GEOGRAPHIC ANALYSIS

Lynn R. Goldman, MD, MPH
Unlike most other chronic diseases, cancer is a disease for which public health officials have established a national system for tracking mortality. Cancer kills: According to the American Cancer Society (ACS) estimates, in 2000, 1,220,100 people were diagnosed with cancer for the first time and 563,100 died from it.[1] It is estimated that environmental factors account for 72% of cancers.[2] Cancer mortality data provide a useful illustration for how tracking efforts could be improved to put together a better picture of how the environment affects disease rates. Based on the NCI Atlas of Cancer Mortality in the U.S. (www.nci.nih.gov/atlas), Health-Track has mapped the mortality rates of eight cancers from 1970-94, the most current rates available to the public.[3] Health-Track chose cancers that are common and are suspected to have strong environmental components. Cancers mapped are: bladder, brain, breast (female), Hodgkin’s disease, leukemia, liver, non-Hodgkin’s lymphoma, and prostate (male). Taken together, these eight cancers account for an estimated 44.6% of cancer incidence and 27.6% of cancer deaths this year.[1] Each mortality rate is mapped separately for race (black/white) and gender.

Cancer rates have been increasing in the U.S. The age-adjusted rate of cancer mortality in the U.S. increased 4.7% between 1950 and 1997 but much of this increase was due to lung cancer, and probably related to smoking.[3,4] Excluding lung cancer, mortality from cancer dropped 19% over this period.[4] At the same time, overall incidence from cancer (other than lung) increased by 45%.[4] The most important environmental cause of cancer in the U.S. is tobacco smoking. Diet and other lifestyle factors are also significant contributors. Other environmental factors, like occupational and community exposures to radiation and chemicals in products and pollutants, are conservatively estimated to account for between 8-16% of cancer incidence.[5]

Eight cancers were chosen for examination because of a likelihood of being environmentally related. However, two of them, breast and prostate, are much more common than the others and it is expected that the geographic distribution of the combined cancers will reflect the distribution of those two types. The table below gives some perspective on this and shows that the cancers in this study comprise about 44.6% of all new cancers NCI predicted for 2000 and 27.6% of deaths.[1]
Table 1. Cancer Diagnoses and Deaths for 2000 (1)

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Diagnoses 2000</th>
<th>Deaths 2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>53,200</td>
<td>12,200</td>
</tr>
<tr>
<td>Brain/Nervous System</td>
<td>16,500</td>
<td>13,000</td>
</tr>
<tr>
<td>Breast (female)</td>
<td>182,800</td>
<td>40,800</td>
</tr>
<tr>
<td>Hodgkin’s Disease</td>
<td>7,400</td>
<td>1,400</td>
</tr>
<tr>
<td>Leukemia</td>
<td>30,800</td>
<td>21,700</td>
</tr>
<tr>
<td>Liver</td>
<td>10,000</td>
<td>8,500</td>
</tr>
<tr>
<td>Non-Hodgkin’s Lymphoma (NHL)</td>
<td>54,900</td>
<td>26,100</td>
</tr>
<tr>
<td>Prostate</td>
<td>188,400</td>
<td>31,900</td>
</tr>
<tr>
<td>Total Subset</td>
<td>544,000</td>
<td>155,600</td>
</tr>
<tr>
<td>All Cancers</td>
<td>1,220,100</td>
<td>563,100</td>
</tr>
</tbody>
</table>

Percent of All Cancers 44.6% 27.6%

Regions: The Centers for Disease Control National Center for Health Statistics divides the nation into four regions for the purpose of analysis of national data. These four regions were split by Health-Track into seven areas, for the purpose of examination of national cancer maps to look for geographic patterns of cancer mortality. These areas are shown in the table and map below. For all cancers combined and the eight cancers examined by Health-Track, we looked at the geographic distribution of cancer mortality by region to see where white males, white females, black males and black females had higher rates. Regions with concordance for all groups or where males and females were found to share higher rates were identified.

Table 2. Geographic Regions for Cancer Mortality Map Analysis

<table>
<thead>
<tr>
<th>NCHS Region</th>
<th>Health Track Analysis</th>
<th>States</th>
</tr>
</thead>
<tbody>
<tr>
<td>Southeast</td>
<td>Southeast (SE)</td>
<td>DC, Delaware, Florida, Georgia, Kentucky, Maryland, North Carolina, South Carolina, Tennessee, Virginia, West Virginia</td>
</tr>
<tr>
<td>Southeast</td>
<td>South Central (SC)</td>
<td>Alabama, Arkansas, Louisiana, Mississippi, Oklahoma, Texas</td>
</tr>
<tr>
<td>Midwest</td>
<td>Great Lakes (GL)</td>
<td>Minnesota, Wisconsin, Illinois, Indiana, Michigan, Ohio</td>
</tr>
<tr>
<td>Midwest</td>
<td>Midwest (MW)</td>
<td>Iowa, Missouri, North Dakota, South Dakota, Nebraska, Kansas</td>
</tr>
<tr>
<td>West</td>
<td>Southwest (SW)</td>
<td>Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, Wyoming</td>
</tr>
<tr>
<td>West</td>
<td>West Coast (WC)</td>
<td>Washington, Oregon, California, Alaska, Hawaii</td>
</tr>
</tbody>
</table>
Overall, from 1970-1994 cancer mortality rates seem to be higher in the Northeast, especially among whites, and in the Great Lakes region. The National Cancer Institute notes that, in comparison with the earlier time period 1950-69, there has been major change in that the rates in the Southeast, once very low, are now much higher.[3] They offer no explanation for this change. For all cancers, the percentage of people with cancer who die from cancer (the case fatality ratio) is low, so that incidence data would be more valuable than mortality data for study of environmental patterns.

**Table 3. All Cancer: Areas of Higher Mortality by Race and Sex, 1970-1994**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Black</th>
<th>White</th>
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</thead>
<tbody>
<tr>
<td>Male</td>
<td>GL</td>
<td>NE</td>
</tr>
<tr>
<td>Female</td>
<td>GL, MW</td>
<td>NE, GL, WC</td>
</tr>
</tbody>
</table>

**Table 4. All Cancer: Regions with Higher Mortality Rates, 1970-1994**

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Region(s) with higher rates across the board</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>Northeast</td>
</tr>
<tr>
<td>Brain</td>
<td>Midwest</td>
</tr>
<tr>
<td>Breast</td>
<td>Northeast, Great Lakes, West Coast</td>
</tr>
<tr>
<td>Hodgkin’s Disease</td>
<td>Northeast, Great Lakes</td>
</tr>
<tr>
<td>Leukemia</td>
<td>Great Lakes, Midwest</td>
</tr>
<tr>
<td>Liver</td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin’s Lymphoma</td>
<td>Northeast, Great Lakes</td>
</tr>
<tr>
<td>Prostate</td>
<td>Southeast</td>
</tr>
</tbody>
</table>


**Public Health Concerns:** Bladder cancers are the fourth most common among males, and while less than half as common in women, they are nonetheless the number nine cause for women in 2000.[1] Between 1950-97 the incidence of new bladder cancers increased by 53% while the mortality rate fell by 35%. [4] Bladder cancer incidences are about twice as common among whites than blacks, but death rates are roughly equivalent. In 2000, the ACS estimates that there were 53,200 people diagnosed with new bladder cancers and 12,200 deaths.[1] There are many types of bladder cancers but 90% are “transitional cell carcinomas.” Men have higher rates than women and bladder cancer in humans has been shown to be caused by certain occupational exposures like benzidine dyes and among certain occupational groups like people in the rubber, chemical and leather industry.[6,7] There is some evidence for genetic predisposition being involved as well. Cigarette smoking is also known to be an important risk factor for bladder cancer.[8]

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**Interpretation:** From 1970-1994, the Northeast and Great Lakes areas seem to overall have the highest rates of bladder cancer death. Although smoking is an important cause of bladder cancer, the map for bladder cancer does not resemble the map for lung cancer, which is almost solely smoking related. This strongly suggests a role for non-smoking exposures in bladder cancers. According to the National Cancer Institute, bladder cancer among men has tended to cluster in the urban Northeast since the 1950s, particularly in areas with chemical industries.[9] 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, including an increased risk among truck drivers and other workers exposed to motor exhausts.[10] Of particular interest might be to take a closer look at Health-Track maps for releases from chemical industries and for levels of air pollutants likely to be a marker for motor exhaust pollution, for example, ozone.


**Public Health Concerns:** Brain cancers are rare; they are the second most common type of cancer for children however. Between 1950-97 the incidence of new brain cancer cases increased by 71% while the mortality rate rose by 45%.[4] The ACS estimates that in 2000 there were 16,500 people newly diagnosed with brain (and other nervous system) cancers, and 13,000 brain deaths in the U.S.[1] Overall, brain cancers occur somewhat more frequently in males. Brain cancer incidence and death rates for whites are 66% higher than black rates.[1] There are many types of brain cancers, some benign and some malignant. Mortality statistics mostly reflect malignant brain tumors. In addition, the brain is frequently the site of metastases (spread) from other primary tumor sites; this analysis is restricted to primary brain cancers. Although the incidence of brain cancers has been increasing steadily over the last decade, it is not known whether this increase is “real” or due to diagnostic improvements like the MRI (magnetic resonance imaging) technologies.[11]

Brain cancers occur at all ages and do not occur with clear genetic patterns, implying environmental causes. Brain cancer is known to result from excessive exposures of the brain directly to radiation as occurred with therapeutic uses of radiation in the mid 1900s. Studies of childhood brain cancers have found associations with pesticide exposures, electric blanket usage and consumption of foods with nitrates, but these are not considered to constitute definitive proof of causation.[12, 13] Workers in certain industries – oil refineries, rubber manufacturing and drug manufacturing – and chemists have been found to have a higher risk of developing brain cancer but no specific agents in these work environments have been pinpointed as being causal factors. Brain tumors have been observed to occur among several members of the same family raising the possibility of genetics playing a role as well. However, in most cases, the cause of brain cancer is unknown and may be due to environmental or other factors yet to be discovered.

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**Interpretation:** From 1970-1994, there are generally higher brain cancer mortality rates in the Midwest for all groups, the Southeast and Great Lakes region for blacks and the West Coast for whites. There are higher rates of smoking in the Southeast but brain cancer is not known to be related to smoking. One could speculate about other possibilities such as pesticides used for farming in these regions, or toxic chemicals used in industries and so forth. According to the National Cancer Institute, “it is possible that variations in diagnosis and reporting practices as well as survival experience contribute to the patterns observed”. [3] To understand these patterns more clearly it would have been helpful if the NCI Cancer Atlas had allowed for a separation between adult and childhood brain cancers since they are likely to have different causes.


**Public Health Concerns:** Breast cancer is the most common type of cancer for women and second highest cause of cancer deaths in women. Between 1950-97 the incidence of new breast cases increased by 59% while the mortality rate fell by 12%. [4] The NCI estimates that approximately 1 in 8 women in the U.S. will develop breast cancer during her lifetime. [4] In 2000, it is estimated that 182,800 women were newly diagnosed with breast cancer and 40,800 died from it. [1] While blacks have a somewhat lower incidence rate of breast cancer, the death rate is 30% higher. [1] There are several types of breast cancer, the most common being “ductal carcinoma.” Early age of menarche, later age of menopause, late childbearing, smaller numbers of pregnancies, and long-term usage of hormonal therapies are associated with elevated breast cancer risk but do not explain the major proportion of breast cancer. Women with first and second-degree relatives with breast cancer also have higher risk of breast cancer. Certain genes have been identified that confer a higher risk of breast cancer and it is estimated that 27% of breast cancer is attributable to heritable causes. [2] Therefore, most of breast cancer risk is not explained and is believed to be due to environmental exposures. Some studies also implicate diets high in fat and high levels of alcohol consumption as risk factors for breast cancer. There is epidemiologic evidence that excess exposures to radiation at a young age cause earlier and a higher incidence of breast cancer. [14] It has been hypothesized on a theoretical basis that environmental hormones may also play a role, but to date the epidemiologic evidence has not clearly supported that hypothesis.


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**Interpretation:** Between 1970-1994, the Northeast, Great Lakes and West Coast have elevated breast cancer mortality rates for white and black women. Mortality rates for breast cancer reflect not only the underlying incidence but also differences in identification and
treatment; early identification does result in a better treatment outcome. However, the areas with higher mortality are similar to areas known to have higher incidence rates as well. According to the NCI, “the regional excess of breast cancer across the Northeast, especially in urban centers, has persisted for over four decades. The pattern is most pronounced among postmenopausal women, with little geographic variation among premenopausal women.”[3, 15-17] The NCI believes that this regional variation is attributed in part to differences in known risk factors like age of woman at menarche, at first birth, and menopause, as well as factors related to treatment (education and mammography history).[18]


Public Health Concerns: Hodgkin’s disease is a relatively rare cancer. Between 1950-97 the incidence of new Hodgkin’s cases increased by 15% while the mortality rate fell by 74%. [1] For 2000 the ACS estimated that 7,400 people were newly diagnosed with Hodgkin’s in the U.S. and that there were 1,400 deaths. [4] It is somewhat more common among males. While blacks have somewhat lower incidence rates for Hodgkin’s, the mortality rates are about the same. [4] Known risk factors for Hodgkin’s disease include familial factors (there is evidence for a hereditary component), acquired or congenital immunodeficiency syndromes and infection with the Epstein-Barr virus (EBV). [19] However, these risk factors are not believed to account for the majority of the disease and therefore studies are underway to attempt to elucidate environmental or other causal factors.


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Interpretation: Between 1970-1994, the highest mortality rates of Hodgkin’s Disease for all groups are in the Northeast and Great Lakes, and for whites in the Midwest as well. However, these numbers should be interpreted with caution given that they are small numbers over a large number of geographic areas. According to the National Cancer Institute, the higher rates in the north for whites are most pronounced for the peak occurrence in young people, which is suspected to be related to infectious agents, including EBV. [20] The NCI believes that the rates for blacks are based on sparse data and are therefore more difficult to interpret but nonetheless do not show the same “north-south gradient.”[3]


Public Health Concerns: Leukemia is the tenth most common cancer among men and women in the U.S., newly affecting an estimated 30,800 and resulting in an estimated 21,700 deaths in 2000. [1] Overall, it is somewhat more common among males. Between 1950-97 the incidence of new leukemia cases increased by 7% while the mortality rate fell by 4%. [4] Whites have a 25% higher incidence of leukemia than blacks and a 10% higher rate of death. [1] There are several types of leukemia. In childhood, the most common type is acute lymphocytic leukemia (ALL), which is the most common type of cancer among children. Today the survival
rate for ALL with appropriate identification and treatment is very high so that leukemia mortality rates will be much lower than childhood leukemia incidence rates. Survival rates for other types of leukemia are low, however. There are carcinogens known to cause leukemia in humans including high-energy radiation,[14, 21] benzene, and certain anti-cancer drugs. Studies have suggested associations between exposure to certain herbicides and pesticides[22] and exposure to electromagnetic fields as well[23, 24]. There is evidence for a genetic component for certain leukemias, for example, children born with trisomy 21 have higher rates of leukemia and there are certain rare inherited diseases that are associated with adult leukemias. In most cases, we do not know the cause of leukemia, however.


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<td>GL, MW</td>
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</table>

Interpretation: Between 1970 and 1994, the highest mortality rates for leukemia are found in the Midwest and Great Lakes areas. For childhood ALL, the ratio between cases and mortality (the case fatality ratio) is low, so that incidence data would be more valuable than mortality data for study of environmental patterns. However, the NCI notes that “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)”. This implies that leukemia incidence follows a similar geographic distribution as mortality. According to the NCI, “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.”[3] Because leukemia is a mix of different diseases, it is possible that “real” geographic relationships could be obscured by the mixing of different leukemia types on one map. According to the NCI, it was not possible to distinguish the patterns for the major cell types of leukemia from the available mortality data.[3] Despite these limitations the Health-Track maps could be employed to explore in depth whether there might be associations between leukemia mortality rates and emissions of benzene and other solvents, for example. To understand these patterns more clearly it would have been helpful if the NCI Cancer Atlas had allowed for a separation between adult and childhood leukemias since they are likely to have different causes.


Public Health Concerns: Liver cancer is the ninth most common cancer among men in the U.S.; it is estimated that there were 10,000 new diagnoses and 8,500 deaths in 2000.[1] Although less frequent among women, there will nonetheless be an estimated 5,300 new diagnoses and 5,300 deaths.[1] Between 1950-97 the incidence of new liver cases increased by 172% while the mortality rate rose by 34%.[4] Blacks have a 70% higher rate of liver cancer diagnosis and a 50% higher rate of death.[1] Primary liver cancer in children is usually a type called hepatoblastoma; for adults it is usually hepatocellular carcinoma. In addition, the liver is frequently the site of metastases (spread) from other primary tumor sites; this analysis is restricted to primary liver cancers. The causes of childhood liver cancer (hepatoblastoma) are unknown but in Japan it has been found to occur more frequently among low birth weight children[25]. For adults, a number of factors, exposure to aflatoxins in the diet (toxins that are
produced by a fungus on food grains and peanuts); diseases that damage the liver (chronic hepatitis B and cirrhosis of the liver); arsenic in drinking water; oral contraceptives; and anabolic steroids have been associated with liver cancer.[26] Vinyl chloride is a known cause of angiosarcoma of the liver. However, in most cases, there is not a known cause. In animal tests the liver is frequently a target site for chemical carcinogens, however, some believe that there are different metabolic mechanisms in mice that account for the cancers. Little work has been done to link rates of liver cancer to environmental data or to study more intensively with case control studies if one had a hypothesis to test that might explain these differences.


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</tr>
<tr>
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<td>SC, GL</td>
<td>SC, GL</td>
</tr>
</tbody>
</table>

Interpretation: Between 1970 and 1994, liver cancer mortality rates are highest in the South Central region for whites and for the Great Lakes region for blacks. According to the NCI, “liver cancer is particularly subject to misspecification on death certificates, but it is unclear whether diagnostic and reporting practices have varied geographically.”[3] SEER data indicate that liver cancer incidence rates are higher among Hispanic than non-Hispanic whites.[27] The Health-Track maps could be used to further explore whether areas with higher liver cancer rates also have higher releases of chemical carcinogens.


Public Health Concerns: The incidence of non-Hodgkin’s lymphoma (NHL) has increased sharply over the last 20 years, for unknown reasons, and it is now the fifth most common cancer in the U.S. for both males and females.[1] Between 1950-97 the incidence of new NHL cases increased by 191% while the mortality rate rose by 33%.[4] In 2000 in the U.S., there were an estimated 54,900 people newly diagnosed with NHL and 26,100 deaths.[1] Males are somewhat more at risk. Whites have a 25% higher rate of NHL incidence and a 40% higher rate of death than blacks.[1] There are many types of NHL, which have varying cell types and degrees of aggressiveness. Those with weaker immune systems, either because of infection (HIV, EB Virus), medications (transplant drugs), or inherited immune deficiency disorders, are known to be at greater risk. The AIDS epidemic currently accounts for 20% of NHL, however, this ratio has changed over the time of the Cancer Atlas as the epidemic has evolved.[28, 29] Occupational studies have found that people who report working with pesticides,[30, 31] fertilizers, or solvents (notably, benzene) are at greater risk. Most cases are not explained by known risk factors and environmental and other agents may be involved.

Table 11. NHL: Areas of Higher Mortality by Race and Sex, 1970-1994

<table>
<thead>
<tr>
<th>Sex</th>
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<tbody>
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<tr>
<td>Female</td>
<td>NE, GL, MW, WC</td>
<td>NE, GL, MW, WC</td>
</tr>
</tbody>
</table>
**Interpretation:** Between 1970-1994, there are overall higher rates of NHL mortality for all race/sex groups in the Northeast and the Great Lakes regions. White males and females have higher rates in the Midwest and the West Coast. According to the NCI, geographic patterns for NHL “have been positively correlated with urbanization and socioeconomic status, 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.”[3] The higher rate of NHL among white males in Northern California has previously been attributed to the epidemic of HIV and the large number of people with AIDS who are cared for in those communities. Health-Track maps could be used to examine releases of chemical carcinogens in areas with higher rates of NHL. However, very few data on pesticide exposures are available on a national basis.


**Public Health Concerns:** Prostate cancer is the most common type of cancer among men in the U.S. Between 1950-97, the incidence of new prostate cases increased by 193% while the mortality rate rose by 4%[4]. In 2000, it is predicted that 188,400 men were newly diagnosed and 31,900 died from prostate cancer.[1] The causes are not well understood. However, incidence rates are 70% higher among blacks and death rates 140% higher.[1] A man has a higher risk if he has a family member with prostate cancer. Studies have suggested a number of risk factors for prostate cancer, including high fat diets, work exposure to cadmium, work in the rubber industry, farming,[32] and exposure to various sexually transmitted viruses. Diets higher in fruits and vegetables and lower in fat seem to be protective but it is unknown why that is the case. There are very possibly other genetic, environmental or lifestyle factors that contribute to the incidence of the disease. Rates of prostate cancer appear to be rising but this increase may be due at least in part to the application of early detection methods.

**Table 12. Prostate Cancer: Areas of Higher Mortality by Race, 1970-1994**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Black</th>
<th>White</th>
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<tbody>
<tr>
<td>Male</td>
<td>SE</td>
<td>NE, SE, SW, NW</td>
</tr>
</tbody>
</table>

**Interpretation:** For 1970-1994, higher rates of prostate cancer mortality are present for blacks and whites in the Southeast and for whites in the Northeast and Southwest. According to the NCI, “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 and among blacks in the southeastern states”.[3, 33] Health-Track maps could be used to evaluate whether higher rates are occurring in areas with more releases from rubber industry and other possible industrial sources of exposure, but would not include agricultural exposures that have been hypothesized to play a role by the NCI.
REFERENCES