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Lead Article

Breast cancer and dietary patterns: a systematic review

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This systematic review collates research on the topic of dietary patterns and breast cancer risks. The literature search targeted epidemiological studies published up to December 2012 and was conducted using the Medline (U.S. National Library of Medicine, Bethesda MD, USA) and Lilacs (Latin American and Caribbean Health Sciences, São Paulo, Brazil) databases. The following search terms were used: breast cancer, breast neoplasm, breast carcinoma, diet, food, eating habits, dietary patterns, factor analysis, and principal component analysis. Only studies that used factor analysis techniques and/or principal component analysis were eligible, and a total of 26 studies were included. The findings of these studies suggest the Mediterranean dietary pattern and diets composed largely of vegetables, fruit, fish, and soy are associated with a decreased risk of breast cancer. There was no evidence of an association between traditional dietary patterns and risk of breast cancer, and only one study showed a significant increase in risk associated with the Western dietary pattern. Diets that include alcoholic beverages may be associated with increased risk.

INTRODUCTION

Worldwide, breast cancer is the most frequently diagnosed cancer and the leading cause of cancer deaths in women.[1] The etiology of breast cancer is multifactorial, and includes interactions between genetic and behavioral factors as well as environmental exposure. Well-established risk factors for breast cancer, which include age, family and reproductive history, obesity in the post-menopausal phase, height reached at adult age, and exposure to high doses of ionizing radiation, are mostly difficult to modify.[2,3] Diet stands out among the modifiable risk factors[4] and has thus been investigated in numerous studies,[5–8] mostly with a focus on specific nutrients or components. However, food and nutrients are not consumed in isolation and, from an epidemiological point of view, form a complex web of correlated influences. Therefore, researchers have recently sought to study dietary patterns,[9,10] which simultaneously reflect these exposures. The objective of these studies is to reduce a large amount of original data (items and food groups) in order to build synthetic indices (factors) that might reflect the dietary behaviors of individuals.[9] Strongly correlated variables are grouped to each factor. The food items contained in the instruments used to assess food intake are grouped according to the degree of correlation among them. A factor score for each factor is estimated and can be used in any correlation or regression analysis of the relationships among dietary patterns and the various issues of interest.[9,11,12]

The global consensus on food, nutrition, physical activity, and the prevention of cancer published in 2007[3] considered that the evidence for a relationship between dietary patterns and the risk of breast cancer was inconclusive. In recent years, two systematic reviews[13,14] including 19 and 16 articles evaluated the evidence for this

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relationship. However, additional research has been published since then, indicating a need exists for an updated review. The objective of the present systematic review was to critically evaluate the currently available literature in order to collate the existing research on this subject.

METHODS

Epidemiological studies of dietary patterns and breast cancer risk were selected from the Medline (U.S. National Library of Medicine, Bethesda, MD, USA) and Lilacs (Latin American and Caribbean Health Sciences, São Paulo, Brazil) databases using the following combinations of search terms: breast cancer and diet, breast neoplasm and diet, breast carcinoma and diet, breast cancer and food, breast neoplasm and food, breast carcinoma and food, eating habits and breast cancer, eating habits and breast neoplasm, eating habits and breast carcinoma, dietary patterns and breast cancer, dietary patterns and breast neoplasm, dietary patterns and breast carcinoma, breast cancer, diet and factor analysis and breast cancer, diet and principal component analysis. The search was restricted to female breast cancer studies in humans that were published up to December 2012. The titles and abstracts of the located documents were initially reviewed and the reference lists of selected papers were searched to identify additional articles. Only studies that assessed dietary patterns through factor analysis techniques and/or principal components analysis and that reported risk estimates of breast cancer (odds ratio [OR] or relative risk [RR]) with a 95% confidence interval (CI) or standard error were included. Studies that evaluated both pre- and postmenopausal women with all primary breast cancer subtypes were also included. Literature reviews, experimental studies, and reports of survival and tumor recurrence and/or metastasis were excluded from this systematic review (Figure 1). The literature search, selection of studies, and data extraction were performed by two researchers (RCRA and DMLM). The protocol used was created in accordance with the PRISMA Statement.[15] The quality of the studies was evaluated according to the STROBE[16] recommendations, with the following factors being assessed: participant selection criteria, clarity in the definition of variables and measurements of exposure and effect, strategies for confounding controls, descriptions of statistical methods, and discussions of possible limitations.

Information about each study's location and design, sample size and characteristics, methods employed in the evaluation of food consumption, the period of evaluation, the nomenclature of the dietary patterns, and the main findings were extracted (Table 1). The dietary patterns were named according to the similarities in factor loadings of the constituent foods, regardless of the original nomenclature used in the revised studies. Food items with a factor loading rotated of ≥|0.30| in the correlation matrix were considered to be significant contributors to the dietary pattern composition. Table 2 describes all of the evaluated dietary patterns and their food-item components. Since there were methodological differences among the studies, such as the questionnaires used, the food items evaluated, the cut-off points defined for consumption categorization (tertiles and quartiles), and the variables used for confounding controls, and these could affect the evaluated relationships,[17,18] a summary measure was not calculated.

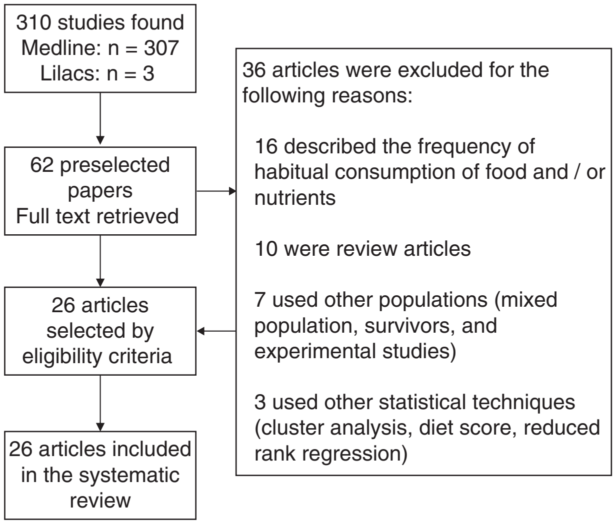

Figure 1 **Flow chart of the search and selection process for articles included in the systematic review.**

RESULTS

The initial search identified 310 articles, of which 62 were considered eligible for further evaluation. Of these, 36 were excluded because they did not fulfill the inclusion criteria (Figure 1); therefore, a total of 26 articles published between 2001 and 2012 (11 cohort studies and 15 case-control studies) were selected.[19–44] These 26 studies were conducted in Europe ($n = 8$), North America ($n = 7$), Asia ($n = 5$), South America ($n = 4$), Africa ($n = 1$), and Oceania ($n = 1$). In total, the studies included 584,437 women and there were 28,962 incident cases of breast cancer (Table 1).

The food frequency questionnaire was the most common dietary assessment tool used in the studies ($n = 24$), while the dietary history questionnaire was used in two studies. The number of food items in various versions of the food frequency questionnaire varied from 30 to 985,[24,29] the period of evaluated diet exposure was

Table 1 **Characteristics of epidemiological studies investigating dietary patterns and breast cancer risk that utilized factor analysis techniques and/or principal component analysis.**

Reference	Location	Study design	Sample size and characteristics	Method and period of dietary evaluation	Information on validation and reproducibility	Method of analysis	Dietary patterns investigated and associated risk[a]	Variables for adjustment (multivariate analysis)
Terry et al. (2001)[19]	Sweden	Cohort	61,463 women (1,328 cases)	FFQ (67 food items); 6 previous months	No information	PCA	Western: RR 0.98 (95% CI 0.74–1.28) Healthy: RR 0.91 (95% CI 0.72–1.16) Ethylic: RR 1.31 (95% CI 1.05–1.63)	Age, energy, BMI, schooling, family history and mother's age at first childbirth
Sieri et al. (2004)[20]	Italy	Cohort	8,984 women (207 cases) stratified according to BMI	FFQ (107 food items); previous year	Validation and reproducibility	FA	Salad and vegetables: RR 0.66 (95% CI 0.47–0.94) Western: RR 0.90 (95% CI 0.58–1.41) Canteen: RR 0.95 (95% CI 0.63–1.45) Prudent: RR 1.28(95% CI 0.90–1.83)	Schooling, parity, weight, menarche age, smoking, energy, menopause status
Adebamowo et al. (2005)[21] Adebamowo et al. (2005)[21] Continuation	United States	Cohort	90,638 women (710 cases)	FFQ (133 food items in 1991 and 142 food items in 1995); previous year	Validation and reproducibility	PCA	Prudent: RR 0.90 (95% CI 0.68–1.18) Western: RR 0.97 (95% CI 0.71–1.33)	Menarche age, parity, age at first childbirth, family history, history of benign mammary illness, contraceptive use, alcohol consumption, energy, BMI, weight, smoking, physical activity, multivitamin use
Fung et al. (2005)[22]	United States	Cohort	71,058 women (3,026 cases) stratified according to hormonal receptor	FFQ (116 food items); previous year	Validation	PCA	Prudent: RR 0.62 (95% CI 0.45–0.88) Western: RR 1.18 (95% CI 0.77–1.82)	Age, smoking, BMI, multivitamin use, energy, physical activity, family history, personal history of benign mammary illness, age at menopause, hormonal replacement therapy, menarche age, parity and age at first childbirth
Männistö et al. (2005)[23]	Holland (NLCS)	Cohort	1,598 women (1,127 cases)	FFQ (150 food items); previous year	Validation	PCA	Vegetables: RR 0.90 (95% CI 0.67–1.2) Processed pork and potatoes: RR 0.69 (95% CI 0.52–0.92)	Age, BMI, weight, schooling, smoking, family history, menarche age, menopause age, age at first childbirth, contraceptive use, replacement therapy, alcohol, energy
	Italy (ORDET)	Cohort	10,788 women (212 cases)	FFQ (107 food items); previous year	Validation		Vegetables: RR 0.79 (95% CI 0.50–1.27) Processed pork and potatoes: RR 1.07 (95% CI 0.58–1.98)	
	Sweden (SMC)	Cohort	66,651 women (1,932 cases)	FFQ (67 food items); 6 previous months	Validation		Vegetables: RR 0.91 (95% CI 0.79–1.05) Processed pork and potatoes: RR 0.92 (95% CI 0.78–1.09)	
Nkondjock and Ghadirian. (2005)[24]	Canada	Hospital-based case-control	414 cases and 429 controls	FFQ (985 food items); 2 years before diagnosis for cases and corresponding period for controls	Validation and reproducibility	FA	Chocolate and cereals: OR 1.14 (95% CI 0.76–1.71) Processed pork: OR 0.85 (95% CI 0.54–1.34) Ethylic: OR 0.92 (95% CI 0.62–1.38)	Energy, family history, marital status, physical activity, smoking, BMI, age at first gestation to term, history of benign mammary illness, number of full-term gestations
Velie et al. (2005)[25]	United States	Cohort	40,559 women (1,868 cases) stratified according to menopause status and hormonal receptor	FFQ (61 food items); previous year	Validation and reproducibility	PCA	Vegetables, fish, fruit, and fowl: RR 1.03 (95% CI 0.88–1.20) Pork and potatoes: RR 1.03 (95% CI 0.89–1.20) Southern traditional: RR 0.89 (95% CI 0.76–1.05)	Age, energy, schooling, family history, BMI, weight, parity, age at first childbirth, menarche age, hormonal replacement, weekly vigorous physical activity, smoking and alcohol
Ronco et al. (2006)[26]	Uruguay	Hospital-based case-control	442 cases and 442 controls stratified according to menopause status	FFQ (64 food items); habitual diet	Reproducibility	PCA	Traditional: OR 0.77 (95% CI 0.64–0.93) Healthy: OR 0.84 (95% CI 0.73–0.98) Western: OR 2.03 (95% CI 1.11–3.72) Stewed: OR 0.71 (95% CI 0.47–1.06) Fatty: OR 2.72 (95% CI 1.16–6.37) Ethylic: OR 1.04 (95% CI 0.92–1.16)	Age, rural/urban residence, schooling, family history, menopause status, menarche age, parity and energy

Table 1 **Continued**

Reference	Location	Study design	Sample size and characteristics	Method and period of dietary evaluation	Information on validation and reproducibility	Method of analysis	Dietary patterns investigated and associated risk[a]	Variables for adjustment (multivariate analysis)
Sant et al. (2007)[27]	Italy	Cohort	8,861 women (238 cases with information about HER-2 expression)	FFQ (107 food items); previous year	Validation and reproducibility	FA	Salad and vegetables: HER-2 +: RR 0.25 (95% CI 0.10–0.64)/HER-2 -: RR 0.71 (95% CI 0.48–1.03) Western: HER-2 +: RR 0.75 (95% CI 0.27–2.08)/HER-2 -: RR 0.88 (95% CI 0.55–1.40) Canteen: HER-2 +: RR 1.39 (95% CI 0.50–3.84)/HER-2 -: RR 1.14 (95% CI 0.75–1.75) Prudent: HER-2 +: RR 0.72 (95% CI 0.35–1.48)/HER-2 -: RR 1.36 (95% CI 0.93–1.98)	Age, energy, schooling, parity, height, weight, menarche age, smoking and menopause status
Cui et al. (2007)[28]	Shanghai	Population-based case-control	1,446 cases and 1,549 controls stratified according to BMI, WHR, menopause status, and hormonal receptor	FFQ (76 food items); 5 years before diagnosis for cases and corresponding period for controls	Validation	PCA	Vegetables and soy: OR 1.0 (95% CI 0.8–1.2) Meat and sweets: OR 1.3 (95% CI 1.0–1.7)	Family history, personal history of fibroadenoma, number of childbirths and age at first childbirth, menopause status, age of menopause start, regular physical activity in last 10 years, BMI, WC, schooling
Hirose et al. (2007)[29]	Japan	Hospital-based case-control	1,885 cases and 22,333 controls stratified according to BMI	FFQ (13 dietary factors and 17 food items); previous year to diagnosis for cases and corresponding period for controls	No information	PCA	Prudent: OR 0.73 (95% CI 0.63–0.84) Fatty: OR 0.99 (95% CI 0.85–1.14) Japanese: OR 1.04 (95% CI 0.90–1.2) Salty: OR 1.04 (95% CI 0.90–1.19)	Age, BMI, menopause status, parity, age at first gestation to term, menarche age, smoking, alcohol, physical activity, family history
Marchioni et al. (2008)[30]	Brazil	Hospital-based case-control	89 cases and 94 controls	FFQ (68 food items); previous year to diagnosis for cases and corresponding period for controls	Validation	PCA	Factor 1: OR 7.28 (95% CI 2.06–25.66) Factor 2: OR 0.20 (95% CI 0.06–0.61)	Age, residence region, contraceptive use, menarche age, BMI, energy
Murtaugh et al. (2008)[31]	United States	Population-based case-control	2,281 cases and 2,465 controls stratified according to BMI and menopause status	Dietary history questionnaire; previous year to diagnosis for cases and corresponding period for controls	No information	FA	Western: OR 1.32 (95% CI 1.04–1.68) Prudent: OR 1.42 (95% CI 1.14–1.77) Native Mexican: OR 0.68 (95% CI 0.55–0.85) Mediterranean: OR 0.76 (95% CI 0.63–0.92)	Age, schooling, family history, smoking, physical activity, energy, dietary fiber, dietary calcium, weight, parity, recent hormonal exposure, BMI, interaction between BMI and recent hormonal exposure
Wu et al. (2009)[32]	United States	Population-based case-control	1,248 cases and 1,148 controls stratified according to menopause status and hormonal receptor	FFQ (174 food items); habitual diet	Validation	PCA	Western (meat/starches): RR 1.10 (95% CI 0.80–1.51) Ethnic (meat/starches): RR 1.41 (95% CI 1.05–1.89) Vegetables: RR 0.72 (95% CI 0.54–0.96)	Age, Asian ethnicity, schooling, date of birth, years living in USA, physical activity, parity, menarche age, type and age at menopause, BMI, WC, tea ingestion, and history of diabetes

Cottet et al. (2009)[33]	France	Cohort	65,374 women (2,381 cases) stratified according to hormonal receptor	Dietary history questionnaire (208 items); habitual diet	Validation and reproducibility	PCA	Alcohol: RR 1.20 (95% CI 1.03–1.38) Healthy: RR 0.85 (95% CI 0.75–0.95)	Age, schooling, BMI, weight, family history, menarche age, age of first childbirth to term combined with number of births, hormonal replacement, benign mammary illness, lobular carcinoma in situ, contraceptive use, breastfeeding duration, frequency of Papanicolau test as indicator of adherence to gynecological screening, physical activity, smoking, energy, use of phytosterol supplements, and use of vitamin and mineral supplements
Agurs-Collins et al. (2009)[34]	United States	Cohort	50,778 women (1,094 cases) stratified according to BMI	FFQ (68 items); previous year to diagnosis for cases and corresponding period for controls	No information	FA	Western: RR 1.06 (95% CI 0.81–1.37) Prudent: RR 0.86 (95% CI 0.68–1.08)	Age, BMI, alcohol, schooling, menarche age, parity and age at first childbirth, family history, physical activity, energy, menopause status, smoking, use of feminine hormone
De Stefani et al. (2009)[35]	Uruguay	Hospital-based case-control	461 cases and 2,532 controls	FFQ (64 items); habitual diet	Reproducibility	PCA	Prudent: OR 0.63 (95% CI 0.47–0.85) Traditional: OR 0.53 (95% CI 0.36–0.77) Western: OR 1.81 (95% CI 1.32–2.50) Ethylic: OR 1.40 (95% CI 1.05–1.87)	Age, place of residence, rural/urban, schooling, BMI, smoking, number of cigarettes/day, energy
Ronco et al. (2010)[36]	Uruguay	Hospital-based case-control	111 cases and 222 controls (only ductal carcinoma cases)	FFQ (120 items); 5 years before diagnosis for cases and corresponding period for controls	Reproducibility	PCA	Low fat: OR 0.30 (95% CI 0.16–0.60) Fried white meat: OR 2.28 (95% CI 1.22–4.25) Non-alcoholic beverages: OR 0.45 (95% CI 0.23–0.89) Western: OR 2.13 (95% CI 1.09–4.15) Fatty cheeses: OR 4.17 (95% CI 1.95–8.90) Prudent: OR 0.90 (95% CI 0.48–1.66)	Age, schooling, family history, BMI, smoking, alcohol, menarche age, parity, menopause status, energy
Butler et al. (2010)[37]	Singapore	Cohort	34,028 women (629 cases) stratified according to menopause status and hormonal receptor (included only women who speak the two main Chinese dialects: Hokkiens and Cantonese)	FFQ (165 items); previous year to diagnosis for cases and corresponding period for controls	Validation	PCA	Vegetables, fruit, and soy: OR 0.82 (95% CI 0.63–1.05) Dim sum meat: OR 0.84 (95% CI 0.65–1.10)	Age, group dialect (Cantonese, Hokkien), interview year, schooling, parity, BMI, family cancer history, and total daily energy consumption
Cho et al. (2010)[38]	Korea	Hospital-based case-control	35 cases and 357 controls stratified according to menopause status and hormonal receptor	FFQ (103 items); previous year to diagnosis for cases and corresponding period for controls	Validation	PCA	Vegetables and seafood: OR 0.14 (95% CI 0.08–0.25) Meat and starches: OR 0.69 (95% CI 0.40–1.16)	Age, BMI, family history, supplement use, schooling, occupation, smoking, alcohol, physical activity, menopause status
Baglietto et al. (2011)[39]	Australia	Cohort	20,967 women (815 cases) stratified according to hormonal receptor	FFQ (124 items); habitual diet	No information	PCA	Vegetables: RR 0.98 (95% CI 0.76–1.28) Fruit and salad: RR 0.81 (95% CI 0.63–1.03) Australian traditional: RR 1.25 (95% CI 0.90–1.74) Meat: RR 1.12 (95% CI 0.85–1.46)	Country of birth, menarche age, breastfeeding duration, contraceptive use and hormonal replacement, menopause status, physical activity, alcohol, smoking, schooling, energy, BMI

Table 1 **Continued**

Reference	Location	Study design	Sample size and characteristics	Method and period of dietary evaluation	Information on validation and reproducibility	Method of analysis	Dietary patterns investigated and associated risk[a]	Variables for adjustment (multivariate analysis)
Zhang et al. (2011)[40]	China	Hospital-based case-control	438 cases and 438 controls	FFQ (81 items); previous year to diagnosis for cases and corresponding period for controls	Validation and reproducibility	PCA	Vegetables, fruit, soy, milk, fowl, and fish: OR 0.26 (95% CI 0.17–0.42) Refined grains, meat, and canned foods: OR 2.58 (95% CI 1.53–4.34)	Menarche age, number of childbirths and live births, breastfeeding duration, BMI, family history, history of benign mammary illness, physical activity, passive smoking and energy
Buck et al. (2011)[41]	Germany	Population-based case-control	2,884 cases and 5.509 controls stratified according to hormonal receptor	FFQ (176 items); previous year to diagnosis for cases and corresponding period for controls	Validation	PCA	Healthy: OR 1.04 (95% CI 0.88–1.23) Non-healthy: OR 0.96 (95% CI 0.81–1.13)	Year of birth, BMI, menopause status, schooling, family history, history of benign illness, number of gestations, menarche age, breastfeeding, total mammographies, smoking, energy
Demetriou et al. (2012)[42]	Cyprus	Population-based case-control	1,109 cases and 1,177 controls	FFQ (32 items); previous year to diagnosis for cases and corresponding period for controls	No information	PCA	Fruit, vegetables, fish, and legumes: OR 0.67 (95% CI 0.49–0.92); $p < 0.0001$[b]	
Bessaoud et al. (2012)[43]	France	Population-based case-control	437 cases and 922 controls	FFQ (162 items); previous year to diagnosis for cases and corresponding period for controls	Validation	PCA	Mediterranean: OR 1.03 (95% CI 0.71–1.44) Western: OR 0.88 (95% CI 0.73–1.06) Meat and drinkers: OR 2.56 (95% CI 1.54–4.27)	Total energy intake, education, parity, breast-feeding age at first full-term pregnancy, duration of ovulatory activity, BMI, physical activity, first-degree family history of breast cancer
Jordan et al. (2012)[44]	Tanzania	Hospital-based case-control	115 cases and 230 controls	FFQ (65 items); previous year to diagnosis for cases and corresponding period for controls	Validation	PCA	Fatty: OR 1.42 (95% CI 1.08–1.87) $p = 0.01$ Fruity: OR 1.61 (95% CI 1.14–2.28) $p = 0.01$	Age, place of living, age at menarche, menopausal status, *Mbege*[c], beer and wine

[a] Association for the highest consumption percentile in the multivariate model.
[b] Three other patterns did not present an association with breast cancer, so the authors presented detailed results only for the "fruit, vegetables, fish, and legumes" pattern.
[c] Homemade opaque beer made from bananas and millet.
Abbreviations: BMI, body mass index; FA, factor analysis; FFQ, food frequency questionnaire; NLCS, The Netherlands Cohort Study on Diet and Cancer; ORDET, Ormoni e Dieta nella Eziologia dei Tumori in Italy; PCA, principal components analysis; SMC, The Swedish Mammography Cohort; WC, waist circumference; WHR, waist to hip ratio.

Table 2 **Characteristics of the dietary patterns and their component foods with factor loadings ≥|0.30|.**

Reference	Country	Dietary pattern	Component foods
Terry et al. (2001)[19]	Sweden	Healthy	Fruit, vegetables, fish, chicken, whole grains, cereals, eggs, meat, fruit juices, low-fat dairy products
		Western	Processed meats, soft drinks, desserts, meat, refined grains, pea soup, potatoes, dairy products with a high fat content
		Ethylic	Wine, liquor, beer, savory snacks
Sieri et al. (2004)[20]	Italy	Salad, vegetables	Raw and cooked vegetables, raw tomato, raw carrot, cooked carrot, olive oil
		Western	Potato, beef, pork, processed meats, offal, eggs, butter, margarine, soybean oil, cheese, stuffed pasta, pizza, cakes
		Canteen	Spaghetti, cooked tomato, bread, olive oil, tomato sauce, wine
		Prudent	Cooked vegetables, cooked carrot, beans, legumes, fruit, milk, rice, chicken, fish, cooked carrot, yoghurt, low consumption of alcoholic beverages
Adebamowo et al. (2005)[21]	United States	Prudent	Eggplant, corn, vegetables, dark yellow vegetables, cruciferous vegetables, legumes, tomatoes, onion, garlic, fish, chicken, whole grains, fruit juice, salad dressings, low-fat dairy products
		Western	Refined grains, red and processed meats, French fries, pizza, potato, eggs, dairy products with a high fat content, desserts, savory snacks, sugary drinks, margarine, mayonnaise
Fung et al. (2005)[22]	United States	Prudent	Fruit, yellow vegetables, cruciferous vegetables, legumes, vegetables, tomatoes, whole grains, fish, chicken, low-fat dairy products, salad dressings, fruit juices
		Western	Processed meats, red meats, refined grains, desserts and sweets, French fries, pizza, condiments, potatoes, dairy products with a high fat content, sugary drinks, mayonnaise, margarine, savory snacks, eggs
Männisto et al. (2005)[23]	Holland (NLCS)	Vegetables	Legumes, cabbage, cooked and raw vegetables, garlic, carrots, tomato, mushroom, rice, spaghetti, fish, oil
		Pork, processed meat, and potatoes	Pork, processed meats, potatoes, coffee, margarine, and low consumption of rice and butter
	Italy (ORDET)	Vegetables	Raw vegetables, carrots, tomatoes, citrus fruits, vegetable oil, desserts
		Pork, processed meat, and potatoes	Processed meats, potatoes, red meat, spaghetti, rice, butter
	Sweden (SMC)	Vegetables	Cabbage, raw vegetables, carrots, tomatoes, citrus fruits, apples and pears, fish
		Pork, processed meat, and potatoes	Pork, processed meats, potatoes, red meat, spaghetti, rice, offal,
Nkondjock et al. (2005)[24]	Canada	Chocolates and cereals	Chocolate bars, morning cereal, water, fruit and fruit-based products, fish, vegetables and vegetable-based products, yoghurt, whole grain bread, seafood, nuts, salad dressing, low consumption of white bread
		Processed pork	Pork, white bread, processed meat, baked products, spaghetti, rice, frozen desserts (ice cream and pies), French fries, snacks, sweets and candies, fatty sauces, soft drinks, coffee, eggs, pudding, chicken, butter, low consumption of whole grain bread
		Ethylic	Wine, liquor, beer
Velie et al. (2005)[25]	United States	Vegetables, fish, chicken, and fruit	Green salad, broccoli, baked or grilled fish, grilled or baked chicken, carrots and selected legumes, tomato and tomato juice, raw and cooked spinach, apples and pears, cabbage, grapefruit, melon, orange, low consumption of cookies, cakes and donuts, ice cream, pies, whole milk, chocolate, white bread
		Red meat and starches	Pork ribs and baked pork, beef, bacon, hamburger, French fries, sausages, fried chicken, hot dog, eggs, offal, ham and sausages, meat pie and stew and low consumption of granola and cereal bran, apples, skimmed milk, black bread, grilled or baked fish and chicken
		Southern traditional	Cooked vegetables, cooked beans and legumes, sweet potato, cornbread, cooked cabbage, sauerkraut, cabbage salad, fried fish and chicken, rice, meat pie and stew, and low consumption of cheese, mayonnaise and salad dressing, savory snacks, wine, liquor and beer
Ronco et al. (2006)[26]	Uruguay	Traditional	Grilled meats, grains, cooked vegetables and tubers
		Healthy	White meats, raw and cooked vegetables, fruit
		Western	Fried red meats, barbecue, processed meats
		Stewed	Grilled meats, legumes, low consumption of white meat
		Fatty	Dairy products, eggs, desserts
		Ethylic	Alcoholic beverages
Sant et al. (2007)[27]	Italy	Salad, vegetables	Raw and cooked vegetables, raw tomato, raw carrot, cooked carrot, olive oil
		Western	Potato, beef, pork, processed meat, offal, eggs, butter, margarine, soybean oil, cheese, stuffed pasta, pizza, cakes
		Canteen	Spaghetti, cooked tomato, bread, olive oil, tomato sauce, wine
		Prudent	Cooked vegetables, cooked carrot, beans, legumes, fruit, milk, rice, chicken, fish, cooked carrot, yoghurt, low consumption of alcoholic beverages
Cui et al. (2007)[28]	China	Vegetables and soy	Tofu, cauliflower, lotus root, freshwater fish, celery, fresh soy grain, turnip, tomato, cucumber, beans, Chinese cabbage, carrots, wild rice stem, beansprouts, vegetables, soy milk
		Meat and sweets	Shrimp, crab, canned sweets and fruit, chicken, dessert, milk, red meat, saltwater fish, bread, pork chops and ribs
Hirose et al. (2007)[29]	Japan	Prudent	Carrot, vegetables, potato, pumpkin, cabbage, tofu, fruit, tubers, fish, milk, lettuce, low preference for fatty and salty foods
		Fatty	Pork, beef, chicken, ham, sausage, eggs, instant noodles, preference for fatty foods
		Japanese	Boiled rice, miso, and low consumption of coffee, raw vegetables, alcoholic beverages, and lettuce.
		Savory	Salt-preserved vegetables, pickles, dried salted fish, preference for savory foods
Marchioni et al. (2008)[30]	Brazil	Factor 1	Vegetables, juice and fruit, dairy products, white and red meat, fats and sauces, and low bean consumption
		Factor 2	Sugars and sweets, beans, sausage and meat sandwiches, cereals, roots and tubers, and low red meat consumption
Murtaugh et al. (2008)[31]	United States	Western	Eggs, dairy products with high fat content, refined grains, savory snacks, refined cereals, fats and sauces, tomato soups, French fries, hamburger, fried chicken, bacon, sausage, cold cuts, potato, margarine, hydrogenated vegetable fat, polyunsaturated oils, sugar, desserts, cola-based soft drinks, meats
		Prudent	Low-fat dairy products, whole grains, vegetables, vegetable juice, citric fruit juice, fruit juice, fresh, dried and canned fruit, legumes, soups, nuts
		Native Mexican	Cheeses, refined grains, Mexican soups, legumes, Mexican meats, tomato-based sauces, pig fat
		Mediterranean	Chicken and turkey, fish and seafood, soy and tofu, green salads, lettuce, butter, olive oil, fatty salad dressings, coffee, tea, vegetables and alcoholic beverages
Wu et al. (2009)[32]	United States	Western	Lettuce, spaghetti with meat, red meat, French fries, baked potato, salad dressing, pizza, mashed potatoes, burritos, tacos, meatballs, hamburger, pancake, fruit pie, cheese, popcorn, chili, mayonnaise, sour cream, refried beans, cookies, butter, bacon, turkey, pasta in tomato sauce
		Ethnic	Vegetable, fish and pork soup, offal, vegetable oil, rice, pork chops, chicken wings, fried noodles, hot dog, sweets, pineapple, dried salted fish, fried seafood, mango, papaya, orange, melon
		Vegetables and soy	Carrots, green vegetables, green beans, cabbage, green peppers, tofu, tomatoes, broccoli, cauliflower, green leaves, soy in grains, soy milk, oranges, apples, yoghurt

Table 2 **Continued**

Reference	Country	Dietary pattern	Component foods
Cottet et al. (2009)[33]	France	Alcohol/Western	Potatoes, beans, rice, pasta, French fries, pizza, pies, sandwiches, cakes, processed meat, ham, offal, eggs, pickled fish, mayonnaise, butter, high consumption of alcoholic beverages
		Healthy/Mediterranean	Fruit, raw and cooked vegetables, crustaceans, fresh fish, olive oil, sunflower oil
Agurs-Collins et al. (2009)[34]	United States	Western	Refined grains, dairy products with a high fat content, red meat and processed meat, eggs, margarine, butter, mayonnaise, potato, French fries, sweets, soft drinks, savories
		Prudent	Cruciferous vegetables and other vegetables, fruit, tomatoes, whole grains, cereals, low-fat dairy products, fish, chicken, fruit juices, soup, beans, pasta
De Stefani et al. (2009)[35]	Uruguay	Prudent	Chicken, fish, raw and cooked vegetables
		Traditional	Eggs, grains, tubers, fruit, dairy products
		Western	Fried red meat, barbecue, processed meats, desserts
		Ethylic	Beer, wine, spirits
Ronco et al. (2010)[36]	Uruguay	Low fat	Skinless chicken, skimmed milk, skimmed yogurt, coffee, low consumption of chicken skin and whole milk
		Fried white meat	Breaded meat, hamburger, chicken skin, fried fish, baked fish, oil, potato, low consumption of olive oil, vegetables, and fruit
		Non-alcoholic drinks	Ricotta cheese, whole yogurt, boiled eggs, soft drinks, tea, mate, low consumption of red meat
		Western	Beef, lamb, hamburger, processed meats, butter, fried eggs, desserts, French fries
		Fatty cheeses	Quartiolo cheese, cheese with high fat content, Parma cheese, low ricotta cheese consumption
		Prudent	Grains, tubers, cooked vegetables, legumes, citrus fruits, fruit
Butler et al. (2010)[37]	Singapore	Vegetables, fruit, and soy	Cauliflower, broccoli, carrot, beans, peas, tofu, mushrooms, tomato, corn, lettuce, potato, cabbage, watercress, celery, cucumber, dark green leafy vegetables, apple, papaya, melon, banana
		Dim sum meat	Seasoned fish paste, spaghetti in sauce, chicken rice, fried chicken, rice dumpling, coconut desserts, coconut rice, chicken and lamb with curry, pickled eggs, baked duck and geese, pork offal
Cho et al. (2010)[38]	Korea	Vegetables and seafood	Yellow and green vegetables, spices, seafood, mushrooms, tubers, algae, tofu, soy milk, lean and fatty fish, fruit
		Meats and starches	Cakes, pizzas, processed meats, red meat, bread, spaghetti, chicken, fatty meat, red meat-based products, dairy products, oils, savories, soft drinks, sweets, eggs
Baglietto et al. (2011)[39]	Australia	Vegetables	Peppers, green salads, celery, cucumber, fennel, beetroot, cabbage salad, potato cooked without fat, carrot, cauliflower, broccoli, green leaves, beans, peas, pumpkin, zucchini, eggplant
		Fruits, salads	Orange, tangerine, apple, banana, peach, nectarine, pear, melon, strawberry, fig, grapes, plums, apricot
		Australian traditional	Cookies, cakes, pudding, cheddar cheese, margarine, lamb, sausage, bacon, chocolate, tea, jam, honey, and low consumption of olive oil and green salads
		Meat	White bread, pizza, fried rice, savory pastries, Feta cheese, fried eggs, preparations with eggs, red and processed meats, fried fish, fried chicken, potato cooked with fat, canned vegetables
Zhang et al. (2011)[40]	China	Vegetables, fruit, milk, soy, fowl, and fish	Dairy products, fruit, eggs, fruit juices, vegetables, fowl, soy, fish and seafood
		Refined grains, meat, canned foods	Refined grains, processed meats, pork, veal and beef, canned vegetables
Buck et al. (2011)[41]	Germany	Healthy	Fish, tea, fruit, cabbage, leafy vegetables, tomato sauce, tomato, mushrooms, salad, sprouts, beans and legumes, soy, morning cereals, sauces based on olive oil and vinegar, garlic and onion, mayonnaise, soup
		Non-healthy	Processed meats, red meats, offal, eggs, fowl, butter, beer, coffee, vegetable and animal fat for frying
Demetriou et al. (2012)[42]	Cyprus	Meat, potatoes	Red meat, fowl, potatoes, sausages, sweets and desserts, rabbit meat
		Cereals, dairy	Low-fat yogurt, lower fat cheese, skimmed milk, whole milk fat (cream), fatty cheese, cereals
		Cakes, sweets, nuts, cookies, pasta, and rice	Cakes, chocolate, bread, nuts, cookies, rice, and pasta
		Fruit, vegetables, fish, legumes	Fish fillet, other fish, fruit, vegetables and salads, legumes
Bessaoud et al. (2012)[43]	France	Mediterranean	Fruits, dried fruits, raw vegetables, cooked vegetables, legumes, fatty fish, lean fish, olive oil
		Western	Cereals, cheese, eggs, processed meats, butter, oil other than olive oil, sweets, pizzas
		Meat-eaters and drinkers	Mollusc and shellfish, meat, offal and giblets, wine, alcohol other than wine
Jordan et al. (2012)[44]	Tanzania	Fatty	Milk, butter and lard, meat, mixed vegetables fat, low consumption of sunflower oil and tea
		Fruity	Fish, mango, papaya, avocado, orange, watermelon, pineapple, banana, Green cooked banana, starchy tubers, pulses, sugar, *Mbege*[a]

[a] Homemade opaque beer made from bananas and millet.

recent (6 months to 1 year before recruitment), and few investigations evaluated previous food consumption.[24,28,36] Information on validation was presented for 10 (38.5%) studies,[22,23,27,28,30,32,37,38,43,44] seven (26.9%) presented information on validation and reproducibility,[20,21,24,25,27,33,40] reproducibility alone was reported in three (11.5%),[26,35,36] and six (23.1%) did not present such information.[19,29,31,34,39,42]

Vegetables, fruits, fish, and soy

Twenty-two studies (10 cohort studies and 12 case-control studies) that evaluated the association of dietary patterns comprised of fruits, vegetables, fish, and soy and its derivatives with breast cancer were selected. The dietary patterns that presented high factor loadings for the above-mentioned foods were assigned different names such as "healthy," "prudent," "vegetables," "salads," and "fruits," among others. Among the studies investigating increased consumption of grains, cereals, vegetables, and fruit, 10 found a significant inverse association with breast cancer,[20,22,26,27,29,32,35,38,40,42] one found no association,[28] and two found a positive association (Figure 2).[31,44]

In nine other studies,[19,22,23,25,34,36,37,39,41] no statistically significant differences between the evaluated dietary patterns and breast cancer were observed.

Using a subsample of The Nurse's Health Study cohort, Fung et al.[22] measured the risk associated with

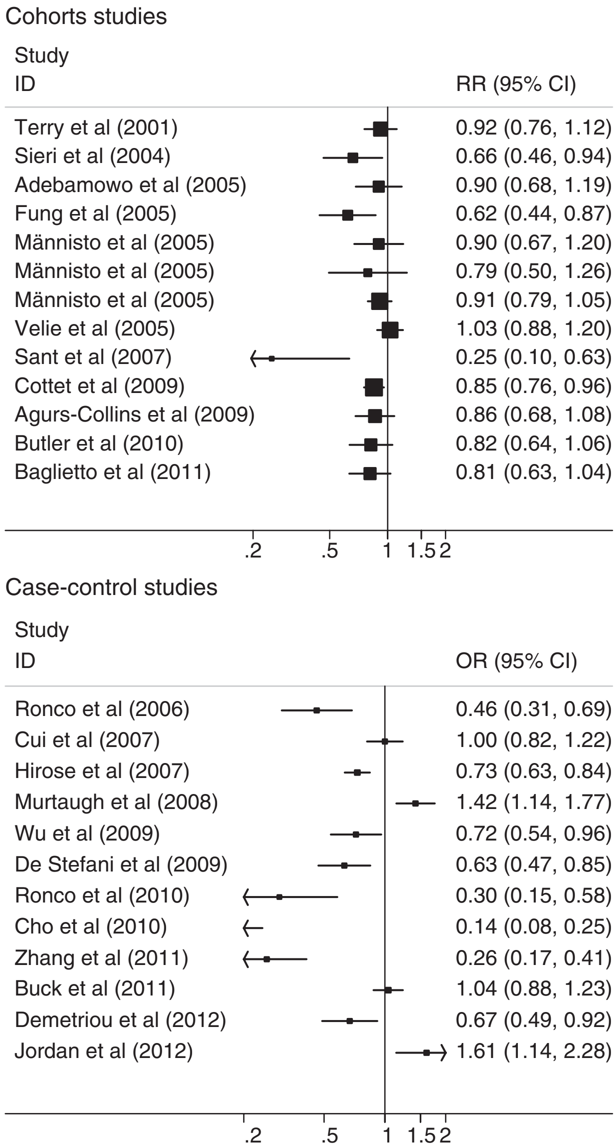

Figure 2 **Forest plot of the highest versus the lowest level of consumption of the fruits, vegetables, fish, and soy dietary pattern.**

food consumption in 3,026 postmenopausal women with breast cancer. The researchers found that the dietary pattern comprised of fruit, vegetables, whole grains, products with low-fat contents, fish, and fowl was inversely associated with estrogen receptor-negative (ER-) tumors. In another cohort with 8,984 Italian women, the dietary pattern comprised of vegetables and salads (upper tertile versus lower tertile of consumption) was inversely associated with breast cancer risk and, when stratified by body mass index (BMI), the relationship was strongest for subjects with a BMI of <25.[20] Sant et al.[27] analyzed the same Italian cohort and observed that this dietary pattern presented a stronger inverse association with HER-2-positive tumors than with tumors of the HER-2-negative subtype ($p = 0.039$ for heterogeneity).

Findings from a recent case-control study of 935 cases and 817 controls in Cyprus corroborated the findings of Fung et al.[22] Demetriou et al.[42] verified a 33% reduction in the risk of breast cancer in association with the highest-quartile consumption of the dietary pattern with high factor loadings for fruit, vegetables, fish, and legumes.

Similar to the studies above from Europe and North America, two studies conducted in South America found an inverse association with breast cancer. In a multicenter case-control study in Uruguay, the dietary pattern comprised of chicken, fish, and raw and cooked vegetables was significantly inversely correlated with breast cancer occurrence.[35] Ronco et al.[26] also found an inverse association between breast cancer and high consumption of white meats, raw and cooked vegetables, and fruit in a Uruguayan population; when stratified by menopause status, this association was verified only in postmenopausal women.

In four case-control studies of Asian populations, an inverse association was found between breast cancer risk and the highest consumption of patterns comprising fruit, vegetables, soy, and soy-bean derivatives.[28,29,32,38,40] Wu et al.[32] studied women of Asian descent and verified an inverse association for the "vegetables and soy" dietary pattern (highest quartile versus lowest quartile of consumption). Hirose et al.,[29] in a study of Japanese women, also found evidence of a strong inverse association for the "prudent" dietary pattern (defined in Table 2), especially among women over 50 years of age and those with a BMI of <25. Cho et al.,[38] in a study of Korean women, also found a negative association with the pattern named "vegetables and seafood"; in this study, the strong inverse association was maintained for all subtypes in the analyses stratified by menopause status and hormonal receptor tumor subtype. Similar results were presented by Zhang et al.[40] from a study of Chinese women; specifically, these researchers found a lower cancer risk among subjects with higher consumption of vegetables, fruit, soy, milk, chicken, and fish. This inverse association remained significant among both pre- and postmenopausal women and for all hormonal receptor tumor subtypes. However, in a study of Chinese women in Shanghai, no association was verified between breast cancer risk and the highest quartile consumption of the "vegetable and soy" pattern.[28]

Unlike the results presented above, in a North American case-control study of Latino and non-Latino Caucasian women,[31] the pattern comprised of low-fat dairy products, whole grains, whole cereals, vegetables, vegetable juices, citrus fruit juices, fruit (fresh, dry, and canned), legumes, soups, and nuts, which was labeled "prudent," was positively associated with breast cancer. The researchers verified a 42% increase in the risk of breast cancer development in women who belonged to the highest quartile of this pattern's consumption. In the analyses stratified by menopause status and BMI, there was a positive association in postmenopausal women with a BMI of <25 and in those with a BMI between 25 and 29.9. According to the authors, this unexpected result could be explained by the greater contribution of fruit and vegetables in the "prudent" pattern, rather than legumes, which reflects a higher carbohydrate intake. However, the authors did not discard the possibility of memory bias in the participants' reporting of previous food consumption.

In a case-control study performed in Tanzania,[44] the pattern characterized by high consumption of fish, mango, papaya, avocado, orange, watermelon, and pineapple was also positively associated with breast cancer. The authors believed that despite being composed of foods rich in vitamins and other micronutrients, which are considered potentially protective against breast cancer, the "fruit" pattern had a high concentration of polyunsaturated fatty acids and perhaps a low ratio of polyunsaturated to saturated fatty acids would be more important for preventing the development of breast cancer.

It was recently suggested that carbohydrate consumption might promote tumor growth due to the effect on circulating insulin levels.[45] Some diseases that are known to be associated with hyperinsulinemia, such as obesity and diabetes mellitus, are associated with an increased risk of breast cancer[46] because insulin could act as a tumor growth factor by stimulating tumor growth via DNA synthesis, altering the hormonal environment, and inhibiting apoptosis.[47] Another hypothesis for the influence of carbohydrates on cancer risk is related to the quality of this nutrient; this suggests that, rather than measuring the absolute carbohydrate intake, one should measure the glycemic index or glycemic load and thus evaluate the glucose absorption and insulin responses of the subjects.[48] In a recent literature review of the impact of diet on breast cancer risk,[49] no association was observed between carbohydrate intake, glycemic index, glycemic load, and general breast cancer risk in most studies. However, the authors found that, under the same conditions mentioned previously,[50] the results corroborated the hypothesis that an association exists between carbohydrates, glycemic index, and/or glycemic load and breast cancer, particularly among premenopausal women with a BMI of >25 and a high-glycemic index diet,[51] and among women <50 years of age. The authors also highlighted results[52] suggesting that high carbohydrate consumption and a high-glycemic index diet could increase the risk of breast cancer with the estrogen receptor-positive/progesterone receptor-negative (ER+/PR-) subtype due to interactions between carbohydrates and hormone modulation.

Mediterranean diet

Only one prospective cohort and two case-control studies were found that described the association between breast cancer and the Mediterranean dietary pattern (Figure 5).[31,33,43]

On the basis of data from a French cohort, the association between breast cancer in postmenopausal women and consumption of the dietary pattern named "healthy/Mediterranean," characterized by fruit, raw and cooked vegetables, fish and crustaceans, olive oil, and sunflower oil, was investigated.[33] The Mediterranean pattern was found to be inversely associated with breast cancer risk in postmenopausal women, especially those with ER+/PR- tumors. A relevant finding of this study was the significant interaction between consumption of the Mediterranean pattern and energy consumption (interaction in Cox regression with $p = 0.03$). In those with a below-median energy consumption level (2,037 kcal/day), the Mediterranean pattern was inversely associated with breast cancer (upper quartile versus lower quartile); the same was not observed in those with a higher level of energy consumption. The researchers then compared the participants' consumption of food items classified as below and above the energy median and found that the difference between the subgroups was the concomitant consumption of foods with high energy densities (e.g. cakes, sandwiches, French fries, and processed meats) by women with higher levels of energy consumption.

In a case-control study performed in the United States to investigate the role of the Mediterranean diet among Latino and non-Latino Caucasian women,[31] a reduction in the risk of breast cancer was observed in association with a dietary pattern comprising alcoholic beverages, chicken, seafood, vegetables, green salads, olive oil, and salad oil; this reduction was most evident among postmenopausal Latino women. However, Bessaoud et al.[43] examined breast cancer risk relative to the consumption of fruits, raw and cooked vegetables, fish, and olive oil in France and found no association between this dietary pattern and breast cancer.

Traditional diet

Four prospective cohort studies[20,25,27,39] and six case-control studies[26,29–32,35] were found among the studies that investigated dietary patterns designated as "traditional" and those that described the typical food consumption patterns of the studied regions (Figure 3).

In an Italian cohort analyzed by Sieri et al.,[20] a pattern characterized by high consumption of pasta, cooked

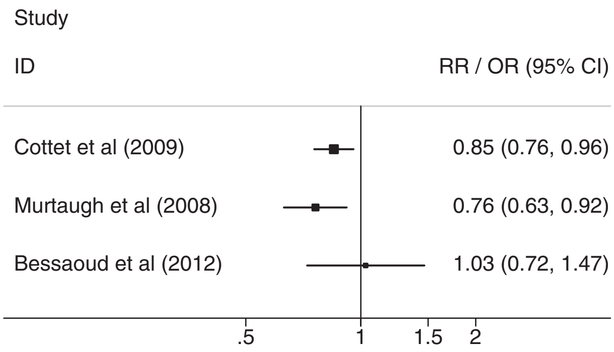

Figure 3 **Forest plot of the highest versus the lowest level of consumption of the Mediterranean dietary pattern.** Case-control and cohort studies were grouped in the same analysis.

tomatoes, tomato sauce, bread, olive oil, and wine was observed and named "canteen." The authors found no association between this pattern and breast cancer risk, even after adjusting for possible confounding variables. However, in the analysis stratified by cancer subtype,[27] a positive association was found between consumption of the "canteen" pattern (highest tertile versus lowest tertile) and the HER-2-positive cancer subtype, in particular ($n = 12$); this suggests that the effects of diet on breast cancer risk might be underestimated when the HER-2-positive and HER-2-negative subtypes are considered together.

Baglietto et al.[39] identified a pattern with high positive factor loadings for cereals, desserts, cheddar cheese, dairy products, margarine, green beans, peas, pumpkin, lamb, sausages, bacon, and baked potatoes, as well as high negative loadings for olive oil, pasta, leafy green vegetables, legumes, and fish. This pattern was named "Australian traditional" since women in Australia and New Zealand consume this pattern frequently. The authors did not observe an association between this traditional pattern and breast cancer among the evaluated women.

In a study developed by Velie et al.,[25] the pattern named "Southern traditional," which was characterized by high consumption of traditional foods from the rural southern region of the United States such as cooked vegetables, beans and legumes, sweet potatoes, cabbage, rice, cornbread, fried fish, and chicken, as well as low consumption of cheese, mayonnaise, salad dressing, wine, liquor, and savory snacks, was associated with a decreased risk of in situ and invasive breast cancer. In the analyses stratified by BMI and hormonal receptor subtypes, risk reductions were observed among women with a BMI of <25 ($p = 0.02$) and those with ER+ tumors ($p = 0.01$), PR+ tumors ($p = 0.003$), and ER-/PR+ tumors ($p = 0.01$).

A similar result was observed in a case-control study developed by Murtaugh et al.[31] The traditional pattern included typical Mexican foods such as cheeses, meats, Mexican soups, legumes, refined grains, and tomato-based sauces and was named "native Mexican." Regardless of ethnicity (Latino or non-Latino Caucasian) and menopause status, the subjects with the highest quartile consumption of this pattern had a lower risk of breast cancer. In the analysis stratified by BMI and menopause status, a significant inverse association was observed among premenopausal women with a BMI of <25.

In a study by Ronco et al.,[26] the "traditional" pattern included cooked red meat, cereals, cooked legumes, and tubers and represented, according to the authors, a food combination that was recognized as habitual among the Uruguayan population. This pattern was inversely associated with the risk of breast cancer occurrence, especially among postmenopausal women, and was similar to the findings reported by De Stefani et al.[35]; their evaluation of a "traditional" pattern comprised of grains, tubers, fruit, desserts, eggs, milk, and milk derivatives was also inversely associated with the risk of breast cancer (highest tertile versus lowest tertile of consumption).

In a study performed in northeastern Brazil, a traditional Brazilian dietary pattern comprised of rice, beans, milk and its derivatives, roots, and tubers was identified.[30] The researchers verified an inverse association of this dietary pattern with breast cancer and highlighted that the results reflected the nutritional transition taking place in the country.

Although most of these findings indicate an inverse association between breast cancer and traditional food patterns, two case-control studies presented opposing results.[29,32] In the first,[29] the pattern designated "Japanese" reflected high consumption of typically Japanese foods such as cooked rice and miso, as well as low consumption of coffee, alcoholic beverages, and raw vegetables. No association between this pattern and breast cancer was found, even after adjusting for potential confounding factors; however, in the stratified analysis, women with a BMI of ≥25 had a significantly higher odds ratio for breast cancer. In an analysis performed by Wu et al.,[32] the "ethnic" (meat and starches) pattern, comprised of typical Asian foods such as vegetable soup, pork, dried and salted fish, fried rice, and noodles, was associated with an increased risk of breast cancer (highest quartile versus lowest quartile of consumption).

Western diet

A total of 24 studies (10 cohort studies and 14 case-control studies) were evaluated that identified a Western dietary pattern with high factor loadings for red and processed meats, refined grains, potatoes and starches, snacks, sweets, fried foods, and soft drinks. Of these, eight showed a positive association between the Western

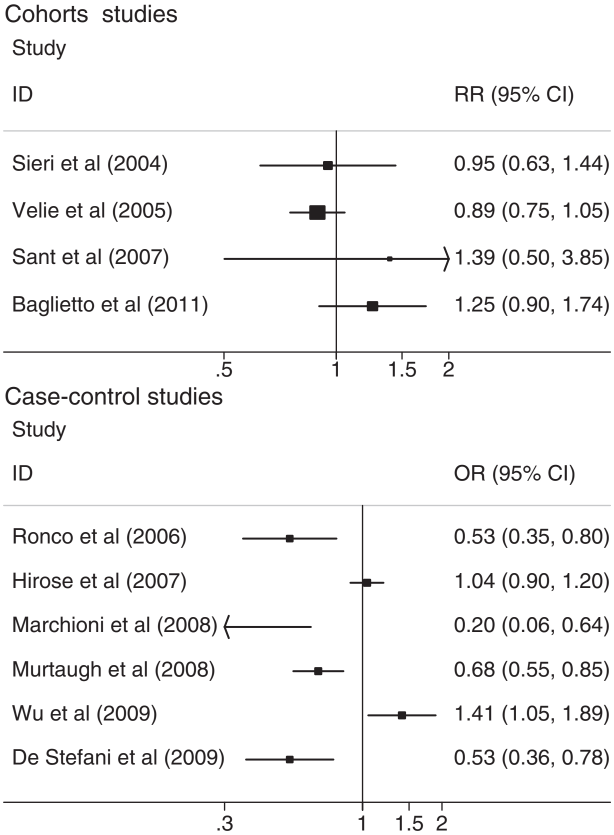

Figure 4 **Forest plot of the highest versus the lowest level of consumption of the traditional dietary pattern.**

dietary pattern and breast cancer,[26,28,30,31,35,36,40,44] one study reported an inverse association,[24] and 15 did not find any association between high consumption of the Western pattern and breast cancer (Figure 4).[19–24,27,29,32,34,37–39,41,43]

Some studies of Latin American and North American populations presented similar results. Ronco et al.[26] observed a twofold increase in breast cancer among women in Argentina who consumed high amounts of the pattern including fried red meat, barbecued meat, and processed meats, especially among postmenopausal women. Another analysis of ductal carcinoma cases only[36] showed that Argentine women with high consumption rates of beef, lamb, hamburger, processed meats, butter, fried eggs, desserts, and French fries also had a twofold higher risk of breast cancer. In a study conducted by Marchioni et al.,[30] a positive association was verified between breast cancer and elevated consumption of a pattern comprised of red and white meat, dairy products, and foods with high energy densities, such as sweets and sausages. The pattern described as "Western" by De Stefani et al.[35] comprised fried red meat, barbecued meat, processed meat, and desserts and was associated with an 81% increase in the risk of breast cancer among the women consuming this pattern most frequently (highest tertile versus lowest tertile). Murtaugh et al.[31] also verified a 32% increase in the risk of breast cancer among American women consuming the "Western" pattern most frequently, regardless of ethnicity. This result remained significant only in postmenopausal non-Latino Caucasian women with a BMI of <25.

In a case-control study of an African population,[44] the "fatty" pattern, characterized by high consumption of red meat, milk, butter, lard, and mixed vegetable oils and low consumption of sunflower oil and tea, showed a significant positive association with breast cancer development ($P = 0.01$).

A positive association with breast cancer was observed in two studies that evaluated the "Western" consumption pattern in Asian populations.[28,40] In one

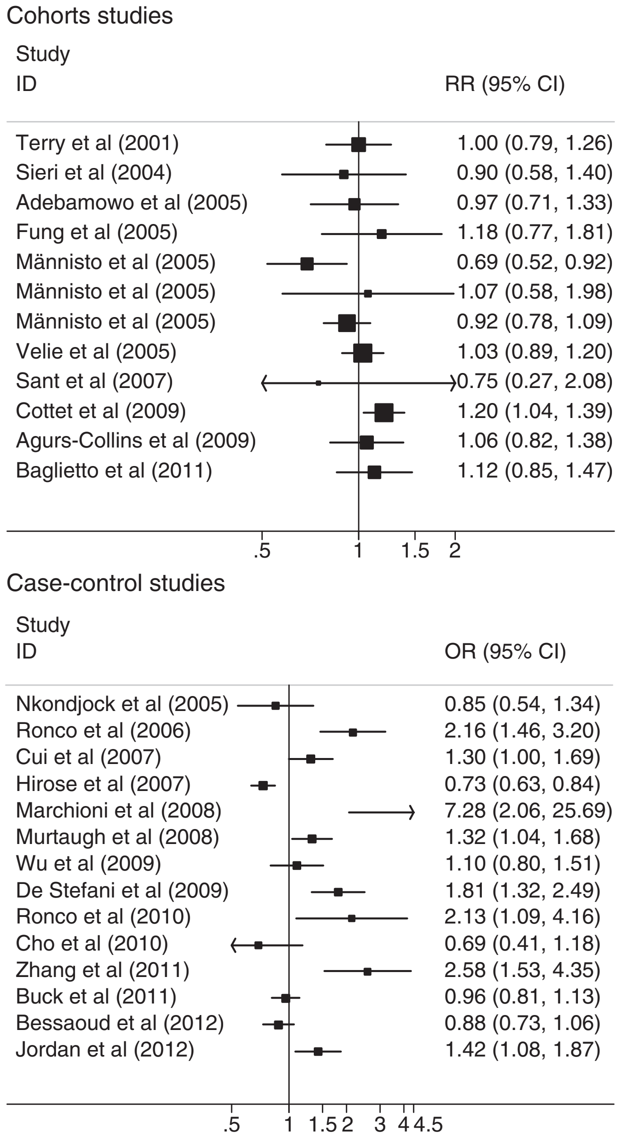

Figure 5 **Forest plot of the highest versus the lowest level of consumption of the Western dietary pattern.**

population study performed in Shanghai,[28] the researchers verified a positive association between breast cancer and high consumption of a pattern comprised of sweets, canned fruit, chicken, desserts, milk, red meat, shrimp, crab, saltwater fish, bread, and pork ribs. In the stratified analysis, the association remained significant only for postmenopausal women with ER+ tumors and a BMI of ≥25. A positive association with breast cancer was also observed in a hospital-based study of Chinese women.[40] The highest consumption (highest quartile versus lowest quartile) of the pattern called "refined grains, meat, and canned products" increased the risk of breast cancer 2.6-fold, and the associations remained significant even in the analyses stratified by menopause status, BMI, and hormone receptor tumor subtypes.

The only study that observed a significant inverse association with consumption of the Western pattern included three of the four European cohorts (NCLS, ORDET, and SMC) that participated in the DIETSCAN project.[23] Each cohort was analyzed separately by exploratory factor analysis to identify patterns common to the three populations. The pattern with high factor loadings for pork and processed meats, coffee, and margarine and low factor loadings for rice and butter was named "pork, processed meats, and potatoes." In the Dutch cohort (NCLS), researchers observed a different result from that found in the other cohorts; namely, an inverse association was observed between consumption (upper quartile versus lower quartile) of the above-mentioned pattern and the risk of breast cancer. According to the researchers, this unexpected result might be explained by the type of fat consumed. The item butter (rich in saturated fatty acids) had high and positive factor loadings in the Italian (ORDER) and Swiss (SMC) cohorts and a negative loading in the Dutch (NCLS) cohort, but in the Dutch cohort butter seemed to have been replaced by margarine (rich in polyunsaturated fatty acids).

Among the 14 studies that did not display a statistically significant association between the Western pattern and breast cancer, the association was direct in four[25,32,34,39] and inverse in 10.[19–21,23,24,27,29,38,41,43]

Since the 1970s, interest has been expressed in the role of dietary fats in the development of breast cancer. More recently, researchers have been analyzing specific types of fat, but the results of these studies remain inconsistent.[49,53] The molecular mechanisms by which dietary fatty acids could influence the process of carcinogenesis, i.e., by modifying the structural components of the cell (membrane lipids), metabolic effects, translation signals, and gene expression, have been proposed. In addition to assuming energy functions, structural lipids can modulate the intracellular signaling cascades that control gene expression and cellular functions. Fatty acids that are incorporated into membrane phospholipids can be separated by the action of phospholipases and thus modulate signals from other pathways. It is well established that the lipid composition of biological membranes influences the inflammatory process, since polyunsaturated fatty acids are the precursors of eicosanoids. Furthermore, lipids with similar properties to hormones can also modulate inflammatory responses and play important roles in cell growth and differentiation.[49]

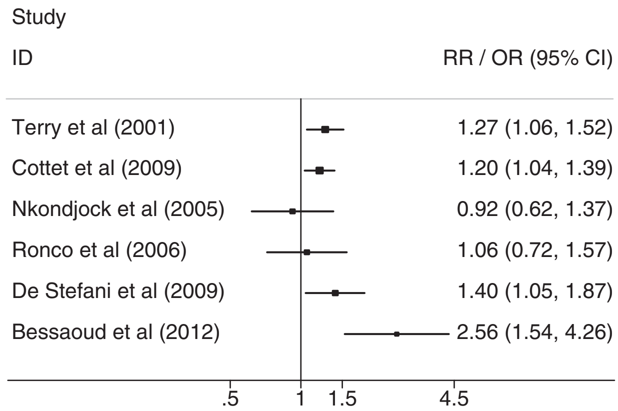

Figure 6 **Forest plot of the highest versus the lowest level of consumption of the alcoholic dietary pattern.** Case-control and cohort studies were grouped in the same analysis.

Alcoholic beverages

Two cohort studies[19,33] and four case-control studies[24,26,35,43] identified a pattern of alcoholic beverage consumption. In four of the six studies, an increase in breast cancer risk was verified when the highest level of consumption was compared with the lowest level (Figure 6). These findings reinforced the verdict of the most recent WCRF/AICR[3] report, which indicated consumption of alcoholic beverages is a significant risk factor for breast cancer in pre- and postmenopausal women.

In a prospective cohort study of 61,463 Swiss women, including 1,328 incident cases of breast cancer, Terry et al.[19] found that consumption of the "alcoholic" pattern increased breast cancer risk by 27%. Among older women (>50 years), the estimated risk increase was 31%.

Similarly, Cottet et al.[33] studied 2,381 cases of invasive breast cancer in postmenopausal women in France and observed a significant positive association with higher consumption of the "alcoholic" pattern. In the stratified analysis, this association was only significant for ER+/PR+ tumors.

Similar findings were observed in Uruguay by De Stefani et al.[35] in a study with 461 cases of breast cancer and 2,532 controls. This study found a significant increase in the risk of breast cancer associated with elevated consumption of the "alcoholic" pattern.

In a case-control study developed by Bessaoud et al.,[43] a positive association was also found between consumption of the "alcohol" pattern and the risk of breast cancer among French women, even after adjusting for potential confounders.

However, in a study of 414 French Canadian cases and 429 controls, no association[24] with alcohol consumption was identified. The authors posited that this finding was due to the relative stability and homogeneity of the study population's lifestyle and dietary habits.

Similarly, Ronco et al.[26] did not find an association between the "alcoholic" dietary pattern and breast cancer, even when the analysis was stratified by menopause status. These authors suggested the absence of an effect was due to the low prevalence of alcohol consumption among Uruguayan women (approximately 20%).

DISCUSSION

The findings reported here are in agreement with previously published systematic reviews. Edefonti et al.[13] analyzed 19 articles published between 1995 and 2008 that identified dietary patterns defined *a priori* (dietary indexes) and *a posteriori* (principal component analysis, factor analysis, cluster analysis, and reduced rank regression). A systematic review with meta-analysis conducted by Brennan et al.[14] included 16 studies published between 2001 and 2009 on dietary patterns defined *a posteriori* (principal component analysis and factor analysis). Both reviews reported a possible inverse association between breast cancer and a dietary pattern characterized by vegetables, fruit, legumes, whole cereals, fish, fowl, and foods with a low fat content.

The findings of some epidemiological studies suggest an association exists between high consumption of fruits and vegetables and reduced risk of breast cancer.[54] These foods contain substances with anticarcinogenic properties, such as phytosterols, vitamins C and E, and beta-carotene, which could have protective functions via antioxidant effects on estrogen metabolism and the reduction of cell proliferation. According to the latest global consensus,[3] fruit and vegetable consumption is likely associated with a reduced risk of breast cancer. High intakes of soy and its derivatives have been proposed to contribute to the low risk of breast cancer in Asian countries; however, the results of epidemiological studies regarding this association are highly variable. [55] In a meta-analysis of 18 studies (12 case-control studies and 6 cohort studies),[56] the combined analyses for all women showed an inverse association of soy intake with breast cancer (RR = 0.86, 95% CI 0.75–0.99). In women from Asian countries, this association was not statistically significant (RR = 0.89, 95% CI 0.71–1.12). In analyses stratified by menopausal status, the inverse association was confirmed to be slightly stronger among premenopausal women (RR = 0.70, 95% CI 0.58–0.85) compared to postmenopausal women (RR = 0.77, 95% CI 0.60–0.98). There are few known modifiable risk factors related to the ER+ and ER- breast cancer subtypes. Thus, large combined analyses are needed to accurately assess the possibility of an inverse association between fruit and vegetable consumption and the risk of ER- breast cancer. The Pooling Project of Prospective Studies of Diet and Cancer, an international consortium, analyzed data collected from 993,466 women in 20 cohort studies, in which 19,869 cases of ER+ cancer and 4,821 cases of ER- cancer were documented.[57] The total fruit consumption was inversely associated with risk of ER- breast cancer (RR = 0.94, 95% CI 0.85–1.04) but not breast cancer in general (RR = 0.99, 95% CI 0.95–1.03) or the ER+ subtype (RR = 0.99, 95% CI 0.93–1.07). The combined total consumption of fruits and vegetables was inversely associated with the risk of ER- breast cancer (RR = 0.90, 95% CI 0.81–1.01), but not with the risk of breast cancer in general (RR = 0.98, 95% CI 0.93–1.02) or ER+ tumors (RR = 1.00, 95% CI 0.94–1.07). The pooled RRs from a comparison of the highest versus the lowest quintiles of total vegetable intake were 0.82 (95% CI 0.74–0.90) for the ER- subtype and 1.04 (95% CI 0.97–1.11) for the ER+ subtype.

In the present systematic review, studies that described the dietary patterns typical for each studied region were designated as traditional. The traditional dietary model refers to typical and traditional foods, preparation methods, and food combinations. Some of the traditional dietary patterns were as follows: rice, beans, roots, and tubers in the Brazilian population; pasta, olive oil, tomatoes, and tomato sauce in the Italian population; and red meat, vegetables, cereals, tubers, and legumes in the Argentinean population. Dietary acculturation has been observed worldwide.[58] Migrant studies have shown that environmental and behavioral factors are decisive in the development of breast cancer, such that, upon migrating to countries with high rates of breast cancer, populations from countries with low rates were found to have an increased risk within one or two generations.[59] In general, the process of acculturation is most strongly associated with unhealthy dietary changes. Thus, the maintenance of traditional food habits could reduce the risk of breast cancer in migrant populations or in individuals who have adopted alternative dietary patterns.[58]

The data are still controversial with regard to the role of dietary fat in the risk of breast cancer. Results of experimental and ecological studies suggest that fat intake is positively associated with the risk of breast cancer, but study designs based on individual exposures (case-control and cohort studies) have shown conflicting results. Most international case-control studies have observed a positive association; however, it is necessary to consider the methodological difficulties inherent in this design, such as recall bias in reports of past exposure. Some prospective studies reported no association between fat intake and the risk of tumor development.[60] In a recent meta-analysis of 31 case-control and 14 cohort studies, Boyd et al.[61] found that the risk estimates were similar. The summary RR for a comparison of the highest and lowest levels of total fat consumption was 1.13 (95% CI 1.03–1.25). Cohort studies had a RR of 1.11 (95% CI 0.99–1.25), while the case-control studies had a RR of 1.14 (95% CI 0.99–1.32). The summary measures for the analyses of saturated fat and meat consumption also showed positive associations with a RR of 1.19 (95% CI 1.06–1.35) and 1.17 (95% CI 1.06–1.29), respectively. In a randomized, controlled trial of primary breast cancer prevention at 40 clinical centers in the United States, researchers found a 9% reduction in the incidence of breast cancer among women who consumed a reduced-fat diet, compared to the control group, during an 8.1-year follow-up period; this was in the Women's Health Initiative Dietary Modification Trial),[62] which included 48,835 postmenopausal women aged 50–79 years with no history of breast cancer. However, the researchers noted that this result could not be attributed solely to reduced fat intake, since the intervention group also reduced their total energy consumption and body weight and increased their consumption of fruits, vegetables, fiber, and folic acid relative to the control group. Thus, the researchers suggested that all of these dietary and behavioral changes contributed to the reduced incidence of breast cancer in the intervention group. In another prospective study (National Institutes of Health – AARP Diet and Health Study),[63] the association between fat intake and the incidence of breast cancer was assessed in 188,736 postmenopausal American women; 3,501 cases of invasive breast cancer were observed after a follow-up period of 4.4 years. The hazard risk (HR) for women with the highest levels of total fat consumption compared to the lowest was 1.11 (95% CI 1.00–1.24, $P = 0.017$). Positive associations were also found for the subtypes of fat consumed (saturated fat: HR 1.13, 95% CI 1.05–1.22; monounsaturated fat: HR 1.12, 95% CI 1.03–1.21; and polyunsaturated fat: HR 1.10, 95% CI 1.01–1.20). These results corroborate the earlier finding that fat consumption is directly associated with the risk of breast cancer in postmenopausal women.

According to the WCRF/AICR,[3] alcohol consumption is a risk factor for breast cancer in both pre- and postmenopausal women. The association of alcohol consumption with an increased risk of breast cancer has been a consistent finding in most epidemiological studies.[53,64] Increased estrogen and androgen levels in women who consume alcohol seem to be important underlying mechanisms for this association.[65,66] Other plausible mechanisms include increased susceptibility to mammary gland carcinogenesis, increased DNA damage, and a higher metastatic potential of breast cancer cells; the magnitude of these processes likely depends on the amount of alcohol consumed.[53,67] The susceptibility of alcohol drinkers to tumor development might also be affected by other factors, including diet (low folic acid intake), lifestyle habits (use of hormone replacement therapy), or biological features (hormone receptor status of the tumor).[68–71]

The main advantage of dietary pattern analyses is the global evaluation of diets, since dietary behaviors are dissected according to the whole population in order to preserve the correlations among individual food items consumed. The method involves important and arbitrary decisions made by the researchers, including the number of factors to extract, the rotation method, and the dietary pattern nomenclature. Comparisons of results and reproducibility can therefore be difficult to achieve, and different populations present with distinct dietary patterns.[10,72]

The present systematic review sought to update the discussion of dietary patterns and breast cancer risk; it includes 10 recently published articles, not included in prior reviews, and by expanding the search to include the Lilacs database, regional publications were also included that might not have otherwise been discovered.[26,36–44] The variability and quality of the studies, which represent the populations of five continents, are outstanding.

The choice to include only studies that defined patterns *a posteriori* and to exclude others that evaluated nutrients and food components demonstrates a meticulous approach to ensuring design homogeneity. The decision to group patterns according to similar factor loading permitted analyses to be performed according to the composition of food items and not simply by the group's name given by each author.

Heterogeneity in the designs, data collection methods, items, and factor loadings among the different studies impeded the calculation of a summary measure. Meta-analyses of published data are generally limited and of little use for the production of valid quantitative estimates or even the investigation of exposure relationships, since it is not possible to ensure that the various variables (factors) measure similar exposures.[17,18]

This analysis has several limitations. First, the instruments used to collect dietary information differed among the studies. Although the food frequency questionnaire was used in most cases, this tool is known to be subject to measurement error and, thus, might not detect a significant association between exposure and breast cancer risk. In addition, the numbers of food items in the instruments varied greatly, which might have resulted in the underrepresentation or overrepresentation of some food groups in the described patterns. Furthermore, few of the instruments were valid and reproducible. These aspects are relevant when ensuring the reliability of the identified dietary patterns.

Additionally, few investigations contemplated previous food consumption. It is known that evaluations performed at a specific point in time do not consider changes in eating habits over time, although these changes might be especially relevant to cancer development. For example, childhood and adolescent eating habits have been associated with early menarche, which is a risk factor for breast cancer.[73]

On the other hand, the studies included in this review incorporated meticulous scientific methodology that included the control of important confounding variables (e.g., age, BMI, menopause status, and hormonal receptor and HER-2 expression subtypes). The limited consistency of the findings can likely be explained by the disease etiology as a result of variations in many of the associated factors and genetic characteristics.

CONCLUSION

The results of this systematic review suggest that consumption of a dietary pattern characterized by vegetables, fruit, fish, and soy and its derivatives, as well as patterns designated as traditional and Mediterranean, reduces the risk of breast cancer, while consumption of the alcoholic pattern is associated with increased risk of breast cancer. A positive association was observed relative to the Western dietary pattern; however, most of these results were not statistically significant. There is no evidence for an association between traditional dietary patterns and breast cancer occurrence.

Generally, the observed findings are consistent with factors currently advocated as protective against most types of cancer and specifically for those that are believed to pose the greatest risk for breast cancer.[74–76] Despite the recently conducted investigations, the evidence for associations between various dietary patterns and breast cancer risk, estimated via factor analysis in various populations, is not conclusive. New studies are required, along with a collective effort by nutritional epidemiology scholars to improve the collection instruments and existing methods for the definition of dietary patterns. Efforts in this regard are underway,[77] and are expected to aid future research efforts and outcomes.

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