Supplementary Table 1. Quality assessment of the included studies with the Newcastle-Ottawa scale

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| First author | Representation of the exposed cohort | Selection of the unexposed cohort | Ascertainment  of exposure | Demonstration that outcome of interest at start of study | Comparability of cohorts on the basis of the design or analysis | Outcome assessment | Follow-up long enough for the outcomes to occur | Adequacy of follow-up of cohorts | Total quality score |
| Ding |  | ☆ |  | ☆ | ☆☆ | ☆ | ☆ | ☆ | ☆☆☆☆☆☆☆ |
| Grosso, | ☆ | ☆ |  | ☆ | ☆☆ |  |  |  | ☆☆☆☆☆ |
| Kataja-  Tuomola |  | ☆ |  |  | ☆☆ | ☆ | ☆ | ☆ | ☆☆☆☆☆☆ |
| Knekt | ☆ | ☆ |  |  | ☆☆ | ☆ | ☆ | ☆ | ☆☆☆☆☆☆☆ |
| Song |  | ☆ |  |  | ☆☆ |  | ☆ | ☆ | ☆☆☆☆☆ |
| Tresserra-  Rimbau |  | ☆ |  |  | ☆☆ | ☆ |  |  | ☆☆☆☆ |
| Wedick, |  | ☆ |  | ☆ | ☆☆ | ☆ | ☆ | ☆ | ☆☆☆☆☆☆☆ |
| Zamora-Ros | ☆ | ☆ |  | ☆ | ☆☆ | ☆ | ☆ | ☆ | ☆☆☆☆☆☆☆☆ |



Supplementary Figure 1. Forest plot to quantify the association between quercetin intake and T2DM risk.



Supplementary Figure 2. Forest plot to quantify the association between kaempferol intake and T2DM risk.



Supplementary Figure 3. Forest plot to quantify the association between myricetin intake and T2DM risk.



Supplementary Figure 4. Sensitivity analysis with respect to flavanols intake.

Supplementary Figure 5. Sensitivity analysis with respect to flavonols intake



Supplementary Figure 6. Sensitivity analysis with respect to flavanones intake.



Supplementary Figure 7. Sensitivity analysis with respect to flavan-3-ols intake.



Supplementary Figure 8. Sensitivity analysis with respect to isoflavones intake.



Supplementary Figure 9. Sensitivity analysis with respect to flavones intake.



Supplementary Figure 10. Sensitivity analysis with respect to quercetin intake.



Supplementary Figure 11. Sensitivity analysis with respect to kaempherol intake.



Supplementary Figure 12. Sensitivity analysis with respect to myricerin intake.

**The protocol of the present meta-analysis**

|  |  |
| --- | --- |
| Review question | Considering that subclasses of flavonoids have different chemical structures, dietary intakes of these flavonoids might have differential effects associated with type 2 diabetes mellitus (T2DM). Prospective cohort studies have suggested controversial associations between flavonoid subclasses and T2DM risk. Therefore, the present study aimed to clarify whether flavonoid subclasses were associated with type 2 diabetes mellitus risk. |
| Searches | (((((((((flavanol) OR flavonol) OR flavan-3-ol) OR isoflavone) OR flavanone) OR flavone) OR quercetin) OR kaempferol) OR myricetin) AND diabetes |
| URL to search strategy | <https://www.ncbi.nlm.nih.gov/pubmed>;  http://www.scopus.com |
| Condition or domain being studied | Type 2 diabetes mellitus (T2DM) is a major contemporary public issue because it is generally associated with diverse complications leading to premature mortality and morbidity. As one of the most common non-communicable diseases, the prevalence of T2DM is expected increase to 592 million in 2035 all over the world. Although a meta-analysis of prospective cohort studies indicated that flavonoid intake was inversely associated with T2DM risk, epidemiological studies have suggested controversial associations between flavonoid subclasses and T2DM risk. |
| Participants/population | Adults of any age across different countries |
| Intervention(s), exposure(s) | The highest category of flavonoid subclasses, including flavanol, flavonol, flavan-3-ol, isoflavone, flavanone, flavone, quercetin, kaempferol and myricetin |
| Comparator(s)/control | The lowest category of flavonoid subclasses |
| Types of study to be included | Prospective cohort study, including prospective cohort, nested case-control and case-cohort studies |
| Primary outcome(s) | Type 2 diabetes mellitus |
| Secondary outcome(s) | None |
| Risk of bias (quality) assessment | Begg's rank correlation test |
| Strategy for data synthesis | Quantitative synthesis |
| Analysis of subgroups or subsets | Duration of follow-up (≤ 10 or > 10 years), region (Europe or U.S), study quality (moderate or high quality) and mean age of participants (≤ 50 or > 50 years) |
| Type of review | Meta-analysis |
| Health area of the review | Endocrine and metabolic disorders |
| Language | There is an English language summary |
| Keywords | Flavonoid subclasses; type 2 diabetes mellitus; prospective cohort study; meta-analysis |
| Current review status | Completed but not published |