SECTION 4

BREAST CANCER

Diet and breast cancer has been investigated extensively, although the overall evidence surrounding the potential relation between dietary factors and breast cancer carcinogenesis has resulted in the identification of very few risk factors.

Breast cancer is a malignancy that forms in the tissues of the breast. Both women and men may develop breast cancer; however, this malignancy is rare among men. Thus, this section focuses on female breast cancer.

A woman's breast is composed of lobules (glands that produce milk), ducts, fatty and connective tissue, blood vessels, and lymph vessels. Most breast tumors begin in the ducts, although some tumors begin in the lobules and other breast tissues. Breast cancer is the most common malignancy among U.S. women, accounting for approximately 180,000 cases, or one-quarter of all female cancers, in 2008 (Jemal et al. 2008).

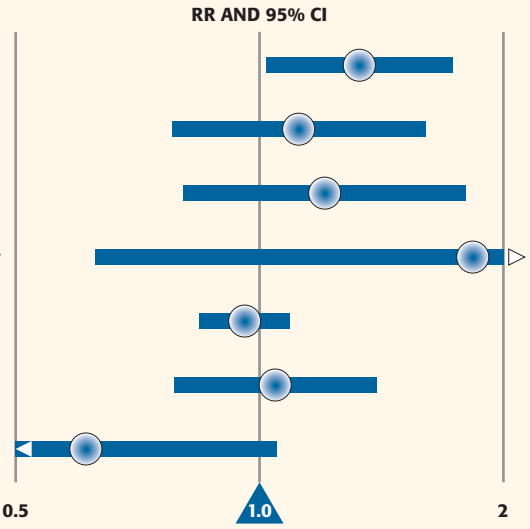
This malignancy is the second leading cause of cancer mortality among women (ACS 2008). Internationally, age-standardized incidence rates of breast cancer are generally higher in North America, Europe, Australia and New Zealand, as compared to Africa, South America, and Asia (Parkin et al. 2005), with rates varying five-fold among different populations worldwide (Key et al. 2001; Lacey et al. 2002). Migrant studies, which evaluate changes in rates of breast cancer in women who move from countries with low breast cancer rates to those with high rates (or vice versa), have shown that rates become similar to those of the population in the new country, suggesting that environmental and lifestyle factors may partially explain some of this observed variation (Tominaga 1985; Ziegler et al. 1993).

Several important factors associated with increasing the risk of breast cancer have been identified, including having a first-degree family history of breast cancer, inherited genetic mutations, such as those in tumor suppressor genes BRCA1 and BRCA2, endogenous and exogenous hormone exposures, and clinico-pathological traits (Key et al. 2001; Collaborative Group 1997). High body mass index (BMI) has been associated with decreasing the risk of premenopausal breast cancer; conversely, high BMI has been associated with increased risks of postmenopausal breast cancer (Hankinson and Hunter 2002). Physical inactivity has been associated with increased risk of breast cancer, with more consistent results in studies of postmenopausal women than premenopausal women (van den Brandt et al. 2000).

FIGURE 4.1
PROSPECTIVE STUDIES OF ANIMAL FAT INTAKE AND BREAST CANCER

AUTHOR AND YEAR	COHORT
Cho 2003	Nurses' Health Study II
Graham 1992	New York State Cohort Study
Mills 1989	Adventist Health Study
Sieri 2002	Hormones and Diet in the Etiology of Breast Cancer Study
Smith-Warner 2001	Pooling Project of Prospective Studies*
Voorrips 2005	Netherlands Cohort Study
Wakai 2005	Japan Collaborative Cohort Study

*Includes data pooled from eight cohorts



Diet and breast cancer has been investigated extensively, although the overall evidence surrounding the potential relation between dietary factors and breast cancer carcinogenesis has resulted in the identification of very few risk factors. The most consistent dietary factor associated with increasing the risk of breast cancer is alcohol consumption (Key et al. 2001; Hankinson and Hunter 2002). Vitamin D intake may be associated with reducing the risk of breast cancer but more research is needed (Shin et al. 2002). No remarkable findings have been observed among the more well-studied foods and nutrients, such as fruits and vegetables, carbohydrates, fiber, or dietary fat.

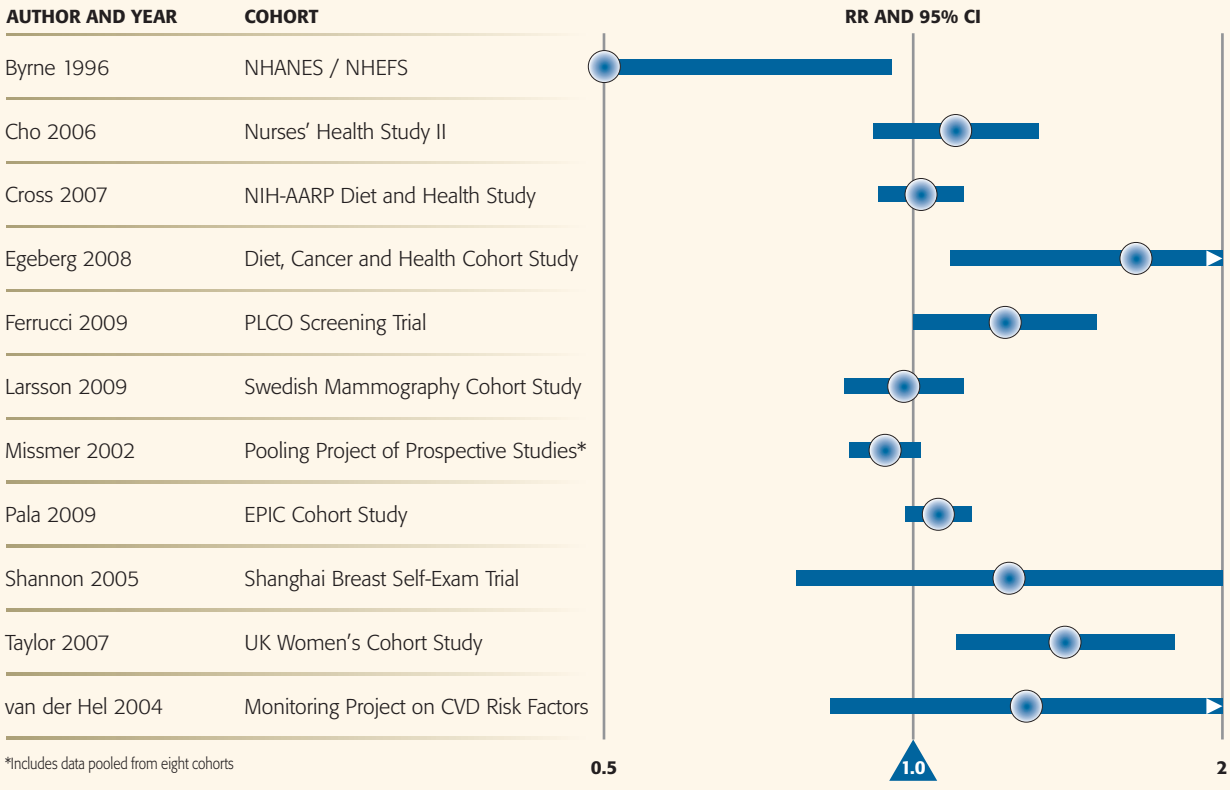
In an analysis of the Pooling Project of Prospective Studies of Diet and Cancer, in which a standardized exposure and analytical methodology was implemented and primary data from eight large prospective cohort studies were analyzed, no significant associations between total fat or specific types of dietary fat were observed (Smith-Warner et al. 2001). In the recent Women's Health Initiative Randomized Controlled Dietary Modification Trial in which the effects of a low-fat diet intervention among postmenopausal aged women were evaluated, a non-significant reduction of breast cancer risk (HR = 0.91, 95% CI: 0.83-1.01) among women in the intervention group was observed (Prentice et al. 2006). There is no consistent epidemiologic evidence indicating that consumption of fat from animal sources, a dietary correlate of red and processed meat intake, is associated with an increased risk of breast cancer (Lowe et al. 2009).

There is no consistent epidemiologic evidence indicating that consumption of fat from animal sources, a dietary correlate of red and processed meat intake, is associated with an increased risk of breast cancer.

As with most dietary factors, the association between meat consumption and breast cancer has been equivocal (Morimoto et al. 2009). The relationship between red meat or processed meat consumption and female breast cancer has been evaluated in numerous studies. Some U.S. and international ecologic studies have reported positive correlations between rates of breast cancer and per capita intake of meat (Armstrong and Doll 1975; Gray et al. 1979; Hems 1970); however, data at the individual level were not analyzed in these studies. Indeed, analytical epidemiologic studies that assessed individual dietary intake have not corroborated these findings, as associations across cohort and case-control studies have been variable.

In a 1993 meta-analysis of case-control and cohort studies, Boyd et al. reported a statistically significant positive association (summary estimate = 1.54, 95% CI: 1.31-1.82) between red meat intake and breast cancer. However, most recent cohort studies have not consistently observed positive associations between red meat or processed meat consumption and breast cancer. In fact, slight inverse associations for consumption of red meat (summary RR for each 100 g/day increment = 0.98, 95% CI: 0.93-1.04) or processed meat (summary RR for each 10 g/day increment = 0.98, 95% CI: 0.96-1.00) were reported in the comprehensive analysis of the Pooling Project of Prospective Studies of Diet and Cancer (Missmer et al. 2002). The Pooling Project analysis included data from eight cohorts in North America and Western Europe, and more than 7,000 women diagnosed with invasive breast cancer were analyzed.

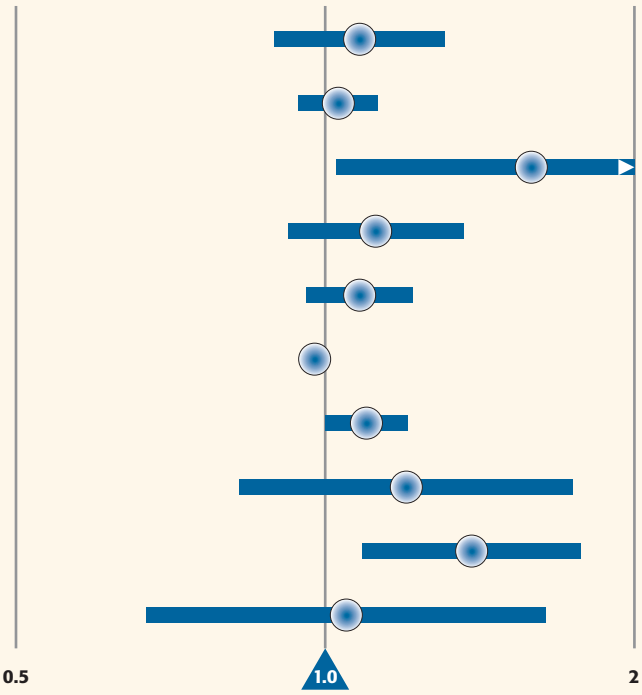
FIGURE 4.2
PROSPECTIVE STUDIES OF RED MEAT INTAKE AND BREAST CANCER



*Includes data pooled from eight cohorts

FIGURE 4.3
PROSPECTIVE STUDIES OF PROCESSED MEAT INTAKE AND BREAST CANCER

AUTHOR AND YEAR	COHORT
Cho 2006	Nurses' Health Study II
Cross 2007	NIH-AARP Diet and Health Study
Egeberg 2008	Diet, Cancer and Health Cohort Study
Ferrucci 2009	PLCO Screening Trial
Larsson 2009	Swedish Mammography Cohort Study
Missmer 2002	Pooling Project of Prospective Studies*
Pala 2009	EPIC Cohort Study
Shannon 2005	Shanghai Breast Self-Exam Trial
Taylor 2007	UK Women's Cohort Study
van der Hel 2004	Monitoring Project on CVD Risk Factors



*Includes data pooled from seven cohorts

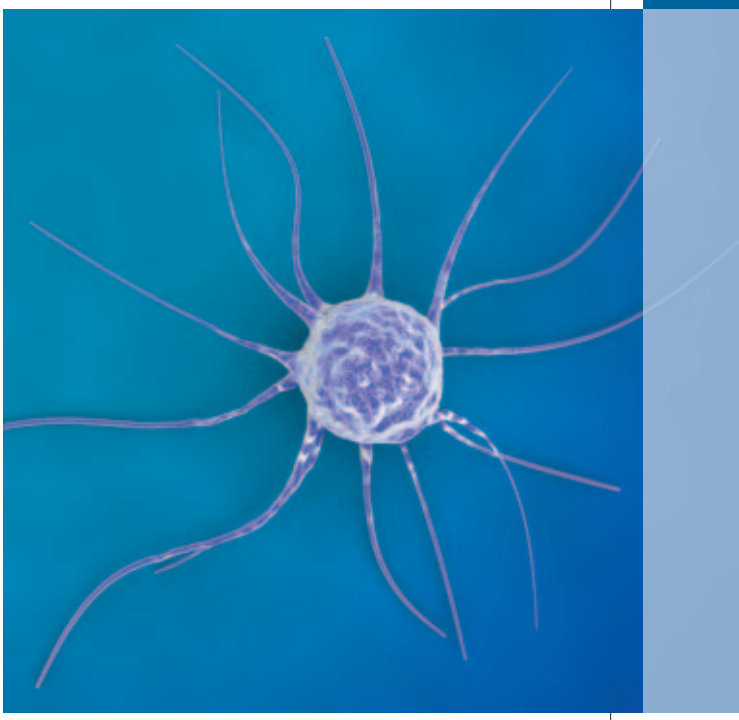
Since the Pooling Project publication, numerous analyses between meat intake and breast cancer have been conducted across large-scale prospective cohorts. In a 2007 publication of the National Institutes of Health (NIH)-AARP (formerly the American Association for Retired Persons) Diet and Health Study, in which approximately 200,000 women (and almost 6,000 breast cancer cases) were analyzed, no association between the highest intake quintiles for red meat (RR = 1.02, 95% CI: 0.93-1.12) or processed meat (RR = 1.03, 95% CI: 0.94-1.12) were found (Cross et al. 2007). Furthermore, no intake-response patterns for red or processed meat were observed. In a sub-group analysis of postmenopausal women from the NIH-AARP cohort, no associations were reported for red meat (RR = 1.05, 95% CI: 0.93-1.18) or processed meat (RR = 1.00, 95% CI: 0.90-1.12) and breast cancer (Kabat et al. 2009). Furthermore, cooking methods, meat doneness, or dietary mutagens were not associated with increasing the risk of breast cancer among postmenopausal women in this study.

In an analysis of the EPIC cohort, non-significant relative risks close to the null value were reported for red meat intake, and marginally significant, albeit weakly elevated relative risks were observed for processed meat consumption (Pala et al. 2009). No association between red or processed meat and breast cancer was observed in an analysis of the Swedish Mammography Cohort (Larsson et al. 2009). Non-significant weak-to-modest positive associations for red meat and processed meat were reported in Dutch (van der Hel et al. 2004) and Chinese (Shannon et al. 2005) cohort studies. In an analysis of the UK Women's Cohort Study, Taylor et al. (2007) observed statistically significant positive associations among the highest consumers of red meat (RR = 1.41, 95% CI: 1.11-1.81) and processed meat (RR = 1.39, 95% CI: 1.09-1.78). Twelve percent and 59% statistically significant increased risks of breast cancer were reported for each increment of 50 g/day for red meat and processed meat, respectively. In the Diet, Cancer and Health Cohort Study, significant positive associations between red meat (RR = 1.65, 95% CI: 1.09-2.50) and processed meat (RR = 1.59, 95% CI: 1.02-2.47) and breast cancer were reported (Egeberg et al. 2008).

Overall, more positive associations are observed among the case-control studies than are inverse associations, but no clear or consistent evidence regarding patterns of increased risks of breast cancer are apparent. Collectively, the case-control studies are more variable than the more rigorous cohort studies in regards to the geographic location of the study, collection of dietary information, type of red/processed meat variables that are analyzed, analytical comparisons, reporting of results data, range of associations, and degree of statistical adjustment.

Because female breast tissue may have increased mammary susceptibility to potential carcinogens during adolescence and early life (Linos and Willett 2007), there is increased interest in how and/or whether diet early in life may contribute to the development of adult cancer. In a case-control study nested within the Nurses' Health Study I and II cohorts, the mothers of study participants were asked about their daughters' perinatal and early childhood dietary habits (Michels et al. 2006). Pre-school intake of ground beef was associated with a non-significant 44% increased risk of adult breast cancer, while consumption of meat (as a main dish or as a sandwich or mixed dish) or hot dogs was associated inversely, albeit non-significantly, with subsequent breast cancer risk. In another study (Frazier et al. 2004), participants were asked to complete a questionnaire regarding diet during high school, a life period that may be affected by micronutrient intake during adolescent growth, and a non-significant positive association between the highest intake of red meat and subsequent risk of breast cancer was reported (RR = 1.22, 95% CI: 0.82-1.82), but no trend based on incremental intake was observed (p-value for trend = 0.17). Results from these studies may be subject to poor recall because study participants (or mothers of cases) reported dietary habits that likely occurred 30 to 40 or more years prior to information ascertainment and breast cancer diagnosis.

Another area of increasing scientific interest is the potential relation between dietary factors and breast cancer risk according to tumor hormone receptor status. Although breast tumors differ clinically and biologically by hormone receptor status (Cho et al. 2006), there is little evidence regarding the potential association between red/processed meat and hormone-receptor-status cancer. In an analysis of the Nurses' Health Study II, a non-significant positive association between the highest intake quintile of red meat and total breast cancer was found (RR = 1.27, 95% CI: 0.96-1.67) (Cho et al. 2006). However, the positive association observed in this study was restricted to women with hormone receptor-positive cancer (ER+: estrogen receptor/PR+: progesterone receptor) (RR = 1.97, 95% CI: 1.35-2.88).



Breast cancer cell

A non-significant inverse association was reported among women with hormone receptor-negative cancer (ER-/PR-) (RR = 0.89, 95% CI: 0.43-1.84). Positive associations were also reported for pork (as a main dish), hamburger, bacon, hot dogs, and other processed meats (e.g., sausage, salami, bologna) among women with ER+/PR+ cancer, while inverse associations for these same meat groups were observed among women with ER-/PR- cancer. The authors suggest that mutagenic by-products from cooked meat (e.g., heterocyclic amines), exogenous hormone residues, heme iron, or fat intake may affect breast cancer through hormone receptors, although additional prospective cohort studies are necessary to confirm or refute these hypotheses. Ferrucci et al. (2009) reported a significant positive association between red meat intake and breast cancer (RR = 1.59, 95% CI: 1.03-2.48) among women with ER+/PR+ cancer. Larsson et al. (2009), however, did not observe a significant positive association among women with ER+/PR+ cancer (RR = 1.10, 95% CI: 0.90-1.34).

The relationship between red meat and processed meat consumption and breast cancer has been the focus of several epidemiologic investigations, although the consortium of scientific evidence is not supportive of an independent association. Of note, breast cancer is a heterogeneous disease with differing etiologies; thus, the potential role that diet may play in the development of breast cancer among subgroups is of great public health importance. Menopausal status does not appear to appreciably modify the risk between red or processed meat intake and breast cancer. Recent studies have suggested that meat consumption may affect breast cancer risk through hormone receptor status, and that diet early in life may influence adult breast cancer; however, epidemiologic data for these hypotheses are limited and additional prospective studies are needed before conclusions can be drawn. In summary, on the basis of the available scientific evidence, primarily from prospective cohort studies and nested case-control studies, red meat or processed meat intake does not appear to be associated with breast cancer risk.

The relationship between red meat and processed meat consumption and breast cancer has been the focus of several epidemiologic investigations, although the consortium of scientific evidence is not supportive of an independent association.