Urban-rural Gradients in Cancer Incidence and Mortality in the United States

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1 Abstract

This study describes urban-rural gradients in cancer incidence and mortality in the United States.

Method. The 1995-1999 North American Association of Central Cancer Registries (NAACCR) data set covering 34% of the U.S. population and 2.1 million cancer cases and 1996-99 cancer deaths for the United States as compiled by the National Vital Statistics System were used for the analyses. Cancer incidence and death rates were calculated by sex, site, race, and Beale category. The Beale urban-rural continuum assigns U.S. counties into one of 10 categories based on population count, proximity to larger metropolitan areas, and work commuting patterns. The gradients in rates of the site- and sex-specific cancer rates by Beale categories were compared using linear regression and were considered statistically significant at $p < 0.05$, with the adjusted R^2 used to explain the strength of the gradient. Further several area socioeconomic measures for the white population were examined for their linear association with the Beale urban-rural indicator.

Results. Statistically significant urban-rural trends occurred similarly for age-adjusted cancer incidence and cancer death rates. Nearly all incidence trends declined from urban to rural areas, with the exception of lip cancer in males and lung and oral cavity cancers in females. The gradients in age-adjusted cancer death rates had more increasing urban-rural trends than did cancer incidence rates. The increasing trends for deaths included cancers of the lip, liver, and lung, and non-Hodgkin lymphoma in males and cancers of

the cervix and breast, and non-Hodgkin lymphoma in females. The urban-rural measure correlated strongly with all area SES indicators.

Conclusion. Urban-rural gradients are evident for many incident cancers and cancer deaths. The gradients differ among different cancer types, although most suggest higher age-adjusted rates among more urban populations.

2 Background

Urban-rural gradients in cancer incidence statistics have been described. *[1-4]* Data definition, however, has varied widely, limiting comparability of results across studies. *[2-4]* Further, since many studies were conducted before 1995 or were based on data from these earlier years, incomplete reporting, and particularly differential incomplete reporting from small rural facilities may have biased results. With the advent of the National Program of Cancer Registries, more states have complete data from 1995 forward, as evidenced by the increasing number of registries that achieve certification from the North American Association of Central Cancer Registries (NAACCR), from 14 states and 3 additional metropolitan areas in 1997 to 41 states and one metropolitan area (not located in a certified state registry) in 2003. *[5]*

The purpose of this study was to describe urban-rural gradients in cancer incidence and mortality in the United States. Secondarily, the use of the Beale urban-rural continuum measure was evaluated in terms of its association with county measures of area socioeconomic status (SES). This assessment was to enlighten whether the urban-rural continuum might be confounded by similar gradients in measures of area SES.

3 Method

3.1 Data Sources and Measures

The NAACCR data set for 1995-1999 is comprised of 26 population-based cancer registries meeting NAACCR standards for high data quality for each of the years in the five-year interval *[6]* and among them, the 20 registries listed in Table 1 provided consent to use their data in this study. Specific cancer cases were categorized according

to SEER site groups for 1995-1999, The file used for the urban-rural analyses included registries covering about 34% of the U.S. population and more than 2.1 million cancer cases.

Table 1. Participating Central Cancer Registries

Colorado	Kentucky	North Carolina	Wisconsin
Connecticut	Louisiana	Pennsylvania	Wyoming
GA: Atlanta	Michigan (includes Detroit Metro area)	Rhode Island	
Idaho	Nebraska	Utah	
Illinois	New Jersey	WA: Seattle	
Iowa	New Mexico	West Virginia	

Cancer deaths in the United States are reported to state vital statistics offices and consolidated into a database by the National Vital Statistics System (NVSS). *[7]* Mortality data were not accessible for the same five-year, 1995-1999 interval as the incidence data, so the death data for 1996-1999 were used. Specific cancer deaths were categorized according to SEER site groups for 1996-1999. *[8]*

Incidence and death rates are expressed per 100,000 population. Rates for sex-specific cancers were computed using the same sex population counts for the denominator. Average annual incidence rates were calculated adjusted to the 2000 U.S. standard million population. Age-specific rates were calculated for five-year age groups, 00-04, 05-09 ….85+.

Population counts, used as denominators for calculating the cancer rates included in this report, were derived from post-1990 census estimates produced by the Population Estimates Program of the U.S. Census Bureau. *[9]* County rates for various socioeconomic indicators in the white population were obtained from the 2000 U.S. Census. These ecologic variables reflect composite area measures of the social-economic environment. The specific area SES indicators for the white population were: the county median percent below poverty level; the county median household income; and the county median per capita income. Each of these county area measures was averaged within each Beale category.

3.1.1 Beale Categories

The 1993 rural-urban continuum codes form a classification scheme that distinguishes metropolitan counties by size, and non-metropolitan counties by degree of urbanization, proximity to metro areas, and work commuting patterns. This indicator, known as the Beale urban/rural continuum, was developed by the U.S. Department of Agriculture. *[10]* It is consistent with the Office of Management and Budget (OMB) standard metro and non-metro categories, with the metro group subdivided into four categories and the non-metro group subdivided into six categories. The Beale continuum has been found to be useful in identifying urbanicity differentials in cancer incidence. *[4]*

The rural-urban continuum code scheme includes 813 metro counties and 2,288 non-metro counties for the US as a whole, according to the following classification. *[10]* The table also summarizes the number of US counties in each of the 10 Beale categories.

Table 2. Distribution of U.S. counties and population counts by the 1993 Beale urban-rural continuum

Beale Code	Description	Population Count	No. Counties
Metro counties:			
0	Central counties of metro areas of 1 million population or more.	483,739,395	176
1	Fringe counties of metro areas of 1 million population or more.	43,234,404	132
2	Counties in metro areas of 250,000 to 1 million population.	234,545,848	323
3	Counties in metro areas of fewer than 250,000 population.	84,970,297	205
Non-metro counties:			
4	Urban population of 20,000 or more, adjacent to a metro area.	40,323,044	138
5	Urban population of 20,000 or more, not adjacent to a metro area.	25,415,803	116
6	Urban population of 2,500 to 19,999, adjacent to a metro area.	68,997,796	618
7	Urban population of 2,500 to 19,999, not adjacent to a metro area.	53,324,545	653
8	Completely rural or less than 2,500 urban population, adjacent to a metro area.	11,026,012	247
9	Completely rural or less than 2,500 urban population, not adjacent to a metro area.	14,598,445	531

The Beale code was incorporated into the NAACCR standard data items (item 3300) in 2003 as a variable derived from reported county codes. All registries use a standard computer algorithm to make this assignment. *[11]* Registries first submitted the code in the 1995-1999 NAACCR data set. The Beale code, but not the county identifier, was available on the data set for analysis.

3.2 Statistics and Analytic Tools

Cancer incidence and death rates were calculated by race, sex, site, and Beale category, using SEER*Stat software. Linear regressions of the sex- and site- specific age-adjusted rates were computed using SAS® software. These regressions were weighted by the population counts in each Beale category and were calculated for all races and for the white population only. Race groups, other than white, are more likely to cluster within Beale categories and since this clustering could confound trends, only the results for the white population are presented. Statistically significant linear gradients were determined using a probability level of $p < .05$. The explained variance in the trends, as measured by the adjusted R^2, was calculated for all trends. Figures of selected sites with statistically significant trends are presented.

4 Results

Of the 21 cancer sites in white males and 24 cancer sites in white females, more than half demonstrated urban-rural gradients in age-adjusted incidence rates, as shown in Table 3. Figure 1 highlights the cancer types with statistically significant urban-rural incidence trends for white males and white females. Nearly all gradients for cancer incidence showed a decline in age-adjusted rates from urban to rural counties, with the exception of the increases in age-adjusted rates for male lip and female lung cancer incidence. Seven cancer sites that occur in both men and women had urban-rural gradients in only one of the sexes: in males, cancers of the colorectum, liver, and lip and melanoma and in females, cancer of the esophagus, Hodgkin disease, and multiple myeloma. With the exception of colorectal cancer in males and Hodgkin disease and

multiple myeloma in females, each of the statistically significant urban-rural gradients explained 50 percent or more of the variance in the rates.

The declining urban-rural trend for all cancers combined was statistically significant for both genders, however among females, about 70 percent of the variance in incidence rates was explained by the Beale categories while among males, there was more unexplained variation. Male lip cancer incidence rates increased as urbanicity decreased, with 80 percent of the variance explained by the urban-rural continuum measure. Female breast cancer incidence was associated with urbanicity with 72 percent of the variance explained by the urban-rural measure. Although cervical cancer rates had a significant negative association with urbanicity, a polynomial model offered a better explanation of the variation in cervical cancer incidence (i.e., a U-shaped curve), with the highest rates in the most urban and most rural counties. The polynomial model explained 66 percent of the variance in cervical cancer incidence rates, while the linear model explained 51 percent.

Of the 21 causes of death in white males and 24 in white females, more than half demonstrated urban-rural gradients in the age-adjusted rates, as shown in Table 4. Figure 2 highlights the cancer types with statistically significant urban-rural incidence trends for white males and white females. Nearly all urban-rural gradients for cancer deaths showed a decline in age-adjusted rates, with the exception, in males, of cancers of the lip, liver, and lung, and non-Hodgkin lymphoma, and in females, cancers of the lung and brain, and non-Hodgkin lymphoma. Seven cancer sites that occur in both white men and white women had urban-rural gradients in only one of the sexes: in white males, cancers of the liver and lip, melanoma, and Hodgkin disease, and in white females, cancers of all sites

combined, oral cavity, pancreas, and brain. With the exception of liver cancer and lymphomas in white males and oral cancer and Hodgkin disease in white females, the statistically significant urban-rural gradients explained 50 percent or more of the variance in the death rates.

The site- and gender-specific urban-rural gradients were compared between age-adjusted incidence and death rates. Only leukemia and cancer of the gallbladder did not have any urban-rural gradients in either cancer incidence rates or cancer death rates. Three cancer sites had opposite gender-specific gradients for incidence and mortality, for example, a declining incidence gradient and in increasing mortality gradient. These included liver cancer in males; lung cancer in males and females; and non-Hodgkin lymphoma in males and females. Many cancers had similar increasing or decreasing urban-rural gradients for both incidence and mortality: in males, cancers of the lip (increasing) and prostate (decreasing), melanoma (decreasing), and lymphoma (decreasing); in females, cancers of all sites combined (decreasing), oral cavity (increasing), pancreas (decreasing), and breast (decreasing); and in both genders, cancers of the stomach and urinary bladder (both decreasing).

Finally, the Beale urban-rural continuum measure was strongly correlated with each area SES indicator. In Figure 3, the median county household income declined with decreasing urbanicity, with 87 percent of the variation explained. Although not shown in the figure, an even stronger association was found when a curvilinear relationship was applied, with a dramatic decrease across the first-five urban categories, the decline tapering across the remaining 4 categories, explaining almost 97 percent of the variance. Similarly, county per capita income was also strongly associated with declining

urbanicity, as shown in Figure 3, with 83 percent of the variance explained. Conversely, area poverty levels increased with decreasing urbanicity as shown in Figure 3 with about 87 percent of the variance explained.

5 Discussion

Statistically significant urban-rural gradients were found for the majority of age-adjusted cancer incidence and death rates in the white population. Nearly all the significant trends in both incidence and mortality showed a decline in the continuum from urban to rural counties. The strongest cancer incidence urban-rural gradients based on explained variance in the linear regression were seen for cancers of the lip, pancreas, and bladder in white males; and cancers of all sites combined, breast, ovary, and urinary bladder, and non-Hodgkin lymphoma in white females. The strongest cancer mortality gradients in age adjusted cancer death rates were seen for cancer of the lip, stomach, urinary bladder, and kidney for males; and cancers of the stomach, lung, breast, cervix, and brain (including other nervous system sites) for females.

The Beale categories were also highly correlated with the selected area SES measures. This could potentially confound interpretation of the urban-rural gradients such that the risk may not be entirely related to urban or rural factors, per se, but rather to the economic climate of the areas.

Although age-adjusted rates were used in the analyses, it is possible that residual age effects within the categories, and particularly in the group of 85 year old persons and older, might contribute to urban-rural variation in cancer rates if the age distributions of the population were also different between urban and rural residents. To address this, the age-specific cancer death rates were examined for the collapsed Beale categories of metro

(groups 0 to 3) and non-metro (groups 4 to 9) counties. The slight differences found were not sufficiently large to explain the urban-rural gradients reported.

Explanations for the site-specific incidence differentials in urban-rural gradients might be related to differences in exposure, risk, cancer screening, access to physicians and facilities to obtain a timely cancer diagnosis, or they could be related to different characteristics of the populations at risk between the urban and rural areas, including, ethnic origin, population diversity, or culture and lifestyle choices. Mortality is not only related to all the aforementioned factors, but it is also impacted by accessibility to treatment and availability of state-of-the-art treatment regimens.

Differences in incidence and mortality gradients could reflect in- and out-migration between the time and place of a cancer diagnosis and the time and place of a person's death. Further, mortality in rural areas may benefit from lower risk to putagenic exposures but this benefit is tempered by poorer access to cancer care, including greater difficulty in obtaining or complying with state-of-the-art multi-modality treatment protocols. In other words, urban exposures or increased penetration of screening modalities could make incidence rates higher in urban than rural areas, and yet lower access to care and quality treatment could make mortality rates higher in rural than urban areas. The former contributes to declining urban-rural gradients in incidence and the latter to different gradients observed for mortality.

Large geographic differentials in site-specific cancer death rates were observed in the early 1950s, with many forms of cancer exhibiting higher death rates in strongly urban counties than moderately urban counties. *[12]* By the early 1970s, many of these differentials had diminished substantially. *[12]*

In 1997, Fulton and colleagues evaluated urbanicity differentials in a multi-registry data set of cancer incidence and mortality for 1988-1992. *[3]* Urbanization was measured by the proportion of the population served by the registry (usually a state) that resided in urban areas. Regardless of the differences in measures, the results were similar to those reported earlier by Greenberg. *[12]* However, decreasing urban-rural differentials in incidence were evident and included cancers of the bladder, brain, liver, pancreas, and stomach, and Hodgkin and non-Hodgkin lymphomas in white males and cancers of the bladder, breast, cervix, corpus uterus, liver, lung, ovary, pancreas, and stomach among white females. The study reported here used a more precise measure of urbanicity (county rather than state) than did Fulton et al. *[3]*, with some similar results. We did not find gradients for cancer of the liver in females or cancers of the pancreas or brain in males. In addition, we report incidence differentials for esophageal and oral cavity cancers, and Hodgkin disease, non-Hodgin lymphoma, and myeloma in females; and colorectal and lung cancers in males. Further, a statistically significant increasing urban-rural gradient in male lip cancer and female oral cancer was identified in the current study.

Howe and colleagues examined 1990-1994 incidence data for selected cancer sites from 12 U.S. registries, involving 400 U.S. counties (i.e., female breast, colo-rectal, prostate, cervix, bladder, and lung). Decreasing urban-rural gradients using the Beale indicator were found for all site-sex-race groups, except lung cancer in white males and colorectal cancer in white females. *[4]*

5.1 Limitations

Because cancer rates vary by race and because race groups other than white also cluster in different Beale categories, race-specific urban-rural gradients in incidence and mortality were calculated. Only gradients for white were presented due to the lack of sufficient data across the 10-category Beale continuum for other race groups.

Group variables always raise the specter of ecologic fallacy and certainly using area measures, rather than individual measures of SES does that. However, in the context of this project, the social-economic context in which an individual resides may be as important an indicator of SES than one's personal education achievement or household income.

In the spring 2003, the population counts used for cancer statistics were revised as were the estimates for all years 1991-1999 between the decennial censuses. These revised estimates were not available for the incidence and mortality data set (in SEER*Stat software) used for the analysis. It is not known what impact the revised state and county estimates would have on the average rate for each of the 10-points on the urban-rural continuum measure, nor on the relation of rates among the 10 groups.

Individual indicators of SES are not available in cancer registries. In this file, neither was the area (county) SES variables linked to each case. Without this, the analysis could not separate the potential SES contributions to the trends from the urbanicity trends. Recently, Singh and colleagues *[13]* published an extensive analysis of the relation of several area SES measures with cancer incidence, mortality, extent of disease at diagnosis, and survival. Area SES gradients in both incidence and mortality varied by cancer site, sex, and race/ethnicity. The authors concluded that area SES measures

enhanced cancer research and surveillance activities when linked to cancer incidence and mortality records. In the future, such linkage would be very useful for analyses of both SES and urban-rural contributions to cancer statistics.

5.2 Conclusion

Advocacy groups often refer to white, rural inhabitants as the hidden minority of underserved populations with a variety of risk, economic, and access issues that contribute to differential cancer burden. *[14]* The National Cancer Institute's SEER program was expanded in 2001 to increase representation or poor, rural white populations, among other under-represented groups.*[15]* The North American Association of Central Cancer Registries responded to the need and the requests for data about rural populations by defining a standard measure of ruralicity in 2003 for all cancer incidence surveillance systems in the United States, and this indicator is the Beale Urban-rural continuum *[10]*. The gradients reported here support the perception urban-rural incidence patterns are different. They do, however, raise the question of what factors contribute to these differences: ruralicity, poverty, or a more complicated mix that differs by cancer type. With estimates of burden, like those reported here, more research can be conducted to advance the understanding of contributing etiologies.

In conclusion, urban-rural gradients are evident for many, but not all cancer incidence and death rates. The gradients differ among different cancer types, although most suggest higher age-adjusted rates among more urban populations.

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Table 3. Urban-rural Linear Trends* in Age-adjusted (2000 U.S. population standard million)

Cancer Incidence Rates, Whites Only, Selected Areas in the United States, 1995-1999

	White Males			White Females		
Site	**Count**	**Trend**	**Adj R^2**	**Count**	**Trend**	**Adj R^2**
All Cancer	958,467	-	0.46	924,421	--	0.70
Oral	27,367	NS	0.10	13,507	+	0.47
Lip	3,329	++	0.80	831	NS	0.23
Esophagus	14,032	NS	0.11	4,402	--	0.62
Stomach	17,658	--	0.63	10,681	-	0.49
Colorectal	115,060	-	0.34	114,775	NS	0.11
Liver/IHB	10,024	--	0.51	5,588	NS	0.16
Gallbladder	1,429	NS	0.21	3,501	NS	0.10
Pancreas	20,693	--	0.77	21,595	-	0.45
Lung	163,303	-	0.65	118,340	+	0.48
Melanoma	33,474	-	0.58	26,206	NS	0.33
Breast (Female)				282,238	--	0.72
Cervix				18,544	NS	0.51
Corpus, Uterus NOS				56,227	-	0.60
Ovarian				36,690	--	0.71
Prostate	266,788	--	0.48			
Bladder	68,512	--	0.77	24,154	-	0.78
Kidney	28,360	NS	0.23	18,708	NS	0.16
Brain/ONS	14,272	NS	0.17	11,873	NS	0.10
Thyroid	6,369	-	0.46	18,423	NS	0.29
Lymphomas	51,141	-	0.52	42,247	--	0.69
Hodgkins	6,280	NS	0.34	5,377	--	0.39
NHL	39,628	-	0.53	36,870	--	0.70
Myeloma	10,578	NS	0.08	9,301	--	0.34
Leukemias	27,255	NS	0.21	21,151	NS	0.10

* Regression trend weighted by population size

\- $p < .05$ for trend of higher urban rates to lower rural rates

-- $p < .01$ for trend of higher urban rates to lower rural rates

\+ $p < .05$ for trend of lower urban rates to higher rural rates

++ $p < .01$ for trend of lower urban rates to higher rural rates

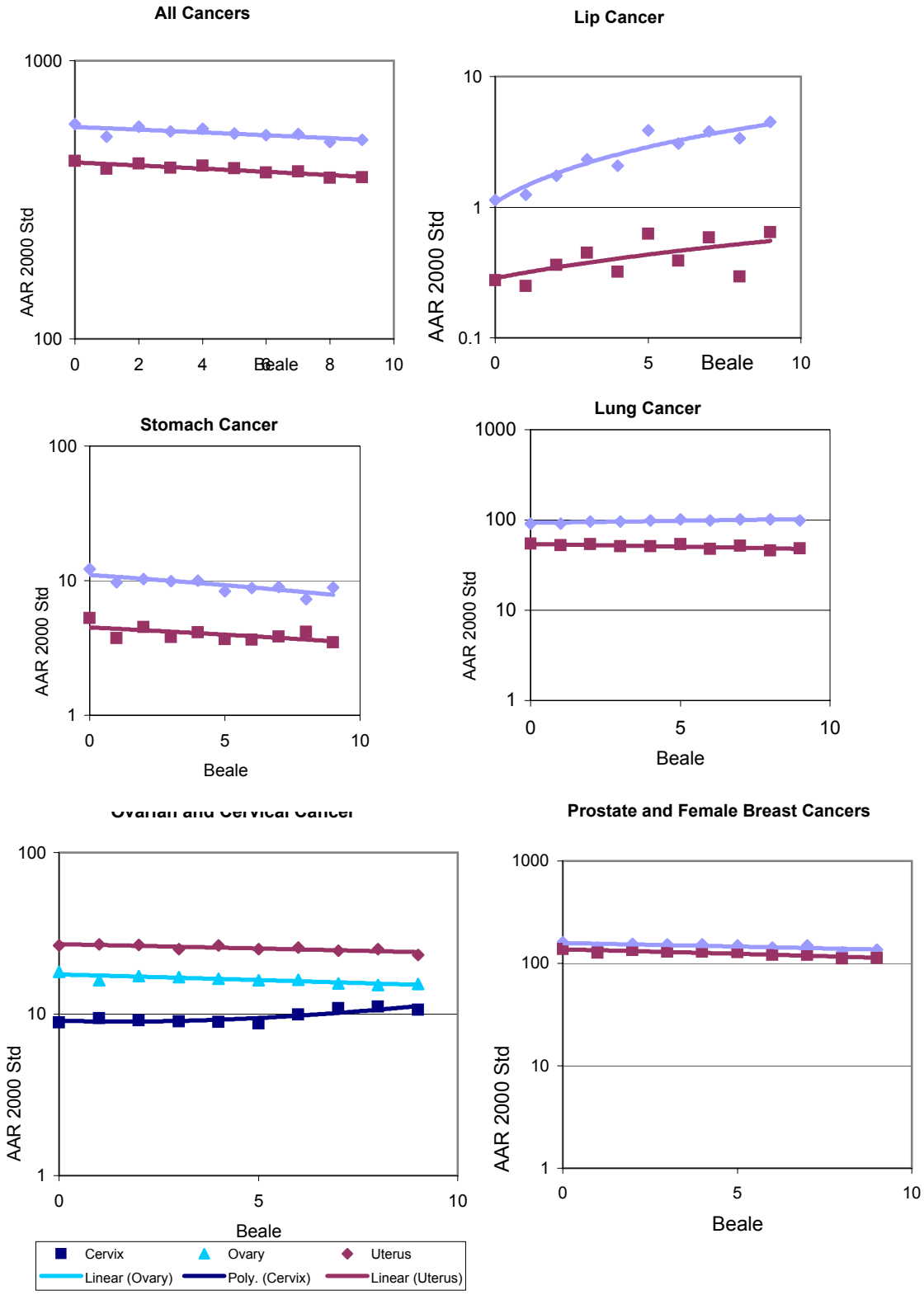
NS no significant trend

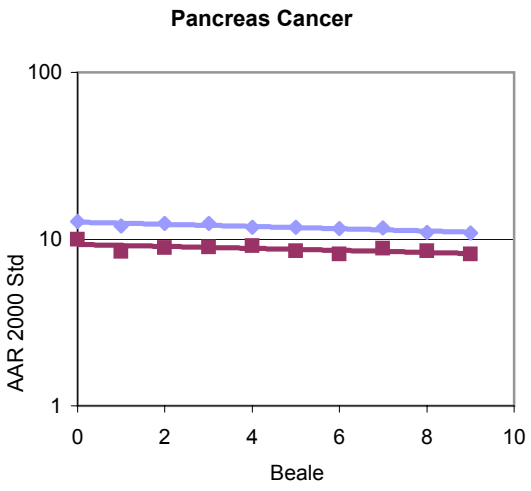
Table 4. Linear trends in site- and gender-specific age-adjusted cancer death rates, White Race, United States, 1996-1999

Cause of Death	White Males All Deaths	White Males All Trend	White Males All Adj R^2	White Females All Deaths	White Females All Trend	White Females All Adj R^2
All Cancer	2,399,091	NS	0.36	2,197,441	--	0.81
Oral	42,400	NS	-0.16	23,140	-	0.48
Lip	622	++	0.73	211	NS	0.01
Esophagus	66,240	--	0.66	21,269	-	0.61
Stomach	62,860	--	0.84	43,066	--	0.85
Colorectal	246,179	NS	0.35	249,678	NS	-0.04
Liver/IHB	52,046	+	0.48	33,967	NS	0.15
Gallbladder	4,955	NS	0.06	13,029	NS	-0.02
Pancreatic	112,111	NS	0.32	118,837	-	0.54
Lung	791,346	++	0.67	514,800	--	0.88
Melanoma	41,727	-	0.58	25,207	NS	0.27
Breast (Female)				369,439	--	0.84
Cervix				33,745	++	0.82
Corpus, Uterus NOS				51,430	NS	-0.13
Ovarian				118,972	NS	0.31
Prostate	275,286	--	0.69			
Bladder	69,186	--	0.94	31,947	--	0.74
Kidney	58,568	--	0.89	37,309	-	0.56
Brain/ONS	61,282	NS	-0.08	51,314	++	0.87
Lymphoma	108,917	-	0.48	101,125	NS	0.41
Hodgkin	7,313	-	0.52	5,793	NS	0.35
NHL	101,604	+	0.44	95,332	+	0.46
Myeloma	41,321	NS	0.08	39,158	NS	0.17
Leukemia	98,401	NS	-0.07	79,840	NS	0.39

- $p < .05$ for trend of higher urban rates to lower rural rates
-- $p < .01$ for trend of higher urban rates to lower rural rates
--- $p < .001$ for trend of higher urban rates to lower rural rates
+ $p < .05$ for trend of lower urban rates to higher rural rates
++ $p < .01$ for trend of lower urban rates to higher rural rates
NS no significant trend

Figure 1. Selected age-adjusted incidence rates by site, gender, and urbanicity, white race, United States, 1995-1996

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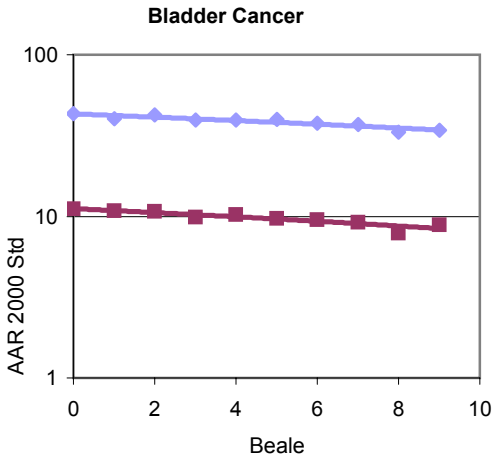
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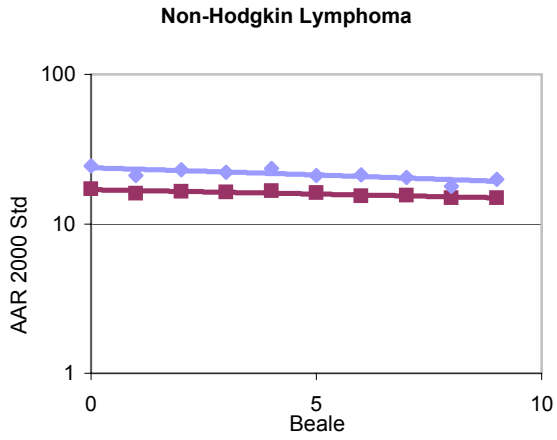
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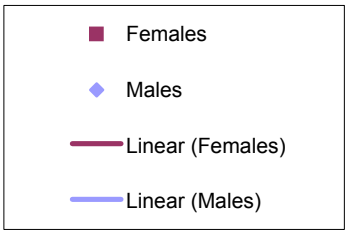
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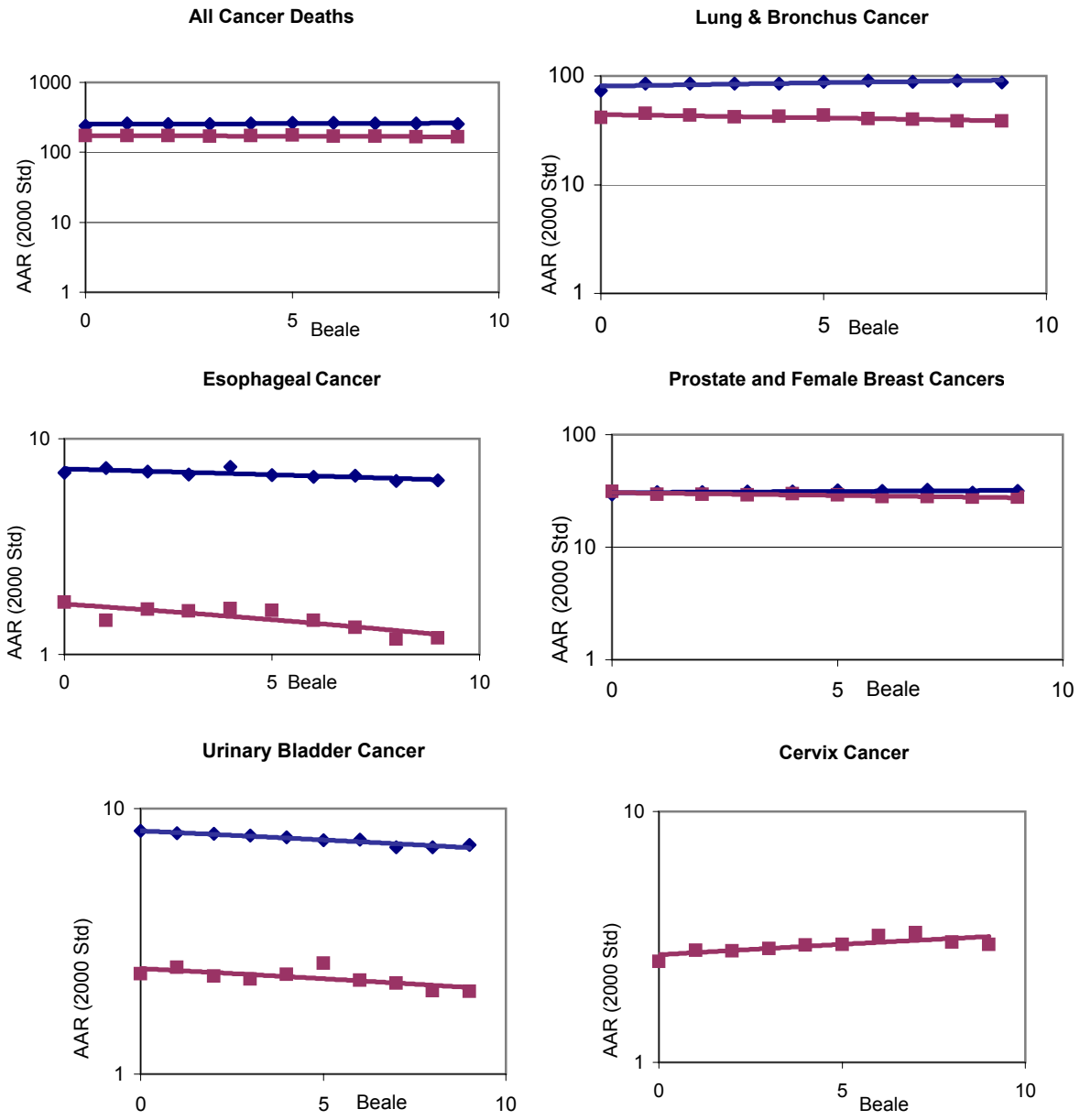
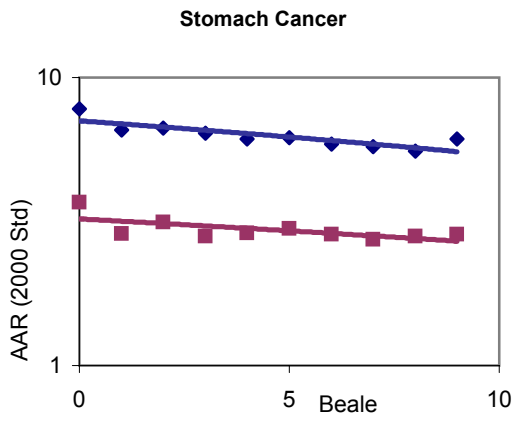
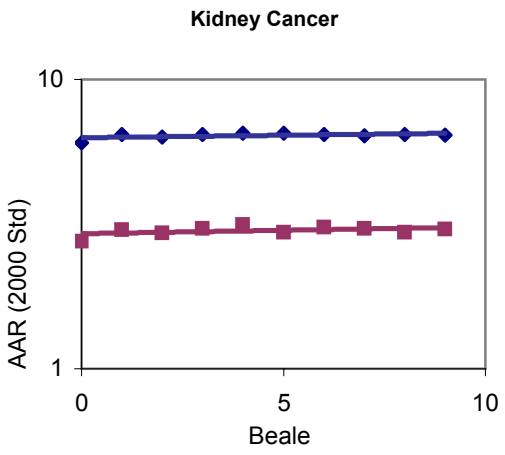
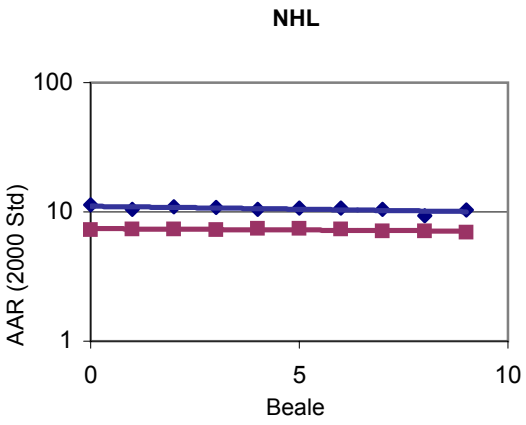
Linear (Males)

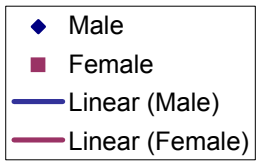
Figure 2. Selected age-adjusted cancer death rates by site, gender, and urbanicity, white race, United States, 1996-1999




Stomach Cancer
10
1
AAR (2000 Std)
0
5
10
Beale


Kidney Cancer
10
1
AAR (2000 Std)
0
5
10
Beale


NHL
100
10
1
AAR (2000 Std)
0
5
10
Beale


Male
Female
Linear (Male)
Linear (Female)

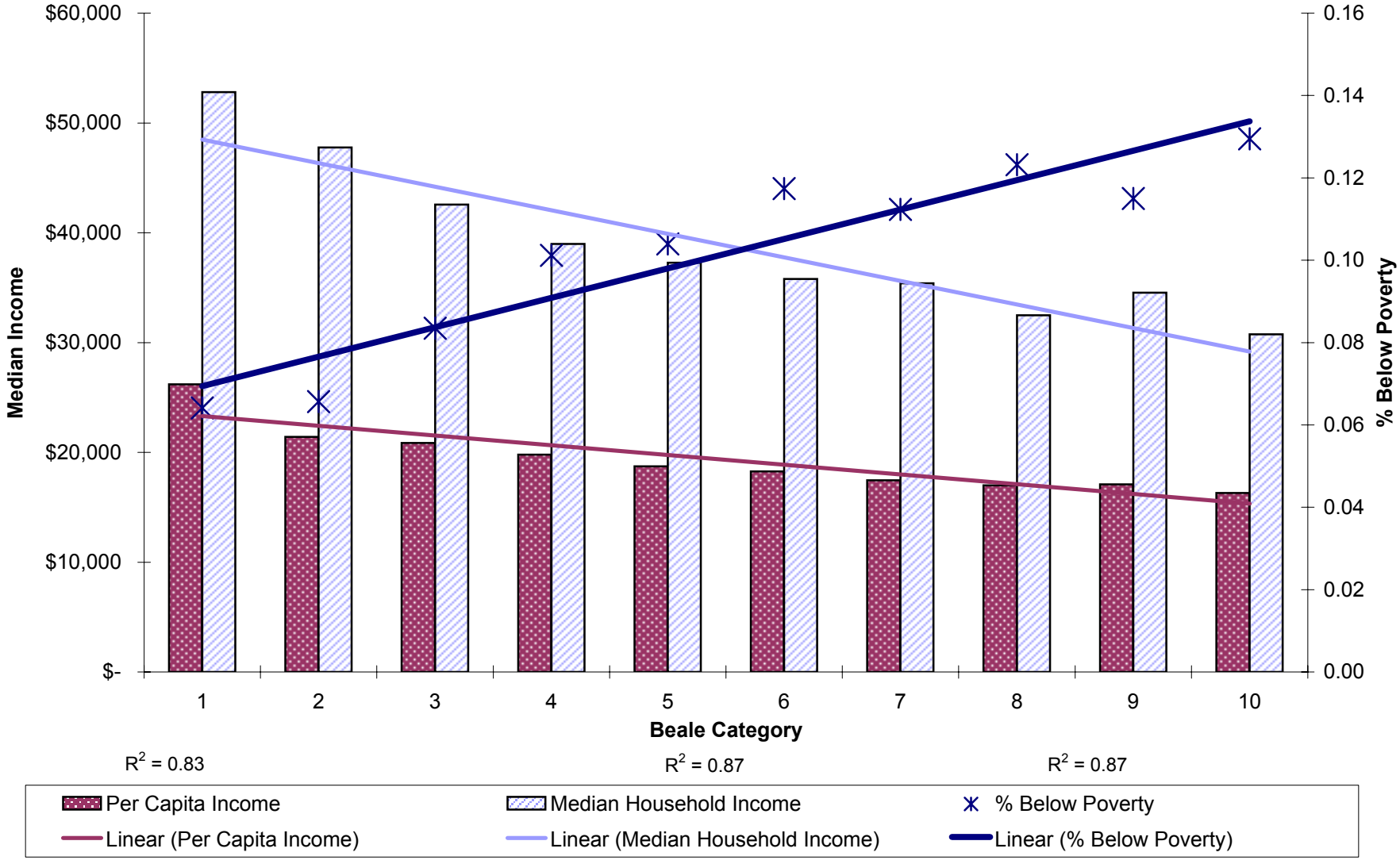



Figure 3. Median County Area Income Indicators by Beale Category, U.S. Census 2000