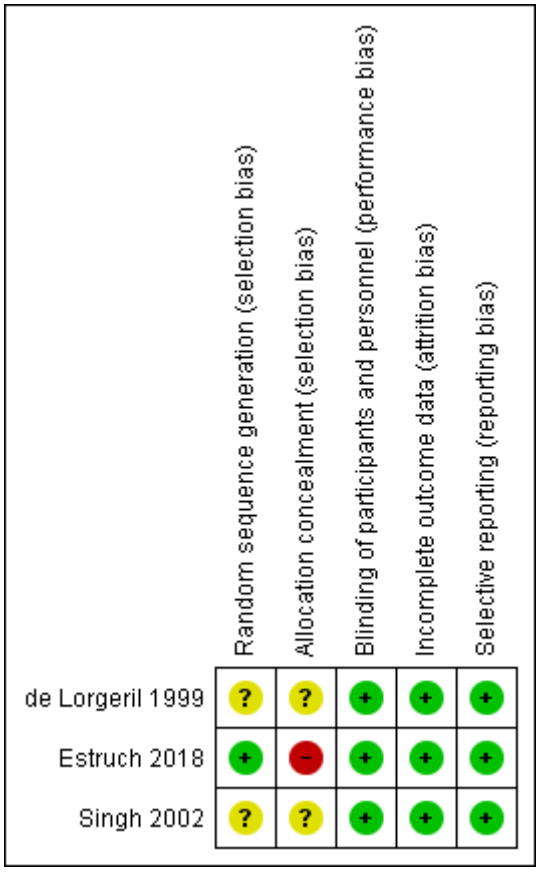
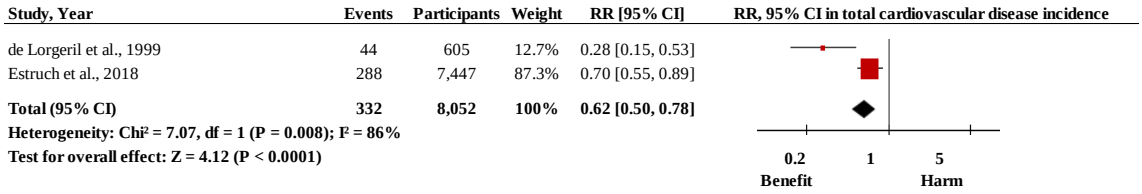
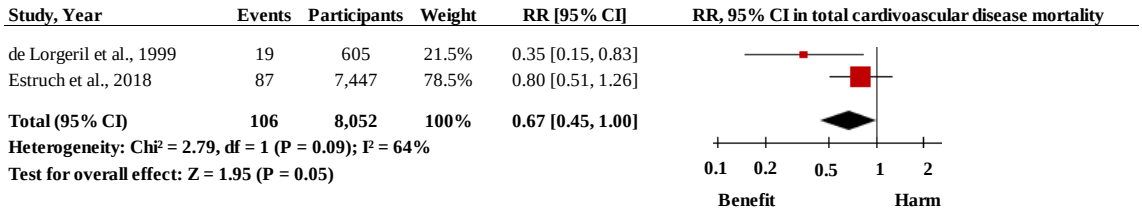


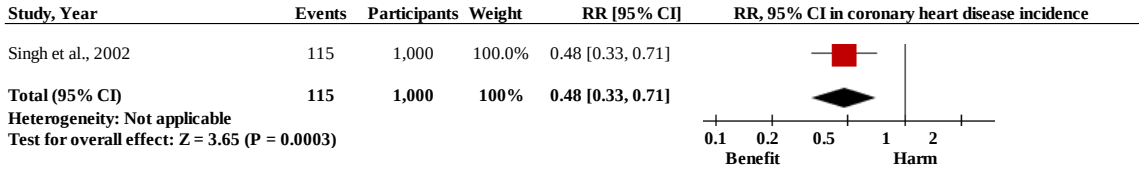
Supplemental figure 1. Risk of bias assessment for randomized clinical trials



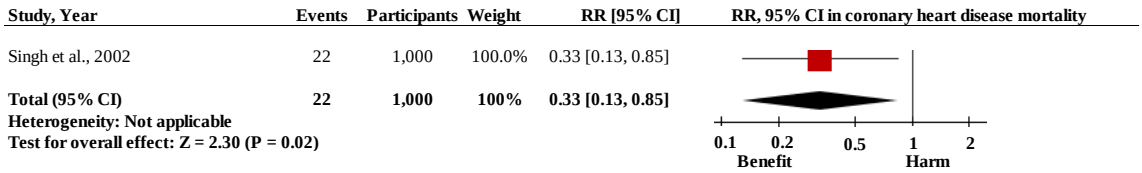
Supplemental figure 2. Effect of Mediterranean diet on total cardiovascular disease incidence risk. The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic.



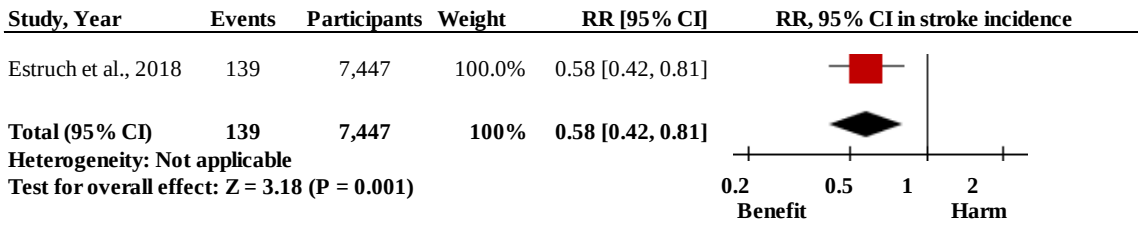
Supplemental figure 3. Effect of Mediterranean diet on total cardiovascular disease mortality risk. The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic



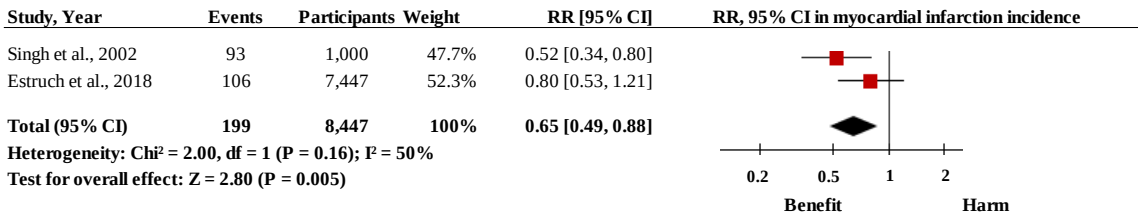
Supplemental figure 4. Effect of Mediterranean diet on coronary heart disease incidence risk. The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic



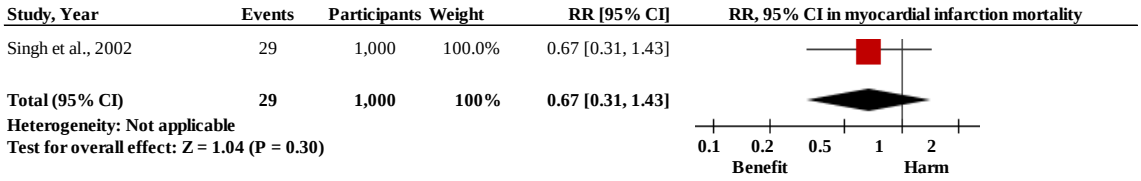
Supplemental figure 5. Effect of Mediterranean diet on coronary heart disease mortality risk. The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic



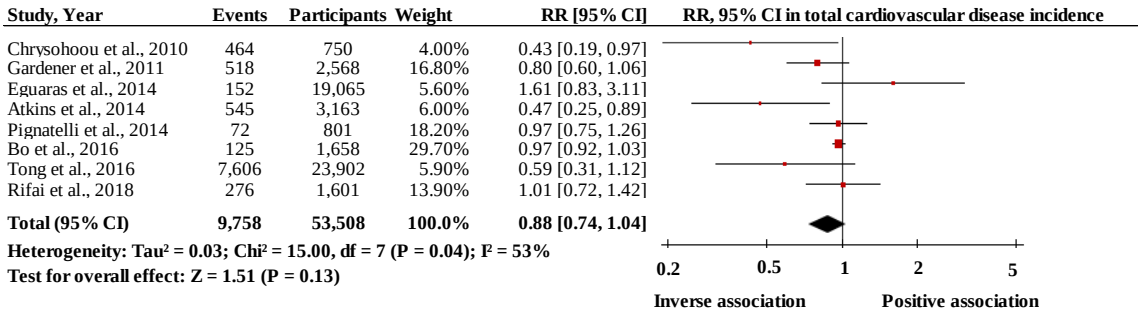
Supplemental figure 6. Effect of Mediterranean diet on total stroke incidence risk. The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic



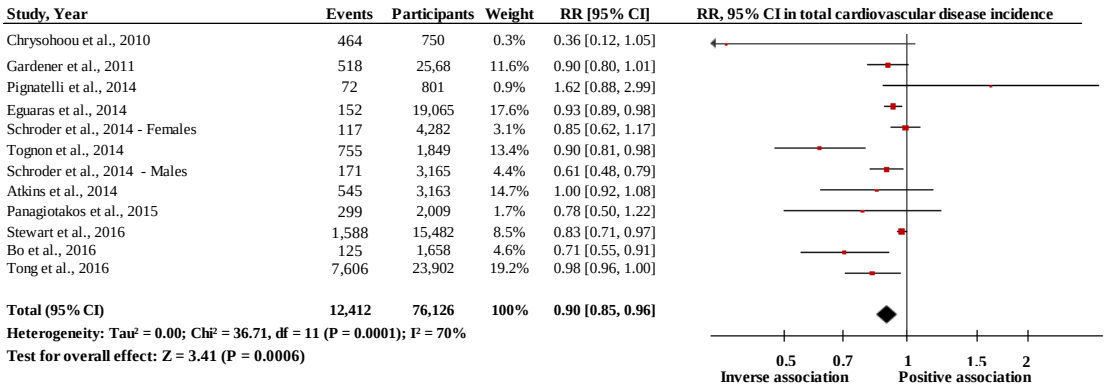
Supplemental figure 7. Effect of Mediterranean diet on myocardial infarction incidence risk. The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic



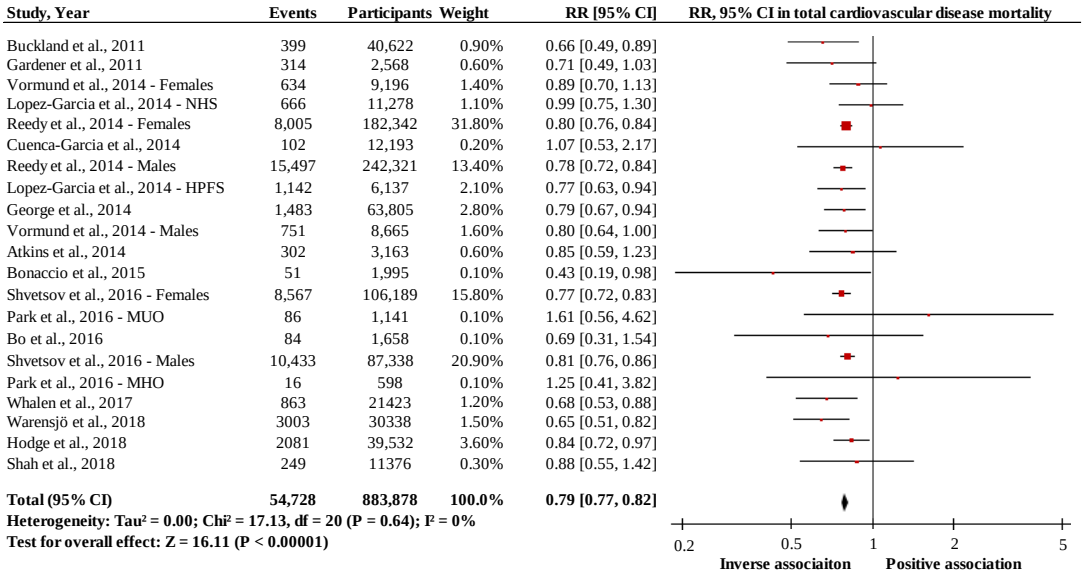
Supplemental figure 8. Effect of Mediterranean diet on myocardial infarction mortality risk. The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic



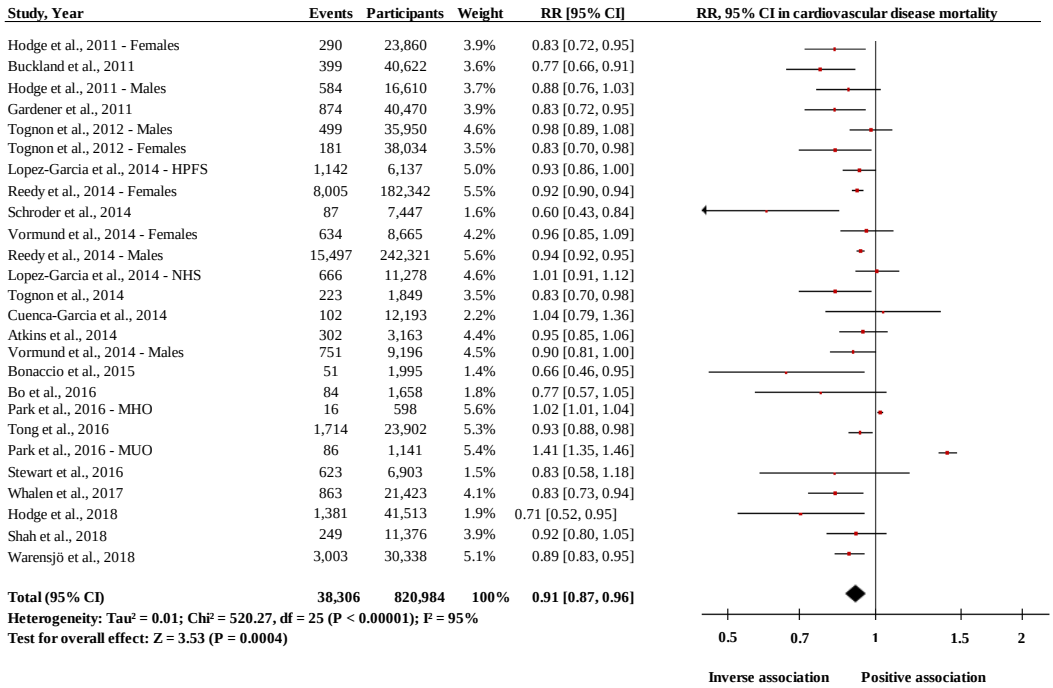
Supplemental figure 9. Association between adherence to Mediterranean diet and total cardiovascular disease incidence (high *vs* low categories). The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic.



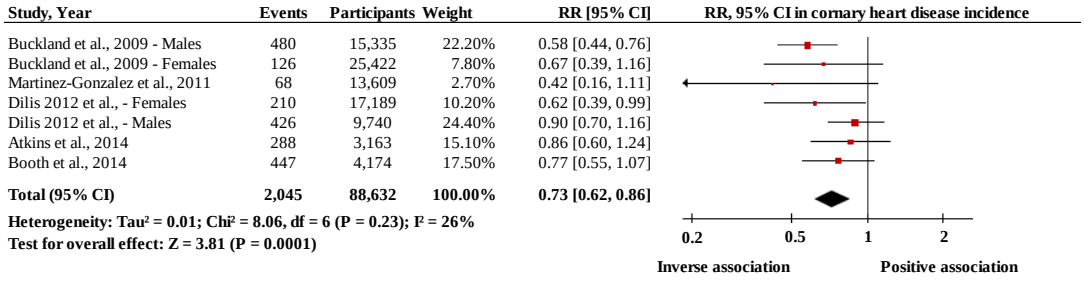
Supplemental figure 10. Forest plots for all prospective cohort studies assessing the association between 2-point increase in the adherence to the Mediterranean diet and total cardiovascular disease incidence risk. Data are expressed as relative risk and 95% confidence interval by using generic inverse-variance random-effects model. Diamond represents the pooled effect estimates. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic. RR, relative risk.



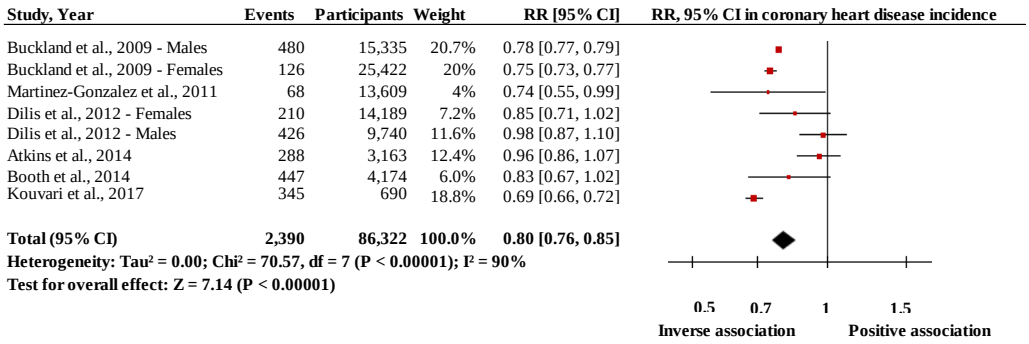
Supplemental figure 11. Association between adherence to Mediterranean diet and total cardiovascular disease mortality risk (high *vs* low categories). The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic.



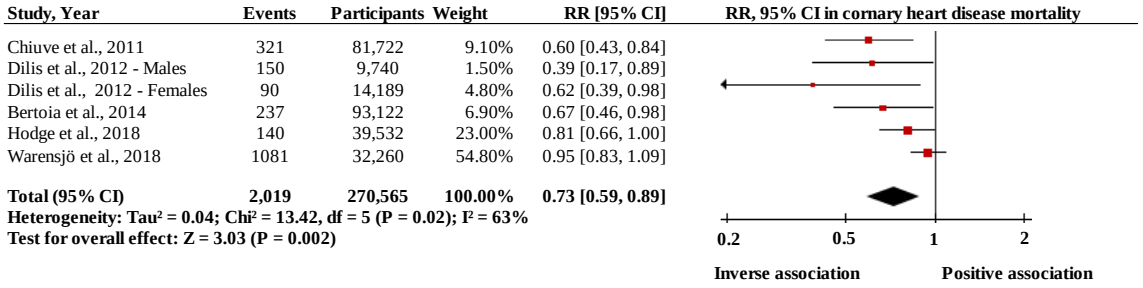
Supplemental figure 12. Forest plots for all prospective cohort studies assessing the association between 2-point increase in the adherence to the Mediterranean diet and total cardiovascular disease mortality risk. Data are expressed as relative risk and 95% confidence interval by using generic inverse-variance random-effects model. Diamond represents the pooled effect estimates. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic.RR, relative risk.



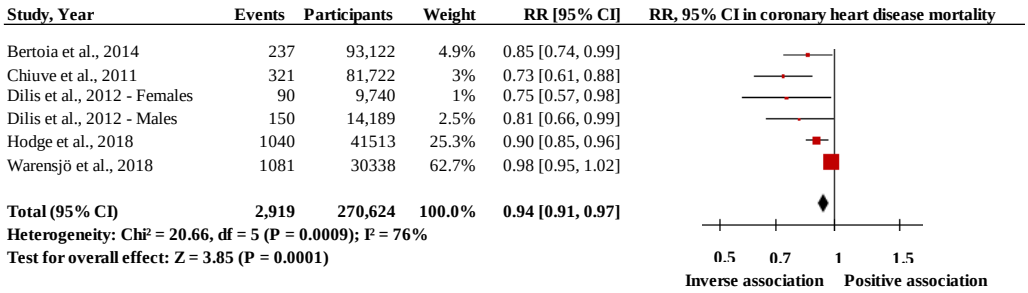
Supplemental figure 13. Association between adherence to Mediterranean diet and coronary heart disease risk (high *vs* low categories). The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic.



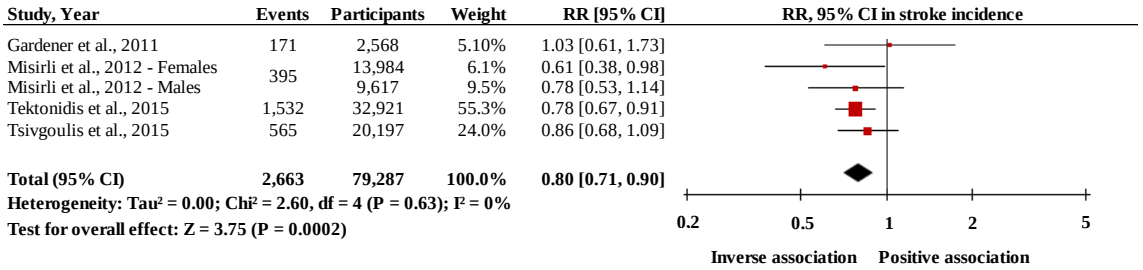
Supplemental figure 14. Forest plots for all prospective cohort studies assessing the association between 2-point increase in the adherence to the Mediterranean diet and coronary heart disease incidence risk. Data are expressed as relative risk and 95% confidence interval by using generic inverse-variance random-effects model. Diamond represents the pooled effect estimates. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of P < 0.10, and quantified by the I^2 statistic. RR, relative risk.



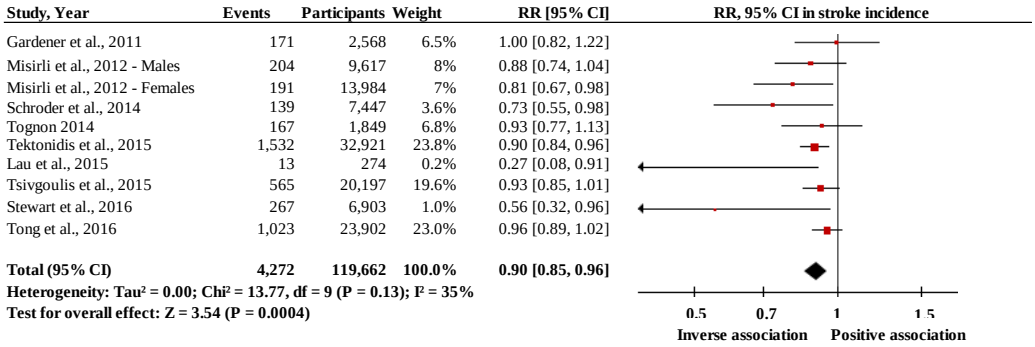
Supplemental figure 15. Association between adherence to Mediterranean diet and coronary heart disease mortality risk (high *vs* low categories). The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi2) at a significance level of P < 0.10, and quantified by the I2 statistic.



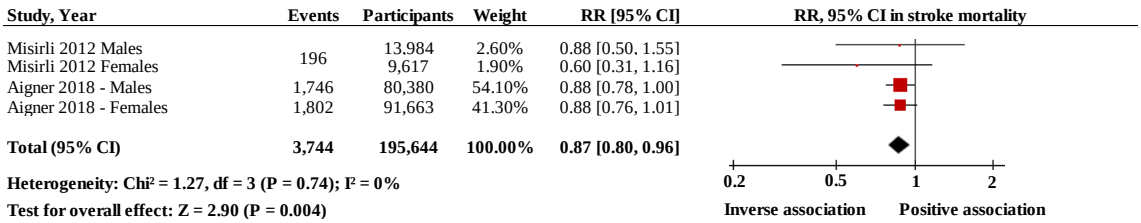
Supplemental figure 16. Forest plots for all prospective cohort studies assessing the association between 2-point increase in the adherence to the Mediterranean diet and coronary heart disease mortality risk. Data are expressed as relative risk and 95% confidence interval by using generic inverse-variance fixed-effects model. Diamond represents the pooled effect estimates. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic. RR, relative risk.



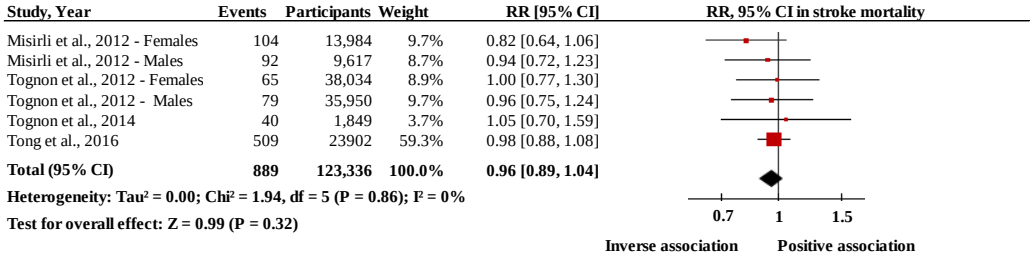
Supplemental figure 17. Association between adherence to Mediterranean diet and stroke incidence risk (high *vs* low categories). The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic.



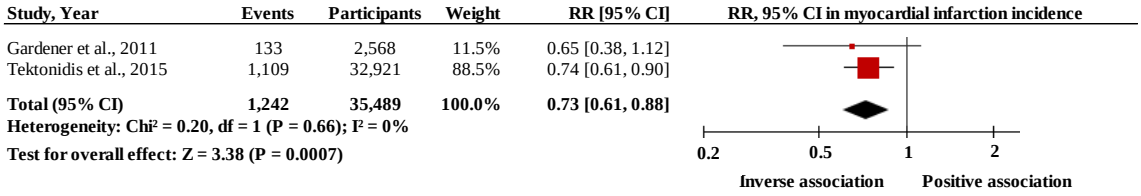
Supplemental figure 18. Forest plots for all prospective cohort studies assessing the association between 2-point increase in the adherence to the Mediterranean diet and stroke incidence risk. Data are expressed as relative risk and 95% confidence interval by using generic inverse-variance random-effects model. Diamond represents the pooled effect estimates. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic. RR, relative risk.



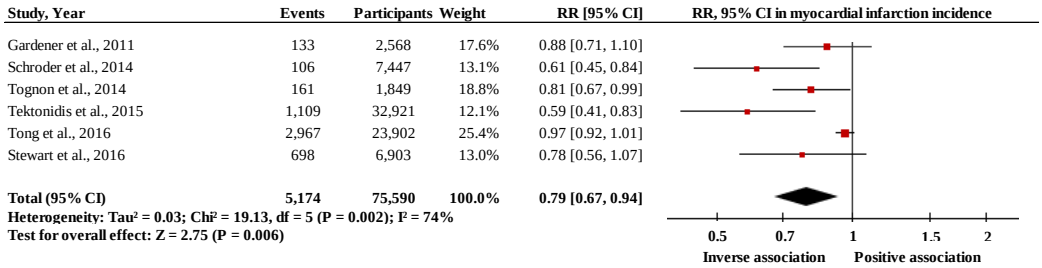
Supplemental figure 19. Association between adherence to Mediterranean diet and stroke mortality risk (high *vs* low categories). The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic.



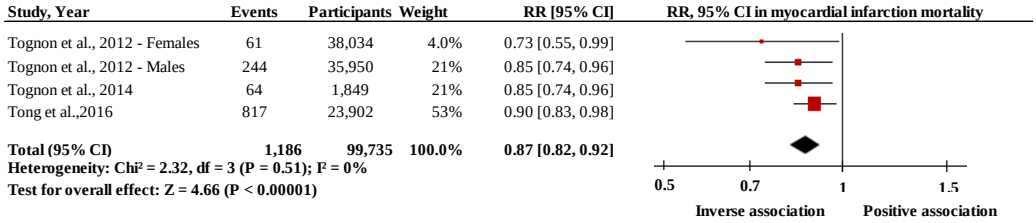
Supplemental figure 20. Forest plots for all prospective cohort studies assessing the association between 2-point increase in the adherence to the Mediterranean diet and stroke mortality risk. Data are expressed as relative risk and 95% confidence interval by using generic inverse-variance random-effects model. Diamond represents the pooled effect estimates. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic. RR, relative risk.



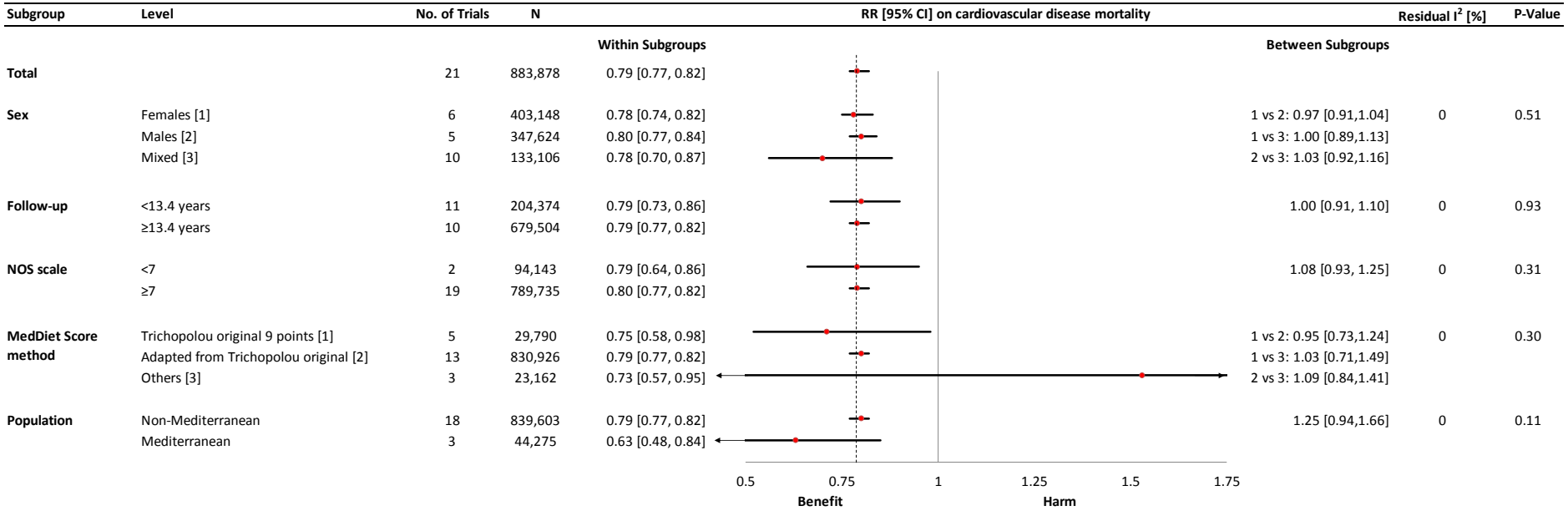
Supplemental figure 21. Association between adherence to Mediterranean diet and total myocardial infarction risk (high *vs* low categories). The diamond represents the pooled risk estimate. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic.



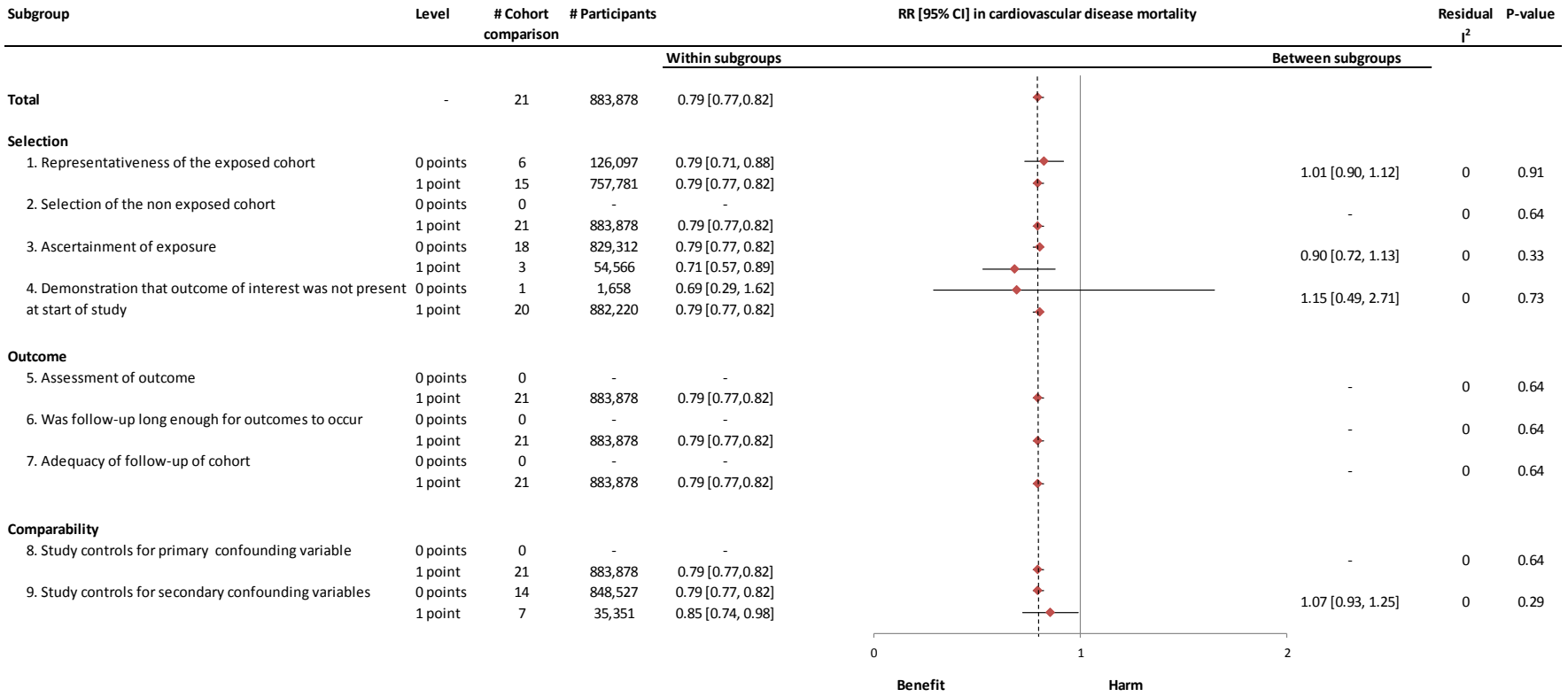
Supplemental figure 22. Forest plots for all prospective cohort studies assessing the association between 2-point increase in the adherence to the Mediterranean diet and myocardial infarction incidence risk. Data are expressed as relative risk and 95% confidence interval by using generic inverse-variance random-effects model. Diamond represents the pooled effect estimates. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic. RR, relative risk.



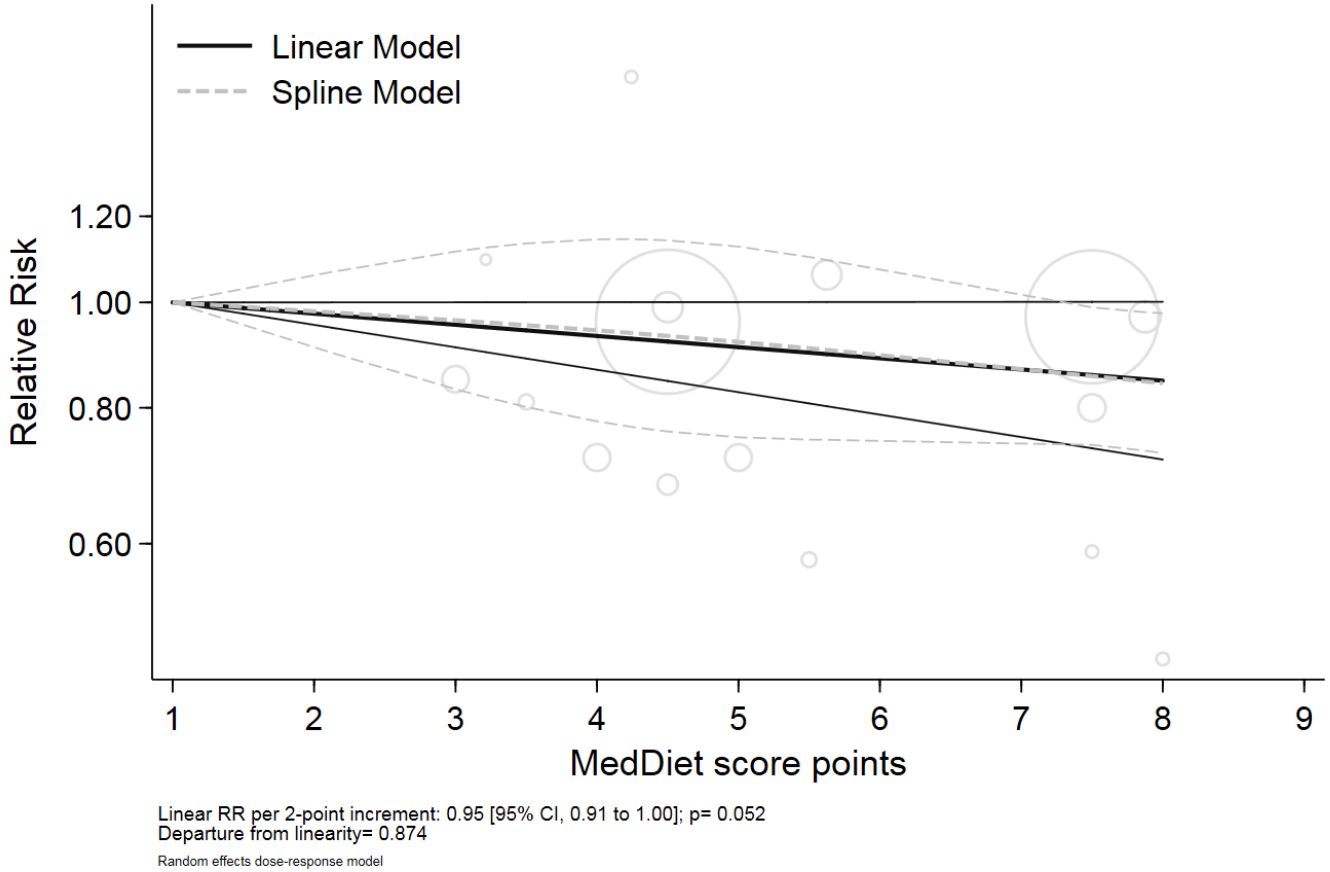
Supplemental figure 23. Forest plots for all prospective cohort studies assessing the association between 2-point increase in the adherence to the Mediterranean diet and myocardial infarction mortality risk. Data are expressed as relative risk and 95% confidence interval by using generic inverse-variance fixed-effects model. Diamond represents the pooled effect estimates. Inter-study heterogeneity was tested using the Cochran Q statistic (Chi^2) at a significance level of $P < 0.10$, and quantified by the I^2 statistic. RR, relative risk.



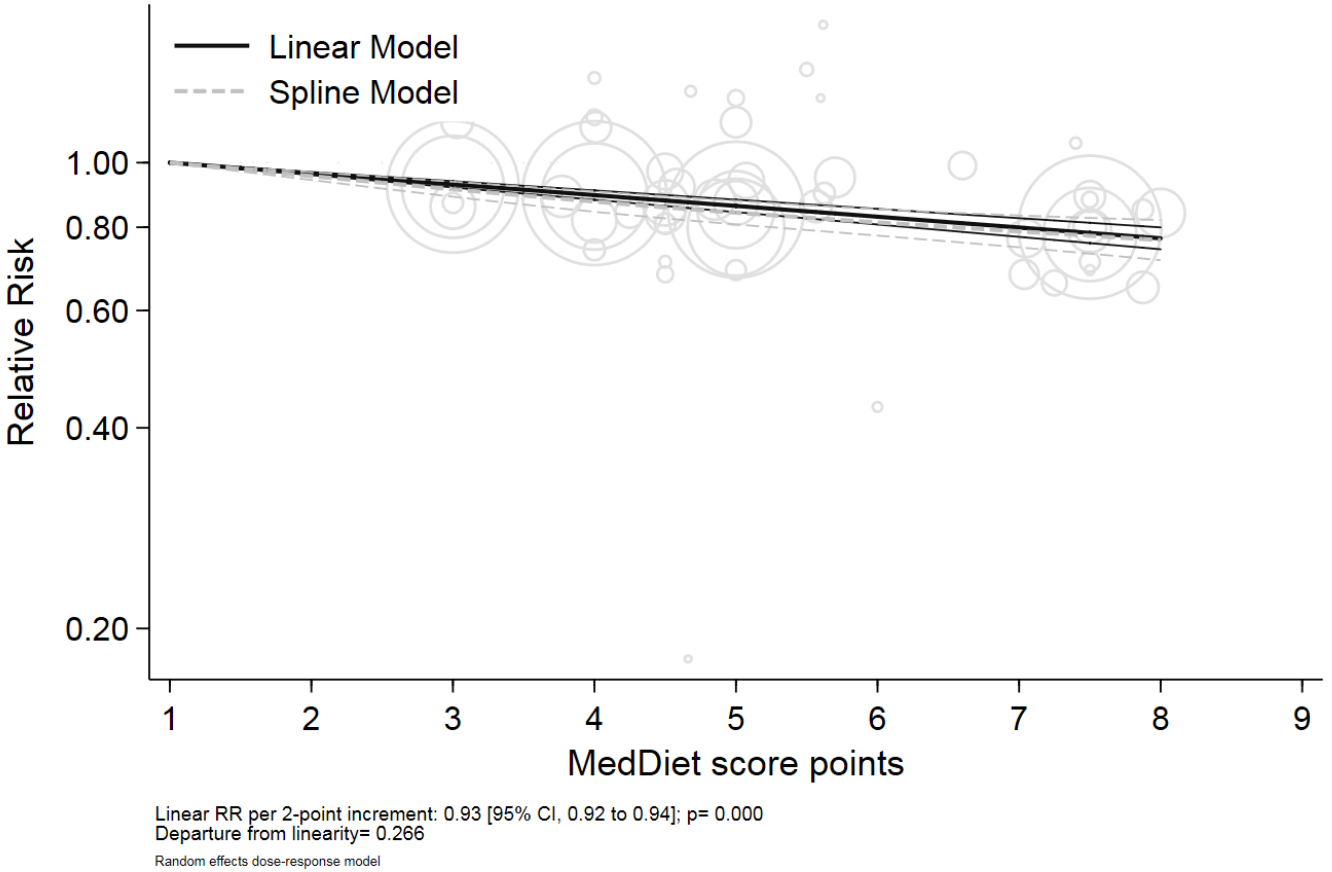
Supplemental figure 24. Subgroup analyses of Mediterranean diet and total cardiovascular mortality. NOS means Newcastle-Ottawa Scale. Diamonds for each subgroup levels represents the pooled effect estimates. The dashed line represents the pooled effect estimated for the overall analysis. RR, relative risk.



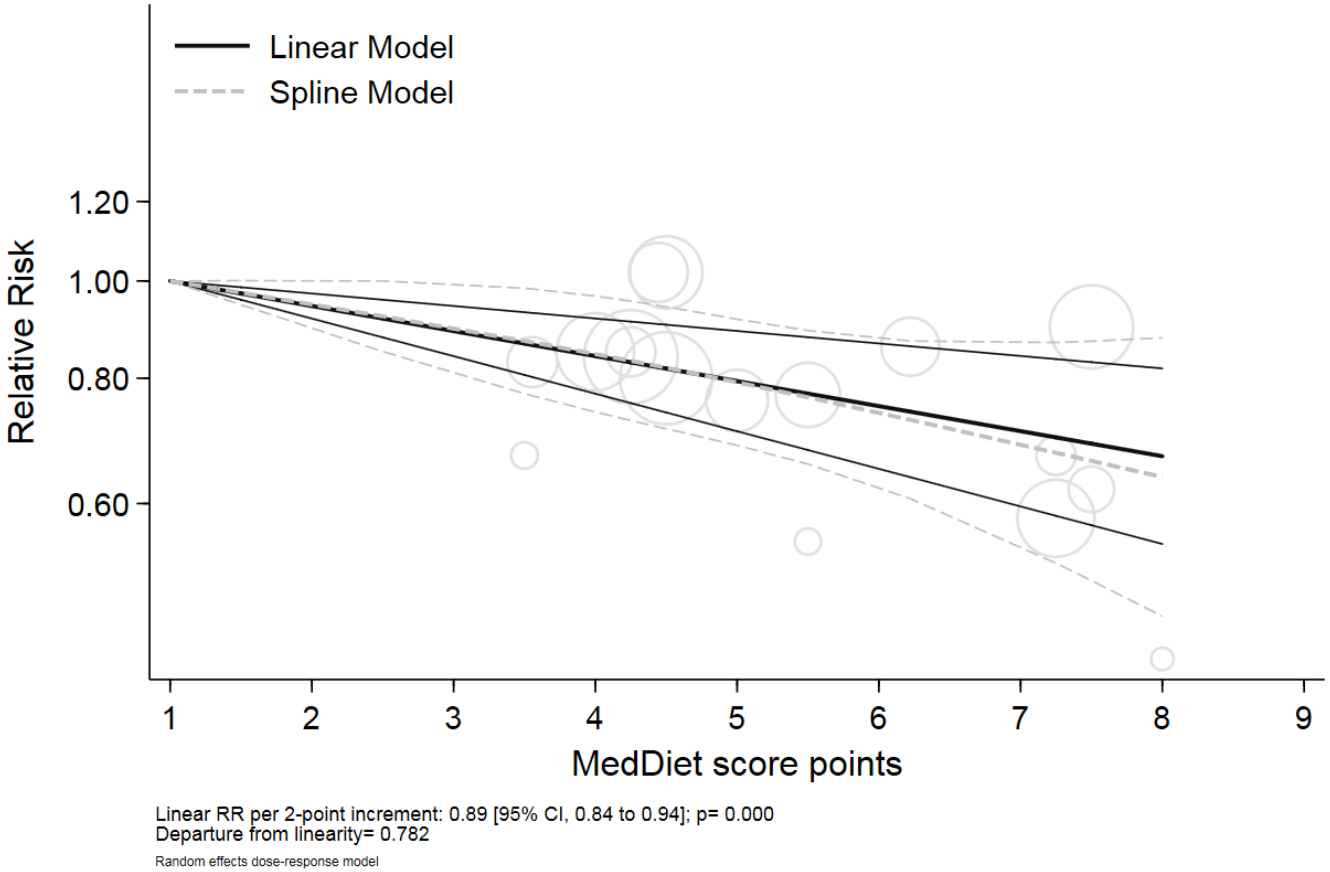
Supplemental figure 25. Risk of bias (using Newcastle-Ottawa Scale [NOS]) subgroup analysis for studies investigating the association of Mediterranean diet adherence and cardiovascular disease mortality. One point was given for comparability if study adjusted for the pre-specified primary confounding variable (age) and a second point if the study adjusted for 4 of the 5 pre-specified secondary variables (gender, physical activity, family history of cardiovascular disease, markers of obesity/overweight and dyslipidemia). Diamonds for each subgroup level represents the pooled effect estimates. The dashed line represents the pooled effect estimates for the overall analysis. RR, relative risk.



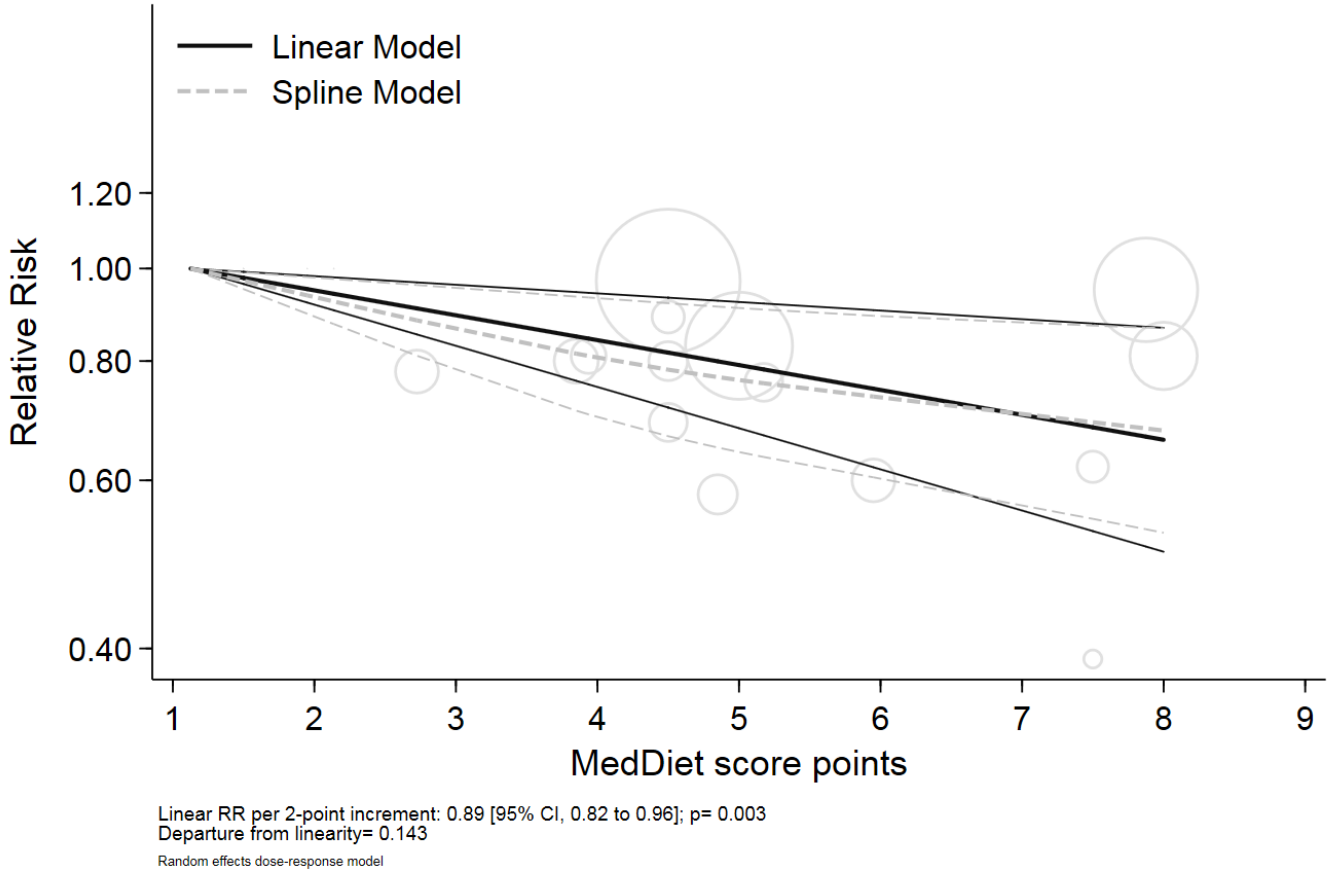
Supplemental figure 26. Linear and non-linear dose-response relation between increasing 2-point of Mediterranean diet score and the risk of total cardiovascular disease incidence (n=6 studies). Each study was centered to the baseline reference dose for the estimation of increasing dose risk.



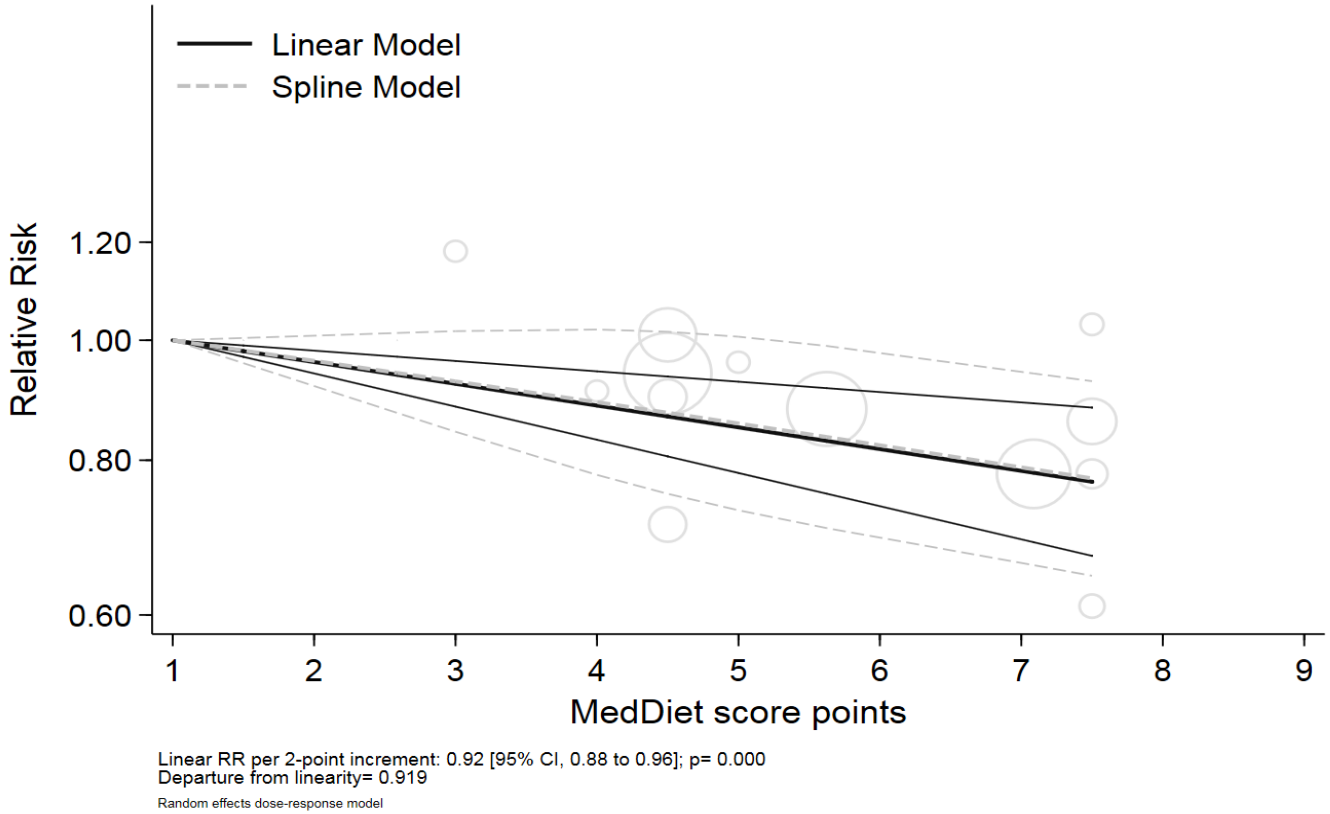
Supplemental figure 27. Linear and non-linear dose-response relation between increasing 2-point of Mediterranean diet score and the risk of total cardiovascular disease mortality (n=19 studies). Each study was centered to the baseline reference dose for the estimation of increasing dose risk.



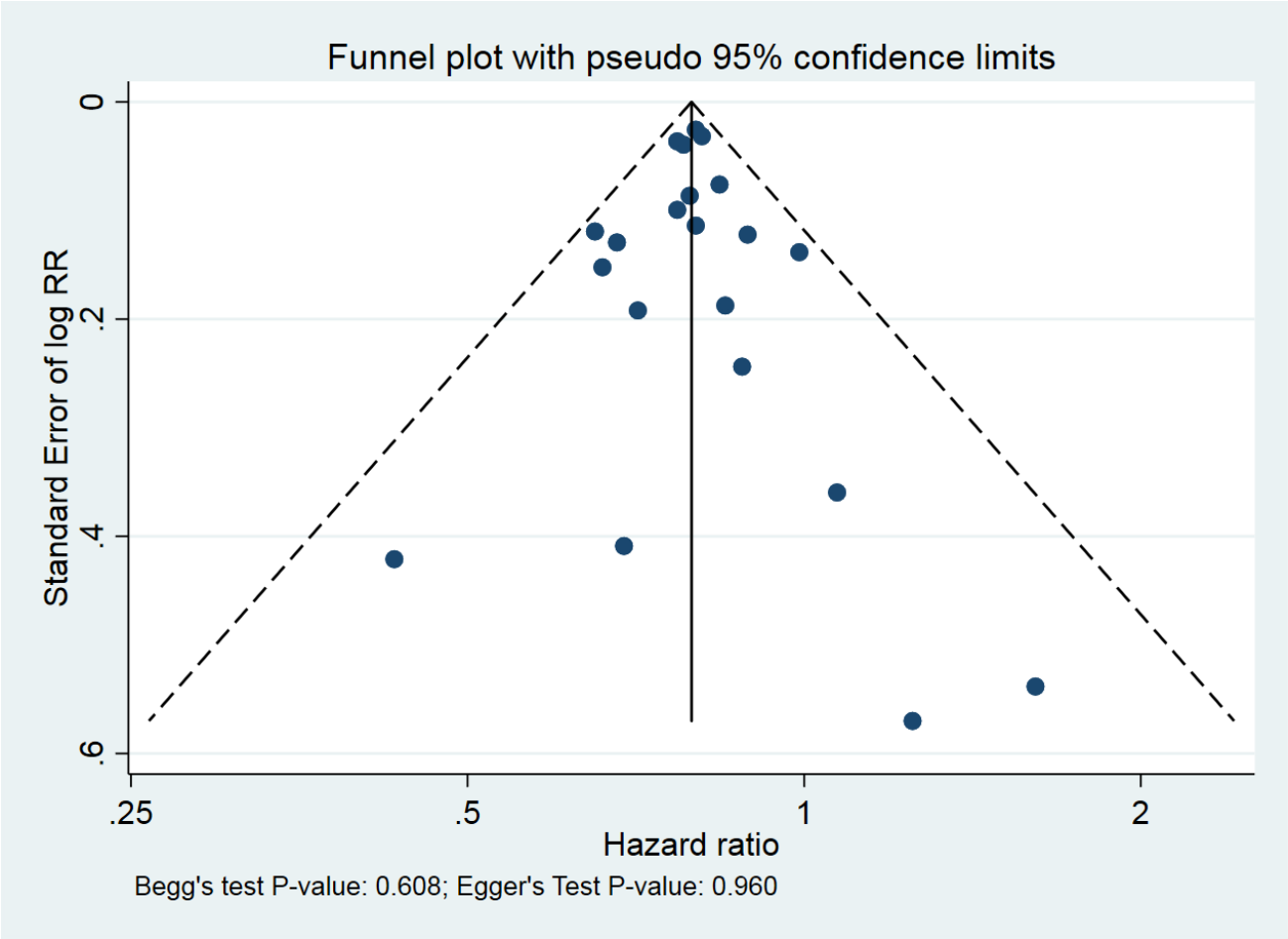
Supplemental figure 28. Linear and non-linear dose-response relation between increasing 2-point of Mediterranean diet score and the risk of coronary heart disease incidence (n=7 studies). Each study was centered to the baseline reference dose for the estimation of increasing dose risk.



Supplemental figure 29. Linear and non-linear dose-response relation between increasing 2-point of Mediterranean diet score and the risk of coronary heart disease mortality (n=6 studies). Each study was centered to the baseline reference dose for the estimation of increasing dose risk.



Supplemental figure 30. Linear and non-linear dose-response relation between increasing 2-point of Mediterranean diet score and the risk of stroke incidence (n=5 studies). Each study was centered to the baseline reference dose for the estimation of increasing dose risk.



Supplemental figure 31. Funnel plot of natural logarithm relative risk (RR) for total cardiovascular disease mortality. The vertical line represents the pooled effect estimates expressed as a lnRR. Dash lines represents pseudo-95% confidence intervals. The circles represent risk estimates for each cohort, and the horizontal lines represent standard errors of the lnRR.

Medline	
1	exp Diet, Mediterranean/
2	(mediterranean adj3 diet).mp.
3	mediterranean diet*.mp.
4	or/1-3
5	exp Stroke/
6	(fatal adj3 stroke).mp.
7	non fatal stroke.mp.
8	hemorrhagic stroke.mp.
9	exp Intracranial Hemorrhages/
10	exp Intracranial arterial diseases/
11	ischemic stroke.mp.
12	exp Brain Ischemia/
13	exp Cerebral Infarction/
14	exp Peripheral Arterial Disease/
15	peripheral artery disease.mp.
16	exp Heart Failure/
17	heart failure.mp.
18	exp myocardial ischemia/
19	exp myocardial infarction/
20	cardiovascular disease mortality.mp.
21	cardiovascular disease death.mp.
22	CVD death.mp.
23	CVD mortality.mp.
24	cardiovascular disease.mp.
25	exp cardiovascular disease/
26	CVD.mp.
27	coronary disease.mp.
28	exp Coronary Disease/
29	cerebrovascular.mp.
30	cerebral vascular.mp.
31	or/5-30
32	exp cohort studies/
33	cohort$.tw.
34	controlled clinical trial.pt.
35	epidemiologic methods/
36	limit 35 to yr=1971-1988
37	32 or 33 or 34 or 36
38	4 and 31 and 37
39	"randomized controlled trial".pt.
40	(random$ or placebo$ or single blind$ or double blind$ or triple blind$).ti,ab.
41	(retraction of publication or retracted publication).pt.
42	or/39-41
43	(animals not humans).sh.
44	((comment or editorial or meta-analysis or practice-guideline or review or letter or journal correspondence) not "randomized controlled trial").pt.
45	(random sampl$ or random digit$ or random effect$ or random survey or random regression).ti,ab. not "randomized controlled trial".pt.
46	42 not (43 or 44 or 45)
47	4 and 31 and 46
48	38 or 47

Embase	
1	exp Mediterranean diet/
2	(mediterranean adj3 diet).mp.
3	mediterranean diet*.mp.
4	or/1-3
5	exp cerebrovascular accident/
6	stroke.mp.
7	(fatal adj3 stroke).mp.
8	non fatal stroke.mp.
9	hemorrhagic stroke.mp.
10	exp brain hemorrhage/
11	intracranial hemorrhage.mp.
12	exp cerebral artery disease/
13	intracranial arterial disease.mp.
14	ischemic stroke.mp.
15	exp brain ischemia/
16	exp brain infarction/
17	exp peripheral occlusive artery disease/
18	peripheral artery disease.mp.
19	exp heart failure/
20	heart failure.mp.
21	exp heart muscle ischemia/
22	exp heart infarction/
23	cardiovascular disease mortality.mp.
24	cardiovascular disease death.mp.
25	CVD mortality.mp.
26	CVD death.mp.
27	cardiovascular disease.mp.
28	exp cardiovascular disease/
29	CVD.mp.
30	coronary disease.mp.
31	exp coronary artery disease/
32	cerebrovascular.mp.
33	cerebral vascular.mp.
34	or/5-33
35	exp cohort analysis/
36	exp longitudinal study/
37	exp prospective study/
38	exp follow up/
39	cohort$.tw.
40	or/35-39
41	4 and 34 and 40
42	(random$ or placebo$ or single blind$ or double blind$ or triple blind$).ti,ab.
43	RETRACTED ARTICLE/
44	or/42-43
45	(animal$ not human$).sh,hw.
46	(book or conference paper or editorial or letter or review).pt. not exp randomized controlled trial/
47	(random sampl$ or random digit$ or random effect$ or random survey or random regression).ti,ab. not exp randomized controlled trial/
48	44 not (45 or 46 or 47)
49	4 and 34 and 48
50	41 or 49

Cochrane	
1	Diet, Mediterranean/
2	(mediterranean adj3 diet).mp
3	mediterranean diet*.mp.
4	or/1-3
5	Stroke/
6	stroke.mp.
7	cerebrovascular accident.mp.
8	(fatal adj3 stroke).mp.
9	Cerebral Hemorrhage/
10	hemorrhagic stroke.mp.
11	Intracranial Hemorrhages/
12	Brain Ischemia/
13	brain ischemia.mp.
14	Cerebral Infarction/
15	Peripheral Arterial Disease/
16	peripheral arterial disease.mp.
17	Heart Failure/
18	Myocardial Ischemia/
19	myocardial ischemia.mp.
20	Myocardial Infarction/
21	myocardial infarction.mp.
22	cardiovascular disease mortality.mp.
23	cardiovascular disease death.mp.
24	CVD mortality.mp.
25	Cardiovascular Diseases/
26	cardiovascular disease.mp.
27	CVD.mp.
28	Coronary Disease/
29	coronary disease.mp.
30	cerebrovascular.mp.
31	or/5-30
32	4 and 31

Supplemental Table 1. Search strategy. The original search date was January 16, 2017 for MEDLINE and EMBASE databases and February 9, 2017 for the Cochrane Library Database. Updated searches were performed on April 20, 2018 and May 7, 2018, respectively.

Supplemental Table 2: Newcastle-Ottawa Scale (NOS) assessment for the quality of cohort studies.

Study	Selection[a]	Outcome[b]	Comparability[c]	Total[d]
Buckland et al, 2009	4	3	2	9
Chrysohoou et al, 2010	2	1	2	5
Buckland et al, 2011	4	3	1	8
Chiuve et al, 2011	2	3	1	6
Gardener et al, 2011	4	3	1	8
Martinez-Gonzalez et al, 2011	3	3	2	8
Dilis et al, 2012	4	3	1	8
Misirli et al, 2012	4	3	1	8
Tognon et al, 2012	3	2	1	6
Atkins et al, 2014	2	3	2	7
Bertoia et al, 2014	2	3	1	6
Booth et al, 2014	2	3	1	6
Cuenca-Garcia et al, 2014	3	3	1	7
George et al, 2014	2	3	1	6
Lopez-Garcia et al, 2014	2	3	2	7
Reedy et al, 2014	3	3	1	7
Schroder et al, 2014	4	3	2	9
Tognon et al, 2014	3	3	1	7
Vormund et al, 2014	3	3	1	7
Bonaccio, et al 2015	3	3	1	7
Eguaras et al, 2015	2	3	1	6
Lau et al, 2015	1	3	2	6
Panagiotakos et al, 2015	3	3	2	8
Pignatelli et al, 2014	1	3	1	5
Tektonidis, et al 2015	3	3	2	8
Tsivgoulis et al, 2015	3	3	1	7
Bo et al, 2016	2	3	2	7
Park et al, 2016	3	3	2	8
Shvetsov et al, 2016	3	3	1	7
Stewart et al, 2016	2	2	2	6
Tong et al, 2016	3	3	2	8
Kouvari et al, 2017	2	3	2	7

Whalen et al, 2017	3	3	1	7
Hodge et al, 2018	3	3	1	7
Shah et al, 2018	3	3	2	8
Warensjö et al, 2018	2	3	1	6
Rifai et al, 2018	2	3	1	6
Aigner et al, 2018	3	3	1	7

[a]Maximum of 4 points could be given for cohort representativeness, selection of non-exposed cohort, exposure assessment and demonstration outcome not present at baseline

[b]Maxium of 3 points could be given for follow-up length, adequacy of follow-up and outcome assessment

[c]Maximum of 2 points could be given for controlling for the pre-specified primary confounding (age) and ≥4 of the secondary confounding variables (sex, family history of cardiovascular disease, physical activity, markers of obesity/overweight and dyslipidemia)

[d]A maximum of 9 points could be given

Supplemental Table 3: Significant results of sensitivity analysis by the systematic removal of one study at a time from the analysis[a].

Removal of	RR	95% CI	P-value*	I^2	P-heterogeneity**	Comment
Total CVD incidence						
Eguaras et al., 2014	0.92	(0.79, 1.07)	0.27	41	0.12	Heterogeneity was explained
CHD mortality						
Warensjo et al., 2018	0.70	(0.61, 0.82)	<0.01	19	0.30	Heterogeneity was explained

[a]Sensitivity analysis consisted in the removal of a single study at a time from the meta-analyses and recalculating the summary relative risk. A comparison whose removal changed the significance of the heterogeneity, or changed the significance, direction or magnitude (by more than 20%) of the pooled effect estimate, was considered as influential. Only comparisons that are influential are presented in the table.

*p<0.05 is considered significant.

** <0.10 is considered significant

CI, confidence interval; CHD, coronary heart disease; CVD, cardiovascular disease; I^2, Heterogeneity; RR, Relative risk.

Supplemental Table 4 GRADE assessment of the systematic review and meta-analysis of randomized clinical trials assessing the effect of the Mediterranean diet on cardiovascular disease outcomes

Outcome	№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative (95% CI)	Quality
Total cardiovascular disease incidence	2	randomized trials	not serious	serious[a]	not serious	not serious	none	**RR 0.62** (0.50 to 0.78)	⨁⨁⨁◯ MODERATE
Total cardiovascular disease mortality	2	randomized trials	not serious	serious[b]	not serious	serious[c]	none	**RR 0.67** (0.45 to 1.00)	⨁⨁◯◯ LOW
Coronary heart disease incidence	1	randomized trials	serious[d]	not serious	serious[e]	not serious	none	**RR 0.48** (0.33 to 0.70)	⨁⨁◯◯ LOW
Coronary heart disease mortality	1	randomized trials	serious[f]	not serious	serious[g]	not serious	none	**RR 0.33** (0.13 to 0.85)	⨁⨁◯◯ LOW
Stroke incidence	1	randomized trials	not serious	not serious	serious[h]	not serious	none	**RR 0.58** (0.42 to 0.81)	⨁⨁⨁◯ MODERATE
Myocardial infarction incidence	2	randomized trials	serious[i]	not serious	not serious	not serious	none	**RR 0.65** (0.49 to 0.88)	⨁⨁⨁◯ MODERATE
Myocardial infarction mortality	1	randomized trials	serious[j]	not serious	serious[k]	serious[l]	none	**RR 0.67** (0.31 to 1.43)	⨁◯◯◯ VERY LOW

CI: Confidence interval; **RR:** Risk ratio

a. Serious inconsistency for total cardiovascular disease events risk due to high heterogeneity (I^2=86%, P=0.007)

b. Serious inconsistency for cardiovascular mortality risk due to high heterogeneity (I^2=67%, P=0.08)

c. Serious imprecision for cardiovascular mortality, as the 95% CIs (0.47, 1.02) overlap with the minimally important difference of 5% (RR 0.95 to 1.05)

d. Serious risk of bias for coronary heart disease events risk, since there is only one study which also appears to have unreliable data.

e. Serious indirectness for coronary heart disease events risk, as there is only 1 available study which also appears to have unreliable data

f. Serious risk of bias for coronary heart disease mortality risk, since there is only one study which also appears to have unreliable data.

g. Serious indirectness for coronary heart disease mortality risk, as there is only 1 available study which also appears to have unreliable data

h. Serious indirectness for stroke events risk, as there is only 1 available study

i. Serious risk of bias for MI events risk, since there are only 2 studies and 1 of them (Singh et al,) appears to have unreliable data

j. Serious risk of bias for MI mortality, since there is only one study which also appears to have unreliable data

k. Serious indirectness for MI mortality risk, as there is only 1 available study which also appears to have unreliable data

l. Serious imprecision for MI mortality risk, as the 95% CIs (0.31, 1.43) include both clinically important benefit (RR 0.95) and harm (RR 1.05)

Supplemental Table 5. GRADE assessment of the systematic review and meta-analysis of prospective cohort studies assessing the association between Mediterranean diet adherence and cardiovascular disease outcomes.

Outcome	№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative (95% CI)	Quality
Total cardiovascular disease incidence	8	observational studies	not serious	not serious[a]	not serious	serious[b]	none	**RR 0.88** (0.74 to 1.04)	⊕◯◯◯ VERY LOW
Total cardiovascular disease mortality	21	observational studies	not serious	not serious	not serious	not serious	dose response gradient	**RR 0.79** (0.77 to 0.82)	⊕⊕⊕◯ MODERATE
Coronary heart disease incidence	7	observational studies	not serious	not serious	not serious	not serious	dose response gradient	**RR 0.73** (0.62 to 0.86)	⊕⊕⊕◯ MODERATE
Coronary heart disease mortality	6	observational studies	serious[c]	not serious[d]	not serious	not serious	dose response gradient	**RR 0.83** (0.75 to 0.92)	⊕⊕◯◯ LOW
Stroke incidence	5	observational studies	not serious	not serious	serious[e]	not serious	dose response gradient	**RR 0.80** (0.71 to 0.90)	⊕⊕◯◯ LOW
Stroke mortality	4	observational studies	not serious	not serious	not serious	serious[f]	none	**RR 0.87** (0.80 to 0.96)	⊕◯◯◯ VERY LOW
Myocardial infarction incidence	2	observational studies	not serious	not serious	serious[g]	not serious	none	**RR 0.73** (0.61 to 0.88)	⊕◯◯◯ VERY LOW

CI: Confidence interval; **RR:** Risk ratio

a. Although there was high heterogeneity (I^2=53%, p=0.04), we did not downgrade for inconsistency because removal of one study (Eguaras et al. 2014) explained some of the heterogeneity (I^2=41%, p=0.12)

b. Serious imprecision as the 95%CIs (0.74, 1.04) overlap with the minimally important difference of 5% (RR 0.95 to 1.05)

c. Serious risk of bias for coronary heart disease mortality risk, as 50% of the studies were low-quality (NOS<7)

d. Although there was high heterogeneity (I^2=53%, p=0.02), we did not downgrade for inconsistency because removal of one study (Warensjo et al. 2018) explained some of the heterogeneity (I^2=19%, p=0.30)

e. Serious indirectness as studies contributing >50% of the weight (64.1%) were conducted in females.

f.. Serious imprecision as the 95%CIs (0.80, 0.96) overlap with the minimally important difference of 5% (RR 0.95 to 1.05)

g. Serious indirectness as 97% of the participants across the 2 studies were female.