

Supplemental Table 1: Example of the search strategy

((((((((((((((((((((((((((((((((((((((("immunoglobulins"[MeSH Terms]) OR Immunoglobulin*) OR IgE) OR IgD) OR IgM) OR IgA) OR IgG) OR Platelet[MeSH Terms]) OR Platelet*) OR Basophil[MeSH Terms]) OR Basophil*) OR Eosinophil[MeSH Terms]) OR Eosinophil*) OR "t lymphocyte subsets"[MeSH Terms]) OR t cell*) OR "b lymphocyte subsets"[MeSH Terms]) OR B cell*) OR Monocyte[MeSH Terms]) OR Monocyte*) OR Neutrophil[MeSH Terms]) OR Neutrophil*) OR Leukocyte[MeSH Terms]) OR Lymphocyte*) OR Lymphocyte*[MeSH Terms]) OR Leukocyte*) OR white blood cells) OR "white blood cells") OR white blood cell) OR "white blood cell") OR NK) OR "natural killer t cells"[MeSH Terms]) OR "natural killer cells") OR natural killer cells) OR natural killer cell) OR "natural killer cell") OR "immunity"[MeSH Terms]) OR immune)) OR (((tumor necrosis factor[MeSH Terms]) OR interleukin[MeSH Terms]) OR (((((((((((((((((((("fibrinogen"[MeSH Terms]) OR fibrinogen) OR TNF) OR "tumor necrosis factor alpha"[MeSH Terms]) OR tumour necrosis factor) OR "tumour necrosis factor") OR "tumor necrosis factor") OR IL-6) OR interleukin) OR "interleukin") OR CRP) OR "c reactive protein") OR C-Reactive Protein[MeSH Terms]) OR inflammat*) OR "inflammation"[MeSH Terms]))) AND ((((((("plant based") OR "plant-based") OR vegan*) OR "vegans"[MeSH Terms]) OR *vegetarian) OR vegetarian*) OR vegetarian[MeSH Terms])

Supplementary Data

Supplemental Table 2. Modified Newcastle Ottawa Scale assessing of the quality of studies

	Acosta-Navarro et al (42), Navarro et al. (48) ¹	Justification	Ambroszkiewicz et al. (43)	Justification	Chen et al. (45)	Justification	Chen et al. (44)	Justification	Chuang et al. (46)	Justification	Dong and Scott (47)	Justification
Sample selection criteria Selection: (Maximum 3 stars)												
<i>1) Representativeness of the sample:</i> a) Truly representative of the average in the target population. ★ (all subjects or random sampling) b) Somewhat representative of the average in the target population. ★ (non-random sampling) c) Selected group of users. d) No description of the sampling strategy.	1b ★	small sample size	1b ★	children aged 4.5-9	1b ★	All pts undergoing general health examination, but enrolled first come, first served	1b ★	females only	1b ★	large sample based on health records of pts in clinics, but not clear how vegetarian and non-vegetarian cases/controls were identified	1c	pts of a vegetarian society conference + very small non-veg group
<i>2) Non-respondents:</i> a) Comparability between respondents and non-respondents characteristics is established, and the response rate is satisfactory. ★ b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory. c) No description of the response rate or the characteristics of the responders and the non-responders.	2a ★	-	2c	no description of those not enrolled	2c	no description of those not enrolled	2c	no description of those not enrolled	2c	no description of those not enrolled	2c	no description of those not enrolled
<i>3) Ascertainment of the exposure (risk factor):</i> a) Validated measurement tool. ★ b) Non-validated measurement tool, but the tool is available or described. c) No description of the measurement tool. NOTE - Study must say 'validated' to score star	3b	-	3b	tool described, but not clear if validated	3c	No description - general diet only	3c	No description of questionnaire used	3a ★	validated tool	3b	tool described, but not clear if validated

Supplementary Data

Supplemental Table 2. Modified Newcastle Ottawa Scale assessing of the quality of studies - Continued

<p>Comparability: (Maximum 2 stars) <i>1) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.</i> a) The study controls for the most important factor (BMI). ★ b) The study controls for any additional factors. ★ (Smoking and physical activity) Note: for ★ on 1b - both PA and smoking needs to be controlled</p>	1b ★	ANOVA analysis performed due to differences in PA	1a ★	PA not considered BMI similar between groups, other factors not discussed	1a ★	Sig. differences in smoking	1a ★ 1b ★	Did not statistically adjust, but exclusion criteria would have limited confounders somewhat	1b ★	Did not adjust for BMI (differed significantly between groups), but did adjust for age, sex, PA, alcohol and study site	-	Does not appear to adjust for confounders
<p>Outcome: (Maximum 2 stars)</p>												
<p><i>1) Assessment of the outcome:</i> a) Independent blind assessment. ★ b) Record linkage. ★ c) Self report. d) No description. <i>2) Statistical test:</i> a) The statistical test used to analyse the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). ★ b) The statistical test is not appropriate, not described or incomplete.</p>	1a ★ 2a ★	-	1a ★ 2a ★	-	1a ★ 2a ★	-	1a ★ 2a ★	-	1a ★ 2a ★	-	1a ★ 2b	-
<p>Total ★ (/7)²</p>	5		4		4		5		5		1	

Supplemental Table 2. Modified Newcastle Ottawa Scale assessing of the quality of studies - Continued

	Famodu et al. (49)	Justification	Fontana et al. (50)	Justification	Fontana et al. (51)	Justification	Franco-de-Moraes et al. (52)	Justification	Gorczyca et al. (53)	Justification	Haddad et al. (54)	Justification
Sample selection criteria Selection: (Maximum 3 stars)												
<i>1) Representativeness of the sample:</i> a) Truly representative of the average in the target population. ★ (all subjects or random sampling) b) Somewhat representative of the average in the target population. ★ (non-random sampling) c) Selected group of users. d) No description of the sampling strategy.	1d	no description of sampling strategy (states members of Adventist Seminary Institute of West Africa.) + non-vegetarians	1c	small select sample, not representative raw vegans	1c	small sample, not clear how controls recruited, not representative	1b ★	convenience sample	1c	parents of non-vegetarian children not randomly selected	1c	small sample, unlikely to be representative
<i>2) Non-respondents:</i> a) Comparability between respondents and non-respondents characteristics is established, and the response rate is satisfactory. ★ b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory. c) No description of the response rate or the characteristics of the responders and the non-responders.	2c	no description of those not enrolled	2c	no description of those not enrolled	2c	no description of those not enrolled	2c	no description of those not enrolled	2c	no description of those not enrolled	2c	no description of those not enrolled
<i>3) Ascertainment of the exposure (risk factor):</i> a) Validated measurement tool. ★ b) Non-validated measurement tool, but the tool is available or described. c) No description of the measurement tool. NOTE - Study must say 'validated' to score star	3b	tool described in supporting reference, but not described if validated	3b	WFR - but no mention of validating	3b	WFR but no mention of validation	3c	-	3b	FR used but unsure if validated	3b	FR (trained) but no mention of validation

Supplementary Data

Supplemental Table 2. Modified Newcastle Ottawa Scale assessing of the quality of studies - Continued

<p>Comparability: (Maximum 2 stars) <i>1) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.</i> a) The study controls for the most important factor (BMI). ★ b) The study controls for any additional factors. ★ (Smoking and physical activity) Note: for ★ on 1b - both PA and smoking needs to be controlled</p>	1a ★	did not adjust for confounders, although no difference in BMI. No description of smoking status or PA	-	Did not adjust for confounders (differences in BMI) smoking same between groups however no description of PA between Ve and NV	-	Did not adjust for confounders (differences in BMI) smoking same between groups however no description of PA between Ve and NV	Nil	BMI and PA not controlled	1a ★	did not adjust for confounders, or control for PA or smoking. Height and weight not sig different between groups	1b ★	BMI sig diff between groups. PA and Smoking no sig diff
<p>Outcome: (Maximum 2 stars)</p>												
<p><i>1) Assessment of the outcome:</i> a) Independent blind assessment. ★ b) Record linkage. ★ c) Self report. d) No description. <i>2) Statistical test:</i> a) The statistical test used to analyse the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). ★ b) The statistical test is not appropriate, not described or incomplete.</p>	1a ★ 2a ★	-	1a ★ 2a ★	-	1a ★ 2a ★	-	1a ★ 2a ★	-	1a ★ 2a ★	-	1a ★ 2a ★	-
<p>Total ★ (/7)</p>	3		2		2		3		3		3	

Supplementary Data

Supplemental Table 2. Modified Newcastle Ottawa Scale assessing of the quality of studies - Continued

	Krajcovicova-Kudlackova et al. (55)	Justification	Malter et al. (56)	Justification	Mezzano et al. (57)	Justification	Montalcini et al. (58)	Justification	Ou et al. (59)	Justification	Paalani et al. (60)	Justification
Sample selection criteria Selection: (Maximum 3 stars)												
1) <i>Representativeness of the sample:</i> a) Truly representative of the average in the target population. ★ (all subjects or random sampling) b) Somewhat representative of the average in the target population. ★ (non-random sampling) c) Selected group of users. d) No description of the sampling strategy.	1b ★	random sampling but no description of strategy	1c	small sample, not clear how selected from Heidelberg study (veg) or research centre (non-veg)	1d	not described	1b ★	small sample, but recruited following newspaper ads	1c	chronic dialysis patients	1a ★	-
2) <i>Non-respondents:</i> a) Comparability between respondents and non-respondents characteristics is established, and the response rate is satisfactory. ★ b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory. c) No description of the response rate or the characteristics of the responders and the non-responders.	2c	No description of those not enrolled	2c	No description of those not enrolled	2c	No description of those not enrolled	2c	No description of those not enrolled	2c	No description of those not enrolled	2a ★	-
3) <i>Ascertainment of the exposure (risk factor):</i> a) Validated measurement tool. ★ b) Non-validated measurement tool, but the tool is available or described. c) No description of the measurement tool. NOTE - Study must say 'validated' to score star	3c	tool not described	3c	no tool	3b	tool described, but not clear if validated	3b	tool described, but not clear if validated	3c	tool not described	3b	tool described, unclear if validated
Comparability: (Maximum 2 stars)												
1) <i>The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.</i> a) <i>The study controls for the most important factor (BMI). ★</i> b) <i>The study controls for any additional factors. ★ (Smoking and physical activity)</i> Note: for ★ on 1b - both PA and smoking needs to be controlled	-	smoking controlled for, however BMI sig difference and no description of PA	-	did not adjust for confounders (differences in other risk factors between groups)	1a ★	matched by BMI, age, sex - no mention of PA	1a ★	matched by BMI, age, sex. PA sig different between groups	-	age and sex matched, but BMI still sig different between groups, and not adjusted	-	Baseline data not available

Supplementary Data

Supplemental Table 2. Modified Newcastle Ottawa Scale assessing of the quality of studies - Continued

<p>Outcome: (Maximum 2 stars) <i>1) Assessment of the outcome:</i> a) Independent blind assessment. ★ b) Record linkage. ★ c) Self report. d) No description. <i>2) Statistical test:</i> a) The statistical test used to analyse the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). ★ b) The statistical test is not appropriate, not described or incomplete.</p>	<p>1a ★ 2b</p>	<p>-</p>	<p>1a ★ 2a ★</p>	<p>-</p>	<p>1a ★ 2a ★</p>	<p>-</p>	<p>1a ★ 2a ★</p>	<p>-</p>	<p>1a ★ 2a ★</p>	<p>-</p>	<p>1a ★ 2a ★</p>	<p>-</p>
<p>Total ★ (/7)</p>	<p>2</p>		<p>2</p>		<p>3</p>		<p>4</p>		<p>2</p>		<p>4</p>	

Supplementary Data

Supplemental Table 2. Modified Newcastle Ottawa Scale assessing of the quality of studies - Continued

	Pinto et al. (61)	Justification	Pongstaporn et al. (62)	Justification	Refsum et al. (63)	Justification	Sebekova et al. (64)	Justification	Sebekova et al. (65)	Justification	Su et al. (66)	Justification
Sample selection criteria Selection: (Maximum 3 stars)												
1) <i>Representativeness of the sample:</i> a) Truly representative of the average in the target population. ★ (all subjects or random sampling) b) Somewhat representative of the average in the target population. ★ (non-random sampling) c) Selected group of users. d) No description of the sampling strategy.	1b ★	recruited via email, adverts and email circulation	1d	-	1b ★	large numbers but obtained from cardiac clinic	1d	-	1d	-	1c	small select sample
2) <i>Non-respondents:</i> a) Comparability between respondents and non-respondents characteristics is established, and the response rate is satisfactory. ★ b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory. c) No description of the response rate or the characteristics of the responders and the non-responders.	2c	no description of those not enrolled	2c	no description of those not enrolled	2c	no description of those not enrolled	2c	no description of those not enrolled	2c	no description of those not enrolled	2c	no description of those not enrolled
3) <i>Ascertainment of the exposure (risk factor):</i> a) Validated measurement tool. ★ b) Non-validated measurement tool, but the tool is available or described. c) No description of the measurement tool. <i>NOTE - Study must say 'validated' to score star</i>	3a ★	validated FFQ	3c	tool not described	3b	tool described, but not clear if validated	3b	tool described, but not clear if validated	3b	tool described, but not clear if validated	3c	tool not described
Comparability: (Maximum 2 stars)												
1) <i>The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.</i> a) <i>The study controls for the most important factor (BMI). ★</i> b) <i>The study controls for any additional factors. ★ (Smoking and physical activity)</i> <i>Note: for ★ on 1b - both PA and smoking needs to be controlled</i>	1a ★	BMI controlled - Nil for PA	-	-	-	does not control for confounders, unclear if potential confounders differed between groups	-	BMI sig different. Smoking controlled but not PA	-	does not control for confounders	1a ★	BMI not sig diff

Supplementary Data

Supplemental Table 2. Modified Newcastle Ottawa Scale assessing of the quality of studies - Continued

<p>Outcome: (Maximum 2 stars)</p> <p>1) <i>Assessment of the outcome:</i></p> <p>a) Independent blind assessment. ★</p> <p>b) Record linkage. ★</p> <p>c) Self report.</p> <p>d) No description.</p> <p>2) <i>Statistical test:</i></p> <p>a) The statistical test used to analyse the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). ★</p> <p>b) The statistical test is not appropriate, not described or incomplete.</p>	<p>1a ★</p> <p>2a ★</p>	<p>-</p>	<p>1a ★</p> <p>2a ★</p>	<p>-</p>	<p>1a ★</p> <p>2a ★</p>	<p>-</p>	<p>1a ★</p> <p>2a ★</p>	<p>-</p>	<p>1a ★</p> <p>2a ★</p>	<p>-</p>	<p>1a ★</p> <p>2a ★</p>	<p>-</p>
<p>Total ★ (/7)</p>	<p>5</p>		<p>2</p>		<p>3</p>		<p>2</p>		<p>2</p>		<p>3</p>	

Supplementary Data

Supplemental Table 2. Modified Newcastle Ottawa Scale assessing of the quality of studies - Continued

	Suwannuruks et al. (67)	Justification	Szeto et al. (68)	Justification	Tungtrongchitr et al. (69)	Justification	Wu et al. (70)	Justification	Yang et al. (71)	Justification
Sample selection criteria Selection: (Maximum 3 stars)										
<i>1) Representativeness of the sample:</i> a) Truly representative of the average in the target population. ★ (all subjects or random sampling) b) Somewhat representative of the average in the target population. ★ (non-random sampling) c) Selected group of users. d) No description of the sampling strategy.	1c	small select sample	1c	small select sample	1c	small select sample, not clear how controls recruited	1b ★	patients on HD	1c	select sample, not representative
<i>2) Non-respondents:</i> a) Comparability between respondents and non-respondents characteristics is established, and the response rate is satisfactory. ★ b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory. c) No description of the response rate or the characteristics of the responders and the non-responders.	2c	no description of those not enrolled	2c	no description of those not enrolled	2c	no description of those not enrolled	2a ★	-	2c	no description of those not enrolled
<i>3) Ascertainment of the exposure (risk factor):</i> a) Validated measurement tool. ★ b) Non-validated measurement tool, but the tool is available or described. c) No description of the measurement tool. <i>NOTE - Study must say 'validated' to score star</i>	3c	tool not described	3c	tool not described	3c	tool not described	3b	tool described, but not clear if validated	3b	tool described, but not clear if validated

Supplementary Data

Supplemental Table 2. Modified Newcastle Ottawa Scale assessing of the quality of studies - Continued

<p>Comparability: (Maximum 2 stars)</p> <p>1) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.</p> <p>a) The study controls for the most important factor (BMI). ★</p> <p>b) The study controls for any additional factors. ★ (Smoking and physical activity)</p> <p>Note: for ★ on 1b - both PA and smoking needs to be controlled</p>	-	not adjusted for confounders	-	-	-	-	-	some differences between groups, did not adjust	1a ★ 2a ★	Table 1 footnotes suggest adjusted for covariates
<p>Outcome: (Maximum 2 stars)</p>										
<p>1) Assessment of the outcome:</p> <p>a) Independent blind assessment. ★</p> <p>b) Record linkage. ★</p> <p>c) Self report.</p> <p>d) No description.</p> <p>2) Statistical test:</p> <p>a) The statistical test used to analyse the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). ★</p> <p>b) The statistical test is not appropriate, not described or incomplete.</p>	1a ★ 2b	stats test not described	1a ★ 2a ★	-	1a ★ 2a ★	-	1a ★ 2a ★	-	1a ★ 2a ★	-
<p>★Total = /7</p>	1		2		2		4		4	

BMI, body mass index; diff, difference; FFQ, food frequency questionnaire; FR, food record; HD, hemodialysis; NV, Non-vegetarian; PA, physical activity; Pts, patients; sig, significant; ve, vegan; veg, vegetarian; WFR, weighted food record.

¹ Two separate papers identified reporting on same study participants, with different outcome marker/s

² Studies assessed using the modified Newcastle Ottawa Scale can achieve 7 stars in total. Studies attracting 7 stars are of high quality while studies attracting 0 stars are of low quality. The criteria in the first column explains the criteria to attain a star.

★, Sample selection criteria met

Supplementary Data

Supplemental Table 3: GRADE assessment of the quality of the body of evidence in observational studies for each outcome

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vegetarian-based	control	Relative (95% CI)	Absolute (95% CI)		
CRP												
19	Observational studies	serious ^a	serious ^b	not serious	not serious	None ³	1844	4736	-	MD 0.62 lower (0.93 lower to 0.30 lower)	⊕○○○ VERY LOW	IMPORTANT
Fibrinogen												
3	Observational studies	serious ¹	not serious ⁴	not serious	serious	none ³	112	96	-	MD 0.22 lower (0.41 lower to 0.04 lower)	⊕○○○ VERY LOW	IMPORTANT
Thrombocytes												
7	Observational studies	serious ¹	not serious ⁴	not serious	not serious	none	663	507	-	MD 8.24 higher (3.35 lower to 19.82 higher)	⊕○○○ VERY LOW	IMPORTANT
Leukocytes												

Supplementary Data

Quality assessment							N ^o of patients		Effect		Quality	Importance
N ^o of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vegetarian-based	control	Relative (95% CI)	Absolute (95% CI)		
11	Observational studies	serious ¹	serious ²	not serious ³	not serious	none	944	970	-	MD 0.62 lower (1.13 lower to 0.10 lower)	⊕○○○ VERY LOW	IMPORTANT

CI, Confidence interval; MD, Mean difference

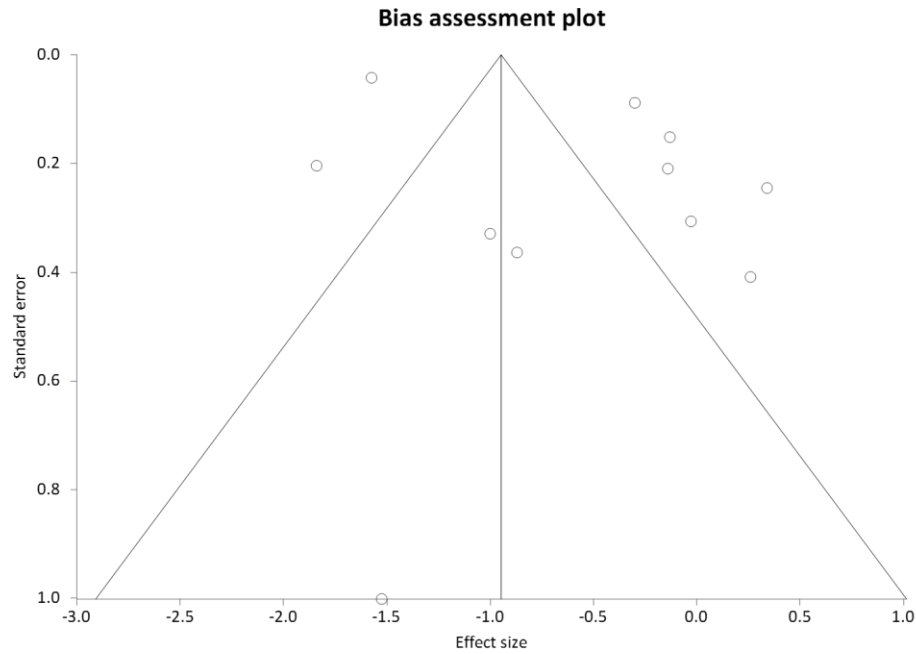
¹ The studies were viewed as being in the category of 'serious limitation'. This category was selected as the risk of bias assessments for each study using a modified Newcastle Ottawa Scale resulted in many studies scoring poorly (majority 4 or less /7). In accordance with the GRADE guidelines, 'high risk' needed to be categorized 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.

² I squared value of 100%, indicating considerable heterogeneity

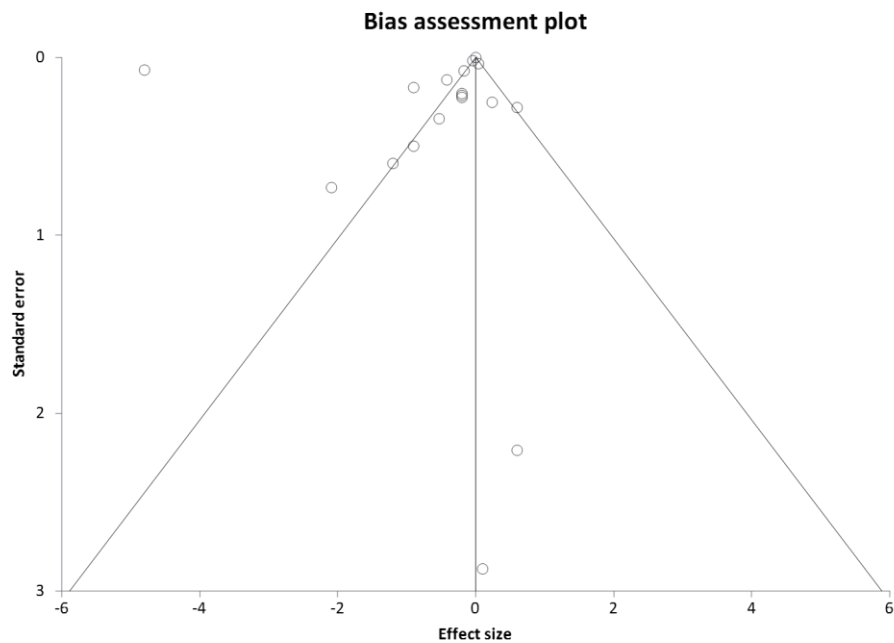
³ Funnel plot does not indicate publication bias

⁴ I squared value of <50% indicating minimal heterogeneity

Supplemental Figure 1 A-B. Funnel plot and Risk of bias

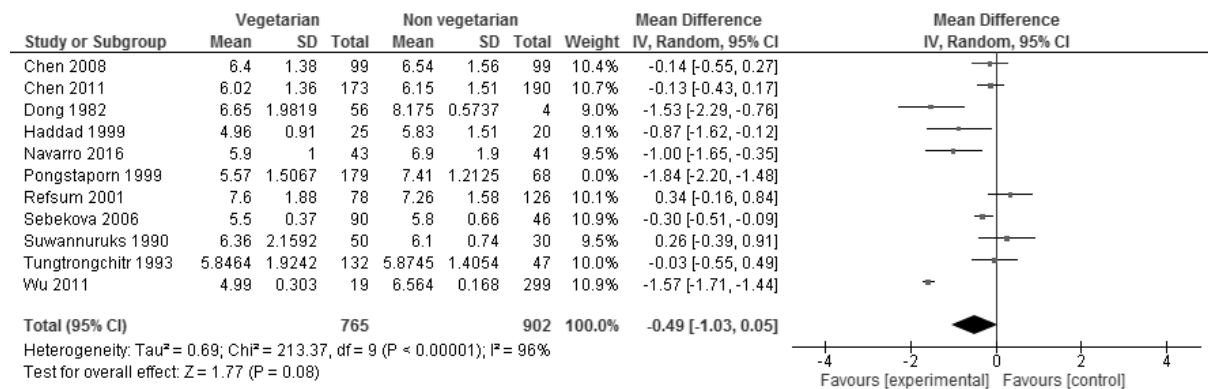


Supplemental Figure 1A. Bias assessment plot for leukocyte concentration with Egger's test applied. Egger bias 4.439487; 95% CI: -0.439381, 9.318356; $P = 0.0697$

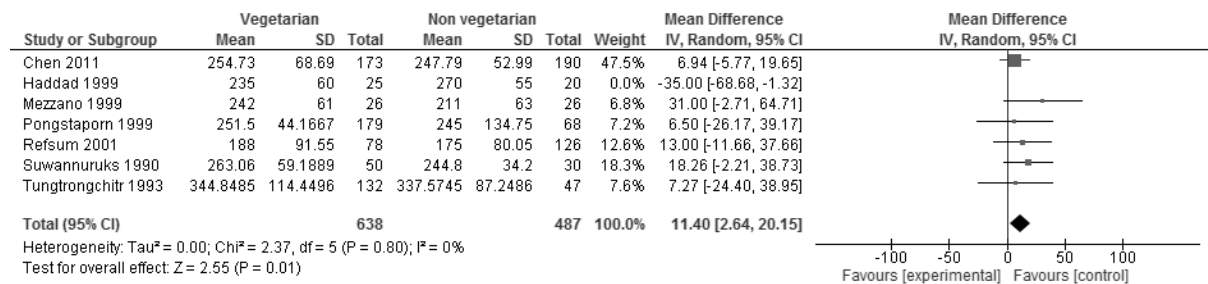


Supplemental Figure 1B. Bias assessment plot for CRP concentration with Egger's test applied. Egger bias: -5.165008; 95% CI: -13.583609, 3.253593; $P = 0.2118$

Supplemental Figure 2 A-B. Sensitivity analysis based on individual study weightings

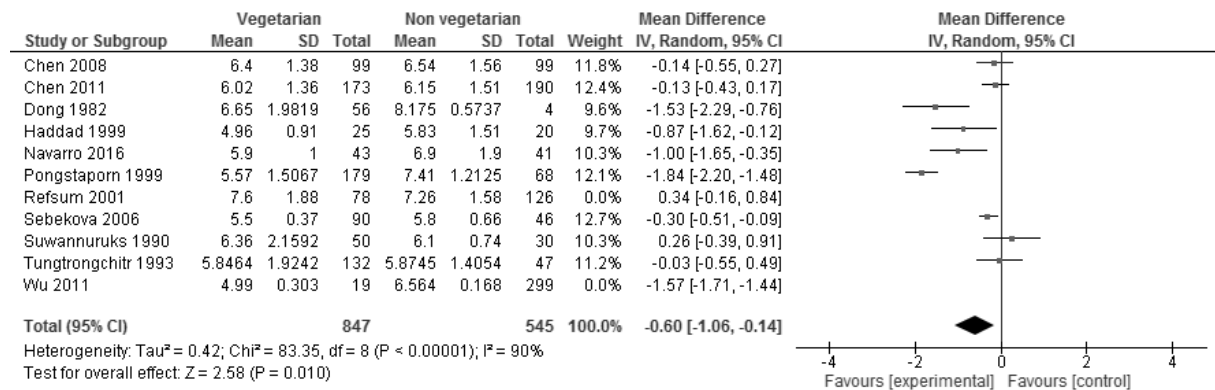


Supplemental figure 2A. Sensitivity analysis for leukocyte ($10^3/\mu\text{L}$) values between those following vegetarian-based dietary patterns and non-vegetarian dietary patterns (cross-sectional studies) with Pongstaporn et al omitted. Diamond indicates weighted mean difference with 95% confidence intervals.

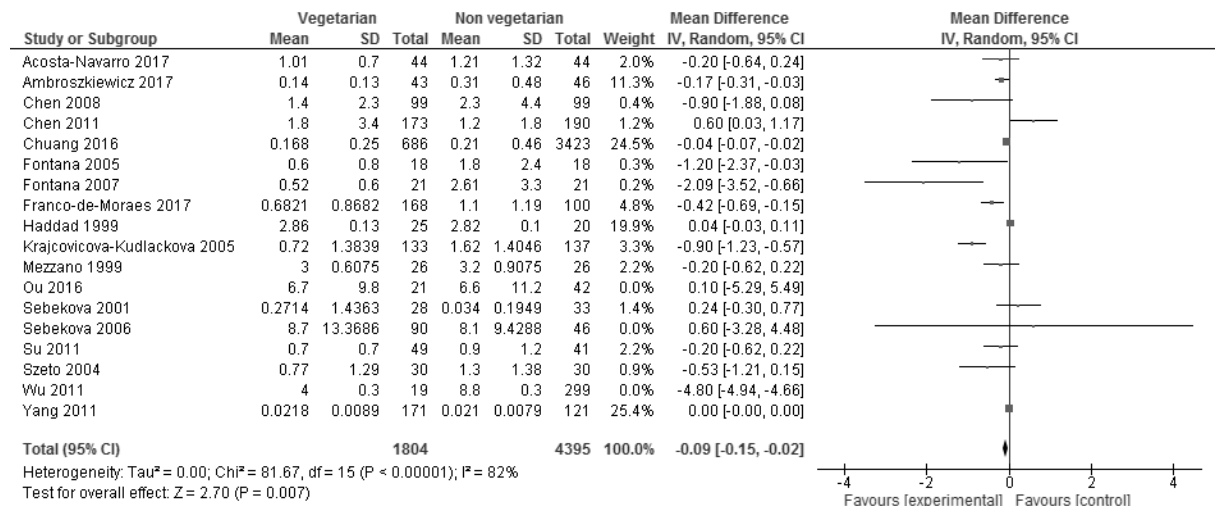


Supplemental figure 2B. Sensitivity analysis for thrombocyte ($\times 10^9/\text{L}$) counts between those following vegetarian-based dietary patterns and non-vegetarian dietary patterns (cross-sectional studies) with Haddad et al omitted. Diamond indicates weighted mean difference with 95% confidence intervals.

Supplemental Figure 3 A-B. Sensitivity analysis based on participant's co-morbidities.

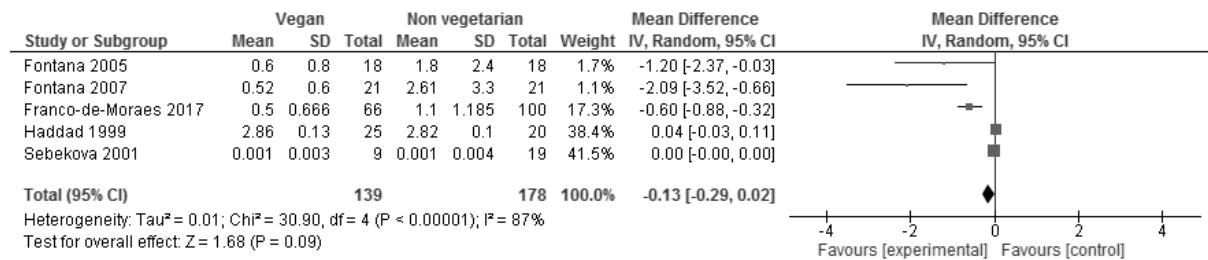


Supplemental figure 3A. Sensitivity analysis for leukocytes ($10^3/\mu\text{L}$) between those following vegetarian-based and non-vegetarian based dietary patterns (cross-sectional studies) with studies omitted where participants were receiving haemodialysis treatment, CVD and/or T2DM were omitted. Diamond indicates weighted mean difference with 95% confidence intervals.

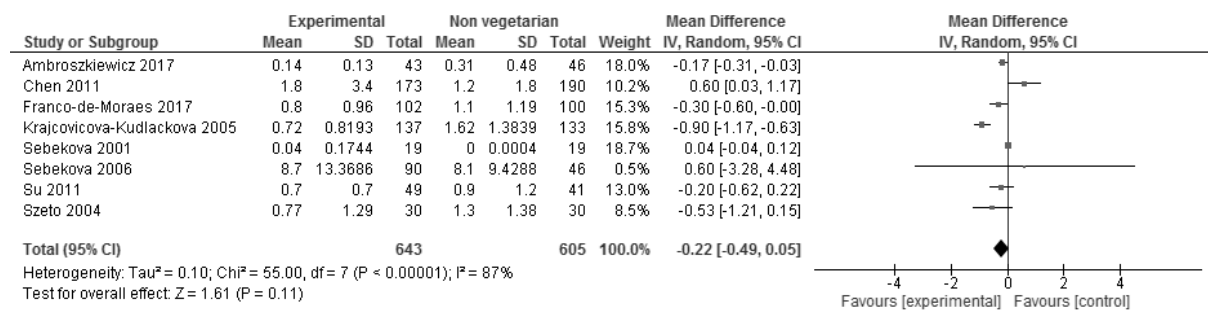


Supplemental figure 3B. Sensitivity analysis for CRP (mg/L) between those following vegetarian-based and non-vegetarian based dietary patterns (cross-sectional studies) with studies omitted where participants were receiving haemodialysis treatment, CVD and/or T2DM were omitted. Diamond indicates weighted mean difference with 95% confidence intervals.

Supplemental Figure 4 A-B. Sub-group analyses based on diet type



Supplemental Figure 4A. Difference in CRP (mg/L) values between those following vegan dietary patterns and non-vegetarian dietary patterns (cross-sectional studies). Diamond indicates weighted mean difference with 95% confidence intervals



Supplemental Figure 4B. Difference in CRP (mg/L) values between those following Lacto-ovo-vegetarian dietary patterns and non-vegetarian dietary patterns (cross-sectional studies). Diamond indicates weighted mean difference with 95% confidence interval.

Supplementary Data

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vegetarian Diet	Mixed non-vegetarian diet	Relative (95% CI)	Absolute (95% CI)		
CRP												
4	randomized trials	serious ¹	serious ²	serious ³	serious ⁴	nil	114	116	-	MD 1.07 lower (2.75 lower to 0.61 higher)	⊕○○ VERY LOW	IMPORTANT

MD – mean difference,

¹ The studies were viewed as bring in the category of 'serious'. This category was selected as despite risk of bias assessments for each study mainly compromising of 'low risk' and 'unclear risk' (see risk of bias assessment charts) the 'other bias's domain had 100% of studies in the 'high risk category'. In accordance with the GRADE guidelines, 'high risk' should be downgraded by one level when "one criterion or some limitations for multiple criteria, sufficient to lower confidence in the estimate of effect" was selected.

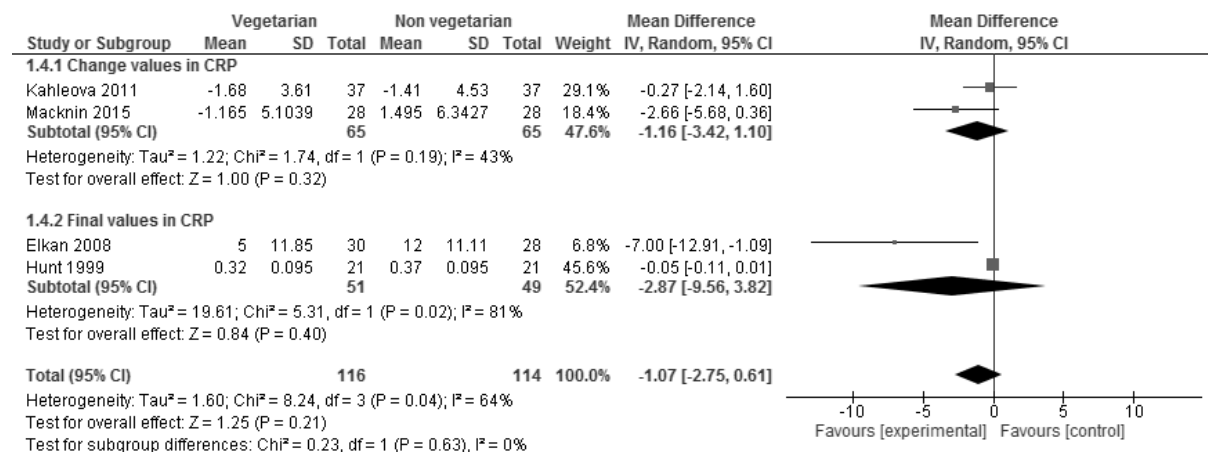
² Inconsistency was deemed to be 'not serious' as the I squared value of 53%, which only slightly exceeded the range (50%-75%) which "likely indicates substantial heterogeneity" as outlined in the Cochrane handbook.

³ The studies were viewed as bring in the category of 'serious'. This category was selected, as there was considerable inconsistency between the populations regarding the main review question. For example, Elkan et al, 2008 study examined participants with rheumatoid arthritis, Kahleova et al, had patients had T2DM and Macknin et al, 2015 had participants who were children with a BMI > 95th % for age/sex + cholesterol >169mg/dL.

⁴ 95% CI does not include an effect, 95% CI does not include appreciable benefit or harm, however less than 400 participants available, therefore the decision was made to downgrade the quality of evidence.

Supplemental Figure 5. GRADE assessment of the quality of the body of evidence – CRP intervention studies

Supplementary Data



Supplemental Figure 6. Change in C-reactive protein (mg/L) between vegetarian dietary patterns and non-vegetarian control dietary patterns (presented as sub-groups based on mean final or change values for readability). Diamond indicates weighted mean difference with 95% confidence intervals.

Supplemental Table 4. Cochrane risk of bias assessment of interventional studies

Elkan et al. (72)		
Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Unclear risk	"Participants were randomly assigned using a minimization technique" - no specific detail on how this was performed.
Allocation concealment (selection bias)	Unclear risk	Not Specified
Blinding of participants and researchers (performance bias)	High risk	Participants aware of dietary group after first check-up (3 months into 1-year trial) - No description of blinding by researchers.
Blinding of outcome assessment (detection bias)	Low risk	Not stated - although outcomes unlikely to be influenced by blinding (blood bio-markers)
Incomplete outcome data (attrition bias)	High Risk	Dropout rate >25% in vegan group after 1 year. Intention-to-treat (ITT) not used
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Other bias	High Risk	CRP appears significantly higher in control group at baseline.
Kahleova et al. (73)		
Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Unclear risk	Stated to be randomized, no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and researchers (performance bias)	Unclear risk	Not possible to blind personnel, unclear if patients blinded
Blinding of outcome assessment (detection bias)	Low risk	Not stated - although outcomes unlikely to be influenced by blinding (blood bio-markers)
Incomplete outcome data (attrition bias)	Low risk	16% drop out, but similar between groups and ITT used
Selective reporting (reporting bias)	Unclear risk	Protocol available, but insufficient information to determine if all outcomes reported
Other bias	High risk	Smoking higher in Control group at baseline
Hunt & Roughead. (81)		
Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Unclear risk	Stated to be randomized, no details of randomisation method given
Allocation concealment (selection bias)	Unclear Risk	Not stated

Supplemental Table 4 – Continued

Blinding of participants and researchers (performance bias)	High Risk	Not possible to blind researchers. Not possible to blind participants (cross-over) which may have affected performance in different arms
Blinding of outcome assessment (detection bias)	Low risk	Not stated - although outcomes unlikely to be influenced by blinding (blood bio-markers)
Incomplete outcome data (attrition bias)	Low risk	Nil drop out
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Other bias	High Risk	Nil washout period
Kjeldsen-Kragh et al. (74, 75) ¹		
Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Unclear Risk	Stated to be randomized, no details of randomisation method given
Allocation concealment (selection bias)	Unclear Risk	Not stated
Blinding of participants and researchers (performance bias)	High risk	Single blind trial - Participants aware of dietary group after first check-up (3 months into 1-year trial).
Blinding of outcome assessment (detection bias)	Low risk	Clinicians/GP's blinded + outcomes unlikely to be influenced by blinding (blood bio-markers)
Incomplete outcome data (attrition bias)	High risk	30% drop out (even though ITT used and similar between groups)
Selective reporting (reporting bias)	Unclear Risk	The study protocol is not available
Other bias	High Risk	Insufficient baseline data reported to determine differences between groups + substantial difference in kJ intake between interventions and control
Macknin et al. (76)		
Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Low Risk	Randomized using an SAS computer program 1:1 in blocks of 4 families stratified by the child's age group (age strata 9-13 years vs 14-18 years)
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and researchers (performance bias)	Unclear risk	Not stated
Blinding of outcome assessment (detection bias)	Low risk	Not stated - although outcomes unlikely to be influenced by blinding (blood bio-markers)
Incomplete outcome data (attrition bias)	High Risk	>10% drop out, both in intervention group, no ITT
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	Baseline CRP and IL-6 does not appear to be similar.
Nenonen et al. (77)		
Bias	Authors' judgment	Support for judgment

Supplemental Table 4 – Continued

Random sequence generation (selection bias)	Unclear risk	Stated to be randomized, no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and researchers (performance bias)	Unclear risk	Not stated
Blinding of outcome assessment (detection bias)	Low risk	Not stated - although outcomes unlikely to be influenced by blinding (blood bio-markers)
Incomplete outcome data (attrition bias)	High risk	higher drop out in intervention, related to intervention
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Other bias	Unclear risk	Baseline CRP between groups unclear
Richter et al (78)		
Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Unclear Risk	Not stated
Allocation concealment (selection bias)	Unclear Risk	Not stated
Blinding of participants and researchers (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	Not stated - although outcomes unlikely to be influenced by blinding (blood bio-markers)
Incomplete outcome data (attrition bias)	Low risk	No missing outcome data
Selective reporting (reporting bias)	Unclear Risk	The study protocol not available
Other bias	Low risk	4-week washout period,
Sköldstam et al. (80)		
Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Unclear Risk	Not stated
Allocation concealment (selection bias)	Unclear Risk	Not stated
Blinding of participants and researchers (performance bias)	Unclear Risk	Not stated
Blinding of outcome assessment (detection bias)	Low Risk	Not stated - although outcomes unlikely to be influenced by blinding (blood bio-markers)
Incomplete outcome data (attrition bias)	Low risk	<5% drop out rate

Supplementary Data

Supplemental Table 4 - Continued

Selective reporting (reporting bias)	Unclear risk	Protocol not described
Other bias	High Risk	Some bio-markers not comparable at baseline

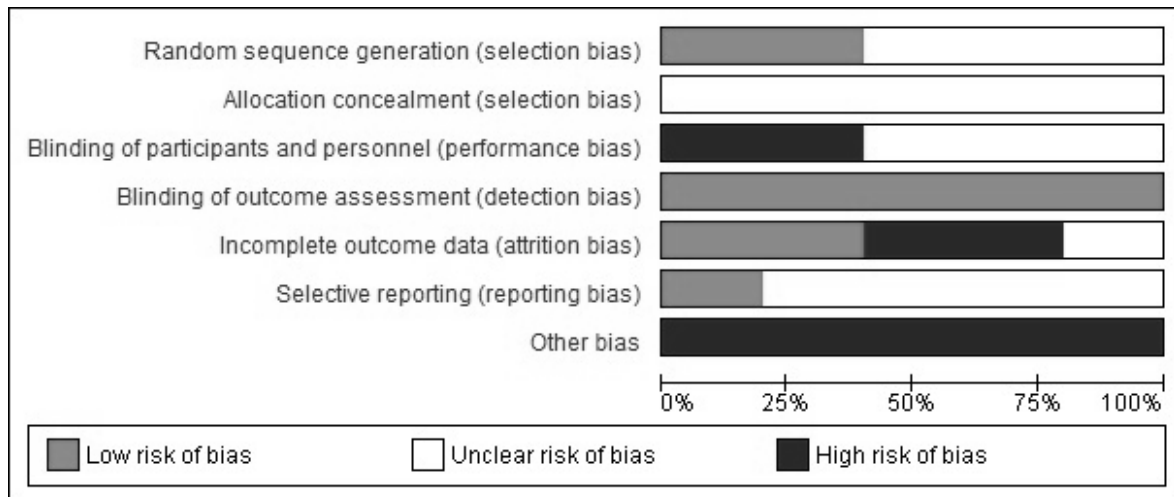
Sköldstam (79)

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Unclear	Not stated
Allocation concealment (selection bias)	Unclear Risk	Not stated
Blinding of participants and researchers (performance bias)	high risk	Not possible to blind researchers. Not possible to blind participants (pre-post) which may have affected performance in different arms
Blinding of outcome assessment (detection bias)	Low Risk	Not stated - although outcomes unlikely to be influenced by blinding (blood bio-markers)
Incomplete outcome data (attrition bias)	unclear risk	<10%, but unclear at which time pts dropped out
Selective reporting (reporting bias)	Unclear Risk	Protocol not described
Other bias	Unclear Risk	Base line data not reported

CRP, C-Reactive Protein; ITT, intention to treat; SAS, Statistical Analysis System.

¹ Kjeldsen-Kragh et al 1995 and 1991 - same participants/study, different outcomes reported

Supplementary Data



Supplemental Figure 7. Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.