

Breast Cancer Risk and Mortality and Adherence to Plant-Based Diets: A Systematic Review and Meta-Analysis

Mariana Del Carmen Fernández-Fígares Jiménez ¹; José Francisco López-Gil ^{2,3,*}; Paula Marrero-Fernández^{4,5}; Miguel López-Moreno ⁵

¹School of Medicine, University of Granada, Granada, 18016, Spain; ²School of Medicine, Universidad Espíritu Santo, Samborondón, 092301, Ecuador; ³Faculty of Health Sciences, Universidad Autónoma de Chile, Santiago, 7500000, Chile; ⁴Department of Chemical Engineering and Pharmaceutical Technology, University of La Laguna, Santa Cruz de Tenerife, 38001, Spain; ⁵Diet, Planetary Health and Performance, Faculty of Health Sciences, Universidad Francisco de Vitoria, Pozuelo, Madrid, 28223, Spain

*Corresponding Author: José Francisco López-Gil, School of Medicine, Universidad Espíritu Santo, Km 2.5 Vía La Puntilla, Samborondón 092301, Ecuador (josefranciscolopezgil@gmail.com).

Context: Plant-based dietary patterns have been associated with a lower risk of several types of cancer. Yet, their specific association with breast cancer (BC) risk and survival remains unclear.

Objective: To evaluate the association of adherence to a plant-based diet index (PDI), unhealthy plant-based diet index (uPDI), and healthy plant-based diet index (hPDI) with BC risk and BC-specific mortality.

Data sources: The Web of Science, Scopus, and PubMed databases were searched from inception to August 2025.

Data extraction: Case-control and cohort studies evaluating the association among the PDI, hPDI, and uPDI with BC risk and BC mortality in cancer-free participants at baseline and in BC survivors were reviewed. Details of the studies and main outcomes were extracted independently by 2 researchers.

Data analysis: Among 3020 records screened, 5 cohort and 4 case-control studies met the inclusion criteria. The PDI was not associated with BC risk in case-control (odds ratio [OR] = 0.72; 95% CI, 0.42-1.25) and cohort studies (hazard ratio [HR] = 0.96; 95% CI, 0.90-1.03). Participants with higher adherence to the hPDI had a lower BC risk in case-control (OR = 0.61; 95% CI, 0.49-0.77) and cohort studies (HR = 0.91; 95% CI, 0.86-0.97). Higher adherence to the uPDI was associated with increased BC risk in case-control (OR = 1.63; 95% CI, 1.20-1.22) and cohort studies (HR = 1.06; 95% CI, 0.98-1.15).

Conclusions: Higher adherence to the hPDI was associated with reduced BC risk, whereas adherence to the uPDI was associated with increased BC risk. Studies are needed to evaluate the role of plant-based diets in BC prognosis and survival.

Systematic Review Registration: PROSPERO registration No. CRD420251115296

Key words: diet, plant-based, breast cancer, breast cancer survival, breast cancer mortality, unhealthy plant-based diet, healthy plant-based diet.

INTRODUCTION

Globally, cancer represents the second leading cause of death after cardiovascular diseases.¹ In 2023, there were 18.5 million incident cases of cancer and 10.4 million

deaths, contributing to 271 million disability-adjusted life-years worldwide.¹ Breast cancer (BC) accounts for 11.6% of all cancer cases, representing the most frequently diagnosed malignancy and the leading cause of cancer-related death among women.² This disease is

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influenced by hormonal factors, such as age at menarche and menopause, and circulating estrogen levels, as well as by metabolic factors, including insulin growth factor 1, obesity, and insulin resistance.^{3–8} Lifestyle, particularly diet, may modulate many of these determinants and therefore plays an important role in BC risk.⁹

Plant-based diets emphasize the consumption of foods derived from plants, such as vegetables, fruits, legumes, whole grains, nuts, and seeds, while limiting or excluding animal products.¹⁰ These diets range from fully vegan patterns, which exclude all animal foods, to predominantly plant-based patterns that include moderate amounts of animal products.¹⁰ Contrary to animal foods, whole plant foods provide dietary fiber, folate, and phytochemicals, with recognized anticancer properties, and have a lower or negligible content in saturated fat, cholesterol, and cancer-promoting compounds, such as advanced glycation end products, aromatic polycyclic hydrocarbons, oncogenic viruses, and heme iron.¹¹ Compared with animal food-containing diets, adherence to a plant-based diet has been associated with improvements in several established BC risk factors, including body fat mass, insulin resistance, and systemic inflammation.^{12–15} Moreover, cohort studies have observed that substituting animal protein sources with plant-based proteins, such as legumes and nuts, is associated with a reduced risk of BC.^{16–19} In line with this evidence, current dietary guidelines for cancer prevention, including the European Code Against Cancer developed by the International Agency for Research on Cancer, recommend following a diet based on vegetables, whole grains, legumes, and fruits; limiting the consumption of red meat, salty foods, and foods high in added sugars and fats; and avoiding processed meat.²⁰

To assess the adherence and quality of plant-based diets, a plant-based diet index (PDI), healthful plant-based diet index (hPDI), and unhealthful plant-based diet index (uPDI) have been developed and are widely used in epidemiological research.²¹ The PDI captures overall adherence to plant-based eating, the hPDI emphasizes higher intake of whole and minimally processed plant foods, and the uPDI reflects diets rich in refined grains, sugary beverages, and other less healthful plant foods. Distinguishing between hPDI and uPDI is relevant because not all plant-based diets confer the same health effects, and dietary quality may substantially influence cancer risk. Notably, higher scores on the PDI and the hPDI have been associated with lower risk of several cancers, including lung, prostate, breast, and digestive cancers.^{22–25}

Previous meta-analyses have reported that higher adherence to the PDI is associated with reduced overall cancer risk²⁶ and mortality.²⁷ However, these analyses did not specifically examine BC risk and survival. Addressing this gap is essential to provide a comprehensive assessment

of the potential role of plant-based diets in BC prevention, particularly given that BC represents the largest global burden in terms of incident cases. Accordingly, in this systematic review and meta-analysis, we examined the associations of adherence to plant-based dietary patterns, as assessed by the PDI, hPDI, and uPDI, with BC risk and mortality.

METHODS

This systematic review and meta-analysis were registered in the International Prospective Register of Systematic Reviews (identifier CRD420251115296) and carried out following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, as well as the Strengthening the Reporting of Observational Studies in Epidemiology checklist.²⁸

Information Sources and Search Strategy

Three electronic databases (Web of Science, Scopus, and PubMed) were examined from inception to August 24, 2025, by 2 independent researchers (M.C.F.-F.J. and P.M.-F.). These databases were chosen because they provide structured indexing and reliable filtering tools, ensuring a more comprehensive, accurate, and replicable search. Moreover, the reference lists of the included articles were also checked to ensure we did not miss potentially eligible studies. The search strategy was based on the following groups of search terms: (a) plant-based diet*, healthy plant-based diet*, unhealthy plant-based diet*, Plant Diet Index*, unhealthful Plant Diet Index*, healthful Plant Diet Index*, vegan diet*, vegetarian diet*; (b) breast cancer*, breast neoplasms*, breast cancer survival*, breast cancer mortality*. The specific search terms and the number of records found in each of the mentioned databases are detailed in [Table S1](#).

Selection Criteria

Studies were eligible for inclusion in this meta-analysis if they met the following PICOS criteria: (1) population: cancer-free individuals and BC survivors (individuals who have received a BC cancer diagnosis) aged >18 years; (2) exposure: adherence to PDI, hPDI, and uPDI; (3) outcome: BC risk and BC-specific mortality; and (4) study design: cohort and case-control studies were included ([Table 1](#)). The exclusion criteria included the following: editorials, abstracts, grey literature (ie, theses, conference proceedings, preprints), cross-sectional analysis, systematic reviews and/or meta-analyses, narrative reviews, and experimental and qualitative studies. Only studies that assessed adherence using the PDI, the uPDI, and the hPDI were included.

Table 1. PICOS Criteria for Inclusion and Exclusion of Studies

Parameter	Inclusion criterion	Exclusion criterion
Population	Cancer-free individuals aged ≥ 18 y BC survivors aged ≥ 18	Individuals aged < 18 y
Intervention/ exposure	PDI, hPDI, uPDI	Studies using other indices (eg, glycemic index, dietary inflammatory index)
Comparison	Studies that compared different levels of adherence to the PDI, hPDI, and uPDI	Studies that did not compare different levels of adherence to the PDI, hPDI, and uPDI
Outcome	BC risk BC-specific mortality	Health outcomes other than BC incidence and BC mortality
Study design	Case-control Cohort	Editorials, abstracts, congress communications, theses, preprints, cross-sectional analysis, systematic reviews and/or meta-analyses, narrative reviews, and experimental and qualitative studies

Abbreviations: BC, breast cancer; PDI, plant-based diet index; hPDI, healthy plant-based diet index; uPDI, unhealthy plant-based diet index.

Studies using other indices were excluded. No language restrictions were applied.

Rayyan software was used to remove duplicate records after the identification of eligible studies in each database. Titles and abstracts were independently screened by 2 researchers (M.C.F.-F.J. and P.M.-F.) to identify potentially relevant articles. Full texts of the studies selected by both reviewers were then independently assessed for eligibility, with any disagreements resolved through discussion with a third researcher (M.L.-M.).

Data Extraction Process and Data Items

Data extraction was conducted independently by 2 researchers (M.C.F.-F.J. and M.L.-M.) to ensure accuracy and reliability. One researcher (M.C.F.-F.J.) performed the data extraction, and a second researcher (M.L.-M.) double-checked the extracted data. In cases of disagreement, the 2 investigators reached a consensus.

Data were extracted into a structured database using Excel (Microsoft, Redmond, WA). Extracted variables included design, year of publication, sample size, mean age, country, duration, plant-based diet adherence outcomes, type of effect size reported, and adjustment covariates. One author (M.C.F.-F.J.) performed the data extraction, and another (M.L.-M.) reviewed the adequacy of the variables. Studies excluded after full-text review, along with the reasons for their exclusion, are provided in [Table S2](#).

Risk of Bias

The risk of bias was assessed by 1 researcher (M.C.F.-F.J.) and reviewed by a second (M.L.-M.) to ensure accuracy, using the Risk of Bias in Nonrandomized Studies of Exposure (ROBINS-E) tool, which encompasses the following 7 domains: bias due to confounding, departure from intended exposures, missing data, bias in the selection of participants, classification of exposures, measurement of outcomes, and the selection of reported results.²⁹ Studies were classified as low risk, moderate

risk, serious risk, and critical risk of bias under each domain. The detailed results of the risk-of-bias evaluation are presented in [Table S3](#).

Statistical Analysis

All analyses were performed using R software (version 4.3.0; R Core Team, Vienna, Austria) and RStudio (version 2023.03.1; Posit, Boston, MA). Effect sizes were expressed as odds ratios (ORs) with 95% CIs for case-control studies and as hazard ratios (HRs) with 95% CIs for cohort studies. For case-control studies, we used the effect estimates as reported by the original authors. For longitudinal studies, data from the latest available follow-up were prioritized. Whenever studies provided both adjusted and unadjusted results, we extracted the adjusted estimates to maximize comparability across studies. When available, we used the effect estimates reported by the authors derived from comparisons between extreme quintiles of the exposure. If such estimates were not provided, we used those corresponding to a 10-point increase in the index.

Pooled analyses were conducted separately for ORs and HRs using random- and fixed-effects inverse-variance models, with between-study variance estimated by the restricted maximum likelihood method. Between-study heterogeneity was assessed using the Cochran's Q test, with statistical significance determined by a P value of $< .05$, and quantified with the inconsistency statistic (I^2). Thresholds for I^2 values were interpreted as follows: 0%-40% (might not be important), 30%-60% (moderate heterogeneity), 50%-90% (substantial heterogeneity), and 75%-100% (considerable heterogeneity). $P < .05$ was considered statistically significant.

RESULTS

Study Selection

A total of 6411 records were identified through the initial search ([Figure 1](#)). After removing duplicates, 3020

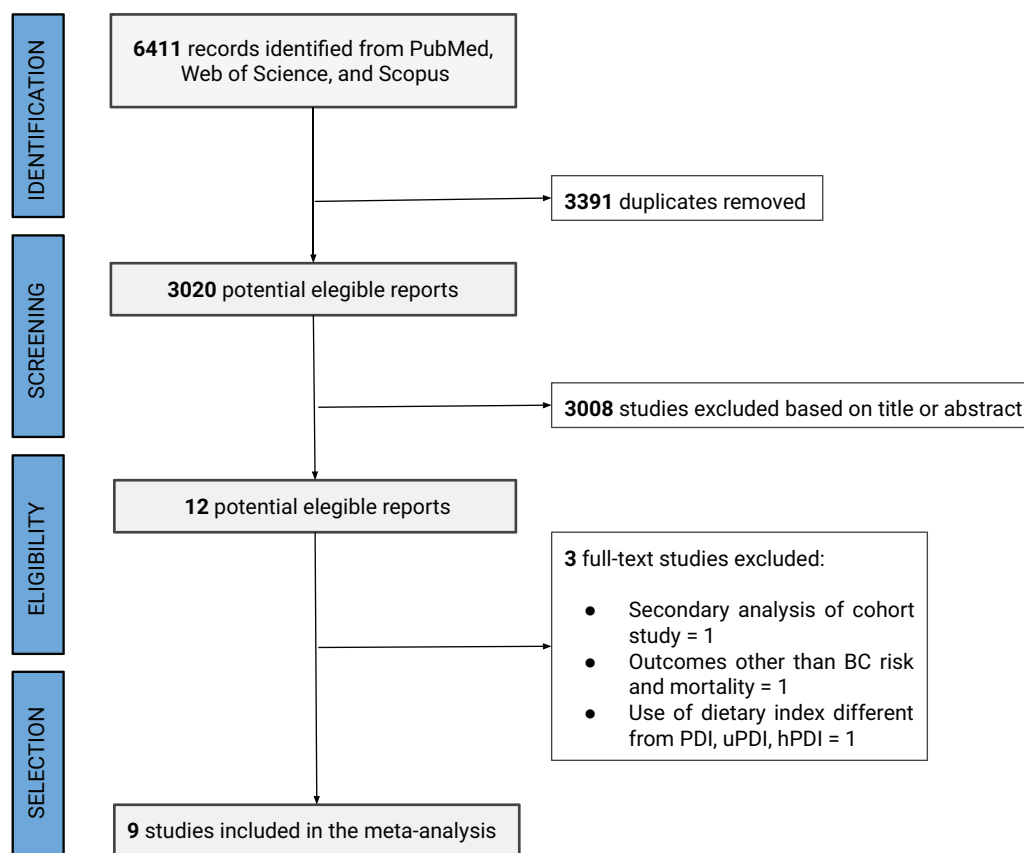


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses Flow Diagram

Abbreviations: BC, breast cancer; hPDI, healthful plant-based diet index; PDI, plant-based diet index; uPDI, unhealthful plant-based diet index.

records remained and were screened by title and abstract. Twelve full-text articles were subsequently assessed for eligibility, of which 9 were included in the systematic review and meta-analysis. The reasons for excluding articles at the full-text stage are presented in Table S2.

Study Characteristics

The characteristics of the 9 studies included are summarized in Table 2. Four studies were conducted in Iran,^{30–33} 2 in the United States,^{25,34} 1 in France,³⁵ 1 in the United Kingdom,³⁶ and 1 included data from a variety of European countries participating in the European Prospective Investigation into Cancer and Nutrition.³⁷ Five articles reported on cohort studies,^{25,34–37} and 4 reported on case-control studies.^{30–33} Eight studies evaluated BC risk,^{25,30–33,35–37} and 1 study evaluated BC recurrence and mortality.³⁴ Because only 1 study evaluated mortality, the meta-analysis was restricted to BC risk. The study evaluating BC recurrence was considered in the meta-analysis because it addresses BC risk among BC survivors.³⁴

Participants in the included studies were women; none evaluated BC in men.

A total of 7 studies applied the PDI, the uPDI, and the hPDI,^{25,30–34,37} and 2 studies evaluated only the uPDI and the hPDI.^{35,36} Multivariate analysis for the adjustment of potential confounders was conducted in all the studies. Established BC risk factors, such as physical activity, body mass index, and hormonal therapy use, were uniformly adjusted in the included studies.

Plant-Based Diets and BC Survival

Anyene et al³⁴ evaluated BC recurrence and BC-specific mortality among BC survivors. Higher adherence to the hPDI, the overall PDI, and the uPDI was not significantly associated with either outcome.

Plant-Based Diets and BC Risk

Higher adherence to the PDI was not significantly associated with BC risk (for case-control studies, OR = 0.72 [95% CI, 0.42–1.25]^{30–33}; for cohort studies, HR = 0.96

Table 2. Baseline Characteristics of Published Studies Examining Plant-Based Dietary Patterns and Breast Cancer Cases

Reference	Study name	Region	Disease outcome	No. of cases/Total	Mean age (SD), y	Mean BMI (SD), kg m ⁻²	Follow-up (y)	Diet assessment	Exposure	Disease ascertainment	Model adjustment
Anyene et al., 2021	Pathways Study	Kaiser Permanente Northern California	BC recurrence; all-cause BC-specific; non-BC mortality	461/3646 recurrences; 653/3646 deaths	60 (SD 12)	28 (SD 7)	Median 9.51 (deaths), 9.2 (recurrence). Range 0.05-12.9	Validated FFQ. Used to compute PDI, hPDI, uPDI.	PDI, hPDI, uPDI	BC diagnosis characteristics (stage, ER, HER2 status) from VDW tumor file, based on KPNC Cancer Registry	M1: age at diagnosis, total energy intake, physical activity M2: M1 plus education, race/ethnicity, smoking status, menopausal status, HER2 status, and stratified by tumor stage and ER status
Payandeh et al., 2021	Hospital-based case-control study	Tehran, Iran	BC incidence	150 BC cases/300 total participants (n = 150 control participants)	46.6 (SD 10.7) (for both case and control participants)	28.0 (SD 5.21) for control participants, 28.1 (SD 4.66) for case participants	Case-control study (cases had a 3-mo history of diagnosis)	Semi-quantitative FFQ	PDI, hPDI, uPDI	Newly diagnosed BC cases	M1: age, energy intake, BMI M2: M1 plus physical activity, education, marital status, alcohol use, smoking status, dietary supplements, and medication use, comorbidities, HRT history, oral contraceptive use, age at menarche, time since menopause, weight at age 18 y, first pregnancy age, breastfeeding length, family history of BC
Rigi et al., 2021	Population-based case-control study	Isfahan, Iran	BC risk	350 BC case patients/1050 total participants (n = 700 control participants)	Overall: 62.4; control participants, 61.4 (SD 10.3); case patients, 65.2 (SD 11.2)	Control participants 25.5 (SD 5); case patients 21.8 (SD 4.8)	Case-control study (case patients had a maximum 6-mo history of diagnosis)	Semi-quantitative dish-based FFQ	PDI, hPDI, uPDI	Diagnosis confirmed by physical examination, mammography, and pathological verification	M1: age, energy intake M2: M1 plus education, socioeconomic status, residential area, supplement use, family history of BC, disease history, physical activity, marital status, smoking status, alcohol consumption, breastfeeding history, menopausal status
Romanos-Nanclares et al., 2021	Nurses' Health Studies	United States	Incident invasive BC (total, ER-positive, ER-negative)	12 482 incident invasive BC cases/169 985 total participants (76 690 from NHS; 93 295 from NHSII)	NHS: 50.2 (SD 7); NHSII 36.5 (SD 4.8)	Not explicitly stated as a single mean, but participants with higher BMI had lower BMI	Up to 2016 (NHS) or 2017 (NHSII)	FFQ	PDI, hPDI, uPDI	Self-reported cases confirmed by medical records (pathology reports)	M3: M2 plus BMI Multivariate model: race, socioeconomic status, age at menarche, age at menopause, postmenopausal hormone use, oral contraceptive use, parity, age at first birth, breastfeeding history, height, alcohol intake, total caloric intake, physical activity, BMI at age 18 y

(continued)

Table 2. Continued

Reference	Study name	Region	Disease outcome	No. of cases/Total	Mean age (SD), y	Mean BMI (SD), kg m ⁻²	Follow-up (y)	Diet assessment	Exposure	Disease ascertainment	Model adjustment
Sasanfar et al., 2021	Case-control	Tehran, Iran	BC risk	412 case patients/ 868 total (456 control participants)	Case patients: 46.2 (SD 10.3); control participants 44.2 (SD 11.1)	Case patients 28.1 (SD 5.2), control participants 28.7 (SD 6.1)	Not applicable (case-control, cases diagnosed within past year)	Validated FFQ	PDI, hPDI, uPDI	Pathologically confirmed BC in case patients (within past year), healthy control participants with no other cancers or dietary restrictions	Age and energy adjusted M1: age, energy, physical activity, family history of BC, education, parity, marital status M2: M1 plus BMI
Shah et al., 2023	E3N Cohort Study	France	Incident postmenopausal BC	3968 cases/65 574 participants	52.9 (SD 6.7) at baseline	22.92 (SD 3.22)	Mean: 21 y (1993-2014)	Validated FFQ at baseline (1993) and follow-up (2005)	PDI, hPDI, uPDI	Self-reported on questionnaires, confirmed by pathological reports (ER, PR, histology)	M1: age-adjusted M2: M1 cov plus physical activity, educational level, smoking status, family history of BC, age at menarche, age at first childbirth, ever breastfeeding, ever use of MHT, ever use of contraceptive pill, past history of benign breast disease, mammography in last follow-up-cycle M3: M2 cov plus BMI, energy intake (excluding alcohol), alcohol
Shah et al., 2025	EPIC	European (multi-country)	Incident invasive BC	1005 cases/ 25 8343 women	50.9 (SD 10.0) at baseline	24.9 (SD 4.4)	Median 14.9	Validated dietary questionnaire (both quantitative and semi-quantitative FFQ)	PDI, hPDI, uPDI	Population-based cancer registries or a combination of methods (health insurance records, cancer/pathology registries, active contact)	M1: center and age M2: M1 plus height, educational level, physical activity index, smoking status, family history of BC, age at menarche, parity, age at first full-term birth, ever breastfeeding, menopausal status at baseline, age at menopause, ever use of contraceptive pill, ever use of menopausal hormone therapy, alcohol intake. M3: M2 plus BMI

(continued)

Table 2. Continued

Reference	Study name	Region	Disease outcome	No. of cases/Total	Mean age (SD), y	Mean BMI (SD), kg m ⁻²	Follow-up (y)	Diet assessment	Exposure	Disease ascertainment	Model adjustment
Souni et al., 2025	Case-control	Tehran, Iran	BC odds/risk	133 case patients/ 398 total (265 control participants)	Case patients: 49.5 (SD 10.7), control patients: 47.1 (SD 10.1)	Case patients: 29.6 (SD 7.6), control patients: 28.9 (SD 6.2)	Not applicable (case-control, cases diagnosed within the past 6 mo)	FFQ	PDI, hPDI, uPDI	Case patients: women diagnosed within the past 6 mo histologically. Control participants: women with nonneoplastic diseases from the same hospitals	Age, BMI, family history of cancer, energy intake, fiber intake, menopausal status, vitamin D supplement, physical activity, and smoking
Thompson et al., 2023	UK Biobank	United Kingdom	Postmenopausal BC incidence	1083 cases/ 12 6394 participants	56.1 (SD 7.8)	26.7 (SD 4.6)	10.6 (SD 1.6)	Oxford WebQ tool (based on mean food intakes from a minimum of 2 24-h dietary assessments)	PDI, hPDI, uPDI	Incident postmenopausal BC cases identified by the National Cancer Registries in England, Wales, and Scotland	M1: region, education, sex M2: energy intake, BMI, smoking status, alcohol intake, ethnicity, physical activity, morbidity, polypharmacy, menopausal hormone therapy use, menopausal status at recruitment, age at menarche, ever use of oral contraception, age at first live birth, polygenic risk score for BC

Abbreviations: BC, breast cancer; BMI, body mass index; E3N, Étude épidémiologique auprès de femmes de la Mutuelle Générale de l'éducation Nationale; EPIC, European Prospective Investigation into Cancer and Nutrition; ER, estrogen receptor; FFQ, food frequency questionnaire; hPDI, healthful plant-based diet index; HRT, hormone replacement therapy; HER2, Human Epidermal Growth Factor Receptor 2; KPNC, Kaiser Permanente Northern California; VDW, Virtual Data Warehouse; M1, Model 1; M2, Model 2; M3, Model 3; MHT, Menopausal Hormone Therapy; NHS, Nurses' Health Study; NHSII, Nurses' Health Study II; PDI, plant-based diet index; PR, progesterone; uPDI, unhealthful plant-based diet index.

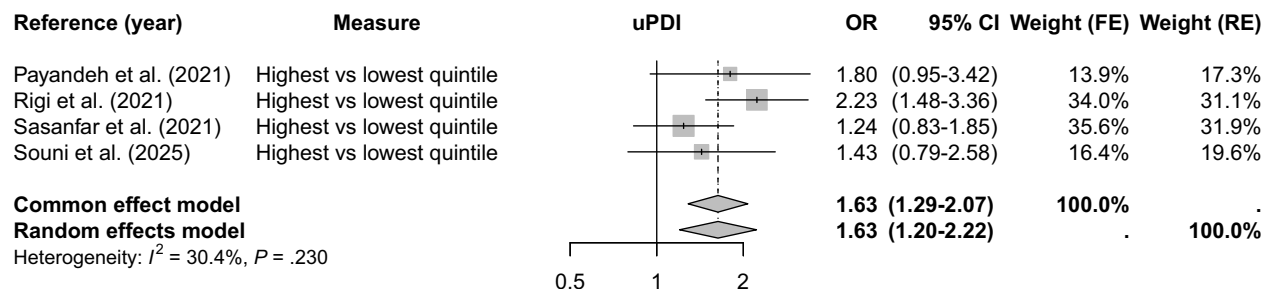


Figure 2. Meta-Analysis: Adherence to a Plant Diet Index and Breast Cancer Risk in Case-Control Studies.

Abbreviations: FE, fixed-effects; RE, random effects; HR, hazard ratio; OR, odds ratio; uPDI, unhealthful plant-based diet index.

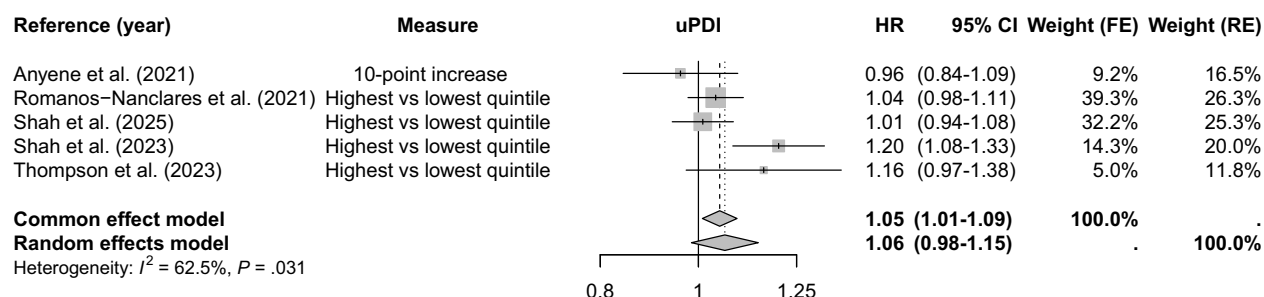


Figure 3. Meta-Analysis: Adherence to a Plant Diet Index and Breast Cancer Risk in Cohort Studies.

Abbreviations: FE, fixed-effects; RE, random effects; HR, hazard ratio; OR, odds ratio; uPDI, unhealthful plant-based diet.

[95% CI, 0.90-1.03]]³⁵⁻³⁷ (Figures 2 and 3). The heterogeneity was high for both study types (for case-control studies, $I^2 = 82.4\%$, $P = .001$; for cohort studies, $I^2 = 76.5\%$, $P = .005$).

Considering the uPDI, a significant positive association with BC risk was observed (for case-control studies, OR = 1.63 [95% CI, 1.20-2.22]³⁰⁻³³; for cohort studies, HR = 1.0 [95% CI, 0.98-1.15])³⁵⁻³⁷ (Figures 4 and 5). Heterogeneity was modest (for case-control studies, $I^2 = 30.4\%$, $P = .23$; for cohort studies, $I^2 = 62.5\%$, $P = .03$). In the case of the hPDI, a significant inverse association with BC risk was observed (for case-control studies, OR = 0.61 [95% CI, 0.49-0.77]³⁰⁻³³; for cohort studies, HR = 0.91 [95% CI, 0.86-0.97])³⁵⁻³⁷ (Figures S1 and S2). Inconsistency was low in case-control studies ($I^2 = 0.0\%$, $P = .51$),³⁰⁻³³ and moderate in cohort studies³⁵⁻³⁷ ($I^2 = 48.6\%$; $P = .10$).

Risk of Bias in Studies

The risk of bias was assessed by applying the ROBINS-E tool to the 9 included studies. Among these studies, 5 were classified as having a low risk of bias, and 4 were identified as having a moderate risk of bias (Table S3).

DISCUSSION

This study represents the first comprehensive meta-analysis examining the association between plant-based diets, assessed via the PDI, the uPDI, and the hPDI, and BC outcomes. We found that overall adherence to a plant-based diet was not associated with BC risk. However, when diet quality was considered, higher adherence to a healthful plant-based diet, characterized by greater intake of fruits, vegetables, whole grains, nuts, and legumes, was associated with a reduced risk of BC. Conversely, higher adherence to an unhealthful plant-based diet, characterized by greater intake of sugar-sweetened beverages, potato products, sweets/desserts, and refined grains, was associated with an increased BC risk. These results underscore the potential role of a healthful plant-based diet in BC prevention, aligning with previous evidence suggesting that plant-based dietary patterns are associated with lower overall cancer risk.

A previous systematic review evaluated the association between plant-based diets and BC recurrence and mortality and found an inverse association.³⁸ However, that study differed from ours in that it also considered other diets, such as the low-fat and prudent dietary patterns, did not assess the relation with primary BC risk,

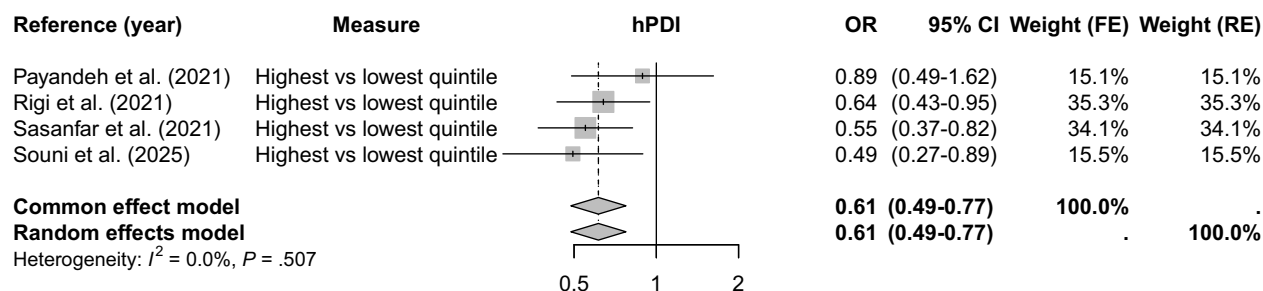


Figure 4. Meta-Analysis: Adherence to an Unhealthful Plant Diet Index and Breast Cancer Risk in Case-Control Studies

Abbreviations: FE, fixed-effects; RE, random effects; HR, hazard ratio; OR, odds ratio; hPDI, healthful plant-based diet.

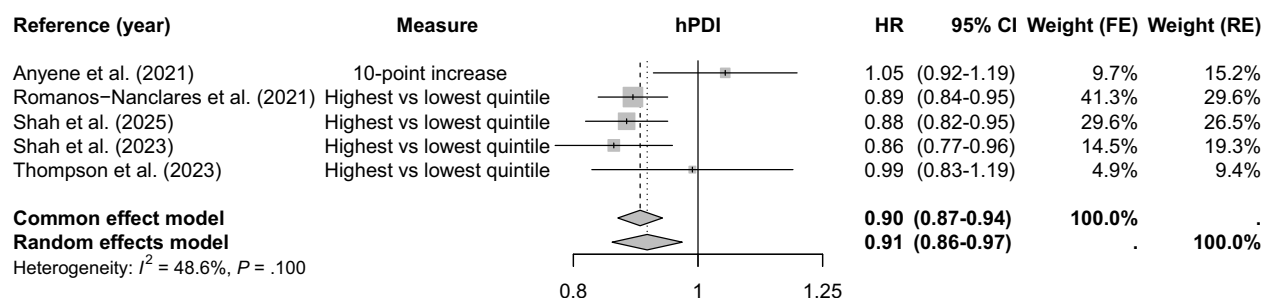


Figure 5. Meta-Analysis: Adherence to an Unhealthful Plant Diet Index and Breast Cancer Risk in Cohort Studies

Abbreviations: FE, fixed-effects; RE, random effects; HR, hazard ratio; OR, odds ratio; hPDI, healthful plant-based diet.

and did not perform a meta-analysis.³⁸ Meta-analyses have explored the association between BC risk and certain food groups and dietary patterns, such as the animal food pattern, the Western pattern, and the Healthy Eating Index, but none of them, to our knowledge, has yet evaluated the relation between the PDI, the hPDI, the uPDI, and BC risk.³⁹

Several cohort studies have shown that greater adherence to a pro-inflammatory diet, measured by the dietary inflammatory index, is associated with higher BC risk and BC-specific mortality.^{40,41} These findings align with our meta-analysis, because dietary compounds present in healthful plant foods, particularly dietary fiber and phytochemicals, are scored as anti-inflammatory in the dietary inflammatory index, whereas compounds typically found in animal foods and unhealthful plant foods, such as saturated fat, dietary cholesterol, and refined carbohydrates, score as pro-inflammatory.⁴² In this line, adherence to the Mediterranean diet has been associated with a reduced risk of BC in various cohort studies, particularly among postmenopausal women.⁴³ Considering the 14-item Mediterranean Diet Adherence Screener, greater adherence to a Mediterranean diet implies increased consumption of vegetables, whole grains, legumes, and nuts, and lower intake of red meats, butter, and other saturated fat-rich sources, sugar-sweetened beverages, and refined grains. Furthermore, cohort studies using substitution

analysis have found that the replacement of animal sources of protein, such as red meat and cow's milk, with plant sources of protein, such as legumes and nuts, is associated with decreased risk of BC.^{16,18,19} These observations support the notion that the health benefits of the Mediterranean diet are largely mediated by its plant-based components, which is consistent with the results of our meta-analysis.

Several mechanisms may explain the protective effects of plant-based diets on BC risk. Compared with diets containing animal foods, entirely plant-based diets emphasizing whole plant foods have been shown to reduce levels of visceral, hepatocellular, and intramyocellular lipids, total body fat, and insulin resistance¹²⁻¹⁴—all recognized BC risk factors.^{6,7} In patients with BC, the adoption of a whole-foods plant-based diet has been associated with lower testosterone and higher sex-hormone-binding globulin concentrations, indicative of enhanced insulin sensitivity, as well as reduced levels of tumor markers.¹⁵ Additionally, increasing the intake of fiber-rich plant foods, specifically whole grains and legumes, lowers circulating estrogen levels by promoting fecal excretion, which may contribute to BC prevention.⁴⁴ Specifically, soluble (ie, β -glucans, xylogalacturonans) and nonsoluble (ie, arabinoxylans) fibers in whole grains and legumes modulate bacterial β -glucuronidase activity within the gut and increase fecal mass, thus favoring estrogen elimination through feces.¹¹

The benefits of higher adherence to a healthful plant-based diet may be further supported by the concomitant reduction in animal-food intake. Diets high in animal foods and saturated fat increase levels of inflammatory endotoxins, ectopic fat, and insulin resistance.^{45,46} Furthermore, dairy and overall animal protein intakes are associated with increased height, earlier age at menarche,^{47–50} and higher levels of circulating insulin growth factor 1^{50,51} and free estradiol,⁵² all of which are consistently linked to higher BC risk.^{3,4,8,53} In addition, animal foods promote endogenous acid generation, due to their higher protein content (particularly sulfur-chain amino acids), phosphorus, and their lower content in potassium and magnesium.⁵⁴ Cohort studies suggest that increased scores in potential renal acid load and net endogenous acid production, meaning an acidogenic diet, are associated with an augmented risk of BC.⁵⁵ Furthermore, animal foods contribute positively to the Empirical Dietary Index for Hyperinsulinemia, which is associated with increased BC risk and worse BC survival.^{56,57}

In our study, greater adherence to the PDI was not associated with BC risk, and, in the case of the uPDI, it was even associated with a higher risk, highlighting that the quality of the plant foods included is also crucial for BC prevention. This is consistent with previous cohort studies showing that increased total sugar and added sugar intakes are associated with increased BC risk.⁵⁸ Furthermore, unhealthful plant foods commonly contain additives, such as mono- and diglycerides of fatty acids, which have been positively associated with BC risk.⁵⁹ It is also worth mentioning the case of sweets and desserts, including chocolates, cookies, brownies, doughnuts, cake, sweet rolls, and pie, which are classified as unhealthful plant foods, even though they are not strictly plant-based, because they frequently contain animal-origin ingredients such as eggs, butter, cream, and milk.²¹ Therefore, the unfavorable associations observed for some unhealthful plant foods may be mediated, at least in part, by the presence of animal-derived ingredients, despite their classification within the uPDI as plant-based items.

Strengths and Limitations

To our knowledge, this is the first meta-analysis specifically assessing the association between PDI, hPDI, and uPDI and BC risk. Dietary indexes evaluated in previous meta-analyses, such as the Mediterranean Diet Adherence Screener and Healthy Eating Index, do not classify animal and plant foods in distinct groups, making it difficult to determine their differential effects on BC. The present work addresses such a limitation, because only studies that used a PDI, hPDI, or

uPDI were included. Additional strengths include that all included studies conducted multivariable adjustment for potential confounders and that a systematic risk of bias assessment was performed using the ROBINS-E tool.

However, several limitations should be considered. First, dietary exposures in the included studies were assessed through food frequency questionnaires, which may introduce recall bias, response bias, social desirability bias, and misclassification.⁶⁰ Considering that the dietary information obtained through food frequency questionnaires may not accurately reflect what participants are actually consuming, it would be valuable for future observational studies also to incorporate objective measures (eg, urine, blood, or stool biomarkers). Second, although all studies performed multivariable adjustment for potential confounders, their observational nature means residual or unmeasured confounding cannot be excluded. Third, high heterogeneity across studies was found when considering the PDI, although it became low and modest when assessing the hPDI and uPDI. Fourth, the included studies used different comparison approaches (eg, per unit increase, first vs fifth quintile), and categories such as quintiles or tertiles varied across studies, meaning the lowest quintile in 1 study may not be comparable to the lowest quintile in another. Therefore, researchers are encouraged to report results using both categorical (eg, quintiles or tertiles) and continuous (per unit increase) exposures. Fifth, only studies conducted in Europe, Iran, and the United States were found, which limits the generalizability of our results to other world regions, such as Africa and Latin America. Finally, it was not possible to conduct a meta-analysis for BC-specific mortality, because only 1 study assessed this outcome.

CONCLUSIONS

Our findings suggest that adherence to a healthful plant-based diet is associated with a lower risk of BC, whereas an unhealthful plant-based diet is associated with an increased risk. Given the limited feasibility of randomized clinical trials directly testing the effects of plant-based diets on BC risk, the present systematic review and meta-analysis of observational studies provide important supporting evidence on the potential beneficial effects of this dietary pattern, particularly those emphasizing healthful plant foods, against BC development. Based on the current evidence, dietary guidelines for BC prevention should promote the substitution of animal foods and unhealthful plant foods with healthful plant foods. Cohort and intervention studies are needed to assess the impact of plant-based diets on BC prognosis and survival.

Author Contributions. All authors were involved in the design and critical revision of the manuscript. M.C.F.-F. J. drafted the manuscript. M.C.F.-F.J. and P.M.-F. conducted the data search, screening, and study selection. J. F.L.-G. conducted the statistical analysis. M.L.-M. participated in the drafting of the manuscript and supervised the entire process.

Supplementary Material

Supplementary Material is available at *Nutrition Reviews* online.

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Conflicts of Interest

M.L.-M. reports having received funding from Danone and Foods For Tomorrow for previous research projects. M.L.-M. did not receive any funding for the present systematic review and meta-analysis. All other authors reported no conflicts of interest.

Data Availability

This systematic review does not include original data. Data were extracted from the literature and are publicly available. The data set generated for the present analyses is available upon request to the corresponding author.

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Meta-Analysis