Dietary flavonoid intake and the risk of digestive tract cancers: a systematic review and meta-analysis

Yacong Bo1, Jinfeng Sun2, Mengmeng Wang3, Jizhe Ding4, Quanjun Lu5 & Ling Yuan6

Several epidemiological studies have investigated the association between dietary flavonoid intake and digestive tract cancers risk; however, the results remain inconclusive. The aim of our study was to evaluate this association. PubMed and the Web of Knowledge were searched for relevant publications from inception to October 2015. The risk ratio (RR) or odds ratio (OR) with the 95% confidence interval (95% CI) for the highest versus the lowest categories of flavonoid intake were pooled using a fixed-effects model. A total of 15 articles reporting 23 studies were selected for the meta-analysis. In a comparison of the highest versus the lowest categories of dietary flavonoid intake, we found no significant association between flavonoid intake and oesophageal cancer (OR = 0.91, 95% CI = 0.75–1.10, I² = 0.0%), colorectal cancer (OR = 1.02, 95% CI = 0.92–1.14, I² = 36.2%) or gastric cancer (OR = 0.88; 95% CI = 0.74–1.04, I² = 63.6%). The subgroup analysis indicated an association between higher flavonoid intake and a decreased risk of gastric cancer in the European population (OR = 0.78, 95% CI = 0.62–0.97). In conclusion, the results of this meta-analysis do not strongly support an association between dietary flavonoid intake and oesophageal or colorectal cancer. Furthermore, the subgroup analysis suggested an association between higher dietary flavonoid intake and decreased gastric cancer risk in European population.

Digestive tract cancers are very common malignant tumours worldwide and are an important cause of cancer-related death1,2. Globocan 2012 showed that the standardised incidences of colorectal cancer, gastric cancer, and oesophageal cancer placed them in the 4th, 6th, and 10th positions among all tumours, respectively3.

Epidemiological evidence suggests that diet may play an important role in the aetiology of digestive tract cancer risk1–6. Diets high in fruits and vegetables are inversely associated with the incidence of digestive tract cancers5–8. Flavonoids are a group of bioactive polyphenols that are abundant in plant-based foods, such as fruits and vegetables1. The biological effects of flavonoids for cancer prevention include the regulation of cell signaling and the cell cycle, antimitogenic and antiproliferative properties, free radical scavenging, and inhibition of angiogenesis9,10.

Several epidemiological studies have investigated the relationship between flavonoid intake and digestive tract cancer risk. However, these results are controversial. A systematic review of the literature to date might be helpful for confirming any such association. Therefore, the objective of the present study was to determine, in a meta-analysis, whether an association exists between dietary flavonoid intake and cancers of the digestive tract.

1Department of Nutrition and Food Hygiene, College of Public Health, Zhengzhou University, 450001 Zhengzhou, Henan, China. 2Department of Social Medicine and Health Service Management, College of Public Health, Zhengzhou University, Zhengzhou, PR China. 3Department of Nutrition and Food Hygiene, College of Public Health, Zhengzhou University, 450001 Zhengzhou, Henan, China. 4Department of Nutrition and Food Hygiene, College of Public Health, Zhengzhou University, 450001 Zhengzhou, Henan, China. 5Department of Nutrition and Food Hygiene, College of Public Health, Zhengzhou University, 450001 Zhengzhou, Henan, China. 6Department of radiotherapy, Affiliated Tumor Hospital of Zhengzhou University, Henan Tumor Hospital, 450003 Zhengzhou, Henan, China. Correspondence and requests for materials should be addressed to Q.L. (email: lqjnutr@zzu.edu.cn) or L.Y. (email: hnyl2001@126.com)
Materials and Methods

Search strategy. The electronic databases PubMed and Web of Knowledge (through October 2015) were searched to identify eligible studies. The following keywords were used: “flavonoids” OR “flavanones”, OR “flavones”, “anthocyanidins” OR “catechin” combined with “oesophagus cancer” OR “oesophageal squamous cell carcinoma”, “colorectal cancer” OR “colon cancer” OR “rectal cancer”, “gastric cancer” OR “stomach cancer”. Besides, we checked the reference list of all articles of interest to identify additional eligible publications.

Study selection. The articles selected met the following criteria: (1) the studies were designed as cohort or case–control studies; (2) the exposure of interest was total dietary flavonoid intake; (3) the outcome of interest was the incidence of digestive tract cancers, including oesophageal cancer, gastric cancer, and colorectal cancer; (4) the odds ratios (ORs) or relative risk (RR) estimates with 95% confidence intervals (95% CI) were reported or could be calculated. If data were duplicated in more than one study, the one with the largest number of cases or the longest follow-up period was included in the meta-analysis.

Data extraction. Two authors (Yacong Bo and Jinfeng Sun) independently extracted the following information from each study: the first author's last name, year of publication, country, study design (case-control or cohort), patient characteristics (including sample size, gender, and mean age), the reported ORs (RRs) with 95% CIs for the highest versus the lowest categories of flavonoid intake, and variables adjusted in the analysis of each study. The ORs (RRs) that reflected the greatest degree of control for potential confounders were adopted in this meta-analysis. Any disagreements were resolved by a third investigator.

Statistical analysis. The pooled ORs with 95% CIs (highest compared to the lowest category of flavonoid intake) were computed from the adjusted ORs and RRs to measure the association between dietary flavonoid intake and the risk of digestive tract cancers.

The extent of heterogeneity across studies was determined using a chi-square test and an I² test; if I² < 0.05 and/or I² > 50%, indicating significant heterogeneity, a random-effect model was selected. Otherwise, a fixed-effect model was applied. Meta-regression and subgroup analyses were performed to explore the possible source of heterogeneity, such as geographic region, experimental design, sample size and publication year. Subgroup analyses were also performed to evaluate the potential effect of the modification of variables, including the study design, geographic region, cancer subtype, and dose. Begg's funnel plots and Egger's linear regression test were performed to assess the publication bias. A value of P < 0.05 was considered statistically significant.

All analyses were conducted using STATA software (version 12.0; StatCorp, College Station, TX, USA) and a value of P < 0.05 was considered as statistically significant.

Results

Literature search and study characteristics. The electronic search of PUBMED and web of knowledge identified a total of 1595 potentially relevant articles. Fifty-one articles were reviewed in full after reviewing the title and abstract. Among them, 7 articles were reviews, 27 articles reported sub-class flavonoids, and 2 articles reported flavonoid supplements. As a result, 15 articles reporting 23 studies, encompassing 312,734 digestive tract cancer cases and 1,142,276 controls were selected for the meta-analysis. The detailed steps of our literature search are shown in Fig. 1, and the main characteristics of the included studies are shown in Table 1.

Flavonoid intake and overall digestive tract cancer risk. We pooled the study-specific ORs using a fixed-effect model. No significant associations were detected between the highest compared with the lowest category of flavonoid intake and digestive tract cancers (overall OR = 0.96, 95% CI = 0.89–1.05, I² = 36.1%) (Fig. 2).

Flavonoid intake and oesophageal cancer risk. Seven studies examined the association between flavonoid intake and oesophageal cancer risk. The pooled OR of oesophageal cancer for the highest versus lowest categories of flavonoid intake was 0.91 (95% CI = 0.75–1.10, I² = 0.0%), suggesting that flavonoid intake was not significantly associated with the risk of oesophageal cancer (Fig. 2).

As shown in Table 2, a subgroup analysis was conducted by geographic location, study design, and histological type. However, non-significant associations of dietary flavonoid intake with oesophageal cancer were detected among all strata for the between-study subgroup analyses.

Flavonoid intake and colorectal cancer risk. A total of eight studies assessed the association between dietary flavonoid intake and colorectal cancer risk. The pooled OR of colorectal cancer risk for the highest versus the lowest categories of flavonoid intake was 1.02 (95% CI = 0.92–1.14, I² = 36.2%), indicating that flavonoid intake was not significantly associated with colorectal cancer risk.

The subgroup analysis indicated that dietary flavonoid intake has no significant effect on colorectal cancer risk in the US or European population. For colorectal cancer subtypes, no significant association was found between flavonoid intake and colon cancer (pooled OR = 0.92, 95% CI = 0.80–1.05) or rectal cancer (pooled OR = 0.90, 95% CI = 0.75–1.08), as shown in Table 2.

Flavonoid intake and gastric cancer risk. Six studies investigated flavonoid intake and gastric cancer risk. As shown in Fig. 2, the meta-analyses demonstrated no significant association between gastric cancer risk and flavonoid intake (OR = 0.88; 95% CI = 0.74–1.04, I² = 63.6%) for a comparison of the highest to the lowest category of intake.

In the subgroup analysis, we found that flavonoid intake was significantly associated with gastric cancer risk in Europe (pooled OR = 0.78, 95% CI = 0.62–0.97), but not in the United States or Asia (Table 2). With respect
to study design, we did not find that flavonoid intake was statistically associated with gastric cancer in either the cohort (pooled OR = 0.86, 95% CI = 0.67–1.09) or case-control studies (pooled OR = 0.90, 95% CI = 0.72–1.13).

**Heterogeneity analysis.** For most of the outcomes of digestive tract cancer, the I² values of heterogeneity were lower than 50%. Only the levels of heterogeneity for gastric cancer were intermediate (I² = 63.6%). To explore the sources of heterogeneity, we performed subgroup analyses with stratification by geographic location and study design. We found that flavonoid intake was significantly associated with gastric cancer risk in Europeans (pooled OR = 0.78, 95% CI = 0.62–0.97) but not in Americans or Asians. Therefore, geographic location may partially account for the appreciable heterogeneity. Meta-regression showed that study design, geographic location, source of controls, and publication year had no significant impact on heterogeneity. Moreover, the leave-one-out analysis showed that the key contributor to heterogeneity was the study conducted by Zamora-Ros16. After excluding this study, the heterogeneity was reduced to I² = 23.4%, and the summary OR for oesophageal cancer was 1.304 (95% CI = 0.807–1.325), which was similar to the main finding.

**Publication bias.** Egger’s test showed no significant publication bias in this meta-analysis (t = −1.46, P = 0.158 for digestive tract cancers, t = −0.49, P = 0.644 for oesophageal cancer, t = −0.06, P = 0.951 for colorectal cancer, and t = −1.56, P = 0.170 for gastric cancer), and the funnel plots are shown in Fig. 3.

**Discussion**

The present meta-analysis first evaluated the association between dietary flavonoid intake and the risk of digestive tract cancers based on the highest versus the lowest categories. We found no significant association between the highest dietary flavonoid intake and oesophageal cancer, colorectal cancer, or gastric cancer. However, studies conducted in European populations indicated an association between higher flavonoid intake and a decreased risk of gastric cancer.

Previous epidemiological studies have suggested that flavonoid intake has no significant effect on breast cancer (RR = 0.98, 95% CI = 0.86–1.13) or colorectal neoplasms (RR = 1.03, 95% CI = 0.88–1.20)22. The meta-analysis also suggested a significant association between the highest category of flavonoid intake and a reduced risk of lung cancer (RR = 0.76, 95% CI = 0.63–0.92)23. The association between dietary flavonoid intake and the risk...
| First author, year | Country     | Cancer site | Study design | Dietary assessment | Participants (cases) | Intake comparison, High vs. low (mg/d) | RR (95% CI) for highest vs lowest category | Adjustment for covariates                                                                                                                                                                                                 |
|---------------------|-------------|-------------|--------------|--------------------|----------------------|-----------------------------------------|-------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| Bobe27              | America     | EC          | Case–control | 75-item FFQ        | 2406 (493)           | White: >107 vs < 43.0 Black: >99.6 vs < 38.6 | White-EAC:0.71 (0.36–1.42), White-ESCC: 1.19 (0.50–2.81), Black-ESCC: 0.72 (0.35–1.46) | smoking duration and intensity, geographical area, age, body mass index, hot tea consumption, hard liquor consumption, beer consumption, red wine consumption, white wine consumption |
| Vermeulen26         | European    | EC          | Cohort       | Validated FFQ      | 477312 (341)         | NR                                      | 0.96 (0.66–1.39)                                                                                   | center, age, sex, energy intake, body mass index, smoking intensity, educational level, physical activity, alcohol, red and processed meat, fiber, vitamin C, and carotenoids intake. |
| Petrick28           | America     | EC and GC   | Case–control | 104-item FFQ       | ≥217.36 vs. 0–63.81  | ≥217.36 vs. 0–63.81                      | EAC:0.92 (0.63–1.37) ESCC: 0.87 (0.53–1.41) GCA: 1.32 (0.87–2.00) OGA: 1.08 (0.73, 1.58) | age, sex, race, geographic centre, cigarette smoking, and dietary energy intake                                                                                                                                     |
| Rossi25             | Italy       | EC          | Case–control | 78-item FFQ        | 107 (304)            | >217.4 vs < 96.5                          | 0.99 (0.55–1.79)                                                                                   | age, sex, study center, education, alcohol consumption, tobacco smoking, body mass index and energy intake                                                                                     |
| Hirvonen19          | Finland     | CC and GC   | Cohort       | 276-item FFQ       | 25776 (CC: 133, GC: 111) | 16.3 vs. 4.2 (median)                      | CC: 1.7 (1.0–2.7) GCA: 1.2 (0.71–1.9)                                                                 | age and supplementation group                                                                                                                                                                        |
| Rossi24             | Italy       | CC          | Case–control | 78-item FFQ        | 6107 (1953)          | >191.1 vs < 75.3                          | 0.97 (0.81–1.16)                                                                                   | age, sex, study center, family history of colorectal cancer, education, alcohol consumption, body mass index, occupational physical activity, and energy intake, according to the residual model |
| Zamora-Ros23        | Spain       | CC          | Case–control | 600-item FFQ       | 825 (424)            | >167.9 vs < 68.9                          | 0.59 (0.35–0.99)                                                                                   | sex, age, BMI, energy intake, alcohol and fiber intake, red and processed meat intake, tobacco consumption, physical activity, regular drugs, and family history of colorectal cancer |
| Lin22               | America     | CC          | Cohort       | 131-item FFQ       | 107401 (878)         | >30.5 vs < 10.7                           | 1.19 (0.94–1.49)                                                                                   | adjusted for age, body mass index, family history of colorectal cancer, history of colorectal polyps, prior sigmoidoscopy screening, physical activity, smoking status, red meat intake, alcohol consumption, total energy, calcium, folate, and fiber intake, aspirin use, and multivitamin use |
| Mursu21             | Finland     | CC          | Cohort       | 4-day food recording | 2590 (55)           | NR                                      | 1.16 (0.58–2.34)                                                                                   | age and examination years, BMI, smoking status, pack-years of smoking, physical activity, alcohol, total fat, saturated fat, energy adjusted intake of fiber, vitamin C and E. |
| Simon18             | Netherlands | CC          | Cohort       | 150-item FFQ       | 3906 (2219)          | 36.0–105.0 vs. 1.4–16.0                    | 0.97 (0.76–1.23)                                                                                   | age, family history of colorectal cancer, smoking status, alcohol intake, nonoccupational physical activity, BMI and processed meat intake |
| Wang17              | America     | CC          | Cohort       | 131-item FFQ       | 38408 (3234)         | 34.55–236.38 vs. 0–11.55                  | 0.93 (0.83–1.03)                                                                                   | Age, race, total energy intake, randomized treatment assignment, smoking, alcohol use, physical activity, postmenopausal status, hormone replacement therapy use, multivitamin use, BMI, family history of colorectal cancer, ovary cancer, and breast cancer, and intake of fruit and vegetables, fiber, folate, and saturated fat |
| Knekt30             | Finnish     | CC and GC   | Cohort       | >100-item FFQ      | 10054 (CC: 90, GC: 74) | NR                                      | CC: 0.84 (0.43, 1.64) GC: 0.87 (0.44, 1.75)                                                                                           | sex, age, geographic area, occupation, smoking, and BMI                                                                                                                                 |
| Garcia-Closas29     | Spain       | GC          | Case–control | 77-item FFQ        | 708 (354)            | NR                                      | 0.44 (0.25–0.78)                                                                                   | intake of nitrates, nitrosamines, vitamin C, total energy, and total carotenoids                                                                                                                                                                |
| Woo18               | Korea       | GC          | Case–control | 103-item FFQ       | 668 (334)            | 152.3 vs. 52.5 (median)                   | 0.62 (0.36–1.09)                                                                                   | Total energy intake, H. pylori, age, sex, education, smoking status, alcohol consumption, BMI, physical activity, and consumption of pickled vegetable and red and processed meat, fruits and vegetable consumption. |

Continued
of digestive cancers identified in our meta-analysis adds new information regarding the relationship between flavonoid intake and cancer risk.

The lack of a strong association between flavonoid intake and oesophageal or colorectal cancer is particularly surprising because numerous in vitro and animal studies have demonstrated an inverse association between flavonoid and oesophageal or colorectal cancer34–37. However, many flavonoids present in foods cannot be absorbed in their native form, including esters, glycosides, and polymers38. It has been demonstrated that the amount of flavonoids that are bioavailable is only a small proportion of the ingested amount, ranging from 0.2–0.9% for tea catechins to 20% for quercetin and isoflavones39,40. In in vitro and animal studies, the intake of flavonoids is much higher than that in humans, and it remains unclear whether the beneficial antiproliferative and antioxidative effects observed during in vitro studies are also present in humans41. Other studies have also suggested that flavonoids have weaker actions in vivo than in vitro42.

Table 1. Characteristics of studies on flavonoids intake and digestive tract cancers risk. Abbreviations: FFQ, Food Frequency Questionnaire; OR, Odds Ratio; CI, Confidence Interval; GCA, Gastric Cardia Adenocarcinoma; OGA, Other Gastric Adenocarcinoma; EAC, Esophageal Adenocarcinoma; ESCC, Esophageal Squamous Cell Cancer, CC, Colorectal cancer; GC, Gastric Cancer.

| First author, year | Country  | Cancer site | Study design | Dietary assessment | Participants (cases) | Intake comparison, High vs. low (mg/d) | RR (95% CI) for highest vs lowest category | Adjustment for covariates |
|---------------------|----------|-------------|--------------|-------------------|----------------------|--------------------------------------|----------------------------------------------|---------------------------------------------|
| Zamora-Ros16        | European | GC          | Cohort       | Validated FFQ      | 477386 (683)         | >595.5 vs < 200.4                     | 0.97 (0.67–1.41) for men, 0.49 (0.30–0.80) for women | center, age, and sex and adjusted for energy intake, body mass index, smoking intensity, educational level, physical activity, alcohol, and red and processed meat intake, fiber, vitamin C, and carotenoids |

Figure 2. The forest plot between highest versus lowest categories of flavonoids intake and digestive tract cancers risk.
In the subgroup analysis by geographic location, we found an inverse association between flavonoid intake and gastric cancer in Europe but not in America or Asia. The reasons for this may include the complexity due to the presence of flavonoids from various food sources, the occurrence of a large amount of flavonoids in nature, and the diversity of dietary culture. The main dietary sources of flavonoids are fruits, vegetables, tea, and red wine. However, the flavonoids in vegetables and fruits depend on the type of cultivation, crop variety and location, as well as the specific morphological part of the plant. Moreover, we could not exclude cultural differences in the storage and preparation of foods, particularly vegetables, which may also lead to this result.

Medium heterogeneity was detected for the association between flavonoid intake and gastric cancer. A meta-regression was used to explore the sources of heterogeneity, which showed that the study design, geographic location, source of controls, and publication year had no significant impact on heterogeneity. Then, we performed subgroup analyses by study design and geographic location and found that flavonoid intake was significantly associated with gastric cancer risk in Europe, but not in America or Asia, suggesting that the intermediate heterogeneity is partially explained by geographic location. Moreover, the leave-one-out analysis showed that the key contributor to heterogeneity was the study conducted by Zamora-Ros. After excluding this study, the summary estimate was not materially altered, but the I² of heterogeneity was reduced from 63.6% to 23.4%.

The role of flavonoids in gastric carcinogenesis has been attributed to several mechanisms. Flavonoids have anticarcinogenic effects by way of their antioxidant properties, which are attributed to their ability to modulate antioxidant pathways. Moreover, flavonoids can regulate cell proliferation and apoptosis, modulate phase I and II metabolic enzymes, and affect inflammatory pathways. Another possible explanation for the protective effects of flavonoids may be their potential anti-Helicobacter pylori effect, including direct bactericidal activity, the neutralisation of VacA, the reduction of urease secretion, and interference with Toll-like receptor 4 signaling, which is unique to gastric cancer. Therefore, high dietary flavonoids intakes can possibly reduce the risk of gastric but not esophageal or colorectal cancer.

Several potential limitations of our meta-analyses should be acknowledged. The relatively small number of studies analysed makes it difficult to evaluate heterogeneity. Furthermore, we only compared the risk of cancer for those in the highest category of flavonoid intake with that of those in the lowest category of flavonoid intake, and the definition of these intake categories varied between studies. In addition, only published studies were included in the meta-analysis, which may have biased the results.

**Conclusion**

In summary, this meta-analysis provides little evidence of an association between the highest category of dietary flavonoid intake and the risk of esophageal cancer or colorectal cancer. However, a subgroup analysis...
demonstrated that dietary flavonoids could reduce the risk of gastric cancer in the European population although not the U.S. or Asian populations.

References

1. Torre, L. A. et al. Global cancer statistics, 2012. CA Cancer J Clin 65, 87–108 (2015).
2. Glade, M. J. Food, nutrition, and the prevention of cancer: a global perspective. American Institute for Cancer Research/World Cancer Research Fund, American Institute for Cancer Research, 1997. Nutrition (Burbank, Los Angeles County, Calif) 15, 523–526 (1999).
3. Woo, H. D. & Kim, J. Dietary Flavonoid Intake and Smoking-Related Cancer Risk: A Meta-Analysis. Plos One 8, e75604 (2013).
4. Vial, M., Grande, L. & Pera, M. Epidemiology of adenocarcinoma of the esophagus, gastric cardia, and upper gastric third. Recent Results Cancer Res 182, 1–17 (2010).
5. Li, B. et al. Intake of vegetables and fruit and risk of esophageal adenocarcinoma: a meta-analysis of observational studies. Eur J Nutr 53, 1511–1521 (2014).
6. Pericleous, M., Mandair, D. & Caplin, M. E. Diet and supplements and their impact on colorectal cancer. J Gastrointest Oncol 4, 409–423 (2013).
7. Luo, W.-P. et al. High consumption of vegetable and fruit colour groups is inversely associated with the risk of colorectal cancer: a case-control study. Br J Nutr 113, 1129–1138 (2015).
8. Vuong, Q. V. et al. Fruit-derived phenolic compounds and pancreatic cancer: Perspectives from Australian native fruits. J Ethnopharmacol 152, 227–242 (2014).
9. Neuhouser, M. L. Dietary flavonoids and cancer risk: Evidence from human population studies. Nutr Cancer 50, 1–7 (2004).
10. Moon, Y. J., Wang, X. D. & Morris, M. E. Dietary flavonoids: Effects on xenobiotic and carcinogen metabolism. Toxicol In vitro 20, 187–210 (2006).
11. Higgins, J. P. T., Thompson, S. G., Deeks, J. J. & Altman, D. G. Measuring inconsistency in meta-analyses. BMJ 327, 557–560 (2003).
12. Higgins, J. P. T. & Thompson, S. G. Controlling the risk of spurious findings from meta-regression. Stat Med 23, 1663–1682 (2004).
13. Li, P. et al. Association between dietary antioxidant vitamins intake/blood level and risk of gastric cancer. Int J Cancer 135, 1444–1453 (2014).
14. Begg, C. B. & Mazumdar, M. Operating characteristics of a rank correlation test for publication bias. Biometrics 50, 1088–1101 (1994).
15. Egger, M., Davey Smith, G., Schneider, M. & Minder, C. Bias in meta-analysis detected by a simple, graphical test. BMJ 315, 629–634 (1997).
16. Zamora-Ros, R. et al. Dietary flavonoid and lignan intake and gastric adenocarcinoma risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Am J Clin Nutr 96, 1398–1408 (2012).
17. Wang, L. et al. Dietary intake of selected flavonols, flavones, and flavonoid-rich foods and risk of cancer in middle-aged and older women. Am J Clin Nutr 89, 905–912 (2009).
18. Woo, H. D. et al. Dietary Flavonoids and Gastric Cancer Risk in a Korean Population. Nutrients 6, 4961–4973 (2014).
19. Hirvonen, T., Virtamo, J., Korhonen, P., Albanes, D. & Pietinen, P. Flavonol and flavone intake and the risk of cancer in male smokers (Finland). Cancer Causes Control 12, 789–796 (2001).
20. Simons, C. C. M. et al. Dietary flavanol, flavone and catechin intake and risk of colorectal cancer in the Netherlands Cohort Study. Int J Cancer 125, 2945–2952 (2009).
Dietary flavonoid intake and the risk of digestive tract cancers: a systematic review and meta-analysis

Y. Bo, M. W., J. D., Q. L., and L. Y.

Author Contributions

Q.L. and L.Y. designed the study. Y.B. and J.S. assessed the studies for inclusion, extracted the data, and assessed the validity. Y.B. and M.W. conducted the meta-analyses and tabulated the data. Y.B. and J.D. wrote the first draft of the manuscript. Q.L. and L.Y. provided critical review of the manuscript.

Additional Information

Competing financial interests: The authors declare no competing financial interests.

How to cite this article: Bo, Y. et al. Dietary flavonoid intake and the risk of digestive tract cancers: a systematic review and meta-analysis. Sci. Rep. 6, 24836; doi: 10.1038/srep24836 (2016). This work is licensed under a Creative Commons Attribution 4.0 International License. The images or other third party material in this article are included in the article’s Creative Commons license, unless indicated otherwise in the credit line; if the material is not included under the Creative Commons license, users will need to obtain permission from the license holder to reproduce the material. To view a copy of this license, visit http://creativecommons.org/licenses/by/4.0/