Veettil SK, Wong TY, Loo YS, et al. Role of diet in colorectal cancer incidence: umbrella review of meta-analyses of prospective observational studies. JAMA Netw Open. 2021;4(2):e2037341. doi:10.1001/jamanetworkopen.2020.37341

eAppendix. Supplementary Methods
eTable 1. Search Strategy
eFigure. Study Flow Diagram
eTable 2. Excluded Studies
eTable 3. Descriptive Characteristics of Included Meta-analyses
eTable 4. Associations With Nonsignificant Evidence
eTable 5. Sensitivity Analyses for Associations With Class I, II, or III Evidence
eTable 6. Evidence Criteria: Difference Between and Comparison of WCRF and Present Review
eTable 7. Summary Estimates for Concordance in Meta-analyses: Red Meat Intake and Incidence of CRC
eReferences.

This supplemental material has been provided by the authors to give readers additional information about their work.
eAppendix. Supplementary Methods

We followed relevant sections of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines.

Umbrella reviews are useful tools that provide a comprehensive overview of evidence of published systematic reviews and meta-analyses on a specific topic. They can elucidate the strength of evidence and the precision of the estimates, and evaluate risk of bias of the published reports. Our objective in this study is to grade the evidence from published meta-analyses of prospective observational studies that assessed the association between dietary patterns, specific foods, food groups, beverages (including alcohol), macronutrients, and micronutrients and incidence of colorectal cancer (CRC). Definition of different dietary patterns is provided below:

**Research questions:** 1) Which dietary factors are associated with the incidence of colorectal cancer in the general adult population? 2) How credible is the evidence behind these associations in published meta-analyses of prospective observational studies?

**Eligibility criteria:** PICO characteristics: population-adults of any age; exposure-any dietary patterns, pre-specified diet quality indices, specific foods, food groups, beverages (including alcohol), macronutrients (i.e., carbohydrate, fat, protein), and micronutrients (vitamins, minerals, antioxidants, polyphenols); comparison of this study-1) exposed group to any of the aforementioned factors versus the non-exposed group and 2) high intake of any of the aforementioned diet groups versus a low intake group; and primary outcome-incidence of colorectal cancer.

Studies were included that met the following criteria: 1) meta-analysis of prospective observational studies (i.e., cohort design) among adults with multivariable-adjusted summary risk estimates and corresponding 95% confidence intervals; and 2) investigated the association of dietary factor(s) with the incidence of CRC. Studies were excluded if they were primary studies, or if no summary estimate was reported (e.g., systematic reviews without meta-analysis). We also excluded (1) meta-analyses of studies with other study designs; and (2) meta-analyses that provided insufficient or inadequate data for quantitative synthesis. We also excluded meta-analyses published in languages other than English. When more than one meta-analysis on the same research question was eligible, only one meta-analysis was selected for each exposure to avoid the inclusion of duplicate studies. In that case, the meta-analysis with the largest number of primary studies was selected. If more than one published meta-analysis on the same exposure included an equal number of studies, the one with the largest number of CRC cases was chosen. If more than one published meta-analysis fulfilled both criteria, the one with more comprehensive information on primary studies was selected.
**Search strategy:** We searched Medline, Embase and the Cochrane Library from database inception to September 2019. We also manually searched the cited references of the retrieved articles and reviews.

**Data extraction:** Data were extracted by two authors (Y.S. and T.Y.) and double-checked by a third author (S.V.). From each eligible article, we recorded the following: name of the first author, publication year, diet exposure, number of included studies, the total number of CRC cases and participants, type of comparison (e.g., high versus low), study-specific summary risk estimates (i.e., risk ratio (RR), odds ratio (OR), hazard ratio (HR), or incident rate ratio (IRR)) together with the corresponding confidence intervals, and estimates of publication bias. For each primary study included in the published meta-analysis, we noted whether relevant confounders were accounted for in adjusted summary estimates and reported. We communicated with authors to obtain data for evidence synthesis if it was not clearly reported in the published meta-analysis.

**Definition of important dietary patterns:**

| Dietary pattern          | Study                     | Exposure definition                                                                                                                                 |
|-------------------------|---------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|
| Dietary calcium         | Meng 2019[218]            | The comparison of elemental intake of dietary calcium from each study included in the meta-analysis classified as highest categories (Q3, Q4, and Q5 [up to 2057 mg/day]) and the lowest categories (Q1 and Q2 [<228 mg/day]). |
| Dietary glycemic load   | Reynolds 2019[182]        | Based on WHO Nutrition Guidance Expert Advisory Group                                                                                               |
| Dietary glycemic load   | Reynolds 2019[182]        | Based on WHO Nutrition Guidance Expert Advisory Group                                                                                               |
| Healthy diet            | Feng 2017[179]            | High intakes of vegetables, fruits, whole grains, olive oil, fish, soy, poultry, and low-fat dairy                                                                 |
| Heavy alcohol drinking  | Fedirko 2011[201]         | Consumption of ≥4 drinks/day (≥50 g/day of ethanol)                                                                                                 |
| Light alcohol drinking  | Fedirko 2011[201]         | Consumption of ≤1 drink/day (≤12.5 g/day of ethanol)                                                                                                 |
| Mediterranean diet      | Schwingshackl 2017[178]   | High consumption of plant-based foods, especially whole grain products, vegetables, fruits, nuts, and legumes with regular intake of fish and seafood. Eggs, red and processed meat as well as high-fat dairy products are consumed in low amounts |
| Moderate alcohol drinking| Fedirko 2011[201]         | Consumption of 2–3 drinks/day (12.6–49.9 g/day of ethanol)                                                                                            |
| Western diet            | Feng 2017                 | High consumption of red and/or processed meat, refined grains, sweets, high-fat dairy products, butter, potatoes and high-fat gravy, and low intake of fruits and vegetables |
| Non-vegetarian diet     | Godos 2016[181]           | Eating meat more than once per week                                                                                                                  |
| Pesco-vegetarian diet   | Godos 2016[181]           | Consumption of fish more than once per month in those following vegetarian diet                                                                      |
| Semi-vegetarian diet    | Godos 2016[181]           | Low consumption of meat (more than once per month but less than once per week)                                                                        |
| Suppemental calcium     | Heine-Bröring 2015[216]   | Use of calcium in supplement form. Mean level of intake:145 mg/day to 1,130 mg/day                                                                     |
| Unhealthy diet          | Grosso 2017[180]          | High intakes of red and processed meat, sugary drinks and salty snacks, starchy foods, and refined carbohydrates                                         |
| Vegetarian diet         | Godos 2016[181]           | Eating meat less than once per month                                                                                                                  |
### eTable 1. Search Strategy

| No. | Search term                                                                 | Embase 1974 | CDSR  | MEDLINE  |
|-----|----------------------------------------------------------------------------|-------------|-------|----------|
| 1   | exp Systematic Review/*CDSR: systematic review.mp.                         | 219179      | 7127  | 112213   |
| 2   | systematic review.ti,ab.                                                  | 170483      | 794   | 130108   |
| 3   | exp Meta Analysis/*CDSR: meta analysis.mp.                                | 171779      | 8406  | 104669   |
| 4   | meta-analysis.ti,ab.                                                     | 174319      | 1843  | 127415   |
| 5   | exp Colorectal Neoplasms/*CDSR: Colorectal Neoplasms.mp.                 | 27509       | 60    | 192528   |
| 6   | exp Colonic Neoplasms/*CDSR: Colonic Neoplasms.mp.                       | 304714      | 12    | 72783    |
| 7   | exp Rectal Neoplasms/*CDSR: Rectal Neoplasms.mp.                         | 240553      | 27    | 45779    |
| 8   | exp Adenomatous Polyps/*CDSR: Adenomatous Polyps.mp.                     | 8868        | 19    | 7822     |
| 9   | exp Adenocarcinoma/*CDSR: Adenocarcinoma.mp.                             | 208037      | 286   | 365492   |
| 10  | exp Intestinal Polyps/*CDSR: Intestinal Polyps.mp.                       | 30058       | 3     | 14332    |
| 11  | exp Colonic Polyps/*CDSR: Colonic Polyps.mp.                              | 19381       | 9     | 8126     |
| 12  | colorectal cancer$.tw.                                                   | 143433      | 280   | 92873    |
| 13  | colorectal tumo$.tw.                                                     | 9331        | 18    | 6648     |
| 14  | colorectal neoplas$.tw.                                                  | 5617        | 64    | 3574     |
| 15  | colon cancer$.tw.                                                        | 65894       | 103   | 44261    |
| 16  | colon tumo$.tw.                                                          | 6699        | 11    | 4907     |
| 17  | colon neoplas$.tw.                                                       | 599         | 5     | 380      |
| 18  | colonic cancer$.tw.                                                      | 3567        | 10    | 2808     |
| 19  | colonic tumo$.tw.                                                        | 2450        | 1     | 1759     |
| 20  | colonic neoplas$.tw.                                                     | 1679        | 19    | 1183     |
| 21  | rectal cancer$.tw.                                                       | 34633       | 70    | 21678    |
| 22  | rectal tumo$.tw.                                                         | 3399        | 11    | 2160     |
| 23  | rectal neoplas$.tw.                                                      | 560         | 31    | 370      |
| 24  | rectum cancer$.tw.                                                       | 929         | 18    | 520      |
| 25  | rectum tumo$.tw.                                                         | 171         | 11    | 92       |
| 26  | rectum neoplas$.tw.                                                      | 23          | 0     | 13       |
| 27  | polyps$.tw.                                                              | 39414       | 110   | 268025   |
| 28  | adenoma$.tw.                                                             | 108700      | 129   | 80009    |
| 29  | adenomatous$.tw.                                                         | 19048       | 40    | 13997    |
| 30  | exp Adenoma/*CDSR: Adenoma.mp.                                           | 110273      | 79    | 98362    |
| 31  | or/1-4                                                                   | 377143      | 9104  | 236427   |
| 32  | or/5-30                                                                  | 667370      | 689   | 898844   |
| 33  | 31 and 32                                                                | 12909       | 663   | 8899     |
| 34  | Limit “33” to humans                                                     | 1661        | (exclude MEDLINE journals) | 7954     |
Screening Records after duplicates removed (n = 9954)

Records identified through database searching
MEDLINE = 7954
Embase = 1661
CDSR = 663

Records screened (n = 9954)

Records excluded based on title and abstract (n = 9732)

Full-text articles assessed for eligibility (n = 222)

Full-text articles excluded (n = 177)
23 Not a relevant study design
38 Outcome of interest on incidence of colorectal cancer not reported
69 Not the largest systematic review or meta-analysis investigating outcome of interest
20 Exposure of interest not reported
21 No meta-analysis
4 Non-English publication
2 Insufficient data reported

Studies included in quantitative synthesis (n = 45 meta-analyses)
### eTable 2. Excluded Studies

| Reason                                      | References |
|---------------------------------------------|------------|
| Outcome of interest on incidence of colorectal cancer not reported | (1)(2)(3)(4)(5)(6)(7)(8)(9)(10)(11)(12)(13)(14)(15)(16)(17)(18)(19)(20)(21)(22)(23)(24)(25)(26)(27)(28)(29)(30)(31)(32)(33)(34)(35)(36)(37)(38) |
| Not a relevant study design                 | (39)(40)(41)(42)(43)(44)(45)(46)(47)(48)(49)(50)(51)(52)(53)(54)(55)(56)(57)(58)(59)(60)(61) |
| No meta-analysis                            | (62)(63)(64)(65)(66)(67)(68)(69)(70)(71)(72)(73)(74)(75)(76)(77)(78)(79)(80)(81)(82) |
| Exposure of interest not reported           | (83)(84)(85)(86)(87)(88)(89)(90)(91)(92)(93)(94)(95)(96)(97)(98)(99)(100)(101)(102) |
| Non-English publication                     | (103)(104)(105)(106) |
| Not the largest systematic review or meta-analysis investigating outcome of interest | (107)(108)(109)(110)(111)(112)(113)(114)(115)(116)(117)(118)(119)(120)(121)(122)(123)(124)(125)(126)(127)(128)(129)(130)(131)(132)(133)(134)(135)(136)(137)(138)(139)(140)(141)(142)(143)(144)(145)(146)(147)(148)(149)(150)(151)(152)(153)(154)(155)(156)(157)(158)(159)(160)(161)(162)(163)(164)(165)(166)(167)(168)(169)(170)(171)(172)(173)(174)(175) |
| Insufficient data reported                  | (176)(177) |
### eTable 3. Descriptive Characteristics of Included Meta-analyses

| Exposure | Author; publication year | No. of primary studies | No. of participant cases | No. of cases | Duration of follow-up (range in years; mean in years) | Adjustment for confounding variables |
|----------|--------------------------|------------------------|--------------------------|--------------|--------------------------------------------------------|-------------------------------------|
| Dietary behaviours or diet quality indices |
| Adherence to Mediterranean diet | Schwingshackl 2017(178) | 6 | 1410030 | 1610 | 5 - 26; 15.5 | Age, sex, race/ethnicity, BMI, physical activity, educational level, socioeconomic status, smoking status, alcohol intake, family history of CRC, use of aspirin or other NSAIDs, colonoscopy, history of polyps, multivitamin use, energy intake, menopausal status, HRT use |
| Adherence to healthy diet | Feng 2017(179) | 15 | 1182930 | 1153 | 1.7 - 14; 8.5 | Age, sex, race/ethnicity, educational level, occupation, diabetes, BMI, smoking status, alcohol intake, physical activity, colorectal adenoma history, extent of colon resection, family history of CRC, energy intake, use of aspirin, use of HRT, multivitamin use, endoscopy |
| Adherence to unhealthy diet | Grosso 2017(180) | 7 | 979243 | 9104 | 5 - 14; 9.5 | Age, sex, race/ethnicity, BMI, energy intake, diabetes, educational level, smoking status, alcohol intake, occupation, physical activity, family history of CRC, use of aspirin or other NSAIDs, use of HRT |
| Adherence to Western diet | Feng 2017(179) | 15 | 1182930 | 1153 | 1.7 - 14; 8.5 | Age, sex, race/ethnicity, BMI, diabetes, smoking status, colorectal adenoma history, extent of colon resection, alcohol intake, educational level, occupation, physical activity, family history of CRC, energy intake, use of aspirin, menopausal status, use of HRT, multivitamin use, endoscopy |
| Adherence to alcohol drinking | Feng 2017(179) | 9 | 718248 | 3965 | 5 - 16; 9.7 | Age, sex, race/ethnicity, BMI, family history of CRC, educational level, smoking status, energy intake, physical activity, meat intake (red or processed meat), consumption of vegetables, fruit intake, use of aspirin, multivitamin use including dietary folate, total milk intake; intakes of fibre, fat, calcium |
| Vegetarian diet | Godos 2016(181) | 3 | 149516 | 1506 | 7.3 - 20.3; 14.2 | Age, sex, race/ethnicity, BMI, educational level, smoking status, alcohol intake, physical activity, family history of CRC, history of peptic ulcer, history of inflammatory bowel disease, treatment for diabetes mellitus within the past year, aspirin use, statin therapy, prior colonoscopy or flexible sigmoidoscopy, supplemental calcium consumption, supplemental vitamin D, energy intake, use of HRT, fibre intake |
| Pesco-vegetarian diet | Godos 2016(181) | 3 | 149516 | 1506 | 7.3 - 20.3; 14.2 | Age, sex, race/ethnicity, BMI, educational level, smoking status, alcohol intake, physical activity, family history of CRC, history of peptic ulcer, history of inflammatory bowel disease, treatment for diabetes mellitus within the past year, aspirin use, statin therapy, |
prior colonoscopy or flexible sigmoidoscopy, supplemental calcium consumption, supplemental vitamin D, energy intake, use of HRT, fibre intake

| Food groups or foods | Dietary glycaemic index | Dietary glycaemic load | Eating frequency (3 vs <3 daily meals) | Eating frequency (4 vs <3 daily meals) | Eating frequency (≥5 vs <3 daily meals) |
|---------------------|-------------------------|-----------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Semi-vegetarian diet | Godos 2016<sup>(181)</sup> | 3                     | 580175                                | 4062                                  | 5 - 20.3; 10.9                        |
|                     |                         |                       | Age, sex, race/ethnicity, total energy intake, smoking status, alcohol intake, BMI, physical activity, educational level, family history of CRC, history of peptic ulcer, history of inflammatory bowel disease, treatment for diabetes mellitus within the past year, aspirin use, statin therapy, prior colonoscopy or flexible sigmoidoscopy, supplemental calcium consumption, supplemental vitamin D, HRT use, intake of fibre |
| Dietary glycaemic index | Reynolds 2019<sup>(182)</sup> | 10                    | 941652                                | 1121                                  | 6.9 - 15.7; 11.2                      |
|                     |                         |                       | Age, sex, race/ethnicity, BMI, educational level, alcohol consumption, smoking status, BMI, use of NSAIDs, history of diabetes, colorectal screening, family history of any cancer, physical activity, energy intake, menopausal status, HRT use, multivitamin use, waist:hip ratio, calcium |
| Dietary glycaemic load | Reynolds 2019<sup>(182)</sup> | 12                    | 1181780                               | 1421                                  | 6.9 - 16.5; 11.4                      |
|                     |                         |                       | Age, sex, race/ethnicity, educational level, alcohol consumption, smoking status, BMI, history of diabetes, family history of any cancer, history of colorectal polyp, physical activity, colorectal screening, menopausal status, hormone therapy (OC or HRT), parity, energy intake, use of NSAIDs, multivitamin use including folic acid, waist:hip ratio, calcium, red meat |
| Eating frequency (3 vs <3 daily meals) | Liu 2014<sup>(183)</sup> | 2                     | 77641                                 | 550                                   | 5.8 - 10; 7.9                        |
|                     |                         |                       | Age, sex, race/ethnicity, educational level, BMI, physical activity, smoking status, energy intake, calcium intake, vitamin D intake, alcohol intake, fruit intake, vegetable intake, red/processed meat intake, use of aspirin or other NSAIDs, family history of CRC, history of sigmoidoscopy/colonoscopy, total fat |
| Eating frequency (4 vs <3 daily meals) | Liu 2014<sup>(183)</sup> | 3                     | 112609                                | 1133                                  | 5.8 - 14; 9.9                        |
|                     |                         |                       | Age, sex, race/ethnicity, educational level, BMI, physical activity, smoking status, energy intake, calcium intake, alcohol intake, fruit intake, vegetable intake, meat intake (red or processed meat), use of aspirin or other NSAIDs, family history of CRC, history of sigmoidoscopy or colonoscopy, total fat, use of supplements containing antioxidants, vitamin intake (dietary folate, vitamin D), dietary approaches to stop hypertension (DASH) score |
| Eating frequency (≥5 vs <3 daily meals) | Liu 2014<sup>(183)</sup> | 2                     | 77641                                 | 550                                   | 5.8 - 10; 7.9                        |
|                     |                         |                       | Age, sex, race/ethnicity, educational level, BMI, physical activity, smoking status, energy intake, calcium intake, vitamin D intake, alcohol intake, fruit intake, vegetable intake, meat intake (red or processed meat), use of aspirin or other NSAIDs, family history of CRC, history of sigmoidoscopy/colonoscopy, total fat |
| Food Type     | Reference          | N  | Year | Study ID | Ages | Age-adjusted HR (95% CI) |
|--------------|--------------------|----|------|----------|------|--------------------------|
| Red meat     | Schwingshackl 2018 | 21 | 2018 | 2154027  | 6    | 4.8 - 32; 11.3           |
| Processed    | Schwingshackl 2018 | 15 | 2018 | 1910983  | 6    | 4.8 - 20; 10.2           |
| Beef         | Carr 2016          | 4  | 2016 | 654521   | 6    | 4.8 - 13.4; 10.1         |
| Pork         | Carr 2016          | 4  | 2016 | 654521   | 6    | 4.8 - 13.4; 10.1         |
| Poultry      | Carr 2016          | 13 | 2016 | 1492358  | 6    | 4.8 - 32; 11.3           |
| Fish         | Wu 2012            | 18 | 2012 | 1083264  | 6    | 4.8 - 24; 11.5           |

Age, sex, race/ethnicity, energy intake, educational level, BMI, waist circumference, family history of CRC, history of colorectal polyps, diabetes, smoking status, alcohol intake, physical activity, screening and examinations, multivitamin use (vitamin B6, folate, vitamin D), use of aspirin or other NSAIDs, use of hormone therapy (OC or HRT), menopausal status, fruits, vegetables, grain foods including cereal, fibre intake, dietary calcium, dietary fat intake, tea consumption, intake of dried and salted fish.
| Group                | Study Year | Study ID | Study Size | Age Range | Variables                                                                                           |
|----------------------|------------|----------|------------|-----------|-----------------------------------------------------------------------------------------------------|
| Fruits and vegetables| Aune 2011  | 1522363  | 11543      | 4.3 - 16; 9.5 | Age, sex, race/ethnicity, family history of CRC, history of colorectal polyps, menopausal status, HRT use, energy intake, BMI, physical activity, smoking status, alcohol consumption, meat intake (red and processed meat), fish intake, dietary fibre from cereal sources, educational level, dietary calcium, aspirin use, multivitamin use (including folate, vitamin D), consumption of dairy products, sigmoidoscopy |
| Fruits               | Schwingshackl 2018 | 1924385  | 19114      | 5 - 26; 11 | Age, sex, race/ethnicity, diabetes, BMI, smoking status, alcohol intake, educational level, physical activity, energy intake, family history of CRC, multivitamin use (including folate, vitamin D), use of aspirin or other NSAIDs, intake of grains and cereal, meat intake including red and processed meat, calcium, screening and examinations, history of polyps or adenoma, menopausal status, HRT use, vegetable intake, intake of dairy products, fish intake, year of follow-up |
| Vegetables           | Schwingshackl 2018 | 1924385  | 19114      | 5 - 26; 11 | Age, sex, race/ethnicity, diabetes, BMI, smoking status, alcohol intake, educational level, physical activity, energy intake, family history of CRC, multivitamin use (including folate, vitamin D), use of aspirin or other NSAIDs, intake of grains and cereal, meat intake including red and processed meat, calcium, screening and examinations, history of polyps or adenoma, menopausal status, HRT use, vegetable intake, intake of dairy products, fish intake, year of follow-up |
| Cruciferous vegetables| Wu 2013     | 1117353  | 8021       | 4.3 - 20; 9 | Age, race/ethnicity, family history of CRC, history of colorectal polyp, smoking status, BMI, physical activity, use of aspirin or other NSAIDs, multivitamin use (including folate, vitamin D), menopausal status, HRT use, energy intake, alcohol consumption, red meat, calcium, educational level, CRC screening, intake of fruits, consumption of grains |
| Broccoli             | Wu 2013     | 278338   | 2807       | 5 - 8.5; 6.9 | Age, race/ethnicity, family history of CRC, history of colorectal polyp, BMI, smoking status, physical activity, use of aspirin or other NSAIDs, multivitamin use (including folate, vitamin D), HRT use, energy intake, alcohol consumption, red meat, calcium, intake of fruits, grain intake, educational level |
| Allium vegetables    | Zhu 2014    | 552180   | 5458       | 3.3 - 24; 14 | Age, sex, energy intake, occupation, income, history of colorectal polyps, diabetes, BMI, physical activity, alcohol intake, smoking status, use of aspirin or other NSAIDs, HRT use, intake of calcium, fruits, vegetables, meat intake (including red or processed meat), family history of CRC or intestinal cancers, educational level, history of chronic intestinal disease or cholecystectomy, screening and examinations, fibre intake, multivitamin use (including folate, vitamin C, vitamin D) |
| Garlic               | Chiavarini 2016 | 330731   | 4141       | 5 - 24; 12.3 | Age, sex, BMI, smoking status, family history, endoscopy, use of aspirin or other NSAIDs, physical activity, HRT use, meat intake (red or processed meat), alcohol consumption, calcium, energy intake, consumption of fruits, vegetable intake, previous polyps, vitamin intake (including folate, vitamin D) |
| Food Group | Study Reference | N | Age, Sex Distribution | Smoking Status | BMI | Alcohol Intake | Family History | Physical Activity | Energy Intake | Other Relevant Factors |
|------------|-----------------|---|-----------------------|----------------|-----|---------------|---------------|-------------------|---------------|-----------------------|
| Onion      | Turati 2014     | 2 | 4 - 10; 7             |                |     |               |               |                   | 1321          | Age, educational level, BMI, smoking status, alcohol intake, beta-carotene; history of cholecystectomy, chronic intestinal disease, colorectal polyps; family history of CRC, physical activity, energy intake, red meat, calcium, fibre, multivitamin use including vitamin C, aspirin use, sigmoidoscopy, HRT use |
| Legumes    | Zhu 2015        | 13| 5 - 16; 8.9           |                |     |               |               |                   | 1782607       | Age, sex, BMI, energy intake, history of colorectal polyps, physical activity, family history of CRC, smoking status, alcohol consumption, use of aspirin or other NSAIDs, sigmoidoscopy, menopausal status, HRT use, multivitamin use (including folate, vitamin D), meat intake (red or processed meat, pork), educational level; intakes of fruits, grains, calcium, dairy products, vegetables, fish, fibre; coffee intake, income, diabetes |
| Nuts       | Schwingshackl 2018 | 6 | 4.8 - 30; 13.1        |                |     |               |               |                   | 1152672       | Age, sex, BMI, alcohol intake, family history of CRC, physical activity, aspirin use, history of colorectal polyps, smoking status, energy intake, multivitamin use, fruit intake, intake of dietary fibre, HRT use, screening and examinations, history of ulcerative colitis, cholesterol and triglyceride |
| Soy products | Lu 2017        | 5 | 8 - 13; 10            |                |     |               |               |                   | 281425        | Age, sex, race/ethnicity, educational level, household income, physical activity, BMI, menopausal status, HRT use, family history of CRC, energy intake; intakes of fruits, vegetables, non-soy calcium, non-soy fibre; vitamin use (non-soy folic acid, vitamin D), dairy products, meat intake including red meat, fish intake, smoking status, alcohol consumption, diabetes, coffee intake |
| Whole grains | Schwingshackl 2018 | 9 | 5 - 26; 14.1          |                |     |               |               |                   | 970927        | Age, sex, BMI, smoking status, educational level, alcohol consumption, fibres from foods other than whole-grain bread, calcium, energy intake, HRT use, family history of CRC, physical activity, aspirin use, colonoscopy, history of polyps, multivitamin use including folate; intakes of saturated fats, fruits, vegetables; meat intake (red or processed meat) |
| Refined grains | Schwingshackl 2018 | 2 | 14 - 14.8; 14.4       |                |     |               |               |                   | 72431         | Age, race/ethnicity, BMI, physical activity, smoking status, educational level, energy intake; intakes of saturated fat, calcium, red meat, fruits, vegetables; family history of CRC, endoscopy, aspirin use |
| Eggs       | Schwingshackl 2018 | 3 | 7.4 - 32; 18.8        |                |     |               |               |                   | 94181         | Age, sex, BMI, educational level, occupation, smoking status, geographic region, energy intake; intakes of vegetables, fruits, cereals; tea consumption, use of NSAIDs, fibre intake, alcohol consumption |
| Dairy products | Schwingshackl 2018 | 17 | 3.3 - 26; 11.7       |                |     |               |               |                   | 1629366       | Age, sex, race/ethnicity, occupation, geographical area, diabetes at baseline, smoking status, BMI, alcohol intake, educational level, physical activity, family history of CRC, energy intake, use of aspirin or other NSAIDs, colonoscopy, history of polyps, multivitamin use (including vitamin B6, folate, vitamin D), history of gallbladder surgery, intake of fat, dietary fibre, meat intake (red or processed meat), intake of fruits, vegetable intake, tea consumption, menopausal status, use of hormone therapy (OC or HRT) |
| Cheese     | Aune 2012       | 7 | 3.3 - 19.6; 11.2      |                |     |               |               |                   | 234759        | Age, sex, BMI, occupation, smoking status, geographical area, energy intake, family history of CRC, fat intake, dietary fibre, gallbladder surgery, alcohol intake, physical activity, educational level, red meat, history of colon polyps, multivitamin use (including vitamin B6, folate), HRT use, menopausal status, diabetes, aspirin use, intake of fruits, vegetable intake |
| Beverage               | Study Year | Study ID | n   | Mean Age | Characteristics                                                                 |
|------------------------|------------|----------|------|----------|---------------------------------------------------------------------------------|
| Yogurt                 | Zhang 2019 | 698366   | 5    | 3.3 - 12; 7.7 | Age, sex, family history of CRC or other cancers, previous polyp, screening, smoking status, alcohol intake, aspirin use, physical activity, BMI, meat intake (including red or processed meat), fat intake, dietary fibre, gallbladder surgery, energy intake, educational level, menopausal status, hormone therapy (OC or HRT), dietary calcium, simple sugars, history of diabetes, vegetables, fruits, nuts and legumes, cereals, fish |
| Beverages              |            |          |      |          |                                                                                 |
| Tea                    | Chen 2017  | 1208316  | 15   | 1 - 15; 8.6 | Age, sex, race/ethnicity, family history of CRC, BMI, intake of fibre, coffee intake, alcohol intake, diabetes, educational level, smoking status, physical activity, intake of fruits, vegetable intake, calcium, energy intake, meat intake (including red meat and pork), radiation exposure, use of aspirin or other NSAIDs, fat intake, vitamin supplement intake, menopausal status, HRT use, household income, history of colorectal polyps and chronic ulcerative colitis, occupation, colorectal screening |
| Green tea              | Wang 2012  | 352275   | 5    | 6 - 15; 9.2 | Age, sex, family history of CRC, smoking status, alcohol intake, BMI, meat consumption including red meat, intake of black tea, intake of fruits, vegetable intake, coffee consumption, radiation exposure, menopausal status, use of NSAIDs, vitamin supplement use, history of colorectal polyps and chronic ulcerative colitis, energy intake |
| Black tea              | Sun 2006   | 274975   | 6    | 8 - 20; 13 | Age, sex, race/ethnicity, educational level, family history of CRC, history of sigmoidoscopy or colonoscopy, BMI, smoking status, physical activity, aspirin use, vitamin supplement intake, alcohol consumption, red meat consumption, total energy intake, menopausal status, HRT use; intakes of fat, fibre, calcium; fruit intake, vegetable intake, waist/hip circumference ratio |
| Coffee                 | Gan 2017   | 2046575  | 19   | 4.5 - 18; 10.1 | Age, sex, race/ethnicity, BMI, smoking status, alcohol intake, educational level, serum cholesterol, physical activity, calcium intake, tea consumption, energy intake, family history of CRC, use of aspirin or other NSAIDs, colorectal screening, vitamin intake (including vitamin B6, folic acid, vitamin C, vitamin D), fat intake, fibre intake, menopausal status, HRT use, diabetes, fruits, vegetables, meat intake including red or processed meat and pork, number of pregnancies and deliveries, age at menarche, age at first delivery, intake of dairy products |
| Non-fermented milk     | Ralston 2014 | 892569  | 14   | 5 - 24; 11.3 | Age, sex, race/ethnicity, occupation, smoking status, geographical area, BMI, total energy intake, family history of CRC, previous intestinal polyp, screening, use of aspirin or other NSAIDs, physical activity, saturated fat, dietary fibre intake, alcohol intake, red meat consumption, educational level, history of diabetes, fruits, vegetables, multivitamin use |
| Food                  | Source               | N    | Median Age or Range | OES or N  | Variables                                                                 |
|----------------------|----------------------|------|---------------------|-----------|---------------------------------------------------------------------------|
| Fermented milk       | Ralston 2014          | 7    | 328750              | 1876      | Age, sex, occupation, smoking status, geographical area, BMI, total energy intake, family history of CRC, previous intestinal polyp, screening, aspirin use, physical activity, saturated fat, dietary fibre intake, alcohol intake, red meat consumption, educational level, history of diabetes, fruits, vegetables, multivitamin use (including folic acid, vitamin C, vitamin D), menopausal status, HRT use |
| Alcohol (Moderate)    | Fedirko 2011          | 22   | 2798092             | 1912      | Age, sex, race/ethnicity, smoking status, BMI, coffee intake, educational level, cholesterol, history of gall bladder surgery, energy intake; intakes of fats, protein, dietary fibre; family history of CRC, physical activity, history of polyps, multivitamin use (including folate and vitamin D), meat intake (including poultry/non-poultry meat, processed meat), seafood intake, calcium, occupation, intake of vegetables, fruit intake, diabetes, menopausal status, use of hormone therapy (OC or HRT), socioeconomic status, aspirin use, screening and examinations |
| Alcohol (Heavy)       | Fedirko 2011          | 7    | 738539              | 5078      | Age, sex, family history of CRC, BMI, smoking status, physical activity, educational level, sedentary work, consumption of vegetables, meat consumption (including red or processed meat), fruit intake, energy intake, aspirin use, screening and examinations, intake of calcium, multivitamins (including folate, vitamin D) |
| Beer                 | Zhang 2015            | 7    | 805177              | 5149      | Age, sex, race/ethnicity, family history of CRC, smoking status, coffee intake, total serum cholesterol, educational level, BMI, non-contraceptive oestrogen use, physical activity, history of colorectal polyps, energy intake, intake of fats, dietary fibre, calcium, other types of alcohol |
| Wine                 | Xu 2019               | 9    | 973286              | 7511      | Age, sex, race/ethnicity, smoking status, coffee intake, total serum cholesterol, educational level, BMI, non-contraceptive oestrogen use, history of colorectal polyps, physical activity, intake of other types of alcohol, meat consumption including poultry, seafood consumption, multivitamin use, energy intake, family history of CRC, intake of fat, dietary fibre, calcium, fruit intake, vegetable intake, diabetes |
| Wine (Light to moderate) | Xu 2019              | 4    | 676331              | 4559      | Age, sex, race/ethnicity, smoking status, BMI, intake of other types of alcohol, physical activity, educational level, energy intake, family history of CRC, intake of fat, dietary fibre, calcium, fruit intake, vegetable intake, meat intake, multivitamin use, diabetes |
| Wine (Heavy) | Xu 2019<sup>(203)</sup> | 5 | 686749 | 4670 | 5.3 - 14.7; 9.9 | Age, sex, race/ethnicity, smoking status, BMI, intake of other types of alcohol, educational level, meat consumption including poultry, seafood consumption, multivitamin use, history of colonic polyps, physical activity, energy intake, family history of CRC, intake of fat, dietary fibre, calcium, fruit intake, vegetable intake, diabetes |
| --- | --- | --- | --- | --- | --- | --- |
| **Macronutrients** | | | | | | |
| Total dietary fat | Liu 2011<sup>(204)</sup> | 13 | 459910 | 3635 | 3 - 32; 11.5 | Age, sex, BMI, energy intake, parity, fibre intake, smoking status, educational level, alcohol intake, physical activity, calcium intake, geographical area, occupation; consumption of fruits, vegetables, cereals; family history of CRC, history of colorectal polyps, hormone therapy, diabetes, vitamin use (including vitamin A, vitamin E) |
| Saturated fatty acids | Liu 2011<sup>(204)</sup> | 12 | 451956 | 3182 | 3 - 32; 9.9 | Age, sex, total energy intake, parity, fibre intake, BMI, smoking status, education, alcohol consumption, physical activity, calcium intake, geographical area, occupation; intakes of fruits, vegetables, cereals; family history of CRC, history of colorectal polyps, hormone therapy, diabetes, vitamin use (vitamin A, vitamin E) |
| Monounsaturated fatty acids | Liu 2011<sup>(204)</sup> | 11 | 399687 | 3048 | 3 - 32; 11.9 | Age, sex, total energy intake, parity, fibre intake, BMI, smoking status, education, alcohol consumption, physical activity, calcium intake, geographical area, occupation; intakes of fruits, vegetables, cereals; family history of CRC, history of colorectal polyps, hormone therapy, diabetes, vitamin use (vitamin A, vitamin E) |
| Polyunsaturated fatty acids | Kim 2018<sup>(205)</sup> | 14 | 933712 | 1003 | 3.3 - 32; 13 | Age, sex, race/ethnicity, dietary fibre intake, Dutch Healthy Diet index, energy intake, BMI, educational level, family history of CRC, screening and examinations, use of aspirin or other NSAIDs, intake of alcohol, smoking status, physical activity, hormone therapy, calcium, multivitamin use (including folate, vitamin D), fruit intake, vegetable intake, meat intake (red or processed meat), history of polyps, cereal intake, cardiovascular disease, memory loss, use of cholesterol-lowering drugs, omega-6 (linoleic + arachidonic) intake, menopausal status, past history of or medication use for diabetes, intake of low-fat dairy products, geographical area, occupation |
| Total n-3 polyunsaturated fatty acids | Chen 2015<sup>(206)</sup> | 8 | 579427 | 6807 | 4.8 - 22; 10.8 | Age, sex, parity, total energy intake, BMI, smoking status, alcohol intake, educational level, physical activity, calcium intake, meat intake (red or processed meat), dietary fibre, intake of fat (saturated fat, monounsaturated fat, n-6 PUFA), diabetes, family history of CRC, menopausal status, use of hormone therapy, multivitamin use (including vitamin A, folate, vitamin C, vitamin D, vitamin E), use of aspirin or other NSAIDs, screening and examinations, low-fat dairy products, fruits, vegetables |

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| Dietary Factor                          | Study Reference       | N  | Median Age (Range) | Covariates                                                                 | Notes                                                                 |
|----------------------------------------|-----------------------|----|--------------------|----------------------------------------------------------------------------|----------------------------------------------------------------------|
| Marine n-3 polyunsaturated fatty acids | Chen 2015[206]        | 10 | 666713             | Age, sex, race/ethnicity, BMI, educational level, alcohol intake, energy intake, dietary fibre, calcium, fat intake (saturated fat, monounsaturated fat, n-6 PUFA), family history of CRC, history of colorectal polyps, physical activity, smoking status, hormone therapy, multivitamin use (including folate, vitamin C, vitamin D), diabetes, use of aspirin or other NSAIDs, menopausal status, low-fat dairy products, fruits, vegetables, cardiovascular disease, memory loss, use of cholesterol-lowering drugs, screening and examinations, meat intake (red or processed meat) |                                                                 |
| Cholesterol                            | Liu 2011[204]         | 7  | 261260             | Age, sex, total energy intake, parity, educational level, BMI, smoking status, alcohol consumption, physical activity, calcium intake, family history of CRC, history of colorectal polyps, hormone therapy, occupation, geographical area; consumption of vegetables, fruits, cereals; vitamin intake (vitamin A, vitamin E) |                                                                 |
| Carbohydrate                           | Aune 2012[207]        | 11 | 806647             | Age, race/ethnicity, educational level, income, BMI, physical activity, family history of CRC, hormone therapy (OC or HRT), total energy intake, colorectal polyps, smoking status, use of aspirin or other NSAIDs, multivitamin use (including folate, vitamin D), alcohol intake, meat intake (red or processed meat), calcium, dietary fibre, diabetes, colorectal screening, magnesium, total fat, parity |                                                                 |
| Sucrose                                | Aune 2012[207]        | 5  | 831687             | Age, race/ethnicity, BMI, family history of CRC or other cancers, smoking status, educational level, physical activity, total energy intake, alcohol intake, colorectal polyps, use of aspirin or other NSAIDs, multivitamin use (including folate, vitamin D), hormone therapy (OC or HRT), meat intake (red or processed meat), calcium, dietary fibre, diabetes, prior endoscopy screening, total fat |                                                                 |
| Fructose                               | Aune 2012[207]        | 4  | 640683             | Age, race/ethnicity, BMI, family history of CRC or other cancers, smoking status, educational level, physical activity, total energy intake, alcohol intake, colorectal polyps, use of aspirin or other NSAIDs, multivitamin use (including folate, vitamin D), diabetes, prior endoscopy screening, use of aspirin or other NSAIDs, calcium, meat intake (red or processed meat), hormone therapy (OC or HRT), total fibre, total fat |                                                                 |
| Dietary protein                        | Lai 2017[208]         | 3  | 207068             | Age, sex, energy intake, dietary fibre intake, supplement intake, smoking status, BMI, alcohol intake, educational level, physical activity, calcium intake (except for milk protein and milk products) |                                                                 |
| Total dietary fibre                    | Reynolds 2019         | 21 | 2259486            | Age, sex, race/ethnicity, physical activity, smoking status, meat intake (red and processed meat), total energy intake, calcium, BMI, educational level, alcohol intake, family history, colorectal polyp, use of multivitamin (including folate, vitamin C, vitamin D), aspirin or other anti-inflammatory use, hormone therapy (OC or HRT), menopause, colonoscopy, dietary assessment, fat |                                                                 |
| Cereal fibre                           | Aune 2011[209]        | 7  | 1471756            | Age, sex, race/ethnicity, family history of CRC, history of colorectal polyps, smoking status, BMI, physical activity, use of aspirin or other NSAIDs, multivitamin use (including folate, vitamin D), meat intake (red and processed meat), menopausal status, HRT use, alcohol intake, calcium intake, energy intake, educational level, sigmoidoscopy or colonoscopy, glycaemic load, consumption of dairy products |                                                                 |

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| Nutrient Type | Source | Study Year | Participants | Follow-Up | Age and Other Covariates |
|---------------|--------|------------|--------------|-----------|--------------------------|
| Fruit fibre   | Aune 2011 | 2011       | 8            | 1514871   | 9930; 4.5 - 16; 9.3      |
|               |         |            |              |           | Age, sex, race/ethnicity, family history of CRC, history of colorectal polyps, smoking status, BMI, physical activity, use of aspirin or other NSAIDs, multivitamin use (including folate, vitamin D), alcohol intake, menopausal status, HRT use, meat intake (red or processed meat, pork), calcium intake, energy intake, education, sigmoidoscopy or colonoscopy, glycaemic load, consumption of dairy products |
| Vegetable fibre | Aune 2011 | 2011       | 8            | 1514871   | 9930; 4.5 - 16; 9.3      |
|               |         |            |              |           | Age, sex, race/ethnicity, family history of CRC, history of colorectal polyps, smoking status, BMI, physical activity, use of aspirin or other NSAIDs, multivitamin use (including folate, vitamin D), alcohol intake, menopausal status, HRT use, meat intake (red or processed meat, pork), calcium intake, energy intake, education, sigmoidoscopy or colonoscopy, glycaemic load, consumption of dairy products |
| Legume fibre  | Reynolds 2019 | 2019 | 4            | 1104339   | 5651; 5 - 12.1; 8.3      |
|               |         |            |              |           | Age, sex, physical activity, smoking status, menopause, HRT use, meat intake (red or processed meat), folate, calcium, energy intake, alcohol intake, educational level, BMI, family history, history of colon polyps, aspirin use |
| Soluble fibre | Reynolds 2019 | 2019 | 3            | 204243    | 2580; 7.6 - 11.7; 9.1   |
|               |         |            |              |           | Age, sex, energy intake, BMI, educational level, family history, colonoscopy, anti-inflammatory use, consumption of alcohol, smoking status, physical activity, HRT use, calcium, red meat, vitamin intake (folate, vitamin D) |
| Insoluble fibre | Reynolds 2019 | 2019 | 3            | 204243    | 2580; 7.6 - 11.7; 9.1   |
|               |         |            |              |           | Age, sex, energy intake, BMI, educational level, family history, colonoscopy, anti-inflammatory use, consumption of alcohol, smoking status, physical activity, HRT use, calcium, red meat, vitamin intake (folate, vitamin D) |

### Micronutrients

| Micronutrient Type | Source | Study Year | Participants | Follow-Up | Age and Other Covariates |
|--------------------|--------|------------|--------------|-----------|--------------------------|
| Flavonoids         | Bo 2016 | 2016       | 6            | 188135    | 6609; 6.1 - 28; 14.2    |
|                    |         |            |              |           | Age, race/ethnicity, BMI, occupation, geographic area, family history of CRC, history of colorectal polyps, prior sigmoidoscopy screening, physical activity, smoking status, alcohol consumption, intake of meat, intake of fruits, vegetables, intake of fibre, total fat, total energy, calcium, vitamin use (folate, vitamin C, vitamin E), aspirin use, HRT use |
| Flavonols          | Chang 2018 | 2018 | 5            | 729461    | 9720; 11 - 28; 18.9     |
|                    |         |            |              |           | Age, sex, geographic area, occupation, smoking, physical activity, education, BMI, history of CRC, history of endoscopy, alcohol consumption, total energy intake, total fat, intake of meat, fibre, calcium intake, menopausal status, hormone therapy (OC or HRT), regular aspirin use, vitamin intake (vitamin C, vitamin D, vitamin E) |
| Quercetin          | Grosso 2017 | 2017 | 2            | 117266    | 463; 10 - 28; 19        |
|                    |         |            |              |           | Age, sex, geographic area, occupation, smoking status, BMI, family history of CRC, history of colorectal polyps, prior sigmoidoscopy screening, physical activity, alcohol consumption, meat intake, total energy intake, total calcium intake, total fibre intake, aspirin use, vitamin intake, HRT use |
| Kaempferol         | Grosso 2017 | 2017 | 2            | 117266    | 472; 10 - 28; 19        |
|                    |         |            |              |           | Age, sex, geographic area, occupation, smoking status, BMI, family history of CRC, history of colorectal polyps, prior sigmoidoscopy screening, physical activity, alcohol consumption, meat intake, total energy intake, total calcium intake, total fibre intake, aspirin use, vitamin intake, HRT use |
| Phytochemicals | Authors | Year | n | OCP | Age Group | Variables Studied |
|----------------|---------|------|----|-----|-----------|-------------------|
| Myricetin      | Grosso 2017 | 2   | 117266 | 466 | 10 - 28; 19 | Age, sex, geographic area, occupation, smoking status, BMI, family history of CRC, history of colorectal polyps, prior sigmoidoscopy screening, physical activity, alcohol consumption, meat intake, total energy intake, total calcium intake, total fibre intake, aspirin use, vitamin intake, HRT use |
| Flavones       | Chang 2018 | 3   | 598744 | 7091 | 11 - 26; 17.7 | Age, sex, history of CRC, history of endoscopy, smoking status, physical activity, education, BMI, alcohol consumption, total energy, total fat, intake of meat, fibre intake, calcium intake, menopausal status, hormone therapy (OC or HRT), regular aspirin use, vitamin intake (vitamin C, vitamin D, vitamin E) |
| Flavanones     | Chang 2018 | 4   | 608609 | 7181 | 11 - 28; 20.3 | Age, sex, geographic area, occupation, history of CRC, history of endoscopy, smoking, physical activity, education, BMI, alcohol consumption, total energy, total fat, intake of meat, fibre intake, calcium intake, menopausal status, hormone therapy (OC or HRT), regular aspirin use, vitamin intake (vitamin C, vitamin D, vitamin E) |
| Flavan-3-ols   | Chang 2018 | 4   | 719596 | 9576 | 11 - 26; 16.6 | Age, sex, family history of CRC, history of CRC, history of endoscopy, smoking, physical activity, education, BMI, alcohol consumption, total energy, total fat, intake of meat, fibre intake, calcium intake, menopausal status, hormone therapy (OC or HRT), regular aspirin use, vitamin intake (vitamin C, vitamin D, vitamin E) |
| Catechin       | Grosso 2017 | 2   | 155503 | 3249 | 13 - 13.3; 13.2 | Age, occupation, BMI, family history of CRC, waist-to-hip ratio, physical activity, smoking, alcohol intake, total fruit intake, vegetable consumption, meat intake, total energy intake |
| Flavanols      | He 2016    | 3   | 242284 | 5059 | 13.3 - 26; 18.5 | Age, BMI, family history of CRC, history of endoscopy, alcohol consumption, physical activity, smoking, fibre intake, meat intake, total energy intake, use of NSAIDs, dietary supplement (calcium, n-3 polyunsaturated fatty acids, manganum, riboflavin, vitamin C, vitamin E, folate) |
| Anthocyanins   | He 2016    | 2   | 121432 | 2574 | 16.2 - 26; 21.1 | Age, BMI, family history of CRC, history of endoscopy, alcohol consumption, physical activity, smoking, fibre intake, meat intake, total energy intake, use of NSAIDs, dietary supplement (calcium, n-3 polyunsaturated fatty acids, manganum, riboflavin, folate, vitamin C, vitamin E) |
| Anthocyanidins | Chang 2018 | 3   | 598744 | 7091 | 11 - 26; 17.7 | Age, sex, history of CRC, history of endoscopy, smoking, physical activity, education, BMI, alcohol consumption, total energy, total fat, intake of meat, fibre intake, calcium intake, menopausal status, hormone therapy (OC or HRT), regular aspirin use, vitamin intake (vitamin C, vitamin D, vitamin E) |
| Phyto-oestrogens| Jiang 2017 | 5   | 275443 | 2485 | 6.4 - 19; 10.2 | Age, sex, household income, dialect group, diabetes at baseline, smoking, BMI, alcohol intake, education, physical activity, family history of CRC, daily energy intake, menopausal status, average intakes of fruits, vegetables, meat intake, fibre intake, non-soya calcium, fats, vitamin intake (non-soya folic acid, vitamin D), use of NSAIDs, hormone therapy |
| Isoflavones    | Grosso 2017 | 5   | 292616 | 2587 | 6.4 - 19; 10.2 | Age, education, alcohol intake, smoking status, BMI, physical activity, household income, family history of CRC, history of diabetes mellitus, total energy intake, intakes of fruits, vegetables, meat, non-soya calcium, fibre, coffee intake, fats, dairy products, individual phytoestrogens, menopausal status, HRT use, vitamin intake (folic acid, vitamin D) |
| Component                  | Study                  | N  | Year   | Code   | Age, sex, race/ethnicity, education level, family history of CRC, BMI, physical activity, smoking status, alcohol consumption, energy intake, dietary factor, use of NSAIDs, menopausal status |
|----------------------------|------------------------|----|--------|--------|----------------------------------------------------------------------------------------------------------------------------------|
| Combined carotenoids       | Panic 2017(215)        | 2  | 2017   | 196383 | 2673 8.2 - 11; 9.6 Age, education level, smoking status, BMI, physical activity, family history of CRC, history of intestinal polyps, alcohol intake, total energy intake, total fat intake, meat intake, dietary fibre intake, total calcium intake, hormone therapy (HRT), use of NSAIDs, vitamin intake (folate, vitamin D) |
| Alpha-carotene             | Panic 2017(215)        | 3  | 2017   | 223334 | 2857 8 - 11; 9.1 Age, education level, smoking status, BMI, physical activity, family history of CRC, history of intestinal polyps, serum cholesterol, alcohol consumption, total energy intake, total fat intake, meat intake, dietary fibre intake, total calcium intake, HRT use, use of NSAIDs, vitamin intake (folate, vitamin D) |
| Beta-carotene              | Panic 2017(215)        | 4  | 2017   | 279666 | 3605 8 - 11; 9.5 Age, education level, smoking status, BMI, physical activity, family history of CRC, history of intestinal polyps, serum cholesterol, alcohol intake, total energy intake, meat intake, dietary fibre intake, total calcium intake, hormone therapy (HRT), use of NSAIDs, vitamin intake (folate, vitamin D) |
| Lycopene                   | Panic 2017(215)        | 3  | 2017   | 223334 | 2857 8 - 11; 9.1 Age, education level, smoking status, BMI, physical activity, family history of CRC, history of intestinal polyps, serum cholesterol, alcohol consumption, total energy intake, total fat intake, meat intake, dietary fibre intake, total calcium intake, hormone therapy (HRT), use of NSAIDs, vitamin intake (folate, vitamin D) |
| Beta-cryptoxanthin         | Panic 2017(215)        | 2  | 2017   | 196383 | 2673 8.2 - 11; 9.6 Age, education level, smoking status, BMI, physical activity, family history of CRC, history of intestinal polyps, alcohol intake, total energy intake, total fat intake, meat intake, dietary fibre intake, total calcium intake, hormone therapy (HRT), use of NSAIDs, vitamin intake (folate, vitamin D) |
| Lutein and zeaxanthin      | Panic 2017(215)        | 3  | 2017   | 223334 | 2857 8 - 11; 9.1 Age, education level, smoking status, BMI, physical activity, family history of CRC, history of intestinal polyps, serum cholesterol, alcohol consumption, total energy intake, total fat intake, meat intake, dietary fibre intake, total calcium intake, hormone therapy (HRT), use of NSAIDs, vitamin intake (folate, vitamin D) |
| Multivitamin               | Heine-Bröring 2015(216) | 7  | 2015   | 670513 | 8737 5 - 24; 12.7 Age, sex, race/ethnicity, education, family history of CRC, BMI, physical activity, smoking status, alcohol consumption, energy intake, dietary factor, use of NSAIDs, menopausal status |
| Multivitamin               | Liu 2015(217)          | 5  | 2015   | 522507 | 3584 5 - 16; 9 Age, race/ethnicity, BMI, education level, alcohol consumption, smoking status, physical activity, family history of CRC, meat intake, total energy intake, fruit intake, vegetable intake, intake of saturated fat, dietary fibre, vitamin intake (vitamin B6, folate, vitamin C, vitamin E), calcium, menopausal status, hormone therapy, aspirin use |
| Vitamin A                  | Heine-Bröring 2015(216) | 2  | 2015   | 46796  | 443 8 - 10; 9 Age, smoking status, energy intake |
| Vitamin A                  | Liu 2015(217)          | 6  | 2015   | 208536 | 1206 4.5 - 10; 7 Age, smoking status, education level, physical activity, alcohol consumption, family history of CRC, menopausal status, total energy intake, intake of meat, hormone therapy (HRT) |
| Vitamin B2                 | Liu 2015(217)          | 5  | 2015   | 392184 | 4939 5.74 - 13.3; 10 Age, educational level, BMI, household income, smoking status, alcohol intake, physical activity, family history of CRC, diabetes history, energy intake, vegetables, fruits, meat, calcium, fibre, iron, fats, menopausal status, hormone therapy (HRT), use of NSAIDs |
| Vitamin       | Reference                      | Sample Size | Study Population                                                                 |
|---------------|--------------------------------|-------------|-----------------------------------------------------------------------------------|
| Vitamin B3    | Liu 2015<sup>(217)</sup>      | 2           | Age, educational level, BMI, household income, smoking status, alcohol intake, physical activity, family history of CRC, diabetes history, energy intake, vegetables, fruits, meat, calcium, fibre, iron, fats, menopausal status, hormone therapy (HRT), use of NSAIDs |
| Vitamin B6    | Liu 2015<sup>(217)</sup>      | 11          | Age, sex, BMI, education, household income, smoking status, alcohol consumption, physical activity, family history of CRC, diabetes history, total intake of energy, intake of vegetables, fruits, meat, fats, iron, calcium, use of aspirin or other NSAIDs, vitamin use (vitamin B, vitamin E), hormone therapy (HRT), menopausal status |
| Folic acid    | Liu 2015<sup>(217)</sup>      | 19          | Age, sex, BMI, education, household income, smoking status, alcohol consumption, physical activity, family history of CRC, diabetes history, past medical history of colonoscopy, total intake of energy, intake of vegetables, fibre, fruits, meat, fats, iron, calcium, use of aspirin or other NSAIDs, vitamin use (vitamin B, vitamin C, vitamin E), hormone therapy (HRT), menopausal status |
| Vitamin B12   | Liu 2015<sup>(217)</sup>      | 5           | Age, BMI, race/ethnicity, past medical history of colonoscopy, smoking status, physical activity, alcohol consumption, diabetes history, energy intake, intake of vegetables, fruits, meat, calcium, use of NSAIDs, vitamin use, hormone therapy (HRT), menopausal status |
| Vitamin C     | Heine-Bröring 2015<sup>(216)</sup> | 3           | Age, BMI, educational level, physical activity, smoking status, alcohol consumption, energy intake, dietary factors, menopausal status |
| Vitamin C     | Liu 2015<sup>(217)</sup>      | 9           | Age, BMI, occupation, education level, smoking level, alcohol consumption, physical activity, family history of CRC, energy intake, intake of fibre, vegetables, multivitamin intake, menopausal status, serum cholesterol concentration, hormone therapy (HRT), use of aspirin |
| Vitamin D     | Heine-Bröring 2015<sup>(216)</sup> | 5           | Age, race/ethnicity, sex, family history of CRC, BMI, physical activity, smoking status, alcohol intake, energy intake, dietary factors, menopausal status, use of NSAIDs |
| Vitamin D     | Liu 2015<sup>(217)</sup>      | 14          | Age, sex, geographical area, occupation, race/ethnicity, BMI, physical activity, smoking status, educational level, total energy intake, fruits, meat, vegetables, alcohol intake, fat intake, dietary fibre intake, calcium intake, CRC screening, menopausal status, family history of CRC, history of intestinal polyps, use of aspirin or other NSAIDs, hormone therapy (HRT), vitamin use |
| Vitamin E     | Heine-Bröring 2015<sup>(216)</sup> | 4           | Age, BMI, family history of CRC, physical activity, smoking status, educational level, energy intake, alcohol consumption, dietary factors, menopausal status, use of NSAIDs |
| Vitamin E     | Liu 2015<sup>(217)</sup>      | 10          | Age, sex, BMI, educational level, alcohol intake, smoking status, physical activity, family history of CRC, history of colorectal polyps, serum cholesterol, energy intake, intake of meat, vegetable consumption, intake of fibre, vitamin intake, hormone therapy (HRT), menopausal status, aspirin use |
| Dietary calcium | Meng 2019<sup>(218)</sup> | 8 | 1449526 | 13640 | 7 - 16.4; 10 | Age, sex, race/ethnicity, BMI, waist:hip ratio, education, smoking status, tea intake, alcohol consumption, physical activity, family history of CRC or other cancers, history of intestinal polyps, CRC screening, diabetes, total energy intake, fat intake, intake of meat, intake of fruits, vegetables, whole grains, fibre, intake of phosphorus, retinol, sodium, potassium, zinc, use of calcium supplement, multivitamin use, use of ginseng, menopausal status, hormone therapy (OC or HRT), statin use, use of aspirin or other NSAIDs |
| Supplemental calcium | Heine-Bröring 2015<sup>(216)</sup> | 7 | 1064458 | 9862 | 3.3 - 16; 8.4 | Age, race/ethnicity, BMI, physical activity, educational level, family history of CRC, smoking status, alcohol consumption, energy intake, dietary factors, menopausal status, use of NSAIDs |
| Supplemental calcium | Heine-Bröring 2015<sup>(216)</sup> | 6 | 929116 | 8837 | 5 - 10; 8 | Age, race/ethnicity, BMI, physical activity, educational level, family history of CRC, smoking status, alcohol consumption, energy intake, dietary factors, menopausal status, use of NSAIDs |
| Heme iron | Qiao 2013<sup>(219)</sup> | 6 | 646901 | 8022 | 7.2 - 22; 15.7 | Age, sex, BMI, education level, physical activity, smoking status, alcohol consumption, family history of CRC, history of endoscopy, diabetes, intake of total energy, fat, calcium, fibre, zinc, magnesium, hormone therapy (HRT), regular aspirin use, menopausal status, vitamin intake |
| Magnesium | Chen 2012<sup>(220)</sup> | 7 | 336463 | 7435 | 7.9 - 28; 15.9 | Age, sex, BMI, geographic region, alcohol intake, physical activity, education, smoking status, diabetes, history of CRC, screening for CRC, magnesium, calcium, fibre intake, fat intake, total energy intake, vitamin intake (vitamin B6, folate, vitamin B12, vitamin D, vitamin E), HRT use, use of aspirin or other NSAIDs |
| Zinc | Li 2014<sup>(221)</sup> | 5 | 350507 | 5676 | 9.5 - 22; 15.7 | Age, BMI, geographic region, alcohol intake, physical activity, education, smoking status, diabetes, history of CRC, screening for CRC, magnesium, calcium, fibre intake, fat intake, total energy intake, vitamin intake (vitamin B6, folate, vitamin B12, vitamin D, vitamin E), HRT use, use of aspirin or other NSAIDs |
| Methionine | Zhou 2013<sup>(222)</sup> | 7 | 431029 | 6331 | 5.8 - 22; 13.3 | Age, income, waist:hip ratio, BMI, physical activity, smoking status, education, alcohol consumption, family history of CRC, history of CRC, history of colorectal polyps, screening, diabetes, energy intake, calcium, meat, fat intake, fibre intake, iron, vegetables, fruits, vitamin intake (vitamin B6, folate, vitamin D, vitamin E), menopausal status, hormone therapy (OC or HRT), use of aspirin or other NSAIDs |
| Garlic supplement | Chiavarini 2016<sup>(110)</sup> | 4 | 304677 | 2703 | 3.3 - 24; 9.8 | Age, sex, BMI, smoking status, educational level, family history, history of chronic intestinal disease or cholecystectomy, screening, physical activity, fruits, vegetables, total energy intake, alcohol intake, calcium, meat, hormone therapy (HRT), vitamin intake (folate, vitamin C, vitamin D), use of aspirin or other NSAIDs |

**Abbreviations:** BMI, body mass index; CRC, colorectal cancer; HRT, hormone replacement therapy; NSAIDs, non-steroidal anti-inflammatory drugs; OC, oral contraceptive; PUFA, polyunsaturated fatty acid
| Exposure                                      | Author; year | Comparison | Summargy metric | Credibility assessment | AMSTAR-2 |
|----------------------------------------------|--------------|------------|-----------------|------------------------|----------|
|                                              |              |            |                 |                         | 2        |
| Dietary glycaemic index                      | Reynolds 2019 | High vs low | RR 1.10 (0.99-1.22) | p-value 0.08955 | I² 56.0% | Largest study (95% CI) 1.06-1.27 | Predictive interval (95% CI) 0.81-1.47 | Egger's p-value 0.868 | Excess significance test O/E 3/NA | Quality of evidence p-value NA | NS | High |
| Dietary glycaemic load                       | Reynolds 2019 | High vs low | RR 0.93 (0.85-1.01) | p-value 0.080955 | I² 32.0% | Largest study (95% CI) 0.70-0.95 | Predictive interval (95% CI) 0.76-1.14 | Egger's p-value 0.139 | Excess significance test O/E 2/NA | Quality of evidence p-value NA | NS | High |
| Eating frequency (3 vs <3 daily meals)       | Liu 2014     | High vs low | RR 0.85 (0.66-1.31) | p-value 0.47531 | I² 63.4% | Largest study (95% CI) 0.78-1.36 | Predictive interval (95% CI) NA | Egger's p-value NA | Excess significance test O/E 0/NA | Quality of evidence p-value NA | NS | Moderate |
| Eating frequency (4 vs <3 daily meals)       | Liu 2014     | High vs low | RR 0.88 (0.65-1.19) | p-value 0.40383 | I² 65.7% | Largest study (95% CI) 0.91-1.32 | Predictive interval (95% CI) 0.03-24.69 | Egger's p-value 0.069 | Excess significance test O/E 0/NA | Quality of evidence p-value NA | NS | Moderate |
| Eating frequency                               | Liu 2014 (183) | High vs low | RR  | 0.75 (0.54-1.05) | 0.09413 | 0.0% | 0.51-1.14 | NA  | NA  | 0/NA | NA  | NS   | Moderate |
|-----------------------------------------------|----------------|-------------|-----|-----------------|---------|------|-----------|-----|-----|-------|-----|-------|----------|
| Vegetarian diet                               | Godos 2016 (181) | Yes vs no   | RR  | 0.88 (0.74-1.05) | 0.14873 | 21.3% | 0.64-0.98 | 0.21-3.67 | 0.919 | 1/NA | NA   | NS   | Low  |

| Food groups or foods                          |                |             |     |                 |         |      |           |     |     |       |     |       |          |
|-----------------------------------------------|----------------|-------------|-----|-----------------|---------|------|-----------|-----|-----|-------|-----|-------|----------|
| Nuts                                          | Schwingshackl 2018 (184) | High vs low | RR  | 0.96 (0.90-1.02) | 0.15397 | 3.7% | 0.85-1.02 | 0.87-1.05 | 0.478 | 0/NA | NA   | NS   | High |
| Refined grains                                | Schwingshackl 2018 (184) | High vs low | RR  | 1.46 (0.80-2.67) | 0.21776 | 71.4% | 0.85-1.50 | NA  | NA  | 1/NA | NA   | NS   | High    |
| Cruciferous vegetables                        | Wu 2013 (188)  | High vs low | RR  | 0.96 (0.86-1.08) | 0.50786 | 39.6% | 0.86-1.09 | 0.73-1.27 | 0.398 | 0/NA | NA   | NS   | Moderate   |
| Broccoli                                     | Wu 2013 (188)  | High vs low | RR  | 0.91 (0.80-1.03) | 0.14492 | 0.0%  | 0.80-1.08 | 0.39-2.10 | 0.920 | 0/NA | NA   | NS   | Moderate |
| Beef                                          | Carr 2016 (185) | High vs low | RR  | 1.10 (0.98-1.23) | 0.12048 | 13.7% | 0.86-1.24 | 0.80-1.51 | 0.458 | 1/NA | NA   | NS   | Low  |
| Poultry                                       | Carr 2016 (185) | High vs low | RR  | 0.97 (0.89-1.07) | 0.57776 | 44.2% | 0.86-1.01 | 0.75-1.26 | 0.302 | 2/NA | NA   | NS   | Low  |
| Fish                                          | Wu 2012 (186)  | High vs low | OR  | 0.93 (0.82-1.05) | 0.22129 | 37.2% | 0.54-0.88 | 0.64-1.34 | 0.817 | 3/NA | NA   | NS   | Low  |
| Fruits and vegetables                         | Aune 2011 (187) | High vs low | RR  | 0.93 (0.86-1.01) | 0.08766 | 28.1% | 0.85-1.09 | 0.77-1.12 | 0.492 | 1/NA | NA   | NS   | Low  |
| Soy products | Lu 2017(193) | High vs low | RR 0.86 (0.72-1.03) | 0.10126 | 44.7 % | 0.78-1.16 | 0.55-1.36 | 0.422 | 2/NA | NA | NS | Low |
|--------------|--------------|-------------|----------------------|---------|--------|----------|---------|-------|------|-----|-----|     |
| Cheese       | Aune 2012(194) | High vs low | RR 0.94 (0.75-1.18) | 0.59378 | 38.5 % | 0.56-1.12 | 0.54-1.65 | 0.122 | 1/NA | NA | NS | Low |
| **Beverages** |              |             |                      |         |        |          |         |       |      |     |     |     |
| Wine         | Xu 2019(203) | Yes vs no   | RR 1.01 (0.90-1.13) | 0.89148 | 59.0 % | 0.93-1.11 | 0.75-1.35 | 0.257 | 2/NA | NA | NS | Moderate |
| Wine         | Xu 2019(203) | <2 drinks/d vs non-drinkers | RR 0.94 (0.84-1.05) | 0.27068 | 25.4 % | 0.83-1.08 | 0.67-1.32 | 0.226 | 0/NA | NA | NS | Moderate |
| Wine         | Xu 2019(203) | ≥2 drinks/d vs non-drinkers | RR 1.03 (0.85-1.24) | 0.79103 | 41.8 % | 1.04-1.40 | 0.62-1.71 | 0.439 | 1/NA | NA | NS | Moderate |
| Coffee       | Gan 2017(199) | High vs low | RR 0.98 (0.90-1.06) | 0.63354 | 41.4 % | 0.95-1.18 | 0.77-1.24 | 0.764 | 3/NA | NA | NS | Moderate |
| Fermented milk | Ralston 2014(200) | High vs low | RR 1.01 (0.89-1.15) | 0.83901 | 0.0%  | 0.86-1.34 | 0.86-1.19 | 0.351 | 0/NA | NA | NS | Moderate |
| Tea          | Chen 2017(196) | High vs low | OR 0.94 (0.86-1.03) | 0.17801 | 32.7 % | 0.90-1.05 | 0.74-1.20 | 0.328 | 3/NA | NA | NS | Moderate |
| Green tea    | Wang 2012(197) | High vs low | RR 0.93 (0.77-1.12) | 0.44432 | 59.2 % | 0.97-1.45 | 0.53-1.62 | 0.653 | 2/NA | NA | NS | Critically low |
| Black tea    | Sun 2006(198) | High vs low | OR 1.05 (0.75-1.46) | 0.77918 | 75.1 % | 0.83-1.22 | 0.37-2.99 | 0.704 | 2/NA | NA | NS | Critically low |

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| Nutrition Factor                  | Study Reference | Consumption Comparison | RR (95% CI)   | %Change | 95% Lower CI | 95% Upper CI | P Value | Risk Classification |
|-----------------------------------|-----------------|-------------------------|---------------|---------|--------------|--------------|---------|---------------------|
| Legume fibre                      | Reynolds 2019   | High vs low             | 0.91 (0.81-1.02) | 38.0%   | 0.83-1.04    | 0.60-1.36    | 0.214  | High                |
| Soluble fibre                     | Reynolds 2019   | High vs low             | 0.84 (0.67-1.05) | 38.2%   | 0.69-1.03    | 0.10-7.29    | 0.904  | High                |
| Insoluble fibre                   | Reynolds 2019   | High vs low             | 0.86 (0.74-1.01) | 0.0%    | 0.72-1.06    | 0.31-2.39    | 0.893  | High                |
| Dietary protein                   | Lai 2017        | High vs low             | 0.94 (0.73-1.21) | 0.0%    | 0.64-1.44    | 0.54-1.63    | 0.454  | Moderate            |
| Polyunsaturated fatty acids       | Kim 2018        | High vs low             | 0.99 (0.93-1.04) | 22.0%   | 0.98-1.03    | 0.85-1.14    | 0.965  | Moderate            |
| Monounsaturated fatty acids       | Liu 2011        | High vs low             | 1.04 (0.93-1.16) | 0.0%    | 0.87-1.29    | 0.92-1.18    | 0.214  | Low                 |
| Saturated fatty acids             | Liu 2011        | High vs low             | 1.00 (0.90-1.12) | 0.0%    | 0.77-1.14    | 0.89-1.13    | 0.037  | Low                 |
| Total dietary fat                 | Liu 2011        | High vs low             | 0.99 (0.89-1.11) | 6.9%    | 0.78-1.17    | 0.84-1.17    | 0.092  | Low                 |
| Total n-3 polyunsaturated fatty acids | Chen 2015     | High vs low             | 1.00 (0.93-1.07) | 8.6%    | 0.92-1.17    | 0.89-1.13    | 0.773  | Low                 |
| Marine n-3 polyunsaturated fatty acids | Chen 2015     | High vs low             | 1.00 (0.93-1.07) | 0.0%    | 0.89-1.20    | 0.92-1.08    | 0.728  | Low                 |
| Cholesterol                       | Liu 2011        | High vs low             | 1.14 (0.88-1.47) | 49.8%   | 0.70-1.60    | 0.56-2.30    | 0.057  | Low                 |
| Carbohydrate                      | Aune 2012       | High vs low             | 0.93 (0.84-1.04) | 39.8%   | 0.75-1.10    | 0.70-1.25    | 0.049  | Low                 |
| Sucrose                           | Aune 2012       | High vs low             | 1.01 (0.87-1.17) | 63.5%   | 0.97-1.20    | 0.65-1.56    | 0.949  | Low                 |
| Fructose            | Aune 2012(207) | High vs low | RR  | 1.06 (0.87-1.28) | 0.5765 (0.87-1.28) | 72.5% | 0.90-1.13 | 0.56-1.99 | 0.353 | 2/NA NA NS Low |
|---------------------|----------------|-------------|-----|------------------|-------------------|-------|-----------|-----------|-------|---------------|
| Fruit fibre         | Aune 2011(209) | High vs low | RR  | 0.94 (0.85-1.04) | 0.2080 (0.85-1.04) | 39.1% | 0.95-1.23 | 0.73-1.20 | 0.913 | 2/NA NA NS Low |
| Vegetable fibre     | Aune 2011(209) | High vs low | RR  | 0.98 (0.91-1.06) | 0.6317 (0.91-1.06) | 0.0%  | 0.89-1.15 | 0.90-1.07 | 0.514 | 0/NA NA NS Low |

**Micronutrients**

| Garlic supplement  | Chiavarini 2016(190) | Yes vs no | RR  | 1.07 (0.91-1.26) | 0.4170 (0.91-1.26) | 27.8% | 1.01-1.81 | 0.74-1.55 | 0.634 | 1/NA NA NS Moderate |
|---------------------|-----------------------|------------|-----|------------------|-------------------|-------|-----------|-----------|-------|---------------------|
| Flavanols           | He 2016(213)          | High vs low | OR  | 1.00 (0.66-1.28) | 0.9558 (0.66-1.28) | 41.3% | 0.95-1.21 | 0.22-4.68 | 0.924 | 0/NA NA NS Moderate |
| Anthocyanins        | He 2016(213)          | High vs low | OR  | 0.92 (0.66-1.28) | 0.6205 (0.66-1.28) | 17.0% | 0.81-1.91 | NA        | NA    | 0/NA NA NS Moderate |
| Quercetin           | Grosso 2017(212)      | High vs low | OR  | 0.98 (0.75-1.29) | 0.8941 (0.75-1.29) | 29.6% | 0.75-1.36 | 0.08-11.45 | 0.430 | 0/NA NA NS Low    |
| Kaempferol          | Grosso 2017(212)      | High vs low | OR  | 1.12 (0.91-1.38) | 0.2893 (0.91-1.38) | 0.0%  | 0.85-1.53 | 0.29-4.32 | 0.984 | 0/NA NA NS Low    |
| Myricetin           | Grosso 2017(212)      | High vs low | OR  | 1.10 (0.82-1.48) | 0.5096 (0.82-1.48) | 42.4% | 0.67-1.18 | 0.06-19.82 | 0.541 | 0/NA NA NS Low    |
| Catechin            | Grosso 2017(212)      | High vs low | OR  | 0.89 (0.71-1.11) | 0.3047 (0.71-1.11) | 57.0% | 0.77-1.21 | 0.36-2.17 | 0.271 | 1/NA NA NS Low    |
| Phyto-oestrogens    | Jiang 2017(214)       | High vs low | RR  | 0.93 (0.83-1.05) | 0.2313 (0.83-1.05) | 0.0%  | 0.79-1.14 | 0.78-1.12 | 0.993 | 0/NA NA NS Low    |
| Nutrient                        | Study                      | Outcome                | RR   | 95% CI        | p-value | I² % | RR   | 95% CI        | p-value | I² % | RR   | 95% CI        | p-value | I² % | Whether Significant
|-------------------------------|----------------------------|------------------------|------|---------------|---------|------|------|---------------|---------|------|------|---------------|---------|------|------------------|
| Isoflavones                   | Grosso 2017(212)           | High vs low            | OR 0.92 (0.82-1.03) | 0.1522 4 | 0.0% | 0.79-1.14 | 0.78-1.08 | 0.668 | 0/NA | NA   | NS Low         |
| Combined carotenoids          | Panic 2017(215)            | High vs low            | RR 1.08 (0.93-1.26) | 0.3171 1 | 0.0% | 0.93-1.28 | NA   | NA   | 0/NA | NA   | NS Low         |
| Alpha-carotene                | Panic 2017(215)            | High vs low            | RR 1.05 (0.92-1.21) | 0.4647 7 | 0.0% | 0.88-1.20 | 0.43-2.59 | 0.190 | 0/NA | NA   | NS Low         |
| Beta-carotene                 | Panic 2017(215)            | High vs low            | RR 0.98 (0.87-1.11) | 0.7854 2 | 0.0% | 0.78-1.08 | 0.74-1.30 | 0.090 | 0/NA | NA   | NS Low         |
| Lycopene                      | Panic 2017(215)            | High vs low            | RR 1.08 (0.94-1.23) | 0.2601 1 | 0.0% | 0.94-1.26 | 0.45-2.56 | 0.309 | 0/NA | NA   | NS Low         |
| Beta-cryptoxanthin            | Panic 2017(215)            | High vs low            | RR 0.99 (0.74-1.34) | 0.9585 7 | 38.8% | 0.78-1.06 | NA   | NA   | 0/NA | NA   | NS Low         |
| Lutein and zeaxanthin         | Panic 2017(215)            | High vs low            | RR 1.05 (0.91-1.20) | 0.5221 0 | 0.0% | 0.88-1.20 | 0.43-2.57 | 0.585 | 0/NA | NA   | NS Low         |
| Multivitamin                  | Liu 2015(217)              | High vs low            | RR 0.83 (0.65-1.05) | 0.1211 6 | 68.5% | 0.83-1.17 | 0.42-1.62 | 0.121 | 2/NA | NA   | NS Low         |
| Vitamin A                     | Liu 2015(217)              | High vs low            | RR 0.89 (0.77-1.03) | 0.1323 0 | 0.0% | 0.70-1.50 | 0.75-1.06 | 0.304 | 1/NA | NA   | NS Low         |
| Vitamin B2                    | Liu 2015(217)              | High vs low            | RR 0.89 (0.78-1.00) | 0.0572 3 | 4.2% | 0.66-0.99 | 0.72-1.08 | 0.159 | 1/NA | NA   | NS Low         |
| Vitamin B3                    | Liu 2015(217)              | High vs low            | RR 1.18 (0.76-1.84) | 0.4568 3 | 31.0% | 0.70-1.60 | NA   | NA   | 0/NA | NA   | NS Low         |
| Vitamin B12                   | Liu 2015(217)              | High vs low            | RR 1.10 (0.92-1.32) | 0.3114 5 | 49.1% | 0.72-1.08 | 0.67-1.80 | 0.018 | 0/NA | NA   | NS Low         |
| Vitamin C                     | Heine-Bröring 2015(216)    | Yes vs no              | RR 0.92 (0.75-1.11) | 0.3779 9 | 42.2% | 0.73-1.49 | 0.55-1.53 | 0.231 | 1/NA | NA   | NS Low         |
| Vitamin     | Author            | High vs low | RR     | 95% CI         | p     | O/E | OR     | 95% CI         | p     | O/E | NA | NS       | Score | Critical \( p \) |
|-------------|-------------------|-------------|--------|----------------|-------|-----|--------|----------------|-------|-----|----|----------|-------|------------------|
| Vitamin C   | Liu 2015(217)     | High vs low | 0.92   | (0.80-1.07)    | 0.3068| 40.0%| 0.73-1.09 | 0.62-1.38     | 0.954 | 2/NA | NA | NS | Low      |
| Vitamin D   | Heine-Bröring 2015(216) | Yes vs no | RR     | 0.90 (0.81-1.02) | 0.0939| 46.3%| 0.80-1.06 | 0.67-1.23     | 0.487 | 2/NA | NA | NS | Low      |
| Vitamin E   | Liu 2015(217)     | High vs low | 0.88   | (0.75-1.04)    | 0.1217| 49.3%| 0.85-1.38 | 0.54-1.43     | 0.264 | 1/NA | NA | NS | Low      |
| Flavonoids  | Bo 2016(210)      | High vs low | OR     | 1.10 (0.95-1.28) | 0.1933| 5.0% | 0.95-1.50 | 0.87-1.40     | 0.825 | 1/NA | NA | NS | Critically low |
| Flavonols   | Chang 2018(212)   | High vs low | RR     | 1.00 (0.92-1.08) | 0.9497| 6.6% | 0.89-1.14 | 0.85-1.17     | 0.777 | 0/NA | NA | NS | Critically low |
| Flavones    | Chang 2018(212)   | High vs low | RR     | 1.02 (0.94-1.12) | 0.6262| 0.0% | 0.92-1.17 | 0.58-1.80     | 0.202 | 0/NA | NA | NS | Critically low |
| Flavanones  | Chang 2018(212)   | High vs low | RR     | 0.99 (0.91-1.06) | 0.7128| 0.0% | 0.91-1.10 | 0.83-1.17     | 0.485 | 0/NA | NA | NS | Critically low |
| Flavan-3-ols| Chang 2018(212)   | High vs low | RR     | 1.02 (0.93-1.12) | 0.6260| 20.4% | 0.95-1.21 | 0.78-1.34     | 0.908 | 0/NA | NA | NS | Critically low |
| Anthocyanidins | Chang 2018(212)   | High vs low | RR     | 1.00 (0.91-1.09) | 0.9457| 0.0% | 0.91-1.13 | 0.54-1.83     | 0.125 | 0/NA | NA | NS | Critically low |
| Methionine  | Zhou 2013(222)    | High vs low | RR     | 0.89 (0.77-1.03) | 0.1118| 29.1%| 0.76-1.28 | 0.64-1.24     | 0.632 | 2/NA | NA | NS | Critically low |

NA = not applicable because of non-significant effect estimate/data unavailability; NS = not significant; O/E = observed/expected number of studies with significant results; OR = odds ratio; RR = risk ratio
### eTable 5. Sensitivity Analyses for Associations With Class I, II, or III Evidence

| Exposure          | Author; year | No. of primary studies | No. of study participants | No. of cases | Comparison | Summary metric | Credibility assessment | AMSTAR-2 |
|-------------------|--------------|------------------------|---------------------------|--------------|------------|---------------|------------------------|-----------|
| Alcohol (Moderate) | Fedirko 2011(201) | 17                     | 2754534                   | 18420        | >1-3 drinks/d vs non/occasion drinkers | RR 1.17 (1.08-1.26) | 0.0000 6 | 37.3 % | 1.01-1.13 | 0.96-1.42 | 0.014 | 5/2.5 | 1.00 | Class III Moderate |
| Supplemen- tal calcium | Heine-Börning 2015(216) | 6                      | 1029242                   | 9621         | Yes vs no | RR 0.89 (0.84-0.95) | 0.0005 1 | 47.5 % | 0.88-1.05 | 0.73-1.09 | 0.252 | 2/3.2 | NP   | Class III Low |
| Whole grains      | Schwingshackle 2018(184) | 7                      | 932818                    | 8943         | High vs low | RR 0.87 (0.82-0.94) | 0.0001 1 | 48.3 % | 0.88-0.99 | 0.73-1.04 | 0.018 | 4/0.9 | 0.06 | Class III High |

**Exclusion of primary studies with number of study participants lower than 25th percentile** (applicable to those meta-analyses with evidence of small-study effects in primary analysis)
Primary studies adjusted for confounding variables

| Study Description                        | Authors        | Year | Participants | High vs Low | RR  | 95% CI   | P Value | % Change | 95% CI   | Class | Critically low |
|------------------------------------------|----------------|------|--------------|-------------|-----|----------|---------|----------|----------|-------|----------------|
| Adherence to Mediterranean diet          | Schwingshackl  | 2017 | 16102        | High vs low | 0.86| (0.80-0.92)|<10^-6  | 29.7     | 0.80-0.99| 0.74-1.00| 0.841 | 3/5.0          |
| Adherence to Western diet                | Feng           | 2017 | 11537        | High vs low | 1.28| (1.13-1.45)|<10^-4  | 72.2     | 1.09-1.44| 0.79-2.07| 0.173 | 8/6.5          |
| Adherence to healthy diet                | Feng           | 2017 | 11537        | High vs low | 0.84| (0.76-0.92)|<10^-4  | 56.2     | 0.69-0.90| 0.60-1.17| 0.602 | 5/7.5          |
| Pesco-vegetarian diet                    | Godos          | 2016 | 1506         | Yes vs no   | 0.67| (0.53-0.83)|<10^-3  | 0.0      | 0.48-0.94| 0.15-2.89| 0.437 | 2/1.7          |
| Semi-vegetarian diet                     | Godos          | 2016 | 4062         | Yes vs no   | 0.86| (0.79-0.94)|<10^-2  | 0.0      | 0.76-0.95| 0.72-1.04| 0.964 | 1/1.2          |
| Red meat                                | Schwingshackl  | 2018 | 21326        | High vs low | 1.13| (1.08-1.19)|<10^-8  | 20.5     | 1.15-1.19| 1.02-1.26| 0.175 | 3/6.0          |
| Processed meat                          | Schwingshackl  | 2018 | 18646        | High vs low | 1.14| (1.07-1.23)|<10^-3  | 25.9     | 1.09-1.32| 0.97-1.35| 0.981 | 4/6.9          |
| Whole grains                            | Schwingshackl  | 2018 | 9223         | High vs low | 0.88| (0.83-0.94)|<10^-6  | 34.9     | 0.88-0.99| 0.77-1.01| 0.067 | 4/1.0          |
| Dairy products                          | Schwingshackl  | 2018 | 16910        | High vs low | 0.83| (0.76-0.89)|<10^-6  | 60.3     | 0.83-0.95| 0.65-1.04| 0.170 | 8/4.0          |
| Yogurt                                  | Zhang          | 2019 | 5432         | High vs low | 0.81| (0.76-0.86)|<10^-6  | 0.0      | 0.75-0.87| 0.72-0.90| 0.835 | 2/1.8          |

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| Variable                          | Study                                                                 | N  | HR 5/20  | Adherence | RR 9/20  | P-value | Class | Study quality |
|----------------------------------|-----------------------------------------------------------------------|----|----------|------------|-----------|---------|-------|---------------|
| Alcohol (Moderate)               | Fedirko 2011                                                        | 22 | RR 1.24  | <10\(^{-6}\) | 49.3%    | 0.95-1.61 |               | Class II Moderate |
|                                   | Fedirko 2011                                                        | 22 | RR 1.24  | <10\(^{-6}\) | 49.3%    | 0.95-1.61 |               | Class II Moderate |
| Alcohol (Heavy)                  | Fedirko 2011                                                        | 7  | RR 1.58  | <10\(^{-6}\) | 0.0%     | 1.27-2.16 | Class I | Moderate |
| Non-fermented milk               | Ralston 2014                                                        | 14 | RR 0.85  | 0.0004    | 0.0%     | 0.78-1.18 | Class III | Moderate |
| Total dietary fibre              | Reynolds 2019                                                       | 21 | RR 0.84  | <10\(^{-6}\) | 18.1%    | 0.65-0.85 | Class I  | High |
| Dietary calcium                  | Meng 2019                                                           | 8  | HR 0.77  | <10\(^{-6}\) | 0.0%     | 0.75-0.94 | Class I  | Moderate |
| Supplementation calcium          | Heine-Bröning 2015                                                   | 7  | RR 0.88  | 0.0009    | 51.7%    | 0.88-1.05 | Class III | Low |
| Supplementation calcium          | Heine-Bröning 2015                                                   | 6  | RR 0.80  | 0.0002    | 30.9%    | 0.72-1.02 | Class III | Low |
| **Primary studies with high quality** |                                                                       |     |          |            |          |         |       |               |
| Adherence to Mediterranean diet* | Schwingshack 2017                                                   | 6  | RR 0.86  | 8.4 \times 10^{-6} | 29.7% | 0.80-0.99 | Class III | Critically Low |

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| Dietary Pattern                        | Source             | N     | Cases    | Controls | High vs low | OR     | 95% CI  | P         | Adjustment | N      | NP   | Class | Moderate |
|---------------------------------------|--------------------|-------|----------|----------|-------------|--------|---------|-----------|------------|--------|------|-------|----------|
| Adherence to Western diet             | Feng 2017(179)     | 13    | 1181915  | 11449    | High vs low | OR 1.23 (1.09-1.40) | 0.0001 | 71.6% | 1.09-1.44 | 0.78-1.95 | 0.457 | 6/6.9 | Class III | Moderate |
| Pescovegetarian diet                  | Godos 2016(181)    | 3     | 149516   | 1506     | Yes vs no   | RR 0.67 (0.53-0.83)  | 0.0004 | 0.0%  | 0.48-0.94 | 0.15-2.89 | 0.437 | 2/1.7 | Class III | Low      |
| Semi-vegetarian diet                  | Godos 2016(181)    | 3     | 580175   | 4062     | Yes vs no   | RR 0.86 (0.79-0.94)  | 0.0007 | 0.0%  | 0.76-0.95 | 0.72-1.04 | 0.964 | 1/1.2 | NP       | Class III Low |
| Red meat*                             | Schwingshackle 2018(184) | 21   | 2154027  | 21326    | High vs low | RR 1.13 (1.08-1.19)  | <10^-6 | 20.5% | 1.15-1.19 | 1.02-1.26 | 0.175 | 3/6.0 | NP       | Class I High |
| Processed meat*                       | Schwingshackle 2018(184) | 15   | 1910983  | 18646    | High vs low | RR 1.14 (1.07-1.23)  | 0.0001 | 25.9% | 1.09-1.32 | 0.97-1.35 | 0.981 | 4/6.9 | NP       | Class III High |
| Whole grains*                         | Schwingshackle 2018(184) | 9    | 970927   | 9223     | High vs low | RR 0.88 (0.83-0.94)  | 0.00006 | 34.9% | 0.88-0.99 | 0.77-1.01 | 0.067 | 4/1.0 | 0.26    | Class III High |
| Dairy products*                       | Schwingshackle 2018(184) | 17   | 1629366  | 16910    | High vs low | RR 0.83 (0.76-0.89)  | <10^-6 | 60.3% | 0.83-0.95 | 0.65-1.04 | 0.170 | 8/4.0 | 0.99    | Class II High |
| Yogurt*                               | Zhang 2019(195)    | 5     | 698366   | 5432     | High vs low | OR 0.81 (0.76-0.86)  | <10^-6 | 0.0%  | 0.75-0.87 | 0.72-0.90 | 0.835 | 2/1.8 | 1.00    | Class I Low |
| Alcohol (Moderate)                    | Fedirko 2011(201)  | 10    | 1061631  | 7809     | >1-3 drinks/d vs non/occasional drinkers | RR 1.36 (1.16-1.58) | 0.00013 | 55.3% | 0.93-1.29 | 0.88-2.10 | 0.016 | 5/1.4 | 0.29    | Class III Moderate |

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| Alcohol (Heavy) | Fedirko 2011 (201) | 4 | 637367 | 3724 | ≥4 drinks/d vs non/occasion al drinkers | RR | 1.73 (1.47–2.04) | <10⁻⁶ | 0.0% | 1.27–2.16 | 1.21–2.49 | 0.248 | 4/3.5 | 0.90 | Class I | Moderate |
|----------------|-------------------|---|--------|------|----------------------------------------|----|-----------------|-------|------|-----------|-----------|------|------|------|---------|---------|
| Non-fermented milk | Ralston 2014 (200) | 10 | 751312 | 4184 | High vs low | RR | 0.83 (0.74–0.94) | 0.0034 | 27.9% | 0.78–1.18 | 0.63–1.10 | 0.577 | 3/0.6 | 0.42 | Class III | Moderate |
| Total dietary fibre | Reynolds 2019 (182) | 17 | 2071669 | 20961 | High vs low | RR | 0.85 (0.79–0.90) | <10⁻⁶ | 10.5% | 0.65–0.85 | 0.76–0.95 | 0.642 | 5/10.5 | NP | Class I | High |
| Dietary calcium* | Meng 2019 (218) | 8 | 1449526 | 13640 | High vs low | HR | 0.77 (0.73–0.82) | <10⁻⁶ | 0.0% | 0.75–0.94 | 0.72–0.83 | 0.598 | 5/3.9 | 1.00 | Class I | Moderate |
| Supplemen tal calcium* | Heine-Bröring 2015 (216) | 7 | 1064458 | 9862 | Yes vs no | RR | 0.88 (0.82–0.94) | 0.0000 | 51.7% | 0.88–1.05 | 0.70–1.09 | 0.071 | 3/3.4 | NP | Class III | Low |
| Supplemen tal calcium* | Heine-Bröring 2015 (216) | 6 | 929116 | 8837 | High vs low | RR | 0.80 (0.72–0.89) | 0.0000 | 30.9% | 0.72–1.02 | 0.63–1.01 | 0.884 | 4/2.7 | 0.95 | Class III | Low |

* Not performed due to limited number of primary studies
*Sensitivity analysis is not possible because no information on quality assessment of primary studies
* Sensitivity analysis is not possible because meta-analysis only included good-quality studies

NP = not pertinent, because estimated number is larger than observed, and there is no evidence of excess significance based on assumption made for plausible effect size; O/E = observed/expected number of studies with significant results; OR = odds ratio; RR = risk ratio.
### eTable 6: Evidence Criteria: Difference Between WCRF and Present Review

| WCRF<sup>(223)</sup> | Umbrella review |
|------------------------|----------------|
| • Evidence from more than one study | • Number of cases >1,000 |
| • Evidence from at least two independent cohort studies | • p <10<sup>−6</sup> |
| • No substantial heterogeneity | • I<sup>2</sup> <50% |
| • Good quality studies to exclude with confidence the possibility that the observed association results from random or systematic error, including confounding, measurement error, and selection bias | • 95% prediction interval excluding the null |
| • Dose-response relationship | • No small-study effects |
| • Strong and plausible experimental evidence | • No excess significance bias |

### eTable 6.1: Comparison with WCRF meta-analyses for associations with class I evidence in primary analysis

| Association | WCRF<sup>(223)</sup> | Present review |
|-------------|-------------------------|----------------|
|             | Author (Year) | Number of studies reported | Author (Year) | Number of studies reported |
| Red meat    | Alexander (2015) | 17 | Schwingshakl (2018) | 21 |
|             | Chan (2011) | 8 |                      |     |
| Alcohol beverages (heavy intake) | Only dose-response meta-analysis found | - | Fedirko (2011) | 7 |
| Total dietary fibre | Aune (2011) | 16 | Reynolds (2019) | 21 |
| Dietary calcium | Only dose-response meta-analysis found | - | Meng (2019) | 8 |
| Yogurt      | Only dose-response meta-analysis found | - | Zhang (2019) | 5 |

**Explanation:**

Although WCRF is the latest report, the meta-analyses they used for the intake of red meat and total dietary fibre are different from ours. According to the published methodology by WCRF, the search for articles was updated to April 2015. For our current review paper, a systematic literature search up to September 2019 was performed. Hence, the meta-analyses included for the intake of red meat, total dietary fibre, yogurt, and dietary calcium are from recent papers published between 2018 to 2019, except for heavy alcohol intake which was published in 2011. The meta-analyses included in our review are chosen based on specified selection criteria: meta-analysis with the largest number of primary studies and the one with the largest number of colorectal cancer cases. However, the selection criteria
in the WCRF report are unclear. We followed exactly the protocol as suggested by recent umbrella reviews for selection of meta-analysis for evidence grading. We excluded the meta-analyses used by WCRF and they are shown in the exclusion references in this supplementary material. For all of the associations, we used summary estimates for high versus low intake instead of dose-response meta-analysis.
eTable 7. Summary Estimates for Concordance in Meta-analyses: Red Meat Intake and Incidence of CRC

| Author          | Year | RR  | 95% CI       | P-value | Class of evidence          |
|-----------------|------|-----|--------------|---------|---------------------------|
| Larsson(175)    | 2006 | 1.20| 1.11 - 1.31  | >10^-6  | Class III                 |
| Chan (173)      | 2011 | 1.17| 1.09 - 1.25  | >10^-6  | Class III                 |
| Pham(141)       | 2014 | 1.18| 0.92- 1.53   | NS      | Not significant (only Japanese population included): excluded in this comparison |
| Alexander(168)  | 2015 | 1.16| 1.10 - 1.23  | NA      | Data not available to grade the evidence |
| Schwingshackl(184) | 2018 | 1.14| 1.07 - 1.23  | >10^-6  | Class III                 |

**Abbreviations:** NA: not available; RR, relative risk; 95% CI, 95% confidence interval

*Please note: Dose-response meta-analyses were not included in our review.*
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