

## TECHNICAL NOTES

There are four measures that are commonly used to assess the impact of a cancer in the general population. The **incidence rate** is the number of new cases per year per 100,000 persons. The **death (or mortality) rate** is the number of deaths per year per 100,000 persons. The survival estimate is the proportion of patients alive at some point subsequent to the diagnosis of their cancer. The **prevalence count** is the number of people alive that have ever been diagnosed with a cancer. All four measures are employed in this report. The Surveillance, Epidemiology, and End Results (**SEER**) Program (<http://seer.cancer.gov>) (based within the Surveillance Research Program (**SRP**) at the National Cancer Institute (**NCI**)) collects incidence and survival data for all areas that participate in the Program. The National Center for Health Statistics (**NCHS**) provides mortality data for the entire United States (**US**). All incidence and mortality rates in this report are age-adjusted (see below) to the 2000 US standard population (see Appendix) unless otherwise specified. Age-adjustment minimizes the effect of a difference in age distributions when comparing rates.

### ***THE SEER PROGRAM***

The National Cancer Act of 1971 mandated the collection, analysis, and dissemination of data useful in the prevention, diagnosis, and treatment of cancer. This mandate led to the establishment of the SEER Program. The population-based cancer registries participating in NCI's SEER Program routinely collect data on all cancers occurring in residents of the participating areas. Trends in cancer incidence and patient survival in the US are derived from this database. See the SEER Research Data (<http://seer.cancer.gov/data/>) for more information.

The SEER Program is a sequel to two earlier NCI programs—the End Results Program and the Third National Cancer Survey. The initial SEER reporting areas were the States of **Connecticut, Iowa, New Mexico, Utah, and Hawaii**; the metropolitan areas of **Detroit, Michigan, and San Francisco-Oakland, California**; and the Commonwealth of Puerto Rico. Case ascertainment began with January 1, 1973, diagnoses.

In 1974-1975, the program was expanded to include the metropolitan area of New Orleans, Louisiana, the thirteen-county **Seattle-Puget Sound** area in the State of Washington, and the metropolitan area of **Atlanta, Georgia**. New Orleans participated in the program only through the 1977 data collection year. In 1978, ten predominantly African-American counties in **rural Georgia** were added. **American Indian residents of Arizona** were added in 1980. In 1983, four counties in New Jersey were added with coverage retrospective to 1979. New Jersey and Puerto Rico participated in the program until the end of the 1989 reporting year. The National Cancer Institute also began funding a cancer registry that, with technical assistance from SEER, collects information on cancer cases among **Alaska Native** populations residing in Alaska. In 1992, the SEER Program was expanded to increase coverage of minority populations, especially Hispanics, by adding **Los Angeles County** and four counties in the **San Jose-**

**Monterey** area south of San Francisco. In 2001, the SEER Program expanded coverage to include **Kentucky, Greater California** (the counties of California that were not already covered by SEER), **New Jersey**, and **Louisiana**.

The long-term incidence trends and survival data for this report are from five states (Connecticut, Hawaii, Iowa, New Mexico, and Utah) and four metropolitan areas (Detroit, Atlanta, San Francisco-Oakland, and Seattle-Puget Sound) (Fig. I-1); this set of registries is called the **SEER 9**. Additional tables show more recent incidence trends for the **SEER 13** areas (the 9 areas above plus Los Angeles, San Jose-Monterey, Alaska Native Registry, and rural Georgia) since 1992 and additional information on race and ethnicity. Other tables give statistics for the **SEER 17** areas; these are the SEER 13 plus Kentucky, Greater California, New Jersey, and Louisiana.

The participating regions were selected principally for their ability to operate and maintain a population-based cancer reporting system and for their epidemiologically significant population subgroups. With respect to selected demographic and epidemiologic factors, they are when combined a reasonably representative subset of the US population. Data from the 9, 13, or 17 SEER geographic areas are used in this report; the given areas contain, respectively, approximately 9, 14, or 26 percent of the US population. By the end of the 2006 diagnosis year, the database of 13 SEER and 4 expansion registries (plus Arizona Indians) contained information on over 7 million cases diagnosed since 1973. New cases added in the most recent data year numbered over 385,000.

The goals of the SEER Program are:

- 1) to assemble and report, on a periodic basis, estimates of cancer incidence, mortality, survival, and prevalence in the US;
- 2) to monitor annual cancer incidence trends to identify unusual changes in specific forms of cancer occurring in population subgroups defined by geographic and demographic characteristics;
- 3) to provide continuing information on trends over time in the extent of disease at diagnosis, trends in therapy, and associated changes in patient survival; and
- 4) to promote studies designed to identify factors amenable to cancer control interventions, such as: (a) environmental, occupational, socioeconomic, dietary, and health-related exposures; (b) screening practices, early detection and treatment; and (c) determinants of the length and quality of patient survival.

## ***DATA SOURCES***

### **INCIDENCE AND SURVIVAL DATA**

The SEER Program contracts with nonprofit, medically-oriented organizations having statutory responsibility for registering diagnoses of cancer among residents of their respective geographic coverage areas. Each SEER contractor:

- 1) maintains a cancer information reporting system;
- 2) abstracts records for *resident* cancer patients seen in every hospital both inside and outside the coverage area;
- 3) abstracts all death certificates of *residents* (dying both inside and outside the coverage area) on which cancer is listed as a cause of death;
- 4) strives for complete ascertainment of cases by searching records of private laboratories, radiotherapy units, nursing homes, and other health services units that provide diagnostic service;
- 5) registers all in situ and malignant neoplasms (with the exceptions of certain histologies for cancer of the skin and—beginning in 1996—in situ neoplasms of the cervix uteri);
- 6) records data on all newly diagnosed cancers, including selected patient demographics, primary site, morphology, diagnostic confirmation, extent of disease, and first course of cancer-directed therapy;
- 7) provides active follow-up on all living patients (except for those with in situ cancer of the cervix uteri);
- 8) maintains confidentiality of patient records;
- 9) at least annually submits electronically to NCI data on all reportable diagnoses of cancer made in residents of the coverage area.

For 1992 to 2000 diagnoses, the SEER program codes site and histology by the *International Classification of Diseases for Oncology*, second edition (**ICD-O-2**) (Percy, Van Holten, & Muir, 1990). All cases before 1992 were machine-converted to ICD-O-2. Beginning with 2001 diagnoses, cases have been coded according to the third edition (**ICD-O-3**) (Fritz et al., 2000). The primary site groupings used for incidence are found in the Appendix. Changes were made to the site recode for ICD-O-2 for comparability with cases coded to ICD-O-3. Follow-up rates are also in the Appendix.

**Underreporting Adjustment for Veterans Affairs Cases:** A recent policy change of the Department of Veterans Affairs (VA) regarding sharing of VA cancer data has resulted in incomplete reporting of VA hospital cases in some central cancer registries. The issue began to affect reporting in the 3<sup>rd</sup> quarter of 2004 diagnosis year and continues to be a concern through the 2007 diagnosis year. The section on VA reporting quantifies the missing number of VA patients in the SEER registries and provides adjustments of new case counts for 2005 and 2006 based on prior years information. These VA adjustment factors may be used to correct for underreporting of 2005, 2006, and 2007 age-specific incidence rates or age-adjusted incidence

rates for SEER-9 and SEER-17 regions. Underreporting appears more extensive for some population subgroups (e.g, adult Black males) and cancer sites (e.g., Lung and Bronchus, Prostate, and Liver and Intrahepatic Bile Duct). Additional details can be found in Howlader et al, 2009.

**Excluded cancers:** Some cancers were excluded from most of the analyses.

Myelodysplastic syndrome (MDS), for example, was reclassified in ICD-O-3 (effective diagnosis year 2001) from nonmalignant to malignant; other cancers so reclassified include endometrial stromal sarcoma (low grade), papillary ependymoma, papillary meningioma, polycythemia vera, chronic myeloproliferative disease (NOS), myelosclerosis with myeloid metaplasia, essential thrombocythemia, refractory anemia, refractory anemia with sideroblasts, refractory anemia with excess blasts, and refractory anemia with excess blasts in transformation. In contrast, borderline tumors of the ovary were reclassified from malignant to nonmalignant at the same time. In addition, benign brain/CNS tumors were collected beginning for 2004 diagnoses. All of these cancers were excluded from most of the analyses, especially time trends. Pilocytic astrocytoma, although reclassified in ICD-O-3, was not excluded. Separate tables for MDS and benign brain/CNS are shown.

## **MORTALITY DATA**

The SEER Program annually obtains from the National Center for Health Statistics (NCHS) a file containing information on all deaths occurring in the US by calendar year. Information on each death includes age at death, sex, geographic area of residence, and underlying and contributing causes of death. For this publication, only the underlying cause of death is used in the calculation of death rates. Cause of death for 1969-1978 was coded according to ICD-8; for 1979-1998, ICD-9 was used; beginning with deaths in 1999, ICD-10 was used. Mortality rates for the SEER geographic areas, for each state, and for the entire US are obtained from these data. A list of the mortality site groupings used in this publication is in the Appendix and reflects updates made in 2004.

## **POPULATION DATA**

The population estimates used in the SEER\*Stat software to calculate cancer incidence and mortality rates for this report are a modified version of the annual time series of July 1 county population estimates by age, sex, race, and Hispanic origin that are produced by the Population Estimates Program of the US Census Bureau (<http://www.census.gov/popest/estimates.php>) with support from the NCI through an interagency agreement. Descriptions of the methodologies employed by the Census Bureau for various sets of estimates may be found on the same website. County population estimates for 2000 and later years must be bridged from 31 race categories used in Census 2000 to the four race categories specified under earlier OMB

standards in order to report long-term cancer trends. The bridging methodology was developed by the National Center for Health Statistics and is described in a report (Ingram et al., 2003) and on their website <http://www.cdc.gov/nchs/about/major/dvs/popbridge/popbridge.htm>.

Modifications made by the NCI to the population estimates are documented in "Population Estimates Used in NCI's SEER\*Stat Software" (<http://seer.cancer.gov/popdata/methods.html>) and the population data files are available for download (see "Download US Population Data" from <http://seer.cancer.gov/popdata/download.html>). Several of the modifications pertaining to the grouping of specific counties needed to assure the compatibility of all incidence, mortality and population datasets. Another modification affects only population estimates for the State of Hawaii. The Epidemiology Program of the Hawaii Cancer Research Center has developed its own set of population estimates, based on sample survey data collected by the Hawaii Department of Health. This effort grew out of a concern that the native Hawaiian population has been vastly undercounted in previous censuses. The "Hawaii-adjustment" to the Census Bureau's estimates has the net result of reducing the estimated white population and increasing the estimated Asian and Pacific Islander population for the state. The estimates for the total population, black population, and American Indian and Alaska Native populations in Hawaii are not modified.

The cancer incidence and mortality rates for American Indians and Alaska Natives (AI/AN) are based on the geographic areas (counties) included in the Indian Health Service's Contract Health Service Delivery Area (CHSDA). This reflects a concern that previously reported AI/AN rates were underestimated due to racial/ethnic misclassification of American Indian cases in geographic areas outside of CHSDA. This change has the net effect of higher, and more accurate, incidence and mortality rates for this population.

Usually the use of a population estimate for July 1 of a particular year reflects the average population of that area for the year. Both Hurricane Katrina and Hurricane Rita struck the Gulf Coast area of the United States in 2005. This had the effect of displacing large populations. Since there weren't any population estimates by age, race, sex, and county for time periods just after the hurricanes, it is very difficult to estimate the actual population at risk for certain areas along the Gulf Coast for 2005. For Louisiana, only the first six months of incidence data for 2005 coupled with ½ of the population estimate for July 1, 2005, were used to calculate cancer incidence. For death rate calculations, no adjustments were made to the total U.S. population, but for the Gulf area, an adjustment for displaced populations was made for 2005 state rates. For more details, see <http://seer.cancer.gov/popdata/methods.html>.

## **2000 US STANDARD POPULATION**

Starting with the November 2004 SEER submission of data (diagnoses through 2002), the SEER Program age-adjusts using the 2000 US standard population based on single years of

age from the Census P25-1130 series estimates of the 2000 US population (Day, 1996). For the CSR, 19 age groupings were used for age-adjustment: <1, 1–4, 5–9, ... , 80–84, 85+.

## ***STATISTICAL METHODS***

### **ESTIMATED CANCER CASES AND DEATHS IN 2009**

The American Cancer Society (**ACS**) projects the numbers of new cancer cases and cancer deaths in the US in 2009 (American Cancer Society, 2009). The ACS projects incidence in 2009 based on incidence rates for 1995-2005 from 41 states, representing about 85% of the US population. These high quality incidence data were submitted to the North American Association of Central Cancer Registries (NAACCR) by 41 states belonging to the SEER Program and/or the National Program of Cancer Registries (NPCR). For additional details please refer to [http://www.cancer.org/docroot/STT/STT\\_0.asp](http://www.cancer.org/docroot/STT/STT_0.asp)

### **LONG-TERM TRENDS, 1950-2007**

Trends in cancer mortality from 1950 to 2007 are summarized by age both for all cancers combined and for lung cancer (Table I-2). These cancer mortality trends are based on the mortality experience in the entire US. Summaries of long-term trends back to 1950 in cancer survival are also shown for whites.

*Use caution when interpreting these statistics. Evaluating trends over a long period of time may hide recent changes in the trends.*

### **YEARS OF LIFE LOST DUE TO PREMATURE DEATH FROM VARIOUS CAUSES**

Death rates alone give an incomplete picture of the burden that deaths impose on the population. Another measure, which adds a different dimension, is the years of life lost due to premature death. This shows the extent to which life is cut short by a particular cause or disease.

This measure is estimated by linking life table data to each death of a person of a given age and sex. The life table permits a determination of the number of additional years an average person of that age, race, and sex would be expected to live. In this report, the age groups used in the calculation were 1-year intervals. These remaining years of life left are summed over all deaths due to a particular cause, yielding the estimate of the number of person-years of life lost (**PYLL**). The average years of life lost (**AYLL**) is obtained by dividing the PYLL by the number of deaths. Both of these measures can be calculated for any cause of death.

## CAUSE-SPECIFIC SURVIVAL

Cancer survival estimates differ substantially among race and ethnic groups in the United States. Evaluation of these differences via the relative survival method, however, is hampered by the non-availability of expected life tables for races other than White or Black. The relative survival method assumes a valid life-table for each race and ethnic group. Furthermore, the U.S. National Center for Health Statistics estimates (Rosenberg et al, 1999) that the published mortality rates are overstated for Whites (1%) and Blacks (5%), and grossly under-stated for American Indians (21%) and Asian Pacific Islanders (11%). Cause-specific can serve as an alternative method to estimate survival within diverse subgroups of the U.S. populations. However, this measure has not been systematically used in population-based registries because of misclassification of cause of death on death-certificates. For example, the site of metastasis might be reported as the cause of death as opposed to the original site of disease (Percy et al, 1981) creating ambiguity when attempting to define endpoints for reliable survival estimates.

Here we describe a new endpoint for calculating cause-specific survival that uses a broad definition of cause of death (COD) based on death certificate. The COD chosen varies depending on the sequence of the tumor and the site of the original cancer diagnosis. For those with one and only one cancer (i.e., sequence number 00), the end point of death is any cancer or HIV/AIDS with cancer. The rationale for including all malignant cancers or an AIDS/HIV diagnosis with cancer is that among patients diagnosed with only one cancer, cause of death coded to another cancer site is likely to be a misclassification, such as one due to metastatic disease (Percy et al, 1981). For those individuals who had more than one cancer, (i.e., sequence number 01, 02, 03, and beyond) cause-specific survival was calculated only for the first cancer diagnosed (sequence number 01) and the cause of death was limited to deaths due to that cancer, site-specific disorders, and to multiple cancers of known or unknown site. The cause of death classification and detailed ICD codes by primary cancer site can be found in the Appendix.

## CANCER PREVALENCE

**Methods:** In this report prevalence is calculated at 1/1/2007. **Limited-duration prevalence** is calculated using the counting method implemented in the SEER\*Stat software. This method calculates the number or proportion of people alive at the prevalence date who had a diagnosis of the disease within the past  $x$  years (e.g.,  $x = 5, 10, 20$ , or the full history of the registry). Because SEER has available information for the various racial/ethnic groups for different numbers of years, different years and registries were used to estimate limited duration prevalence. Prevalence estimates for all races combined, for whites, and for blacks use cases from 1975 through 2006 from the SEER 9 registries; prevalence estimates for Asian Pacific Islanders and Hispanics use cases diagnosed from 1990 through 2006 from the SEER 11 areas and rural Georgia.

The limited duration prevalence method includes a correction for people lost to follow-up. For each individual lost to follow-up, a probability of being alive at the prevalence date is estimated from an appropriate survival function stratified by age at diagnosis (0–59, 60–69, 70+), sex, cancer site, year of diagnosis, and race, conditional on being alive at the time of loss to follow-up. Year of diagnosis is stratified into 5-year groups from the prevalence date, with the least recent interval being of varying length (4-8 years), depending on the length of years used to calculate prevalence. Race is stratified into white, black, other (American Indian/Alaska Native, Asian/Pacific Islander), and unknown/other-unspecified. When we use the SEER 11 registries, the same stratification as before is used, with American Indian/Alaska Native separated from Asian/Pacific Islander. Prevalence calculations for Hispanics use race stratified into: white, non-white, and unknown.

Different methods can be used to determine which tumors are to be included for people diagnosed with multiple tumors. Unless otherwise specified, prevalence calculations included only the *first malignant tumor per person*; that is, in situ cancers and second-or-later primary cancers were not included. Thus, if a woman had a melanoma prior to a breast cancer diagnosis, her melanoma would contribute to the prevalence of melanoma and to the prevalence of all sites, but the breast cancer would not contribute to the prevalence of breast cancer. Counting only one cancer per individual avoids some ambiguity in prevalence counts, and allows the counts for individual sites to sum to the all sites total. Prevalence using different selection criteria is compared in a table in the overview chapter. For more information on tumor selection criteria refer to <http://srab.cancer.gov/prevalence/methods.html>.

**Complete prevalence** is an estimate of the number of persons (or the proportion of population) alive on a specified date who had been diagnosed with the given cancer, no matter how long ago that diagnosis was. It was estimated for all races, whites, and blacks by applying the *completeness index method* (Capocaccia & De Angelis, 1997; Merrill et al., 2000; Mariotto et al., 2002) to limited-duration prevalence. The completeness index method is implemented in the COMPREV software which can be found at <http://srab.cancer.gov/comprev/>. Validation of the completeness index for all races and for whites was made by using data from the Connecticut Tumor Registry (CTR) beginning with 1940; for blacks, SEER 9 data beginning with 1975 were used. Identification of blacks is not possible in the CTR data prior to 1970. To validate the completeness index for blacks, we have compared the performance of the method to obtain 24-year prevalence from 10-year limited-duration prevalence. For all races combined and for whites, in cases where the validation indicated some lack of fit of the model, an approximation to the completeness index was derived from the CTR data. If there was a lack of fit for blacks, no estimate of complete prevalence was reported. Complete prevalence for Asian/Pacific Islanders and Hispanics is not available at this time. Complete prevalence by age for all races combined was validated by comparing estimated 10-year complete prevalence with observed prevalence from the CTR data. Prevalence by age is reported for the sites that validated well.



The US cancer prevalence counts at 1/1/2007 *were estimated* by multiplying the SEER age- and race-specific prevalence proportions by the corresponding US population estimates based on the average of 2006 and 2007 population estimates from the US Bureau of the Census. US cancer prevalence counts for all races were estimated by summing the US estimated counts for whites/unknown, blacks, and other races. For Hispanics, the estimates for Hispanics of white or unknown race and for Hispanics of other races were summed.

Complete prevalence estimates of the number of individuals in the U.S. diagnosed with cancer as children (ages 0-19), including those surviving for more than 32 years, is introduced this year using a statistical method that estimates the number of childhood survivors diagnosed before 1975 (Simonetti et al. 2008, Mariotto et al 2009). Limited-duration prevalence proportions by age at prevalence are not shown for childhood cancers (age at diagnosis 0-19) since many of these estimates are not informative. For example, the number of people diagnosed with childhood cancers in the last 25 years and who are currently age 50-59 is zero by definition. For more details on available prevalence estimates, see <http://srab.cancer.gov/prevalence/index.html>.

The overview chapter contains two prevalence tables. The first table reports US complete prevalence counts by age at prevalence and sex for some main cancer sites. The second table reports US prevalence counts for people diagnosed in the 5 years and 32 years prior to the prevalence date using different tumor inclusion criteria. Each site-specific chapter contains a prevalence table that reports limited-duration US prevalence counts by time since diagnosis for different racial/ethnic groups. US complete prevalence estimates are also reported when available. The second part of the site-specific tables displays the percent of the population in the SEER 11 areas diagnosed in the previous 17 years with the specific cancer by 10-year age groups for the different racial/ethnic groups.

## **PROBABILITY OF BEING DIAGNOSED WITH OR DYING FROM CANCER**

**Lifetime and interval risks of being diagnosed with cancer:** The probability of being diagnosed with cancer is computed by applying cross-sectional age-specific 2005-2007 incidence rates from the SEER 17 areas and death rates from those same areas to a hypothetical cohort of 10,000,000 live births. This cohort is considered to be at risk for two mutually exclusive events: (1) developing the specified cancer, and (2) dying of other causes without developing the specified cancer. Using these two types of events, a standard **multiple decrement life table** (with 20 age groups from 0-4 to 90-94 and 95+) is derived. For each age interval, the number alive and free of the specified cancer at the beginning of the interval is decremented by the number who develop the specified cancer and the number who die of other causes. The lifetime risk of being diagnosed with the specified cancer is derived by summing all cancer cases from age 0-4 through age 95+ and dividing by 10,000,000. This calculation does

not assume that an individual lives to any particular age; rather, it is the sum over all age intervals of the probability of living to the beginning of that interval without developing the given cancer times the probability of developing the cancer in that interval. The probability of developing cancer during any time period (e.g., between age 50 and age 60) is calculated by adding up all the cancers in the life table over the specified age range and dividing by the number of individuals alive and free of the specified cancer at the beginning of the period. The methodology is described in detail in Fay (2003, 2004). To improve the precision of the calculations, rates were calculated beyond the usual last open ended age interval (i.e. 85+) for the age groups 85-89, 90-94, and 95+.

**Lifetime risk of dying from cancer:** The lifetime risk of dying from a specified cancer is derived using a standard multiple decrement life table (Elandt-Johnson & Johnson, 1980). For each age, the risks of dying of the specified cancer and of all other causes are calculated, based on mortality data from the entire United States.

**Detailed methodology and software:** The estimates of developing and dying from cancer are implemented in DevCan (Probability of DEVeloping or dying from CANcer software). More details on the software, various databases, and the methodology can be found at <http://srab.cancer.gov/devcan/>.

## U.S. CANCER DEATH RATES BY STATE

Each cancer-site-specific section presents the death rate for the given cancer for each state and the District of Columbia, specifying the five highest and the five lowest death rates by state for the most recent 5-year period for all persons, males only, and females only. The rates are per 100,000 persons; they are age-adjusted to the 2000 US standard population. (In some previous editions of the CSR, the 1970 US standard million population was used; *death rates standardized to the 2000 US standard million population cannot be compared to death rates standardized to the 1970 US standard million population.*)

The **percent difference (PD)** between a state rate and the rate for the total US is given by the formula:

$$PD = [(State\ Rate - Total\ US\ Rate)/Total\ US\ Rate] * 100$$

The **standard error** for each age-adjusted state death rate is calculated, based on the assumptions that (1) for each age-specific rate, the number of deaths is a Poisson random variable (Keyfitz, 1966) and (2) the variance of the age-adjusted rate is a linear combination of the variances of the age-specific rates (Snedecor & Cochran, 1980; pp. 188-9).

The **standard error of the difference (SE<sub>d</sub>)** between a state rate and the total US rate is given by the formula

$$SE_d = \text{Square Root of } [SE_s^2 + SE_U^2 - 2 * \text{Cov}_{s,U}]$$

where SE<sub>s</sub> and SE<sub>U</sub> are the standard errors of a state rate and of the total US rate, respectively, and Cov<sub>s,U</sub> is the covariance between the two rates. The variance of each rate (i.e., the square of the standard error) and the covariance between the two rates are based on the Poisson assumption. The standard error does not represent the total error that may be present in the age-adjusted rate; it is merely the square root of the variance associated with the rates. In addition to this variance, there also exist potential biases and errors in the measurement of the rate that are difficult to assess accurately and probably impact differently on the error calculations for different states.

The difference between each age-adjusted state rate and the age-adjusted US rate is tested for statistical significance (see below) by calculating a **Z** (standard normal) statistic from the formula:

$$Z = (\text{State rate} - \text{Total US rate}) / SE_d$$

Although the rates being compared are not independent because each state is part of the US, the statistical test may not be substantially affected if the state represents a small proportion of the total US. There is also an adjustment for multiple comparisons; see below under *Statistical Significance*.

## JOINPOINT REGRESSION ANALYSIS OF CANCER TRENDS

An advance in the presentation of cancer trends is the use of joinpoint models (Kim et al., 2000). In some past issues of the *Cancer Statistics Review*, certain time intervals (e.g., 1973–1996) were specified and the annual percent changes (APC) were computed over those intervals. The choices of where to start and where to end an interval were arbitrary and sometimes did not give an accurate picture of the trend for a given cancer site. For example, the rates might be increasing and decreasing in different parts of the same interval. For some sites, increases occurred in the earlier years, followed by declines in more recent years.

To achieve greater descriptive accuracy, a statistical algorithm finds the optimal number and location of places where a trend changes. The point (in time) where a trend changes is called a **joinpoint**. Trends may change in different ways at a joinpoint: from up to down, from down to up, from up to up at a different rate, or from down to down at a different rate. A **joinpoint regression model** describes the trends by a sequence of connected segments where each segment is connected by a straight line on a log scale. Adjacent segments are connected at a joinpoint. The segments are connected because we assume that rates generally change smoothly, rather than “jump” abruptly. The rates are assumed to grow or decay exponentially, i.e., to change by a constant percentage each year. Thus the slope in each segment can be associated with a fixed annual percent change (**APC**).

Joinpoint analysis first assumes no joinpoints are needed to describe the data accurately, i.e., the trend over the entire interval 1975-2007 does not change. Joinpoints are added in turn if they are statistically significant. Thus, in the final model, each joinpoint represents a significant change in trend. Computational considerations currently limit the maximum possible number of segments to be no larger than five, with four joinpoints. Smoother polynomial models may provide a good fit overall, but are less sensitive to what is occurring at the ends of the data.

In running the Joinpoint program, we set the program parameters as follows: maximum number of joinpoints 4, minimum interval between joinpoints 2 years, minimum interval between a joinpoint and an endpoint 2 years, joinpoints occurring only at exact years. These restrictions provide some added stability to the resultant models. Different values for these parameters may yield a different joinpoint model. Since the test statistic to determine if additional joinpoints are necessary cannot be compared against any known standard distribution to determine significance, (e.g., the normal, t, or f) a permutation test is used which simulates the distribution of the test statistic under the null hypothesis. Thus an element of randomness is introduced by the random number stream used. However, for greater consistency in the p-values obtained if one were to change the random seed for each run, we run the program for 4499 permutations.

**Average Annual Percent Change (AAPC)** is a summary measure of a trend over a pre-specified fixed interval based on an underlying joinpoint model. It allows us to use a single number to describe the average trend over a period of multiple years. It can be estimated even if the joinpoint model indicates that there were changes in trends during those years, since it is estimated as a geometric weighted average of the joinpoint APCs, with the weights equal to the lengths of each segment over the pre-specified fixed interval. In this report, we have included AAPCs as an addendum to the underlying joinpoint trends, and as a summary measure to compare fixed interval trends by race/ethnicity. For more information on how the AAPC is calculated and the advantages of reporting an AAPC over APCs, see <http://srab.cancer.gov/joinpoint/aapc.html>.

A Windows-based program, *Joinpoint*, is freely available at <http://srab.cancer.gov/joinpoint/>; it accepts data from the *SEER\*Stat* program, as well as user defined data. Further details on joinpoint regression may be found at the web site.

## REPORTING DELAY

Timely and accurate calculation of cancer incidence rates is hampered by **reporting delay**, the time lapse before a diagnosed cancer case is reported to the NCI or the delay in receiving updated information for an existing case. Currently, the NCI allows a standard delay of 22 months between the end of the diagnosis year and the time the cancers are reported to the NCI in November, almost two years later. The data are released to the public in the spring of the following year. For example, cases diagnosed in 2007 were first reported to the NCI in

November 2009 and released to the public in April 2010. However, in each subsequent release of the SEER data, *records from all prior diagnosis years* (e.g., diagnosis years 2006 and earlier in the 2009 submission to the NCI) *are updated* as either new cases are found or new information is received about previously submitted cases.

The submissions for the most recent diagnosis year are, in general, about two percent below the total number of cancers that will eventually be submitted for that year, although this varies by cancer site and other factors.

The idea behind modeling reporting delay is *to adjust the recent rates to anticipate future corrections (additions, changes, and deletions) to the data*. These adjusted rates and the associated delay model are valuable in more precisely determining current cancer trends, as well as in monitoring the timeliness of data collection—an important aspect of quality control (Clegg et al., 2002). Reporting delay models have been previously used in the reporting of AIDS cases (Brookmeyer & Damiano, 1989; Pagano et al., 1994; Harris, 1990).

In this report, we show SEER age-adjusted incidence rates and trends, along with their calculated delay adjustments for SEER 9 and SEER 13 areas. The adjusted rates, factors, and trends are available for all cancers combined (malignant only except for urinary bladder), for female breast in situ, for urinary bladder (in situ and malignant), and for 22 malignant cancer sites: melanoma (for all races combined and whites only), lung/bronchus, colon/rectum, prostate, female breast, liver and intrahepatic bile duct, pancreas, cervix uteri, corpus and uterus, ovary, testis, kidney and renal pelvis, brain and other nervous system, Hodgkin lymphoma, non-Hodgkin lymphoma, all leukemias, esophagus, larynx, myeloma, oral cavity and pharynx, thyroid, and stomach.

For more information on cancer incidence rates adjusted for reporting delay, see <http://srab.cancer.gov/delay/>. Estimates of observed incidence rates, delay-adjusted incidence rates, and delay-adjustments factors may be found in the Cancer Query Systems at <http://seer.cancer.gov/canques/>

## **Adjustment for VA Case Backlog, Submission Year 2009**

A policy change of the Department of Veterans Affairs (VA) regarding data sharing on VA cancer cases resulted in underreporting on VA hospital cases for submission years 2006-2008. Section 33 of this report provides factors to adjust for the lack of reporting of VA cases. In addition to the adjustments made in Section 33, some special adjustments to case counts are necessary to fit the delay adjustment model. In the 2009 submission of SEER data, some SEER registries began accounting for VA cases. This caused a backlog on the VA case reporting, i.e., the cases that would have been reported in 2006-2008 were reported in 2009. This sudden upsurge in cases could cause perturbation in the delay model if fit on the usual manner.

To take into account the VA backlog in the 2009 submission in the delay adjustment model, the counts are adjusted by re-distributing VA cases in the 2009 submission to previous submission years according to the expected counts from the delay distribution conditional on the current submission. More specifically, for each of the diagnosis years 2004-2006, given the total cancer count in submission year 2009, the proportion of cumulative cancer count in each subsequent submission year is calculated based on the estimated parameters from previous year's reporting delay model. The VA cases in 2009 are re-distributed to each of the submission years according to this proportion. The adjusted total cancer count in that submission year was then calculated by combining the non-VA cases and the re-distributed VA counts. Overall, the VA delay-adjustment is modest for the November 2009 submission. It was integrated into SEER 9 and SEER 13 delay models presented throughout the CSR. More details can be found at <http://srab.cancer.gov/delay/vabacklog.html>.

### **The SEER 9 delay model**

For each cancer site, many combinations of covariates were considered in prediction models of delay probabilities. Potential covariates included delay time, year of diagnosis, age at diagnosis, sex, race, and reporting year effect [Zou et al, 2009]. Models were evaluated by fitting the SEER 9 models using 1983 and 2008 annual submissions, with a maximum 26 year delay, then predicting the counts for the 2009 submission. For each cancer site, the model that minimized the sum of squared prediction errors was chosen as the default final model. However, to choose a more parsimonious model, we added an additional selection step in which possible competing models were selected using the following criteria:

- the competing model had fewer number of parameters of the default model, and
- the percent change between the prediction errors of the competing and the default models per extra parameter (i.e., percent change in prediction errors divided by the difference in the numbers of parameters between the two models) was less than 1 percent.

If more than one competing model met the criteria, the model with the smallest percentage change per extra parameter was generally selected. However, if there are other competing models that had fewer parameters and the differences between their percentage changes per extra parameter and the smallest one did not exceed 0.02, the competing model with the fewest number of parameters (rather than the model with the smallest percentage change per extra parameter) was selected. The chosen model was then refitted using all data (1983-2009 submissions, 1981-2007 diagnosis years) to estimate delay distributions and calculate delay adjusted estimates of the cancer counts.

Age-adjusted (using the 2000 US standard population) cancer incidence rates were then calculated with and without adjusting for reporting delay. Joinpoint linear regression was used to obtain the annual percentage changes for the 1975-2007 incidence rates for the data series with

and without delay adjustment. Because the delay distribution was assumed complete after 27 years, incidence rates for diagnosis years prior to 1982 were not reporting-adjusted. In joinpoint regression analyses, up to four change points (i.e., 5 trend-line segments) were allowed, and these were modeled to fall at either whole years or midway between diagnosis years. Change points were constrained to be at least 2 years away from both the beginning and the end of the data series and at least 2 years apart. Models were fitted using weighted least squares (weighted by appropriate variances of age-adjusted incidence rates) of the joinpoint regression software.

Results show that adjusting for delay tends to raise cancer incidence rates in more current reporting years. While this adjustment increases the rate of change over the most recent diagnosis years, it probably will only rarely cause the detection of a new joinpoint, although this is possible. See Clegg et al. (2002) for details on the impact of reporting-delay adjustment to SEER cancer incidence rates.

### The SEER 13 Delay Model

Starting with the April 2009 release of the *Cancer Statistics Review* we estimated delay adjusted rates for SEER 13 registries. SEER 13 consists of SEER 9 registries, covering diagnosis years 1975 through the present, plus 4 newer registries (Los Angeles, San Jose-Monterey, Rural Georgia, Alaska Native Tumor Registry) covering diagnosis years 1992 through the present. These four registries will be referred to here as SEER 13-9.

Delay-adjusted rates for SEER 13 were obtained through a 2 step process. First, the delay adjustment factors are derived separately for SEER 9 and SEER13-9. Delay adjusted age specific case counts are computed for SEER 9 and SEER 13-9 using their respective delay adjustment factors and then summed to get the delay-adjusted case counts for SEER 13. These adjusted case counts are then paired with the appropriate denominator to obtain age-specific rates, and are age-adjusted in the usual manner. The formula to compute the age-adjusted combined SEER 13 rates is:

Delay adjusted rate for *i*th age group =

$$\frac{\sum_j \text{delay counts for SEER 9 for age/stratum } (i, j) + \sum_j \text{delay counts for SEER 13-9 for age/stratum } (i, j)}{\sum_j \text{population for age/stratum } (i, j)}$$

$$\text{AAR} = \sum_i \frac{\text{Standard Population in } i\text{th age group}}{\text{Total Standard Population}} \times (\text{delay adjusted rate for } i\text{th age group})$$

*i* is for age, *j* is for stratum defined by multiple variables included in the delay model.



Future developments will include an application program to allow the computation of SEER 13 combined delay adjusted rates based on this formula.

Consecutive data submissions were not available for the Alaska Native Tumor Registry for the entire period of interest. Modeling SEER 13-9, therefore, was conducted using only Los Angeles, San Jose-Monterey and Rural Georgia though the final delay-adjustment factors were applied across the four registries.

In creating the SEER 13-9 model, we first followed the same process of model selection and delay adjustment factor estimation as is used in SEER 9. We then modified the SEER 13-9 factors to share the same delay adjustment factors as SEER 9 under the assumption that the data have the same delay distribution prior to 1992. The modified delay adjusted factors are then the final estimated factors for SEER 13-9. As with SEER 9, we also assume that in SEER 13-9 there is no delay after 27 year of reporting.

## **Cancer Sites and Variables**

Delay-adjusted incidence rates and trends are reported for all cancers combined (malignant only except for urinary bladder), for female breast in situ, for urinary bladder (in situ and malignant), and for 22 malignant cancer sites: melanoma (for all races combined and whites only), lung/bronchus, colon/rectum, prostate, female breast, liver and intrahepatic bile duct, pancreas, cervix uteri, corpus and uterus, ovary, testis, kidney and renal pelvis, brain and other nervous system, Hodgkin lymphoma, non-Hodgkin lymphoma, all leukemias, esophagus, larynx, myeloma, oral cavity and pharynx, thyroid, and stomach.

A delay distribution models the probability of a cancer being reported after a delay of  $d$  years ( $d = 2, 3, \dots, 25$ ). The number of cancers reported at each delay year is assumed to follow a Poisson distribution. Cases are removed as corrections to the data are made, and the probability of removing cases is modeled as a binomial distribution. To reduce the number of parameters that have to be estimated and to achieve stability in the tails of the delay distributions, an assumption is made that all cancer cases will be reported within 25 years of diagnosis.

The delay distributions were modeled as a function of covariates using a discrete-time proportional hazards model. The following potential covariates are included: age at diagnosis, sex, diagnosis year, delay times, and race/ethnicity. For each cancer site, a delay distribution was calculated for all races combined and a separate delay distribution was calculated for whites and blacks. In the distributions for all races combined, if a patient's race value changed between two submission years the change of value does not contribute to the delay model. For melanoma, only all races combined and whites were analyzed because melanoma is rare for blacks. A complete list of covariates and as well this year's models for each cancer site can be found at <http://srab.cancer.gov/delay/covariates.html>



## STATISTICAL SIGNIFICANCE

Errors may be made in the estimation of a given statistic. In order to test whether two groups (such as the populations of a state and the entire US) have the same or different *actual* rates, the *observed* rates for the groups are compared. Statisticians consider that a difference in observed rates can be explained by one of two hypotheses: ( $H_0$ ) The actual rates are really the same, but the observed rates are different because of some combination of error-causing factors, or ( $H_1$ ) the actual rates of the groups are really different.  $H_0$  is called the **null hypothesis** (because it says there is *no* real difference);  $H_1$  is called the **alternate hypothesis**. Typically,  $H_0$  is rejected only if there is strong evidence in favor of  $H_1$ . (Thus, if the observed rates are equal, we cannot reject  $H_0$ .)

Using statistical theory, one can determine the distribution of the rate difference under the assumption that  $H_0$  is true. Then values of the rate difference that are very unlikely to occur if  $H_0$  is true are identified. More specifically, a small positive number, called **alpha** ( $\alpha$ ), is chosen; usually,  $\alpha$  is 0.05 or 0.01. (Alpha is called the **significance level** of the hypothesis test.) One can then identify limits for the difference in rates such that, if  $H_0$  is true, the probability of the difference being outside of those limits is  $\alpha$ . If the observed difference is *outside* of these limits, then the observed result is *very unlikely* to happen if  $H_0$  is true, so  $H_0$  is rejected.

Another way of looking at the same process is to calculate, assuming  $H_0$  is true, the probability that the observed difference or any greater observed difference would occur; this number is called the **P-value** of the observed result. If the *P*-value of a comparison is less than  $\alpha$  (that is, the observed difference is *very unlikely* to happen if the null hypothesis is true),  $H_0$  will be rejected. If the *P*-value of a test is greater than the significance level  $\alpha$ ,  $H_0$  will not be rejected. When a difference in rates is sufficiently large to cause the null hypothesis to be rejected for a given value of  $\alpha$  (usually 0.05), it is called a **statistically significant** difference.

When a null hypothesis is rejected, there remains a small chance that a wrong decision has been made. If many statistical comparisons are done, even with  $\alpha = 0.01$ , the chance of making at least one wrong decision becomes a concern. In testing the differences between the total US rate and the rate for each state (or for the District of Columbia) for a given cancer, 51 statistical comparisons of the type described above are performed. Based on one of Bonferroni's inequalities (if there are  $n$  events and  $p_i$  is the probability of success in event  $i$ , then  $P(\text{at least 1 success}) < p_1 + \dots + p_n$ ) (Snedecor & Cochran, 1980; p. 115-117), the significance level  $\alpha$  for each individual comparison was set equal to  $0.01/51 \approx 0.0002$ . Thus, only individual-state-to-total-US comparisons with an associated *P*-value less than 0.0002 are considered to be statistically significant. That is, a *very small* significance level  $\alpha$  (0.0002) is used in order to minimize the total risk (0.01) of falsely deciding that some pair of equal rates are unequal.

*Use caution in assessing statistically significant differences.* Population size has an important role in any calculation of statistical significance. Some states may have estimated rates that are

very close to the estimated total US rate, but because of their large population, the difference between their estimated rate and the estimated total US rate is found to be statistically significant. In this case, the true state rate and the true US rate are almost certainly different, because the observed difference, though small, is nearly impossible if the null hypothesis (equal rates) is true. A small difference in rates, however, may have no practical importance. On the other hand, some smaller states may have estimated rates that differ substantially from the estimated total US rate, but because of their relatively small population, the differences are found to be statistically nonsignificant. When this happens, if the true state rate and the true US rate were equal, the probability of obtaining a difference at least as large as what has been observed is greater than  $\alpha \approx 0.0002$ . Therefore, *because the evidence against it isn't strong enough, the null hypothesis (equal rates) is not rejected.*

If the percent difference (PD) between the two rates is small, there may be some question about the importance of the difference. It is difficult to specify a minimally significant absolute PD, below which the difference would always be unimportant, because the observed PD will depend on the populations of the areas involved. It may be of value to consider the size of the PD between a state rate and the US rate in assessing the importance of a statistically significant difference.

Comparing individual state rates with the US rate and assessing statistical significance is not an appropriate procedure for assessing geographic clustering of state rates. Identification of states which may represent regional clusters of high or low rates would require additional statistical and graphical analyses.

For a number of cancers, the District of Columbia has the highest death rates. *Use caution when comparing cancer rates for the District with those from the 50 states.* The District is an entirely urban area, whereas a state includes urban, suburban, and rural areas. Mortality rates for many cancers are higher in urban areas. Also, the District has a higher percentage of blacks (58% of the total population in 2005) than any state. In addition, their higher mortality rates for several types of cancer elevate the overall rate for the District.

## STANDARD ERRORS OF RATES

**Survival rates:** In the tables presenting survival estimates, the magnitude of the standard error is given as a clue to the reliability of a given rate: the greater the standard error, the less reliable the rate. In addition, if there were fewer than 25 diagnoses in the first interval of the life table constructed to calculate survival, or if all cases became lost to follow-up within an interval, a valid survival estimate could not be calculated, as is noted in the table footnotes.

The **standard error (SE)** of a relative survival estimate is obtained as follows (Ederer et al., 1961):

$$SE(CR_t) = CR_t * \text{square root of } [q_1/(e_1-d_1) + q_2/(e_2-d_2) + \dots + q_t/(e_t-d_t)]$$

where  $CR_t$  is the  $t$ -year relative survival estimate, and for  $i = 1, \dots, t$ ,  
 $q_i$  is the probability of dying in year  $i$  after diagnosis,  
 $e_i$  is the effective number of patients at risk in year  $i$  after diagnosis, and  
 $d_i$  is the number of deaths in year  $i$  after diagnosis.

**Incidence and mortality rates:** The standard errors of age-adjusted incidence and mortality rates are often not specified. However, the reader can approximate the SE of a particular incidence or mortality rate by the SE of a crude incidence or mortality rate (Keyfitz, 1966), that is, the SE can be approximated by the rate divided by the square root of the number of cancer cases (or the number of deaths).

Appendix tables provide numbers of cancer diagnoses within SEER areas and numbers of deaths in the entire US, respectively, by race and sex for the most recent 5-year period. These can be used to obtain approximations of the standard errors for associated age-adjusted rates for the same time period using the above formula. To approximate the standard error of a rate for a single year, use the formula but replace the number of cancer cases or deaths with the number of cancer cases or deaths divided by 5.

## ***DEFINITIONS***

Several technical terms are used in presenting the data in this report. Their definitions are presented here to clarify them for the reader.

**Incidence rate:** The cancer incidence rate is the number of new cancers of a specific site/type occurring in a specified population during a year, usually expressed as the number of cancers per 100,000 persons at risk. That is,

$$\text{Incidence rate} = (\text{New cancers} / \text{Population}) * 100,000.$$

The *numerator* of the incidence rate is the number of new cancers; the *denominator* of the incidence rate is the size of the population. The number of new cancers may include multiple primary cancers occurring in one patient. The primary site reported is the site of origin and not the metastatic site. In general, the incidence rate would not include recurrences. *The population used depends on the rate to be calculated.* For cancer sites that occur in only one sex, the sex-specific population (e.g., females for cervical cancer) is used.

The incidence rate can be computed for a given type of cancer or for all cancers combined. Except for 5-year age-specific rates, all incidence rates in this report are *age-adjusted* (see

below) to the 2000 US standard population (or, where appropriate, to the world standard million population). (In some previous editions of the *CSR*, the 1970 US standard million population was used; therefore, *incidence rates in this edition cannot be compared to rates published in those editions.*) Incidence rates are for *invasive cancer only*, unless otherwise specified. (Exceptions are the incidence rate for cancer of the urinary bladder (where both in situ and invasive cancers are counted) and breast cancer in situ, which is shown separately.)

**Death rate:** The cancer death (or mortality) rate is the number of deaths with cancer given as the underlying cause of death occurring in a specified population during a year, usually expressed as the number of deaths due to cancer per 100,000 persons. That is,

$$\text{Death Rate} = (\text{Cancer Deaths} / \text{Population}) * 100,000.$$

The *numerator* of the death rate is the number of deaths; the *denominator* of the death rate is the size of the population. As with the incidence rate, *the population used depends on the rate to be calculated.* The death rate can be computed for a given cancer site or for all cancers combined. Except for 5-year age-specific rates, all death rates in this report are *age-adjusted* (see below) to the 2000 US standard population (or, where appropriate, to the world standard million population). (In some previous editions of the *CSR*, the 1970 US standard million population was used; therefore, *death rates in this edition cannot be compared to rates published in those editions.*)

**Age distribution:** A table showing a partition of the entire lifespan into disjoint age intervals, along with the proportion of the population in each interval.

**Median age:** The age at which half of a population is younger and half is older.

**Standard population:** A **standard population** for a geographic area, such as the US or the world, is a table giving the proportions of the population falling into the age groups 0, 1-4, 5-9, ..., 80-84, and 85+. A **standard million population** for a geographic area is a table giving the number of persons in each age group 0, 1-4, ... , 85+ out of a theoretical cohort of 1,000,000 persons that is distributed by age in the same proportions as the standard population. Table A-7 shows the US 2000 standard population and the world standard million population. (Some World Health Organization mortality publications use a different world standard million population.)

**Age-adjusted rate:** An age-adjusted incidence or mortality rate is a weighted average of the age-specific incidence or mortality rates, where the weights are the counts of persons in the corresponding age groups of a standard population. The potential confounding effect of age is reduced when comparing age-adjusted rates based on the same standard population. For this report, the 2000 US standard population (or, where appropriate, the world standard million population) is used in computing age-adjusted rates, unless otherwise noted.

**Percent change:** The percent change (**PC**) in a statistic over a given time interval is

$$\text{Percent change} = (\text{Final value} - \text{Initial value}) / \text{Initial value} * 100.$$

A positive PC corresponds to an increasing trend, a negative PC to a decreasing trend.

**Annual percent change:** The annual percent change (**APC**) is calculated by first fitting a regression line to the natural logarithms of the rates ( $r$ ) using calendar year ( $x$ ) as a regressor variable. In this report the method of *weighted least squares* is used to calculate the regression equation. If  $\ln(r) = mx + b$  is the resulting regression equation (with slope  $m$ ), then

**APC = 100 \* (e<sup>m</sup> - 1).** A positive APC corresponds to an increasing trend, a negative APC to a decreasing trend.

Because the methods used in their calculation are mathematically different, *the signs of the PC and the APC for a given statistic and time interval may differ*, as occurs in a few of the tables presented. That is, one of these statistics may show an increasing trend, the other a decreasing trend.

Testing the hypothesis that the actual mean annual percent change is 0 is equivalent to testing the hypothesis that the theoretical slope estimated by the slope  $m$  of the line representing the equation  $\ln(r) = mx + b$  is 0. The latter hypothesis is tested using the  $t$  distribution of  $m / SE_m$  with  $n - 2$  degrees of freedom. The standard error of  $m$ , called  $SE_m$ , is obtained from the fit of the regression (Kleinbaum et al., 1988). (This calculation assumes that the rates increased or decreased at a constant rate over the entire calendar year interval; the validity of this assumption was not assessed.) In those few instances where at least one of the rates was 0, the linear regression was not calculated.

**Average Annual Percent Change:** The average annual percent change (**AAPC**) is a summary measure of a trend over a pre-specified fixed interval based on an underlying joinpoint model. It allows us to use a single number to describe the average trend over a period of multiple years. It can be estimated even if the joinpoint model indicates that there were changes in trends during those years, since it is estimated as a weighted average of the joinpoint APCs, with the weights equal to the lengths of each segment over the pre-specified fixed interval.

**Life table:** A table for a given population listing, for each sex and each age from 0 to 120, how many members die at that age and how many survive one more year.

**Observed survival:** The observed survival estimate represents the proportion of cancer patients surviving for a specified time interval after diagnosis. Note that some of those not surviving died of the given cancer and some died of other causes.

**Relative percent:** The relative survival estimate is calculated using a procedure (Ederer et al., 1961) whereby the observed survival estimate is adjusted for expected mortality. The relative survival estimate approximates the likelihood that a patient cohort will not die from causes associated specifically with the given cancer before some specified time after diagnosis. It is always larger than the observed survival estimate for the same group of patients.

**Standard error:** The standard error of a rate is a measure of the sampling variability of the rate.

**Person-years of life lost:** The person-years of life lost (**PYLL**) is calculated as follows: For each individual who dies of the cancer of interest, the number of years of expected additional life for an average person of that age, race, and sex is obtained from life tables for the US population (available from the NCHS). The PYLL in the general population associated with a particular cancer for a given year is simply the sum of this expectation over all those individuals who died of that cancer in that year.

**Average years of life lost:** The average years of life lost (**AYLL**) associated with a particular cancer for a given year is the PYLL associated with that cancer in the general population divided by the number of deaths from that cancer in the general population in that year.

**Prevalence:** Prevalence is defined as the number or percent of people alive on a certain date in a population who previously had a diagnosis of the disease. It includes new (incident) and pre-existing cases and is a function of past incidence, past survival, and the size and age structure of the population. *Limited-Duration Prevalence* represents the proportion of people alive on a certain day who had a diagnosis of the disease within the past  $x$  years (e.g.  $x = 5, 10,$  or  $20$  years). *Complete prevalence* is an estimate of the number of persons (or the proportion of the population) alive on a specified date who had been diagnosed with the given disease, no matter how long ago that diagnosis was. For more details on cancer prevalence definitions and methods, refer to <http://srab.cancer.gov/prevalence/>.

**Stage of disease at diagnosis:** Extent-of-disease information determines stage of disease at diagnosis. The **SEER summary stage** presented has four levels. An invasive neoplasm confined entirely to the organ of origin is said to be **localized**. A neoplasm that has extended beyond the limits of the organ of origin, either directly into surrounding organs or tissues or into regional lymph nodes, is said to be **regional**. A neoplasm that has spread to parts of the body remote from the primary tumor, either by direct extension or by discontinuous metastasis, is said to be **distant**. When information is not sufficient to assign a stage, a neoplasm is said to be **unstaged**. In situ tumors (except those of the cervix uteri) are also collected by SEER but generally are not published in this series. For some cancers and diagnosis years, the extent of

disease information can also be converted to Stages 0-IV as defined by the American Joint Committee on Cancer (Greene et al, 2002).

### ***SOFTWARE USED TO GENERATE THE SEER CANCER STATISTICS REVIEW***

The SEER Cancer Statistics Review includes statistics generated by a variety of statistical software including:

- [SEER\\*Stat](#), statistical software for the analysis of SEER and other cancer databases, was used to generate incidence, mortality, prevalence, and survival statistics presented in the CSR.
- Analysis generated by the [Joinpoint Regression Program](#) are presented to better describe trends that are not constant over time.
- The [DevCan](#) system generated the probability of developing cancer from twelve SEER areas and the probability of dying from cancer from the total United States.
- The [ComPrev](#) software was used to calculate complete prevalence estimates.

Additional statistics can be obtained via SEER's [Cancer Query Systems](#). These data retrieval applications provide access to pre-calculated cancer statistics stored in online databases.

## **REFERENCES**

- Baquet CR, Horm JW, Gibbs T, Greenwald P. Socioeconomic factors and cancer incidence among blacks and whites. *J Natl Cancer Inst.* 1991; 83:551-557.
- Breslow L (Chairman, Extramural Committee to Assess Measures of Progress Against Cancer). Measurement of progress against cancer: Final report to the Senate Appropriations Committee. Bethesda: National Cancer Institute; 1988.
- Brookmeyer R, Damiano A. Statistical methods for short-term projections of AIDS incidence. *Stat Med.* 1989;8:23-34.
- Byrne J, Kessler LG, Devesa SS. The prevalence of cancer among adults in the United States: 1987. *Cancer.* 1992;68:2154-9.
- Capocaccia R, De Angelis R. Estimating the completeness of prevalence based on cancer registry data. *Stat Med.* 1997;16:425-40.
- Clegg LX, Feuer EJ, Midthune D, Fay MP, Hankey BF. Impact of reporting delay and reporting error on cancer incidence rates and trends. *J Natl Cancer Inst.* 2002;94:1537-1545.
- Clegg L, Gail M, Feuer EJ. Estimating the variance of disease prevalence estimates from population-based registries. *Biometrics.* 2002;58(3):684-8.
- Day, Jennifer Cheeseman, *Population Projections of the United States by Age, Sex, Race, and Hispanic Origin: 1995 to 2050*, U.S. Bureau of the Census, Current Population Reports, P25-1130, U.S. Government Printing Office, Washington, DC, 1996. Available from: <http://www.census.gov/prod/1/pop/p25-1130/p251130.pdf>
- Ederer F, Axtell LM, Cutler SJ. The relative survival rate: A statistical methodology. *J Natl Cancer Inst. Monogr* 1961;6:101-121.
- Elandt-Johnson RC, Johnson NL. *Survival Models and Data Analysis*. New York (NY): Wiley; 1980.
- Fay MP. Estimating age conditional probability of developing disease from surveillance data. *Popul Health Metr.* 2004 Jul 27;2(1):6. Available from: <http://www.pophealthmetrics.com/content/2/1/6>
- Fay MP, Pfeiffer R, Cronin KA, Le C, Feuer EJ. Age-conditional probabilities of developing cancer. *Stat Med.* 2003;22(11):1837-48.



Feinstein AR, Sosin DM, Wells CK. The Will Rogers phenomenon: Stage migration and new diagnostic techniques as a source of misleading statistics for survival of cancer. *New Engl J Med*. 1985;312:1604-1608.

Feldman AR, Kessler L, Myers M, Naughton MD. The prevalence of cancer: Estimates based on the Connecticut Tumor Registry. *New Engl J Med*. 1986; 315:1394-1397.

Feuer EJ, Wun L-M, Boring CC. Probability of developing cancer. In: Miller BA, Ries LAG, Hankey BF, Kosary CL, Edwards BK, editors. *Cancer Statistics Review: 1973-1989*, National Cancer Institute, NIH Pub. No. 92-2789, 1992. p. 1-8.

Feuer EJ, Wun L-M, Boring CC, Flanders WD, Timmel MJ, Tong T. The lifetime risk of developing breast cancer. *J Natl Cancer Inst*. 1993;85:892-897.

Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, Whelan S, editors. *International Classification of Diseases for Oncology, 3rd ed*. Geneva: World Health Organization; 2000.

Gail MH, Kessler L, Midthune D, Scoppa S. Two approaches for estimating disease prevalence from population-based registries of incidence and total mortality. *Biometrics*. 1999;55:1137-44.

Greene FL, Page DL, Fleming ID, Fritz AG, Balch CM, Haller DG, Morrow M, editors. *AJCC Cancer Staging Manual, 6th ed*. New York (NY): Springer; 2002.

Hahn RA, Mulinare J, Teutsch SM. Inconsistencies in coding of race and ethnicity between birth and death in U.S. infants. *JAMA*. 1992;267:259-263.

Harris JE. Reporting delays and the incidence of AIDS. *J Am Stat Assoc*. 1990;85:915-924.

Howlader H, Ries LA, Stinchcomb DG, Edwards BK. The Impact of Underreported Veterans Affairs Data on National Cancer Statistics: Analysis Using Population-Based SEER Registries. *J Natl Cancer Inst*. 2009 101(7):533-536.

Ingram DD, Parker JD, Schenker N, Weed JA, Hamilton B, Arias E, Madans JH. United States Census 2000 population with bridged race categories. *Vital Health Stat 2*. 2003 Sep;(135):1-55.

Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, Thun MJ. Cancer statistics, 2008. *CA Cancer J Clin*. 2008;58:71-96.

Keyfitz N. Sampling variance of standardized mortality rates. *Hum Biol*. 1966;38:309-317.

Kim H-J, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med*. 2000;19:335-351.

Kleinbaum DG, Kupper LL, Muller KE. Applied Regression Analysis and Other Multivariable Methods, 2nd ed. Mariotto A, Gigli A, Capocaccia R, Clegg L, Scoppa S, Ries LA, Tesauro GS, Rowland JS, Feuer EJ. Complete and limited duration prevalence estimates. SEER Cancer Statistics Review, 1973-1999. 2002;19.

Merrill RM, Feuer EJ, Capocaccia R, Mariotto A. Cancer prevalence estimates based on tumor registry data in the SEER Program. *Int J Epidemiol.* 2000;29:197-207.

Midthune DN, Fay MP, Clegg LX, Feuer EJ. Modeling reporting delays and reporting corrections in cancer registry data. *J Am Stat Assoc.* 2005;100(469):61-70.

Pagano M, Tu XM, De Gruttola V, & MaWhinney S. Regression analysis of censored and truncated data: estimating reporting-delay distributions and AIDS incidence from surveillance data. *Biometrics.* 1994;50:1203-1214.

Percy C, Ries LAG, Van Holten VD. The accuracy of liver cancer as the underlying cause of death on death certificates. *Public Health Rep.* 1990;105:361-368.

Percy C, Stanek E, Gloeckler L. Accuracy of cancer death certificates and its effect on cancer mortality statistics. 1981. *Am J Public Health,* 71: 3242-3250.

Percy C, Van Holten V, Muir C, editors. International Classification of Diseases for Oncology, 2nd ed. Geneva: World Health Organization;1990.

Ries LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg LX, Edwards BK (eds). SEER Cancer Statistics Review, 1973-1997. National Cancer Institute. NIH Pub. No. 00-2789. Bethesda, MD, 2000.

Robinson JG, West KK, Adlakha A. Coverage of the population in Census 2000: Results from demographic analysis. *Population Res Policy Rev.* 2002;21:19-38.

Rosenberg HM, Maurer JD, Sorlie PD, Johnson NJ, MacDorman MF, Hoyert DL, Spitler JF, Scott C. Quality of death rates by race and Hispanic origin: A summary of current research. Hyattsville (MD): National Center for Health Statistics; Vital and Health Statistics, Series 2, No. 128, 1999.

Snedecor GW, Cochran WG. Statistical Methods, 7th ed. Ames (IA): Iowa State University Press; 1980.

US Cancer Statistics Working Group. *United States Cancer Statistics: 1999-2002 Incidence and Mortality Web-based Report Version.* Atlanta: Department of Health and Human Services, Centers for Disease Control and Prevention, and National Cancer Institute; 2005. Available from: <http://www.cdc.gov/cancer/npcr/uscs/index.htm>

US Bureau of the Census. Current Population Reports; Series P-25 No. 985. Washington (DC): US Government Printing Office; 1986.

Zelen M. Theory of early detection of breast cancer in the general population. In: Heuson J-C, Mattheiem WH, Rozenzweig M, editors. Breast Cancer: Trends in Research and Treatment. New York (NY): Raven Press; 1976. p. 287-299.

Zou J, Huang L, Midthune D, Horner MJ, Krapcho M, Feuer EJ. Effect of reporting year on delay modeling. Statistical Research and Applications Branch, National Cancer Institute; 2009. Technical Report #2009-01. Available from: <http://srab.cancer.gov/reports/>.