Chapter 29
Diet Before and After Breast Cancer

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Abstract The incidence of breast cancer has dramatically increased recently in several Asian countries. This region has experienced rapid economic growth and demographic and environmental changes. Breast cancer rates vary substantially among countries, with a lower incidence in developing countries than that in Western countries. Given the upward trend of breast cancer incidence in Asian countries and the large variation in incidence around the world, dietary changes may contribute to breast cancer development. In particular, nutrients and foods from animal sources have drawn attention as potential causes of breast cancer given that obesity and energy balance appear to be important factors associated with breast cancer risk. However, prospective cohort and intervention studies do not support the hypothesis that diet in middle life influences breast cancer development. However, recent studies have provided better insight into the roles of dietary factors in specific types of breast cancers, such as estrogen receptor-negative (ER-) breast cancer. Some studies suggest that diet in early life may play a substantial role in breast cancer development, but data and evidence remain limited.

Although etiologic and epidemiologic studies have long studied modifiable risk factors for breast cancer incidence, much remains to be explored regarding the role of diet after a breast cancer diagnosis. Several epidemiologic studies have explored the factors that improve breast cancer survival rates, including diet, physical activity, and body mass index (BMI). While there is evidence of the effect of BMI on breast cancer mortality, the effects of changing dietary habits after a breast cancer diagnosis on survival or recurrence are less clear. A report of the World Cancer Research Fund stated that evidence was not sufficient to draw firm conclusions about the effect of diet and nutrition on breast cancer prognosis, but it did suggest a link between diet and breast cancer survival.

The global burden of breast cancer is increasing and breast cancer is a major and emerging health problem in both developed and developing countries. For example, the five-year survival rate for Korean breast cancer patients has improved from

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78.0% in 1993–1995 to 92.7% in 2012–2016. This improvement emphasizes the importance of supportive care, diet, and quality of life for breast cancer survivors. However, we have limited data of non-Western breast cancer survivors. There is a need to examine the role of diet in breast cancer survival in both Western and non-Western regions.

Keywords Diet · Breast cancer incidence · Breast cancer survival · Cohort study · Intervention study

29.1 Introduction

The incidence of breast cancer has dramatically increased in recent years in several Asian countries, where there has been rapid economic growth and demographic and environmental changes. In Korea, the incidence of breast cancer is the highest in women in 2016. The age-standardized incidence rate of breast cancer has steadily increased, reaching 54.9 per 100,000 in 2016 with an average annual increase of 7.8% from 1999 to 2016 [1]. However, the incidence rate in Korea remains still lower than that of Western countries. The age-standardized incidence rates of breast cancer (per 100,000) were 105.0 in Denmark, 95.0 in U.K., 92.9 in the US, and 86.0 in Australia in 2012 [2]. This large international variation in incidence, with incidence lower in developing countries than in Western countries, and the rapid upward trend in parts of Asia may suggest the important roles of dietary factors in breast cancer development.

The association between dietary factors and breast cancer risk has long been studied in epidemiologic research. Accumulating evidence suggests that maintaining healthy body weight and abstaining from alcohol can help to prevent breast cancer [3]. However, there is limited evidence regarding the association of diet in adulthood, including intake of fruit and vegetables, dairy products, and micronutrients. Future research should examine the role of soy products, vitamin D, diet during childhood and adolescence, and the interaction of diet with genetic and microbiological effects. In particular, dietary exposure in early life is of great interest.

Early detection, treatment improvement, and social support have contributed to improvement of breast cancer outcomes. The global comparison of population-based cancer survival (CONCORD)-2 study showed that five-year survival from breast cancer has increased steadily in most developed countries and the age-standardized 5-year survival from breast cancer was 80% or higher in 34 countries in women diagnosed between 2005–2009, including Korea [4]. Survival statistics based on the Korea Central Cancer Registry data linked to mortality data from Ministry of the Interior and Safety reported that five-year survival rate for Korean breast cancer patients has improved from 78.0% in 1993–1995 to 92.7% in 2012–2016 [1]. Global survival improvements emphasize the importance of supportive care, diet, and quality of life for breast cancer survivors. However, although evidence that maintaining a healthy weight and engaging in regular physical activity improved breast cancer prognosis, the association between diet after breast cancer diagnosis and survival or recurrence of breast cancer is less clear.

29.2 Diet before Breast Cancer and Breast Cancer Risk

29.2.1 Fat Intake

Ecologic studies suggested that dietary fat was associated with an increased risk of breast cancer, and several case-control studies supported this hypothesis [5]. However, total fat intake did not appear to prevent breast cancer in several prospective cohort studies [6], which are less prone to recall bias and selection bias than case-control studies. In a pooled analysis of seven prospective cohort studies, including 4980 cases from studies involving 337,819 women, RR (95% CI) for comparing the highest and the lowest quintiles was 1.05 (0.94–1.16) [6]. When different latencies between total fat intake and occurrence of breast cancer (0–4, 4–8, 8–12, 12–16, and 16–20 years) were taken into account, there was still no association between total fat intake and breast cancer in a cohort study [7]. The Women's Health Initiative Dietary Modification Trial found that reducing dietary fat did not reduce the risk of breast cancer in 48,835 postmenopausal women, randomly assigned to the dietary modification intervention group ($n = 19{,}541$) or the comparison group ($n = 29{,}294$) [8].

Regarding types of fat, the Pooling Project, an international consortium of prospective cohort studies, reported a weak positive association between saturated fat and breast cancer risk (RR = 1.09; 1.00–1.19 for 5% energy increment from saturated fat), but no such association for monounsaturated or polyunsaturated fat intake [9]. When investigators in the Nurses' Health Study analyzed diet only during premenopausal period, animal fat intake was associated with increasing risk of breast cancer (RR = 1.33 for the highest vs. the lowest quintiles), but vegetable fat intake was not [10].

In summary, considerable evidence supports that fat intake in middle life does not increase the risk of breast cancer, but fat from animal sources in early adulthood may be associated with breast cancer risk. The important effects of diet in early adulthood warrant further research.

29.2.2 Fruits and Vegetables

Prospective cohort studies indicate that total fruit and total vegetable intake in adulthood do not appear to prevent breast cancer [11, 12]. However, a recent cohort study found that this association might vary by type of breast cancer. A pooled analysis of 20 cohort studies including 993,466 women followed for 11 to 20 years found an inverse association between total fruit and vegetable intake and risk of ER− breast cancer, but there was no association with risk of breast cancer overall or estrogen receptor (ER) + tumors [13]; RRs (95% CIs) for the highest vs. the lowest quintiles of total vegetable intake were 0.82 (0.74–0.90) for ER− breast cancer and 1.04 (0.97–1.11) for ER+ breast cancer. In the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort, including 10,197 incident invasive breast cancers with a median follow-up of 11.5 years, total vegetable intake had a stronger association with a lower risk of ER− progesterone receptor (PR)-breast cancer (RR = 0.74; 95% CI = 0.57–0.96 for the highest vs. the lowest quintiles) than ER +PR+ breast cancer [14].

29.2.3 Carbohydrate and Carbohydrate Quality

The hypothesis that cancer arises partly through insulin and the insulin-like growth factor axis has inspired research on the associations of carbohydrate and carbohydrate quality, as measured by glycemic index and glycemic load, with breast cancer risk. Although individual cohort studies have reported contradictory findings, a recent meta-analysis suggested a potential link of carbohydrate intake and glycemic load with ER-breast cancer [15]. As part of the World Cancer Research Fund/American Institute for Cancer Research Continuous Update Project, Schlesinger S et al. conducted a systematic review and meta-analysis and found that glycemic load and carbohydrate intake were positively associated with breast cancer in postmenopausal women with ER− tumors; summary RRs (95% CIs) were 1.28 (1.08–1.52) for per 50 units/day of glycemic load and 1.13 (1.02–1.25) for per 50 g/day of carbohydrate intake [15].

29.2.4 Soy Product

Soy products have potential anti- and pro-estrogenic effects due to isoflavones, the major flavonoids of soy products. Isoflavones have been suggested to stimulate tumor growth [16, 17] because of their structural similarity to estrogen and high affinity for the estrogen receptor [18]. In vitro and in vivo studies suggested that isoflavones might exert anti-estrogenic effects on breast tissue by competing with the estrogen receptor, therefore blocking the action of endogenous estrogens, or other mechanisms including antioxidative potency [19] or inhibition of angiogenesis [20] or inhibition of tyrosine kinase [21]. Several cohort studies examined whether isoflavones were associated with breast cancer risk; however, the results were not consistent [22–24]. A recent report from the World Cancer Research Fund concluded that there is limited evidence to support the benefit or harm of soy products for breast cancer prevention [3].

29.2.5 Dietary Patterns

Dietary patterns have been attractive for both researchers and public because it deals with the effects of diet as a whole rather the effects of individual nutrients or foods. People often want to hear how to eat overall to improve their health, and dietary pattern analysis identifies overall diets that lower the risk of poor health outcomes [25]. The US Nurses' Health Study observed no significant association for either Prudent or Western dietary patterns in relation to overall breast cancer risk. However, when investigators categorized breast cancers into ER− and ER+ breast cancers, they found an inverse association between the Prudent dietary pattern and ER− breast cancer risk [26]. Likewise, a priori dietary quality indices (Alternate Healthy Eating Index, Recommended Food Score, and the alternate Mediterranean Diet Score) were inversely associated with ER− breast cancer risk; RRs for the highest vs. the lowest quintiles ranged from 0.69 to 0.79 for these indices with a statistically significant trend [27]. The PREDIMED study, a randomized, single-blind, controlled trial conducted in Spain, found that a Mediterranean diet lowered primary breast cancer risk [28]. The association between dietary patterns and breast cancer incidence remains to be explored in terms of the effect modification by other health-related behaviors, histological types, genetic and metabolic profiles.

29.2.6 Micronutrients

Dietary calcium has been suggested to prevent breast cancer as intake of dairy products showed an inverse association with breast cancer [29]. Also, dietary intake and circulating levels of vitamin D, which is often added to dairy products in the US, were associated with a lower risk of breast cancer in some observational studies [30–32], but not in others [33, 34]. The World Cancer Research Fund suggested that diets high in calcium may be inversely associated with the risk of premenopausal breast cancer, but there is limited evidence to draw conclusions about vitamin D [3]. In the Women's Health Initiative trial, calcium and vitamin D supplementation did not reduce breast cancer incidence among postmenopausal women [35].

Carotenoids, known for their antioxidant properties, are abundant in fruits and vegetables. Many observational studies have examined the role of carotenoids in cancer prevention. A pooled analysis of 18 prospective cohort studies found that inverse associations for α-carotene, β-carotene, and lutein/zeaxanthin intakes were limited to ER− breast cancer, whereas no associations were noted for ER+ breast cancer risk [36]. In a pooled analysis of prospective data, circulating levels of carotenoids were inversely associated with overall breast cancer risk and inverse associations were more apparent for ER− breast cancer than ER+ breast cancer for α-carotene and β-carotene [37]. Similarly, the European Prospective Investigation into Cancer and Nutrition cohort showed that higher concentrations of plasma β-carotene and α-carotene were associated with a lower risk of ER− breast cancer

[38]. Other antioxidant nutrients, including vitamins C and E and selenium, did not show consistent results in prospective cohort studies [3].

29.2.7 Diet in Early Life

In the 1980s, Willett [39] and DeWaard and Trichopoulos [40] proposed a relationship between breast cancer risk with an energy-rich diet during puberty and adolescence. Taller height, which reflects childhood nutrition, is an independent risk factor for breast cancer [41]. The potential plausible explanation is that early life around the time of mammary gland development may be a critical period in breast cancer development. A prospective cohort study in Denmark found that high stature at 14 years of age and peak growth at an early age were associated with the risk of breast cancer [42], suggesting that growth during adolescence is an important factor for breast cancer.

Limited prospective cohort studies have reported a potential link between diet in early life and breast cancer risk. Red meat intake in adolescence was significantly associated with a higher premenopausal breast cancer risk (RR = 1.43; 95%CI, 1.05–1.94 for the highest vs. the lowest quintiles), but not with postmenopausal breast cancer risk [43]. Total fruit intake [44] and dietary fiber intake [45] in adolescence lowered the risk of breast cancer. Whole-grain intake during adolescent and early adulthood was inversely associated with premenopausal breast cancer risk (RR = 0.74; 95% CI 0.56–0.99 for the highest vs. the lowest quintiles), but not with overall or postmenopausal breast cancer risk [46]. A comparison of the findings on dietary factors in adolescence and adulthood in relation to breast cancer incidence in the Nurses' Health Study I and II is presented in Table 29.1.

29.3 Diet after Breast Cancer and Breast Cancer Survival

Several prospective cohort and intervention studies have investigated the role of diet in breast cancer prognosis (Table 29.2). Although evidence regarding diet and breast cancer survival has been accumulating, the data are mainly from studies of Western populations. Few Asian studies have explored the association between diet and breast cancer survival.

29.3.1 Dietary Patterns

Recent prospective cohort studies reported that dietary patterns are an important component in addressing a healthy diet for breast cancer survivors (Table 29.3). Relatively consistent findings showed that healthy dietary patterns lowered the risk

Table 29.1 Comparison of the results; dietary factors during adolescence and during adulthood in relation to breast cancer incidence in the Nurses' Health Study I and II

Dietary factors	Study Characteristics	Dietary intake during mid-life or later adulthood	Dietary intake during adolescence
Meat	First author	Holmes MD [47]	Farvid MS [43]
	No. of participants	88,647 women	44,231 premenopausal women
	No. of breast cancer cases	4107 cases	1132 cases
	Follow-up period	1980–1998	1998–2011
	Results	• RR (95% CI) for the highest vs. the lowest quintile of red meat intake = 0.94 (0.84–1.05)	• RR (95% CI) for the highest vs. the lowest of red meat intake = 1.43 (1.05–1.94) for premenopausal breast cancer • RR (95%CI) for replacement of one serving/day of total red meat with one serving of combination of poultry, fish, legumes, and nuts = 0.85 (0.74–0.96) for overall breast cancer and 0.77 (0.64–0.92) for premenopausal breast cancer
Fruit and vegetable	First author	Smith-Warner SA [11]	Farvid MS [44]
	No. of participants	89,046 women in the NHS I (a) and 68,817 women in the NHS I (b)	44,223 premenopausal women
	No. of breast cancer cases	1023 cases in the NHS I (a) and 1638 cases in the NHS I (b)	1347 cases
	Follow-up period	1980–1986 in the NHS I (a) and 1986–1996 in the NHS I (b)	1998–2013
	Results	• RR (95% CI) for 100 g/day intake increment of total fruits = 0.98 (0.95–1.02) NHS I (a) and 0.98 (0.95–1.01) NHS I (b) • RR (95% CI) for 100 g/day intake increment of total vegetables = 1.01 (0.95–1.07) NHS I (a) and 1.01 (0.98–1.05) NHS I (b)	• RR (95% CI) for the highest vs. the lowest of total fruit intake = 0.75 (0.62–0.90). • RR (95% CI) for the highest vs. the lowest of total vegetable intake = 0.85 (0.71–1.01)
Dietary fiber	First author	Holmes MD [48]	Farvid MS [45]
	No. of participants	88,678 women	44,263 premenopausal women
	No. of breast cancer cases	4092 cases	1118 cases
	Follow-up period	1980–1998	1998–2011

(continued)

Table 29.1 (continued)

Dietary factors	Study Characteristics	Dietary intake during mid-life or later adulthood	Dietary intake during adolescence
	Results	• RR (95% CI) for the highest vs. the lowest quintile of total fiber intake = 0.98 (95% CI: 0.87, 1.11)	• RR (95% CI) for the highest vs. the lowest quintile of total fiber intake = 0.84 (0.70–1.01)

Investigators divided Nurses' Health Study (NHS) I into two studies; NHS I (a) and NHS I (b)

of non-breast cancer deaths in observational studies of breast cancer survivors. The US Nurses' Health Study (NHS), a large cohort study of female nurses from 11 US states, found that adherence to healthy dietary guidelines, the Dietary Approaches to Stop Hypertension (DASH) and the Alternative Healthy Eating Index (AHEI)-2010, after breast cancer diagnosis was associated with reduced risk of non-breast cancer mortality in women with breast cancer, but not with the risk of breast cancer death or recurrence [52]. Similarly, other cohort studies found a lower risk of death from non-breast cancer causes with healthy dietary pattern [58, 61, 62]. Inflammatory potential of diet after breast cancer diagnosis was associated with mortality from cardiovascular disease, but not with breast cancer-specific mortality or all-cause mortality among women diagnosed with invasive breast cancer in the Women's Health Initiative (WHI) [67]; compared to high inflammatory diet, low inflammatory diet (low vs. high quartile) had a 56% lower risk of cardiovascular disease mortality among breast cancer survivors.

29.3.2 Soy Products

A recent pooled analysis of three cohort studies (Life After Cancer Epidemiology, Shanghai Breast Cancer Survival Study, and Women's Healthy Eating and Living) suggested a potential benefit of consuming soy products for breast cancer survival; hazard ratio (HR)s (95% CIs) for comparing $\geq$10 mg/day of isoflavones vs. <4 mg/day were 0.87 (0.70–1.10) for all-cause mortality, 0.83 (0.64–1.07) for breast cancer-specific mortality, and 0.75 (0.61–0.92) for breast cancer recurrence [68]. In that study, the inverse association was slightly stronger among women with ER$-$ breast cancer. When stratified by tamoxifen use, although the test for interaction was not statistically significant, an inverse association between isoflavone intake and breast cancer recurrence was stronger for tamoxifen users than non-users. The Breast Cancer Family Registry, containing 6235 women with breast cancer enrolled, found that post-diagnostic isoflavone intake reduced the risk of all-cause deaths [69]. Two Chinese cohort studies of breast cancer survivors in which investigators examined a larger contrast of soy product intake compared to Western studies observed an inverse association of isoflavone intake with breast

Table 29.2 Intervention and prospective cohort studies regarding post-diagnostic diet and breast cancer survival

Intervention study				
Study name	*Location*	*Design article or example article*	*Baseline number of breast cancer survivors*	*Intervention*
Women's Intervention Nutrition Study (WINS)	US	Chlebowski RT et al. [49]	2437	Reduction in fat intake
Women's Healthy Eating and Living (WHEL)	US	Pierce JP et al. [50]	3088	Increase in vegetable, fruit, and fiber intake and a decrease in dietary fat intake
Prospective cohort study				
Study name	*Location*	*Design article or example article*	*Baseline number of breast cancer survivors*	*Method and timing of dietary assessment*
DietCompLyf	UK	Swann R et al. [51]	3159	FFQ at baseline for pre and post-diagnosis FFQs at 1-year, 1.5-year, and every year up to 6-year post-diagnosis
Nurses' Health Study (NHS)	US	Izano MA et al. [52]	More than 2000 (increasing across time because new cases occur during follow-up)	FFQs at various time points before and after diagnosis
Health, Eating, Activity, and Lifestyle (HEAL)	US	Belle FN et al. [53]	1183	FFQ at 24 months after diagnosis
Shanghai Breast Cancer Survival Study (SBCSS)	China	Shu XO et al. [54]	5042	FFQs at 6-, 18-, 36-, and 60-month post-diagnosis
Women's Healthy Eating and Living (WHEL)	US	Caan BJ et al. [55]	3088	FFQ at baseline post-diagnosis
Life After Cancer Epidemiology Study (LACE)	US	Caan B et al. [56]	2321	FFQs at baseline post-diagnosis
Collaborative Women's Longevity Study (CWLS)	US	Beasley JM et al. [57]	5791	FFQ (42% of women completed within 5 years of diagnosis of breast cancer; range: 1–16 years)
Women's Health Initiative	US	George SM et al. [58]	More than 2000 (increasing across time because new cases occur during follow-up)	FFQs administered, on average, 1.5 years after diagnosis

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Table 29.2 (continued)

The Pathways Study	US	Kwan ML et al. [59]	1539	FFQs at baseline, 6 and 24 months after baseline
After Breast Cancer Pooling Project[a]	US and China	Nechuta SJ et al. [60]	More than 18,000 (increasing across time because new cases occur during follow-up)	FFQs after diagnosis
American Cancer Society's Cancer Prevention Study-II (CPS-II) Nutrition Cohort	US	McCullough ML et al. [61]	2152	FFQs after diagnosis

[a]After Breast Cancer Pooling Project is a collaborative work of SBCSS, LACE, WHEL, and NHS

cancers-specific mortality [70] or with breast cancer recurrence among postmenopausal patients [71]. A summary of the results is presented in Table 29.4.

29.3.3 Fruits and Vegetables and their Components

Total fruit and vegetable intake was not associated with breast cancer survival in observational [57, 61, 72] and intervention studies [73]. A recent meta-analysis of nine cohort studies and one randomized trial reported no associations between pre- or post-diagnostic intake of vegetables and fruits and overall survival among breast cancer survivors; HRs (95% CIs) of overall survival comparing the highest vs. the lowest categories were 1.01 (0.72–1.42) for vegetables and fruits combined, 0.96 (0.83–1.12) for vegetables alone, and 0.99 (0.89–1.11) for fruit alone [74]. In a randomized controlled trial of the Women's Healthy Eating and Living Study, an intervention that promoted a diet high in vegetables, fruits, and fiber and low in fat did not improve breast cancer prognosis [50]. Also, the After Breast Cancer Pooling Project did not support any association between cruciferous vegetable intake after diagnosis and breast cancer prognosis [75].

Although the evidence does not suggest benefit of overall fruit and vegetable intake for breast cancer prognosis, the results regarding components abundant in fruits and vegetables are mixed. The Women's Healthy Eating and Living (WHEL) study found that plasma levels of total carotenoids, measured from blood samples during the baseline visit, were inversely associated with breast cancer recurrence among women with a history of early-stage breast cancer [73]; HR (95% CI) was 0.57 (0.37–0.89) for the highest vs. the lowest quartiles of plasma total carotenoid levels. However, intakes of carotenoids were not associated with breast cancer prognosis in other observational studies [57, 72].

The association between dietary fiber intake and breast cancer survival was examined in several cohort studies of breast cancer survivors. These studies reported

Table 29.3 The association between dietary patterns and breast cancer survival

Authors, year	Study name	Location	Baseline number of women with breast cancer	Follow-up period	Results
Kwan ML et al. [62]	LACE	US	1901	Median follow-up of 3.17 years	Healthy dietary pattern was associated with improved overall survival and non-breast cancer survival
Kroenke CH et al. [63]	NHS	US	2619	Median follow-up of 9 years	A higher intake of the prudent pattern and a lower intake of the Western pattern were associated with lower risk of death from causes other than breast cancer
Izano MA et al. [52]	NHS	US	4103	Median follow-up of 112 months	Healthy dietary choices after breast cancer were associated with reduced risk of non-breast cancer mortality
Kim EH et al. [64]	NHS	US	2729	1978–1998 to 2004	A higher alternate Mediterranean Diet Score was associated with a lower risk of non-breast cancer death in women with low physical activity
George SM et al. [65]	HEAL	US	670	6 years	Women consuming better quality diets, as defined by higher Healthy Eating Index-2005 scores, had a reduced risk of death from any cause and a reduced risk of death from breast cancer
George SM et al. [58]	WHI	US	2317	Median follow-up of 9.6 years	Better quality diet had a lower risk of death from any cause and death from non-breast cancer causes
Vrieling A et al. [66][a]	N/A	Germany	2522	Median of 5.5 years	Increasing consumption of an unhealthy dietary pattern was associated with an increased risk of non-breast cancer mortality
McCullough ML et al. [61]	CPS-II nutrition	US	2152	Mean of 3.3 years	Diets consistent with guidelines for cancer prevention were associated with non-breast cancer mortality

Study abbreviations: *LACE* Life After Cancer Epidemiology Study, *HEAL* Health, Eating, Activity, and Lifestyle, *NHS* Nurses' Health Study; and *CPS-II Nutrition* American Cancer Society's Cancer Prevention Study-II Nutrition Cohort

[a]A follow-up of cases from a case-control study

no statistically significant association with overall survival [53, 57] or with breast cancer-specific survival [76], and a statistically significant inverse association with overall survival [72, 77] or with recurrence among women with late stage breast cancer [78].

29.3.4 Fats

The possible link between total fat intake and breast cancer survival has long been the focus of attention. However, the evidence remains inconclusive [79]. For types of fat, several cohort studies examining the associations between intakes of saturated fat, unsaturated fat, and trans-fat and breast cancer-specific and overall mortality among breast cancer survivors had inconsistent findings. The Collaborative Women's Longevity Study reported an increased risk of overall mortality with increasing intakes of saturated fat and trans-fat, but no association for mono- or polyunsaturated fat intake [57]. Other studies have reported no statistically significant associations [72, 76] or increased risk of all-cause mortality for increasing saturated fat intake [77, 80], A U-shaped association has been reported for the polyunsaturated to saturated ratio [81]. Marine fatty acids from food were associated with a reduced risk of recurrences and deaths in the in the Women's Healthy Eating and Living (WHEL) Study. Women with higher intakes of EPA and DHA from food had a 28% lower risk of breast cancer recurrence (HR comparing top vs. bottom tertiles = 0.72 (95% CI = 0.57–0.90)) and 41% lower risk of all-cause mortality (HR comparing top vs. bottom tertiles = 0.59 (95% CI = 0.43–0.82) [82]. Further research is warranted on omega-3 fatty acids.

29.3.5 Vitamin D

Vitamin D has been hypothesized to decrease cancer risk from ecologic [83] and observational studies [84] because of its anti-carcinogenic properties, including inhibition of angiogenesis and proliferation and promotion of differentiation and apoptosis. Goodwin PJ et al. reported that breast cancer survivors with low prognostic levels of 25-hydroxyvitamin D (<50 nmol/L), a good indicator of vitamin D status, had 1.71 times higher risk of distant recurrence and 1.60 times higher risk of death compared to those with sufficient levels (≥72 nmol/L) [85]. A meta-analysis involving five studies of 4413 women with breast cancer reported that pooled hazard ratios (95% confidence intervals) comparing the highest with lowest categories were 0.62 (0.49–0.78) for all-cause mortality and 0.58 (0.38–0.84) for breast cancer-specific mortality [86].

Table 29.4 Prospective cohort studies regarding the association between isoflavones or soy products and breast cancer survival

Authors, year	Study name	Location	Ethnicity	Baseline number of women with breast cancer	Follow-up period	No. of endpoints	Results (HR and 95% CI)
Shu XO et al. [54]	Shanghai Breast Cancer Survival Study (SBCSS)	China	Asian	5042	2002–2009 (median follow-up of 3.9 years)	444 deaths 534 recurrence or breast cancer-related death	Soy food intake All-cause deaths: 0.71 (95% CI, 0.54–0.92) for $\geq$15.31 g/day vs. $\leq$5.31 g/day Recurrence/breast cancer-specific deaths: 0.68 (95% CI, 0.54–0.87) for $\geq$15.31 g/day vs. $\leq$5.31 g/day Isoflavones All-cause deaths: 0.79 (95% CI, 0.61–1.03) for $\geq$62.68 mg/day vs. $\leq$20.00 mg/day Recurrence/breast cancer-specific deaths: 0.77 (95% CI, 0.60–0.98) for $\geq$62.68 mg/day vs. $\leq$20.00 mg/day
Nechuta SJ et al. [68]	After Breast Cancer Pooling Project	US and China	White, Black, Asian, Hispanic, and other	9514	Mean follow-up of 7.4 years	1171 total deaths 881 breast cancer-specific deaths 1348 recurrences	Isoflavones All-cause deaths: 0.87 (95% CI, 0.70–1.10) for $\geq$10 mg/day vs. <4 mg/day Breast cancer-specific deaths: 0.83 (95% CI, 0.64–1.07) for $\geq$10 mg/day vs. <4 mg/day Recurrence: 0.75 (95% CI, 0.61–0.92) for $\geq$10 mg/day vs. <4 mg/day

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Table 29.4 (continued)

Authors, year	Study name	Location	Ethnicity	Baseline number of women with breast cancer	Follow-up period	No. of endpoints	Results (HR and 95% CI)
Zhang YF et al. [70]	N/A	China	Asian	616	2004–2006 to 2011	79 breast cancer-specific deaths	Isoflavones Breast cancer-specific deaths: 0.62 (95% CI, 0.42–0.90) for >28.83 mg/day vs. <7.56 mg/day Soy protein Breast cancer-specific deaths: 0.71 (95% CI, 0.52–0.98) for >13.03 mg/day vs. <2.12 mg/day
Kang X et al. [71]	N/A	China	Asian	524	2002–2003 to 2008	154 overall deaths 185 recurrence	Isoflavones Among premenopausal patients ($n = 248$) All-cause mortality: 1.05 (95% CI, 0.78–1.71) for >42.3 mg/day vs. <15.2 mg/day Recurrence: 0.88 (95% CI, 0.61–1.23) for >42.3 mg/day vs. <15.2 mg/day Among postmenopausal patients ($n = 276$) All-cause mortality: 0.88 (95% CI, 0.56–1.24) for >42.3 mg/day vs. <15.2 mg/day Recurrence: 0.67 (95% CI, 0.54–0.85) for >42.3 mg/day vs. < 15.2 mg/day

Zhang FF et al. [69]	The Breast Cancer Family Registry	US	White 58.5% Hispanics 16.6% Blacks 12% Asians 11.1% other 1.8%	6235	Median of 9.4 years	1224 deaths	Pre-diagnostic total isoflavones ($n = 4769$) All-cause mortality: 0.84 (0.66–1.06) for ≥1.494 mg/day vs. <0.342 mg/day Post-diagnostic total isoflavones ($n = 1466$) All-cause mortality: 0.65 (0.41–1.00) for ≥1.494 mg/day vs. <0.342 mg/day

After Breast Cancer Pooling Project included data from 2 US cohorts (WHEL and LACE) and 1 Chinese cohort (SBCSS)
N/A not applicable

29.3.6 Dietary Supplement

Cancer survivors tended to use dietary supplements more than general populations, and the prevalence of dietary supplement use was relatively higher in breast cancer survivors than survivors of cancer in other sites [87, 88]. The American Cancer Society guidelines suggests that taking a dietary supplement should be considered only when there is a nutrient deficiency and cancer survivors need to obtain nutrients mainly from dietary sources [89]. Evidence for dietary supplements improving prognosis after a cancer diagnosis is lacking. For example, the After Breast Cancer Pooling Project suggested a better prognosis with vitamins C and E, but an attenuated association of vitamins C and E with recurrence after mutual adjustment [90].

29.4 Research in Asia

Breast cancer in Asian individuals has a different profile than breast cancer in Western individuals. For example, the incidence of newly diagnosed breast cancer was the highest among women aged 40–49 years and the median age at diagnosis was 50 years in Korea, which is younger than Western women [91]. Given that Asian women have different patterns of breast cancer compared to Western women and breast cancer incidence is predicted to continue to increase in Asian regions, it is important to identify a healthy diet after diagnosis that is customized to Asian women.

However, evidence on the effect of diet on breast cancer survival in Asia is limited. The Shanghai Breast Cancer Survival Study [54] and a few Chinese [70, 71] and Japanese hospital-based study [92] have examined the relationship between dietary factors and breast cancer prognosis among breast cancer survivors. Soy products and isoflavones are of particular interest in Asian studies because these foods are widely consumed in Asia. This research has contributed to the understanding of the roles of soy products and isoflavones in breast cancer prognosis [54, 70, 71]. A few cross-sectional studies or small scale intervention studies reported on diet and quality of life among breast cancer survivors in Korea [93–95]. However, these studies warrant further prospective cohort and large-scale intervention studies to provide evidence on how Korean diet and dietary behaviors affect breast cancer survival.

29.5 Future Research Direction

Breast cancer is a major and emerging health problem in both developed and developing countries. The high incidence and prevalence of breast cancer and improved cancer treatment require a better understanding of breast cancer risk factors and lifestyle management for breast cancer survivors. Given that a few, limited cohort studies suggest that diet in early life may play a critical role in breast cancer development, further long-term follow-up studies are needed. The effects of pre- and post-diagnostic diet on quality of life, recurrence, and mortality among breast cancer survivors need to be characterized. In particular, little is known about dietary guidelines for Asian breast cancer survivors, who have different diagnostic, genetic, and anthropometric profiles from Western women. Survival strategies for breast cancer survivors may differ by genetic profiles and treatment type, but data on interaction factors are sparse. In conclusion, identifying the role of diet in breast cancer prevention and prognosis and its interaction with clinical and genetic factors remain important as the global burden of breast cancer is increasing.

29.6 Summary

The global burden of breast cancer is increasing and it is a major and emerging health problem in both developed and developing countries. Therefore, identifying the role of diet in breast cancer prevention and prognosis and its interaction with clinical and genetic factors are of great importance.

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