20% arise in the renal pelvis (2).

In 2006, cancer of the kidney and renal pelvis was the 9th most common incident malignancy (estimated 38,890 new cancers) and the 12th most common cause of cancer death (estimated 12,840 deaths) in the United States (3). However, increasing incidence rates of renal cell and renal pelvis carcinoma have been reported during more recent years (1,4,5,6). Although the use of abdominal imaging has increased, leading to more renal cancers being detected at local or regional stages of disease, the incidence of cancer presenting at a distant stage has not declined (6). This finding suggests that a true increase in renal cancer has occurred that cannot be solely attributed to changes in diagnostic practices.

Regardless of race, age-adjusted incidence rates have remained higher in males compared with females (4). Among cancers of the kidney, age-adjusted incidence rates in white males and females have remained lower compared with black males and females (4). However, among renal pelvis carcinomas, white males and females have higher age-adjusted incidence rates compared with black males and females.

Rising mortality rates from cancers of the kidney and renal pelvis have also been observed (4). During more recent years, similar age-adjusted mortality rates have been reported in white males and black males, as well as in white females and white males. In both white and blacks, mortality rates were significantly higher in males compared with females.

Although incidence and mortality from cancers of the kidney and renal pelvis have increased, 5-year relative survival rates in whites have improved over time (4). However, significant changes in survival among blacks have not been observed.

Table 24.1: Cancer of the Kidney and Renal Pelvis : Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
47,220	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
38,329	8,891	Select first primary only
37,583	746	Exclude death certificate only or at autopsy
37,443	140	Exclude unknown race
37,392	51	Exclude alive with no survival time
36,431	961	Exclude children (Ages 0-19)
35,786	645	Exclude in situ cancers for all except breast & bladder cancer
32,755	3,031	Exclude no or unknown microscopic confirmation
32,603	152	Exclude sarcomas
32,583	20	Exclude carcinoids

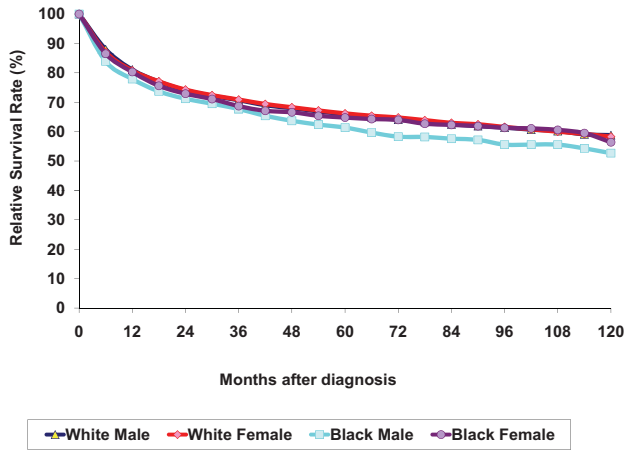
Table 24.2: Cancer of the Kidney and Renal Pelvis: Number and Distribution of Cases by Age (20+), Race and Sex, 12 SEER Areas, 1988-2001

	Total		Race/Sex							
			White				Black			
			Male		Female		Male		Female	
Age Group (Years)	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	32,583	100.0	17,221	100.0	10,228	100.0	1,876	100.0	1,268	100.0
20-29	228	0.7	78	0.5	81	0.8	22	1.2	28	2.2
30-39	1,263	3.9	607	3.5	366	3.6	111	5.9	91	7.2
40-49	4,209	12.9	2,271	13.2	1,108	10.8	351	18.7	214	16.9
50-59	7,200	22.1	4,006	23.3	1,962	19.2	525	28.0	272	21.5
60-69	8,845	27.1	4,879	28.3	2,638	25.8	470	25.1	293	23.1
70-79	8,006	24.6	4,109	23.9	2,833	27.7	323	17.2	280	22.1
80+	2,832	8.7	1,271	7.4	1,240	12.1	74	3.9	90	7.1

MATERIALS AND METHODS

The material and methods follow the description provided in the introductory chapter. Topographic codes used at this site within the SEER Program permit separation of kidney (C64) and renal pelvis (C65). The number of persons with cancers of the kidney and renal pelvis from this population for the period from 1988 to 2001 is provided in Table 24.1, accompanied by the numbers and reasons for those excluded for this survival analysis.

Figure 24.1: Cancer of the Kidney & Renal Pelvis: Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001



RESULTS

All Kidney and Renal Pelvis Cancers

Distribution and survival by age, sex and race

Eighty-two percent of adults were diagnosed at age 50 and older (Table 24.2). The greatest numbers occurred in the 60-69 age group, and the 50-79 age group contained 73.8% of all kidney and renal pelvis cancers. The male to female ratio was 1.7:1 for whites and 1.5:1 for blacks. White males alone accounted for 52.9% of all eligible persons. Whereas 15.2% of the cancers occurred under age 50 in white females, 26.3% occurred under age 50 in black females.

Relative survival curves were similar by race and sex (Figure 24.1). Five to ten years after diagnosis, black males have the poorest relative survival rates. The five-year relative survival rates ranged from a low of 59% for black males aged 50+ to a high of 78% for white females aged 20-49 (Table 24.3). Under age 50, median survival times were greater than 10 years for both races and sexes. For ages 50 and older, median survival times and 5-year relative survival rates were lowest for black males and highest for white females. Overall for ages 20+, five-year relative survival rates varied by age, race, and sex.

Survival by histology

Of the 32,583 adult cases, 87.7% were diagnosed with adenocarcinoma (Table 24.4). Pathologists specify adenocarcinoma through several different terms, which relate to histologic features representing the different cells of origin recapitulated in differentiation. The most common coded term was renal cell carcinoma (ICD-O-3 M-8312,

Table 24.3: Cancer of the Kidney and Renal Pelvis: Number of Cases, Median Survival Time (Months) and 5-Year Survival Rates (%) by Race, Sex, and Age Group (20+), 12 SEER Areas, 1988-2001

Race, Sex and Age Group	Cases	Median Survival Time (Months)	5-Year Survival Rate (%)		
			Observed	Expected	Relative
White Females, 20-49	1,555	> 120	77.4	99.0	78.3
White Males, 20-49	2,956	> 120	71.1	97.9	72.6
Black Females, 20-49	333	> 120	70.5	97.9	71.4
Black Males, 20-49	484	> 120	63.4	95.2	66.4
White Females, 50+	8,673	77.2	54.7	85.8	63.8
White Males, 50+	14,265	67.6	52.6	81.8	64.3
Black Females, 50+	935	70.4	52.3	84.6	61.8
Black Males, 50+	1,392	51.7	47.2	79.7	59.2
White Females, 20+	10,228	92.6	58.1	87.8	66.2
White Males, 20+	17,221	79.8	55.7	84.6	65.9
Black Females, 20+	1,268	91.9	57.1	88.1	64.8
Black Males, 20+	1,876	64.4	51.4	83.7	61.4

8316-8319) followed by clear cell adenocarcinoma (ICD-O-3 M-8310). The second most common histologic type, accounting for nearly 10% of all cancers, was transitional cell carcinoma. Most of these cancers were coded as papillary transitional cell carcinoma (ICD-O-3 M-8130) or transitional cell carcinoma (ICD-O-3 M-8120). Squamous cell carcinoma was rare and most commonly was reported as having arisen in the renal pelvis, where it has been often associated with squamous metaplasia, renal calculi, and chronic infection (7). Oxyphilic adenocarcinoma, also known as oncocytic carcinoma, in the ICD-O coding scheme, probably consists largely of renal oncocytoma, a tumor distinct from renal cell carcinoma because it typically has a benign behavior (8). The occasional malignant cases are thought to be most likely chromophobe renal cell carcinomas (ICD-O-3 M-8270) (9). Nephroblastoma, also known as Wilms tumor, rarely occurs in adults, but is the most common form of renal cancer in children (10). Oxyphilic adenocarcinoma and nephroblastoma arose only in the kidney. We classified 2.4% of kidney and renal pelvis cancers to an "other" category. Within this category, carcinoma not otherwise specified (ICD-O-3 M-8010) was the most common histologic type.

Five-year relative survival rates were greatest for oxyphilic adenocarcinoma followed by nephroblastoma/Wilms tumor (Table 24.5). Squamous cell carcinoma had the poorest survival rate. Median survival rates for these histologic types followed a similar pattern. The two most common histologic types, adenocarcinoma and transitional cell carcinoma, had observed survival rates that were about 10 percentage points lower than their corresponding relative rates. Median survival for adenocarcinoma (92 months) was more than double that for transitional cell carcinoma (45 months).

Relative survival curves for each of these histologic types showed oxyphilic adenocarcinoma with the best survival and squamous cell carcinoma with the worst (Figure 24.2). Eighteen or more months after diagnosis, the relative survival rates for adenocarcinoma was significantly better than transitional cell carcinoma.

Adenocarcinoma

Survival by age, race, sex, and laterality

Of the 28,560 persons with adenocarcinoma, 81.3% were diagnosed when at least 50 years old (Table 24.6). Persons in the 50-79 year age groups were diagnosed with almost three-quarters of all adenocarcinomas. The male to female ratio was 1.75:1. White males alone accounted for 53.4% of all adenocarcinomas. Whereas 17.6% of adenocarcinomas occurred in whites under age 50, 26.8% occurred in blacks under age 50.

Over 99% of adenocarcinomas with classifiable laterality (n = 28,078) were coded as arising in the kidney (Table 24.7). Right kidney was a slightly more common location (50.7%). The median survival time was slightly higher for adenocarcinomas of the right kidney compared with the left kidney.

In the 20-49, 50+ and 20+ age groups, five-year observed and relative survival rates were highest among white females and lowest among black males (Table 24.8). In each of these age groups, five-year survival rates for white males and black females were similar. For each race-sex group, survival rates were highest in the 20-49 age group. Relative survival curves for adenocarcinoma by race and

Table 24.4: Cancer of the Kidney and Renal Pelvis: 5-Year Relative Survival Rate (RSR) and Distribution of Cases by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology/ICD-O Code	Cases	Percent	5-Year RSR (%)
Total	32,583	100.0	65.5
Adenocarcinoma	28,560	87.7	67.5
Renal Cell Carcinoma (8312,8316-8319)	20,045	61.5	65.6
Adenocarcinoma, NOS (8140)	684	2.1	39.1
Tubular Adenocarcinoma (8211)	96	0.3	79.5
Papillary Adenocarcinoma (8260)	371	1.1	74.1
Clear Cell Adenocarcinoma, NOS (8310)	6,445	19.8	75.4
Granular Cell Carcinoma (8320)	748	2.3	72.2
Other Adeno (8141,8190,8200,8251,8255,8270,8280,8323,8370,8440,8450, 8480-8481,8490,8500,8504,8510,8521,8550,8570,8940)	171	0.5	68.6
Transitional Cell Carcinoma	3,049	9.4	57.5
Transitional Cell Carcinoma, NOS (8120)	1,495	4.6	38.2
Papillary Transitional Cell Carcinoma (8130)	1,550	4.8	75.4
Other Transitional (8121-8122)	<5	~	~
Squamous Cell Carcinoma	93	0.3	4.0
Squamous Cell Carcinoma, NOS (8070)	78	0.2	4.7
Other Squamous (8052,8071)	15	0.0	~
Oxyphilic Adenocarcinoma (8290)	65	0.2	94.9
Nephroblastoma/Wilms Tumor (8960)	42	0.1	78.1
Other Histologies (8000-8001,8004,8010,8012,8020-8022,8030,8032-8033, 8041,8046,8050,8560,8933,8935,8963-8964,8990,9082,9364,9473)	774	2.4	23.8

~ Statistic not displayed due to less than 25 cases.

Table 24.5: Cancer of the Kidney and Renal Pelvis: Number and Distribution of Cases, Median Survival Time (Months) and 5-Year Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology	Cases	Percent	Median Survival Time (Months)	5-Year Survival Rate (%)		
				Observed	Expected	Relative
Total	32,583	100.0	83.3	56.3	86.0	65.5
Adenocarcinoma	28,560	87.7	91.9	58.6	86.9	67.5
Transitional cell carcinoma	3,049	9.4	45.4	45.5	79.1	57.5
Squamous cell carcinoma	93	0.3	5.2	3.2	80.7	4.0
Oxyphilic adenocarcinoma	65	0.2	> 120	81.1	79.9	94.9
Nephroblastoma/Wilms tumor	42	0.1	> 120	76.9	97.5	78.1
Other Histologies	774	2.4	6.7	19.3	81.2	23.8

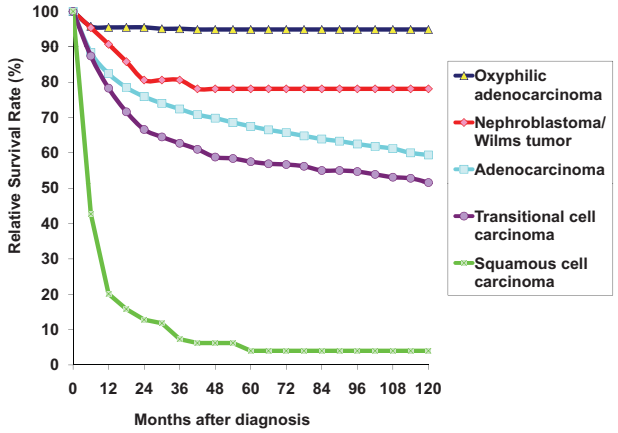
sex (Figure 24.3) were almost identical to those for all histologic types combined (Figure 24.1).

Survival by stage

Staging information for adenocarcinoma was available for 78.3% of the 26,824 patients in the comparison of stage for white patients and black patients (Table 24.9). For each of these race and sex subgroups, the greatest percentages of adenocarcinomas were diagnosed at stage I, 30.6% among white males, 35.0% among black males, 35.5% among white females, and 35.6% among black females (Table 24.9). Overall, 40.4% of adenocarcinomas in white males, 45.2% in black males, 45.3% in white females, and 47.3% in black females were diagnosed at AJCC stages I & II. The percentages of stage III adenocarcinomas ranged from 9.5% in black females to 15.6% in white males, whereas for stage IV adenocarcinomas the percentages were in a much tighter range of 19.1% in black females to 22.7% in white males.

For Stages I and II, 5-year relative survival varied more by race than stage for males. Relative survival curves were higher for white males compared with black males for Stages I, II, and III but similar for Stage IV (Figure 24.4). Analogous curves for females were different at stage III up until 10 years but similar for other stages (Figure 24.5).

Figure 24.2: Cancer of the Kidney & Renal Pelvis: Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001



Transitional Cell Carcinoma

Survival by age, race, sex, and laterality

Among persons with transitional cell carcinoma, 92.9% occurred in patients at least 50 years old (Table 24.10). The male to female ratio was 1.2:1. The under 60 age group comprised only 14.5% in white females, whereas 23.4%, 26.3%, and 31.4% occurred in white males, black females, and black males, respectively.

About 99% (n = 3,019) of the transitional cell carcinomas were coded as arising in the right or left kidney and right or left renal pelvis (Table 24.11). Most of these (80.3%) were classifiable to renal pelvis with the right renal pelvis being the preferred side (50.8%). The median survival times were similar between the right and left renal pelves. Median survival times for transitional cell carcinomas that arose in the kidney were less than half that of those arising in the renal pelvis.

Age-specific five-year relative survival rates ranged from a low of 36% for black males aged 70+ to a high of 64% for white males in the 20-69 age group (Table 24.12). Observed and relative survival rates were greater for

Table 24.6: Adenocarcinoma of the Kidney and Renal Pelvis: Number and Distribution of Cases by Age (20+), Race and Sex, 12 SEER Areas, 1988-2001

Age Group (Years)	Total		Race/Sex							
			White				Black			
			Male		Female		Male		Female	
	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	28,560	100.0	15,252	100.0	8,707	100.0	1,723	100.0	1,142	100.0
20-29	198	0.7	63	0.4	74	0.8	20	1.2	23	2.0
30-39	1,179	4.1	561	3.7	347	4.0	100	5.8	88	7.7
40-49	3,964	13.9	2,126	13.9	1,048	12.0	335	19.4	202	17.7
50-59	6,648	23.3	3,713	24.3	1,785	20.5	493	28.6	249	21.8
60-69	7,860	27.5	4,369	28.6	2,310	26.5	425	24.7	274	24.0
70-79	6,652	23.3	3,472	22.8	2,282	26.2	287	16.7	235	20.6
80+	2,059	7.2	948	6.2	861	9.9	63	3.7	71	6.2

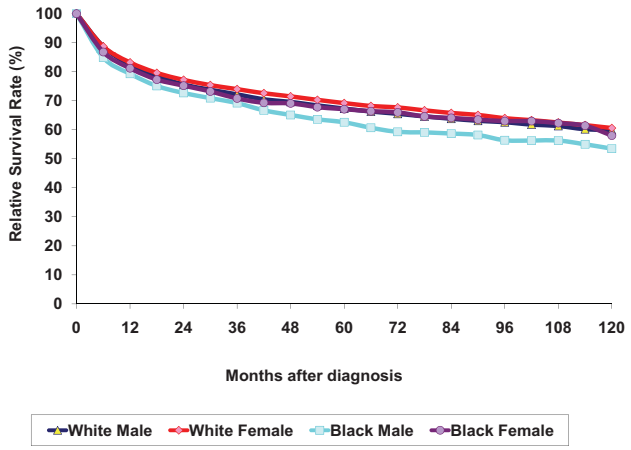
Table 24.7: Adenocarcinoma of the Kidney and Renal Pelvis: 5-Year Relative Survival Rate (RSR), Distribution of Cases with Classifiable Laterality and Median Survival Time (Months) by Laterality and Subsite, Ages 20+, 12 SEER Areas, 1988-2001

Laterality	Kidney				Renal Pelvis			
	Cases	Percent	Median Survival Time (Months)	5-Year RSR (%)	Cases	Percent	Median Survival Time (Months)	5-Year RSR (%)
Total (with classifiable laterality)	28,014	100.0	95.1	68.4	64	100.0	34.5	47.7
Right	14,217	50.7	99.8	69.5	37	57.8	34.4	46.0
Left	13,797	49.3	89.7	67.2	27	42.2	47.1	47.0

Table 24.8: Adenocarcinoma of the Kidney and Renal Pelvis: Number and Distribution of Cases, Median Survival Time (Months) and 5-Year Survival Rates (%) by Race, Sex and Age (20+), 12 SEER Areas, 1988-2001

Race, Sex and Age Group (Years)	Cases	Percent	Median Survival Time (Months)	5-Year Survival Rate (%)		
				Observed	Expected	Relative
All	28,560	100.0	91.9	58.6	86.9	67.5
White Females, 20-49	1,469	5.1	> 120	78.3	99.0	79.1
White Males, 20-49	2,750	9.6	> 120	71.7	97.9	73.2
Black Females, 20-49	313	1.1	> 120	71.8	97.9	72.8
Black Males, 20-49	455	1.6	> 120	64.6	95.1	67.7
White Females, 50+	7,238	25.3	89.6	58.3	87.0	67.0
White Males, 50+	12,502	43.8	73.5	54.4	82.7	65.8
Black Females, 50+	829	2.9	75.7	54.8	85.3	64.3
Black Males, 50+	1,268	4.4	54.8	48.3	80.0	60.4
White Females, 20+	8,707	30.5	105.0	61.6	89.0	69.2
White Males, 20+	15,252	53.4	86.1	57.5	85.4	67.3
Black Females, 20+	1,142	4.0	104.7	59.5	88.7	67.1
Black Males, 20+	1,723	6.0	66.0	52.6	84.0	62.6

Figure 24.3: Adenocarcinoma of the Kidney & Renal Pelvis: Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001



males than females in each of these age groups except blacks 70+. Survival rates were higher for the younger age group by race and sex.

Black and white males had the best relative survival rates 2 to 6 years after diagnosis (Figure 24.6). Thereafter, relative survival rates in black males tailed off and were similar to black and white females. Overall, black and white males had better relative survival rates than black and white females and higher median survival times.

Survival by sex, stage, and grade

Staging information was available for 65.0% of the 3,049 transitional cell carcinomas. AJCC (5th edition) stage I transitional cell carcinomas were slightly more frequent in males (17.2%) compared with females (14.5%), whereas stage IV transitional cell carcinomas were slightly more frequent in females (29.1%) than males (25.4%) (Table 24.13). AJCC (5th edition) stage distribution was similar for blacks and whites except blacks had a higher percentage unknown, 41.5% and 35.2%, respectively. Survival rates for blacks with stages II and III could not be calculated due to insufficient case numbers for analysis (Table 24.13, Figure 24.8).

Males had slightly better relative survival rates than females for each stage of disease with the exception of stage II and III (Figure 24.7). Coupled with the slightly larger percentage of tumors in the early stage, this, at least in part, explained the overall better survival rates for males compared with females (Figure 24.6). Relative survival differences between blacks and whites were not substantial, in part due to low numbers of blacks at each stage (Figure 24.8).

Within both sexes, low grade (grades I & II) transitional cell carcinomas had better survival than high grade (grades III & IV) at each stage (Figures 24.9 & 24.10).

DISCUSSION

During 2006, cancers of the kidney and renal pelvis were the 9th most common incident malignant cancer and the 12th most common cause of cancer death. Of the 32,583 patients, 84.2% were white, 9.6% black, and 6.2% other races. The greatest number of these cancers was diagnosed in the 60-69 age group. Adenocarcinoma was the most common histologic type, accounting for 87.7% of

Table 24.9: Adenocarcinoma of the Kidney and Renal Pelvis: Number and Distribution of Cases, 5-Year Relative Survival Rates (%), and Median Survival Time (Months) by AJCC Stage (5th Edition), Race, and Sex, Ages 20+, 12 SEER Areas, 1988-2001

	Race/Sex											
	White						Black					
	Male			Female			Male			Female		
AJCC Stage	Cases	Percent	5-Year Relative Survival Rate (%)	Cases	Percent	5-Year Relative Survival Rate (%)	Cases	Percent	5-Year Relative Survival Rate (%)	Cases	Percent	5-Year Relative Survival Rate (%)
Total	15,252	100.0	67.3	8,707	100.0	69.2	1,723	100.0	62.6	1,142	100.0	67.1
Stage I	4,674	30.6	94.6	3,088	35.5	93.3	603	35.0	84.9	407	35.6	91.0
Stage II	1,490	9.8	86.1	856	9.8	88.2	175	10.2	79.8	134	11.7	88.8
Stage III	2,372	15.6	66.5	1,137	13.1	62.1	188	10.9	60.2	109	9.5	48.2
Stage IV	3,460	22.7	11.1	1,723	19.8	9.4	381	22.1	9.5	218	19.1	8.1
Unstaged/ Unknown	3,256	21.3	80.2	1,903	21.9	80.0	376	21.8	73.0	274	24.0	74.3

	Median Survival Time (Months)			
AJCC Stage	White Males	White Females	Black Males	Black Females
Total	86.1	105.0	66	104.7
Stage I	> 120	> 120	116.4	> 120
Stage II	> 120	> 120	112.5	> 120
Stage III	76.6	74.9	58.7	35.9
Stage IV	8.1	7.0	5.6	5.8
Unstaged/ Unknown	116.6	> 120	99.7	110.1

all cancers, followed by transitional cell carcinoma, which accounted for 9.4%. Squamous cell carcinoma, oxyphilic adenocarcinoma, and nephroblastoma/Wilms tumor accounted for less than 1%. Oxyphilic adenocarcinoma had the highest 5-year relative survival rate (95%), followed by nephroblastoma/Wilms tumor (78%), adenocarcinoma (68%), transitional cell carcinoma (58%), and squamous cell carcinoma (4%). The male:female ratio was 1.75:1 for adenocarcinoma and 1.2:1 for transitional cell carcinoma.

For adenocarcinomas, blacks had a slighly higher percentage of stage I & II disease than whites. Nevertheless, their overall relative survival was slightly less than whites because of lower survival rates by stage. Females had a slightly higher relative survival percentage than males except for stage III. Part of the explanation for this was a higher percentage of stages I & II adenocarcinomas in females compared with males for both blacks and whites.

For transitional cell carcinoma, low grade tumors had better relative survival rates than high grade tumors within each stage. Overall, relative survival was higher among males than females. This was, at least in part, explained by males 1) having a greater percentage diagnosed under age 60, 2) having a lower percentage of stage IV cancers, and 3) having a higher percentage of low grade cancers.

Figure 24.4: Male Adenocarcinoma of the Kidney & Renal Pelvis: Relative Survival Rates (%) by AJCC Stage (5th Edition) and Race, Ages 20+, 12 SEER Areas, 1988-2001

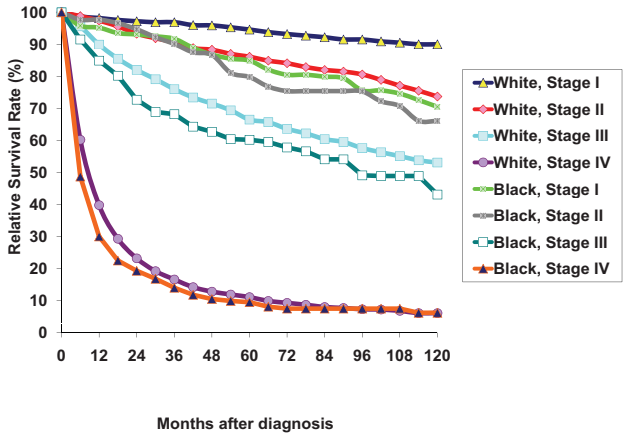


Figure 24.5: Female Adenocarcinoma of the Kidney & Renal Pelvis: Relative Survival Rates (%) by AJCC Stage (5th Edition) and Race, Ages 20+, 12 SEER Areas, 1988-2001

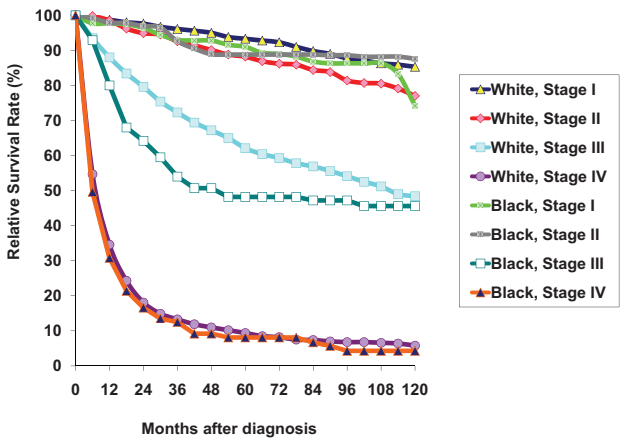


Table 24.10: Transitional Cell Carcinoma of the Kidney and Renal Pelvis: Number and Distribution of Cases by Age (20+), Race and Sex, 12 SEER Areas, 1988-2001

Age Group (Years)	Total		Race/Sex							
			White				Black			
			Male		Female		Male		Female	
	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	3,049	100.0	1,501	100.0	1,192	100.0	83	100.0	76	100.0
20-49	216	7.1	144	9.6	46	3.9	11	13.3	6	7.9
50-59	383	12.6	207	13.8	126	10.6	15	18.1	14	18.4
60-69	766	25.1	385	25.6	269	22.6	29	34.9	14	18.4
70-79	1,069	35.1	512	34.1	444	37.2	20	24.1	29	38.2
80+	615	20.2	253	16.9	307	25.8	8	9.6	13	17.1

Table 24.11: Transitional Cell Carcinoma of the Kidney and Renal Pelvis: 5-Year Relative Survival, Distribution of Cases with Classifiable Laterality and Median Survival Time (Months) by Laterality and Subsite, Ages 20+, 12 SEER Areas, 1988-2001

Laterality	Kidney				Renal Pelvis			
	Cases	Percent	Median Survival Time (Months)	5-Year Relative Survival	Cases	Percent	Median Survival Time (Months)	5-Year Relative Survival
Total	596	100.0	25.3	44.4	2,423	100.0	54.9	60.9
Right	302	50.7	25.9	44.2	1,230	50.8	56.0	61.6
Left	294	49.3	23.6	44.0	1,193	49.2	54.1	60.2

Table 24.12: Transitional Cell Carcinoma of the Kidney and Renal Pelvis: Number and Distribution of Cases, Median Survival Time (Months) and 5-Year Survival Rates (%) by Race, Sex, and Age (20+), 12 SEER Areas, 1988-2001

Race, Sex and Age Group (Years)	Cases	Percent	Median Survival Time (Months)	5-Year Survival Rate (%)		
				Observed	Expected	Relative
All	3,049	100.0	45.4	45.5	79.1	57.5
White Females, 20-69	441	14.5	85.9	53.5	94.2	56.6
White Males, 20-69	736	24.1	94.7	58.4	91.1	64.0
Black Females, 20-69	34	1.1	> 120	52.3	92.0	55.8
Black Males, 20-69	55	1.8	81.4	54.8	86.8	63.1
White Females, 70+	751	24.6	29.7	36.5	72.0	50.6
White Males, 70+	765	25.1	33.8	37.3	64.2	58.1
Black Females, 70+	42	1.4	21.0	36.3	70.7	46.9
Black Males, 70+	28	0.9	30.0	23.1	62.0	35.9
White Females, 20+	1,192	39.1	39.3	42.7	80.2	53.3
White Males, 20+	1,501	49.2	50.8	47.7	77.4	61.5
Black Females, 20+	76	2.5	44.0	43.4	80.2	51.7
Black Males, 20+	83	2.7	43.9	43.9	78.5	56.0

Figure 24.6: Transitional Cell Carcinoma of the Kidney & Renal Pelvis: Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

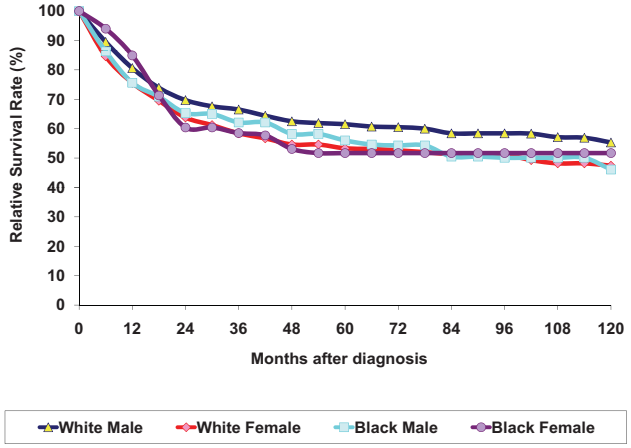


Figure 24.7: Transitional Cell Carcinoma of the Kidney & Renal Pelvis: Relative Survival Rates (%) by AJCC Stage (5th Edition) and Sex, Ages 20+, 12 SEER Areas, 1988-2001

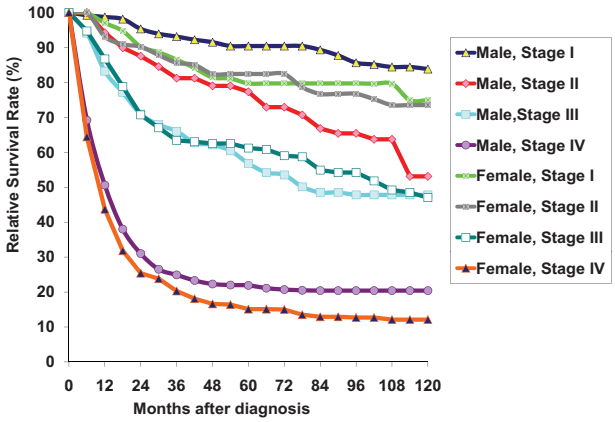


Figure 24.8: Transitional Cell Carcinoma of the Kidney & Renal Pelvis: Relative Survival Rates (%) by AJCC Stage (5th Edition) and Race, Ages 20+, 12 SEER Areas, 1988-2001

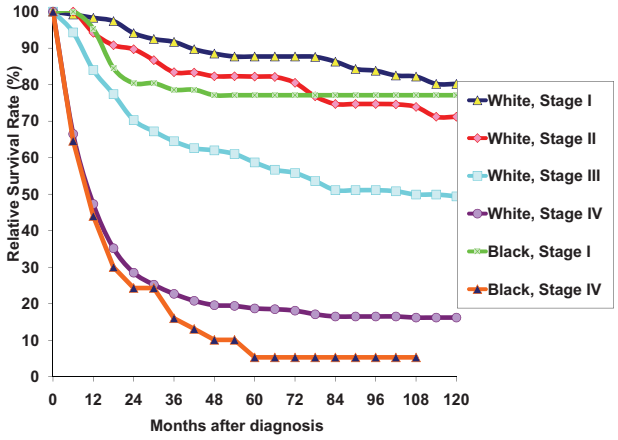


Figure 24.9: Male Transitional Cell Carcinoma of the Kidney & Renal Pelvis: Relative Survival Rates (%) by AJCC Stage (5th Edition) and Grade, Ages 20+, 12 SEER Areas, 1988-2001

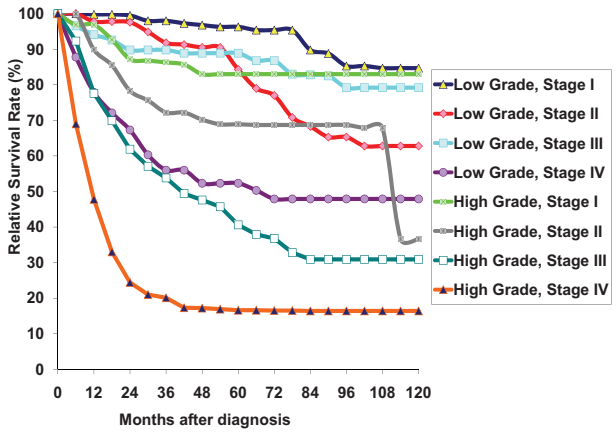


Figure 24.10: Female Transitional Cell Carcinoma of the Kidney & Renal Pelvis: Relative Survival Rates (%) by AJCC Stage (5th Edition) and Grade, Ages 20+, 12 SEER Areas, 1988-2001

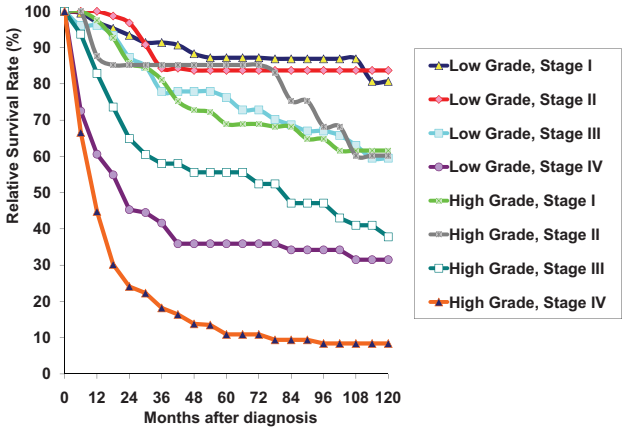


Table 24.13: Transitional Cell Carcinoma of the Kidney and Renal Pelvis: Number and Distribution of Cases, 5-Year Relative Survival Rates (%), and Median Survival Time (Months) by AJCC Stage (5th Edition), Sex, and Race, Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage (5th Edition)	Sex						Race					
	Male			Female			White			Black		
	Cases	Percent	5-Year Relative Survival Rate (%)	Cases	Percent	5-Year Relative Survival Rate (%)	Cases	Percent	5-Year Relative Survival Rate (%)	Cases	Percent	5-Year Relative Survival Rate (%)
Total	1,704	100.0	61.1	1,345	100.0	53.2	2,693	100.0	57.9	159	100.0	55.0
Stage I	293	17.2	90.4	195	14.5	79.7	422	15.7	87.7	25	15.7	77.1
Stage II	97	5.7	77.3	62	4.6	82.4	143	5.3	82.2	6	3.8	~
Stage III	298	17.5	56.8	215	16.0	61.2	459	17.0	58.7	24	15.1	~
Stage IV	432	25.4	21.9	391	29.1	15.1	722	26.8	18.7	38	23.9	5.3
Unstaged/ Unknown	584	34.3	72.1	482	35.8	64.3	947	35.2	69.0	66	41.5	67.5

Median Survival Time (Months)				
AJCC Stage	White Males	White Females	Black Males	Black Females
Total	51.6	39.9	45.1	43.8
Stage I	> 120	> 120	> 120	116.0
Stage II	77.9	104.0	97.2	~
Stage III	50.2	65.0	53.1	~
Stage IV	11.2	9.3	10.3	9.0
Unstaged/ Unknown	79.9	65.2	74.0	91.3

~Statistic not displayed due to less than 25 cases.

REFERENCES

1. Lynch CF, Cohen MB. Urinary system. Cancer 1995; 75(1Suppl):316-29.
2. Devesa SS, Silverman DT, McLaughlin JK, Brown CC, Connelly RR, Fraumeni JF Jr. Comparison of the descriptive epidemiology of urinary tract cancers. Cancer Causes Control 1990;1:1133-1141.
3. American Cancer Society. Cancer facts & figures 2006, The American Cancer Society, Atlanta, (GA), 2006.
4. Chow, WH, Devesa SS, Warren JL, Fraumeni JF Jr. Rising incidence of renal cell carcinoma in the United States. JAMA 1999; 281:1628-31
5. McCredie M. Bladder and kidney cancers. Cancer Surv. 1994;19:343-368.
6. Hock LM, Lynch J, Balaji KC. Increasing incidence of all stages of kidney cancer in the last 2 decades in the United States: An analysis of surveillance, epidemiology, and end results program data. J Urol 2002;167:57-60.
7. Peterson RO. Renal pelvis. In: Urologic Pathology, 2nd ed. Philadelphia: JB Lippincott Co., 1992, pp. 170-212.
8. Eble JN. Neoplasms of the kidney. In: Urologic Surgical Pathology, Bostwick DG and Eble JN (eds). Mosby-Year Book, Inc., 1997, pp. 83-148.
9. Lieber MM, Hosaka Y, Tsukamato T. Renal oncocytoma. World J Urol 1987; 5:71-9.
10. Ries LAG, Smith MA, Gurney JG, Linet M, Tamra T, Young JL, Bunin GR (eds). Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975-1995, National Cancer Institute, SEER Program. NIH Pub. No. 99-4649. Bethesda, MD, 1999.

Chapter 25
Cancer of the Brain and Other Central Nervous System

Jill S. Barnholtz-Sloan, Andrew E. Sloan, and Ann G. Schwartz

INTRODUCTION

This study provides survival analysis for 19,774 histologically confirmed first primary brain and other central nervous system (CNS) cancers diagnosed from 1988 through 2001 from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). The analysis performed in this study attempts to better understand the influence of morphologic and demographic factors on survival. Other CNS cancers include cancers of the central nervous system and malignant meningiomas of the brain. Benign and borderline tumors are not included in these analyses.

Brain and other CNS cancers are considered to be rare compared to prostate, lung, breast, or colon cancer. It is estimated there will be 18,820 new cases diagnosed of and 12,820 deaths from brain and other CNS cancer in the United States each year (1). The average annual age-adjusted incidence rate for brain and other CNS cancer in the United States is 7.6 per 100,000 for males and 5.4 per 100,000 for females (white males: 8.3 per 100,000; white females: 5.9 per 100,000; black males: 4.9 per 100,000; black females: 3.5 per 100,000) (2). The average annual age-adjusted mortality rate is approximately 4.5 per 100,000 for all races combined, with males having a higher mortality rate as compared to females (2).

Histologic type of tumor, age at diagnosis, race and treatment are all important predictors of survival, with a large variation in survival by histologic type of tumor (3, 4, 5, 6). The most common histologic subtypes of brain cancer are astrocytoma and glioblastoma multiforme (GBM), while the most common histologic subtypes of other CNS cancer are meningioma and ependymoma (3, 4, 7, 8, 9). Patients with GBM have the worst survival compared to any other histologic subtype (8).

No risk factor accounting for a large number of brain and other CNS cancers has been identified. There has been some evidence for inherited factors, with approximately 16% of families studied having a family history of cancer (5, 10, 11). The only known risk factor for primary brain and other CNS cancers is exposure to therapeutic ionizing radiation. Other factors have been shown to cause increased risk, including exposure to synthetic rubber manufacturing, to vinyl chloride, to petroleum refining/production work, or to pesticides and consumption of cured foods, but the data are inconsistent (5). Exposure to filtered cigarettes, diagnostic ionizing radiation, residential electromagnetic fields, formaldehyde, cell phone use and active or passive maternal tobacco smoking are not proven risk factors (5). The most common presenting symptoms, progressive neurological deficit, motor weakness, headache and seizure, do not appear to be independent risk factors (5, 11).

MATERIALS AND METHODS

Exclusions

Between 1988 and 2001, 29,335 adult cases of malignant brain and other CNS cancer were diagnosed and reported to the NCI SEER Program. Children (aged less than 20) were excluded because brain and other CNS cancer are different in children compared to adults in terms of incidence and survival (8, 12). Patients were followed for vital status until 2001. The survival analysis was based on relative survival rates calculated by the life-table method (13). The relative rate was used to estimate the effect of cancer on the survival of the cohort. Relative survival, defined as observed survival divided by expected survival, adjusts for the expected mortality that the cohort would experience. Further descriptions of the NCI SEER program, data selection and relative survival analysis can be found in Chapter 1. Table 25.1 details the exclusions from this group of patients that resulted in a final group of 19,774 total patients, 18,669 brain cancer and 1,105 other CNS cancer.

Histologic Type of Tumor Classification

For brain and other CNS cancer, histologic type is one of three important clinical factors (the others are age at diagnosis and grade). In the SEER database, histologic classification for years of diagnosis 1988-2001 follows the ICD-O-2 and ICD-O-3 morphology codes. For the brain cancer cases, the histologic types were coded in the following manner: 9380, 9381, 9382 – glioma; 9390, 9443, 9473 – glioma, other; 9391, 9392, 9393 – ependymoma; 9400-9430 – astrocytoma; 9440-9442 – glioblastoma; 9450-9460 – oligodendroglioma; 9470-9472 – medulloblastoma; 9060-9085, 9490-9506, 8000-8002, 8680, 9364, 9370 – Other. For the other CNS cancer cases, the histologic types were coded in the following manner: 9391-9394 – ependymoma; 9400-9421 – astrocytoma; 9380-9382, 9473, 9440, 9450 – glioma; 9530-9539 – meningioma; 9490-9522, 8680-8693, 800-8001, 8990, 9064, 9364, 9370 – other.

Primary Site Classification

For brain cancers, primary site of tumor is classified as the following: C710 – Cerebrum, C711 - Frontal Lobe, C712 - Temporal Lobe, C713 - Parietal Lobe, C714 - Occipital Lobe, C715 – Ventricle, Not Otherwise Specified (NOS), C716 - Cerebellum, NOS, C717 - Brain Stem, C718 - Overlapping lesion of brain and C719 - Brain, NOS. For other CNS cancers, primary site of tumor is classified as the following: BRAIN: C700 - Cerebral meninges, C709 - Meninges, NOS, C710 – Cerebrum, C711 - Frontal Lobe, C712 - Temporal Lobe, C713 - Parietal Lobe, C714 - Occipital Lobe, C715 - Ventricle, NOS, C716 - Cerebellum, NOS, C717 - Brain Stem, C718 - Overlapping lesion of brain and C719 - Brain, NOS; SPINE: C701 - Spinal meninges, C720 - Spinal Cord and C721 - Cauda equine and OTHER: C723 - Optic nerve, C724 - Acoustic nerve, C725 - Cranial nerve, NOS, C728 - Overlapping lesion of brain and CNS and C729 – Nervous system, NOS.

Stage Classification

Stage is not presented for brain cancer; however, stage is presented for other CNS cancer. In the SEER database, the categories for SEER stage are in situ, localized, regional, distant and unstaged. In situ cases are excluded from this study as seen in Table 25.1. Localized stage is defined as an invasive neoplasm confined entirely to the organ. Regional stage is defined as a neoplasm that has extended either beyond the organ or into regional lymph nodes. Distant stage is defined as a neoplasm that has spread to parts of the body remote from the primary tumor. Unstaged cancers lack sufficient information to assign stage. The American Joint Committee on Cancer (AJCC) TNM staging system, 5th Edition, (14) is also used.

RESULTS

In general, 24% and 69% of patients survived 5 years for brain cancer and other CNS cancer, respectively (Table 25.2). Figure 25.1 shows the 10-year relative survival curves for these two distinct types of cancer.

Table 25.1: Cancer of the Brain & Other Central Nervous System: Number of Cases and Exclusions, 12 SEER Areas, 1988-2001

Brain		Other CNS		
Number Selected/ Remaining	Number Excluded	Number Selected/ Remaining	Number Excluded	Reason for Exclusion/selection
27,479	0	1,856	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
25,159	2,320	1,680	176	Select first primary only
24,647	512	1,656	24	Exclude death certificate only or at autopsy
24,562	85	1,644	12	Exclude unknown race
24,502	60	1,639	5	Active follow-up and exclude alive with no survival time
20,937	3,565	1,306	333	Exclude children (000-019)
20,937	0	1,306	0	Exclude in situ cancers
18,740	2,197	1,196	110	Exclude no or unknown microscopic confirmation
18,674	66	1,118	78	Exclude sarcomas
18,669	5	1,105	13	Exclude Melanomas

For all analyses, brain cancer and other CNS cancer are analyzed separately because of the distinct differences between these two groups in clinical presentation, treatment patterns, response to treatment, and survival (12). In some of the tables, 1-, 2-, 3-, 5-, 8-, and 10-year relative survival rates are presented and in the figures, they are presented annually.

Brain Cancer

The prognostic factors of interest for the brain cancer analysis were: race, sex, age at diagnosis, histologic type, grade and primary site. The combinations of particular interest were: race and sex, histologic type and sex and histologic type and race. Size of tumor information was not analyzed because of the large amount of missing data (46.8%) (Table 25.3).

Race and Sex

For the analyses of relative survival, SEER classifies patients by race in three basic categories: white, black and other. For all race specific analyses, only white and black patients are used because the other category is made up of a mix of racial groups. In general, whites will develop brain cancer more often than blacks and survival in blacks was similar to whites (5-year relative survival rate: 23%). Males generally had a slightly higher incidence of brain cancer as compared to females, and females had better survival than males (5-year relative survival rate: 25% versus 23%). 5-year relative survival rate was highest for black males. Tables 25.3 and 25.4 show the relative survival rates for brain cancer by race and gender.

Age at Diagnosis

The average age of onset for adult brain cancer is in the mid-fifties, although this does vary by histologic subtype of tumor. As with most other cancer sites, survival decreased as age at diagnosis increased. The 5-year relative survival rates (%) for brain cancer by age at diagnosis categories 20-29, 30-39, 40-49, 50-59, 60-69, 70-79 and 80+ were 64%, 55%, 33%, 14%, 6%, 2% and 1%, respectively (Table 25.3). Figure 25.2 shows the 10-year relative survival curves by age at diagnosis.

Figure 25.1: Brain & Other Central Nervous System Cancer: Relative Survival by Primary Site, Ages 20+, 12 SEER Areas, 1988-2001

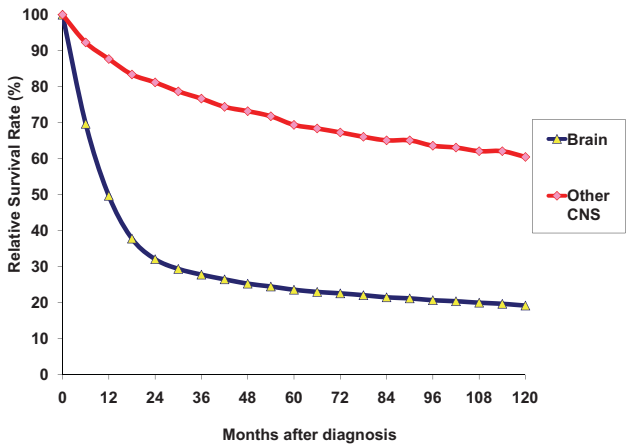


Table 25.2: Cancer of the Brain & Other CNS : 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Site, Ages 20+, 12 SEER Areas, 1988-2001

Site	Cases	% of Cases	Relative Survival Rate (%)					
			1-Year %	2-Year %	3-Year %	5-Year %	8-Year %	10-Year %
Total	19,774	100.0	51.8	34.9	30.5	26.2	23.2	21.6
Brain	18,669	94.4	49.7	32.1	27.8	23.6	20.7	19.2
Other Central Nervous System	1,105	5.6	87.7	81.2	76.7	69.5	63.7	60.6

Table 25.3: Cancer of the Brain: Race, Sex, Age (20+), Grade and Tumor Size, 12 SEER Areas, 1988-2001

Characteristics	Cases	% of Cases	Relative Survival Rate 5-Year (%)
Total Brain	18,669	100.0	23.6
Race			
White	16,824	90.1	23.4
Black	924	4.9	22.8
Other	921	4.9	29.2
Sex			
Male	10,701	57.3	22.9
Female	7,968	42.7	24.6
Age			
20-29	1,504	8.1	64.4
30-39	2,469	13.2	55.2
40-49	3,011	16.1	32.8
50-59	3,521	18.9	13.6
60-69	3,854	20.6	5.8
70-79	3,388	18.1	1.9
80+	922	4.9	1.3
Grade (Differentiation)			
Well differentiated; Grade I	478	2.6	77.0
Moderately differentiated; Grade II	1,885	10.1	62.4
Poorly differentiated; Grade III	1,642	8.8	18.3
Undifferentiated; anaplastic; Grade IV	7,442	39.9	13.1
Unknown	7,222	38.7	21.1
Size of tumor			
<=2cm	1,110	5.9	31.5
2-5 cm	6,201	33.2	19.8
>5 cm	2,619	14.0	20.8
Unknown	8,739	46.8	26.1

Grade

Tumors are graded as Grades 1, 2, 3, 4, and unknown. Grade 1 tumors are well differentiated, grade 2 tumors are moderately differentiated, grade 3 tumors are poorly differentiated and grade 4 tumors are undifferentiated. A tumor that has an unknown grade means that there was insufficient information to grade the tumor. It is important to note that for brain cancer, grade is directly correlated with the histologic type of tumor classification.

Survival for patients with brain cancer decreased from grade 1 to grade 4. The 5-year relative survival rates (%) for grade 1, grade 2, grade 3, grade 4 and unknown were 77%, 62%, 18%, 13% and 21%. However, it is important to note that 39% of patients had unknown grade in this study sample. Figure 25.3 shows the 10-year relative survival curves by grade.

Table 25.4: Cancer of the Brain: 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

			Relative Survival Rate (%)					
		% of	1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Sex/Race	Cases	Cases	%	%	%	%	%	%
All	18,669	100.0	49.7	32.1	27.8	23.6	20.7	19.2
Male	10,701	57.3	50.5	31.7	27.2	22.9	19.8	18.3
White	9,670	51.8	49.9	31.0	26.7	22.5	19.5	18.0
Black	491	2.6	54.1	34.4	29.7	24.8	20.8	20.8
Female	7,968	42.7	48.6	32.7	28.4	24.6	21.9	20.3
White	7,154	38.3	47.9	32.3	28.2	24.5	21.9	20.3
Black	433	2.3	49.3	31.3	25.4	20.7	19.1	16.6

Figure 25.2: Brain Cancer: Relative Survival Rates by Age Group, Ages 20+, 12 SEER Areas, 1988-2001

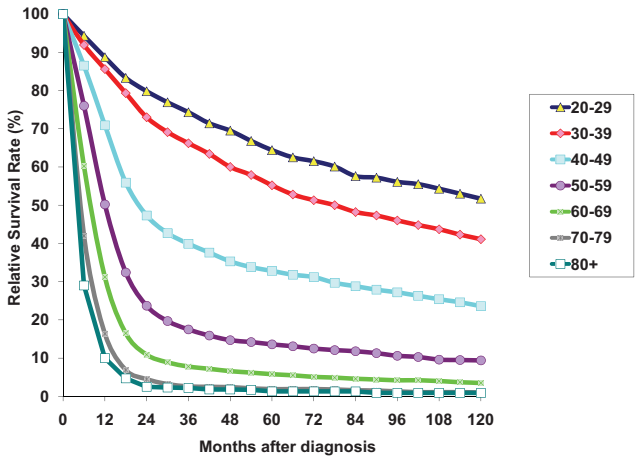
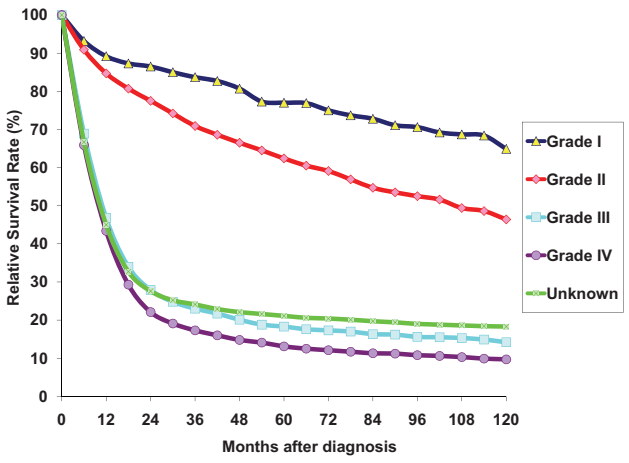


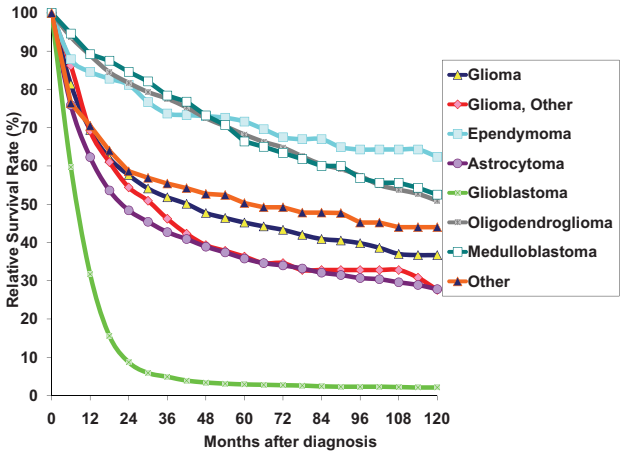
Figure 25.3: Brain Cancer: Relative Survival Rates by Grade, Ages 20+, 12 SEER Areas, 1988-2001



Histology

An individual's course of treatment, response to treatment and expected survival are all highly dependent on histologic type. Relative survival rates (%) varied greatly by histologic type (Table 25.5). The categories of histologic types of tumor used in this analysis (for brain cancer cases) were: glioma, glioma (other), ependymoma, astrocytoma, glioblastoma, oligodendroglioma, medulloblastoma, and other (germ cell neoplasms, neuroepitheliomatous neoplasms, other). Figure 25.4 shows the 10-year relative survival curves by histologic type.

Figure 25.4: Brain Cancer: Relative Survival Rates by Histology, Ages 20+, 12 SEER Areas, 1988-2001



Histology and Sex

Males had similar proportions of astrocytomas (26-27%) and glioblastomas (53-54%) as compared to females. Survival rates by histologic type were similar or slightly higher for females compared to males except for ependymoma where males had a 5-year relative survival rate of 75% compared to 68% for females. Figures 25.5 and 25.6 show the 10-year relative survival rate (%) by histologic type and sex (males and females, respectively).

Histology and Race

Whites had a higher frequency of oligodendrogliomas and glioblastomas as compared to blacks (oligodendroglioma: 9.5% vs. 8.2% and glioblastoma: 54.3% vs. 49.6%, respectively) and a lower frequency of astrocytoma as compared to blacks (astrocytoma: 26.5% vs. 28.5%). Relative survival rates (%) did differ by race for each histologic type. Table 25.5 shows the relative survival rates for invasive brain cancer by histologic type and race.

Primary Site

Brain cancer occurring in the frontal lobes (25.8% of total), temporal lobe (20.1% of total), parietal lobe (14.6% of total) and overlapping lesions of the brain (19.8% of total) were the most common. Relative survival rates (%) did differ by primary site, with tumors in the cerebrum, parietal lobe, occipital lobe, brain NOS, and overlapping lesions of the brain having the poorest survival, less than 20% at 5 years.

Figure 25.5: Male Brain Cancer: Relative Survival Rates by Histology, Ages 20+, 12 SEER Areas, 1988-2001

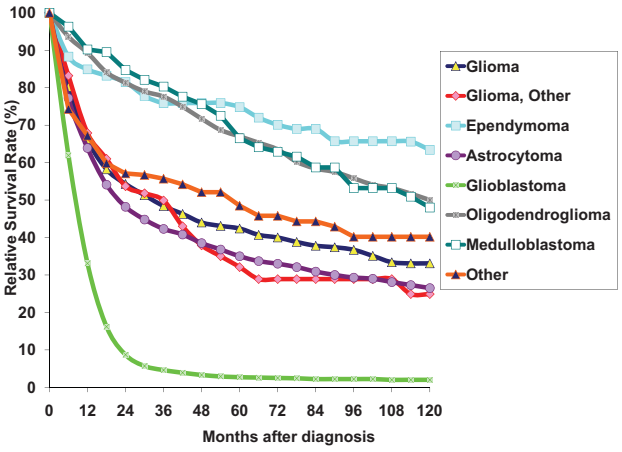


Figure 25.6: Female Brain Cancer: Relative Survival Rates by Histology, Ages 20+, 12 SEER Areas, 1988-2001

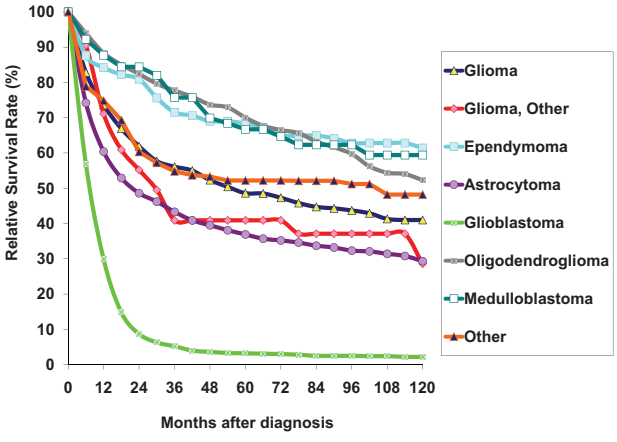


Table 25.5: Cancer of the Brain: 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Race and Histology, Ages 20+, 12 SEER Areas, 1988-2001

Race/ Histology	Cases	% of Cases	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Races	18,669	100.0	49.7	32.1	27.8	23.6	20.7	19.2
Glioma	1,076	5.8	69.4	57.6	51.8	45.2	39.8	36.7
Glioma, Other	100	0.5	69.2	54.4	46.2	36.3	32.8	27.6
Ependymoma	282	1.5	84.6	81.2	73.7	71.6	64.3	62.4
Astrocytoma	4,972	26.6	62.3	48.4	42.7	35.8	30.7	27.8
Glioblastoma	10,037	53.8	31.7	8.7	4.9	2.9	2.3	2.1
Oligodendroglioma	1,796	9.6	88.9	81.7	77.6	68.2	57.4	50.9
Medulloblastoma	216	1.2	89.2	84.6	78.4	66.4	56.8	52.5
Other	190	1.0	70.5	58.6	55.4	50.3	45.2	44.0
White	16,824	100.0	49.1	31.6	27.4	23.4	20.5	19.0
Glioma	966	5.7	68.5	57.3	51.2	44.9	39.4	36.3
Glioma, Other	85	0.5	69.9	55.2	47.3	37.5	35.6	29.5
Ependymoma	238	1.4	85.8	82.7	75.2	73.0	65.9	63.5
Astrocytoma	4,465	26.5	61.7	47.9	42.6	35.9	30.5	27.6
Glioblastoma	9,135	54.3	31.3	8.4	4.6	2.8	2.2	2.0
Oligodendroglioma	1,590	9.5	89.1	81.7	77.9	68.8	58.7	52.2
Medulloblastoma	195	1.2	89.6	85.5	79.2	65.5	57.2	52.2
Other	150	0.9	71.0	59.9	57.2	53.0	47.2	45.4
Black	924	100.0	51.8	32.9	27.7	22.8	20.0	19.4
Glioma	60	6.5	67.8	49.1	43.6	31.0	31.0	31.0
Glioma, Other	9	1.0	~	~	~	~	~	~
Ependymoma	22	2.4	~	~	~	~	~	~
Astrocytoma	263	28.5	64.4	48.1	40.6	33.3	29.5	27.5
Glioblastoma	458	49.6	33.9	10.1	7.1	5.3	3.0	3.0
Oligodendroglioma	76	8.2	79.6	71.9	63.1	50.2	37.6	28.5
Medulloblastoma	12	1.3	~	~	~	~	~	~
Other	24	2.6	~	~	~	~	~	~

~ Statistic not displayed due to less than 25 cases.

Other CNS Cancer

The prognostic factors of interest for the other CNS cancer analysis were: race, sex, age at diagnosis, histologic type, grade, SEER stage of disease and primary site. Size of tumor information was not analyzed because of the large amount of missing data (65.9%) (Table 25.7).The combinations of interest were: race and sex, SEER stage and sex, SEER stage and grade, histologic type, race and sex and histologic type and SEER stage.

Race and Sex

For all race specific analyses of the 1,105 patients, only white and black patients (91%) are used, because the other category is made up of a mix of racial groups. As with the brain cancer group, the proportion of whites with other CNS cancer was much higher than the proportion of blacks with the same disease. However, survival was worse in blacks than in whites with other CNS cancer (5-year relative survival rate: 59% vs. 72%). Males and females develop other CNS cancer in comparable proportions and the relative survival rate was the same (69.5%). 5-year relative survival rate was shortest for black males. Table 25.7 and 25.8 show the relative survival rates for other CNS cancer by race and sex.

Age at Diagnosis

Survival for patients diagnosed with other CNS cancer decreased as age at diagnosis increased except for ages 20-29 which had poorer survival than 30-39, 40-49 and 50-59 year olds and 80+ which had better survival than 70-79 years of age. The 5-year relative survival rate (%) for other CNS cancer by age at diagnosis categories 20-29, 30-39, 40-49, 50-59, 60-69, 70-79 and 80+ were 70%, 81%, 77%, 72%, 66%, 41% and 58%, respectively (Table 25.7). Figure 25.7 shows the 10-year relative survival curves by age at diagnosis.

Grade

Survival for patients with other CNS cancer decreased from grade 1 to grade 4. The 5-year relative survival rate (%) for grade 1, grade 2, grade 3, grade 4 and unknown were 86%, 80%, 43%, 35% and 72%. However, it is important to note that 71.0% of patients had unknown grade in this study sample. Figure 25.8 shows the 10-year relative survival curves by grade.

Table 25.6: Cancer of the Brain: 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Primary Site, Ages 20+, 12 SEER Areas, 1988-2001

Primary Site	Cases	% of Cases	Relative Survival Rate					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	18,669	100.0	49.7	32.1	27.8	23.6	20.7	19.2
Cerebrum	844	4.5	37.5	21.8	16.3	12.7	11.6	9.9
Frontal Lobe	4,812	25.8	58.9	42.9	37.9	32.4	27.8	25.6
Temporal Lobe	3,759	20.1	50.8	28.1	24.2	20.4	18.1	17.1
Parietal Lobe	2,735	14.6	43.5	23.9	19.8	16.1	13.8	12.8
Occipital Lobe	584	3.1	42.8	19.9	14.6	13.4	12.3	10.7
Ventricle, NOS	227	1.2	66.8	57.8	55.4	50.3	45.0	43.2
Cerebellum, NOS	545	2.9	82.4	74.6	68.4	62.9	58.0	55.4
Brain Stem	374	2.0	68.8	59.2	55.6	50.7	45.2	43.8
Overlapping lesion of brain	3,695	19.8	40.5	23.4	19.0	15.2	12.3	10.6
Brain, NOS	1,094	5.9	38.4	26.3	23.1	19.8	16.8	15.4

* NOS, Not Otherwise Specified

Table 25.7: Cancer of the Other Central Nervous System: Distributions and 5-Year Relative Survival Rates (%) by Race, Age(20+), Grade, and Tumor Size, 12 SEER Areas, 1988-2001

Characteristics	Cases	% of Cases	Relative Survival Rate 5-Year (%)
All Cases	1,105	100.0	69.5
Race			
White	886	80.2	71.5
Black	120	10.9	59.1
Other	99	9.0	62.9
Sex			
Male	565	51.1	69.5
Female	540	48.9	69.5
Age			
20-29	114	10.3	70.1
30-39	167	15.1	80.8
40-49	248	22.4	77.1
50-59	202	18.3	72.4
60-69	164	14.8	66.2
70-79	154	13.9	40.7
80+	56	5.1	57.5
Grade (Differentiation)			
Well differentiated; Grade I	73	6.6	85.5
Moderately differentiated; Grade II	113	10.2	79.7
Poorly differentiated; Grade III	40	3.6	43.3
Undifferentiated; anaplastic; Grade IV	95	8.6	35.4
Unknown	784	71.0	72.3
Size of tumor			
<=2cm	78	7.1	89.2
2-5 cm	198	17.9	71.2
>5 cm	101	9.1	58.3
Unknown	728	65.9	68.1

Figure 25.7: Other Central Nervous System Cancer: Relative Survival Rates by Age Group (20+), 12 SEER Areas, 1988-2001

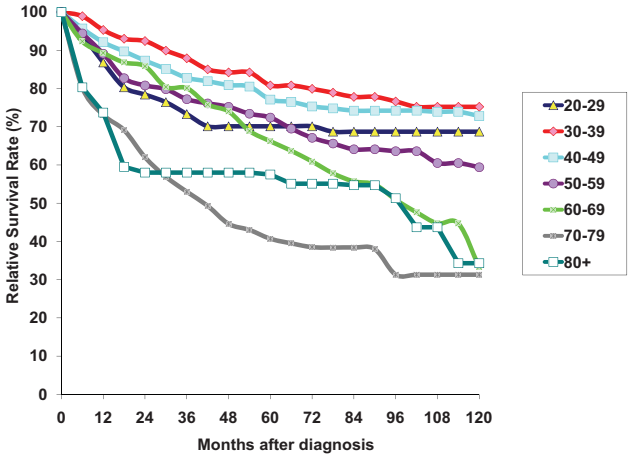


Figure 25.8: Other Central Nervous System Cancer: Relative Survival Rates by Grade, Ages 20+, 12 SEER Areas, 1988-2001

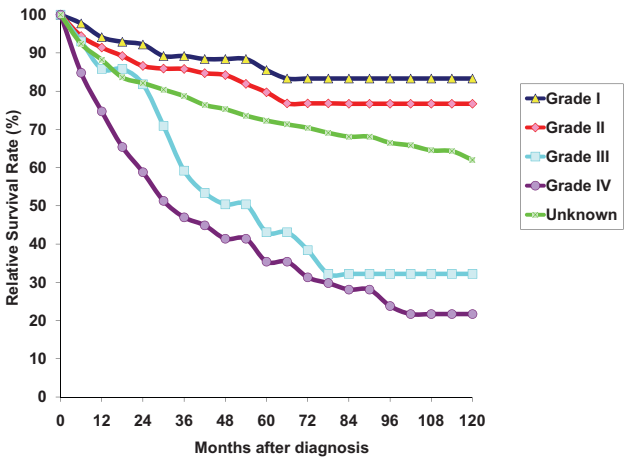


Table 25.8: Cancer of the Other Central Nervous System Cancer: 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Sex/Race	Cases	% of Cases	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All	1,105	100.0	87.7	81.2	76.7	69.5	63.7	60.6
Male	565	51.1	88.0	82.5	77.6	69.5	66.6	64.0
White	476	43.1	88.9	85.3	80.3	72.4	69.2	67.0
Black	49	4.4	87.1	65.4	63.9	57.9	57.2	49.5
Female	540	48.9	87.3	79.9	75.7	69.5	60.1	56.9
White	410	37.1	88.2	81.6	76.9	70.5	61.4	60.4
Black	71	6.4	83.2	68.1	67.3	59.7	53.9	47.5

Table 25.9: Cancer of the Other Central Nervous System Cancer: 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by SEER Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001

Stage	Cases	% of Cases	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	1,105	100.0	87.7	81.2	76.7	69.5	63.7	60.6
Localized	680	61.5	90.8	85.1	80.4	75.1	70.2	66.6
Regional	192	17.4	79.2	71.3	67.3	57.0	45.9	45.2
Distant	81	7.3	76.6	70.9	69.4	60.2	53.5	53.5
Unstaged	152	13.8	90.0	81.5	74.9	65.0	60.0	52.4

Table 25.10: Cancer of the Other Central Nervous System : Distribution of Cases by SEER Stage, Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

SEER Stage	Total		Race/Sex							
			White				Black			
			Male		Female		Male		Female	
	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	1,105	100.0	476	100.0	410	100.0	49	100.0	71	100.0
Localized	680	61.5	303	63.7	257	62.7	30	61.2	40	56.3
Regional	192	17.4	77	16.2	65	15.9	11	22.4	9	12.7
Distant	81	7.3	35	7.4	28	6.8	<5	-	7	9.9
Unstaged	152	13.8	61	12.8	60	14.6	<5	-	15	21.1

Table 25.11: Cancer of the Other Central Nervous System: Distribution of Cases by Histology, Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Histology	Total		Race/Sex							
			White				Black			
			Male		Female		Male		Female	
	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	1,105	100.0	476	100.0	410	100.0	49	100.0	71	100.0
Ependymoma	355	32.1	190	39.9	130	31.7	7	14.3	11	15.5
Astrocytoma	167	15.1	75	15.8	53	12.9	13	26.5	13	18.3
Glioma	65	5.9	28	5.9	21	5.1	<5	-	<8	-
Meningioma	456	41.3	152	31.9	182	44.4	23	46.9	38	53.5
Other	62	5.6	31	6.5	24	5.9	<5	-	<5	-

SEER Stage of Disease

SEER classifies invasive stage of disease into 4 categories: localized, regional, distant and unstaged. Survival decreased as the staging category progressed from localized to regional to distant. The 5-year relative survival rates (%) for other CNS cancer patients with localized, regional, distant and unknown stages of disease were 75%, 57%, 60% and 65%, respectively. It is also important to note that the majority of the other CNS patients were in the localized SEER stage category. Relative survival rates for other CNS cancer are shown by stage (Table 25.9) and stage by race/sex (Table 25.10).

Histology

As previously noted, relative survival varied greatly by histology. The categories of histology of tumor used in this analysis, for other CNS cancer patients only, were: glioma, ependymoma, astrocytoma, meningioma and other (other, neuroepitheliomatous neoplasms, paragangliomas, and glomus tumors). Figure 25.9 shows the 10-year relative survival curves by histologic type. Tables 25.11 and 25.12 show the distribution of patients by histology, race and sex and by histology and SEER stage of disease, respectively.

Primary Site

For patients with other CNS cancer, the spine was the most common primary site (53.9% of total), followed by the brain (41.3% of total) and other (4.8% of total). Other CNS cancers in the brain (malignant meningiomas) had worse survival compared to other CNS cancers in the spine (Table 25.13).

Figure 25.9: Other Central Nervous System Cancer: Relative Survival Rates by Histology, Ages 20+, 12 SEER Areas, 1988-2001

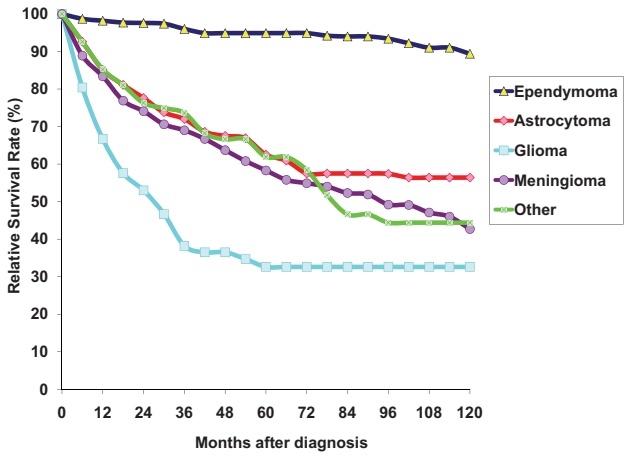


Table 25.12: Cancer of the Other Central Nervous System: Distribution of Cases by Histology and SEER Summary Stage, Ages 20+, 12 SEER Areas, 1988-2001

	SEER Summary Stage									
	Total		Local		Regional		Distant		Unstaged	
Histology	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	1,105	100.0	680	100.0	192	100.0	81	100.0	152	100.0
Ependymoma	355	32.1	287	42.2	25	13.0	14	17.3	29	19.1
Astrocytoma	167	15.1	127	18.7	10	5.2	8	9.9	22	14.5
Glioma	65	5.9	37	5.4	11	5.7	5	6.2	12	7.9
Meningioma	456	41.3	208	30.6	136	70.8	40	49.4	72	47.4
Other	62	5.6	21	3.1	10	5.2	14	17.3	17	11.2

Table 25.13: Cancer of the Other Central Nervous System: 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Primary Site, Ages 20+, 12 SEER Areas, 1988-2001

			Relative Survival Rate (%)					
Primary Site	Cases	% of Cases	1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	1,105	100.0	87.7	81.2	76.7	69.5	63.7	60.6
Brain	456	41.3	83.0	73.8	68.2	56.9	48.0	41.7
Spine	596	53.9	92.1	87.9	83.5	78.8	74.8	73.0
Other	53	4.8	77.9	68.8	68.8	65.1	57.9	57.9

DISCUSSION

Brain and other CNS cancer are rare, occurring at an incidence rate of approximately 6 cases per 100,000 per year. Malignant brain cancer cases excluding malignant meningiomas comprised 94% of the sample used for this analysis (18,669 patients out of 19,774 total combined patients). Five-year relative survival rate after diagnosis with brain cancer or other CNS cancer was 24% and 69%, respectively. Hence, individuals with brain cancer have a very poor prognosis as compared to individuals with other CNS cancer. These relative survival estimates show the distinct difference between the two types of cancer even though they both affect the central nervous system; therefore, brain cancer and other CNS cancer were analyzed separately.

For the brain cancer patients, survival varied only slightly by race and sex. Blacks had a similar 5-year relative survival rate as compared to whites and females had a slightly better 5-year relative survival rate as compared to males. Black males had a 5-year relative survival rate of 25%, which is higher than black females (21%) or white males (23%) and similar to white females (25%). Survival differed the most by age at diagnosis, grade, and histologic type. As age increased the 5-year relative survival rate decreased from 64% for ages 20-29 to 1% for ages 80+, with the highest proportion of patients diagnosed at age 60-69 (20.6% of total). Relative survival decreased as the grade of the tumor progressed from 1 to 4. Most of the patients had grade 4 or grade unknown tumors (39.9% and 38.7%).

For brain cancer patients, survival also differed by histologic type of tumor and race, although most differences were small. Glioblastomas had the worst 5-year relative survival rate of 3% and ependymomas had the best 5-year relative survival rate of 74%. Fifty-four percent had glioblastomas and 1.5% had ependymomas. The distribution of histologic type by race differed slightly for whites and blacks. Malignant brain tumors in the temporal, frontal, parietal lobes and overlapping lesions of the brain were the most common locations in the brain. Malignant tumors in cerebrum and tumors in the occipital lobe had the worst survival at 5 years.

For the other CNS cancer patients, survival varied more by race than by sex. Whites had a better 5-year relative survival rate as compared to blacks (72% vs. 59%), and males and females had the same 5-year relative survival rate (70%). Black males had a 5-year relative survival rate of 58%, which was lower than black females (60%), or white males (72%) or females (71%). Survival differed most by age at diagnosis, grade, histologic type and SEER stage. As age increased the 5-year relative survival rate decreased from 81% for ages 30-39 to 41% for ages 70-79, with the highest proportion of patients being diagnosed at age 40-49 (22.4% of total). Relative survival decreased as the grade of the tumor progressed from 1 to 4. However, over 70% of the 1,103 total patients had unknown grade information. Five-year relative survival rate decreased as SEER stage of disease became more advanced (localized 75%; regional 57% and distant 60%). There was no difference in the distribution of SEER stage by race and sex. Patients in the glioma category had the worst 5-year relative survival rate of 33% and ependymoma patients had the best 5-year relative survival rate of 95%. Less than 6% had glioma tumors and 32.1% had ependymomas. Black males and females had a higher proportion of astrocytomas and meningiomas as compared to white males and females. Whites had a much higher proportion of ependymomas. Tumors of the spine were the most common site with other CNS cancers, although malignant meningiomas of the brain had worse survival than those with malignant tumors in the spine.

Hence, race, age at diagnosis, grade, histologic type and primary site for both brain and other CNS cancers, and SEER stage (for other CNS cancers only) are all important predictors of survival, concurring with previous literature studying survival in brain and other CNS cancer patients (3, 4, 5, 6, 15). These variables are all used to determine one's course of treatment and prognosis after diagnosis. The slight differences in survival by race and by race and histologic type of tumor for brain and other CNS cancers could be due to access to health care and/or socioeconomic status differences. However, recent studies suggest that these differences by race cannot be completely attributed to access to health care and/or diagnostic practices (6, 9) and may in fact be caused by biological differences. Older men and women would be more likely to have competing risks of death as compared to younger individuals with the same diagnosis, which would negatively affect their survival. Though competing risk information was unavailable for this analysis, performing relative survival analysis rather than absolute survival analysis allows for the adjustment of the expected mortality that the cohort would experience. Having a higher grade of tumor or a higher stage of cancer directly correlates with worse survival for almost every type of cancer (2). The patterns seen in this analysis for survival by histologic type for brain and other CNS cancers have been shown previously (3, 4, 6, 8), where brain cancer patients with GBM have the poorest survival, patients with oligodendroglioma have the best survival compared to any other histologic subtype, and other CNS cancer patients with ependymoma have the best survival compared to any other histologic subtype. Similar patterns by primary site of tumor have been seen previously also (8, 4, 15).

REFERENCES

1. American Cancer Society. Cancer Facts and Figures 2006. Atlanta: American Cancer Society; 2006.
2. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Eisner MP, Horner MJ, Howlader N, Hayat M, Hankey BF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site, 2006.
3. Davis FG, Freels S, Grutsch J, Barlas S, Brem S. Survival rates in patients with primary malignant brain tumors stratified by patient age and tumor histological type: an analysis based on Surveillance, Epidemiology, and End Results (SEER) data, 1973-1991. J Neurosurg 1998;88:1-10
4. Surawicz TS, Davis F, Freels S, Laws ER Jr, Menck HR. Brain tumor survival: results from the National Cancer Data Base. J Neurooncol 1998; 40:151-60.
5. Wrensch M, Minn Y, Chew T, Bondy M, Berger MS. Epidemiology of primary brain tumors: current concepts and review of the literature. Neuro-oncol 2002; 4:278-99.
6. Barnholtz-Sloan JS, Sloan AE, Schwartz AG. Racial differences in survival after diagnosis with primary malignant brain tumor. Cancer 98:603-609, 2003a.
7. Polednak AP, Flannery BS. Brain, other central nervous system and eye cancer. Cancer Suppl 1995; 75:330-337.
8. Central Brain Tumor Registry of the United States (CBTRUS). Statistical Report: Primary Brain Tumors in the United States, 1992-1997, Central Brain Tumor Registry of the United States (CBTRUS), www.cbtrus.org, 2003.
9. Surawicz TS, McCarthy BJ, Kupelian V, Jukich PJ, Bruner JM, Davis FG. Descriptive epidemiology of primary brain and CNS tumors: results from the Central Brain Tumor Registry of the United States, 1990-1994. Neuro-oncol. 1999; 1:14-25.
10. Mahaley MS Jr, Mettlin C, Natarajan N, Laws ER Jr, Peace BB. National survey of patterns of care for brain-tumor patients. J Neurosurg 1989; 71:826-36
11. Mahaley MS Jr, Mettlin C, Natarajan N, Laws ER Jr, Peace BB. Analysis of patterns of care of brain tumor patients in the United States: a study of the Brain Tumor Section of the AANS and the CNS and the Commission on Cancer of the ACS. Clin Neurosurg 1990;36:347-52.
12. Gurney JG, Smith MA, Bunin GR. Chapter III: CNS and Miscellaneous Intracranial and Intraspinal Neoplasms. In: Ries LAG, Smith MA, Gurney JG, Linet M, Tamra T, Young JL, Bunin GR (eds). Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975-1995, National Cancer Institute, SEER Program. NIH Pub. No. 99-4649. Bethesda, MD, 1999.
13. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958; 53:457-481.
14. Fleming ID, Cooper JS, Henson DE, Hutter RVP, Kennedy BJ, Murphy GP, O'Sullivan B, Sobin LH, Yarbro, JW (Eds.) AJCC Cancer Staging Manual, 5th edition. American Joint Committee on Cancer. Philadelphia: Lippincott-Raven, 1997.
15. Barnholtz-Sloan JS, Sloan AE, Schwartz AG. Relative survival and patterns of diagnosis by time period for individuals with primary malignant brain tumor 1973-1997. Journal of Neurosurgery 99:458-466, 2003b.

ACKNOWLEDGEMENTS

This work was supported by NCI contract number N01 PC35145 to the Metropolitan Detroit Cancer Surveillance System (Detroit SEER Registry).

We would like to thank Jennifer Brooks, Huong Do, and William Cheng for their assistance in preparing this chapter.

Chapter 26
Cancer of the Thyroid

Carol L. Kosary

INTRODUCTION

Cancers of the thyroid are rare, accounting for approximately 2% of all diagnosed cancers, but account for over 93% of all cancers of the endocrine system (1). Approximately 30,180 cases and 1,500 deaths occur each year in the United States (1). Thyroid cancer is nearly 3 times more common in women than men (1). Differentiated tumors, predominantly diagnosed as either papillary or follicular, are the most commonly diagnosed. Poorly or undifferentiated tumors, predominantly diagnosed as either medullary or anaplastic, are much less common, are aggressive with a tendency for early metastasis, and have a much poorer prognosis.

RESULTS

Exclusions

Between 1988-2001, there were 29,345 thyroid cancers diagnosed in SEER . The following were excluded from the analysis: patients for whom thyroid cancer was not the first primary, cases identified through autopsy or death certificate only, persons of unknown race, cases without active follow-up or alive with no survival time, patients less than 20 years old, cases without microscopic confirmation, sarcomas and carcinoids. After these exclusions, 25,396 adult cases remained for analysis (Table 26.1).

Age and Sex

Cancers of the thyroid were three times more likely to be diagnosed in women than in men (19,162 cases versus 6,234) during the time frame examined. Almost 54% of the cancers in women were diagnosed between the ages of 20 to 44 compared to nearly 40% of those diagnosed in men while a higher percentage of men were diagnosed in the older age groups (Table 26.2).

For both sexes, together and separately, survival declines slightly with age. In women under age 45, 5-year relative survival rate is nearly 100% compared to 97% in women 45-64 and 84% in women aged 65 and older. In men under age 45, 5-year relative survival rate is 98% compared to 92% in men 45-64 and 83% in men aged 65 and older (Table 26.3).

Table 26.1: Cancer of the Thyroid: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/selection
29,345	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
26,812	2,533	Select first primary only
26,521	291	Exclude death certificate only or at autopsy
26,271	250	Exclude unknown race
26,195	76	Exclude alive with no survival time
25,509	686	Exclude children (Ages 0-19)
25,485	24	Exclude in situ cancers
25,416	69	Exclude no or unknown microscopic confirmation
25,403	13	Exclude sarcomas
25,396	7	Exclude carcinoids

Table 26.2: Cancer of the Thyroid: Number and Distributions of Cases by Age (20+) and Sex, 12 SEER Areas, 1988-2001

Age Group (Years)	Total		Male		Female	
	Cases	Percent	Cases	Percent	Cases	Percent
Total 20+	25,396	100.0	6,234	100.0	19,162	100.0
20-44	12,730	50.1	2,469	39.6	10,261	53.5
45-64	8,536	33.6	2,499	40.1	6,037	31.5
65+	4,130	16.3	1,266	20.3	2,864	14.9

Geographic Location

Five-year relative survival rates in the 12 SEER regions represented in this study ranged from 98% in Seattle (Puget Sound) to 89% in Rural Georgia (Table 26.4).

Histology

Distribution by histology, overall and by sex, is presented in Table 26.5. In both males and females, a majority of the tumors are classified as papillary, although the percent is higher in females (83.7%) than males (76.5%). Males are slightly more likely to be diagnosed with tumor classified as follicular (14.1% versus 11.0%), medullary (0.5% vs 0.3%) and anaplastic (2.5% versus 1.3%)

Similar comparisons between the sexes can be made when histology distribution is examined by age (Table 26.6). A higher percent of tumors are classified as papillary in both males and females under the age of 45 years compared to those over the age of 45 years (83.4% for males and 88.5% for females under the age of 45 versus 71.9% for males and 78.3% for females ages 45 and older). Opposite findings are seen for those tumors classified as follicular and medullary. For ages under 45, 10.8% of the tumors are classified as follicular in males and 8.7% in females compared to 16.3% in males ages 45 and older and 13.7% in females. Tumors classified as medullary account for 0.4% in males under age 45 and 0.2% in females versus 0.6% in males ages 45 and older and 0.4% in females.

Of the 399 cases of anaplastic tumors, 95% were seen in individuals ages 45 and older. For males 45 and older, 3.8% of all tumors were classified as anaplastic compared to 2.7% in females.

Staging

The American Joint Committee on Cancer (AJCC) has designated staging for cancers of the thyroid (2). Separate stage groupings are recommended for papillary, follicular, medullary and anaplastic cell types. In addition, within papillary and follicular, separate stage groupings are recommended based on age at diagnosis (20-44 and 45+). The SEER modified fifth edition AJCC staging comprises:

Primary tumor (T):

TX: Primary tumor cannot be assessed

T0: No evidence of primary tumor

T1: Tumor 1 cm or less in greatest dimension limited to the thyroid

T2: Tumor more than 1 cm but not more than 4 cm in greatest dimension limited to the thyroid

T3: Tumor more than 4 cm in greatest dimension limited to the thyroid

T4: Tumor of any size extending beyond the thyroid capsule

Table 26.3: Cancer of the Thyroid: Number of Cases, Median Survival Time (Months) and 5-year Survival Rates (%) by Sex and Age (20+), 12 SEER Areas, 1988-2001

Sex and Age Group (Years)	Cases	Median Survival Time (Months)	5-Year Survival Rate (%)		
			Observed	Expected	Relative
Both sexes, 20-44	12,730	> 120	98.6	99.3	99.3
Male, 20-44	2,469	> 120	96.9	98.7	98.1
Female, 20-44	10,261	> 120	99.0	99.5	99.6
Both sexes, 45-64	8,536	> 120	92.4	96.3	95.9
Male, 45-64	2,499	> 120	87.2	94.5	92.2
Female, 45-64	6,037	> 120	94.5	97.1	97.3
Both Sexes, 65+	4,130	114.2	66.4	79.2	83.8
Male, 65+	1,266	92.7	62.4	74.9	83.3
Female, 65+	2,864	> 120	68.2	81.1	83.9

Table 26.4: Cancer of the Thyroid: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by SEER Geographic Area, Ages 20+, 12 SEER Areas, 1988-2001

SEER Geographic Area	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	25,396	100.0	97.0	96.5	96.4	96.0	95.8	95.6
Atlanta and Rural Georgia	1,666	6.6	97.7	97.2	96.5	95.5	95.1	95.1
Atlanta (Metropolitan) - 1988+	1,614	6.4	97.6	97.1	96.7	95.7	95.2	95.2
Rural Georgia - 1988+	52	0.2	98.9	97.9	92.3	89.4	89.4	88.2
California								
Los Angeles - 1992+	4,762	18.8	96.9	96.3	95.8	95.0	94.4	93.7
Greater Bay Area	4,437	17.5	96.7	96.3	96.3	95.9	95.7	95.4
San Francisco-Oakland SMSA - 1988+	2,832	11.2	96.5	96.3	96.1	95.5	95.1	95.1
San Jose-Monterey - 1988+	1,605	6.3	97.2	96.2	96.2	96.2	96.2	95.4
Connecticut - 1988+	2,521	9.9	94.8	94.2	94.0	93.9	93.6	93.6
Detroit (Metropolitan) - 1988+	2,916	11.5	96.6	96.4	96.1	95.6	95.3	94.5
Hawaii - 1988+	1,164	4.6	96.9	96.4	96.2	95.2	94.1	92.8
Iowa - 1988+	2,158	8.5	97.6	96.9	96.7	96.6	96.6	96.6
New Mexico - 1988+	1,375	5.4	97.4	97.1	97.1	96.8	96.8	96.7
Seattle (Puget Sound) - 1988+	2,842	11.2	98.3	98.0	97.9	97.7	96.8	96.4
Utah - 1988+	1,555	6.1	97.4	97.1	97.1	96.9	96.9	96.8

Table 26.5: Cancer of the Thyroid: Number and Distribution of Cases by Histology and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Histology	ICD-O Code	Total		Male		Female	
		Cases	Percent	Cases	Percent	Cases	Percent
Total	8000-9989	25,396	100.0	6,234	100.0	19,162	100.0
Epidermoid	8051-8130	58	0.2	26	0.4	32	0.2
Adenocarcinoma	8050,8140-8147,8160-8162,8180-8221,8250-8506,8520-8550,8560,8570-8573,8940-8941	24,587	96.8	5,935	95.2	18,652	97.3
Papillary	8050,8260,8340,8350,8450	20,814	82.0	4,767	76.5	16,047	83.7
Follicular	8290,8330-8332	2,991	11.8	880	14.1	2,111	11.0
All Other Adenocarcinoma	8140-8147,8160-8164,8180-8221,8250-8259,8261-8289,8291-8329,8333-8339,8341-8349,8351-8449,8451-8506,8520-8550,8560,8570-8573,8940-8941	782	3.1	288	4.6	494	2.6
Other Specified Carcinomas	8033-8045,8150-8155,8170-8171,8230-8248,8510-8512,8561-8562,8580-8671	95	0.4	41	0.7	54	0.3
Medullary	8510-8511	86	0.3	34	0.5	52	0.3
All Other Specified Carcinomas	8033-8045,8150-8155,8170-8171,8230-8248,8512,8561-8562,8580-8671	9	0.0	7	0.1	<5	0.0
Carcinoma, NOS*	8004,8010-8022,8030-8032	613	2.4	218	3.5	395	2.1
Anaplastic	8004,8012,8020-8021,8030-8032	399	1.6	155	2.5	244	1.3
All Other Carcinoma, NOS*	8010-8011,8013-8019,8022	214	0.8	63	1.0	151	0.8
Unspecified Other Specified Types	8000-8003, 8720-8790,8932-8933,8950-8982,9000-9030,9060-9110,9350-9364,9380-9512,9530-9539	43	0.2	14	0.2	29	0.1

* NOS: Not Otherwise Specified

Table 26.6: Cancer of the Thyroid: Number and Distribution of Cases by Histology, Age (20+) and Sex, 12 SEER Areas, 1988-2001

	Age (Years)							
	20-44				45+			
	Male		Female		Male		Female	
Histology	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	2,469	100.0	10,261	100.0	3,765	100.0	8,901	100.0
Epidermoid	<5	~	5	0.0	22	0.6	27	0.3
Adenocarcinoma	2,425	98.2	10,176	99.2	3,510	93.2	8,476	95.2
Papillary	2,059	83.4	9,078	88.5	2,708	71.9	6,969	78.3
Follicular	266	10.8	894	8.7	614	16.3	1,217	13.7
All Other Adenocarcinoma	100	4.1	204	2.0	188	5.0	290	3.3
Other Specified Carcinomas	10	0.4	19	0.2	31	0.8	35	0.4
Medullary	10	0.4	19	0.2	24	0.6	33	0.4
All Other Specified Carcinomas	0	0.0	0	0.0	7	0.2	<5	~
Carcinoma, NOS*	25	1.0	55	0.5	193	5.1	340	3.8
Anaplastic	11	0.4	7	0.1	144	3.8	237	2.7
All Other Carcinoma, NOS*	14	0.6	48	0.5	49	1.3	103	1.2
Other Specified Types	<5	~	<5	~	0	0.0	0	0.0
Unspecified	<5	~	5	0.0	9	0.2	23	0.3

* NOS: Not Otherwise Specified
~ Statistic not displayed.

Table 26.7: Thyroid Papillary Adenocarcinoma (with Established Stage): Number and Distribution of Cases by Age (20+) and AJCC Stage (SEER modified 5th Edition), 12 SEER Areas, 1988-2001

	AJCC Stage									
	Total with Established Stage		I		II		III		IV	
Age Group (Years)	Cases	Row Percent	Cases	Row Percent	Cases	Row Percent	Cases	Row Percent	Cases	Row Percent
Total w/ Established Stage	19,607	100.0	13,289	67.8	3,195	16.3	2,870	14.6	253	1.3
20-44	10,822	100.0	10,740	99.2	82	0.8	*	*	*	*
45-64	6,374	100.0	1,961	30.8	2,368	37.2	1,923	30.2	122	1.9
65+	2,411	100.0	588	24.4	745	30.9	947	39.3	131	5.4

* Under 45 Age Group Only Staged at I or II

Table 26.8: Thyroid Papillary Adenocarcinoma (with Established Stage) : Number of Cases and 5-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 5th Edition) and Age (20+), 12 SEER Areas, 1988-2001

	Age (Years)							
	Total		20-44		45-64		65+	
AJCC Stage	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)
Total w/ Established Stage	19,607	98.7	10,822	99.7	6,374	98.3	2,411	94.2
Stage I	13,289	99.8	10,740	99.8	1,961	99.3	588	98.1
Stage II	3,195	99.9	82	86.7	2,368	99.9	745	100.0
Stage III	2,870	93.3	*	*	1,923	96.3	947	86.6
Stage IV	253	46.4	*	*	122	57.0	131	33.6

* Under 45 Age Group Only Staged at I or II

Regional lymph nodes (N) (Note: Regional lymph nodes are the cervical and upper mediastinal lymph nodes.)

NX: Regional lymph nodes cannot be assessed
N0: No regional lymph node metastasis
N1: Regional lymph node metastasis
N1a: Metastasis in ipsilateral cervical lymph node(s)
N1b: Metastasis in bilateral, midline, or contralateral cervical or mediastinal lymph node(s)

Distant metastases (M)
MX: Distant metastasis cannot be assessed
M0: No distant metastasis
M1: Distant metastasis

Papillary or follicular
Under 45 years
Stage I: Any T, any N, M0
Stage II: Any T, any N, M1
45 years and older
Stage I : T1, N0, M0
Stage II : T2, N0, M0
T3, N0, M0
Stage III : T4, N0, M0
Any T, N1, M0
Stage IV: Any T, any N, M1

Medullary
Stage I: T1, N0, M0
Stage II: T2, N0, M0
T3, N0, M0
T4, N0, M0
Stage III: Any T, N1, M0
Stage IV: Any T, any N, M1

Anaplastic [Note: All cases are stage IV]
Stage IV: Any T, any N, any M

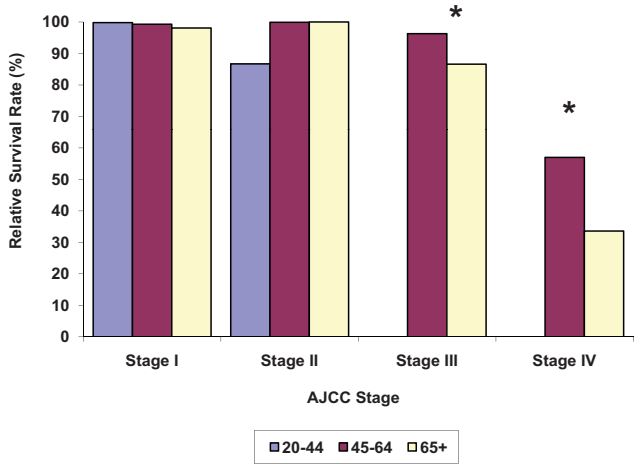
Papillary

Survival by Age and Stage

Of the 20,814 cases of papillary, enough information to establish stage at diagnosis was available for 19,607 (94%). The staging scheme for individuals diagnosed under the age of 45 places individuals in either stage I or II depending in the presence or absence of metastasis. Most of the cases diagnosed in this age group were stage I (99.2%).

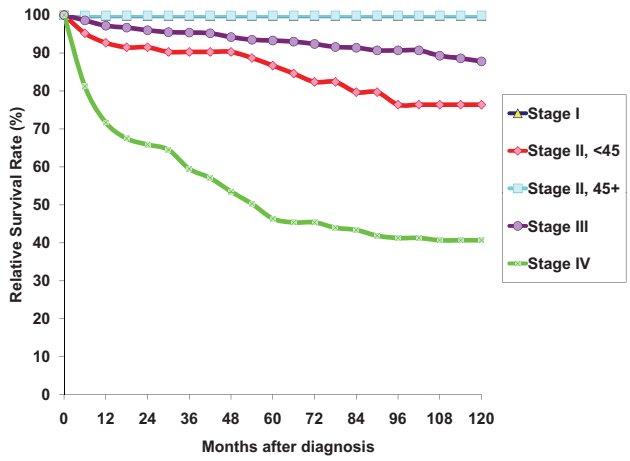
For ages 45 and older, the percent diagnosed in stage I declines with age, from 30.8% in ages 45-64 to 24.4% in ages 65+. At the same time the percent diagnosed stage IV increases from 1.9% in ages 45-64 to 5.4% in ages 65+ (Table 26.7).

Figure 26.1: Papillary Cancer of the Thyroid: 5-Year Relative Survival Rate (%) by AJCC Stage (5th Edition) and Age Group (20+), 12 SEER Areas, 1988-2001



* Under 45 age group only staged at I or II

Figure 26.2: Papillary Cancer of the Thyroid: Relative Survival Rates (%) by AJCC Stage (5th Edition), Ages 20+, 12 SEER Areas, 1988-2001



No survival differentials by age are seen in both stages I and II, with the exception of those diagnosed 20-44 years of age, where stage II consists of those with metastasis at the time of diagnosis. Higher survival in both stages III and IV is observed in those diagnosed in the 45-64 age group compared to those 65+. Since stage II in those diagnosed 20-44 years of age is equivalent to a stage IV diagnosis in those 45 and older, a large survival differential is observed in those with metastases at diagnosis who are 20-44 years of age compared to those 45 and older. (Table 26.8 and Figure 26.1)

Survival by Stage

Table 26.9 and Figure 26.2 show the contrast between stage at diagnosis and years since diagnosis (with stage II broken out for those 20-44 versus 45+). The steepest declines in survival rates are observed within 5 years of

Table 26.9: Thyroid Papillary Adenocarcinoma (with Established Stage): Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total with Established Stage	19,607	100.0	99.1	99.0	99.0	98.7	98.4	98.2
Stage I	13,289	67.8	99.8	99.8	99.8	99.8	99.8	99.8
Stage II, 20-44	82	0.4	92.7	91.5	90.3	86.7	76.4	76.4
Stage II, 45+	3,113	15.9	99.9	99.9	99.9	99.9	99.9	99.9
Stage III	2,870	14.6	97.2	96.0	95.4	93.3	90.7	87.8
Stage IV	253	1.3	71.7	65.9	59.5	46.4	41.3	40.7

Table 26.10: Thyroid Follicular Adenocarcinoma (with Established Stage): Number of Distribution of Cases by Age (20+) and AJCC Stage (5th Edition), 12 SEER Areas, 1988-2001

Age Group (Years)	AJCC Stage									
	Total with Established Stage		I		II		III		IV	
	Cases	Row Percent	Cases	Row Percent	Cases	Row Percent	Cases	Row Percent	Cases	Row Percent
Total 20+	2,718	100.0	1,205	44.3	1,032	38.0	299	11.0	182	6.7
20-44	1,143	100.0	1,129	98.8	14	1.2	*	*	*	*
45-64	911	100.0	54	5.9	658	72.2	135	14.8	64	7.0
65+	664	100.0	22	3.3	360	54.2	164	24.7	118	17.8

* Under 45 Age Group Only Staged at I or II

Table 26.11: Thyroid Follicular Adenocarcinoma (with Established Stage): Number of Cases and 5-Year Relative Survival Rates (%) by AJCC Stage (5th Edition) and Age (20+), 12 SEER Areas, 1988-2001

AJCC Stage	Age (Years)							
	Total		20-44		45-64		65+	
	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)	Cases	5-Year Relative Survival Rate (%)
Total with Established Stage	2,718	95.6	1,143	99.2	911	95.9	664	86.8
Stage I	1,205	99.6	1,129	99.5	54	100.0	22	~
Stage II	1,032	99.9	14	~	658	99.6	360	99.8
Stage III	299	83.7	*	*	135	87.8	164	79.1
Stage IV	182	45.5	*	*	64	54.0	118	40.4

* Under 45 Age Group Only Staged at I or II

~ Statistic not displayed due to less than 25 cases.

diagnosis for those diagnosed in stage IV. The favorable outcome for stage II in those diagnosed under the age of 45 is evident when compared to the outcome of the comparable stage IV in those age 45 and older.

Follicular

Survival by Age and Stage

Of the 2,991 cases of follicular, enough information to establish stage at diagnosis was available for 2,718 (91%). The staging scheme for individuals diagnosed under the age of 45 places individuals in either stage I or II depending in the presence or absence of metastasis. Most of the cases diagnosed in this age group were stage I (98.8%).

For ages 45 and older, the percent diagnosed in stages I and II declines with age from 5.9% for ages 45-64 to 3.3% for ages 65+ in stage I and 72.2% for ages 45-64 to 54.2% for ages 65+ in stage II. At the same time the percent diagnosed stage III & IV increases from 14.8% for ages 45-64 to 24.7% for ages 65+ in stage III and 7.0% for ages 45-64 to 17.8% for ages 65+ in stage IV (Table 26.10).

No survival differentials by age are seen in both stage I and II between those age groups where enough cases are available for analysis. Higher survival rates in both stages III and IV is observed in those diagnosed in the 45-64 age group compared to those 65+. Unfortunately, not enough cases are available to make any observations concerning stage II in individuals under the age of 45 or stage I on individuals ages 65 and older (Table 26.11 and Figure 26.3)

Survival by Stage

Table 26.12 shows the contrast between stage at diagnosis and years since diagnosis. A steady decline in survival rate is observed in stage IV throughout most of the 10 years observed. The favorable outcome for stages I-III is also evident. Figure 26.4 shows 5-year relative survival rates by stage and time since diagnosis.

Medullary

Survival by Stage

Of the 86 cases of medullary, enough information to establish stage at diagnosis was available for 80 (93%). Most cases were diagnosed in either stage II or III (42.5% and 43.8% respectively) (Table 26.13).

Only small differentials in 5-year relative survival rates are observed between stages II and III (Table 26.14 and Figure 26.5). This is also evident for longer survival periods (Table 26.14 and Figure 26.5).

Anaplastic

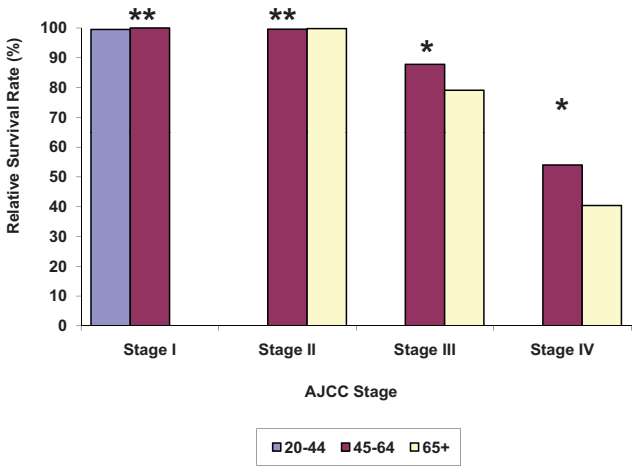
Survival by Age

All anaplastic tumors are categorized as stage IV. Of the 399 cases observed, approximately 67% were diagnosed in individuals ages 65 and older (Table 26.15). Five-year relative survival rates could be calculated for ages 45 and older only (accounting for 96% of the cases). Survival rates were higher for those diagnosed between the ages of 45-65 compared to those aged 65 and older (Table 26.15). This was also evident for shorter and longer periods of survival (Table 26.16 and Figure 26.6).

REFERENCES

1. American Cancer Society, Cancer Facts and Figures, 2006, American Cancer Society, Atlanta, 2006.
2. Fleming ID, Cooper JS, Henson DE, Hutter RVP, Kennedy BJ, Murphy GP, O'Sullivan B, Sobin LH, Yarbro, JW (eds). AJCC Cancer Staging Manual, Fifth edition, American Joint Committee on Cancer. Philadelphia: Lippincott-Raven, 1997.

Figure 26.3: Follicular Cancer of the Thyroid: 5-Year Relative Survival Rate (%) by AJCC Stage (SEER modified 5th Edition) and Age Group (20+), 12 SEER Areas, 1988-2001



* Under 45 age group only staged at I or II

** Statistic not displayed due to less than 25 cases for ages 20-44 Stage II and age 65+ Stage II

Table 26.12: Thyroid Follicular Adenocarcinoma (with Established Stage): Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (5th Edition), 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total with Established Stage	2,718	100.0	97.4	96.7	96.1	95.6	94.2	94.0
Stage I	1,205	44.3	99.6	99.6	99.6	99.6	99.6	99.3
Stage II	1,032	38.0	100.0	99.9	99.9	99.9	99.3	98.8
Stage III	299	11.0	90.0	87.5	86.1	83.7	80.3	80.3
Stage IV	182	6.7	77.7	70.3	61.1	45.5	32.8	24.5

Table 26.13: Thyroid Medullary Carcinoma (with Established Stage): Number, Distribution, and 5-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 5th Edition), 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	5-Year Relative Survival Rate (%)
Total with Established Stage	80	100.0	82.1
Stage I	<7	-	~
Stage II	34	42.5	89.6
Stage III	35	43.8	82.3
Stage IV	<5	-	~

~ Statistic not displayed due to less than 25 cases.

Table 26.14: Thyroid Medullary Carcinoma: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by AJCC Stage (SEER modified 5th Edition), 12 SEER Areas, 1988-2001

AJCC Stage	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total with Established Stage	80	100.0	97.0	91.5	83.9	82.1	81.3	77.9
Stage I	<5	-	~	~	~	~	~	~
Stage II	34	42.5	97.5	94.5	89.6	89.6	86.3	77.1
Stage III	35	43.8	100.0	95.4	89.8	82.3	82.3	82.3
Stage IV	<8	-	~	~	~	~	~	~

~ Statistic not displayed due to less than 25 cases.

Table 26.15: Thyroid Anaplastic Carcinoma: Number, Distribution, and 5-Year Relative Survival Rates (%) by Age (20+), 12 SEER Areas, 1988-2001

Age (Years)	Cases	Percent	5-Year Relative Survival Rate (%)
Total 20+	399	100.0	9.1
20-44	18	4.5	~
45-64	113	28.3	13.7
65+	268	67.2	4.0

Table 26.16: Thyroid Anaplastic Carcinoma: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Age (20+), 12 SEER Areas, 1988-2001

Age (Years)	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total 20+	399	100.0	19.4	13.0	11.1	9.1	9.1	9.1
20-44	18	4.5	~	~	~	~	~	~
45-64	113	28.3	24.4	20.8	19.0	13.7	13.7	13.7
65+	268	67.2	14.7	7.2	5.0	4.0	3.5	3.5

~ Statistic not displayed due to less than 25 cases.

Figure 26.4: Follicular Cancer of the Thyroid: Relative Survival Rates (%) by AJCC Stage (SEER modified 5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

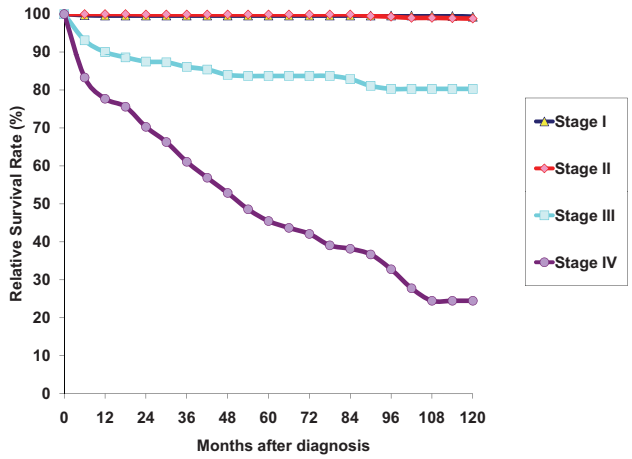


Figure 26.5: Medullary Cancer of the Thyroid: Relative Survival Rates (%) by AJCC Stage (SEER modified 5th Edition), Ages 20+, 12 SEER Areas, 1988-2001

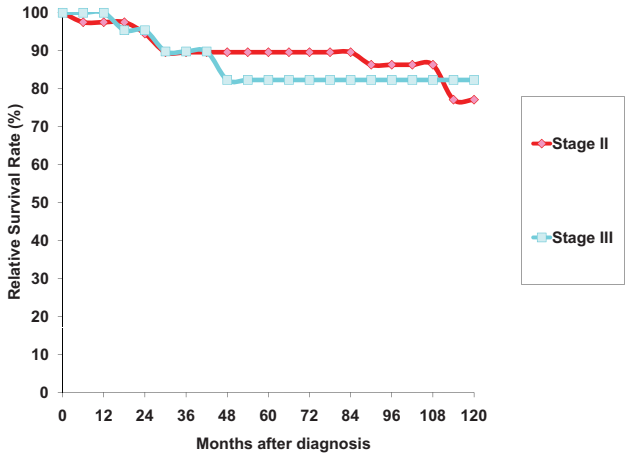
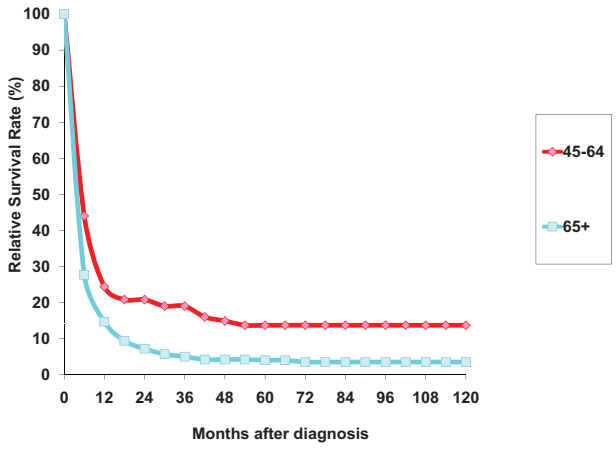


Figure 26.6: Anaplastic Cancer of the Thyroid: Relative Survival Rates (%) by Age Group (20+), 12 SEER Areas, 1988-2001



Chapter 27
Hodgkin Lymphoma

Christina Clarke, Cynthia O'Malley, and Sally Glaser

INTRODUCTION

Hodgkin Lymphoma (HL) is a cancer of the lymphoid cells with which an estimated 7,800 persons are diagnosed each year in the United States (1). Although it is a relatively rare cancer in the general population, it is one of the most common cancers diagnosed in young persons. A hallmark feature of HL epidemiology is its bimodal age-specific incidence pattern, in which incidence is highest between the ages of 15 and 34 years, declines between ages 35 and 54 years and increases again after age 55 years. Indeed, HL is unique among cancers in that over two-thirds of patients are diagnosed before 50 years of age. HL is also notable among cancers for the availability of curative therapy, which has resulted in relatively favorable outcomes. Despite its relatively low level of occurrence and high curability, it is the propensity of HL to occur in the productive years of life that makes it a significant source of cancer-related morbidity and mortality in the US. In fact, HL ranks third behind childhood cancers and testicular cancer in the average years of life lost to a cancer (2). This chapter examines survival characteristics in a large, population-based cohort of patients diagnosed with HL between 1988 and 2001 and reported to the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program.

MATERIALS AND METHODS

Patients

Analyses included all patients aged 15 years or over diagnosed with HL between 1988 and 2001 and reported to the SEER program. Patients were followed for vital status until 2002. Table 27.1 details exclusions, resulting in a final series of 11,720 patients. The majority of the eligible patients were young adults, defined as ages 15-44 at diagnosis (n=8,001, 68%), and of white race/ethnicity (n=10,154, 87%). In addition, there were slightly more male (n= 6,428, 55%) than female patients.

Stage classification

HL tumors almost always develop in a lymph node or other lymphoid structure and spread contiguously to nearby nodes (3). In the SEER database, classification of stage of disease at diagnosis for HL follows the Ann Arbor guidelines (4). In brief, the Ann Arbor system provides four stages of tumor spread relative to the diaphragm: I--involvement of a single lymph node region, II-- involvement of two or more lymph node regions on one side of the diaphragm, III--involvement of lymph node regions on both sides of the diaphragm, IV--disseminated

Table 27.1: Hodgkin Lymphoma: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number selected/remaining	Number excluded	Reason for exclusion/selection
13,302	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
12,560	742	Select first primary only
12,498	62	Exclude death certificate only or at autopsy
12,384	114	Exclude unknown race
12,361	23	Exclude alive with no survival time
11,777	584	Exclude children (Ages 0-14)
11,777	0	Exclude in situ cancers for all except breast & bladder cancer
11,720	57	Exclude no or unknown microscopic confirmation
11,720	0	Exclude sarcomas

disease. Each stage can be subclassified as AA" or AB" type according to the absence or presence of B-symptoms, respectively; these include fever, night sweats, generalized pruritus or weight loss of greater than 10 percent of total body mass. In these analyses, stage information was incomplete for 485 patients (4%), while information regarding B-symptoms was incomplete for 3,188 patients with known stage, or 27% of the total. Patients with incomplete stage or B-symptom information were excluded only from analyses addressing those variables.

Histologic classification

HL is distinguished from other lymphomas by the histologic presence of malignant Hodgkin and Reed-Sternberg (HRS) cells. The relative proportion of HRS cells to reactive cells and fibrosis within the tumor define the main histologic subtypes of HL. In this analysis, we defined histologic subtypes according to the WHO classification system (5): nodular sclerosing (NS), mixed cellularity (MC), nodular lymphocyte predominance (nodular LP) and lymphocyte depletion (LD). Beginning with 2001 data, lymphocyte rich (LR) could not be separated out. The subtypes were assigned using ICD-O-2 morphology codes (6): NS (M-9663-9667), MC (M-9652), nodular LP (M-9659) and LD (M-9653-9655). Patients with unknown histologic subtype were described as HL, not otherwise specified (NOS), ICD-O-2 code M-9650, and included in all analyses.

Statistical methods

Survival over time was measured by the relative survival rate, which measures the percentage of cancer patients surviving a given time from diagnosis adjusted for the survival experience of an age-, sex-, race-, and calendar year-matched cohort as determined from US vital statistics life tables. Detailed information regarding the calculation of the relative survival rate is provided in the introduction to this monograph.

RESULTS

Between 1988 and 2001, the availability of effective therapy for HL is reflected in the favorable relative survival rates for patients diagnosed in SEER areas. Ninety-two percent of all patients survived beyond one year after diagnosis, relative to the general population. However, this rate decreased steadily with time since diagnosis. Relative survival rate was 83% at five years and 78% at ten years (Table 27.2). As detailed below, relative survival for HL varies by age, sex, race/ethnicity, and stage of disease (Table 27.2). Relative survival was not observed to vary substantially by SEER region (data not shown).

Table 27.2: Hodgkin Lymphoma: Number and Distribution of Cases and Relative Survival Rates (%) by Sex, Race, Age (15+), Ann Arbor Stage, and Symptoms, 12 SEER Areas, 1988-2001

Characteristics	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	11,720	100.0	92.0	88.3	86.2	83.0	79.1	78.1
Sex								
Male	6,428	54.8	91.2	87.0	84.5	80.8	76.3	75.5
Female	5,292	45.2	92.9	89.9	88.2	85.6	82.3	81.1
Race								
White	10,154	86.6	92.2	88.6	86.5	83.7	80.2	79.3
Black	1,129	9.6	90.3	85.8	83.9	77.5	70.7	69.4
Age (Years)								
15-44	8,001	68.3	97.3	94.5	92.8	89.9	86.6	85.4
45-64	2,165	18.5	89.1	83.5	79.9	74.8	67.4	64.9
65+	1,554	13.3	67.6	60.2	56.3	50.6	40.4	36.6
Ann Arbor Stage								
I	2,778	23.7	95.9	93.4	91.7	89.0	85.1	84.7
II	4,344	37.1	96.6	93.7	92.1	89.3	85.5	84.4
III	2,220	18.9	90.4	86.4	84.1	80.8	77.5	75.7
IV	1,893	16.2	77.7	71.0	67.4	62.6	57.3	56.0
Unknown	485	4.1	90.0	85.4	82.3	78.4	74.0	74.0
Symptoms								
A	4,015	34.3	96.4	94.5	93.2	91.1	87.7	87.2
B	4,139	35.3	88.0	83.1	80.1	76.2	71.9	69.9
Unknown	3,566	30.4	91.6	87.3	85.1	81.5	77.5	76.8

In general, young-adult female patients with early stage disease were observed to have the most favorable relative survival, while older, male patients with late stage disease had the least favorable survival rates.

Age at diagnosis

Age at diagnosis substantially impacted relative survival. Figure 27.1 shows five and ten-year relative survival rates by detailed age at diagnosis. Both five and ten-year estimates declined with advancing age at diagnosis. Ten-year relative survival rates generally exceeded 80% for persons 15-24, 25-34, and 35-44 years at diagnosis, but were substantially lower in older age groups. For persons diagnosed at age 75 or older, relative survival was poor, 38% at five years and 21% at 10 years.

Based both on observations from Figure 27.2 as well as epidemiologic features, the data were stratified into three age groups for further analysis: young adults (ages 15-44 at diagnosis), middle-aged adults (ages 45-64), and older adults (ages 65+). Figure 27.2 shows relative survival over time for patients diagnosed in these age groupings. In the first two years after diagnosis, relative survival decreased more sharply for older adults (65+) than young or middle-aged adults. At six months after diagnosis, the relative survival rates for older adults was lower than 80%, and at 24 months, had decreased further to nearly 60%. In contrast, relative survival rate exceeded 80% for young-adult patients across the entire ten-year follow-up period. Figure 27.2 also shows that relative survival does not stabilize but rather declines continuously over the ten-year follow-up period irrespective of age at diagnosis.

Sex

Figure 27.2 also shows that sex differentially impacts relative survival rate among young, middle-aged, and older adults. In young adults, females exhibit more favorable survival across the entire ten-year follow-up period, while male-female relative survival differences are smaller for middle-aged HL patients. These patterns are also evident in the five-year relative survival rates for males and females by age group. In young adults, five-year relative survival rate was 87% for males and 93% for females. In middle-aged adults, five-year rates were 74% for males and 77% for females, and females continued to exhibit better survival than males between five and ten years after diagnosis (Figure 27.2). There was little evidence of an influence by sex on relative survival among older adult patients aged 65 across the follow-up period, particularly at 48 months (males, 53%; females, 53%).

Race

The small numbers of non-white patients diagnosed with HL (total n=1,566) hinders detailed comparison of relative survival rates between racial/ethnic groups, particularly within older age groups. Regardless, relative survival rates was generally lower for persons of black race than for persons of white or "other" race/ethnicity. Among young adults aged 15-44 years at diagnosis, five-year relative survival rate for black males was 76%, substantially lower than the 88% rate observed in white males These racial/ethnic differences appeared to be independent of sex (Figure 27.3).

Figure 27.1: Hodgkin Lymphoma: 5- and 10-Year Relative Survival Rates (%) by Age at Diagnosis (15+), 12 SEER Areas, 1988-2001

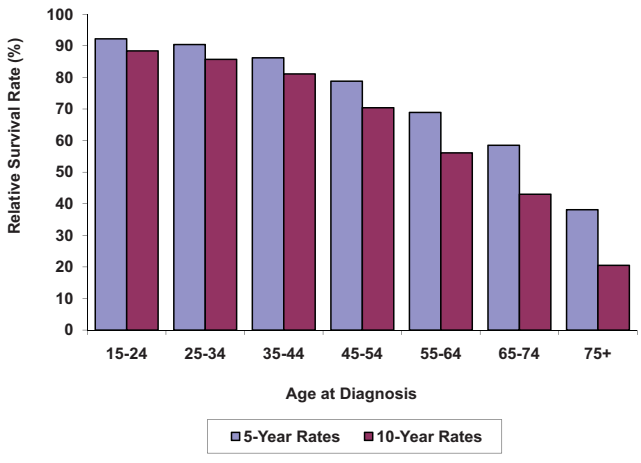


Figure 27.2: Hodgkin Lymphoma: Relative Survival Rates (%) by Age Group (15+) and Sex, 12 SEER Areas, 1988-2001

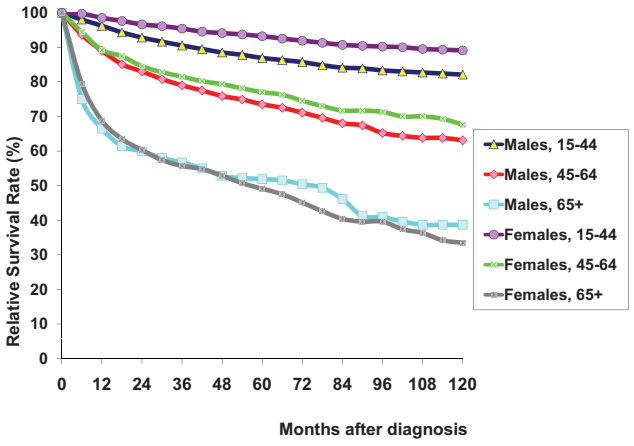


Table 27.3: Hodgkin Lymphoma: Number of Cases and 5-Year (Yr) Relative Survival Rates (RSR) (%) by Sex, Age (15+) and Ann Arbor Stage, 12 SEER Areas, 1988-2001 (Patients with Complete Stage Information: 8,047 Cases)

Sex/Age (Years)	Stage									
	Stages I-IV		IA		IB		IIA		IIB	
	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)
Total	8,047	83.7	1,125	93.5	424	81.2	1,957	92.9	1,458	85.7
15-44	5,618	90.3	705	96.8	274	88.0	1,564	95.8	1,151	89.4
45-64	1,463	74.1	271	90.7	86	72.0	272	87.3	187	77.2
65+	966	51.5	149	79.1	64	56.9	121	58.5	120	52.2
Male	4,464	81.9	685	94.1	252	77.0	856	93.4	781	84.1
15-44	3,030	87.7	424	96.9	163	84.6	663	94.4	589	88.3
45-64	927	73.6	186	89.2	51	66.0	142	90.4	124	76.0
65+	507	53.0	75	84.1	38	52.2	51	73.5	68	49.9
Female	3,583	86.0	440	92.6	172	86.6	1,101	92.4	677	87.4
15-44	2,588	93.3	281	96.5	111	92.7	901	96.7	562	90.6
45-64	536	75.0	85	94.0	35	80.3	130	83.6	63	79.1
65+	459	49.2	74	71.7	26	61.0	70	43.2	52	52.9

~ Statistic not displayed due to less than 25 cases.

Table 27.3 (continued): Hodgkin Lymphoma: Number of Cases and 5-Year (Yr) Relative Survival Rates (RSR) (%) by Sex, Age (15+) and Ann Arbor Stage, 12 SEER Areas, 1988-2001 (Patients with Complete Stage Information: 8,047 Cases)

Sex/Age (Years)	Stage									
	Stages I-IV		IIIA		IIIB		IVA		IVB	
	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)
Total	8,047	83.7	622	88.0	1,109	77.3	259	75.7	1,093	60.1
15-44	5,618	90.3	436	95.6	736	87.1	158	88.2	594	71.0
45-64	1,463	74.1	121	73.8	201	63.6	53	60.6	272	52.5
65+	966	51.5	65	53.5	172	39.7	48	42.5	227	33.5
Male	4,464	81.9	332	87.8	690	76.8	142	72.6	726	58.2
15-44	3,030	87.7	230	94.7	461	84.9	83	85.3	417	66.8
45-64	927	73.6	69	77.1	139	66.2	32	60.4	184	50.5
65+	507	53.0	33	51.0	90	40.6	27	35.7	125	32.2
Female	3,583	86.0	290	88.1	419	77.7	117	79.1	367	63.8
15-44	2,588	93.3	206	96.6	275	90.7	75	91.3	177	80.9
45-64	536	75.0	52	69.6	62	58.3	21	~	88	56.5
65+	459	49.2	32	53.6	82	38.2	21	~	102	34.2

~ Statistic not displayed due to less than 25 cases.

Stage and B-symptoms

Certain clinical presentations of HL had substantially worse five-year survival than others. Patients diagnosed with disseminated disease, stage IV (n=1,893) had markedly worse outcome than those with earlier stage disease, stage I (n= 2,778), stage II (n=4,344), and stage III (n=2,220), as captured by five-year relative survival rates (63% vs. 89%, 89%, and 81%, respectively) (Table 27.2). However, the presence of B-symptoms was a potent modifier of stage-specific survival, particularly for stage IV. Among the 8,047 patients with known stage and B-symptom status, comprising 69% of the HL patients in this analysis, patients with B-symptoms showed poorer survival across the ten-year follow-up period when compared to patients with similarly staged disease but without B-symptoms (Figure 27.4). In fact, patients with stage IIIA disease showed better survival than patients with stages IB and IIB disease. Survival curves for patients with stage IIIB disease were similar to those for patients with IVA, and survival time was substantially worse for patients with stage IVB than any of the other stages. Relative survival rate for patients with stage IVB was 76% at one year, 60% at five years, and 53% at ten years.

Figure 27.3: Hodgkin Lymphoma: 5-Year Relative Survival Rate (%) for Ages 15-44 by Race and Sex, 12 SEER Areas, 1988-2001

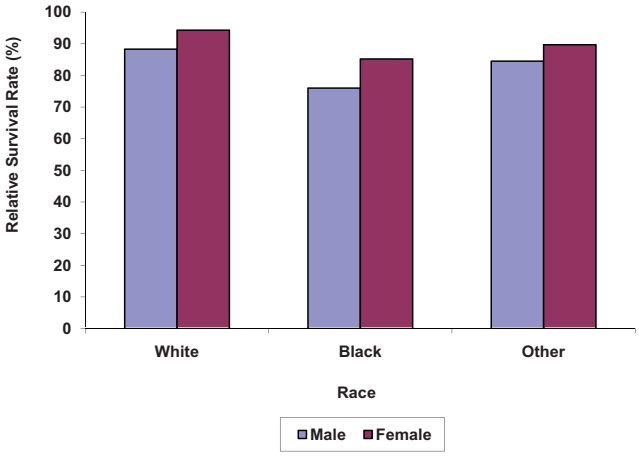


Figure 27.4: Hodgkin Lymphoma: Relative Survival Rates (%) by Stage and B-Symptoms, Ages 15+, 12 SEER Areas, 1988-2001 (Patients with Complete Stage & B Symptom Information: 8,047)

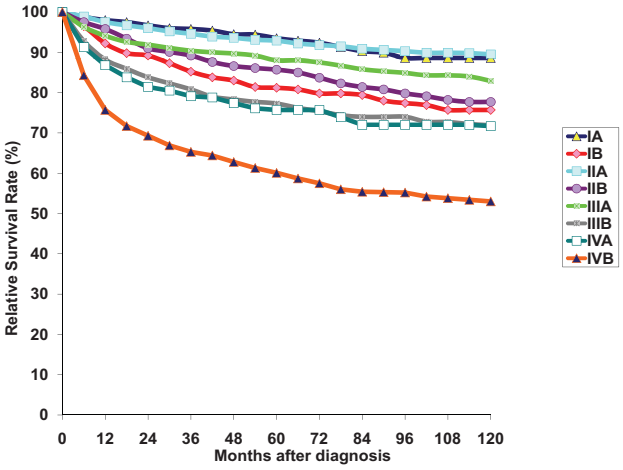


Table 27.4: Hodgkin Lymphoma: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Age (15+) and Histology, 12 SEER Areas, 1988-2001

Age (Years) /Histology (ICD-O Code)	Cases	Percent	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Ages	11,720	100.0	92.0	88.3	86.2	83.0	79.1	78.1
Unknown HD, NOS (9650-9651,9661-9662)	1,666	14.2	84.9	80.4	77.8	74.0	69.5	68.3
HD MC (9652)	2,097	17.9	87.0	82.0	79.5	74.7	69.5	68.1
HD LD (9653-9655)	209	1.8	57.1	52.2	51.0	48.6	46.1	44.0
HD NS (9663-9667)	7,435	63.4	95.6	92.4	90.4	87.6	84.1	83.2
Nodular LP (9659)	313	2.7	98.1	96.9	95.0	91.2	88.4	85.7
Ages 15-44	8,001	100.0	97.3	94.5	92.8	89.9	86.6	85.4
Unknown HD, NOS (9650-9651,9661-9662)	908	11.3	92.3	88.6	86.4	83.5	79.5	78.5
HD MC (9652)	986	12.3	95.2	92.6	90.9	86.4	81.9	80.7
HD LD (9653-9655)	71	0.9	80.5	74.8	71.9	67.1	65.3	65.3
HD NS (9663-9667)	5,833	72.9	98.5	95.9	94.2	91.7	88.6	87.4
Nodular LP (9659)	203	2.5	97.7	96.8	95.9	92.5	90.9	89.8

Figure 27.5: Hodgkin Lymphoma: Relative Survival Rates (%) by Age Group (15+) and Stage, 12 SEER Areas, 1988-2001 (Patients with Complete Stage & B Symptom Information: 8,047)

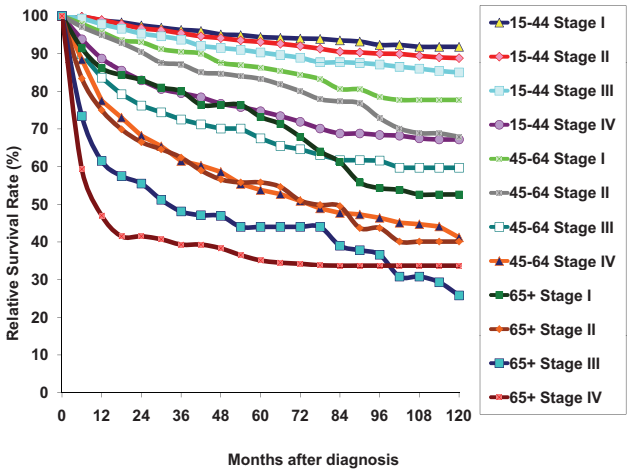
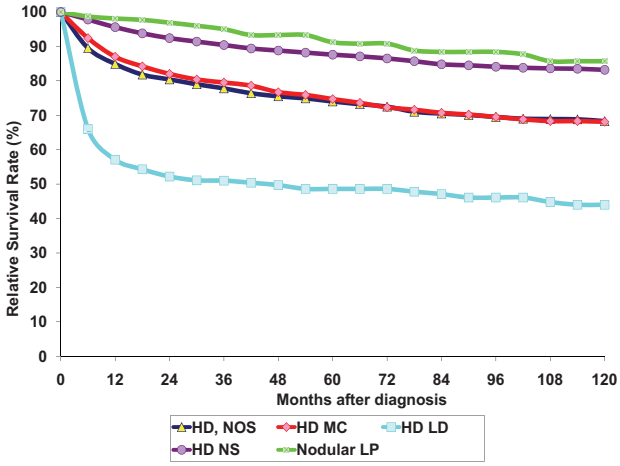


Figure 27.6: Hodgkin Lymphoma: Relative Survival Rates (%) by Histologic Subtype, Ages 15+, 12 SEER Areas, 1988-2001



However, like most features of HL, stage-specific survival is influenced strongly by age at diagnosis. Relative survival curves for young, middle-aged, and older adult HL patients by stage are shown in Figure 27.5. These curves show that stage at diagnosis modifies relative survival differently in young adults as compared to middle-aged and older adults. For young adults, there was little difference in relative survival rate over time for stages I, II, or III disease, but substantially poorer survival for persons with stage IV disease. For middle-aged and older adults, survival patterns were well-differentiated by stage and tended to show steeper declines in the first two years after diagnosis. Figure 27.5 also shows that relative survival did not level off but rather continually declined over time for nearly all age and stage groups, with the possible exception of stage IV disease in older adults. When B-symptoms are considered in addition to age and stage, it is additionally evident that age generally influences relative survival independently of these factors. Matched for stage and B-symptom status, relative survival rate decreased with increasing age at diagnosis. The survival deficit experienced by older adult patients became more profound with increasing disease spread. In patients with stage IA, five-year relative survival rate was 18 percentage points lower in older adults (79%) than in young adults (97%), but was 31-37 percentage points lower for patients with stages IB (57% vs. 88%), IIA (59% vs. 96%), and IIB (52% vs. 89%), and 37-47% lower for stages IIIA (54% vs. 96%), IIIB (40% vs. 87%), IVA (43% vs. 88%) and IVB (34% vs. 71%) (Table 27.3). Table 27.3 also shows five-year relative survival rates by stage and B-symptom status by age and sex. These data show that five-year relative survival rate were generally lower for males than females matched for stage/B-symptom status and age, although male-female differences were more pronounced for some age/stage combinations than for others. For example, relative survival rates for young adult males with stage IA or IIA disease were nearly equivalent to those for young adult females, but the rate for young adult males with stage IVB disease was 14 percentage points lower than that for young adult females. Overall, the range of five-year relative survival rates was wide; with the most favorable survival rates (97%) observed in young adult females and males with stage IA disease, and the poorest rates observed in older adult males with stage IVB (32%).

Histology

Histologic subtype additionally influences relative survival rates, although the relative rarity of some subtypes and the strong association of subtype with other prognostic factors (e.g., age, sex, race) make this influence difficult to examine. As shown in Table 27.4, NS comprised 73% of all young-adult cases and 63% of all ages, while the second most common subtype, MC, was observed in only 12% of young-adult patients, and 18% overall. The other specific subtypes, nodular LP, and LD, together comprised less than 5% of all cases. Across all ages, five-year relative survival was higher for NS (88%) and nodular LP (91%) subtypes and was intermediate for the MC subtype (75%) and non-specified types (74%). These patterns were additionally evident when limiting the series to young adults only (Table 27.3). The LD histologic subtype represented less than 2% of all cases but exhibited a substantially poorer five-year relative survival rate than other subtypes both in young adults (67%) and across all ages (49%). Figure 27.6 shows relative survival rates for

histologic subtypes across the ten-year follow-up period. The starkly different survival profile of the LD subtype is evident throughout the ten years.

DISCUSSION

Compared to other cancers, the one-year relative survival rate for HL was generally favorable at 92%. This relatively good survival rate reflects the availability of curative therapies for HL, including radiation or combination chemotherapeutic regimens, the introduction of which in the 1960's resulted in immediate reductions in HL mortality rates (2). Additionally, the 5-year relative survival rate after diagnosis has improved markedly from 40% in the early 1960's to 84 % in 1999 (2).

However, unlike some other cancers, relative survival rates after HL declined steadily with time since diagnosis, to 83% at five years and 78% at ten years. The fact that relative survival does not level off for most groups likely reflects ongoing risks of disease recurrence and long-term complications of treatment. Because most HL patients are young adults at the time of diagnosis, exposure to radiation and chemotherapy intended to cure HL at young ages has been shown to substantially increase risks of second or later malignancies (7) particularly breast cancer in young women (8). Other second malignancies observed in cohorts treated for HL include acute leukemias and non-Hodgkin's lymphomas (9). Within the first 15 years after diagnosis, HL is the major cause of death among HL patients, but soon after this time, cumulative mortality from second malignancies exceeds cumulative mortality from HL (10). Long-term risks of treatment-associated heart disease (11) and reproductive sterility are additionally important quality-of-life issues for HL survivors.

We observed substantial variation in relative survival rates by age at diagnosis. Most epidemiologic and clinical features of HL differ between young and older-adults (12), and relative survival is no different. The relative ten-year survival rate was nearly 90% for ages 15-24, but only 21% for persons diagnosed at age 75 or older. Age differences in survival patterns have been examined in detail by other authors and have also been interpreted as further evidence of the "two-disease" theory holding that young-adult and older-adult HL are etiologically distinct diseases (13).

As is the case with most cancers, stage or degree of disease spread at time of diagnosis profoundly impacts survival after HL, as patients with stage IVB disseminated disease had significantly shorter 5-year survival rate (60%) than those with less advanced disease, regardless of age (76-94%). The impact of stage on survival, however, was modified by age, reflecting the clinically more aggressive nature of the disease in older adults.

In these data, B-symptom status clearly altered survival, and like age, it modified the impact of stage on survival. Patients with no B-symptoms but diagnosed with stage III disease had higher survival rates than those diagnosed with early stage (I and II) disease with B-symptoms. B-symptom status has been long associated with poor prognosis in lymphoma patients and may be caused by tumor-related dysregulation of certain cytokines.

HL survival also varied by histology. Histologic subtypes were strongly associated with age, with younger patients more likely to have NS, the subtype associated with the most favorable survival rate. However, within histologic categories, younger patients consistently had higher survival rates than older patients. Patients with the LD subtype had considerably worse survival than patients with other subtypes, as described previously (14).

In this relatively large, population-based series of patients, we were able to examine the influences of demographic characteristics like race and sex. The poorer survival rates observed for blacks than whites have been reported previously and appear to be independent of stage and other prognostic factors (15). We also observed intriguing differences by sex in survival after HL. Males exhibited poorer relative survival rates than females in young adults across nearly all stages of disease, but not in persons over 45 years of age. In young adults, male sex has been shown to be associated with HL survival independently of other factors in previous analyses using SEER data (13).

In summary, survival following HL is relatively favorable, and the 83% five-year relative survival rate observed in this population-based cohort is comparable to those reported in clinical settings. However, relative survival rate was observed to vary substantially with sex, stage at diagnosis, B-symptom status, histology, and, especially, age at diagnosis. Indeed, the generally good average survival rates for HL largely represent the outcome of patients diagnosed at ages 45 and younger, who comprise the majority of patients in the US. However, the relatively young average age of the HL patient amplifies the effect of this cancer on the overall cancer burden; it ranks third in the average years of life lost to a cancer. Although substantial progress has been made against HL, the current challenges facing HL clinicians and researchers include reducing treatment-related side effects to improve the quality-of-life for long-term HL survivors and improving outcomes for older patients.

REFERENCES

1. American Cancer Society. Cancer facts and figures 2006. Atlanta: American Cancer Society, 2006.
2. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Eisner MP, Horner MJ, Howlader N, Hayat M, Hankey BF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site, 2006.
3. Mauch, P. M., Kalish, L. A., Kadin, M., Coleman, C. N., Osteen, R., and Hellman, S. Patterns of presentation of Hodgkin disease. Implications for etiology and pathogenesis [see comments]. Cancer, 71: 2062-71, 1993.
4. Carbone, P. P., Kaplan, H. S., Musshoff, K., Smithers, D. W., and Tubiana, M. Report of the committee on Hodgkin's disease staging classification. Cancer Research, 31: 1860-1861, 1971.
5. Harris, N. L., Jaffe, E. S., Diebold, J., Flandrin, G., Muller-Hermelink, H. K., Vardiman, J., Lister, T. A., and Bloomfield, C. D. World Health Organization classification of neoplastic diseases of the hematopoietic and lymphoid tissues: report of the Clinical Advisory Committee meeting-Airlie House, Virginia, November 1997. Journal of Clinical Oncology, 17: 3835-49, 1999.
6. Percy, C., Van Holten, V., and Muir, C. International classification of diseases for oncology--second edition. Geneva: World Health Organization, 1990.
7. Hodgson DC, Gilbert ES, Dores GM, Schonfeld SJ, Lynch CF, Storm H, Hall P, Langmark F, Pukkala E, Andersson M, Kaijser M, Joensuu H, Fossa SD, Travis LB. Long-term solid cancer risk among 5-year survivors of Hodgkin's lymphoma. J Clin Oncol. 2007 Apr 20;25(12):1489-97.
8. Aisenberg, A. C., Finkelstein, D. M., Doppke, K. P., Koerner, F. C., Boivin, J. F., and Willett, C. G. High risk of breast carcinoma after irradiation of young women with Hodgkin's disease. Cancer, 79: 1203-10, 1997.
9. Boivin, J. F., Hutchison, G. B., Zauber, A. G., Bernstein, L., Davis, F. G., Michel, R. P., Zanke, B., Tan, C. T., Fuller, L. M., Mauch, P., and et al. Incidence of second cancers in patients treated for Hodgkin's disease. Journal of the National Cancer Institute, 87: 732-41, 1995.
10. Mauch, P. M., Kalish, L. A., Marcus, K. C., Shulman, L. N., Krill, H., Tarbell, N. J., Silver, B., Weinstein, H., Come, S., and Canellos, G. P. Long term survival in Hodgkin's disease: relative impact of mortality, second tumors, infection and cardiovascular disease. The Cancer Journal from Scientific American, 1: 33-42, 1995.
11. Swerdlow AJ, Higgins CD, Smith P, Cunningham D, Hancock BW, Horwich A, Hoskin PJ, Lister A, Radford JA, Rohatiner AZ, Linch DC. Myocardial infarction mortality risk after treatment for Hodgkin disease: a collaborative British cohort study. J Natl Cancer Inst. 2007 Feb 7;99(3):206-14.
12. Glaser, S. L., and Jarrett, R. F. The epidemiology of Hodgkin's disease. Baillieres Clinical Haematology, 9: 401-16, 1996.
13 Clarke, C. A., Glaser, S. L., and Prehn, A. W. Age and patterns of survival after Hodgkin's disease. Cancer Causes and Control, in press, 2001.
14. Medeiros, L. J., and Greiner, T. C. Hodgkin's disease. Cancer, 75: 357-69, 1995.
15. Zaki, A., Natarajan, N., and Mettlin, C. J. Early and late survival in Hodgkin disease among whites and blacks living in the United States. Cancer, 72: 602-6, 1993.

ACKNOWLEDGEMENTS

The authors would like to acknowledge Angela Prehn Ph.D and Erin Eberle for their contributions to this chapter.

Chapter 28
Non-Hodgkin Lymphoma

Christina Clarke and Cynthia O'Malley

INTRODUCTION

Lymphomas are malignancies of the lymphoid cells and can be divided on the basis of pathologic features into Hodgkin and non-Hodgkin lymphomas (NHL), the latter an umbrella designation for at least 30 types of distinct B- and T-cell neoplasms. Although it was recently determined to be a B-cell lymphoma, Hodgkin lymphoma or Hodgkin's disease differs substantially from other lymphomas with respect to epidemiologic and survival characteristics, and so it is discussed in a separate chapter. Altogether, NHLs are substantially more common and, when grouped together as a single entity, represent one of the top five sources of cancer morbidity and mortality in the US population.

NHLs are also a growing component of the cancer burden; incidence rates increased over 80% between 1973 and 1999, one of the most rapid increases observed among all cancers. Some of the rapid increase in NHL incidence can be attributed to improvements in diagnostic practice and disease classifications, as well as to the HIV epidemic, as NHL is at least 100-times more likely to occur in the context of HIV-related immunosuppression. However, other reasons for the increasing incidence remain unclear. The extraordinary heterogeneity of NHLs has hindered our progress in its description and study. We took advantage of this unique opportunity to use the large, population-based SEER registry to examine survival patterns for NHLs considered together as a single entity as well as by separate histologic subtypes.

MATERIALS AND METHODS

Patients

Analyses included all patients aged 20 or over diagnosed with NHL (ICD-O-2 codes 9590-9595, 9670-9717) between 1988 and 2001 and reported to the SEER program. Patients were followed for vital status until 2002. Table 28.1 details exclusions from the case series, which resulted in a final series of 65,932 patients. Patients without histologic confirmation of lymphoma diagnosis were excluded from analysis.

Presence of HIV/AIDS

Persons with HIV infection have substantially elevated risks of developing and dying from NHL. In addition to its poorer prognosis, HIV/AIDS-related NHL differs from unrelated NHL with respect to epidemiologic, histologic, and clinical characteristics to be elucidated below. Although the SEER program has formally collected information regarding HIV/AIDS as part of the extent of disease information for lymphoma cases diagnosed in 1990 and beyond, this information tends to be somewhat incomplete in the SEER database. Therefore, all cases with evidence of positive HIV/AIDS status based on the extent of disease information or underlying cause of death (ICD-9 codes 0420-0449 or ICD-10 codes B020-B024) were separated from cases without any evidence of HIV for stratified analyses (1).

Table 28.1: Non-Hodgkin Lymphoma: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
81,867	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
70,531	11,336	Select first primary only
69,699	832	Exclude death certificate only or at autopsy
69,020	679	Exclude unknown race
68,920	100	Active follow-up and exclude alive with no survival time
67,568	1,352	Exclude children (Ages 0-19)
67,568	0	Exclude in situ cancers for all except breast & bladder cancer
65,932	1,636	Exclude no or unknown microscopic confirmation
65,932	0	Exclude sarcomas

Stage classification

NHL tumors usually begin in lymph nodes or other lymphoid tissue but spread to extranodal sites, including organs. In the SEER database, classification of stage of disease at diagnosis for all lymphomas follows guidelines set forth at the 1971 Ann Arbor conference (2). In brief, it provides four stages of tumor spread relative to the diaphragm: I--involvement of a single lymph node region, II--involvement of two or more lymph node regions on one side of the diaphragm, III--involvement of lymph node regions on both sides of the diaphragm, IV--disseminated disease. Each stage can be subclassified as A or B type according to the absence or presence, respectively, of symptoms such as fever, night sweats, pruritus or weight loss of greater than 10 percent of total body mass. In the analyses below, stage information was complete for 90% and B-symptom information for 46% of the cohort without evidence of HIV/AIDS (Table 28.2).

Histologic classification

NHL has long been recognized as a heterogeneous group of lymphoid malignancies, and multiple classification schemes have been developed over the past several decades. In 1994 an international group of expert hemato-

Table 28.2: Non-Hodgkin Lymphoma: Number of Cases, Distribution and 5-Year Relative Survival Rates (RSR) (%) by Sex, Race, Age (20+), Ann Arbor Stage, and HIV/AIDS Status, Ages 20+12 SEER Areas, 1988-2001

	Total			non-HIV/AIDS			HIV/AIDS		
Characteristics	Cases	Percent	5-Year RSR (%)	Cases	Percent	5-Year RSR (%)	Cases	Percent	5-Year RSR (%)
Total	65,932	100.0	56.3	61,214	100.0	60.0	4,718	100.0	14.8
Sex									
Male	36,354	55.1	52.5	31,982	52.2	58.7	4,372	92.7	13.8
Female	29,578	44.9	60.9	29,232	47.8	61.3	346	7.3	27.2
Race									
White	56,851	86.2	57.1	53,040	86.6	60.6	3,811	80.8	15.0
Black	4,502	6.8	48.2	3,724	6.1	56.2	778	16.5	13.2
Race/sex									
White male	31,232	47.4	53.4	27,620	45.1	59.4	3,612	76.6	14.3
White female	25,619	38.9	61.5	25,420	41.5	61.8	199	4.2	29.7
Black male	2,605	4.0	43.4	1,955	3.2	55.0	650	13.8	11.6
Black female	1,897	2.9	54.8	1,769	2.9	57.5	128	2.7	20.5
Age (20+)									
20-34	4,522	6.9	53.6	3,246	5.3	69.8	1,276	27.0	12.8
35-49	11,646	17.7	59.7	9,090	14.8	72.4	2,556	54.2	14.1
50-64	16,925	25.7	63.6	16,196	26.5	65.7	729	15.5	17.4
65-79	23,591	35.8	53.7	23,453	38.3	53.8	138	2.9	35.2
80+	9,248	14.0	37.9	9,229	15.1	37.9	19	0.4	~
Ann Arbor Stage									
I	19,971	30.3	69.4	18,463	30.2	74.5	1,508	32.0	15.7
IA	7,238	11.0	77.5	6,781	11.1	81.6	457	9.7	24.5
IB	1,926	2.9	50.7	1,592	2.6	60.4	334	7.1	10.6
II	9,098	13.8	61.1	8,685	14.2	63.0	413	8.8	25.4
IIA	3,357	5.1	68.1	3,256	5.3	69.2	101	2.1	34.6
IIB	2,018	3.1	50.5	1,858	3.0	53.4	160	3.4	20.9
III	7,910	12.0	49.7	7,407	12.1	51.9	503	10.7	21.6
IIIA	2,573	3.9	59.5	2,452	4.0	61.2	121	2.6	28.1
IIIB	2,240	3.4	38.3	2,001	3.3	41.5	239	5.1	15.0
IV	22,558	34.2	42.4	20,610	33.7	46.0	1,948	41.3	9.5
IVA	5,119	7.8	51.2	4,781	7.8	53.8	338	7.2	17.9
IVB	6,203	9.4	30.0	5,328	8.7	34.1	875	18.5	7.9
Unstaged	6,395	9.7	65.7	6,049	9.9	68.9	346	7.3	17.8

pathologists proposed the first international consensus classification system, now known as the WHO classification. The WHO system has been incorporated into the newest (third) edition of the coding system used by all cancer registries: the International Classification of Diseases—Oncology (ICD-O). However, data available for analysis were collecting using the more obsolete ICD-O, second edition (ICD-O-2) system. We used the ICD-O-2 to ICD-O-3 conversion tables to create histologic groupings base on ICD-O-2 that are more reflective of the WHO concepts. These groupings, with their associated ICD-O-2 codes, are as follows: small B-lymphocytic lymphoma (9670,9823), lymphoplasmacytic lymphoma (9671), mantle cell lymphoma (9673, 9674, 9677), mixed small/large cell diffuse lymphoma (9675-76), large B-cell diffuse lymphoma (9680-81, 9683-84, 9688, 9712), Burkitt's lymphoma (9687), follicular grade 2 (9691), follicular grade 1 (9695, 9696), follicular grade 3 (9697-9698, 9693), all follicular combined (9690-9693, 9695-9698), marginal zone (9710-9711, 9715), mycosis fungoides/Sezary's syndrome (9700-9701), other mature T-cell lymphomas (9702-04, 9706-08, 9716), angioblastic T-cell (9705), cutaneous T-cell (9709), anaplastic T-cell (9714), other T-cell (9708, 9716-9718,9827), NK/null cell (9713), precursor B-cell lymphoma/leukemias (9685,9821), and unspecified lymphomas (9590-9592, 9672,9682,9694).

RESULTS

Patients with evidence of HIV/AIDS

Of the 65,932 adult patients with NHL in this analysis, 4,718 (over 7%) had some evidence of HIV/AIDS on the basis of the medical record or cause of death information. These patients were more likely than patients without evidence of HIV/AIDS to be male (93% vs. 52%), aged 20-50 at diagnosis (81% vs. 20%) and black (17% vs. 6%). Survival was very poor for these patients, with relative survival rate of 15% at five years (Table 28.2). Figure 28.1 shows the relative survival curves for black and white male patients with and without evidence of HIV/AIDS.

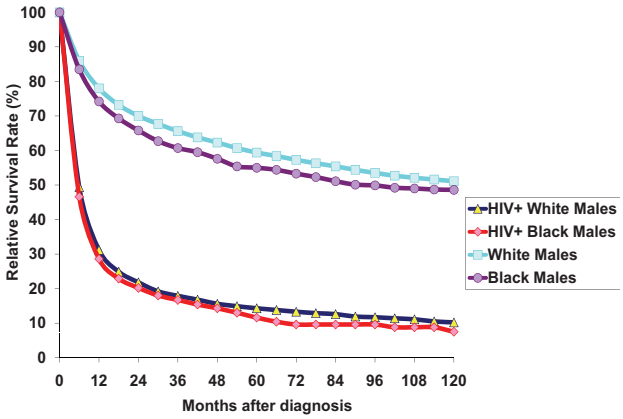
Patients without evidence of HIV/AIDS

Patients without evidence of HIV/AIDS numbered 61,214; 80% were aged 50 years or older at diagnosis, 52% were male, and 87% were of white race. Overall, survival rates for these patients were moderate, with 78% surviving one year after diagnosis relative to the general population, but this rate declined to 60% at five years and 51% at ten years. Relative survival after NHL is influenced by age, sex, race/ethnicity, stage of disease, and histologic type and the relative survival curves for NHL patients continue to decline as years since diagnosis increases irrespective of these factors.

Age, sex and race

Table 28.2 shows survival by age, sex, and race. Overall, females had somewhat higher five-year relative survival rates (61%) than males (59%), and whites (61%) had slightly higher rates than blacks (56%). Assessing survival jointly by sex and race shows that these factors influence survival subtly but independently. Relative survival rates for white females (62%) were slightly higher than those for white males (59%), black females (58%), and black males (55%). Without consideration of factors possibly associated with race and sex like stage at diagnosis, whites

Figure 28.1: Non-Hodgkin Lymphoma: Relative Survival Rates (%) for Males by Race and HIV Status, Ages 20+, 12 SEER Areas, 1988-2001



demonstrated better survival rates than blacks, and females survived better than males.

Patient age at diagnosis strongly influences survival patterns after NHL diagnosis. Figure 28.2 shows survival curves by sex for detailed age groups over time, showing generally linear associations of increasing age with poorer survival, particularly as regards survival in the first 5 years after diagnosis.

The female survival advantage was also apparent across age groups. Figure 28.2 shows that females generally have better survival than males over time. Some of the differences by sex observed in persons aged 20-49 years may relate to HIV/AIDS-related lymphoma that could not be identified in the SEER database. In addition, all age groups individually demonstrated consistently declining relative survival with time since diagnosis. As described below, age at diagnosis additionally impacted relative survival regardless of stage of disease spread and symptomatology.

Stage of disease at diagnosis

Like most other cancers, outcome after NHL is impacted largely by the extent of disease spread at time of diagnosis. Figure 28.3 shows relative survival curves for younger (ages 20-64 years) and older (ages 65+) patients by Ann Arbor stage of disease. Younger and older patients had essentially similar distributions of stage at diagnosis (Stage I: 30% vs. 30%, Stage II: 14% vs. 14%, Stage III: 12% vs. 12%, Stage IV: 34 % vs. 34%, unknown: 10% vs. 10%). Relative survival rates decreased incrementally with increasing stage, with the exception of older patients, for whom survival patterns were similar in stages III and IV, with equivalent survival in the long-term (10 years after diagnosis). Additionally important to outcome was the presence or absence of B-symptoms. Although B-symptom status was unknown for a large proportion of patients, we examined stage and B-symptom specific survival curves for the patients with complete information (Figure 28.4). Stage for stage, patients with B-symptoms had substantially poorer survival than patients without symptoms. For example, the 5-year relative survival rate for patients with stage IA was 82%, compared to the 60% for patients with stage IB (Table 28.2).

Table 28.3: Non-Hodgkin Lymphoma: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by Age (20+) and Ann Arbor Stage, 12 SEER Areas, 1988-2001 (Patients with Complete Stage Information and No Evidence of HIV/AIDS: 28,049 Cases)

Age Group (Years)	Ann Arbor Stage									
	Total		IA		IB		IIA		IIB	
	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)
All Ages (20+)	28,049	58.6	6,781	81.6	1,592	60.4	3,256	69.2	1,858	53.4
20-34	1,758	69.0	368	86.7	141	70.5	222	83.3	183	68.9
35-49	4,617	70.4	1,142	87.1	264	75.0	487	81.5	323	61.5
50-64	7,632	63.8	1,821	86.2	350	68.7	908	74.0	474	57.8
65-79	10,243	51.3	2,479	78.6	589	50.0	1,173	63.8	648	44.4
80+	3,799	36.7	971	62.9	248	38.1	466	41.0	230	31.5

Table 28.3 (continued)

Age Group (Years)	Ann Arbor Stage									
	Total		IIIA		IIIB		IVA		IVB	
	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)
All Ages (20+)	28,049	58.6	2,452	61.2	2,001	41.5	4,781	53.8	5,328	34.1
20-34	1,758	69.0	116	78.3	137	67.8	242	58.5	349	45.5
35-49	4,617	70.4	407	79.2	326	63.1	740	68.1	928	46.2
50-64	7,632	63.8	712	67.3	532	41.4	1,377	60.7	1,458	38.9
65-79	10,243	51.3	874	48.8	716	31.2	1,795	45.7	1,969	25.2
80+	3,799	36.7	343	35.7	290	14.5	627	28.0	624	13.7

Stage, age, and B-symptom status

Table 28.3 shows the relationship of age to NHL survival, within stage and B-symptom strata. For patients diagnosed at age 50 or older, survival decreased with age within each stage/ B-symptom category. The poorer survival of patients with B-symptoms is observed across all age groups and stages. Sex did not appear to appreciably modify these differences (data not shown).

Histology

As described above, NHL is a category blanketing more than 30 different B and T-cell malignancies, many of which are still being distinguished and described as new molecular diagnostic tools become available. Table 28.4 shows counts and five-year relative survival rates for distinct NHL subtypes as recorded by the SEER database. Seventeen percent of patients were reported as having lymphoma, not otherwise specified (NOS) and were not assigned a histologic subtype, which limits the interpretability of the distribution of other specified subtypes. Regardless, large B-cell lymphoma (36.6%) and follicular lymphoma (19.3%) were the two most common subtypes. Five-year relative survival rates for follicular lymphomas, particularly grades 1 (80%) and 2 (76%) were substantially higher than that for large B-cell lymphomas (50%). In general, lymphoma subtypes can be grouped into indolent subtypes with more favorable survival features, or as aggressive lymphomas with poorer outcomes.

Figure 28.2: Non-Hodgkin Lymphoma: Relative Survival Rates (%) by Age Group (20+) and Sex, 12 SEER Areas, 1988-2001 (Patients with No Evidence of HIV/AIDS: 61,214)

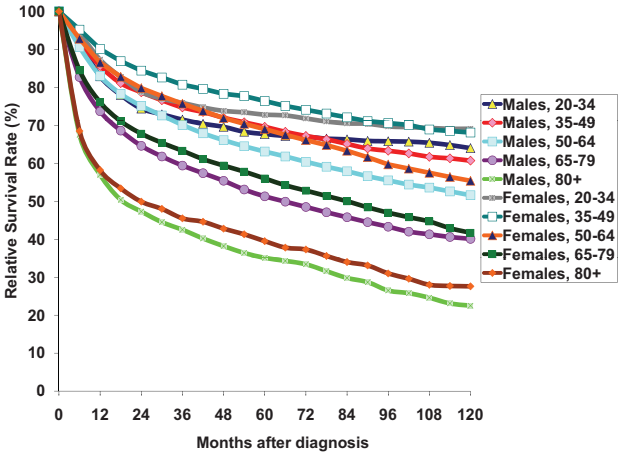


Figure 28.3: Non-Hodgkin Lymphoma: Relative Survival Rates (%) by Stage and Age Group (20+), 12 SEER Areas, 1988-2001 (Patients with Complete Stage Information and No Evidence of HIV/AIDS)

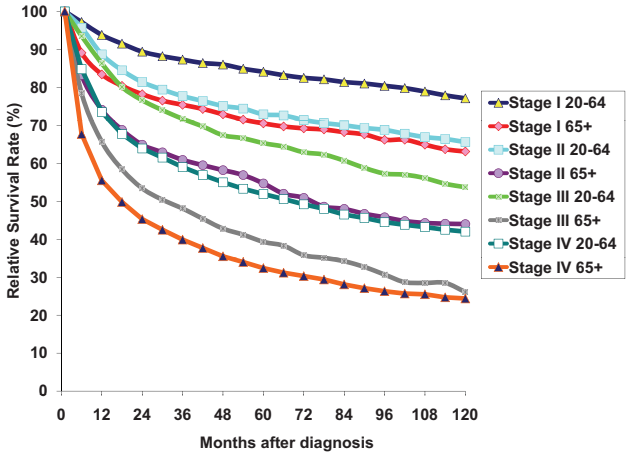


Figure 28.4: Non-Hodgkin Lymphoma: Relative Survival Rates (%) by Stage and B-Symptoms, Ages 20+, 12 SEER Areas, 1988-2001 (Patients with Complete Stage Information and No Evidence of HIV/AIDS)

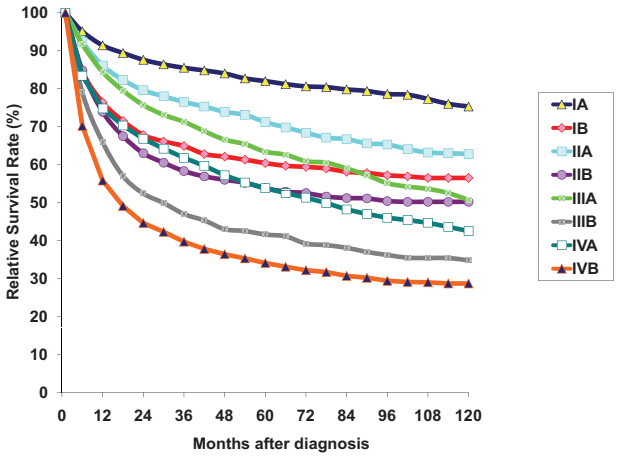


Table 28.4: Non-Hodgkin Lymphoma: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Histologic Subtype, Ages 20+, 12 SEER Areas, 1988-2001
(Patients with No Evidence of HIV/AIDS: 61,214 Cases)

Histology (ICD-O Code)	Cases	Percent	Relative Survival Rate (%) 1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	61,214	100.0	77.5	69.9	65.8	60.0	53.5	50.8
Small B Lymphocytic (9670,9823)	4,586	7.5	87.8	82.1	77.2	67.9	55.4	49.5
Lymphoplasmacytic (9671)	802	1.3	86.0	80.5	74.9	64.6	50.6	45.5
Mantle cell (9673)	1,558	2.5	83.9	72.6	65.2	51.1	37.4	34.3
Mixed small/large diffuse (9675)	2,219	3.6	77.5	68.1	62.4	55.5	49.4	47.7
Large B-cell diffuse, NOS* (9679,9680,9684)	22,390	36.6	67.0	57.1	53.8	50.4	47.3	45.9
Burkitts (9687)	508	0.8	53.5	47.8	47.4	45.4	45.1	45.1
Follicular grade 2 (9691)	3,701	6.0	94.6	88.5	83.2	75.7	67.1	61.6
Follicular grade 1 (9695)	4,649	7.6	95.9	92.2	88.1	79.8	68.4	63.8
Follicular grade 3 (9698)	2,170	3.5	88.5	81.5	76.2	69.2	61.9	60.8
All follicular combined (9690-9691, 9695-9698)	11,784	19.3	93.6	88.2	83.6	75.8	66.3	61.6
Marginal zone (9689,9699)	2,646	4.3	93.8	91.6	88.7	83.7	80.6	64.2
Mycosis fungoides, Sezary (9700-9701)	1,815	3.0	97.1	95.1	92.4	88.4	84.5	82.6
Mature T-cell, NOS* or other (9702)	725	1.2	61.9	48.8	43.6	38.1	34.3	32.5
Angioblastic T (9705)	144	0.2	61.1	55.4	49.0	38.3	28.4	28.4
Cutaneous T (9709)	738	1.2	92.7	88.8	86.6	84.4	79.8	77.8
Anaplastic T (9714)	605	1.0	69.0	59.8	56.6	53.9	52.7	43.9
Other specified T (9708,9716-9718,9827)	66	0.1	67.7	64.2	56.1	42.5	33.4	0.0
NK/null T (9719)	75	0.1	53.1	48.1	47.3	40.6	32.2	32.2
Precursor cells (9727-9729)	394	0.6	66.8	49.6	45.6	40.3	38.5	38.0
Lymphoma, NOS* (9590-9591,9596)	10,159	16.6	70.6	62.9	58.3	51.6	44.7	42.5

* NOS: Not Otherwise Specified
~ Statistic not displayed due to less than 25 cases.
! Not enough intervals to produce rate.

Table 28.5: Non-Hodgkin Lymphoma: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Predominant Extranodal NHL Sites, Ages 20+, 12 SEER Areas, 1988-2001
(Patients with No Evidence of HIV/AIDS: 61,214 Cases)

Primary Site (ICD-O Code)	Cases	Percent	Relative Survival Rate (%) 1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	61,214	100.0	77.5	69.9	65.8	60.0	53.5	50.8
Nodes (C770-C779)	40,797	66.6	76.1	67.3	62.6	56.0	49.0	46.0
Skin (C440-C449)	3,879	6.3	94.1	91.2	88.7	84.9	80.6	78.9
Stomach (C160-C169)	3,233	5.3	74.4	70.8	69.2	67.4	63.3	62.3
Small Intestine (C170-C179)	1,220	2.0	72.6	66.7	64.7	62.6	61.0	59.0
Brain (C710-C719)	1,014	1.7	50.6	38.0	30.8	21.2	13.5	10.4
Lung (C340-C349)	705	1.2	75.5	69.8	65.8	61.6	50.9	50.9
Colon (C180-C189, C260)	728	1.2	73.8	67.4	65.7	61.4	56.6	53.3
Bone Marrow (C421)	542	0.9	69.3	62.5	56.8	45.2	40.5	40.3
Spleen (C422)	610	1.0	81.8	74.7	71.8	67.5	60.8	57.7
Liver (C220)	224	0.4	49.7	45.3	43.6	40.0	33.9	33.4
Mediastinum (C380-C389)	211	0.3	75.2	67.2	63.4	59.6	57.5	57.5

Figure 28.5 shows relative survival curves for indolent lymphomas, including the cutaneous lymphomas like mycosis fungoides, while Figure 28.6 shows relative survival curves for aggressive lymphomas. Indolent lymphomas, particularly follicular, small B-lymphocytic, and lymphoplasmacytic lymphomas, were observed to have nearly linear declines in relative survival over time, while relative survival curves for aggressive lymphomas, particularly large –cell and most T cell lymphomas, were observed to level off with time.

Extranodal site of diagnosis for extranodal lymphoma

Nodal or extranodal site at primary diagnosis of lymphoma influences survival outcomes. More than 20% of NHL patients in this series were observed to have some extranodal presentation (n=12,366). Table 28.5 shows counts and five-year survival rates for nodal or common extranodal sites of presentation. Lymphoma present in the central nervous system (CNS) or brain had the worst five-year relative survival rate (21%) while skin, the most common site of extranodal presentation, had the most favorable (85%). About 5.3% of all lymphomas presented in the stomach and had a five-year relative survival rate of 67%.

DISCUSSION

Overall, more than half of the patients diagnosed with NHL survive five years after diagnosis. However, relative survival rates after most types of NHL declined consistently over time, rather than leveling off as do survival curves for some solid tumors. Decreasing relative survival over time reflects the ongoing risks of disease recurrence, treatment sequelae, and health outcomes noted to follow treatment for lymphoma.

Survival patterns after NHL are heterogeneous and vary enormously by HIV status, age at diagnosis, stage, presence of B-symptoms, histologic type, and to a lesser extent, sex and race. This substantial variation is demonstrated by five-year survival rates ranging from 82% with Stage IA disease to 8% in patients with HIV-associated NHL and Stage IVB.

Over 7% of the patients that were eligible for this survival analysis had some evidence of HIV-associated disease, which was shown to prognosticate extremely poor survival. This proportion is probably not reflective of the overall contribution of HIV/AIDS-associated lymphoma to the total burden of NHL, as many patients with evidence of HIV/AIDS were diagnosed without histologic confirmation and were excluded from analysis. In addition, there is an under ascertainment of the HIV/AIDS cases. HIV-associated NHL is considerably more aggressive than sporadic NHL, and treatment choices are constrained by the weakened immune system, causing poor survival. A further limitation of this analysis is the assessment of outcomes over a time period when highly active antiretroviral therapies were introduced for treatment of HIV/AIDS. These therapies have been shown to improve survival after HIV/AIDS related lymphoma substantially (3). While caution must be used in interpreting these results, the main point is that for total NHL survival is heavily influenced by HIV/AIDS.

Figure 28.5: Indolent Non-Hodgkin Lymphoma: Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001
(Patients with No Evidence of HIV/AIDS: 61,214)

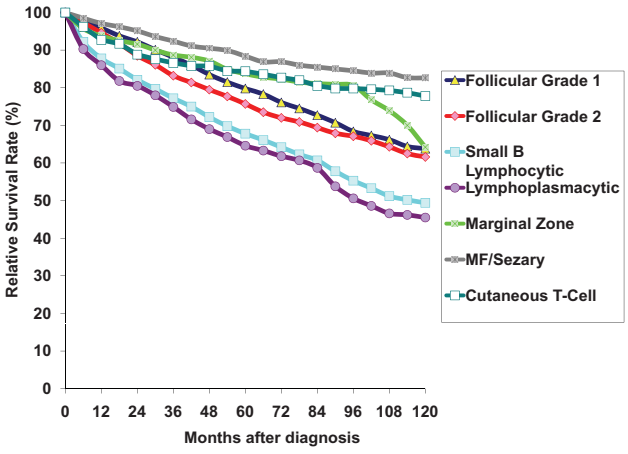
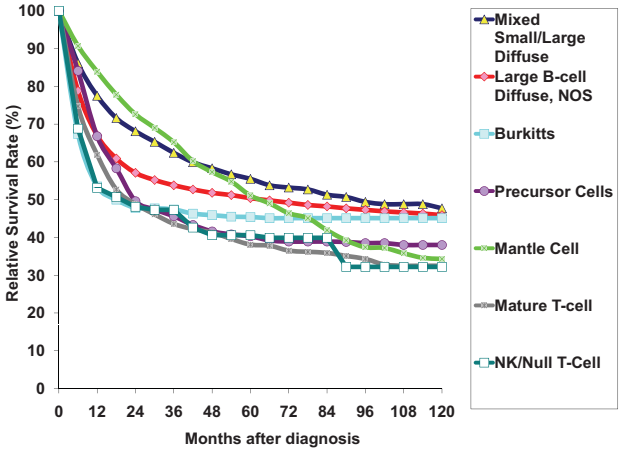


Figure 28.6: Aggressive Non-Hodgkin Lymphoma Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001
(Patients with No Evidence of HIV/AIDS: 61,214)



Age strongly influenced survival as older persons typically experienced poorer survival, and even within stage, older persons had lower survival rates. NHL incidence rates were higher in males than females across the age spectrum, but females had slightly higher survival rates. As with most cancers, stage at diagnosis exerted considerable impact on survival. The presence of B-symptoms dramatically lowered survival within all stage and age groups.

The heterogeneity of NHL is particularly evident when considering the different patterns of survival by histologic subtypes. The survival curves of aggressive NHLs declined rapidly in the early months following diagnosis, but leveled off over time, a pattern similar to that of many solid tumors. This pattern contrasted dramatically with that of the indolent lymphomas, where a gradual steady decline was observed over the entire period of follow-up. While rarely cured, patients with indolent lymphomas typically have long periods of remission (4). The site of extranodal involvement was also observed to strongly influence survival.

Standard treatment choices for NHL are determined primarily by histologic subtype and stage and generally include both chemotherapy and radiation therapy. While treatment has improved survival after diagnosis with lymphoma, it may cause additional health problems. A significantly increased risk of second primary cancers has been noted in persons surviving 15 years or more after diagnosis with NHL (5), and cardiac toxicity has been reported (6). The monoclonal antibody rituximab has been shown to be helpful in assisting immune responses against lymphoma cells, thereby providing a treatment choice with fewer side effects than other therapies for a subset of NHLs expressing the CD20 antigen (7). Other treatment innovations include novel chemotherapy agents and regimens including bone marrow or peripheral blood stem cell transplantation. The high and increasing incidence of NHLs underscores the importance of continuing efforts to develop therapies that will improve survival and reduce adverse treatment effects.

These population-based data are based on nearly 66,000 patients diagnosed between 1988 and 2001. While the SEER data provide a large representative sample to examine numerous clinical and demographic predictors of survival after diagnosis with NHL, especially for rare subtypes, data were not available on treatment differences and comorbidity, two additional factors which impact survival and could explain some of the observed patterns. These analyses do, however, provide evidence of the considerable variation in survival patterns for NHL patients, reflecting the incredible heterogeneity of this disease entity.

REFERENCES

1. Clarke CA, Glaser SL. Population-based surveillance of HIV-associated cancers: utility of cancer registry data. J Acquir Immune Defic Syndr. 2004 Aug 15;36(5):1083-91
2. Carbone PP, Kaplan HS, Musshoff K, Smithers DW, Tubiana M. Report of the committee on Hodgkin's disease staging classification. Cancer Research 1971;31(11)1860-1861.
3. Diamond C, Taylor TH, Aboumrad T, Anton-Culver H. Changes in acquired immunodeficiency syndrome-related non-Hodgkin lymphoma in the era of highly active antiretroviral therapy: incidence, presentation, treatment, and survival. Cancer. 2006 Jan 1;106(1):128-35.
4. Skarin AT, Dorfman DM. Non-Hodgkin's lymphomas: current classification and management. Ca Cancer J Clin 47(6): 351-372,1997
5. Travis LB, Curtis RE, Glimelius B, et al.: Second cancers among long-term survivors of non-Hodgkin's lymphoma. JNCI 85(23): 1932-1937, 1993.
6. Haddy TB, Adde MA, McCalla J, Domanski MJ, Datiles M 3rd, Meehan SC, Pikus A, Shad AT, Valdez I, Lopez Vivino L, Magrath IT Late effects in long-term survivors of high-grade non-Hodgkin's lymphomas. J Clin Oncol; 16(6):2070-9 1998
7. Schulz H, Bohlius JF, Trelle S, Skoetz N, Reiser M, Kober T, Schwarzer G, Herold M, Dreyling M, Hallek M, Engert A. Immunochemotherapy with rituximab and overall survival in patients with indolent or mantle cell lymphoma: a systematic review and meta-analysis. J Natl Cancer Inst. 2007 May 2;99(9):706-14

ACKNOWLEDGEMENTS

The authors would like to acknowledge Angela Prehn, PhD and Erin Eberle for their contributions to this chapter.

Chapter 29
Leukemia

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INTRODUCTION

Leukemias are malignancies that affect the blood-forming stem cells found in bone marrow. Myeloid leukemias are cancers that arise from myeloid stem cells, which normally mature into red blood cells, white blood cells, and platelet-producing cells. Lymphoblastic leukemias are cancers that arise from lymphocyte stem cells, which normally mature into white blood cells, also known as leukocytes. Leukemias are a heterogeneous group of cancers in terms of both biological and clinical features. Acute types refer to cancers arising in immature stem cells, while chronic types refer to cancers arising in mature stem cells.

Acute leukemias have been linked with several occupational and environmental exposures, and certain carcinogenic therapies. Radiation from the atom bomb (1) has been associated with an increased risk for acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML), but not for chronic leukemias. The risk from low-dose radiation seen in occupational settings (2) and from electromagnetic fields (3, 4) is controversial. Smoking has been linked to acute leukemia (5-7). As much as 20% of AML cases may be due to smoking (6). Certain chemotherapy agents are associated with an increased risk of secondary leukemias, in particular AML, following treatment for ALL (8-10) and Hodgkin lymphoma (11).

The average age-adjusted incidence for leukemia during the period 1975-2003 is 12.8 per 100,000 persons (12). The American Cancer Society (ACS) estimates that in 2006 there will be 35,070 leukemias diagnosed in the United States: 13,950 lymphoblastic leukemias, 16,430 myeloid leukemias, and 5,690 "other" leukemias (13). Leukemias considered together are one of the top 10 cancers in the United States.

ACS shows the most common leukemia to be acute myeloid leukemia (AML) (11,930 cases) followed by chronic lymphoblastic leukemia (CLL) (10,020 cases) (13). The incidence of the different types of leukemia, varies by age. When age-adjusted rates were used CLL had the highest incidence rate, 4.3 per 100,000 (12), compared to 3.4 per 100,000 for acute myeloid leukemia (AML), 1.8 per 100,000 for chronic myeloid leukemia (CML), and 1.3 per 100,000 for acute lymphoblastic leukemia (ALL) in 1975-2003. The 2000-2003 average incidence of all leukemias in persons over 65 years of age was 54.8 per 100,000 compared to 6.0 for persons less than 65 years. However, of all types of leukemia, acute lymphoblastic leukemia impacted children and young adults the most. Acute lymphoblastic leukemia was responsible for more deaths in this age group than any other cancer site. The median age at diagnosis for ALL was 13 years and 61.1% of incident cases for 2000-2003 occurred in children/young adults <20 years of age (12).

This chapter provides survival analysis for 42,678 histologically confirmed cases of primary leukemia diagnosed from 1988 through 2001 from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). This chapter highlights the influence of type of leukemia, race and ethnicity, age, and sex on survival outcomes.

MATERIALS AND METHODS

Exclusions

Analyses for all categories of leukemia, with the exception of acute lymphoblastic leukemia, included patients aged 20 years or over diagnosed with leukemia between 1988 and 2001 and reported to the SEER program. Analysis for acute lymphoblastic leukemia also included cases less than 20 years of age, since children and young adults represent nearly two-thirds of cases for this histological type and since their incidence and survival differ from those of adults. Patients were followed for vital status until 2002. Patients with unknown race, death certificate only cases, those without histologic confirmation of a leukemia diagnosis, or those alive with no survival time were excluded from analysis. Table 29.1 details the counts for these exclusions with 42,678 cases for analyses.

Table 29.1: Leukemia: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number selected/remaining	Number excluded	Reason for selection/exclusion
54,899	-	Diagnosed 1988-2001 (Los Angeles for 1992-2001 only)
47,631	7,268	Select first primary only
46,486	1,145	Exclude death certificate only or at autopsy
46,083	403	Exclude unknown race
46,009	74	Exclude alive with no survival time
44,667	1,342	Exclude children (Ages 0-19, except for Acute Lymphocytic Leukemia
44,667	0	Exclude in situ cancers
44,667	0	Exclude sarcomas
42,678	1,989	Exclude no or unknown microscopic confirmation

The survival analysis was based on relative survival rates calculated by the life-table method (14).The relative rate was used to estimate the effect of cancer on the survival of the cohort. Relative survival, defined as the ratio of observed survival to expected survival, adjusts for the expected mortality that the cohort would experience from other causes of death.

Histologic classification

Leukemia is a heterogeneous group of malignancies. Multiple classification schemes have been developed over the past several decades. The 1988-2000 data were collected using the International Classification of Diseases for Oncology, second edition (ICD-O-2) schema (12) and the 2001 data use the International Classification of Diseases for Oncology, third edition (ICD-O-3) (15). The French-American-British (FAB) classification of leukemias uses cytogenetic and molecular elements and has been included in the latest ICD edition, ICD-O-3, which was implemented in 2001 (15). We used the ICD-O-2 to ICD-O-3 conversion tables to create histologic groupings that are more reflective of the current World Health Organization classification of hematopoietic diseases.

Leukemia subtypes generally fall into one of the major cell type groups and will be analyzed as such: acute lymphoblastic leukemia (ALL), chronic lymphoblastic leukemia (CLL), "other" lymphoblastic leukemia, acute myeloid leukemia (AML), acute monocytic leukemia, chronic myeloid (or granulocytic) leukemia (CML), "other" myeloid/monocytic leukemia, "other" acute leukemia, and aleukemic, subleukemia, not otherwise specified (NOS) leukemia(12). Histologic categories, with their associated ICD-O-3 codes, are summarized in table 29.2.

RESULTS

Histology

For each type of leukemia, there was a slightly higher proportion of men than women, except for "other" lymphocytic leukemia where nearly three-fourths were men. The age distribution at diagnosis for adults with leukemia varies widely by type of leukemia. For example, the percentage 75 years of age and over ranged from 14.1% of adults with ALL to over 35% for CLL, "other" myeloid/

Table 29.2: Leukemia: Number of Cases by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology Group	Histology (ICD-O Code)	Cases
Lymphocytic Leukemia	Children and young adults 0-19 years Acute Lymphocytic Leukemia (9826,9835-9837)	4,418
	Adults 20+ years Acute Lymphocytic Leukemia (9826,9835-9837)	2,312
	Chronic Lymphocytic Leukemia (9823)	13,145
	Other Lymphocytic Leukemia (9820,9832-9834, 9940)	1,686
Myeloid and Monocytic Leukemia	Acute Myeloid Leukemia (9840,9861,9866,9867,9871-9874, 9895-9897, 9910, 9920)	11,459
	Acute Monocytic Leukemia (9891)	738
	Chronic Myeloid Leukemia (9863,9875, 9876, 9945,9946)	6,028
	Other Myeloid/Monocytic Leukemia (9860,9930)	507
Other Leukemia	Other Acute Leukemia (9801, 9805, 9931)	1,474
	Aleukemic, Subleukemic and NOS (9733,9742, 9800, 9827,9831, 9870, 9948, 9963-9964)	911
Total		42,678

Table 29.3: Number and Distribution of Cases by Sex, Race, Age at Diagnosis (20+, except for Acute Lymphocytic Leukemia) and Histology, 12 SEER Areas, 1988-2001

Characteristics	Histology									
	Acute Lymphocytic Leukemia				Chronic Lymphocytic Leukemia		Other Lymphocytic Leukemia		Acute Myeloid Leukemia	
	0-19 years		>20 years		All Ages 20+					
	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	4,418		2,312		13,145		1,686		11,459	
Sex										
Male	2,509	56.8	1,357	58.7	7,801	59.3	1,231	73.0	6,240	54.5
Female	1,909	43.2	955	41.3	5,344	40.7	455	27.0	5,219	45.5
Race*										
White	3,681	83.3	1,943	84.0	11,997	91.3	1,548	91.8	9,607	83.8
Black	298	6.7	150	6.5	851	6.5	72	4.3	814	7.1
Age at diagnosis (Years)										
20-39	N/A	N/A	887	38.4	143	1.1	139	8.2	1,536	13.4
40-59	N/A	N/A	665	28.8	2,754	21.0	645	38.3	2,675	23.3
60-74	N/A	N/A	433	18.7	5,611	42.7	523	31.0	3,869	33.8
75+	N/A	N/A	327	14.1	4,637	35.3	379	22.5	3,379	29.5

* Relative survival rate for "other" race not calculated

Table 29.3: (continued)

Characteristics	Histology									
	Acute Monocytic Leukemia		Chronic Myeloid Leukemia		Other Myeloid/ Monocytic Leukemia		Other Acute Leukemia		Aleukemic, Subleukemic and NOS	
	All Ages									
	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	738		6,028		507		1,474		911	
Sex										
Male	435	58.9	3,499	58.0	287	56.6	800	54.3	491	53.9
Female	303	41.1	2,529	42.0	223	44.0	674	45.7	420	46.1
Race*										
White	646	87.5	5,010	83.1	419	82.6	1,268	86.0	762	83.6
Black	42	5.7	553	9.2	50	9.9	102	6.9	96	10.5
Age at diagnosis (Years)										
20-39	99	13.4	995	16.5	39	7.7	115	7.8	59	6.5
40-59	191	25.9	1,588	26.3	81	16.0	197	13.4	123	13.5
60-74	231	31.3	1,774	29.4	182	35.9	472	32.0	310	34.0
75+	217	29.4	1,671	27.7	205	40.4	690	46.8	419	46.0

* Relative survival rate for "other" race not calculated

Table 29.4: Acute Lymphocytic Leukemia: Number of Cases and 1-, 3-, 5- and 10-Year Relative Survival Rates (%) by Sex, Age (20+), and Race, 12 SEER Areas, 1988-2001

Characteristics	Cases	Relative Survival			
		1-Yr	3-Yr	5-Yr	10-Yr
Total	6,730	79.8	66.7	62.2	60.1
Sex					
Male	3,866	79.9	65.7	60.9	58.6
Female	2,864	79.7	68.1	64.1	61.9
Age (Years)					
0-19	4,418	94.5	85.3	80.2	76.5
20-39	887	70.8	43.4	37.3	33.4
40-59	665	55.5	28.0	22.0	17.2
60-74	433	29.4	14.1	9.9	5.9
75+	327	16.1	5.8	4.0	3.3
Race					
White	5,624	80.1	67.3	63.2	60.9
Black	448	77.1	59.1	51.7	49.3
Race/Sex					
White males	3,235	80.2	66.3	61.8	59.6
White females	2,389	79.8	68.7	65.1	62.6
Black males	245	78.5	59.6	52.0	47.8
Black females	203	75.3	58.6	51.2	50.1

Table 29.5: Chronic Lymphocytic Leukemia: Number of Cases and 1-, 3-, 5- and 10-Year Relative Survival Rates (%) by Sex, Age (20+) and Race, 12 SEER Areas, 1988-2001

Characteristics	Cases	Relative Survival Rate (%)			
		1-Yr	3-Yr	5-Yr	10-Yr
Total	13,145	92.3	86.7	74.9	54.2
Sex					
Male	7,801	92.3	83.7	75.5	52.5
Female	5,344	91.4	83.4	75.4	56.5
Age (Years)					
20-39	143	94.6	86.7	83.4	64.8
40-59	2,754	97.0	90.0	82.6	60.8
60-74	5,611	95.0	86.6	78.0	55.4
75+	4,637	85.7	74.4	62.0	40.0
Race					
White	11,997	92.8	84.7	76.3	56.1
Black	851	86.2	71.4	58.0	30.0
Race/Sex					
White males	7,120	93.4	85.1	76.3	54.7
White females	4,877	92.0	84.1	76.3	58.0
Black males	490	87.5	68.9	53.1	25.7
Black females	361	84.2	74.9	64.5	35.1

Table 29.6: Acute Myeloid Leukemia: Number of Cases and 1-, 3-, 5- and 10- Year Relative Survival Rates (%) by Sex, Age (20+) and Race, 12 SEER Areas, 1988-2001

Characteristics	Cases	Relative Survival Rate (%)			
		1-Yr	3-Yr	5-Yr	10-Yr
Total	11,459	34.4	18.9	16.5	16.1
Sex					
Male	6,240	33.7	17.7	15.1	14.8
Female	5,219	35.3	20.2	18.0	17.2
Age (Years)					
20-39	1,536	67.3	46.2	42.1	38.3
40-59	2,675	50.6	29.6	25.1	21.7
60-74	3,869	29.0	11.0	7.3	5.3
75+	3,379	11.0	2.9	1.9	0.8
Race					
White	9,607	34.1	18.7	16.3	15.8
Black	814	34.7	17.0	14.5	13.1
Race/Sex					
White males	5,276	33.6	17.3	15.0	14.6
White females	4,331	34.7	20.2	17.8	17.1
Black males	395	34.6	18.3	14.6	11.1
Black females	419	34.8	15.7	14.2	14.2

Table 29.7: Acute Monocytic Leukemia: Number of Cases and 1-, 3-, 5-and 10-Year Relative Survival Rates (%) by Sex, Age (20+) and Race, 12 SEER Areas, 1988-2001

Characteristics	Cases	Relative Survival Rate (%)			
		1-Yr	3-Yr	5-Yr	10-Yr
Sex					
Male	435	30.8	17.0	15.1	13.6
Female	303	26.2	14.7	13.2	12.1
Age (Years)					
20-39	99	43.3	30.9	24.4	24.4
40-59	191	45.3	24.9	22.2	21.4
60-74	231	26.2	11.7	9.0	3.3
75+	217	9.1	2.9	2.9	!
Race					
White	646	29.5	16.4	15.2	13.7
Black	42	24.6	19.8	11.1	11.1
Race/Sex					
White males	386	31.9	17.4	16.0	14.0
White females	260	26.1	14.9	13.7	12.7
Black males	19	~	~	~	~
Black females	23	~	~	~	~

~ Statistic not displayed due to less than 25 cases

Figure 29.1: Leukemia: Relative Survival Rates (%) by Histology, Ages 20+ plus Acute Lymphoblastic Leukemia for Ages 0-19, 12 SEER Areas, 1988-2001

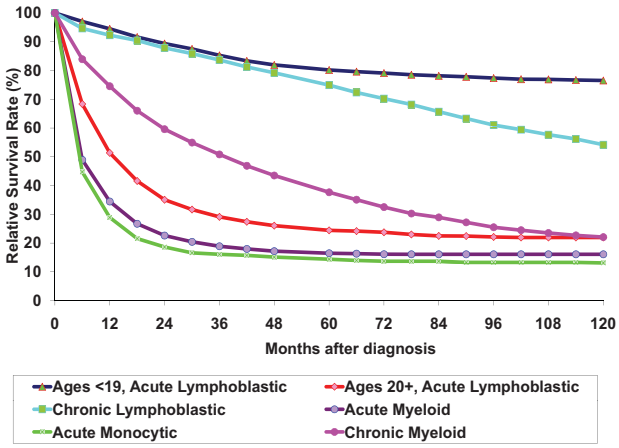


Figure 29.2:"Other" Leukemia: Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

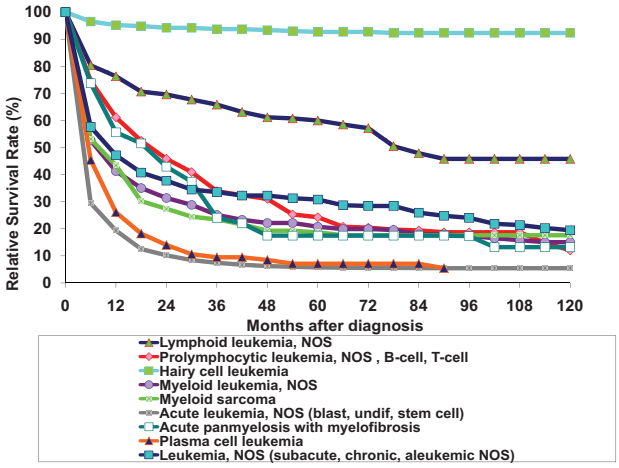


Figure 29.3: Acute Lymphocytic Leukemia: Relative Survival Rates (%) by Race and Sex, Ages 0-19, 12 SEER Areas, 1988-2001

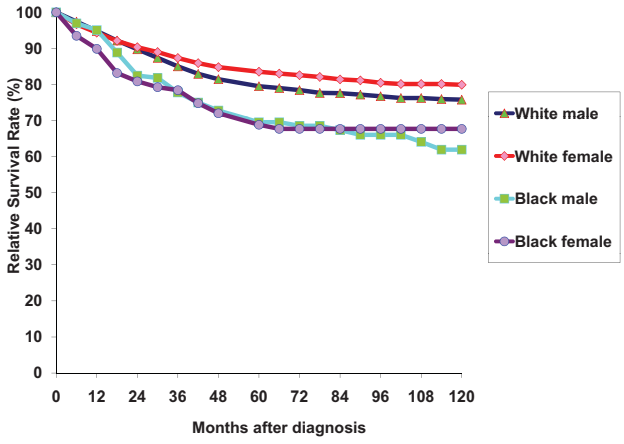
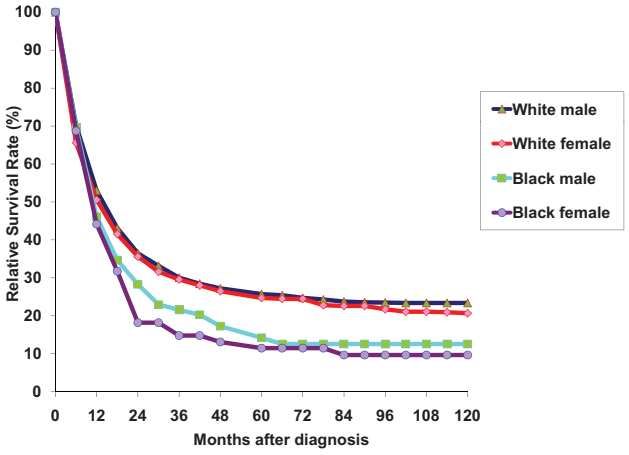


Figure 29.4: Acute Lymphocytic Leukemia: Relative Survival Rates (%) by Race and Sex, Ages 20+12 SEER Areas, 1988-2001



monocytic, "other" acute, and aleukemic leukemia (Table 29.3). One-, three-, five-, and ten-year relative survival rates, are presented in tables by type of leukemia: ALL (Table 29.4), CLL (Table 29.5), AML (Table 29.6), acute monocytic (Table 29.7), CML (Table 29.8) and other leukemias including "other" lymphocytic, "other" myeloid, "other" acute, and aleukemic, subleukemic, and not otherwise specified (NOS) (Table 29.9).

Lymphoblastic leukemias, notably CLL, have the most favorable survival outcomes during the first twelve months following diagnosis. The 1-year relative survival rates for CLL and ALL were 92% and 80%, respectively (Tables 29.4, 29.5, 29.9; Figure 29.1). Myeloid and monocytic leukemias have the least favorable survival rates during the first year following diagnosis, with a 1-year relative survival rate of 34% for AML, 30% for acute monocytic, and 76% for CML (Tables 29.6-29.7; Figure 29.1).

Five years after diagnosis, patients with CLL and ALL still fared better than those diagnosed with myeloid and monocytic types of leukemia. The 5-year relative survival rates for CLL and ALL were 75% and 62% respectively, compared to 38% and 17% for CML and AML (Tables 29.4-29.8). Figure 29.1 shows the 10-year relative survival curves for distinct histological types of leukemia.

"Other" lymphoblastic leukemia had the most favorable among "other" types of leukemia, for 1- and 5- years after diagnosis (Table 29.9). The 1-year survival rate for "other" lymphoblastic leukemia is 88%, while that of "other" myeloid is 42% and that of aleukemic, subleukemic, and

Table 29.8: Chronic Myeloid Leukemia: Number of Cases and 1-, 3-, 5-and 10-Year Relative Survival Rates (%) by Sex, Age (20+) and Race, 12 SEER Areas, 1988-2001

Characersitics	Cases	Relative Survival Rate (%)			
		1-Year	3-Year	5-Year	10-Year
Total	6,028	75.5	50.8	37.7	22.1
Sex					
Male	3,499	75.5	50.4	37.4	23.0
Female	2,529	74.6	51.4	38.1	20.8
Age (Years)					
20-39	995	89.8	65.3	55.0	41.1
40-59	1,588	86.3	63.1	48.1	29.6
60-74	1,774	71.9	46.7	30.5	8.6
75+	1,671	55.5	30.0	16.9	2.9
Race					
White	5,010	74.2	50.6	37.6	21.7
Black	553	76.6	49.8	36.6	20.9
Race/Sex					
White males	2,901	74.1	50.2	37.4	22.9
White females	2,109	74.3	51.2	38.0	20.1
Black males	320	77.0	49.6	34.1	20.0
Black females	233	76.1	50.0	39.8	21.9

Table 29.9: "Other" leukemias: Number of Cases and 1-, 3-, 5- and 10-Year Relative Survival Rate (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001

Histology	Cases	Relative Survival Rate (%)			
		1-Year	3-Year	5-Year	10-Year
"Other" lymphocytic	1,686	87.7	81.8	79.5	77.5
Lymphoid leukemia, NOS	238	76.3	65.8	60.0	45.8
Prolymphocytic, NOS [3]	249	61.5	33.9	24.3	12.0
Hairy cell leukemia	1,199	95.2	93.7	92.7	92.3
Other myeloid	507	41.7	24.8	20.3	15.8
Myeloid leukemia, NOS *	400	41.3	25.1	20.8	15.1
Myeloid sarcoma	107	43.4	23.5	18.7	17.6
Other acute	1,474	21.1	8.3	6.4	6.2
Acute leukemia, NOS[1]	1,402	19.4	10.2	5.8	5.5
Acute panmyelosis with myelofibrosis	65	55.6	24.0	17.5	13.2
Aleukemic, Subleukemic, and NOS*	911	45.1	30.0	27.1	17.3
Leukemia, NOS[4]	712	47.1	33.6	30.8	19.5
Plasma cell leukemia	103	26.1	9.5	7.1	!

*NOS, not otherwise specified
[1] Blast cell, undifferentiated, Stem cell
[2] Subacute NOS, Chronic NOS, Aleukemic NOS
[3] Includes Prolymphocytic B-cell, Prolymphocytic T-cell
[4] Subacute NOS, Chronic NOS, Aleukemic NOS
! Not enough intervals to produce rate

NOS is 45%. "Other" acute leukemia fares the worst 1-year after diagnosis, with a 1-year survival rate of 21%. These differences in survival widen 5 and 10 years after diagnosis.

In terms of specific histologies in "other" lymphoblastic leukemia, hairy cell leukemia had the most optimistic survival rates, 1-year (95%) and 5-years after diagnosis (93%), compared to lymphoid leukemia, NOS, and prolymphocytic leukemia, NOS (Table 29.9). Figure 29.2 shows the relative survival of specific histologies for "other" lymphoblastic, "other" myeloid leukemia, "other" acute leukemia, and aleukemic, subacute and NOS leukemia.

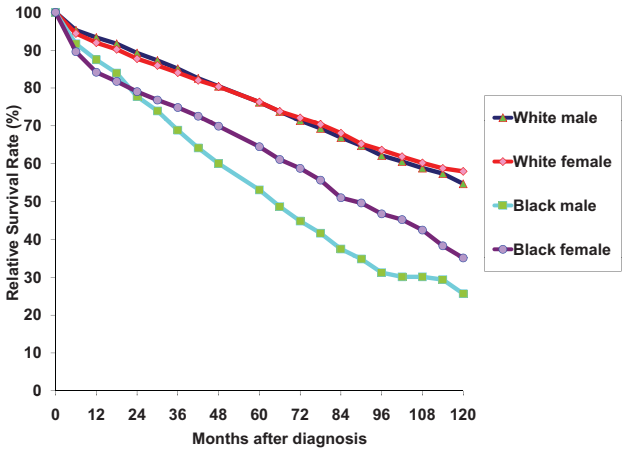
Age at diagnosis

Patient age at diagnosis strongly influences survival patterns after leukemia diagnosis. Increasing age at diagnosis had a general linear association with poorer survival over 10 years after diagnosis for all categories of leukemia. These differences in relative survival become more apparent with increasing time since diagnosis.

Lymphoblastic leukemias

Approximately two-thirds of persons diagnosed with acute lymphoblastic leukemia were children and young adults. The survival among those less than 20 years of age is distinctly higher than the survival in any other age group (Table 29.4). As age of diagnosis increases, survival de-

Figure 29.5: Chronic Lymphocytic Leukemia: Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001



clines. The 1-year relative survival rate in ALL patients aged 0-19 years is 95%, while the same 1-year survival rate in 20-39 year olds is 71%. In the two oldest age groups, 60-74 and 75+ years of age, the 1-year survival rate is 29% and 16%, respectively. These large differences by age remain pronounced over the three, five, and ten year period following diagnosis.

Chronic lymphoblastic leukemia had the best overall survival for all age groups. At 12 months after diagnosis, the difference between the relative survivals among age groups is not pronounced until 10 years after diagnosis (Table 29.5). The 1-year survival rates for CLL is slightly more favorable for patients diagnosed at 40-59 years (97%) compared to those diagnosed at 20-39 years (95%), 60-74 (95%) and 75+ years of age (86%). However, as with ALL, the long-term survival patterns favor those diagnosed at a younger age. The 5- and 10-year relative survival rates were highest among patients diagnosed at 20-39 years (5-year, 83%; 10-year, 65%) compared to patients diagnosed at 75+ years (5-year, 62%; 10-year, 40%).

Myeloid and monocytic leukemias

The 1-year survival rate for acute myeloid leukemia was most favorable for those in the 20-39 years age group (67%), compared to those in the 75+ age group (11%). This discrepancy persists over 5- and 10-year period following diagnosis (Table 29.6). Similarly for acute monocytic, the survival rates vary greatly between the youngest age group and the oldest; the 1-year relative survival rate was 43% for 20-39 and only 9% for those 75 years and older. For acute monocytic leukemia the survival rates were similar for ages 20-39 and 40-59 (Table 29.7).

The survival curves for chronic myeloid leukemia were very similar for 20-39 and 40-59 age groups for years 1 through 5, after which they slightly diverge, with the 40-59 age group faring slightly worse than their younger counterparts. Overall, the lowest survival rate was found in the age group of 75+, and becomes more pronounced over the long-term. The 1-year survival rate for persons in age groups 20-39 and 40-59 years was 90% and 86% compared to 56% for the 75+ age group. The 5-year relative survival rate for persons in age groups 20-39 and 40-59 years was 55% and 48% compared to 17% for the 75+ age group (Table 29.8).

Histology, gender, and race

Lymphoblastic leukemias

Overall, whites had more favorable 5-year survival rates for childhood lymphoblastic leukemias (Figure 29.3) than black children. Adult lymphoblastic leukemias (5-year ALL, 63%; CLL, 76%) had more favorable 5-year survival rates than blacks (5-year ALL, 52%; CLL, 58%) (Figures 29.4 and 29.5, respectively). The gender difference slightly favored females diagnosed with ALL (5-year survival rate, 64%; males 5-year survival 61%) was not seen among persons diagnosed with CLL (male 5-year survival rate 76%; female 5-year survival rate 75%). Within racial categories, the female survival advantage in survival became more apparent, but was limited to whites (Tables 29.4, 29.5).

Myeloid and monocytic leukemias

Whites diagnosed with myeloid and monocytic leukemias had a slight 5-year survival advantage (5-year survival rates: AML,16%; acute monocytic, 15%, CML, 38%) compared to blacks (5-year AML, 15%; acute monocytic, 11%; CML, 37%). Females also showed a slight 5-year survival advantage compared to males (Tables 29.6, 28.7).

DISCUSSION

These population-based data were based on 42,678 adult leukemia cases diagnosed between 1988 and 2001. While the SEER data provide a large representative sample to examine numerous demographic predictors of survival after diagnosis with leukemia, data were not available on treatment differences and comorbidity, two additional factors that impact survival and could explain some of the patterns we observed. These analyses provide evidence of the considerable variation in survival patterns for leukemia patients, reflecting the heterogeneity of this disease entity.

Leukemia had a combined incidence of 12.2 per 100,000 per year for the period 2000-2003 (12). Relative survival estimates show distinct differences between histologic groups. Survival outcome varies widely between groups, with the lymphoblastic leukemias having the highest 5-year relative survival rates, in particular childhood and young adult ALL (80%). There were large differences in survival by age-group. The older the patient's age was at diagnosis, the lower the relative survival curve for all histology groups. Older patients also had a greater incidence of the cytogenetic abnormalities associated with poor prognosis, namely the Philadelphia chromosome found in cases of ALL (16). Previous reports on AML

indicate that age is inversely associated with cancer remission (17, 18).

The incidence in men is 15.9 per 100,000, while that of women is lower, at 9.4 per 100,000. Overall, there is little gender difference in survival. By race, whites had a higher incidence (12.7 per 100,000) than blacks (10.1 per 100,000). Survival varies by race and gender, but these differences were most pronounced for lymphoblastic leukemias, especially at the 5- and 10-year period after diagnosis. In general, black males and black females tended to fare worse than white males and females. As with other cancer sites, some of these differences in survival outcomes may be due to issues related to access to care and socioeconomic status.

REFERENCES

1. Ron, E., et al. Cancer incidence in atomic bomb survivors. Part IV: Comparison of cancer incidence and mortality. Radiat Res, 1994. 137(2 Suppl): p. S98-112.
2. Sandler, D.P. Recent studies in leukemia epidemiology. Curr Opin Oncol, 1995. 7(1): p. 12-8.
3. Feychting, M. and A. Ahlbom. Magnetic fields and cancer in children residing near Swedish high-voltage power lines. Am J Epidemiol, 1993. 138(7): p. 467-81.
4. Taubes, G. Another blow weakens EMF-cancer link. Science, 1995. 269(5232): p. 1816-7.
5. Sandler, D.P., et al. Cigarette smoking and risk of acute leukemia: associations with morphology and cytogenetic abnormalities in bone marrow. J Natl Cancer Inst, 1993. 85(24): p. 1994-2003.
6. Siegel, M. Smoking and leukemia: evaluation of a causal hypothesis. Am J Epidemiol, 1993. 138(1): p. 1-9.
7. Kabat, G.C., A. Augustine, and J.R. Hebert, Smoking and adult leukemia: a case-control study. J Clin Epidemiol, 1988. 41(9): p. 907-14.
8. Pui, C.H., et al., Secondary acute myeloid leukemia in children treated for acute lymphoid leukemia. N Engl J Med, 1989. 321(3): p. 136-42.
9. Pui, C.H., et al., Characterization of childhood acute leukemia with multiple myeloid and lymphoid markers at diagnosis and at relapse. Blood, 1991. 78(5): p. 1327-37.
10. Tucker, A., Cancers of the haematopoietic and lymphatic systems. Br J Hosp Med, 1977. 18(1): p. 95-6.
11. van Leeuwen, F.E., et al., Second cancer risk following Hodgkin's disease: a 20-year follow-up study. J Clin Oncol, 1994. 12(2): p. 312-25.
12. Ries, L.A.G., et al. (ed), SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site,2006.
13. (ACS), A.C.S., Cancer Facts & Figures – 2006. 2006, Atlanta, Georgia.
14. Kaplan, E.L. and P. Meier, Nonparametric estimation from incomlpete observations. J Am Stat Assoc, 1958. 53: p. 457-481.
15. Fritz, A., et al., International Classification of Diseases for Oncology, Third Edition. 2000, Geneva: World Health Organization.
16. Cancer principles & practice of oncology, fourth edition, ed. T.J. DeVita, S. Hellman, and S.A. Rosenbreg. 1993, Philadelphia: J.B. Lippencott.
17. Yates, J., et al., Cytosine arabinoside with daunorubicin or adriamycin for therapy of acute myelocytic leukemia: a CALGB study. Blood, 1982. 60(2): p. 454-62.
18. Rai, K.R., et al., Treatment of acute myelocytic leukemia: a study by cancer and leukemia group B. Blood, 1981. 58(6): p. 1203-12.

Chapter 30
Cancers of Rare Sites

John L. Young, Jr., Kevin C. Ward, and Lynn A. Gloeckler Ries

INTRODUCTION

There are some anatomic sites in which cancer rarely occurs, for example, the eye, the ureter, the pituitary gland, etc. Most of these rare sites have been excluded from other chapters in this monograph due to the small number of cases involved. This chapter provides a limited analysis of survival for these rare sites and for cancers which could not be assigned to a specific anatomic location at the time of diagnosis due to the advanced stage of the tumor. Cases were obtained from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI).

MATERIALS AND METHODS

The NCI contracts with medically-oriented, nonprofit institutions located in specific geographic areas to obtain data on all cancers diagnosed in residents of the SEER geographic areas. SEER collects data on all invasive and in situ cancers except basal cell and squamous cell carcinomas of the skin (of non-genital anatomic sites) and in situ carcinomas of the uterine cervix. SEER actively follows all previously diagnosed patients on an annual basis to obtain vital status allowing the calculation of observed and relative survival rates.

This analysis is based on data from 12 SEER geographic areas which collectively cover about 14% of the total US population. The areas are the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Michigan; Atlanta, Georgia; San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; and 10 counties in rural Georgia. Los Angeles contributed data for diagnosis years 1992 to 2001, all other areas for 1988-2001.

With the exception of male breast cancers, in situ diagnoses have been excluded. Cases diagnosed in children and adolescents aged 0-19 have also been excluded. Some patients have more than one diagnosis of cancer, but only the first diagnosis of cancer has been included. Death certificate only cases, autopsy only cases, and alive cases with no survival time have been excluded. All sarcomas arising in these rare sites have been excluded since they are included in the chapter on sarcomas included elsewhere in this monograph (1). Finally, with the exception of cancers where the primary site could not be determined, cases with no microscopic confirmation have been included.

Survival analysis is based on relative survival rates calculated by the life-table (actuarial) method. Relative survival, defined as observed survival in the cohort divided by expected survival in the cohort, adjusts for the expected mortality that the cohort would experience from other causes of death. Expected survival is based on decennial life tables for the United States in 1990.

In many of the chapters in this monograph, data on stage are presented using the Stage I-IV definitions of the American Joint Committee on Cancer (AJCC) 3rd or 5th Editions. However, for many of the rare tumor sites there are no appropriate AJCC staging definitions. Therefore, the staging definitions utilized in this chapter are those of the 1977 Summary Staging Guide (2). For simplicity, all categories of regional disease have been added together into a single group.

RESULTS

Table 30.1 shows the anatomic sites included in this analysis along with the numbers of cases diagnosed during 1988-2001 classified by sex, by race, and by stage of diagnosis. The sites have been arranged by body systems and show the specific rare cancer sites under the appropriate body system. Relative survival rates at 1, 3, 5, and 10 years are shown in Table 30.2 for both sexes and for males and females separately where appropriate. Table 30.3 presents rates for whites and for blacks where the number of cases permitted meaningful analyses. Finally, Table 30.4 presents relative survival rates by SEER Summary Stage.

Table 30.1: Cancers of rare sites: Number and Distribution of Cases by Primary Site, Sex, Race and SEER Summary Stage 1977 (2), Ages 20+, 12 SEER Areas, 1988-2001

Primary Site	Total	Sex		Race		Stage (%)			
		Male	Female	White	Black	Loc	Reg	Dis	Uns
Respiratory and Intrathoracic Organs									
Nose, Nasal Cavity and Middle Ear	2,299	1,329	970	1,842	223	25.8	51.3	14.1	8.7
Nasal Cavity	1,009	571	438	868	59	46.2	30.7	12.0	11.1
Middle Ear	82	38	44	67	8	17.1	50.0	20.7	12.2
Trachea, Mediastinum and Other Respiratory	573	427	146	474	50	20.8	33.0	24.6	21.6
Trachea	211	112	99	173	20	24.2	42.2	16.1	17.5
Squamous Cell	105	65	40	89	12	21.0	41.9	20.0	17.1
Mediastinum	315	282	33	258	27	21.6	30.5	30.8	17.1
Mediastinum - Germ	250	236	14	205	20	24.4	28.4	28.8	18.4
Other Respiratory	47	33	14	43	<5	0.0	8.5	21.3	70.2
Pleura*	49	28	21	40	<5	16.3	14.3	24.5	44.9
Skin^	2,793	1,517	1,276	2,539	105	73.4	7.4	5.9	13.4
Merkel Cell	1,076	617	459	1,021	9	66.5	11.1	8.2	14.2
Skin Appendage Adenocarcinoma	383	199	184	356	13	77.0	7.6	0.8	14.6
Sweat Gland Adenocarcinoma	208	125	83	185	13	77.4	6.3	2.9	13.5
Sebaceous Adenocarcinoma	458	229	229	413	13	79.9	1.7	6.8	11.6
Peritoneum and Retroperitoneum*	1,461	209	1,252	1,300	80	7.3	15.1	70.9	6.6
Papillary Serous Cystadenocarcinoma	636	<5	635	579	24	1.1	11.3	85.7	1.9
Male Breast (including in situ)	1,905	1,905	0	1,578	232	43.6	37.9	5.2	2.5
In situ	205	205	0	177	20	0.0	0.0	0.0	0.0
Invasive	1,700	1,700	0	1,401	212	48.8	42.5	5.9	2.8
Female Genital									
Ligaments and Adnexa	49	0	49	37	8	44.9	10.2	40.8	4.1
Overlapping	60	0	60	49	7	35.0	21.7	31.7	11.7
Other and Not Otherwise Specified	192	0	192	160	20	0.5	12.0	50.0	37.5
Male Genital									
Penis	1,132	1,132	0	976	94	61.2	29.9	4.3	4.6
Penis - Squamous Cell Carcinoma	996	996	0	858	87	60.5	31.1	4.3	4.0
Scrotum	233	233	0	149	22	69.5	19.3	3.0	8.2
Scrotum - Squamous Cell Carcinoma	87	87	0	65	18	67.8	21.8	4.6	5.7
Scrotum - Paget Disease	74	74	0	34	0	70.3	21.6	1.4	6.8
Other and Not Otherwise Specified	27	27	0	24	0	48.1	18.5	14.8	18.5

* Excludes mesotheliomas and sarcomas
^ Excludes Basal, Squamous, Kaposi sarcoma & Melanoma

Respiratory and Intrathoracic Organs

Cancer of the nose and nasal cavities had the best survival among this group of rare sites. Five-year relative survival rate was 54% overall and was similar for males and females but was better for whites vs. blacks. Cancers of the nasal cavity tended to be diagnosed at an earlier stage which doubtless contributed to a better overall 5-year relative survival rate of 70%. Cancers of the middle ear were much rarer (82 cases during the time period) and relative survival rate was much poorer, 34% at five years (Table 30.2). Some additional tables for nose and nasal cavities are found in the chapter on head and neck cancer (3).

Relative survival rates for cancers of the trachea and pleura were poor (35 % and 28%, respectively, at five years) but were better than that for lung cancer (16%) (4). Not surprisingly, most cases were diagnosed with regional or distant disease. For cancers of the mediastinum, the five-year relative survival rate was 48% and was higher among males (50%) than among females (30%). For all respiratory sites, survival was markedly lower for patients diagnosed

Table 30.1 (continued): Cancers of Rare Sites: Number and Distribution of Cases by Primary Site, Sex, Race and SEER Summary Stage 1977 (2), Ages 20+, 12 SEER Areas, 1988-2001

Primary Site	Total	Sex		Race		Stage (%)			
		Male	Female	White	Black	Loc	Reg	Dis	Uns
Urinary System									
Ureter	1,333	808	525	1,158	42	52.6	28.5	10.4	8.6
Ureter - Papillary Transitional Cell	1,251	770	481	1,086	37	54.1	28.5	9.4	7.9
Other Urinary	850	539	311	626	174	27.4	24.8	14.0	33.8
Other Urinary - Papillary Transitional Cell	445	339	106	355	63	28.8	18.9	12.1	40.2
Eye and Orbit	1,904	1,069	835	1,824	33	77.6	7.2	3.0	12.2
Eye and Orbit - Squamous Cell Carcinoma	305	240	65	278	7	74.1	9.5	3.3	13.1
Eye and Orbit - Melanoma	1,504	779	725	1,469	17	80.3	5.3	2.3	12.1
Other Endocrine	1,727	921	806	1,301	184	29.6	36.5	24.8	9.1
Thymus	826	465	361	558	101	20.0	50.6	20.2	9.2
Thymus - Thymoma	678	367	311	441	89	18.9	52.1	19.3	9.7
Adrenal Gland	598	283	315	513	47	37.3	16.9	37.3	8.5
Adrenal Gland - Adrenal Cortical	387	170	217	340	21	43.4	20.2	31.5	4.9
Adrenal Gland - Pheochromocytoma	66	34	32	46	15	40.9	12.1	25.8	21.2
Parathyroid Gland	115	56	59	89	16	51.3	40.0	4.3	4.3
Pituitary Gland	52	25	27	37	8	26.9	40.4	9.6	23.1
Pineal Gland	95	68	27	71	8	48.4	27.4	14.7	9.5
Mesothelioma	3,562	2,795	767	3,239	182	10.9	18.5	58.5	12.1
Mesothelioma - Pleura and Lung	3,148	2,548	600	2,860	160	11.0	19.0	58.4	11.5
Mesothelioma - Peritoneum and Retroperitoneum	354	212	142	328	15	6.5	14.1	65.3	14.1
Reticuloendothelial System Tumors	1,297	779	779	1,174	51	0.0	0.0	99.7	0.3
Waldenstrom's Macroglobulinemia	1,161	709	452	1,050	46	0.0	0.0	100.0	0.0
Myeloma	18,446	9,879	8,567	14,282	3,024	4.5	0.0	95.5	0.0
Solitary Myeloma	526	328	198	433	54	87.3	0.0	12.7	0.0
Multiple Myeloma	17,217	9,103	8,114	13,281	2,870	0.0	0.0	100.0	0.0
Unknown or Ill-defined Primary Site	39,140	18,587	20,553	32,097	4,310	0.0	0.0	0.1	99.9
Microscopically confirmed	30,382	14,917	15,465	24,852	3,334	0.0	0.0	0.1	99.9
Carcinomas	10,700	6,090	4,610	8,891	1,096	0.0	0.0	0.0	100.0
Adenocarcinomas	16,654	7,286	9,368	13,494	1,875	0.0	0.0	0.0	100.0
Other	3,028	1,541	1,487	2,467	363	0.0	0.0	1.3	98.7
Non-microscopically confirmed	8,758	3,670	5,088	7,245	976	0.0	0.0	0.0	100.0

* Excludes mesotheliomas and sarcomas
^ Excludes Basal, Squamous, Kaposi sarcoma & Melanoma
Loc, Localized; Reg, Regional; Dis, Distant; Uns, Unstaged

with distant disease, especially for patients with tracheal cancer (3% at 5 years) (Table 30.4).

Skin

Basal and squamous cell skin cancers are not reported to the SEER program except those of the genital sites. Melanomas of the skin and Kaposi sarcoma of the skin and of visceral organs are discussed elsewhere in this monograph. Still there are other types of cancers which occur, albeit rarely, on the skin. The four major types are Merkel cell, skin appendage adenocarcinomas, sweat gland adenocarcinomas, and sebaceous adenocarcinomas. Among this group of cancers, patients diagnosed with Merkel cell survived more poorly than those with other histologic types; there were more patients with Merkel cell diagnosed at regional or distant stages when compared to the other three groups. The overall 5-year relative rates for the various subtypes were Merkel cell, 63% ; skin appendage 98%; sweat gland, 95%; and sebaceous, 95% (Table 30.2). In general, females

Table 30.2: Cancers of Rare Sites: 1-, 3- ,5- and 10-Year (Yr) Relative Survival Rates (%) by Primary Site and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Primary Site	Relative Survival Rate (%)											
	Total				Male				Female			
	1-Yr	3-Yr	5-Yr	10-Yr	1-Yr	3-Yr	5-Yr	10-Yr	1-Yr	3-Yr	5-Yr	10-Yr
Respiratory and Intrathoracic Organs												
Nose, Nasal Cavity and Middle Ear	79.8	61.9	54.0	46.4	80.8	62.4	54.4	47.2	78.3	61.1	53.6	44.9
Nasal Cavity	89.9	77.6	70.1	61.7	89.9	77.6	69.4	62.8	89.9	77.5	70.8	59.7
Middle Ear	68.7	38.5	33.8	27.7	65.7	36.7	36.7	29.6	71.3	39.9	30.4	27.0
Trachea, Mediastinum and Other Respiratory	60.6	45.0	42.3	37.0	61.2	46.1	43.9	38.9	59.0	41.8	37.1	30.6
Trachea	57.7	40.2	34.6	25.5	55.5	36.7	30.5	20.5	60.2	43.8	38.7	28.0
Squamous Cell	47.4	27.6	20.4	13.2	46.6	28.4	21.2	16.2	48.6	26.4	19.1	7.5
Mediastinum	65.5	49.9	48.2	44.0	66.7	51.8	50.3	45.6	55.2	32.9	30.1	25.1
Mediastinum - Germ	69.5	56.8	55.6	51.5	69.4	57.7	56.3	52.0	~	~	~	~
Other Respiratory	39.8	31.0	31.0	15.2	31.6	24.1	24.1	8.3	~	~	~	~
Pleura *	40.4	29.9	28.2	21.2	30.0	19.6	19.6	0.0	~	~	~	~
Skin ^	94.2	85.9	84.0	81.2	93.3	83.5	81.1	79.3	95.2	88.6	87.1	81.9
Merkel Cell	87.4	68.6	62.8	57.5	87.2	65.1	58.6	55.2	87.6	73.2	67.8	60.0
Skin Appendage Adenocarcinoma	99.8	99.1	97.5	97.2	99.8	99.8	97.8	97.8	99.0	96.4	95.7	90.5
Sweat Gland Adenocarcinoma	97.8	94.9	94.5	83.6	95.6	91.8	91.6	78.2	100.0	99.1	97.3	88.9
Sebaceous Adenocarcinoma	98.2	94.6	94.6	87.3	95.2	90.5	90.5	82.8	100.0	98.7	98.7	91.2
Peritoneum and Retroperitoneum *	78.1	49.0	34.3	28.5	78.8	60.6	54.5	51.4	77.9	46.9	30.4	22.8
Papillary Serous Cystadenocarcinoma	84.8	49.5	26.9	17.2	~	~	~	~	84.8	49.6	26.9	17.3
Male Breast (including in situ)	97.3	93.0	85.6	74.2	97.3	93.0	85.6	74.2	N/A	N/A	N/A	N/A
In situ	99.1	99.1	99.1	96.9	99.1	99.1	99.1	96.9	N/A	N/A	N/A	N/A
Invasive	97.0	92.0	83.6	71.3	97.0	92.0	83.6	71.3	N/A	N/A	N/A	N/A
Female Genital												
Ligaments and Adnexa	87.1	72.2	67.1	53.2	N/A	N/A	N/A	N/A	87.1	72.2	67.1	53.2
Overlapping	70.7	55.2	48.8	33.0	N/A	N/A	N/A	N/A	70.7	55.2	48.8	33.0
Other and Not Otherwise Specified	50.4	28.8	25.6	19.1	N/A	N/A	N/A	N/A	50.4	28.8	25.6	19.1
Male Genital												
Penis	88.8	79.1	73.5	64.0	88.8	79.1	73.5	64.0	N/A	N/A	N/A	N/A
Penis - Squamous Cell Carcinoma	87.4	76.7	71.7	62.6	87.4	76.7	71.7	62.6	N/A	N/A	N/A	N/A
Scrotum	94.7	82.0	77.5	62.5	94.7	82.0	77.5	62.5	N/A	N/A	N/A	N/A
Scrotum - Squamous Cell Carcinoma	85.4	63.4	58.6	38.5	85.4	63.4	58.6	38.5	N/A	N/A	N/A	N/A
Scrotum - Paget Disease	100.0	93.0	89.0	82.3	100.0	93.0	89.0	82.3	N/A	N/A	N/A	N/A
Other and Not Otherwise Specified	73.0	62.1	51.8	34.1	73.0	62.1	51.8	34.1	N/A	N/A	N/A	N/A

* Excludes mesotheliomas and sarcomas
^ Excludes Basal, Squamous, Kaposi sarcoma & Melanoma
~ Statistic not displayed due to less than 25 cases.

had better survival rates at both 5 and 10 years. Overall, blacks had higher relative survival rates than whites at 1, 3, and 5 years, but whites had higher rates after 10 years. With the exception of patients with Merkel cell, 5-year relative survival was 97% or higher for all other types diagnosed while localized to the skin.

Peritoneum and Retroperitoneum

Over 70% of cancers occurring in the retroperitoneum were already distant at the time of diagnosis accounting for overall poor relative survival rate, 34% at five-years. Over forty percent of these tumors were papillary serous cystadenocarcinomas which are probably extra-ovarian tumors. Survival from these cancers was even poorer, 27% at five-years. For peritoneum and retroperitoneum

Table 30.2 (continued): Cancers of Rare Sites: 1-, 3- ,5- and 10-Year (Yr) Relative Survival Rates (%) by Primary Site and Sex, Ages 20+, 12 SEER Areas, 1988-2001

	Relative Survival Rate (%)											
	Total				Male				Female			
Primary Site	1-Yr	3-Yr	5-Yr	10-Yr	1-Yr	3-Yr	5-Yr	10-Yr	1-Yr	3-Yr	5-Yr	10-Yr
Urinary System												
Ureter	82.3	63.4	55.9	49.6	82.4	63.4	55.6	50.2	82.1	63.3	56.0	46.7
Ureter - Papillary Transitional Cell	83.5	64.6	57.8	51.4	83.4	64.7	57.7	52.1	83.7	64.6	57.5	48.1
Other Urinary	80.5	67.0	60.5	54.2	82.7	71.4	67.6	60.8	76.8	59.5	48.5	42.2
Other Urinary - Papillary Transitional Cell	81.4	68.4	63.8	60.0	83.6	71.9	68.2	62.1	74.2	57.3	49.5	46.3
Eye and Orbit	97.4	85.2	75.4	63.1	97.4	85.9	77.1	65.8	97.3	84.3	73.0	59.8
Eye and Orbit - Squamous Cell Carcinoma	96.5	90.4	86.8	77.3	98.0	91.6	87.7	82.6	90.9	85.2	83.6	54.9
Eye and Orbit - Melanoma	97.8	84.5	73.6	61.1	97.5	84.9	74.8	62.5	98.1	84.1	72.1	59.4
Other Endocrine	78.2	66.2	58.9	47.2	79.2	66.3	59.6	47.5	77.0	66.0	58.1	46.8
Thymus	87.4	74.5	66.3	51.3	88.9	75.0	68.5	54.5	85.5	73.9	63.4	46.8
Thymus - Thymoma	89.0	77.4	70.0	55.7	90.8	76.8	71.4	60.7	86.9	78.3	68.2	49.5
Adrenal Gland	59.4	45.5	38.7	29.6	55.7	40.9	34.1	22.7	62.6	49.6	42.5	35.4
Adrenal Gland - Adrenal Cortical	66.0	48.5	41.2	31.3	62.9	43.7	37.9	27.0	68.4	52.1	43.6	34.6
Adrenal Gland - Pheochromocytoma	84.5	73.0	64.8	44.0	83.9	73.4	67.3	29.7	85.1	72.6	62.4	58.9
Parathyroid Gland	94.1	94.1	93.1	81.6	93.8	93.8	89.6	71.7	94.0	93.1	93.1	88.4
Pituitary Gland	83.7	74.9	63.8	41.7	85.5	70.9	52.6	25.7	81.9	78.9	74.4	53.4
Pineal Gland	87.7	76.2	71.7	63.9	90.1	80.0	75.2	69.8	81.7	66.2	62.4	47.8
Mesothelioma	39.0	12.8	8.2	5.6	37.0	9.8	5.5	3.0	46.1	23.1	17.3	12.9
Mesothelioma - Pleura and Lung	38.2	10.5	6.4	4.3	36.9	8.5	4.8	2.4	43.7	18.7	12.8	9.9
Mesothelioma - Peritoneum and Retroperitoneum	41.8	25.9	18.4	9.5	34.1	19.0	11.7	5.6	53.1	35.6	28.2	14.7
Reticuloendothelial System Tumors	88.0	78.5	66.6	44.0	88.9	77.3	65.6	45.6	86.6	80.3	67.9	41.9
Waldenstrom's Macroglobulinemia	90.2	81.0	69.3	45.6	91.6	80.0	67.9	47.4	88.1	82.6	71.3	43.1
Myeloma	74.7	48.1	31.7	14.2	75.1	49.4	33.4	15.7	74.1	46.7	29.8	12.6
Solitary Myeloma	90.3	73.7	64.9	44.1	90.4	78.8	69.1	52.8	90.0	65.2	57.5	29.1
Multiple Myeloma	73.7	46.4	29.4	11.7	74.0	47.2	30.6	12.3	73.4	45.6	28.3	11.1
Unknown or Ill-defined Primary Site	24.2	13.5	11.3	9.8	25.2	14.8	12.8	11.7	23.2	12.4	10.0	8.1
Microscopically confirmed	27.4	15.0	12.4	10.6	28.4	16.5	14.1	12.7	26.5	13.6	10.7	8.8
Carcinomas	35.9	23.4	20.9	18.3	39.6	26.6	24.0	21.7	30.9	19.3	16.8	14.0
Adenocarcinomas	19.4	7.5	5.2	4.1	16.3	5.8	4.0	3.3	21.8	8.7	6.0	4.7
Other	41.2	26.6	21.8	18.5	40.9	27.1	22.6	19.9	41.5	26.1	21.0	16.7
Non-microscopically confirmed	12.5	7.7	6.6	5.4	12.0	7.0	5.9	5.4	12.9	8.1	7.1	5.4

* Excludes mesotheliomas and sarcomas
^ Excludes Basal, Squamous, Kaposi sarcoma & Melanoma
~ Statistic not displayed due to less than 25 cases.

combined, males had a survival advantage at 1, 3, 5, and 10 years, and the relative survival rate for whites was considerably higher than that of blacks at five years, 35% vs. 24% (Table 30.3).

Male Breast

About one percent of all breast cancers occur among males. As among females, some cases are diagnosed at the in situ stage. The majority of male breast cancers are ductal carcinomas. Relative survival rates for cases diagnosed at the in situ stage are quite good, overall, 99% at five-years. Among the invasive tumors, almost half were diagnosed while still localized. Five-year relative survival for all males was 84% (compared to 89% in females) (5) with white males having a survival advantage of 86% vs. 67% among black males. A similar advantage existed at 10 years also, 73% among whites vs. 52% among blacks. Five-year relative survival for males with localized breast cancer was 97%.

Female genital

Survival from cancers of the vagina, vulva, uterus, ovary, fallopian tube, and placenta are included in other chapters in this monograph. Among the remaining cases occurring within specific female genital sites – round and broad ligaments, parametrium, and adnexa – there were too few cases for a separate analysis, so these sites have been grouped together. The five-year relative survival rate for this group of 67% was intermediate to that for ovary (44%) (6) vs. cervix (72%) (7) and corpus uteri (85%) (8), this despite the fact that over 40% of the patients were diagnosed at an advanced stage. For those women whose cancer overlapped two or more sites within the female genital tract, relative survival rate was much poorer, 49% at five years, even though only one third of these women were diagnosed with distant disease. The poorest relative survival rate was experienced by those women whose cancer could not be specifically assigned to any specific genital site at the time of diagnosis, only

Table 30.3: Cancers of Rare Sites: 1,3,5 and 10-Year Relative Survival Rates (%) by Site and Race, 12 SEER Areas, 1988-2001

Site	Relative Survival Rate (%)							
	White				Black			
	1-Year	3-Year	5-Year	10-Year	1-Year	3-Year	5-Year	10-Year
Respiratory and Intrathoracic Organs								
Nose, Nasal Cavity and Middle Ear	80.4	63.5	56.4	48.1	70.4	47.1	36.3	30.5
Nasal Cavity	90.0	77.9	71.0	61.4	81.3	64.1	59.1	58.4
Middle Ear	68.8	41.1	39.2	31.5	~	~	~	~
Trachea, Mediastinum and Other Respiratory	61.4	45.8	43.5	39.0	51.1	30.2	21.1	17.4
Trachea	55.8	38.9	35.1	27.8	~	~	~	~
Squamous Cell	47.8	29.0	23.5	15.0	~	~	~	~
Mediastinum	68.3	52.1	50.0	46.0	52.6	31.6	31.6	22.8
Mediastinum - Germ	71.1	58.2	56.7	53.3	~	~	~	~
Other Respiratory	41.1	31.4	31.3	9.7	~	~	~	~
Pleura *	39.0	25.0	22.2	12.8	~	~	~	~
Skin ^	94.1	85.4	83.3	81.3	97.1	87.7	87.7	70.9
Merkel Cell	87.6	68.4	62.5	57.2	~	~	~	~
Skin Appendage Adenocarcinoma	99.7	98.8	96.6	96.5	~	~	~	~
Sweat Gland Adenocarcinoma	97.8	95.3	94.8	85.4	~	~	~	~
Sebaceous Adenocarcinoma	97.8	94.1	94.1	91.2	~	~	~	~
Peritoneum and Retroperitoneum *	78.1	49.3	35.0	28.9	80.6	45.5	23.5	9.6
Papillary Serous Cystadenocarcinoma	83.7	48.9	27.0	16.7	~	~	~	~
Male Breast (including in situ)	98.1	94.5	87.7	75.1	92.6	81.8	70.4	58.1
In situ	99.2	99.2	99.2	93.2	~	~	~	~
Invasive	97.9	93.7	85.9	72.6	92.1	80.2	67.2	52.4
Female Genital								
Ligaments and Adnexa	93.4	72.9	70.5	54.3	~	~	~	~
Overlapping	71.6	57.4	51.9	36.3	~	~	~	~
Other and Not Otherwise Specified	50.7	30.7	27.4	21.4	47.2	25.7	25.7	16.9
Male Genital								
Penis	90.0	79.9	73.9	64.6	77.3	64.3	64.3	52.4
Penis - Squamous Cell Carcinoma	88.6	77.6	71.9	62.9	77.3	64.3	64.3	52.4
Scrotum	97.5	88.3	82.5	67.0	~	~	~	~
Scrotum - Squamous Cell Carcinoma	90.4	72.8	67.0	47.5	~	~	~	~
Scrotum - Paget Disease	100.0	100.0	94.4	86.8	~	~	~	~
Other and Not Otherwise Specified	~	~	~	~	~	~	~	~

* Excludes mesotheliomas and sarcomas
^ Excludes Basal, Squamous, Kaposi sarcoma & Melanoma
~ Statistic not displayed due to less than 25 cases.

26% at five years. There were too few cases occurring among blacks to allow a comparison of white vs. black females.

Male genital

Survival from cancers of the prostate and testis are analyzed elsewhere in this monograph. Cancer of the penis is indeed rare within the United States, and the majority of the tumors occurs on the skin of the penis and is of squamous cell origin. Relative survival rates were quite high and were better for white males than for black males. Similarly, the majority of other cancers occurring in the remainder of the male genital system was of the skin of the scrotum and was squamous cell in origin. However, men with squamous cell carcinoma of the scrotum versus the penis survived more poorly at 5 years with relative rates of 59% vs. 72%, respectively. Men with localized squamous cell carcinoma of the scrotum had much poorer 5-year

Table 30.3 (continued): Cancers of Rare Sites: 1,3,5 and 10-Year Relative Survival Rates (%) by Site and Race, 12 SEER Areas, 1988-2001

Site	Relative Survival Rate (%)							
	White				Black			
	1-Year	3-Year	5-Year	10-Year	1-Year	3-Year	5-Year	10-Year
Urinary System								
Ureter	82.8	64.6	57.2	50.7	72.5	53.9	40.3	39.0
Ureter - Papillary Transitional Cell	84.3	66.2	59.1	52.6	68.3	51.7	44.2	42.5
Other Urinary	81.3	68.9	63.9	58.8	77.2	58.5	48.1	40.3
Other Urinary - Papillary Transitional Cell	82.3	69.3	64.9	61.9	76.8	60.2	55.6	47.6
Eye and Orbit	97.5	85.1	75.7	63.7	89.7	75.8	41.7	10.1
Eye and Orbit - Squamous Cell Carcinoma	96.0	89.9	86.4	76.7	~	~	~	~
Eye and Orbit - Melanoma	97.9	84.5	74.2	61.7	~	~	~	~
Other Endocrine	76.5	64.3	57.5	46.4	79.5	70.4	61.5	44.8
Thymus	86.8	73.6	65.9	49.4	85.5	76.2	66.7	51.1
Thymus - Thymoma	87.9	77.0	70.1	54.2	90.2	79.4	71.1	54.6
Adrenal Gland	58.5	45.3	39.1	31.1	64.9	47.6	37.3	13.1
Adrenal Gland - Adrenal Cortical	65.9	50.0	43.5	33.5	~	~	~	~
Adrenal Gland - Pheochromocytoma	81.6	66.9	60.3	44.9	~	~	~	~
Parathyroid Gland	94.2	93.7	92.8	86.5	~	~	~	~
Pituitary Gland	89.9	78.0	66.3	40.4	~	~	~	~
Pineal Gland	87.7	73.3	67.5	60.2	~	~	~	~
Mesothelioma	39.4	12.8	8.1	5.3	37.9	12.0	11.7	8.6
Mesothelioma - Pleura and Lung	38.8	10.7	6.3	4.1	37.3	9.4	8.8	6.2
Mesothelioma - Peritoneum and Retroperitoneum	40.7	24.4	17.4	8.4	~	~	~	~
Reticuloendothelial System Tumors	87.8	78.9	66.7	43.9	95.6	76.1	68.2	46.6
Waldenstrom's Macroglobulinemia	90.3	81.5	69.7	45.4	94.9	77.3	71.4	51.6
Myeloma	74.2	48.0	31.2	13.7	76.4	49.5	34.1	15.7
Solitary Myeloma	89.8	74.1	63.7	42.1	92.9	68.7	68.0	40.3
Multiple Myeloma	73.2	46.2	28.8	11.0	75.7	48.5	32.6	14.1
Unknown or Ill-defined Primary Site	24.5	13.9	11.6	10.0	21.6	11.0	8.9	7.8
Microscopically confirmed	28.1	15.7	12.9	11.0	22.2	10.6	8.6	7.7
Carcinomas	37.4	24.9	22.3	19.4	24.9	13.5	11.4	10.1
Adenocarcinomas	19.6	7.5	5.2	4.0	16.9	5.7	4.1	3.5
Other	41.4	26.7	21.6	18.3	40.8	26.2	23.0	19.9
Non-microscopically confirmed	11.3	6.8	5.9	4.6	19.6	12.6	10.1	8.4

* Excludes mesotheliomas and sarcomas
^ Excludes Basal, Squamous, Kaposi sarcoma & Melanoma
~ Statistic not displayed due to less than 25 cases.

Table 30.4: Cancers of Rare Sites: 5- & 10-Year (Yr) Relative Survival Rates (%) by Primary Site and SEER Summary Stage 1977 (2), 12 SEER Areas, 1988-2001

Primary Site	Summary Stage									
	Total		Local		Regional		Distant		Unstaged	
	Relative Survival Rate (%)		Relative Survival Rate (%)		Relative Survival Rate (%)		Relative Survival Rate (%)		Relative Survival Rate (%)	
	5-Yr	10-Yr	5-Yr	10-Yr	5-Yr	10-Yr	5-Yr	10-Yr	5-Yr	10-Yr
Respiratory and Intrathoracic Organs										
Nose, Nasal Cavity and Middle Ear	54.0	46.4	82.5	77.4	47.3	37.6	25.3	21.7	55.6	45.6
Nasal Cavity	70.1	61.7	86.3	79.4	57.5	47.0	37.6	29.7	73.2	63.6
Middle Ear	33.8	27.7	~	~	37.7	29.2	~	~	~	~
Trachea, Mediastinum and Other Respiratory	42.3	37.0	66.2	60.0	44.2	36.2	17.1	13.6	43.5	35.8
Trachea	34.6	25.5	59.7	43.5	31.2	20.7	3.4	!	32.8	21.6
Squamous Cell	20.4	13.2	~	~	12.4	12.4	~	~	~	~
Mediastinum	48.2	44.0	69.9	67.7	54.6	46.0	23.3	17.5	53.0	50.6
Mediastinum - Germ	55.6	51.5	73.4	70.9	62.0	59.8	29.5	21.5	60.1	57.7
Other Respiratory	31.0	15.2	!	!	~	~	~	~	36.1	18.1
Pleura *	28.2	21.2	~	~	~	~	~	~	~	~
Skin ^	84.0	81.2	91.7	87.6	62.1	58.3	46.4	44.1	70.0	68.8
Merkel Cell	62.8	57.5	74.7	68.4	38.7	32.4	28.4	28.4	45.6	39.2
Skin Appendage Adenocarcinoma	97.5	97.2	99.1	98.6	88.2	79.1	~	~	86.8	84.7
Sweat Gland Adenocarcinoma	94.5	83.6	97.4	87.9	~	~	~	~	80.9	73.6
Sebaceous Adenocarcinoma	94.6	87.3	97.1	84.2	~	~	85.4	85.4	86.0	86.0
Peritoneum and Retroperitoneum *	34.3	28.5	77.7	74.1	52.6	41.5	25.0	18.9	39.5	36.5
Papillary Serous Cystadenocarcinoma	26.9	17.2	~	~	46.3	!	23.8	16.4	~	~
Male Breast (including in situ)	85.6	74.2	96.9	92.1	78.1	58.1	23.0	5.8	64.2	34.8
In situ	99.1	96.9	!	!	!	!	!	!	!	!
Invasive	83.6	71.3	96.9	92.1	78.1	58.1	23.0	5.8	64.2	34.8
Female Genital										
Ligaments and Adnexa	67.1	53.2	~	~	~	~	~	~	~	~
Overlapping	48.8	33.0	~	~	~	~	~	~	~	~
Other and Not Otherwise Specified	25.6	19.1	~	~	~	~	13.9	13.1	43.0	31.8
Male Genital										
Penis	73.5	64.0	84.9	74.5	59.2	52.6	11.4	!	68.2	54.4
Penis - Squamous Cell Carcinoma	71.7	62.6	84.5	75.9	55.8	47.9	11.9	!	61.5	40.5
Scrotum	77.5	62.5	88.5	70.6	56.4	34.3	~	~	~	~
Scrotum - Squamous Cell Carcinoma	58.6	38.5	67.0	48.2	~	~	~	~	~	~
Scrotum - Paget Disease	89.0	82.3	98.3	86.3	~	~	~	~	~	~
Other and Not Otherwise Specified	51.8	34.1	~	~	~	~	~	~	~	~

* Excludes mesotheliomas and sarcomas
^ Excludes Basal, Squamous, Kaposi sarcoma & Melanoma
~ Statistic not displayed due to less than 25 cases.
! Not enough intervals to produce rate

Table 30.4 (continued): Cancers of Rare Sites: 5- & 10-Year (Yr) Relative Survival Rates (%) by Primary Site and SEER Summary Stage 1977 (2), 12 SEER Areas, 1988-2001

Primary Site	Summary Stage									
	Total		Local		Regional		Distant		Unstaged	
	Relative Survival Rate (%)		Relative Survival Rate (%)		Relative Survival Rate (%)		Relative Survival Rate (%)		Relative Survival Rate (%)	
	5-Yr	10-Yr	5-Yr	10-Yr	5-Yr	10-Yr	5-Yr	10-Yr	5-Yr	10-Yr
Urinary System										
Ureter	55.9	49.6	76.6	65.5	35.6	32.6	9.8	9.4	44.7	41.4
Ureter - Papillary Transitional Cell	57.8	51.4	77.3	66.5	36.3	33.6	10.1	9.7	50.4	46.3
Other Urinary	60.5	54.2	80.1	70.0	50.5	45.2	15.9	12.7	69.2	63.4
Other Urinary - Papillary Transitional Cell	63.8	60.0	77.6	70.7	52.8	43.3	4.8	!	73.9	70.2
Eye and Orbit	75.4	63.1	79.6	69.1	56.0	37.3	30.2	24.3	69.2	45.7
Eye and Orbit - Squamous Cell Carcinoma	86.8	77.3	89.2	82.2	64.3	!	~	~	88.5	57.8
Eye and Orbit - Melanoma	73.6	61.1	77.3	66.2	57.2	34.2	14.8	14.8	65.7	42.4
Other Endocrine	58.9	47.2	77.6	69.3	68.6	51.2	22.5	15.2	54.7	42.4
Thymus	66.3	51.3	88.8	82.1	70.5	48.6	35.4	24.3	61.6	51.6
Thymus - Thymoma	70.0	55.7	87.8	86.1	74.4	52.6	41.4	29.8	65.1	56.3
Adrenal Gland	38.7	29.6	65.5	52.6	45.7	39.2	8.6	3.4	31.4	19.4
Adrenal Gland - Adrenal Cortical	41.2	31.3	64.7	51.5	43.9	36.3	7.1	2.0	~	~
Adrenal Gland - Pheochromocytoma	64.8	44.0	83.0	60.5	~	~	~	~	~	~
Parathyroid Gland	93.1	81.6	95.6	85.8	95.5	82.2	~	~	~	~
Pituitary Gland	63.8	41.7	~	~	~	~	~	~	~	~
Pineal Gland	71.7	63.9	81.1	78.5	69.5	49.6	~	~	~	~
Mesothelioma	8.2	5.6	19.3	16.2	10.3	9.0	4.9	2.1	10.1	5.4
Mesothelioma - Pleura and Lung	6.4	4.3	15.2	11.9	9.1	7.8	3.7	1.4	6.6	3.3
Mesothelioma - Peritoneum and Retroperitoneum	18.4	9.5	~	~	24.8	14.3	13.1	5.3	26.6	16.9
Reticuloendothelial System Tumors	66.6	44.0	!	!	!	!	66.6	43.9	~	~
Waldenstrom's Macroglobulinemia	69.3	45.6	!	!	!	!	69.3	45.6	!	!
Myeloma	31.7	14.2	68.4	51.8	!	!	30.0	12.3	!	!
Solitary Myeloma	64.9	44.1	64.9	47.1	!	!	64.0	25.0	!	!
Multiple Myeloma	29.4	11.7	!	!	!	!	29.4	11.7	!	!
Unknown or Ill-defined Primary Site	11.3	9.8	~	~	!	!	46.7	41.6	11.2	9.7
Microscopically confirmed	12.4	10.6	~	~	!	!	47.2	47.2	12.3	10.6
Carcinomas	20.9	18.3	!	!	!	!	!	!	20.9	18.3
Adenocarcinomas	5.2	4.1	!	!	!	!	!	!	5.2	4.1
Other	21.8	18.5	~	~	!	!	47.2	47.2	21.4	18.0
Non-microscopically confirmed	6.6	5.4	!	!	!	!	~	~	6.6	5.4

* Excludes mesotheliomas and sarcomas
^ Excludes Basal, Squamous, Kaposi sarcoma & Melanoma
~ Statistic not displayed due to less than 25 cases.
! Not enough intervals to produce rate

relative survival than men with localized squamous cell carcinoma of the penis (67% vs. 85%, respectively).

Urinary System

Cancers of the ureter, urethra, urachus and other urinary organs were diagnosed most commonly as localized or regional disease and occurred more commonly among males. The majority of these cancers were papillary transitional cell carcinomas. Five-year relative survival rates from cancers of the ureter were similar among males vs. females, but for the other rare urinary sites, males had a distinct survival advantage at 5 years, 68% vs. 49%. The survival rates among whites were consistently higher than those for blacks. Five-year relative survival rates were uniformly poor for patients diagnosed with distant disease.

Eye and Orbit

Since children are excluded from this analysis, by definition, retinoblastomas are excluded as well. Among adults, nearly 80% of the malignancies of the eye were melanomas with most of the remainder being squamous cell carcinomas. Over 70% of all eye tumors were diagnosed while still localized, resulting in five-year relative survival rates of 87% for squamous cell carcinomas and 74% for melanomas. For melanomas of the eye 1, 3, and 5-year rates were quite similar in males and females while for squamous cell carcinomas of the eye, there appears to be a male survival advantage. There were very few cases among blacks, but for these few, survival was much poorer than among whites, especially at 5 and 10 years. Patients with squamous cell carcinoma of the eye had higher relative survival rates than patients with melanoma of the eye.

Endocrine System

Cancers of the thymus gland were primarily thymomas and patients tended to be diagnosed with regional disease. For thymomas, males and females survived similarly at 1, 3, and 5 years and the survival rates were similar among whites and blacks at 1, 3, 5, and 10 years. Sixty-five percent of adrenal gland malignancies were of the adrenal cortical type while another 10 percent were malignant pheochromocytomas. Relative 5-year survival rates were much better for the pheochromocytomas, 65% than for the adrenal cortical carcinomas, 41%. Males with pheochromocytomas had a survival advantage at 5 years compared to females, but at 10 years, the advantage was in favor of females, 59% vs. 30%. There were too few cases of pheochromocytomas among blacks to yield meaningful comparisons by race.

For adrenal cortical carcinomas, females had a survival advantage at 1, 3, 5, and 10 years. Malignant tumors of the parathyroid, pituitary, and pineal glands were indeed rare with too few cases to allow comparisons by race. The majority of these tumors were diagnosed at either the localized or regional stage with relative 5-year survival rates of 93%, 64%, and 72% respectively. For malignancies of the parathyroid and the pituitary, females survived better than males at 5 and 10 years whereas the opposite was true for pineal malignancies. For each stage, patients with adrenal gland cancers had much poorer survival than patients with other endocrine tumors.

Mesothelioma

Mesotheliomas arose more frequently in the pleura for both males (91%) and females (78%) with most of the remaining mesotheliomas arising from the (retro)peritoneum. The majority of mesotheliomas were diagnosed as distant disease. While uniformly dismal, the 5- and 10-year relative survival rates for females were more than triple those for males. Survival rates were slightly higher for blacks compared to whites. Interestingly for all races combined and both sexes combined, 5-year relative survival rates from mesotheliomas which arose in the (retro)peritoneum were at least double those which arose in the pleura. This was true even for patients diagnosed with regional or distant disease (Table 30.2).

Reticuloendothelial System

Survival from leukemias and multiple myeloma are discussed elsewhere. Ninety percent of the remaining tumors occurring in the reticuloendothelial system were classified as Waldenstrom's macroglobulinemia, a systemic disease always staged as distant at the time of diagnosis. Survival rates were similar among males and females (Table 30.2) and whites versus blacks (Table 30.3).

Myelomas

Multiple myelomas accounted for 93% of the myelomas. Patients with multiple myeloma survived much more poorly than patients with a solitary myeloma, especially at 5 (29% vs. 65%) and 10 (12% vs. 44%) years. For multiple myeloma survival was similar among males and females and blacks had slightly higher survival rate compared to whites. However, for solitary myeloma, males had a distinct survival advantage at 10 years, 53% vs. 29% for females.

Ill-defined and Unknown Sites

Some tumors are so disseminated at the time of diagnosis that it is impossible to determine the exact anatomic site in which the tumor arose. Sometimes these tumors can be ascribed to a body region such as the abdomen, but still, an exact primary site cannot be determined with certainty. For this group of tumors only, those without microscopic confirmation have been included but are shown separately in Tables 1-3. Twenty-two percent of these tumors did not have microscopic confirmation. By convention, these tumors are always classified with an unknown stage.

Not surprisingly, relative survival rates for this group as a whole were poor – 11% at five years. Patients whose disease was classified as "carcinoma" had a better survival than those with "adenocarcinoma" – 21% vs. 5% at five years. Patients with non-microscopically confirmed cancers experienced a five-year survival rate of only 7% vs. 12% for those with microscopic confirmation. Survival was essentially equal for males and for females, but whites had a slight survival advantage when compared to blacks, especially those with a tumor classified as carcinoma, 22% vs. 11% at five years.

DISCUSSION

It is not clear as to why there are certain anatomic sites in which cancer rarely arises. This is particularly curious in systems such as the endocrine system where with the exception of the thyroid gland few tumors arise, particularly in the pituitary and pineal glands. However, when cancer does arise in one of these rare sites, survival, in general, is similar to survival from other primary sites in the same system. For example survival from cancers of the pleura and from pleural mesotheliomas was very similar to survival from lung cancers.

Survival from cancer of the male breast, in general was similar to survival among females with breast cancer.

Among females, survival from cystadenocarcinomas of the (retro)peritoneum was very similar to survival from cystadenocarcinomas of the ovary. Roffers et al. documented that these tumors are actually extra ovarian tumors (9).

The extremely poor survival among patients with unknown or ill-defined primary site was probably reflective of the fact that the disease was already widely disseminated at the time of diagnosis so that the site of origin could not be identified. While this group was the largest of the rare site groups, overall unknown site accounts for less than 3% of all primary cancers.

Because of the small numbers of cases involved, detailed analysis of survival by races other than white cannot be made. Further, time trends in survival are also difficult due to the small numbers involved. As more survival data are accumulated from a larger group of registries for a longer time period, these analyses should be repeated.

REFERENCES

1. Ries LAG, Ward KC and Young JL Jr., Chapter 11: Sarcomas in Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner, M-J (editors). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program. NIH Pub. No. 07-6215, 2007.
2. Shambaugh, EM, Weiss, MA. Axtell, LM (eds), The 1977 Summary Staging Guide for the Cancer Surveillance, Epidemiology and End Results Reporting (SEER) Program, National Cancer Institute, Bethesda, MD, April 1977.
3. Piccirillo JF, Costas I, and Reichman ME, Chapte 2 Cancer of the Head and Neck in Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner, M-J (editors). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program. NIH Pub. No. 07-6215, 2007.
4. Ries LAG, and Eisner MP, Chapter 9: Cancer of the Lung in Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner, M-J (editors). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program. NIH Pub. No. 07-6215, 2007.
5. Ries, LAG and Eisner MP, Chapter13: Cancer of the Female Breast in Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner, M-J (editors). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program. NIH Pub. No. 07-6215, 2007.
6. Kosary CL, Chapter 16: Cancer of the Ovary in Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner, M-J (editors). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program. NIH Pub. No. 07-6215, 2007.
7. Kosary CL, Chapter 14: Cancer of the Cervix Uteri in Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner, M-J (editors). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program. NIH Pub. No. 07-6215, 2007.
8. Kosary CL, Chapter 15: Cancers of the Corpus Uteri in Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner, M-J (editors). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program. NIH Pub. No. 07-6215, 2007.
9. Roffers SD, Wu XC, Johnson CH, and Correa CN. Incidence of Extraovarian Primary Cancers in the United States, 1992-1997. Cancer; Vol. 15;97(10 Suppl):2643-7; May 2003.

Chapter 31
Race and Ethnicity

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INTRODUCTION

Cancer is the second leading cause of death in the U.S., and accounts for approximately one-fourth of all deaths. In 2006, an estimated 1.4 million Americans will be diagnosed with cancer (other than carcinomas of the skin) and 564,830 people will die of cancer (1). The most common cancers among men are carcinomas of the prostate, lung (including bronchus), and colon/rectum, whereas women are most likely to develop carcinomas of the breast, lung, and colon/rectum (1). Published SEER data show that for most cancers, including the four major ones (colon/rectum, lung and bronchus, female breast, and prostate), relative survival rates among African-American patients were poorer than for white patients, although survival improved in recent years for both groups (2). Published information on patient survival among other racial/ethnic minorities is limited.

This chapter describes and compares cancer-specific survival rates by racial/ethnic group among adult patients (aged 20 or older at disease diagnosis) diagnosed with a first malignant neoplasm during the period between 1988 and 2001 in 12 SEER geographic areas. The cancer-specific survival measure used in this study quantifies the likelihood that a cancer patient will not die of the neoplasm within a specified time after diagnosis. The cancers included in this chapter are all cancers combined and individual cancers by body system for 6 race/ethnicity groups (white, black, Asian/Pacific Islander (API), American Indian/Alaska Native (AI/AN), Hispanic and non-Hispanic). Note that these groupings are not mutually exclusive in that Hispanic or non-Hispanic can be of any race. For the four major cancers: female breast, colorectal, lung (including bronchus), and prostate, the API group is broken into Asian and Pacific Islanders with specific Asian and Pacific Islander groups shown separately and whites are subdivided by Hispanic and non-Hispanic.

MATERIALS AND METHODS

Study Populations and Data Sources

The NCI SEER Program currently collects cancer incidence and survival information from 18 geographic areas that encompass nearly 26% of the total U.S. population. This study utilizes the data from 12 geographic areas that include the States of Connecticut, Hawaii, Iowa, New Mexico, and Utah; the metropolitan areas of Atlanta, Detroit, Seattle-Puget Sound, San Francisco-Oakland, Los Angeles, San Jose-Monterey, and Rural Georgia. Data are included for adults who resided in these areas and were diagnosed with their first invasive cancer between 1988 and 2001, except for Los Angeles for which data are only included from 1992-2001. These patients were followed for vital status through December 31, 2002.

The first part of this chapter focuses on anatomic systems and the major sites within them by race/ethnicity (white, black, American Indian/Alaska Native (AI/AN), Asian/Pacific Islander (API), Hispanic, and non-Hispanic).

The second part focuses on detailed race/ethnicity for cancers of the breast (females), lung (including bronchus), prostate, and colon/rectum. These four cancers accounted for more than 50% of all incident cancers diagnosed in the SEER areas during these years. Since this part of the analyses separates Asians from Pacific Islanders, the cases used were limited to 1991-2001 years of diagnosis when this detail was collected. The race/ethnicity codes used were: white; white non-Hispanic, white Hispanic, black, AI/AN, Asian, and Pacific Islanders. The Asian group was further classified by Asian Indian/Pakistani, Chinese, Filipino, Korean, Japanese, Vietnamese, and other Asian. The Pacific Islanders were further classified by Hawaiian and other Pacific Islander.

Excluded from the study were cancer patients whose initial diagnosis was found on the death certificate or at autopsy, patients who were not under active follow-up or alive with no survival time, patients who were diagnosed under age 20, in situ cancers, and no microscopic confirmation or unknown. Unlike other chapters, sarcomas were included and cases with unknown or missing cause of death were also excluded because it would not be possible to classify the case as a death due to the cancer vs. not due to the cancer. Cancer site and morphology were coded according to the International Classification of Diseases for Oncology, Second edition (ICD-O-2) up to 2001 or Third edition (ICD-O-3) for 2001.

Cancer Staging

Cancer stage was determined by extent of cancer spread from the site of origin at initial diagnosis. The SEER historic staging scheme classified invasive cancers into four stages: localized to the primary tumor site, tumor with regional spread or metastases to regional lymph node, tumor with distant metastases, or unknown stage (when relevant data were unavailable, or stage was assigned more than four months after initial diagnosis). Data on cancer stage were included for breast, colorectal, lung, and prostate cancers. For prostate cancer, local and regional stages were combined because these two stages were not consistent over time.

Statistical Analysis

This analysis utilized cancer-specific survival rates rather than relative survival rates (2). The relative survival rate was used in the other chapters of this monograph and it is defined as the ratio of observed all-cause survival to expected survival (3). For this analysis, cause-specific (c-s) survival rates were calculated based on the underlying cause of death as coded based on the death certificate. Any cancer listed as the underlying cause of death was considered a death due to the cancer. In addition, some AIDS deaths and benign/borderline/in situ and unspecified cancers were included as a death due to cancer. Kaposi sarcoma was excluded from all sites and the specific diagnoses because many times the death certificate is signed out to HIV/AIDS or some other cause and rarely is Kaposi sarcoma listed as the underlying cause of death.

The cause-specific (c-s) survival rate uses the actuarial or lifetable method with deaths not associated with the cancer censored at time of death. Deaths which were considered to be attributed to the cancer were treated as deaths and other deaths were considered losses to follow-up at the date of death. Survival times were measured in months and were censored at the date of a patient being lost to follow-up, the date of death from causes not considered as deaths due to the cancer, or on December 31, 2002, whichever occurred first. While c-s rates were calculated monthly, only the 5-year c-s rates are shown due to lack of space. Survival rates are not shown for less than 25 cases and frequencies are not shown for under 5 cases.

RESULTS

A total of 1,595,392 adult men and women were included who were diagnosed with an incident malignant cancer in the 12 SEER areas during the period 1988-2001. Table 31.1 shows the 5-year cause-specific survival rates by anatomic system and major sites within those systems for males and females combined by race/ethnicity. Survival rates for males are shown in table 31.2 and for females in table 31.3. For all sites combined, the 5-year c-s survival was highest for white patients (65%) and lowest for AI/AN (54%). The overall rates for Hispanics and non-Hispanics were similar. While the c-s rate for all sites is interesting by race/ethnicity, emphasis should be on evaluating c-s rates for individual primary sites among the racial/ethnic groups since there is a different distribution of sites for each race/ethnicity. Therefore, c-s rates are shown for a very detailed list of primary sites. The following four cancers represented over half of the cancer diagnoses included for study in 1991-2001: lung/bronchus (162,121 cases) (Tables 31.4, 31.5, and 31.6), female breast (215,368) (Table 31.7), prostate (237,138) (Table 31.8), and colon/rectum (147,323) (Table 31.9).

Table 31.4 shows the distributions of cancer stage at diagnosis and 5-year c-s survival by more detailed race/ethnicity for males and females diagnosed with lung cancer. Tables 31.5 and 31.6 show lung cancer for males and females, respectively. For males and females combined, the 5-year c-s rates ranged from a low of 11.9% for Other Pacific Islanders to a high of 23.0% among Asian Indian/Pakistanis. Most of the rates were in the 12-17% range. The overall low survival rates were associated with a high proportion of regional and distant disease. Asian Indians/Pakistanis had the lowest percentage of distant disease, 35%, and the highest regional disease, 44%, contributing to their higher overall survival rate. While the survival rates were much higher for localized disease (41-69%), less than 20% were diagnosed while the tumor was confined to the lung for each of the race/ethnicities. For most groups, females (Table 31.6) had a higher percentage of localized disease compared to males (Table 31.5). Even within stage females had higher survival rates than males for lung cancer. For females, 5-year c-s survival rates for localized disease ranged from 44% for Pacific Islander to 84% for Other Asians (based on few cases).

Table 31.7 shows the distributions of cancer stage at diagnosis and 5-year c-s survival by race/ethnicity for female breast cancer. Unlike lung cancer, a high proportion of breast cancer cases were localized at diagnosis and a very small percentage were distant (under 10% for each group). Five-year c-s survival rates were high for localized disease, over 90% for all except blacks and AI/AN.

Table 31.8 shows the distributions of cancer stage at diagnosis and 5-year c-s survival by race/ethnicity for prostate cancer. Over 80% of the prostate cases were localized/regional at diagnosis. Survival rates were very high for localized/regional disease and ranged from 88% for Other Pacific Islander to 97% for Other Asian. Only a small percentage of cases were distant and even distant survival rates were higher than distant for most other sites.

Table 31.9 shows the distributions of cancer stage at diagnosis and 5-year c-s survival by race/ethnicity for males and females for cancer of the colon and rectum. Since survival rates were similar by sex, survival rates are not shown separately by sex. There was a fairly even split between localized and regional disease for each of the race/ethnicity groups. Only a small proportion were unstaged.

DISCUSSION

This chapter describes racial/ethnic patterns in cancer-specific survival rates by primary site and gender. It expands on the findings from an earlier report of population-based data on cancer-specific survival for the six major racial/ethnic groups in the U.S. (4). Many report have focused largely on whites and African-Americans (5-8). This study was facilitated by the intentional coverage by the SEER Program of certain geographic areas with relatively large racial/ethnic population subgroups so that information on the cancer burden would be available for these groups (9). Although geographic areas included in the SEER Program were not selected randomly, they include various levels of urbanization and socioeconomic status. Thus, descriptive studies based on SEER data, which covers large percentages of the populations being studied, provide insights into patterns at the national level.

In many of SEER publications, expected survival data were calculated using 1970, 1980, and 1990 US decennial life tables matched on age, race, and sex. However for these years, reliable expected life tables are not available for Hispanic whites, Native-Hawaiians, American Indians/Alaska Natives, and Asian Americans and these would be needed to generate valid relative survival estimates. Estimation of expected life tables depends on US mortality rates from all causes. Based on its current research on the quality and reliability of US mortality rates (from all causes) by race and Hispanic origin, however, the National Center for Health Statistics estimates that the published mortality rates for the white and African American population are overstated in official publications by an estimated 1.0% and 5.0%, respectively, resulting principally from undercounts of these population groups in the census. Mortality rates for other minority groups are understated in official publications, approximately by 21% for American Indians and 11% for Asian and Pacific Islanders (10). For these reasons, c-s rates were chosen to compare survival patterns among racial/ethnic groups, since they do not require race/ethnicity specific life tables.

To obtain reliable estimates of cancer-specific survival, it is essential that classification of the underlying cause of death on death certificates is accurate. For colorectal, lung, breast, and prostate cancers, levels of accuracy exceed 90% for the underlying cause of death (11). There is no definitive answer on what causes of death should be included to indicate that an individual died of their cancer based on the death certificate. In some instances, the cause of death may reflect the site to which the cancer metastasized rather than the primary site. There are other primary site/histology groups where the cause of death may be less specific than the original diagnosis such as leukemia on the death certificate instead of the more specific diagnosis of acute lymphoblastic leukemia. In ICD-10, a cause of death ascribed to multiple cancers would go to C97 and therefore, for persons with more than one cancer, C97 was considered a death due to the cancer. An example of a site-specific decision would be a diagnosis of primary invasive brain tumor but for which the cause of death is brain tumor which would place it in the benign or not specified benign or malignant category which is generally not considered as cancer for mortality data. For brain, one would want to include these but for other cancers, one might not want to include all in situ and benign cancers as death attributed to the invasive cancer. For this analyses, all were included no matter what the original cancer site was.

Since expected rate tables are not readily available for races other than white or black, other methodology was needed to evaluate survival differences by specific race/ethnicity groups. Therefore, cause-specific rates were used in this chapter. Since there isn't a standard set of causes of death to use as deaths due to the disease under study, a study is underway to evaluate which causes would be optimal for each individual primary site. For this chapter, a more generic set of causes of death were used, namely, any cancer cause of death plus AIDS and benign/borderline/in situ cancer deaths. Therefore, the survival rates presented here will be slightly lower than if a more site-specific approach were used because for persons with multiple primaries, the cancer death due to the second primary would be considered

Table 31.1: Number of Cases and 5-Year (5-Yr) Cause-Specific (C-S) Survival Rates (%) Using the Actuarial Method by Selected Primary Site and Race/Ethnicity, Males & Females, Ages 20+, 12 SEER Areas, 1988-2001.

	All races		White		Black		AI/AN	
Primary Site	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)
All Sites excluding KS	1,595,392	61.7	1,336,148	62.7	147,982	53.1	5,128	52.4
Oral Cavity and Pharynx	38,367	58.3	30,926	60.5	4,137	39.1	145	46.6
Lip	3,953	91.0	3,864	91.3	39	74.9	13	~
Tongue	8,560	53.9	7,062	56.1	903	34.9	24	~
Nasopharynx	2,857	57.0	1,250	49.0	247	48.9	27	48.8
Digestive System	289,603	44.1	231,220	45.1	29,563	36.7	1,127	31.9
Esophagus	14,749	13.8	11,438	14.5	2,367	10.5	43	12.0
Stomach	31,117	22.3	21,851	20.2	3,690	22.3	192	13.8
Small Intestine	4,817	52.2	3,807	52.8	695	52.0	20	~
Colon and Rectum	179,453	59.9	147,992	60.3	16,545	52.3	519	52.7
Colon excluding Rectum	127,087	60.1	104,792	60.6	12,487	52.3	350	54.0
Rectum/Rectosigmoid	52,366	59.4	43,200	59.6	4,058	52.2	169	50.2
Liver/Intrahepatic Bile Duct	13,347	10.2	8,668	9.8	1,491	6.0	103	10.1
Gallbladder & Other Biliary	8,720	17.4	6,950	17.1	610	16.4	113	13.6
Pancreas	29,180	4.4	23,565	4.3	3,383	3.8	106	5.1
Respiratory System	215,839	19.7	177,767	20.1	24,289	16.8	533	14.6
Larynx	14,788	65.7	12,058	67.3	2,129	55.3	31	42.0
Lung and Bronchus	197,654	15.6	162,978	16.0	21,823	12.6	482	12.7
Bones and Joints	3,457	66.5	2,881	66.3	305	68.9	23	~
Soft Tissue including Heart	10,070	64.1	8,164	65.0	1,076	58.5	62	62.4
Skin except Basal/Squamous	60,765	86.1	59,126	86.2	765	84.2	82	77.1
Melanoma of the Skin	55,137	86.0	54,284	86.2	308	68.6	65	72.6
Other Non-Epithelial Skin	5,628	87.2	4,842	86.0	457	94.7	17	~
Breast	257,436	83.9	217,297	84.9	21,690	72.2	793	74.6
Female Genital System	103,856	67.7	87,441	68.3	8,250	56.9	466	63.6
Cervix Uteri	21,240	72.0	16,058	73.1	2,789	63.2	139	69.6
Corpus and Uterus, NOS	48,820	80.9	42,302	82.2	3,138	60.1	161	77.4
Ovary	27,275	41.4	23,477	40.7	1,752	38.4	137	40.5
Male Genital System	286,438	87.2	237,885	87.7	33,108	82.8	676	81.6
Prostate	272,580	86.9	225,162	87.4	32,681	82.8	600	80.9
Testis	12,241	95.5	11,379	95.8	293	87.4	65	90.0
Urinary System	102,313	72.5	90,831	73.2	6,498	64.1	337	66.4
Urinary Bladder	66,937	77.1	61,113	77.8	3,023	63.0	96	69.1
Kidney and Renal Pelvis	33,224	64.3	27,961	64.1	3,260	66.0	234	66.1
Eye and Orbit	2,375	76.4	2,175	75.9	96	79.2	18	~
Brain and Other Nervous	23,018	32.7	20,330	31.6	1,415	40.1	90	44.3
Endocrine System	28,327	91.0	23,107	91.2	1,602	87.7	146	91.9
Thyroid	25,919	93.9	21,274	94.0	1,352	92.1	132	94.0
Myeloma	18,044	31.7	13,985	30.7	2,960	34.9	85	21.4
Leukemia	42,994	47.4	37,011	48.5	3,103	39.7	187	37.0
Acute Lymphocytic	6,640	63.1	5,549	63.9	442	53.5	59	46.7
Chronic Lymphocytic	12,903	71.6	11,787	72.5	825	58.5	29	58.7
Acute Myeloid	12,056	18.5	10,039	18.0	890	19.0	52	19.1
Chronic Myeloid	6,013	41.1	4,967	41.1	564	39.8	30	28.4
Mesothelioma	3,488	7.2	3,175	7.0	179	12.1	16	~
Miscellaneous	31,032	15.8	25,559	16.4	3,303	11.4	129	10.0
Hodgkin Lymphoma	12,172	85.1	10,551	85.4	1,170	82.7	21	~
Non-Hodgkin Lymphoma	65,798	58.2	56,717	58.4	4,473	57.1	192	46.2

~ Statistic not displayed due to less than 25 cases.

AI/AN: American Indian/Alaska Native; API: Asian/Pacific Islander; NOS: Not otherwise specified.

Table 31.1 (continued): Number of Cases and 5-Year (5-Yr) Cause-Specific (C-S) Survival Rates (%) by Selected Site and Race/Ethnicity, Males & Females, Ages 20+, 12 SEER Areas, 1988-2001.

	API		Hispanic		Non-Hispanic	
Primary Site	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)
All Sites excluding KS	106,134	60.5	109,356	61.7	1,486,036	61.7
Oral Cavity and Pharynx	3,159	61.6	2,203	57.2	36,164	58.3
Lip	37	85.3	195	90.7	3,758	91.1
Tongue	571	56.9	475	50.6	8,085	54.1
Nasopharynx	1,333	66.1	157	45.0	2,700	57.7
Digestive System	27,693	44.3	21,249	39.3	268,354	44.5
Esophagus	901	13.8	824	13.7	13,925	13.8
Stomach	5,384	30.8	3,787	23.0	27,330	22.2
Small Intestine	295	46.0	309	51.4	4,508	52.3
Colon and Rectum	14,397	64.4	10,684	58.4	168,769	60.0
Colon excluding Rectum	9,458	64.6	7,054	59.0	120,033	60.2
Rectum/Rectosigmoid	4,939	63.9	3,630	57.2	48,736	59.5
Liver/Intrahepatic Bile Duct	3,085	12.9	1,713	12.8	11,634	9.8
Gallbladder & Other Biliary	1,047	20.3	1,253	18.7	7,467	17.2
Pancreas	2,126	6.0	2,050	6.8	27,130	4.2
Respiratory System	13,250	19.7	9,622	20.4	206,217	19.7
Larynx	570	71.6	883	62.9	13,905	65.9
Lung and Bronchus	12,371	16.3	8,368	14.1	189,286	15.7
Bones and Joints	248	68.3	511	66.4	2,946	66.5
Soft Tissue including Heart	768	62.7	1,160	65.5	8,910	63.9
Skin except Basal/Squamous	792	83.2	1,937	83.3	58,828	86.2
Melanoma of the Skin	480	76.4	1,581	81.1	53,556	86.2
Other Non-Epithelial Skin	312	93.2	356	92.8	5,272	86.8
Breast	17,656	86.9	17,178	81.4	240,258	84.1
Female Genital System	7,699	72.8	9,985	70.8	93,871	67.4
Cervix Uteri	2,254	75.4	4,190	76.0	17,050	71.1
Corpus and Uterus, NOS	3,219	82.8	3,154	79.6	45,666	80.9
Ovary	1,909	52.9	2,120	48.8	25,155	40.8
Male Genital System	14,769	87.9	18,288	87.5	268,150	87.2
Prostate	14,137	87.7	16,538	87.2	256,042	86.9
Testis	504	94.2	1,537	93.0	10,704	95.8
Urinary System	4,647	71.3	6,067	69.6	96,246	72.7
Urinary Bladder	2,705	77.0	2,843	75.0	64,094	77.2
Kidney and Renal Pelvis	1,769	64.4	3,111	65.4	30,113	64.2
Eye and Orbit	86	87.4	232	86.3	2,143	75.5
Brain and Other Nervous	1,183	42.0	2,225	42.9	20,793	31.7
Endocrine System	3,472	91.4	3,402	91.1	24,925	91.0
Thyroid	3,161	93.9	3,132	93.7	22,787	93.9
Myeloma	1,014	39.3	1,408	33.5	16,636	31.6
Leukemia	2,693	41.6	4,277	51.0	38,717	47.0
Acute Lymphocytic	590	64.2	1,713	64.6	4,927	62.5
Chronic Lymphocytic	262	74.0	475	66.6	12,428	71.8
Acute Myeloid	1,075	23.2	1,141	29.6	10,915	17.3
Chronic Myeloid	452	43.5	609	46.4	5,404	40.5
Mesothelioma	118	7.9	309	6.7	3,179	7.3
Miscellaneous	2,041	15.6	2,427	15.8	28,605	15.8
Hodgkin Lymphoma	430	81.8	1,362	81.5	10,810	85.5
Non-Hodgkin Lymphoma	4,416	57.9	5,514	57.6	60,284	58.3

Table 31.2: Number of Cases and 5-Year (5-Yr) Cause-Specific (C-S) Survival Rates (%) Using the Actuarial Method by Selected Primary Site and Race/Ethnicity, Males, Ages 20+, 12 SEER Areas, 1988-2001.

	All races		White		Black		AI/AN	
Primary Site	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)
All Sites excluding KS	828,041	60.4	690,875	61.6	81,571	53.7	2,435	49.7
Oral Cavity and Pharynx	25,899	56.4	20,770	59.3	2,964	34.8	105	45.5
Lip	3,210	91.1	3,162	91.1	17	~	12	~
Tongue	5,700	51.9	4,690	54.5	670	32.5	15	~
Nasopharynx	1,980	56.5	848	50.0	176	48.5	19	~
Digestive System	154,650	42.1	122,891	43.2	15,234	33.7	605	32.0
Esophagus	11,028	13.6	8,587	14.4	1,670	9.4	37	14.2
Stomach	19,281	20.3	13,779	18.3	2,204	19.8	113	14.7
Small Intestine	2,520	51.5	1,986	51.6	357	52.7	13	~
Colon and Rectum	91,330	59.4	75,434	59.8	7,726	51.3	275	53.2
Colon excluding Rectum	61,761	59.9	51,066	60.4	5,604	51.9	179	55.4
Rectum/Rectosigmoid	29,569	58.3	24,368	58.7	2,122	49.6	96	49.1
Liver/Intrahepatic Bile Duct	9,085	9.6	5,765	9.0	1,062	5.5	70	8.6
Gallbladder & Other Biliary	3,459	18.6	2,709	18.8	234	17.2	35	14.5
Pancreas	14,719	4.2	11,967	4.2	1,625	3.2	45	5.7
Respiratory System	129,278	19.3	104,595	19.8	15,715	16.0	330	14.4
Larynx	11,848	65.9	9,657	67.6	1,673	54.3	26	46.3
Lung and Bronchus	115,384	13.8	93,290	14.1	13,852	11.0	294	11.3
Bones and Joints	1,970	65.2	1,650	65.0	162	66.0	10	~
Soft Tissue including Heart	5,532	63.8	4,503	64.9	570	57.5	33	56.3
Skin except Basal/Squamous	33,199	83.1	32,407	83.1	365	82.3	36	75.4
Melanoma of the Skin	30,143	82.9	29,726	83.1	155	65.8	31	74.6
Other Non-Epithelial Skin	3,056	84.5	2,681	83.3	210	94.3	5	~
Breast	1,680	79.5	1,383	81.6	211	63.6	<5	~
Male Genital System	286,438	87.2	237,885	87.7	33,108	82.8	676	81.6
Prostate	272,580	86.9	225,162	87.4	32,681	82.8	600	80.9
Testis	12,241	95.5	11,379	95.8	293	87.4	65	90.0
Urinary System	71,903	73.8	64,453	74.4	3,968	65.7	222	67.6
Urinary Bladder	49,973	78.4	45,934	78.9	1,943	67.0	81	71.9
Kidney and Renal Pelvis	20,601	63.4	17,406	63.4	1,912	64.7	138	65.7
Eye and Orbit	1,307	77.2	1,208	77.1	48	74.8	11	~
Brain and Other Nervous	13,066	31.6	11,610	30.6	742	40.7	46	43.8
Endocrine System	7,632	84.9	6,383	85.4	401	78.1	36	85.9
Thyroid	6,291	90.2	5,361	90.5	284	83.6	27	88.6
Myeloma	9,653	32.9	7,634	31.8	1,418	36.0	46	22.7
Leukemia	24,772	47.6	21,420	48.9	1,676	39.6	102	35.5
Acute Lymphocytic	3,803	61.8	3,183	62.6	241	55.0	34	45.4
Chronic Lymphocytic	7,677	70.5	7,014	71.6	477	54.6	14	~
Acute Myeloid	6,518	17.2	5,469	16.9	432	19.4	28	21.8
Chronic Myeloid	3,492	39.7	2,875	39.7	326	36.9	16	~
Mesothelioma	2,741	4.8	2,505	4.5	131	10.3	12	~
Miscellaneous	15,365	18.0	12,612	19.2	1,646	10.2	53	14.9
Hodgkin Lymphoma	6,667	83.8	5,799	84.3	630	80.2	10	~
Non-Hodgkin Lymphoma	36,289	57.4	31,167	57.7	2,582	56.0	99	40.5

~ Statistic not displayed due to less than 25 cases.

AI/AN: American Indian/Alaska Native; API: Asian/Pacific Islander; NOS: Not otherwise specified.

Table 31.2 (continued): Number of Cases and 5-Year (5-Yr) Cause-Specific (C-S) Survival Rates (%) by Selected Site and Race/Ethnicity, Males, Ages 20+, 12 SEER Areas, 1988-2001.

	API		Hispanic		Non-Hispanic	
Primary Site	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)
All Sites excluding KS	53,160	55.2	53,674	59.6	774,367	60.4
Oral Cavity and Pharynx	2,060	58.6	1,494	53.2	24,405	56.6
Lip	19	~	159	89.8	3,051	91.2
Tongue	325	54.0	302	45.2	5,398	52.3
Nasopharynx	937	63.7	103	43.7	1,877	57.2
Digestive System	15,920	42.2	11,487	38.2	143,163	42.4
Esophagus	734	13.3	653	13.4	10,375	13.6
Stomach	3,185	29.8	2,187	21.1	17,094	20.3
Small Intestine	164	50.6	158	51.4	2,362	51.6
Colon and Rectum	7,895	63.4	5,728	57.9	85,602	59.5
Colon excluding Rectum	4,912	64.4	3,568	59.1	58,193	60.0
Rectum/Rectosigmoid	2,983	61.8	2,160	56.1	27,409	58.5
Liver/Intrahepatic Bile Duct	2,188	13.2	1,143	12.0	7,942	9.3
Gallbladder & Other Biliary	481	18.5	405	18.7	3,054	18.6
Pancreas	1,082	5.0	965	5.7	13,754	4.1
Respiratory System	8,638	19.4	5,930	20.7	123,348	19.3
Larynx	492	72.0	740	63.4	11,108	66.1
Lung and Bronchus	7,948	15.2	4,933	12.2	110,451	13.9
Bones and Joints	148	69.5	295	66.3	1,675	65.1
Soft Tissue including Heart	426	60.7	626	64.4	4,906	63.8
Skin except Basal/Squamous	391	79.6	814	77.5	32,385	83.2
Melanoma of the Skin	231	71.5	643	73.8	29,500	83.1
Other Non-Epithelial Skin	160	91.1	171	91.5	2,885	84.1
Breast	83	83.2	71	70.0	1,609	79.9
Male Genital System	14,769	87.9	18,288	87.5	268,150	87.2
Prostate	14,137	87.7	16,538	87.2	256,042	86.9
Testis	504	94.2	1,537	93.0	10,704	95.8
Urinary System	3,260	72.1	3,986	69.7	67,917	74.0
Urinary Bladder	2,015	78.5	2,079	77.0	47,894	78.5
Kidney and Renal Pelvis	1,145	62.6	1,839	62.1	18,762	63.6
Eye and Orbit	40	87.0	136	89.8	1,171	75.9
Brain and Other Nervous	668	39.6	1,215	41.8	11,851	30.6
Endocrine System	812	84.7	749	83.2	6,883	85.1
Thyroid	619	90.4	589	90.4	5,702	90.1
Myeloma	555	40.8	764	35.0	8,889	32.7
Leukemia	1,574	40.2	2,435	51.0	22,337	47.3
Acute Lymphocytic	345	60.6	992	63.2	2,811	61.2
Chronic Lymphocytic	172	71.1	283	66.6	7,394	70.6
Acute Myeloid	589	18.7	599	28.3	5,919	16.1
Chronic Myeloid	275	43.9	361	43.6	3,131	39.2
Mesothelioma	93	6.1	237	5.5	2,504	4.7
Miscellaneous	1,054	16.3	1,170	16.7	14,195	18.1
Hodgkin Lymphoma	228	79.0	803	78.9	5,864	84.4
Non-Hodgkin Lymphoma	2,441	55.7	3,174	55.9	33,115	57.5

Table 31.3: Number of Cases and 5-Year (5-Yr) Cause-Specific (C-S) Survival Rates (%) Using the Actuarial Method by Selected Primary Site and Race/Ethnicity, Females, Ages 20+, 12 SEER Areas, 1988-2001.

	All races		White		Black		AI/AN	
Primary Site	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)
All Sites excluding KS	767,351	63.1	645,273	64.0	66,411	52.5	2,693	54.8
Oral Cavity and Pharynx	12,468	62.0	10,156	62.8	1,173	49.9	40	50.2
Lip	743	90.7	702	92.0	22	~	1	~
Tongue	2,860	57.7	2,372	59.0	233	41.5	9	~
Nasopharynx	877	58.2	402	46.8	71	49.9	8	~
Digestive System	134,953	46.4	108,329	47.2	14,329	39.9	522	31.9
Esophagus	3,721	14.6	2,851	14.9	697	13.2	6	~
Stomach	11,836	25.5	8,072	23.6	1,486	26.0	79	12.8
Small Intestine	2,297	52.9	1,821	54.1	338	51.1	7	~
Colon and Rectum	88,123	60.4	72,558	60.8	8,819	53.1	244	52.1
Colon excluding Rectum	65,326	60.2	53,726	60.8	6,883	52.6	171	52.5
Rectum/Rectosigmoid	22,797	60.8	18,832	60.7	1,936	55.0	73	51.8
Liver/Intrahepatic Bile Duct	4,262	11.2	2,903	11.5	429	6.6	33	13.7
Gallbladder & Other Biliary	5,261	16.6	4,241	16.1	376	15.9	78	13.2
Pancreas	14,461	4.6	11,598	4.4	1,758	4.4	61	4.8
Respiratory System	86,561	20.3	73,172	20.5	8,574	18.3	203	14.9
Larynx	2,940	64.8	2,401	65.8	456	58.9	5	~
Lung and Bronchus	82,270	18.1	69,688	18.5	7,971	15.4	188	14.4
Bones and Joints	1,487	68.2	1,231	68.0	143	72.0	13	~
Soft Tissue including Heart	4,538	64.4	3,661	65.0	506	59.5	29	69.4
Skin except Basal/Squamous	27,566	89.8	26,719	89.9	400	85.9	46	78.3
Melanoma of the Skin	24,994	89.7	24,558	90.0	153	71.4	34	70.7
Other Non-Epithelial Skin	2,572	90.3	2,161	89.3	247	94.9	12	~
Breast	255,756	84.0	215,914	84.9	21,479	72.3	790	74.5
Female Genital System	103,856	67.7	87,441	68.3	8,250	56.9	466	63.6
Cervix Uteri	21,240	72.0	16,058	73.1	2,789	63.2	139	69.6
Corpus and Uterus, NOS	48,820	80.9	42,302	82.2	3,138	60.1	161	77.4
Ovary	27,275	41.4	23,477	40.7	1,752	38.4	137	40.5
Urinary System	30,410	69.4	26,378	70.2	2,530	61.7	115	64.1
Urinary Bladder	16,964	73.0	15,179	74.2	1,080	55.8	15	~
Kidney and Renal Pelvis	12,623	65.8	10,555	65.5	1,348	67.8	96	66.5
Eye and Orbit	1,068	75.5	967	74.4	48	83.4	7	~
Brain and Other Nervous	9,952	34.2	8,720	33.1	673	39.4	44	43.6
Endocrine System	20,695	93.3	16,724	93.4	1,201	91.0	110	93.8
Thyroid	19,628	95.1	15,913	95.2	1,068	94.4	105	95.4
Myeloma	8,391	30.5	6,351	29.3	1,542	33.8	39	20.4
Leukemia	18,222	47.0	15,591	48.0	1,427	39.9	85	38.9
Acute Lymphocytic	2,837	64.9	2,366	65.7	201	51.7	25	47.8
Chronic Lymphocytic	5,226	73.3	4,773	73.9	348	63.7	15	~
Acute Myeloid	5,538	20.0	4,570	19.2	458	18.6	24	~
Chronic Myeloid	2,521	43.1	2,092	43.1	238	44.0	14	~
Mesothelioma	747	15.8	670	15.9	48	16.6	4	~
Miscellaneous	15,667	13.7	12,947	13.8	1,657	12.5	76	7.1
Hodgkin Lymphoma	5,505	86.6	4,752	86.8	540	85.4	11	~
Non-Hodgkin Lymphoma	29,509	59.2	25,550	59.2	1,891	58.4	93	51.9

~ Statistic not displayed due to less than 25 cases.

AI/AN: American Indian/Alaska Native; API: Asian/Pacific Islander; NOS: Not otherwise specified.

Table 31.3 (continued): Number of Cases and 5-Year (5-Yr) Cause-Specific (C-S) Survival Rates (%) by Selected Site and Race/Ethnicity, Females, Ages 20+, 12 SEER Areas, 1988-2001.

	API		Hispanic		Non-Hispanic	
Primary Site	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)	Cases	5-Yr C-S Rate (%)
All Sites excluding KS	52,974	65.7	55,682	63.7	711,669	63.0
Oral Cavity and Pharynx	1,099	67.3	709	65.5	11,759	61.8
Lip	18	~	36	93.5	707	90.5
Tongue	246	60.3	173	59.8	2,687	57.6
Nasopharynx	396	72.3	54	47.0	823	58.9
Digestive System	11,773	47.0	9,762	40.6	125,191	46.8
Esophagus	167	15.8	171	14.9	3,550	14.6
Stomach	2,199	32.4	1,600	25.7	10,236	25.5
Small Intestine	131	40.3	151	51.4	2,146	53.0
Colon and Rectum	6,502	65.5	4,956	58.9	83,167	60.4
Colon excluding Rectum	4,546	64.9	3,486	58.9	61,840	60.3
Rectum/Rectosigmoid	1,956	66.9	1,470	58.9	21,327	60.9
Liver/Intrahepatic Bile Duct	897	12.4	570	14.1	3,692	10.8
Gallbladder & Other Biliary	566	21.9	848	18.5	4,413	16.3
Pancreas	1,044	7.1	1,085	7.7	13,376	4.4
Respiratory System	4,612	20.1	3,692	20.0	82,869	20.3
Larynx	78	69.4	143	60.3	2,797	65.0
Lung and Bronchus	4,423	18.2	3,435	16.8	78,835	18.2
Bones and Joints	100	66.7	216	66.6	1,271	68.5
Soft Tissue including Heart	342	64.8	534	66.5	4,004	64.1
Skin except Basal/Squamous	401	86.8	1,123	87.4	26,443	89.9
Melanoma of the Skin	249	81.2	938	86.0	24,056	89.9
Other Non-Epithelial Skin	152	95.5	185	93.8	2,387	90.0
Breast	17,573	86.9	17,107	81.5	238,649	84.1
Female Genital System	7,699	72.8	9,985	70.8	93,871	67.4
Cervix Uteri	2,254	75.4	4,190	76.0	17,050	71.1
Corpus and Uterus, NOS	3,219	82.8	3,154	79.6	45,666	80.9
Ovary	1,909	52.9	2,120	48.8	25,155	40.8
Urinary System	1,387	69.5	2,081	69.5	28,329	69.4
Urinary Bladder	690	72.5	764	69.6	16,200	73.2
Kidney and Renal Pelvis	624	67.6	1,272	70.3	11,351	65.3
Eye and Orbit	46	88.6	96	82.0	972	75.0
Brain and Other Nervous	515	45.4	1,010	44.3	8,942	33.0
Endocrine System	2,660	93.3	2,653	93.3	18,042	93.3
Thyroid	2,542	94.7	2,543	94.5	17,085	95.2
Myeloma	459	37.6	644	31.8	7,747	30.3
Leukemia	1,119	43.5	1,842	51.1	16,380	46.6
Acute Lymphocytic	245	69.2	721	66.5	2,116	64.3
Chronic Lymphocytic	90	79.8	192	66.5	5,034	73.6
Acute Myeloid	486	28.5	542	31.1	4,996	18.7
Chronic Myeloid	177	43.1	248	50.5	2,273	42.3
Mesothelioma	25	16.2	72	10.5	675	16.4
Miscellaneous	987	15.0	1,257	15.0	14,410	13.6
Hodgkin Lymphoma	202	85.2	559	85.1	4,946	86.8
Non-Hodgkin Lymphoma	1,975	60.6	2,340	59.7	27,169	59.2

Table 31.4: Cancer of the Lung - Males & Females: 5-Year Cause-Specific Survival Rates (%) by Race/Ethnicity and Historic Stage, Ages 20+, 12 SEER Areas, 1991-2001.

		Stage Distribution				5-Year Cause-Specific Survival Rate (%)				
		Loc	Reg	Dist	Uns	All	Loc	Reg	Dist	Uns
Race/Ethnicity	Cases	Percent	Percent	Percent	Percent	Rate (%)	Rate (%)	Rate (%)	Rate (%)	Rate (%)
All Races	162,121	16.4	38.0	39.2	6.4	15.6	49.9	15.7	1.9	11.2
White	132,779	16.9	37.8	38.9	6.5	16.0	50.5	16.0	1.8	11.1
White non-Hispanic	125,570	17.0	37.7	38.8	6.4	16.1	50.7	16.2	1.8	10.9
White Hispanic	7,209	14.2	38.0	40.6	7.2	13.6	47.0	13.1	2.0	14.6
Black	18,202	14.2	38.5	40.8	6.5	12.6	43.4	12.9	1.6	11.0
AI/AN	399	16.8	37.1	40.6	5.5	13.4	41.7	13.5	1.6	~
Asian	9,490	14.4	40.7	39.1	5.8	17.0	52.8	17.5	3.4	11.6
Asian Indian/Pakistani	151	16.6	44.4	35.1	4.0	23.0	54.8	18.2	9.7	~
Chinese	2,864	13.2	40.1	39.6	7.2	15.5	50.0	16.8	2.7	10.8
Filipino	2,470	14.6	41.1	38.5	5.8	18.8	53.6	19.1	5.3	11.5
Korean	753	11.7	43.4	38.5	6.4	13.9	50.0	13.6	3.4	11.7
Japanese	2,157	16.6	40.4	39.2	3.9	17.5	55.9	17.8	2.0	4.9
Vietnamese	659	15.2	37.6	42.3	4.9	16.3	43.0	18.2	4.9	22.9
Other Asian	436	13.8	41.5	37.6	7.1	18.1	68.7	17.0	1.8	14.1
Pacific Islander	1,251	13.2	38.1	43.3	5.4	12.6	43.8	14.0	2.3	8.3
Hawaiian	1,010	13.8	37.9	42.6	5.7	12.8	44.4	13.7	2.3	9.5
Other Pacific Islander	241	10.8	39.0	46.5	3.7	11.9	41.0	15.8	!	~

! Not enough intervals to produce rate.
~ Less than 25 cases.
AI/AN: American Indian/Alaska Native; Loc: Localized; Reg: Regional; Dis: Distant; Uns: Unstaged.

a cancer death for the first. Using only the specific cancer as the cause of death, however, overestimates the c-s survival rates. The main point is that if the same definitions for what is considered a 'cancer' death are used across all of the racial groups, then the survival rates can be compared for the racial/ethnic groups. An assumption is that the assignment of the cause of death does not vary across racial/ethnic groups. Another assumption is that there is access to the underlying cause of death for all of the racial/ethnic groups. Several years ago, it was difficult to obtain the underlying cause of death if the person moved out of the state where they were diagnosed and died. However, the National Death Index is now being used to obtain these, A concern, however, would be if there are subgroups who would be more likely than others to return to their original or ancestral country to die. Research is on-going to try to evaluate differences in follow-up rates and non-access to causes of death by race/ethnicity to evaluate the impact on survival differences.

Differences in access to and utilization of effective cancer screening and treatment services by race/ethnicity might explain some of our findings. Other possible explanations for the observed racial/ethnic differences in survival include differences in access to optimal treatments that reduce cancer mortality. In addition, unmeasured biological determinants might partly explain our findings.

Limitations of our study include the relatively small number of cancers diagnosed in some minorities, particularly Native-Americans and Native-Hawaiians. In addition, our analyses only considered tumor stage at diagnosis and not other potential prognostic factors such as tumor size, grade, lymph node status, other patient characteristics such as age, socioeconomic status, co-morbid diseases, and health insurance status. Additional research is needed to clarify the role of socioeconomic, medical, biological, cultural and other determinants of racial/ethnic differences in cancer patient survival described in this report.

Table 31.5: Cancer of the Lung - Males: 5-Year Cause-Specific Survival Rates (%) by Race/Ethnicity and Historic Stage, Ages 20+, 12 SEER Areas, 1991-2001.

		Stage Distribution				5-Year Cause-Specific Survival Rate (%)				
		Loc	Reg	Dist	Uns	All	Loc	Reg	Dist	Uns
Race/Ethnicity	Cases	Percent	Percent	Percent	Percent	Rate (%)	Rate (%)	Rate (%)	Rate (%)	Rate (%)
All Races	93,248	15.0	38.6	40.1	6.4	13.8	45.6	14.6	1.7	9.6
White	74,732	15.4	38.4	39.8	6.4	14.1	46.3	15.0	1.6	9.5
White non-Hispanic	70,499	15.5	38.4	39.7	6.4	14.2	46.6	15.1	1.5	9.1
White Hispanic	4,233	12.9	38.1	41.7	7.3	11.9	41.2	12.1	1.9	14.8
Black	11,420	13.1	38.3	42.2	6.3	10.9	39.1	11.7	1.3	9.2
AI/AN	245	16.7	38.4	40.8	4.1	12.5	39.3	13.1	1.2	~
Asian	6,080	14.1	41.3	38.7	6.0	15.8	47.3	16.4	3.5	12.6
Asian Indian/Pakistani	97	17.5	49.5	30.9	2.1	25.7	~	17.1	!	~
Chinese	1,724	14.0	40.6	37.9	7.4	14.9	43.7	15.6	2.8	12.3
Filipino	1,719	13.7	41.1	39.2	6.0	17.4	49.5	18.3	5.2	14.3
Korean	485	11.1	46.0	36.3	6.6	11.7	40.0	11.5	2.9	11.6
Japanese	1,337	14.8	41.1	39.4	4.6	15.4	53.9	16.0	1.4	4.5
Vietnamese	460	17.2	38.3	40.9	3.7	16.7	35.3	19.8	5.9	~
Other Asian	258	12.0	40.3	40.7	7.0	15.2	54.0	14.2	3.2	~
Pacific Islander	771	12.1	38.7	42.9	6.4	11.4	43.8	11.4	2.8	5.4
Hawaiian	620	13.1	38.2	41.9	6.8	12.0	44.2	11.5	3.3	6.1
Other Pacific Islander	151	7.9	40.4	47.0	4.6	8.8	~	12.0	0.0	~

!Not enough intervals to produce rate.
~Less than 25 cases.
AI/AN: American Indian/Alaska Native; Loc: Localized; Reg: Regional; Dis: Distant; Uns: Unstaged.

Table 31.6: Cancer of the Lung - Females: 5-Year Cause-Specific Survival Rates (%) by Race/Ethnicity and Historic Stage, Ages 20+, 12 SEER Areas, 1991-2001.

		Stage Distribution				5-Year Cause-Specific Survival Rate (%)				
		Loc	Reg	Dist	Uns	All	Loc	Reg	Dist	Uns
Race/Ethnicity	Cases	Percent	Percent	Percent	Percent	Rate (%)	Rate (%)	Rate (%)	Rate (%)	Rate (%)
All Races	68,873	18.3	37.3	37.9	6.5	18.1	54.6	17.2	2.2	13.2
White	58,047	18.8	36.9	37.7	6.5	18.4	54.9	17.4	2.2	13.2
White non-Hispanic	55,071	19.0	36.9	37.6	6.5	18.5	54.9	17.5	2.2	13.1
White Hispanic	2,976	16.1	37.9	39.0	7.0	16.0	53.8	14.7	2.2	14.0
Black	6,782	15.9	38.9	38.5	6.8	15.5	49.5	14.8	2.1	13.9
AI/AN	154	16.9	35.1	40.3	7.8	14.5	44.5	13.6	!	~
Asian	3,410	15.0	39.6	39.9	5.5	19.1	61.9	19.5	3.3	10.5
Asian Indian/Pakistani	54	14.8	35.2	42.6	7.4	21.2	~	~	~	~
Chinese	1,140	11.8	39.4	42.0	6.8	16.3	62.0	18.5	2.6	8.5
Filipino	751	16.8	41.0	36.9	5.3	21.8	60.8	20.8	5.3	8.0
Korean	268	12.7	38.8	42.5	6.0	18.1	66.0	17.4	4.4	~
Japanese	820	19.4	39.1	38.8	2.7	20.8	58.4	20.9	2.9	~
Vietnamese	199	10.6	36.2	45.7	7.5	15.6	~	14.0	2.5	~
Other Asian	178	16.3	43.3	33.1	7.3	22.5	84.1	20.6	0.0	~
Pacific Islander	480	15.0	37.3	44.0	3.8	14.6	44.1	18.3	!	~
Hawaiian	390	14.9	37.4	43.6	4.1	14.2	45.0	17.5	!	~
Other Pacific Islander	90	15.6	36.7	45.6	2.2	17.4	~	22.5	!	~

! Not enough intervals to produce rate.
~ Less than 25 cases.
AI/AN: American Indian/Alaska Native; Loc: Localized; Reg: Regional; Dis: Distant; Uns: Unstaged.

Table 31.7: Cancer of the Female Breast: 5-Year Cause-Specific Survival Rates (%) by Race/Ethnicity and Historic Stage, Ages 20+, 12 SEER Areas, 1991-2001.

		Stage Distribution				5-Year Cause-Specific Survival Rate (%)				
		Loc	Reg	Dist	Uns	All	Loc	Reg	Dist	Uns
Race/Ethnicity	Cases	Percent	Percent	Percent	Percent	Rate (%)	Rate (%)	Rate (%)	Rate (%)	Rate (%)
All Races	215,368	62.7	30.0	5.5	1.8	84.2	93.2	77.4	22.9	63.1
White	180,640	63.7	29.4	5.2	1.7	85.1	93.5	78.8	24.1	64.8
White non-Hispanic	165,465	64.4	28.8	5.1	1.7	85.5	93.6	79.2	24.0	64.9
White Hispanic	15,175	55.7	35.7	6.5	2.1	81.6	92.3	75.7	25.5	64.2
Black	18,539	52.9	35.3	8.7	3.1	72.5	88.3	64.4	15.0	53.4
AI/AN	692	54.0	34.7	8.8	2.5	73.2	89.6	61.8	22.1	~
Asian	14,027	64.2	30.2	4.3	1.3	87.8	95.2	81.0	28.0	68.6
Asian Indian/Pakistani	571	53.4	37.8	7.0	1.8	82.3	94.7	75.4	29.9	~
Chinese	3,244	63.2	31.2	4.3	1.3	87.9	94.8	83.2	26.3	68.4
Filipino	3,714	60.4	33.5	4.7	1.3	86.5	95.3	78.7	28.5	74.1
Korean	781	61.6	32.5	3.7	2.2	86.9	93.7	82.4	19.5	~
Japanese	4,004	71.8	23.8	3.5	0.9	90.6	95.9	84.6	29.1	63.1
Vietnamese	642	57.3	37.1	4.5	1.1	81.7	94.2	68.7	34.7	~
Other Asian	1,071	64.1	30.3	4.2	1.3	87.9	94.4	83.7	29.1	~
Pacific Islander	1,470	59.5	33.1	6.1	1.3	81.9	93.7	76.9	8.4	~
Hawaiian	1,209	61.6	32.2	5.4	0.8	83.4	93.7	78.1	9.9	~
Other Pacific Islander	261	49.4	37.5	9.6	3.4	74.6	93.8	71.9	4.6	~

~ Less than 25 cases.

AI/AN: American Indian/Alaska Native; Loc: Localized; Reg: Regional; Dis: Distant; Uns: Unstaged.

REFERENCES

1. American Cancer Society. Cancer Facts and Figures 2006. Atlanta: American Cancer Society, 2006.
2. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Eisner MP, Horner MJ, Howlader N, Hayat M, Hankey BF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site, 2006.
3. Ederer F, Axtell LM, Cutler SJ. The relative survival rate: A statistical methodology. Natl.Cancer.Inst.Monogr., 6: 101-121.
4. Clegg LX, Li FP, Hankey BF, Chu K, Edwards BK. Cancer Survival Among US Whites and Minorities: A SEER (Surveillance, Epidemiology, and End Results) Program Population-Based Study.PG -. Arch.Intern.Med., 162: 1985-1993.
5. Eley JW, Hill HA, Chen VW et al. Racial differences in survival from breast cancer. Results of the National Cancer Institute Black/White Cancer Survival Study. JAMA, 272: 947-954.
6. Yood MU, Johnson CC, Blount A et al. Race and differences in breast cancer survival in a managed care population. J Natl Cancer Inst, 91: 1487-1491.
7. Ragland KE, Selvin S, Merrill DW. Black-white differences in stage-specific cancer survival: analysis of seven selected sites. Am.J.Epidemiol., 133: 672-682.
8. Optenberg SA, Thompson IM, Friedrichs P, Wojcik B, Stein CR, Kramer B. Race, treatment, and long-term survival from prostate cancer in an equal-access medical care delivery system. JAMA, 274: 1599-1605.
9. Hankey BF, Ries LAG, Edwards BK. The SEER Program: A national resource. Cancer Epidemiology, 12: 1117-1121.
10. Rosenberg, H. M., Maurer, J. D., Sorlie, P. D., Johnson, N. J., MacDorman, M. F., Hoyert, D. L., Spitler, J. F., and Scott, C. Quality of Death Rates by Race and Hispanic Origin: a Summary of Current Research, 1999. 128. 9-1-1999. Hyattsville, MD, DHHS/CDC. Data Evaluation and Methods.
11. Percy C, Stanek E, Gloeckler L. Accuracy of cancer death certificates and its effect on cancer mortality statistics. Am J Public Health, 71: 242-250.

Table 31.8: Cancer of the Prostate: 5-Year Cause-Specific Survival Rates (%) by Race/Ethnicity and Historic Stage, Ages 20+, 12 SEER Areas, 1991-2001.

Race/Ethnicity	Cases	Stage Distribution			5-Year Cause-Specific Survival Rate (%)			
		Loc/Reg	Dist	Uns	All stages	Loc/Reg	Dis	Uns
		Percent	Percent	Percent	Rate (%)	Rate (%)	Rate (%)	Rate (%)
All Races	237,138	87.6	5.4	7.0	88.1	91.9	34.1	83.0
White	194,529	88.3	4.9	6.8	88.6	92.1	33.5	83.7
White non-Hispanic	179,510	88.4	4.8	6.8	88.7	92.0	33.3	84.1
White Hispanic	15,019	87.0	6.5	6.5	87.8	92.5	34.8	78.1
Black	29,487	83.5	7.7	8.8	84.5	90.1	31.5	78.9
AI/AN	496	87.5	9.3	3.2	82.9	89.0	20.6	~
Asian	11,768	86.9	7.5	5.6	89.3	93.2	49.2	83.6
Asian Indian/Pakistani	485	88.0	6.6	5.4	90.3	93.5	43.2	100.0
Chinese	2,848	87.3	7.8	5.0	90.6	94.2	47.0	91.9
Filipino	3,490	84.6	9.1	6.3	87.4	92.5	48.7	77.8
Korean	371	87.6	6.2	6.2	86.0	91.3	~	~
Japanese	3,741	88.1	6.3	5.6	90.3	93.1	54.6	87.4
Vietnamese	318	88.7	8.2	3.1	82.2	86.8	35.7	~
Other Asian	515	89.9	5.0	5.0	92.1	96.7	47.2	67.6
Pacific Islander	858	85.7	11.3	3.0	81.0	88.5	30.8	69.7
Hawaiian	639	87.5	10.2	2.3	83.1	88.7	36.1	~
Other Pacific Islander	219	80.4	14.6	5.0	74.4	87.7	21.1	~

~ Less than 25 cases.

AI/AN: American Indian/Alaska Native; Loc: Localized; Reg: Regional; Dis: Distant; Uns: Unstaged.

Table 31.9: Cancer of the Colon/rectum - Males & Females: 5-Year Cause-Specific Survival Rates (%) by Race/Ethnicity and Historic Stage, Ages 20+, 12 SEER Areas, 1991-2001.

Race/Ethnicity	Cases	Stage Distribution				5-Year Cause-Specific Survival Rate (%)				
		Loc	Reg	Dist	Uns	All	Loc	Reg	Dist	Uns
		Percent	Percent	Percent	Percent	Rate (%)	Rate (%)	Rate (%)	Rate (%)	Rate (%)
All Races	147,323	38.7	38.5	18.8	3.9	60.0	85.4	61.6	8.4	41.8
White	120,411	39.0	38.7	18.5	3.8	60.4	85.5	62.1	8.5	41.6
White non-Hispanic	111,058	39.3	38.6	18.3	3.8	60.6	85.5	62.2	8.3	41.7
White Hispanic	9,353	35.9	39.7	20.6	3.8	58.5	84.8	61.1	10.9	41.4
Black	14,052	35.3	35.8	23.2	5.7	52.4	81.2	55.0	6.7	42.3
AI/AN	440	32.3	40.0	25.9	1.8	51.3	84.7	52.8	6.7	~
Asian	11,641	39.6	40.6	16.3	3.5	64.8	88.8	64.6	10.1	42.6
Asian Indian/Pakistani	235	39.1	40.4	15.3	5.1	73.4	98.1	74.9	10.5	~
Chinese	3,385	38.3	41.2	16.4	4.1	63.7	89.3	63.0	8.8	44.6
Filipino	2,168	37.6	39.7	18.2	4.5	62.5	88.3	62.9	12.9	39.8
Korean	838	36.5	43.9	15.4	4.2	62.9	82.7	67.7	10.1	31.2
Japanese	3,881	42.5	39.9	15.3	2.2	65.9	88.9	64.2	8.0	40.4
Vietnamese	515	38.6	41.6	17.3	2.5	66.9	91.7	66.0	14.8	~
Other Asian	619	39.9	40.5	15.3	4.2	69.5	90.3	72.1	12.8	44.0
Pacific Islander	779	37.4	37.1	22.0	3.6	56.0	87.1	56.7	7.0	30.4
Hawaiian	650	37.5	37.1	21.5	3.8	57.1	87.5	58.7	7.1	33.8
Other Pacific Islander	129	36.4	37.2	24.0	2.3	50.0	85.1	45.5	6.8	~

~ Less than 25 cases.

AI/AN: American Indian/Alaska Native; Loc: Localized; Reg: Regional; Dis: Distant; Uns: Unstaged.