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Index-based dietary patterns in relation to gastric cancer risk: a systematic review and meta-analysis

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Abstract

Dietary indices are widely used in diet quality measurement, and the index-based dietary patterns are related to gastric cancer risk. To evaluate the relationship between different kinds of index-based dietary patterns and gastric cancer risk, we systematically searched four English-language databases and four Chinese-language databases. The quality of studies was assessed by the Newcastle–Ottawa Scale. Meta-analyses were performed to estimate the association between gastric cancer incidence and different types of index-based dietary patterns. The OR and hazard ratios (HR) of gastric cancer incidence were calculated by regression models in case–control studies and prospective cohort studies, respectively. The studies were pooled in the random effects model to calculate the summarised risk estimate of the highest quantile interval of dietary indices, taking the lowest as the referent. The dietary indices included different versions of Mediterranean diet score (MDS) and dietary inflammatory index (DII), healthy eating index, Chinese Food Pagoda score and food index score. The meta-analysis was carried out for studies on MDS and DII. The combined OR of gastric cancer for the highest MDS *v.* the referent was 0·42 (95 % CI 0·2, 0·86), and the combined HR was 0·89 (95 % CI 0·68, 1·17). The combined OR for DII was 2·11 (95 % CI 1·41, 3·15). Higher Mediterranean dietary pattern consumption might reduce gastric cancer risk, while higher inflammatory diet pattern consumption might increase gastric cancer risk.

Key words: **Gastric cancer: Index-based dietary patterns: Systematic reviews: Meta-analyses**

Gastric cancer is the fifth most common cancer and the third leading cause of cancer-related death worldwide. The incidence is significantly elevated in Eastern Asia, compared with North America and Europe[1]. Increasing evidence has shown that gastric cancer was induced by synergistic effects of *Helicobacter pylori* infection, dietary factors and genetic instability[2–4]. Since *H. pylori* eradication has been applied, the morbidity of gastric cancer has decreased[5]. However, the eradication of *H. pylori* is becoming more difficult[6,7].

Different sorts of food patterns and foods have various effects on gastrointestinal tumours[8,9]. Previous studies on diet and gastric cancer mainly used *a posteriori* methods to study the association between gastric cancer risk and dietary patterns[10]. Diets were generally categorised into healthy/prudent patterns (rich in fruit and vegetables), Western/unhealthy patterns (rich in starchy foods, meat and fat) and alcohol-drinking patterns (high consumption of alcohol). The healthy/prudent pattern showed a protective effect on gastric cancer, while the Western and alcohol-drinking patterns were risk factors. This method summarises the dietary consumption via factor analysis, principal component analysis or cluster analysis and correlated the dietary patterns with diseases' risk. However, the *a posteriori* method defined dietary patterns empirically, for example, in Bahmanyar & Ye's study[11], the Western pattern mainly included processed meat, red meat, sweets, high-fat dairy, high-fat gravy, high-energy drinks, whole grains and coffee, while in Kim *et al.*'s study[12], the Western pattern mainly included butter, mayonnaise, cheese, beef, pork, poultry, bacon, liver, soda beverages, fruit juice, vegetable juice and instant noodles, which added the heterogeneity of the study.

Abbreviations: CHFP, Chinese Food Pagoda; DII, dietary inflammatory index; GCA, gastric cardia adenocarcinoma; GNCA, gastric non-cardia adenocarcinoma; HEI, Healthy Eating Index; HR, hazard ratio; MDP, Mediterranean dietary pattern; MDS, Mediterranean diet score; NOS, Newcastle–Ottawa Scale.

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The *a priori* method assesses the dietary quality by a unified scoring system. For example, the Mediterranean diet score (MDS) system includes vegetables, legumes, fruits and nuts, dairy products, cereals, meat and meats products, alcohol and olive oil.

The *a priori* methods, namely dietary indices, were hypothesis-driven and were used to quantify dietary quality according to dietary guidelines or certain types of diets. The dietary management would be more precise and practical by using this method. So, the dietary indices could be used for chronic disease prevention and management by not only nutritionists but also clinicians and gastropathy patients. Increasing evidence has indicated the correlation between these index-based dietary patterns and the risk of gastric cancer, such as the MDS[13,14], the healthy eating index (HEI)[15] and the dietary inflammatory index (DII)[16–18]. The Mediterranean dietary pattern (MDP), which is characterised by a high intake of vegetables, fruits, legumes, non-refined cereals, nuts, olive oil, moderate intake of fish and dairy products and low intake of red meat, could prevent gastric cancer. Because these ingredients containing an abundance of antioxidants could reduce DNA damage, they could also reduce *H. pylori* infection[19] and inhibit the angiogenesis process of tumours[20]. The DII, however, could reflect the inflammatory effect caused by diet[21], which was a key process in gastric cancer initiation and progression[22]. However, to date, there is no systematic review and meta-analysis on the association between index-based dietary patterns and gastric cancer risk. In order to quantify the general effects of high consumption of different index-based dietary patterns on gastric cancer, we carried out a systematic review and meta-analysis of observational studies on the relationship between the index-based dietary patterns and gastric cancer incidence.

Materials and methods

The protocol was registered in PROSPERO International Prospective Register of systematic reviews (ID: CRD 42018100575).

Inclusion and exclusion criteria

Studies were included if they met the following SPIDER[23] (Sample, Phenomenon of Interest, Design, Evaluation, Research type) criteria: (1) Sample: for cohort studies, the general population without gastric cancer; for case–control studies, patients who were diagnosed with gastric cancer. (2) The Phenomenon of Interest: the incidence of gastric cancer. (3) Design: studies using index-based dietary patterns to reflect dietary quality. (4) Evaluation: the consumption of certain index-based dietary patterns, such as the Mediterranean diet (reflected by the MDS) and the inflammatory diet (reflected by DII). (5) Research type: prospective cohort, retrospective cohort, case–control.

Studies were excluded for: (1) cellular, animal experiments; (2) studies on the other risk or protective factors for gastric cancer; (3) studies on certain drugs, foods, nutrients or eating behaviours; (4) studies that used *a posteriori* methods to identify dietary patterns.

Search strategy

A comprehensive search of literature published before December 2018 was performed in PubMed (https://www.ncbi.nlm.nih.gov/pubmed), Embase (https://www.embase.com), Web of Science (https://www.webofknowledge.com), Cochrane Library (https://www.cochranelibrary.com), CNKI (https://www.cnki.net), VIP (http://www.cqvip.com), WAN FANG (http://www.wanfangdata.com.cn) and SinoMed (http://www.sinomed.ac.cn). Publications with title and abstract containing the keywords 'diet', 'gastric', 'cancer' were identified. The full list of the searching strategy was as follows: (diet* OR food OR eat*) AND (quality OR pattern OR score OR index OR indices) AND (gastric OR stomach) AND (cancer OR neoplasm OR tumor OR carcinoma). There were no restrictions on the types of publications or the participants' characteristics, but only studies published in English and Chinese were considered.

Screening

Two authors screened all the identified literature by title and abstract independently and selected articles according to the inclusion and exclusion criteria. Then, a full-text screen was made on all possibly eligible papers. Relevant studies in reference lists that met the inclusion criteria were also included. Finally, all eligible articles were collected, and disagreements that could not be resolved by discussion were presented to a third person for the final decision.

Data extraction

Data extracted included general information (authors and year of publication, time of enrollment or follow-up time and the regions of the study), participants (numbers of participants), dietary assessment (data collection method and dietary indices used for assessment), adjusted variables (factors related to gastric cancer, such as *H. pylori* infection, age, sex, alcohol intake, smoking, physical activity, etc.), main findings (conclusion of the relation of dietary indices to gastric cancer incidence, OR, risk ratio or hazard ratio (HR) of the highest quantile interval compared with the referent or one-unit increase in the score, 95 % CI, *P* value), subgroup analysis (female and male, gastric cardia adenocarcinoma (GCA) and gastric non-cardia adenocarcinoma (GNCA), intestinal type and diffuse type). Data not shown in the publication were acquired by sending an email to the author.

Quality assessment

The quality and risk of bias of the included studies were assessed using a modified Newcastle–Ottawa Scale (NOS) for assessing the quality of non-randomised studies[24]. Two researchers independently assessed the quality of the studies using the NOS, and the disagreement was resolved by discussion with the third person. Three aspects, namely, selection, comparability and outcomes, were assessed using this scale, with a maximum score of nine. Studies scored six or more stars were considered as having high quality.

Statistical analysis

We first categorised all the retrieved dietary indices used in gastric cancer incidence studies. Then for each type of indices, mean difference with 95 % CI was pooled into the relevant effect models.

For heterogeneity assessment, we first carried out a Q test. As the test detected moderate degrees of heterogeneity and there were not many included studies, $P \leq 0{\cdot}1$ was considered of significant heterogeneity. Then, the I^2 statistic was calculated. I^2 equaling 0–25 % indicates that the heterogeneity might not be important; 25–50 % represents moderate heterogeneity; 50–75 % represents substantial heterogeneity and 75–100 % represents considerable heterogeneity[25]. When heterogeneity was more than 25 %, a random effect model was used for meta-analysis. A fixed effects model was used when the heterogeneity was less than 25 %[26]. Publication bias would be assessed by Begg's and Egger's tests if the included studies were ten studies or more.

All calculations and graphs were performed using Review Manager version 5.3 (Nordic Cochrane Center).

Subgroup analysis and sensitivity analysis

In order to deal with heterogeneity, subgroup analysis is necessary. These will focus on four aspects: (1) patterns of diets (MDP and inflammatory diet pattern); (2) types of study (cohort study or case–control study); (3) types of gastric cancer (GCA and GNCA, intestinal type and diffuse type) and (4) regions of study. In order to explore the influence of the methodological quality of the study on effect size, sensitivity analyses might be performed. Pre-specified sensitivity analyses will be performed by removing one study at a time and determining the influence of a single article on the overall pooled estimate.

Results

Study characteristics and quality assessment

As shown in the flow chart (Fig. 1), eleven publications were selected from 4104 pieces of the article identified by the systematic review. The main characteristics and NOS scores of each study are shown in Tables 1 and 2, respectively. According to NOS assessment, all studies were eligible, among which nine were considered as high quality. Among these, five studies focused on the association between gastric cancer and Mediterranean diet using different versions of the MDS created by Trichopoulou *et al.*[32]. They are the relative MDS in Buckland's studies[13,14]; the alternate MDS[33] in Li *et al.*'s study[15]; the MDS in the first case–control study in Praud *et al.*'s study[29]; the MDS, MDP adherence index[34] and Mediterranean Adequacy Index[35] in the second case–control from the same article[29] and Literature-based adherence score to the Mediterranean Diet[36,37] in Stojanovic *et al.*'s study[30]. Other widely applied dietary indices were different versions of DII[21], such as the Literature-derived Population-based DII[38] used in the case–control study by Shivappa *et al.*[17], as well as another two case–control studies by Lee *et al.*[18] and Vahid *et al.*[31]; and Inflammatory Score of the Diet in Agudo's cohort study, which is mainly based on DII and changed according to local dietary habits[16]. There were three other types of dietary indices, the food index score used in Campbell *et al.*'s study[28], the HEI-2005[39] used in Li *et al.*'s cohort study[15] and the Chinese Food Pagoda (CHFP) score[40] used in Zhang *et al.*'s cohort study[27].

In the studies on indices based on MDP and gastric cancer incidence, there were different conclusions. Three case–control studies and two cohort studies indicated that high adherence to the Mediterranean diet was associated with reducing gastric cancer risk, while the other cohort study on the American population demonstrated that Mediterranean diet was associated with increased risk of GCA and decreasing risk of GNCA. In the studies related to DII, the score was associated with increased gastric cancer risk. The HEI, based on the American dietary guidelines, showed a protective effect in the cohort study. What is more, the food index score was inversely associated with gastric cancer incidence. There was only one piece of study on HEI and one piece of study on food index score, other studies focused on MDS and DII. Therefore, we carried out a meta-analysis on the studies using MDS (including MDS, relative MDS, alternate MDS, and Literature-based adherence score to the Mediterranean Diet) or DII (including Literature-derived Population-based DII and Inflammatory Score of the Diet). The analysis was carried out for case–control and cohort studies, respectively.

Meta-analysis

Since the included studies focused on different versions of dietary indices, and only the studies on MDS and DII have more than one study, we included the studies on MDS and the studies on DII in the meta-analysis. Because two pieces of Buckland *et al.*'s literature (2010[13] and 2015[14]) were from the same study[41] (the one published in 2015 has a larger population), two cohort studies on MDS, two case–control studies on MDS and three case–control studies on DII were included in meta-analysis, respectively.

The estimated OR and HR for the highest quantile interval *v.* the lowest values of MDS and DII are shown in Figs. 2 and 3, respectively. For MDS and gastric cancer risk, there were two case–control studies and two cohort studies focusing on the association between MDP and gastric cancer risk. For the case–control studies, groups with a high MDS had a significantly lower odds of developing gastric cancer than those with a low score (OR 0·42 (95 % CI 0·20, 0·86), $P = 0{\cdot}02$). For the cohort studies, there was a similar tendency in both GCA (HR 0·84 (95 % CI 0·47, 1·49), $P = 0{\cdot}54$) and GNCA (HR 0·92 (95 % CI 0·63, 1·35), $P = 0{\cdot}67$); the combined HR was 0·89 (95 % CI 0·68, 1·17), $P = 0{\cdot}4$. However, the tendency was not significant. There was a substantial heterogeneity in both case–control ($I^2 = 77$ %) and cohort studies ($I^2 = 52$ %). As there were only two studies for each meta-analysis, the sensitivity analysis could not be carried out. The subgroup analysis did not show any reduction of heterogeneity for the cohort studies (for GCA $I^2 = 73$ %; for GNCA $I^2 = 59$ %). As two cohort studies were carried out in America (USA) and Europe (ten different countries), respectively, and two case–control studies were all in Italy, the subgroup analysis on the region of study is impossible to carry out. The heterogeneity might be caused by different versions of

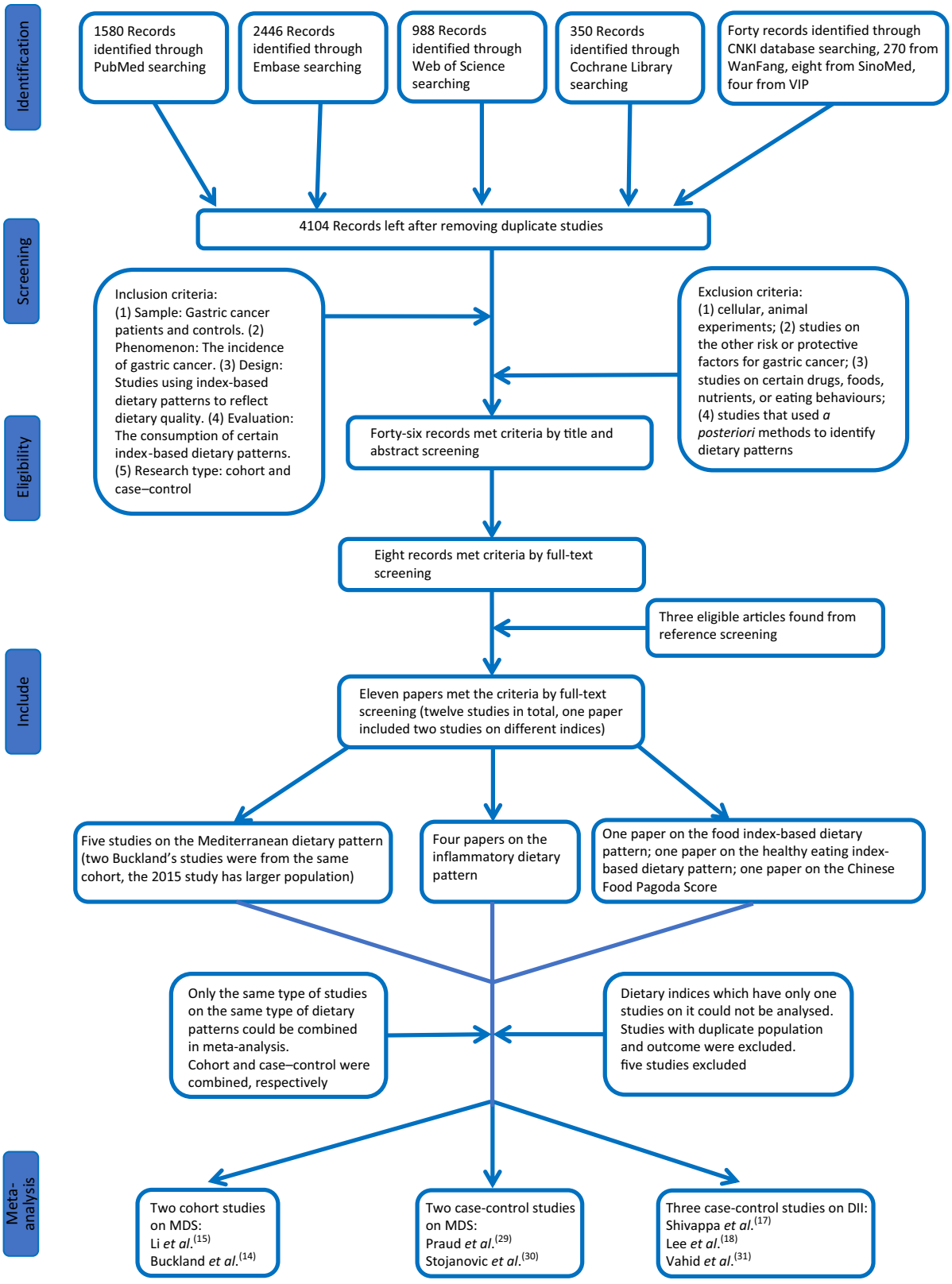

Fig. 1. Flow chart of the literature search. MDS, Mediterranean Diet Score.

Table 1. Main characteristics of eleven studies in the systematic review*

General information	Participants	Dietary assessment	Adjusted variables	Main findings	Subgroup analyses
Cohort studies					
Buckland *et al.*[13], 1992–1998, followed up to 2003–2006 Ten European countries (UK, France, Denmark, Sweden, Germany, Italy, Spain, the Netherlands, Norway and Greece)	485 044 participants (29·8 % men) including 449 incident cases	Validated country-specific questionnaires (88–266 different foods in the past 12 months) and 24-h diet recall rMED score (range 0–18)	Sex, BMI, education level, smoking status and intensity and energy intake	rMED score associated with a significant reduction in gastric cancer risk (HR 0·67; 95 % CI 0·47, 0·94) A one-unit increase in rMED score was associated with a 7 % reduced risk of GC (95 % CI 0·89, 0·99)	High adherence was associated with a reduced risk of GCA compared with a low rMED adherence (HR 0·45; 95 % CI 0·21, 0·91), while an inverse trend was found for GNCA (HR 0·71; 95 % CI 0·44, 1·17; $P = 0·148$)
Li *et al.*[15], 1995–1996, followed up to 2006 USA	494 968 participants (295 300 men) including 453 GCA and 501 GNCA	FFQ (124 food items over the past year) and calibrated with 24-h dietary recalls HEI-2005 (0–100) and aMED (0–9)	Age, sex, race, smoking, alcohol intake, education, BMI, vigorous physical activity, usual activity and total energy intake	Neither HEI-2005 nor aMED scores were significantly associated with GC	HEI-2005: GCA (HR 0·92; 95 % CI 0·67, 1·27; $P = 0·56$); GNCA (HR 0·88; 95 % CI 0·65, 1·2; $P = 0·15$) aMED: GCA (HR 1·10; 95 % CI 0·76, 1·61; $P = 0·90$); GNCA (HR 0·75; 95 % CI 0·52, 1·09; $P = 0·11$)
Buckland *et al.*[14], 1992–2000, followed up to 2010 Ten European countries (UK, France, Denmark, Sweden, Germany, Italy, Spain, the Netherlands, Norway and Greece)	461 550 participants, including 662 incident cases	Validated country-specific questionnaires (88–266 different foods in the past 12 months) and 24-h diet recall rMED score (excluding alcohol intake, range 0–16)	Sex, BMI, education level, smoking status and intensity and energy intake	Higher rMED score associated with reduction in gastric cancer risk (HR 0·87; 95 % CI 0·69, 1·09)	High adherence associated with reduced risk of GCA compared with low rMED adherence (HR 0·61; 95 % CI 0·38, 0·97), while an inverse trend was found for GNCA (HR 1·11; 95 % CI 0·80, 1·54)
Zhang *et al.*[27], 2002–2006, followed up to 2013 Shanghai, China	59 503 participants (all male) including 477 with gastric cancer	FFQ (semiquantitative contained eighty-one items) CHFP score (on the basis of 2007 CHFP, contained ten components, range 0–45)	Age, education, occupation, income, tea drinking habits, digestive diseases, smoking status, alcohol consumption, BMI, physical exercise	CHFP score associated with increased gastric cancer risk in men (OR 1·02; 95 % CI 0·82, 1·28; $P = 0·843$)	Without subgroup analysis
Agudo *et al.*[16], 1992–2000, with an average of 14 years follow-up Ten European countries (UK, France, Denmark, Sweden, Germany, Italy, Spain, the Netherlands, Norway and Greece)	476 160 subjects (29 % men) including 913 incident cases (56 % men)	FFQ or diet-history questionnaires 24-h dietary recall measurements ISD (assessing twenty-eight food items available in the EPIC databases)	Sex and energy intake, educational level, tobacco smoking, BMI, alcohol consumption, as well as intake of red meat, processed meat, citrus fruit and other fresh fruit Red meat and processed meat were not adjusted in CGC; BMI was not adjusted in NCGC	ISD is associated with an increased risk of gastric cancer (HR 1·66; 95 % CI 1·26, 2·20; $P < 0·001$) ISD as a continuous variable (HR 1·25; 95 % CI 1·12, 1·39)	ISD and CGC: HR = 1·94 (95 % CI 1·14, 3·30) $P = 0·011$. HRcon = 1·30 (95 % CI 1·06, 1·59). ISD and NCGC: HR = 1·07 (95 % CI 0·67, 1·70) $P = 0·55$. HRcon = 1·07 (95 % CI 0·89, 1·28). ISD and intestinal type: HR = 1·65 (95 % CI 1·18, 2·31) $P = 0·002$. HRcon = 1·18 (95 % CI 1·03, 1·34). ISD and diffuse type: HR = 1·30 (95 % CI 0·73, 2·31) $P = 0·34$. HRcon = 1·33 (95 % CI 1·06, 1·67)
Case–control studies					
Campbell *et al.*[28], 1995–1997 Canada	373 female cases and 1131 female controls; 796 male cases and 1201 male controls	FFQ (sixty-nine different foods in the past 2 years) Food index score (based on putative dietary risk factors for gastric cancer, range 0–58)	Age, strenuous physical activity, BMI, income, education, province of residence, smoking status and total energy intake	Food index score was significantly associated with decreased gastric cancer risk	Women: OR = 0·4, 95 % CI 0·27, 0·59; distal GC (OR 0·44; 95 % CI 0·23, 0·85); cardia GC (OR 0·63; 95 % CI 0·24, 1·67) Men: OR = 0·63, 95 % CI 0·45, 0·88; Distal GC (OR 0·61; 95 % CI 0·35, 1·09); cardia GC (OR 0·56; 95 % CI 0·32, 0·99)

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Table 1. (*Continued*)

General information	Participants	Dietary assessment	Adjusted variables	Main findings	Subgroup analyses
Praud *et al.*[29], 1985–1997 and 1997–2007 (two case–control studies) Italy	769 incident (469 men) and 2081 (1220 men) controls in the first study 230 incident (143 men) and 547 controls (286 men) in the second study 999 incident cases and 2628 controls in total	First study, FFQ (twenty-nine selected food items over the past 2 years) Second study, another FFQ (seventy-eight foods and beverages and a range of recipes) to collect weekly frequency of food consumption MDS (0–9) for both studies. MDPAI and MAI only for the second study	Age, sex, study, year of interview, education, BMI, tobacco smoking, family history and total energy intake	MDS associated with significantly reduced risk of gastric cancer (OR 0·57; 95 %CI 0·45, 0·70; $P < 0·0001$) First study: OR = 0·51; 95 %CI 0·39, 0·65; $P < 0·0001$ Second study: OR = 0·84; 95 %CI 0·54, 1·31; $P = 0·41$ MDPAI and MAI were associated with reduced risk of gastric cancer. MDPAI (OR 0·58; 95 %CI 0·34, 0·98; $P = 0·05$) and MAI (OR 0·71; 95 %CI 0·41, 1·23; $P = 0·06$)	Without subgroup analysis
Shivappa *et al.*[17], 1997–2007 Italy	230 incident cases (143 men) with 547 controls (286 men)	FFQ (consisting of seventy-eight items, including the most common Italian recipes and beverages) DII score (range 4·78 to –4·71) including thirty-one food parameters was used to compare the inflammatory potential of diets	Education, year of interview, BMI, smoking, total energy intake	DII score significantly associated with increased gastric cancer risk (OR 2·35; 95 %CI 1·32, 4·20; $P = 0·004$) DII as a continuous variable (OR 1·19; 95 %CI 1·06, 1·34)	Without subgroup analysis
Lee *et al.*[18], 2011–2014 South Korea	388 cases (249 men) with 776 controls (498 men)	FFQ (semi-quantitative questionnaire including 106 food items) DII score including thirty-five food parameters was used	Total energetic intake, BMI, education, smoking, alcohol intake, physical activity, *Helicobacter pylori* infection and first-degree family history of gastric cancer	DII score significantly associated with increased gastric cancer risk (OR 1·63; 95 %CI 1·15, 2·29; $P = 0·007$)	Intestinal type gastric cancer, OR = 2·33; 95 % CI 1·37, 3·96; $P = 0·002$ Diffuse type gastric cancer, OR = 1·49; 95 % CI 0·95, 2·35; $P = 0·077$
Stojanovic *et al.*[30], 2003–2015 Italy	223 cases (117 men) with 223 controls (132 men)	FFQ MEDI-LITE score (based on six components of the MD, range 0–12)	Sex, tobacco smoking and total energy intake	MEDI-LITE score associated with reduced risk of gastric cancer (OR 0·27; 95 % CI 0·14, 0·49) MEDI-LITE as a continuous variable (OR 0·70; 95 % CI 0·61, 0·81)	Without subgroup analysis
Vahid *et al.*[31]	Case–control study (2014–2016, matched on sex and age)	Eighty-two patients (thirty-seven men) with gastric cancer with ninety-five (forty-three men) controls Iran	FFQ (168 food items 1 year prior to assessment) DII (thirty-one food parameters)	Sex, BMI, education, smoking, alcohol consumption, *H. pylori* infection, physical activity, aspirin/NSAID use and total energetic intake	DII associated with increased risk of gastric cancer (OR 3·39; 95 % CI 1·59, 7·22; $P < 0·0001$) DII as continuous variable, OR = 2·65; 95 % CI 1·73, 4·07 Without subgroup analysis

GC, gastric adenocarcinoma; EPIC, Europe Prospective Investigation into Cancer and Nutrition Cohort; GCA, gastric cardia adenocarcinoma; GNCA, gastric non-cardia adenocarcinoma; CGC, cardia gastric cancer; NCGC, non-cardia gastric cancer; HRcon, Hazard Ratio for continuous variable; MDS, Mediterranean Diet Score; rMED, relative MDS; aMED, alternate MDS; MDPAI, Mediterranean Dietary Pattern Adherence Index; MAI, Mediterranean Adequacy Index; MEDI-LITE, Literature-based adherence score to the Mediterranean Diet; DII, Dietary Inflammatory Index; ISD, Inflammatory Score of the Diet; HEI-2005, Healthy Eating Index-2005; CHFP, Chinese Food Pagoda.

* All OR represents the OR of the highest quantile compared with the referent, and the lowest quantile was considered as the referent. All HR represents the HR of the highest quantile compared with the referent, and the lowest quantile was considered as a referent.

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Table 2. Newcastle–Ottawa Scale of eleven studies in the systematic review

Cohort studies	Selection				Comparability	Outcome			Total no. of stars
	Exposed cohort	Non-exposed cohort	Ascertainment of exposure	Outcome of interest		Assessment of outcome	Length of follow-up	Adequacy of follow-up	
Buckland *et al.*[13]	*	*		*	* *	*	*	*	8
Li *et al.*[15]	*	*		*	**	*	*	*	8
Buckland *et al.*[14]	*	*		*	**	*	*	*	8
Zhang *et al.*[27]	*	*	*	*	*	*	*	*	8
Agudo *et al.*[16]	*	*	*	*	**	*	*	*	9

Case–control studies	Selection				Comparability	Exposure			Total no. of stars
	Definition of cases	Representativeness of cases	Selection of controls	Definition of controls		Assessment of outcome	Method of ascertainment	Non-response rate	
Campbell *et al.*[28]	*	*	*	*	**		*		7
Praud *et al.*[29]	*	*		*	**		*	*	7
Shivappa *et al.*[17]	*	*		*	**		*	*	7
Lee *et al.*[18]	*	*	*	*	**		*		7
Stojanovic *et al.*[30]	*	*		*	**		*		6
Vahid *et al.*[31]		*	*	*	**		*		6

MDS (alternate MDS in Li *et al.*'s study[15], relative MDS in Buckland *et al.*'s study[14], MDS in Praud *et al.*'s study[29] and Literature-based adherence score to the Mediterranean Diet in Stojanovic *et al.*'s study[30]). According to the NOS system, all studies included are of high quality. Stojanovic *et al.*'s case–control study scored lower for lack of non-response rate description.

For DII and gastric cancer risk, there were three case–control studies included in the meta-analysis. High DII dietary patterns showed significantly higher odds of gastric cancer risk than lower DII dietary patterns (OR 2·11 (95 % CI 1·41, 3·15), $P = 0{\cdot}0003$. As there existed moderate heterogeneity ($I^2 = 41\,\%$), a sensitivity analysis was carried out. When Shivappa *et al.*'s study[17] was removed, the heterogeneity increased ($I^2 = 65\,\%$), while heterogeneity reduced when Lee *et al.*'s study or Vahid *et al.*'s study was removed ($I^2 = 0\,\%$ or $I^2 = 12\,\%$). Since three studies were taken in different continents, and only Lee *et al.*'s study has subgroup analysis based on the intestinal type and diffuse type, the subgroup analysis was not able to be taken. According to NOS, all these studies were of high quality. Vahid *et al.*'s study quality was relatively lower; considering the result of sensitivity analysis, the heterogeneity might be caused by Vahid *et al.*'s study. The publication bias could not be assessed, as there were less than ten studies included.

Discussion

We retrieved studies on different types of index-based dietary patterns related to gastric cancer incidence. The study populations were from Asia, North America and Europe. The results indicated that the MDP has a preventing effect on gastric cancer, while inflammatory dietary pattern promoted gastric cancer. There was one study on the HEI, one study on the CHFP score and one study on the food index score.

We combined the HR or OR for different types of dietary patterns and obtained a general trend. However, the studies were separated into different types of dietary patterns; thus, each meta-analysis had a limited number of included studies. Our study showed all kinds of index-based dietary patterns in relation to gastric cancer and offered practical ways for gastric cancer prevention. However, as we mentioned, different dietary patterns were based on the geographic and cultural characteristics of the local population; thus, whether one particular dietary index could also predict gastric cancer risk in another population requires further verification. For example, the study on MDS and gastric cancer was based on American and European populations, and whether the index could be used for gastric cancer prevention in Asia needs to be verified.

The MDP was based on the dietary habits of residents in most parts of Greece and Southern Italy, where adults have a longer life expectancy and lower rates of chronic diseases. Characters of this dietary pattern are abundant vegetables and fresh fruit, low in saturated fat, with low to moderate amounts of dairy products, fish, poultry and wine[42]. A large variety of studies have indicated the positive roles of the Mediterranean diet in health status[36,43]. In 1995, Trichopoulou *et al.* food index score first devised the scoring system, MDS, finding a significant protective

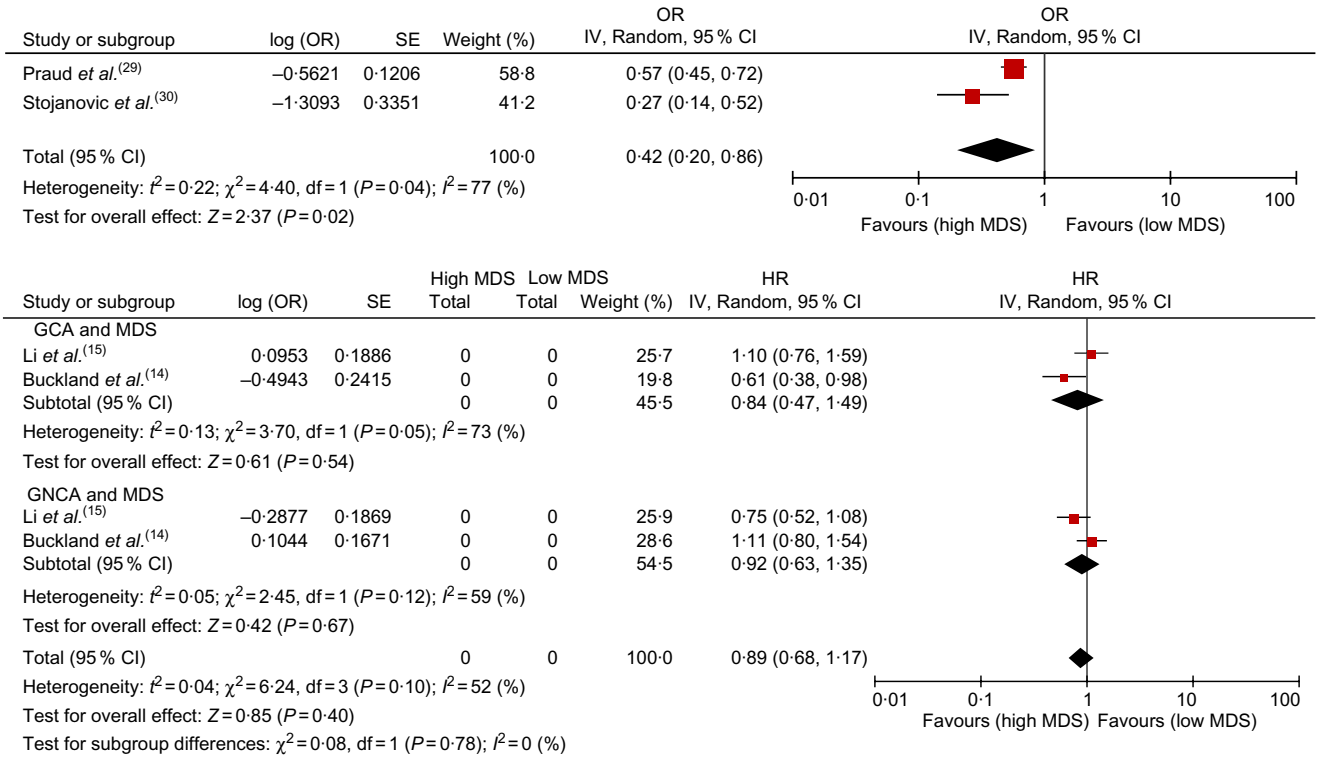

Fig. 2. Forest plot for the Mediterranean diet patterns and gastric cancer risk studies. HR, hazard ratio; MDS, Mediterranean Diet Score; IV, inverse variance; Random, random-effect methods; GCA, gastric cardia adenocarcinoma; GNCA, gastric non-cardia adenocarcinoma.

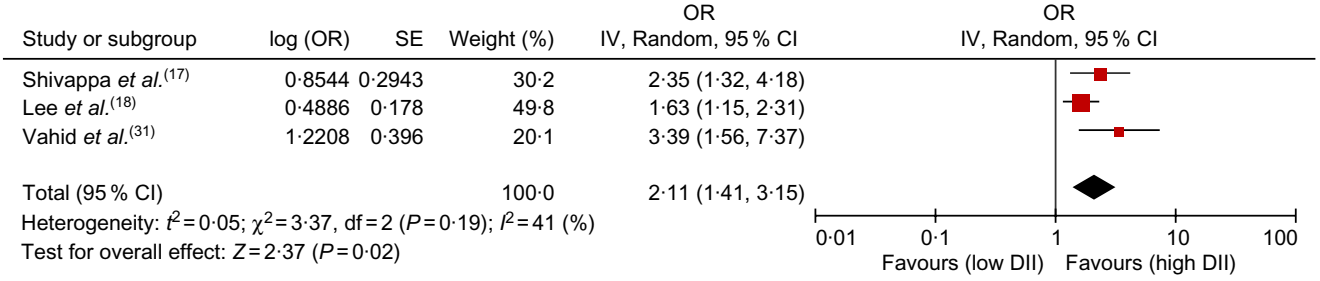

Fig. 3. Forest plot for the inflammatory dietary patterns and gastric cancer risk studies. DII, Dietary Inflammatory Index.

effect against overall mortality (risk ratio$_{\text{for 1 unit increasing}}$ = 0·83, 95 % CI 0·69, 0·99) in the Mediterranean region[32]. Since then, numerous variations of this score have been proposed[13,34–37], which are suitable for different countries and areas.

According to the anatomical location, gastric adenocarcinoma is classified into two main types, gastric cardia (proximal) and gastric non-cardia (distal) adenocarcinoma[44]. Different types of gastric adenocarcinoma have different epidemiological characteristics and aetiology, for example, GCA is more susceptible in people with high BMI and obesity[45,46], whereas gastric GNCA is more related to *H. pylori* infection[47]. Buckland *et al.*'s cohort study[14] indicated that high adherence to a Mediterranean diet was associated with a reduced risk of both GCA and GNCA in a European population, while Li *et al.*[15] found a protective effect of the Mediterranean diet in the American population, but only for gastric GNCA. Since Li *et al.*'s result was not statistically significant, further well-designed prospective studies with a larger population are needed. Different versions of the scores added to the heterogeneity. So, a more precise definition of the Mediterranean diet and a more unified standard should be developed[48,49].

The DII was first proposed by Cavicchia through a literature search on foods and constituents related to IL-1β, IL-4, IL-6, IL-10, TNF-α and C-reactive protein[21]. The scale was then validated by high-sensitivity C-reactive protein level from 494 healthy participants. The DII was improved by Shivappa *et al.*, who developed a scale with forty-five parameters, including protein, total fat, carbohydrate, cholesterol and caffeine[38], which is now widely used in different studies. DII was based on data collected from FFQ, and the data were converted into a *Z* score and centred percentiles for each component, according to the average and standard deviation derived from regionally representative world databases. The food parameter-specific DII was obtained by multiplying the percentiles of each component by its

inflammatory effect score and eventually summed to create an overall DII for each individual. By using this approach, the problem of non-comparability of units was resolved; thus, DII could reflect the proinflammatory effects of diet worldwide.

Inflammation induces cancer in various ways, including DNA damage, avoidance of immune surveillance and synergistic effects with commensal microbiota[50]. Anti-inflammatory drugs can significantly reduce gastrointestinal cancer[51]. However, the adverse effects of aspirin and non-steroidal anti-inflammatory drugs, such as peptic ulcer, cannot be neglected. Hence, avoiding an inflammatory diet and taking more anti-inflammatory food are a better choice.

There were also other types of dietary indices used in gastric cancer studies, which were the food score index[28], the HEI-2005[15] and the CHFP score[27]. In 2007, Campbell *et al.*[28] designed the food index score based on previous studies on dietary components and gastric cancer risk in order to avoid the data-driven problem from *a posteriori* approach. The result indicated that the food index score was an efficient tool for gastric cancer prevention, and this was the first study that we could find that used an *a priori* approach to study the association between dietary pattern and gastric cancer. However, as the food index score was not derived from dietary guidelines, it was not widely applied in further studies.

The HEI was designed by the US Department of Agriculture on the basis of local dietary guidelines and used to monitor dietary intake and quality[52]. HEI-2005 was a revised version based on the 2005 American Dietary Guidelines, but with the same principle. There was only one study on the association between the HEI and gastric cancer incidence. Although not significant, the result showed both GCA and GNCA incidence were related to lower HEI-2005 score and further studies should be carried out to verify this conclusion.

In China, the first dietary guidelines were devised by the Chinese Nutrition Society in 1989, which consisted of eight entries[53]. After several revisions, the newest version was published by the Chinese Nutrition Society in 2016. The Chinese Nutrition Society also published the new dietary pagoda, which showed the appropriate amount of food consumption[54]. The CHFP scoring method is similar to the HEI[40]. Zhang *et al.*'s cohort study showed that higher quantiles in CHFP score had lower gastric cancer risk in men, but after adjusting for age, education level, occupation, income, tea-drinking habits, smoking habits, physical exercise, BMI and alcohol consumption, the result became confused (risk ratio highest quantile *v.* lowest = 1·02, risk ratio middle quantile *v.* lowest = 0·9). Further studies should be carried out to resolve this problem.

There were several limitations to our meta-analysis. First, the studied populations were different (America, Europe and Asia). The prevalence of *H. pylori* infection was quite different[55]; however, only two studies[18,31] on DII considered this factor as a covariate. Second, as the dietary habits of different populations vary from each other, the dietary indices were calculated on the basis of each local food consumption database, collected by FFQ. Third, although the HR and OR were all from the highest quantile (taking the lowest as the referent), different studies divided the score range into different intervals. These caused substantial heterogeneity. Fourth, the data collection procedure was based on the self-report of participants. The participants may record what they believe the researchers want them to put rather than actually eat. Thus, inherent recall bias existed. What is more, the unexpected and non-significant association between index-based dietary indices and gastric cancer incidence may not be published and only published literature in English or Chinese was included in the present study, so there might exist publication bias.

Our meta-analysis indicated that MDS and DII were the most widely used dietary indices in gastric cancer prevention, and higher MDP consumption might reduce gastric cancer risk, while higher inflammatory diet pattern consumption might increase gastric cancer risk. Whether these indices could be applied in a worldwide population still remained to be verified in larger cohort studies. Future cohort and case–control studies should focus on the application of these dietary patterns in different populations, regions, cultures and the effects on gastric cancer prevention or progression.

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X. D. and S. D. formulated the research question. S. D. and Y. F. designed the study. S. D., Y. L., Z. S., X. S., N. J., P. L., Y. Z., Q. Z. and L. W. conducted the study and analysed the data. S. D. and X. Z. evaluated the quality of included studies. S. D., Y. L., X. D., Y. F., K. L. and Y. C. discussed the results and wrote the paper. All of the authors contributed to the revision of the manuscript and approved the final version.

None of the authors has any conflicts of interest to declare.

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