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

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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. A total of 16 reviews were included for dietary food item and all-cause mortality and 17 reviews for cardiovascular disease. Carbohydrates were associated with a reduced risk of all-cause mortality (whole grain bread: relative risk (RR) 0.85, 95% confidence interval (CI) 0.82–0.89; breakfast cereal: RR 0.88, 95% CI 0.83–0.92; oats/oatmeal: RR 0.88, 95% CI 0.83–0.92). Fish consumption was associated with a small benefit (RR 0.98, 95% CI 0.97–1.00) and processed meat appeared to be harmful (RR 1.25, 95% CI 1.07–1.45). Root vegetables (RR 0.76, 95% CI 0.66–0.88), green leafy vegetables/salad (RR 0.78, 95% CI 0.71–0.86), cooked vegetables (RR 0.89, 95% CI 0.80–0.99) and cruciferous vegetables (RR 0.90, 95% CI 0.85–0.95) were associated with reductions in all-cause mortality. Increased mortality was associated with the consumption of tinned fruit (RR 1.14, 95% CI 1.07–1.21). Nuts were associated with a reduced risk of mortality in a dose–response relationship (all nuts: RR 0.78, 95% CI 0.72–0.84; tree nuts: RR 0.82, 95% CI 0.75–0.90; and peanuts: RR 0.77, 95% CI 0.69–0.86). For cardiovascular disease, 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 cardiovascular disease and mortality, including grains, fish, nuts and vegetables, but processed meat and tinned fruit appear to be harmful.

Keywords
Diet, epidemiology, systematic review

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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 health.[3] There has been exponential growth in the nutritional literature evaluating diet and CVD. There have been reviews

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for specific food groups and their influence on cardiovascular health,[4] and further reviews of individual components of diet such as fish intake,[5] cheese intake,[6] butter[7] and less frequently consumed components such as soy products.[8] One of the advantages of evaluating individual food components is that overall dietary 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 the risk of CVD 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 CVD and mortality. The aim of this review was to summarize collectively 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 the risk of CVD 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 Americans[11] 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 in which 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 four levels in which 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 the inclusion of prospective cohorts, the number of studies and the presence of statistical heterogeneity ($I^2 \leq 30\%$ vs. $I^2 > 30\%$) is shown in Supplementary Table 2.

The included studies had to have the dietary component of interest and some form of quantitative association with either CVD or mortality. Food item consumption and its association with outcome can be quantified as a dose–response relationship and highest compared to lowest consumers of food items. We chose studies that considered a dose–response relationship when 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 (RRs) and 95% confidence intervals (CIs) from the most adjusted models presented in the review; the evidence of heterogeneity (I^2) was obtained from the original source meta-analyses and reported in 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 that reported associations of the increased risk of harm were colored in red, those that showed beneficial associations were colored in green, and those that 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 3011 studies were reviewed from the search shown in Supplementary Table 1. After detailed review of relevant studies, a total of 16 reviews[7,14–28] were included for all-cause mortality and 17

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

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 April 2016	Dose–response per 90 g/day RR 0.85 (0.82–0.89), $I^2 = 0\%$	Aune, 2016[14]
	Pasta	2	265,457	Prospective cohort studies up to April 2016	Dose–response per 150 h/day RR 0.85 (0.74–0.99), $I^2 = 54\%$	
	Whole grain breakfast cereal	2	206,200	Prospective cohort studies up to April 2016	Dose–response per 30 g/day RR 0.87 (0.84–0.90), $I^2 = 0\%$	
	Oats/oatmeal	1	120,010	Prospective cohort studies up to April 2016	Dose–response per 20 g/day RR 0.88 (0.83–0.92)	
	Refined grain	4	163,634	Prospective cohort studies up to April 2016	Dose–response per 90g/day RR 0.95 (0.91–0.99), $I^2 = 20\%$	
	Rice	5	453,723	Cohort studies up to July 2014	High vs. low intake RR 0.97 (0.88–1.06), $I^2 = 39.4\%$	Saneei, 2017[15]
	Fibre	8	875,390	Prospective cohort studies up to May 2014	Dose–response per 10 g/day RR 0.90 (0.86–0.94), $I^2 = 77.2\%$	Yang, 2015[16]
Meat & eggs	Fish	14	911,348	Prospective cohort studies up to Sept 2016	Dose–response per 20 g/day RR 0.98 (0.97–1.00), $I^2 = 81.9\%$	Jayedi, 2018[17]
	White meat	5	1,156,644	Prospective cohort studies up to Aug 2013	Dose–response per 100 g/day RR 0.90 (0.73–1.11), $I^2 = 92.1\%$	Abete, 2014[18]
	Red meat	6	1,277986	Prospective cohort studies up to Aug 2013	Dose–response per 100 g/day RR 1.04 (0.92–1.17), $I^2 = 95\%$	
	Processed meat	5	1,143,696	Prospective cohort studies up to Aug 2013	Dose–response per 50 g/day RR 1.25 (1.07–1.45), $I^2 = 95.7\%$	
	Eggs	4	853,974	Prospective cohort studies up to Mar 2016	High vs. low HR 1.09 (0.997–1.20), $I^2 = 59.1\%$	Xu, 2018[19]
Fruits & vegetables	Root vegetables	1	451,151	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.76 (0.66–0.88)	Aune, 2017[20]
	Green leafy vegetables/salad	7	568,725	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.78 (0.71–0.86), $I^2 = 11.1\%$	
	Cooked vegetables	4	631,480	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.89 (0.80–0.99), $I^2 = 94\%$	
	Cruciferous vegetables	6	531,147	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.90 (0.85–0.95), $I^2 = 35.2\%$	
	Raw vegetables	2	602,120	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.91 (0.80–1.02), $I^2 = 90.8\%$	
	Mushrooms	2	495,001	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.74 (0.46–1.20), $I^2 = 77.7\%$	

(continued)

Table 1. Continued

Food group	Food item	Number of studies	Sample size	Inclusion criteria	Risk estimate and statistical heterogeneity	Reference
	Onion/allium vegetables	2	453,051	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.76 (0.40–1.46), $I^2 = 50.3\%$	
	Apples/pears	3	462,571	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.80 (0.64–1.01), $I^2 = 95.3\%$	
	Berries	2	461,115	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.85 (0.70–1.03), $I^2 = 0\%$	
	Citrus fruits	7	509,708	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.94 (0.88–1.00), $I^2 = 49.9\%$	
	Fruit juice	1	109,076	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.88 (0.84–0.92)	
	Non-cruciferous vegetables	2	61,436	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.95 (0.89–1.02), $I^2 = 83.1\%$	
	Bananas	2	11,420	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.95 (0.80–1.14), $I^2 = 70.5\%$	
	Tinned fruits	4	147,712	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 1.14 (1.07–1.21), $I^2 = 0\%$	
	Potatoes	5	486,865	Prospective cohort studies, up to May 2018	Dose–response per 150 g/day RR 0.88 (0.69–1.12), $I^2 = 81\%$	Schwingshackl, 2018[21]
Beverages	Alcohol	31	844,414	Prospective cohort studies up to Sept 2009	High vs. low intake RR 0.87 (0.83–0.92), $I^2 = 68\%$	Ronksley, 2011[22]
	Coffee	16	941,247	Prospective cohort studies up to June 2013	Dose–response per cup/day RR 0.96 (0.94–0.97). I^2 not reported	Je, 2014[23]
	Green tea	5	205,761	Prospective cohort studies up to April 2015	Dose–response per cup/day RR 0.96 (0.94-0.98), $I^2 = 77.5\%$	Tang, 2015[24]
	Black tea	12	349,508	Prospective cohort studies up to April 2015	Dose–response per cup/day RR 0.97 (0.94-0.99), $I^2 = 84.4\%$	
	Sugar-sweetened beverages	3	187,402	Prospective cohort studies up to July 2015	High vs. low intake RR 1.03 (0.91–1.18), $I^2 = 75\%$	Narain, 2016[25]
	Artificially sweetened beverages	2	173,778	Prospective cohort studies up to July 2015	High vs. low intake RR1.09 (0.92–1.30), $I^2 = 73\%$	

(continued)

Table 1. Continued

Food group	Food item	Number of studies	Sample size	Inclusion criteria	Risk estimate and statistical heterogeneity	Reference
Dairy	Yogurt	3	40,460	Prospective cohort studies up to Sept 2016	Dose–response per 50 g/day RR 0.97 (0.85–1.11), $I^2 = 65.8\%$	Guo, 2017[26]
	Cheese	11	256,091	Prospective cohort studies up to Sept 2016	Dose–response per 10 g/day RR 0.99 (0.96–1.01), $I^2 = 93.3\%$	
	Milk	10	268,570	Prospective cohort studies up to Sept 2016	Dose–response per 244 g/day RR 1.00 (0.93–1.07), $I^2 = 97.4\%$	
	Butter	9	379,763	Prospective cohort studies up to May 2015	Dose–response per 14 g/day RR 1.01 (1.00–1.03), $I^2 = 0\%$	Pimpin, 2018[7]
Nuts & other	Nuts	16	819,448	Prospective cohort studies up to July 2016	Dose–response per 28 g/day RR 0.78 (0.72–0.84), $I^2 = 66.0\%$	Aune, 2016[27]
	Tree nuts	4	202,751	Prospective cohort studies up to July 2016	Dose–response per 10 g/day RR 0.82 (0.75–0.90), $I^2 = 70.0\%$	
	Peanuts	5	265,252	Prospective cohort studies up to July 2016	Dose–response per 10 g/day RR 0.77 (0.69–0.86), $I^2 = 64.0\%$	
	Peanut butter	2	83,789	Prospective cohort studies up to July 2016	Dose–response per 10 g/day RR 0.94 (0.86–1.02), $I^2 = 0\%$	
	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), $I^2 = 61\%$	Aburto, 2013[28]

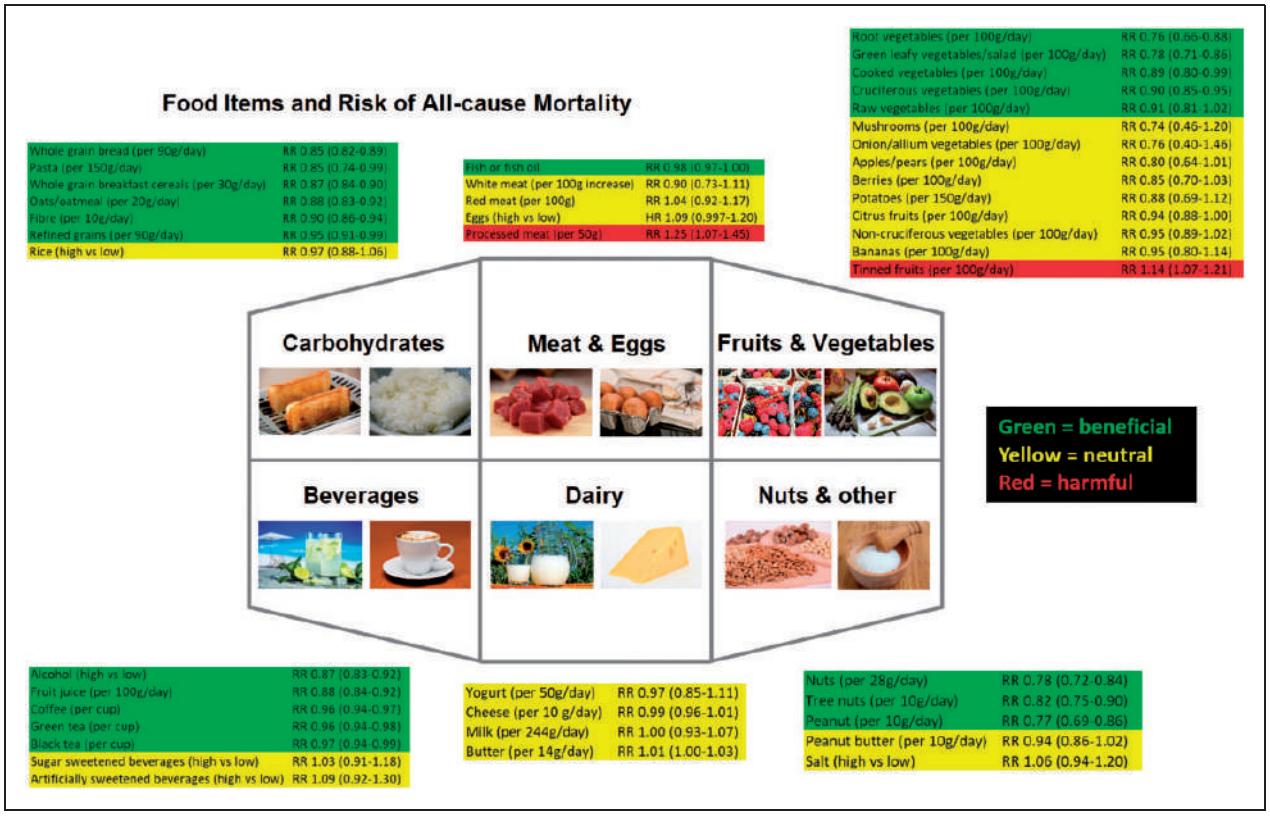

Figure 1. Food items and risk of all-cause mortality.

reviews[7,8,14,17–20,22,24–32] for CVD (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 four 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 CVD 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 two 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 a reduced risk of all-cause mortality (whole grain bread: RR 0.85, 95% CI 0.82–0.89; pasta: RR 0.85, 95% CI 0.74–0.99; whole grain breakfast cereal: RR 0.88. 95% CI 0.83–0.92; oats/oatmeal: RR 0.88, 95% CI 0.83–0.92). Both the intake of refined grains and fibre were associated with a significant dose–response reduction in all-cause mortality (RR 0.95, 95% CI 0.91–0.99, four studies and RR 0.90, 95% CI 0.86–0.94, eight studies, respectively). Rice was evaluated in five 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, 95% CI 0.97–1.00) and processed meat appeared to be harmful (RR 1.25, 95% CI 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, 95% CI 0.66–0.88, one study), green leafy vegetables/salad (RR 0.78, 95% CI 0.71–0.86, seven studies), cooked vegetables (RR 0.89, 95% CI 0.80–0.99, four studies) and cruciferous vegetables (RR 0.90, 95% CI 0.85–0.95, six 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, 95% CI 1.07–1.21, four studies). Comparing the highest and lowest consumers of alcohol there appeared to be a reduction in all-cause mortality among the highest consumers (RR 0.87, 95%

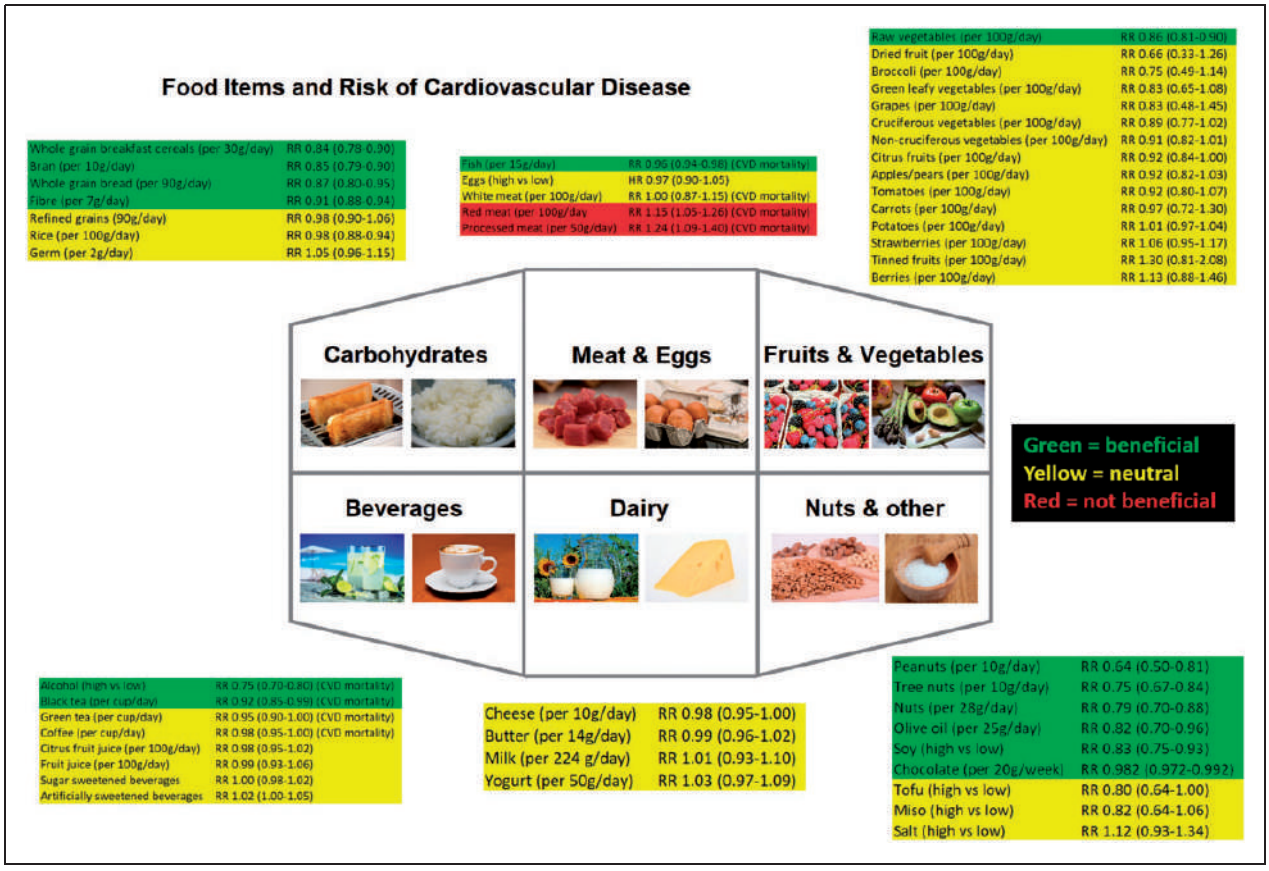

Figure 2. Food items and the risk of cardiovascular disease.

CI 0.83–0.92, 31 studies). Coffee also showed a dose–response association for the reduced risk of all-cause mortality (RR 0.96, 95% CI 0.94–0.97, 16 studies). For dairy products, there was no significant difference in the risk of mortality with yogurt, cheese, milk or butter consumption. The data from nuts appeared to be associated with a reduced risk of mortality in a dose–response relationship (all nuts: RR 0.78, 95% CI 0.72–0.84, 16 studies; tree nuts: RR 0.82, 95% CI 0.75–0.90, four studies; and peanuts: RR 0.77, 95% CI 0.69–0.86, five studies).

The associations between CVD and food items are shown in Figure 2 and Table 2. Among carbohydrates, there was a dose–response association for the benefit for whole grain bread (RR 0.87, 95% CI 0.80–0.95, three studies), whole grain breakfast cereals (RR 0.84, 95% CI 0.78–0.90, two studies), bran (RR 0.85, 95% CI 0.79–0.90, two studies) and fibre (RR 0.91, 95% CI 0.88–0.94, 10 studies). Red meat (RR 1.15, 95% CI 1.05–1.26), six studies) and processed meat (RR 1.24, 95% CI 1.09–1.40), six studies) appeared to be harmful. Out of all the fruits and vegetables only one study on raw vegetables suggested a dose–response association of benefit (RR 0.86, 95% CI 0.81–0.90). Alcohol consumption for the highest compared to the lowest consumers showed an association of a reduced risk of CVD (RR 0.75, 95% CI 0.70–0.80, 21 studies). Black tea was associated with a dose–response benefit for cardiovascular mortality (RR 0.92, 95% CI 0.85–0.99, seven studies). Dairy products (yogurt, cheese, milk and butter) showed no evidence of a dose–response association for benefit or harm. The intake of nuts was associated with a reduced risk of CVD (all nuts: RR 0.79, 95% CI 0.70–0.88, 12 studies; tree nuts: RR 0.75, 95% CI 0.67–0.84, three studies; peanuts: RR 0.64, 95% CI 0.50–0.81, five studies). In addition, olive oil showed a dose–response benefit in CVD (RR 0.82, 95% CI 0.70–0.96, nine studies) and soy products as compared by the highest and lowest consumers showed a lower risk of CVD (RR 0.83, 95% CI 0.75–0.93). Finally, an association for a dose–response benefit was observed for chocolate (RR 0.982, 95% CI 0.972–0.992, 12 studies).

The additional analysis considering differences in results based on sex showed no major differences

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 April 2016	Dose–response per 90 g/day RR 0.87 (0.80–0.95), $I^2 = 0\%$	Aune, 2016[14]
	Whole grain breakfast cereal	2	206,200	Prospective cohort studies up to April 2016	Dose–response per 30 g/day RR 0.84 (0.78–0.90), $I^2 = 0\%$	
	Bran	2	118,085	Prospective cohort studies up to April 2016	Dose–response per 10 g/day RR 0.85 (0.79–0.90), $I^2 = 0\%$	
	Germ	2	118,085	Prospective cohort studies up to April 2016	Dose–response per 2 g/day RR 1.05 (0.96–1.15), $I^2 = 0\%$	
	Refined grain	3	171,842	Prospective cohort studies up to April 2016	Dose–response per 90 g/day RR 0.98 (0.90–1.06), $I^2 = 56\%$	
	Rice	3	133,393	Prospective cohort studies up to April 2016	Dose–response per 100 g/day RR 0.98 (0.95–1.00), $I^2 = 0\%$	
	Fibre	10	1,279,690	Prospective cohort studies up to Aug 2013	Dose–response per 7 g/day RR 0.91 (0.88–0.94), $I^2 = 45\%$	Threapleton, 2013[29]
Meat & eggs	Fish	8	331,239	Prospective cohort studies up to Sept 2016	Dose–response per 20 g/day RR 0.96 (0.94–0.98) for cardiovascular mortality, $I^2 = 0\%$	Jayedi, 2018[17]
	White meat	5	1,197,805	Prospective cohort studies up to Aug 2013	Dose–response per 100 g/day RR 1.00 (0.87–1.15) for cardiovascular mortality, $I^2 = 36.6\%$	Abete, 2014[18]
	Red meat	6	1,319,147	Prospective cohort studies up to Aug 2013	Dose–response per 100 g/day RR 1.15 (1.05–1.26) for cardiovascular mortality, $I^2 = 76.6\%$	
	Processed meat	6	1,186,761	Prospective cohort studies up to Aug 2013	Dose–response per 50 g/day RR 1.24 (1.09–1.40) for cardiovascular mortality, $I^2 = 76.4\%$	
	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, 2018[19]

(continued)

Table 2. Continued

Food group	Food item	Number of studies	Sample size	Inclusion criteria	Risk estimate for cardiovascular disease unless otherwise specified	Reference
Fruits & vegetables	Raw vegetables	1	451,151	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.86 (0.81–0.90)	Aune, 2017[20]
	Dried fruit	1	30,458	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.66 (0.33–1.26)	
	Broccoli	2	72,665	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.75 (0.49–1.14), $I^2 = 0\%$	
	Green leafy vegetables	5	204,508	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.83 (0.65–1.08), $I^2 = 66.7\%$	
	Grapes	3	74,713	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.83 (0.48–1.45), $I^2 = 66.7\%$	
	Cruciferous vegetables	9	371,431	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.89 (0.77–1.02), $I^2 = 65.1\%$	
	Non-cruciferous vegetables	2	134,796	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.91 (0.82–1.01), $I^2 = 74.5\%$	
	Citrus fruits	8	239,724	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.92 (0.84–1.00), $I^2 = 65.8\%$	
	Citrus fruit juice	2	102,368	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.98 (0.95–1.02), $I^2 = 6.9\%$	
	Fruit juice	2	53,989	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.99 (0.93–1.06), $I^2 = 0\%$	
	Apples/pears	7	124,710	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.92 (0.82–1.03), $I^2 = 46.9\%$	
	Tomatoes	4	85,225	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.92 (0.80–1.07), $I^2 = 52.6\%$	
	Carrots	1	9766	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 0.97 (0.72–1.30)	
	Strawberries	1	38,176	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 1.06 (0.95–1.17)	
	Tinned fruits	4	106,017	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 1.30 (0.81–2.08), $I^2 = 66.0\%$	
	Berries	2	40,224	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 1.13 (0.88–1.46), $I^2 = 0\%$	
	Potatoes	4	202,479	Prospective cohort studies up to Sept 2016	Dose–response per 100 g/day RR 1.01 (0.97–1.04), $I^2 = 13.4\%$	

(continued)

Table 2. Continued

Food group	Food item	Number of studies	Sample size	Inclusion criteria	Risk estimate for cardiovascular disease unless otherwise specified	Reference
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, $I^2 = 72.2\%$	Ronksley, 2011[22]
	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, $I^2 = 87.8\%$	Malerba, 2013[30]
	Green tea	5	197,957	Prospective cohort studies up to April 2015	Dose–response per cup/day RR 0.95 (0.90–1.00) for cardiovascular mortality, $I^2 = 83.8\%$	Tang, 2015[24]
	Black tea	7	162,230	Prospective cohort studies up to April 2015	Dose–response per cup/day RR 0.92 (0.85–0.99) for cardiovascular mortality, $I^2 = 75.6\%$	
	Sugar-sweetened beverages	1	2564	Prospective cohort studies up to July 2015	High vs. low intake RR 1.00 (0.98–1.02) for vascular event	Narain, 2016[25]
	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 50 g/day RR 1.03 (0.97–1.09), $I^2 = 0\%$	Guo, 2017[26]
	Cheese	9	234,447	Prospective cohort studies up to Sept 2016	Dose–response per 10 g/day RR 0.98 (0.95–1.00), $I^2 = 82.6\%$	
	Milk	9	249,779	Prospective cohort studies up to Sept 2016	Dose–response per 244 g/day RR 1.01 (0.93–1.10), $I^2 = 92.4\%$	
	Butter	2	147,297	Prospective cohort studies up to May 2015	Dose–response per 14 g/day RR 0.99 (0.96–1.02), $I^2 = 0\%$	Pimpin, 2018[7]

(continued)

Table 2. Continued

Food group	Food item	Number of studies	Sample size	Inclusion criteria	Risk estimate for cardiovascular disease unless otherwise specified	Reference
Nuts & Other	Nuts	12	376,228	Prospective cohort studies up to July 2016	Dose–response per 28 g/day RR 0.79 (0.70–0.88), $I^2 = 59.6\%$	Aune, 2016[27]
	Tree nuts	3	130,987	Prospective cohort studies up to July 2016	Dose–response per 10 g/day RR 0.75(0.67–0.84), $I^2 = 0\%$	
	Peanuts	5	265,252	Prospective cohort studies up to July 2016	Dose–response per 10 g/day RR 0.64 (0.50–0.81), $I^2 = 77.0\%$.	
	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), $I^2 = 61\%$	Aburto, 2013[28]
	Olive oil	9	476,714	Case–control, prospective studies and randomized trials up to Dec 2013	Dose–response per 25 g/day RR 0.82 (0.70–0.96), $I^2 = 77\%$	Martinez-Gonzalez, 2014[31]
	Soy	20	718,279	Prospective cohort and case control studies up to Feb 2016	High vs. low RR 0.83 (0.75–0.93), $I^2 = 71.4\%$	Yan, 2017[8]
	Tofu	4	260,607	Prospective cohort and case control studies up to Feb 2016	High vs. low RR 0.80 (0.64–1.00), $I^2 = 75.1\%$	
	Miso	2	42,371	Prospective cohort and case control studies up to Feb 2016	High vs. low RR 0.82 (0.64–1.06), $I^2 = 29.8\%$	
	Chocolate	12	369,599	Prospective cohort studies up to Jun 2018	Dose–response per 20 g/week 0.982 (0.972–0.992), $I^2 = 50.4\%$	Ren, 2018[32]

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 CVD and all-cause mortality. Many fruits and vegetables that 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 CVD.

Our results are important as diet is complex, and it appears that there may be dissonance between foods that are beneficial for all-cause mortality and CVD. We speculate that this may be because the major causes of all-cause mortality are likely to be a composite of CVD and those of cancer etiology. While oxidative stress plays an important role in both atherosclerosis[33] and oncogenesis[34] and both CVD and cancer share risk factors such as obesity,[35] physical inactivity, diabetes[36] and smoking,[37] hypertension is common and is strongly associated with CVD but the evidence of its link to cancer is less strong. Dietary elements which affect blood pressure may have greater benefits for CVD risk while 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 used by the public when interpreting healthy eating messages.[38] We found that dietary nuts appear to be beneficial for both all-cause mortality and CVD. 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] The consumption of nuts is 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 individuals 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 needed to examine different types of tree nuts as there were insufficient data on important nuts such as 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 is 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 a lower education level, have a higher body mass index and is 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 the effects of variation on exposure over time so caution may be needed when interpreting the risk of exposures measured only once at baseline.[51] This may apply for items that are not consumed on a regular basis or food items in which 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 population 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 into consideration of patients' overall nutritional 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, are more likely to exercise regularly, are more likely to be of normal weight and body mass index, are more likely be non-smokers 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 attract media attention disproportionately 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 CVD. 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 CVD risk.[52] Considering this finding, the overall CVD risk is likely to incorporate 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 were no data on seafood other than fish. More importantly, many reviews only had level 4 or limited evidence because there were fewer than four 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 CVD. A further limitation is that we are unable to assess on the individual study level the impact of the 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 CVD, 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 CVD. Our review provides a comprehensive summary of the evidence of benefit or harm of food items that may help physicians counsel their patients better about dietary advice.

Author 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 the work ensuring integrity and accuracy.

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References

1. Roth GA, Johnson C, Abajobir A, et al. Global, regional and national burden of cardiovascular disease for 10 causes, 1990 to 2015. *J Am Coll Cardiol* 2017; 70: 1–25.
2. Verschuren WMM. Diet and cardiovascular disease. *Curr Cardiol Rep* 2012; 14: 701–708.
3. Anand SS, Hawkes C, de Souza RJ, et al. Food consumption and its impact on cardiovascular disease: importance of solutions focused on the globalized food system. *J Am Coll Cardiol* 2015; 66: 1590–1614.
4. Bechthold A, Boeing H, Schwedhelm C, et al. Food groups and risk of coronary heart disease, stroke and heart failure: a systematic review and doseresponse meta-analysis of prospective studies. *Crit Rev Food Sci Nutr*. Epub ahead of print 17 October 2017. DOI: 10.1080/10408398.2017.1392288.
5. Mozaffarian D and Rimm EB. Fish intake, contaminants, and human health: evaluating the risks and benefits. *JAMA* 2006; 296: 1885–1899.
6. Chen GC, Wang Y, Tong X, et al. Cheese consumption and risk of cardiovascular disease: a meta-analysis of prospective studies. *Eur J Nutr* 2017; 56: 2565–2575.
7. Pimpin L, Wu JH, Haskelberg H, et al. Is butter back? A systematic review and meta-analysis of butter consumption and risk of cardiovascular disease, diabetes and total mortality. *PLoS One* 2016; 11: e0158118.
8. Yan Z, Zhang X, Li C, et al. Association between consumption of soy and risk of cardiovascular disease: a meta-analysis of observational studies. *Eur J Prev Cardiol* 2017; 24: 735–747.
9. Schulze Matthias B, Martínez-González Miguel A, Fung Teresa T, et al. Food based dietary patterns and chronic disease prevention. *BMJ* 2018; 361: k2396.
10. GOV.UK. *The Eatwell Guide*. www.gov.uk/government/publications/the-eatwell-guide (accessed 22 October 2018).
11. Office of Disease Prevention and Health Promotion. *2015–2020 Dietary guidelines for Americans*. https://health.gov/dietaryguidelines/2015/ (accessed 22 October 2018).

12. United States Department of Agriculture. Center for Nutrition Policy and Promotion. *Food Guide Pyramid*. www.cnpp.usda.gov/FGP (accessed 22 October 2018).
13. Grosso G, Godos J, Alvano F, et al. Coffee, caffeine, and health outcome: an umbrella review. *Ann Rev Nutr* 2017; 37: 131–156.
14. Aune D, Keum N, Gionvannucci E, et al. Whole grain consumption and risk of cardiovascular disease, cancer and all cause and cause specific mortality: systematic review and dose–response meta-analysis of prospective studies. *BMJ* 2016; 353: i2716.
15. Saneei P, Larijani B and Esmaillzadah A. Rice consumption, incidence of chronic diseases and risk of mortality: meta-analysis of cohort studies. *Public Health Nutr* 2017; 20: 233–244.
16. Yang Y, Zhao LG, Wu Q, et al. Association between dietary fiber and lower risk of all-cause mortality: a meta-analysis of cohort studies. *Am J Epidemiol* 2015; 181: 83–91.
17. Jayedi A, Shab-Bidar S, Eimeri S, et al. Fish consumption and risk of all-cause and cardiovascular mortality: a dose–response meta-analysis of prospective observational studies. *Public Health Nutr* 2018; 21: 1297–1306.
18. Abete I, Romaguera D, Vieira AR, et al. Association between total, processed, red and white meat consumption and all-cause, CVD and IHD mortality: a meta-analysis of cohort studies. *Br J Nutr* 2014; 112: 762–775.
19. Xu L, Lam TH, Jiang CQ, et al. Egg consumption and the risk of cardiovascular disease and all-cause mortality: Guangzhou Biobank Cohort Study and meta-analysis. *Eur J Nutr* 2019; 58: 785–796.
20. Aune D, Giovannucci E, Boffetta P, et al. Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality – a systematic review and dose–response meta-analysis of prospective studies. *Int J Epidemiol* 2017; 46: 1029–1056.
21. Schwingshackl L, Schwedhelm C, Hoffmann G, et al. Potatoes and risk of chronic disease: a systematic review and dose–response meta-analysis. *Eur J Nutr*, Epub ahead of print 9 July 2018. DOI: 10.1007/s00394-018-1774-2.
22. Ronksley PE, Brien SE, Turner BJ, et al. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. *BMJ* 2011; 342: d671.
23. Je Y and Giovannucci E. Coffee consumption and total mortality: a meta-analysis of twenty prospective cohort studies. *Br J Nutr* 2014; 111: 1162–1173.
24. Tang J, Zheng JS, Fang L, et al. Tea consumption and mortality of all cancers, CVD and all causes: a meta-analysis of eighteen prospective cohort studies. *Br J Nutr* 2015; 114: 673.
25. Narain A, Kwok CS and Mamas MA. Soft drinks and sweetened beverages and the risk of cardiovascular disease and mortality: a systematic review and meta-analysis. *Int J Clin Pract* 2016; 70: 791–805.
26. Guo J, Astrup A, Lovegrove JA, et al. Milk and dairy consumption and risk of cardiovascular diseases and all-cause mortality: dose–response meta-analysis of prospective cohort studies. *Eur J Epidemiol* 2017; 32: 269–287.
27. Aune D, Keum N, Giovannucci E, et al. Nut consumption and risk of cardiovascular disease, total cancer, all-cause and cause-specific mortality: a systematic review and dose–response meta-analysis of prospective studies. *BMC Med* 2016; 14: 207.
28. Alburto NJ, Ziolkovska A, Hooper L, et al. Effect of lower sodium intake on health: systematic review and meta-analyses. *BMJ* 2013; 346: f1326.
29. Treapleton DE, Greenwood DC, Evans CE, et al. Dietary fibre intake and risk of cardiovascular disease: systematic review and meta-analysis. *BMJ* 2013; 347: f6879.
30. Malerba S, Turati F and Galeone C. A meta-analysis of prospective studies and coffee consumption and mortality for all causes, cancers and cardiovascular diseases. *Eur J Epidemiol* 2013; 28: 527–539.
31. Martinez-Gonzalez MA, Dominguez LJ and Delgado-Rodriguez M. Olive oil consumption and risk of CHD and/or stroke: a meta-analysis of case-control, cohort and interventional studies. *Br J Nutr* 2014; 112: 248–259.
32. Ren Y, Liu Y, Sung XZ, et al. Chocolate consumption and risk of cardiovascular disease: a meta-analysis of prospective studies. *Heart* 2019; 105: 49–55.
33. Kattoor AJ, Pothineni NVK, Palagiri D, et al. Oxidative stress in atherosclerosis. *Curr Atheroscler Rep* 2017; 19: 42.
34. Reuter S, Gupta SC, Mhaturvedi MM, et al. Oxidative stress, inflammation, and cancer: how are they linked? *Free Radic Biol Med* 2010; 49: 1603–1616.
35. Basen-Engquist K and Chang M. Obesity and cancer risk: recent review and evidence. *Curr Oncol Rep* 2011; 13: 71–76.
36. Vigneri P, Fasca F, Sciacca L, et al. Diabetes and cancer. *Endocrine-Related Cancer* 2009; 16: 1103–1123.
37. Carbone D. Smoking and cancer. *Am J Med* 1992; 93: S13–S17.
38. Bisogni CA, Jastran M, Seligson M, et al. How people interpret healthy eating: contributions of qualitative research. *J Nutr Educ Behav* 2012; 44: 282–301.
39. Ros E. Health benefits of nut consumption. *Nutrients* 2010; 2: 652–682.
40. Kris-Etherton PM, Zhao G, Binkoski AE, et al. The effect of nuts on coronary heart disease risk. *Nutr Rev* 2001; 59: 103–111.
41. Rajaram S and Sabete J. Nuts, body weight and insulin resistance. *Br J Nutr* 2006; 96: S79–S86.
42. Ros E. *The Mediterranean Diet*. Chapter 17 – Contribution of Nuts to the Mediterranean Diet. Academic Press; 2015; pp. 175–184.
43. Micha R, Michas G and Mozaffarian D. Unprocessed red and processed meats and risk of coronary artery disease and type 2 diabetes – an updated review of the evidence. *Curr Atheroscler Rep* 2012; 14: 515–524.
44. Sacks FM and Campos H. Dietary therapy in hypertension. *N Engl J Med* 2010; 362: 2102–2112.
45. Forstermann U. Oxidative stress in vascular disease: causes, defense mechanisms and potential therapies. *Nat Clin Pract Cardiovasc Med* 2008; 5: 338–349.

46. McGrowder D, Ragoobirsingh D and Dasgupta T. Effects of S-nitrosoN-acetyl-penicillamine administration on glucose tolerance and plasma levels of insulin and glucagon in the dog. *Nitric Oxide* 2001; 5: 402–412.
47. Portha B, Giroix MH, Cros JC, et al. Diabetogenic effect of N-nitrosomethylurea and N-nitrosomethylurethane in the adult rat. *Ann Nutr Aliment* 1980; 34: 1143–1151.
48. Aasheim ET, Sharp JS, Appleby PN, et al. Tinned fruit consumption and mortality in three prospective cohorts. *PLoS One* 2015; 10: e0117796.
49. Yang Q, Zhang Z, Gregg EW, et al. Added sugar intake and cardiovascular diseases mortality among US adults. *JAMA Intern Med* 2014; 30341: 1–9.
50. Mozaffarian S and Foroughi N. Dietary guidelines and health – is nutrition science up to the task? *BMJ* 2018; 360: k822.
51. Britton A, Marmot MG and Shipley MJ. How does variability in alcohol consumption over time affect the relationship with mortality and coronary heart disease? *Addiction* 2010; 105: 639–645.
52. Alvarez-Alvarez I, de Rojas JP, Fernandez-Montero A, et al. Strong inverse associations of Mediterranean diet, physical activity and their combination with cardiovascular disease: the Seguimiento Universidad de Navarra (SUN) cohort. *Eur J Prev Cardiol* 2018; 25: 1186–1197.