Supplementary material

Search strategy

Pubmed

(colorectal[All Fields] OR ("colon"[MeSH Terms] OR "colon"[All Fields]) OR ("rectum"[MeSH Terms] OR "rectum"[All Fields])) AND (("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields]) OR ("tumour"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "tumor"[All Fields]) OR ("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "neoplasm"[All Fields]) OR ("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "malignancy"[All Fields]) OR ("adenoma"[MeSH Terms] OR "adenoma"[All Fields])) AND (("phytoestrogens"[Pharmacological Action] OR "phytoestrogens"[MeSH Terms] OR "phytoestrogens"[All Fields] OR "phytoestrogen"[All Fields]) OR ("isoflavones"[MeSH Terms] OR "isoflavones"[All Fields] OR "isoflavone"[All Fields]) OR ("lignans"[MeSH Terms] OR "lignans"[All Fields] OR "lignan"[All Fields])).

Embase

colorectal OR 'colon'/exp OR colon OR 'rectum'/exp OR rectum AND ('cancer'/exp OR cancer OR 'tumor'/exp OR tumor OR 'neoplasm'/exp OR neoplasm OR malignancy OR 'adenoma'/exp OR adenoma) AND ('phytoestrogen'/exp OR phytoestrogen OR 'isoflavone'/exp OR isoflavone OR 'lignan'/exp OR lignan)

The Newcastle-Ottawa quality assessment Scale (NOS)

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

**CASE-CONTROL STUDIES**

**Selection**

1) Is the case definition adequate?

a) yes, with independent validation **☆**

b) yes, eg record linkage or based on self reports

c) no description

2) Representativeness of the cases

a) consecutive or obviously representative series of cases **☆**

b) potential for selection biases or not stated

3) Selection of Controls

a) community controls **☆**

b) hospital controls

c) no description

4) Definition of Controls

a) no history of disease (endpoint) **☆**

b) no description of source

**Comparability**

1) Comparability of cases and controls on the basis of the design or analysis

a) study matches/adjusts for age, sex **☆**

b) study adjusts for any additional factor **☆**

**Exposure**

1) Ascertainment of exposure

a) secure record (eg surgical records) **☆**

b) structured interview where blind to case/control status **☆**

c) interview not blinded to case/control status

d) written self report or medical record only

e) no description

2) Same method of ascertainment for cases and controls

a) yes **☆**

b) no

3) Non-Response rate

a) same rate for both groups **☆**

b) non respondents described

c) rate different and no designation

**COHORT STUDIES**

**Selection**

1) Representativeness of the exposed cohort

a) representative of the general population **☆**

b) selected group of users eg nurses, volunteers

c) no description of the derivation of the cohort

2) Selection of the non exposed cohort

a) drawn from the same community as the exposed cohort **☆**

b) drawn from a different source

c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure

a) secure record (eg surgical records) **☆**

b) structured interview **☆**

c) written self report

d) no description

4) Demonstration that outcome of interest was not present at start of study

a) yes **☆**

b) no

**Comparability**

1) Comparability of cohorts on the basis of the design or analysis

a) study adjusts for age,sex **☆**

b) study adjusts for any additional factor **☆**

**Outcome**

1) Assessment of outcome

a) independent blind assessment **☆**

b) record linkage **☆**

c) self report

d) no description

2) Was follow-up long enough for outcomes to occur

a) yes (>5 years) **☆**

b) no

3) Adequacy of follow up of cohorts

a) complete follow up - all subjects accounted for **☆**

b) subjects lost to follow up unlikely to introduce bias ( small number lost, > 80% follow up, or description provided of those lost) **☆**

c) follow up rate < 80% and no description of those lost

d) no statement

Table S1 Meta-analyses of the association (highest vs. lowest categories) between exposure to overall phytoestrogens and colorectal cancer by adjustment factors from random-effect models

|  |  |  |  |
| --- | --- | --- | --- |
| **Group** | **Colorectal cancer only** |  | **Colorectal cancer and adenoma** |
|  | **No. of studies** | **Pooled RR****(95% CI)** | **I2 (%)** | **P-h\*** |  | **No. of studies** | **Pooled RR** **(95% CI)** | **I2 (%)** | **P-h\*** |
| ***Cohort studies*** | 6 | 0.95 (0.85-1.06) | 0 | 0.35 |  | 6 | 0.95 (0.85-1.06) | 0 | 0.35 |
| *BMI* |  |  |  |  |  |  |  |  |  |
| No | 0 | NA | NA | NA |  | 0 | NA | NA | NA |
| Yes | 6 | 0.95 (0.85-1.06) | 0 | 0.35 |  | 6 | 0.95 (0.85-1.06) | 0 | 0.35 |
| *Physical activity* |  |  |  |  |  |  |  |  |  |
| No | 0 | NA | NA | NA |  | 0 | NA | NA | NA |
| Yes | 6 | 0.95 (0.85-1.06) | 0 | 0.35 |  | 6 | 0.95 (0.85-1.06) | 0 | 0.35 |
|  *Total energy intake* |  |  |  |  |  |  |  |  |  |
| No | 0 | NA | NA | NA |  | 0 | NA | NA | NA |
| Yes | 6 | 0.95 (0.85-1.06) | 0 | 0.35 |  | 6 | 0.95 (0.85-1.06) | 0 | 0.35 |
|  *Family history of colorectal cancer* |  |  |  |  |  |  |  |
| No | 4 | 1.01 (0.87-1.20) | 0 | 0.45 |  | 4 | 1.01 (0.87-1.20) | 0 | 0.45 |
| Yes | 2 | 0.88 (0.71-1.08) | 38 | 0.20 |  | 2 | 0.88 (0.71-1.08) | 38 | 0.20 |
| *NSAIDs use* |  |  |  |  |  |  |  |  |  |
| No | 5 | 0.94 (0.84-1.05) | 0 | 0.65 |  | 5 | 0.94 (0.84-1.05) | 0 | 0.65 |
| Yes | 1 | 1.70 (0.88-3.28) | 0 | 1.00 |  | 1 | 1.70 (0.88-3.28) | 0 | 1.00 |
| ***Case-control studies*** | 6 | 0.76 (0.69-0.84) | 0 | 0.51 |  | 8 | 0.75 (0.68-0.82) | 0 | 0.67 |
| *BMI* |  |  |  |  |  |  |  |  |  |
| No | 2 | 0.72 (0.62-0.84) | 0 | 0.85 |  | 2 | 0.72 (0.62-0.84) | 0 | 0.85 |
| Yes | 4 | 0.79 (0.69-0.90) | 0 | 0.33 |  | 6 | 0.76 (0.68-0.86) | 0 | 0.49 |
| *Physical activity* |  |  |  |  |  |  |  |  |  |
| No | 1 | 0.71 (0.59-0.86) | 0 | 1.00 |  | 2 | 0.70 (0.59-0.83) | 0 | 0.75 |
| Yes | 5 | 0.77 (0.69-0.87) | 0 | 0.45 |  | 6 | 0.77 (0.69-0.86) | 0 | 0.54 |
|  *Total energy intake* |  |  |  |  |  |  |  |  |
| No | 0 | NA | NA | NA |  | 1 | 0.66 (0.44-0.99) | 0 | 1.00 |
| Yes | 6 | 0.76 (0.69-0.84) | 0 | 0.51 |  | 7 | 0.75 (0.69-0.83) | 0 | 0.61 |
|  *Family history of colorectal cancer* |  |  |  |  |  |  |  |
| No | 2 | 0.72 (0.62-0.84) | 0 | 0.85 |  | 2 | 0.72 (0.62-0.84) | 0 | 0.85 |
| Yes | 4 | 0.78 (0.69-0.90) | 0 | 0.33 |  | 6 | 0.77 (0.68-0.86) | 0 | 0.49 |
| *NSAIDs use* |  |  |  |  |  |  |  |  |  |
| No | 4 | 0.74 (0.66-0.82) | 0 | 0.96 |  | 4 | 0.74 (0.66-0.82) | 0 | 0.96 |
| Yes | 2 | 0.74 (0.45-1.22) | 66 | 0.09 |  | 4 | 0.74 (0.60-0.92) | 36 | 0.22 |
| Abbreviations: RR Relative risk; CI confidence interval; NA not applicable; NSAID Nonsteroidal anti-inflammatory drug |
| **\***Heterogeneity within subgroup |  |  |  |  |