



Dietary Patterns and Risk of Lung Cancer: A Systematic Review and Meta-Analyses of Observational Studies

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Abstract

Purpose of Review Previous literature reviews summarized the associations between individual foods or food groups and lung cancer risk, but the relationship between dietary patterns and lung cancer risk has received less attention. We conducted a systematic review and meta-analyses of observational studies on the associations between dietary patterns and lung cancer risk.

Recent Findings PubMed, Embase, and Web of Science were systematically searched from inception to February 2023. Random-effects models were used to pool relative risks (RR) on associations with at least two studies. Twelve studies reported on data-driven dietary patterns, and 17 studies reported on *a priori* dietary patterns. A prudent dietary pattern (high in vegetables, fruit, fish, and white meat) tended to be associated with a lower risk of lung cancer (RR = 0.81, 95% confidence interval [CI] = 0.66–1.01, $n = 5$). In contrast, Western dietary patterns, characterized by higher intakes of refined grains and red and processed meat, were significantly positively associated with lung cancer (RR = 1.32, 95% CI = 1.08–1.60, $n = 6$). Healthy dietary scores were consistently associated with a lower risk of lung cancer (Healthy Eating Index [HEI]: RR = 0.87, 95% CI = 0.80–0.95, $n = 4$; Alternate HEI: RR = 0.88, 95% CI = 0.81–0.95, $n = 4$; Dietary Approaches to Stop Hypertension: RR = 0.87, 95% CI = 0.77–0.98, $n = 4$; Mediterranean diet: RR = 0.87, 95% CI = 0.81–0.93, $n = 10$) while the dietary inflammatory index was associated with a higher risk of lung cancer (RR = 1.14, 95% CI = 1.07–1.22, $n = 6$).

Summary Our systematic review indicates dietary patterns characterized by a higher intake of vegetables and fruits, a lower intake of animal products, and anti-inflammation may be associated with a reduced risk of lung cancer.

Keywords Dietary patterns · Lung cancer · Systematic review · Meta-analysis

Abbreviations

AHEI	Alternate Healthy Eating Index
CI	Confidence intervals
DASH	Dietary Approaches to Stop Hypertension
DII	Dietary Inflammatory Index
EDIP	Empirical Dietary Inflammation Pattern
HEI	Healthy Eating Index
NOS	Newcastle-Ottawa scale
RR	Relative risk

Introduction

Lung cancer was the most common cancer among men and the third most common cancer among women (following breast and colorectal cancers) globally in 2020 [1]. In the USA, lung cancer incidence has been decreasing dramatically from 64.4 (1992) to 41.6 (2019) per 100,000 in the last three decades [2]. However, it is still the second leading incident cancer among both men and women and the leading cause of cancer death in the USA. [3]. The most well-established risk factor for lung cancer is tobacco smoking, which is attributed to 80–90% of lung cancer deaths among US men and women [4]. However, over 15% of men and over 50% of women with lung cancer are nonsmokers [5]. Therefore, identification of other lifestyle factors besides smoking that are associated with lung cancer is critical for informing prevention efforts.

The World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) summarized the evidence

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on dietary factors and lung cancer risk, concluding with limited suggestive evidence that red meat and processed meat might increase the risk of lung cancer and higher intake of fruits/vegetables might decrease the risk of lung cancer [6]. However, individual foods or food groups can be highly correlated or have components which interact biologically which cannot be captured by studying them in isolation.

Rather than focusing on a single food or nutrient, dietary pattern analysis captures the quality of the overall diet [7•, 8, 9]. Generally, two types of dietary patterns are commonly used in nutritional studies: *a priori* (literature-, guideline-, or index-based methods) and data-driven methods (also called *a posteriori*). *A priori* dietary patterns use scoring methods based on existing dietary guidelines or literature and include the commonly studied Healthy Eating Index (HEI) [10], alternate HEI (AHEI), Dietary Approaches to Stop Hypertension (DASH) [11], Mediterranean diet [12], and dietary inflammatory index (DII) [13]. Data-driven dietary patterns are derived from statistical analyses such as factor analysis and cluster analysis based on dietary intake data from a specific study. Other methods combine *a priori* knowledge and the data itself using reduced rank regression, such as used in the creation of the empirical dietary inflammation pattern (EDIP) [14].

To our knowledge, only two systematic reviews have focused on associations between dietary patterns and lung cancer risk. One review, published in 2016, involved only eight observational studies [15]. Another recently published review summarized the associations between the Mediterranean diet and lung cancer with eight cohort and one case–control studies [16•]. Several additional prospective cohort studies have investigated the association between *a priori* dietary patterns and lung cancer risk [17–19, 20•, 21]. Therefore, we aimed to conduct a systematic review and meta-analysis to summarize the available evidence on associations between dietary patterns and lung cancer risk.

Methods

The current review was conducted and reported in accordance with standard criteria (Preferred Reporting Items for Systematic Reviews and Meta-Analyses, PRISMA) [22]. The protocol was registered in PROSPERO (CRD42021242842).

Search Strategy

We searched PubMed, Embase, and Web of Science up to February 2, 2023. Generally, the search terms included the following components: cohort or case–control study, lung cancer, and dietary patterns. Details about the search terms could be found in the Supplemental Table 1. We only included studies written in English and did not restrict on

year of publication. The references of the retrieved studies also were searched for any additional studies.

Study Selection and Inclusion Criteria

The study selection was performed with the following steps. First, authors (LZ and BK) scanned the title and abstract to obtain the relevant literature for further full-text review. Second, the authors downloaded the identified literature and read the full text carefully to ascertain eligibility based on our inclusion criteria. The inclusion criteria included as follows: (1) participants who were free of lung cancer at baseline for cohort studies and controls without lung diseases for case–control studies; and (2) the exposure of interest was any dietary patterns or scores including Western diet, prudent diet, HEI, AHEI, DASH, Mediterranean diet, DII, or other dietary patterns derived from data-driven methods including factor analysis or cluster analysis; and (3) the outcome of interest was the incidence of lung cancer; and (4) the study design was cohort design or case–control design; and (5) the study reported adjusted relative risk (RR) including odds ratio (OR) or hazard ratio (HR) and 95% confidence intervals (CI).

The exclusion criteria included: (1) studies that focused on children or adolescents (age ≤ 18 years); or (2) the exposures were food items, or food groups, or glycemic index/load; or (3) the outcome was lung cancer death or mortality, or recurrence or metastasis of lung cancer; or (4) the study design was experiments, ecological studies, or meta-analysis; or (5) studies lacked information on RR or OR or HR and their 95% CIs. An exclusion list of full-text review was provided in Supplemental Table 2.

Data Extraction and Quality Assessment

We used an *a priori* abstract table to obtain the following information: last name of the first author, publication year, study location or cohort name, study design, study duration or follow-up period, total number of cases, cohort size or number of controls, study population, median age, sex, exposure assessment method, deriving methods of dietary patterns and scoring details, outcome and outcome assessment method, contrast groups, main results for adjusted models, confounders included in analyses, and results stratified by sex and smoking status. We used the Newcastle–Ottawa scale (NOS) to assess the study quality of the included studies based on selection bias, comparability, and outcome assessment [23]. In questions for comparability of the NOS, the most important confounders are age and smoking. The second most important confounders are energy intake and family history of lung cancer. We considered studies with 0–3, 4–6, and 7–9 points to represent low-, medium-, and high-quality studies, respectively (Supplemental Table 3).

Statistical Analyses

All data were shown as abstracted and displayed according to the study design and exposure types (data-driven and *a priori* dietary patterns). We conducted meta-analyses to combine the available evidence on associations with at least two studies using random-effects models [24] and in sensitivity analyses combined results for prospective cohort studies only. We evaluated heterogeneity by estimating the variance between studies using Cochran's Q test and the *I*-squared (I^2) statistic [25]. We did not assess small study effects and perform meta-regression because of the limited number of studies for each association. We used command "metan" in STATA (version 15, StataCorp) to perform the meta-analyses. A 2-sided *P* value < 0.05 was considered statistically significant.

Results

Study Characteristics

After removing the duplicates, we identified 573 records by searching PubMed, Embase, and Web of Science (Fig. 1). Another two papers were added from the manual reference review [26]. We identified 47 articles for further full-text review, of which 19 articles were excluded (Supplemental Table 2). Finally, we included 28 studies in the current review [17–19, 20•, 21, 26–48]. Characteristics of each of the studies, including covariates adjusted for in multivariable models, are shown in Table 1. There were 17 cohort studies [17, 19, 20•, 21, 26, 28, 34–37, 40, 42–45, 47, 48], nine case–control studies [27, 30–33, 38, 39, 41, 46], and two case-cohort studies [17, 28]. The publication years ranged from 2003 to 2022. Two case-cohort studies were performed in the Netherlands [17, 28]. Only five case–control studies [30–32, 39, 46] and five cohort studies [19, 20•, 36, 42, 48] were conducted outside the USA or European countries. The median follow-up years of prospective studies was 12 years, ranging from 4.3 to 20.3 years. Most of these studies (26 out of 28) used food frequency questionnaires (FFQs) to collect the diet information.

We obtained 12 studies on data-driven dietary patterns and 17 studies on *a priori* dietary patterns (one study reported two types of dietary patterns). Eleven studies focused on factor analysis [28, 30–34, 38, 39, 41, 47, 48], and one focused on cluster analysis [27]. Four studies reported on HEI [20•, 21, 35, 45], four on AHEI [20•, 21, 35, 45], and four on DASH [20•, 21, 35, 45]. Nine studies evaluated the associations between the Mediterranean diet and lung cancer [17, 18, 20•, 21, 26, 35–37, 45]. Six articles assessed the associations between DII and lung cancer [18, 19, 21, 36, 37, 46]. We

classified over 80% of studies (23/28) as high-quality studies with the NOS ≥ 7 (Supplemental Table 3).

Dietary Patterns and Lung Cancer Among Case–Control Studies

Associations between dietary patterns and lung cancer among case–control studies were summarized in Fig. 2. Three of four studies indicated an inverse association between prudent diet and lung cancer [31, 32, 41] and two of them were statistically significant [32, 41]. Three studies focusing on a vegetable dietary pattern found significant inverse associations with lung cancer (all *P* values for trend < 0.01) [32, 38, 39]. Two studies showed that high meat or high quality protein-based dietary patterns were significantly associated with a higher risk of lung cancer [30, 39]. Similarly, four of five studies showed the Western diet was associated with higher lung cancer risk [31, 32, 38, 41]. One study reported associations between *a priori* dietary patterns and lung cancer using a case–control design (Fig. 2) [41]. The study suggested conformity to the Polish-adapted Mediterranean diet was associated with a lower risk of lung cancer [41]. One case–control study showed positive association between DII and lung cancer risk [46].

Dietary Patterns and Lung Cancer Among Prospective Studies

Figure 3 showed associations between data-driven dietary patterns and lung cancer using a prospective design. Prudent dietary patterns (two studies) [47, 48] and dietary patterns high in vegetables (two studies) [28] and fiber (two studies) [34, 48] showed significant inverse associations with lung cancer. In contrast, dietary patterns high in animal products [34], fructose [48], and meat [28], as well as a Western diet [47, 48] were associated with a higher risk of lung cancer.

Associations between *a priori* dietary patterns and lung cancer risk among cohort studies were shown in Fig. 4. Four studies reported associations for HEI [20•, 21, 35, 45] and four reported on AHEI [20•, 21, 35, 45]. Except for the Women's Health Initiative (WHI) [45], the other three studies indicated inverse associations of HEI with lung cancer risk with RRs for the highest category compared with the lowest category ranging from 0.79 to 0.86 [20•, 21, 35]. The findings from the WHI observational study with 86,090 postmenopausal women suggested null associations between HEI or AHEI and lung cancer risk [45]. A lower risk of lung cancer was found among higher DASH scores in three out of four studies [20•, 21, 35, 45]. Mediterranean diet was associated with a reduced lung cancer risk in six out of nine studies [17, 18, 20•, 26, 35–37, 45]. Among five studies on DII [18, 19, 21, 36, 37], all were positively associated with lung cancer

Table 1 Characteristics of included studies on associations between dietary patterns and lung cancer risk

Author, year [reference]	Study location or cohort name	Dates of enrollment or follow-up duration	Cases/Cohort or controls	Study participants, median/mean age or range, sex	Exposure assessment	Dietary pattern scoring details	Outcome assessment, ICD codes (if reported)	Confounders included in analyses
Case-control study								
Tsai, 2003 [27]	USA	1995–1996	254/184	Newly diagnosed lung cancer patients and healthy controls among individuals attending cancer screening clinics or wellness programs at the same hospitals, 50.9 (case), Both	A validated 64-item FFQ	Healthy high-fiber low-fat dietary patterns was derived using cluster analysis	Clinical diagnosis	Age, sex, smoking.
De Stefani, 2008 [30]	Uruguay	1996–2004	846/846	Patients were identified in the four major hospitals, and controls were selected in the same time period and in the same hospitals, 30–89, Men	A 64-item FFQ	Factor analysis (30 nutrients and bioactive substances) identified three dietary patterns: high-meat, antioxidants, carbohydrate	Newly diagnosed and microscopically confirmed cases of lung cancer	Age, residence, urban/rural status, education, family history of lung cancer among first-degree relative, BMI, smoking status, years since cessation, number of cigarettes smoked per day among current smokers, age at start smoking, alcohol drinking, mate consumption, total energy intake and for each score.
De Stefani, 2009 [31]	Uruguay	1996–2004	920/2532	Patients were identified in the four major hospitals, and controls were selected in the same time period and in the same hospitals, 30–89, Both	A 64-item FFQ	Factor analysis (17 foods) identified four dietary patterns: prudent, traditional, western, drinker	Newly diagnosed and microscopically confirmed cases of lung cancer	Age, residence, urban/rural status, education, body mass index, smoking status, years since stopping, number of cigarettes/day among current smokers, total energy intake and all other dietary patterns.
De Stefani, 2011 [32]	Uruguay	1996–2004	200/3874	Patients were identified in the four major hospitals, and controls were selected in the same time period and in the same hospitals, 30–79, Men	A 64-item FFQ	Factor analysis (17 foods) identified four dietary patterns: western, starchy vegetables, prudent, milk/coffee	Newly diagnosed and microscopically confirmed adenocarcinomas of the lung	Age, residence, interviewers, hospital, education, family history of lung cancer, body mass index, smoking, and total energy intake, and all other dietary patterns.

Table 1 (continued)

Author, year [reference]	Study location or cohort name	Dates of enrollment or follow-up duration	Cases/Cohort or controls	Study participants, median/mean age or range, sex	Exposure assessment	Dietary pattern scoring details	Outcome assessment, ICD codes (if reported)	Confounders included in analyses
Gorlova, 2011 [33]	USA	1995–2008	299/317	Cases are never smoker lung cancers, and controls are healthy physicians, 61.5, Both	A 214-item FFQ	Factor analysis (201 food items) identified two dietary patterns: principal component 1 (high in vegetables and low in animal foods), principal component 2 (other plant-based foods)	Historically confirmed, newly diagnosed and previously untreated lung cancer	Age, gender, caloric intake, and education.
Tu, 2016 ^a [38]	USA	1995–1996	2139/2163	Newly diagnosed and histologically confirmed NSCLC patients and age-matched healthy controls from same clinics, 61.8 (case), Both	A validated FFQ designed by NIH	Factor analysis (117 food items) identified three DPs: Fruits/vegetables, American/Western, Tex-Mex	Historically confirmed NSCLC	Age, sex, education, smoking status, pack-years, family history of lung cancer among 1st relatives, body mass index, physical activity, and total energy intake.
He, 2018 [39]	China	2006–2013	1166/1179	Newly diagnosed cancer and healthy controls randomly selected from the community, 58.3 (case), Both	Interview-based validated FFQ	Factor analysis (11 food groups) identified four DPs: High quality protein, fruits/vegetables, cereals/wheat/meat, frugal pattern	Cases were collected from three area hospitals	Age, sex, incomes, occupation, education, family history of lung cancer, history of lung diseases, environmental tobacco smoke, smoking status, BMI.
Hawrysz, 2020 [41]	Poland	2013–2017	187/252	Newly diagnosed and histologically confirmed lung cancer and controls from who attended national screening programs, 62.6, Men	A 62-item FFQ	Polish-aMED (23 food groups) was modified from aMED by substituted one item; Factor analysis identified three DPs: prudent, Westernized traditional, sweet dairy	Newly primarily diagnosed (with digital X-ray examination and CT of the chest) and histologically confirmed lung cancer	Age, BMI, current smoking status, socioeconomic status, overall physical activity, the occurrence of lung cancer in relatives, and occupational exposure in the workplace.

Table 1 (continued)

Author, year [reference]	Study location or cohort name	Dates of enrollment or follow-up duration	Cases/Cohort or controls	Study participants, median/mean age or range, sex	Exposure assessment	Dietary pattern scoring details	Outcome assessment, ICD codes (if reported)	Confounders included in analyses
Sadeghi, 2022 [46]	Iran	2020–2021	140/140	Historically and pathologically confirmed lung cancer during last 6 months and controls from the general adult population with no family relationship with lung cancer patients	A dish-based FFQ with 84 food items and 58 mixed dishes	DII based on 32 of 45 specific foods and nutrients;	Histologically and pathologically confirmed lung cancer	Age, energy intake, and gender, marital status, smoking, physical activity, family history of lung cancer, family history of any other cancers, diabetes, hypertension, aspirin use, dietary supplement use, and BMI.
Cohort study								
Mai, 2005 [29]	USA; BCDDP	9.5 yr	353/42,254	Women recruited from breast cancer-screening programme, 61, Women	A 62-item Block/NCI FFQ	RFS (23 food items) reflects compliance with the current dietary guidance; 0–1 for each; total score: 0–23	90% of the case identifications included a self-report from the follow-up questionnaires	Energy intake, smoking, NSAID use, and BMI, smoking duration, and cigarettes/day.
Gnagnarella, 2013 [26]	Italy; COSMOS	5.7 yr	178/4336	Asymptomatic heavy smokers from a lung cancer screening programme, 57, Both	A validated self-administered FFQ with 188 food items	aMED: 9 food items; 0–1 for each; total score: 0–9	Lung cancer identified from annual low-dose CT	Baseline lung cancer risk probability and total energy intake. Baseline lung cancer risk probability was calculated using information on age, sex, smoking history, and asbestos exposure.
Gnagnarella, 2013 [34]	Italy; COSMOS	5.7 yr	178/4336	Asymptomatic heavy smokers from a lung cancer screening programme, 57, Both	A validated self-administered FFQ with 188 food items	Factor analysis (27 nutrients) identified four dietary patterns: Animal products, vitamins and fiber, starch-rich, other PUFA	Lung cancer identified from annual low-dose CT	Baseline lung cancer risk probability and other nutrient patterns. Baseline lung cancer risk probability was calculated using information on age, sex, smoking history, and asbestos exposure.

Table 1 (continued)

Author, year [reference]	Study location or cohort name	Dates of enrollment or follow-up duration	Cases/Cohort or controls	Study participants, median/mean age or range, sex	Exposure assessment	Dietary pattern scoring details	Outcome assessment, ICD codes (if reported)	Confounders included in analyses
Anic, 2016 [35]	USA; NIH-AARP	10.5 yr	9272/460,770	Members of the AARP, 50–71 years, Both	A validated 124-item FFQ	HEI-2010 based the Dietary Guidelines for Americans-2010; 12 diet components; 0–5 for six components, 0–10 for five components, 0–20 for one component; total score: 0–100 AHEI-2010 based on epidemiologic studies of foods and nutrients associated with chronic disease risk: 11 components; 0–10 for each; total score: 0–110 aMED assesses conformity to a traditional Mediterranean diet: 9 components; 0–1 for each; total score: 9 DASH: 8 components; 1–5 for each; total score: 8–40	The cancer registry case ascertainment for this cohort is around 90%; ICD-O, C34.0-C34.9	Age, sex, race, education, BMI, physical activity, total energy, smoking status, cigarettes per day, time since quitting smoking, and regular use of cigars/pipes. The HEI-2010 and DASH models were also adjusted for alcohol intake.
Hodge, 2016 [36]	Australia; MCCS	18 yr	403/35,303	Residents of Melbourne, 40–69, Both	A 121-item FFQ	DII based on 29 of 45 specific foods and nutrients; adapted MDS included 10 components ranging from 0 to 9	Victorian Cancer Registry, ICD-O, C33/C34	Age, pack-years, years since quit smoking, smoking status, country of birth, education, BMI, alcohol intake, physical activity, sex, socioeconomic index quintile, energy.

Table 1 (continued)

Author, year [reference]	Study location or cohort name	Dates of enrollment or follow-up duration	Cases/Cohort or controls	Study participants, median/mean age or range, sex	Exposure assessment	Dietary pattern scoring details	Outcome assessment, ICD codes (if reported)	Confounders included in analyses
Maisonneuve, 2016 [37]	Italy; COSMOS	8.5 yr	200/4336	Asymptomatic heavy smokers from a lung cancer screening programme, 57, Both	A validated self-administered FFQ with 188 food items	DII based on 24 of 45 specific foods and nutrients; adapted MDS included 10 components ranging from 0 to 9	Lung cancer identified from annual low-dose CT	Baseline risk probability (based on age, sex, smoking duration, smoking intensity, years of smoking cessation, and asbestos exposure), and total energy. aMED and DII scores mutual adjusted.
Deschasaux, 2018 [44]	Europe; EPIC	15.3 yr	3654/471,495	Multicentre prospective cohort study in 10 European countries, 51.2, Both	Country-specific and validated dietary questionnaires including FFQ and 7-day dietary records	FSAm-NPS score, measuring the conformity to nutritional recommendations. Points (0–10) are allocated for the content per 100 g in total sugars, saturated fatty acids, sodium, and energy and opposite points (5–0) allocated for dietary fibers, proteins, and fruits/vegetables/legumes/nuts	Combined methods include record linkage with population-based cancer registries, health insurance records, pathology registries, and active follow-up of study subjects	Age, sex, center, BMI, height, alcohol, physical activity, smoking status and intensity of smoking, educational level.
Kane-Diallo, 2018 [40]	France; The NutriNet-Sante study	4.3 yr	68/42,544	Participants aged over 18 years with access to the Internet from general population, 56.9, Both	Three 24-h dietary records	Pro plant-based dietary score (7 vegetable groups and 5 animal groups); 1–5 for each; total score: 12–60	Medical records were obtained for > 90% of cancer cases	Age, sex, energy intake without alcohol, number of 24-h dietary records, smoking status, educational level, physical activity, height, BMI, alcohol intake, family history of cancers, lipids intake, and for breast cancer analyses, hormone replacement therapy, number of children, contraception use.
Bodén, 2019 [18]	Sweden; VIP	15 yr	442/35,393	Population-based study from a decennial health examination, 47, Both	A validated FFQ with 64–84 food items	DII based on 30 of 45 specific foods and nutrients; adapted MDS included 9 components ranging from 0 to 8	Swedish Cancer Registry, C32–34	Age, sex, energy intake, BMI, physical activity, smoking, educational status.

Table 1 (continued)

Author, year [reference]	Study location or cohort name	Dates of enrollment or follow-up duration	Cases/Cohort or controls	Study participants, median/mean age or range, sex	Exposure assessment	Dietary pattern scoring details	Outcome assessment, ICD codes (if reported)	Confounders included in analyses
Shivappa, 2019 [19]	Singapore; SCHS	17.6 yr	1851/60,232	Population-based cohort study among general population, 45–74, Both	A validated 165-item semi-quantitative FFQ	DII based on 36 of 45 specific foods and nutrients	Singapore Cancer Registry, C34	Age, dialect group, sex, interview year, education, BMI, physical activity, total energy intake, number of cigarettes per day, number of years of smoking, and number of year since quitting smoking for former smokers.
Myneni, 2021 [45]	USA; WHI	16.8 yr	1491/86,090	Prospective cohort study with postmenopausal women recruited from 40 clinical centers across 24 US states and the District of Columbia, 50–79, Women	A validated 122-item semi-quantitative FFQ	HEI-2015 based the Dietary Guidelines for Americans-2015; 13 diet components; 0–5 for six components, 0–10 for 8 components; total score: 0–100 AHEI-2010 based on epidemiologic studies of foods and nutrients associated with chronic disease risk: 11 components; 0–10 for each; total score: 0–110 aMED assesses conformity to a traditional Mediterranean diet: 9 components; 0–1 for each; total score: 0–9 DASH: 8 components; 1–5 for each; total score: 8–40	Self-reported lung cancer from follow-up form accompanied by medical records	Age, race, education, BMI, physical activity, active smoking, years of exposure to secondhand smoke during childhood and as an adult, and energy intake.

Table 1 (continued)

Author, year [reference]	Study location or cohort name	Dates of enrollment or follow-up duration	Cases/Cohort or controls	Study participants, median/mean age or range, sex	Exposure assessment	Dietary pattern scoring details	Outcome assessment, ICD codes (if reported)	Confounders included in analyses
Park, 2021 [21]	USA; The Multiethnic Cohort Study	17.5 yr	5350/179,318	Population-based prospective cohort, 45–75, Both	A validated 180-item quantitative FFQ	HEI-2015 based the Dietary Guidelines for Americans-2015; 13 diet components; 0–5 for six components, 0–10 for 8 components; total score: 0–100 AHEI-2010 based on epidemiologic studies of foods and nutrients associated with chronic disease risk: 11 components; 0–10 for each; total score: 0–110 aMED assesses conformity to a traditional Mediterranean diet: 9 components; 0–1 for each; total score: 0–9 DASH: 8 components; 1–5 for each; total score: 8–40 DII: with 28 of 45 specific foods and nutrients	Lung cancer cases were identified by linkage of the cohort to the Surveillance, Epidemiology, and End Results Program (SEER) tumor registries	Age, sex, race/ethnicity, family history of lung cancer, education, BMI, physical activity, and total energy intake, and smoking status, average number of cigarettes per day, squared average number of cigarettes per day, number of years smoked, number of years since quitting, and interactions between race/ethnicity and smoking status, average number of cigarettes per day, squared average number of cigarettes per day and number of years smoked. For HEI-2015 and DASH, additionally adjusted for alcohol intake.

Table 1 (continued)

Author, year [reference]	Study location or cohort name	Dates of enrollment or follow-up duration	Cases/Cohort or controls	Study participants, median/mean age or range, sex	Exposure assessment	Dietary pattern scoring details	Outcome assessment, ICD codes (if reported)	Confounders included in analyses
Wang, 2021 [20•]	Iran; GCS	12 yr	136/48,421	Prospective population-based cohort on general population, 40–75, Both	A 116-item FFQ	HEI-2015 based the Dietary Guidelines for Americans-2015; 13 diet components; 0–5 for six components, 0–10 for 8 components; total score: 0–100 AHEI-2010 based on epidemiologic studies of foods and nutrients associated with chronic disease risk: 11 components; 0–10 for each; total score: 0–110 aMED assesses conformity to a traditional Mediterranean diet: 9 components; 0–1 for each; total score: 0–9 DASH: 8 components; 1–5 for each; total score: 8–40	Two external internists reviewed death or occurrence of lung cancer; ICD-10 codes C34	Age, sex, race/ethnicity, BMI, education, place of residence, socioeconomic score, marital status, opium usage, alcohol consumption, total energy intake, physical activity, smoking status.
Wei, 2021 [47]	UK; UK Biobank	7.13 yr	1782/416,588	Prospective study of >500,000 participants from 22 health assessment centers across Great Britain, 40–69, Both	A FFQ included 29 questions about diet and 18 questions about alcohol	PCA (16 food items) derived dietary patterns: prudent pattern, western pattern, open-sandwich pattern	Cases were linked to cancer and death registries. ICD-10 codes C33 and C34	Age, sex, geographical region, smoking status and ethnicity, Townsend deprivation index, education, BMI, alcohol, family history of lung cancer, and for women, menopause status and hormone replacement therapy use.

Table 1 (continued)

Author, year [reference]	Study location or cohort name	Dates of enrollment or follow-up duration	Cases/Cohort or controls	Study participants, median/mean age or range, sex	Exposure assessment	Dietary pattern scoring details	Outcome assessment, ICD codes (if reported)	Confounders included in analyses
Willemsen, 2022 [48]	Canada; The Alberta's Tomorrow Project cohort	13.3 yr	252/26,462	Prospective cohort study with 55,530 Albertan, 50.8, Both	A validated 124-item FFQ	PCA revealed three dietary patterns (western, prudent, and "sugar, fruits, and dairy") and RRR resulted in four patterns (dietary fiber, vitamin D, fructose, and discretionary fat)	Incident cases were obtained by data linkage with the Alberta Cancer Registry	Age, sex, BMI, energy intake, smoking status, physical activity.
Zhang, 2022 [43]	USA; The Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial	8.8 yr	1632/98,159	Prospective cohort study with 98,159 participants, 65.5, Both	A validated dietary history questionnaire	Diabetes risk reduction diet, the sum of the quintile values from 1 to 5 of 9 dietary variables including cereal fiber, nuts, coffee, whole fruits, and ratio of polyunsaturated to saturated fat; and GI, trans-fat, SBs/fruit juices, and red and processed meats	Incident cases were from annual study update forms, and then the diagnosis was confirmed in relevant medical records	Age, sex, BMI, energy intake, family history of lung, marital status, race/ethnicity, smoking status, pack-years of cigarettes, alcohol intake, history of diabetes.
Cai, 2022 [42]	Japan; The Japan Public Health Center-based prospective study	17.0 yr	Not reported/90,171	Prospective cohort study with 90,171 participants, 50.4, Both	A validated 147-item FFQ	Low-carbohydrate diet based on the	Incident cases were from medical records and cancer registries	Age, sex, smoking, drinking, BMI, total physical activity levels, history of diabetes, total energy intake, green tea consumption, and coffee consumption.

Table 1 (continued)

Author, year [reference]	Study location or cohort name	Dates of enrollment or follow-up duration	Cases/Cohort or controls	Study participants, median/mean age or range, sex	Exposure assessment	Dietary pattern scoring details	Outcome assessment, ICD codes (if reported)	Confounders included in analyses
Case-cohort study								
Balder, 2005 [28]	Netherlands; The Netherlands Cohort Study on Diet and Cancer	9.3 yr	1426/2190	Population-based, 61.3 (sub-cohort), Men	A 9-day diet record	Factor analysis (51 food groups) identified five stable dietary patterns: (salad) vegetables, (cooked) vegetables, pork/processed meat/potatoes, sweet foods, white/brown bread substitution	The Netherlands Cancer Registry, ICD-O, T162.2-T162.9	Age, total energy intake, current cigarette smoker, number of cigarettes smoked per day, years of smoking cigarettes, higher vocational or university education, family history of lung cancer, physical activity. DPs were mutually adjusted.
Schulpen, 2018 [17]	Netherlands; The Netherlands Cohort Study	20.3 yr	2861/3720	Population-based, 55–69, Both	A validated self-administered, 150-item, semi-quantitative FFQ	aMED: 9 food items; 0–1 for each; total score: 0–9 mMED: collapsed fruit and vegetables into one group, added total meat, dairy, refined grains, and UFA:SFA	Netherlands Cancer Registry, ICD-O, C34	Age, cigarette smoking status, cigarette smoking duration, cigarette smoking frequency, energy intake, alcohol consumption, BMI, non-occupational physical activity, highest level of education, family history of lung cancer, history of physician-diagnosed chronic bronchitis.

AHEI-2010 Alternate Healthy Eating Index-2010, *aMED* alternate Mediterranean diet score, *BCDDP* The Breast Cancer Detection Demonstration Project, *BMI* body mass index, *COSMOS* The Continuous Observation of Smoking Subjects study, *CT* computed tomography, *DASH* Dietary Approaches to Stop Hypertension, *DII* Dietary inflammatory index, *DP*'s dietary patterns, *EPIC* The European Prospective Investigation into Cancer and Nutrition, *FFQ* food frequency questionnaire, *HEI-2015* Healthy Eating Index-2015, *GCS* The Golestan Cohort Study, *MCCS* The Melbourne Collaborative Cohort Study, *MDS* Mediterranean diet score, *mMED* modified Mediterranean diet, *NIH-AARP* The NIH-AARP diet and health study, *NSAID* non-steroidal anti-inflammatory drugs, *NSCLC* non-small cell lung cancer, *PCA* principal component analysis, *RFS* Recommended Food Score, *RRR* reduced rank regression, *SCHC* The Singapore Chinese Health Study, *SFA* saturated fatty acids, *UFA* unsaturated fatty acids, *VIP* The Vasterbotten Intervention Programme, *WHI* The Women's Health Initiative Observational Study

^aOutcome is NSCLC

risk but only two of them were statistically significant [18, 21]. Three other studies reported that conformity to the Recommended Food Score [29] or a plant-based diet [40] or diabetes risk reduction diet [43] were related to a lower risk of lung cancer.

Dietary Patterns and Lung Cancer Stratified by Sex or Smoking Status

Among studies that evaluated results stratified by sex, similar results for males and females were reported (Supplemental Table 4). Considering the impact of smoking on associations between dietary patterns and lung cancer, we further summarized the evidence stratified by smoking status (Supplemental Table 5). For data-driven dietary patterns, the proportion of studies reporting statistically significant findings (approximately 43–55%) were similar between smoking subgroups, with 11 out of 20 studies for former smokers, eight out of 16 studies among current smokers, and six out of 14 studies for never smokers. For the *a priori* dietary patterns, there were more statistically significant associations observed among former smokers (nine out of 17 studies) and current smokers (seven of 16 studies) than never smokers (four out of 18 studies).

Meta-Analyses on Associations of Dietary Patterns with Lung Cancer

Table 2 shows the pooled results between dietary patterns and lung cancer risk when there were at least two studies reporting associations. Fruits/vegetables patterns (RR = 0.56, 95% CI = 0.36–0.87) were inversely associated with lung cancer risk, while high meat/protein patterns (RR = 1.58, 95% CI = 1.10–2.26) and Western dietary patterns (RR = 1.32, 95% CI = 1.08–1.60) were positively associated with lung cancer. Higher dietary quality measured by HEI (RR = 0.87, 95% CI = 0.80–0.95), AHEI (RR = 0.88, 95% CI = 0.81–0.95), DASH (RR = 0.87, 95% CI = 0.77–0.98), and Mediterranean Diet Score (MDS; RR = 0.87, 95% CI = 0.81–0.93) were significantly associated with lower risk of lung cancer, while higher DII (i.e., more pro-inflammatory diet) was associated with a higher risk of lung cancer (RR = 1.14, 95% CI = 1.07–1.22). The forest plots were shown in Supplemental Fig. 1. We found a high heterogeneity between studies for fruit/vegetables patterns ($I^2 = 91$, $P < 0.001$) and high meat/protein patterns ($I^2 = 75$, $P = 0.007$). After we excluded the He et al. study and De Stefani et al. 2008 study, the I^2 decreased, and results were similar with our main estimates (fruit/vegetables patterns: RR = 0.71, 95% CI = 0.62–0.82, $I^2 = 0$, P for $Q = 0.46$;

Table 2 Meta-analyses on associations of dietary patterns with lung cancer risk

Dietary patterns	No. of studies	RR (95% CI)	I^2	P for Q
Data-driven dietary patterns				
Prudent pattern	5	0.81 (0.66–1.01)	65	0.01
Fruits/vegetables pattern ^a	5	0.56 (0.36–0.87)	91	<0.001
High meat/protein pattern ^b	4	1.58 (1.10–2.26)	75	0.007
Western pattern	6	1.32 (1.08–1.60)	68	0.04
Traditional pattern ^c	2	1.08 (0.82–1.42)	0	0.33
Drinker patterns ^d	2	1.28 (1.03–1.59)	0	0.51
A priori dietary patterns				
HEI ^e	4	0.87 (0.80–0.95)	42	0.16
AHEI	4	0.88 (0.81–0.95)	40	0.17
DASH	4	0.87 (0.77–0.98)	72	0.01
MDS ^f	10	0.87 (0.81–0.93)	35	0.08
DII	6	1.14 (1.07–1.22)	0	0.61

AHEI alternate Healthy Eating Index, CI confidence intervals, DASH Dietary Approaches to Stop Hypertension, DII dietary inflammatory index, HEI Healthy Eating Index, MDS Mediterranean diet score, RR relative risk

^aFruits/vegetables patterns included fruits/vegetables pattern, starchy vegetables pattern, high in vegetables and low in animal products pattern, (cooked) vegetables pattern, (salad) vegetables pattern

^bHigh meat/protein pattern included high quality protein pattern, high-meat pattern, animal products pattern, pork/processed meat/potatoes pattern

^cTraditional pattern was highly related to desserts, total grains, and all tubers

^dDrinker pattern was highly related to beer, wine, and hard liquor intake

^eHEI included HEI-2010 and HEI-2015

^fMDS included Polish-adapted MDS, alternate Mediterranean diet score, modified Mediterranean diet

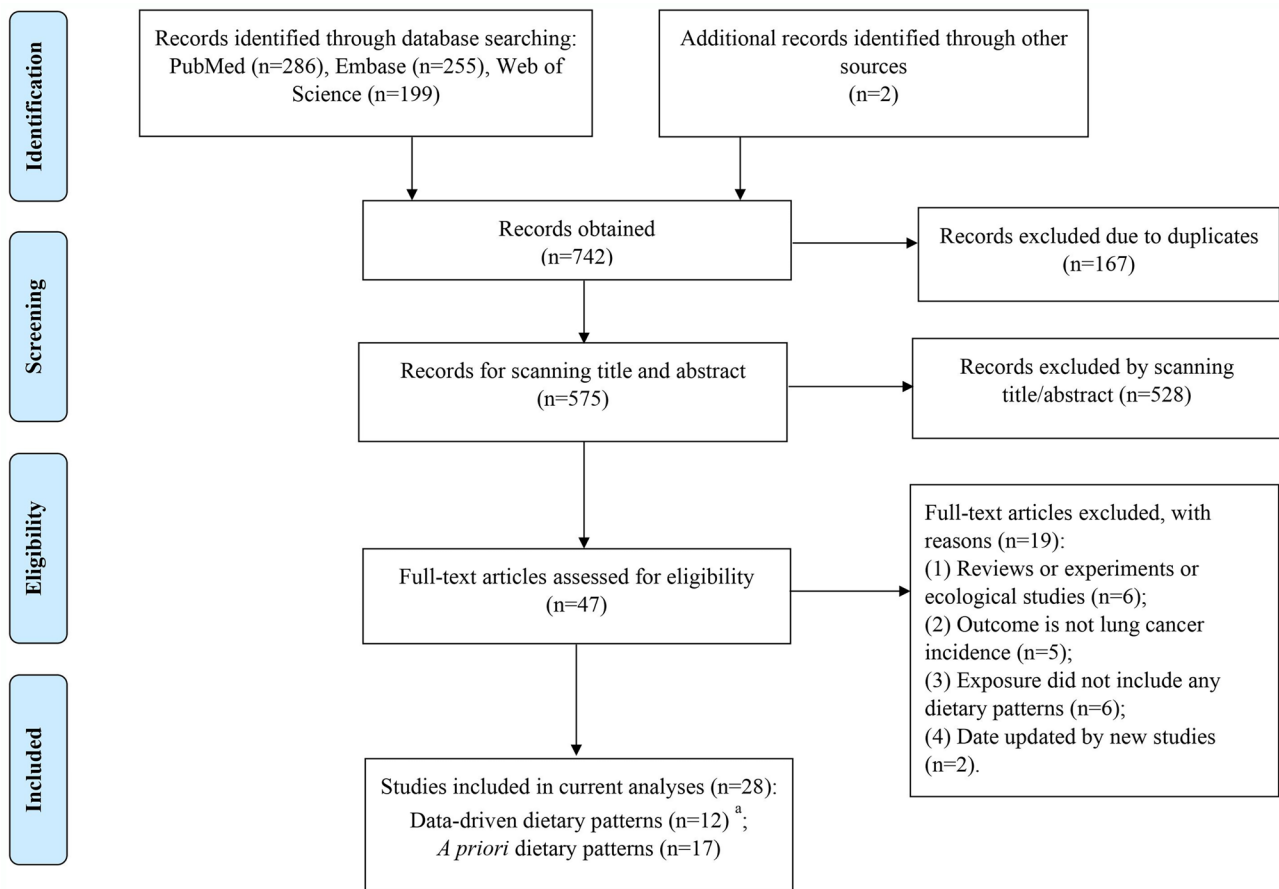


Fig. 1 Flow chart of study selection. ^a One article provided results from both Mediterranean diet and factor analysis. Only one study used reduced rank regression and we grouped it into data-driven dietary patterns

high meat/protein patterns: RR = 1.31, 95% CI = 1.09–1.58, $I^2 = 0$, P for $Q = 0.83$). These observed associations were similar when we restricted the analyses to prospective studies (Supplemental Table 6).

We further pooled studies stratified by sex (Supplemental Table 7) or smoking status (Supplemental Table 8). Consistent with our summary results, the associations between dietary patterns and lung cancer did not differ much across sex. However, significant associations were more likely to be found among former and current smokers than among never smokers.

Discussion

Summary of Results

Based on this systematic review of the evidence on associations between dietary patterns and lung cancer risk, we found that dietary patterns characterized by high intake of fruits or vegetables and low intake of animal-based foods

were associated with a lower risk of lung cancer. Conformity of diet to a healthy dietary pattern including HEI, AHEI, DASH, and Mediterranean diet was associated with a lower risk of lung cancer, while a more pro-inflammatory diet (i.e., higher DII) was associated with a higher risk of lung cancer in the majority of studies reported to date.

Explanations and Comparison

Our review indicates dietary patterns with higher fruits and vegetables and lower animal products are associated with a lower risk of lung cancer, which is generally consistent with previous evidence on these individual food groups [49]. Recently, an umbrella review summarized the associations between fruit and vegetable intake and health outcomes [50]. The study found higher fruit intake or vegetable intake is associated with a lower risk of lung cancer. Another umbrella review that focused on the associations between red meat and cancer risk found higher intake of red meat was associated with a higher risk of lung cancer [51]. A prudent diet and HEI, AHEI, DASH, and Mediterranean diet scores are all

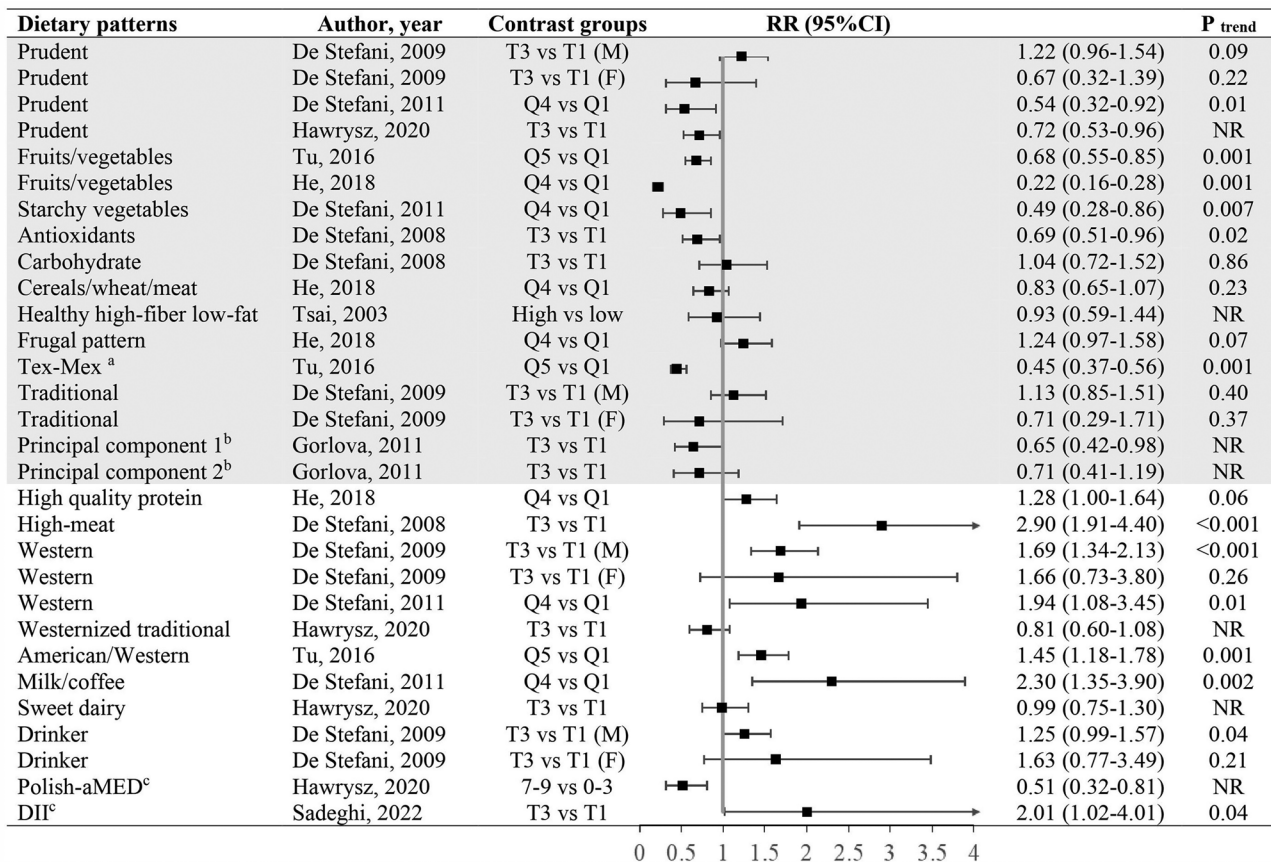


Fig. 2 Associations between dietary patterns and lung cancer risk among case–control studies. CI confidence intervals, F female, M male, Q4 vs Q1 Quartile 4 vs. Quartile 1, Q5 vs Q1 Quintile 5 vs. Quintile 1, RR relative risk, T3 vs T1 Tertile 3 vs. Tertile 1. ^a Tex-Mex pattern is character-

ized by its heavy use of legumes, spices, and shredded cheese. ^b Principal component 1: High in vegetables and low in animal products. Principal component 2: High in other plant food except for vegetables. ^c Except for these two studies, all others are data-driven dietary patterns

characterized by higher intakes of fruits and vegetables, and lower intakes of red/processed meat, and the consistent lower risk of lung cancer with these dietary patterns in our review supports the previous reviews of the individual food groups.

Our findings on the Mediterranean diet and lung cancer corroborate the conclusions of a review published in 2022 which included nine studies (eight cohort and one case–control studies) [16•]. Our review included an additional cohort study published in 2021 [20•]. Besides Mediterranean diet, in the current systematic review, conformity to a healthy diet as assessed by the HEI, AHEI, and DASH is consistently associated with a lower risk of lung cancer. These dietary patterns give higher scores for plant-based foods, such as whole grains, vegetables, fruits, and nuts [52] and emphasize moderation of red and processed meat intake. The DASH diet also emphasizes reduced intake of sugar-sweetened beverages and sodium. Chronic inflammation plays a critical role in carcinogenesis [53]. Recently, an umbrella review suggested compelling evidence on the link between DII and respiratory (including lung) cancers

[54]. A meta-analyses of multiple cancer types reported a positive association between DII and lung cancer in three cohorts (pooled RR = 1.30, 95% CI = 1.13–1.50) [55]. In our systematic review, six studies indicate positive associations between DII and lung cancer risk with three of them statistically significant (pooled RR = 1.14, 95% CI = 1.07–1.22).

We found that among studies that reported on *a priori* dietary patterns, more statistically significant associations were observed among former and current smokers than never smokers, which was somewhat consistent with a previous systematic review on the Mediterranean diet and lung cancer that identified inverse associations among former smokers but not among never smokers or current smokers [16•]. However, among previous studies, only one study reported a statistically significant interaction between HEI and smoking on lung cancer ($P_{interaction} = 0.03$) [20•]. For data-driven dietary patterns, results were similar between smoking subgroups. Thus, more studies are needed that stratify results by smoking status to determine whether associations may differ by tobacco exposure. Studies evaluating the effect modification

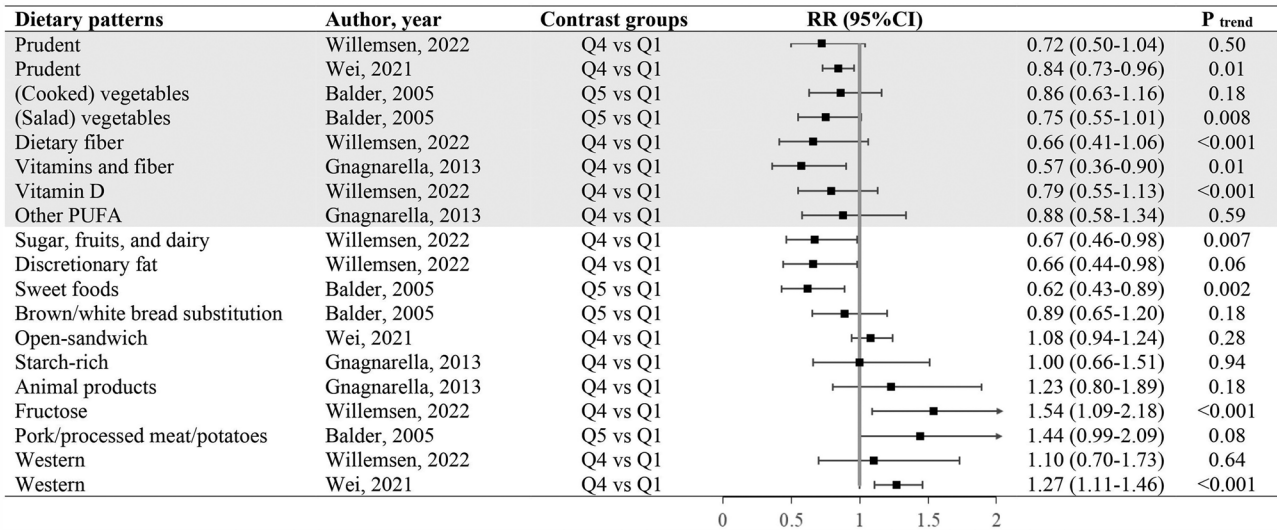


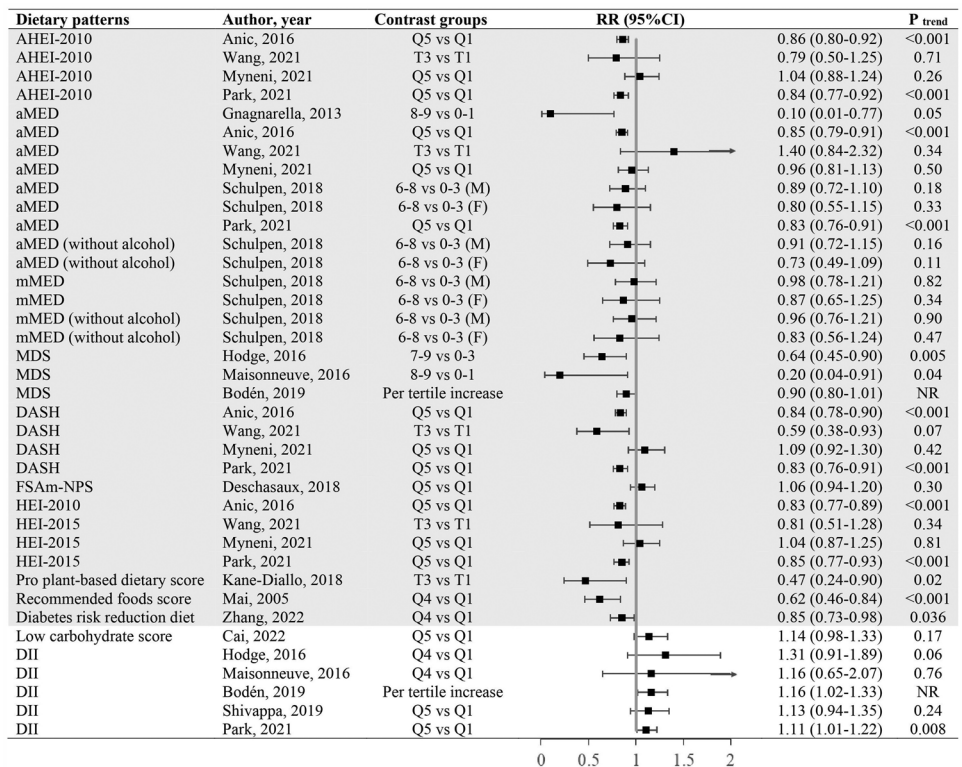
Fig. 3 Associations between data-driven dietary patterns and lung cancer risk among prospective studies. CI confidence intervals, PUFA polyunsaturated fatty acids, Q4 vs Q1 Quartile 4 vs. Quartile 1, Q5 vs Q1 Quintile 5 vs. Quintile 1, RR relative risk

role of sex on the associations between dietary patterns and lung cancer reported similar results between males and females without significant interactions [19, 21, 47].

The inverse associations of diets high in plant-based foods and low in red meat or animal products with lung cancer risk are biologically plausible. A diet high in fruits, vegetables, and whole grains is higher in bioactive compounds like carotenoids, flavonoids, and polyphenols, which display anticarcinogenic

properties in animal studies [56]. In addition, dietary components like fiber may affect inflammation which is a hallmark of cancer and is implicated in the etiology of lung cancer [57, 58]. Potential biological mechanisms have been proposed to support the positive association between diets high in red or processed meat and lung cancer risk. Multiple carcinogens like heme iron, heterocyclic amines, and N-nitroso compounds were found in red and processed meat [59]. Epidemiological studies

Fig. 4 Associations between *a priori* dietary patterns and lung cancer risk among prospective studies. AHEI Alternate Healthy Eating Index-2010, aMED alternate Mediterranean diet, CI confidence intervals, DASH Dietary Approaches to Stop Hypertension, DII Dietary inflammatory index, FSAm-NPS the Nutrient Profiling System of the British Food Standards Agency (modified version), F female, HEI-2010 Healthy Eating Index-2010, HEI-2015 Healthy Eating Index-2015, M male, mMED modified alternate Mediterranean diet, MDS adapted Mediterranean diet score, Q4 vs Q1 Quartile 4 vs. Quartile 1, Q5 vs Q1 Quintile 5 vs. Quintile 1, RR relative risk, T3 vs T1 Tertile 3 vs. Tertile 1



also showed heme iron from red or processed meat was positively associated with a higher risk of lung cancer [60].

Limitations

Several limitations of the review and of the individual studies should be noted. First, due to the observational study designs of the included studies, we cannot rule out residual confounding of healthy lifestyles. Previous studies reported cigarette smoking is significantly associated with unhealthy diet [61–63]. Even though most of the included studies have adjusted for important confounders, such as smoking, physical activity, body mass index, and family history of cancer, the observed association could still be biased by unmeasured confounders or residual confounding. Second, we observed an inverse association between some dietary patterns and lung cancer with a limited number of studies, such as the pro plant-based dietary score which calculates the relative contribution of plant foods versus animal products in the diet and the Recommended Food Score. We cannot draw definitive conclusions based on only one or two studies, and more research is needed among different populations. Third, we did not have enough information to further explore the association between dietary patterns and subtypes of lung cancer. Lung cancer is a complex disease including small cell lung cancer (accounts for 15–17%) and non-small cell lung cancer (> 85%) like adenocarcinoma, squamous cell carcinoma, and large cell carcinoma [64]. Those histologic subtypes may have different etiology. Only five studies in our review reported results stratified by histologic subtypes [19, 39, 43, 45, 47], and none of them observed significant differences in these subgroup analyses, which may be due to the limited numbers in each subgroup. More studies with larger sample sizes are needed to examine whether associations differ by histologic subtype. Finally, we did not have enough information to address the role of race and ethnicity in the associations between dietary patterns and lung cancer risk. Among those studies in our systematic review, none of case–control studies reported information on race and ethnicity and only six of 17 cohorts further controlled for race and ethnicity in multivariable models [20, 21, 35, 43, 45, 47]. Of these six studies, four studies [21, 43, 45, 47] examined the interaction between dietary patterns and race and ethnicity with only one study reporting a significant interaction between Western dietary pattern and ethnicity [47]. Further research is needed to evaluate the role of race and ethnicity in associations between diet and lung cancer risk.

Conclusion

Our systematic review indicated healthy dietary patterns characterized by high fruits and vegetables and low in red meat and animal products are associated with a lower risk of lung cancer.

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Author Contribution Study conception and design: LZ and SS; study protocol: LZ and SS; literature research and data extraction: LZ and BK; data analyses: LZ and BK; results interpretation: LZ, BK, JZ, and SS; draft: LZ; review and critical revision: LZ, BK, JZ, and SS; read and approved the version of the manuscript being submitted: LZ, BK, JZ, and SS.

Data Availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Compliance with Ethical Standards

Conflict of Interest All authors have no conflict of interest to declare.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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