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Abstract

We extend a prior analysis on the relation between poverty and cancer incidence in a sample of 2.90 million cancers diagnosed in 16 U.S. states plus Los Angeles over the 2005-2009 period by additionally considering stage at diagnosis. Recognizing that higher relative disparities are often found among less-common cancer sites, our analysis incorporated both relative and absolute measures of disparities. Fourteen of the 21 cancer sites analyzed were found to have significant variation by stage; in each instance, diagnosis at distant stage was more likely among residents of high-poverty areas. If the incidence rates found in the lowest-poverty areas for these 21 cancer sites were applied to the entire country, 18,000 fewer distant-stage diagnoses per year would be expected, a reduction of 8%. Conversely, 49,000 additional local-stage diagnoses per year would be expected, an increase of 4%. These figures, strongly influenced by the most common sites of prostate and female breast, speak to the trade-offs inherent in cancer screening. Integrating the type of analysis presented here into routine cancer surveillance activities would permit a more complete understanding of the dynamic nature of the relationship between socioeconomic status and cancer incidence.

Introduction

In order to better understand and ameliorate cancer disparities, it is essential to track the relationship between cancer incidence and socioeconomic status (SES).[1,2] A recent United States-based study found that nearly all of the most common anatomic sites of cancer displayed a significant relationship with poverty, with the rates differing by as much as a factor of two between the poorest and most affluent groups.[3] A shortcoming of this study is that it did not consider stage at diagnosis, which itself often correlates with SES. Specifically, worse stage distributions (that is, a tendency toward more advanced stage at diagnosis) are often characteristic of poorer populations. To characterize a disease such as prostate cancer as "affluent"[4] is misleading because a large majority of prostate cancers are diagnosed at early stage. Late-stage prostate cancer, in contrast, is more characteristic of poorer populations,[5] but this detail is lost when all prostate cancers are grouped together. Here we make use of the same data set used in the recent US study to measure the role of stage in the cancer incidence-poverty relationship.

A novel element of our analysis is that we report both absolute and relative measures of SES disparities. Cancer sites previously identified as having the largest disparities are, in many cases, quite rare in absolute terms (as with Kaposi sarcoma and larynx, for example), making them less amenable to high-impact public health interventions, except insofar as they share risk factors with more common cancer types. There have been numerous calls in recent years for the inclusion of both absolute and relative measures in published research[6-9], but these calls have not been widely heeded: a recent review found only 7% of publications reported an absolute measure.[10]

Material and Methods

We used a data file containing 2.90 million incident cancers diagnosed in 16 participating US states (Arizona, Colorado, Connecticut, Florida, Georgia, Hawaii, Idaho, Iowa, Louisiana, Minnesota, New Hampshire, New Jersey, New York, Texas, Utah, West Virginia) plus Los Angeles County, California between 2005 and 2009.[3] Together, these areas include about 42% of the United States population for this time period and collectively have a poverty rate of 13.5%, similar to the national average of 13.3% as measured by the American Community Survey (ACS) during these same years. Cancer cases in the central tumor registries of these states were geocoded to the census tract and assigned to one of four categories based on the percentage of households below the poverty threshold as measured by the ACS: 0-<5%, 5-<10%, 10-<20%, and over 20%. These categories have been widely used in cancer surveillance and epidemiological research generally and have been shown to be a simple and effective measure of SES.[11-12] The 20% poverty threshold is also used as a criteria for some federal aid programs.[13] The categories also conveniently divide the nation into four roughly equal parts, ranging from 22

to 30 percent of the population. Census tracts are relatively homogeneous and stable geographic units with an average population of about 4,000.

Using poisson regression, we modeled the cancer rate for each anatomic site of cancer by stage for each of the four poverty categories, using a widely used list of sites developed by the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program[14], after excluding those cancer sites which are not staged or rarely staged (myeloma, leukemia, and miscellaneous sites), leaving 2.72 million tumors for analysis. We focused our analysis on the 21 most common cancer sites that collectively account for 97% of all stageable tumors. These sites and their shorthand names used subsequently in this paper are given in Table 1. Sites less common than these had stage-specific rates with very wide confidence intervals and were not informative. Stage was classified using the derived SEER Summary Stage 2000 staging system into local, regional, distant and unknown.[15] The models estimated cancer rates for each site as a function of the population size, age (5-year age groups through 85+), sex, race/ethnicity (white, black, Hispanic, American Indian/Alaska Native, Asian and Pacific Islander), and poverty category. The populations were obtained from a custom file developed by Woods & Poole, Inc. for the use of the SEER program that has been described elsewhere.[3,16] We additionally modeled the cancer rates for three site groupings: all stageable sites combined, tobacco-related sites (oral, esophagus, larynx, lung, and bladder), and HPV-related sites (penis, vagina, vulva, cervix, anus, and the oral cancer subsites nasopharynx, oropharynx, hypopharynx, and tonsil). Breast cancer was limited to females only; male breast cancer was included in all stageable sites combined. The cancer counts and populations used in the models are available in an online data repository associated with this project.[17]

We computed the relative risk of the highest poverty category to the lowest poverty category by stage for each site and site grouping. In addition to this relative measure of disparity, we also computed an absolute measure, consisting of a comparison of the total number of cases by site/stage with the total number predicted by the model after discounting the effects of poverty (that is, if the parameter estimates for all variables in the model for the lowest poverty category were applied to the age, race, and sex counts and populations for the other three poverty categories). To make this number more interpretable, we converted the counts from five-year totals based on 42% of the US population to single-year totals based on the entire US population, assuming that our sample was representative of the nation as a whole. That is, we took the five-year totals, divided by five, then divided by 0.42.

Results

The relative measure of disparity is shown in Figure 1. For clarity, only local and distant stage are depicted here; values for all stages and sites are available in the project data repository.[17] For 14 of the 21 sites (larynx, cervix, oral, lung, prostate, kidney, bladder, colorectal, female breast,

testis, uterus, melanoma, thyroid, NHL), as well as for HPV-related, tobacco-related, and all stageable sites combined, diagnosis at distant stage was more strongly associated with poverty than diagnosis at early stage, as determined by the presence of non-overlapping confidence intervals in Figure 1. For 7 sites (liver, esophagus, stomach, brain, HL, pancreas, ovary), there was no significant difference in stage distribution by poverty. There were no sites where diagnosis at local stage was more strongly associated with poverty.

Of the 14 sites with a stage disparity by poverty, 7 (prostate, kidney, bladder, female breast, testis, uterus, and melanoma) had a more pronounced form, with higher-poverty areas having both a significantly elevated risk of distant-stage diagnosis and a significantly diminished risk of early-stage diagnosis. For example, for prostate cancer, the relative risk of diagnosis at distant stage was 1.27 times higher in the highest poverty category than in the lowest poverty category (95% confidence interval: 1.20-1.34), while the relative risk of early stage prostate cancer was 0.77 (0.76-0.78). This characteristic was also true of tobacco-related cancers and all cancers combined.

The absolute measure of disparity is presented in Figure 2 (the raw counts used to develop this figure are available in the project data repository).[17] Note that the scale in the top row was compressed by a factor of 2.5 in order to fit all sites onto a single page. The figure shows that discounting the effects of poverty would result in large increases in the numbers of local and regional stage prostate and breast cancers, as well as early stage bladder, melanoma, and thyroid cancers. The only major decreases would be found among regional, distant, and unstaged lung cancers. For most sites, the absolute changes for all stages would be small, even though they may be large in relative terms. For example, late-stage oral cancer counts would decrease by about 1,000, barely discernable in the figure but representing a decrease of 22%.

Discounting poverty would result in an absolute reduction in cancer at local, regional, and distant stage for seven sites (lung, colorectal, oral, liver, esophagus, cervix, larynx). For prostate, breast, and kidney there would be a reduction in distant stage tumors but an even larger increase in the number of local-stage tumors. For six sites, there would be an increase in local-stage tumors and almost no change in the number of distant stage tumors (bladder, melanoma, uterus, thyroid, brain, testis). Ovary, HL, and NHL would see an increase in tumors at all stages. Pancreas would have small increases in regional and distant stage, and stomach would remain essentially unchanged.

For these 21 sites combined, discounting poverty would be expected to result in nearly 46,000 additional tumors, or a 4% increase. Tumors diagnosed at early stage would increase by 64,000 (10%) and at regional stage by 3,000 (1%). Tumors diagnosed at distant stage would decrease by 18,000 (8%) and at unknown stage by 4,000 (3%).

Discussion

We found that, in general, high poverty areas tended to have worse stage distributions than low poverty areas. This was apparent whether the data were presented on a relative scale (Figure 1) or absolute scale (Figure 2), though the relative scale may exaggerate the apparent importance of poverty by presenting all cancer sites on a seemingly equal basis. If we consider only the four most common cancer sites (prostate, breast, lung, and colorectal) that account for roughly half of all cancers, for two of these (lung and colorectal) there would be an unqualified benefit accompanying any reduction in poverty, as the numbers of tumors at every stage would be expected to diminish. For the other two (breast and prostate), we would expect a tradeoff between a modest reduction in distant-stage diagnoses and a much larger number of local-stage diagnoses. This resembles the tradeoff seen with certain modes of cancer screening, where each probable life saved (that is, each late-stage cancer detected earlier) must be balanced against a larger number of lives harmed (that is, clinically insignificant early-stage cancer or pre-cancers that need not have been detected at all).[18] Notably, for the three sites most often diagnosed at distant stage (ovary and the two lymphomas), poverty appeared to be protective. Each of these sites are difficult to detect at an early stage, and it appears that for these sites this is true irrespective of SES.

The generally worse stage distributions seen in areas with the highest poverty rates would be expected to translate into higher cancer mortality rates in these areas. Unfortunately, we were not able to measure mortality directly because geocoded vital statistics data at the national level are not presently available at the census tract level. Even so, higher mortality rates can reasonably be inferred from the dramatic differences in survival by stage seen for nearly all cancer sites. For example, the 5-year relative survival for local-stage prostate cancer is at least 100% (meaning those with this diagnosis actually tend to outlive their similarly-aged counterparts without prostate cancer), while distant-stage is 28%.[19] For breast cancer, the corresponding values are 99% and 26%, and for lung cancer, 55% and 4%.[20,21] In addition, recent work by Singh et al. at the county level found that cancer mortality in the lowest-income decile was higher than that in the highest-income decile for all cancers combined and for lung, colorectal, prostate, breast, and cervix.[22]

Cancer sites that would be expected to have more local-stage diagnoses and the same or fewer distant-stage diagnoses after discounting poverty overlap substantially with cancer sites known to be overdiagnosed, or detected in the absence of symptoms and unlikely or contribute to death.[23] Among these sites are prostate, breast, kidney, thyroid, and melanoma. For these sites, the "better" stage distribution found in the most affluent group does not necessarily constitute an advantage. For example, the rates of early-stage thyroid cancer are more than 30% higher in the most affluent group compared with the poorest group, while the rates of distant-stage thyroid cancer are nearly identical in both groups. To discount the effects of poverty here would only result in an increase in the number of early (and regional) stage diagnoses. This relationship can

be inferred from Figure 1, as the relative risk of distant-stage thyroid cancer is close to 1, with wide confidence intervals indicating rarity, while local-stage thyroid cancer is centered below 0.7, with narrow confidence intervals indicating it is more common. Figure 2, however, shows the relationship much more directly.

We included unknown stage in Figure 2 as an illustration of how even a data element as fundamental to cancer surveillance as stage is not always well-collected - often the number of unknown stage equal or exceed the number of regional or distant stage. For most sites, the expected change in the number of cases with unknown stage after discounting the effects of poverty tracks the expected change in the most frequent stage. Pancreas is one exception - even as the number of cases would increase by 5% after discounting poverty, the number with unknown stage would decrease by 7%, suggesting the presence of a SES-based disparity in data quality for this site.

We note that our findings are specific to the period 2005-2009, and that the dynamic nature of cancer screening and prevention efforts and behavioral risk factors mean that the results would not necessarily apply to the current year. For example, local-stage prostate cancer incidence in the United States dropped by 25% between 2011 and 2012 following the United States Preventive Services Task Force recommendation against PSA testing.[24] Were we to repeat our analysis with 2012 data, we would expect to find the projected number of additional local-stage prostate cancer cases diagnosed after discounting poverty to diminish considerably, reducing or perhaps even eliminating the SES disparity for local disease, while leaving the disparity for distant disease intact. Similarly, the introduction of vaccinations against HPV-related cancers are expected to exert substantial downward pressure on the absolute numbers of these cancers, even as relative disparities may rise, at least temporarily, as those at greater risk for the disease may be less likely to receive the vaccinations.[25] The dynamic nature of the cancer-SES relationship argues in favor of it becoming a routine part of national cancer surveillance rather than the subject of an occasional focused investigation such as this one.

Overall, these findings support the general conclusion that poorer populations are more likely to die of cancer while wealthier populations are more likely to die with it. The poor are not simply at higher risk of more fatal cancers, but also at higher risk of being diagnosed with more fatal forms of less-fatal cancers. Specifically, our results suggest that poverty contributes to an additional 18,000 distant-stage cancers in the United States each year while protecting against 64,000 early-stage cancers. Reducing these disparities will require both improvements in primary prevention and improvements in the sensitivity of cancer screening.

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Table 1. Included cancer sites.

Cancer site name[14]	Short name used throughout this paper
Oral cavity and pharynx	Oral
Esophagus	Esophagus
Stomach	Stomach
Colon and rectum	Colorectal
Liver and intrahepatic bile duct	Liver
Pancreas	Pancreas
Larynx	Larynx
Lung and bronchus	Lung
Melanoma of the skin	Melanoma
Breast	Breast
Cervix Uteri	Cervix
Corpus and uterus, NOS	Uterus
Ovary	Ovary
Prostate	Prostate
Testis	Testis
Urinary bladder	Bladder
Kidney and renal pelvis	Kidney
Brain and other nervous system	Brain
Thyroid	Thyroid
Hodgkin lymphoma	HL
Non-Hodgkin lymphoma	NHL
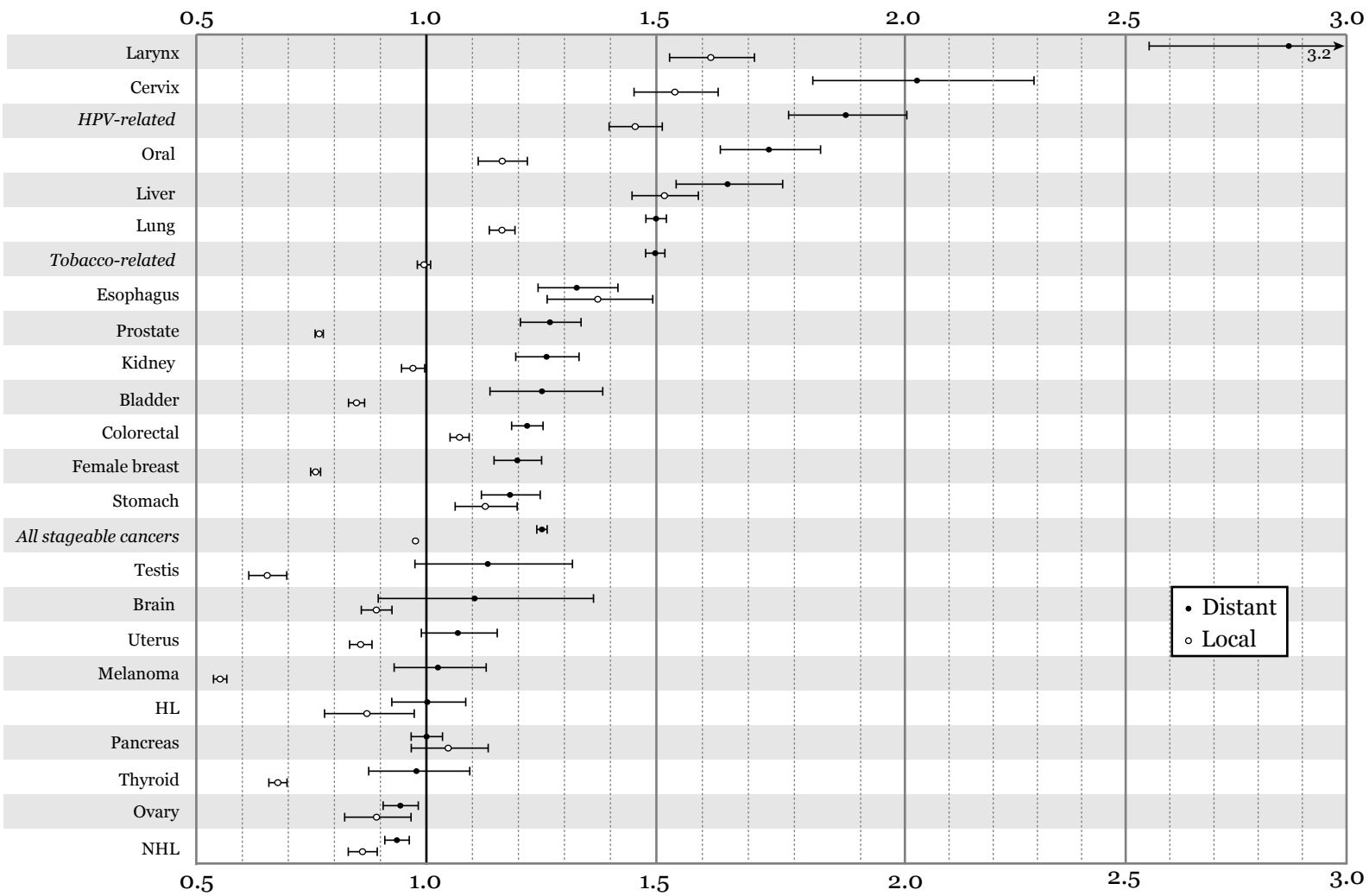
Figure 1. Relative risk of cancer incidence between highest (over 20%) and lowest (<5%) poverty category, by site and stage, United States, 2005-2009.
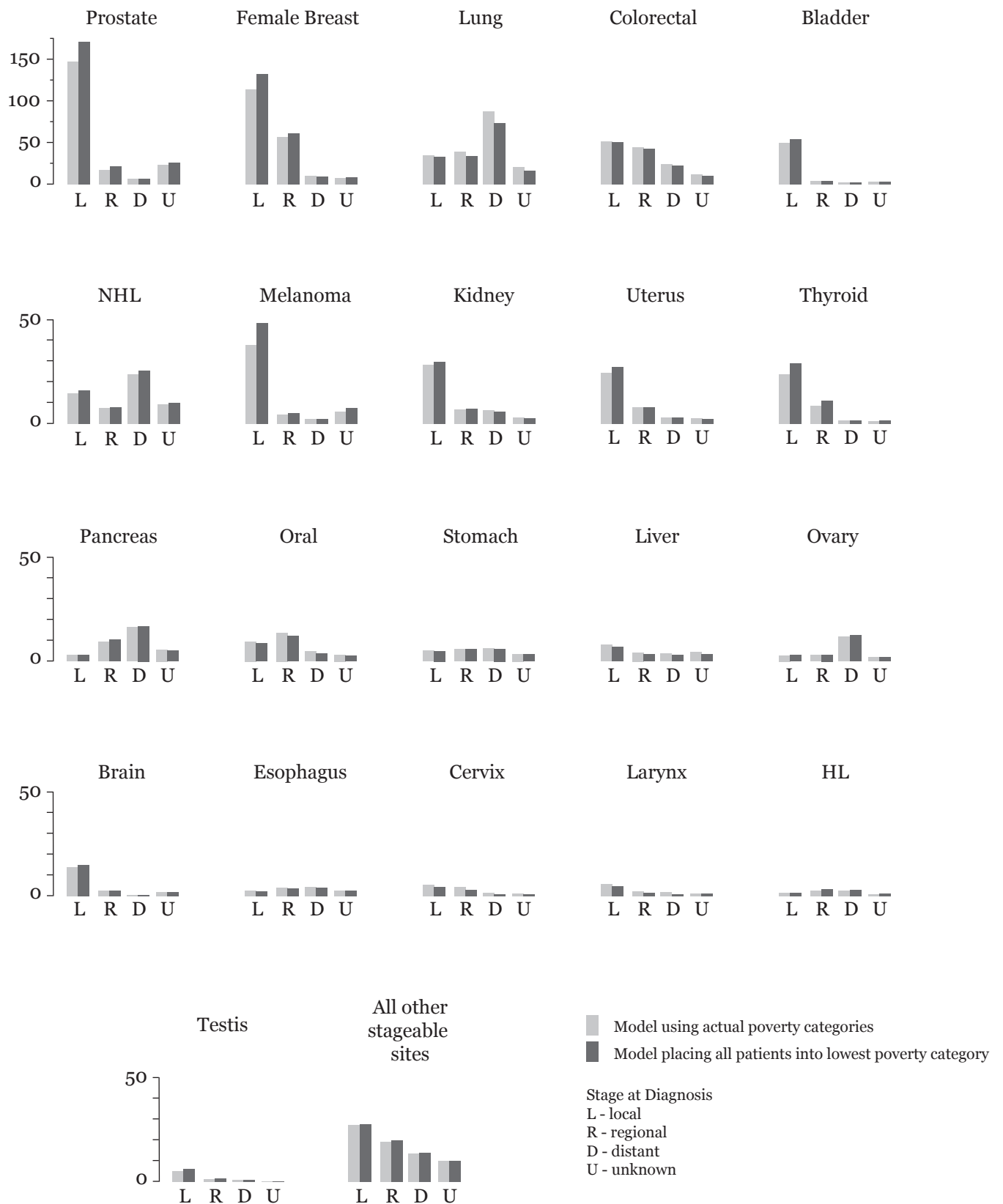
Figure 2. Estimated number of newly diagnosed cancers per year (in thousands), by site and stage, United States, 2005-2009, showing the influence of poverty.