Lung Cancer in Kentucky
Policy Brief
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The severity of lung cancer in the Commonwealth

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Lung cancer accounts for 13% of all new cancer cases – but 28% of all cancer deaths – in the United States. It ranks third in incidence, yet first in mortality. The reason for the discrepancy between the incidence and mortality rates is clear: Not only is lung cancer a common disease, it is also a severe disease with lower survival rates than other major cancers. In this issue we use data from the Kentucky Cancer Registry[1] and the Surveillance, Epidemiology, and End Results Program[2] to look at the severity of lung cancer. We start by comparing survival rates in Kentucky with those from SEER, then relate these rates to the stage of tumor development when the disease is diagnosed.

Measuring the severity of disease

Survival rates are commonly used to measure the degree of severity of disease in a population, rather than to determine the fate of an individual patient. This population-based approach generally leads to estimating the outcome of a disease probabilistically. For example, a patient may be told that, given the extent of disease, she has a 50% chance of being alive in five years. This estimate is based on the experience observed across a large number of patients under similar disease conditions and following them over time after diagnosis. For diseases with poor prognoses they may be expressed as the three-month, six-month or one-year survival rates. For cancer it is common to use the five-year survival rate either as a measure of successful treatment or as an approximation for being cured if one is free of the disease. For example, the five-year survival rate for female breast cancer is 85%, meaning that 85 of every 100 women with a diagnosis of this cancer probably will be alive five years after diagnosis.

Over the past 25 years great strides have been made in increasing the survival rates of cancer patients. Advances in both screening and treatment have made significant contributions to these improvements: Better screening allows for detection of tumors at earlier stages, before they have spread to other organs, and more successful treatment increases the chances of eradicating or controlling the disease.

Unequal improvement

But the improvements in survival rates have not been equally shared among the various types of cancer. And, unfortunately, the situation for lung cancer has remained grim for decades. Figure 1 shows the five-year survival rates in the U.S. (as estimated from SEER data) for selected cancers from 1974 to 1996, divided into three time periods. A comparison over time reveals obvious disparities in improvement across different cancers. Major progress is evident for prostate

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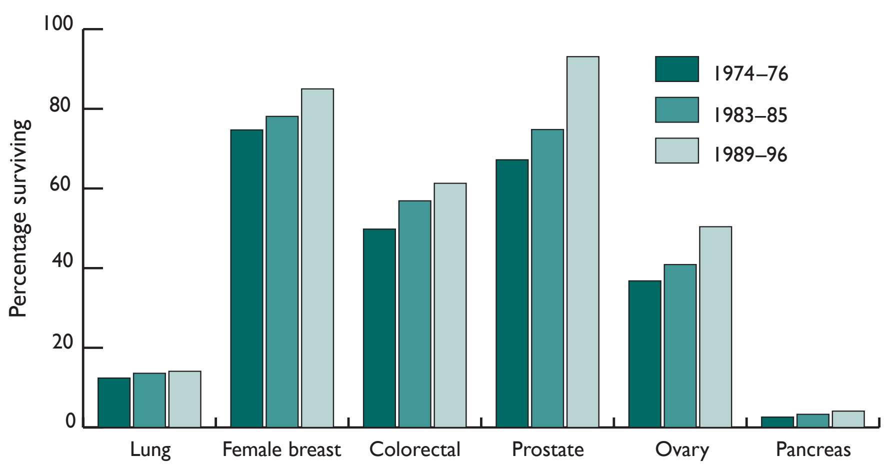

Fig. 1. Five-year survival rates by cancer site and year of diagnosis (Source: SEER, 1974–96).

[1] The Kentucky Cancer Registry collects data on all cancers diagnosed in residents of Kentucky, recording about 95% of all new cases in the state.

[2] The SEER — Surveillance, Epidemiology, and End Results — Program, started in 1973 by the National Cancer Institute, is the most comprehensive source of nationwide information on diagnosed cancers and survival rates in the United States. SEER compiles data on cancers from 14% of the U.S. population. In these briefs we often state *SEER rates*, which are thought to approximate the cancer rates in the nation as a whole.

cancer survival rates, which increased from 67.2% to 93.1%. Female breast, colorectal and ovarian cancers have also had marked improvements. But advances in lung cancer survival pale in comparison, with a dismal increase of less than two percentage points — from 12.4% to just 14.1% — over those years. Although the increase in survival for pancreatic cancer was even lower than for lung cancer, it is a much less common cancer, so its burden on the population is correspondingly lower than is the burden for lung cancer. Applying the 1989–96 survival rates from Figure 1 to the 3,616 Kentuckians who had a diagnosis of lung cancer in 1998, an estimated 3,100 will have died within five years, compared with the estimated 350 individuals with a diagnosis of pancreatic cancer who will have died that same year. In fact, of those 3,616 lung cancer patients about 2,130 will not have survived even one year.

What explains the low survival and the lack of more substantial improvement in survival over time for lung cancer, a disease that kills more than 150,000 people in the United States each year? Two factors are largely responsible:

- Lack of practical and successful screening methods to detect lung cancer early.
- Less successful treatment methods to cure or control lung cancer compared with other cancers.

This is partly the case because the molecular mechanisms underlying the development of lung cancer and the mechanisms of resistance to drug and radiation therapy are still poorly understood. Thus, the relatively slow progress in detection of lung cancer and in its treatment largely explain the low improvement in survival over the past 25 years.

Stage and extent of spread

Survival rates are greatly influenced by stage of development at diagnosis or how much a tumor has spread. Stages are assigned to cancers based on the extent of the disease using such characteristics as the size of tumor, whether lymph nodes are involved, and if and where the tumor has spread or *metastasized*. We use the commonly grouped classifications of local, regional and distant stages used by SEER and the American Cancer Society.

Cancers in the *local stage* are confined to the site or organ where they originated, while those in the *regional stage* have spread to adjacent tissues, nearby lymph nodes, or both. *Distant-staged* cancers have metastasized beyond adjacent tissues to other tissues or organs, such as the liver or brain. A certain percentage of cancers are classified as *unstaged* or *unknown*, either because the information was not recorded or because they cannot be assigned a stage. For lung cancer the proportion of unstaged tumors tends to be greater than for other cancers mainly because of the relatively large number of inoperable cases, where the extent of the disease's spread cannot be assessed by clinicians or pathologists.

As expected, survival rates typically decrease as a tumor grows and spreads from the local to regional to distant stage at diagnosis. Figure 2 shows the distribution by stage of selected cancers using data from SEER for 1994–98. As mentioned in volume 1, issue 1 of these policy briefs, almost 50% of lung cancers are diagnosed in the distant stage, a startlingly high proportion when compared with the 4.3% of breast cancers and 5.6% of prostate cancers diagnosed in this stage. And the reverse is true for the proportion of cancers diagnosed at the local stage: Only 17.1% of lung cancers are diagnosed this early, compared with the 63.8% of female breast and 71.4% of prostate cancers diagnosed at the local stage. This difference in distribution of stage partly explains why lung cancer has comparatively lower survival rates than other major cancers.

The stage-specific survival rates, however, are not the same across different cancers. An analysis of survival rates by stage at diagnosis shows that lung cancer lags behind other cancers. SEER data show that only about 50% of lung cancer patients diagnosed at the local stage survive past five years. This contrasts starkly with the five-year survival rates for other major cancers diagnosed at the local stage: 90% for colorectal, 92% for cervical, 97% for female breast, and 100% for prostate cancers.

Given that Kentucky has the highest incidence rates of lung cancer in the United States, the evidence points to an urgent need to find ways to reduce the burden of this disease. Fortunately, one statistical finding for Kentucky is positive: The Commonwealth has a larger proportion lung cancers diagnosed in

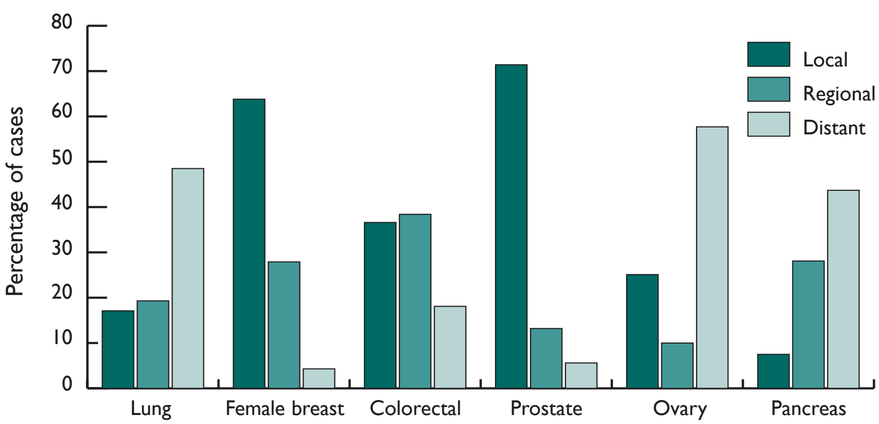

Fig. 2. Distribution by cancer site and stage at diagnosis, 1994–98 (Source: SEER data).

the early stage, when treatment is modestly successful, than does SEER (20.7% for Kentucky versus 17.1% for SEER – see Table 1 for a comparison of lung cancer stage at diagnosis between Kentucky and SEER).

When analyzed by age, the stage at diagnosis reveals a disturbing trend. For both Kentucky and SEER data the proportion of distant-stage lung cancers is higher among younger patients. In other words, younger age groups are diagnosed with advanced-stage lung cancer proportionally more frequently than are older age groups. In Kentucky 44.2% of patients diagnosed with lung cancer under 55 years of age are in the distant stage, compared with 34.7% of those aged 75 to 84. The SEER figures for the same groups are more alarming: 56.1% for those under 55 years of age versus 45.3% for those aged 75 to 84. This suggests that younger patients are more likely than their older counterparts to have more aggressive, advanced-staged and, consequently, untreatable lung cancers.

Another interesting finding is that the proportion of individuals with a diagnosis of lung cancer in the unstaged or unknown group increases with age. In Kentucky, for those aged 85 or older, 42.4% are in this category, whereas for those aged 54 or younger the proportion is 10.7%. It is possible, however, that older patients are less likely to receive surgery as the first step in therapy, so a greater proportion of their lung cancers might fall into the unstaged or unknown group.

Other factors also affect the stage and aggressiveness of lung cancer and, therefore, the success of treatment and survival. Lung cancer is generally thought of as one disease, but there are several kinds of lung cancer, depending on the types of cancer cells, their location in the lung where they develop, and their cause or *etiology*. Lung cancer is, therefore, a heterogeneous disease with several sub-types (*e.g.* adenocarcinoma versus small cell carcinoma), and this may at least partly explain some of the differences seen across age groups described earlier. We will discuss this in more detail in a subsequent issue.

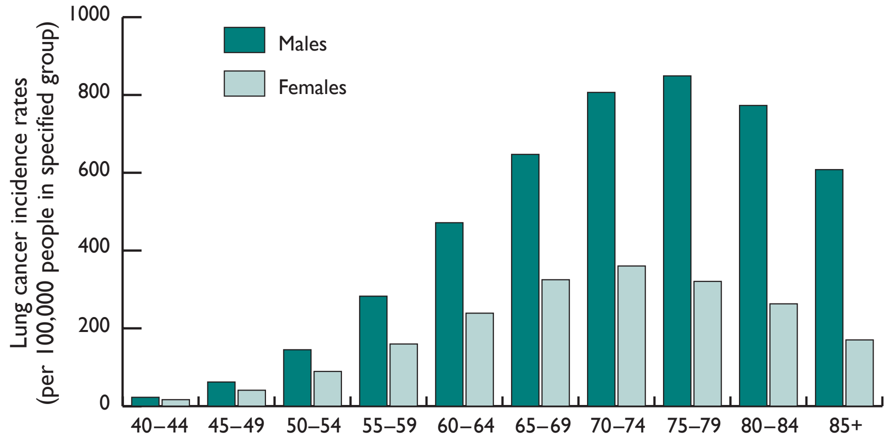

Fig 3. Lung cancer incidence rates by gender and age group in Kentucky, 1994–98 (Source: KCR data).

More on demographic patterns

In volume 1, issues 1 and 2 of the policy brief we examined patterns in distribution of lung cancer. We now compare age-specific lung cancer incidence rates in Kentucky by gender for 1994–98 (Fig. 3). Overall, the rates peak at an earlier age group for women (70–74) than for men (75–79), but this seems to be specific to Kentucky as similar SEER data show the peak age to be the same for men and women (75–79). Figure 3 also shows that the difference in incidence rates between the sexes increases with age.

Table 1. Lung cancer by stage at diagnosis, 1994–98 (Source: SEER and KCR data).

Stage of tumor	SEER	Kentucky
Local	17.1%	20.7%
Regional	19.3%	24.8%
Distant	48.5%	38.1%
Unknown or unstageable	15.1%	16.4%

Conclusion

These survival data indicate that in the last two to three decades no significant improvements have occurred in reducing the high severity and fatality of lung cancer. Lung cancer remains a common type of cancer, diagnosed in more than 3,600 Kentuckians every year. Moreover, the disease's five-year survival rates are only slowly improving, to just 14.1%, with increases in survival continuing to lag behind most other cancers. Together, these facts underscore the urgent need for improvement in the prevention, detection and treatment of lung cancer. Indeed, even when lung cancer is detected in the localized stage of development, its survival rates are still far below those of other cancers.

A recent report from the National Cancer Institute stated that improvements are needed in several areas, particularly in the development of effective and practical screening methods to detect the disease earlier and of more successful therapies to threat those with cancer. Underlying these is the necessity to more fully understand the biological and molecular mechanisms of lung cancer development. The Lung Cancer Research Project, established by the General Assembly, is currently addressing these needs. Visit LCRP's site at **www.mc.uky.edu/markey/Research/KLCR/** for more info.

From the Governance Board

In the first cycle of submissions for proposals to the Lung Cancer Research Project, 20 projects were funded to conduct investigations by research groups from both the University of Kentucky and the University of Louisville (see list of funded projects by university and researcher below). The projects span a number of areas — detection by investigating innovative, potential lung cancer vaccines; biological mechanisms; better understanding of lung cancer development; behavioral research; understanding how psychosocial effects of patients may affect treatment and outcome; and novel approaches to developing more effective treatment protocols. (More information about the Lung Cancer Research Project can be found at **www.mc.uky.edu/markey/Research/KLCR/**.)

We congratulate these investigators for their leading roles in lung cancer research in Kentucky. The Board is now reviewing the second cycle of proposals, which includes 41 proposed projects submitted from both universities.

Researcher at UK	Project title
Mansoor Ahmed	TGF-beta signaling and radiation response in lung carcinoma
Douglas Andres	Novel Ras-related GTPase in lung cancer
Stephen A. Brown	Radioprotective agents in NSCLC therapy
Ramesh C. Gupta	Etiology and prevention of lung cancer: Biomarker development in clinical studies
Louis B. Hersh	A gene therapeutic investigation of dendritic cell vaccines in NSCLC
Edward A. Hirschowitz	Therapeutic investigation of dendritic cell vaccines in NSCLC
Marcos A. Oliveira	A novel chemo/radio sensitizing target: PARP-1 activation domain
H. Peter Spielmann	Pre-clinical studies of novel Ras function inhibitors to treat lung cancer
William St. Clair	Novel anti-cancer agents to promote the efficacy of contemporary or GRID radiation therapy for treatment of lung cancer
John R. Yannelli	Use of dendritic cells to present non-small cell lung cancer associated antigens

Researcher at UofL	Project title
Paula J. Bates	Nucleolin: A novel marker and therapeutic target for lung cancer
Haribabu Bodduluri	Role of G-protein coupled receptor mediated motility in lung cancer
John W. Eaton	Pro-inflammatory and clastogenic actions of smoke-borne free fatty acids
H. Leighton Grimes	Involvement of the GFI1 oncoprotein in human lung cancer
David A. Hein	Environmental genomics and molecular epidemiology in lung cancer: Functional characterization of N-acetyltransferase-1 and -2 genetic polymorphisms
W. Glenn McGregor	Mechanisms of BPDE-induced mutagenesis and mutation avoidance
Stephen C. Peiper	Role of G-protein coupled receptors in lung cancer biology: Novel approaches to block proliferation and spread
Gordon D. Ross	Oral adjuvant immunotherapy of lung carcinoma
Sandra Sephton	Psychosocial effects of lung cancer outcomes
Haval Shirwan	A novel approach to tumor vaccination

Lung Cancer Policy Brief is a joint publication of the University of Kentucky and the University of Louisville.

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Previous issues of the brief are available on-line at **ukprc.uky.edu/publications.htm**.

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