HEALTH CONSULTATION

ASSESSMENT OF CANCER INCIDENCE IN COUNTIES ADJACENT TO OAK RIDGE RESERVATION, U.S. DEPARTMENT OF ENERGY

OAK RIDGE, ANDERSON COUNTY, TENNESSEE

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Prepared by: Division of Health Studies Agency for Toxic Substances and Disease Registry

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INTRODUCTION

Residents of the communities surrounding the U.S. Department of Energy's Oak Ridge Reservation in Oak Ridge, Tennessee, are concerned about a perceived increase in cancer in their area. To address these concerns, the Oak Ridge Reservation Health Effects Subcommittee (ORRHES) requested that the Agency for Toxic Substances and Disease Registry (ATSDR) and the Tennessee Cancer Registry (TCR) of the Tennessee Department of Health assess the incidence of cancer in this area. Cancer incidence refers to newly diagnosed cases of cancer that are reported to the TCR. This assessment was conducted using data that are already collected by the TCR, providing a general picture of the occurrence of cancer in the area.

The purpose of this report is to give residents of the Oak Ridge area information about cancer rates in their county compared with the State of Tennessee. This assessment examined cancer rates at the population level and cannot be used to evaluate individual risk. Also, it cannot be used to determine why an individual develops cancer, because (1) information on individual exposure data or risk factors is not available, (2) cancer takes time to develop, usually 20–40 years, (3) different types of cancer have different causes, and (4) we do not know the causes of most types of cancer. However, scientific studies have identified risk factors for various cancers. A risk factor is something that may increase an individual's risk of developing a specific type of cancer. Cancer risk factors include heredity, geographic area, diet, occupational exposures, environmental factors, tobacco smoke, sexual practices, and alcohol consumption. Appendix A contains information about the most commonly diagnosed cancers.

MATERIALS AND METHODS

Geographic Area

The geographic area for this assessment of cancer incidence includes eight counties surrounding the Oak Ridge Reservation: Anderson, Blount, Knox, Loudon, Meigs, Morgan, Rhea, and Roane. Figure 1 in Appendix B shows the locations and boundaries of the eight counties.

Tennessee Cancer Registry

All cancer data were provided by the TCR of the Tennessee Department of Health. The TCR has maintained data on cancer incidence (new cases of cancer) for the State of Tennessee since 1986. Cancer incidence data are acquired under the Tennessee Cancer Reporting System Act of 1983 (T.C.A. 68-1-1001 et seq.), which requires that all general and specialty hospitals, clinical laboratories, and cancer treatment centers report all cases of cancer to the Tennessee Department of Health. Every inpatient or outpatient case diagnosed with or treated for cancer must be reported to the TCR within 6 months of the diagnosis date.

The TCR relies on each institution to supply data on the cancer cases. The number of expected reports from each institution is monitored, however, and the TCR contacts facilities that fail to report. The number of reports expected is based on national trends and mortality data.

The registry information available for each newly diagnosed cancer case is abstracted from the patient's medical record and includes demographic and medical data on each individual cancer patient such as name, address at time of diagnosis, primary cancer site, histology type, date of diagnosis, age at diagnosis, birth date, race, sex, and registry identification number. To ensure that reported data are complete and accurate, TCR staff members perform case-finding and other quality control checks at these institutions. All abstracts are reviewed for completeness of required items, and if discrepancies suggest a reporting error, the TCR contacts the registrars at the reporting facility for clarification and changes. Currently all abstracts must pass the edits recommended by the North American Association of Central Cancer Registries.

Cancer Incidence Data

This assessment used cancer incidence data supplied by the TCR for the years 1991–2000. A "case" was defined as a diagnosis of a new primary malignant cancer in an individual residing in one of the selected counties. Analysis was conducted for 42 cancer types, listed in Appendix C.

Statistical Methods

The procedure for analyzing and interpreting cancer incidence data is to compare the number of cancer cases in the population living in the area of concern with a reference population to determine whether an excess of a particular type of cancer exists. Ratios are used to compare the observed number of cancer cases with the "expected" number of cases. The expected number of cancer cases is calculated based on the observed occurrence in a reference population. The expected number of cancers is defined as the number of cancers that would be observed in a particular county, if the county cancer rate was identical to the state rate.

For this analysis, the area of concern consists of eight counties surrounding the Oak Ridge Reservation, and the reference population is the population of the State of Tennessee as a whole. For each county, the ratio of the observed to the expected number of cancer cases was examined for males and females, and the information was further standardized to control for the effects of race and age. Standardized or adjusted rates are used to control for demographic differences between populations being compared. These adjusted ratios are referred to as the standardized incidence ratio (SIR).

Specifically, the SIR is the observed number of cases divided by the expected number of cases. A ratio of 1.0 indicates that the number of cases observed in the population being evaluated is equal to the number of cases expected based on the rate of disease in the reference population. A ratio greater than 1.0 indicates that more cases occurred than expected; and a ratio less than 1.0 indicates that fewer cases occurred than expected. Accordingly, a ratio of 1.5 is interpreted as one-and-a-half times as many cases as the expected number, and a ratio of 0.9 indicates nine-tenths as many cases as the expected number. Results were considered statistically significant if the confidence interval did not include 1.0, and results were considered borderline statistically significant if either the lower or upper limit of the confidence interval was 1.0. More detailed information regarding the calculation and interpretation of SIRs, including statistical significance, is included in Appendix D.

RESULTS

ATSDR analyzed the data for 42 cancer types in the eight counties surrounding the Oak Ridge Reservation (Anderson, Blount, Knox, Loudon, Meigs, Morgan, Rhea, and Roane). Tables 1–16 present the results of the analyses for cancer types with more than 5 observed cases. The tables present the results for each county individually by gender. For reasons of confidentiality, and the instability of data with small numbers, the TCR requires that more than 5 cases be observed for results to be reported. The total number of new cases of cancer presented below for each county includes all cancers. These numbers may not add up to the totals presented in the tables since cancer types with 5 or fewer cases were not included in the tables.

Anderson County

During the period of 1991–2000, 3501 new cases of cancer were reported in Anderson County. Of these, 1682 occurred in females and 1819 occurred in males. The most frequently reported cancers in this county among females were breast, colon, and lung cancer, and among males were colon, bladder, lung, and prostate cancer.

Table 1 shows the number of observed and expected cancer incidence cases in Anderson County for females based on Tennessee state cancer incidence rates. Breast and ovarian cancer occurred more often than expected, although these results were of borderline statistical significance. No significant excess of the remaining types of cancer was observed among females in this county during this same time period. Melanomas occurred significantly less often than expected among females during the 10-year time period evaluated.

A significantly greater than expected number of bladder cancer cases were observed among males residing in Anderson County compared with the State of Tennessee, as shown in Table 2. Colon and lung cancer occurred more often than expected among males during this time period, although the results were of borderline statistical significance. No significant excess of the remaining types of cancer was observed in males during this time period. Melanomas occurred significantly less often than expected in males during the 10-year time period evaluated.

Blount County

During the period of 1991–2000, 4413 new cases of cancer were reported in Blount County. Of these, 2072 occurred in females and 2341 occurred in males. The most frequently reported cancers in this county among females were breast, colon, and lung cancer, and among males were colon, bladder, lung, and prostate cancer.

Table 3 shows the observed and expected number of cancer incidence cases in Blount County for females based on Tennessee state cancer incidence rates. Melanomas occurred significantly more often than expected among females during the 10-year time period evaluated. No significant excess of the remaining types of cancer was observed among females in this county during this same time period. Lung, corpus uteri and thyroid gland cancer occurred significantly less often

than expected. Ovarian, breast, and colon cancer occurred less often than expected among females, although these results were of borderline statistical significance.

Cancer incidence occurred at about expected rates for males in Blount County when compared with the State of Tennessee, as shown in Table 4. Melanomas occurred more often than expected among males, although this result was of borderline statistical significance. No significant excess of any type of cancer was observed among males in this county. Colon, lung, prostate, and tongue cancer occurred less often than expected among males, although these results were of borderline statistical significance.

Knox County

During the period of 1991–2000, 15,886 new cases of cancer were reported in Knox County. Of these, 7951 occurred in females and 7935 occurred in males. The most frequently reported cancers in this county among females were breast, colon, and lung cancer, and among males were colon, bladder, lung, and prostate cancer.

Table 5 shows the observed and expected cancer incidence cases in Knox County for females based on Tennessee state cancer incidence rates. No significant excess of cancer was observed among females in this county. Breast, colon, lung, and corpus uteri cancer occurred more often than expected, although these results were of borderline statistical significance.

No significant excess of cancer was observed among males in this county, as Table 6 illustrates. Colon, lung, melanoma, soft tissue, and prostate cancer, as well as non-Hodgkin lymphoma, occurred more often than expected, although these results were of borderline statistical significance.

Loudon County

During the period of 1991–2000, 1966 new cases of cancer were reported in Loudon County. Of these, 922 occurred in females and 1044 occurred in males. The most frequently reported cancers in this county among females were breast and lung cancer, and among males were lung and prostate cancer.

Table 7 shows the observed and expected cancer incidence cases in Loudon County for females based on Tennessee state cancer incidence rates. No significant excess of cancer was observed among females in this county. Rectum cancer occurred more often than expected among females in this county during this same time period, although these results were of borderline statistical significance.

Table 8 shows that the overall cancer incidence rates for males were about what would be expected when compared with rates for the State of Tennessee. No significant excess in cases of cancer of any type was observed among males in this county. Gum cancer occurred more often than expected, although these results were of borderline statistical significance.

Note: An analysis of cancer incidence in Loudon County was also presented in a public health assessment released May 17, 2005 (<u>http://www2.state.tn.us/health/CEDS/list.htm</u>). The results presented in the public health assessment were crude rates of cancer (i.e., number of cancer cases per 100,000 population) while the results presented in this document are standardized incidence ratios which compare the occurrence of cancer in a county to the state, taking into account differences due to age and race.

Meigs County

During the period of 1991–2000, 395 new cases of cancer were reported in Meigs County. Of these, 178 occurred in females and 217 occurred in males. For the majority of cancer types, 5 or fewer cases were reported for either males or females.

No significant excess of cases of any type of cancer was observed among females or males in this county during the 10-year time period evaluated, as shown in Tables 9 and 10. Colon cancer among females occurred significantly less often than expected when compared with cancer incidence rates for the State of Tennessee.

Morgan County

During the period of 1991–2000, 577 new cases of cancer were reported in Morgan County. Of these, 260 occurred in females and 317 occurred in males. The most frequently reported type of cancer in this county among females was breast cancer, and the most frequently reported types among males were lung and prostate cancer.

No significant excess of cases of any type of cancer was observed among females or males in this county during this time period when compared with cancer incidence rates for the State of Tennessee, as Tables 11 and 12 illustrate. Breast cancer in females and colon and prostate cancer in males occurred significantly less often than expected in Morgan County when compared with cancer incidence rates for the State of Tennessee.

Rhea County

During the period of 1991–2000, 1186 new cases of cancer were reported in Rhea County. Of these, 558 occurred in females and 628 occurred in males. The most frequently reported cancers in this county among females were breast, colon, and lung cancer, and among males were lung and prostate cancer.

A significantly greater than expected number of cervical cancer cases were observed among females, as shown in Table 13. No significant excess in cases of the remaining types of cancer was observed in females during this time period. Breast and lung cancer among females occurred less often than expected during this time period, although the results were of borderline statistical significance.

A significantly greater than expected number of cases of cancer of the floor of the mouth and of cancer of the small intestine were observed among males residing in Rhea County when compared with cancer incidence rates for the State of Tennessee, as shown in Table 14. Chronic lymphocytic leukemia occurred more often than expected among males during this time period, although the results were of borderline statistical significance. No significant excess in cases of the remaining types of cancer was observed in males during this time period. Prostate cancer occurred less often than expected during the 10-year time period evaluated, although this result was of borderline statistical significance.

Roane County

During the period of 1991–2000, 2380 new cases of cancer were reported in Roane County. Of these, 1127 occurred in females and 1253 occurred in males. The most frequently reported cancers in this county among females were breast and lung cancer, and among males were colon, lung, and prostate cancer.

Table 15 shows that kidney cancer occurred significantly more often than expected among females in Roane County when compared with cancer incidence rates for the State of Tennessee. No significant excess in cases of the remaining types of cancer was observed among females in this county during this same time period. Pancreatic cancer occurred significantly less often than expected among females during this time period. Breast and colon cancer and non-Hodgkin lymphoma occurred less often than expected among females during the 10-year time period evaluated, although these results were of borderline statistical significance.

No significant excess in cases of any type of cancer was observed in males in Roane County, as shown in Table 16. Lung cancer occurred more often than expected, although this result was of borderline statistical significance. Melanomas and prostate cancer occurred significantly less often than expected among males residing in Roane County when compared with cancer incidence rates for the State of Tennessee.

DISCUSSION

An assessment of cancer incidence gives a general picture of the occurrence of cancer in a community, and it may confirm the presence of excess cancer in a community. However, the cause of elevated rates of a particular cancer cannot be determined by cancer incidence data. Many other risk factors, such as socioeconomic status, occupation, and personal habits (for example, diet and smoking), influence the development of cancer. Information on risk factors was not available and therefore was not analyzed in this assessment of cancer incidence.

Advantages

Advantages of conducting an analysis of this type is that it responds to community members' concerns about a potential excess of cancer in their county. It also provides specific information about the status of cancer rates in a particular county, and it can be used to identify areas where further public health investigations or actions may be warranted. Analyzing cancer incidence

data is better than examining deaths caused by cancer, because people with cancer may not die from their cancer; therefore, information about their cancer would not be captured in the death certificate. Also, making comparisons using the number of people in a county who have been diagnosed with cancer presents a truer picture of cancer rates in a county.

Limitations

Several limitations are associated with the data available for this analysis:

- The data from 1991–2000 are estimated to be 85% complete based on the Centers for Disease Control and Prevention (CDC) projections. There was under-ascertainment for the time period considered for this analysis because information on new cases of cancers was collected from area hospitals but was not available from other facilities such as laboratories until 2005.
- 2. Some of the reported numbers of specific types of cancer are very small, making the rates unstable; and
- 3. Information on risk factors was not available, making it impossible to evaluate the potential causes of cancer in the counties around the Oak Ridge Reservation or to identify all the risk factors that may have influenced the rate of cancer in the population.

Another limitation of this type of investigation is that cancer is a chronic disease that takes many years to manifest as a clinical disease. The information supplied by the TCR provides an address at the time of diagnosis for each person diagnosed with cancer but does not give information on the length of time a person may have lived at the address before being diagnosed. This lack of information about the length of time a person has resided at an address is an issue with any type of cancer incidence analysis, because population mobility cannot be accounted for. In other words, some reported cases of cancer may be for residents who have recently moved into the area, so including those cases in the data analysis would result in an overcount of cancer cases. Similarly, cancers could have developed among persons who lived in an area in the past but who have moved away. If so, the analysis would have missed these persons, creating an undercount of cancer cases.

In addition, there are many factors that can affect the magnitude of an SIR in one direction or the other (not necessarily larger) including confounding, bias, exposure misclassification, data quality, random error, and small sample sizes. We controlled for potential confounders such as age and race since this information was available from the TCR. However, there are other factors such as income, education, and place of residence which could affect access to care and hence reporting of cancer cases, but was not available for analysis. It is unknown what effect this information could have on the results.

CONCLUSIONS

The objective of this analysis was to determine whether elevated rates of cancer are present in the counties around the Oak Ridge Reservation as compared with cancer incidence in the State of Tennessee. The results show that higher rates of some cancers and lower rates of some cancers

were found in several of the counties for which data were analyzed, although there was no consistent pattern in cancer occurrence.

The reasons for the higher rates of some cancers are unknown. It is not possible to determine why people in the Oak Ridge area developed cancer, or whether the Oak Ridge Reservation could be the cause of the higher number of cancers observed, because (1) information on individual exposure data is not available, (2) it takes time for cancer to develop, usually 20 to 40 years, (3) different types of cancer have different causes, and (4) the causes of most types of cancer are unknown. Scientific studies have identified factors that may increase the risk of developing specific types of cancer. Cancer risk factors include heredity, geographic area of residence, diet, environmental causes, tobacco smoke, sexual practices, and alcohol consumption. Increases in rates of cancer reported in certain areas also could be due simply to increased awareness and screening in those areas.

The statistically significant findings from this assessment are as follows:

- 1. For two counties, Meigs and Morgan, limited information was available for the analysis because 5 or fewer cases of several cancer types were reported in those counties during 1991–2000.
- 2. In Anderson County, melanomas occurred less often than expected among males and females, and bladder cancer occurred more often than expected among males.
- 3. In Blount County, lung, thyroid, and corpus uteri cancer occurred less often than expected among females, and melanomas occurred more often than expected among females.
- 4. In Knox County, no type of cancer occurred more often than expected among females or males.
- 5. In Loudon County, no type of cancer occurred more often than expected among females or males.
- 6. In Meigs County, colon cancer occurred less often than expected among females.
- 7. In Morgan County, colon and prostate cancer occurred less often than expected among males, and breast cancer occurred less often than expected among females.
- 8. In Rhea County, cancer of the floor of the mouth and cancer of the small intestine occurred more often than expected among males, and cervical cancer occurred more often than expected among females.
- 9. In Roane County, melanomas and prostate cancer occurred less often than expected among males, and pancreatic cancer occurred less often than expected among females. Kidney cancer occurred more often than expected among females.

ANSWERS TO COMMUNITY HEALTH CONCERNS

1. What were the results from this investigation for each county?

The main findings from this analysis that were statistically significant are as follows:

- In Anderson County, melanomas occurred less often than expected among males and females, and bladder cancer occurred more often than expected among males.
- In Blount County, lung, thyroid, and corpus uteri cancer occurred less often than expected among females, and melanomas occurred more often than expected among females.
- In Knox County, no type of cancer occurred more often than expected among females or males.
- In Loudon County, no type of cancer occurred more often than expected among females or males.
- In Meigs County, colon cancer occurred less often than expected among females.
- In Morgan County, colon and prostate cancer occurred less often than expected among males, and breast cancer occurred less often than expected among females.
- In Rhea County, cancer of the floor of the mouth and cancer of the small intestine occurred more often than expected among males, and cervical cancer occurred more often than expected among females.
- In Roane County, melanomas and prostate cancer occurred less often than expected among males, and pancreatic cancer occurred less often than expected among females. Kidney cancer occurred more often than expected among females.

2. Should the community be worried about these findings? What do they mean?

Although higher rates of certain cancers were found in several of the counties for which data were analyzed, no consistent pattern was observed in cancer occurrence. For this analysis, data on 42 cancer types were evaluated for the eight counties surrounding the Oak Ridge Reservation during the period 1991–2000. Given the large number of statistical analyses performed, it is not unusual to find some increases and some decreases in rates of occurrence.

These findings provide a picture of cancer in the population living in the eight counties surrounding the Oak Ridge Reservation. Although incidence rates of certain cancers were higher in several counties than would be expected, the reasons for these increases are

unknown and could be simply because of increased awareness and screening in these areas.

Also, community residents should be aware that scientific studies have identified a number of factors for various cancers which may increase an individual's risk of developing a specific type of cancer. These risk factors include such things as diet, age (cancer risk increases with age), family history, exposure to certain chemicals (only a limited number of chemicals show definite evidence of human carcinogenicity), exposure to radiation, alcohol use, and tobacco smoke. Appendix A contains information regarding the 10 most commonly reported cancers. Additional information on prevention, genetics, and causes of cancer can be found on the Web site of the National Cancer Institute (*http://www.cancer.gov/cancertopics/prevention-genetics-causes*).

3. Could the Oak Ridge Reservation be the cause of the higher number of cancers observed?

This analysis could not determine why people living in the eight counties surrounding the Oak Ridge Reservation developed cancer, because (1) information on individual exposure data or risk factors is not available, (2) cancer takes time to develop, usually 20–40 years, (3) different types of cancer have different causes, and (4) we do not know the causes of most types of cancer. Scientific studies have identified risk factors for developing various cancers. Cancer risk factors include heredity, geographic area of residence, diet, environmental causes, tobacco smoke, sexual practices, and alcohol consumption.

4. Why did you standardize?

The reason for standardizing is to take into account differences among people in the population such as age, race, ethnicity, or sex to see if there are still elevated rates of a disease. In this analysis, we wanted to standardize because the counties we were concerned with may be very different demographically from the State of Tennessee as a whole, which was the comparison population, and we wanted to account for these differences. If we had not standardized, we would not have been able to draw meaningful conclusions from our analysis. For example, if we were to examine the cancer rates in a community predominantly of older people, we would expect higher rates because cancer is more common in older people. However, if our comparison population was predominantly younger, we would not expect much cancer. To get an accurate cancer rate, we must make adjustments for differences in age and/or other characteristics between the groups being compared.

5. Why do the results for Loudon County presented in this report differ from those presented in the public health assessment? (http://www2.state.tn.us/health/CEDS/list.htm)

The cancer analysis in the Loudon County public health assessment examined the crude rates of cancer incidence in the area and did not take into account differences due to age or race/ethnicity.

6. Why were the 49 census tracts surrounding the Oak Ridge Reservation not included in the analysis as requested by the Oak Ridge Reservation Health Effects Subcommittee?

Though we had hoped to conduct a census tract analysis, the Tennessee Cancer Registry collects cancer data at the county level and is not intended for census-tract level analysis. Although an attempt was made to geocode addresses, the quality of address data was insufficient to guarantee reliable census tract data, rendering any results uninterpretable. The reason for this was that a high percentage of the addresses for several counties were for either post office boxes or rural routes, which could not be geocoded to the census tract level.

7. Who can I contact if I have additional questions about cancer?

If you are concerned about your risk of developing cancer, you should discuss this with your physician. If you want more information about cancer, you can contact the following agencies:

American Cancer Society 1-800-227-2345 (or 1-866-228-4327 for TTY) www.cancer.org

National Cancer Institute 1-800-422-6237 (or 1-800-332-8615 TTY) www.cancer.gov

PREPARERS OF THE REPORT

Dhelia Williamson, Ph.D. Epidemiologist Surveillance and Registries Branch

Michael Lewin, M.S. Statistician Health Investigations Branch

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TABLES

S	tandardized Inciden	ce Ratios, Andersor	County, 1991–200	0^1
		FEMALES		
Site	Observed	Expected	SIR*	95% CI
Anus	6	6.1	1.0	0.4 - 2.2
Bladder	39	43.8	0.9	0.6 - 1.2
Brain	18	22.1	0.8	0.5 - 1.3
Breast	578	519.9	1.1	1.0 - 1.2‡
Cervix	30	33.6	0.9	0.6 - 1.3
Colon	157	152.1	1.0	0.9 - 1.2
Corpus uteri	96	90.9	1.1	0.9 - 1.3
Esophagus	9	9.5	0.9	0.4 - 1.8
Gallbladder	8	4.8	1.7	0.7 - 3.3
Gum and other	8	9.6	0.8	0.4 - 1.6
mouth				
Hodgkin disease	11	9.9	1.1	0.6 - 2.0
Kidney	31	34.5	0.9	0.6 - 1.3
Larynx	15	12.1	1.2	0.7 - 2.0
Leukemia†				
AML	9	8.7	1.0	0.5 - 2.0
CLL	6	8.2	0.7	0.3 – 1.6
Lung and	241	244.5	1.0	0.9 – 1.1
bronchus				
Melanoma	8	31.0	0.3	0.1 - 0.5
Multiple	11	17.5	0.6	0.3 - 1.1
myeloma				
Non-Hodgkin	58	62.5	0.9	0.7 - 1.2
lymphoma				
Ovary	81	62.0	1.3	1.0-1.6‡
Pancreas	29	35.6	0.8	0.5 - 1.2
Rectum	38	44.2	0.9	0.6 - 1.2
Soft tissue	9	8.9	1.0	0.5 – 1.9
Stomach	17	15.5	1.1	0.6 - 1.8
Thyroid gland	40	31.7	1.3	0.9 – 1.7
Tongue	6	6.9	0.9	0.3 - 1.9

Table 1: Number of Observed and Expected New Cancer Cases and Race- and Age-Adjusted

¹Cancers with \leq 5 cases were not included in the analysis.

* SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0. † AML: acute myeloid leukemia; CLL: chronic lymphocytic leukemia

Bold type indicates statistical significance.

‡ Borderline statistical significance

Standardized Incidence Ratios, Anderson County, 1991–2000 ¹				
		MALES		
Site	Observed	Expected	SIR*	95% CI
Bladder	147	112.0	1.3	1.1 – 1.5
Bones and joints	6	3.3	1.8	0.7 - 3.9
Brain	24	27.8	0.9	0.6 – 1.3
Colon	168	145.3	1.2	1.0 - 1.3 ‡
Esophagus	30	25.7	1.2	0.8 - 1.7
Gum and other	7	7.0	1.0	0.4 - 2.1
mouth				
Hodgkin disease	8	10.5	0.8	0.3 – 1.5
Hypopharynx	6	4.7	1.3	0.5 - 2.8
Kidney	47	51.2	0.9	0.7 - 1.2
Larynx	34	35.3	1.0	0.7 – 1.3
Leukemia†				
CLL	8	11.2	0.7	0.3 - 1.4
AML	7	8.8	0.8	0.3 – 1.6
Liver	8	9.0	0.9	0.4 - 1.7
Lung and	438	401.7	1.1	1.0 - 1.2‡
bronchus				
Melanoma	23	38.3	0.6	0.4 - 0.9
Multiple	18	18.9	1.0	0.6 – 1.5
myeloma				
Non-Hodgkin	60	65.7	0.9	0.7 - 1.2
lymphoma				
Pancreas	31	34.0	0.9	0.6 - 1.3
Prostate	483	478.3	1.0	0.9 – 1.1
Rectum	52	51.0	1.0	0.8 – 1.3
Small intestine	6	6.4	0.9	0.3 - 2.0
Soft tissue	9	10.2	0.9	0.4 - 1.7
Stomach	25	28.5	0.9	0.6 - 1.3
Testis	14	15.0	0.9	0.5 - 1.6
Thyroid gland	17	11.0	1.5	0.9 - 2.5
Tongue	8	10.5	0.8	0.3 - 1.5
Ureter	6	3.0	2.0	0.7 - 4.4

Table 2[·] Number of Observed and Expected New Cancer Cases and Race- and Age-Adjusted

¹Cancers with ≤5 cases were not included in the analysis. * SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0.

† CLL: chronic lymphocytic leukemia; AML: acute myeloid leukemia

Bold type indicates statistical significance.

Sta	ndardized Incide	ince Ratios, Blount (County, $1991-2000^{11}$	lind Age-Adjusted
		FEMALES	,	
Site	Observed	Expected	SIR*	95% CI
Anus	7	8.4	0.8	0.3 - 1.7
Bladder	53	57.9	0.9	0.7 - 1.2
Bones and joints	8	4.7	1.7	0.7 - 3.3
Brain	32	31.0	1.0	0.7 - 1.5
Breast	678	717.9	0.9	0.9 - 1.0*
Cervix	40	48.3	0.8	0.6 - 1.1
Colon	176	197.2	0.9	0.8 - 1.0*
Corpus uteri	92	123.5	0.7	0.6 - 0.9
Esophagus	8	12.4	0.6	0.3 - 1.3
Gum and other	17	12.3	1.4	0.8 - 2.2
mouth				
Hodgkin disease	10	14.6	0.7	0.3 - 1.3
Kidney	38	46.5	0.8	0.6 - 1.1
Larynx	17	16.6	1.0	0.6 - 1.6
Leukemia†				
ALL	11	6.8	1.6	0.8 - 2.9
CLL	12	10.7	1.1	0.6 - 2.0
AML	17	11.7	1.5	0.8 - 2.3
CML	7	4.0	1.8	0.7 - 3.6
Lung and bronchus	267	326.4	0.8	0.7 - 0.9
Melanoma	67	43.8	1.5	1.2 – 1.9
Multiple myeloma	27	22.9	1.2	0.8 - 1.7
Non-Hodgkin	97	83.3	1.2	0.9 - 1.4
lymphoma				
Ovary	69	85.1	0.8	0.6 - 1.0‡
Pancreas	51	46.1	1.1	0.8 - 1.5
Rectum	49	58.9	0.8	0.6 - 1.1
Soft tissue	9	12.2	0.7	0.3 - 1.4
Stomach	15	20.1	0.7	0.4 - 1.2
Thyroid gland	30	47.0	0.6	0.4 - 0.9
Tongue	10	9.4	1.1	0.5 - 2.0

Table 3. Number of Observed and Expected New Cancer Cases and Race- and Age-Adjusted

¹Cancers with \leq 5 cases were not included in the analysis.

* SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0.

[†] ALL: acute lymphocytic leukemia; CLL: chronic lymphocytic leukemia; AML: acute myeloid leukemia;

CML: chronic myeloid leukemia

Bold type indicates statistical significance.

‡ Borderline statistical significance

Table 4: Number of Observed and Expected New Cancer Cases, and Race- and Age-Adjusted Standardized Incidence Ratios, Blount County, 1991–2000 ¹				
		MALES	<i></i>	
Site	Observed	Expected	SIR*	95% CI
Bladder	147	151.7	1.0	0.8 - 1.1
Brain	51	40.9	1.2	0.9 - 1.6
Colon	171	196.9	0.9	0.7 - 1.0‡
Esophagus	44	35.7	1.2	0.9 - 1.7
Eye	6	5.3	1.1	0.4 - 2.5
Floor of mouth	7	7.3	1.0	0.4 - 2.0
Gum and other	9	9.9	0.9	0.4 - 1.7
mouth				
Hodgkin disease	18	15.9	1.1	0.7 - 1.8
Hypopharynx	7	6.7	1.0	0.4 - 2.1
Kidney	77	71.8	1.1	0.8 - 1.3
Larynx	55	49.8	1.1	0.8 - 1.4
Leukemia†				
ALL	11	8.3	1.3	0.7 - 2.4
CLL	14	15.2	0.9	0.5 - 1.5
AML	12	12.2	1.0	0.5 - 1.7
CML	10	5.3	1.9	0.9 - 3.5
Lip	6	7.0	0.9	0.3 – 1.9
Liver	8	12.4	0.6	0.3 – 1.3
Lung and bronchus	496	549.4	0.9	0.8 - 1.0 ‡
Melanoma	67	54.3	1.2	1.0 - 1.6‡
Multiple myeloma	30	25.2	1.2	0.8 - 1.7
Non-Hodgkin	80	91.9	0.9	0.7 - 1.1
lymphoma				
Pancreas	55	46.5	1.2	0.9 - 1.5
Prostate	620	646.5	1.0	0.9 - 1.0‡
Rectum	66	70.4	0.9	0.7 – 1.2
Small intestine	8	8.9	0.9	0.4 - 1.8
Soft tissue	9	14.2	0.6	0.3 - 1.2
Stomach	36	39.0	0.9	0.6 - 1.3
Testis	26	24.4	1.1	0.7 – 1.6
Thyroid gland	13	16.2	0.8	0.4 - 1.4
Tongue	7	15.0	0.5	0.2 - 1.0‡

¹Cancers with ≤ 5 cases were not included in the analysis. * SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0

† ALL: acute lymphocytic leukemia; CLL: chronic lymphocytic leukemia; AML: acute myeloid leukemia;

CML: chronic myeloid leukemia

Table 5: Number of Observed and Expected New Cancer Cases, and Race- and Age-Adjusted Standardized Incidence Ratios, Knox County, 1991–2000 ¹				
		FEMALES		
Site	Observed	Expected	SIR*	95% CI
Anus	34	27.2	1.3	0.9 - 1.7
Bladder	196	188.4	1.0	0.9 - 1.2
Bones and Joints	15	16.0	0.9	0.5 - 1.5
Brain	110	102.0	1.1	0.9 - 1.3
Breast	2498	2378	1.1	1.0-1.1‡
Cervix	165	173.8	0.9	0.8 - 1.1
Colon	698	656.6	1.1	1.0-1.1‡
Corpus uteri	434	404.8	1.1	1.0-1.2‡
Esophagus	47	43.3	1.1	0.8 - 1.4
Floor of mouth	9	8.9	1.0	0.5 - 1.9
Gallbladder	17	20.0	0.8	0.5 - 1.4
Gum and other	35	40.2	0.9	0.6 - 1.2
mouth				
Hodgkin disease	62	55.2	1.1	0.9 - 1.4
Kidney	160	156.1	1.0	0.9 - 1.2
Larynx	53	57.0	0.9	0.7 - 1.2
Leukemia†				
ALL	22	22.6	1.0	0.6 - 1.5
CLL	41	34.4	1.2	0.9 – 1.6
AML	36	39.0	0.9	0.6 - 1.3
CML	13	13.4	1.0	0.5 - 1.7
Lip	10	5.4	1.8	0.9 - 3.4
Liver	39	30.6	1.3	0.9 - 1.7
Lung and	1188	1087	1.1	1.0-1.2‡
bronchus				
Major salivary	12	12.8	0.9	0.5 - 1.6
gland				
Melanoma	159	143.8	1.1	0.9 - 1.3
Multiple	89	80.8	1.1	0.9 - 1.4
myeloma	• • • •	0.50 (1.0	<u> </u>
Non-Hodgkin	286	273.1	1.0	0.9 – 1.2
Iymphoma	202	201.2	1.0	0.0 1.1
Ovary	282	281.3	1.0	0.9 - 1.1
Pancreas	174	158.9	1.1	0.9 - 1.3

Table 5: Number	of Observed and Ex	xpected New Cance	r Cases, and Race- a	nd Age-Adjusted
Stand	ardized Incidence R	latios, Knox County	7, 1991–2000 ¹ (conti	nued)
		FEMALES		
Site	Observed	Expected	SIR*	95% CI
Rectum	192	190.3	1.0	0.9 - 1.2
Soft tissue	42	41.5	1.0	0.7 - 1.4
Small intestine	18	18.5	1.0	0.6 - 1.5
Stomach	72	67.7	1.1	0.8 - 1.3
Thyroid gland	165	159.1	1.0	0.9 - 1.2
Tongue	35	31.1	1.1	0.8 - 1.6
Ureter	11	9.3	1.2	0.6 - 2.1

¹Cancers with \leq 5 cases were not included in the analysis.

* SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0. † ALL: acute lymphocytic leukemia; CLL: chronic lymphocytic leukemia; AML: acute myeloid leukemia;

CML: chronic myeloid leukemia

Table 6: Number	of Observed and Ex Standardized Incide	xpected New Cance ence Ratios, Knox (r Cases, and Race- a County, 1991–2000 ¹	and Age-Adjusted
		MALES	<u>,</u>	
Site	Observed	Expected	SIR*	95% CI
Anus	18	15.0	1.2	0.7 - 1.9
Bladder	439	459.0	1.0	0.9 - 1.1
Bones and joints	16	16.6	1.0	0.6 - 1.6
Brain	129	131.3	1.0	0.8 - 1.2
Breast	24	17.4	1.4	0.9 - 2.0
Colon	645	615.8	1.0	1.0 - 1.1‡
Esophagus	101	111.5	0.9	0.7 - 1.1
Eye	19	15.9	1.2	0.7 - 1.9
Floor of mouth	21	24.1	0.9	0.5 - 1.3
Gallbladder	7	9.0	0.8	0.3 - 1.6
Gum and other	28	31.2	0.9	0.6 - 1.3
mouth				
Hodgkin disease	56	56.6	1.0	0.7 – 1.3
Hypopharynx	23	22.5	1.0	0.6 - 1.5
Kidney	222	228.4	1.0	0.8 - 1.1
Larynx	160	159.7	1.0	0.9 - 1.2
Leukemia†				
ALL	28	28.0	1.0	0.7 - 1.4
CLL	53	47.8	1.1	0.8 - 1.5
AML	40	38.6	1.0	0.7 - 1.4
CML	16	17.1	0.9	0.5 - 1.5
Lip	28	21.2	1.3	0.9 - 1.9
Liver	42	40.0	1.1	0.8 - 1.4
Lung and bronchus	1719	1716	1.0	1.0-1.1‡
Major salivary	24	22.3	11	07-16
gland	27	22.5	1.1	0.7 1.0
Melanoma	190	167.7	11	$10 - 13^{+}$
Multiple	86	81.1	1.1	0.8 - 1.3
mveloma	00	01.1		0.0 1.5
Nasopharvnx	10	10.3	1.0	0.5 - 1.8
Non-Hodgkin	323	289.8	1.1	1.0 - 1.2‡
lymphoma				
Öropharynx	11	7.5	1.5	0.7 - 2.6
Pancreas	158	146.6	1.1	0.9 - 1.3
Penis	8	10.4	0.8	0.3 - 1.5

Table 6: Number of Observed and Expected New Cancer Cases, and Race- and Age-Adjusted					
Stand	Standardized Incidence Ratios, Knox County, 1991–2000 ¹ (continued)				
		MALES			
Site	Observed	Expected	SIR*	95% CI	
Prostate	2217	2045	1.1	1.0-1.1‡	
Rectum	227	223.4	1.0	0.9 - 1.2	
Small intestine	27	28.5	0.9	0.6 - 1.4	
Soft tissue	61	48.7	1.3	1.0 - 1.6‡	
Stomach	126	123.7	1.0	0.8 - 1.2	
Testis	95	89.8	1.1	0.9 - 1.3	
Thyroid gland	51	51.5	1.0	0.7 – 1.3	
Tongue	62	50.9	1.2	0.9 - 1.6	
Ureter	7	12.4	0.6	0.2 - 1.2	

¹Cancers with \leq 5 cases were not included in the analysis.

* SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0.

[†] ALL: acute lymphocytic leukemia; CLL: chronic lymphocytic leukemia; AML: acute myeloid leukemia; CML: chronic myeloid leukemia

Table 7: Number	of Observed and E	xpected New Cance	r Cases, and Race- a	and Age-Adjusted
	Standardized Incide	nce Ratios, Loudon	County, 1991–2000	-
		FEMALES	1	
Site	Observed	Expected	SIR*	95% CI
Bladder	27	24.2	1.1	0.7 - 1.6
Brain	15	12.4	1.2	0.7 - 2.0
Breast	286	294	1.0	0.9 - 1.1
Cervix	20	18.2	1.1	0.7 - 1.7
Colon	84	80.0	1.0	0.8 - 1.3
Corpus uteri	58	51.6	1.1	0.9 - 1.5
Esophagus	7	5.1	1.4	0.6 - 2.8
Gum and other mouth	8	5.1	1.6	0.7 – 3.1
Kidney	16	19.1	0.8	0.5 - 1.4
Leukemia† AML	6	4.6	1.3	0.5 - 2.8
Lung	134	138.2	1.0	0.8 - 1.1
Melanoma	11	17.1	0.6	0.3 - 1.2
Multiple myeloma	10	9.2	1.1	0.5 - 2.0
Non-Hodgkin lymphoma	27	34.2	0.8	0.5 – 1.1
Ovary	36	34.7	1.0	0.7 - 1.4
Pancreas	24	18.6	1.3	0.8 - 1.9
Rectum	34	24.7	1.4	1.0 - 1.9‡
Stomach	10	8.0	1.2	0.6 - 2.3
Thyroid gland	14	18	0.8	0.4 - 1.3

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 ¹Cancers with \leq 5 cases were not included in the analysis.

 * SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0.

 † AML: acute myeloid leukemia

 ‡ Borderline statistical significance

	Standardized Incide	ence Ratios, Loudon	County, 1991–2000) ¹
		MALES		
Site	Observed	Expected	SIR*	95% CI
Bladder	63	65.2	1.0	0.7 - 1.2
Brain	17	17.3	1.0	0.6 - 1.6
Colon	86	83.9	1.0	0.8 - 1.3
Esophagus	17	15.3	1.1	0.6 - 1.8
Gum and other mouth	9	4.2	2.1	1.0-4.0‡
Hodgkin disease	7	6	1.2	0.5 - 2.4
Kidney	40	31.0	1.3	0.9 - 1.8
Larynx	19	21.7	0.9	0.5 - 1.4
Leukemia† CLL AML	6 8	6.5 5.2	0.9 1.5	0.3 - 2.0 0.7 - 3.0
Liver	6	5.3	1.1	0.4 - 2.5
Lung and bronchus	238	243.2	1.0	0.9 – 1.1
Melanoma	24	22.8	1.1	0.7 - 1.6
Multiple myeloma	11	10.7	1.0	0.5 – 1.8
Non-Hodgkin lymphoma	41	38.8	1.1	0.8 - 1.4
Pancreas	18	19.8	0.9	0.5 - 1.4
Prostate	277	287.9	1.0	0.9 – 1.1
Rectum	33	30.4	1.1	0.7 – 1.5
Stomach	17	16.3	1.0	0.6 - 1.7
Testis	10	8.7	1.1	0.5 - 2.1
Thyroid gland	6	6.6	0.9	0.3 – 2.0
Tongue	6	6.3	1.0	0.3 - 2.1

Table 8: Number of Observed and Expected New Cancer Cases and Race- and Age-Adjusted

¹Cancers with ≤5 cases were not included in the analysis. * SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0.

† CLL: chronic lymphocytic leukemia; AML: acute myeloid leukemia

Table 9: Number of Observed and Expected New Cancer Cases, and Race- and Age-Adjusted				
	Standardized Incide	ence Ratios, Meigs	County, 1991–2000 ¹	
		FEMALES		
Site	Observed	Expected	SIR*	95% CI
Bladder	8	5.2	1.5	0.7 - 3.1
Breast	58	68.0	0.9	0.6 - 1.1
Cervix	9	4.6	1.9	0.9 - 3.7
Colon	7	16.9	0.4	0.2 - 0.9
Corpus uteri	12	11.6	1.0	0.5 - 1.8
Lung	23	30.0	0.8	0.5 – 1.1
Ovary	8	8.0	1.0	0.4 - 2.0
Rectum	7	5.3	1.3	0.5 - 2.7

¹Cancers with ≤5 cases were not included in the analysis. * SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0. **Bold** type indicates statistical significance.

Table 10: Number	Table 10: Number of Observed and Expected New Cancer Cases, and Race- and Age-Adjusted					
	Standaruized metu		County, 1991–2000			
	[MALES	Γ	[
Site	Observed	Expected	SIR*	95% CI		
Bladder	12	14.7	0.8	0.4 - 1.4		
Brain	6	4.4	1.3	0.5 - 2.9		
Colon	14	19.3	0.7	0.4 - 1.2		
Esophagus	6	3.6	1.7	0.6 - 3.6		
Kidney	9	7.4	1.2	0.6 - 2.3		
Lung	44	56.1	0.8	0.6 – 1.1		
Melanoma	7	5.6	1.2	0.5 - 2.6		
Non-Hodgkin	7	9.4	0.7	0.3 – 1.5		
lymphoma						
Prostate	61	64.8	0.9	0.7 - 1.2		
Stomach	8	3.7	2.1	0.9 - 4.2		

¹Cancers with ≤ 5 cases were not included in the analysis. * SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0.

Table 11: Number of Observed and Expected New Cancer Cases, and Race- and Age-Adjusted Standardized Incidence Ratios Morgan County 1991–2000 ¹				
		FEMALES		
Site	Observed	Expected	SIR*	95% CI
Bladder	6	9.0	0.7	0.2 - 1.5
Breast	78	114.6	0.7	0.5 - 0.8
Cervix	8	7.7	1.0	0.4 - 2.0
Colon	25	29.7	0.8	0.5 – 1.2
Corpus uteri	17	19.6	0.9	0.5 - 1.4
Lung and	45	50.7	0.9	0.6 - 1.2
bronchus				
Non-Hodgkin	12	13.0	0.9	0.5 - 1.6
lymphoma				
Ovary	9	13.6	0.7	0.3 - 1.3
Rectum	6	9.3	0.6	0.2 - 1.4
Thyroid gland	7	7.9	0.9	0.4 - 1.8

¹Cancers with ≤5 cases were not included in the analysis. * SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0. **Bold** type indicates statistical significance.

Table 12: Number of Observed and Expected New Cancer Cases, and Race- and Age-Adjusted						
	Standardized Incide	nce Ratios, Morgan	County, 1991-2000)1		
		MALES				
Site	Observed	Expected	SIR*	95% CI		
Bladder	25	25.4	1.0	0.6 - 1.5		
Brain	6	7.8	0.8	0.3 – 1.7		
Colon	18	33.4	0.5	0.3 - 0.9		
Kidney	10	12.8	0.8	0.4 - 1.4		
Lung and	90	94.5	1.0	0.8 - 1.2		
bronchus						
Melanoma	6	9.9	0.6	0.2 - 1.3		
Prostate	69	108.3	0.6	0.5 - 0.8		
Rectum	15	12.4	1.2	0.7 - 2.0		

¹Cancers with ≤ 5 cases were not included in the analysis. * SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0. **Bold** type indicates statistical significance.

Table 13: Number of Observed and Expected New Cancer Cases, and Race- and Age-Adjusted Standardized Incidence Ratios, Rhea County, 1991–2000 ¹				
		FEMALES		
Site	Observed	Expected	SIR*	95% CI
Bladder	12	15.3	0.8	0.4 - 1.4
Brain	8	8.2	1.0	0.4 - 1.9
Breast	157	186.5	0.8	0.7 - 1.0 ‡
Cervix	24	12.3	1.9	1.2 - 2.9
Colon	56	51.8	1.1	0.8 - 1.4
Corpus uteri	31	32.3	1.0	0.7 - 1.4
Kidney	14	12.1	1.2	0.6 - 1.9
Lung and bronchus	70	84.8	0.8	0.6 - 1.0‡
Melanoma	11	11.3	1.0	0.5 - 1.7
Non-Hodgkin lymphoma	26	21.8	1.2	0.8 - 1.7
Ovary	23	22.2	1.0	0.7 - 1.6
Pancreas	9	12.0	0.7	0.3 - 1.4
Rectum	14	15.4	0.9	0.5 - 1.5
Soft tissue	6	3.2	1.9	0.7 - 4.1
Stomach	6	5.3	1.1	0.4 - 3.5
Thyroid gland	14	12.2	1.1	0.6 - 1.9

¹Cancers with ≤ 5 cases were not included in the analysis. * SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0. **Bold** type indicates statistical significance. ‡ Borderline statistical significance

Table 14: Number of Observed and Expected New Cancer Cases, and Race- and Age-Adjusted Standardized Incidence Ratios, Rhea County, 1991–2000 ¹				
		MALES		
Site	Observed	Expected	SIR*	95% CI
Bladder	36	40.1	0.9	0.6 - 1.2
Brain	15	11.0	1.4	0.8 - 2.3
Colon	40	51.8	0.8	0.6 - 1.1
Esophagus	7	9.4	0.7	0.3 - 1.5
Floor of mouth	7	2.0	3.6	1.4 - 7.3
Hodgkin disease	7	4.3	1.6	0.7 - 3.4
Kidney	16	19.2	0.8	0.5 - 1.4
Larynx	17	13.3	1.3	0.7 - 2.0
Leukemia†				
CLL	9	4.0	2.2	1.0 - 4.3 ‡
Lung and	163	146.6	1.1	0.9 - 1.3
bronchus				
Melanoma	17	14.3	1.2	0.7 - 1.9
Non-Hodgkin	21	24.4	0.9	0.5 - 1.3
lymphoma				
Pancreas	7	12.3	0.6	0.2 - 1.2
Prostate	142	172.5	0.8	0.7 - 1.0 ‡
Rectum	11	18.7	0.6	0.3 - 1.1
Small intestine	7	2.3	3.0	1.2 - 6.3
Stomach	11	10.3	1.1	0.5 - 1.9

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 ¹ Cancers with ≤ 5 cases were not included in the analysis.
 *
 SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0.

 † CLL: chronic lymphocytic leukemia
 Bold type indicates statistical significance.
 ‡

 Borderline statistical significance
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Table 15: Number	of Observed and I Standardized Incide	Expected New Cancelence Ratios Roane	er Cases, and Race-	and Age-Adjusted		
FFMALES						
Site	Observed	Expected	SIR*	95% CI		
Bladder	34	31.3	1.1	0.8 - 1.5		
Brain	9	16.2	0.6	0.3 - 1.1		
Breast	328	382.2	0.9	0.8 - 1.0*		
Cervix	27	24.4	1.1	0.7 - 1.6		
Colon	87	105.8	0.8	0.7 - 1.0‡		
Corpus uteri	61	66.8	0.9	0.7 - 1.2		
Esophagus	6	6.6	0.9	0.3 - 2.0		
Gum and other	9	6.6	1.4	0.6 - 2.6		
mouth						
Hodgkin disease	9	7.1	1.3	0.6 - 2.4		
Kidney	38	25.0	1.5	1.1 – 2.1		
Larynx	12	9.0	1.3	0.7 – 2.3		
Lung and	173	179.6	1.0	0.8 - 1.1		
bronchus						
Melanoma	19	22.5	0.8	0.5 - 1.3		
Multiple	13	12.4	1.1	0.6 - 1.8		
myeloma						
Non-Hodgkin	31	44.6	0.7	0.5 - 1.0 ‡		
lymphoma						
Ovary	44	45.2	1.0	0.7 – 1.3		
Pancreas	13	25.0	0.5	0.3 - 0.9		
Rectum	40	31.9	1.3	0.9 - 1.7		
Soft tissue	7	6.3	1.1	0.4 - 2.3		
Stomach	10	10.7	0.9	0.4 - 1.7		
Thyroid gland	30	23.4	1.3	0.9 - 1.8		

¹Cancers with \leq 5 cases were not included in the analysis.

* SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0. **Bold** type indicates statistical significance. ‡ Borderline statistical significance

Table 16: Number of Observed and Expected New Cancer Cases, and Race- and Age-Adjusted				
	Standardized metac	MALES	County, 1771–2000	
Site	Observed	Expected	SIR*	95% CI
Bladder	82	82.8	1.0	0.8 - 1.2
Brain	14	21.6	0.6	0.4 - 1.1
Colon	112	107.7	1.0	0.9 - 1.3
Esophagus	18	19.5	0.9	0.5 - 1.5
Hodgkin disease	7	7.8	0.9	0.4 - 1.8
Kidney	40	39.2	1.0	0.7 - 1.4
Larynx	26	27.2	1.0	0.6 - 1.4
Leukemia†				
ALL	6	4.1	1.5	0.5 - 3.2
CLL	6	8.3	0.7	0.3 – 1.6
Liver	6	6.7	0.9	0.3 – 1.9
Lung and	325	305.1	1.1	1.0 - 1.2
bronchus				
Melanoma	8	29.0	0.3	0.1 – 0.5
Multiple	10	13.9	0.7	0.3 – 1.3
myeloma				
Non-Hodgkin	49	49.3	1.0	0.7 - 1.3
lymphoma				
Pancreas	21	25.3	0.8	0.5 – 1.3
Prostate	296	361.6	0.8	0.7 - 0.9
Rectum	45	38.5	1.2	0.9 – 1.6
Soft tissue	6	7.4	0.8	0.3 - 1.8
Stomach	21	21.0	1.0	0.6 - 1.5
Testis	10	11.3	0.9	0.4 – 1.6
Thyroid gland	7	8.5	0.8	0.3 - 1.7
Tongue	8	8.1	1.0	0.4 - 2.0

¹Cancers with ≤5 cases were not included in the analysis. * SIR: standardized incidence ratio; when the number of observed cases equals the number expected, the SIR=1.0. † ALL: acute lymphocytic leukemia; CLL: chronic lymphocytic leukemia **Bold** type indicates statistical significance. ‡ Borderline statistical significance

APPENDIX A

MOST COMMON TYPES OF CANCER

The Surveillance, Epidemiology, and End Results (SEER) Cancer Statistics Review (CSR) is a report of the most recent cancer incidence, mortality, survival, prevalence, and lifetime risk statistics published annually by the Cancer Statistics Branch of the National Cancer Institute. According to the SEER results for 1998–2002, cancer of the prostate gland has become the most common type of cancer among both black and white males (see table below). Lung cancer and colorectal cancer are the second and third highest, respectively, for both black and white males. Bladder cancer is the fourth most commonly diagnosed cancer in white males, but ranks seventh for black males.

Breast cancer is by far the most common cancer among both black and white females. Lung cancer and colorectal cancer are the second and third highest cancers, respectively, among white females compared with ranks of third and second highest, respectively, for black females. The fourth most common cancer for females is corpus uteri (endometrial) for both whites and blacks.

10 Most Commonly Diagnosed Cancers in the United States as Measured by Number of Incident Cancer Cases, 1998–2002, By Race and Gender National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Cancer Statistics Review 1975–2002*

Black Males	White Males	Black Females	White Females
1. prostate gland	prostate gland	breast	breast
2. lung & bronchus	lung & bronchus	colon/rectum	lung & bronchus
3. colon/rectum	colon/rectum	lung & bronchus	colon/rectum
4. oral cavity & pharynx	urinary bladder	corpus uteri	corpus uteri
5. non-Hodgkin lymphoma	melanoma of skin	pancreas	non-Hodgkin lymphoma
6. kidney/renal	non-Hodgkin lymphoma	cervix	melanoma of skin
7. urinary bladder	kidney/renal	non-Hodgkin lymphoma	ovary
8. stomach	leukemia	ovary	thyroid
9. pancreas	oral & pharynx	kidney/renal	urinary bladder
10. leukemia	pancreas	stomach	leukemia

* http://www.seer.cancer.gov/cgi-bin/csr/1975_2002/search.pl#results

APPENDIX B

FIGURE 1. MAP OF COUNTIES INCLUDED IN ANALYSIS



APPENDIX C

LIST OF CANCER SITES INCLUDED IN ANALYSIS

- 1. acute lymphocytic leukemia
- 2. acute myeloid leukemia
- 3. anus
- 4. bladder
- 5. bones and joints
- 6. brain
- 7. breast
- 8. cervix
- 9. chronic lymphocytic leukemia
- 10. chronic myeloid leukemia
- 11. colon (excluding rectum)
- 12. corpus uteri
- 13. esophagus
- 14. eye
- 15. floor of mouth
- 16. gallbladder
- 17. gum and other mouth
- 18. Hodgkin disease
- 19. hypopharynx
- 20. kidney
- 21. larynx
- 22. lip
- 23. liver
- 24. lung and bronchus
- 25. major salivary gland
- 26. melanomas
- 27. multiple myeloma
- 28. nasopharynx
- 29. non-Hodgkin lymphoma
- 30. oropharynx
- 31. ovary
- 32. pancreas
- 33. penis
- 34. prostate
- 35. rectum and rectosigmoid
- 36. soft tissue
- 37. small intestine
- 38. stomach
- 39. testis
- 40. thyroid gland
- 41. tongue
- 42. ureter

APPENDIX D

METHODS FOR ANALYZING AND INTERPRETING CANCER INCIDENCE DATA

A standardized incidence ratio (SIR) is the ratio of the incident number of cases of a specified condition in the study population to the incident number that would be expected if the study population had the same incidence rate as a standard or other population for which the incidence rate is known. Standardization (or adjustment) helps control for demographic differences between populations being compared. Standardized incidence rates estimate what the incidence rates for populations would be if their composition were similar to that of a comparison, or standard, population (and, therefore, to each other). Adjustment can be made for various characteristics that influence incidence rates, including age, race or ethnicity, and gender.

Although an unadjusted (or crude rate) is a valuable summary measure, comparison of crude rates between populations can be problematic if demographic characteristics, such as age distribution, that affect health outcome differ between the populations. The overall crude incidence rate for a population depends on not only the incidence rate for each age group but also the proportion of people in each age group. Age-adjustment helps control for differences in the age distribution of populations. Age-adjusted incidence rates for two populations are calculated by multiplying the incidence rates for each age group by the proportion of people in the same age group in the standard population. The sum of these products is the age-adjusted, or age-standardized, incidence rate for each of the populations.

Statistical significance implies that less than a certain percent chance (usually selected as 5%) exists that the observed difference is merely the result of random fluctuation in the number of observed cancer cases. Statistical significance can be determined by examining the confidence interval, which is the computed interval with a given confidence (usually 95%) that the true value of an estimate is contained within the interval. For example, if the confidence interval does not include 1.0 and the interval is below 1.0, then the number of cases is significantly lower than expected. Similarly, if the confidence interval does not include 1.0 and the interval is above 1.0, then a statistically significant excess exists in the number of cases. If the confidence interval includes 1.0, then the true ratio may be 1.0, and the conclusion cannot be made with sufficient confidence that the observed number of cases reflects a real excess or deficit. As long as the 95% confidence interval contains 1.0, the indication is that the SIR is still within the range expected on the basis of the disease experience of the comparison population.

The width of the confidence interval also reflects the stability of the ratio estimate. For example, a narrow confidence interval (e.g., 1.03-1.15) allows a fair level of certainty that the calculated ratio is close to the true ratio for the population. A wide interval (e.g., 0.85-4.50) leaves considerable doubt about the true ratio, which could be much lower or much higher than the calculated ratio.

APPENDIX E

CALCULATION OF STANDARDIZED INCIDENCE RATIOS (SIRs)

- SIRs are standardized ratios of observed cases to expected cases.
- The ratio is standardized to the age-distribution of the county.
- Because standardization is based on the county population, SIRs from different counties should not be compared.
- The formula for the SIR is:

$$SIR = \frac{observed}{expected} = \frac{\sum_{i} (\# \text{ of observed cases in age - group i for the county})}{\sum_{i} [(\text{person - years in age - group i for the county}) \cdot (\text{state rate in age - group i})]}$$

• Example using data from Rothman (1986):

Age-group	County Person-Years	State Rate (1991-2000)	County Observed Cases
1	1000	.0005	5
2	10,000	.002	40

 $SIR = \frac{5+40}{1000 \cdot (.0005) + 10,000 \cdot (.002)} = 2.195$

Interpretation: The number of cases observed in the county is greater than expected. The expected number is based on state rates that have been standardized to the age-distribution found in the county.

But is the result due to chance? To answer this question, calculate 95% confidence intervals. If the 95% confidence interval includes the value 1.0, then one can conclude that the observed SIR of 2.195 may be due to chance.

• Several formulas are available for calculating confidence intervals for SIRs. Exact confidence intervals are based on the Poisson distribution and have iterative solutions. Closed-form solutions exist which provide good approximations to the exact methods (Breslow and Day 1980). Byron's approximation has been shown to give good approximations to exact confidence intervals, even for small numbers of observed cases, and was used in this report (Breslow and Day 1980).

The $100(1-\alpha)$ % confidence interval is given by:

$$SIR_{L} = SIR \cdot \left(1 - \frac{1}{9C} - \frac{Z_{\frac{q}{2}}}{3\sqrt{C}}\right)^{3}$$
$$SIR_{U} = SIR \cdot \left(\frac{C+1}{C}\right) \left(1 - \frac{1}{9(C+1)} + \frac{Z_{\frac{q}{2}}}{3\sqrt{C+1}}\right)^{3}$$

where:

C = observed number of cases $Z_{\alpha/2}$ = critical point of the inverse N(0,1) density function $Z_{\alpha/2}$ = 1.96 when α = .05

For our example:

$$Z_{\frac{6}{2}} = 1.96$$

 $C = 45$
SIR = 2.195

so:

SIR_L =
$$2.195 \cdot (1 - .00247 - .0974)^3 = 1.6$$

SIR_U = $2.195 \cdot (1.022) \cdot (1 - .00241 + .096)^3 = 2.9$

Consequently the 95% confidence interval is (1.6, 2.9). Since this interval does not include the value 1.0, we conclude that the observed SIR of 2.195 is *probably* not due to chance alone. It could be caused by any number of reasons including biases in the data, incomplete data, confounding variables, or real difference in rates between the county and the state.

APPENDIX F

RESPONSES TO PUBLIC COMMENTS

The Assessment of Cancer Incidence for the Eight Counties Surrounding the Oak Ridge Reservation Public Health Consultation (PHC) was available for public review and comment from March 1 to April 14, 2006. The public comment period was announced in local newspapers and flyers summarizing the report were sent to residents living in the area. In addition, the PHC was sent to several state and local health officials. The following comments were received:

- <u>Comment:</u> There appears to be a mistake in Table 7. The expected number, SIR and 95% confidence intervals for bladder, brain, and breast cancer are the same.
- <u>Response:</u> Correct. We found that there was a data entry problem with this table. The table has been modified to include the proper values. After correcting the table, the conclusions for all of the cancer types did not change except for that of acute myeloid leukemia (AML). The corrected values are 6 observed cases, 4.6 expected cases, standardized incidence ratio of 1.3, and a 95% confidence interval of 0.5–2.8. The conclusions were modified to state that there were no statistically significant excesses in cancer among females in Loudon County.

Other data entry errors in the tables include:

Table 1: SIR for AML is 1.0 and the SIR for CLL is 0.7.
Table 2: Expected value for Hodgkin disease is 10.5, the SIR is 0.8, and the 95% CI is 0.3–1.5.
Table 5: Observed number of breast cancer cases is 2498.

- <u>Comment:</u> In browsing the text of the cancer incidence study some more, I found a difference in numbers that is probably worthy of an explanation. On page 7, the total numbers of cancers for females and males in Anderson County are given, respectively, as 1682 and 1819. But in Tables 1 and 2, summing the observed numbers of cancers analyzed, for females and males, respectively, gives 1559 and 1690. The differences in the corresponding numbers are 123 and 129. The numbers given on page 7 may be crude numbers, and the numbers given in Tables 1 and 2 are definitely age-adjusted, with counts for individual types of cancers of 5 or less also removed. Whatever the cause(s) of the differences, adding an explanation at the top of page 7 would be helpful.
- <u>Response:</u> At the end of each table there is a footnote stating that cancer types with 5 or fewer cases are not included. Therefore, the number of cancers presented in the table may not add up to the total number of cancers stated

in the text. This information has also been reiterated in the Results section of the document.

- <u>Comment:</u> Although the report focuses on incidence of specific types of cancer, it doesn't clearly show how the individual counties or the eight-county area compare to the state for overall reported cancers. Can the county numbers be aggregated and compared against state totals for a "big picture" view of cancer incidence in this area (i.e., total area/county cancers vs. total state cancers)?
- <u>Response:</u> We did not conduct an analysis for overall reported cancers because different types of cancer have different causes, take different lengths of time to develop, affect men and women differently, and occur in racial/ethnic groups differently. Therefore, they could actually be considered different diseases and should be examined individually and not aggregated. We did not combine specific cancer types for the entire eightcounty area because the community was concerned about cancer rates in the specific counties individually.
- <u>Comment:</u> How do the results look when expressed as cases per thousand population? Would values be added to the report by presenting population-adjusted results, and if not, why not?
- Response: We did not calculate crude rates of cancer (i.e., the number of cancer cases per 100,000 population) in the eight counties because this information is very general and does not answer the question of whether there is an excess of a particular type of cancer in the community. This report compared the occurrence of cancer types in each county to what would be "expected" based on the occurrence of cancer in the State of Tennessee. We adjusted for age and race to take into account differences in the population.
- <u>Comment:</u> Page 5, 1st paragraph, last sentence. For clarification, it may be helpful to mention by whom and how the data were "already collected."
- <u>Response:</u> The Introduction section has been modified to state that the data were collected by the Tennessee Cancer Registry of the Tennessee Department of Health. A description of the methods used to collect this information is included in the Methods section of the report.
- <u>Comment:</u> Page 6, 1st paragraph. Probably need to at least acknowledge here that the TCR data have some weaknesses and limitations.
- <u>Response:</u> The limitations of the data used for this analysis are listed in the Discussion section on page 11.

<u>Comment:</u> Page 6, 2nd paragraph. Explain in the text the significance of 80% completeness and how it may or may not affect this incidence assessment.

<u>Response:</u> Further explanation regarding this issue has been added to the Limitations section of the report.

- <u>Comment:</u> Page 6, 3rd paragraph. Explain/illustrate how the "expected cases" were determined. Since the State of Tennessee is the reference population, explain what level of confidence can be placed on the "expected" numbers of cases reported for Tennessee as a whole and how that may or may not affect this assessment.
- Response:Expected cases of a particular cancer type were calculated separately for
males and females. They were determined by multiplying the age-specific
statewide incidence rate for the years 1991–2000 by the corresponding
age-specific population totals for the county. This calculation was
performed separately for each of 23 age groups (0–4, 5–9, 10–14,..., 80–
84, and 85+), and then summed to yield the expected number of cases. The
Tennessee Cancer Registry provided all numerator data for this analysis
(population estimates were based on US Census data). Data limitations
are noted in the Discussion section of the report.
- <u>Comment:</u> Page 6. The Statistical Methods section would benefit by including a graphic(s) depicting a sample SIR calculation and interpretation (similar to what you showed ORRHES once before). Also, it is not clear from the discussion how the 95% confidence interval or statistical significance is determined. Clarification might help lay readers better understand the meaning of statistical significance when used in the Results section and tables.
- <u>Response:</u> The report has been modified to include an additional appendix illustrating the calculation and interpretation of an SIR, and how the 95% confidence intervals and statistical significance are determined.
- <u>Comment:</u> Results section. While I understand the meaning of "expected" throughout the report, frequent repetition of the word might cause some lay readers to associate "expected" with acceptability. It may be helpful to remind those readers more frequently that "expected" refers to statewide comparisons.
- <u>Response:</u> The report has been modified to help clarify this issue: page 6, paragraph 3, in the Statistical Methods section includes the following addition: "The expected number of cancers is defined as the number of cancers that would be observed in a particular county, if the county cancer rate was identical to the state rate."

- <u>Comment:</u> Page 11, Conclusions. This would be a good place to reiterate the overall incidence of total area/county cancers as compared to state totals. Also, given the appropriate organizational mandates and responsibilities, maybe include contact information for the state and local agencies that should be contacted for follow-up to issues outside the scope of this assessment.
- <u>Response:</u> As stated previously, the purpose of this report was to determine if there were elevated rates of cancer in the counties surrounding the Oak Ridge Reservation compared with cancer incidence in the State of Tennessee. Therefore, the Conclusions section focused on the results from each county.

We have included an additional section to the Answers to Community Health Concerns regarding whom to contact about questions regarding cancer.

- <u>Comment:</u> Page 14, Question 5. Since the Loudon County PHA was not mentioned elsewhere in this report, nor was it part of the DOE Oak Ridge Area PHA, please provide in the written response a complete citation for the Loudon County PHA and a brief statement of its scope. Maybe this should be included in the Loudon County portion of the Results section.
- <u>Response:</u> The report has been modified to include an explanation after the Loudon County Results section describing the differences between the results presented in the Loudon County public health assessment and this report.
- <u>Comment:</u> Page 37. Re-title the table to clarify that these cancers are ranked as diagnosed nationwide, not locally. Also minor typographical editing is needed in the first paragraph.
- <u>Response:</u> The title of the table has been modified to state that the information presented is for the United States. The typographical errors were corrected.
- <u>Comment:</u> Appendix D. Provide more illustrative and descriptive detail on the derivation and interpretation of SIRs and CIs calculated for this report. Inclusion of raw data tables may be useful for those who'd like to check the math.
- <u>Response:</u> Appendix E has been added to the report providing details on the derivation and interpretation of SIRs and CIs.
- <u>Comment:</u> One of the original goals of this exercise was to critique cancer incidence at the census tract level of the subject counties. However, this goal was abandoned for good reason in my opinion but the topic has received short shrift in the document. The explanation for this failure should be more

complete stating why NO census tracts were suitable for analysis lest it become a general perception problem with the public. The Tennessee Registry personnel admitted in Oak Ridge to the census tract data insufficiencies and I believe they have documented their opinion in correspondence. Their opinion should be cited in support of the ATSDR actions. It should be made clear that when the number of suspect tracts gets large that all tracts become suspect.

<u>Response:</u> Additional detail regarding this issue was included in the Answers to Community Health Concerns section of the report (Question 6).

- <u>Comment:</u> The document should explain that the omission of entries of less than six cancer cases biases the composite data distribution and the dependent SIRs on the high side. Sigmas and dependent confidence limits are likewise biased to the narrow side. Thus higher values of SIRs occur more frequently than the actual rate and appear more reliable than they really are.
- Response: Cancer types with less than six cases were omitted from the analysis due to reasons of confidentiality and the instability of the SIRs that would be calculated. The value of the SIR is influenced by the expected value of the cancer type. If the expected value is much lower than the observed value, then the resulting SIR would be high. Conversely, if the expected value is high and the observed value is low, then the resulting SIR would be small. It is unclear how the omission of these data would affect the distribution of the SIRs.
- <u>Comment:</u> The reasons for the numbers of SIRs and confidence limits excluding the value 1 should be more fully described to prevent public misinterpretation. The number and direction of these values should be tallied in a table.
- <u>Response:</u> The report was modified to include Appendix E which describes the calculation of an SIR and a confidence interval in more detail.

For this analysis, 338 SIRs are presented in the tables. By chance alone, we expect approximately 5% to be statistically significant (n=17). We found 19 statistically significant results. These results are completely in line with what is expected by chance.

Of the 19 statistically significant results, 12 of the SIRs were less than 1.0 (protective). Of the 7 SIRs greater than 1.0, only 2 were greater than 2.0. However, both of those SIRs were based on case counts of only 7 and are therefore unstable results.

- <u>Comment:</u> There should be more discussion of confounders and the lack of correction thereof as well as other things that influence statistical conclusions. Most of these will be in the direction of making the incidence of cancer appear larger than it really is.
- <u>Response:</u> The report has been modified to include more discussion of this issue in the Limitations section.
- Comment:It would be worth mentioning the decision guidelines mentioned in:
 Taube, Gary; Special News Report Epidemiology Faces Its Limits;
 Science, Vol 269, 1995/7/14, p.164. The public needs to understand that

 epidemiology is a blunt tool and what this means to studies of this type.

 The public needs to understand that statistical conclusions about

 "confidence limits" and other statistical parameters are valid only under

 the correct assumption of distribution function and the absence of

 confounding effects. The current document is adequate for knowledgeable

 readers but is wide of the mark for others.
- <u>Response:</u> To assist readers of this report in understanding how the conclusions were drawn, information regarding the methods used to conduct the analysis, as well as the guidelines used to interpret these results, were provided.
- <u>Comment:</u> One should not give the public the belief that they know more about the "true value" than they really do. Statements about confidence usually refer to sample estimates not to true values which are known only under special conditions.
- <u>Response:</u> The explanation in Appendix D has been modified by replacing the word "probability" with "confidence." Also, in the same paragraph the term "significant" was changed to "statistically significant."
- <u>Comment:</u> The conclusion that no consistent pattern of cancer incidence exists in the counties studied is particularly significant, especially since the statistics include both on-site workers as well as off-site non-worker residents. I believe that the observed lack of any consistent pattern in the data might be further strengthened and substantiated by treating all the standard incidence ratios themselves as random variables, either by gender and county, by county, or in total. In doing so, it could be determined whether or not these numbers fit normal or log-normal distributions, and whether there are any outliers. I suspect that there would not be any. I suggest that ATSDR consider doing such calculations.

<u>Response:</u> This is beyond the scope of this report.