SECTION 7
# LUNG CANCER

*Cancer of the lung is the most commonly diagnosed cancer in the United States, accounting for an estimated 15% of all cancer diagnoses in 2008, which is second only to prostate and breast cancer for men and women, respectively (ACS 2008). In addition, lung cancer is the most common cause of cancer death with a five year survival rate of approximately 15% for all stages combined (ACS 2008).*

Lung cancer is cancer that forms in the tissue of the lung. The lungs are responsible for the exchange of gases in the air with the circulatory system.

The rate of lung cancer increases with increasing age; however, a recent decline in the incidence among older age groups appears to correspond with the declining rates of tobacco use (Adami et al. 2002; Schottenfeld and Fraumeni 1996). Worldwide, this malignancy is at least two times more common among men than women, although the incidence among women in the United States has increased due to a higher prevalence of tobacco use (Jemal et al. 2008; Schottenfeld and Fraumeni 1996). Tobacco smoking is the strongest and most established risk factor for lung cancer, contributing to approximately 87% of lung cancer deaths in the United States (ACS 2008). Risk of lung cancer increases with duration and quantity of tobacco smoking, and cessation of smoking results in a decrease in cancer risk over time (Adami et al. 2002; Jemal et al. 2008).

Some occupational and environmental factors, such as radon, secondhand smoke, certain metals, and air pollution, have been associated with increasing the risk of lung cancer (Adami et al. 2002). A variety of food groups, individual food items, and specific micronutrients have been evaluated with respect to lung cancer risk in numerous epidemiologic studies and experimental trials. Collectively, associations for most factors have been equivocal, although high-dose supplementation with beta-carotene likely increases the risk of lung cancer and high intake of fruits or foods containing carotenoids may decrease risk (WCRF/AICR 2007).

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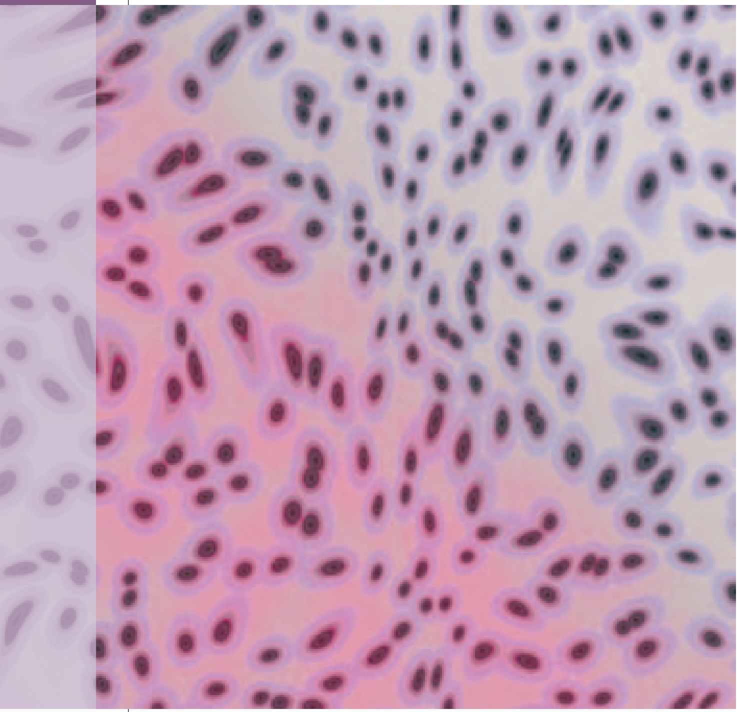
Although lung cancer is the most commonly diagnosed cancer in the United States, the epidemiologic cohort data for meat intake is relatively sparse. Indeed, in the 2007 WCRF/AICR report on diet and cancer, it was stated that the evidence surrounding red/processed meat intake and lung cancer was limited and inconsistent. In a large prospective cohort study, Cross et al. (2007) reported a statistically significant 20% increased risk of lung cancer among the highest consumers of red meat (RR = 1.20, 95% CI: 1.10-1.31). In an analysis of lung cancer mortality using data from the 1987 National Health Interview Survey, a marginally significant positive association was reported for a broad category of red meats (RR = 1.6, 95% CI: 1.0-2.6), and positive associations of 1.6, 1.3, and 2.0 were observed for pork, beef (e.g., roasts and steak), and ground beef (e.g., hamburgers, meatloaf), respectively (Breslow et al. 2000). Non-significant associations of 1.1 and 1.3 for a variable labeled "meat (except chicken)" were reported among men and women, respectively, in a Japanese cohort study (Khan et al. 2004).



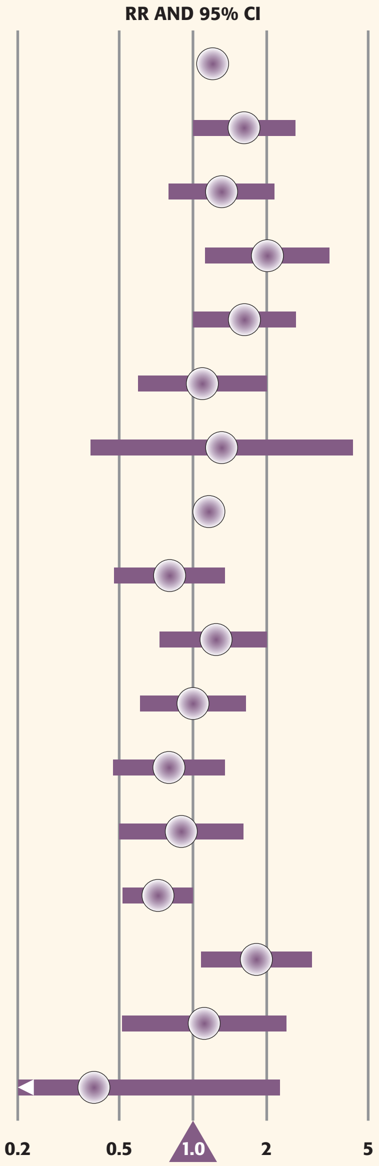
Cancer cells

The association between red meat and lung cancer has been evaluated in approximately 12 case-control studies, and although the results have been variable, most associations are positive. In the most recent case-control study, Lam et al. (2009) analyzed approximately 2,000 lung cancer cases who were recruited from 13 hospitals in Italy. A statistically significant positive association was observed among the highest consumers of red meat (OR = 1.8, 95% CI: 1.5-2.2). When analyzed by histologic subtype, significant positive associations were restricted to adenocarcinomas and squamous cell carcinomas, but not small cell lung cancer.

Associations between processed meat intake and lung cancer have been more heterogeneous than results for red meat consumption. Cross et al. (2007) reported a statistically significant 16% increased risk of lung cancer among persons in the highest processed meat intake category (RR = 1.16, 95% CI: 1.06-1.26). In contrast, Breslow et al. (2000) observed an inverse association between the highest quartile of processed meat intake and lung cancer mortality (OR = 0.8, 95% CI: 0.5-1.4). The authors also reported non-significant relative risks of 0.8, 0.9, 1.0, and 1.2 for the highest intake categories of hot dogs, ham/lunch meats, sausage, and bacon respectively. Conflicting associations for ham/sausage intake were reported in two Japanese cohort studies: Ozasa et al. (2001) observed a statistically significant inverse association among men (RR = 0.72, 95% CI: 0.52-0.99) and a significant positive association among women (RR = 1.79, 95% CI: 1.07-3.01), and Khan et al. (2004) reported a non-significant positive association among men (RR = 1.1, 95% CI: 0.5-2.3) and a non-significant inverse association among women (RR = 0.4, 95% CI: 0.1-3.1). In a cohort of Norwegian men and women, five or more "main meals with meat" were associated with a non-significant 10% decreased risk of lung cancer, but specific meat categories (i.e., red or processed) were not analyzed (Veierod et al. 1997). In the same study, intake of five or more frankfurters per month was associated with a marginally significant two-fold risk of lung cancer.

## FIGURE 7.1
## PROSPECTIVE STUDIES OF RED AND PROCESSED MEAT INTAKE AND LUNG CANCER

| AUTHOR AND YEAR | COHORT | COMPARISON* |
|---|---|---|
| Cross 2007 | NIH-AARP Diet and Health Study | Red Meat |
| Breslow 2000 | National Health Interview Survey | Red Meat |
| | | *Beef (steaks and roasts)* |
| | | *Ground Beef (burgers/meatloaf)* |
| | | *Pork (chops and roasts)* |
| Khan 2004 (M) | Japan Cohort Study | Meat (except chicken) |
| Khan 2004 (W) | Japan Cohort Study | Meat (except chicken) |
| Cross 2007 | NIH-AARP Diet and Health Study | Processed Meat |
| Breslow 2000 | National Health Interview Survey | Processed Meat |
| | | *Bacon* |
| | | *Sausage* |
| | | *Hot Dogs* |
| | | *Ham/Lunch Meat* |
| Ozasa 2001 (M) | Japan Collaborative Cohort Study | Ham/Sausage |
| Ozasa 2001 (W) | Japan Collaborative Cohort Study | Ham/Sausage |
| Khan 2004 (M) | Japan Cohort Study | Ham/Sausage |
| Khan 2004 (W) | Japan Cohort Study | Ham/Sausage |




*Comparisons based on high vs. low intake
M: men; W: women

Similar to the cohort studies, findings for processed meat and individual processed meat items have been inconsistent across the case-control studies. For example, Lam et al. (2009) reported a statistically significant positive association among persons in the highest processed meat intake category (OR = 1.7, 95% CI: 1.4-2.1) in a case-control study conducted in Italy, while De Stefani et al. (2002) reported an inverse association (OR = 0.83, 95% CI: 0.55-1.26) for processed meat in a study conducted in Uruguay.

When interpreting results between dietary factors and lung cancer, a central focus should be on the adequacy of adjustment and/or control for smoking history. Indeed, in the aforementioned evaluation by Cross et al. (2007), detailed control for smoking history did not attenuate their results but the authors indicated that residual confounding remains a potential issue because smoking is such a strong risk factor. Smokers generally have less healthy diets, are more sedentary, and may be leaner than non-smokers; thus, interpretation of the nutritional epidemiology literature with respect to lung cancer (and other smoking-related malignancies for that matter) should consider the potential confounding influence of smoking status.

Postulated mechanisms for which meat intake may be associated with lung carcinogenesis include exposure to meat mutagens, such as heterocyclic amines and polycyclic aromatic hydrocarbons produced by high temperature cooking, intake of dietary heme iron, and endogenous formation of N-nitroso compounds (Lam et al. 2009). However, none of these factors have been established as contributing to an increased risk of lung cancer among consumers of red or processed meat. Lam et al. (2009) reported positive associations with intakes of the meat mutagens PhIP, MeIQx, and Bap derived from high cooking temperatures. Sinha et al. (2000) reported a positive association for MeIQx but not for DiMeIQx or PhIP. Findings for meat mutagens should be interpreted with some reservation as these chemicals are commonly quantified based on indirect estimates.

It remains unclear whether confounding and/or residual confounding by smoking status, or low fruit and vegetable (to a lesser extent) consumption may have contributed to the observed positive associations across the epidemiologic literature. In addition, cooking practices, particularly for red meat, that result in the production of heterocyclic amines or polycyclic aromatic hydrocarbons may contribute to the pattern of positive associations. More prospective cohort studies are needed to clarify any potential associations between red meat or processed meat consumption and lung cancer, independent of the effects of smoking, low intake of fruits and vegetables, and cooking practices.