SUPPLEMENTAL MATERIAL

Table S1. Checklist: PRISMA 2020 Main Checklist.

Topic	No.	Item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Line 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Line 50-64
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Line 69-72
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Line 81-89
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Line 77-80
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Line 77-78 and Table S2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Line 80-81
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Line 92-93
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Line 93-96
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Line 96-97
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Line 89-90

Topic	No.	Item	Location where item is reported
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Line 99-102
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item 5)).	Line 125-128, Table S3
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Line 107-108; Line 110-114
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Line 110-114
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Line 110-114 and Line 120-121
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Line 114-120
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Line 107-108
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Line 104-107
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Line 125-128 Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Line 125-128, Figure S1
Study characteristics	17	Cite each included study and present its characteristics.	Supp. references and Table S3
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table S4
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Line 129-149 and Table 1, S3
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Line 198-199

Topic	No.	Item	Location where item is reported
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Line 151-196
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Line 168-196
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Line 203-205
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Line 198-203
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Line 151-166
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Line 208-262
	23b	Discuss any limitations of the evidence included in the review.	Line 263-273
	23c	Discuss any limitations of the review processes used.	Line 263-273
	23d	Discuss implications of the results for practice, policy, and future research.	Line 274-282
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	N/A
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	N/A
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Line 284-285
Competing interests	26	Declare any competing interests of review authors.	Line 286
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

PRIMSA Abstract Checklist

Topic	No.	Item	Reported?
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	No
Synthesis of results	6	Specify the methods used to present and synthesize results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	No
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	No
Registration	12	Provide the register name and registration number.	No

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. MetaArXiv. 2020, September 14. DOI: 10.31222/osf.io/v7gm2. For more information, visit: www.prisma-statement.org

Table S2. Literature retrieval strategies for online databases.

Database	Search Strategy
PubMed	#1 (“Dietary fats, unsaturated” [MH] OR “fish oils” [MH] OR “fish oil” [tiab] OR “fatty acids, omega-3”[MH] OR "Docosahexaenoic Acids" [tiab] OR “PUFA” [tiab] OR “DHA” [tiab] OR “EPA” [tiab] OR “long chain omega-3 fatty acids” [tiab] OR “polyunsaturated fatty acid” [tiab] OR "Docosahexaenoic Acids" [tiab] OR “eicosapentaenoic acid” [tiab]) #2 (“blood pressure”[MH] OR “blood pressure determination”[MH] OR “arterial pressure”[MH] OR “hypertension”[MH] OR “blood pressure”[tiab] OR “hypertension”[tiab]) #1 AND #2 AND “human study”
Embase	#1 (‘fish oils’:ab,ti) OR (‘omega-3 fatty acids’:ab,ti) OR (‘docosahexaenoic acids’:ab,ti) OR (‘PUFA’:ab,ti) OR (‘DHA’:ab,ti) OR (‘EPA’:ab,ti) OR (‘ALA’:ab,ti) OR (‘long chain omega-3 fatty acids’:ab,ti) OR (‘polyunsaturated fatty acid’:ab,ti) OR (‘eicosapentaenoic acid’:ab,ti) OR (‘alpha linolenic acid’:ab,ti) #2 (‘blood pressure’:ab,ti) OR (‘blood pressure determination’:ab,ti) OR (‘arterial pressure’:ab,ti) OR (‘hypertension’:ab,ti) #1 AND #2 AND 'human'/de

Table S3. Summary of study characteristics of 71 trials.

Author	Year	Country	n, M/F	Age[a], y Mean (SE/SD) range	Design	HTN	HL	Device	Intervention type	DHA dose d/day	EPA dose d/day	Total dose d/day	Control	Duration, week
Albert [36]	2015	Australia	M47	35-55	Crossover	No	No	Automatic	Supplementation	0.15	0.23	0.38	Canola oil	8
Armstrong [37]	2012	United States	M35/F81	20-59	Parallel	No	No	Automatic	Supplementation	1.00	2.00	3.00	Corn + soy oil	6
Bach[38]	1989	United States	M16/F14	31(9)	Parallel	No	Yes	NR	Supplementation	1.44	1.08	2.52	Neutral oil	5
Barcelo-Coblijn[39]	2008	Canada	MF62	36-44	Parallel	No	No	NR	Supplementation	0.13	0.25	0.38	Sunflower oil	12
					Parallel	No	No	NR	Supplementation	0.25	0.50	0.76	Sunflower oil	12
Blonk[40]	1990	Netherland	M45	22-48	Parallel	No	No	Manual	Supplementation	0.60	0.90	1.50	Not specified	12
					Parallel	No	No	Manual	Supplementation	1.20	1.80	3.00	Not specified	12
					Parallel	No	No	Manual	Supplementation	2.40	3.60	6.00	Not specified	12
Bonaa[41]	1990	Netherland	MF156	20-61	Parallel	Yes	No	Automatic	Supplementation	1.82	3.26	5.08	Corn oil	10
Buckley[42]	2009	Australia	M25	22(1)	Parallel	No	No	Automatic	Supplementation	1.56	0.36	1.92	Sunflower oil	5
Burgin-Maunder[43]	2015	Australia	M23/F19	45-58	Parallel	No	No	Automatic	Supplementation	0.84	1.68	2.52	Canola oil	12
					Parallel	Yes	No	Automatic	Supplementation	0.84	1.68	2.52	Canola oil	12
Carter[44]	2012	United States	M18/F20	24(2)	Parallel	No	No	Automatic	Supplementation	1.10	1.60	2.70	Olive oil	8
Chin[45]	1993	Australia	M29	18-32	Parallel	No	No	Manual	Supplementation	0.58	0.89	1.47	Palm+safflower+olive oil	4
					Parallel	No	No	Manual	Supplementation	1.16	1.78	2.94	Palm+safflower+olive oil	4
					Parallel	No	No	Manual	Supplementation	2.32	3.56	5.88	Palm+safflower+olive oil	4
Cobiac[46]	1991	Australia	M31	30-60	Parallel	No	Yes	Automatic	Diet	3.00	1.50	4.50	Vegetable oil	5
					Parallel	No	Yes	Automatic	Supplementation	1.74	3.08	4.82	Vegetable oil	5
Cobiac[47]	1992	Australia	M36/F19	60-80	Parallel	No	No	Automatic	Supplementation	1.70	2.50	4.20	Sunflower oil	4
Conquer[48]	1999	Canada	M19	30(2)	Parallel	No	No	NR	Supplementation	1.70	1.30	3.00	Vegetable oil	6
Dart[49]	1989	United Kingdom	M14/F7	46(2)	Crossover	No	Yes	NR	Supplementation	2.50	3.52	6.02	Olive oil	8.5
Demke[50]	1988	United States	M8/F23	18-60	Parallel	No	Yes	NR	Supplementation	0.79	0.93	1.72	Safflower oil	4
Derosa[51]	2009	Italy	M164/F169	≥18	Parallel	No	Yes	Manual	Supplementation	1.50	0.90	2.40	Sucrose, mannitol and mineral salt	26
Derosa[52]	2012	Italy	M82/F85	18-75	Parallel	No	Yes	NR	Supplementation	1.35	1.20	2.55	Sucrose, mannitol and mineral salt	26

Dewell[53]	2011	United States	M64/F36	50(10)	Parallel	No	No	NR	Supplementation	0.50	0.70	1.20	Soybean oil	6
					Parallel	No	No	NR	Supplementation	1.50	2.10	3.60	Soybean oil	6
Dyerberg[54]	2004	Denmark	M51	20-60	Parallel	No	No	Automatic	Supplementation	1.40	2.20	3.60	Palm oil	8
Flaten[55]	1990	Norway	M56	35-45	Parallel	No	No	Manual	Supplementation	2.87	3.60	6.47	Olive oil	6
Geelen[56]	2003	Netherland	M36/F38	50-70	Parallel	No	No	Automatic	Supplementation	0.56	0.70	1.26	Sunflower oil	12
Grieger[57]	2014	Australia	MF80	70(6)	Parallel	No	No	Automatic	Diet	NR	NR	0.80	Usual diet	8
Grimsgaard[58]	1998	Norway	M234	36-56	Parallel	No	No	Automatic	Supplementation	—	3.80	3.80	Corn oil	7
					Parallel	No	No	Automatic	Supplementation	3.60	—	3.60	Corn oil	7
Grundt[59]	1995	Norway	M51/F6	18-70	Parallel	No	Yes	Manual	Supplementation	1.28	2.07	3.35	Corn oil	12
Hallund[60]	2010	Denmark	M45	40-70	Parallel	No	No	Automatic	Diet	2.00	0.90	2.90	Chicken	8
Harris[61]	2008	United States	M9/F13	21-70	Parallel	No	No	NR	Supplementation	—	0.98	0.98	Soybean oil	16
Hellsten[62]	1993	Sweden	MF40	30-60	Parallel	No	Yes	NR	Supplementation	NR	NR	2.00	Corn oil	21
Hill[63]	2007	Australia	M28/F53	25–65	Parallel	Yes	Yes	Automatic	Supplementation	1.56	0.36	1.92	Sunflower oil	12
Howe[64]	2018	Australia	M26/F12	40-85	Parallel	Yes	No	Automatic	Supplementation	1.60	0.40	2.00	Corn oil	20
Huerta[65]	2015	Spain	F77	20-50	Parallel	No	No	Manual	Supplementation	0.04	1.30	1.34	Sunflower oil	10
Hughes[66]	1990	United States	M13	32(9)	Crossover	No	No	Automatic	Supplementation	1.50	3.50	5.00	Wheat germ oil	4.3
					Crossover	Yes	No	Automatic	Supplementation	1.50	3.50	5.00	Wheat germ oil	4.3
Jones[67]	2014	United States and Canada	M60/F70	46(14)	Crossover	No	No	Automatic	Supplementation	0.35	0.01	0.36	Oleic acid	4
Kelley[68]	2007	United States	M34	39-66	Parallel	No	Yes	Automatic	Supplementation	3.00	—	3.00	Olive oil	14
Kestin[69]	1990	Australia	M33	46(2)	Parallel	No	No	Automatic	Supplementation	1.30	2.10	3.40	Linoleic acid	6
Knapp[23]	1989	United States	M36	30-71	Parallel	Yes	No	Automatic	Supplementation	1.20	1.80	3.00	Safflower oil	4
					Parallel	Yes	No	Automatic	Supplementation	6.00	9.00	15.00	Safflower oil	4
Kristensen[70]	2016	Denmark	M60/F83	52(12)	Parallel	No	No	Automatic	Supplementation	1.50	1.50	3.00	Olive oil	24
Lee[71]	2019	Canada	M45/F45	18-30	Parallel	No	No	Automatic	Supplementation	—	0.81	0.81	Olive oil	12
					Parallel	No	No	Automatic	Supplementation	0.81	—	0.81	Olive oil	12
Levinson[24]	1990	United States	MF17	18-75	Parallel	Yes	No	Automatic	Supplementation	6.00	9.00	15.00	Vegetable oil	6
Lindqvist[72]	2009	Sweden	M35	35-60	Crossover	No	No	NR	Diet	NR	NR	1.20	Baked lean pork + chicken	6
Lofgren[73]	1993	United States	M23	≤60	Crossover	No	No	Manual	Supplementation	2.40	3.60	6.00	Safflower oil	12
					Crossover	Yes	No	Manual	Supplementation	2.40	3.60	6.00	Safflower oil	12

Logan[74]	2015	Canada	F26	60-76	Parallel	No	No	Automatic	Supplementation	1.00	2.00	3.00	Olive oil	12
Maki[75]	2009	United States	M13/F63	35-64	Parallel	No	No	Automatic	Supplementation	0.09	0.22	0.31	Olive oil	4
					Parallel	No	No	Automatic	Supplementation	0.18	0.21	0.39	Olive oil	4
Meland[76]	1989	Norway	M40	26-66	Parallel	Yes	No	Manual	Supplementation	2.40	3.60	6.00	Corn + olive oil	6
Mills[77]	1990	Canada	M29	19-31	Parallel	No	No	Automatic	Supplementation	0.51	0.81	1.32	Safflower oil	4
Monahan[78]	2004	United States	M10/F8	18-35	Parallel	No	No	Automatic	Supplementation	2.00	3.00	5.00	Olive oil	4
Mori[79]	1999	Australia	M56	20-65	Parallel	No	Yes	Automatic	Supplementation	—	3.84	3.84	Olive oil	6
					Parallel	No	Yes	Automatic	Supplementation	3.68	—	3.68	Olive oil	6
Murphy[80]	2007	Australia	M41/F43	20-65	Parallel	No	No	Automatic	Diet	0.60	0.40	1.00	Control diet	26
Neff[81]	2011	United States	M15/F21	18-65	Parallel	No	No	Automatic	Supplementation	2.00	—	2.00	Corn + soybean oil	16
Nestel[82]	2002	Australia	M21/F17	40-69	Parallel	No	Yes	Automatic	Supplementation	—	3.04	3.04	Olive oil	7
					Parallel	No	Yes	Automatic	Supplementation	2.83	—	2.83	Olive oil	7
Noreen[83]	2012	United States	M14/F26	19-55	Parallel	No	No	Automatic	Supplementation	0.80	1.60	2.40	Safflower oil	6
Pase[84]	2015	Australia	M75/F85	50-70	Parallel	No	No	Automatic	Supplementation	0.48	0.48	0.96	Monounsaturated acid	16
Passfall[85]	1993	Germany	M4/F6	40-61	Crossover	Yes	No	Automatic	Supplementation	0.90	1.26	2.16	Olive oil	6
Prisco[86]	1998	Italy	M16	33-56	Parallel	Yes	No	Automatic	Supplementation	1.40	2.04	3.44	Olive oil	17
Radack[87]	1991	United States	M19/F14	≥18	Crossover	Yes	No	Manual	Supplementation	0.80	1.20	2.00	Safflower oil	12
Ryu[88]	1990	United States	M20	20-39	Parallel	No	No	Manual	Supplementation	0.90	2.10	3.00	Wheat germ oil	4
Sagara[89]	2011	United Kingdom	M38	45-59	Parallel	Yes	Yes	Automatic	Supplementation	2.00	—	2.00	Olive oil bread	5
Sanders[90]	2006	United Kingdom	M39/F40	33	Parallel	No	No	Automatic	Supplementation	1.50	—	1.50	Olive oil	4
Sanders[91]	2011	United Kingdom	M142/F225	45-70	Parallel	No	No	Automatic	Supplementation	0.18	0.27	0.45	Olive oil	52
					Parallel	No	No	Automatic	Supplementation	0.36	0.54	0.90	Olive oil	52
					Parallel	No	No	Automatic	Supplementation	0.72	1.08	1.80	Olive oil	52
Shabrina[92]	2020	China	M21	>30	Parallel	Mixed	No	Automatic	Supplementation	0.85	1.28	2.13	Caloric restriction	12
Shen[93]	2017	China	M48/F49	63(10)	Parallel	No	No	NR	Supplementation	0.20	0.31	0.51	Soybean oil	12
Sjoberg[94]	2010	Australia	M36/F31	53(2)	Parallel	No	No	Automatic	Supplementation	0.52	0.10	0.62	Sunola oil	12
					Parallel	No	No	Automatic	Supplementation	1.04	0.20	1.24	Sunola oil	12
					Parallel	No	No	Automatic	Supplementation	1.56	0.30	1.86	Sunola oil	12

Stark[95]	2004	Canada	F32	45-70	Crossover	No	No	Automatic	Supplementation	2.80	—	2.80	Corn and soy oil	4
Sveinsdottir[96]	2016	Iceland	M30/F69	>50	Parallel	Mixed	No	NR	Diet	0.50	1.00	1.50	Olive oil	4
Theobald[97]	2007	United Kingdom	M20/F19	45-65	Crossover	No	No	NR	Supplementation	0.70	—	0.70	Olive oil	13
Toft[98]	1995	Norway	M50/F28	21-61	Parallel	Yes	No	Manual	Supplementation	1.20	2.10	3.30	Corn oil	16
TOHP[99]	1992	United States	MF350	30-54	Parallel	No	No	Manual	Supplementation	0.90	2.10	3.00	Olive oil	24
Vandongen[100]	1993	Australia	M51	30-60	Parallel	No	No	Automatic	Supplementation	0.90	1.30	2.20	Olive, palm, safflower oils	12
					Parallel	No	No	Automatic	Supplementation	1.70	2.60	4.30	Olive, palm, safflower oils	12
					Parallel	No	No	Automatic	Diet	0.90	1.30	2.20	Olive, palm, safflower oils	12
Vericel[101]	1999	France	MF20	70-83	Parallel	Yes	No	NR	Supplementation	0.15	0.03	0.18	Sunflower oil	6
von Houwelingen[102]	1987	Norway and Netherland	M82	20-45	Parallel	No	No	Manual	Diet	3.00	1.70	4.70	Meat paste	6
Wang[103]	2008	China	M37/F6	42(3)	Parallel	Yes	Yes	Manual	Supplementation	0.36	0.54	0.90	Vegetable oil	8
Wu[104]	2014	United Kingdom	M29/F55	21-65	Crossover	No	No	Automatic	Supplementation	0.60	0.90	1.50	Corn oil	8

Abbreviations: DHA, docosahexaenoic acid; DBP, diastolic blood pressure; EPA, eicosapentaenoic acid; HTN, hypertension; HL, hyperlipidemia; NR, not reported; —, not administered.

Note: a, The age is expressed as Mean (SD/SE), SD, standard deviation and SE, standard error.

Table S4. Risk of bias of included trials.

Author	Year	Randomiz-ation	Blinding	Missing outcome	Measure-ment	Selection of results	Overall
Albert [36]	2015	low	low	low	low	low	low
Armstrong [37]	2012	some concern	some concern	low	low	low	low
Bach[38]	1989	some concern	low	low	some concern	low	low
Barcelo-Coblijn[39]	2008	some concern	some concern	low	some concern	low	low
Blonk[40]	1990	some concern	medium	low	moderate	some concern	moderate
Bonaa[41]	1990	low	low	low	low	low	low
Buckley[42]	2009	some concern	some concern	low	low	low	low
Burgin-Maunder[43]	2015	some concern	some concern	low	some concern	low	low
Carter[44]	2012	some concern	some concern	low	low	low	low
Chin[45]	1993	some concern	some concern	low	low	low	low
Cobiac[46]	1991	low	some concern	low	low	low	low
Cobiac[47]	1992	some concern	some concern	low	low	low	low
Conquer[48]	1999	moderate	some concern	low	some concern	low	moderate
Dart[49]	1989	moderate	some concern	low	some concern	low	moderate
Demke[50]	1988	some concern	low	low	some concern	low	low
Derosa[51]	2009	low	low	low	low	low	low
Derosa[52]	2012	low	some concern	low	some concern	low	low
Dewell[53]	2011	some concern	low	low	some concern	low	low
Dyerberg[54]	2004	low	some concern	low	some concern	low	low
Flaten[55]	1990	some concern	some concern	low	low	low	low
Geelen[56]	2003	some concern	some concern	low	some concern	low	low
Grieger[57]	2014	some concern	low	low	low	low	low
Grimsgaard[58]	1998	low	some concern	low	low	low	low
Grundt[59]	1995	some concern	high	low	low	low	low
Hallund[60]	2010	low	low	low	low	low	low
Harris[61]	2008	some concern	some concern	some concern	some concern	low	moderate
Hellsten[62]	1993	some concern	low	low	some concern	low	low
Hill[63]	2007	low	low	low	low	low	low
Howe[64]	2018	some concern	some concern	low	low	low	low
Huerta[65]	2015	low	some concern	some concern	some concern	low	moderate
Hughes[66]	1990	some concern	low	low	low	low	low
Jones[67]	2014	low	low	low	some concern	low	low
Kelley[68]	2007	some concern	low	low	some concern	low	low
Kestin[69]	1990	some concern	low	some concern	low	low	low
Knapp[23]	1989	low	low	low	low	low	low
Kristensen[70]	2016	low	low	low	some concern	low	low
Lee[71]	2019	some concern	low	low	low	low	low
Levinson[24]	1990	some concern	high	low	low	low	low
Lindqvist[72]	2009	some concern	some concern	low	some concern	low	low

Lofgren[73]	1993	some concern	medium	low	low	low	low
Logan[74]	2015	some concern	some concern	low	low	low	low
Maki[75]	2009	some concern	some concern	low	low	low	low
Meland[76]	1989	some concern	low	low	low	low	low
Mills[77]	1990	low	some concern	low	low	low	low
Monahan[78]	2004	some concern	low	low	low	low	low
Mori[79]	1999	some concern	low	low	low	low	low
Murphy[80]	2007	some concern	some concern	low	low	low	low
Neff[81]	2011	some concern	some concern	low	some concern	low	low
Nestel[82]	2002	low	some concern	low	some concern	low	low
Noreen[83]	2012	some concern	low	low	some concern	low	low
Pase[84]	2015	low	some concern	low	low	low	low
Passfall[85]	1993	some concern	some concern	low	low	low	low
Prisco[86]	1998	some concern	low	low	low	some concern	low
Radack[87]	1991	low	some concern	low	low	low	low
Ryu[88]	1990	low	some concern	low	low	low	low
Sagara[89]	2011	some concern	low	low	some concern	low	low
Sanders[90]	2006	low	low	low	low	low	low
Sanders[91]	2011	some concern	some concern	low	low	low	low
Shabrina[92]	2020	some concern	low	low	some concern	low	low
Shen[93]	2017	low	some concern	low	some concern	low	low
Sjoberg[94]	2010	some concern	low	low	low	low	low
Stark[95]	2004	low	some concern	low	low	low	low
Sveinsdottir[96]	2016	some concern	low	low	low	low	low
Theobald[97]	2007	some concern	low	low	low	low	low
Toft[98]	1995	low	low	low	low	low	low
TOHP[99]	1992	some concern	some concern	low	low	low	low
Vandongen[100]	1993	some concern	high	low	low	low	low
Vericel[101]	1999	high	medium	low	some concern	low	high
von Houwelingen[102]	1987	some concern	some concern	low	low	low	low
Wang[103]	2008	some concern	some concern	low	low	low	low
Wu[104]	2014	low	low	low	low	low	low

Note: Two review authors independently assessed risk of bias of each included trials in the domains of randomization (random sequence generation); blinding (allocation concealment, blinding of participants and personnel, and blinding of outcome assessors); missing outcome (incomplete outcome data); measurement (method and measurement bias); and selection of results (reporting bias).

Figure S1. Histogram of dose and duration distribution. A, Histogram of trial duration (week). B, Histogram of the total dose (DHA+EPA, g/day).

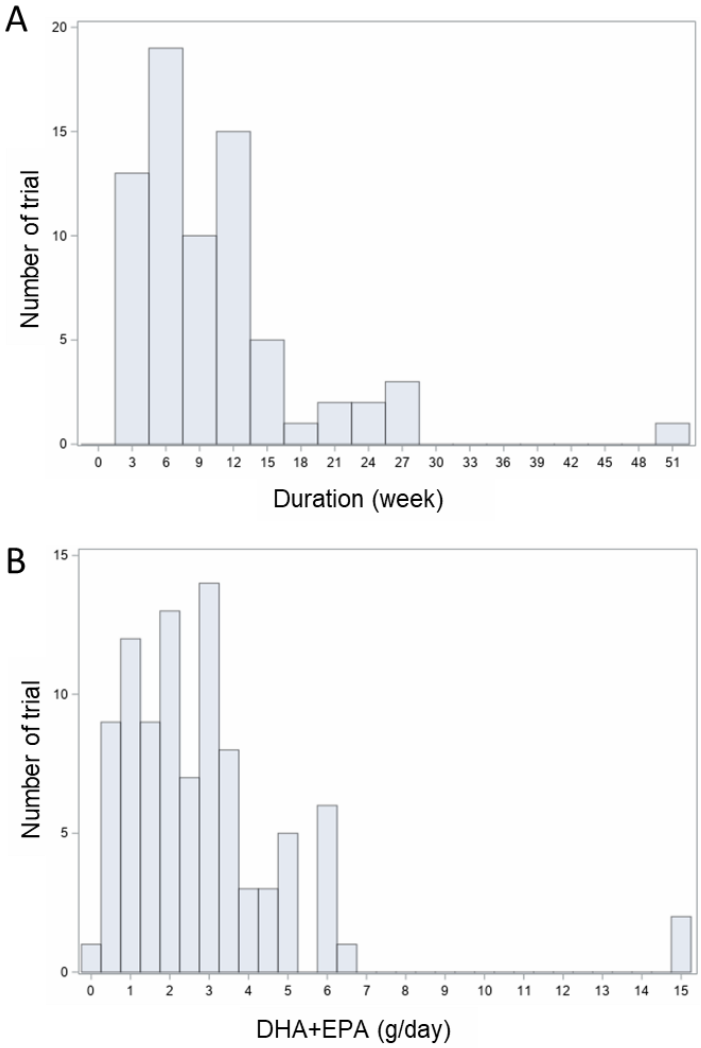
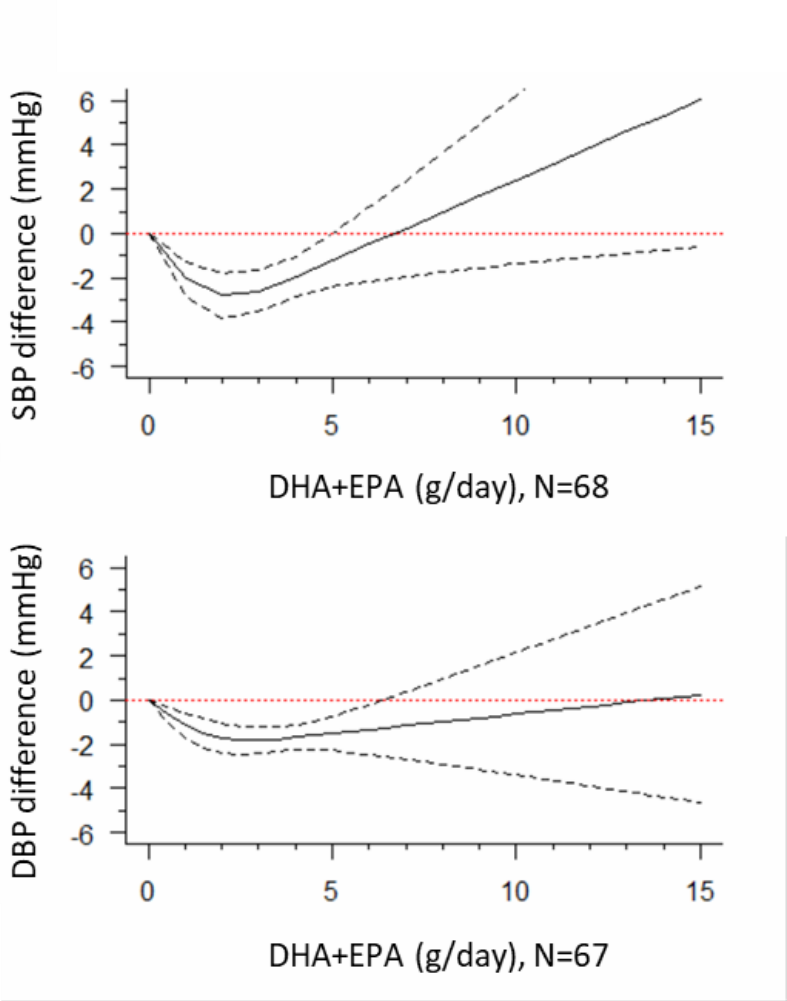
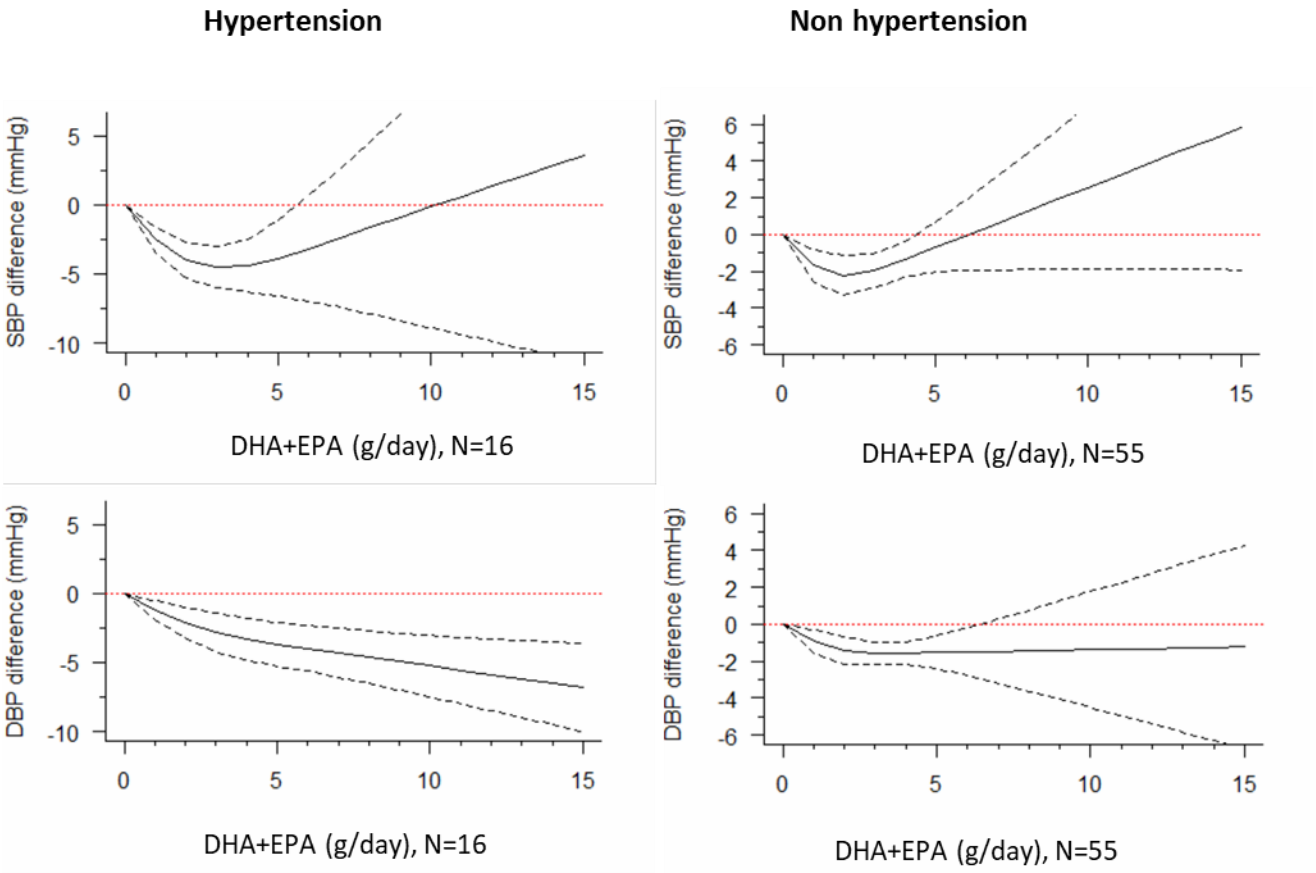


Figure S2. Dose-response relation between changes in blood pressure and combined DHA+EPA intake, after excluding the two trials with a dose of 15 g/day.



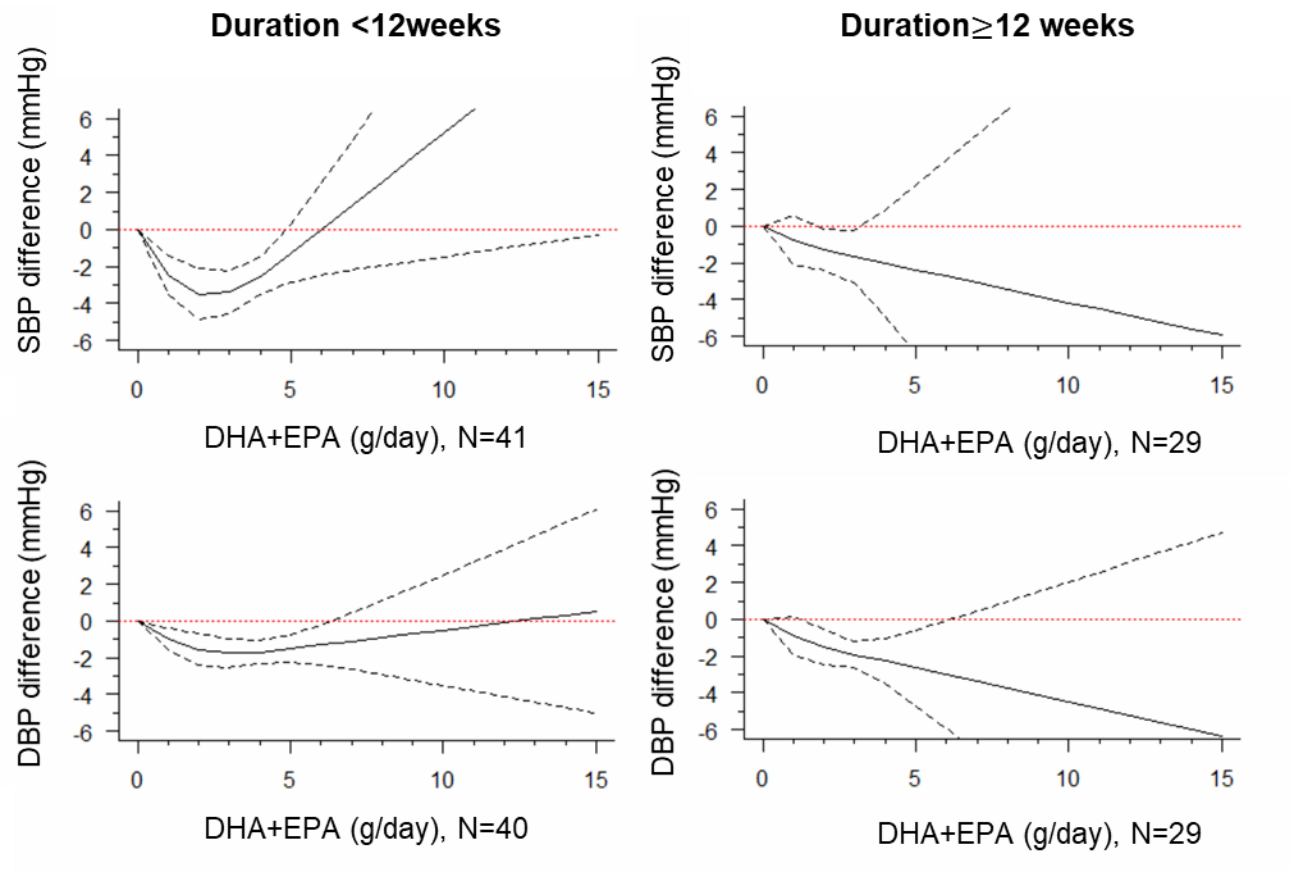
Marginal average dose-response curve (solid line) with 95% point-wise confidence intervals (dashed lines) estimated by a one-stage random-effects restricted cubic spline model, using 0 g/day as the referent. DBP, diastolic blood pressure; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; SBP, systolic blood pressure. Studies included N=69 for SBP and N=68 for DBP.

Figure S3. Dose-response relation between changes in blood pressure and combined DHA+EPA intake of the studies stratified by the status of hypertension



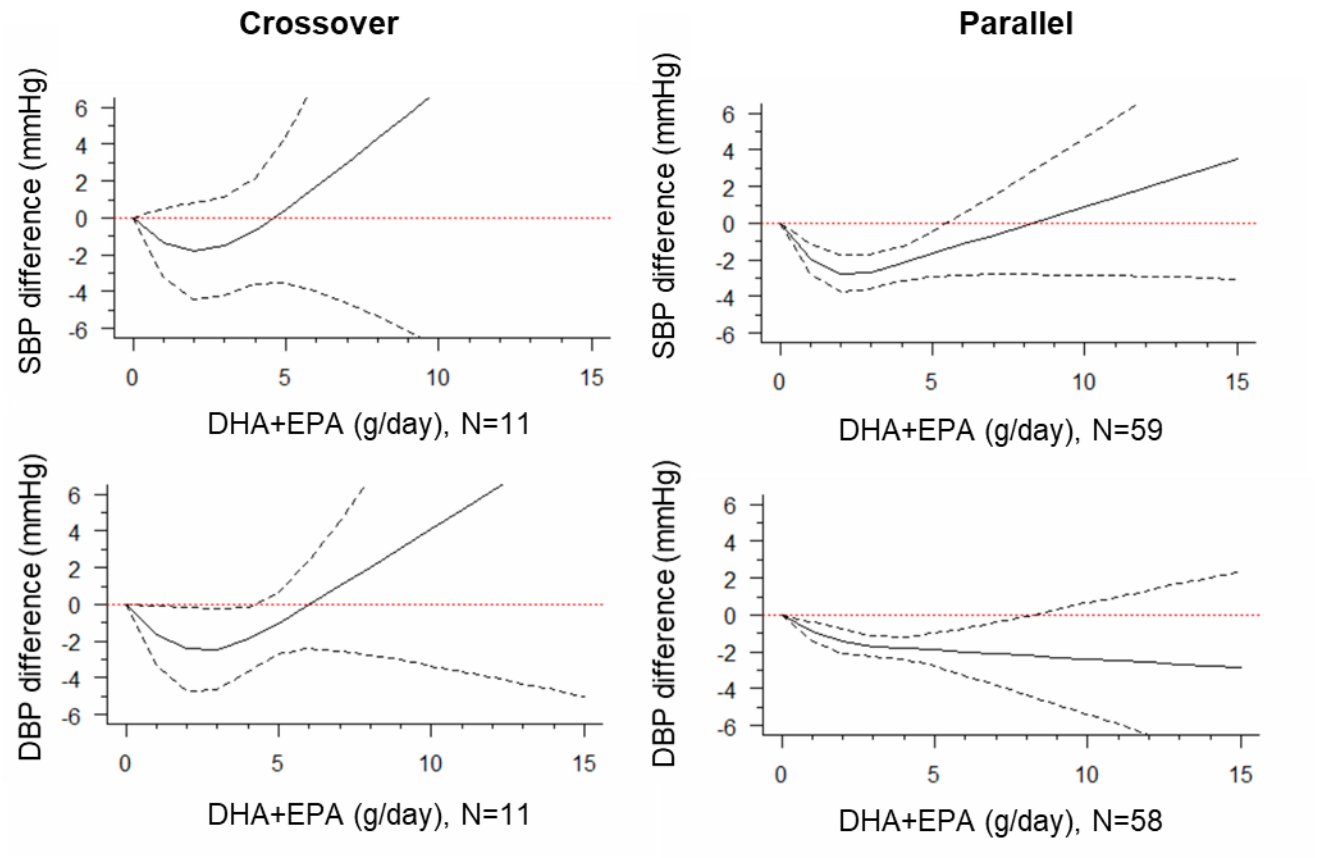
Marginal average dose-response curve (solid line) with 95% point-wise confidence intervals (dashed lines) estimated by a one-stage random-effects restricted cubic spline model, using 0 g/day as the referent, in participants with or with on hypertension, baseline SBP ≥ 140 mmHg or DBP ≥ 90 mmHg. DBP, diastolic blood pressure; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; SBP, systolic blood pressure. N, number of the included study.

Figure S4. Dose-response relation between changes in blood pressure and combined DHA+EPA intake of the studies stratified by trial duration.



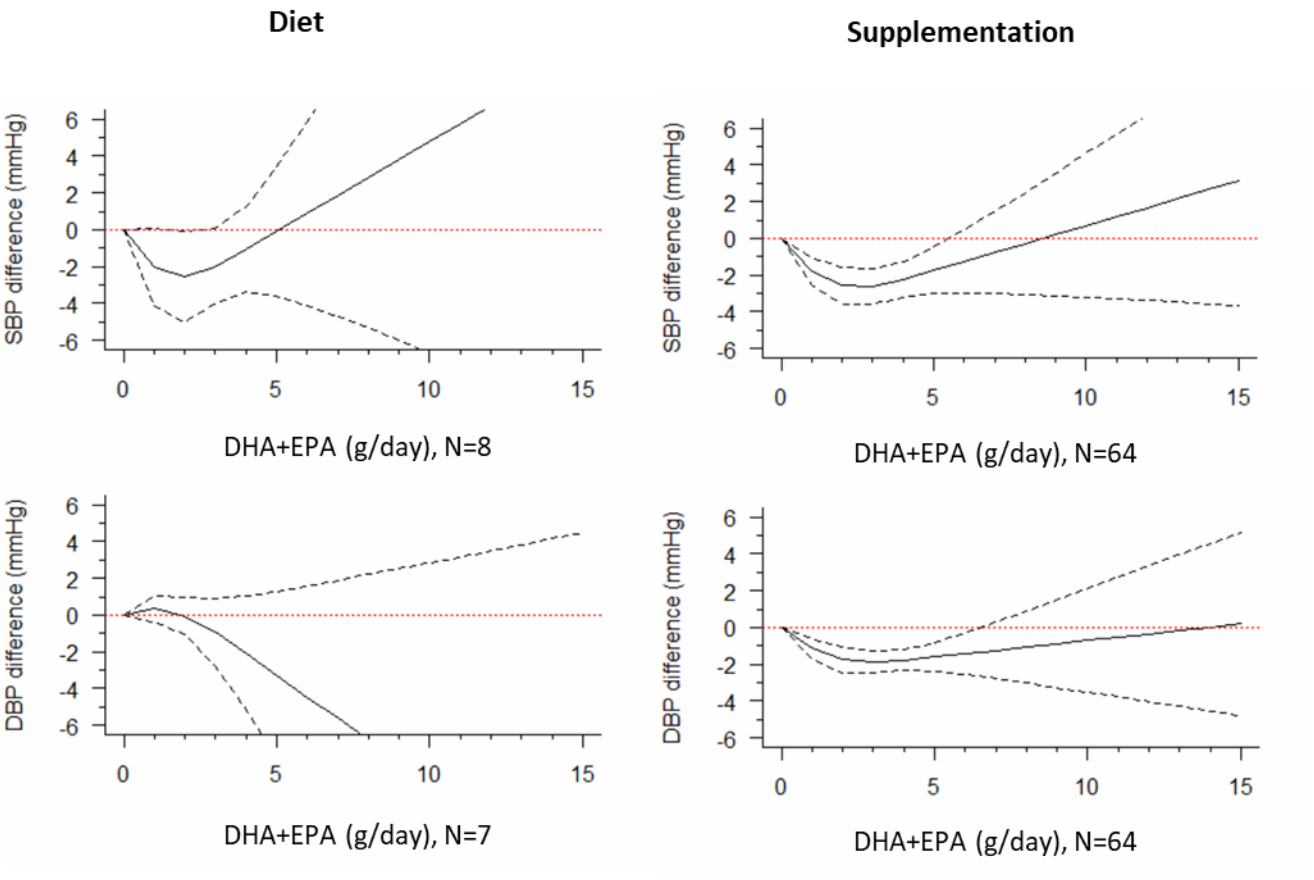
Marginal average dose-response curve (solid line) with 95% point-wise confidence intervals (dashed lines) estimated by a one-stage random-effects restricted cubic spline model, using 0 g/day as the referent, in participants with trial duration ≥ or <12 weeks. DBP, diastolic blood pressure; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; SBP, systolic blood pressure. N, number of the included study.

Figure S5. Dose-response relation between changes in blood pressure and combined DHA+EPA intake in studies stratified by study design.



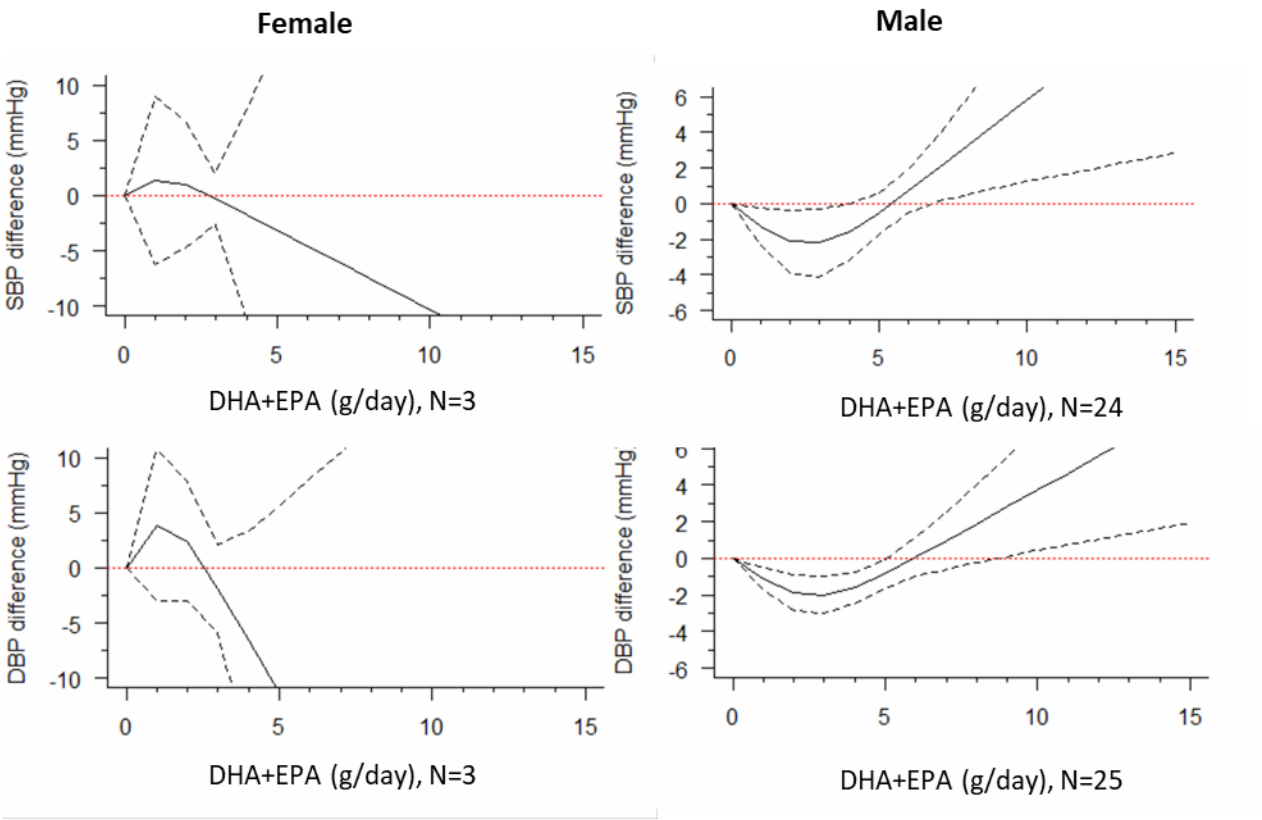
Marginal average dose-response curve (solid line) with 95% point-wise confidence intervals (dashed lines) estimated by a one-stage random-effects restricted cubic spline model, using 0 g/day as the referent, in studies stratified by study design (crossover or parallel). DBP, diastolic blood pressure; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; SBP, systolic blood pressure. N, number of the included study.

Figure S6. Dose-response relation between changes in blood pressure and combined DHA+EPA intake of the studies stratified by the intervention type.



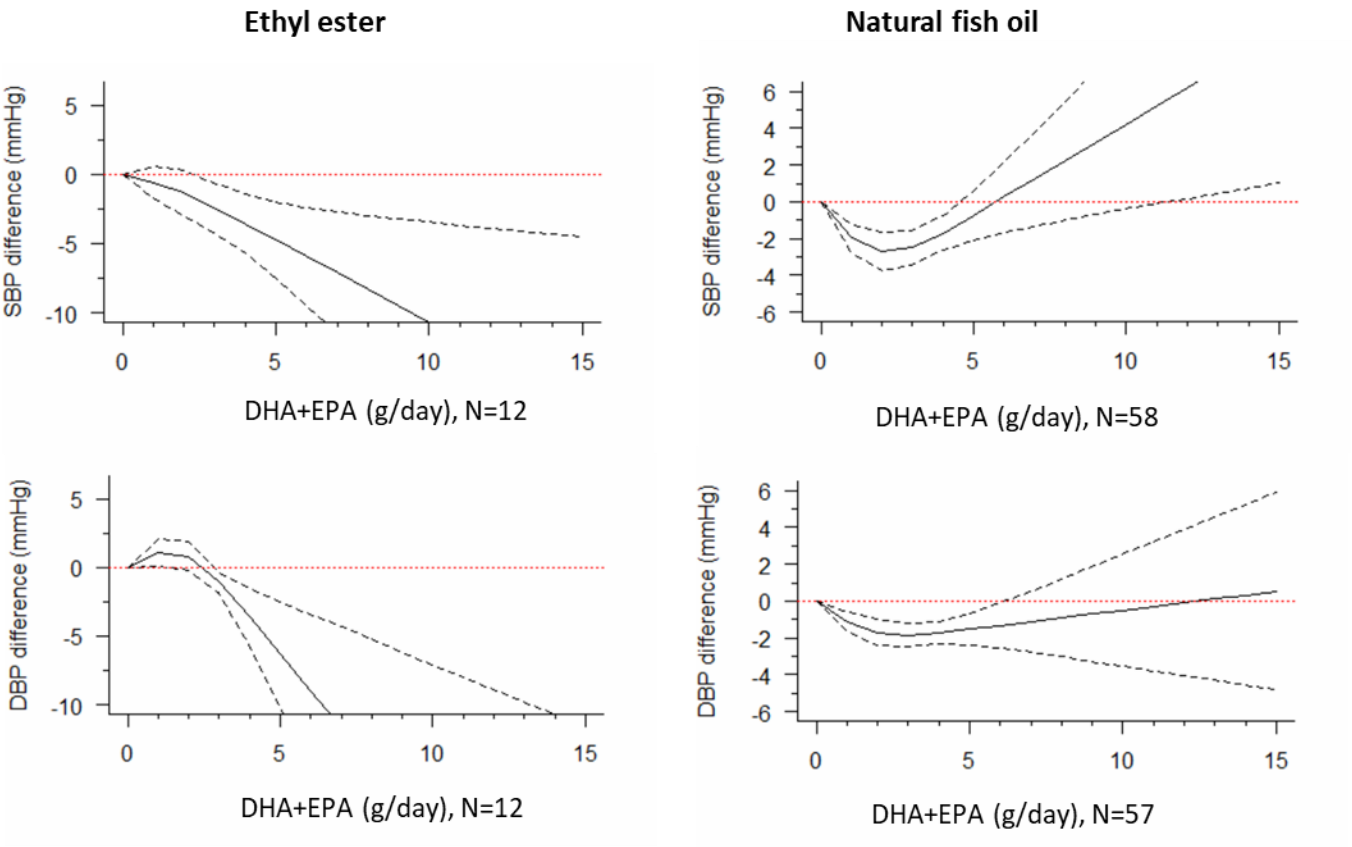
Marginal average dose-response curve (solid line) with 95% point-wise confidence intervals (dashed lines) estimated by a one-stage random-effects restricted cubic spline model, using 0 g/day as the referent, in studies restricted to different intervention types (diet-based or supplementation). DBP, diastolic blood pressure; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; SBP, systolic blood pressure. N, number of the included study.

Figure S7. Dose-response relation between changes in blood pressure and combined DHA+EPA intake of the studies stratified by sex.



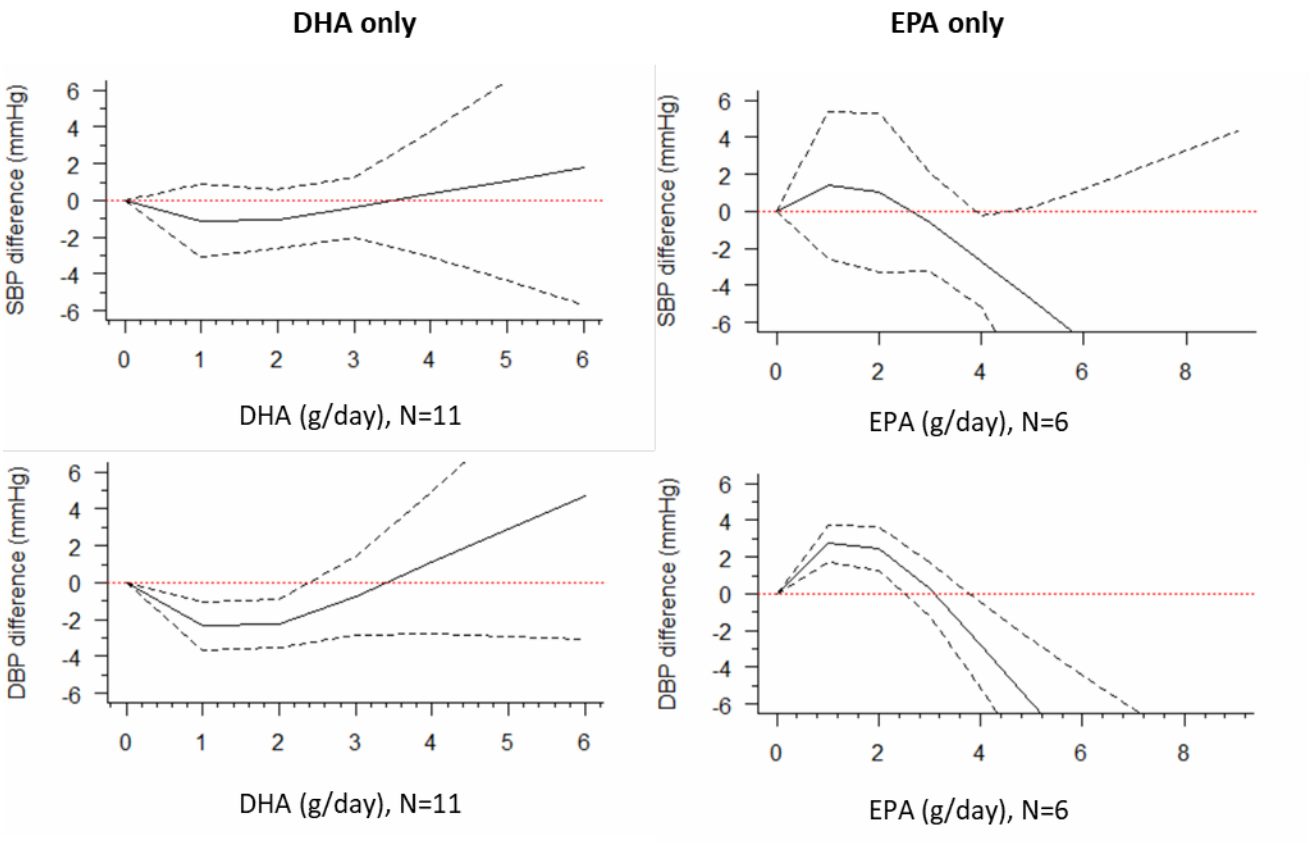
Marginal average dose-response curve (solid line) with 95% point-wise confidence intervals (dashed lines) estimated by a one-stage random-effects restricted cubic spline model, using 0 g/day as the referent, among female- or male-only participants. DBP, diastolic blood pressure; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; SBP, systolic blood pressure. N, number of the included study.

Figure S8.Dose-response relation between changes in blood pressure and combined DHA+EPA intake of the studies stratified by the fish oil composition.



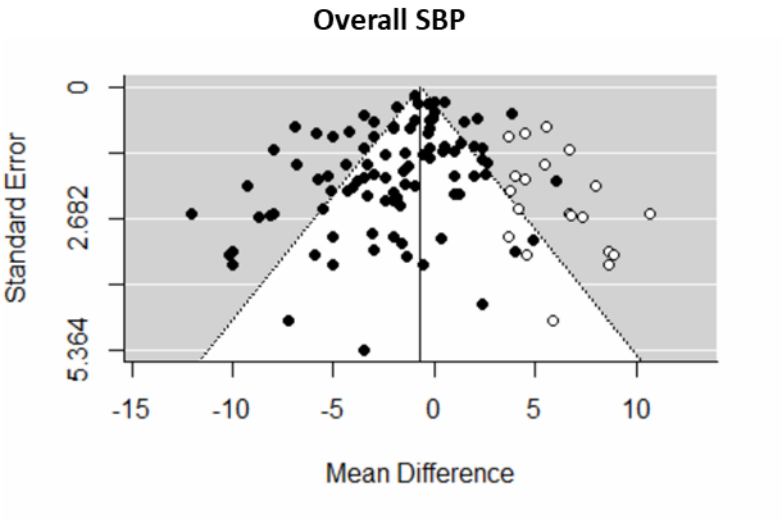
Marginal average dose-response curve (solid line) with 95% point-wise confidence intervals (dashed lines) estimated by a one-stage random-effects restricted cubic spline model, using 0 g/day as the referent, in studies either using purified ethyl esters or natural fish oils. DBP, diastolic blood pressure; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; SBP, systolic blood pressure. N, number of the included study.

Figure S9. Dose-response relation between changes in blood pressure and DHA/EPA intake of the studies stratified by the individual fish oils.

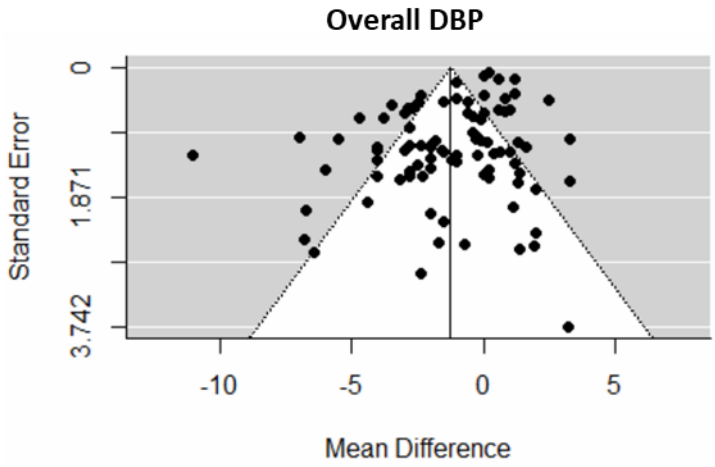


Marginal average dose-response curve (solid line) with 95% point-wise confidence intervals (dashed lines) estimated by a one-stage random-effects restricted cubic spline model, using 0 g/day as the referent, in studies using DHA or EPA alone. DBP, diastolic blood pressure; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; SBP, systolic blood pressure. N, number of the included study.

Figure S10. Funnel plot for assessment of overall publication bias.



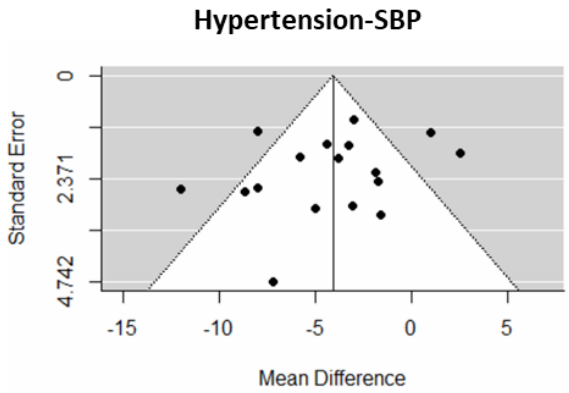
Estimated number of missing studies: 20 ;
Test for funnel plot asymmetry: : z = -3.05, p = 0.002



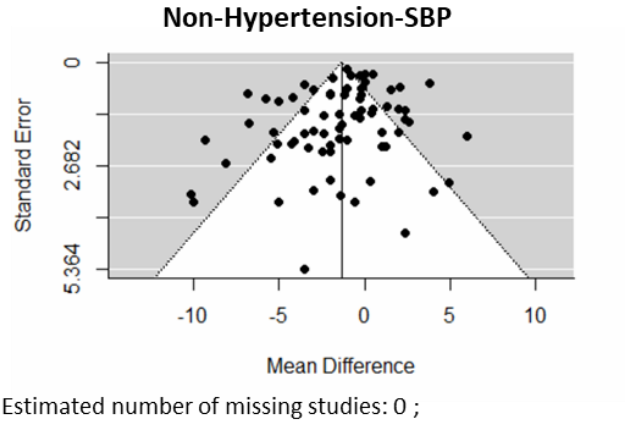
Estimated number of missing studies: 0 ;
Test for funnel plot asymmetry: z = -1.38, p = 0.17

The plots are generated for the mean difference of changes in systolic (SBP) and diastolic (DBP) blood pressure levels as mmHg and its standard error using the trim-and-fill method. No imputed studies are predicted in both plots. Filled dots indicate observed studies. The Grey area indicates $p \leq 0.05$. The plot asymmetry analysis was performed by Egger's regression test.

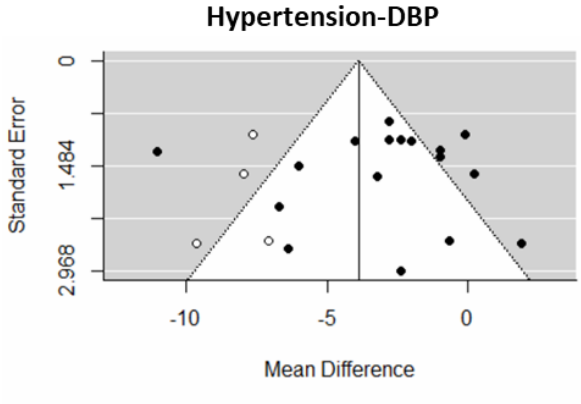
Figure S11. Funnel plot for assessment of publication bias in studies with stratification of hypertension status.



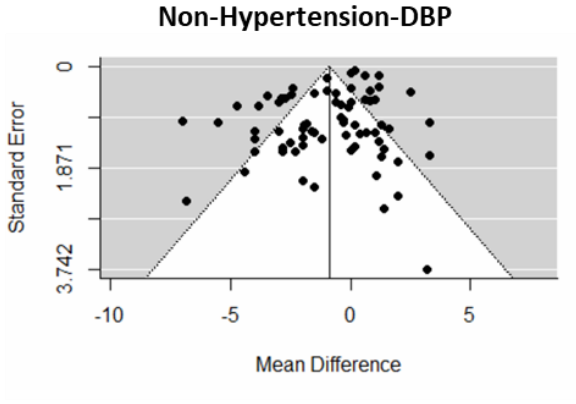
Estimated number of missing studies: 0 ;
Test for funnel plot asymmetry: z = -1.08, p = 0.28



Estimated number of missing studies: 0 ;
Test for funnel plot asymmetry: z = -1.70, p = 0.09



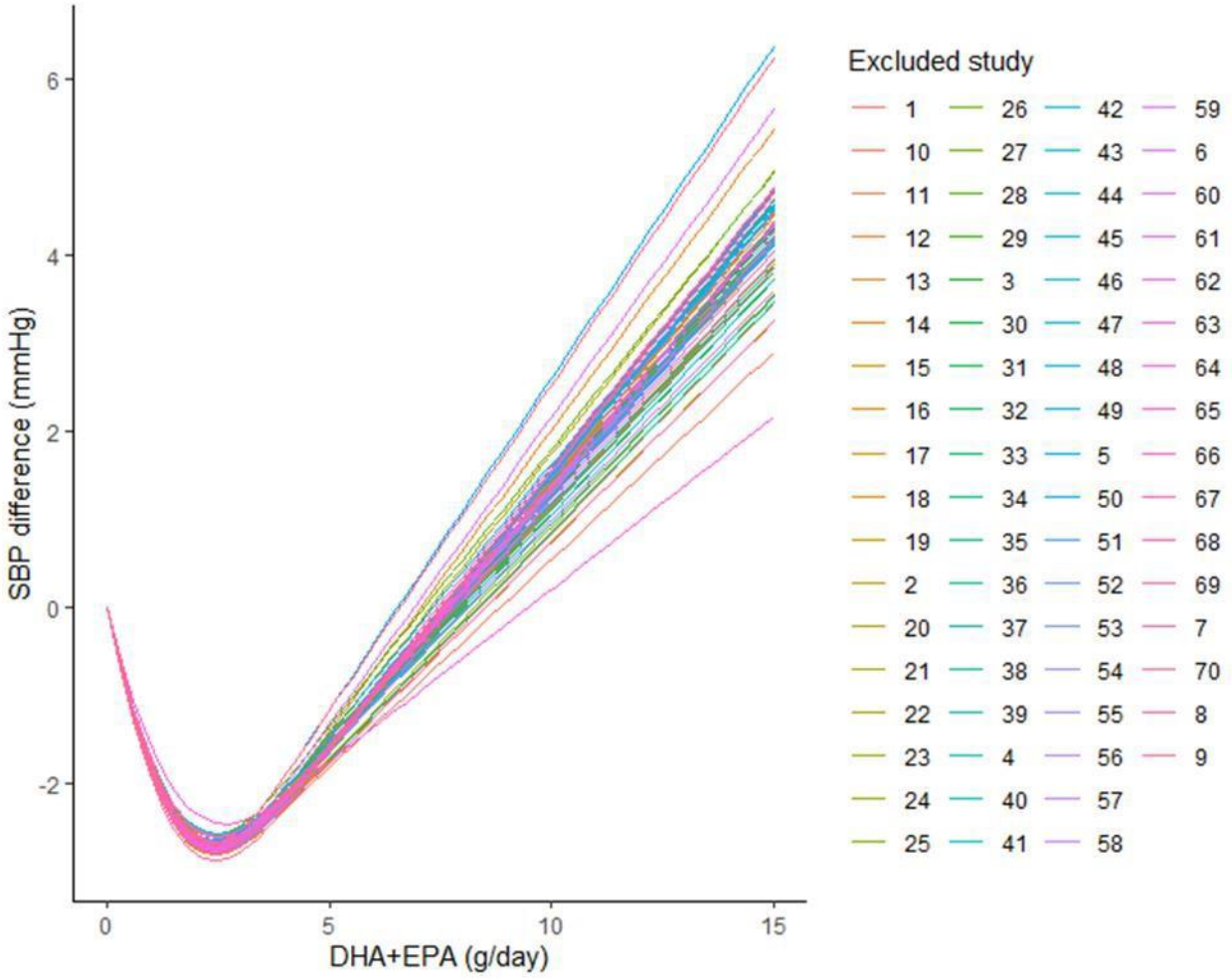
Estimated number of missing studies: 4 ;
Test for funnel plot asymmetry: z = 0.14, p = 0.89



Estimated number of missing studies: 0;
Test for funnel plot asymmetry: z = -0.63, p = 0.53

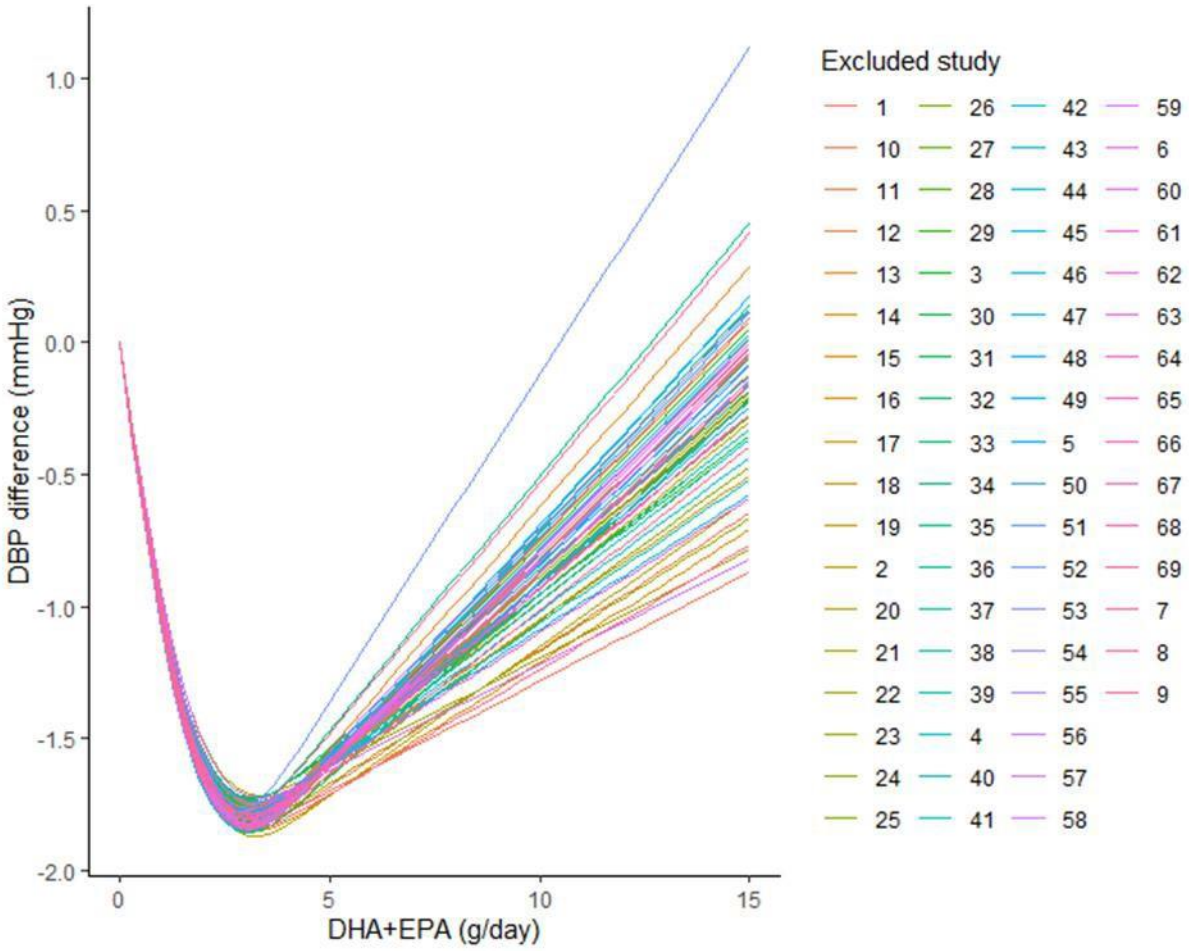
The plots are generated for the mean difference of changes in systolic (SBP) and diastolic (DBP) blood pressure levels as mmHg and its standard error using the trim-and-fill method for studies divided by hypertension status. Imputed studies are shown as empty dots. Solid dots indicate observed studies. The Grey area indicates $p \leq 0.05$. The asymmetry analysis was performed by Egger's regression test.

Figure S12. Sensitivity analysis of overall effects of EPA+DHA on SBP.



Sensitivity analysis of mean difference for changes in systolic blood pressure (SBP) levels between DHA+EPA treatment and placebo groups, using the leave-one-out method where each time one study is omitted to compute the pooled estimate in the one-stage regression model.

Figure S13. Sensitivity analysis of overall effects of EPA+DHA on DBP.



Sensitivity analysis of mean difference for changes in diastolic blood pressure (DBP) levels between DHA+EPA treatment and placebo groups, using the leave-one-out method where each time one study is omitted to compute the pooled estimate in the one-stage regression model.