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REVIEW ARTICLE

Dietary patterns derived from principal component analysis (PCA) and risk of colorectal cancer: a systematic review and meta-analysis

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Abstract

Background and aim Colorectal cancer (CRC) is highly prevalent worldwide, with dietary habits being a major risk factor. We systematically reviewed and meta-analysed the observational evidence on the association between CRC and dietary patterns (DP) derived from principal component analysis.

Design PRISMA guidelines were followed. Web of Science, Medline/PubMed, EMBASE, and The Cochrane Library were searched to identify all eligible papers published up to the 31st July 2017. Any pre-defined cancer of the colon was included, namely colon-rectal cancer (CRC), colon cancer (CC), rectal cancer (RC), or proximal and distal CC, if available. Western (WDP) and prudent (PDP) dietary patterns were compared as a proxy to estimate "unhealthy" (Rich in meat and processed foods) and "healthy" diets (containing fruits or vegetables), respectively. Meta-analyses were carried out using random effects model to calculate overall risk estimates. Relative risks (RR) and 95% confidence intervals were estimated comparing the highest versus the lowest categories of dietary patterns for any of the forms of colon cancer studied.

Results 28 studies were meta-analysed. A WDP was associated with increased risk of CRC (RR 1.25; 95% CI 1.11, 1.40), and of CC (RR 1.30; 95% CI 1.11, 1.52). A PDP was negatively associated with CRC (RR 0.81; 95% CI 0.73, 0.91). Sensitivity analyses showed that individuals from North-and South-American countries had a significantly higher risk of CRC than those from other continents.

Conclusion A PDP might reduce the risk of CRC. Conversely, a WDP is associated with a higher risk of disease.

Introduction

Colorectal cancer (CRC) represents a major health and social burden around the world, being the second most common cancer in women and the third in men [1, 2]. The highest CRC incidence rates are reported in Europe, North America, and Oceania (>40 per 100,000), whilst Sub-Saharan Africa has the lowest incidence of this disease (<2 per 100,000) [3]. Developing regions that have undergone industrialization and urbanization have seen a significant increase in CRC prevalence, suggesting that the adoption of a more "Westernised" lifestyle could be a contributing factor [2, 4, 5].

Changes in dietary habits, along with changes in related lifestyle factors such as obesity, alcohol, and tobacco consumption, have been proposed to influence the increase in CRC [5–7]. Diet has been shown to be one of the most important modifiable risk factors in CRC [5, 8–12], with numerous epidemiological studies investigating the association between specific components of diet and risk of

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CRC [13–18]. Although research has demonstrated that some food groups, such as red meat, have been associated with CRC risk [19], studies focusing on individual components of diet may not provide a reflection of the overall diet nor take into account the complex interactions from other dietary components. This might be one of the reasons that observational studies of single food analysis and CRC have been inconclusive [13, 20, 21].

Limitations in the study of single foods and single nutrients have motivated the use of alternative methods to facilitate a more exhaustive approach to investigating the association between diet and disease. In recent years, with the introduction of principal component analysis (PCA) as a statistical tool to examine the relation between diet and disease, observational studies have used this approach to derive dietary patterns. PCA allows the investigation of diet as a whole, by aggregating the foods or food groups that are commonly eaten together as part of an underlying dimension of food consumption, defined as a dietary pattern [21]. With the use of this approach, several associations have been observed between dietary patterns and the risk of several cancers [22]. It is possible that PCA might deal with the complexity of diet and tackle confounding issues better than single food or nutrient analysis.

The objective of this study was to systematically analyse and interpret the existing scientific evidence from observational studies published up to July 2017 that examined the association of dietary patterns derived with the use of PCA, with CRC in adults.

Methods

Search strategy

This systematic review was carried out in accordance with the PRISMA guidelines for systematic reviews [23]. An electronic search was carried out using four databases, namely Web of Science, Medline (via OVID), Embase (via OVID), and The Cochrane Library, to identify all potentially eligible papers published up to the 31st July 2017.

We used a pre-defined strategy and protocol to carry out this systematic review. Details of the search strategies used to capture relevant studies are included in Appendix 1. Briefly, the following expressions were used to search for dietary patterns: ((principal component analysis OR principal component OR PCA OR factor analysis OR factorial analysis) AND (diet OR nutr OR dietary pattern OR eating pattern OR food pattern OR Diet OR food habits OR feeding behavior)). The search strategy was piloted several times before the final search terms were used. Only studies that defined dietary patterns *a posterior* were considered eligible for the systematic review. Reference lists of eligible studies were scanned to identify additional relevant studies. There were no language restrictions. Papers published in a language other than English were translated with the help of a native speaker.

Inclusion criteria

After de-duplication checks, titles and abstracts of all original studies were examined and selected for inclusion if they met the following criteria: empirical papers that derived dietary patterns with the use of PCA; empirical papers with the objective of illustrating, testing, criticizing or appraising PCA compared to other methods being employed for dietary pattern; analysis papers where colorectal cancer is a primary or secondary outcome. Only studies that reported risk estimates [hazards ratios, odds ratios (ORs), and relative risks] of colorectal, colon and rectal cancer and measures of variability (SEs or 95% CIs from which these could be derived) were included. The exclusion criteria for the systematic review was defined as follows: conceptual papers on methodological issues of the dietary patterns approach using PCA including think pieces and reviews of methods papers without original data; conceptual papers comparing methods of identifying dietary patterns without original data; studies that used *a priori* dietary patterns such as quality index, Mediterranean diet score or healthy eating index; studies that were using data-driven methods other than PCA, articles that provided only abstracts, articles presented only to conferences. Eligible papers were fully examined for data extraction.

Data extraction

Data from eligible studies were extracted according to recommended guidelines [23]. These included: author; year; paper title; country; study design; outcome; study population; characteristics of dietary patterns, including the number of dietary patterns, label of each pattern and food groups that correlated highly with this pattern, PCA information and percentage of total variance of original food items being explained by the dietary patterns in each study (if available); statistical adjustments made in the analysis, and the main findings, including risk estimates [hazards ratios, odds ratios (ORs), and relative risks] with 95% confidence intervals and *p* values.

To make the results more interpretable and meaningful, dietary patterns were labeled "Western" and "Prudent", as these tend to be frequently reported across studies. The factor loadings for each dietary pattern labeled in selected studies were also considered. Dietary patterns were labeled as "Western" when correlated highly with red and processed meat, refined grains, and high-fat dairy. Dietary patterns characterized by higher principal component loadings of

fruit, vegetables, whole grains, low-fat dairy, and fish were labeled as "Prudent".

Risk of bias (quality) assessment

The risk of bias was examined using as reference the National Institute for Clinical Excellence (NICE) methodological checklist for cohort and case–control studies. Areas of bias examined included subject selection, exposure and outcome assessment, and confounding [23]. Studies were considered at low risk of bias if most of the criteria in the checklist were addressed. For cohort studies, a level of <20% loss to follow up was accepted as representing low risk of bias from incomplete outcome data.

Statistical analysis

All studies in the meta-analysis reported dietary pattern results in terms of tertiles, quartiles or quintiles, apart from one study, Flood et al. [17], which reported the highest versus the lowest scores and colorectal cancer risk. Therefore, in the meta-analysis we compared the highest versus the lowest categories of Western and prudent dietary patterns to estimate the pooled effect estimate for colorectal cancer (CRC), colon cancer (CC), and rectal cancer (RC). Distinctions between different outcome measures of relative risks (RR), including odds ratios (OR), relative risks (RR), and hazard ratios (HR), were treated the same, assuming that CRC is a rare disease as recommended in previous meta-analyses [24–28]. Multivariable adjusted ORs, HRs, and RRs with 95% CIs from individual studies were weighted and combined to produce an overall RR. The random effects model by DerSimonian and Laird method [29] was used to in order to account for heterogeneity between studies. The percentage of heterogeneity between studies was quantified by the I-squared statistic (I^2) and heterogeneity was tested with a chi-squared test [30]. Each study was weighted and the effect sizes and confidence intervals were displayed in forest plots, along with the pooled overall effect. Publication bias was assessed through funnel plots using the Egger test [31]. Meta-regression was performed by study design and gender. Subgroup analyses were performed to investigate associations between the dietary patterns and distal and proximal CC and CRA risk as well as for a "drinker" dietary pattern (containing wine, beer, spirits and in some occasions, other foods). All statistical analyses were conducted with STATA, version 12.0 (2012; StataCorp, College Station, TX).

The codes used to perform the analyses can be requested to the corresponding author.

Results

Inclusion

A total of 4824 papers were retrieved from the search strategy (after deduplication). After checking all titles and abstract for eligibility, 38 studies were fully examined, of which 28 met the inclusion criteria and their data were extracted and meta-analysed (Fig. 1). The summary characteristics of included and excluded studies and their methodology are described in detail as supplementary files. Amongst included studies, sixteen were cohort studies [12, 15–18, 32–42], ten were case–control studies [13, 43–51], and two were of cross-sectional design [52, 53]. The geographical provenance of the studies included North America and South America, Europe, and Asia.

Quality assessment was examined in relation to confounding, selection and assessment bias, most of which showed an overall low risk of bias (Fig. 2). All of the studies in this review were of low risk of confounding bias, as considerations were made in statistical models for the main confounding factors, including age, gender, total energy intake, physical activity, and body mass index. There was low risk of assessment in all studies because the exposure measures (dietary intake) were determined using validated FFQs or similar data collection methods, and the outcome measures (cancer) were either confirmed histologically, through medical records or cancer registries, which are all considered reliable and valid. Selection bias, from source populations, in case–control studies was generally low as cases and controls were from comparable populations and cases are clearly defined and differentiated from controls. However, it was difficult to detect in some case-controls studies the exact participation rate and if the authors had adjusted for exposure differences between study participants and non-participants. In cohort studies there were some methodological issues with confirmation of patients without cancer at follow up, which led to the majority of studies being classed as "unclear" and "high" for selection bias.

Outcomes and dietary exposures

Studies with varying outcomes of interest were included in the systematic review, including CRC, CC, RC, proximal, and distal CC. The majority of studies (76.9%) used either histology/pathology or medical records to confirm cases of CRC. Only 15.4% used cancer registries only as confirmation of the study outcome.

Table 1 summarizes the characteristics of the included studies. The majority of studies used semi-quantitative FFQs and quantitative FFQs to ascertain dietary intake ($n =$ 23). Two studies used qualitative and quantitative diet

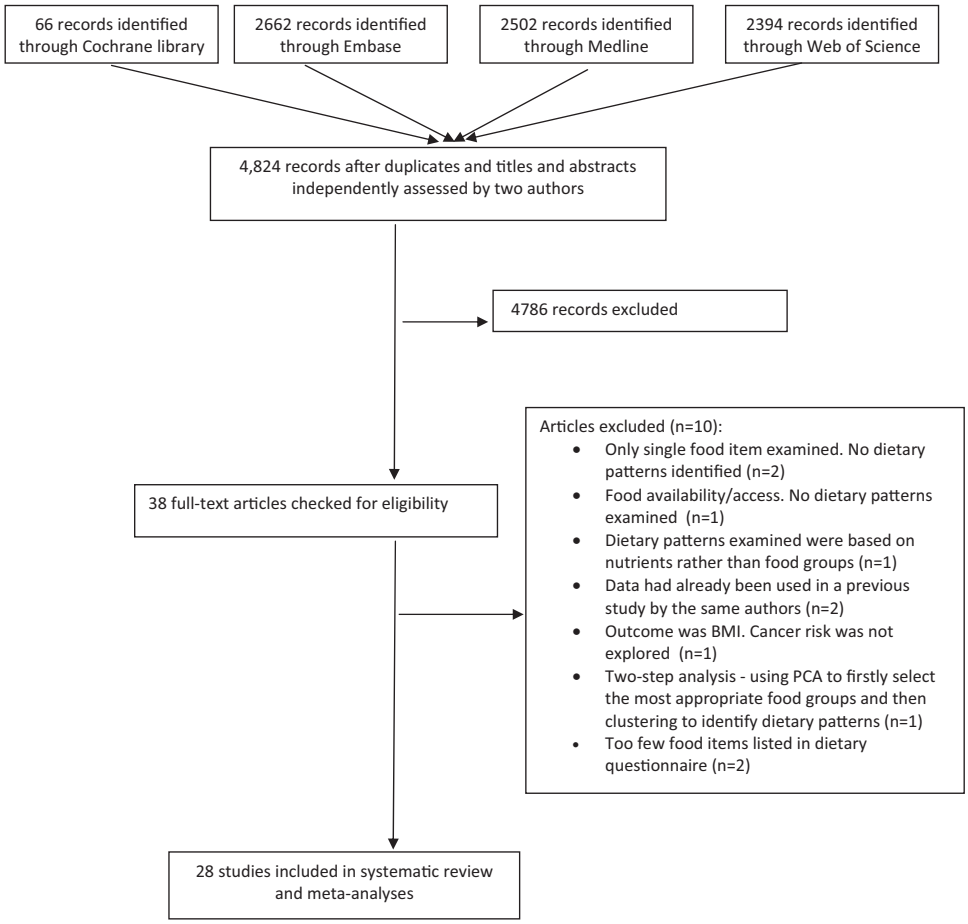

Fig. 1 PRISMA flowchart for selection of eligible papers on colorectal cancer and dietary patterns derived from principal component analysis (PCA)

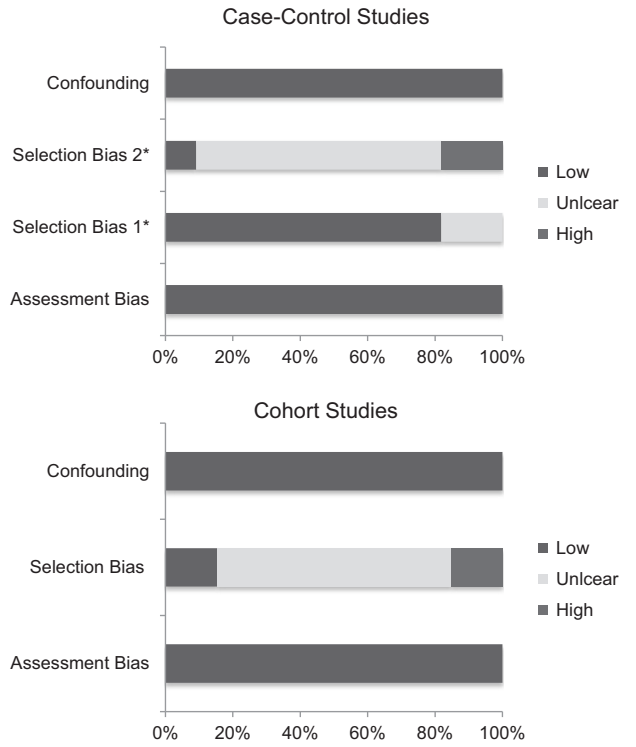

Fig. 2 Quality assessment of included studies using the NICE Guidelines on systematic reviews

history questionnaires [12, 51]; one ascertained dietary intake using an adaptation of the validated diet history questionnaire of the Coronary Artery Risk Development in Young Adults (CARDIA) Study [13]; one used a dietary questionnaire that comprised of quantitative and qualitative questions on food intake [18]; and one paper used a semi-quantitative food frequency instrument [48]. The number of food items enquired across dietary questionnaires ranged between 40 and 267.

All papers reported a "Western" and a "Prudent" dietary pattern. The number of dietary patterns in each study varied between 2 and 14, with a mean of 4 dietary patterns (Table 1). In some studies, dietary patterns were labeled qualitatively corresponding to the foods or foods groups that are considered to provide some benefit to health (namely prudent). These were generally characterized by higher factor loadings of fruit, vegetables, whole grains, low-fat dairy products, poultry and fish. Other dietary patterns following similar dietary features that were also classed as prudent for this review were labeled "healthy", "healthful", "vegetable-fruit-soy", "Mediterranean", "vegetable", "fruit-vegetable", "fruit and vegetable", "prudent vegetable", "high-dairy", "high-fruit and -vegetable, high-starch, low-alcohol

Table 1 General characteristics of included studies

Author, (Year) Country	Study design and population	Outcome	Characteristics of Dietary patterns (DPs) 1. Number of DPs 2. Label of each DP and food items included 3. PCA information (including % of total variance of original food items being explained by the DPs, if available	Adjustments	Main findings
Botma et al.[32] The Netherlands	Prospective cohort (20 month FU) Data collected between 2007 and 2009 Participants selected from a Lynch Syndrome cohort via the GEOLynch cohort study, who were identified from families registered at the NFDHT $n = 486$ 34.4–59.6% = men (varied between DPs)vAge = 18–80 years BMI = 24.5–25.6 (varied between DPs)	CRA All participants had Lynch Syndrome and were MMR gene mutation carriers All were Dutch-speaking and Caucasian/white Colonoscopy follow-up data was collected at the LS family registry at the NFDHT and from medical records For each colonoscopy, information on the number of neoplasms, and the location, size and histology were collected CRA were histologically confirmed	Self-administered FFQ (183 items) at baseline to assess food intake during the previous month (validated) 1. Four 2. Prudent; fruits and vegetables (including legumes, cruciferous, allium, leafy vegetables, carrots, tomatoes, citrus and kiwi fruit, apples and pears, other fruits), whole grain pasta, rice, noodles, non-fat yogurt, custard and curd, low-fat cheese, poultry, oils, fish dressings, green and herbal tea and added sweets Meat; poultry, beef, pork, minced meat, processed meat, and coffee. Snack; chips, fried snacks, fast food snacks, spring rolls, mayonnaise-based sauces, cooking fat and butter, peanut sauce, ketchup, sweets, and diet sodas. Cosmopolitan; leafy vegetables, tomatoes, allium vegetables, refined grains, fish, dressings, tomato sauce, cream, low-fat margarine, sweet sandwich spread and wine 3. Eigenvalues > 1.0 were selected and foods with individual loading ≥ 3.0 were included in the model (factor loadings > 0.15 were excluded) DP scores were calculated by summing participants" food intake, multiplied by its component (DP) loading for each food group. DPs were grouped into tertiles, with the lowest being the reference group	Two adjustment models: Model 1; age and sex Model 2; added smoking habits, CRA history, and the extent of colon resection The following variables were not considered for the multivariate adjustment model as they changed the HR by <10%: regular use of non-steroidal anti-inflammatory drugs, PA, BMI, and the number of endoscopies	58 participants developed CRA Risk of CRA was estimated by calculating HR and 95% CI, using Cox regression None of the multivariate-adjusted findings reached statistical significance, other than the "snack" DP, which was associated with an increased CRA risk (HR 2.16; 95% CI 1.03–4.49) The "prudent" DP was associated with a reduced risk of CRA (HR 0.73; 95% CI 0.32–1.66; p for trend 0.78) The "meat" and "cosmopolitan" DPs were associated with an increased risk of CRA, (HR 1.70; 95% CI 0.83–3.52; p for trend 0.21), and HR 1.25 (95% CI 0.61–2.55; p for trend 0.56), respectively.
Butler et al. [33] Singapore	Prospective cohort (9,8 years FU) Data collected between 1993 and 2005 Participants selected from the Singapore Chinese Health Study $n = 61,321$ 31.2–59.6% = men (quartile range) Age = 45–74 years BMI = 28.2–32.6 (varied between DPs)	CRC CRC incidence and deaths identified by record linkage of cohort database with the population-based Singapore Cancer Registry and Singapore Registry of Births and Deaths. Participants were Singapore Chinese and permanent residents or citizens of Singapore	Quantitative FFQ (165 items) administered at baseline to assess food intake during the previous 12 months (validated) 1. Two 2. Vegetable-fruit-soy; (32 items) vegetable, soy and fruit foods. Meat-dim-sum; (31 food items) chicken, pork, fish, rice, noodle dishes and preserved foods 3. Eigenvalues > 1.0 and foods with individual loading ≥ 3.0 were included in the model DP scores were calculated, taking the unweighted sum of standardized frequencies of food intake associated with the DP, then dividing them into quartiles	One adjustment model: Model 1; Sex, age at baseline interview, year of interview (1993-1995, 1996-1998), dialect group (Cantonese, Hokkien), educational level, cigarette smoking, alcohol consumption, BMI, family history of CRC, diabetes at baseline, and weekly PA	961 participants developed invasive CRC Calculating HR and 95% CI, using proportional hazards regression to obtain adjusted HR estimated risk of developing CC. There was no evidence of association between the "vegetable-fruit-soy ; DP (HR 1.02; CI 95% 0.83–1.24) or the "meat-dim sum" DP (HR 0.97; 0.78–1.20) and CRC.
Cottet et al. [12] Europe (Belgium, Denmark, France, Germany, Ireland, Israel, Italy, Portugal, Spain and UK) Cottet et al. (continued)	Prospective cohort (3 years FU) Data collected between 1991 and1997 (1991–1994 baseline) Participants selected from the ECP Intervention Study—an RCT of calcium and fiber supplementation for CRA prevention (3 treatment groups; calcium, fiber, and placebo) $n = 442$ 62.7% = men Age = 35–75 years Mean BMI range = W 25.4–26.4, M 26.2–26.6 (varied between DPs)	CRA Recurrence Participants had histologically confirmed adenomas at the index colonoscopy, showing at least two adenomas or one more than 5 mm in diameter Diagnosis was confirmed by a pathologist Cases were defined as having occurrence of new adenomas and were identified by 3-year follow-up colonoscopy	Qualitative and quantitative diet history questionnaire (validated), assessing diet over the previous 12 months, completed at enrollment and at the end of the study 1. Three (separate for men and women) 2. *Men*: "Mediterranean"; low fat beef, low fat meat, low fat poultry, fish and crustaceans, high fat cheese, olive oil, legumes, rice and pasta, vegetables, fresh fruits, citrus fruits, refined bread and cereals, water, wine, and condiments "Sweets and snacks"; poultry, delicatessen, high fat cheese, nuts, fresh fruits, refined bread and cereals, yogurt, desserts, chocolate, sweets, sodas, water, and condiments "High fat and proteins"; meat, offal, fish and crustaceans, high fat delicatessen, chips, nuts, legumes, chocolate, sodas, and wine *Women*: "Mediterranean"; olive oil, vegetables, fruit, fish, lean meat, low fat beef and poultry, fish and crustaceans, high fat cheese, olive oil, legumes, rice and pasta, vegetables, fresh fruits, citrus fruit whole grain bread and cereals, and water "Western"; meat, poultry, low fat poultry, fish and crustaceans, high fat fish, high fat delicatessen, butter and animal fat, vegetable fat, nuts, legumes, rice and pasta, potatoes, refined bread and cereals, milk, sodas, beer, and condiments. "Snacks"; low fat beef, high fat delicatessen, high fat cheese, butter and animal fat, desserts, sweets, sodas, water, beer, and pickles 3. Eigenvalues > 1.0 and foods with a factor loading > 0.25 and <−0.25 were included in the model. Male dietary patterns explained 21.3% of variability and female dietary patterns explained 21.9% of variability. DP factor scores were divided into tertiles. The reference group was defined as the factor score below the first tertile	One model: Age, treatment group, presence of proximal adenomas (at inclusion). Additional confounders with marginal effect on associations were TEI, geographical area, and smoking status	92 participants presented with new CRA at 3-year colonoscopy follow-up. The overall recurrence rate was 20.8% and was higher in men then in women (23.5% and 16.4% respectively) No significant associations were identified between male dietary patterns and overall occurrence of CRA Mediterranean dietary pattern significantly reduced reoccurrence of CRA in women in the 2nd (OR 0.50; 95% CI 0.18–1.42; p for trend 0.04) and 3rd (OR 0.30; 95% CI 0.09–0.98; p for trend 0.04) tertile There was no association between snack and Western dietary patterns and reoccurrence of CRA in women (3rd tertile), OR 1.11 (95% CI 0.34–3.68; p for trend 0.90) and OR 0.99 (95% CI 0.32–3.05; p for trend 0.99) respectively

Table 1 (continued)

Author, (Year) Country	Study design and population	Outcome	Characteristics of Dietary patterns (DPs) 1. Number of DPs 2. Label of each DP and food items included 3. PCA information (including % of total variance of original food items being explained by the DPs, if available	Adjustments	Main findings
Dixon et al. [16] Finland, Netherlands Sweden	Four prospective cohorts (combined; specific details provided in footnote)[a] ATBC study (men) NLC study (men) NLC (women) SMC study (women)	CRC, CC, RC Follow-up data obtained though record linkage of the cohorts with national cancer registries	The ATBC study used a semi-quantitative FFQ (276 items) at baseline, to assess diet over the previous 12 months. The NLCS study (men and women) used a self-administered FFQ (150 items) at baseline. All FFQ"s were validated. The SMC study used an FFQ (67 items) at baseline, to assess diet over the previous 6 months 1.Two (common to the ATBC, SMC and NLCS cohorts) 2. "Vegetables"; vegetables and legumes, citrus fruits and berries, pasta and rice, poultry and fish, and oil and salad dressings, intake of vitamin A, C and E, folate, and polyunsaturated fatty acids "Pork, processed meats and potatoes (PPP)"; pork, processed meat, potatoes and coffee, and correlated with intakes of energy, protein, carbohydrate, fat, saturated and monounsaturated fatty acids cholesterol, B vitamins, and minerals 3. The vegetables DP accounted for the most variance in dietary intake; 5.6% in NLCS men 9.7% in the ATBC men. The PPP DP was associated with 4-5% of variance in dietary intake across the cohorts Food items were aggregated into 51 food groups—selected as foods common to all countries; specific foods included in each FFQ, and food groups that have a specific role in the diet and potential relevance to cancer etiology Pattern scores assessed by PCA were categorized into quartiles	ATBC Model 1; age and TEI Model 2; age, ATBC treatment group, BMI, level of education, number of cigarettes smoked per day, number of years regularly smoking, occupation in the past year, TEI. NLCS (both genders) Model 1; age and energy. Model 2; age, BMI, education, number of cigarettes smoked per day, number of years smoking regularly, minutes per day of PA outside of the profession, family history of CRC, and TEI SMC Model 1; age and energy. Model 2; age, BMI, education, and TEI	The Vegetable dietary pattern was not associated with CRC in the ATBC (RR 1.22; 95% CI 0.87–1.73, p for trend 0.09), NLCS (men) (RR 1.04; 95% CI 0.78–1.39, p for trend 0.41), NLCS (women) (RR 0.91, 95% CI 0.65–1.27, p for trend 0.78), or the SMC (women) (RR 0.99, 95% CI 0.77–1.27, p for trend 0.90). The PPP dietary pattern was associated with an increased risk of CRC (RR 1.37, 95% CI 1.00–1.89, p for trend 0.03) and CC (RR 1.62, 95% CI 1.12–2.34. PPP was also associated with an increased risk of RC in ATBC (men) (RR 2.21 (95% CI 1.07–4.57, P for trend 0.05) Neither pattern was associated with the risk of CC or RC in NLCS women and men
Flood et al. [17] USA Flood et al. (2008) (continued)	Prospective cohort (5 years FU) Data collected between 1995–2000 Selected participants were part of the NIH-AARP Diet and Health Study. $n = 492,382$ 59.6% = men Age = 50–71 Mean BMI = 26.5–27.8 (varied between dietary patterns)	CRC, proximal CC, distal CC, and RC Cases were identified by linkage between the AARP cohort and cancer registry databases in the places of study participants" residency. Annual linkage of the AARP cohort to the Social Security Administration Death Master File in the US, cancer registry linkage, follow-up searches of the National Death Index Plus, questionnaire responses, and responses to other mailings.	FFQ (124 items) at baseline, to assess diet over the previous 12 months (validated) 1. Three male and 3 female dietary patterns identified 2. Male dietary patterns: Fruit and vegetables; broccoli, lettuce, carrots, tomatoes raw, cauliflower and brussel sprouts, peppers, green beans, vegetable medley, spinach cooked, spinach raw, oranges, apples, grapes, fish, coleslaw, chicken light, and salad dressing (non-fat). Fat-reduced and diet foods; skimmed milk on cereal, margarine, frozen yogurt, cold cut poultry, crackers (low fat), cold cuts low fat, cookies (low fat), chicken light, mayonnaise (diet), turkey, mayonnaise (nonfat), coffee (decaffeinated, no sugar), hot dog (low fat), and salad dressing (non-fat) Red meat and potatoes; green beans, gravy, meat loaf, beef stew, pork, roast beef sandwich, French fries, sausage, ham, macaroni, bacon, roast beef (lean), biscuits, fried fish, hamburger (lean), and potato salad *Female dietary patterns:* Fruit and vegetables; broccoli, carrots, lettuce, peppers, cauliflower and Brussel sprouts, tomatoes raw, and green beans. Fat-reduced and diet foods; gravy, meat loaf, pork, beef stew, French fries, hamburger lean, sausage, chicken (light), margarine, skimmed milk on cereal, salad dressing (nonfat), cold cut poultry, mayonnaise (nonfat, sandwich), turkey, frozen yogurt, crackers (low fat), mayonnaise (non-fat), and tuna (canned in water) Meat and potatoes; spinach (raw and cooked), oranges, cantaloupe, coleslaw, vegetable medley, apples, melon, bacon, hot dog, macaroni, roast beef sandwich, roast beef lean, biscuits, ham, and steak lean 3. Before rotation, the 3 factors explained 35.1% of the variance in men and 34.2% in women Data identified dietary patterns from 181 food groups. A caloric-density approach was used, where daily frequency of the consumption of each food group was divided by the total daily calorie consumption, to adjust for energy. Energy-adjusted frequency values were then standardized and entered into the factor analysis. Pattern scores assessed by PCA were categorized into quintiles	Two adjusted models: Model 1; age Model 2; ethnicity, tobacco use, PA, BMI, education, use of menopausal hormones (women only)	Cox proportional hazards regression generated RR and 95% CI on the 3 dietary patterns separately for men and women CRC was incidence was 2151 in men and 959 in women In men, the fruit and vegetable dietary pattern was associated with a decreased risk of CRC (RR 0.81, 95% CI 0.70–0.93, p for trend 0.004) The fat-reduced and diet foods pattern was associated with a reduced risk in both men (RR 0.82, 95% CI 0.72–0.94, p for trend 0.001) and women (RR 0.87, 95% CI 0.71–1.07, p for trend 0.06). The red meat and potatoes dietary pattern were associated with an increased risk in both men (RR 1.18, CI 1.02–1.35, p for trend 0.14) and women (RR 1.48, CI 1.20–1.83, p for trend 0.0002)
Fung et al. [34] USA	Prospective cohort (12 years FU) Data collected between 1984 and 1996. Participants were selected from The Nurses" Health Study (NHS) cohort $n = 76,399$ (females) Age = 38–63 BMI range = 24.6–25.6 (varied between dietary patterns)	CC and RC Diagnosis obtained from questionnaire and clinically confirmed through medical records. Deaths were reported by family members, the postal service or obtained through National Death Index searches	FFQ (116 items) were used to assess dietary intake over the previous 12 months, updated in 1984 (baseline), 1986, 1990, and1994 1. Two 2. Prudent; fruits, vegetables, legumes, fish, poultry, and whole grains. Western; red and processed meats, sweets and desserts, French fries, and refined grains. 3. Eigenvalue of > 1. Pooled logistic regression used to pool each 2 year time period as an independent follow up. Cumulative averages of dietary pattern scores were calculated from each repeated measurement, i.e., dietary intake assessed in 1984 predicted CC between 1984 and 1986	One adjustment model: Age, family history of CRC, BMI, aspirin use, multivitamin use, PA, alcohol intake, smoking, TEI, and failing to return a FFQ	The prudent DP was inversely associated with CC risk (RR 0.71, 95% CI 0.50–1.00) A borderline significant increased risk of CC was observed for the Western dietary pattern, although this association was not a strong (RR 1.46 95% CI 0.97–2.19 p for trend 0.02). There was no distinct association between dietary patterns and RC risk

Table 1 (continued)

Author, (Year) Country	Study design and population	Outcome	Characteristics of Dietary patterns (DPs) 1. Number of DPs 2. Label of each DP and food items included 3. PCA information (including % of total variance of original food items being explained by the DPs, if available	Adjustments	Main findings
Kesse et al. [18] France	Prospective cohort (7 years FU for CRC) (4 years FU for CRA) Data collected between 1993 and 2000 $n = 72,804$ Age = 40–65 years All females Mean BMI range = 22.5–23.6 Participants selected from E3N cohort Two separate studies were performed; CRA study ($n = 5,320$): CRA identified by reported diagnosis of colorectal polyp and pathology reports. Researchers isolated a group of high-risk of adenomas. CRC study ($n = 67,484$): CRA identified by reported diagnosis of colorectal cancer	CRC and CRA	One dietary questionnaire (validated) comprised of quantitative and qualitative questions on food intake (208 items) 1. 4 2. Healthy; raw and cooked vegetables, legumes, fruit, yogurt, fresh cheese, breakfast cereals, sea products, eggs and vegetables oils (olive oil and others) Western; potatoes, pizzas and pies, sandwiches, legumes, sweets, cakes, cheese, bread, rice, pasta, processed meat, eggs and butter Drinkers; sandwiches, snacks, coffee, processed meat, sea products, wine, and other alcoholic beverages, and low consumption of soup and fruit Meat-eaters; potatoes, legumes, coffee, meat, poultry, vegetable oils (except olive oil) margarine 3. Factor loading defined as >0.2 and <−0.2 Score patterns were categorized into quartiles	Two adjustment models: Model 1; energy and age Model 2; TEI, BMI, family history of CRC, PA, high educational level, and tobacco status	RR were estimated with 95% CI 175 CRA and 172 CRC cases were identified during follow up There was a significant increased risk of CRA observed in the Western (RR 1.39, 95% CI 1.00–1.94, p for trend 0.03) and drinkers dietary patterns (RR 1.42, 95% CI 1.10–1.83, p for trend 0.01) There was a positive association between meat-eaters patterns and CRC (RR 1.58, 95% CI 0.98–2.53, p for trend 0.02) There were no significant associations between CRC and healthy (RR 0.77, 95% CI 0.49–1.20, p for trend 0.20), Western (RR 1.09, 95% CI 0.60–2.00, p for trend 0.40) or drinker (RR 1.36, 95% CI 0.85–2.17, p for trend 0.13) dietary patterns and CRC
Kim et al. [35] Japan	Prospective cohort (10 years FU) Data collected between 1990 and 1999. Participants selected from JPHC Study Cohort I. $n = 42,112$ 48.2% = men Age = 40–59 Mean BMI range = 23–24 (varied between dietary patterns)	CRC, CC, RC, proximal CC, distal CC. Cases identified through continuous surveillance of hospital records, pathologically confirmed diagnosis, population-based cancer registries	Self-administered FFQ (44 items), assessing food consumption over the previous month (validated and reproducible), was completed at baseline (1990) 1. Three 2. Healthy; vegetables, fruits, soy products, seaweeds, mushroom, milk, beans, and yogurt Traditional; pickled vegetables, salted fish and roe, fish, rice, miso soup, low intake of bread and butter for both men and women, and high intake of alcoholic beverages (sake, shochu and beer) only for men. Western; meat, poultry, cheese, bread, and butter 3. Eigenvalue > 1.5 Pattern scores assessed by PCA were categorized into quartiles	One adjustment model: Age, BMI, study area (for Western and healthy diet), TEI, education level, PA, and family history of CRC. Smoking status and alcohol consumption was also adjusted for in men only	Cox"s proportional-hazard model was used to calculate RR. 370 CRC cases were identified during follow up A positive association was identified between the traditional (RR 2.06, 95% CI 1.10–3.84, p for trend 0.11) and Western (RR 2.21, 95% CI 1.10–4.45, p 0.74) dietary patterns and CC risk in women There were no statistically significant associations between the dietary patterns and CRC risk in both men and women
Kumagai et al. [36] Japan	Prospective cohort (11 years FU) Data collected between 1995 and 2005. Participants (47.8% male) were selected from the Ohsaki National health Insurance (NHI) Cohort Study $n = 44,097$ Age = 40–79 years Mean BMI range = 23.4–23.7 (varied between dietary patterns)	CRC, CC, and RC Cases were identified through the Miyagi Prefectural Cancer Registry	A 40 item validated FFQ administered at baseline 1. Three 2. Japanese; egg, milk, deep-fried dishes, tempura, fish (raw, boiled, in soy/paste/dried/roasted), vegetables (green, carrot and pumpkin, tomato, cabbage and lettuce, Chinese cabbage, wild plant, mushrooms, potato, seaweeds, pickles, soybean), orange, other fruits, confectioneries, green tea Animal food; beef, pork, ham and sausage, chicken, liver, egg, cheeses, butter, margarine, deep-fried dishes and tempura, boiled fish paste, food boiled with soy, coffee, and alcoholic beverages High-dairy, High-fruit-and-vegetables, Low-alcohol (DFA); milk, yogurt, cheeses, margarine, carrot and pumpkin, tomato, seaweeds, orange, and other fruits 3. Not specified. Pattern scores assessed by PCA were categorized into quartiles	Two adjustment model: Model 1; age and gender Model 2; age, sex, BMI, smoking status, walking duration, education, TEI, and family history of CRC	The Cox proportional hazard regression model was used to estimate HR and 95% CI. 854 cases of CRC, which included 554 cases of CC and 323 cases of RC. The DFA dietary pattern was inversely associated with CRC risk (HR 0.76, 95% 0.60–0.97). This also the case for RC risk (HR 0.56, 95% CI 0.37–0.84, but not for CC (0.89, 95% CI 0.66–1.19, p for trend 0.43). Not associations were found between CRC, CC or RC risk and the Japanese and animal food DPs
Mehta et al.[40] USA	Prospective cohort (ongoing) Two Studies: (1) The Health Professionals FU Study (HPFS, since 1986). 51,529 US male podiatrists, dentists, osteopathic physicians, veterinarians, pharmacists, and optometrists aged 40–75 years at enrollment (2) The Nurses" Health Study (NHS), (since 1976) 121,700 US female registered nurses aged 30–55 years at enrollment Total sample of 137,217 included in analyses 3260 incident cases of CRC	In both cohorts, incidence of CRC was confirmed by a study physician, blinded to exposure information, who reviewed all records to confirm diagnosis Data on histologic type, anatomic location, and stage were collected Tumors were classified as proximal, distal, or rectal	Both cohort studies used validated FFQs, which were self-administered. In the HPFS study, authors used data from FFQs administered in 1986, 1990, 1994, 1998, 2002, 2006, and 2010. For the NHS study, authors used data from the FFQs administered in 1980, 1984, 1986, 1990, 1994, 1998, 2002, 2006, and 2010 1. Two (characteristics of the patterns were stable across repeated FFQs and in both cohorts) 2. "Western"; red and processed meats, high-fat dairy products, refined grains, and desserts "Prudent"; vegetables, fruits, whole grains, and fish 3. Factor loadings were derived from the correlations between food groups and the 2 derived factors. Each participant was then assigned 2 factor scores, determined by adding the reported frequencies of food group intakes, weighted by the factor loadings for each factor. These factor scores were then standardized using a z-score scale, with a mean of 0 and standard deviation of 1. Higher scores indicated stronger adherence to that particular pattern. To capture long-term habitual consumption, the authors calculated the cumulative average of factor scores, which were then categorized into quartiles to maximize our power for molecular subtype analysis Data from both cohorts were pooled after examining heterogeneity	Two models of adjustments Model 1; TEI, and stratified by age, year of questionnaire return, and sex (in the analysis using combined cohorts) Model 2; BMI, pack years of smoking (never, 0–4 years, 5–19 years 20–39 years, o r >40 years), family history of CRC in any first-degree relative, previous lower gastrointestinal endoscopy, menopausal hormone use, physical activity, and regular aspirin or NSAID use (≥2 tablets/week)	Western DP (highest vs. lowest quartile) was associated with an increased incidence of CRC, with a relative risk (RR) of 1.31 (95% CI, 1.15–1.48) The association of Western DP (highest vs. lowest quartile) with CRC was evident for tumors of the distal colon (RR, 1.55; 95% CI, 1.22–1.96) and rectum (RR, 1.35; 95% CI, 1.03–1.77) but not proximal colon (RR, 1.11; 95% CI, 0.91–1.35) With the "Prudent" DP there was a RR of 0.86 for overall CRC (95% CI, 0.77–0.95)

Table 1 (continued)

Author, (Year) Country	Study design and population	Outcome	Characteristics of Dietary patterns (DPs) 1. Number of DPs 2. Label of each DP and food items included 3. PCA information (including % of total variance of original food items being explained by the DPs, if available	Adjustments	Main findings
Meyerhardt et al. [37] USA	Prospective cohort (5.3 years FU) Data collected period not specified (1999–2001 baseline) $n = 1009$ 56% = men Age = 21–85 BMI = 27.5 mean and 17.6–48.2 range (highest prudent dietary pattern quintile at baseline) BMI = 28.8 mean and 17.6–54.4 range (highest Western dietary pattern quintile at baseline) Participants in this cohort study were participants in a randomized adjuvant chemotherapy trial	CC reoccurrence after stage III Primary end point of study was disease-free survival—defined as the time from completion of FFQ to tumor recurrence, occurrence of a new tumor and death from any cause. Additionally, recurrent-free survival was defined as the time from the completion of the FFQ, to tumor recurrence or occurrence of a new primary colon tumor. Lastly, overall survival was defined as the time from completion of the FFQ to death from any cause	Semi-quantitative FFQ (131 items) (validated and reproducible) mid-way through therapy (4 months following surgical resection) and 6 months after adjuvant chemotherapy (14 months following surgical resection), to assess diet over the immediate previous 6 months. Total dietary intake was averaged using both data from both questionnaires 1. Two 2. Prudent; fruits, vegetables, whole grains, legumes, poultry, and fish Western; processed and red meats, fat, refined grains, high-fat products, desserts, and French fries 3. Eigenvalues of ≥1.5 was used to retain the food in the factor (pattern) Pattern scores assessed by PCA were categorized into quintiles	Two adjustment models: Model 1; TEI Model 2: TEI, PA, BMI, age at study entry, sex, number of positive lymph nodes, baseline performance status, presence of bowel perforation or obstruction at time of surgery, smoking history, treatment group, and weight change between the first and second questionnaire	324 patients had cancer recurrence, 223 patients died with cancer recurrence, and 28 died without documented cancer recurrence Cox proportional hazards regression was used in the analysis Higher intake of Western dietary pattern was associated with significantly worse disease free survival (CC reoccurrence or death). For the Western dietary pattern the adjusted hazard ratio (AHR) for disease-free survival was 3.25 (95% CI 2.04–5.19, p for trend <0.001). Similarly, the AHR for recurrent-free survival was 2.85 (95% CI 1.75–4.63, p for trend <0.001) and overall survival was 2.32 (95% CI 1.36–3.96, p for trend <0.001) The prudent dietary pattern was not significantly associated with disease-free survival (AHR 1.20, 95% CI 0.83–1.75, p for trend 0.78), cancer recurrence-free survival (AHR 1.13; 95% CI 0.77–1.67; p for trend 0.84), or overall survival (AHR 1.32; 95% CI 0.86–2.04; p for trend 0.54)
Nimptsch et al. [38] USA	Prospective cohort (18 years FU) Data collected between 1989 and 2007 Participants were female registered nurses were selected from the NHS II cohort (Nurses" Health Study) $n = 17{,}221$ 0% = men Age = 34–51 years BMI = not clearly specified	CRA, CA and RA Cases were identified by sigmoidoscopies and colonoscopies, and confirmed through medical records	High School (HS) FFQ (124 items) (validated and reproducible) was used to assess diet during high school (ages 13-17). Adult dietary intake was assessed by a FFQ (131 items) to assess diet over the previous 12 months, every 4 years (1991, 1995, 1999, 2003, and 2007). Both FFQ"s were used to identify dietary patterns 1. Two 2. Prudent; vegetables, fruit, better quality grains, fish, and poultry intake Western; desserts and sweets, snack foods, and red and processed meat 3. Eigenvalues > 1 Pattern scores assessed by PCA were categorized into quintiles	Two adjustment models: Model 1; age (at baseline), height, family history of CRC, PA during HS, pack years of smoking (<20 years), and TEI Model 2; BMI, pack-years of smoking, PA, aspirin use, time of endoscopy, two or more endoscopies during the study period, endoscopy prior to 1998, reason for most recent endoscopy (screening vs. symptoms), current cumulative updated average alcohol intake, adult TEI, and the respective dietary pattern during adulthood	Overall 1299 participants were diagnosed with CRC Multivariable logistic regression models adjusting for covariates produced OR, with 95% CI The prudent DP was associated with a significantly reduced risk of CRA (OR 0.82, 95% CI 0.67–1.02, p for trend 0.23) and RC (OR 0.45, 95% CI 0.27–0.75, p for trend 0.005). This was not reflected for CA, although a non-significant reduced risk was observed (OR 0.89, 95% 0.71–1.11, p for trend 0.59) The Western dietary pattern was associated with a significantly higher risk of RA only (OR 1.78, 95% CI 1.12–2.85, p for trend 0.005) There were no associations between DP and proximal CA and distal CA risk
Shin et al. [41] Japan	Prospective cohort (13.8 years FU) Data collected between 1995 and 1998 and 2012. Subjects participated in the Japan Public Health Center-based Prospective Study $n = 93{,}062$ subjects (43,591 men, 49,471 women) Age 40–69 at baseline	CRC, proximal, distal 2482 cases identified at FU Diagnosis was based on the International Classification of Disease for Oncology	Self-administered 138 food item FFQ used as baseline dietary data, which were aggregated into 38 food groups according to culinary preferences 1. Three 2. "Prudent"; vegetables, fruit, noodle, potatoes, soy products, mushrooms, and seaweed "Westernised"; meat, processed meat, eel, dairy foods, fruit juice, coffee, tea, soft beverages, sauces, and alcohol "Traditional"; pickles, seafood, fish (oily, salty, lean, salmon), chicken, and sake (men only) 1. Eigenvalue > 1.75 Test for trend was performed by modeling the quintile medians of each dietary pattern scores as continuous variables	Two adjustment models Model 1; age Model 2; age, BMI, smoking status, total PA, TEI, menopause, use of exogenous female hormones (women only)	The "Prudent" DP pattern was negatively associated with CRC risk in men (HR for highest quintile vs lowest: 0.85; 95% CI 0.72, 1.00) and slightly more strongly with distal colon cancer (p trend <0.05) In women, the "Westernized" DP showed a positive linear trend for CC (p-trend < 0.05) and distal CC (p-trend < 0.05) in women. There was no association of traditional DP on the overall, or any specific sites risk of CRC
Terry et al. [15] Sweden	Prospective cohort (11 years FU) Data collected between 1987 and 1998. Participants selected from a population-based mammography screening program $n = 61{,}463$ (females) Age = 40–74 years Median BMI range = 23.3–24.5	CC [proximal CC and distal CC] (Defined as occurring above (CC) or below (RC) the peritoneal delineation of the abdominal cavity Cases were identified through regional cancer registers for colon and rectal cancer	Self-administered FFQ (67 items) was used to assess diet over the previous 6 months 1. Three 2. Healthy; fruits and vegetables, fish and poultry, cereal and wholegrain breads, fruit juice, and low-fat dairy products. Western; processed and red meats, soda and sweets, refined breads and potatoes, and high-fat dairy products. Drinker; wine, beer, and spirits 3. Eigenvalues > 1. Positive loadings indicated that dietary variable was positively associated with factor, and negative loadings indicated an inverse association with the factor Pattern scores assessed by PCA were categorized into quintiles	Two adjustment models: Model 1; age and TEI Model 2; age, TEI, BMI, and education	Cox proportional hazards models were used to estimate hazard rate ratios and 95% CI There were no clear associations found between dietary patterns and CRC risk, although data suggests that low intakes of foods associated with a healthy dietary pattern maybe increase CC and RC risk For women under 50 years of ages, there was an inverse association was found between the healthy dietary pattern and CRC risk

Table 1 (continued)

Author, (Year) Country	Study design and population	Outcome	Characteristics of Dietary patterns (DPs) 1. Number of DPs 2. Label of each DP and food items included 3. PCA information (including % of total variance of original food items being explained by the DPs, if available	Adjustments	Main findings
Wu et al. [42] USA	Prospective cohort (14 years FU) Data collected between 1986 and 2000 $n = 47{,}311$ (all males) Mean BMI range = 24.8–26.1 Mean age range = 51.5–55.9 years Participants were selected from a male USA health professional's cohort	CC, proximal CC and distal CC Diagnosis was identified by self-reported questionnaire and confirmed though medical records (histology, anatomic location and stage of CC) if not specified on questionnaire Review of death certificate or response was from next of kin was used to identify cases that had died during follow up	FFQ (131 items) was used to assess diet in the previous 12 months, updated in 1986, 1990, and 1994 1. Two 2. Vegetable; vegetables, legumes, fruit, whole grains, fish, and poultry Western; red meat, processed meat, refined grains, French fries, high-fat dairy products, sweets and desserts, high-sugar drinks, and eggs 3. Eigenvalues > 1.0 Pattern scores assessed by PCA were categorized into quintiles	Three adjustment models Model 1; Age Model 2; age, race, family history of CRC in first degree relatives, history of endoscopy, PA, accumulated pack-years of smoking ≤ 30 years of age, aspirin use (at baseline), and TEI Model 3; age, race, family history of CRC in first degree relatives, history of endoscopy, PA, accumulated pack-years of smoking ≤ 30 years of age, aspirin use (at baseline), TEI, and BMI	Multivariate-adjusted RR and 95% CI were calculated using the Cox proportional hazards model Neither dietary pattern was significantly associated with CC risk, nor proximal and distal CC risk The prudent dietary pattern was weakly and non-significantly associated with a reduction in CC risk (RR 0.84, 95% CI 0.64–1.10, p for trend 0.38), proximal CC risk (RR 1.01, 95% CI 0.66–1.55, p for trend 0.66), and distal CC risk (RR 0.89, 95% CI 0.59–1.35, p for trend 0.48). Similarly, the Western pattern was weakly linked to CC risk (RR 1.21, 95% CI 0.91–1.60, p for trend 0.13), proximal CC risk (RR 1.05, 95% CI 0.67–1.65, p for trend 0.54) and distal CC, RR 1.20, 95% CI 0.77–1.86, p for trend 0.53
Zhu et al. [16, 39] Canada	Prospective cohort (6.4 years FU) Data collected between 1999 and 2003 $n = 529$ 60.1% = males Mean age range = 61.7–57.4 years BMI = not clearly specified Participants were selected from the Newfoundland Familial CRC Registry	CRC disease-free Survival (time from cancer diagnosis to first confirmed tumor reoccurrence, metastasis or death from all causes and overall survival) Overall survival (date of cancer diagnosis to the date of death from all causes) Cases were eligible if they were newly diagnosed with CRC, and were confirmed by pathologically confirmed, invasive CRC. Outcomes were ascertained from autopsy, pathology, radiology, surgical reports, physicians" notes, and local newspapers	FFQ (170 items), to assess diet over the 12 months prior to diagnosis 1. Three 2. Processed meat; coffee, soft drinks, cheese, egg, mixed dishes, red meat, cured/processed meat, cured/processed red meat, game, poultry, fish, processed fish, root and other vegetables, beans, peas, pickled vegetables, total cereals and grains, beer, desserts and sweets, and pies and tarts Prudent vegetable; milk, sugar, cheese, mixed dishes, poultry, fish, processed fish, fruit juice, cruciferous vegetables, other fruit, other greens, tomato sauce, other vegetables, bean and peas, pickled vegetables, total cereals and grains, whole grains, citrus, berries, dried fruit, and canned fruit High-sugar; sugar, tea, egg, mixed dishes, red meat, cured/processed red meat, fruit juice, root vegetables, pickled vegetables, total cereals and grains, desserts and sweets, pies and tarts, canned fruit, and jam and jelly 3. Eigenvalue > 1.15 and loading factor ≥ 0.50 Pattern scores assessed by PCA were categorized into quartiles	One adjustment model: Age at diagnosis, sex, stage at diagnosis, BMI, marital status, family history, reporting screening procedure, reported chemo-radiotherapy, MSI status, TEI.	Multivariate Cox proportional hazards models estimated HR and 95% CI Disease-free survival among CRC patients was poorer in the processed meat dietary pattern (HR 1.82; 95% CI 1.07-3.09; p for trend 0.09), when comparing the highest quartile to the lowest Neither the prudent vegetable pattern nor the high-sugar pattern was observed to be significantly associated with disease-free survival and overall survival
Chen et al. [43] Canada	Case–control (Population based) Data collected between 1999 and 2003 Participants were selected using existing data that was collected by the Newfoundland Familial Colorectal Cancer Registry (NFCCR) Cases = 506 Controls = 673 60% men Age 20–74 years 49% of cases had family history of CRC	Patients were newly diagnosed with CRC and enrolled in the NFCCR Registry	A 169 food item FFQ was used, which contained 39 pre-defined food groups 1. Three 2. "Meat-Diet"; red meat, cured/processed red meat, fish, processed fish "Plant-based"; root vegetables, tomato sauce, total cereals and grains, berries, dried fruits, other fruits, other green vegetables, other vegetables "Sugary-diet"; pies, tarts, desserts, sweets 3. Loading ≥ 0.35 (three DPs explained 74% of variance)	Two adjustment models: Model 1; age and TEI Model 2; sex, BMI, marital status, educational attainment, household income status, alcohol intake, smoking, NSAID use, family history of CRC, history of polyps, diabetes, colon screening procedures, high cholesterol, Crohn"s disease or colitis; multivitamin supplement use, PA	The "Meat-diet" and the "Sugary-diet" DPs increased the risk of CRC (OR 1.84 (95% CI: 1.19–2.86) and 2.26 (95% CI: 1.39–3.66, respectively for the highest vs. lowest quintile of DP score The "Plant-based" DP decreased the risk of CRC (OR 0.55, 95% CI 0.35–0.87). Even though ORs were not always statistically significant, largely similar associations across three cancer sites were found: the proximal colon, the distal colon, and the rectum
De Stefani et al. [44]	Case–control (Hospital based) Data collected between 1996 and 2004 Participants were selected from the same hospitals in Montevideo $n = 1830$ Cases = 610 Controls = 1220 59% = men Age = 30–89 BMI range = <23.0 to >28.1 (varied between DPs)	CRC, CC and RC Cases were defined as newly diagnosed and CRC, CC, or RC was confirmed microscopically Controls were selected from the same time period and hospitals as cases, and were admitted for conditions unrelated to smoking or alcohol drinking and without recent changes to their diets	FFQ (64 items) (non-validated, reproducible) 1. Four in men, and three in women 2. Men: "Prudent"; white meat, dairy foods, raw vegetables, and total fruits "Traditional"; desserts, cooked vegetables, all tubers, legumes "Western"; red meat, processed meat, and eggs "Drinker"; beer, wine, and hard liquor Women: Prudent; white meat, dairy foods, desserts, raw and cooked vegetables, and total fruits Western; red meat, white meat, total grains, and all tubers Drinker; beer, wine, and hard liquor 3. Loadings > 0.39. Total variance (including error variance) for men was 40.4% and for women it was 34.3% Pattern scores assessed by PCA were categorized into quartiles. ORs were estimated by logistic regression and polynomial regression	One adjustment model: Age, residence, urban/rural status, education, family history of CRC among first degree relatives, BMI, smoking index, TEI and all dietary patterns	CRC was inversely associated with both prudent and traditional DPs in men, with a reduced risk of 0.56 (OR) (95% CI 0.37–0.84) and 0.60 (OR) (95% CI 0.38–0.93), respectively In women, the "Prudent" DP was inversely associated with CRC (OR 0.53, 95% CI 0.32–0.89) In men, there was no statistically significant association between CRC risk in the "Western" (OR 1.39, 95% CI 0.85–2.26) and "Drinker" DPs (OR 1.41, 95% CI 0.94–2.11). Similar findings were found in women, with no significant associations between CRC cancer risk in the "Western" (OR 1.48, 95% CI 0.83–2.64) and "Drinker" DPs (OR 1.04, 95% CI 0.66–1.64)

Table 1 (continued)

Author, (Year) Country	Study design and population	Outcome	Characteristics of Dietary patterns (DPs) 1. Number of DPs 2. Label of each DP and food items included 3. PCA information (including % of total variance of original food items being explained by the DPs, if available	Adjustments	Main findings
Kurotani et al. [45] Japan	Case–control (Community based) Data collected between 1993 and 2000. Participants were derived from Fukuoka Colorectal Cancer Study $n = 1575$ Cases = 800 Controls = 775 % of men unclear Mean age range = 60.5–61.3 Mean BMI range = 22.6–23.8 (varied between dietary patterns)	CRC, proximal CC, distal CC and RC Cases identified as those admitted to one of the participating hospitals for the first surgical treatment Controls were randomly selected from the community, with no history of CRC	Semi-quantitative FFQ (148 items) (validate and reproducible) assessing diet over the previous 12 months 1. Three 2. Prudent; vegetables, fruits, sea foods and soya foods High-fat; fat and oils, red meat, processed meat and mayonnaise and low intake of rice, poultry, bread, and noodles Light-meal patterns; confectioneries of the Western and Japanese types, dairy products, bread and fruits 3. Eigenvalue > 1.0 After dietary analysis, 29 food groups were identified. Pattern scores assessed by PCA were categorized into quartiles	Two adjustment models: Model 1; sex, age, residential area. Model 2; sex, age, residential area, BMI 10 years earlier, cigarette smoking, alcohol use, type of job, leisure-time, PA, parental CRC, TEI	The "Prudent" DP was negatively associated with overall risk of CRC (OR 0.79, 95% CI 0.58–1.08, p for trend 0.05) Neither the "High-fat" (OR 0.99, 95% CI 0.73–1.34, p for trend 0.96) or the"Light-meal" DPs patterns (OR 1.19, 95% CI 0.86–1.65, p for trend 0.42) were associated with CRC risk
Miller et al. [46] USA	Case–control (Community-based) Data collected between 2007 and 2009 Participants were selected from a 19-county area in central and northeast Pennsylvania $n = 1157$ Cases = 431 (225 men and 206 women) Controls = 726 (330 men and 396 women) 48% = males Mean age range = 57.5–66.2 Mean BMI range = 28.2–29.9	CRC Newly diagnosed (within 12 months of diagnosis) CC and RC cases were confirmed histologically from records of the Pennsylvania State Cancer Registry. Controls identified by random digit dialing (10% nonresponse rate) and resided in the same region as cases, with no history of CRC	Self-administered, validated FFQ (137 items) 1. Three DPs identified for men, and two for women 2. Men: Fruits and vegetables pattern; other vegetables, yellow and orange vegetables, dark green and cruciferous vegetables, other fruit, tomatoes, citrus, berries and melons, starchy vegetables, legumes, vegetable oils, fish, nuts and seeds, and whole grains Meat, potatoes and refined grains pattern; fresh red meat, fried potatoes, white potatoes, refined grains, processed meat, gray, poultry, sweets, butter, pizza, salty snacks sugar-free beverages, and high-fat dairy Alcohol and sweetened beverages; other fruit, citrus, berries, and melon, refined grains, sweets, sugar-sweetened beverages, liquor, mayonnaise, high-fat diary, and beer Women: "Fruits and vegetables"; other vegetables, yellow/orange vegetables, dark green and cruciferous vegetables, other fruit, tomatoes, citrus, berries and melons, starchy vegetables, legumes, vegetable oils, nuts and seeds, whole grains, low-fat dairy Meat, potatoes and refined grains"; fresh and processed red meat, fried potatoes, white potatoes, refined grains, poultry, sweets, butter, pizza, salty snacks sugar-sweetened beverages, high-fat dairy, mayonnaise, and margarine 3. Eigenvalues were > 1.5 and factor loading was ≥ 0.30 Dietary patterns derived from both diet index-based (HEI-05) and PCA. Pattern scores assessed by PCA were categorized into quartiles	Two adjusted models: Model 1; age Model 2; age, BMI, education, TEI, family history of CRC, NSAID, use, PA, and smoking	Logistic regression was sued to estimate OR and 95% CI The "Fruits and vegetables" DP was negatively associated with CRC risk in both men (OR 0.38, 95% CI 0.21–0.69) and women (OR 0.35, 95% CI 0.19–0.65) There was a positive association between the "Meat, potatoes, and refined grains" DP and CRC risk in women (OR 2.20, 95% CI 1.08–4.50) and men (OR 1.56, 95% CI 0.84–2.90) There was no evidence of an association between cancer risk and the alcohol and sweetened beverages pattern
Park et al. [47] Korea	Case–control (Clinic-based) Data collected between 2010 and 2013 Participants were enrolled in the Center for Colorectal Cancer, National Cancer Center Cases were confirmed based on pathology reports and chart review 1846 controls 923 cases	Specific colon sites: Proximal colon (cecum, ascending colon, hepatic flexure, transverse colon, and splenic flexure), distal colon (descending colon, sigmoid-descending colon junction, and sigmoid colon), and rectum Diagnosis obtained from medical records	The 106 food items listed in the semi-quantitative FFQ were categorized into 33 food groups based on nutrient profiles and culinary usage 1. Three DP identified 2. "Traditional"; staple Korean foods including vegetables, tubers, seaweeds, fish, soy, mushrooms, and seasonings. " Westernised"; red meat, meat by-products, poultry, cakes, pizza, bread, hamburger, noodles, oil, and sugar "Prudent"; fruits, milk and dairy products, cereals, nuts 3. Eigenvalues > 02.0 The proportion of total variation explained by these DPs was 24.2% for men and 25.3% for women. DP were analysed as intake tertiles of DP scores	One multivariate model including as potential confounders: BMI (defined by the criteria for the Asia-Pacific region), smoking status, alcohol consumption, physical activity, a first-degree family history of CRC, education level, occupation, marital status, monthly income, and total energy intake	The "Traditional" and "Prudent" DPs (highest vs lowest tertile) were inversely associated with CRC risk [OR 0.35 (95% CI 0.27–0.46) and 0.37 (95% CI 0.28–0.48), respectively] the " Westernised" DP was positively associated with CRC in women (OR 2.13 (95% CI 1.35–3.34) A decrease in CRC risk among those with the highest intake of the "Prudent" pattern was observed in all anatomical subsites in both men [OR = 0.36 (95% CI 0.19–0.68) for proximal colon; 0.21 (95% CI 0.12–0.36) for distal colon; 0.28 (95% CI 0.18–0.44) for rectum] and women [OR = 0.28 (95% CI 0.11–0.71); 0.27 (95% CI 0.13–0.54); 0.45 (95% CI 0.25–0.83)

Table 1 (continued)

Author, (Year) Country	Study design and population	Outcome	Characteristics of Dietary patterns (DPs) 1. Number of DPs 2. Label of each DP and food items included 3. PCA information (including % of total variance of original food items being explained by the DPs, if available	Adjustments	Main findings
Randall et al. [48] USA	Case–control study (Community-based) Data was collected between 1975 and 1984 Participants were selected from the Western New York Diet Study $n = 856$ Cases = 428 Controls = 428 47.9% = men Age = not specified BMI = not specified	CC Cases were by identified nurse interviews and hospital medical records Controls were matched on age, gender, and neighborhood residence	Interview-based semi-quantitative, validated 128 food item FFQ enquiring on diet over the previous 12 months 1. Seven DPs in men, and another seven in women 2. Men: "Salad"; lettuce, celery, green pepper, cucumber, tomatoes, radishes, onion, and carrots "Fruit"; peaches, plums, pears, apples, oranges or tangerines, cherries, grapes, melons, bananas, and berries "Healthful"; Broccoli, spinach, cauliflower, rice, poultry, mushrooms, green beans, summer squash, and asparagus "Traditional"; wax beans, green beans, potatoes, peas, beets, cabbage, roast beef, cakes, pies, and corn "Snacks"; cookies, candy, crackers, donuts or pastries, hamburger, ice cream, and baked beans "High fat"; eggs, bacon, sausage, steak, beer, salami or pepperoni, and distilled alcohol "Whole grain"; whole wheat bread, cooked cereal, oatmeal Women: "Salad"; lettuce, celery, green pepper, cucumber, tomato, radishes, onion, carrot, apples, and broccoli "Healthful"; green beans, cauliflower, spinach, beets, summer squash, pineapple, liver, wax beans, broccoli, winter squash, cottage cheese, mushrooms, peas, and cabbage "Low cost"; macaroni, spaghetti, bologna, hot dogs, French fries, noodle, hamburger, processed cheese, salami or pepperoni, canned fish, coffee "Fruit"; pears, peaches, plums, oranges or tangerines, apples bananas, grapes, and grapefruit. "High fat"; pies, candy, cake, potatoes, roast beef, donut or pastries, bacon, rolls, and potato chips "Light"; mushrooms, lemons or limes, hard cheese, fin fish, yogurt, melon, and broccoli "Whole grain"; cooked cereal, cookies, dried fruit, unsweetened cereal, crackers, oat products, whole wheat bread, nuts, and yogurt 3. Eigenvalue ≥ 1.5 and factor loadings were ≥ 0.2	Four models: Model 1; age and education Model 2; added TEI Model 3; age, education, and total fat intake Model 4; age, education, and dietary fiber intake	Bivariate logistic regression was used to calculate OR for adjustment model 1 (women and men separately). Logistic regression analysis was used to calculated OR and 95% CI for adjustment models 2, 3 and 4 "High fat" DP in men associated with CC risk ([model 2] OR 1.26, 95% CI 1.02–1.56), however this association was not identified in women ([model 2] OR 0.86, 95% CI 0.69–1.07) The "Healthful" DP was not associated with CC risk in men ([model 2] OR 0.96, 95% CI 0.79–1.17) or women (OR 0.95, 95% CI 0.78–1.15)
Safari et al. [49] Iran	Case–control (Hospital-based study) Data collected between 2008 and 2010. $n = 213$ Cases = 71 (35 men and 36 women) Controls = 142 (70 men and 72 women) 49.3% = men Mean BMI in controls = 26.67 ± 4.2 Mean BMI in cases = 27.23 ± 4.2 Age = 40–75 years	CRC Cases were pathologically confirmed. Controls were randomly selected from patients admitted to the same hospitals as cases during the same time period, and for acute, non-neoplastic diseases	A 125 food item, semi-quantitative FFQ (validated and reproducible) was used to assess diet over the previous 12 months 1. Two 2. "Healthy"; vegetables, fruits, olives, liquids oils, all fish, low-fat dairy, carrot, nuts, whole grains, and yogurt drink "Western"; sugars, red meat, pickles, refined grains, soft drinks, animal butter mayonnaise, black tea, processed meat, legumes, solid oil, sweets and desserts, and snacks 3. Factor loading was < 0.20. Each DP explained 11.9% (healthy) and 10.3% (Western) of the variation in food intake Pattern scores assessed by PCA were categorized into high and low scores	1 adjustment model: Family history of CRC in first and second degree relatives, vegetables preparation, aspirin, acetaminophen, mineral intake, and TEI	A "Healthy" DP was associated with a reduced CRC risk (OR 0.23; 95% CI 0.11–0.48; $p < 0.001$) The "Western" DP was associated with increased risk of CRC (OR 2.62; 95% CI 1.36-5.03; $p < 0.004$)
Satia et al. [50] USA	Case–control (Community-based) Data collected between 1996 and 2000 Participants were selected from the North Carolina Colon Cancer Study (NCCCS). $n = 1678$ Cases = 636 Controls = 1042 43–56% = men (range across groups and cases and controls) Age = 40–80 years Mean BMI range = 27.6–30.5	CC Cases were those who had historically confirmed invasive adenocarcinoma of the colon between October 1996 and September 2000 Controls were population-based, randomly selected individuals from the North Carolina Division of Motor Vehicle records and the Center for Medicare and Medicaid Services	A semi-quantitative, 100 food item FFQ (validated and reproducible) was used to assess diet over the previous 12 months 1. Three (1 dietary pattern varying in food loadings between White and African American groups) 2. "Western-Southern"; red meats, fried chicken, fish eggs, French fries, cheese dishes, white bread, and sweets "Fruit-vegetable"; fruits and vegetables, legumes, collards, green beans, yams, and cereals "Metropolitan"; salad and seafood. In the White group—Mexican foods, pastas, chicken, turkey, veal, and lamb. In the African American group—cruciferous vegetables, pasta salad, alfalfa sprouts, and yogurt 3. Factor loadings ≥ 0.20 Pattern scores assessed by PCA were categorized into tertiles	2 adjustment models: Model 1; TEI, age, sex, and off-set term Model 2; TEI, age, sex, and off-set term, education, history of CC in first-degree relatives, PA, vitamin/minerals use and BMI	Unconditional logistic regression was used to estimate OR and 95% CI. The fruit-vegetable dietary pattern was associated with a reduced risk of CC in the white sub-group (OR 0.4, 95% CI 0.3–0.6, p for trend 0.0001). This association was not identified in the African American sub-group (OR 1.1, 95% CI 0.7–1.6, p for trend 0.78). There were no other associations between CC and the Western-Southern and Metropolitan dietary patterns in both the white and African American sub-groups.

Table 1 (continued)

Author, (Year) Country	Study design and population	Outcome	Characteristics of Dietary patterns (DPs) 1. Number of DPs 2. Label of each DP and food items included 3. PCA information (including % of total variance of original food items being explained by the DPs, if available	Adjustments	Main findings
Slattery et al. [13] USA	Case–control Data collected between 1991 and 1994 Participants were recruited from the Kaiser Permanente Medical Care Program of Northern California; an eight-county area in Utah and the metropolitan Twin Cities area of Minnesota	CC, proximal, and distal CC Cases were identified by a rapid reporting system. Cases were eligible if the diagnosis with first primary incident CC (October 1, 1991–September 30, 1994) Controls were randomly selected from Kaiser Permanente membership lists, and contacted through random digit dialing, and driver"s license lists	An adapted FFQ from the Coronary Artery Risk Development in Young Adults (CARDIA) Study 1. Four in men, and four in women 2. Men: "Western"; red meat, processed meat, fast food, refined grains, and sugar containing foods, and low levels of vegetables (other than potatoes) and fruits (predominantly canned) "Prudent"; Fruits, vegetables, fish and poultry "Drinker"; alcoholic beverages "Substituter""; fruit, margarine substituted for butter, whole grains substituted for refined grains, low fat dairy products substituted for high fat dairy products, and poultry was substituted for red meat Women: "Western"; red meat, processed meat, fast food, refined grains, and sugar containing foods, and low levels of vegetables (other than potatoes) and fruits (predominantly canned) "Prudent"; Fruits, vegetables, fish and poultry "Drinker"; alcoholic beverages "Substituter"; fruit margarine substituted for butter, whole grains substituted for refined grains, low fat dairy products substituted for high fat dairy products, and poultry was substituted for red meat 3. Eigenvalue > 1.25 and factor loadings > 0.20 Pattern scores assessed by PCA were categorized into quintiles	One adjustment model: Model 1; age, BMI, long term PA, and TEI	Unconditional logistic regression estimated OR and 95% CI The "Western" DP was associated with an increased risk of CC (OR 1.80, 95% CI 1.28–2.53, p for trend < 0.01) and distal CC (OR 2.25, 95% CI 1.47–3.46, p for trend < 0.01) in men, with no significant associations with proximal CC risk There was an increased risk of CC (OR 1.49, 95% CI 1.05–2.12, p for trend 0.02), and proximal CC (OR 1.65, 95% CI 1.06–2.51, p for trend < 0.01) associated with the "Western" DP in women, and there was a weaker association between distal CC and the "Western" DP in women (OR 1.39, 95% CI 0.89–2.18, p for trend 0.05) A significant CC risk reduction was associated with the "Prudent" DP in men (0.66, 95% CI 0.50–0.86, p for trend 0.02), and women (OR 0.73, 95% CI 0.55–0.97, p for trend 0.02). This association was similarly reflected with proximal CC risk in both men (OR 0.55, 95% CI 0.38–0.80, p for trend 0.02) and women (OR0.64, 95% CI 0.45–0.92, p for trend 0.02) There were no significant associations between the prudent dietary pattern and distal CC risk in men or women
Williams et al. [51] USA	Case–control (Population-based) Data collected between May 2001 and September 2006 Non-Hispanic whites and African-Americans participants were identified from the North Carolina Colon Cancer Study (NCCCS) - Phase II	RC Cases identified by the NCC Registry rapid ascertainment system, and included those with cancers of the rectum, sigmoid, and recto-sigmoid junction Cases confirmed through pathology and report notes. Controls were randomly identified from the North Carolina Department of Motor Vehicles and from the Center for Medicaid and Medicare Services	Dietary intake in the previous 12 months was assessed using the Diet History Questionnaire (124 items) (validated and reproducible) 1. Three 2. Different dietary patterns were derived for White and African-American sub-groups Whites: "High fat/meat/ potatoes"; discretionary fat, non-whole grains, white potatoes, red and processed meat, cheese, and added sugar "Vegetable/fish/ poultry"; vegetables, fish and poultry "Fruit/whole grains"; fruit, whole grains, milk and yogurt African-Americans: "High fat/meat/ potatoes"; discretionary fat, non-whole grains, white potatoes, red and processed meat, cheese, and added sugar "Fruit/vegetables"; fruit and vegetables "Legumes/dairy"; nuts, beans, peas, milk, yogurt 3. The three dietary patterns explained 39% of the variance in Whites and 43% of the variance in African-Americans Pattern scores assessed by PCA were categorized into high and low scores	One adjustment model: Age, sex, socioeconomic status, BMI (12 months previous to study), PA, family history, nonsteroidal anti-inflammatory drug use, and TEI	Multivariate logistic regression was used to estimate OR and 95% CI. Results were stratified by race and results showed that cancer risk differed between and White and African-American sub-groups The "High fat/meat/potatoes" DP was associated with an increased risk (OR 1.84, 95% CI 1.08-3.15, p for trend < 0.0001), but only in the white sub-group Amongst white Americans, the "Vegetable/ fish/poultry" DP was negatively associated with RC risk (OR 0.47, 95% CI 0.33–0.67, p for trend < 0.0001). This association was also apparent with the "Fruit/whole grain/dairy" DP (OR 0.65, 95% CI 0.45–0.93, p for trend < 0.0001)
Mizoue et al. [52] Japan	Cross-sectional Data collected between 1999 and 2002 Participants were selected from those in the Self-Defense Forces Health Study cross-sectional survey and health examination (including total colonoscopy) n = 1341 (all male) Age = 40–49 BMI = not specified	CRA, CA, RA proximal CA, and distal CA—findings of adenoma of any size reported here Data identified through results of laboratory tests and colonoscopic findings, including histology for polyp, were extracted form clinical reports	A 74 food item FFQ (validated) enquiring about diet in the previous 12 months. Participants answered it before undergoing total colonoscopy 1. Three 2. "High-dairy, high-fruit and -vegetable, high-starch, low-alcohol" (DFSA); fermented dairy products, confectionaries, fruits (fresh/canned), bread, fruit and vegetable juices, milk, oil dressing, fried foods, processed meat and fish, cooked and raw vegetables, seaweed, potatoes, and garlic "Animal food"; confectionaries, oil dressing, soda/cola, alcoholic beverages, read meat, poultry, fried foods, boiled fish/meat, seaweed, processed meat and fish, gyoza, liver, eggs, cooked vegetables, potatoes, and fish "Japanese"; fruits (not canned), vegetable juice, oil dressing, alcoholic beverages, fried foods, boiled fish/meat, seafood (except fish), processed fish, eggs, soybean products, cooked and raw vegetables, seaweed, pickles, green tea, potatoes, fish, and garlic 3. The proportion explained by the 3 factors was 24% Pattern scores assessed by PCA were categorized into quartiles	One adjustment model: Model 1; Hospital, age, parental history of CRC, occupational rank, BMI, smoking, and leisure-time PA.	Multiple logistic regression analysis used to estimate OR and 95% CI A significant inverse association was identified between the DFSA dietary pattern and risk of CRA (OR 0.62, 95% CI 0.43–0.90, p for trend 0.003). The Japanese (OR 1.18; 95% CI 0.83–1.69; p for trend 0.26) and animal food (OR 0.86; 95% CI 0.60–1.23; p for trend 0.49), dietary patterns were not associated with risk of CRA

Table 1 (continued)

Author, (Year) Country	Study design and population	Outcome	Characteristics of Dietary patterns (DPs) 1. Number of DPs 2. Label of each DP and food items included 3. PCA information (including % of total variance of original food items being explained by the DPs, if available	Adjustments	Main findings
Tazhibi et al. [53] Iran	Cross-sectional $n = 96$ Mean age range = 48–51 years Mean BMI range = 26–28	CC Participants selected from the Poursina Hakim clinic. Diagnosis was self-reported and confirmed by medical records	Semi-quantitative FFQ used to assess diet of past 12 months 1. Four 2. "DP1"; dried fruits, vegetables, legumes, fruits, fish, dairy, spices "DP2"; cream, butter, and animal fats, with lower amounts of legumes, dairy and tea "DP3"; animal fats, tea and red meat, with lower amounts of margarine, and non-hydrogenated vegetable oils "DP4"; hydrogenated and non-hydrogenated oil, with lower amounts of olive, diary and margarine 3. Eigenvalue > 1.5	Three adjustment models Model 1; age and gender Model 2; age, gender, and TEI Model 3; age, gender, TEI and BMI	No significant associations were found between either of the 4 dietary patterns and risk of CC

BMI body mass index, *CC* colon cancer, *CRC* colorectal cancer, *CRA* colorectal adenoma, *DP* dietary pattern, *FFQ* food frequency questionnaire, *FU* follow-up, *NSAID* non-steroidal anti-inflammatory drugs, *PA* physical activity

[a]Dixon et al [9]. was comprised of four cohort studies, namely the ATBC study (men) included in the broader DIETSCAN study. This was an 11-year prospective cohort, and included 27,111 participants aged 50–69 years old, with a mean BMI of 26.3 + 3.8. The data were collected between 1988 and 1999 (1985–1988 baseline), and the population were extracted from a randomized, double blind, placebo controlled chemoprevention trial of male smokers (>5 cigarettes per day).

The second cohort (6 years follow-up) was the NLCS study (men) included in the broader DIETSCAN study. 6-year population-based prospective cohort study and included 1525 subjects aged 55–69 years old, with a mean BMI of 25.0 + 2.6 (varied between dietary patterns). The data were collected between 1986 and 1992. Participants were selected from 204 municipalities in the Netherlands using computerized population registries. Case-cohort approach utilized for data processing and analysis. A sub-cohort was randomly selected from the entire cohort.

The third cohort was the NLCS study (women), which was also part of the DIETSCAN study, and included 1598 females aged 55–69. A case-cohort approach utilized for data processing and analysis. A sub-cohort was randomly selected from the entire cohort. The participants had a mean BMI of 25.1 + 3.5 (varied between dietary patterns)

The fourth cohort was the SMC study (women), also part of the DIETSCAN study, with a follow-up of 11 years, and 61,463 participants aged 40–74 years old, and a BMI of 24.8 + 4.4 (varied between dietary patterns). Data were collected between 1987 and1990. Participants were chosen from a population-based mammography screening program.

(DFSA)", "high-dairy, high-fruit-and-vegetables, low-alcohol (DFA)". Alternatively, dietary patterns were labeled according to the extent they are positively connected with a specific lifestyle, with a "Western" dietary labels being most common. For analysis, the following dietary patterns were grouped into the Western dietary pattern, labeled "meat", "meat-dim-sum", "high-fat and proteins", "western", "Pork, processed meats and potatoes", "red meat and potatoes", "processed meat", and "meat, potatoes, refined grains", "animal food" and "Southern Cone".

Associations of dietary patterns with CRC

The association of CRC and Western and prudent dietary patterns are presented in Fig. 3. When an overall pooled effect was estimated from a random effects model, there was a positive association between Western dietary pattern and CRC (RR 1.25; 95% CI 1.11, 1.40), whereas the prudent dietary pattern had a statistically significant negative association with CRC (RR 0.76; 95% CI 0.68, 0.86). Case–control studies showed a higher heterogeneity than cohort studies in both meta-analyses. Funnel plots showed little evidence of asymmetry and publication bias was only observed when the association between CRC and prudent dietary pattern (Fig. 4).

When combining all the effect of the studies that investigated CC as an outcome, the overall direction of association remained the same as for CRC in both Western and prudent dietary patterns (Fig. 5). There was evidence of 30% increase of risk of CC for Western dietary patterns (RR 1.30; 95% CI 1.11, 1.52), with high heterogeneity in cohort and case-control studies ($I^2 = 69.5\%$ and 71.5%, respectively). A prudent dietary pattern was associated with a 19% reduced risk of CC (RR 0.81; 95% CI 0.73, 0.91), with no evidence of heterogeneity in cohort studies ($I^2 = 0\%$) and high heterogeneity in case-control studies ($I^2 = 78.1\%$).

With regards to RC, there was no evidence of a statistically significant association between this cancer and Western dietary pattern intake, with high overall heterogeneity across studies ($I^2 = 62.8\%$). A prudent dietary pattern was negatively associated with RC in the case–control studies (RR 0.58; 95% CI 0.40, 0.85) but there was no evidence of association in the cohort studies (Fig. 6).

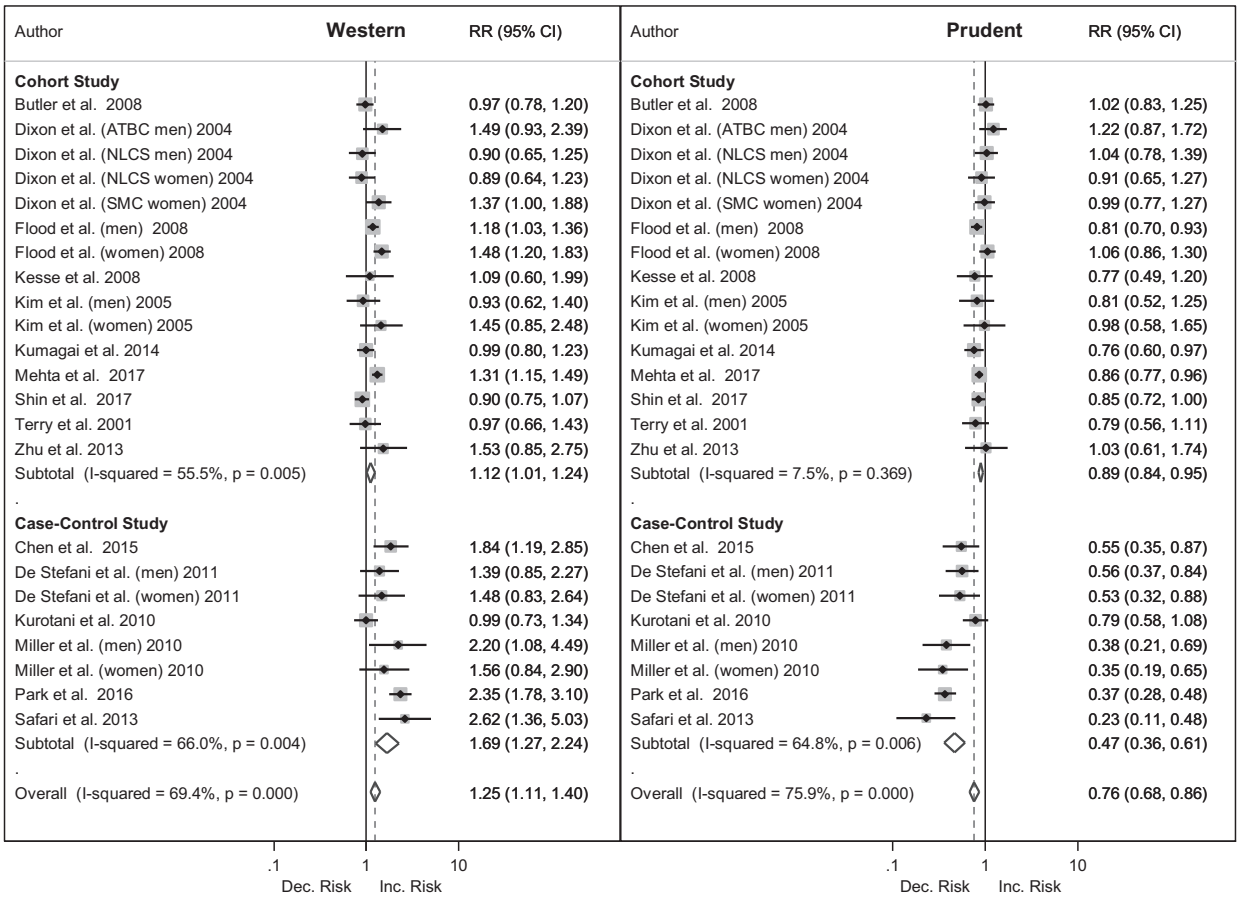

Fig. 3 Meta-analysis of associations between Western and Prudent dietary patterns (highest vs. lowest categories of intake) and CRC risk, stratified by study design

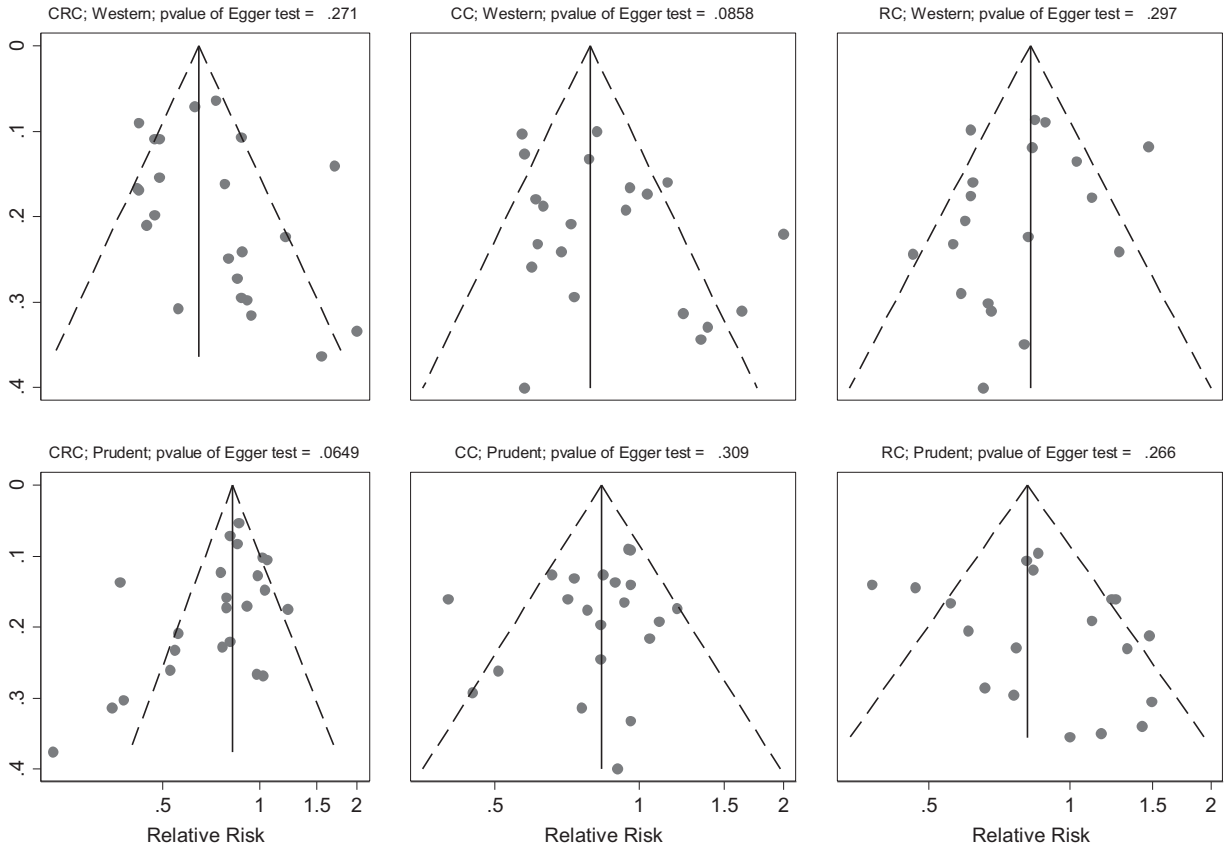

Fig. 4 Illustration of publication bias in included studies (funnel plots with Pseudo 95% confidence intervals) according to Western or Prudent (**a**) or Drinker pattern (**b**)

The results of the analyses with "Drinker" dietary pattern are shown in Figure S1. There was a borderline positive association with risk of CRC (RR 1.19; 95% CI 0.99, 1.43), and no evidence of association with CC or RC. All meta-analyses had very little heterogeneity ($I^2 < 3.0\%$).

Subgroup analyses

When results were analysed by studies that investigated colon cancer sub-sites only, an increased risk of both proximal CC (RR 1.19; 95% CI 1.05, 1.35) and distal CC (RR 1.48; 95% CI 1.23, 1.79) remained, when comparing the highest to the lowest categories of intake score of Western dietary pattern. On the other hand, a prudent dietary pattern was negatively associated with risk of both proximal and distal CC (RR 0.72; 95% CI 0.60, 0.85; and RR 0.80; 95% CI 0.69, 0.93, respectively (Figure S2; supplementary file).

Further sensitivity analyses were carried out stratifying by gender and continent. For both men and women, the risk of CRC and CC with a Western dietary pattern, was statistically significantly higher, whilst the reduced risk of these cancers was also observed for both genders. The risk of RC was unrelated to either males or females when stratifying by sex (Figure S3). When we examined the risk of colon cancer by geographical provenance (Figures S4, S5 and S6) we found that a Western dietary pattern was positively associated with risk of CRC, and CC in individuals from North America and South America. Similarly, in these two regions, a prudent dietary pattern was negatively associated with the risk of both CRC and CC.

Discussion

In this systematic review, we investigated the association of CRC, CC and RC with dietary patterns identified with the use of PCA in observational studies. Both cohort and case–control studies showed that a "Western" dietary pattern was statistically significantly associated with an increased overall risk of CRC and CC. A prudent dietary pattern showed a statistically significant negative association with CRC and CC. Stratified analyses by gender showed that both men and women were at increased risk of CRC and CC if they had a "Western" dietary pattern. Proximal and distal CC were positively associated with

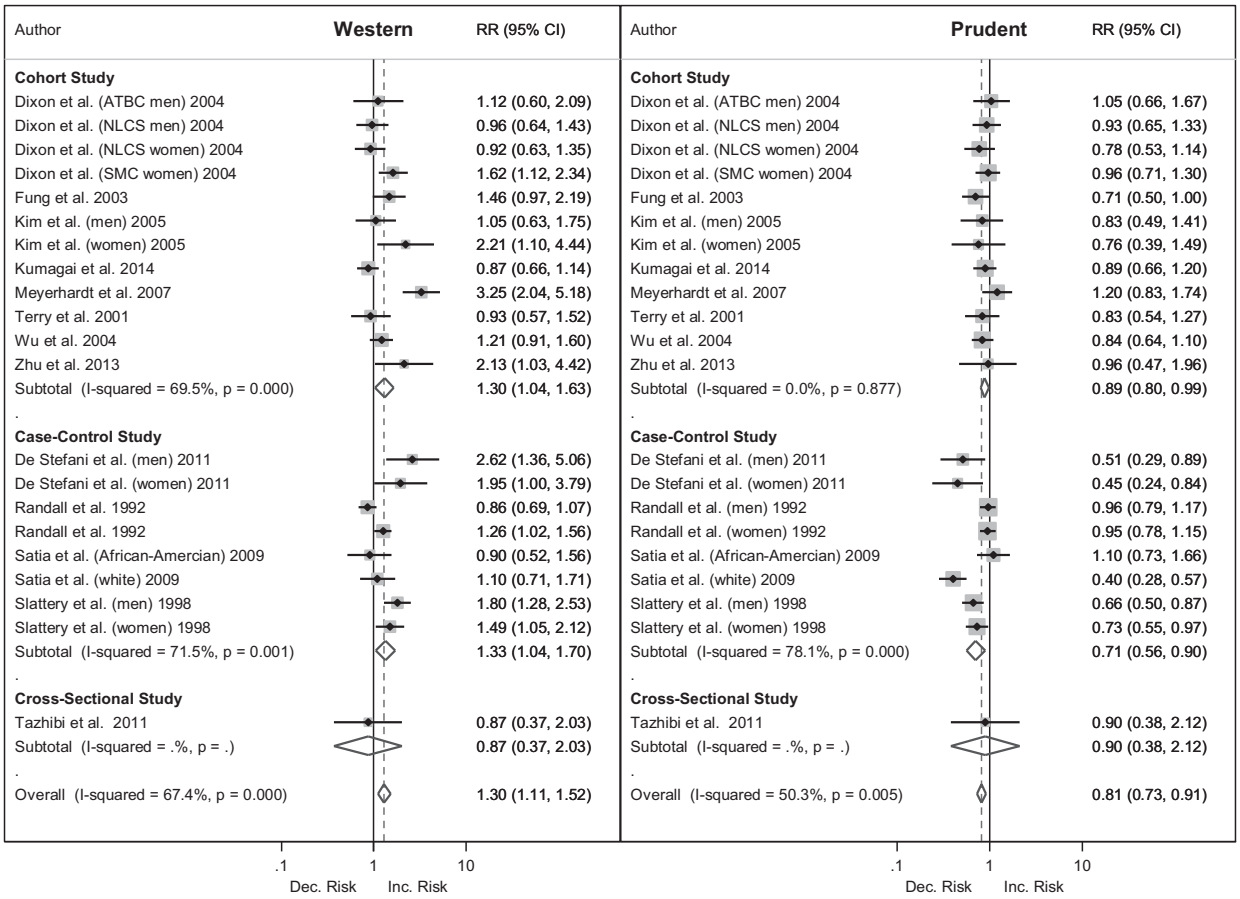

Fig. 5 Forest plot of the highest compared with the lowest categories of intake of the Western dietary pattern and CC risk, stratified by study design

having a Western dietary pattern, whilst the risk of having these cancer sites was reduced in individuals with a prudent dietary pattern. When stratifying by world region, the associations for CRC and CC with "Western" dietary pattern were observed in studies from North America and South America.

"Western" dietary patterns have generally been associated with increased risk of CRC and CC [13, 16, 17, 34, 35, 48, 54]. We found that a "Western" dietary pattern (mostly comprised of red and processed meats) was associated with a 25% higher risk of CRC (95% CI 1.11, 1.40). The case–control study of Carr et al. in German adults reported similar higher risks of CRC in individuals with a higher intake of red and processed meat (OR 1.66; 95% CI 1.34, 2.07) [55]. In our sensitivity analyses, this risk of CRC was stronger in women (OR 1.26). In a large population-based study, Vulcan and colleagues found that intake of pork was associated with a similar higher risk of CRC in Swedish women (HR 1.54; 95% CI 1.12, 2.15) [56].

The definitions used for "Western" dietary pattern varied between the observational studies included in this systematic, but the majority had in common meats (red and poultry), refined grains, and foods rich in sugar. This suggests that there might be a synergic effect of grouped foods on risk of CRC [57]. Refined grains and sugary products (e.g., confectionaries) are known to cause elevated plasma insulin levels and insulin-like growth factor-1, which are both associated with cancer risk, in particular CC [58]. Several epidemiological studies have confirmed a higher risk of disease in individuals who had a higher consumption of refined grains (e.g. wheat) [59], or high intake of carbohydrates [60], whilst adherence to dietary guidelines that restrict intake of sugary drinks has been associated with lower risk of CRC [61].

All the prudent dietary patterns described in this systematic review included fruits and vegetables, and most studies also included legumes. These foods are rich in dietary fiber and flavonoids, which have been suggested to protect against CRC risk [62]. The overall reduced risk we observed for a prudent dietary pattern on CRC and CC cancer (24 and 19%, respectively) is similar to the evidence from observational studies examining the association with fruit and vegetable intake. A recent systematic review on apple intake and cancer risk showed that a higher intake of this fruit was associated with a 33% lower risk of CRC in a meta-analysis of five studies [63].

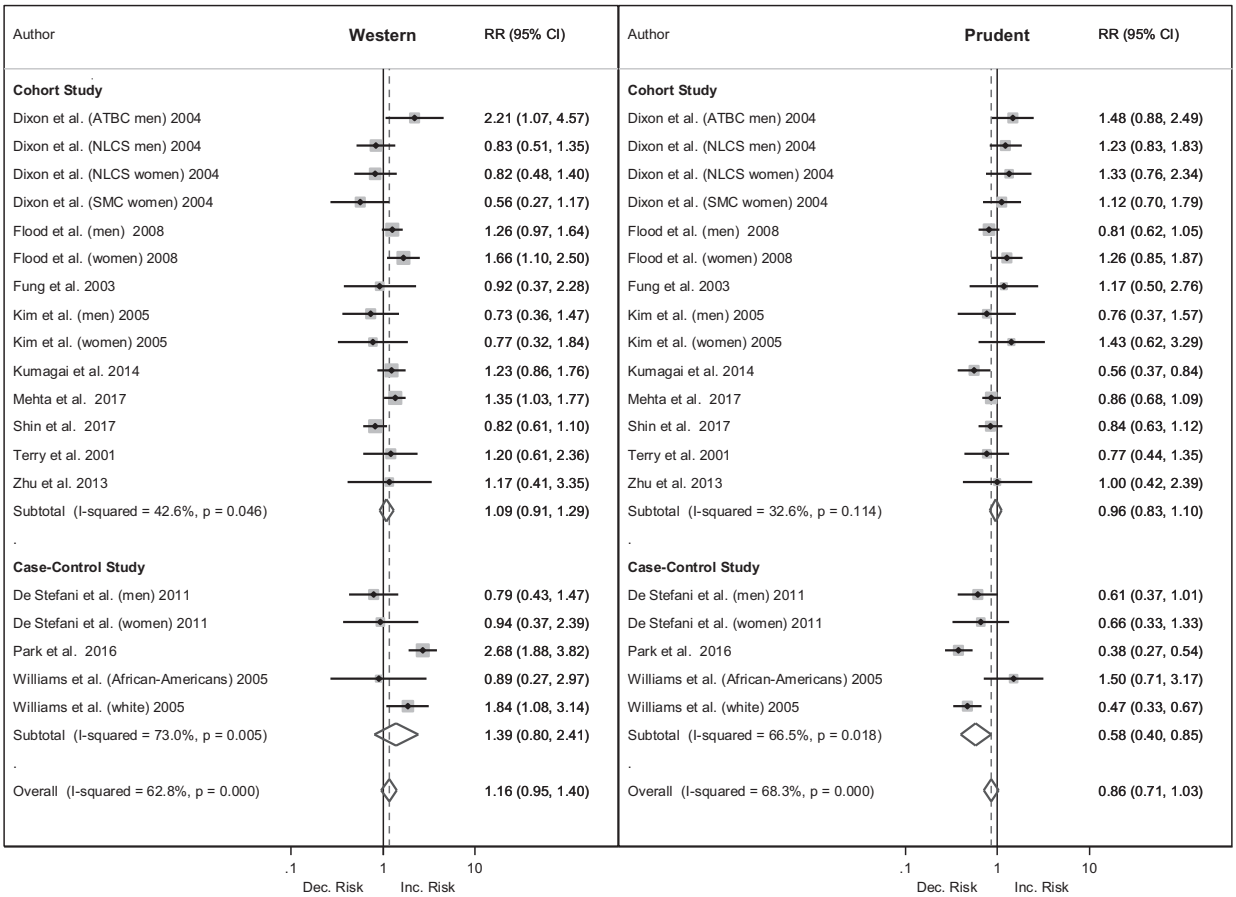

Fig. 6 Forest plot of the highest compared with the lowest categories of intake of the Western dietary pattern and RC risk, stratified by study design

Dietary fiber has been suggested to reduce the risk of CRC through several mechanism including promotion of a healthy gut microbiota [64], facilitating the elimination of faecal carcinogens, and decreasing colonic pH [65, 66]. Fruit fiber in particular, has also shown a strong association with reduced CRC risk, which may be due to its high pectin content, as well as an anti-proliferative effect on short-chain-fatty-acids [65, 67, 68]. Prudent dietary patterns are also considered less likely to contain harmful compounds found in processed foods (including processed meats), such as polycyclic aromatic hydrocarbons [46, 69].

In spite the various biological and chemical mechanisms that support a beneficial effect of fruit and vegetable intake against CRC, such association has not been confirmed in some observational studies [67, 70, 71]. A recent review on vegetable intake and CRC risk suggested that differences in findings might be due to study design, as reduced risks found in case-control studies, are not always confirmed in cohort studies [72]. The reasons for these inconsistencies between case-control and cohort study designs might be methodological, including the inherent recall bias in case-control studies or due to measurement error in cohort studies. These differences can also be due to the variety of foods that are included in fruits, vegetables and whole-grains, which might have different specific health benefits [73].

High alcohol intake has been suggested to be an important risk factor for CRC [5]. The meta-analysis on "drinker" pattern showed that it was associated with a 19% higher risk of CRC, but was not associated to CC or RC risk. Epidemiological studies in The Netherlands [61] and Malaysia [74] have shown that restricting alcohol intake, as part of a healthy diet, is associated with a reduced risk of CRC. Although the detrimental effects of ethanol are well known, it is also acknowledged moderate consumption of red wine and beer might be beneficial for their anti-inflammatory and antioxidant properties [75], which might partly explain the differences in the associations between colon sites.

Strengths of the review

This is the first systematic review and meta-analysis exploring the association between dietary patterns derived from PCA and CRC risk. The review was done following the PRISMA guidelines [23], and four datasets were

searched to identify eligible papers. Every effort was made to include specific country-related dietary habits, therefore no language restrictions were used in the search strategy. The systematic review also included an itemized assessment of the main biases that can be found in epidemiological studies, and used a visual, as well as an objective measurement of publication bias. We examined evidence that has analysed dietary intake using a relatively novel statistical tool in nutritional epidemiology, PCA, which is argued to capture the complexity of the diet of the population [13, 21]. Dietary patterns derived using PCA claims to capture the interactive and additive effects of diet on disease outcomes [13]. Also, meta-regression by study design and gender provided additional insight to the association between dietary patterns and CRC, CC, and RC.

Another strength of this systematic review is that we also examined the association of dietary patterns and CRC by geographical region (continents). The detailed description of dietary patterns in this systematic review confirms that dietary patterns derived from PCA are latent dimensions, which are comprised of different food items across cultures, and they could represent different food items in different contexts. The definitions used by the studies not always represent the traditional understanding of a " Westernised" dietary pattern. This might partly explain the very high heterogeneity across studies in Asia, and in some cases, the lack of association with disease outcomes; for example, dietary patterns in Japanese studies reported that "animal food pattern", containing red meat, but also soy and fish, which are considered "healthy" foods.

We acknowledge some limitations inherent to this systematic review. The analyses used pre-defined dietary patterns and assumed methodological homogeneity in these definitions across studies. In spite of this, there was a relative consistency in the type of foods included under "Western" or "Prudent" patterns, but such pre-definitions prevented us from further exploring the role of specific foods, such as meat. Definitions of components of specific dietary patterns can differ greatly between studies and populations, but foods associated with a high risk of non-communicable diseases tend to naturally correlate between one another. The results of the meta-analyses were fairly consistent in showing that regardless of the components defining a Western dietary pattern, it was related to a higher risk of CRC. The methods to collect the dietary intake that was used to derive dietary patterns also differed between studies. Although food frequency questionnaires were the most commonly used tool, they differed in the number of items considered for analysis and the time period the questionnaire collected data, for example one, six or twelve months previous to completing the questionnaire. These may be problematic when combining data to provide on overall effect estimate, as dietary patterns may be manipulated by differing habits across geographical populations.

We found evidence of heterogeneity shown across studies, regardless of the outcomes studied. High percentage of heterogeneity in the meta-analyses can be explained by a number of factors, including differences in the sample population for each study such as age and sex, whether these samples represented the general population and the variation in severity of disease. Different adjustments in the models might also have a role in the lack of associations observed with some of the specific cancer sites studies. Although all studies took in account confounding variables, some used a more thorough approach to control for potential confounders, including family history of CRC and having first-degree relatives with CRC. Epidemiological studies are also limited by the possibility of unknown confounders blurring associations.

PCA is a popular statistical tool to explore associations between several foods and risk of diseases. In spite of its increasing use, PCAs are not exempt from limitations. During the PCA process, there are a number of assumptions and subjective decisions made to drive dietary patterns. These decisions may impact the type and number of dietary patterns. Furthermore, the criteria to derive loading factors will also influence the dietary components of patterns. It is recommended that a factor loading of 0.3 is used to derive a dietary pattern. However, the cut-off point varied greatly between studies to allocate foods into specific patterns. Recent evidence suggests that other models than PCA can be used to derive dietary patterns and might provide a more accurate reflection on the association between diet and disease [76].

In conclusion, our findings provide evidence of a positive association between "Western" and "drinker" dietary patterns and colorectal cancer, particularly in countries from North- and South America, and a reduced risk of CRC with a prudent dietary patterns. The results of these meta-analyses lend support to the notion that well-designed lifestyle and dietary interventions could contribute to reduce the risk of CRC in the general population.

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Author contributions VGL and IB conceived the study, and VGL designed the systematic review following the PRISMA guidelines. TR designed the search strategies. VGL and VM piloted and carried out the search strategies of eligible studies. VM and VGL extracted the data independently, and discrepancies were discussed and harmonized with IB. VGL, VM, and IB agreed on the final list of eligible papers. VGL and IB discussed the statistical approach for data synthesis and analysis, and IB carried out the statistical analyses. TN, AM, and JP advised on the quality assessment of the studies, and on the interpretation of the results. VGL wrote the first and revised drafts of the manuscript, with contributions from all co-authors. All authors approved the final version of the manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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