Master in Nutrition and Metabolism

MASTER THESIS

Title:

Association between plant-based diet index and cancer risk: A systematic review

Author:

Karina Estefania Gavin Quinchuela

Advisor:

Paula Jakszyn, PhD

Research group:

Nutrition and Cancer Unit (UNAC) - Catalan Institute of Oncology

Bellvitge Biomedical Research Institute (IDIBELL)

September – 2023

INDEX

ABSTRACT

Background:

Plant-based dietary pattern have been recommended for improving health outcomes including cancer. However, not all plant foods are necessarily beneficial for health. The aim of this systematic review is to assess the relationship between healthful and unhealthful plant-based diets and the risk of cancer.

Methods:

A systematic search was conducted in PubMed, and a total of 12 prospective cohort studies and 5 case-control published between 2018 and 2023 were selected. Data of the multivariable-adjusted relative risks (RRs), Hazard ratio (HRs) and odd ratio (ODs) 95% confidence intervals (CIs) comparing the highest and lowest score of plant-based diet index were obtained from the original articles and reported.

Results:

Evidence gathered from prospective and cohort studies showed that a healthy plant-based diet (hPDI) was associated with a decrease of risk breast, colorectal, digestive cancer (gastrointestinal and liver) and lung cancer. In contrast, an unhealthy plant-based diet (uPDI) was associated with a higher risk of breast, colorectal and stomach cancer.

Conclusion:

The available evidence supports the benefits of a healthy plant-based diet with a lower risk of cancer. However, additional research on large and prospective studies is needed to confirm these findings.

Key Words: Plant-based diet index, healthy plant-based diet, unhealthy plant-based diet, cancer risk

INTRODUCTION

Dietary patterns: definition and importance

Dietary patterns are defined as the quantities, proportions, variety, or combination of different foods and drinks in diets and the frequency with which they are habitually consumed [1]. Dietary pattern encompasses the entire diet and considers the interactions and cumulative effects of multiple foods and nutrients on health outcomes. The food combinations consumed in diets reflect individual food preferences modulated by a mix of genetic, cultural, social, health, environmental, lifestyle, and economic determinants and can vary widely between different countries and regions [2].

The study of dietary patterns has gained greater attention and significance in recent decades due to significant changes in eating habits and their impact on public health. Many societies have undergone significant shifts in their dietary habits due to urbanization, globalization, and changes in food production and availability. Traditional diets rich in whole foods, fruits, and vegetables have been replaced by diets high in processed foods, unhealthy fats, added sugars, and low in fiber. This has led to increased rates of obesity, cardiovascular disease, type 2 diabetes, and other diet-related chronic diseases [3,4]. As these health problems have become global epidemics, there has been an urgent need to understand how dietary patterns influence health and how effective strategies can be developed to promote healthy eating habits. Furthermore, dietary patterns research has also been driven by the recognition that nutrition is a multidimensional approach that goes beyond the simple analysis of individual nutrients by taking into account synergistic or antagonistic interactions between different diet components [5]. Understanding how different foods interact and how overall dietary patterns affect health is critical to addressing current nutritional challenges and promoting public health.

Additionally, in the field of nutritional epidemiology, the study of dietary patterns is important because it allows the identification of associations between specific dietary patterns and the risk of developing certain diseases by observing dietary habits and health status of people over time [2,6].

Methods for Defining Dietary Patterns

In the field of studying dietary patterns, several important methodologies have been developed. These methods can be broadly categorized into two main types: 1) a priori methods, also called investigator-defined methods and 2) a posteriori method also referred to as data-driven methods. Each of these methods offers a comprehensive or summary assessment of eating behaviors. However, it is important to recognize that the choice of a specific method will depend on the research question due to each approach gives a different perspective [7].

A priori methods

A priori methods are determined by researchers to characterize intakes based on prior knowledge, hypotheses about diet–disease mechanisms, guidelines, and recommendations using prespecified criteria. The researcher set the attributes, including food components or items, indicators, criteria, and cut points to form the dietary pattern [8]. The classification of the attributes can be based on nutrients, types of food, or a combination of nutrient and food intake. The cut-off points are commonly selected based on national dietary guidelines, food selection guides, and nutrient reference values. Subsequently, based on the pre-established attributes and criteria, the dietary intakes of individuals are scored to assess the degree of alignment with the specified dietary pattern [9]. Dietary quality indices or scores evaluate the degree to which individuals adhere dietary guidelines and recommendations, enabling an assessment of the overall dietary quality in the population and the prediction of potential diseases. There are some commonly used a priori methods for assessing dietary patterns:

Healthy Eating Index (HEI): HEI is a scoring system developed by the United States Department of Agriculture (USDA) to measure adherence to the Dietary Guidelines for Americans. It assesses the intake of various food groups and nutrients, such as fruits, vegetables, whole grains, dairy, protein foods, added sugars, saturated fats, and sodium. The index generates a score that reflects overall diet quality [10].

Mediterranean Diet Score: This scoring system evaluates adherence to the Mediterranean diet, which is characterized by high consumption of fruits, vegetables, whole grains, legumes, nuts, seeds, and olive oil, moderate intake of fish, poultry, and dairy, and limited consumption of red meat and processed foods. The score assigns points based on the consumption of these food groups and nutrients [11].

Dietary Approaches to Stop Hypertension (DASH) Score: The DASH scoring system evaluates adherence to the DASH diet, which aims to reduce blood pressure and promote heart health. It emphasizes fruits, vegetables, whole grains, low-fat dairy products, lean proteins, and limits sodium, saturated fats, and added sugars. The score is derived from the intake of these food groups and nutrients [12].

A posteriori methods

These methods refer to the dietary intake patterns derived from population data using a range of multivariate statistical approaches. These approaches utilize data already collected from food frequency questionnaires, 24-h recall questionnaires or dietary records to obtain dietary patterns. A priori methods offer valuable insights into the dietary behaviors that currently exist [13]. The main limitations of this method is the subjectivity on the part of the researchers. One of the decisions that researchers must make and that influence all data-driven methods is the classification of the food groups used as input variables for statistical analysis. This subjective step is considered since the classification of foods can be based on food composition databases, which could be classified by their nutrient content or other characteristics. Additionally, dietary patterns consider culinary aspects of food, its use, and form of consumption [14]. However, these aspects vary depending on the countries and population groups, so the form of food categorization will depend on the objectives and research questions.

Principal component analysis (PCA) and factor analysis: Principal component analysis is commonly used to define dietary patterns because the principal components are certain mathematical functions of the observed variables. Factor analysis is a multivariate statistical technique to identify common underlying dimensions (factors or patterns) of food consumption. It combines particular food items or food groups based on the extent to which they are correlated with each other in the dataset. Subsequently, a summary score for each pattern is then derived, which can be employed in correlation or regression analysis to investigate the relationships between various dietary patterns and the specific outcome of interest [13].

Cluster analysis: This method combines individuals into relatively homogeneous subgroups (clusters) based on differences and similarities in food intake. Food and drink intakes are considered input variables, are typically represented as intake frequency, percentage of energy intake, and standardized nutrient intakes or a combination of dietary and biochemical measures [15]. By applying cluster analysis to dietary data, experts can uncover commonalities among individuals or food items, making it easier to understand and describe various dietary patterns within a population.

*Reduced rank regression**:*** This method is commonly acknowledged as a hybrid method due to its incorporation of both data-driven techniques and the integration of prior knowledge. This method used to explore the relationships between food intake, health outcomes, and the underlying mechanisms by which diet influences health. Using this method, researchers select specific food groups, the desired health outcome, and a set of intermediary variables based on prior knowledge or previous research [16].

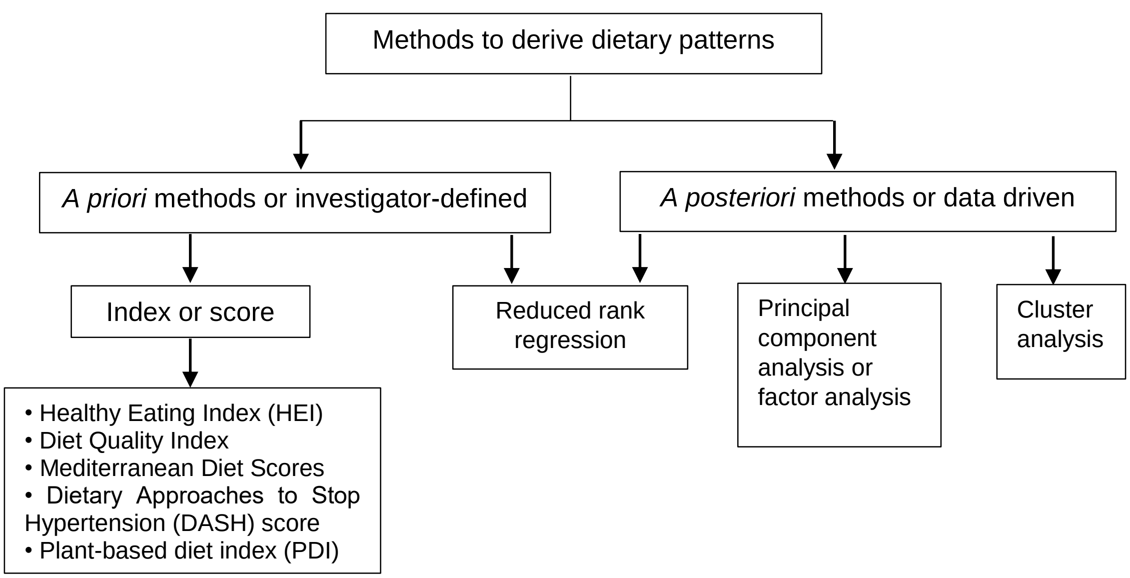

Fig. 1. Approaches to define dietary patterns in observational studies (modified from Schulze et al. 2006) [15]

Plant-based diet index

Plant-based diets are a diverse family of dietary patterns defined as infrequent consumption of animal foods along with frequent intake of plant-based foods in the usual diet. Vegetarian diets are a subset of plant-based diets, in which foods of animal origin are totally or mostly excluded [17]. However, vegetarian diets also include certain plant foods, such as refined grains and sugar-sweetened beverages, which are detrimental to the health [18,19]. Therefore, is important to highlight that nutritional quality is not equal in all plant-based foods. To better account for the quality of plant-based foods Satija and colleagues [20] developed a plant-based diet index, based on the method created by Martínez-González et al [21]. The plant-based diet index is a graded dietary pattern that positively weighs plant foods and negatively weighs animal foods. The plant-based diet index includes an overall plant-based diet index (PDI) which represent the overall intake, healthful plant-based diet index (hPDI) which represent intake of high quality plant foods, and unhealthful plant-based diet index (uPDI) represent less nutritive plant foods. A greater score of the healthy plant-based diet has been associated with reduced risk of type 2 diabetes and cardiovascular disease, whereas a greater score of the unhealthy plant-based diet was associated with incidence of some major chronic diseases [20,22].

To create the plant-based dietary scores first, frequencies of consumption were converted into servings consumed per day, subsequently the number of servings of foods were added up to 18 food groups. Based on nutrient and culinary similarities within larger groups of animal foods and plant foods, the 18 food groups were established, categorizing them into healthy and less healthy options. Healthy plant food groups included (*whole grains, fruits, vegetables, nuts, legumes, vegetable oils, and tea/coffee),* less healthy plant food groups included *(fruit juices, sugar-sweetened beverages, refined grains, potatoes, and sweets/desserts).* Animal food groups included *(animal fats, dairy, eggs, fish/seafood, meat (poultry and red meat), and miscellaneous animal-based food).* The cut points for the quintiles were calculated for each 18 food groups, with assigned score between 1 and 5 for each quintile. Regarding PDI, a score of 5 was dedicated for each plant food group for which they were above the highest quintile of consumption, and a score of 4 was assigned for each plant food group for which they were above the second highest quintile but below the highest quintile, and so on, with a score of 1 for consumption below the lowest quintile (positive scores). In contrast, a score of 1 was allocated to each animal food group for which they were above the highest quintile of consumption, a score of 2 for each animal food group for which they were between the highest and second highest quintiles, and so on, with a score of 5 for consumption below the lowest quintile (reverse scores). For hPDI, positive scores were given to healthy plant food groups, and reverse scores to less healthy plant food groups and animal food groups. Finally, for uPDI, positive scores were given to less healthy plant food groups and reverse scores to healthy plant food groups and animal food groups. The 18 food group scores were summed to obtain the indices, with a theoretical range of 18 (lowest possible score) to 90 (highest possible score) [22].

Cancer and the association with plant-based diets

Cancer continues to rank among the primary causes of death worldwide. According to the International Agency for Research on Cancer (IARC), around 20 million new cancer cases and 9.9 million cancer-related deaths occurred worldwide in 2020. Breast cancer has taken over lung cancer as the most frequently diagnosed cancer, with approximately 2.3 million new cases (11.7%). The leading cause of cancer-related mortality remained lung cancer resulting in around 1.8 million deaths (18%). This was followed by colorectal cancer (9.4%), liver cancer (8.3%), stomach cancer (7.7%), and female breast cancer (6.9%) [23].

Plant-based diets have gained considerable attention in recent years for their potential health benefits, including a potential link to cancer prevention. While the relationship between plant-based diets and cancer is complex and ongoing research is continually expanding our understanding. The benefits of plant-based diets on health may be due to the direct effects of their healthy components such as fiber, sulfur compounds, carotenoids, and polyphenols, present in foods such as cruciferous and allium vegetables, tomatoes, green tea, and whole grain cereal, have well-known anticarcinogenic properties [24]. Some studies support a beneficial role for specific plant-based foods, such as whole grain and fiber intake with gastric and colorectal cancer [25,26]. On the other hand, simple carbohydrates, sugar-sweetened beverages, and saturated fatty acids have been linked with an increased breast cancer risk, digestive system cancer [18,27], and there is evidence linking dairy and red meat with an increased risk of prostate cancer [28]. The World Health Organization (WHO) categorizes processed meat as group 1 carcinogen; red meat is classified as group 2A, probably carcinogenic to humans which are related mainly with colorectal cancer, but some association have been seen for pancreatic and prostate cancer [29].

There is epidemiological evidence on the relationship between the plant-based diets which included (Mediterranean and vegetarian diets) and cancer [30]. However, little is known about the quality of plant-based diets and the impact on cancer. To our knowledge, there is only one systematic review that included the quality of plant-based diets and the relationship with cancer prognosis [31]. Therefore, epidemiological evidence available between plant-based diets quality and different types of cancer must be systematized. The aim of this review is to assess the association between healthy and unhealthful plant-based diets and the risk of cancer.

Objective

To assess the association between healthy and unhealthful plant-based diets and the risk of cancer

Hypothesis

Healthy plant-based diets have a protective factor against cancer risk whereas the unhealthy plant-based diets increase the risk of cancer.

MATERIAL AND METHODS

This systematic review was conducted according to the general methodology of the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Search Strategy

A literature search was performed using the electronic database PubMed from 1 June 2018 until 31 July 2023 to identify epidemiologic studies on the association of plant-based dietary patterns and the risk of cancer. The keywords or phrases used to perform the search were: (Plant-Based Diet OR Plant-Based Diet Index OR Plant-based dietary pattern) AND (cancer OR breast cancer OR colorectal cancer OR digestive cancer OR stomach cancer OR liver cancer OR pancreatic cancer OR bile tract cancer OR prostate cancer OR lung cancer) AND (cancer outcome OR cancer mortality OR cancer recurrence OR cancer incidence OR cancer survivors). The language to search for articles published was English, only sources limited to human adult studies were included. There were excluded reviews and meta-analysis. Further exploration of the reference lists of the identified papers complemented this search.

Study Eligibility Criteria

Studies were included if they met the following inclusion criteria: 1) it was a case-control or a cohort study; 2) the exposure variable was the Plant-based Diet Index (overall plant-based diet index (PDI), healthful plant-based diet index (hPDI), and unhealthful plant-based diet index (uPDI); 3) the outcome of interest was cancer (risk cancer, all-cause mortality, cancer-specific mortality/survival, recurrence); 4) the relative risks (RRs), hazards ratios (HRs), or odds ratios (ORs) and the corresponding 95% confidence intervals (CI) for the highest compared with the lowest score of the Plant-based Diet Index were reported.

Data extraction

The information that was abstracted from each of the articles included: first author, publication year, location of the study, study name, study design, sample size; age and gender of participants; cancer type, type of food pattern, dietary pattern estimation, dietary assessment method, RRs, HRs, and ORs with the corresponding 95% CIs from the fully adjusted model for the highest compared with the lowest category of dietary patterns; and potential confounders adjusted in the multivariate analysis.

Quality of the articles

The quality of the articles was evaluated using the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) methodology for cohort and case-controls studies. The STROBE checklist contains 22 items organized according to the title and abstract, introduction, methods, results, and discussion structure.

RESULTS

Identified Studies

Figure 2 shows the flowchart of the study selection process. From the initial search, 181 records were identified through PupMed and one article was added from reference in total were 182, of which 134 articles were excluded based on title or abstract and duplicated. This left 48 potential relevant studies only the full text of one study could not be obtained. For this, 47 full-length article were selected for further evaluation and 28 of these were excluded because did not meet the inclusion criteria. This resulted in the selection of 19 original research studies for this review (12 cohort and 7 case-control studies).

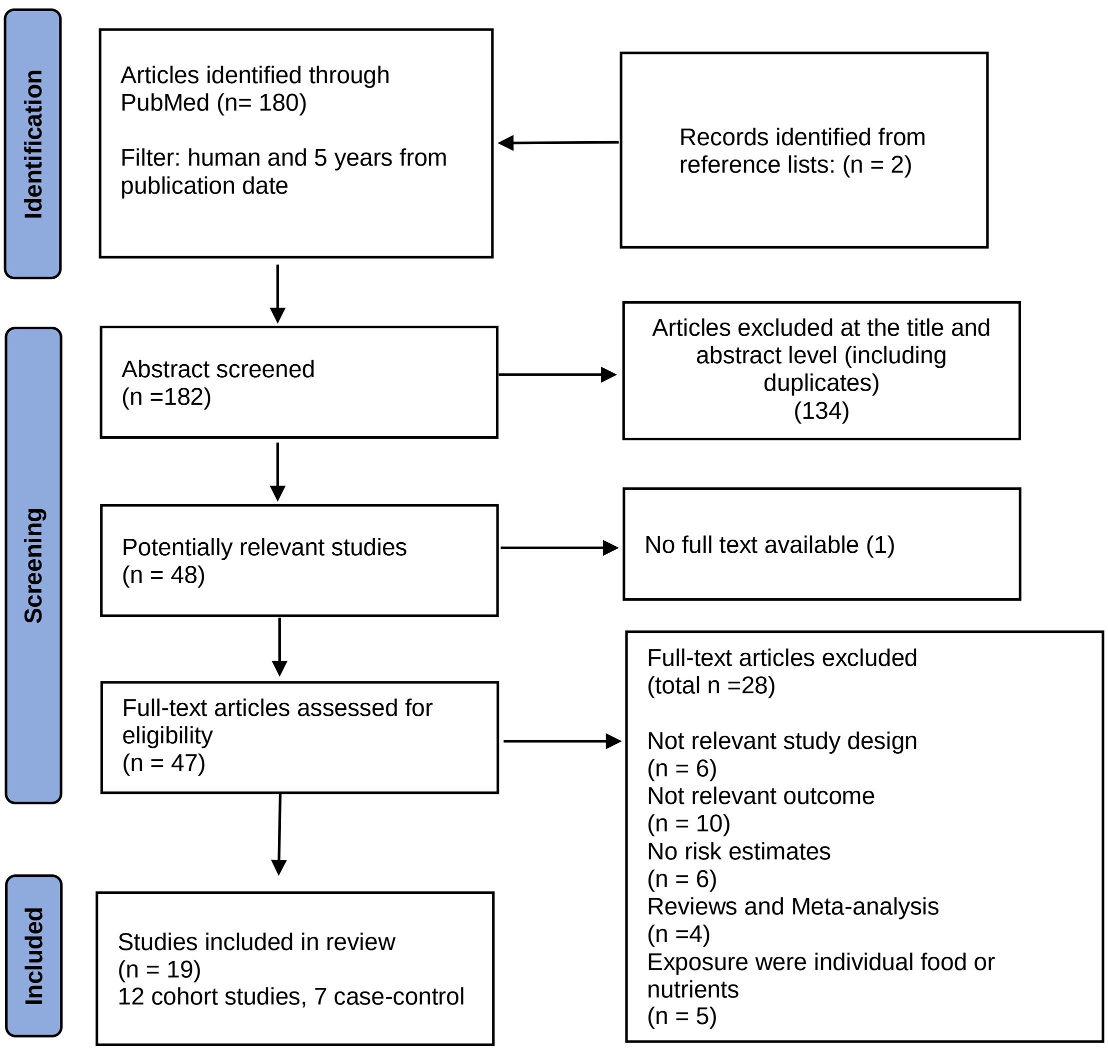

Fig. 2 Adapted flow-chart of the study selection process according to PRISMA 2020 statement.

Table 1. Characteristics of the population in the cohort studies

Author, year, (ref), study, country	Cohort /cases	Outcome	Sex/age	Follow-up	Type of food pattern	Dietary pattern estimation	Dietary assessment method	Covariates included in model
Anyene I.C et al., 2021 [32], Pathway, USA	3,646/(461 recurrence, 653 all cause mortality, 323 Breast cancer-specific mortality, 330 Non-Breast cancer-specific mortality)	Breast cancer recurrence and mortality	Women/ >21years	9.51 years [a]	Plant-Based diet index	Three plant-based diet indices (PDI, hPDI, and uPDI) methodology defined by Satija et al. (18 foods groups). Range: 18–90 y (lowest to highest adherence).	139-item FFQ	Age at diagnosis, total energy intake, and physical activity, race/ethnicity, education, menopausal status, smoking status.
Romanos-Nanclares A. et al., 2020 [33], SUN study, Spain	10,812/101	Breast cancer risk	Women/ 20 years	11.5 years [a]	Pro vege-tarian	The PVG was constructed using the approach of Martínez-Gonzalez et al. and the indices (hPVG and uPVG) following the method by Satija et al. (18 foods groups). Range: PVG (15 lowest and 75 highest), hPVG and uPVG (18 lowest and 90 highest).	136-item FFQ	Height, family history of breast cancer, smoking status, physical activity, alcohol intake, BMI, age at the time of menarche, menopause, number of pregnancies, pregnancy before the age of 30 years, months of breastfeeding, use of hormone replacement therapy, total energy intake.
Romanos-Nanclares A. et al., 2021 [34], NHS and NHSII), USA	99,211/12,248	Breast cancer risk	Women/ 30-55 years (NHS), Women/ 25-42 years (NHSII)	1984-2016 (NHS), 1991 to 2017 (NHSII)	Plant-Based diet index	Three plant-based diet indices (PDI, hPDI, and uPDI) methodology defined by Satija et al. (18 foods groups). Range:18–90 (lowest to highest adherence).	116-item (NHS), >130-items (NHSII) FFQ	Age, weight, height, BMI, personal and family history of breast cancer, breastfeeding, postmenopausal hormone use, physical activity, alcohol intake, total energy intake.
Shah S. et al., 2022 [35], E3N, France	65,574/3,968	Breast cancer risk	Women/ 40-65 years	21 years	Plant-Based diet index	Two Plant-based diet indices (hPDI and uPDI) methodology defined by Satija et al. (18 foods groups). Range:18–90 (lowest to highest adherence).	208-item FFQ	Age, educational level, physical activity, smoking status, family history of BC, breastfeeding, age at menarche, age at first full-term birth, past history of benign breast disease, use of the contraceptive pill, menopausal hormone therapy, and mammography in the last follow-up cycle, BMI, energy intake, and alcohol.

(Continued)

Table 1. Characteristics of the population in the cohort studies

Author, year, (ref), study, country	Cohort /cases	Outcome	Sex/age	Follow-up	Type of food pattern	Dietary pattern estimation	Dietary assessment method	Covariates included in model
Wang F. et al. 2022 [36], NHS and HPFS, USA	123,773/ 3,077	Incidence of Colorectal cancer	Women/30-55 y (NHS) &Men/ 40-75 y (HPFS)	1976 NHS 1986 HPFS	Plant-Based diet index	Plant-based diet indices (hPDI and uPDI) methodology defined by Satija et al. (18 foods groups). Range:18–90 (lowest to highest adherence).	FFQ	BMI, physical activity, smoking status, regular use of aspirin or other non-steroidal anti-inflammatory drugs, family history of colorectal cancer, history of previous lower gastrointestinal endoscopy, alcohol intake, total energy intake.
Zhong Guo-Chao et al., 2022 [37], PLCO, USA	101,748 /421	Pancreas cancer risk	Women & Men /55-74 years	8.86 years b	Plant-Based diet index	The indices PDI, hPDI, and uPDI were constructed using the approach proposed by Satija et al. (18 foods groups). Range:18-72 (lowest to highest adherence).	124-item DHQ	Age, diet history questionnaire completion, sex, race, body mass index, alcohol consumption, smoking status, family history of pancreatic cancer, history of diabetes.
Kim J. et al., 2023 [38], MEC, USA	170,321/ 722	Hepatocellular carcinoma cancer risk	Women & Men /45-75 years	19.6 years b	Plant-Based diet index	Three plant-based diet indices (PDI, hPDI and uPDI) methodology by Satija et al. (16 foods groups, the study combinied sugar sweetened beverages and sweets and desserts into added sugars and excluding miscellaneous animal-based foods) Range: 16-80 (lowest to highest adherence	>180-items FFQ	Age, race and ethnicity, sex, age at cohort entry, family history of liver cancer, history of diabetes, BMI, cigarette smoking, alcohol consumption, total energy intake.
Loeb S. et al. 2021 [39], HPFS, USA	47,239/6,655 (4573 lozalized ,515 advanced, 956 lethal and 806 fatal prostate cancer)	Prostate cancer risk	Men/ 40-75 years (HPFS)	20.7 years b	Plant-Based diet index	Three plant-based diet indices (PDI, hPDI and uPDI) methodology defined by Satija et al. (18 foods groups) Range:18–90 (lowest to highest adherence).	137-152 items FFQ	Age, race, height. BMI, BMI at age 21, smoking status, family history of prostate cancer, PSA test, vitamin E supplement use, alcohol intake, physical activity, aspirin use, anti-cholesterol medication and diabetes.

(Continued)

Table 1. Characteristics of the population in the cohort studies

Author, year, (ref), study, country	Cohort /cases	Outcome	Sex/age	Follow-up	Type of food pattern	Dietary pattern estimation	Dietary assessment method	Covariates included in model
Kane-Diallo A. et al., 2018 [40] NutriNet Santé, France	42,544 /1,591 (173 digestive, 68 lung, 487 Breast, 243 prostate)	Risk of overall and especific cancer:digestive, lung, breast, prostate	Women & men/ >18 years	4.3 years [a]	Pro Plant-based	It was built according to the algorithm proposed by Martinez-Gonzalez et al. modified by considering all vegetables oils and not only olive oil. (12 food groups) Range: 12-60 (lowest to highest adherence).	24h dietary records	Age,sex, energy intake without alcohol, number of 24 h dietary record, smoking status, educational level, physical activity, height, BMI, alcohol intake, family history cancer, lipids intake. for breast cancer analyses, hormone replacement therapy, number of children, contraception use.
Wang Q. et al., 2023 [41], Lung cancer follow-up study, China	408/408	Lung cancer mortality	Women & men/18-79 years	40.97 moths a	Plant-Based diet index	Three scores, PDI, hPDI, and uPDI, were calculated using the method described by Satija et al. (18 foods groups) Range:18–90 (lowest to highest adherence).	111-items FFQ	Age at diagnosis, sex, energy intake, race, region, education, income, marital status, smoking status, alcohol intake, diet change, BMI, physical activity, histological type, AJCC stage, comorbidities, surgery chemotherapy, radiotherapy, targeted treatment and immunotherapy
Kim J. et al., 2023 [42] NHS and HPFS; USA	211,673 / 6518 (490 Oral cavity/ oropharyngeal, 292 esophageal, 319 stomach, 128 small intestine, 3794 colorectal, 2284 colon, 759 rectal, 1541 accessory organ, 1126 pancreatic, 246 biliary tract, 175 liver cancer)	Digestive system cancer risk	Women/ 30-55 years (NHS), Women/ 25-42 years (NHSII), Men/ 40-75 years (HPFS)	1984-2018 NHS 1991-2017 NHSII 1986-2016 HPFS	Plant-Based diet index	Three plant-based diet indices (PDI, hPDI and uPDI) methodology proposed by Satija et al. (18 foods groups) Range:18–90 (lowest to highest adherence).	>130-items FFQ	Age, race, BMI, physical activity, smoking status, alcohol intake, family history of cancer, personal history of diabetes, multivitamin, use, aspirin use, NSAID use, menopausal status, total energy intake and calcium supplement intake. For colorectal cancer (including colon cancer and rectum cancer), family history of colorectal cancer and endoscopy in the past 2 years instead of family history of cancer.

(Continued)

Table 1. Characteristics of the population in the cohort studies

Author, year, (ref), study, country	Cohort /cases	Outcome	Sex/age	Follow-up	Type of food pattern	Dietary pattern estimation	Dietary assessment method	Covariates included in model
Ratjen I. et al. 2021 [43], ,Germany	1,404/1,404	all-cause mortality in CRC survivors	Women & Men	2009-2011	Plant-Based diet index	Three plant-based diet indices (PDI, hPDI and uPDI) methodology defined by Satija et al. (18 foods groups) Range:18–90 (lowest to highest adherence).	112-item FFQ	Sex, age at diet assessment, BMI, physical activity, survival time from CRC diagnosis until diet assessment, tumor location, metastases, other cancer, type of therapy, smoking status, alcohol intake, total energy intake.

Abbreviations: PDI, overall plant-based diet index; hPDI, healthful plant-based diet index; uPDI, unhealthful plant-based diet index; PVG, pro-vegetarian; hPVG, healthful Pro-vegetarian food pattern; uPVG, unhealthful pro-vegetarian food pattern; FFQ, food-frequency questionnaires; DHQ, diet history questionnaire; PSA, prostate-specific antigen; CRC, colorectal cancer; BC, Breast cancer; HCC, hepatocellular carcinoma; AJCC, American Joint Committee on Cancer, BMI, Body Mass Index; NSAID, Nonsteroidal anti-inflammatory drugs. Study names: E3N, Etude Epidemiologique aupres de femmes de la Mutuelle Generale de l'Education Nationale); MEC, Multiethnic Cohort; NHS, Nurses' Health Study; NHSII, Nurses' Health Study II; Pathway; HPFS, Professionals Follow-up Study; PLCO, Prostate, Lung, Colorectal, and Ovarian Randomized control study; SUN, Seguimiento Universidad de Navarra.
[a] median, [b] mean

Table 2. Characteristics of the population in the case- control studies

Author, year, (ref), study country	Study base and period	Case/ control	Outcome	Control information	Type of food pattern	Dietary pattern estimation	Dietary Assessment method	Covariates included in model
Sasanfar B. et al., 2021 [44], Iran	Hospital (2014-2016)	412/456	Breast cancer risk	Women/19-80 y/ matched by age ±10 years and geographic region	Plant-Based diet index	Three plant-based diet indices (PDI, hPDI and uPDI) methodology defined by Satija et al. (18 foods groups) Range: 18–90 (lowest to highest adherence).	168-item FFQ	Age, energy, physical activity, family history of breast cancer, education, parity,marital status, BMI.
Payandeh N. et al., 2021 [45], Iran	Hospital (NA)	150/ 150	Breast cancer risk	Women/ matched by age and socioeconomic status	Plant-Based diet index	Three plant-based diet indices (PDI, hPDI and uPDI) methodology defined by Satija et al. (18 foods groups). Range: 18–90 (lowest to highest adherence).	147-item FFQ	Age, energy intake, BMI, physical activity, family history of cancer, socioeconomic status, smoking, alcohol intake, menopause status, first menstruation age, weight at 18 years, length of breastfeeding, hormone replacement therapy, supplement and medication use, comorbidities.
Rigi S. et al., 2021 [46], Iran	Population (2013-2015)	300/700	Breast cancer risk	Women/>30/ matched by age ±5 years and socioeconomic status	Plant-Based diet index	Three plant-based diet indices (PDI, hPDI and uPDI) methodology defined by Satija et al. (16 food groups). Range:16-80 (lowest to highest adherence).	106-item FFQ	Age and energy intake, education, social economic status, residential area, supplement use, family history of breast cancer, disease history, physical activity, marital status, smoking status, alcohol consumption, history of breast-feeding and BMI.
Oncina-Cánovas A. et al., 2022 [47] PANESOES Study, Spain	Hospital (1995-1999)	778/ 455 (199 esophagus , 414 stomach, 165 pancreas)	Gastro-intestinal cancer risk	Women & men/30-80 y/ matched by age, sex and province	Pro-vegetarian	The PVG food patterns were created following the methodology proposed by Martínez-González, and hPVG and uPVG food patterns by Satija method. (18 foods groups) Range: PVG (12 lowest and 60 highest), h and uPVG (18 lowest and 90 highest).	93-items FFQ	Age, sex, province, education level, tobacco consumption, alcohol intake, and energy intake.

(Continued)

Table 2. Characteristics of the population in the case- control studies

Author, year, (ref), study country	Study base and period	Case/ control	Outcome	Control information	Type of food pattern	Dietary pattern estimation	Dietary Assessment method	Covariates included in model
Leone A. et al., 2020 [48], Spain	Nested case control study (1999- ongoing study)	101/ 404	Risk of basal cell carcinoma (BCC)	Women & men/39-56 y/ matched by sex, age and analysis time)	Pro-vegetarian	To obtain the Provegetarian diet score the approach described by Martínez-González et al. was followed. (12 food groups) Range:16 -60 (lowest to highest adherence).	136-item FFQ	Age, height, smoking, physical activity, recruitment year, total energy intake, family history of melanoma, sunscreen use, during sun exposure, sunburns during childhood and adolescence, number of sunburns during adolescence and presence of freckles.
Mousavi S. et al. 2021 [49], Iran	Hospital (2009-2011)	128/ 256	Glioma cancer risk	Women/20-75 y/ matched by sex and age ±5 years)	Plant-Based diet index	Three plant-based diet indices (PDI, hPDI and uPDI) methodology defined by Satija et al. (18 food groups) Range:18–90 (lowest to highest adherence).	123-item FFQ	Age, sex, energy intake, physical activity, family history of glioma, marital status, high-risk job, high-risk living area, duration of cell phone usage, supplement use, history of exposure to the radiographic X-ray, history of dental photography, history of head trauma, smoking status, exposure to chemicals, personal hair dye use, frequent use of fried food, and microwave.
Wu B. et al,.2022 [50], China	Population (2010-ongoing)	2799/ 2799	Colorectal	Women& men/30-75 y/ matched by sex and age ±5 years)	Plant-Based diet index	The indices were created using a method proposed by Martínez-González et al. and defined by Satija et al. In the study "potatoes group" was classified as a hPDI food group whereas "salted vegetables" were add to uPDI. (16 foods group) Range:16 -80 (lowest to highest adherence).	106-item FFQ	Age, sex, total energy intake, marital status, residence, educational level, occupation, income, BMI, smoking status, alcohol drinking, first degree relative with cancer, occupational activity, and household and leisure-time activities.

Abbreviation: PDI, overall plant-based diet index; hPDI, healthful plant-based diet index; uPDI, unhealthful plant-based diet index; PVG, pro-vegetarian; hPVG, healthful Pro-vegetarian food pattern; uPVG, unhealthful pro-vegetarian food pattern; FFQ, food-frequency questionnaires; BCC, Basal cell carcinoma; BMI, Body Mass Index. Study names; PANESOES, pancreatic, esophageal and stomach cancer study. NA: Not available

Table 3. Risk estimation for cancer within the highest versus lowest range score of plant-based diet index

Author, year (ref), country	N cases	Type of food pattern	Lowest range score	Highest range score	Comparison	Multivariate Adjusted HR/OR/RR (95% CI)	p-trend
Breast cancer							
A: Prospective							
Romanos-Nanclares A. et al., 2020 [33], Spain	101	PVG	22-43	48-66	T3 vs T1	HR: 1.03 (0.67 - 1.60)	0.875
		hPVG	30-51	58-80	T3 vs T1	HR: 0.83 (0.50 - 1.37)	0.466
		uPVG	30-51	52-82	T3 vs T1	HR: 1.31 (0.79 - 2.19)	0.282
Romanos-Nanclares A. et al., 2021 [34] USA	12,482	PDI	41 a	62 a	Q5 vs Q1	HR: 0.89 (0.84 - 0.95)	**0.01***
		hPDI	46 a	64 a	Q5 vs Q1	HR: 0.89 (0.83 - 0.94)	**0.01***
		uPDI	46 a	64 a	Q5 vs Q1	HR: 1.04 (0.97 - 1.10)	0.20
Shah S. et al., 2022 [35], France	3,968	hPDI	27	79	Q5 vs Q1	HR: 0.86 (0.77 - 0.95)	**0.01***
		uPDI	27	78	Q5 vs Q1	HR: 1.20 (1.08 - 1.33)	**0.01***
Kane-Diallo et al., 2018 [40], France	487	PDI	31.2 (1.7)	42.1 (3)	T3 vs T1	HR: 0.86 (0.69 - 1.08)	0.2
Anyene I.C et al., 2021 [32], USA	461 Recurrence of Breast	PDI	32-48	61-79	Q5 vs Q1	HR: 1.17 (0.98 - 1.39)	
		hPDI	31-47	62-81	Q5 vs Q1	**HR: 1.11 (0.97 - 1.26)**	
		uPDI	27-47	62-77	Q5 vs Q1	HR: 0.9 (0.79 - 1.03)	
	563 All cause Mortality of Breast	PDI	32-48	61-79	Q5 vs Q1	HR: 0.96 (0.82 - 1.11)	
		hPDI	31-47	62-81	Q5 vs Q1	HR: 0.93 (0.83 - 1.05)	
		uPDI	27-47	62-77	Q5 vs Q1	HR: 1.07 (0.96 - 1.2)	
	323Breast cancer-specific mortality	PDI	32-48	61-79	Q5 vs Q1	HR: 0.98 (0.79 - 1.22)	
		hPDI	31-47	62-81	Q5 vs Q1	HR: 1.07 (0.91 - 1.25)	
		uPDI	27-47	62-77	Q5 vs Q1	HR: 0.94 (0.8 - 1.11)	
	330 Non-Breast cancer-specific mortality	PDI	32-48	61-79	Q5 vs Q1	HR: 0.9 (0.73 - 1.11)	
		hPDI	31-47	62-81	Q5 vs Q1	HR: 0.83 (0.71 - 0.98)	
		uPDI	27-47	62-77	Q5 vs Q1	**HR: 1.2 (1.02 - 1.41)**	
B: Case- control							
Sasanfar B. et al., 2021 [44], Iran	412	PDI	59	142	Q4 vs Q1	OR: 0.96 (0.65 - 1.42)	
		hPDI	64	157	Q4 vs Q1	**OR: 0.61 (0.40 - 0.93)**	
		uPDI	54	144	Q4 vs Q1	OR: 1.21 (0.80 - 1.84)	

(Continued)

Table 3. Risk estimation for cancer within the highest versus lowest range score of plant-based diet index

Author, year (ref), country	N cases	Type of food pattern	Lowest range score	Highest range score	Comparison	Multivariate Adjusted HR/OR/RR (95% CI)	p-trend
Payandeh N. et al., 2021 [45], Iran	150	PDI	NA	NA	T3 vs T1	OR: 1.00 (0.55 - 1.83)	0.95 [b]
		hPDI	NA	NA	T3 vs T1	OR: 0.89 (0.49 - 1.62)	0.93 [b]
		uPDI	NA	NA	T3 vs T1	OR: 1.80 (0.95 - 3.42)	0.18 [b]
Rigi S. et al., 2021 [46], Iran	300	PDI	21	74	Q4 vs Q1	OR: 0.33 (0.22 - 0.50)	**0.001***
		hPDI	26	77	Q4 vs Q1	OR: 0.64 (0.43 - 0.94)	**0.008***
		uPDI	31	78	Q4 vs Q1	OR: 2.23 (1.48 - 3.36)	**0.001***
Colorectal cancer							
A: Prospective							
Wang F. et al. 2022 [36], USA	3,077	hPDI(NHS)	46.9	63	Q4 vs Q1	HR: 0.92 (0.79 - 1.06)	0.46
		hPDI (HPFS)	46.4	63.5	Q4 vs Q1	HR: 0.82 (0.70 - 0.98)	0.07
		hPDI (pooled)			Q4 vs Q1	HR: 0.86 (0.77 - 1.84)	**0.04***
		uPDI(NHS)	57.8	51.6	Q4 vs Q1	HR: 1.14 (0.98 - 1.32)	0.34
		uPDI (HPFS)	57.1	52.1	Q4 vs Q1	HR: 1.14 (0.96 - 1.34)	0.05
		uPDI (pooled)			Q4 vs Q1	HR: 1.16 (1.04 -1.29)	**0.005***
Kim J. et al., 2023 [42], USA	3,794 colorectal	PDI	47.7 (2.7)	60.5(3.0)	Q4 vs Q1	HR: 0.98 (0.92 - 1.05)	
		hPDI	47.0 (3.2)	62.0 (3.3)	Q4 vs Q1	HR: 0.94 (0.89 - 1.00)	
		uPDI	47.0 (3.2)	62.7 (3.2)	Q4 vs Q1	**HR: 1.07 (1.01 - 1.13)***	
	2284 colon	PDI	47.7 (2.7)	60.5(3.0)	Q4 vs Q1	HR: 0.98 (0.90 - 1.07)	
		hPDI	47.0 (3.2)	62.0 (3.3)	Q4 vs Q1	HR: 0.94 (0.87 - 1.01)	
		uPDI	47.0 (3.2)	62.7 (3.2)	Q4 vs Q1	HR: 1.04 (0.97 - 1.11)	
	759 rectal	PDI	47.7 (2.7)	60.5(3.0)	Q4 vs Q1	HR: 1.02 (0.88 - 1.19)	
		hPDI	47.0 (3.2)	62.0 (3.3)	Q4 vs Q1	HR: 0.99 (0.87 - 1.13)	
		uPDI	47.0 (3.2)	62.7 (3.2)	Q4 vs Q1	HR: 1.08 (0.96 - 1.22)	
	128 small intestine	PDI	47.7 (2.7)	60.5(3.0)	Q4 vs Q1	HR: 0.86 (0.60 - 1.24)	
		hPDI	47.0 (3.2)	62.0 (3.3)	Q4 vs Q1	HR: 0.86 (0.63 - 1.18)	
		uPDI	47.0 (3.2)	62.7 (3.2)	Q4 vs Q1	HR: 0.87 (0.65 - 1.17)	

(Continued)

Table 3. Risk estimation for cancer within the highest versus lowest range score of plant-based diet index

Author, year (ref), country	N cases	Type of food pattern	Lowest range score	Highest range score	Comparison	Multivariate Adjusted HR/OR/RR (95% CI)	p-trend
Ratjen et al. 2021[43],Germany	1,404	PDI	47(44-48) [a]	61 (60-63) [a]	Q4 vs Q1	HR: 0.46 (0.29 - 0.75)	**0.01***
		hPDI	46(43-48) [a]	62 (60-65) [a]	Q4 vs Q1	HR: 0.76 (0.51 - 1.14)	0.20
		uPDI	45(43-47) [a]	62 (60-65) [a]	Q4 vs Q1	HR: 1.29 (0.84 - 1.98)	0.07
B: Case- control							
Wu B. et al,.2022 [50], China	2,799	PDI	40 [a]	56 [a]	Q5 vs Q1	OR: 0.79 (0.66 - 0.95)	**0.001***
		hPDI	40 [a]	55 [a]	Q5 vs Q1	OR: 0.45 (0.38 - 0.55)	**0.001***
		uPDI	38 [a]	58 [a]	Q5 vs Q1	OR: 1.45 (1.18 - 1.78)	**0.001***
Pancreas cancer							
A: Prospective							
Kim J. et al., 2023 [42], USA	1126	PDI	47.7 (2.7)	60.5(3.0)	Q4 vs Q1	**HR: 0.83 (0.73-0.94)***	
		hPDI	47.0 (3.2)	62.0 (3.3)	Q4 vs Q1	HR: 0.91 (0.81-1.01)	
		uPDI	47.0 (3.2)	62.7 (3.2)	Q4 vs Q1	HR: 0.93 (0.84-1.04)	
Zhong Guo-Chao et al., 2022 [37], USA	421	PDI	21-41	48-66	Q4 vs Q1	HR: 0.74 (0.57- 0.96)	**0.023***
		hPDI	23-40	49-67	Q4 vs Q1	HR: 0.56 (0.42- 0.75)	**0.001***
		uPDI	23-40	49-66	Q4 vs Q1	HR: 1.38 (1.20- 1.85)	**0.012***
B: Case- control							
Oncina-Cánovas A.et al.,2022 [47], Spain	165	PVG	<32	>41	Q5 vs Q1	RR: 0.43 (0.35-0.52)	**0.01***
		hPVG	<48	>60	Q5 vs Q1	RR: 0.74 (0.59-0.92)	0.10
		uPVG	<50	>59	Q5 vs Q1	RR: 0.91 (0.72-1.14)	0.10
Liver cancer							
A: Prospective							
Kim J. et al., 2023 [38], USA	722	PDI	24-44	54-71	Q5 vs Q1	HR: 0.77 (0.61-0.98)	**0.02***
		hPDI	26-43	55-75	Q5 vs Q1	HR: 0.81 (0.63-1.03)	0.08
		uPDI	23-43	54-73	Q5 vs Q1	HR: 1.13 (0.88-1.44)	0.23
Kim J. et al., 2023 [42], USA	175	PDI	47.7 (2.7)	60.5(3.0)	Q4 vs Q1	**HR: 0.69 (0.50-0.95)***	
		hPDI	47.0 (3.2)	62.0 (3.3)	Q4 vs Q1	**HR: 0.68 (0.52-0.91)***	
		uPDI	47.0 (3.2)	62.7 (3.2)	Q4 vs Q1	HR: 1.08 (0.83-1.40)	

(Continued)

Table 3. Risk estimation for cancer within the highest versus lowest range score of plant-based diet index

Author, year (ref), country	N cases	Type of food pattern	Lowest range score	Highest range score	Comparison	Multivariate Adjusted HR/OR/RR (95% CI)	p-trend
Prostate cancer							
A: Prospective							
Loeb S. et al. 2021 [39], USA	6,655 total	PDI	-1.3	1.3	Q5 vs Q1	HR: 0.97 (0.90 - 1.05)	0.17
		hPDI	-1.3	1.3	Q5 vs Q1	HR: 0.95 (0.87 - 1.02)	0.11
	4573 localized	PDI	-1.3	1.3	Q5 vs Q1	HR: 0.96 (0.87 - 1.06)	0.18
		hPDI	-1.3	1.3	Q5 vs Q1	HR: 0.91 (0.83 - 1.01)	**0.02***
	515 advanced	PDI	-1.3	1.3	Q5 vs Q1	HR: 0.78 (0.59 - 1.04)	0.06
		hPDI	-1.3	1.3	Q5 vs Q1	HR: 0.93 (0.70 - 1.25)	0.75
	956 lethal	PDI	-1.3	1.3	Q5 vs Q1	HR: 0.83 (0.67 - 1.02)	0.07
		hPDI	-1.3	1.3	Q5 vs Q1	HR: 0.98 (0.79 - 1.21)	0.60
	806 fatal	PDI	-1.3	1.3	Q5 vs Q1	HR: 0.81 (0.64 - 1.01)	**0.04***
		hPDI	-1.3	1.3	Q5 vs Q1	HR: 0.89 (0.71 - 1.13)	0.35
Kane-Diallo A. et al., 2018 [40],France	243	PDI	31.2 (1.7)	42.1 (3)	T3 vs T1	HR: 0.76 (0.55 - 1.06)	0.1
Lung cancer							
Wang Q et al.,, 2023 [41], China	408	PDI	31-46	54-67	Q4 vs Q1	HR: 1.16 (0.76 – 1.75)	0.555
		hPDI	42-56	63-74	Q4 vs Q1	HR: 0.66 (0.45 – 0.97)	**0.042***
		uPDI	35-47	57.5–69	Q4 vs Q1	HR: 1.38 (0.89 – 2.14)	0.168
Kane-Diallo A. et al., 2018 [40],France	68	PDI	31.2 (1.7)	42.1 (3)	T3 vs T1	HR: 0.47 (0.25 - 0.90)	**0.02***
Glioma cancer							
B: Case- control							
Mousavi S. et al. 2021 [49],Iran	128	PDI	<52	>57	T3 vs T1	OR: 0.31 (0.15 - 0.60)	**0.001***
		hPDI	<51	>56	T3 vs T1	OR: 0.28 (0.13 - 0.60)	**0.001***
		uPDI	<51	>57	T3 vs T1	OR: 4.89 (2.33 - 10.28)	**0.001***
Basal cell carcinoma							
B: Case- control							
Leone A et al., 2020 [48], Spain	101	PVG	30 [a]	44 [a]	Q5 vs Q1	OR: 1.54 (0.61-3.91)	0.384

(Continued)

Table 3. Risk estimation for cancer within the highest versus lowest range score of plant-based diet index

Author, year (ref), country	N cases	Type of food pattern	Lowest range score	Highest range score	Comparison	Multivariate Adjusted HR/OR/RR (95% CI)	p-trend
Esophageal cancer							
A: Prospective							
Kim J. et al., 2023 [42], USA	292	PDI	47.7 (2.7)	60.5 (3.0)	Q4 vs Q1	HR: 1.09 (0.86 - 1.40)	
		hPDI	47.0 (3.2)	62.0 (3.3)	Q4 vs Q1	HR: 0.91 (0.74 - 1.12)	
		uPDI	47.0 (3.2)	62.7 (3.2)	Q4 vs Q1	HR: 1.12 (0.91 - 1.37)	
B: Case- control							
Oncina-Cánovas et al.,2022. [47], Spain	199	PVG	<32	>41	Q5 vs Q1	RR:0.37 (0.32 - 0.42)	**0.01***
		hPVG	<48	>60	Q5 vs Q1	RR:0.72 (0.58 - 0.90)	0.10
		uPVG	<50	>59	Q5 vs Q1	RR:1.26 (1.00 - 1.60)	0.10
Stomach cancer							
A: Prospective							
Kim J. et al., 2023 [42], USA	319	PDI	47.7 (2.7)	60.5 (3.0)	Q4 vs Q1	HR: 1.22 (0.97 - 1.54)	
		hPDI	47.0 (3.2)	62.0 (3.3)	Q4 vs Q1	HR: 1.10 (0.90 - 1.35)	
		uPDI	47.0 (3.2)	62.7 (3.2)	Q4 vs Q1	HR: 0.98 (0.81 - 1.19)	
Oncina-Cánovas et al.,2022 [47], Spain	414	PVG	<32	>41	Q5 vs Q1	RR: 0.34 (0.27 - 0.43)	**0.001***
		hPVG	<48	>60	Q5 vs Q1	RR: 0.42 (0.34 - 0.52)	**0.01***
		uPVG	<50	>59	Q5 vs Q1	RR: 1.76 (1.42 - 2.18)	**0.01***
Digestive cancer							
A: Prospective							
Kane-Diallo A. et al., 2018 [40],France	173	PDI	31.2 (1.7)	42.1 (3)	T3 vs T1	HR: 0.68 (0.47 - 0.99)	**0.04**
Others digestive system cancer							
Total digestive cancer							
Kim J. et al., 2023 [42], USA	6,518	PDI	47.7 (2.7)	60.5 (3.0)	Q4 vs Q1	**HR: 0.94 (0.89 - 0.99)***	
		hPDI	47.0 (3.2)	62.0 (3.3)	Q4 vs Q1	**HR: 0.93 (0.89 - 0.97)***	
		uPDI	47.0 (3.2)	62.7 (3.2)	Q4 vs Q1	**HR: 1.04 (0.99 - 1.08)***	

(Continued)

Table 3. Risk estimation for cancer within the highest versus lowest range score of plant-based diet index

Author, year (ref), country	**N cases**	**Type of food pattern**	**Lowest range score**	**Highest range score**	**Comparison**	**Multivariate Adjusted HR/OR/RR (95% CI)**	**p-trend**
Gastrointestinal tract							
		PDI	47.7 (2.7)	60.5 (3.0)	Q4 vs Q1	HR: 0.97 (0.92 - 1.03)	
Kim J. et al., 2023 [42], USA	4,992	hPDI	47.0 (3.2)	62.0 (3.3)	Q4 vs Q1	HR: 0.94 (0.89 - 0.99)	
		uPDI	47.0 (3.2)	62.7 (3.2)	Q4 vs Q1	**HR: 1.06 (1.01 - 1.11)***	
Oral cavity / oropharyngeal							
Kim J. et al., 2023 [42], USA		PDI	47.7 (2.7)	60.5 (3.0)	Q4 vs Q1	**HR: 0.78 (0.65 - 0.95)***	
	490	hPDI	47.0 (3.2)	62.0 (3.3)	Q4 vs Q1	HR: 0.86 (0.73 - 1.02)	
		uPDI	47.0 (3.2)	62.7 (3.2)	Q4 vs Q1	HR: 0.97 (0.83 - 1.13)	
Accessory organ							
Kim J. et al., 2023 [42], USA	1,541	PDI	47.7 (2.7)	60.5 (3.0)	Q4 vs Q1	**HR: 0.84 (0.75 - 0.94)***	
		hPDI	47.0 (3.2)	62.0 (3.3)	Q4 vs Q1	**HR: 0.89 (0.81 - 0.98)***	
		uPDI	47.0 (3.2)	62.7 (3.2)	Q4 vs Q1	HR: 0.97 (0.89 - 1.06)	
Biliary tract							
		PDI	47.7 (2.7)	60.5 (3.0)	Q4 vs Q1	HR: 1.01 (0.77 - 1.32)	
Kim J. et al., 2023 [42], USA	246	hPDI	47.0 (3.2)	62.0 (3.3)	Q4 vs Q1	HR: 0.98 (0.78 - 1.23)	
		uPDI	47.0 (3.2)	62.7 (3.2)	Q4 vs Q1	HR: 1.04 (0.84 - 1.29)	

Abbreviation: PDI, overall plant-based diet index; hPDI, healthful plant-based diet index; uPDI, unhealthful plant-based diet index; PVG, pro-vegetarian; hPVG, healthful Pro-vegetarian food pattern; uPVG, unhealthful pro-vegetarian food pattern. NA, Not available. Values are means ( ) in the lowest and highest range score.

a Median

[b] p- value

* statistically significant

Study characteristics

The provenance of the studies analyzed in this review were from the USA (37%), Europe (32%) specifically from Spain, France, and Germany; and Asia (32%) from Iran and China. Sample sizes of studies ranged from 150 to 170,321. Regarding the type of dietary pattern of the total of 19 studies, 15 were plant based diet index, 3 studies were pro-vegetarian and one study used the pro-plant based score. The construction of each type of pattern and more information is detailed in table 1 and 2. Dietary intake was assessed using food-frequency questionnaire (FFQ) in 17 studies, a diet history questionnaire in one study and 24-h recall in one study. A wide range of potential confounding factors were adjusted depending on the type of cancer: Most of them were based on: sex, race, ethnicity, body mass index, smoking, alcohol consumption, energy intake, family history cancer, physical activity, hormone use, menopausal status, vitamin use or medicament use, among others.

Description of the results for each tumor

Table 3 shows the results of tumors with their respective case numbers classified by study design (A: prospective or B: case-control). Likewise, risk estimation for cancer (Harzard ratio, Odds ratio and Relative risk 95%CI) within the highest versus lowest range score of plant-based diet index.

Breast cancer (BC)

Breast cancer is the most commonly diagnosed cancer and is the most represented cancer type in this review, with eight studies in total (5 cohorts and 3 case-control). Two studies found that a higher adherence to the overall plant-based diet index (PDI) was significantly inverse associated with BC (HR, 0.89; 95% CI: 0.84- 0.95) [34], (OR, 0.33; 95%CI:0.22- 0.50) [46] for participants from the highest quintile compared with the lowest. For the healthy plant-based diet index (hPDI), four studies also found a significantly inverse association with risk BC (HR, 0.89; 95% CI: 0.83- 0.94) [34], (HR, 0.86; 95% CI:0.77- 0.95) [35], (OR, 0.61; 95%CI: 0.40 - 0.93) [44], (OR, 0.64; 95%CI:0.43 - 0.94) [46]. Regarding the unhealthy plant-based diet index (uPDI) and the risk of BC, two studies found a significantly positive association (HR, 1.20; 95% CI: 1.08 - 1.33) [35] and (OR, 2.23; 95%CI: 1.48 - 3.36) [46]. The Pathway study examined the risk of breast cancer recurrence and mortality, according with hPDI, the healthy pattern had a reduced hazard of non-breast-cancer mortality (HR 0.83, 95% CI: 0.71–0.98) but had no association with all-cause mortality (HR 0.93, 95% CI: 0.83, 1.05). In contrast, the uPDI had an increased hazard of non-breast-cancer mortality (HR, 1.20; 95% CI:1.02–1.41) and no association with all-cause mortality (HR, 1.07; 95% CI: 0.96–1.2) [32]. Nevertheless, two studies [33,45] did not find an association between the plant-based diet index and risk cancer. Globally, in relation to breast cancer, data obtained showed a statistically significant inverse association in 5 out 8 studies for the hPDI, and 3 out 8 for uPDI. These results support the potential association of a greater adherence to a healthy plant-based diet lower cancer risk.

Colorectal (CRC) and colon cancer

This review gathered four studies (3 cohorts and 1 case-control). The cohort study, composed of 123,773 participants [36] examined the incidence of CRC. They found a higher adherence to hPDI was associated with a lower incidence (HR, 0.86; 95% CI: 0.77 -1.84) while a higher adherence to uPDI was associated with increased CRC incidence (HR, 1.16; 95% CI:1.04 -1.29) both results were statistically significant. In the large-cohort studies [42], examined the association between plant-based dietary patterns and the risk of digestive system cancers which included colorectal, rectal, colon, and small intestine cancer. The study found an association between the uPDI with a higher risk of colorectal cancer (HR, 1.07; 95% CI:1.01-1.13). There were no other associations between the other tumors and the other two index (PDI and hPDI). Regarding the risk of all-cause mortality in CRC survivors (1,440 cases), the study [43] found a statistically significant association between the PDI and decreased risk of all-cause mortality in CRC, showing that subjects in the top of quartile of PDI had a 54% lower risk of dying from all causes (HR, 0.46; 95% CI: 0.29 - 0.75). For the hPDI and uPDI there were no association. The case-control study carried out in China [50] showed a significant reduction of CRC risk in PDI and hPDI (OR, 0.79; 95%CI: 0.66 - 0.95) and (OR, 0.45; 95% CI:0.38 - 0.55) respectively. By contrast, greater adherence to uPDI was associated with an increased risk (OR, 1.45; 95% CI:1.18 - 1.78). Overall, 3 studies found a statistically significant positive association between unhealthy uPDI and the risk of CRC, and two studies an inverse association for the PDI and hPDI. Despite not having found sufficient epidemiologic evidence, these studies showed a strong association regarding the unhealthy uPDI and increased cancer risk and the decreased risk associated with overall or healthy plant-based diet.

Pancreatic cancer

Three studies (2 cohorts and 1 case-control) researched the association between a plant-based dietary pattern and the risk of pancreas. The prospective cohort study (1,126 cases) [42] showed a 17% reduction of risk pancreatic cancer (HR, 0.83; 95% CI: 0.73 -0.94) for participant who had a greater adherence to PDI. The same tendency was observed for the PDI in the prospective multicenter study [37] with 421 cases. Participants in the highest compared to the lowest quartile of the PDI had a 26% lower risk of pancreatic cancer and 44% lower risk for the healthy hPDI (HR,0.56; 95% CI:0.42-0.75). With reference to the unhealthy uPDI, the study found a positive association (HR,1.38; 95% CI: 1.20- 1.85) which means a 38% of higher risk of cancer. For the three indices (PDI, hPDI and uPDI) the results were statistically significant. The case-control study [47], only found a statistically significant association for the general Pro-vegetarian dietary pattern PVG, with a 57% lower risk of pancreatic cancer (RR, 0.43 95% CI: 0.35-0.52). Globally, 3 studies found a statistically significant association between the PDI and the decreased risk of pancreatic cancer. Only 1 study was statistically significantly associated with the hPDI, and 1 study to the unhealthy uPDI.

Liver cancer

Two cohort studies gathered in this review researched the association between three plant-based diet indices and the risk of liver cancer. The first study was conducted within the Multiethnic Cohort Study (722 cases) and found a statistically significance decrease risk of 23% in the overall PDI (HR,0.77; 95% CI: 0.61-0.98) [38]. Likewise, in the prospective study (175 cases), participants in quintile 5 of PDI and hPDI had a 31% 0.69 (0.50-0.95) and 32 % 0.68 (0.52-0.91) lower risk of liver cancer, respectively, compared to those in quintile 1 [42]. Overall, in both studies the result were statistically significance for the overall PDI, and only one found an inverse association with the hPDI. Both studies highlight adherence to the PDI pattern associated with liver cancer.

Prostate cancer

This review gathered two cohort studies. The study carried out by Loeb and colleagues [39] used data from de HPFS study, and found a significantly inverse association with fatal prostate cancer for PDI (HR,0.81; 95% CI: 0.64 - 1.01), and the healthful hPDI had also an inverse association but was nonsignificance with localized prostate cancer in the overall population (HR,0.91; 95% CI: 0.83 - 1.01). On the other hand, the NutriNet Santé study based in France evaluated the association between the pro-plant-base dietary score and overall cancer risk. Related to the prostate cancer, the study did not find any substantial associations [40]. In general, of the two studies, only one found a statistically significant association among the PDI. Therefore, a definitive conclusion can not be given, more studies are need to better elucidate this association.

Lung cancer

There are two cohort studies in this review. In the lung cancer follow-up study with 408 participants [41] found that a higher adherence to the hPDI is associated with a statistically significant 34% decreased risk of lung cancer mortality (HR, 0.66; 95% CI: 0.45- 0.97). Concerning with uPDI, the study did not find any association. Similar results to the lung cancer follow-up study were observed in the NutriNet-santé cohort study (68 cases). A higher pro-plant-based dietary score was associated with a statistically significant 54% decreased risk of lung cancer (HR, 0.47; 95% CI: 0.25 -0.90) [40]. Overall, both studies showed statistically significant results for the healthy PDI and the pro-plant-based score, which suggest the potential association between plant-based diet index and the decreased of lung cancer risk.

Glioma

The hospital-based case-control study, using a sample of 128 Iranian adults [49], found that greater adherence to PDI and hPDI had a significant inverse association with a chance of glioma cancer (OD, 0.31; 95% CI: 0.15 - 0.60) and (OD, 0.28; 95% CI: 0.13 - 0.60) respectively. By contrast, a higher adherence to uPDI was directly associated with the odds of glioma. Subjects in the highest tertile of uPDI had a 4.89 times higher chance of glioma than those in the lowest tertile (OR, 4.89; 95% CI: 2.33-10.28), and it was a statistically significant. The results showed a significant inverse association between the PDI and hPDI with a lower risk of glioma cancer risk, however more studies are needed.

Basal cell carcinoma (BCC)

A total of 101 adults participated in the nested case-control SUN study [48]. In addition to analyzing the association between Pro-vegetarian dietary patterns and BCC risk, the study included two other patterns (Mediterranean and DASH diet). Regarding the Pro-vegetarian dietary pattern, the results did not show any significant association (OR, 1.54; 95% CI: 0.61-3.91, p-trend 0.384). Overall, there is not a conclusive association with the pro-vegetarian pattern and BCC.

Esophageal and stomach cancer:

The review included two studies (1 cohort and 1 case-control) for both tumors. Regarding esophageal cancer only one study was statistically significate inverse associate with the PVG (RR: 0.37; 95% CI:0.32 - 0.42) [47]. About the stomach cancer, also only the case-control PANESOES study had a statistically significate inverse association for the PVG (RR, 0.34; 95% CI: 0.27-0.43) and hPVG (RR, 0.42; 95% CI: 0.34-0.52) while had a positive association for the uPVG (RR, 1.76; 95% CI: 1.42- 2.18) [47]. Globally, the evidence is insufficient and heterogeneous to lead any conclusion. Although seems to suggest a potential association between healthy (lower risk) and unhealthy (higher risk) plant-based and stomach cancer risk.

Digestive system cancer

This review unified the results of two articles one related only about digestive cancer [40] and one studied with focused on digestive system cancer [42] which included all cancers in gastrointestinal tract and the accessory organs necessary for digestion.

The French study [40] found a strong inverse association between a higher pro-plant based diet score and digestive cancer risk (HR, 0.68; 95% CI:0.47- 0.99). Likewise, the result of the 3 large prospective study [42] showed that subjects in the highest quintile of adherence to hPDI had a significantly inverse association for the total digestive cancer (HR, 0.93; 95% CI: 0.89 -0.97). Respecting to the others digestive system cancer included in the same study [42], result showed an inverse association to the hPDI for gastrointestinal tract (HR, 0.94; 95% CI: 0.89 -0.99) and accessory organ cancer (HR, 0.89; 95% CI:0.81-0.98). About the PDI had also a significantly inverse association in oral cavity/oropharyngeal cancer (HR, 0.78; 95% CI: 0.65-0.95) and accessory organ (HR, 0.84; 95% CI: 0.75 -0.94). In contrast, uPDI had a positive association for gastrointestinal tract cancer (HR, 1.06; 95% CI: 1.01 - 1.11) [42]. No association was found for biliary tract between the three plant-based index [42]. Overall, both studies found a statistically significant inverse association to the pro-plant based score, PDI and hPDI for digestive cancer. Additionally, in one study also found a significant inverse association for the PDI and hPDI in 3 specific digestive organs. Hence, these results support evidence associated with a lower risk of digestive cancer with a healthy plant-based diet.

DISCUSSION

This systematic review summarizes the evidence on the association between healthy and unhealthy plant-based diets and the risk of cancer based upon twelve prospective cohort studies and seven case-control studies. As expected, most of the articles focused on breast and colorectal cancer because they are the most studied.

This review identified evidence of a decreased risk of breast cancer associated with a healthy plant-based diet (hPDI) with a percentage ranging from 11% and 36% [32,34,35,44,46], whereas a adherence to unhealthy uPDI showed an increased risk [32,35,46]. In fact, these findings are in good agreement with previous studies showing an association between high fruit and vegetable consumption may be associated with better overall survival in women with breast cancer [51]. A meta-analysis by Jayedi et al.[52] identified an association between higher fiber intake and improved BC prognosis for all-cause mortality survival in breast cancer survivors. By contrast, a meta-analysis [53] examined the association of different dietary patterns and found that the western pattern (rich in red meat, dairy products, processed foods, and salt, with minimal intake of fruits, and vegetable) increase the risk of BC by 14%.

Regarding to the colorectal cancer, this review found a strong association regarding the unhealthy uPDI and increased cancer risk and a lower risk associated with overall or healthy plant-based diet. Bella et al. showed a 1.7 times increased risk of CRC with high meat compared to plant-based dietary patterns and a 13% reduced risk for CRC in those consuming a plant-based diet compared to a mixed food diet [54]. In a systematic review and meta-analysis evaluated the associations of pre and post-diagnosis dietary intake on all-cause and CRC-specific mortality among colorectal cancer survivors. Regarding post-diagnosis whole grain intake, a high vs. low indicates a 17% reduced risk of all-cause mortality [55] .

This review identified that a hPDI was associated with a lower risk of digestive cancer including some specific organs: gastrointestinal tract (6%), accessory organs (11), and liver cancer (32%). By contrast, uPDI was associated with a higher risk of total gastrointestinal tract cancer (6%). These findings show that quality of plant-based diets may play an important role in the whole digestive system. This is also confirmed by a meta-analysis that found a plant-based diets were protective against cancers of the digestive system, with no significant differences between different types of cancer [56]. In the Adventist Health Study 2, adopting a vegetarian diet was linked to a reduced risk of gastrointestinal tract cancer by 23% and colorectal cancer by 22%, in comparison to those following a non-vegetarian diet [57]. However, in that meta-analysis and the AHS 2 did not differentiate the quality of plant-based food.

Another tumor of interest because it is still the leading cause of death cancer is lung cancer [23]. Only two studies were found for this review of which both showed a protective factor for the risk of this cancer related to adherence to a healthy plant-based diet and pro-plant based score [40,41]. In 2016, a meta-analysis suggested that a healthy dietary pattern is associated with a lower lung cancer risk (19%), and they provided more beneficial evidence for changing the diet pattern in the general population. However, in that meta-analysis consider as a healthy dietary patterns the (HEI, healthy eating index and Prudent pattern).

Concerning of others tumors gathered in this review such as basal cell carcinoma and glioma both were a case-control studies, therefore, more evidence is needed in large prospective cohorts evaluating the quality of plant-based diet and the risk of these cancer. For instance, Mann S et al. found that ketogenic diets improved cancer outcomes in malignant gliomas but did not find association to other dietary pattern [58].

Overall, most of the studies analyzed suggest that a healthy plant-based diet lowers the risk of cancer, whereas adherence to a less healthy diet confers a higher risk. However, more researches are needed.

Several potential biological mechanisms support a protective role of the hPDI toward cancer risk. The healthful plant-predominant dietary pattern is characterized by whole grains, fruits, vegetables, nuts, legumes, vegetable oils, and tea while minimizing the consumption of animal foods. Hence, they are rich sources of dietary fiber, phytochemicals (flavonoids), and vitamins (vitamin C). These bioactive compounds have been identified to have anti-inflammatory and antioxidant abilities, which are capable of attenuating chronic inflammation and DNA oxidative damage and antiproliferative activities [59–61]. A high fiber intake reduces the total body pool of estrogen, thus helping reduce breast cancer risk [62]. Fiber also decreases the risk of colorectal cancer by increasing the volume of feces and decreasing transit time, thus reducing the contact between potential carcinogens and colorectal epithelial cells [63]. In addition, microbial fermentation of fiber produces short-chain fatty acids, which may regulate the immune system. Other beneficial nutritional components for decreasing CRC cancer risk are polyphenols, lignans, and phytoestrogen [64,65]. Polyphenols, for example, exert chemopreventive effects and may induce tumor cell apoptosis [66].

On the other hand, less healthful plant-based foods are poor in fiber and micronutrients and laden with carbohydrates with tumor-promoting potential via effects on circulating insulin and insulin-like growth factor-1 (IGF1) [67]. Trans-fatty acids found in commercially processed salty and sugary foods, as well as other packaged products, influence systemic inflammation, visceral adiposity, body weight, and insulin resistance, which are associated with breast cancer [68]. Diets high in animal products and constituents like saturated fats, dietary cholesterol, antibiotics from meat, heme iron, and chemical contaminants from high-temperature cooking of animal products are also associated with cancer, particularly with colorectal and prostate cancer [69,70]

A limitation of this systematic review was that eligible studies were predominantly prospective, including, in some instances, several publications based on the same cohort. In addition, in these prospective studies, for example (Nurses' Health Study, Professionals Follow-up Study, E3N, SUN study), the population was predominantly white, health professionals and highly educated. For this reason, it is important that future studies be carried out in a diverse racial and ethnic population. In general, most studies derived dietary intake from FFQ that although in most cases the questionnaire was validated and carried out by nutritionists or health professional, in some studies participants made a self-report of the dietary intake that might result in the overestimation or underestimation of actual exposure.

CONCLUSION

Overall, the evidence gathered, although heterogenic and insufficient, seems to suggest a potential association between a healthy plant-based diet and a lower risk of cancer. In contrast, adherence to an unhealthy plant-based diet is associated with a higher risk.

However, additional research on large and prospective studies is needed to confirm these findings. In addition, it is important to consider the plant food quality for making nutrition policies for preventing cancer and support recommendations to shift toward a dietary pattern that promotes healthy plant foods but limits the intake of less healthy plant foods.

REFERENCES:

1. United States Department of Agriculture. A Series of Systematic Reviews on the Relationship Between Dietary Patterns and Health Outcomes. 2014.

2. Kant AK. Dietary patterns and health outcomes. J Am Diet Assoc. 2004;104:615–35.

3. Popkin BM. The nutrition transition and obesity in the developing world. J Nutr. 2001;131:871S-873S.

4. Popkin BM. Nutrition Transition and the Global Diabetes Epidemic. Curr Diab Rep. 2015;15.

5. Hu FB. Dietary pattern analysis: A new direction in nutritional epidemiology. Curr Opin Lipidol. 2002;13:3–9.

6. Michels KB, Schulze MB. Can dietary patterns help us detect diet–disease associations? Nutr Res Rev. 2005;18:241–8.

7. Schulze MB, Martínez-González MA, Fung TT, Lichtenstein AH, Forouhi NG. Food based dietary patterns and chronic disease prevention. BMJ. 2018;361:1–6.

8. Agnoli C, Krogh V, Pounis G. Dietary Pattern Analysis. Anal Nutr Res Princ Stat Methodol Interpret Results. 2019;75–101.

9. McNaughton SA. Dietary patterns. Present Knowl Nutr Clin Appl Top Nutr. Elsevier Inc.; 2020. p. 235–48.

10. Reedy J, Lerman JL, Krebs-Smith SM, Kirkpatrick SI, Pannucci TRE, Wilson MM, et al. Evaluation of the

Healthy Eating Index-2015. J Acad Nutr Diet. 2018;118:1622–33.

11. Bach A, Serra-Majem L, Carrasco JL, Roman B, Ngo J, Bertomeu I, et al. The use of indexes evaluating the adherence to the Mediterranean diet in epidemiological studies: a review. Public Health Nutr. 2006;9:132–46.

12. Fung TT, Chiuve SE, McCullough ML, Rexrode KM, Logroscino G, Hu FB. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. Arch Intern Med. 2008;168:713–20.

13. Zhao J, Li Z, Gao Q, Zhao H, Chen S, Huang L, et al. A review of statistical methods for dietary pattern analysis. Nutr J. 2021;20:1–18.

14. Newby PK, Tucker KL. Empirically Derived Eating Patterns Using Factor or Cluster Analysis: A Review. Nutr Rev. 2004;62:177–203.

15. Schulze MB, Hoffmann K. Methodological approaches to study dietary patterns in relation to risk of coronary heart disease and stroke. Br J Nutr. 2006;95:860–9.

16. Weikert C, Schulze MB. Evaluating dietary patterns: the role of reduced rank regression. Curr Opin Clin Nutr Metab Care. 2016;19.

17. Hargreaves SM, Rosenfeld DL, Moreira AVB, Zandonadi RP. Plant-based and vegetarian diets: an overview and definition of these dietary patterns. Eur J Nutr. 2023;62:1109–21.

18. Romanos-Nanclares A, Toledo E, Gardeazabal I, Jiménez-Moleón JJ, Martínez-González MA, Gea A. Sugar-sweetened beverage consumption and incidence of breast cancer: the Seguimiento Universidad de Navarra (SUN) Project. Eur J Nutr. 2019;58:2875–86.

19. Malik VS, Popkin BM, Bray GA, Després JP, Willett WC, Hu FB. Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: A meta-analysis. Diabetes Care. 2010;33:2477–83.

20. Satija A, Bhupathiraju SN, Rimm EB, Spiegelman D, Chiuve SE, Borgi L, et al. Plant-Based Dietary Patterns and Incidence of Type 2 Diabetes in US Men and Women: Results from Three Prospective Cohort Studies. PLoS Med. 2016;13:1–18.

21. Martínez-González MA, Sánchez-Tainta A, Corella D, Salas-Salvadó J, Ros E, Arós F, et al. A provegetarian food pattern and reduction in total mortality in the Prevención con Dieta Mediterránea (PREDIMED) study. Am J Clin Nutr. 2014;100:320–8.

22. Satija A, Bhupathiraju SN, Spiegelman D, Chiuve SE, Manson JAE, Willett W, et al. Healthful and Unhealthful Plant-Based Diets and the Risk of Coronary Heart Disease in U.S. Adults. J Am Coll Cardiol. 2017;70:411–22.

23. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71:209–49.

24. Subramaniam S, Selvaduray KR, Radhakrishnan AK. Bioactive compounds: Natural defense against cancer? Biomolecules. 2019;9.

25. Zhang XF, Wang XK, Tang YJ, Guan XX, Guo Y, Fan JM, et al. Association of whole grains intake and the risk of digestive tract cancer: A systematic review and meta-analysis. Nutr J. 2020;19:1–14.

26. Vogtmann E, Xiang YB, Li HL, Levitan EB, Yang G, Waterbor JW, et al. Fruit and vegetable intake and the risk of colorectal cancer: Results from the Shanghai Men's Health Study. Cancer Causes Control. 2013;24:1935–45.

27. Sieri S, Krogh V, Ferrari P, Berrino F, Pala V, Thiébaut ACM, et al. Dietary fat and breast cancer risk in the European Prospective Investigation into Cancer and Nutrition. Am J Clin Nutr. 2008;88:1304–12.

28. Aune D, Navarro Rosenblatt DA, Chan DSM, Vieira AR, Vieira R, Greenwood DC, et al. Dairy products, calcium, and prostate cancer risk: A systematic review and meta-analysis of cohort studies. Am J Clin Nutr. 2015;101:87–117.

29. Bouvard V, Loomis D, Guyton KZ, Grosse Y, Ghissassi F El, Benbrahim-Tallaa L, et al. Carcinogenicity of consumption of red and processed meat. Lancet. Oncol. England; 2015. p. 1599–600.

30. Molina-montes E, Salamanca-Fernández E, Garcia-Villanova B, Sánchez MJ. The Impact of Plant-Based Dietary Patterns on Cancer-Related Outcomes: A Rapid Review and Meta-Analysis. Nutrients. 2020;12:1–29.

31. Hardt L, Mahamat-Saleh Y, Aune D, Schlesinger S. Plant-Based Diets and Cancer Prognosis: a Review of Recent Research. Curr Nutr Rep. 2022;11:695–716.

32. Anyene IC, Ergas IJ, Kwan ML, Roh JM, Ambrosone CB, Kushi LH, et al. Plant-based dietary patterns and breast cancer recurrence and survival in the pathways study. Nutrients. 2021;13:1–11.

33. Romanos-Nanclares A, Toledo E, Sánchez-Bayona R, Sánchez-Quesada C, Martínez-González MÁ, Gea A. Healthful and unhealthful provegetarian food patterns and the incidence of breast cancer: Results from a Mediterranean cohort. Nutrition. 2020;79–80.

34. Romanos-Nanclares A, Willett WC, Rosner BA, Collins LC, Hu FB, Toledo E, et al. Healthful and unhealthful plant-based diets and risk of breast cancer in U.S. women: Results from the nurses' health studies. Am Asoc Cancer Res. 2021;30:1921–31.

35. Shah S, Mahamat-Saleh Y, Ait-Hadad W, Koemel NA, Varraso R, Boutron-Ruault MC, et al. Long-term adherence to healthful and unhealthful plant-based diets and breast cancer risk overall and by hormone receptor and histologic subtypes among postmenopausal females. Am J Clin Nutr. 2023;117:467–76.

36. Wang F, Ugai T, Haruki K, Wan Y, Akimoto N, Arima K, et al. Healthy and unhealthy plant-based diets in relation to the incidence of colorectal cancer overall and by molecular subtypes. Clin Transl Med. 2022;12.

37. Zhong GC, Li Z, You AJ, Zhu Q, Wang CR, Yang PF. Plant-based diets and the risk of pancreatic cancer: a large prospective multicenter study. Am J Clin Nutr. 2023;117:235–42.

38. Kim J, Setiawan VW, Wilkens LR, Le Marchand L, Park SY. Healthful Plant-Based Dietary Pattern and Risk of Hepatocellular Carcinoma in a Multiethnic Population: A Cohort Study. Am J Clin Nutr. 2023;

39. Loeb S, Fu BC, Bauer SR, Pernar CH, Chan JM, Van Blarigan EL, et al. Association of plant-based diet index with prostate cancer risk. Am J Clin Nutr. 2022;115:662–70.

40. Kane-Diallo A, Srour B, Sellem L, Deschasaux M, Latino-Martel P, Hercberg S, et al. Association between a pro plant-based dietary score and cancer risk in the prospective NutriNet-santé cohort. Int J Cancer. 2018;143:2168–76.

41. Wang Q, Cui Q, Gao J-P, Zhao Y-H. Plant-based dietary patterns and lung cancer mortality: a perspective cohort study. Food Funct. 2023;6470–81.

42. Kim J, Khil J, Kim H, Keum NN, Zhang X, Giovannucci E. Plant-based dietary patterns and the risk of digestive system cancers in 3 large prospective cohort studies. Eur J Epidemiol. 2023;

43. Ratjen I, Enderle J, Burmeister G, Koch M, Nöthlings U, Hampe J, et al. Post-diagnostic reliance on plant-compared with animal-based foods and all-cause mortality in omnivorous long-term colorectal cancer survivors. Am J Clin Nutr. 2021;114:441–9.

44. Sasanfar B, Toorang F, Booyani Z, Vassalami F, Mohebbi E, Azadbakht L, et al. Adherence to plant-based dietary pattern and risk of breast cancer among Iranian women. Eur J Clin Nutr. 2021;75:1578–87.

45. Payandeh N, Shahinfar H, Amini MR, Jafari A, Safabakhsh M, Imani H, et al. The Lack of Association between Plant-Based Dietary Pattern and Breast Cancer: a Hospital-Based Case-Control Study. Clin Nutr Res. 2021;10:115.

46. Rigi S, Mousavi SM, Benisi-Kohansal S, Azadbakht L, Esmaillzadeh A. The association between plant-based dietary patterns and risk of breast cancer: a case–control study. Sci Rep. 2021;11:1–10.

47. Oncina-Cánovas A, González-Palacios S, Notario-Barandiaran L, Torres-Collado L, Signes-Pastor A, de-Madaria E, et al. Adherence to Pro-Vegetarian Food Patterns and Risk of Oesophagus, Stomach, and Pancreas Cancers: A Multi Case–Control Study (The PANESOES Study). Nutrients. 2022;14.

48. Leone A, Martínez-González M, Martin-Gorgojo A, Sánchez-Bayona R, de Amicis R, Bertoli S, et al. Mediterranean diet, Dietary Approaches to Stop Hypertension, and Pro-vegetarian dietary pattern in relation to the risk of basal cell carcinoma: A nested case-control study within the Seguimiento Universidad de Navarra (SUN) cohort. Am J Clin Nutr. 2020;112:364–72.

49. Mousavi SM, Shayanfar M, Rigi S, Mohammad-Shirazi M, Sharifi G, Esmaillzadeh A. Adherence to plant-based dietary patterns in relation to glioma: a case–control study. Sci Rep. 2021;11:1–11.

50. Wu B, Zhou RL, Ou QJ, Chen YM, Fang YJ, Zhang CX. Association of plant-based dietary patterns with the risk of colorectal cancer: a large-scale case-control study. Food Funct. 2022;13:10790–801.

51. Farvid MS, Holmes MD, Chen WY, Rosner BA, Tamimi RM, Willett WC, et al. Postdiagnostic Fruit and Vegetable Consumption and Breast Cancer Survival: Prospective Analyses in the Nurses' Health Studies. Cancer Res. 2020;80:5134–43.

52. Jayedi A, Emadi A, Khan TA, Abdolshahi A, Shab-Bidar S. Dietary Fiber and Survival in Women with Breast Cancer: A Dose-Response Meta-Analysis of Prospective Cohort Studies. Nutr Cancer. 2021;73:1570–80.

53. Xiao Y, Xia J, Li L, Ke Y, Cheng J, Xie Y, et al. Associations between dietary patterns and the risk of breast cancer: A systematic review and meta-analysis of observational studies. Breast Cancer Res. 2019;21:1–22.

54. Bella F, Godos J, Ippolito A, Di Prima A, Sciacca S. Differences in the association between empirically derived dietary patterns and cancer: a meta-analysis. Int J Food Sci Nutr [Internet]. 2017;68:402–10. Available from: http://dx.doi.org/10.1080/09637486.2016.1261087

55. Hoang T, Kim H, Kim J. Dietary Intake in Association with All-Cause Mortality and Colorectal Cancer Mortality among Colorectal Cancer Survivors: A Systematic Review and Meta-Analysis of Prospective Studies. Cancers (Basel). 2020;12.

56. Zhao Y, Zhan J, Wang Y, Wang D. The Relationship Between Plant-Based Diet and Risk of Digestive System Cancers: A Meta-Analysis Based on 3,059,009 Subjects. Front Public Heal. 2022;10:1–12.

57. Orlich MJ, Singh PN, Sabaté J, Fan J, Sveen L, Bennett H, et al. Vegetarian dietary patterns and the risk of colorectal cancers. JAMA Intern Med. 2015;175:767–76.

58. Mann SDO, Sidhu MDO, Gowin KDO. Understanding the Mechanisms of Diet and Outcomes in Colon, Prostate, and Breast Cancer; Malignant Gliomas; and Cancer Patients on Immunotherapy. Nutrients. 2020;12.

59. Samtiya M, Aluko RE, Dhewa T, Moreno-Rojas JM. Potential health benefits of plant food-derived bioactive components: An overview. Foods. 2021;10:1–25.

60. Liu RH. Health-promoting components of fruits and vegetables in the diet. Adv Nutr. 2013;4:384S-392S.

61. Grosso G, Bella F, Godos J, Sciacca S, Del Rio D, Ray S, et al. Possible role of diet in cancer: Systematic review and multiple meta-analyses of dietary patterns, lifestyle factors, and cancer risk. Nutr Rev. 2017;75:405–19.

62. Moore MA, Park CB, Tsuda H. Soluble and insoluble fiber influences on cancer development. Crit Rev Oncol Hematol. 1998;27:229–42.

63. Aune D, Chan DSM, Lau R, Vieira R, Greenwood DC, Kampman E, et al. Dietary fibre, whole grains, and risk of colorectal cancer: Systematic review and dose-response meta-analysis of prospective studies. BMJ. 2011;343:1082.

64. Slavin JL. Mechanisms for the impact of whole grain foods on cancer risk. J Am Coll Nutr. 2000;19:300S-307S.

65. Webb AL, McCullough ML. Dietary Lignans: Potential Role in Cancer Prevention. Nutr Cancer. 2005;51:117–31.

66. Alam MN, Almoyad M, Huq F. Polyphenols in Colorectal Cancer: Current State of Knowledge including Clinical Trials and Molecular Mechanism of Action. Biomed Res Int. 2018;2018.

67. Bowers LW, Rossi EL, O'Flanagan CH, De Graffenried LA, Hursting SD. The role of the insulin/IGF system in cancer: Lessons learned from clinical trials and the energy balance-cancer link. Front Endocrinol (Lausanne). 2015;6:1–16.

68. Chajès V, Thiébaut ACM, Rotival M, Gauthier E, Maillard V, Boutron-Ruault M-C, et al. Association between serum trans-monounsaturated fatty acids and breast cancer risk in the E3N-EPIC Study. Am J Epidemiol. 2008;167:1312–20.

69. Johnson IT. The cancer risk related to meat and meat products. Br Med Bull. 2017;121:73–81.

70. Harrison S, Lennon R, Holly J, Higgins JPT, Gardner M, Perks C, et al. Does milk intake promote prostate cancer initiation or progression via effects on insulin-like growth factors (IGFs)? A systematic review and meta-analysis. Cancer Causes Control. Springer International Publishing; 2017.