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((((((((((((((((((((("nuts"[MeSH Terms]) OR nut) OR nuts) OR "juglans"[MeSH Terms]) OR walnut*) OR "prunus dulcis"[MeSH Terms]) OR almond*) OR "bertholletia"[MeSH Terms]) OR brazil nut*) OR Amazonia) OR "anacardium"[MeSH Terms]) OR cashew*) OR "corylus"[MeSH Terms]) OR hazelnut*) OR "macadamia"[MeSH Terms]) OR macadamia*) OR "carya"[MeSH Terms]) OR pecan*) OR "pinus"[MeSH Terms]) OR pine nut*) OR "pistacia"[MeSH Terms]) OR pistachio*) OR "arachis"[MeSH Terms]) OR peanut*))

AND

((((((((((((((((((("inflammation"[MeSH Terms]) OR inflammat*) OR endothelial*) OR "adiponectin"[MeSH Terms]) OR adiponectin) OR high molecular weight adiponectin) OR "c reactive protein"[MeSH Terms]) OR c reactive protein) OR c-reactive protein) OR CRP) OR "tumor necrosis factor alpha"[MeSH Terms]) OR tumor necrosis factor*) OR tumour necrosis factor*) OR TNF*) OR "interleukins"[MeSH Terms]) OR interleukin*) OR "cell adhesion molecules"[MeSH Terms]) OR adhesion molecule*) OR flow mediated dilat*) OR flow-mediated dilat*) OR FMD) OR "cytokines"[MeSH Terms]) OR cytokine*)

Supplementary material 3: Differences in CRP, adiponectin, TNF-α, IL-6, ICAM-1, VCAM-1, and FMD following nut consumption, compared to control, using correlation coefficient of 0.5

Outcome	**Number of analyses**	**Number of participants**	**Effect estimate**		**Inconsistency (I^2)**
CRP (mg/L)	26	1578	-0.03 mg/L [-0.09, 0.03], P = 0.30	-5.53 mg/L [-11.96, 0.90] - 0.60 mg/L [-2.44, 3.64]	33%
Total adiponectin (µg/mL)	7	506	0.15 µg/mL [-0.77, 1.07], P = 0.75	-9.80µg/mL [-23.99, 4.39] - 10.60µg/mL [6.39, 14.81]	81%
TNF-α (pg/mL)	8	482	-0.05 pg/mL [-0.12, 0.02], P = 0.17	-3.70pg/mL [-6.93, -0.47] - 0.70 pg/mL [-0.41, 1.81]	7%
IL-6 (pg/mL)	13	906	-0.06 pg/mL [-0.16, 0.04], P = 0.24	-1.55 pg/mL [-2.80, -0.30] - 0.46 pg/mL [-0.22, 1.14]	28%
ICAM-1 (ng/mL)	15	1047	0.62 ng/mL [-0.24, 1.49], P = 0.16	-80.63ng/mL [-209.62, 48.36] - 16.76ng/mL [1.44, 32.08]	0%
VCAM-1 (ng/mL)	14	804	1.25 ng/mL [-12.09, 14.59], P = 0.85	-99.72ng/mL [-316.35, 116.91] - 62.00ng/mL [-39.40, 163.40]	9%

FMD (%)	9	652	0.74 % [0.27, 1.20], P = 0.002	-0.40% [-1.33, 0.53] - 2.36% [-1.71, 6.43]	46%

Supplementary material 4: Results of sub-group analyses

Table 1: Results of sub-group analyses for CRP

Sub-group analysis category	Sub-group	Number of analyses	Number of participants	Effect estimate	Test for sub-group differences
Duration	Less than three months	17	847	-0.00 mg/L [-0.04, 0.03]	Chi^2 = 1.02, df = 1 (P = 0.31), I^2 = 1.9%
	More than three months	9	731	-0.24 mg/L [-0.69, 0.22]	
Risk of bias	Low/unclear	11	588	-0.25 mg/L [-0.53, 0.04]	Chi^2 = 2.82, df = 1 (P = 0.09), I^2 = 64.6%
	High	15	990	0.00 mg/L [-0.00, 0.00]	
Nut type	Almond	7	295	-0.79 mg/L [-1.52, -0.06]	Chi^2 = 10.42, df = 6 (P = 0.11), I^2 = 42.4%
	Walnut	5	336	0.00 mg/L [-0.00, 0.00]	
	Hazelnut	2	163	-0.31 mg/L [-0.79, 0.18]	
	Mixed nut	5	318	0.01 mg/L [-0.03, 0.05]	
	Peanut	2	187	-0.38 mg/L [-0.89, 0.13]	

	Pistachio	4	258	-0.42 mg/L [-1.03, 0.19]	
	Brazil nut	1	21	-0.15 mg/L [-0.90, 0.60]	
Health status	Healthy	2	61	0.00 mg/L [-0.00, 0.00]	Chi^2 = 10.41, df = 5 (P = 0.06), I^2 = 52.0%
	Chronic disease risk factors	14	869	-0.29 mg/L [-0.54, -0.04]	
	T2DM	4	208	-1.18 mg/L [-2.70, 0.35]	
	MetS	4	242	-0.19 mg/L [-0.55, 0.17]	
	CAD	1	90	-0.60 mg/L [-2.53, 1.33]	
	Combination	1	108	0.50 mg/L [-0.34, 1.34]	
Energy value of nuts included in diet	Adjusted	16	1029	-0.23 mg/L [-0.44, -0.01]	Chi^2 = 3.99, df = 1 (P = 0.05), I^2 = 74.9%
	Not adjusted	10	549	-0.00 mg/L [-0.06, 0.05]	
Study design	Parallel	14	828	-0.29 mg/L [-0.58, 0.00]	Chi^2 = 3.84, df = 1 (P = 0.05), I^2 = 74.0%
	Cross-over	12	750	0.00 mg/L [-0.00, 0.00]	
Nut dose	<50g/day	13	828	0.00 mg/L [-0.00, 0.00]	Chi^2 = 5.74, df = 1 (P = 0.02), I^2 = 82.6%
	≥50g/day	13	750	-0.34 mg/L [-0.63, -0.06]	

Table 2: Results of sub-group analyses for FMD

Sub-group analysis category	Sub-group	Number of analyses	Number of participants	Effect estimate	Test for sub-group differences
Duration	Less than three months	6	386	0.77 % [0.17,1.38]	$Chi^2 = 0.01$, df = 1 (P = 0.91), I^2 = 0%
	More than three months	3	266	0.70 % [-0.29, 1.70]	
Risk of bias	Low/unclear	6	480	0.69 % [0.22, 1.16]	$Chi^2 = 1.32$, df = 1 (P = 0.25), I^2 = 24.2%
	High	3	172	1.43 % [0.25, 2.61]	
Nut type	Almond	1	90	0.80 % [-0.75, 2.35]	$Chi^2 = 3.86$, df = 2 (P = 0.15), I^2 = 48.1%
	Walnut	5	404	1.02 % [0.51, 1.53]	
	Pistachio	3	158	-0.11 % [-1.11, 0.90]	
Health status	Chronic disease risk factors	4	230	1.09 % [0.25, 1.92]	$Chi^2 = 0.97$, df = 3 (P = 0.81), I^2 = 0%
	T2DM	2	108	0.38 % [-0.98, 1.74]	

	CAD	1	90	0.80 % [-0.75, 2.35]	
	Combination	2	224	0.60 % [-0.43, 1.62]	
Energy value of nuts included in diet	Adjusted	8	540	0.77 % [0.27, 1.27]	$Chi^2 = 0.00$, df = 1 (P = 1.00), I^2 = 0%
	Not adjusted	1	112	0.77 % [-0.64, 2.18]	
Study design	Parallel	1	42	2.36 % [-1.71, 6.43]	$Chi^2 = 0.58$, df = 1 (P = 0.45), I^2 = 0%
	Cross-over	8	610	0.77 % [0.32, 1.21]	
Nut dose	<50g/day	1	42	2.36 % [-1.71, 6.43]	$Chi^2 = 0.58$, df = 1 (P = 0.45), I^2 = 0%
	≥50g/day	8	610	0.77 % [0.32, 1.21]	

Table 3: Results of sub-group analyses for adiponectin

Sub-group analysis category	Sub-group	Number of analyses	Number of participants	Effect estimate	Test for sub-group differences
Duration	Less than three months	2	130	-0.60 μg/mL [-2.48, 1.28]	$Chi^2 = 1.03$, df = 1 (P = 0.31), I^2 = 3.3%
	More than three months	5	376	1.71 μg/mL [-2.33, 5.75]	
Risk of bias	Low/unclear	3	234	-0.00 μg/mL [-0.00, 0.00]	$Chi^2 = 0.45$, df = 1 (P = 0.50), I^2 = 0%
	High	4	272	1.91 μg/mL [-3.70, 7.53]	
Nut type	Walnut	2	96	-0.52 μg/mL [-3.78, 2.75]	$Chi^2 = 0.57$, df = 2 (P = 0.75), I^2 = 0%
	Mixed nut	3	234	-0.00 μg/mL [-0.00, 0.00]	
	Pistachio	2	176	4.49 μg/mL [-8.30, 17.28]	
Health status	Chronic disease risk factors	2	178	-2.33 μg/mL [-5.28, 0.63]	$Chi^2 = 3.42$, df = 2 (P = 0.18), I^2 = 41.5%
	MetS	3	178	0.53 μg/mL [-0.49, 1.55]	

	Combination	2	150	-2.05 μg/mL [-11.64, 7.54]	
Energy value of nuts included in diet	Adjusted	5	396	0.80 μg/mL [-4.62, 6.22]	Chi^2 = 0.08, df = 1 (P = 0.77), I^2 = 0%
	Not adjusted	2	110	-0.00 μg/mL [-0.00, 0.00]	
Study design	Parallel	5	328	0.53 μg/mL [-0.43, 1.49]	Chi^2 = 3.24, df = 1 (P = 0.07), I^2 = 69.2%
	Cross-over	2	178	-2.33 μg/mL [-5.28, 0.63]	
Nut dose	<50g/day	6	398	0.34 μg/mL [-0.60, 1.28]	Chi^2 = 0.49, df = 1 (P = 0.48), I^2 = 0%
	≥50g/day	1	108	-2.48 μg/mL [-10.31, 5.35]	

Table 4: Results of sub-group analyses for TNF-α

Sub-group analysis category	Sub-group	Number of analyses	Number of participants	Effect estimate	Test for sub-group differences
Duration	Less than three months	5	285	-0.06 pg/mL [-0.12, 0.01]	$Chi^2 = 0.21$, df = 1 (P = 0.65), I^2 = 0%
	More than three months	3	197	-0.70 pg/mL [-3.48, 2.08]	
Risk of bias	Low/unclear	2	148	0.11 pg/mL [-0.51, 0.73]	$Chi^2 = 0.21$, df = 1 (P = 0.65), I^2 = 0%
	High	6	334	-0.04 pg/mL [-0.22, 0.15]	
Nut type	Almond	3	151	-0.06 pg/mL [-0.13, 0.01]	$Chi^2 = 6.75$, df = 4 (P = 0.15), I^2 = 40.8%
	Walnut	2	90	-0.03 pg/mL [-0.21, 0.14]	
	Mixed nut	1	108	0.70 pg/mL [-0.41, 1.81]	
	Peanut	1	65	-0.16 pg/mL [-1.41, 1.10]	
	Pistachio	1	68	-3.70 pg/mL [-6.93, -0.47]	
Health status	Healthy	1	40	-0.01 pg/mL [-0.24, 0.22]	$Chi^2 = 7.08$, df = 5 (P = 0.21), I^2 =

	Chronic disease risk factors	2	115	-0.07 pg/mL [-0.34, 0.20]	29.4%
	T2DM	2	61	-0.06 pg/mL [-0.13, 0.01]	
	MetS	1	68	-3.70 pg/mL [-6.93, -0.47]	
	CAD	1	90	0.10 pg/mL [-0.54, 0.74]	
	Combination	1	108	0.70 pg/mL [-0.41, 1.81]	
Energy value of nuts included in diet	Adjusted	6	421	-0.04 pg/mL [-0.24, 0.15]	$Chi^2 = 0.05$, df = 1 (P = 0.83), I^2 = 0%
	Not adjusted	2	61	-0.01 pg/mL [-0.24, 0.22]	
Study design	Parallel	4	262	-0.27 pg/mL [-1.68, 1.14]	$Chi^2 = 0.09$, df = 1 (P = 0.77), I^2 = 0%
	Cross-over	4	220	-0.05 pg/mL [-0.12, 0.01]	
Nut dose	<50g/day	5	287	-0.02 pg/mL [-0.34, 0.31]	$Chi^2 = 0.06$, df = 1 (P = 0.80), I^2 = 0%
	≥50g/day	3	195	-0.06 pg/mL [-0.13, 0.01]	

Table 5: Results of sub-group analyses for IL-6

Sub-group analysis category	Sub-group	Number of analyses	Number of participants	Effect estimate	Test for sub-group differences
Duration	Less than three months	7	386	0.04 pg/mL [-0.02, 0.09]	$Chi^2 = 2.71$, df = 1 (P = 0.10), I^2 = 63.1%
	More than three months	6	520	-0.19 pg/mL [-0.45, 0.07]	
Risk of bias	Low/unclear	5	314	-0.01 pg/mL [-0.26, 0.23]	$Chi^2 = 0.62$, df = 1 (P = 0.43), I^2 = 0%
	High	8	592	-0.13 pg/mL [-0.29, 0.03]	
Nut type	Almond	4	201	-0.16 pg/mL [-0.44, 0.13]	$Chi^2 = 5.17$, df = 4 (P = 0.27), I^2 = 22.6%
	Walnut	3	216	-0.11 pg/mL [-0.31, 0.10]	
	Hazelnut	2	163	0.05 pg/mL [-0.01, 0.11]	
	Mixed nut	3	218	-0.18 pg/mL [-0.99, 0.63]	
	Pistachio	1	108	-0.14 pg/mL [-0.47, 0.19]	
Health status	Chronic disease risk	6	497	0.04 pg/mL [-0.02, 0.10]	$Chi^2 = 3.09$, df = 5 (P = 0.69), I^2 = 0%

	factors				
	Healthy	1	40	-0.10 pg/mL [-0.39, 0.19]	
	MetS	2	110	-0.47 pg/mL [-2.44, 1.49]	
	T2DM	2	61	-0.14 pg/mL [-0.46, 0.18]	
	CAD	1	90	-0.50 pg/mL [-1.62, 0.62]	
	Combination	1	108	0.00 pg/mL [-0.41, 0.41]	
Energy value of nuts included in diet	Adjusted	8	628	0.03 pg/mL [-0.02, 0.09]	$Chi^2 = 0.68$, df = 1 (P = 0.41), I^2 = 0%
	Not adjusted	5	278	-0.18 pg/mL [-0.68, 0.32]	
Study design	Parallel	7	528	-0.04 pg/mL [-0.29, 0.22]	$Chi^2 = 0.26$, df = 1 (P = 0.61), I^2 = 0%
	Cross-over	6	378	-0.12 pg/mL [-0.27, 0.04]	
Nut dose	<50g/day	9	618	-0.03 pg/mL [-0.17, 0.12]	$Chi^2 = 0.65$, df = 1 (P = 0.42), I^2 = 0%
	≥50g/day	4	288	-0.14 pg/mL [-0.36, 0.09]	

Table 6: Results of sub-group analyses for ICAM-1

Sub-group analysis category	Sub-group	Number of analyses	Number of participants	Effect estimate	Test for sub-group differences
Duration	Less than three months	12	537	0.66 ng/mL [-0.56, 1.88]	$Chi^2 = 0.04$, df = 1 (P = 0.83), I^2 = 0%
	More than three months	3	510	2.35 ng/mL [-13.26, 17.96]	
Risk of bias	Low/unclear	8	660	4.58 ng/mL [-2.68, 11.85]	$Chi^2 = 1.14$, df = 1 (P = 0.29), I^2 = 12.4%
	High	7	387	0.57 ng/mL [-0.66, 1.80]	
Nut type	Almond	3	81	11.65 ng/mL [-1.49, 24.80]	$Chi^2 = 3.34$, df = 4 (P = 0.50), I^2 = 0%
	Walnut	5	244	0.58 ng/mL [-0.65, 1.81]	
	Hazelnut	2	163	-3.32 ng/mL [-22.42, 15.78]	
	Mixed nut	4	499	3.75 ng/mL [-7.31, 14.81]	
	Pistachio	1	60	-2.60 ng/mL [-18.13, 12.93]	

Health status	Healthy	1	40	0.65 ng/mL [-0.59, 1.89]	Chi^2 = 1.02, df = 4 (P = 0.91), I^2 = 0%
	Chronic disease risk factors	9	444	0.86 ng/mL [-6.94, 8.65]	
	T2DM	2	100	-1.67 ng/mL [-16.50, 13.16]	
	MetS	2	110	-13.46 ng/mL [-76.61, 49.70]	
	Combination	1	353	8.00 ng/mL [-8.85, 24.85]	
Energy value of nuts included in diet	Adjusted	9	749	-1.31 ng/mL [-8.90, 6.29]	Chi^2 = 0.48, df = 1 (P = 0.49), I^2 = 0%
	Not adjusted	6	298	2.06 ng/mL [-3.72, 7.84]	
Study design	Parallel	7	667	5.39 ng/mL [-2.46, 13.24]	Test for subgroup differences: Chi^2 = 1.42, df = 1 (P = 0.23), I^2 = 29.6%
	Cross-over	8	380	0.56 ng/mL [-0.66, 1.79]	
Nut dose	<50g/day	9	830	0.62 ng/mL [-0.60, 1.84]	Chi^2 = 0.29, df = 1 (P = 0.59), I^2 = 0%
	≥50g/day	6	217	3.66 ng/mL [-7.32, 14.65]	

Table 7: Results of sub-group analyses for VCAM-1

Sub-group analysis category	**Sub-group**	**Number of analyses**	**Number of participants**	**Effect estimate**	**Test for sub-group differences**
Duration	Less than three months	11	537	2.23 ng/mL [-9.68, 14.13]	$Chi^2 = 0.02$, df = 1 (P = 0.89), I^2 = 0%
	More than three months	3	267	-4.16 ng/mL [-96.76, 88.44]	
Risk of bias	Low/unclear	8	417	2.39 ng/mL [-9.72, 14.50]	$Chi^2 = 0.04$, df = 1 (P = 0.83), I^2 = 0%
	High	6	387	7.42 ng/mL [-38.20, 53.04]	
Nut type	Almond	4	171	1.11 ng/mL [-13.10, 15.33]	$Chi^2 = 1.56$, df = 4 (P = 0.82), I^2 = 0%
	Walnut	3	154	-30.19 ng/mL [-99.92, 39.53]	
	Hazelnut	2	163	17.62 ng/mL [-24.61, 59.85]	
	Mixed nut	4	256	9.30 ng/mL [-21.20, 39.80]	
	Pistachio	1	60	3.40 ng/mL [-60.84, 67.64]	

Health status	Chronic disease risk factors	8	394	3.95 ng/mL [-9.12, 17.02]	Chi^2 = 2.08, df = 4 (P = 0.72), I^2 = 0%
	T2DM	2	100	-17.58 ng/mL [-67.98, 32.82]	
	MetS	2	110	9.61 ng/mL [-23.37, 42.59]	
	CAD	1	90	-48.00 ng/mL [-193.52, 97.52]	
	Combination	1	110	-70.00 ng/mL [-230.43, 90.43]	
Energy value of nuts included in diet	Adjusted	9	546	-12.78 ng/mL [-42.38, 16.83]	Chi^2 = 1.27, df = 1 (P = 0.26), I^2 = 21.0%
	Not adjusted	5	258	5.71 ng/mL [-7.00, 18.42]	
Study design	Parallel	7	424	5.01 ng/mL [-7.27, 17.29]	Chi^2 = 1.26, df = 1 (P = 0.26), I^2 = 20.5%
	Cross-over	7	380	-17.66 ng/mL [-55.33, 20.02]	
Nut dose	<50g/day	7	497	9.74 ng/mL [-14.01, 33.49]	Chi^2 = 0.43, df = 1 (P = 0.51), I^2 = 0%
	≥50g/day	7	307	0.63 ng/mL [-12.78, 14.04]	

Supplementary material 5: Forest plots of difference in CRP after exclusion of individual studies

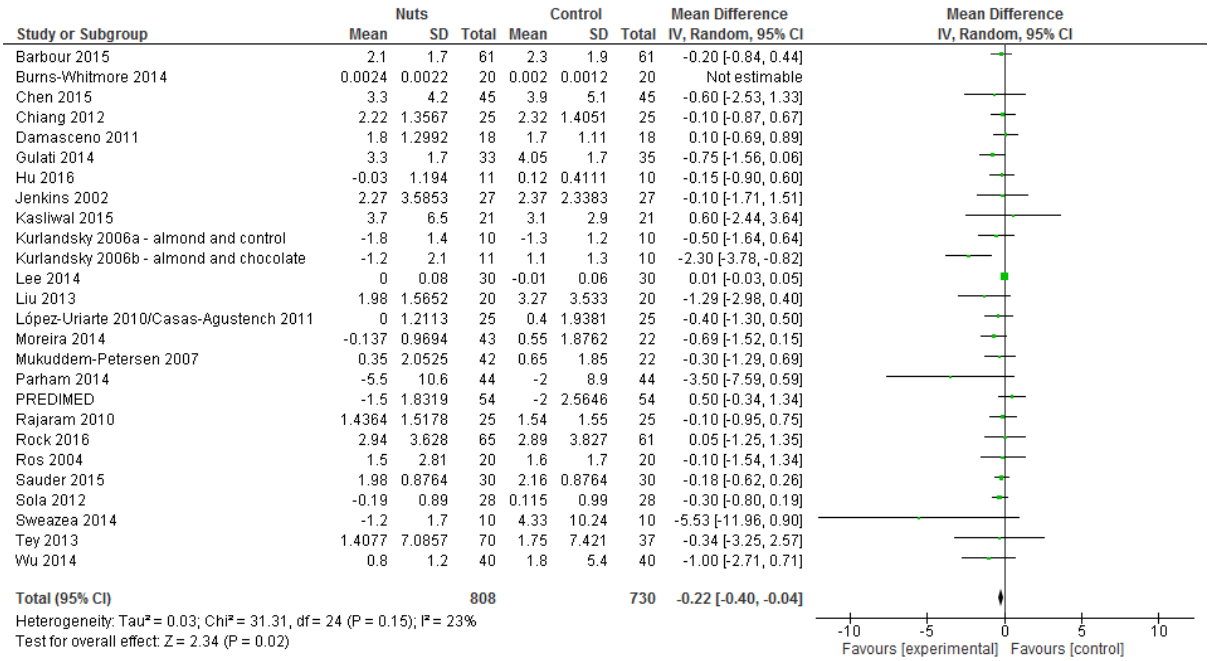

Figure 1: Difference in CRP (mg/L) between nut consumption and control, after exclusion of Burns-Whitmore et al. (2014). Diamond indicates weighted mean difference with 95% confidence intervals.

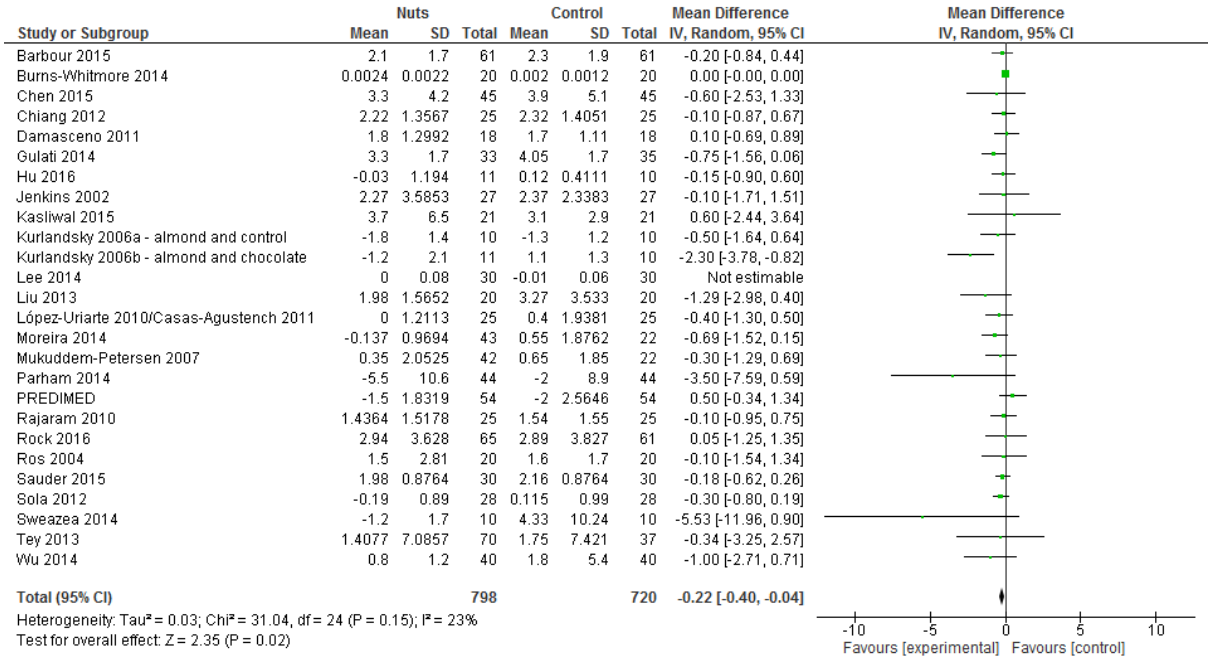

Figure 2: Difference in CRP (mg/L) between nut consumption and control, after exclusion of Lee et al. (2014). Diamond indicates weighted mean difference with 95% confidence intervals.

Supplementary material 6: Forest plots of differences in biomarkers between nut consumption and control

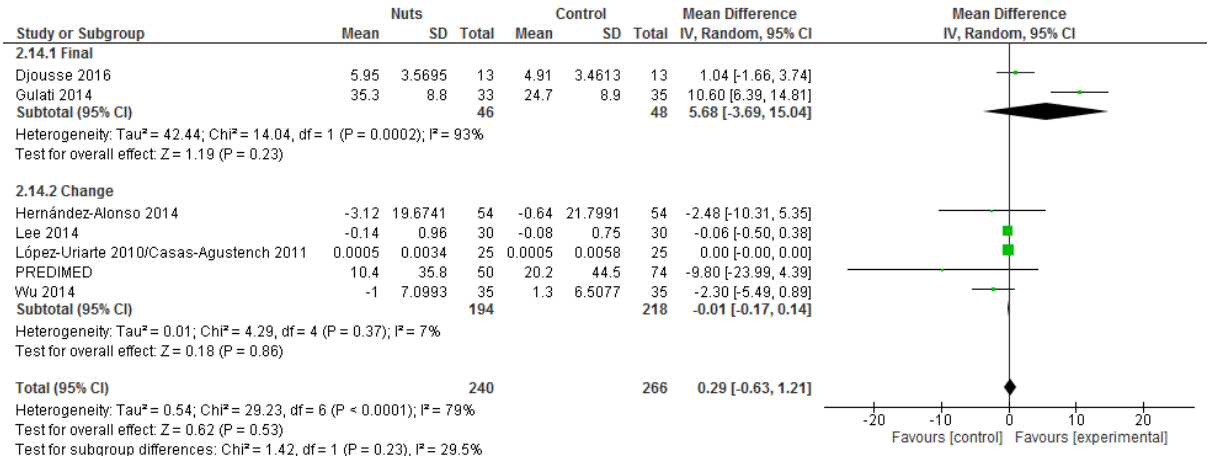

Figure 3: Difference in adiponectin (µg/mL) between nut consumption and control (presented as sub-groups based on mean final or change values for readability). Diamond indicates weighted mean difference with 95% confidence intervals.

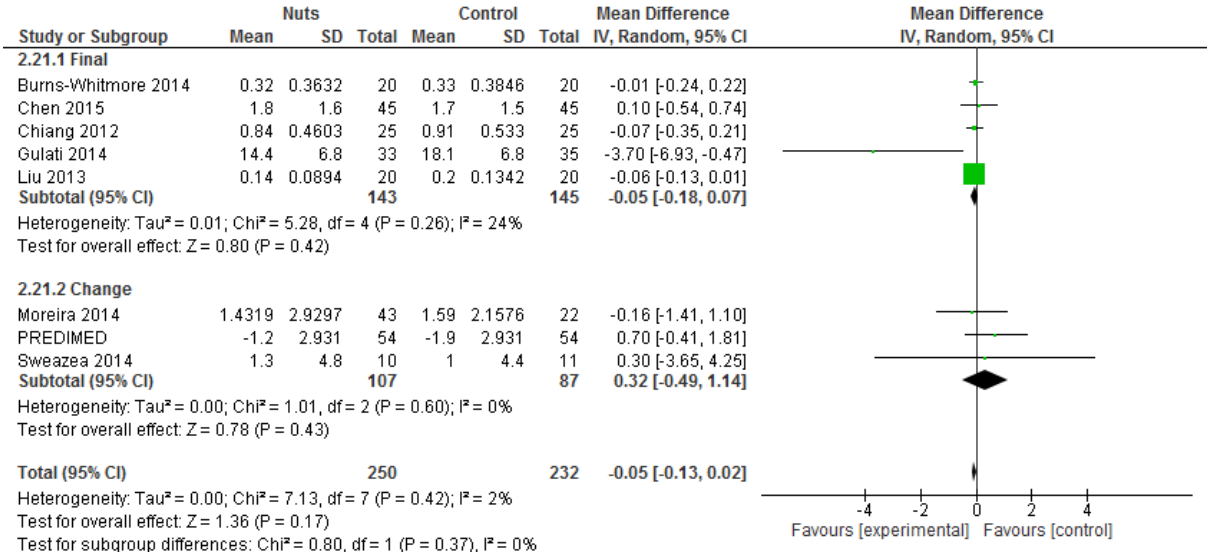

Figure 4: Difference in TNF-α (pg/mL) between nut consumption and control (presented as sub-groups based on mean final or change values for readability). Diamond indicates weighted mean difference with 95% confidence intervals.

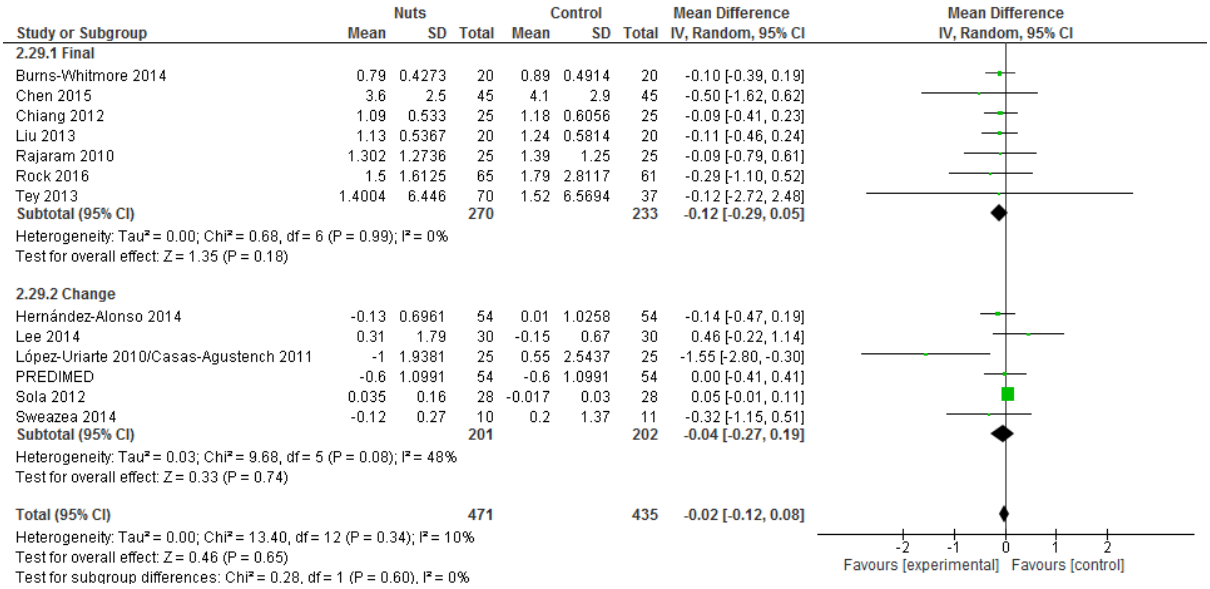

Figure 5: Difference in IL-6 (pg/mL) between nut consumption and control (presented as sub-groups based on mean final or change values for readability). Diamond indicates weighted mean difference with 95% confidence intervals

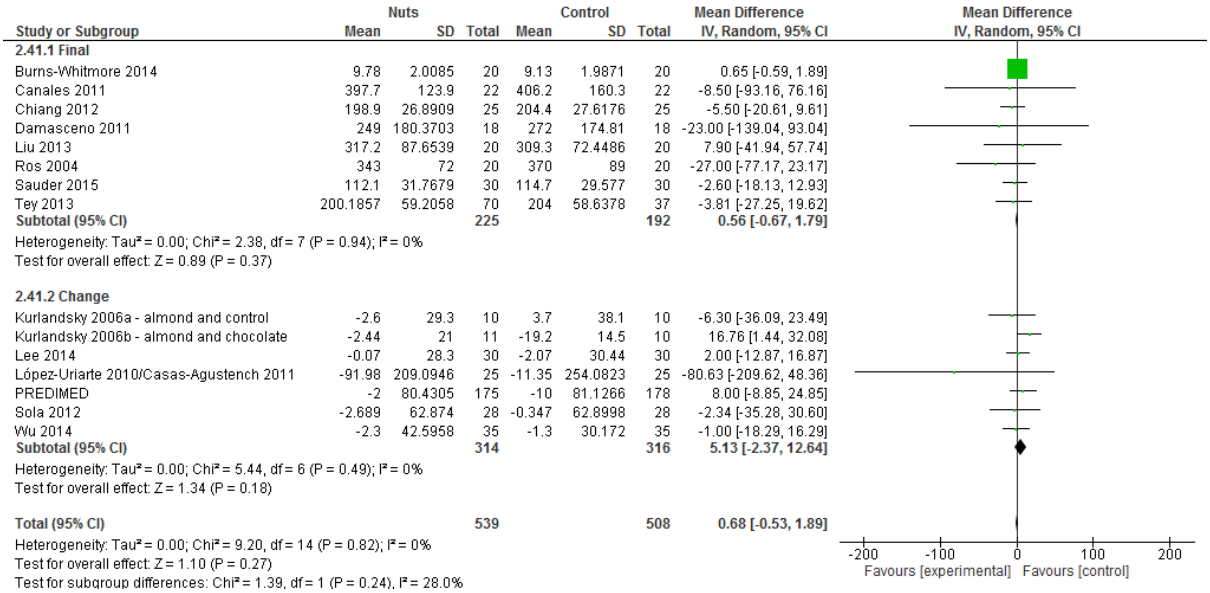

Figure 6: Difference in ICAM-1 (ng/mL) between nut consumption and control (presented as sub-groups based on mean final or change values for readability). Diamond indicates weighted mean difference with 95% confidence intervals

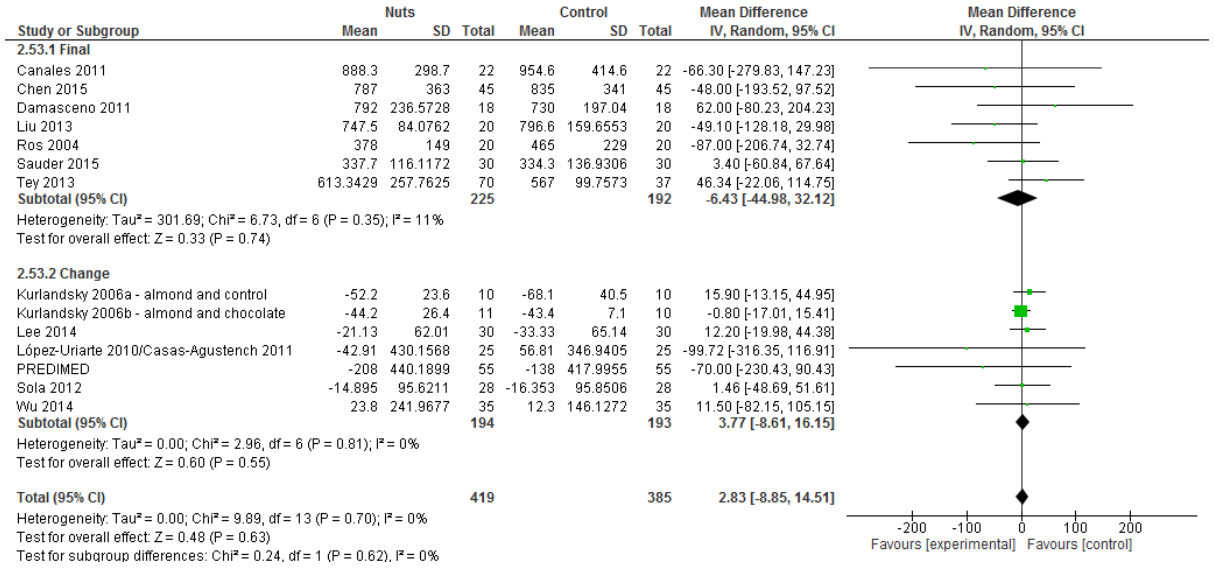

Figure 7: Difference in VCAM-1 (ng/mL) between nut consumption and control (presented as sub-groups based on mean final or change values for readability). Diamond indicates weighted mean difference with 95% confidence intervals

Supplementary material 7: Funnel plots

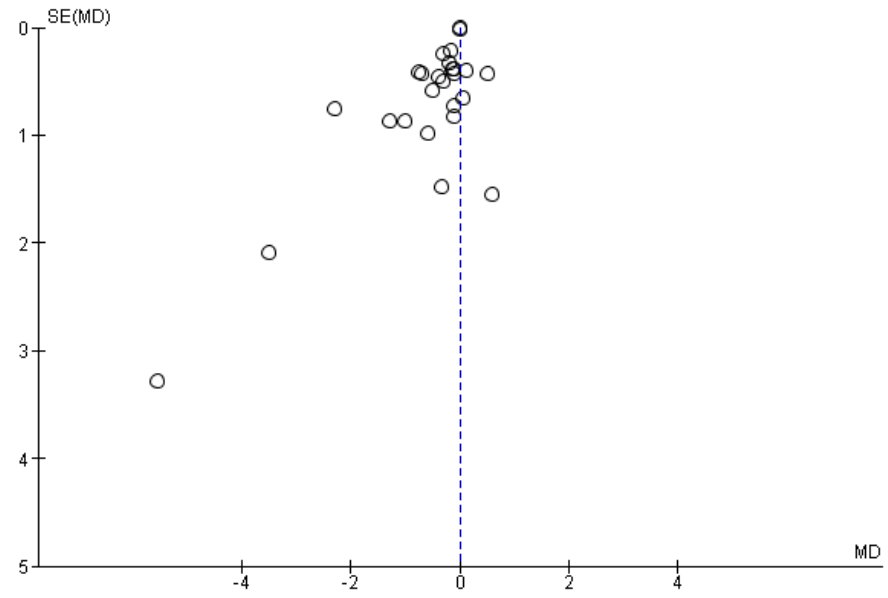

Figure 8: Funnel plot of the effect of nut consumption on CRP (mg/L)

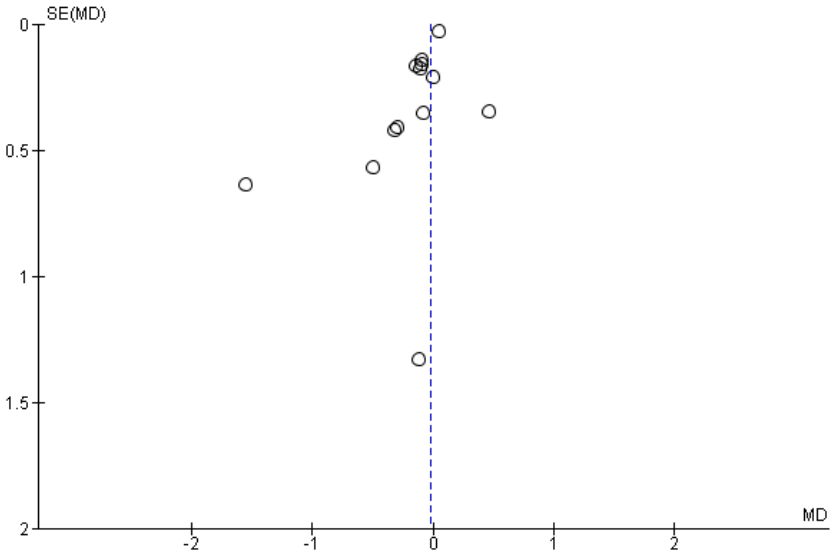

Figure 9: Funnel plot of the effect of nut consumption on IL-6 (pg/mL)

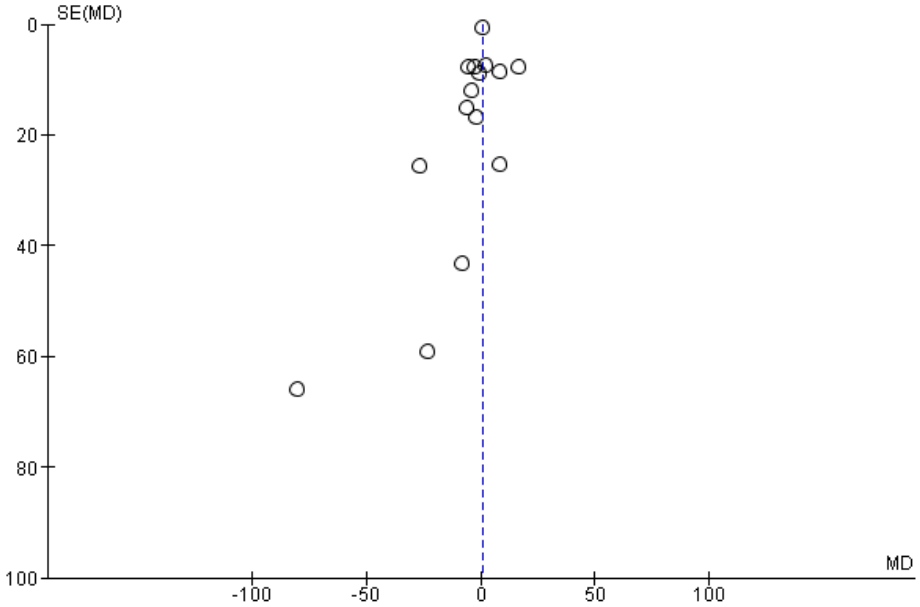

Figure 10: Funnel plot of the effect of nut consumption on ICAM-1 (ng/mL)

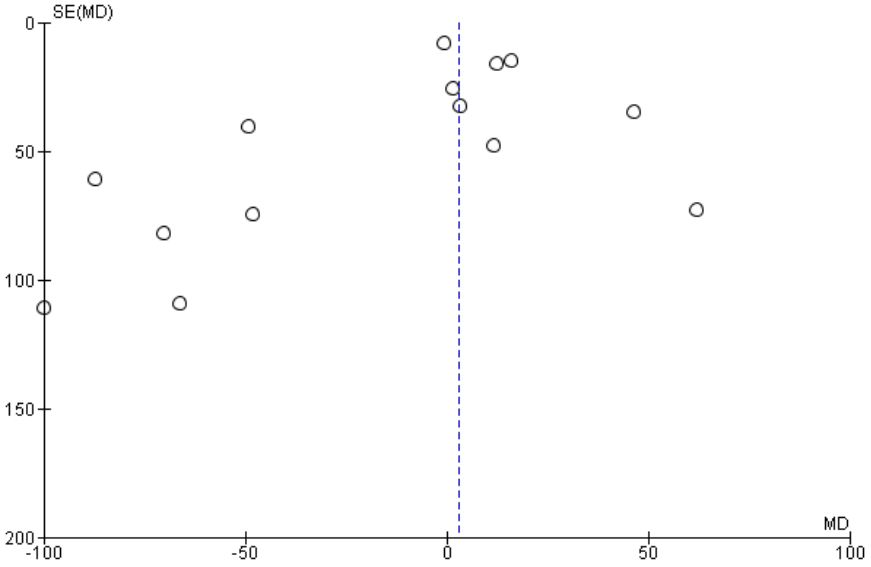

Figure 11: Funnel plot of the effect of nut consumption on VCAM-1 (ng/mL)

Supplementary material 8: Risk of bias assessment summary

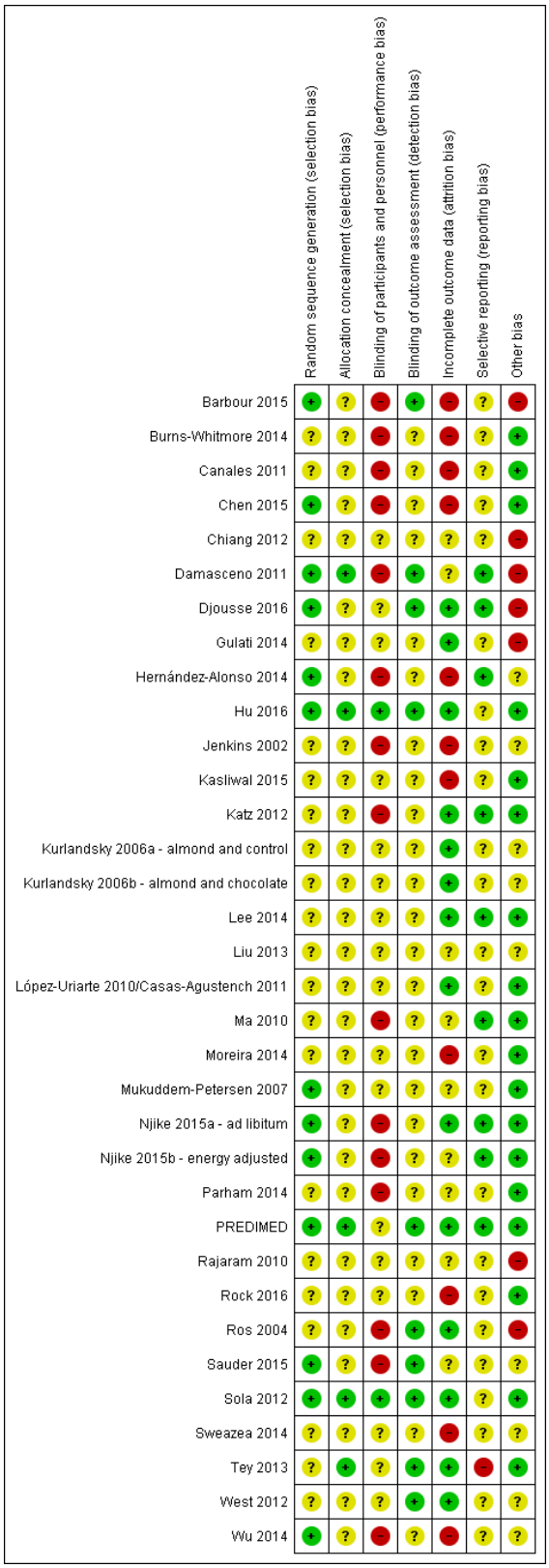

Figure 12: Risk of bias assessment for each study

Supplementary material 9: Justification for risk of bias judgements

Barbour et al., 2015

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Article states: "Subjects were randomised using computer generated software"
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	Would not be possible to blind participants or personnel as food was provided. Whilst this may not have affected measures, it may have affected participant behaviour during intervention and control periods
Blinding of outcome assessment (detection bias)	Low risk	Article states: "Data entry and analysis was blinded to minimise investigator bias"
Incomplete outcome data (attrition bias)	High risk	>10% withdrawal, intention-to-treat (ITT) not used
Selective reporting (reporting bias)	Unclear risk	ANZCTRN registration available, includes pre-specified outcomes not reported in this paper but which may have been reported in unpublished primary paper
Other bias	High risk	No washout period - authors specify 12 week period would have been sufficient to avoid carry over effects but this is not clear

Burns-Whitmore et al., 2014

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, method not given
Allocation concealment (selection bias)	Unclear risk	Not specified

Blinding of participants and personnel (performance bias)	High risk	Would not be possible to blind participants or personnel as food was provided. Whilst this may not have affected measures, it may have affected participant behaviour during intervention and control periods
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although outcomes unlikely to be influenced by blinding
Incomplete outcome data (attrition bias)	High risk	>20% withdrawal, ITT not used (not clear which group participants dropped out of)
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Other bias	Low risk	4 week wash-out period (justified). Did not report baseline results for outcomes of interest, but unlikely to influence as cross-over study

Canales et al., 2011

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, method not given
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	Stated to be non-blinded. Whilst this may not have affected measures, it may have affected participant behaviour during intervention and control periods
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although outcomes unlikely to be influenced by blinding
Incomplete outcome data (attrition bias)	High risk	>10% withdrawal, ITT not used
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Other bias	Low risk	4 -6 week wash-out period (appears suitable)

Chen et al., 2015

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The program in the randomization.com was employed for the randomization
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	Would not be possible to blind participants or personnel as food was provided. Whilst this may not have affected measures, it may have affected participant behaviour during intervention and control periods
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although outcomes unlikely to be influenced by blinding
Incomplete outcome data (attrition bias)	High risk	>10% withdrawal, ITT not used
Selective reporting (reporting bias)	Unclear risk	Clinical trial registration provides insufficient detail to determine if all outcomes reported
Other bias	Low risk	Wash-out period of 4 weeks appears suitable

Chiang et al., 2012

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, method not given
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	Unclear risk	single-blinded, unclear who was blinded (participants vs personnel) as all foods provided
Blinding of outcome assessment (detection bias)	Unclear risk	Stated to be single-blind (assume outcome assessors), outcomes unlikely to be influenced by blinding
Incomplete outcome data (attrition bias)	Unclear risk	<10%, however unclear at which point withdrew
Selective reporting (reporting bias)	Unclear risk	Protocol not available

Other bias	High risk	Wash-out period of 2 days

Damasceno et al., 2011

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization was simple (not stratified) and was based on a random number table prepared by a biostatistician
Allocation concealment (selection bias)	Low risk	"...six possible diet sequences, which were coded and introduced into sealed envelopes"
Blinding of participants and personnel (performance bias)	High risk	Stated as not possible to blind participants or personnel as food was provided. Whilst this may not have affected measures, it may have affected participant behaviour during intervention and control periods
Blinding of outcome assessment (detection bias)	Low risk	Investigators involved in preparation of databases and laboratory determinations, however, were masked with respect to treatment sequence
Incomplete outcome data (attrition bias)	Unclear risk	<10%, however unclear at which point withdrew
Selective reporting (reporting bias)	Low risk	The study protocol is available and all pre-specified outcomes of interest to the review have been reported in the pre-specified way
Other bias	High risk	No washout period. Authors state would not effect, but likely to be carry-over effect

Djousse et al., 2016

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Article states: "computer-generated randomization schedule with balanced blocks, stratified by prevalent DM and coronary artery disease"

Allocation concealment (selection bias)	Unclear risk	Biostatistician generated schedule and did not have contact with study subjects, but not clear how allocation was communicated to researchers
Blinding of participants and personnel (performance bias)	Unclear risk	Unclear if participants blinded, researcher providing intervention not blinded
Blinding of outcome assessment (detection bias)	Low risk	Test completed by blinded staff
Incomplete outcome data (attrition bias)	Low risk	<5% withdrawal
Selective reporting (reporting bias)	Low risk	The study protocol is available and all pre-specified outcomes of interest to the review have been reported in the pre-specified way
Other bias	High risk	Control group had significantly higher proportion with hypercholesterolaemia

Gulati et al., 2014

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, however no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	No details given
Blinding of participants and personnel (performance bias)	Unclear risk	Not stated if participants blinded, would not be possible to blind personnel
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although would be unlikely to affect results
Incomplete outcome data (attrition bias)	Low risk	12% drop-out, but similar between groups and ITT used
Selective reporting (reporting bias)	Unclear risk	protocol not available
Other bias	High risk	CRP significantly higher in control group at baseline

Hernández-Alonso et al., 2014

Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	Low risk	Article states: "randomly assigned to one of the two different intervention periods using a computer generated random number table"
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	High risk	Would not be possible to blind participants or personnel as food was provided. Whilst this may not have affected measures, it may have affected participant behaviour during intervention and control periods
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, however would be unlikely to affect results
Incomplete outcome data (attrition bias)	High risk	10% drop-out (ITT used) - but all dropped out during first pistachio sequence
Selective reporting (reporting bias)	Low risk	The study protocol is available and all pre-specified outcomes of interest to the review have been reported in the pre-specified way
Other bias	Unclear risk	2 week washout period, unclear if sufficient

Hu et al., 2016

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation sequence was computer generated
Allocation concealment (selection bias)	Low risk	Study states: "Allocation concealment was achieved by keeping codes in a sealed envelope by a person who was not in contact with study subjects, and codes were disclosed after the study"
Blinding of participants and personnel (performance bias)	Low risk	Study states: "It was impossible to blind participants because of the nature of the intervention (especially the Brazil nuts), but all data curation, checking, measurements and data analysis were conducted by researchers blinded to treatment allocation of subjects."

Blinding of outcome assessment (detection bias)	Low risk	Study states: "It was impossible to blind participants because of the nature of the intervention (especially the Brazil nuts), but all data curation, checking, measurements and data analysis were conducted by researchers blinded to treatment allocation of subjects."
Incomplete outcome data (attrition bias)	Low risk	<10% drop-out and evenly spread between groups
Selective reporting (reporting bias)	Unclear risk	Protocol available, but not possible to determine if all outcomes reported
Other bias	Low risk	

Jenkins et al., 2002

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	High risk	Would not be possible to blind participants or personnel as food was provided. Whilst this may not have affected measures, it may have affected participant behaviour during intervention and control periods
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, however would be unlikely to affect results
Incomplete outcome data (attrition bias)	High risk	>20% drop-out, and unclear at which point in study participants dropped out
Selective reporting (reporting bias)	High risk	Study protocol is available but unclear if all relevant outcomes have not been reported
Other bias	Unclear risk	2 week washout period, unclear if sufficient

Kasliwal et al., 2015

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	Unclear risk	"open-label", unclear if both participants and personnel unblinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although would be unlikely to affect results
Incomplete outcome data (attrition bias)	High risk	>20% drop-out rate, ITT not used
Selective reporting (reporting bias)	Unclear risk	protocol not available
Other bias	Low risk	

Katz et al., 2012

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	High risk	Would not be possible to blind participants or personnel as food was provided. Whilst this may not have affected measures, it may have affected participant behaviour during intervention and control periods
Blinding of outcome assessment (detection bias)	Unclear risk	Single-blinded (unclear who was blinded though), although would be unlikely to affect results
Incomplete outcome data (attrition bias)	Low risk	13% dropout (ITT used), but similar between groups
Selective reporting (reporting bias)	Low risk	The study protocol is available and all pre-specified outcomes of interest to the review have been reported in the pre-specified way

Other bias	Low risk	Wash-out period of 4 weeks appears suitable

Kurlandsky 2006a - almond and control

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	Unclear risk	Not possible to blind personnel, unclear if participants blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although would be unlikely to affect results
Incomplete outcome data (attrition bias)	Low risk	<5% dropout, although not clear which group dropped out of
Selective reporting (reporting bias)	Unclear risk	protocol not available
Other bias	Unclear risk	Age differed significantly between groups, unclear if impacted on results

Kurlandsky 2006b - almond and chocolate

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	Unclear risk	Not possible to blind personnel, unclear if participants blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although would be unlikely to affect results
Incomplete outcome data (attrition bias)	Low risk	<5% dropout, although not clear which group dropped out of
Selective reporting (reporting bias)	Unclear risk	protocol not available

Other bias	Unclear risk	Age differed significantly between groups, unclear if impacted on results

Lee et al., 2014

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	Unclear risk	Not possible to blind personnel, unclear if participants blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although would be unlikely to affect results
Incomplete outcome data (attrition bias)	Low risk	<5% dropout, group specified
Selective reporting (reporting bias)	Low risk	The study protocol is available and all pre-specified outcomes of interest to the review have been reported in the pre-specified way
Other bias	Low risk	No differences in baseline characteristics

Liu et al., 2013

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	Unclear risk	Unclear if blinded as all foods provided
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although would be unlikely to affect results
Incomplete outcome data (attrition bias)	Unclear risk	<10% dropout, but unclear during which diet participant dropped out

Selective reporting (reporting bias)	Unclear risk	protocol not available
Other bias	Unclear risk	2 week washout period, unclear if sufficient

López-Uriarte et al., 2010/Casas-Agustench et al., 2011

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, method not given
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	Unclear risk	Not possible to blind personnel, unclear if participants blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although outcomes unlikely to be influenced by blinding
Incomplete outcome data (attrition bias)	Low risk	<5% withdrawal
Selective reporting (reporting bias)	Unclear risk	Clinical trial registration provides insufficient detail to determine if all outcomes reported
Other bias	Low risk	

Ma et al., 2010

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	High risk	Would not be possible to blind participants or personnel as food was provided. Whilst this may not have affected measures, it may have affected participant behaviour during intervention and control periods

Blinding of outcome assessment (detection bias)	Unclear risk	Single-blinded (unclear if all outcome assessors blinded), although would be unlikely to affect results
Incomplete outcome data (attrition bias)	Unclear risk	<10% dropout, ITT used (although unclear when participants dropped out)
Selective reporting (reporting bias)	Low risk	The study protocol is available and all pre-specified outcomes of interest to the review have been reported in the pre-specified way
Other bias	Low risk	8 week washout appears adequate

Moreira et al., 2014

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	Unclear risk	Not possible to blind personnel, unclear if participants blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although would be unlikely to affect results
Incomplete outcome data (attrition bias)	High risk	>10% drop out/excluded, not evenly spread across groups
Selective reporting (reporting bias)	Unclear risk	protocol not available
Other bias	Low risk	

Mukuddem-Petersen et al., 2007

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Drawing numbers from a hat
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	Unclear risk	Not possible to blind personnel, unclear if participants blinded

Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although would be unlikely to affect results
Incomplete outcome data (attrition bias)	Unclear risk	<10% drop-out, but unclear during which diet participants dropped out
Selective reporting (reporting bias)	Unclear risk	protocol not available
Other bias	Low risk	

Njike et al., 2015a – non-calorie adjusted

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	study participants were randomized using a SAS-generated random table
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	High risk	Would not be possible to blind participants or personnel as food was provided. Whilst this may not have affected measures, it may have affected participant behaviour during intervention
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, however would be unlikely to affect results
Incomplete outcome data (attrition bias)	Low risk	>10% drop-out, but ITT and similar between groups
Selective reporting (reporting bias)	Low risk	The study protocol is available and all pre-specified outcomes of interest to the review have been reported in the pre-specified way
Other bias	Low risk	

Njike et al., 2015b – calorie adjusted

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	study participants were randomized using a SAS-generated random table

Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	High risk	Would not be possible to blind participants or personnel as food was provided. Whilst this may not have affected measures, it may have affected participant behaviour during intervention and control periods
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, however would be unlikely to affect results
Incomplete outcome data (attrition bias)	Unclear risk	14% drop-out (ITT used) but 3 x in walnut arm
Selective reporting (reporting bias)	Low risk	The study protocol is available and all pre-specified outcomes of interest to the review have been reported in the pre-specified way
Other bias	Low risk	

Parham et al., 2014

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Allocation based on random numbers, but not clear how generated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	High risk	Would not be possible to blind participants or personnel as food was provided. Whilst this may not have affected measures, it may have affected participant behaviour during intervention and control periods
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although would be unlikely to affect results
Incomplete outcome data (attrition bias)	Unclear risk	<10%, but not clear when participants withdrew/were excluded
Selective reporting (reporting bias)	Unclear risk	protocol not available

Other bias	Low risk	washout period of 8 weeks appears appropriate

PREDIMED

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Article states: "Randomization was performed centrally by means of a computer-generated random-number sequence"
Allocation concealment (selection bias)	Low risk	"These tables have been centrally elaborated by the Coordinating Unit and provide a stratified random sequence of allocation for each FC using closed envelopes"
Blinding of participants and personnel (performance bias)	Unclear risk	single-blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors blinded
Incomplete outcome data (attrition bias)	Low risk	participants completers only
Selective reporting (reporting bias)	Low risk	The study protocol is available and all pre-specified outcomes of interest to the review have been reported in the pre-specified way
Other bias	Low risk	

Rajaram et al., 2010

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	3 x 3 Latin square design, no description of method of randomisation
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	Unclear risk	single-blinded, unclear if participants aware as all foods provided

Blinding of outcome assessment (detection bias)	Unclear risk	single-blind (not stated who blinded), although would be unlikely to affect results
Incomplete outcome data (attrition bias)	Unclear risk	<10%, but not clear when participants withdrew/were excluded
Selective reporting (reporting bias)	Unclear risk	protocol not available
Other bias	High risk	washout period not included, Sabate paper states lipids would stabilise but would still impact starting levels

Rock et al., 2016

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Randomised by study statistician, not clear if involved in other aspects of study
Blinding of participants and personnel (performance bias)	Unclear risk	Not possible to blind personnel, unclear if participants blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although would be unlikely to affect results
Incomplete outcome data (attrition bias)	High risk	18% withdrawal, does not appear that ITT used for biomarkers analysis (Table 3)
Selective reporting (reporting bias)	Unclear risk	Protocol is available, but insufficient detail to determine if all outcomes reported
Other bias	Low risk	

Ros et al., 2004

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomised but no additional detail given
Allocation concealment (selection bias)	Unclear risk	Not stated

Blinding of participants and personnel (performance bias)	High risk	Would not be possible to blind participants or personnel as food was provided. Whilst this may not have affected measures, it may have affected participant behaviour during intervention
Blinding of outcome assessment (detection bias)	Low risk	Blinded
Incomplete outcome data (attrition bias)	Low risk	<5% dropout (although not clear when dropped out)
Selective reporting (reporting bias)	Unclear risk	protocol not available
Other bias	High risk	washout period not included, references paper stating lipids would stabilise but would still

Sauder et al., 2015

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Generated via randomization.com
Allocation concealment (selection bias)	Unclear risk	Generated by study coordinator, but not stated if concealed
Blinding of participants and personnel (performance bias)	High risk	"But due to the nature of the dietary intervention, participants were aware of their treatment order assignment"
Blinding of outcome assessment (detection bias)	Low risk	Technicians who measured outcome variables were blinded to treatment assignments
Incomplete outcome data (attrition bias)	Unclear risk	11.7% drop-out, but not clear when participants dropped out
Selective reporting (reporting bias)	Unclear risk	Protocol is available, but insufficient detail to determine if all outcomes reported
Other bias	Unclear risk	washout period of 2 weeks

Sola et al., 2012

Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	Low risk	The randomization code was computer-generated random number sequence in gender-stratified blocks
Allocation concealment (selection bias)	Low risk	Center and treatment assignment codes were allocated via an interactive electronic response system administered by the Barcelona Randomization Unit, which was not further involved in the study.
Blinding of participants and personnel (performance bias)	Low risk	The participants, clinical investigators and laboratory personnel were blinded with respect to the type of cream being consumed
Blinding of outcome assessment (detection bias)	Low risk	The participants, clinical investigators and laboratory personnel were blinded with respect to the type of cream being consumed
Incomplete outcome data (attrition bias)	Low risk	<10% dropout, similar between groups, ITT used
Selective reporting (reporting bias)	Unclear risk	Protocol is available, but insufficient detail to determine if all outcomes reported
Other bias	Low risk	No differences in baseline characteristics

Sweazea et al., 2014

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	Unclear risk	Not possible to blind personnel, unclear if participants blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although would be unlikely to affect results
Incomplete outcome data (attrition bias)	High risk	>10% drop out, ITT not used
Selective reporting (reporting bias)	Unclear risk	protocol not available
Other bias	Unclear risk	Unclear if baseline inflammation levels differ between groups

Tey et al., 2013

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Details of randomisation given, but not how sequence was generated
Allocation concealment (selection bias)	Low risk	Managed by an off-site statistician
Blinding of participants and personnel (performance bias)	Unclear risk	Not possible to blind personnel, unclear if participants blinded
Blinding of outcome assessment (detection bias)	Low risk	Stated to be blinded
Incomplete outcome data (attrition bias)	Low risk	5% drop-out, ITT used, similar drop-out between groups
Selective reporting (reporting bias)	High risk	TNF-α referenced in protocol, not reported in paper.
Other bias	Low risk	controlled for baseline values

West et al., 2012

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised, but no further detail given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	Unclear risk	Unclear if blinded as all foods provided
Blinding of outcome assessment (detection bias)	Low risk	Appears to be blinded (Gebauer et al., 2008)
Incomplete outcome data (attrition bias)	Low risk	<5% drop-out (although not clear which group dropped out of)
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Other bias	Unclear risk	2 weeks compliance break (assume washout)

Wu et al., 2014

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	computer generated randomisation sequence

Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	High risk	Would not be possible to blind participants or personnel as food was provided. Whilst this may not have affected measures, it may have affected participant behaviour during intervention and control periods
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated, although would be unlikely to affect results
Incomplete outcome data (attrition bias)	High risk	~20% drop-out
Selective reporting (reporting bias)	Unclear risk	Protocol available, but not possible to determine if all outcomes reported
Other bias	Unclear risk	2 weeks washout

Supplementary material 10: GRADE assessment of the quality of the body of evidence

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	nut consumption	control	Relative (95% CI)	Absolute (95% CI)		
CRP												
26	randomised trials	serious [a]	not serious [b]	not serious	not serious	publication bias strongly suspected [c]	828	750	-	MD **0.01 lower** (0.06 lower to 0.03 higher)	⨁⨁◯◯ LOW	IMPORTANT
Adiponectin												
7	randomised trials	serious [d]	serious [e]	not serious	serious [f]	none	240	266	-	MD **0.29 higher** (0.63 lower to 1.21 higher)	⨁◯◯◯ VERY LOW	IMPORTANT
TNF-a												
8	randomised trials	serious [g]	not serious	not serious	not serious	none	250	232	-	MD **0.05 lower** (0.13 lower to 0.02 higher)	⨁⨁⨁◯ MODERATE	IMPORTANT
IL-6												
13	randomised trials	serious [h]	not serious	not serious	not serious	publication bias strongly suspected [i]	471	435	-	MD **0.02 lower** (0.12 lower to 0.08 higher)	⨁⨁◯◯ LOW	IMPORTANT
ICAM-1												

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	nut consumption	control	Relative (95% CI)	Absolute (95% CI)		
15	randomised trials	not serious [i]	not serious	not serious	not serious	none	539	508	-	MD **0.68 higher** (0.53 lower to 1.89 higher)	⨁⨁⨁⨁ HIGH	IMPORTANT
VCAM-1												
14	randomised trials	not serious [k]	not serious	not serious	not serious	none	419	385	-	MD **2.83 higher** (8.85 lower to 14.51 higher)	⨁⨁⨁⨁ HIGH	IMPORTANT
FMD												
9	randomised trials	not serious [l]	not serious	not serious	not serious	none	326	326	-	MD **0.79 higher** (0.35 higher to 1.23 higher)	⨁⨁⨁⨁ HIGH	IMPORTANT

CI: Confidence interval; **MD:** Mean difference

a. The studies were viewed as being in the category of 'serious limitation'. This category was selected as the risk of bias assessments for each study resulted in mainly 'high risk' (see risk of bias assessment charts). In accordance with the GRADE guidelines, 'high risk' needed to be categorised as either 'serious limitations' or 'very serious limitations'. In view of the potential implications of the 'high risk' aspects on the quality of the body of evidence, 'serious limitations' was selected

b. I squared value of 20%, indicating minimal heterogeneity

c. Funnel plot indicates likelihood of publication bias

d. The studies were viewed as being in the category of 'serious limitation'. This category was selected as the risk of bias assessments for each study resulted in mainly 'high risk' (see risk of bias assessment charts). In accordance with the GRADE guidelines, 'high risk' needed to be categorised as either 'serious limitations' or 'very serious limitations'. In view of the potential implications of the 'high risk' aspects on the quality of the body of evidence, 'serious limitations' was selected

e. I squared value of 79% indicating considerable heterogeneity

f. Total sample size is greater than 400, however 95% CIs overlap no effect and include appreciable benefit or harm

g. The studies were viewed as being in the category of 'serious limitation'. This category was selected as the risk of bias assessments for each study resulted in mainly 'high risk' (see risk of bias assessment charts). In accordance with the GRADE guidelines, 'high risk' needed to be categorised as either 'serious limitations' or 'very serious limitations'. In view of the potential implications of the 'high risk' aspects on the quality of the body of evidence, 'serious limitations' was selected

h. The studies were viewed as being in the category of 'serious limitation'. This category was selected as the risk of bias assessments for each study resulted in mainly 'high risk' (see risk of bias assessment charts). In accordance with the GRADE guidelines, 'high risk' needed to be categorised as either 'serious limitations' or 'very serious limitations'. In view of the potential implications of the 'high risk' aspects on the quality of the body of evidence, 'serious limitations' was selected

i. Funnel plot indicates likelihood of publication bias

j. The studies were viewed as being in the category of 'no limitation'. This category was selected as the risk of bias assessments for each study resulted in mainly 'unclear risk' (see risk of bias assessment charts). In accordance with the GRADE guidelines, 'unclear risk' needed to be categorised as either 'no limitations' or 'serious limitations'. In view of the potential implications of the 'unclear risk' aspects on the quality of the body of evidence, 'no limitations' was selected

k. The studies were viewed as being in the category of 'no limitation'. This category was selected as the risk of bias assessments for each study resulted in mainly 'unclear risk' (see risk of bias assessment charts). In accordance with the GRADE guidelines, 'unclear risk' needed to be categorised as either 'no limitations' or 'serious limitations'. In view of the potential implications of the 'unclear risk' aspects on the quality of the body of evidence, 'no limitations' was selected

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