Atlas of Cancer Mortality in the United States

1950-94

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Abstract

The geographic patterns of cancer around the world and within countries have provided important clues to the causes of cancer. In the mid-1970s the National Cancer Institute prepared county-based and state economic area (SEA)-based maps of cancer mortality during 1950–69 in the United States that identified distinctive variations for specific tumors, thus prompting a series of analytic studies of cancer in high-risk areas of the country. This new *Atlas of Cancer Mortality in the United States* utilizes 1950–94 mortality data from the National Center for Health Statistics and population estimates from the Census Bureau. Rates per 100,000 person-years, directly standardized using the 1970 U.S. population, are calculated by race (whites, blacks) and sex for 40 forms of cancer. The *Atlas* includes more than 250 computerized color-coded maps showing variations in cancer rates during 1970–94 and compares them with corresponding maps for 1950–69. Summary tables and figures are also presented. Accompanying text describes the observed variations for specific cancers and suggests explanations based in part on the risk factors identified by analytic studies stimulated by the earlier atlases. The updated maps show that the patterns previously observed for several cancers have persisted, such as the broad stretches of high rates for cancers of the breast, colon, and rectum in the Northeast, although the regional variation has diminished somewhat as rates have risen in many areas of the South. For some tumors, the geographic clustering of areas with elevated rates has become more pronounced in the recent time period, as shown for cancers of the corpus uteri, prostate, bladder, and biliary tract. For lung cancer, there have been remarkable changes in the geographic patterns corresponding to regional/temporal variations in smoking trends by sex and race, with the recent emergence of high mortality rates among white men across the South, among white women in the far western states, and among blacks in northern urban areas. The updated geographic patterns should help in formulating etiologic and other hypotheses, and in targeting high-risk populations for further epidemiologic research and cancer control interventions.

Introduction

The study of geographic variation in cancer rates has provided important clues to the role of lifestyle and other environmental factors that affect cancer risk. Earlier atlases of cancer mortality in the United States[1–4] prepared by the National Cancer Institute (NCI) revealed substantial geographic fluctuations in rates from 1950 to 1980 in the white and nonwhite populations, pointing to high-risk areas for epidemiologic studies designed to identify carcinogenic exposures.[5,6] This *Atlas* updates the maps through 1994, presenting for the first time data specifically for blacks. The main focus will be the recent geographic patterns for 1970–94, but we also present maps for 1950–69 prepared in a similar fashion for purposes of comparison. The geographic patterns of cancer displayed in this *Atlas* should help to target further epidemiologic investigations into the causes of cancer and to set priorities for public health activities aimed at cancer prevention and control.

Two Web sites are available to further enhance evaluation of data illustrated in the *Atlas*:

Static Web Site: This Web site contains the entire text of the *Atlas*, as well as the maps for both time periods (1950–69 and 1970–94), tables, and figures. Maps at the state level, which are not included in the *Atlas*, are also available at this Web site. All data used to generate the county, state economic area, and state maps are housed at this site as well. Data, text, maps, tables, and figures can be downloaded. The Table of Contents is hyperlinked to the various sections of the *Atlas*, and references in the text are hyperlinked to the individual citations in the References section of the *Atlas*. The discussion about any specific cancer and the associated maps are interlinked.

Dynamic Web Site: This Web site enables the user to view the maps for both time periods, as well as for the entire period 1950–94. The user can control certain parameters such as number of ranges and colors. Also available is the option to view maps using percentiles based on one of the two time periods versus the entire time period. The user can select (from a drop-down menu) a specific state, state economic area, or county and view a map of the specific geographic unit and a table displaying the mortality rate and number of deaths for the selected unit, as well as the larger areas in which it is contained. Zooming in and out, and panning around the map, are additional options available at this Web site.

Materials and Methods

Sources of data

Data on all deaths among Americans during 1950–94 with cancer as the underlying cause according to age, sex, and race were provided for the 3,053 contiguous U.S. counties by the National Center for Health Statistics. Annual county-, age-, sex-, and race-specific midyear population estimates based on data from the Bureau of the Census were aggregated over the 25-year period 1970–94 and the 20-year period 1950–69 to form the person-years at risk. Data for the recent time period were produced at the county level for whites and at the state economic area (SEA) level for blacks and whites. The 506 contiguous SEAs are individual counties or groups of counties that are relatively homogeneous with respect to various demographic, economic, and cultural factors; they do not cross state lines. For 1950–69, when detailed county-level population estimates were not available specifically for blacks, maps are produced for whites only. Data for all 50 states and the District of Columbia are presented. Since mortality data were available only at the state level for Alaska and Hawaii, each was considered a single unit for county and SEA purposes, resulting in data for 3,055 counties and 508 SEAs. Data for Alaska and Hawaii are available only beginning in 1959 and 1960, respectively, when they became states. Appendix Map 1 of the United States displays the state, SEA, and county boundaries. Appendix Table 1 lists the state economic areas by state, and Appendix Table 2 lists the counties within state economic areas by state. A total of more than 40 cancers (including all forms combined) were considered, as shown in Appendix Table 3 (which also indicates the sixth to ninth revisions of the International Classification of Diseases[7–10] [ICD] codes used for each form of cancer).

Calculation of age-adjusted cancer mortality rates

For each form of cancer, the age-adjusted (direct method, 1970 U.S. population standard—see Appendix Table 4) mortality rate R per 100,000 person-years was calculated by race, sex, and geographic area for each of the time periods 1970–94 and 1950–69, as follows:[3,11,12]

$$R=100{,}000\sum(w_i r_i)=100{,}000\sum(w_i d_i/n_i)$$

where

i=the 18 age groups 0–4, 5–9, …, 85+,

w_i=the proportion of the standard population in age group i,

r_i=the age-specific rate d_i/n_i,

d_i=the number of deaths in age group i, and

n_i=the person-years in age group i

The binomial approximation to the variance of the age-adjusted rate was calculated as:

$$var(R)=100{,}000^2\sum[w_i^2 r_i(1-r_i)/n_i]$$

The 95 percent confidence limits of R were calculated from the square root of the variance as:

$$R \pm 1.96\sqrt{\mathrm{var}(R)}$$

A negative lower confidence limit was replaced by zero. For an area with zero deaths, the rate R was zero and the var(R) was estimated using the national rate. An area-specific age-adjusted rate was deemed significantly different statistically from the U.S. age-adjusted rate if their confidence limits did not overlap. Detailed area-specific data are not presented in this Atlas but are available from the NCI and from the NCI Atlas Static Web site.

Expected numbers of deaths from cancer for each geographic area by race and sex were the sums over age groups of the corresponding national age-specific rates times the age-specific person-years for each area by race and sex.

Male/female and black/white rate ratios (R_1/R_2) were calculated using the national age-adjusted rates rounded to two digits after the decimal point. The 95 percent confidence limits on the rate ratios are not presented but may be calculated as:[13]

$$\exp\left[\ln(R_1/R_2) \pm 1.96\sqrt{1/D_1 + 1/D_2}\right]$$

where

$\exp[x]=e^x$,

$\ln[x]$=the natural logarithm of x, and

D_1,D_2=the deaths associated with R_1,R_2 respectively

Maximum likelihood estimates of the relative risk standard deviations (RRSDs) and their standard errors (SEs) were calculated under the assumption of a mixed effects model. The RRSDs provide a measure of the standard deviation of the underlying area-specific relative risks and serve as quantitative indices to compare geographic variation across maps.[14]

Map production

Maps displaying cancer mortality rates by county and SEA were produced using Atlas Pro and Atlas GIS for Windows software (Strategic Mapping, Inc., now part of ESRI) on a Pentium personal computer. For ease of comparisons and readability, the size of Alaska was reduced and, for the SEA maps, the size of the District of Columbia was increased and separated from adjacent areas. Prior to mapping, rates for an area based on sparse data were deemed unstable if (a) the observed number of deaths was less than 6; (b) the observed number of deaths was less than 12 and the rate was not significantly different statistically from the U.S. rate; or (c) the expected number of deaths was less than 6 and the rate was not significantly different statistically from the U.S. rate. The stable rates were then ranked and partitioned into 10 deciles. The legend for each map portrays the national rate and the range of rates for each decile. Rates per 100,000 person-years are generally presented with 2 digits to the right of the decimal, although for some of the rarer cancers 3 digits are shown. In each map and legend, five shades of red (deciles at the median and above) and five shades of blue (deciles below the median) are used, with the intensity of color reflecting the ranked distance from the median. Gray is used for areas with sparse data (i.e., unstable rates as defined above).

Results

National mortality rates

During the 25-year study period 1970–94, more than 9.5 million whites and 1.1 million blacks died from cancer (Table 1a). The national annual age-adjusted mortality rates per 100,000 person-years for all cancers combined ranged from 136 among white females to 294 among black males. Although counts and rates for more than 40 specific categories of cancer are presented, almost 60 percent of all cancer deaths among males were due to 4 primary sites of cancer: lung, prostate, colon, and pancreas. Among females, nearly 60 percent of all cancer deaths were due to cancers of the breast, lung, colon, ovary, and pancreas. During the 20-year study period 1950–69, more than 4.8 million whites died from cancer; the numbers and rates are presented in Table 1b.

The 1970–94 national mortality rates for all cancers combined were 54 percent higher among white males than females and 84 percent higher among black males than females (Table 2 and Figures 1a-b). Most forms of cancer were more common among males than females, except for cancers of the breast, gallbladder, and thyroid. Among whites, the male/female rate ratio was highest for lip cancer, surpassing 10-fold, while ratios were also notably high for cancers of the larynx, esophagus, and bladder, each exceeding three-fold. Among blacks, the male/female ratio was highest for cancer of the larynx (6.5), followed by cancers of the oral cavity and pharynx, and the esophagus, each ratio being four-fold or greater. The male/female ratio for lung cancer was nearly three-fold among whites and nearly four-fold among blacks. Due to the large numbers of deaths, all male/female rate ratios were significantly different from unity.

The U.S. rates for all cancers combined were 40 percent higher among black than white males and 17 percent higher among black than white females (Table 2 and Figures 2a-b). For most specific forms of cancer, rates were higher among blacks than whites. The excess among blacks was most pronounced for esophageal cancer, with a black/white ratio exceeding three-fold in both males and females. Black/white ratios ranged between two- and three-fold for cancer of the cervix uteri among females; for cancers of the penis, prostate, oral cavity, and stomach among males; and for multiple myeloma in both sexes. On the other hand, rates for about one-third of all the cancers were higher among whites than blacks, most notably for cancers of the lip (males only), testis, eye, and brain, and for melanoma and non-Hodgkin's lymphoma. Most of the black/white rate ratios were significantly different from unity, except for rectal cancer among males, lung cancer among females, and nonmelanoma skin cancer in both sexes. The sex and race ratios varied somewhat with age. For all cancers combined, the higher rates among black than white males were limited to those aged 40 years and older (Figure 3), while the higher rates among males than females were primarily among those aged 60 and older.

Cancer mortality rates increased logarithmically with age, at least up to about age 40 for melanoma of the skin and cervical cancer, age 50 for breast cancer, and age 60 for many other sites (Figure 3). At older ages, the rates for certain cancers, such as cancers of the nasopharynx, oral cavity and pharynx, esophagus, larynx, lung, and brain, and Hodgkin's disease, did not continue to rise. Age-specific rates were bimodal for cancers of the bones and joints, testis, brain, and other endocrine glands, and for Hodgkin's disease and leukemia.

Measures of geographic variation

To assess geographic variability, mortality rates were calculated for counties and SEAs. Appendix Map 1 shows the boundaries for the states, SEAs, and counties, which vary greatly in area and population size. Based on 1980 census figures (the approximate midpoint of the 1970–94 study period), the largest white populations were clustered in counties and SEAs in the northeast, midwest, and west coast areas, with lightly populated areas in the Plains and Rocky Mountain states (Appendix Maps 2a-c). The black populations tended to be concentrated across the South and in urban areas in the East and along the west coast, with few blacks residing in large portions of the rest of the country. All 508 SEAs had at least 10,000 whites, while almost 90 percent had at least 100,000. In contrast, 47 percent of the SEAs had fewer than 10,000 blacks.

Geographic areas (counties or SEAs) with sparse data are shaded gray on the maps. For all cancers combined among whites during 1970–94 and 1950–69, mortality rates for only a few of the 3,055 counties were unstable on the basis of small numbers (Tables 3a-d). At the SEA level, no rates among whites were based on sparse data. Among blacks, however, the total cancer rates during 1970–94 for 61 and 80 of the 508 SEAs among males and females, respectively, were based on data too sparse to analyze, but these areas contributed less than 0.07 percent of all cancer deaths among U.S. blacks. The number of geographic units with sparse data for specific tumors varied considerably, and thus the proportion of areas shaded gray differs among the maps.

County-level maps for a specific form of cancer were included in this volume when less than 10 percent of male or female deaths from that cancer occurred in gray areas during 1970–94. Because of this criterion, county maps are presented only for whites with the more common tumors. Individual SEA-level maps, however, are shown for whites and for blacks if fewer than 50 percent of the deaths from the specific cancer among males or females of that race occurred in gray areas (Tables 3a-d). Thus, the numbers of maps presented vary by site of cancer (Table 4). Maps are not shown at the county or SEA level for the very rare sites: lip and eye.

Measures of the degree of geographic variation in cancer rates are given by the relative range and decile distribution of the rates for each 1970–94 SEA map included in the Atlas (Figures 4a-d). In most of the four race/sex groups, the relative differences were greatest for cancers of the oral cavity and pharynx, esophagus, liver, larynx, and lung. Considerably less variation was apparent for leukemia and cancers of the pancreas, ovary, and brain. Prostate cancer varied relatively little among whites but more among blacks. A closely-packed midrange of rates indicates little geographic variation, whereas a spread out midrange suggests substantial differences in rates across the country. The 95 percent confidence limits on the national rates are not shown because, being based on large numbers of events, they generally are quite narrow. For example, a cancer rate of 1.000 based on 1,000 events would have confidence limits of 0.939 and 1.064, or ±6 percent.

The relative risk standard deviations (RRSDs), an additional measure of the extent of geographic variation, are presented in Table 5 and Figures 5a-d for each 1970–94 SEA map included in the Atlas. Among those 28 cancers with sufficient data to warrant SEA maps for both races, the RRSDs were greatest for cancers of the oral cavity and pharynx, gallbladder, larynx, and (among whites) rectum. Relatively small RRSDs were estimated for leukemia, multiple myeloma, and cancers of the pancreas and prostate (among whites).

Geographic patterns by type of cancer

Following are brief descriptions of the geographic patterns of mortality during 1970–94 by form of cancer. Comparisons are made with the patterns for 1950–69, along with possible explanations suggested by epidemiologic studies prompted by the earlier maps. It should be noted that each map was prepared independently and portrays the geographic variation in rates during the given time period. Thus, for those cancers whose rates have increased or decreased over time, the relative position of a particular rate in a given area may vary when the change is more or less rapid compared to other areas.

All cancers (pages 64–73): In the recent time period 1970–94, rates were elevated among white males in a large proportion of counties across the eastern third of the country, both north and south, and along parts of the lower Mississippi River, while rates were low in most of California and Nevada. By contrast, in the earlier time period 1950–69, rates among white males were relatively low across the Southeast except for coastal areas. In both time periods, rates tended to be low across the upper midwestern states, the Plains, and Rocky Mountain states. Particularly striking was the change from low to high rates across much of the Southeast. Among white females in both periods, high rates were concentrated in the northeastern and mid-Atlantic states and in parts of the upper midwestern states, while in recent years high rates emerged in the far western states and several southeast coastal areas. Relatively low rates persisted in the southern and central regions of the country. Among black males and females, rates tended to be low across the southern parts of the country and elevated in the mid-Atlantic and midwestern areas. There was little geographic concordance at the SEA level between high-rate areas for whites and blacks among either males or females.

Salivary glands (pages 74–77): There was little consistent variation in SEA-level rates among white males or females, although rates were unstable in most areas due to small numbers of deaths. Mortality was elevated in parts of Texas in three of the four maps presented.

Nasopharynx (pages 78–83): There was no evidence of geographic clustering except for some elevated rates among white males along the Gulf coast in the recent time period. Mortality was elevated in Hawaii among white males during both time periods and white females during 1970–94. Since several Asian groups, especially Chinese, have an increased risk of nasopharyngeal cancer,[15] it is possible that the elevated rates reported among whites in Hawaii are related to racial misclassification or admixture. It is noteworthy that nasopharyngeal cancer incidence rates are not elevated among whites in Hawaii,[16] suggesting possible misclassification on Hawaiian death certificates.

Oral cavity and pharynx (pages 84–93): In recent years, geographic variation was pronounced, with high rates along the eastern seaboard among white males and females and elevated rates also among females in the northeastern and several western states, especially along the Pacific coast. In both time periods, low rates were seen across the central, Plains, and Rocky Mountain states in both sexes. The prominent clustering of excess mortality among white females in the Southeast during 1950–69 faded somewhat during 1970–94. Among blacks, the rates were generally low across the South. As the dominant risk factors for oral and pharyngeal cancer, cigarette smoking and alcohol consumption largely account for the higher national rates among blacks than whites and among men than women[17,18] and contribute to the geographic patterns observed.[19] Use of smokeless tobacco has been implicated as the cause of the elevated rates of oral cancer observed since the 1950s among women in the rural South.[20] Despite reductions in the prevalence of snuff dipping among women,[21] there are still patches of elevated oral cancer rates in parts of the Carolinas, Georgia, and Florida in the recent period.

Esophagus (pages 94–103): Marked geographic variation among white males and females was seen in both periods, especially in recent years, with elevated rates primarily in the northeastern and mid-Atlantic states and in scattered midwestern areas. Low rates have persisted among white males in the southern and Rocky Mountain states and among white females in the central portions of the country. The geographic variation has been more pronounced among males than females and among whites than blacks. However, high rates among white females have emerged recently in certain areas along the Gulf coast and in the far western states. Tobacco smoking and alcohol drinking are the major risk factors for esophageal cancer,[22,23] as they are for oral cancer, and they contribute to the high rates in urban areas and to the striking black/white differentials in rates.[24] In Washington, DC, and coastal areas of South Carolina, where the rates are especially high in blacks, case-control studies have revealed strong associations with alcohol consumption and tobacco use along with deficiencies of fruit and vegetable consumption.[25–27] Heavy use of moonshine (home-brewed) whiskeys among blacks in the South Carolina low country appears partly responsible for the elevated rates in that area.[27] Mortality rates for esophageal cancer almost doubled among blacks from the 1950s to their peak in the 1980s, accounting for increases in the black/white rate ratios over time.[23,28]

In recent decades, a remarkable shift has occurred in the histologic patterns of esophageal cancer among whites, as incidence rates for squamous cell cancer have decreased while rates for adenocarcinoma have increased dramatically to surpass the rates for squamous cancer of the esophagus among males.[29,30] The reasons for the upward trend in esophageal adenocarcinoma are not entirely clear but may be related in part to smoking habits[31] and obesity,[32] which appear to promote the development of reflux esophagitis and its evolution to Barrett's esophagus, a precursor state for this cancer.[33,34] Since histologic type is not routinely recorded on death certificates, the geographic differences in the two forms of esophageal cancer could not be evaluated. Incidence rates among white males in the Surveillance, Epidemiology, and End Results (SEER) program during 1973–95 were highest in Connecticut and Seattle for esophageal cancer overall and for esophageal adenocarcinoma, while the rates for squamous cell carcinoma were highest in Hawaii and Connecticut (unpublished SEER data). Rates for total esophageal cancer and both histologic types were lowest in New Mexico and Utah.

Stomach (pages 104–113): The maps for both time periods revealed high rates among whites that stretch across the northeastern and north-central states, especially in urban areas. Rates were elevated also in parts of the Southwest but were generally low across the Southeast. The geographic patterns among blacks were less pronounced, although rates were generally higher than among whites, with clustering in parts of southern Louisiana. The elevated rates in the north-central areas appear to be related to the concentration of Scandinavian and other high-risk ethnic groups from Europe,[35,36] while the elevated rates among whites in the Southwest appear to reflect the excess risk among Hispanics.[37] In high-risk areas of southern Louisiana, case-control studies have suggested protective effects of fruit and vitamin C consumption in whites and blacks, while consumption of smoked foods and home-cured meats was associated with increased risk among blacks but not whites.[38] Although dietary factors may influence the geographic, temporal, and racial patterns of stomach cancer, there is mounting evidence that infection with *Helicobactor pylori*, particularly at young ages, plays a key role in the origins and distribution of gastric cancer.[39,40]

Rates for stomach cancer have been declining for many years.[41] However, the incidence of cancers arising from the gastric cardia has increased along with esophageal adenocarcinoma, both of which appear to share risk factors.[29,30] The location of tumors within the stomach is typically not recorded on death certificates, so that geographic variation by subsite could not be studied. The SEER incidence rates among whites for total stomach cancer during 1973–95 were highest in Hawaii and lowest in Atlanta, whereas rates for tumors of the gastric cardia were highest in Seattle and lowest in Utah (unpublished SEER data).

Colon (pages 114–123): In all four race/sex groups, striking geographic variation was evident, with mortality rates highest in the northeast quadrant of the United States, including parts of New England, and both the mid-Atlantic and the midwestern states. Rates across the South and West have remained relatively low. Colon cancer mortality has been elevated in the Northeast for at least four decades, partly due to increased risks for urban populations with high socioeconomic levels,[42] although the regional variation has diminished somewhat over time as more areas in the South have displayed rising mortality rates than in the North.[3,4] While reasons for the geographic patterns are unclear, dietary and nutritional factors are likely to be involved.[43–45] A diet high in fat and calories was suggested, for example, by a case-control study of colon cancer in a high-risk area of Nebraska with a large concentration of residents of Czechoslovakian background.[46] Of particular note is the lack of high rates in southern retirement areas, suggesting a pattern opposite to the rapid increase in risk reported in population groups migrating from low- to high-risk countries.[47] Colon cancer incidence rates among whites during 1991–95 were relatively high in Connecticut, Detroit, and Iowa, and low in Utah and New Mexico,[48] consistent with the mortality patterns.

Rectum (pages 124–133): Like colon cancer, there was a clear pattern in both periods of elevated rates among whites in the northeastern, mid-Atlantic, and midwestern areas, with low rates across the southern tier. Few of the SEAs west of the Mississippi River had high rates. The similar variations for colon and rectal cancer suggest risk factors in common. Reporting practices may contribute to the similarity in patterns, since rectal cancer is sometimes specified on the death certificate as intestinal cancer, which is then categorized with colon cancer.[49] The geographic variation among blacks was similar to that of whites, although less consistent.

Liver, gallbladder, and other biliary tract (pages 134–143): These sites did not have separate ICD codes until 1958, so that the three sites are grouped together for both time periods and then considered separately for the recent time period 1970–94. Included with primary liver cancers are tumors not stated to be primary in the liver, but excluded are those stated as secondary or metastatic. In the combined categories of liver, gallbladder, and other biliary tract cancers, the rates among white males were elevated during both periods in several Appalachian areas and in southern Louisiana and Texas. High rates among white females were prominent in the midwestern and north-central areas as well as in Appalachia, south Texas, and New Mexico. Rates among blacks were higher in northern urban areas and generally low across the Southeast.

Liver (pages 144–147): Rates were elevated in many areas across the south-central and southwestern states among whites and were generally low in northern areas. Little geographic variation was evident in blacks, whose rates have been higher than those among whites. Liver cancer is particularly subject to misspecification on death certificates,[50] but it is unclear whether diagnostic and reporting practices have varied geographically. In the SEER data, liver cancer incidence rates are higher among Hispanic than non-Hispanic whites,[37] which probably contributes to the excess mortality in the southwestern states. Further work is needed to clarify the role of hepatitis B and C infection, as well as that of alcohol consumption, in the ethnic and geographic patterns of liver cancer.[51]

Gallbladder (pages 148–151): Among whites, rates were elevated in portions of the Appalachian region, the midwestern and north-central regions, and parts of the

Southwest, with generally low rates across the southeastern and far western states. The pattern was more pronounced among females, whose rates of gallbladder disease, including cancer, are higher than those of males and reflect the excess risk of gallbladder cancer in patients with gallstones.[52] Despite the rarity of mortality from gallstones, the geographic patterns have been found to resemble those for gallbladder cancer.[53] The elevated rates of gallstones and gallbladder cancer among Hispanics and American Indians largely account for the excessive mortality seen in the southwestern states, while a high incidence of both conditions has been reported in areas of Appalachia with low socioeconomic levels.[54] The elevated rates in the northeastern and north-central areas may be related to the concentration of high-risk ethnic groups from eastern Europe,[52] but further studies are needed. Among blacks, there was no consistent geographic variation for this rare cancer.

Other biliary tract (pages 152–153): The geographic distribution of other biliary tract cancers (including bile duct and ampulla of Vater) resembles that for gallbladder cancer, especially in females. However, the variation is less pronounced, probably because gallstones are less conspicuous as a risk factor for these tumors.[52]

Pancreas (pages 154–163): In both time periods, geographic variation was less pronounced than for most other cancers. Nevertheless, several high-rate areas were seen among whites in the urban northeastern and south-central areas, including southern Louisiana, along with scattered areas with elevated rates across the north-central and western states (especially for white females in the recent time period). Among blacks, whose rates are higher than those for whites, there was no obvious clustering of high-rate areas, except in southern Louisiana among males, although mortality tended to be low across the South. Ecological studies have suggested that pancreas cancer mortality rates are higher in urban areas and in areas with many persons of Scandinavian and eastern European descent.[55] Although cigarette smoking is an important risk factor for pancreas cancer, the geographic patterns have shown little resemblance to those for lung cancer. In the high-rate area of southern Louisiana, a case-control study revealed elevated risks associated with cigarette smoking and with dietary habits characteristic of the Cajun population, especially the use of pork products and low consumption of fruit.[56]

Nose, nasal cavity, and sinuses (pages 164–167): There were no clear-cut patterns for this uncommon tumor, except for some elevated rates among white males in the eastern part of Texas. However, elevated mortality from sinonasal cancer was found in a correlation study of counties with furniture industries,[57] prompting case-control studies in high-exposure areas of North Carolina and Virginia.[58–61] Work in the furniture industry was found to be associated with an excess risk of nasal adenocarcinoma, resembling the occupational hazard previously reported in England and other countries.[62] In addition, heavy smokers were shown to have an excess risk of squamous cell carcinomas of the nasal passages, the most common form of nasal cancer.[59] Among females, an excess risk of nasal cancer was associated also with work in the textile industry, consistent with results of other studies.[60]

Larynx (pages 168–173): Rates among white males and, to a lesser extent, white females were elevated in scattered areas of the eastern third of the country and in southern Louisiana but tended to be low in central and western areas. The clustering of high rates across the eastern part of the country seemed more pronounced in 1970–94 than in 1950–69. The pattern among white females is less remarkable, with scattered high rates in the Northeast. The geographic patterns of laryngeal cancer have been strongly correlated with those for lung, esophageal, and oral cancers,[63] consistent with the major risk factors of tobacco smoking and alcohol consumption.[64,65] Laryngeal cancer rates were elevated among white men in counties that had shipyard industries during World War II,[66] but a case-control study in Virginia failed to identify an excess risk associated with employment in area shipyards.[67]

Lung, trachea, bronchus, and pleura (pages 174–183): Among white males, rates in the recent time period 1970–94 were elevated across broad stretches of the Southeast, particularly along the eastern seaboard, across the Gulf coast, and along the Mississippi valley. Rates in the upper midwestern, Plains, and Rocky Mountain states were notably low, whereas rates in the northeastern and far western states approximated the national rate. Among white females, elevated rates during 1970–94 tended to cluster along both the Atlantic and Pacific coasts, including most of Florida and California. Among black males and females, rates were elevated in scattered northeastern and midwestern areas, and low across much of the South. These patterns are described in more detail elsewhere.[68] The recent patterns for whites are quite different from those of 1950–69, which showed high lung cancer rates among males in northeastern urban areas, in areas along the southeastern Atlantic and Gulf coasts, and throughout the far western states, but only limited clustering of high rates among females. When data were previously reported through the 1970s, there was a shift towards higher rates in broader areas of the South among men and along the Atlantic and Pacific coastal areas among women.[3,69] The earlier maps for nonwhites[2,4] showed low rates across the South for both males and females, with scattered high rates in other areas of the country.

Since the dominant cause of lung cancer in the United States is cigarette smoking,[70] efforts have been made to correlate the cancer patterns with regional variations in smoking rates identified from population surveys in the 1950s through the 1990s according to area of residence. Since smoking acts at both early and late stages in the process of lung carcinogenesis,[71] the relevant data on smoking for cancers occurring in 1970–94 would be smoking prevalences for this time period *and* for periods 10, 20, and 30 or more years earlier. Limited data from the 1950s indicate that regional differences in smoking patterns among males were rather small, except that smoking was more common in urban than rural areas and the percentage of heavy smokers was greatest in the Northeast.[72] By the late 1970s, the prevalence of current smokers was highest among men in the South under age 65, with little difference at older ages.[73] More recently, in the mid-1980s, it was clear that the South led the nation at all ages in the percentage of adult males who smoked.[74] Hence the smoking trends fit well with an early excess of lung cancer among white men in urban areas, particularly in the North, and the recent emergence of elevated mortality among white men across broad stretches of the South. Smoking data were not specific enough to correlate with the patterns of lung cancer seen along the southeastern coast. However, smoking habits, including the greater use of hand-rolled cigarettes, were found to contribute to the high rates in southern Louisiana, especially in the Cajun population.[75] The prevalence of smoking among black males in 1985 was lowest in the South and highest in the West,[74] where the lung cancer rates are not yet elevated.

Among females, the 1950s' smoking survey found the highest prevalence of current smokers in the West and the lowest in the South.[72] By the 1980s, however, white women in the West, in both the Pacific and Rocky Mountain states, made up the lowest percentage of current smokers among all regions.[74] Thus, the clustering of lung cancer among white women in the recent time period, particularly along the Pacific coast, is consistent with earlier rather than later variations in smoking rates. The 1985 prevalence of smoking among black females was highest in the north-central region and lowest in the South, similar to the geographic patterns of lung cancer.

Although smoking patterns largely account for the regional variation in lung cancer mortality, the early maps[1,3] and subsequent correlation studies also suggested a relation to certain occupational exposures,[35,76] which prompted a series of case-control studies in high-risk areas, particularly along the southern seaboard. In the 1970s and early 1980s, studies in coastal Georgia,[77] Tidewater Virginia,[67] northeast Florida,[78] and southern Louisiana[79] revealed an excess risk of lung cancer associated with work in shipyards, primarily during World War II. Asbestos exposure appeared to be the major hazard, especially since clusters of mesothelioma were also observed in certain coastal areas.[80,81] In the recent maps, the coastal excess of lung cancer among men was less pronounced, perhaps due to a diminished effect of wartime asbestos exposures, since risk of lung cancer is known to decline following cessation of asbestos exposure.[71] Indeed, a case-control study of lung cancer in northeast Florida during the 1990s found no significant excess risk associated with prior work in shipyards.[82] It is possible that the recent clustering of high lung cancer rates among females in certain areas along the southeast coast may be partly related to asbestos exposures associated with the shipbuilding industry, particularly in view of synergistic effects with smoking.[77]

Correlation studies have also revealed elevated rates of lung cancer among males and females residing in counties with arsenic-emitting smelters,[83] prompting case-control studies indicating a carcinogenic effect of neighborhood as well as occupational exposures to inorganic arsenic.[84]

Bones and joints (pages 184–189): High rates among whites were seen in both time periods in portions of Appalachia, extending into the deep South. Rates among blacks also were higher in the South than in the North. It seems likely, however, that the mortality patterns are influenced by the inclusion of tumors metastatic to the bone.[85] In contrast, incidence rates for primary bone cancer during 1973–95 were highest in Utah, Seattle, Connecticut, and San Francisco-Oakland, and lowest in Atlanta (unpublished

SEER data). Despite concerns that fluoridation of drinking water might increase the risk of bone tumors, particularly osteosarcomas, detailed analyses of incidence and mortality rates have revealed no temporal or spatial patterns suggesting a relation to fluoridated supplies of drinking water.[86,87]

Connective tissue (pages 190–195): There was little evidence of geographic variation, except for some elevated rates among white females in the northern Plains and mountain states in the recent time period. The patterns for this uncommon tumor may be influenced by changes in diagnostic and reporting practices.[88]

Melanoma of skin (pages 196–199): During both time periods, a north-south differential was seen among white males and females, with lower rates in the North and higher rates in the southeastern and south-central regions. The low rates in south Texas and south Florida may be due to the concentration of Hispanic populations, which have low rates of melanoma.[37] The persistent latitudinal gradient seen for melanoma has been attributed to ultraviolet radiation from sunlight, especially when exposures occur at young ages.[89] The epidemiologic patterns for melanoma suggest that intermittent or recreational exposures are especially important, along with host susceptibility factors, including light skin pigmentation and dysplastic nevi.[90] Because of the rarity of melanoma among blacks, the data were too sparse for mapping.

Other skin (pages 200–205): The geographic patterns generally resemble melanoma, despite the low case-fatality rates of basal and squamous cell carcinomas. Based on special incidence surveys in the United States, both tumors have shown latitudinal gradients consistent with sunlight exposure.[91] The assignment of Kaposi sarcoma to this category during part of the recent time period is likely to explain the high rates in some urban areas where the AIDS epidemic was most prevalent.[92]

Breast (pages 206–212): Among white females in both time periods, there was a predominance of high rates in the northeastern and north-central regions and in scattered areas of the far western states, as well as low rates across the South and in the Rocky Mountain areas. A north-south gradient in breast cancer risk was also suggested among white males and black females, although not as pronounced as among white females. The regional excess of breast cancer across the Northeast, especially in urban centers, has persisted for over four decades.[1,3,93] The pattern is most pronounced among postmenopausal women, with little geographic variation among premenopausal women.[94] However, the north-south differences have diminished over time as mortality rates have risen in many areas of the South, including rural areas of Appalachia.[3] In a recent correlational analysis, regional variations in breast cancer mortality were attributed mainly, but not totally, to the distribution of established risk factors, including late age at first birth, early menarche, and late menopause, and to certain prognostic factors, including education and mammography history.[95]

Cervix uteri (pages 214–218): Elevated rates among white females tended to cluster across the South, more so in the earlier time period than recently, across Appalachia, parts of the midwestern states, and the upper Northeast. High rates were also seen in the southern part of Texas, perhaps due to the concentration of Hispanic women, who tend to have elevated risks.[37] Low rates occurred in the lower Northeast, northern Plains, and Rocky Mountain states. Among black females, elevated rates were seen in areas across the Southeast. In southern stretches of the Appalachian mountains, incidence and mortality rates for cervical cancer are known to be increased, particularly among rural women of low socioeconomic status.[96,97] The geographic, racial, and socioeconomic patterns of cervical cancer can be attributed mainly to variations in the prevalence of human papillomavirus (HPV) and in the use of Pap smears to detect premalignant lesions, which can then be cured.[98] The prevalence of HPV infection was shown to be 34 percent among Washington, DC, women who attended medical assistance clinics and were presumably at high risk,[99] as compared with 18 percent among low-risk women in Portland, OR.[100] Although mortality from cervical cancer has declined substantially throughout the country,[101] rates in certain areas have decreased less rapidly, mainly due to relative lack of access to screening programs.

Corpus uteri and uterus not otherwise specified (NOS) (pages 220–224): High rates among white females clustered in parts of the northeastern, midwestern, and Plains states, whereas rates generally were low across the South and the Rocky Mountain states. These patterns were more pronounced in recent years than earlier. In the far western states, low rates in the past have given way to intermediate and higher levels of mortality. Among black females, rates appeared high in scattered areas of the eastern half of the country. The clustering of elevated rates among white women in the Northeast, the West, and the midwestern states in recent years appears related to variations in the prevalence of risk factors such as nulliparity, obesity, and hormone replacement therapy.[95,102–104] National mortality rates for cancers of the corpus and uterus NOS have decreased over time,[101] partly due to the pronounced decline in cervical cancer that might have been specified as uterus NOS on death certificates and to earlier diagnoses of corpus cancer with consequent improvements in survival. The incidence trends corresponding to the increase and subsequent decline in use of unopposed menopausal estrogens during the early 1970s had little effect on the mortality trends,[48] since affected cases were largely diagnosed at early stages with a favorable prognosis. The map for blacks shows some resemblance to that for cervical cancer, suggesting problems with reporting and classification.

Ovary (pages 226–230): Mortality rates among white females in both time periods revealed a north-south gradient, with high rates extending across the northern tier and low rates in most of the South. The pattern among black females was similar, with rates being low in most of the Southeast and high in scattered areas elsewhere. The maps resemble those for breast cancer and suggest risk factors in common, such as nulliparity.[105]

Vagina (page 232): Cancer of the vagina was coded with other tumors of the genital tract during the earlier time period, so rates are available only for the recent period. Among white females, elevated rates were seen in parts of northern Appalachia, but the rates in most SEAs are based on sparse data. Like cervical cancer, these tumors have been related to HPV infection.[106] Although the national rate was higher for blacks than whites, the data for black females were too sparse for mapping.

Vulva (page 234): Cancer of the vulva was also coded with other tumors of the female genital tract during the earlier time period. In recent years, high rates clustered not only in parts of northern Appalachia but also in some areas of the northeast quadrant of the country, with generally low rates in the rest of the country. These tumors also have been linked to HPV infection.[107] The data for black females were too limited for presentation.

Prostate gland (pages 236–240): Although geographic variation is generally more limited than for most cancers, a distinct geographic pattern was seen during both time periods among white males, with a concentration of elevated rates in the Northwest, Rocky Mountain, and north-central areas of the United States and low mortality in the south-central areas. An inverse urban-rural gradient was also suggested, with high rates in less populated areas of New England, the midwestern, northern Plains, and Rocky Mountain states, and the West. The recent patterns for white males have revealed more pronounced clustering in the northwest sector of the country than in earlier years. Black males have especially high mortality from prostate cancer at the national level, with pockets of elevated rates in the southeastern part of the country. It is unclear whether the patterns are partly related to screening and treatment practices, but there is some evidence that agricultural exposures may contribute to the geographic variation, including the high rates among whites in farming communities in the north-central and western states[108] and among blacks in the southeastern states.[109,110]

Testis (pages 242–243): In both time periods, scattered high rates were seen among white males in the northern and central areas of the country, while mortality was generally low across the South and close to the national rate in the Northeast. Mortality rates have declined substantially since the early 1970s due to improved treatment and patient survival, whereas incidence rates have risen.[92] During 1973–95, testicular cancer incidence rates among white males were highest in Seattle, Hawaii, and San Francisco-Oakland, and lowest in New Mexico, Atlanta, and Iowa (unpublished SEER data). Testicular cancer is relatively rare among blacks, with the incidence rate among whites more than five times that among blacks,[48] so that the mortality data for blacks were too sparse for mapping.

Penis (page 244): Rates among white males are based on sparse data in most SEAs, but some elevations were seen in midwestern areas, while low rates were noted in the West and in southern Florida. Although rates were higher among blacks than whites, the data for blacks were too limited for mapping. Rates are not available for the earlier time period, since penile cancer was coded with other tumors of the male genital tract.

Bladder (pages 246–255): In both time periods, elevated mortality rates among white males clustered in the northeastern states, especially in New Jersey, New York, and upper New England. High rates also occurred in parts of the midwestern and far western states, whereas rates generally were low across the South, except in Florida. Rates among white females also were elevated in the Northeast, particularly in northern New England and New York, overlapping with the patterns seen in males. North-south gradients were suggested also among black males and females, except for Florida. Bladder cancer among men has tended to cluster in the urban Northeast since the 1950s, particularly in areas with chemical industries.[111] Case-control studies in high-risk areas have revealed excess risks in a variety of occupations, which contribute to about one-quarter of bladder tumors in white males,[112–114] including an increased risk among truck drivers and other workers exposed to motor exhausts.[115] Although cigarette smoking accounts for one-half of bladder cancer,[116] the geographic patterns for lung and bladder cancer are dissimilar. Elevated rates for bladder cancer among males and females in northern New England and New York have become more pronounced over time, and thus cannot be entirely explained by the associations with textile and leather occupations that were once prevalent in this area.[117]

Kidney, renal pelvis, and ureter (pages 256–265): Among white males and females, high rates were most prominent in New England and the upper midwestern and northern Plains states, with scattered elevations in the South and other areas, more so in the recent period than earlier. Among blacks, rates were generally low across the South. The persistently elevated rates among whites in the north-central states may be partly related to ethnic factors, with higher rates among those of northern European ancestry.[118] Cigarette smoking, obesity, and hypertension are important risk factors for renal cell carcinoma, the most common form of kidney cancer, but their contributions to the geographic patterns and upward trends are unclear.[119,120]

Brain and other nervous system (pages 266–275): In both time periods, elevated rates were seen in parts of the upper midwestern and north-central states and the Southeast among white males and females, with rates generally low in most areas of the northeastern, lower midwestern, southwestern, and Rocky Mountain states. Among blacks, the patterns appear fairly random. The causes of brain cancer are not well understood,[121] and it is possible that variations in diagnosis and reporting practices as well as survival experience contribute to the patterns observed.

Thyroid gland (pages 276–279): Consistent geographic patterns are not readily apparent, but in the earlier period there were scattered high rates among whites in the north-central and Rocky Mountain states,[122] where goiters were once more prevalent.[123] Concerns have been raised that thyroid cancer rates may be related to the fallout from radioactive iodine as a result of nuclear test explosions,[124] but the geographic and temporal correlations with mortality and incidence data are inconclusive.[125] Although female thyroid cancer mortality has been higher among blacks than whites, the data for blacks were too sparse for mapping.

Other endocrine glands (pages 280–283): There was little suggestion of a geographic pattern for this heterogeneous category among white males or females, with most rates being unstable due to limited data. Rates among blacks were based on data too sparse to map.

Hodgkin's disease (pages 284–289): Among white males and females, a latitudinal gradient was suggested, with mortality rates tending to be higher in the North than in the South. The clustering of high rates in the midwestern and northeastern states was more pronounced in 1970–94 than in 1950–69. This north-south gradient is most pronounced for the peak occurrence in young people,[126] which is suspected to be related to infectious agents, including Epstein-Barr virus.[127] Although incidence rates have not changed greatly over time, mortality rates have declined due to improvements in treatment and patient survival,[48,92] which may have influenced the geographic patterns. The rates among blacks are based on sparse data and show no evidence of a north-south gradient.

Non-Hodgkin's lymphoma (pages 290–299): In both periods, among white males and females, rates were higher in the northern and central parts of the country, especially in the north-central and upper midwestern states, and were generally low across the South. A north-south gradient was also suggested among blacks. The geographic patterns have been positively correlated with urbanization and socioeconomic status,[128] yet several studies have indicated that farm-related activities, including use of certain pesticides, may contribute to the elevated rates in the central parts of the country.[129–134] It has been suggested also that sunlight exposure may be a risk factor for non-Hodgkin's lymphoma, but the north-south gradients are opposite to those seen for melanoma and other skin cancers.[135] Incidence and mortality rates for this cancer have been increasing for many years,[92,136] and these trends are only partly explained by the AIDS epidemic, which accounts for nearly 20 percent of non-Hodgkin's lymphoma.[137,138] Despite the rising trends for this tumor, the geographic patterns have not significantly changed over time.

Multiple myeloma (pages 300–305): Some geographic clustering among whites was evident in both the 1950–69 and the 1970–94 maps, with rates being relatively high in midwestern areas and the Plains states and low in parts of the South. In early years, the patterns were positively correlated with degree of urbanization and socioeconomic level,[139] probably related to diagnostic factors, but the disease is now more common in persons of low socioeconomic status.[140] Environmental causes are obscure, although an elevated risk has been reported among farmers.[109] North-south gradients are suggested among blacks, whose rates are much higher than those among whites for reasons that are unknown.[141]

Leukemia (pages 306–315): In both time periods, high rates among whites occurred in a central band of the country from the Plains states to the midwestern region and south to the Gulf, along with a scattering of high rates in the East and West. Rates were generally low in the Southwest and much of the East. This pattern was more pronounced among white males than white females. Similarly, leukemia incidence rates among whites during 1973–95 were highest in Detroit and Iowa and lowest in Atlanta, Utah, and New Mexico (unpublished SEER data). Little variation in leukemia mortality was seen among blacks. Although the geographic variation is less pronounced than for other cancers, some studies have suggested that agricultural exposures, including pesticides, may contribute to the patterns.[109] The patterns for the major cell types of leukemia could not be distinguished from the available data. Ionizing radiation may contribute to some forms of leukemia, but a nationwide survey of mortality among populations living near nuclear facilities revealed no excess risk.[142]

Other and unspecified cancers (pages 316–325): Rates for these poorly specified cancers were elevated in several areas across the South, West, and mid-Atlantic regions, while low rates were evident in the north-central and northwest areas of the country. Due to changes in coding specificity, cancers of the vagina, vulva, and penis were included with other and unspecified cancers in the earlier time period, but are presented separately for the recent period. Because of their rarity, these tumors probably had little influence on the 1950–69 maps. In the recent time period, the category of other and unspecified cancers accounted for seven to nine percent of all cancers, and it would appear to represent a very heterogeneous group of tumors.

Discussion

The updated maps presented in this new Atlas continue to display substantial geographic variation in mortality from a number of cancers in the United States. Mortality data are derived from death certificates and, as such, are dependent on the accuracy of the information recorded. However, the precision of demographic data (sex, race, age, address) on the certificates has been found to be quite good,[143–145] and diagnoses of cancer are considered generally reliable. A comparison of the information on the death certificates with autopsy findings revealed that neoplasms were more accurately diagnosed than other causes of death.[146] Although specificity of the site or type of cancer on the death certificate may be less detailed than in the medical record, there is generally good agreement for most forms of cancer.[147,148] Geographic variation in the accuracy of death certificates has not been well studied and may contribute to some of the patterns observed. Coding of the cause of death, however, is conducted nationally according to strict guidelines, using an automated system, and thus should not vary geographically.[149,150]

Mortality data are available for the entire country over a substantial period of time, a key advantage over cancer incidence data that are available for only certain portions of the United States. Furthermore, for the more fatal cancers, mortality approximates incidence. For the less fatal cancers, mortality may reflect not only risk of cancer but also stage of disease at diagnosis, treatment efficacy, and subsequent survival. Thus, geographic variation in patient access to medical facilities, and in diagnostic and treatment practices, may influence the mortality patterns for certain cancers. Residential history is not available in the mortality data, so that migration effects could not be evaluated. In general, however, population movements would tend to reduce the geographic fluctuations in mortality rates.

Despite these limitations, it is likely that the mortality data in this Atlas provide an adequate and appropriate measure of cancer deaths across the United States, and that the site-specific geographic patterns are a meaningful source of clues to the causes and control of cancer. In particular, clustering of adjacent counties or SEAs with elevated rates may provide a signal to lifestyle or other environmental causes of cancer, while aggregation of low rates may reflect a lowered prevalence of risk factors or perhaps a higher prevalence of protective factors. The maps, along with other descriptive and ecologic patterns, cannot serve to identify carcinogenic exposures, but they have proven to be useful as a strategy for generating etiologic leads and identifying areas of the country where hypothesis-testing studies may be targeted.[6]

The updated maps show that the patterns previously observed for several cancers have persisted, such as the broad stretches of high rates for cancers of the breast, colon, and rectum in the Northeast. However, the amount of regional variation has diminished somewhat as rates have risen in many areas of the South. For some tumors, the clustering of areas with elevated rates has become more pronounced in the recent time period, as seen for cancers of the corpus uteri, prostate, bladder, liver, and gallbladder. For lung cancer, there have been remarkable shifts in the geographic patterns corresponding to regional/temporal variations in smoking trends by sex and race, with the recent emergence of high mortality rates among white men across the South, among white women in the far western states, and among blacks in northern urban areas.

The determinants of many geographic patterns remain to be elucidated, but there is little question that variations in cigarette smoking greatly influence the patterns of lung and certain other tobacco-related cancers. In addition, smokeless tobacco use contributes to the patterns of oral cancer, specifically the high rates among women in the Southeast. The patterns of alcohol consumption are responsible in part for the geographic variations in cancers of the oral cavity and pharynx, larynx, esophagus, and liver.[151] Dietary factors, including the protective effects of fruit and vegetable consumption,[152] may affect the patterns of esophageal, stomach, colorectal, and other cancers, while infectious agents probably contribute to the variations seen for cancers of the cervix, liver, and stomach, and the lymphomas.[153,154] Occupational exposures have been implicated in the more localized clusters of high-rate areas, as seen among men with cancers of the lung and bladder and possibly lymphoma. The persistently high rates for bladder cancer among males and females in northern New England suggest the need for further studies to identify environmental pollutants, dietary factors, or other exposures that affect both sexes. For several cancer sites, it is unclear whether the geographic variations in mortality reflect environmental hazards, medical care and delivery systems, reporting practices, or other factors. Whatever the reason, the updated geographic patterns should help in formulating etiologic and other hypotheses, and in targeting high-risk populations for further epidemiologic research and cancer control interventions.

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