

1 **Association between health risk factors and dietary flavonoid intake in**
2 **cohort studies**

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Supplementary Table 1. The Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines.

| Section/topic | # | Checklist item | Reported on page # |
|---------------------------|----|---|-------------------------------|
| TITLE | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 2 |
| ABSTRACT | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| INTRODUCTION | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 3,4 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 4 |
| METHODS | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | NA |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 4,5 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 4,5 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 4,5 and Supplementary Table 2 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 5,6 and Figure 1 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 5,6 |

| | | | |
|------------------------------------|----|--|---|
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 5,6 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | NA |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 5-6 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis. | 6 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | NA |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 6 |
| RESULTS | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 7 and Figure 1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 7 and Table 1, Table 2, Supplementary Table 4 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | NA |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | Figure 2, Figure 3, Table 3 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 8-11 and Figure 2, Figure 3, Table 3, Table 4, and Supporting information |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | NA |

| | | | |
|---------------------|----|--|---------------------------------|
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 8-11 and Supporting information |
| DISCUSSION | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 11-12, 14-15 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 16 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 12-16 |
| FUNDING | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | NA |

Supplementary Table 2 Search on Pubmed database (up to 31 January 2020)

| | |
|--------------|---|
| CVD | (cardiovascular diseases[MeSH Terms] OR “cardiovascular disease”[Title/Abstract] OR “cardiovascular diseases”[Title/Abstract] OR “heart disease”[Title/Abstract] OR “heart diseases”[Title/Abstract] OR stroke*[Title/Abstract] OR “myocardial infarction”[Title/Abstract] OR “myocardial infarctions”[Title/Abstract] OR “heart attack”[Title/Abstract] OR “heart attacks”[Title/Abstract] OR “cerebrovascular disease”[Title/Abstract] OR “cerebrovascular diseases”[Title/Abstract] OR “cerebral infarction”[Title/Abstract] OR “cerebral infarctions”[Title/Abstract] OR “cerebrovascular accident”[Title/Abstract] OR “cerebrovascular accidents”[Title/Abstract] OR “sudden death”[Title/Abstract] OR “sudden deaths”[Title/Abstract] OR diabetes[MeSH Terms] OR diabetes[Title/Abstract] OR mortality[MeSH Terms] OR mortality[Title/Abstract] OR death[MeSH Terms] OR death*[Title/Abstract]) |
| POLYPHENOLS | (polyphenol[Title/Abstract] OR polyphenols[Title/Abstract] OR flavonoid[Title/Abstract] OR lignan[Title/Abstract] OR isoflavone[Title/Abstract] OR anthocyanins[Title/Abstract] OR flavan-3ols[Title/Abstract] OR flavanols[Title/Abstract] OR flavonols[Title/Abstract] OR flavones[Title/Abstract] OR flavanones[Title/Abstract] OR isoflavonoids[Title/Abstract]) |
| STUDY DESIGN | (cohort[Title/Abstract] OR prospective[Title/Abstract] OR follow-up[Title/Abstract] OR longitudinal[Title/Abstract]) |

Supplementary Table 3 Quality included studies - NOS scale

| Author | Representativeness of the exposed cohort | Selection of the non-exposed cohort | Ascertainment of exposure | Demonstration that outcome of interest was not present at start | Comparability of cohorts on the basis of the design or analysis* | Comparability of cohorts on the basis of the design | Assessment of outcome | Was follow-up long enough for outcomes to occur | Adequacy of follow up of cohorts | Total score |
|-------------------------------|--|-------------------------------------|---------------------------|---|--|---|-----------------------|---|----------------------------------|-------------|
| Flavonols and flavones | | | | | | | | | | |
| Knekt, 1996 | * | * | - | * | * | - | * | * | * | 7 |
| Rimm, 1996 | - | * | * | * | * | * | * | * | * | 8 |
| Hirvonen, 2001 | - | * | * | * | * | * | * | * | * | 8 |
| Sesso, 2003 | - | * | * | * | * | * | * | * | * | 8 |
| Flavonoids | | | | | | | | | | |
| Mink, 2007 | - | * | * | * | * | - | * | * | - | 6 |
| Mursu, 2008 | * | * | - | * | * | - | * | * | * | 7 |
| Cassidy, 2012 | - | * | * | * | * | * | * | * | * | 8 |
| McCullough, 2012 | * | * | * | * | * | * | * | * | * | 9 |
| Ivey, 2015 | - | * | * | - | - | - | * | * | * | 5 |
| Ponzo, 2015 | - | * | * | - | * | - | * | * | * | 6 |
| Goetz, 2016 (CHD) | * | * | * | * | * | * | * | * | - | 8 |
| Dalgaard, 2019 | - | * | * | * | * | - | * | * | * | 7 |

* adjustment for sex, age, bmi/energy, ** adjustment for family history of CVD/CVD risk factors

Supplementary Table 4 Source of the information about selected health risk factors

| | |
|---|--|
| BMI [kg/m²] | (Knekt, Jarvinen et al. 1996), (Rimm, Katan et al. 1996), (Sesso, Gaziano et al. 2003), (Mink, Scrafford et al. 2007), (Mursu, Voutilainen et al. 2008), (Cassidy, Rimm et al. 2012), (Rimm et al. 2014), (Ponzo, Goitre et al. 2015), (Goetz, Judd et al. 2016), (Dalgaard, Bondonno et al. 2019), (Hirvonen, Pietinen et al. 2001), (Hirvonen, Pietinen et al. 2001) |
| Vitamin C [mg/d] | (Knekt, Jarvinen et al. 1996), (Mink, Scrafford et al. 2007), (Mursu, Voutilainen et al. 2008), (Ponzo, Goitre et al. 2015), (Goetz, Judd et al. 2016), (Hirvonen, Pietinen et al. 2001) |
| Folate [µg/d] | (Sesso, Gaziano et al. 2003), (Mink, Scrafford et al. 2007), (Mursu, Voutilainen et al. 2008), (Cassidy, Rimm et al. 2012), (Goetz, Judd et al. 2016), |
| Energy intake [kcal/d] | (Knekt, Jarvinen et al. 1996), (Rimm, Katan et al. 1996), (Sesso, Gaziano et al. 2003), (Mink, Scrafford et al. 2007), (Mursu, Voutilainen et al. 2008), (Cassidy, Rimm et al. 2012), (McCullough, Peterson et al. 2012), (Ponzo, Goitre et al. 2015), (Goetz, Judd et al. 2016), (Dalgaard, Bondonno et al. 2019), (Hirvonen, Pietinen et al. 2001) |
| Vitamin E [mg/d] | (Knekt, Jarvinen et al. 1996), (Mursu, Voutilainen et al. 2008), (Ponzo, Goitre et al. 2015), (Goetz, Judd et al. 2016), (Hirvonen, Pietinen et al. 2001) |
| Fiber [g/d] | (Knekt, Jarvinen et al. 1996), (Rimm, Katan et al. 1996), (Sesso, Gaziano et al. 2003), (Mink, Scrafford et al. 2007), (Mursu, Voutilainen et al. 2008), (Cassidy, Rimm et al. 2012), (Ponzo, Goitre et al. 2015), (Goetz, Judd et al. 2016), (Dalgaard, Bondonno et al. 2019), (Hirvonen, Pietinen et al. 2001) |
| Alcohol consumption [g/d] | (Mink, Scrafford et al. 2007), (Mursu, Voutilainen et al. 2008), (Cassidy, Rimm et al. 2012), (Goetz, Judd et al. 2016), (Dalgaard, Bondonno et al. 2019), (Hirvonen, Pietinen et al. 2001) |
| Beta carotene [mg/d] | (Knekt, Jarvinen et al. 1996), (Mink, Scrafford et al. 2007), (Ponzo, Goitre et al. 2015), (Goetz, Judd et al. 2016), (Hirvonen, Pietinen et al. 2001) |
| SFA [g/d] | (Knekt, Jarvinen et al. 1996), (Rimm, Katan et al. 1996), (Sesso, Gaziano et al. 2003), (Mink, Scrafford et al. 2007), (Mursu, Voutilainen et al. 2008), (McCullough, Peterson et al. 2012), (Ponzo, Goitre et al. 2015), (Goetz, Judd et al. 2016), (Hirvonen, Pietinen et al. 2001) |
| Multivitamin supplements use [%] | (Mink, Scrafford et al. 2007), (Cassidy, Rimm et al. 2012), (McCullough, Peterson et al. 2012), (Ponzo, Goitre et al. 2015) |
| Smoking status [%] | (Knekt, Jarvinen et al. 1996), (Rimm, Katan et al. 1996), (Sesso, Gaziano et al. 2003), (Mink, Scrafford et al. 2007), (Mursu, Voutilainen et al. 2008), (Cassidy, Rimm et al. 2012), (McCullough, Peterson et al. 2012), (Ivey, Hodgson et al. 2015), (Ponzo, Goitre et al. 2015), (Goetz, Judd et al. 2016), (Dalgaard, Bondonno et al. 2019) |
| Hypertension [%] | (Knekt, Jarvinen et al. 1996), (Rimm, Katan et al. 1996), (Sesso, Gaziano et al. 2003), (Mink, Scrafford et al. 2007), (Mursu, Voutilainen et al. 2008), (Cassidy, Rimm et al. 2012), (Ponzo, Goitre et al. 2015), (Goetz, Judd et al. 2016), (Dalgaard, Bondonno et al. 2019) |
| Hipercholesterolemia [%] | (Rimm, Katan et al. 1996), (Sesso, Gaziano et al. 2003), (Cassidy, Rimm et al. 2012), (McCullough, Peterson et al. 2012), (Dalgaard, Bondonno et al. 2019) |
| Vitamin E [%] | (Rimm, Katan et al. 1996), (McCullough, Peterson et al. 2012), |
| High physical activity [%] | (Sesso, Gaziano et al. 2003), (Mink, Scrafford et al. 2007), (McCullough, Peterson et al. 2012), (Goetz, Judd et al. 2016), (Hirvonen, Pietinen et al. 2001) |
| Low physical activity [%] | (Sesso, Gaziano et al. 2003), (Ivey, Hodgson et al. 2015), (Goetz, Judd et al. 2016) |
| Diabetes [%] | (Rimm, Katan et al. 1996), (Sesso, Gaziano et al. 2003), (Mink, Scrafford et al. 2007), (Mursu, Voutilainen et al. 2008), (Cassidy, Rimm et al. 2012), (Ponzo, Goitre et al. 2015), (Goetz, Judd et al. 2016), (Dalgaard, Bondonno et al. 2019) |
| Aspirin use [%] | (Mink, Scrafford et al. 2007), (Cassidy, Rimm et al. 2012), (McCullough, Peterson et al. 2012), (Ponzo, Goitre et al. 2015), (Dalgaard, Bondonno et al. 2019) |

Supplementary Table 5 Subgroup analyses by gender for association between selected variables and flavonoid intake, bivariate meta-analysis of linear regression coefficients

| Variable | Males | | | Females | | | Both gender | | |
|-------------------------------------|--------------------|----------------------|-------|--------------------|-----------------------|--------|--------------------|----------------------|--------|
| | datasets (studies) | slope* | p** | datasets (studies) | slope* | p** | datasets (studies) | slope* | p** |
| Multivitamin supplements [%] | 1 (1) | 2.21 (-13.57; 17.99) | 0.326 | 3 (3) | 1.01 (0.17; 1.85) | 0.018 | 1 (1) | 0.02 (-0.09; 0.14) | 0.236 |
| Current smoking [%] | 2 (2) | -2.39 (-5.07; 0.28) | 0.079 | 4 (4) | -0.98 (-1.85; -0.11) | 0.027 | 3 (3) | -1.77 (-3.12; -0.42) | 0.010 |
| Hypertension [%] | 2 (2) | -0.37 (-0.76; 0.01) | 0.059 | 3 (3) | -0.02 (-0.23; 0.2) | 0.888 | 3 (3) | -0.22 (-0.44; -0.01) | 0.044 |
| High physical activity [%] | 1 (1) | 0.99 (-13.61; 15.59) | 0.546 | 2 (2) | 1.98 (0.3; 3.65) | 0.021 | 1 (1) | 0.74 (-0.68; 2.16) | 0.194 |
| Diabetes [%] | 1 (1) | 0.19 (-0.9; 1.29) | 0.526 | 2 (2) | 0.1 (-0.04; 0.24) | 0.176 | 3 (3) | -0.19 (-0.43; 0.05) | 0.114 |
| BMI [kg/m²] | 1 (1) | -0.06 (-0.12; 0.01) | 0.06 | 2 (2) | -0.04 (-0.09; 0) | 0.041 | 3 (3) | -0.11 (-0.14; -0.08) | <0.001 |
| VitaminC [mg/d] | 1 (1) | 2.34 (-16.35; 21.03) | 0.644 | 1 (1) | 12.82 (1.12; 24.53) | 0.040 | 2 (2) | 2.94 (-0.47; 6.35) | 0.091 |
| Folate [µg/d] | 1 (1) | 6.76 (-7.39; 20.9) | 0.176 | 2 (2) | 17.59 (4.33; 30.85) | 0.009 | 1 (1) | 8.91 (-8.81; 26.63) | 0.208 |
| Energy intake [kcal/d] | 2 (2) | -7.59 (-29.58; 14.4) | 0.499 | 3 (3) | 17.28 (-66.7; 101.27) | 0.687 | 3 (3) | 29.27 (8.2; 50.34) | 0.006 |
| VitaminE [mg/d] | 1 (1) | 0.13 (-0.42; 0.69) | 0.413 | - | - | - | 2 (2) | 0.04 (0; 0.08) | 0.051 |
| Fiber [g/d] | 1 (1) | 0.39 (-1.03; 1.82) | 0.355 | 2 (2) | 0.84 (-0.08; 1.76) | 0.074 | 3 (3) | 0.53 (0.14; 0.91) | 0.007 |
| Alcohol [g/d] | 1 (1) | -0.63 (-2.04; 0.78) | 0.194 | 2 (2) | -0.36 (-0.52; -0.19) | <0.001 | 2 (2) | -0.09 (-0.54; 0.35) | 0.679 |
| Beta carotene [mg/d] | - | - | - | 1 (1) | 0.45 (0.14; 0.76) | 0.018 | 2 (2) | 0.14 (0; 0.27) | 0.049 |
| Saturated fat [g/d] | 2 (2) | -0.74 (-1.53; 0.04) | 0.063 | 2 (2) | -0.68 (-0.94; -0.43) | <0.001 | 2 (2) | -0.34 (-1.88; 1.2) | 0.662 |

*per 100 mg flavonoids, **p for significance of slope

Supplementary Table 6 Subgroup analyses by geographical region for association between selected variables and flavonoid intake, bivariate meta-analysis of linear regression coefficients

| Variable | Europe | | | | US | | | |
|-------------------------------------|--------------------|---------------------------|-----------------------|--------|--------------------|----------------------------|----------------------|--------|
| | datasets (studies) | intercept | slope* | p** | datasets (studies) | intercept | slope* | p** |
| Multivitamin supplements [%] | 1 (1) | 3.26 (2.86; 3.67) | 0.02 (-0.09; 0.14) | 0.236 | 4 (3) | 35.94 (30.17; 41.71) | 1.16 (0.35; 1.97) | 0.005 |
| Current smoking [%] | 3 (3) | 37.48 (27.06; 47.9) | -2.43 (-3.05; -1.8) | <0.001 | 5 (4) | 12.05 (6.03; 18.07) | -0.78 (-1.37; -0.19) | 0.010 |
| Hypertension [%] | 3 (3) | 27.56 (2.04; 53.08) | -0.3 (-0.89; 0.29) | 0.314 | 5 (4) | 37.27 (27.67; 46.88) | -0.25 (-0.55; 0.05) | 0.107 |
| High physical activity [%] | - | - | - | - | 4 (3) | 22.5 (16.23; 28.77) | 1.43 (0.49; 2.38) | 0.003 |
| Diabetes [%] | 3 (3) | 3.47 (1.76; 5.18) | 0.06 (-0.06; 0.18) | 0.319 | 3 (3) | 9.24 (-0.47; 18.95) | -0.06 (-0.43; 0.32) | 0.769 |
| BMI [kg/m²] | 3 (3) | 26.56 (26.18; 26.93) | -0.08 (-0.13; -0.04) | <0.001 | 3 (3) | 27.35 (25.41; 29.28) | -0.06 (-0.1; -0.01) | 0.017 |
| VitaminC [mg/d] | 2 (2) | 103.36 (39.77; 166.94) | 2 (-0.32; 4.31) | 0.091 | 2 (2) | 107.04 (81.49; 132.59) | 8.66 (-0.88; 18.2) | 0.075 |
| Folate [µg/d] | 1 (1) | 246.83 (215.31; 278.36) | 6.76 (-7.39; 20.9) | 0.176 | 3 (3) | 353.72 (312.69; 394.75) | 15.36 (5.65; 25.07) | 0.002 |
| Energy intake [kcal/d] | 3 (3) | 2113.39 (1916.1; 2310.68) | 23.95 (-10.06; 57.97) | 0.168 | 5 (4) | 1732.02 (1569.33; 1894.72) | 8.74 (-41.74; 59.23) | 0.734 |
| VitaminE [mg/d] | 2 (2) | 8.42 (7.68; 9.15) | 0.08 (-0.03; 0.18) | 0.174 | 1 (1) | 9.4 (6.9; 11.91) | 0.06 (-0.77; 0.89) | 0.832 |
| Fiber [g/d] | 3 (3) | 20.39 (15.76; 25.01) | 0.48 (0.23; 0.74) | <0.001 | 3 (3) | 15.82 (14.8; 16.85) | 0.69 (0.06; 1.32) | 0.032 |
| Alcohol [g/d] | 2 (2) | 11.75 (9.96; 13.54) | -0.21 (-1.01; 0.58) | 0.599 | 3 (3) | 5.53 (4.71; 6.34) | -0.33 (-0.45; -0.22) | <0.001 |
| Beta carotene [mg/d] | 1 (1) | 2.76 (-1.65; 7.17) | 0.23 (-1.05; 1.52) | 0.261 | 2 (2) | 3.81 (2.77; 4.86) | 0.27 (-0.09; 0.63) | 0.140 |
| Saturated fat [g/d] | 2 (2) | 37.13 (18.18; 56.09) | -0.17 (-1.3; 0.96) | 0.764 | 4 (3) | 22.86 (19.9; 25.81) | -0.74 (-0.98; -0.5) | <0.001 |

*per 100 mg flavonoids, **p for significance of slope

Supplementary Table 7 Subgroup analyses by subclasses of flavonoids included to calculation total sum of flavonoid intake (with or without proanthocyanidins), bivariate meta-analysis of linear regression coefficients

| Variable | Flavonoids with proanthocyanidins | | | | | Flavonoids without proanthocyanidins | | | | |
|-------------------------------------|-----------------------------------|----------------------------|-----------------------|--------|------------------|--------------------------------------|----------------------------|----------------------|--------|------------------|
| | datasets (studies) | intercept | slope* | p** | I ² # | datasets (studies) | intercept | slope* | p** | I ² # |
| Multivitamin supplements [%] | 4 (3) | 27.29 (10.79; 43.79) | 1.24 (0.4; 2.07) | 0.004 | 89.6 | 1 (1) | 36.93 (30.91; 42.94) | 0.27 (-1.24; 1.78) | 0.607 | - |
| Current smoking [%] | 5 (4) | 14.65 (5; 24.29) | -1.07 (-1.99; -0.16) | 0.021 | 83.6 | 4 (4) | 35.34 (20.48; 50.2) | -2.29 (-3.29; -1.28) | <0.001 | 5.2 |
| Hypertension [%] | 5 (4) | 41.87 (31.87; 51.86) | -0.39 (-0.62; -0.17) | <0.001 | 24.1 | 3 (3) | 19.62 (9.97; 29.28) | 0.01 (-0.11; 0.13) | 0.892 | 33.2 |
| High physical activity [%] | 4 (3) | 22.5 (16.23; 28.77) | 1.43 (0.49; 2.38) | 0.003 | 52.3 | - | - | - | - | - |
| Diabetes [%] | 3 (3) | 10.06 (1.08; 19.05) | -0.14 (-0.49; 0.21) | 0.436 | 53.6 | 3 (3) | 3.19 (2.02; 4.36) | 0.1 (-0.04; 0.24) | 0.161 | 91.3 |
| BMI [kg/m²] | 3 (3) | 27.68 (26.17; 29.18) | -0.06 (-0.11; -0.01) | 0.015 | 11.9 | 3 (3) | 26.29 (25.79; 26.79) | -0.08 (-0.13; -0.04) | <0.001 | 80.9 |
| VitaminC [mg/d] | 3 (3) | 119.02 (95.1; 142.94) | 5.57 (-1.28; 12.42) | 0.111 | 85.1 | 1 (1) | 70.64 (28.99; 112.29) | 2.34 (-16.35; 21.03) | 0.644 | - |
| Folate [µg/d] | 2 (2) | 338.1 (293.79; 382.41) | 16.5 (0.69; 32.31) | 0.041 | 85.8 | 2 (2) | 321.63 (173.31; 469.95) | 8.58 (2.11; 15.05) | 0.009 | 25.1 |
| Energy intake [kcal/d] | 5 (4) | 1737.78 (1557.06; 1918.49) | 27.79 (-20.92; 76.49) | 0.263 | 80.5 | 3 (3) | 2094.67 (1844.99; 2344.35) | -4.2 (-35.71; 27.3) | 0.794 | 91.2 |
| VitaminE [mg/d] | 2 (2) | 8.64 (7.34; 9.95) | 0.04 (0; 0.08) | 0.051 | 1.9 | 1 (1) | 8.81 (7.57; 10.06) | 0.13 (-0.42; 0.69) | 0.413 | - |
| Fiber [g/d] | 3 (3) | 15.85 (14.71; 16.99) | 0.97 (0.17; 1.77) | 0.017 | 86.4 | 3 (3) | 19.49 (14.33; 24.66) | 0.47 (0.23; 0.71) | <0.001 | 9.8 |
| Alcohol [g/d] | 2 (2) | 5.24 (4.54; 5.94) | -0.34 (-0.49; -0.19) | <0.001 | 9.6 | 3 (3) | 9.97 (5.97; 13.97) | -0.17 (-0.45; 0.1) | 0.222 | 59.2 |
| Beta carotene [mg/d] | 3 (3) | 3.59 (2.81; 4.36) | 0.22 (-0.01; 0.45) | 0.059 | 91.1 | - | - | - | - | - |
| Saturated fat [g/d] | 5 (4) | 24.32 (21.03; 27.62) | -0.73 (-1.02; -0.44) | <0.001 | 27.3 | 1 (1) | 46.75 (40.99; 52.51) | -0.57 (-3.16; 2.01) | 0.441 | - |

*per 100 mg flavonoids, **p for significance of slope, #I² statistic for heterogeneity of slopes

Supplementary Table 8 Sensitivity analyses for alternatively accounted polyphenol intake as a sum of flavonols and flavones only, bivariate meta-analysis of linear regression coefficients

| Variable | Flavonols and flavones | | | | | Polyphenols | | | | |
|------------------------------|------------------------|-------------------------|---------------------------|-----------------|-----------------|--------------------|----------------------------|---------------------|-----------------|-----------------|
| | datasets (studies) | intercept | slope ^{&} | p ^{**} | I ^{2#} | datasets (studies) | intercept | slope [*] | p ^{**} | I ^{2#} |
| Multivitamin supplements [%] | - | - | - | - | - | 1 (1) | 15.15 (12.72; 17.59) | 0.51 (0.2; 0.82) | 0.014 | - |
| Current smoking [%] | 4 (3) | 25.69 (3.09; 48.28) | -8.2 (-20.91; 4.5) | 0.206 | 99.1 | 4 (4) | 21.43 (13.29; 29.57) | 0.08 (-0.02; 0.18) | 0.129 | 16.6 |
| Hypertension [%] | 4 (3) | 19.63 (14.1; 25.16) | 0.69 (0.37; 1.02) | <0.001 | 47.9 | 3 (3) | 42.43 (-9.7; 94.56) | -0.71 (-1.99; 0.56) | 0.274 | 99.7 |
| High physical activity [%] | 2 (2) | 12.87 (5.74; 19.99) | 1.72 (-0.61; 4.05) | 0.147 | 90.8 | 1 (1) | 21 (14.37; 27.62) | 0.38 (0.07; 0.7) | 0.041 | - |
| Diabetes [%] | 2 (2) | 1.76 (1.54; 1.97) | 0.33 (0.24; 0.41) | <0.001 | 0.0 | 3 (3) | 18.97 (-12.67; 50.62) | -0.1 (-0.4; 0.19) | 0.482 | 99.2 |
| BMI [kg/m ²] | 5 (4) | 25.77 (25.43; 26.12) | 0.03 (-0.02; 0.07) | 0.21 | 17.5 | 3 (3) | 25.29 (20.1; 30.47) | -0.01 (-0.09; 0.07) | 0.812 | 95.4 |
| VitaminC [mg/d] | 3 (2) | 45.84 (30.14; 61.54) | 89.71 (32.52; 146.91) | 0.002 | 98.3 | - | - | - | - | - |
| Folate [μg/d] | 1 (1) | 379.03 (323.63; 434.43) | 21.08 (0.53; 41.64) | 0.047 | - | - | - | - | - | - |
| Energy intake [kcal/d] | 5 (4) | 2158.31 (1798; 2518.62) | 471.39 (-148.86; 1091.65) | 0.136 | 100.0 | 4 (4) | 2148.39 (1785.21; 2511.57) | 3.21 (-4.14; 10.56) | 0.392 | 41.7 |
| VitaminE [mg/d] | 3 (2) | 6.71 (4.41; 9.01) | 4.21 (1.64; 6.77) | 0.001 | 97.9 | - | - | - | - | - |
| Fiber [g/d] | 5 (4) | 19.09 (15.46; 22.72) | 9.39 (0.82; 17.96) | 0.032 | 99.6 | 1 (1) | 15.47 (14.03; 16.91) | 0.14 (-0.05; 0.33) | 0.085 | - |
| Alcohol [g/d] | 1 (1) | 11.52 (10.57; 12.48) | -0.48 (-1.39; 0.43) | 0.194 | - | 2 (2) | 14.86 (-7.26; 36.98) | -0.09 (-0.69; 0.52) | 0.778 | 77.1 |
| Beta carotene [mg/d] | 3 (2) | 0.99 (0.66; 1.31) | 2.23 (0.75; 3.71) | 0.003 | 97.0 | - | - | - | - | - |
| Saturated fat [g/d] | 5 (4) | 43.32 (26.59; 60.05) | 4.26 (-5.43; 13.96) | 0.389 | 99.9 | 1 (1) | 38.94 (28.24; 49.64) | -0.75 (-2.11; 0.61) | 0.178 | - |

[&]per 10 mg flavonols and flavones, ^{*}per 100 mg flavonoids, ^{**}p for significance of slope, [#]I² statistic for heterogeneity of slopes