

# The Leading Cause of Cancer Death in Women

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## Abstract

Lung cancer kills more women than breast cancer, ovarian cancer, and uterine cancer combined. The incidence and mortality rates of lung cancer in women were once much lower. Following the trend of the number of women smokers, lung cancer quickly escalated to epidemic proportions. In 1987, an equality of the sexes occurred when lung cancer became the leading cause of cancer death in women. Recent findings support lung cancer in women to be a different entity than lung cancer in men. There are reported sex dependant differences in incidence, susceptibility, histology, and outcomes. Although a proportion of women with lung cancer are never-smokers, most have significant smoking histories. Proactive measures such as increasing awareness, education, and support for funding can have a positive impact in controlling an epidemic that unnecessarily takes the lives of 70,000 women each year.

## INTRODUCTION

When practitioners discuss cancer risks and preventative measures with females, it should be highlighted that lung cancer is the leading cause of cancer death in U.S. women.

Any diagnosis of cancer can be devastating. At the time of diagnosis, patients inquire about their chances for survival, often conveyed as "How long do I have?" The unfortunate answer for patients diagnosed with lung cancer is that the mortality rate is high. In oncology, survival is key and is one of the main focuses of researchers, clinicians, and patients. Each year, approximately 174,470 people are diagnosed with lung cancer in the United States. Only 15% of those will be alive five years after their diagnosis. This is a stark contrast to a 5-year relative survival rate of 88% for patients diagnosed with breast cancer (SEER Breast Stat Facts, 2006). The incidence of lung cancer in women is 52.3 per 100,000 women (SEER Lung Stat Facts, 2006) and accounts for almost 25% of all cancer deaths in U. S. women (Fu, Kau, Severson, & Kalemkerian, 2005). In the U.S., almost 163,000 people die of lung cancer each year. More than 70,000 of those deaths are women. Not only is this 30,000 more deaths than are attributed to breast cancer each year, it is more than the annual deaths from breast, ovarian, and uterine cancers combined (I-ELCAP, 2006).

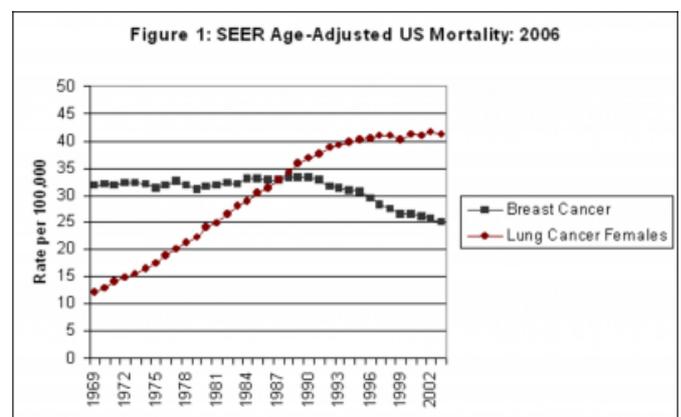
## TREND OF MORTALITY RATE

The alarming statistics of lung cancer in women are relatively new developments. In the 1930s, lung cancer was

only the seventh most lethal cancer in women. The mortality rate grew quickly and it became the first most lethal cancer in women in 1987 (Patel, Bach, & Kris, 2004). While mortality rates from other cancers have declined, the mortality from lung cancer in women began rising in the 1930's and accelerated in the 1960's (Jemal, Ward, & Thun, 2005) with an increase of 600% between 1930 and 1997 (Patel et al., 2004). It maintained an upward trend until it stabilized in the last five years as shown in Figure 1 (SEER Fast Stats Lung, 2006) (SEER Fast Stats Breast, 2006).

## Figure 1

Figure 1: SEER Database of Age-Adjusted US Mortality: 2006



The term epidemic has been used to describe this gross escalation in the incidence of lung cancer in women. This epidemic has been related to an increase in the numbers of

women who smoke (Patel et al., 2004). The incidence has shown a slight decline in the last decade, attributed to a decline in women smokers. In 1965, almost 40% of U.S. women were smokers. This has dropped to approximately 19% in 2003. It is hoped that the rate of smokers will continue to decline and will result in a further decrease in the incidence of lung cancer (Jemal et al., 2005).

### **SEX DIFFERENCES**

A primary topic in lung cancer is whether there are sex-dependant differences. Thomas, Doyle, & Edelman (2005) state that there are sex differences in lung cancer in regards to risk factors, molecular variables, response to therapy, and outcome. Moore, Doherty, Chamberlain, & Khuri (2004) reported a study of 7,553 patients that showed significant sex-dependant differences in non-small cell lung cancer survival. Neugut & Jacobson (2006) concluded that multiple studies report potential differences in the smoking history, incidence, histological type, and outcomes between men and women diagnosed with lung cancer. According to Neugut & Jacobson (2006), "The association between gender and lung cancer survival has been better documented than that between gender and incidence" (p. 219).

### **SMOKING AND SUSCEPTIBILITY**

The association between smoking and lung cancer is well reported. A review of data provided by the American Cancer Society, the Center for Disease Control and Prevention, the National Cancer Institute, and the North American Association of Central Cancer Registries supports that smoking patterns are a primary determinate for lung cancer mortality trends in the United States (Edwards et al., 2005). Based on a review of 228,572 patients, this connection is considered "indisputable" (Fu et al., 2005, p. 774).

In smokers of the same age and tobacco exposure, women have a higher incidence than men (I-ELCAP, 2006). Only 10% of men diagnosed with lung cancer have never smoked. This is in contrast to 20% of women diagnosed with lung cancer who were never-smokers (ACS, 2007). In a study of 975 Asian patients with non-small cell lung cancer, Toh et al. (2006) reported that 32.4% were never-smokers, almost 73% of those never-smokers were female. In agreement with prior studies suggesting a difference in biologic susceptibility, Fu et al. (2005) utilized the SEER database and reported that odds ratio analysis supports that females may have a greater susceptibility to carcinogens. Thomas et al. (2005) report multiple pathobiological factors that can account for the reported sex risk difference. These include

differences in enzymes, molecular abnormalities, growth factor receptors, DNA repair capacity, and hormonal influences. Neugut and Jacobson (2006) state that not all studies agree on this point. They offer the explanation that conflicting results might be due to methodological differences such as biases and confounders in measurement.

### **HISTOLOGY**

There appears to be a relationship between tumor histology and sex. Adenocarcinoma has become the more common type of non-small cell lung cancer in both sexes. Bronchioalveolar carcinoma (BAC) is a subtype of adenocarcinoma that has an indolent growth pattern but is more resistant to conventional chemotherapies (Thomas et al., 2005). Women appear more likely to develop bronchioalveolar tumors than men (Moore et al, 2004). Women with BAC appear to have a better response to newer tyrosine kinase targeted therapies than men (Neugut & Jacobson, 2006). A sex difference is also reported for squamous cell carcinoma, with women having a better prognosis than men (Fu et al., 2005).

### **OUTCOMES AND SURVIVAL**

"Women with lung cancer survive the disease better than men" (I-ELCAP, 2006, p. 183). Although this difference in survival is broader when diagnosed at an earlier stage (I-ELCAP, 2006), Visbal et al. (2004) evaluated 4,618 patients in a prospective study and determined that male sex is an independent unfavorable prognostic factor. He concluded that the survival benefit does not appear to be accounted for by differences in histology, stage at diagnosis, or treatments. An analysis of over 228,000 patients by Fu et al. (2005) also supports sex as an independent prognostic factor. Reviewing the results of seven studies, Thomas et al. (2005) concluded that women have a significant survival advantage regardless of histology, therapy, or disease stage. There are some studies that do not show this survival advantage (Toh et al., 2006) (Barnes, 2004). Neugut and Jacobson (2006) recently reviewed the published data and report that despite different study conclusions, a majority of publications concur that a survival advantage exists. They report that there is no clear consensus on the reasons for difference in survival.

### **CONCLUSION**

Although there remain some unanswered questions about lung cancer in women, there are some important facts that all practitioners should know. Lung cancer is the number one cause of cancer death in U. S. women. The mortality rate of women with lung cancer exceeds the number of deaths from

breast cancer, ovarian cancer, and uterine cancer combined. Smoking is a primary cause of lung cancer. The rate of women who developed and died from lung cancer rose to epidemic proportions as the number of women smokers increased. As the number of women smokers in the U. S. has declined slightly, so has the incidence of lung cancer in women. There is a minority proportion of women with lung cancer who are never-smokers. An increase in susceptibility to carcinogens may account for some of those patients. Women diagnosed and treated for lung cancer have better outcomes than men.

Charged with protecting the health of patients and the public, clinicians are obliged to provide timely and understandable knowledge that can help people make better informed decisions. These decisions can be about lifestyle as well as about treatment options. Discussions about risks of cancer and prevention should be an integral part of regular well-person visits.

Actions can be taken to help control this epidemic. Practitioners must be aware of the problem and knowledgeable about the facts. Patients should be educated and encouraged to prevent, change, and survive this disease. Public awareness needs to be raised about lung cancer in general and specifically its impact on women. Support for public and private funding to needs to be generated.

Resources are available for both professionals and patients. These include the American Cancer Society, the SEER.cancer.gov website, and the National Lung Cancer Partnership. Practical changes can be implemented during patient interactions. When educating female patients, convey this disease as a female epidemic, highlight the association with smoking, and clinically assess for signs of the disease when appropriate. Support never-smokers to remain never-smokers. Inform active smokers that cessation can lead to a significant decrease in cancer risk. With proactive measures at both the individual and the national level, the number of women losing their lives to this predominantly preventable disease can be reduced. Lung cancer does not have to be the leading cause of cancer death in women.

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