**Dietary components and risk of cardiovascular disease and all-cause mortality: A review of evidence from meta-analyses**

Running title: Dietary components and risk of CVD and mortality

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**Abstract**

**Aims:** The optimal diet for cardiovascular health is controversial. The aim of this review is to summarize the highest level of evidence and rank the risk associated with each individual component of diet within its food group.

**Methods and results:** A systematic search of PudMed was performed to identify the highest level of evidence available from systematic reviews or meta-analyses that evaluated different dietary components and their associated risk of all-cause mortality and cardiovascular disease (CVD). A total of 16 reviews were included for dietary food item and all-cause mortality and 17 reviews for CVD. Carbohydrates were associated with reduced risk of all-cause mortality (whole grain bread RR 0.85(95%CI 0.82-0.89), breakfast cereal RR 0.88(0.83-0.92), oats/oatmeal RR 0.88(0.83-0.92)). Fish consumption was associated with a small benefit (RR 0.98 (0.97-1.00)) and processed meat appeared to be harmful (RR 1.25(1.07-1.45)). Root vegetables (RR 0.76(0.66-0.88)), green leafy vegetables/salad (RR 0.78(0.71-0.86)), cooked vegetables (RR 0.89(0.80-0.99)) and cruciferous vegetables (RR 0.90(0.85-0.95)) were associated with reductions in all-cause mortality. Increased mortality was associated with consumption of tinned fruit (RR 1.14(1.07-1.21)). Nuts were associated with a reduced risk of mortality in a dose response relationship (all nuts RR 0.78(0.72-0.84), tree nuts RR 0.82(0.75-0.90), and peanuts RR 0.77(0.69-0.86)). For CVD, similar associations for benefit were observed for carbohydrates, nuts and fish, but red meat and processed meat were associated with harm.

**Conclusions:** Many dietary components appear to be beneficial for CVD and mortality, including grains, fish, nuts and vegetables, but processed meat and tinned fruit appear to be harmful.

**Introduction**

Cardiovascular disease (CVD) is a major global cause of health loss.1 Dietary habits, influence cardiovascular risk either through an effect of risk factors such as serum cholesterol, blood pressure, body weight and diabetes or through an effect independent of these risk factors.2 However, there is still controversy surrounding the optimal diet for cardiovascular health3 There has been exponential growth in the nutritional literature evaluating diet and cardiovascular disease. There have been reviews for specific food groups and their influence on cardiovascular health4 and further reviews of individual components of diet such as fish intake,5 cheese intake,6 butter7 and less frequently consumed components such as soy products.8 One of the advantages of evaluating individual food components, is that overall diary patterns may mask the potential effects of individual food components.9 Nevertheless, as healthcare professionals it is necessary to give more holistic dietary advice rather than just focusing on individual food items / categories. There has yet to be a single review that has collated all available evidence from prior quality meta-analyses evaluating dietary components and risk of cardiovascular disease and all-cause mortality.

We conducted an up-to-date review of systematic reviews and meta-analyses on individual components of diet and their risk of cardiovascular disease and mortality. The aim of this review is to collectively summarize the highest level of evidence from previously conducted systematic reviews and meta-analyses and rank the risk associated with each individual component of diet within its food group.

**Methods**

*Search and study identification*

We carried out a review of the literature to identify the best evidence evaluating individual dietary components and risk of cardiovascular disease or mortality.

We began by identifying the broad categories of food after reviewing the “Eatwell Guide” in the United Kingdom,10 “The Five Food Groups” in the 2015-2020 Dietary Guidelines for Americans11 and the “Food Guide Pyramid” from the Center for Nutrition Policy and Promotion in the United States.12 Once the main groups of food were identified each individual component in a typical Western diet was determined and shown in Supplementary Table 1.

For each individual component of diet, we searched for and identified the most recent and highest quality systematic review and meta-analysis evaluating the dietary component and its associated risk of adverse outcomes. This was a two-step process where first a search was performed and screened independently by two reviewers (CSK and either PW or JP). The search was performed on 13 August 2018 and we used each food category in Supplementary Table 1 as a key word on the Pubmed search. We chose to include the review with the most studies because the number of studies was part of our evidence grading criteria. The quality of the evidence for a systematic review of a food item was graded according to a modified criteria based on Grosso et al.13 The grading method has 4 levels where level 1 represents the highest level of evidence (convincing) and level 4 represents the lowest level of evidence (limited/contrasting). The exact method of grading the reviews based on inclusion of prospective cohorts, number of studies and the presence of statistical heterogeneity (I2≤30% vs I2>30%) is shown in Supplementary Table 2.

Included studies had to have the dietary component of interest and some form of quantitative association with either cardiovascular disease or mortality. Food item consumption and its association with outcome can be quantified as dose-response relationship and highest compared to lowest consumers of food items. We chose studies that considered a dose-response relationship where available.

The search process as described in this paragraph was conducted in August 2018. We initially searched PubMed using the Clinical Queries option to identify systematic reviews using the dietary component as the search term along with the terms related to outcomes. These outcome terms are: (death OR mortality OR stroke OR cerebrovascular disease OR cerebrovascular accident OR coronary heart disease OR ischemic heart disease OR ischaemic heart disease OR coronary artery disease OR acute myocardial infarction OR acute coronary syndrome OR heart failure OR cardiac failure OR cardiac insufficiency). The results of the search process are shown in Supplementary Table 1.

*Evidence synthesis*

Statistical analysis was performed by presenting all the results and ranking them according to effect within each food group. For each included meta-analysis or review for the specific foods groups, we extracted the Relative Risks (RR) and 95% confidence intervals (95% CI) from the most adjusted models presented in the review; the evidence of heterogeneity (I2) was obtained from the original source meta-analyses and reported in our Table 1. We also collected information on the quality assessments of the reviews. Results are presented numerically in Tables and Graphically in Figures. For graphical representation, the studies which reported associations of increased risk of harm were colored in red, those which showed beneficial associations were colored in green, and those which showed no statistical difference were colored in yellow. We performed additional analysis considering the impact of sex-specific differences in outcomes.

**Results**

A total of 3,011 studies were reviewed from the search shown in Supplementary Table 1. After detailed review of relevant studies, a total of 16 reviews7,14-28 were included for all-cause mortality and 17 reviews7,8,14,17-20,22,24-32 for cardiovascular disease (Supplementary Figure 1).

Supplementary Table 3 shows the quality assessment conducted in each included review. The grading of the evidence based on the criteria in Supplementary Table 3 suggested that many analyses showed the lowest or most limited (level 4) evidence mainly because there were fewer than 4 studies (Supplementary Table 4). However, for all-cause mortality, level 2 evidence was present for refined grains, green leafy vegetables/salad and tinned fruit. For cardiovascular disease, there was only level 2 evidence for fish. None of the meta-analyses were based on randomized controlled trial data.

Table 1 and Figure 1 show the food items within different food groups and their risk of all-cause mortality. For carbohydrates, there were 2 or fewer studies for the assessment of whole grain bread, pasta, whole grain breakfast cereals, oats/oatmeal. In the dose-response analysis all of these food items were associated with reduced risk of all-cause mortality (whole grain bread RR 0.85 (95% CI 0.82-0.89), pasta RR 0.85 (0.74-0.99), whole grain breakfast cereal RR 0.88 (0.83-0.92), oats/oatmeal RR 0.88 (0.83-0.92). Both intake of refined grains and fibre were associated with a significant dose response reduction in all-cause mortality (RR 0.95 (0.91-0.99), 4 studies and RR 0.90 (0.86-0.94), 8 studies, respectively). Rice was evaluated in 5 studies in the highest consumer compared to the lowest consumer analysis and no significant difference in mortality was observed.

Among meat, eggs and fish, fish consumption was associated with a small benefit for mortality (RR 0.98 (0.97-1.00)) and processed meat appeared to be harmful (RR 1.25 (1.07-1.45)). No significant differences were observed for white meat, red meat and eggs. Among fruits and vegetables, root vegetables (RR 0.76 (0.66-0.88), 1 study), green leafy vegetables/salad (RR 0.78 (0.71-0.86), 7 studies), cooked vegetables (RR 0.89 (0.80-0.99), 4 studies) and cruciferous vegetables (RR 0.90 (0.85-0.95), 6 studies) were associated with reductions in all-cause mortality. There was an association for increased mortality with a dose-response consumption of tinned fruit (RR 1.14 (1.07-1.21), 4 studies). Comparing the highest and lowest consumers of alcohol there appeared to be reduction in all-cause mortality among the highest consumers (RR 0.87 (0.83-0.92), 31 studies). Coffee also showed a dose-response association for reduced risk of all-cause mortality (RR 0.96 (0.94-0.97), 16 studies). For dairy products, there was no significant difference in risk of mortality with yogurt, cheese, milk or butter consumption. The data from nuts appeared to be associated with reduced risk of mortality in a dose response relationship (all nuts RR 0.78 (0.72-0.84), 16 studies, tree nuts RR 0.82 (0.75-0.90), 4 studies and peanuts RR 0.77 (0.69-0.86), 5 studies).

The associations between cardiovascular disease and food items are shown in Figure 2 and Table 2. Among carbohydrates, there was a dose-response association for benefit for whole grain bread (RR 0.87 (0.80-0.95), 3 studies), whole grain breakfast cereals (RR 0.84 (0.78-0.90), 2 studies), bran (RR 0.85 (0.79-0.90, 2 studies) and fibre (RR 0.91 (0.88-0.94), 10 studies). Red meat (RR 1.15 (1.05-1.26), 6 studies) and processed meat (RR 1.24 (1.09-1.40), 6 studies) appeared to be harmful. Out of all the fruits and vegetables only 1 study on raw vegetables suggested a dose-response association of benefit (RR 0.86 (0.81-0.90)). Alcohol consumption for the highest compared to the lowest consumers showed an association of reduced risk of cardiovascular disease (RR 0.75 (0.70-0.80), 21 studies). Black tea was associated with a dose-response benefit for cardiovascular mortality (RR 0.92 (0.85-0.99), 7 studies). Dairy products (yogurt, cheese, milk and butter) showed no evidence of a dose response association for benefit or harm. Intake of nuts were associated with reduced risk of cardiovascular disease (all nuts RR 0.79 (0.70-0.88), 12 studies, tree nuts RR 0.75 (0.67-0.84), 3 studies, peanuts RR 0.64 (0.50-0.81), 5 studies). In addition, olive oil showed a dose-response benefit in cardiovascular disease RR 0.82 (0.70-0.96), 9 studies and soy products as compared by highest and lowest consumers showed lower risk of cardiovascular disease (RR 0.83 (0.75-0.93)). Finally, an association for a dose response benefit was observed for chocolate (RR 0.982 (0.972-0.992), 12 studies).

The additional analysis considering differences in results based on sex showed no major differences between men and women in most studies (Supplementary Table 5).

**Discussion**

To facilitate clinician-patient communications regarding the impact of diet for cardiovascular health, we have summarized current evidence from the highest quality systematic reviews available by various food groups. We have shown that food components within food groups are associated with different risks for cardiovascular disease and all-cause mortality. Many fruits and vegetables which are presumed to be beneficial as a group actually lack strong evidence of cardiovascular benefit. The best evidence appears to support the intake of green leafy vegetables/salad to reduce all-cause mortality. On the other hand, processed meat appears to be harmful for both all-cause mortality and cardiovascular disease.

Our results are important as diet is complex and it appears that there may be dissonance between foods which are for beneficial for all-cause mortality and cardiovascular disease. We speculate that this may be because the major causes of all-cause mortality are likely a composite of cardiovascular disease and those of cancer etiology. While oxidative stress plays an important role in both atherosclerosis33 and oncogenesis34 and both cardiovascular disease and cancer share risk factors such as obesity,35 physical inactivity, diabetes36 and smoking.37 Hypertension is common and strongly associated with cardiovascular disease but the evidence of its link to cancer is less strong. Dietary elements which affect blood pressure may have greater benefits for cardiovascular disease risk whilst food items that protect from oxidative stress may have a greater protective effect for cancer.

The consideration of individual foods and food components has been highlighted as a key approach use by the public when interpreting healthy eating messages.38 We found that dietary nuts appear to be beneficial for both all-cause mortality and cardiovascular disease. Tree nuts and peanuts are foods rich in high-quality vegetable protein, fiber, minerals, tocopherols, phytosterols and phenoic compounds which beneficially impact health outcomes.39 Consumption of nuts are associated with a favorable fatty acid profile which is high in unsaturated fatty acids and low in saturated fatty acids which contributes to cholesterol lowering.40 Also, nuts have a tendency to lower body weight and fat mass and in the context of calorie-restricted diets, adding nuts promotes weight loss in obese subjects and improves insulin sensitivity.41 It has been further suggested that the benefits of the Mediterranean diet may be partly attributed to nuts.42 We believe more studies are need to examine different types of tree nuts as there was insufficient data on important nuts like almonds, cashews, macadamia nuts, pistachios and walnuts.

We found evidence that processed meat and tinned fruit may be harmful. The biggest difference among constituents of processed and unprocessed meat are sodium and nitrate which are 400% and 50% more per gram of meat.43 Blood pressure and peripheral vascular resistance increase with dietary sodium, and dietary sodium may also impair arterial compliance.44 It is further suggested that nitrates and their by-products may promote endothelial dysfunction, atherosclerosis and insulin resistance.45-47 For tinned fruit, it has been suggested that the population consuming tinned fruit tended to be male, older, report lower education level, have higher body mass index and more likely to have diabetes.48 Compared to fresh fruit, tinned fruit has added sugar which may contribute to cardiovascular mortality.49 There may also be concerns about bisphenol A which is greater in tinned fruit and the acidity of food cans may dissolve lead solder from food cans.48

There are inherent challenges and limitations in analyzing nutritional data from observational studies, yet such research has played a vital role over the years in identifying new links between food and health.50 First, it is possible that some of the food items assessed showed a non-linear dose-response relationship and estimates at high or very low doses may not be accurate. Second, multiple repeat measures are required to explore effects of variation on exposure over time so caution may be needed when interpreting risk of exposures measured only once at baseline.51 This may apply for items which are not consumed on a regular basis or food items where there is major variability such as a person who drinks alcohol regularly at low quantities daily versus a person who drinks less frequently but heavily. Third, some of the food items which show no association of benefit or harm may actually have an impact for the individual cardiovascular risk factors such as blood pressure or cholesterol levels and may be beneficial or harmful for some subgroups of the populations such as patients with diabetes. Fourth, while our results showed that certain foods appear to be beneficial or harmful it is important that these results should be taken in consideration of patients’ overall nutrition status. Fifth, even though lifestyle and socioeconomic factors may be adjusted for in the cohort studies included in our review, it is likely there is residual confounding by sociodemographic and lifestyle factors. Patients who eat “healthier” foods are also more likely to be educated, have greater income, more likely to exercise regularly, more likely to be of normal weight and body mass index, more likely be a non-smoker and have better access to healthcare, and the collective effects of these factors may not be completely accounted for in the adjustments. Sixth, another important consideration is that the comparison group is not the same across each analysis. An obvious difficulty is that eating food is essential to health and wellbeing so it would not be possible to conduct a study comparing individual food items to consuming nothing and there is no obvious single food reference to compare to. Furthermore, there are other limitations such as self-reporting bias, recall bias, and heterogeneity in the way food intake was estimated among the studies. While dietary studies tend to disproportionately attract media attention and often the communicated result is that a specific food will cause or prevent a certain disease, the conclusions and results need to be scrutinized as the case of the current review and methodological limitations of these dietary studies make interpretations of a 'perfect food' very unlikely.

While the current study demonstrates that dietary components have different associations with adverse outcomes, it is important to recognize that our current study only considers the dietary component of associations with overall cardiovascular disease. There has been a study to suggest that the Mediterranean diet and adopting an active lifestyle show a synergistic effect in their inverse association with cardiovascular disease risk.52 Considering this finding, the overall cardiovascular disease risk likely incorporates a variety of factors which would contribute but may or may not further interact to modify the overall risk.

Our study has several limitations. While we were able to cover many different vegetables there was insufficient evidence for many meat types and nuts and there was no data on seafood other than fish. More importantly many reviews only had level 4 or limited evidence because there were fewer than 4 studies. Nevertheless, our review is important as it summarizes in a concise way the evidence for food items that are associated with all-cause mortality and cardiovascular disease. A further limitation is that we are unable to assess on the individual study level the impact of daily calorific content of foods and any clustering effects in dietary intake.

In conclusion, many food items appear to be beneficial in diet including nuts, whole grain foods and fiber. Within the fruit and vegetables category many foods presumed to be beneficial actually have insufficient evidence to suggest benefit in cardiovascular disease but there is modest evidence for benefit for raw vegetables, root vegetables, green leafy vegetables, cooked vegetables and cruciferous vegetables and all-cause mortality. Foods that appear harmful include processed meat and tinned fruit for all-cause mortality and processed meat and red meat for cardiovascular disease. Our review provides a comprehensive summary of the evidence of benefit or harm of food items which may help physicians better counsel their patients about dietary advice.

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**Authors’ Contribution:** CSK designed the study, concept and performed the data analysis. CSK, JP and PW were involved in the data collection. CSK wrote the first draft of the manuscript. All authors critically revised the manuscript and gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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**Figure Legends**

**Figure 1.** Food items and risk of all-cause mortality

**Figure 2.** Food items and risk of cardiovascular disease

**Table 1.** Studies that evaluate food items and non-consumption of food items and all-cause mortality

**Table 2.** Studies that evaluate food items and non-consumption of food items and cardiovascular disease

**Appendices**

**Supplementary Figure 1.** Study selection process

**Supplementary Table 1.** Food categories, food components and search results

**Supplementary Table 2.** Grading of meta-analyses based on Grosso et al.

**Supplementary Table 3:** Quality assessments in the included systematic reviews and meta-analyses

**Supplementary Table 4.** Grading the quality of the evidence for each food component

**Supplementary Table 5:** Consideration of sex differences among included studies

**Figure 1.** Food items and risk of all-cause mortality

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**Figure 2.** Food items and risk of cardiovascular disease

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**Table 1:** Studies that evaluate food items and non-consumption of food items and all-cause mortality

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| --- | --- | --- | --- | --- | --- | --- |
| Food group | Food item | Number of studies | Sample size | Inclusion criteria | Risk estimate and statistical heterogeneity. | Reference |
| Carbohydrate | Whole grain bread | 2 | 153,858 | Prospective cohort studies up to Apr 2016 | Dose-response per 90g/day RR 0.85 (0.82-0.89), I2=0%. | Aune 201614 |
| Pasta | 2 | 265,457 | Prospective cohort studies up to Apr 2016 | Dose-response per 150h/day RR 0.85 (0.74-0.99) , I2=54%. |
| Whole grain breakfast cereal | 2 | 206,200 | Prospective cohort studies up to Apr 2016 | Dose-response per 30g/day RR 0.87 (0.84-0.90), I2=0%. |
| Oats/oatmeal | 1 | 120,010 | Prospective cohort studies up to Apr 2016 | Dose-response per 20g/day RR 0.88 (0.83-0.92). |
| Refined grain | 4 | 163,634 | Prospective cohort studies up to Apr 2016 | Dose-response per 90g/day RR 0.95 (0.91-0.99) , I2=20%. |
| Rice | 5 | 453,723 | Cohort studies up to July 2014 | High vs low intake RR 0.97 (0.88-1.06) , I2=39.4%. | Saneei 201715 |
| Fibre | 8 | 875,390 | Prospective cohort studies up to May 2014. | Dose-response per 10g/day RR 0.90 (0.86-0.94), I2=77.2%. | Yang 201516 |
| Meat & eggs | Fish | 14 | 911,348 | Prospective cohort studies up to Sept 2016 | Dose-response per 20g/day RR 0.98 (0.97-1.00), I2=81.9%. | Jayedi 201817 |
| White meat | 5 | 1,156,644 | Prospective cohort studies up to Aug 2013 | Dose-response per 100g/day RR 0.90 (0.73-1.11), I2=92.1%. | Abete 201418 |
| Red meat | 6 | 1,277986 | Prospective cohort studies up to Aug 2013 | Dose-response per 100g/day RR 1.04 (0.92-1.17), I2=95%. |
| Processed meat | 5 | 1,143,696 | Prospective cohort studies up to Aug 2013 | Dose-response per 50g/day RR 1.25 (1.07-1.45), I2=95.7%. |
| Eggs | 4 | 853,974 | Prospective cohort studies up to Mar 2016 | High vs low HR 1.09 (0.997-1.20), I2=59.1%. | Xu 201819 |
| Fruits & vegetables | Root vegetables | 1 | 451,151 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.76 (0.66-0.88). | Aune 201720 |
| Green leafy vegetables/salad | 7 | 568,725 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.78 (0.71-0.86), I2=11.1%. |
| Cooked vegetables | 4 | 631,480 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.89 (0.80-0.99) , I2=94%. |
| Cruciferous vegetables | 6 | 531,147 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.90 (0.85-0.95), I2=35.2%. |
| Raw vegetables | 2 | 602,120 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.91 (0.80-1.02), I2=90.8%. |
| Mushrooms | 2 | 495,001 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.74 (0.46-1.20), I2=77.7%. |
| Onion/allium vegetables | 2 | 453,051 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.76 (0.40-1.46), I2=50.3%. |
| Apples/pears | 3 | 462,571 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.80 (0.64-1.01), I2=95.3%. |
| Berries | 2 | 461,115 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.85 (0.70-1.03), I2=0%. |
| Citrus fruits | 7 | 509,708 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.94 (0.88-1.00), I2=49.9%. |
| Fruit juice | 1 | 109,076 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.88 (0.84-0.92). |
| Non-cruciferous vegetables | 2 | 61,436 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.95 (0.89-1.02) , I2=83.1%. |
| Bananas | 2 | 11,420 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.95 (0.80-1.14) , I2=70.5%. |
| Tinned fruits | 4 | 147,712 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 1.14 (1.07-1.21) , I2=0%. |
| Potatoes | 5 | 486,865 | Prospective cohort studies, up to May 2018 | Dose-response per 150g/day RR 0.88 (0.69-1.12) , I2=81%. | Schwingshackl 201821 |
| Beverages | Alcohol | 31 | 844,414 | Prospective cohort studies up to Sept 2009 | High vs low intake RR 0.87 (0.83-0.92), I2=68%. | Ronksley 201122 |
| Coffee | 16 | 941,247 | Prospective cohort studies up to June 2013 | Dose-response per cup/day RR 0.96 (0.94-0.97). I2 not reported. | Je 201423 |
| Green tea | 5 | 205,761 | Prospective cohort studies up to Apr 2015 | Dose-response per cup/day RR 1.01 (0.99-1.02), I2=0%. | Tang 201524 |
| Black tea | 12 | 349,508 | Prospective cohort studies up to Apr 2015 | Dose-response per cup/day RR 0.98 (0.86-1.10), I2=84.3%. |
| Sugar-sweetened beverages | 3 | 187,402 | Prospective cohort studies up to July 2015 | High vs low intake RR 1.03 (0.91-1.18), I2=75%. | Narain 201625 |
| Artificially sweetened beverages | 2 | 173,778 | Prospective cohort studies up to July 2015 | High vs low intake RR1.09 (0.92-1.30), I2=73%. |
| Dairy | Yogurt | 3 | 40,460 | Prospective cohort studies up to Sept 2016 | Dose-response per 50g/day RR 0.97 (0.85-1.11), I2=65.8%. | Guo 201726 |
| Cheese | 11 | 256,091 | Prospective cohort studies up to Sept 2016 | Dose-response per 10g/day RR 0.99 (0.96-1.01), I2=93.3%. |
| Milk | 10 | 268,570 | Prospective cohort studies up to Sept 2016 | Dose-response per 244g/day RR 1.00 (0.93-1.07), I2=97.4%. |
| Butter | 9 | 379,763 | Prospective cohort studies up to May 2015 | Dose-response per 14g/day RR 1.01 (1.00-1.03), I2=0%. | Pimpin 20187 |
| Nuts & Other | Nuts | 16 | 819,448 | Prospective cohort studies up to July 2016 | Dose-response per 28g/day RR 0.78 (0.72-0.84), I2=66.0%. | Aune 201627 |
| Tree nuts | 4 | 202,751 | Prospective cohort studies up to July 2016 | Dose-response per 10g/day RR 0.82 (0.75-0.90) , I2=70.0%. |
| Peanuts | 5 | 265,252 | Prospective cohort studies up to July 2016 | Dose-response per 10g/day RR 0.77 (0.69-0.86), I2=64.0%. |
| Peanut butter | 2 | 83,789 | Prospective cohort studies up to July 2016 | Dose-response per 10g/day RR 0.94 (0.86-1.02), I2=0%. |
| Salt | 7 | 21,515 | Cohort studies of adults up to August 2011. | Dose-response per increase in sodium intake RR 1.06 (0.94-1.20), I2=61%.. | Aburto 201328 |

**Table 2:** Studies that evaluate food items and non-consumption of food items and cardiovascular disease

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Food group | Food item | Number of studies | Sample size | Inclusion criteria | Risk estimate for cardiovascular disease unless otherwise specified | Reference |
| Carbohydrate | Whole grain bread | 3 | 177,389 | Prospective cohort studies up to Apr 2016 | Dose-response per 90g/day RR 0.87 (0.80-0.95), I2=0%. | Aune 201614 |
| Whole grain breakfast cereal | 2 | 206,200 | Prospective cohort studies up to Apr 2016 | Dose-response per 30g/day RR 0.84 (0.78-0.90), I2=0%. |
| Bran | 2 | 118,085 | Prospective cohort studies up to Apr 2016 | Dose-response per 10g/day RR 0.85 (0.79-0.90), I2=0%. |
| Germ | 2 | 118,085 | Prospective cohort studies up to Apr 2016 | Dose-response per 2g/day RR 1.05 (0.96-1.15), I2=0%. |
| Refined grain | 3 | 171,842 | Prospective cohort studies up to Apr 2016 | Dose-response per 90g/day RR 0.98 (0.90,1.06), I2=56%. |
| Rice | 3 | 133,393 | Prospective cohort studies up to Apr 2016 | Dose-response per 100g/day RR 0.98 (0.95-1.00), I2=0%. |
| Fibre | 10 | 1,279,690 | Prospective cohort studies up to Aug 2013 | Dose-response per 7g/day RR 0.91 (0.88-0.94), I2=45%. | Threapleton 201329 |
| Meat & eggs | Fish | 8 | 331,239 | Prospective cohort studies up to Sept 2016 | Dose-response per 20g/day RR 0.96 (0.94-0.98) for cardiovascular mortality, I2=0%. | Jayedi 201817 |
| White meat | 5 | 1,197,805 | Prospective cohort studies up to Aug 2013 | Dose-response per 100g/day RR 1.00 (0.87-1.15) for cardiovascular mortality, I2=36.6%. | Abete 201418 |
| Red meat | 6 | 1,319,147 | Prospective cohort studies up to Aug 2013 | Dose-response per 100g/day RR 1.15 (1.05-1.26) for cardiovascular mortality, I2=76.6%. |
| Processed meat | 6 | 1,186,761 | Prospective cohort studies up to Aug 2013 | Dose-response per 50g/day RR 1.24 (1.09-1.40) for cardiovascular mortality, I2=76.4%. |
| Eggs | 9 | 363,565 | Prospective cohort studies up to Mar 2016 | High vs low HR 0.97 (0.90-1.05) for ischemic heart disease mortality. | Xu 201819 |
| Fruits & vegetables | Raw vegetables | 1 | 451,151 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.86 (0.81-0.90). | Aune 201720 |
| Dried fruit | 1 | 30,458 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.66 (0.33-1.26). |
| Broccoli | 2 | 72,665 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.75 (0.49-1.14), I2=0%. |
| Green leafy vegetables | 5 | 204,508 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.83 (0.65-1.08), I2=66.7%. |
| Grapes | 3 | 74,713 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.83 (0.48-1.45), I2=66.7%. |
| Cruciferous vegetables | 9 | 371,431 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.89 (0.77-1.02), I2=65.1%. |
| Non-cruciferous vegetables | 2 | 134,796 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.91 (0.82-1.01), I2=74.5%. |
| Citrus fruits | 8 | 239,724 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.92 (0.84-1.00), I2=65.8%. |
| Citrus fruit juice | 2 | 102,368 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.98 (0.95-1.02), I2=6.9%. |
| Fruit juice | 2 | 53,989 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.99 (0.93-1.06), I2=0%. |
| Apples/pears | 7 | 124,710 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.92 (0.82-1.03), I2=46.9%. |
| Tomatoes | 4 | 85,225 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.92 (0.80-1.07), I2=52.6%. |
| Carrots | 1 | 9,766 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 0.97 (0.72-1.30). |
| Strawberries | 1 | 38,176 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 1.06 (0.95-1.17). |
| Tinned fruits | 4 | 106,017 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 1.30 (0.81-2.08), I2=66.0%. |
| Berries | 2 | 40,224 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 1.13 (0.88-1.46), I2=0%. |
| Potatoes | 4 | 202,479 | Prospective cohort studies up to Sept 2016 | Dose-response per 100g/day RR 1.01 (0.97-1.04), I2=13.4%. |
| Beverages | Alcohol | 21 | 1,184,974 | Prospective cohort studies up to Sept 2009 | High vs low intake RR 0.75 (0.70-0.80) for cardiovascular mortality, I2=72.2%. | Ronksley 201122 |
| Coffee | 16 | 1,029,237 | Prospective cohort studies up to Jan 2013 | Dose-response per cup/day RR 0.98 (0.95-1.00) for cardiovascular mortality, I2=87.8%. | Malerba 201330 |
| Green tea | 5 | 197,957 | Prospective cohort studies up to Apr 2015 | Dose-response per cup/day RR 0.95 (0.90-1.00) for cardiovascular mortality, I2=83.8%. | Tang 201524 |
| Black tea | 7 | 162,230 | Prospective cohort studies up to Apr 2015 | Dose-response per cup/day RR 0.92 (0.85-0.99) for cardiovascular mortality, I2=75.6%. |
| Sugar-sweetened beverages | 1 | 2,564 | Prospective cohort studies up to July 2015 | High vs low intake RR 1.00 (0.98-1.02) for vascular event. | Narain 201625 |
| Artificially sweetened beverages | 1 | 2,564 | Prospective cohort studies up to July 2015 | High vs low intake RR 1.02 (1.00-1.05) for vascular event. |
| Dairy | Yogurt | 3 | 36,624 | Prospective cohort studies up to Sept 2016 | Dose-response per 50g/day RR 1.03 (0.97-1.09), I2=0%. | Guo 201726 |
| Cheese | 9 | 234,447 | Prospective cohort studies up to Sept 2016 | Dose-response per 10g/day RR 0.98 (0.95-1.00), I2=82.6%. |
| Milk | 9 | 249,779 | Prospective cohort studies up to Sept 2016 | Dose-response per 244g/day RR 1.01 (0.93-1.10), I2=92.4%. |
| Butter | 2 | 147,297 | Prospective cohort studies up to May 2015 | Dose-response per 14g/day RR 0.99 (0.96-1.02), I2=0%. | Pimpin 20187 |
| Nuts & Other | Nuts | 12 | 376,228 | Prospective cohort studies up to July 2016 | Dose-response per 28g/day RR 0.79 (0.70-0.88), I2=59.6%. | Aune 201627 |
| Tree nuts | 3 | 130,987 | Prospective cohort studies up to July 2016 | Dose-response per 10g/day RR 0.75(0.67-0.84), I2=0%. |
| Peanuts | 5 | 265,252 | Prospective cohort studies up to July 2016 | Dose-response per 10g/day RR 0.64 (0.50-0.81), I2=77.0%. |
| Salt | 9 | 46,483 | Cohort studies of adults up to August 2011. | Dose-response per increase in sodium intake 1.12 (0.93-1.34), I2=61%. | Aburto 201328 |
| Olive oil | 9 | 476,714 | Case-control, prospective studies and randomized trials up to Dec 2013 | Dose-response per 25g/day RR 0.82 (0.70-0.96), I2=77%. | Martinez-Gonzalez 201431 |
| Soy | 20 | 718,279 | Prospective cohort and case control studies up to Feb 2016 | High vs low RR 0.83 (0.75-0.93), I2=71.4%. | Yan 20178 |
| Tofu | 4 | 260,607 | Prospective cohort and case control studies up to Feb 2016 | High vs low RR 0.80 (0.64-1.00), I2=75.1%. |
| Miso | 2 | 42,371 | Prospective cohort and case control studies up to Feb 2016 | High vs low RR 0.82 (0.64-1.06), I2=29.8%. |
| Chocolate | 12 | 369,599 | Prospective cohort studies up to Jun 2018 | Dose-response per 20g/week 0.982 (0.972-0.992), I2=50.4%. | Ren 201832 |

**Supplementary Figure 1:** Study selection process

3,011 studies retrieved from the search described in the methods and presented in Supplementary Table 1.

17 reviews for cardiovascular disease.

16 reviews for all-cause mortality.

341 reviews or studies reviewed in detail for potential inclusion.

**Supplementary Table 1:** Food categories, food components and search results

|  |  |  |
| --- | --- | --- |
| Food Category | Food component | Search results |
| Fats and Oil | Olive oil | 35 |
| Palm oil | 4 |
| Sunflower oil | 0 |
| Sesame oil | 0 |
| Peanut oil | 0 |
| Butter | 16 |
| Margarine | 5 |
| Dairy | Milk | 140 |
| Yogurt | 11 |
| Ice cream | 2 |
| Cheese | 15 |
| Meat, poultry and beans | Pork or pig | 124 |
| Beef or cow | 84 |
| Lamb or sheep | 53 |
| Chicken | 26 (39 with poultry) |
| Turkey | 257 |
| Duck | 4 |
| Beans or legumes or pulses | 361 |
| Tofu or soybean | 39 |
| Fish and seafood | Salmon | 32 |
| Tuna | 2 |
| Cod or bass | 64 |
| Catfish | 0 |
| Mackerel | 0 |
| Anchovy | 0 |
| Herring | 4 |
| Shark | 1 |
| Shrimp or prawn | 1 |
| Squid or octopus | 4 |
| Shellfish or oyster or mussel or scallop or clams | 6 |
| Crab or lobster | 3 |
| Mussel | 0 |
| Eggs | Eggs | 37 (51 egg) |
| Nuts | Almond | 9 |
| Chestnuts | 0 (26 chestnut) |
| Hazelnuts | 1 |
| Walnuts | 6 |
| Cashews | 0 |
| Pistachios | 2 |
| Pine nuts | 0 |
| Brazil nuts | 0 |
| Macadamia nuts | 1 |
| Peanuts | 5 |
| Vegetables | Broccoli | 5 |
| Cabbage | 2 |
| Carrots | 4 |
| Celery | 0 |
| Corn | 14 |
| Lettuce | 0 |
| Peas | 0 |
| Spinach | 1 |
| Cauliflower | 3 |
| Chickpea | 0 |
| Asparagus | 1 |
| Garlic | 23 |
| Onion | 3 |
| Ginger | 4 |
| Seaweed | 1 |
| Fruit | Apple | 23 |
| Bananas | 9 |
| Blueberry | 0 |
| Blackberry | 2 |
| Cherry | 22 |
| Coconut | 2 |
| Cranberry | 5 |
| Grapes | 6 |
| Figs | 2 |
| Dates | 144 |
| Kiwifruit | 0 |
| Mango | 1 |
| Lychee | 0 |
| Olive | 55 |
| Peach | 6 |
| Pear | 2 |
| Plum | 1 |
| Pineapple | 0 |
| Raspberry | 0 |
| Strawberry | 0 |
| Orange | 106 |
| Lemon | 17 |
| Avocado | 3 |
| Pepper | 0 |
| Melons | 3 |
| Cucumber | 0 |
| Pumpkins | 0 |
| Squash | 0 |
| Tomato | 6 |
| Courgettes or zucchini | 1 |
| Carbohydrate and grains | Bread | 6 |
| Rice | 123 |
| Cereal | 37 |
| Pasta | 3 |
| Fibre or fibre | 177 |
| Potatoes | 6 |
| Noodles | 0 |
| Drinks and beverages | Coffee | 50 |
| Tea | 54 |
| Wine | 38 |
| Beer | 54 |
| Spirits or vodka or gin or whisky or rum | 35 |
| Soft drinks | 3 |
| Snacks and sweets | Crisps | 0 |
| Chocolate | 19 |
| Confectionary or sweets | 21 |
| Biscuits or cookies | 0 |
| Sauces and condiments | Sauces and condiments | 1 |
| Salt | Salt | 495 |
| Fungus | Mushroom | 5 |

Search took place on 13 August 2018.

**Supplementary Table 2:** Grading of meta-analyses based on Grosso et al.

|  |  |  |
| --- | --- | --- |
| Level of evidence | Level | Definition |
| Convincing | 1a (high)  1b (low) | Concordance of meta-analysis of RCTs and meta-analysis of observational studies.  Meta-analysis of RCTs with contrary results to observational studies. |
| Probable | 2 | Meta-analysis of prospective studies with no heterogeneity. |
| Possible | 3 | Meta-analysis of prospective or retrospective study lacking information on statistic heterogeneity or with I2>30%. |
| Limited/contrasting | 4 | Limited studies included in meta-analysis (n≤3). |

Grosso G, Godos J, Alvano F, Giovannucci EL. Coffee, caffeine, and health outcome: an umbrella review. Ann Rev Nutr 2017;37:131-156.

**Supplementary Table 3:** Quality assessments in the included systematic reviews and meta-analyses

|  |  |  |  |
| --- | --- | --- | --- |
| Review ID | Dietary component | Assessment method | Quality assessment |
| Aune 201614 | Grain | Newcastle-Ottawa scale (0-9). | Average quality assessment score for CVD was 7.7/9 and all-cause death 7.9/9. |
| Saneei 201715 | Rice | Hu et al score (out of 15). | Average quality assessment score for mortality was 10.3/15. |
| Yang 201516 | Fibre | No quality score used. | Not performed. |
| Jayedi 201817 | Fish | Newcastle-Ottawa scale (0-9). | Average quality assessment score overall was 7.5/9. |
| Abete 201428 | Meat | No quality score used. | Not performed. |
| Xu 201819 | Eggs | No quality score used. | Not performed. |
| Aune 201720 | Fruits and vegetables | Newcastle-Ottawa scale (0-9). | Quality assessment scores for CVD was 12/13 for fruits/vegetables, 15/17 for fruits and 12/14 for vegetables. For all-cause mortality, it was 14/15 for fruits/vegetables, 20/27 for fruits and 19/22 for vegetables. |
| Schwingshackl 201821 | Potatoes | NutriGrade scoring system (out of 10 but graded as very low (0-3), low (4-5), moderate (6-7) and high (≥8). | Average quality for all-cause mortality was low and CHD was low. |
| Ronksley 201122 | Alcohol | 2 criteria assessed based on Egger et al and Laupacis et al. | 85% of studies had >5 years follow up and 90% of studies adjusted for basic demographic information. |
| Je 201423 | Coffee | Adjustments for potential confounders only factor considered. | All studies adjusted for covariates. |
| Tang 201524 | Tea | Newcastle-Ottawa scale (0-9). | Average quality assessment score overall was 6.1/9. |
| Narain 201625 | Soft drink | 5 areas assessed. | Average quality assessment score overall was 3.6/5. |
| Guo 201726 | Milk | Newcastle-Ottawa quality assessment scale (0-9). | Average quality assessment score overall was 7.9/9. |
| Pimpin 20187 | Butter | Adapted Newcastle-Ottawa quality scale (0-5). | Average quality assessment score overall 4.6/5. |
| Aune 201627 | Nuts | Newcastle-Ottawa scale (0-9). | Average quality assessment score for CVD was 7.6/9 and all-cause death 7.3/9. |
| Aburto 201328 | Salt | GRADE methodology used to assess quality. | Quality of the evidence was very low to moderate for CVD, very low to low for CHD and very low for all-cause mortality. |
| Threapleton 201329 | Fibre | Newcastle-Ottawa scale (0-9). | Average quality assessment score overall 7.2/9. |
| Malerba 201330 | Coffee | No quality score used. | Not performed. |
| Martinez-Gonzalez 201431 | Olive oil | Newcastle-Ottawa scale (0-9). | Average quality assessment score overall 7.8/9. |
| Yan 20178 | Soy | Newcastle-Ottawa scale (0-9). | Average quality assessment score overall 7.7/9. |
| Ren 201832 | Chocolate | Newcastle-Ottawa scale (0-9). | Average quality assessment score overall 8.4/9. |

CVD=cardiovascular disease, CHD=coronary heart disease

**Supplementary Table 4:** Grading the quality of the evidence for each food component

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Food group | Food item | Grade for mortality | Reason | Grade for CVD | Reason |
| Carbohydrate | Whole grain bread | Level 4 limited | Fewer than 4 studies. | Level 4 limited | Fewer than 4 studies. |
| Pasta | Level 4 limited | Fewer than 4 studies. | - | - |
| Whole grain breakfast cereal | Level 4 limited | Fewer than 4 studies. | Level 4 limited | Fewer than 4 studies. |
| Oats/oatmeal | Level 4 limited | Fewer than 4 studies. | Level 4 limited | Fewer than 4 studies. |
| Refined grain | Level 2 probable | 4 prospective studies with I2=20%. | - | - |
| Bran | - | - | Level 4 limited | Fewer than 4 studies. |
| Germ | - | - | Level 4 limited | Fewer than 4 studies. |
| Rice | Level 3 possible | 5 cohort studies with I2=39.4%. | Level 4 limited | Fewer than 4 studies. |
| Fibre | Level 3 possible | 5 prospective studies with I2=77.2%. | Level 3 possible | 10 prospective studies with I2=45%. |
| Meat & eggs | Fish | Level 3 possible | 14 prospective studies with I2=81.9%. | Level 2 possible | 8 prospective studies with I2=0%. |
| White meat | Level 3 possible | 5 prospective studies with I2=92.1%. | Level 3 possible | 5 prospective studies with I2=36.6%. |
| Red meat | Level 3 possible | 6 prospective studies with I2=95%. | Level 3 possible | 6 prospective studies with I2=76.6%. |
| Processed meat | Level 3 possible | 5 prospective studies with I2=95.7%. | Level 3 possible | 6 prospective studies with I2=76.4%. |
| Eggs | Level 3 possible | 4 prospective studies with I2=59.1%. | Level 3 possible | 9 prospective studies with I2 not reported. |
| Fruits & vegetables | Root vegetables | Level 4 limited | Fewer than 4 studies. | - | - |
| Green leafy vegetables/salad | Level 2 probable. | 7 prospective studies with I2=11.1%. | Level 3 possible | 5 prospective studies with I2=66.7%. |
| Cooked vegetables | Level 3 possible | 4 prospective studies with I2=94%. | - | - |
| Cruciferous vegetables | Level 3 possible | 6 prospective studies with I2=35.2%. | Level 3 possible | 9 prospective studies with I2=65.1%. |
| Raw vegetables | Level 4 limited | Fewer than 4 studies. | Level 4 limited | Fewer than 4 studies. |
| Mushrooms | Level 4 limited | Fewer than 4 studies. | - | - |
| Onion/allium vegetables | Level 4 limited | Fewer than 4 studies. | - | - |
| Apples/pears | Level 4 limited | Fewer than 4 studies. | Level 3 possible | 7 prospective studies with I2=46.9%. |
| Berries | Level 4 limited | Fewer than 4 studies. | Level 4 limited | Fewer than 4 studies. |
| Citrus fruits | Level 3 possible | 7 prospective studies with I2=49.9%. | Level 3 possible | 8 prospective studies with I2=65.8%. |
| Fruit juice | Level 4 limited | Fewer than 4 studies. | Level 4 limited | Fewer than 4 studies. |
| Non-cruciferous vegetables | Level 4 limited | Fewer than 4 studies. | Level 4 limited | Fewer than 4 studies. |
| Bananas | Level 4 limited | Fewer than 4 studies. | - | - |
| Tinned fruits | Level 2 probable | 4 prospective studies with I2=0%. | Level 3 possible | 4 prospective studies with I2=66.0%. |
| Carrots | - | - | Level 4 limited | Fewer than 4 studies. |
| Strawberries | - | - | Level 4 limited | Fewer than 4 studies. |
| Tomatoes | - | - | Level 3 possible | 4 prospective studies with I2=52.6%. |
| Citrus fruit juice | - | - | Level 4 limited | Fewer than 4 studies. |
| Grapes | - | - | Level 4 limited | Fewer than 4 studies. |
| Broccoli | - | - | Level 4 limited | Fewer than 4 studies. |
| Dried fruit | - | - | Level 4 limited | Fewer than 4 studies. |
| Potatoes | Level 3 possible | 5 prospective studies with I2=81%. | Level 2 probable | 4 prospective studies with I2=13.4%. |
| Beverages | Alcohol | Level 3 possible | 31 prospective studies with I2=68%. | Level 3 possible | 21 prospective studies with I2=72.2%. |
| Coffee | Level 3 possible | 16 prospective studies with I2 not reported. | Level 3 possible | 16 prospective studies with I2=87.8%. |
| Green tea | Level 2 probable | 5 prospective studies with I2=0%. | Level 3 possible | 5 prospective studies with I2=83.8%. |
| Black tea | Level 3 possible | 12 prospective studies with I2=84.3%. | Level 3 possible | 7 prospective studies with I2=75.6%. |
| Sugar-sweetened beverages | Level 4 limited | Fewer than 4 studies. | Level 4 limited | Fewer than 4 studies. |
| Artificially sweetened beverages | Level 4 limited | Fewer than 4 studies. | Level 4 limited | Fewer than 4 studies. |
| Dairy | Yogurt | Level 4 limited | Fewer than 4 studies. | Level 4 limited | Fewer than 4 studies. |
| Cheese | Level 3 possible | 11 prospective studies with I2=93.3%. | Level 3 possible | 9 prospective studies with I2=82.6%. |
| Milk | Level 3 possible | 10 prospective studies with I2=97.4%. | Level 3 possible | 9 prospective studies with I2=92.4%. |
| Butter | Level 2 possible | 9 prospective studies with I2=0%. | Level 4 limited | Fewer than 4 studies. |
| Nuts & Other | Nuts | Level 3 possible | 16 prospective studies with I2=66.0%. | Level 3 possible | 12 prospective studies with I2=59.6%. |
| Tree nuts | Level 3 possible | 4 prospective studies with I2=70.0%. | Level 4 limited | Fewer than 4 studies. |
| Peanuts | Level 3 possible | 5 prospective studies with I2=64.0%. | Level 3 possible | 5 prospective studies with I2=77.0-%. |
| Peanut butter | Level 4 limited | Fewer than 4 studies. | - | - |
| Salt | Level 3 possible | 7 prospective studies with I2=61%. | Level 3 possible | 9 prospective studies with I2=61%. |
| Olive oil | - | - | Level 3 possible | 9 prospective studies with I2=77%. |
| Soy | - | - | Level 3 possible | 20 prospective studies with I2=71.4%. |
| Tofu | - | - | Level 3 possible | 4 prospective studies with I2=75.1%. |
| Miso | - | - | Level 4 limited | Fever than 4 studies. |
| Chocolate | - | - | Level 3 possible | 12 prospective studies with I2=61%. |

**Supplementary Table 5:** Consideration of sex differences among included studies

|  |  |  |
| --- | --- | --- |
| Review ID | Dietary component | Consideration of sex differences among included studies |
| Aune 201614 | Grain | The authors state that there was little evidence of heterogeneity between subgroups in subgroup and meta-regression stratified by sex. |
| Saneei 201715 | Rice | Risk of mortality in men RR 0.87 (0.81-0.94) and in women RR 1.08 (0.97-1.19). |
| Yang 201516 | Fibre | For top vs bottom tertile, risk of mortality in men RR 0.80 (0.76-0.85) and in women RR 0.83 (0.79-0.86). |
| Jayedi 201817 | Fish | Risk of mortality in men was RR 0.99 (0.96-1.02) and in women it was RR 0.98 (0.95-1.00) |
| Abete 201418 | Meat | Risk of mortality in men for red meat RR 1.21 (1.15-1.26), white meat RR 0.87 (0.65-1.17) and processed meat RR 1.23 (1.10-1.37) and in women for red meat RR 1.14 (1.00-1.30), white meat RR 1.01 (0.89-1.15) and processed meat RR 1.34 (1.09-1.66). Risk of cardiovascular mortality in men for red meat RR 1.20 (1.12-1.30), white meat RR 1.05 (0.74-1.31) and processed meat RR 1.15 (0.96-1.37) and in women for red meat RR 1.26 (1.08-1.47), white meat RR 1.08 (0.94-1.24) and processed meat RR 1.64 (1.25-2.15). |
| Xu 201819 | Eggs | The authors state "As no evidence suggested different associations by sex (P values for interaction from 0.45 to 0.92), all analysis was conducted with both sexes combined, adjusted for sex." |
| Aune 201720 | Fruits and vegetables | Risk of CHD in men for fruits/vegetables RR 0.93 (0.89-0.97), fruits RR 0.91 (0.86-0.97) and vegetables RR 0.77 (0.68-0.89) and in women for fruits/vegetables RR 0.88 (0.82-0.94), fruits RR 0.84 (0.76-0.92) and vegetables RR 0.89 (0.81-0.98). Risk of CVD in men for fruits/vegetables RR 0.93 (0.85-1.03), fruits RR 0.85 (0.70-1.05) and vegetables RR 0.89 (0.78-1.00) and in women for fruits/vegetables RR 0.94 (0.89-0.99), fruits RR 0.83 (0.77-0.90) and vegetables RR 0.92 (0.86-0.98). Risk of mortality in men for fruits/vegetables RR 0.95 (0.91-0.99), fruits RR 0.88 (0.78-1.00) and vegetables RR 0.91 (0.84-0.99) and in women for fruits/vegetables RR 0.94 (0.90-0.98), fruits RR 0.96 (0.90-1.02) and vegetables RR 0.93 (0.86-0.99). |
| Schwingshackl 201821 | Potatoes | Risk of CHD in men RR 1.05 (0.94-1.17) and women RR 1.00 (0.85-1.17). |
| Ronksley 201122 | Alcohol | The authors state that sensitivity analyses confined to only studies of sex revealed generally similar results for all the outcomes. |
| Je 201423 | Coffee | For high vs low consumption, risk of mortality in men RR 0.81 (0.79-0.90) and women RR 0.84 (0.79-0.89). |
| Tang 201524 | Tea | For high vs low consumption, green tea and risk of CVD in men RR 0.72 (0.42-1.23) and women RR 0.54 (0.34-0.84). Green tea and risk of all-cause mortality in men RR 0.80 (0.68-0.95) and women RR 0.74 (0.60-0.93). Black tea and risk of CVD in men RR 1.56 (0.76-3.20) and women RR 1.01 (0.80-1.26). Black tea and risk of all-cause mortality in men RR 1.45 (0.95-1.21) and women RR 1.0 (0.89-1.14). |
| Narain 201625 | Soft drink | Sex differences not explored for myocardial infarction or mortality. |
| Guo 201726 | Milk | No sex specific subgroup analyses were performed. |
| Pimpin 20187 | Butter | No sex specific subgroup analyses were performed. |
| Aune 201627 | Nuts | Risk of CHD in men was RR 0.70 (0.62-0.80) and in women it was RR 0.71 (0.61-0.82). Risk of CVD in men was RR 0.73 (0.66-0.81) and in women it was RR 0.86 (0.72-1.03). Risk of mortality in men was RR 0.76 (0.70-0.83) and in women was RR 0.76 (0.64-0.88). |
| Aburto 201328 | Salt | No sex specific subgroups reported for CVD and mortality. |
| Threapleton 201329 | Fibre | The authors state that for total fibre and CHD risk there was no differences observed between the sexes. |
| Malerba 201330 | Coffee | Risk of mortality with incremental increase in coffee (1 cup/day), for men was RR 0.97 (0.95-0.99) and for women it was RR 0.95 (0.93-0.97). Risk of CVD mortality, for men was RR 0.99 (0.95-1.03) and for women it was RR 0.94 (0.92-0.98). |
| Martinez-Gonzalez 201431 | Olive oil | The authors state that no substantial differences were found for the risk of CVD when separating the studies according to women or men. |
| Yan 20178 | Soy | Risk of CVD for soy intake in men was RR 0.91 (0.79-1.05) and for women it was RR 0.83 (0.69-0.99). |
| Ren 201832 | Chocolate | Risk of CVD for chocolate consumption in men was RR 0.991 (0.964-1.019) and in women it was RR 0.965 (0.931-1.001). |

RR=relative risk, CHD=coronary heart disease, CVD=cardiovascular disease