Online Supporting Material

SUPPLEMENTAL MATERIAL

Article: Dietary and circulating long-chain omega-3 fatty acids and mortality risk after myocardial infarction: a long-term follow up of the Alpha Omega Cohort

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Supplemental Table 1. Percentage contribution of selected food groups to total intakes of EPA+DHA and ALA in the Alpha Omega Cohort

	EPA+DHA	ALA**
Grain products*	-†	19
Meat and poultry	5	7
Eggs	4	-†
Milk and milk products‡	-†	6
Fish§	89	3
Nuts and seeds‖	-†	4
Vegetables and potatoes	-†	6
Legumes	-†	1
Cooking oils	-†	26
Margarine	-†	14
Dressings#	-†	6
Savory spreads	2	3

*Grain products include bread, pie, pancake, pizza, noodle; †contribution <1%; ‡milk and milk products include butter; §fish include oily fish (50%), lean fish and shellfish; ‖nuts and seeds include peanut butter; #dressings include creamy (mayonnaise-based) and oil-vinegar dressings.
**Values for ALA do not add up to 100% because snacks and unknown sources are not in the Table.

Supplemental Table 2. Baseline characteristics of the Alpha Omega Cohort in categories of dietary EPA+DHA intake

	Dietary EPA+DHA intake, adjusted for energy				P^*
	≤50 mg/d (n=1113)	51 to 100 mg/d (n=815)	101 to 200 mg/d (n=1234)	>200 mg/d (n=905)	
Age, y	69.5±5.6	69.3±5.5	68.5±5.6	68.6±5.6	<0.001
Men	882 (79.2)	654 (80.2)	975 (79.0)	710 (78.4)	0.83
Body mass index, kg/m^{2†}	27.6±3.8	27.6±3.7	27.9±3.8	27.7±3.9	0.35
Obese (≥30 kg/m^2)	242 (21.8)	192 (23.6)	304 (24.6)	215 (23.8)	0.42
Time since MI, y†	3.8 (1.8-6.6)	3.8 (1.7-6.1)	3.8 (1.7-6.4)	3.3 (1.5-6.0)	0.15
Smoking status†					0.65
Never	181 (16.3)	119 (14.6)	200 (16.2)	163 (18.0)	
Former	751 (67.5)	559 (68.6)	822 (66.6)	598 (66.1)	
Current	180 (16.2)	137 (16.8)	212 (17.2)	144 (15.9)	
Physical activity†					<0.001
Low	522 (47.3)	373 (46.1)	465 (37.9)	292 (32.3)	
Middle	357 (32.4)	288 (35.6)	505 (41.1)	378 (41.8)	
High	224 (20.3)	149 (18.4)	258 (21.0)	234 (25.9)	
Highest level of education†					<0.001
Primary	265 (23.9)	187 (23.2)	223 (18.1)	128 (14.2)	
Lower secondary	432 (39.0)	318 (39.5)	418 (34.0)	294 (32.6)	
Higher secondary or lower tertiary	308 (27.8)	229 (28.4)	421 (34.2)	317 (35.2)	
Higher tertiary	104 (9.4)	72 (8.9)	168 (13.7)	162 (18.0)	
Alcohol intake					<0.001
No	67 (6.0)	41 (5.0)	51 (4.1)	44 (4.9)	
Low	651 (58.5)	459 (56.3)	622 (50.4)	423 (46.7)	
Moderate	279 (25.1)	194 (23.8)	342 (27.7)	252 (27.9)	
High	116 (10.4)	121 (14.9)	219 (17.8)	186 (20.6)	
Medication use					
Statins	937 (84.2)	692 (84.9)	1068 (86.6)	797 (88.1)	0.06
Antithrombotic drugs	1084 (97.4)	800 (98.2)	1207 (97.8)	887 (98.0)	0.67
Antihypertensive drugs	995 (89.4)	727 (89.2)	1113 (90.2)	815 (90.1)	0.86
Serum lipids, mmol/L‡,§					

	Dietary EPA+DHA intake, adjusted for energy				P^*
	≤50 mg/d (n=1113)	51 to 100 mg/d (n=815)	101 to 200 mg/d (n=1234)	>200 mg/d (n=905)	
Total cholesterol	4.68±0.96	4.74±0.93	4.73±0.94	4.69±0.97	0.79
LDL cholesterol	2.54±0.81	2.61±0.81	2.59±0.80	2.56±0.84	0.92
HDL cholesterol	1.27±0.33	1.25±0.33	1.29±0.33	1.32±0.38	<0.001
Triglycerides	1.68 (1.23-2.32)	1.79 (1.28-2.42)	1.63 (1.20-2.32)	1.57 (1.18-2.21)	0.002
Plasma glucose, mmol/L[‡]	5.63 (5.08-6.59)	5.58 (5.00-6.58)	5.60 (5.08-6.68)	5.59 (5.05-6.46)	0.48
Blood pressure (mmHg)[†]					
Systolic	141±22	142±21	142±21	143±22	0.16
Diastolic	80±11	80±11	80±11	81±11	0.048
Prevalent diabetes	224 (20.1)	172 (21.1)	248 (20.1)	169 (18.7)	0.65
Family history of MI	125 (11.2)	90 (11.1)	139 (11.3)	113 (12.5)	0.76
Family history of diabetes	218 (19.6)	160 (19.6)	250 (20.3)	206 (22.8)	0.28
Dietary factors					
Energy, kcal/d	1959±525	1896±530	1898±505	1931±514	0.65
Protein, en%	14.3±2.7	14.8±2.9	15.1±2.7	15.9±2.8	<0.001
Total fat, en%	34.3±6.4	34.1±6.4	33.7±6.0	33.0±5.9	<0.001
SFAs, en%	13.0±3.2	12.7±3.1	12.4±2.9	11.8±2.9	<0.001
cis MUFAs, en%	9.4±2.2	9.4±2.2	9.5±2.1	9.7±2.2	<0.001
PUFAs, en%	7.3±2.4	7.3±2.2	7.3±2.2	7.1±2.2	0.11
Total n-3 FAs, en%	0.65±0.25	0.67±0.25	0.71±0.24	0.82±0.25	<0.001
ALA, g/d[‖]	1.07±0.53	1.10±0.49	1.11±0.48	1.08±0.47	0.98
EPA+DHA, mg/d[‖]	26 (12-37)	75 (63-87)	141 (121-165)	339 (255-454)	<0.001
Total n-6 FAs, en%	5.6±2.2	5.5±2.1	5.5±2.1	5.3±2.0	<0.001
trans-FAs, g/d[‖]	1.7±0.7	1.6±0.6	1.5±0.6	1.5±0.6	<0.001
Carbohydrates, en%	47.9±6.8	46.7±7.0	46.3±6.6	45.9±6.6	<0.001
Fiber, g/d[‖]	21.9±7.0	21.0±7.0	21.2±6.5	22.1±6.6	0.13
Cholesterol, mg/d[‖]	170±67	180±67	187±67	199±71	<0.001
Total fish (g/d)	1.8 (0.1-4.3)	9.6 (6.3-14.8)	15.6 (12.8-17.8)	39.8 (26.7-44.2)	<0.001
Oily fish (g/d)	0.4 (0-1.2)	3.2 (1.8-4.6)	7.5 (5.9-9.6)	20.6 (14.4-28.3)	<0.001
DHD-15 score	75.2±13.1	77.0±13.0	79.8±12.6	85.4±13.5	<0.001

	Dietary EPA+DHA intake, adjusted for energy				P^*
	≤50 mg/d (n=1113)	51 to 100 mg/d (n=815)	101 to 200 mg/d (n=1234)	>200 mg/d (n=905)	
Circulating FAs, % total FAs					
SFAs	13.1±1.1	13.1±1.3	13.2±1.1	13.2±1.1	0.07
MUFAs	22.4±3.1	22.4±3.3	22.6±3.2	22.7±3.3	0.027
PUFAs	63.1±4.0	63.1±4.2	62.9±4.0	62.7±4.1	0.027
Total n-3 PUFAs	2.02 (1.74-2.43)	2.21 (1.87-2.64)	2.46 (2.08-3.03)	2.94 (2.37-3.70)	<0.001
ALA	0.51±0.15	0.51±0.15	0.50±0.14	0.51±0.14	0.47
EPA	0.88 (0.68-1.13)	0.97 (0.73-1.26)	1.14 (0.85-1.58)	1.48 (1.06-2.07)	<0.001
DHA	0.54 (0.44-0.67)	0.62 (0.52-0.75)	0.71 (0.59-0.85)	0.84 (0.66-0.98)	<0.001
Total n-6 PUFAs	60.7±4.2	60.5±4.5	60.1±4.3	59.4±4.4	<0.001
Linoleic acid, 18:2 n-6	50.3±5.0	50.2±5.0	49.8±4.9	49.6±5.0	0.001
Arachidonic acid, 20:4 n-6	8.6±2.1	8.5±2.1	8.4±2.0	8.0±2.0	<0.001

ALA, alpha-linolenic acid; DHA, docosahexaenoic acid; DHD-15, 2015 Dutch Healthy Diet score; EPA, eicosapentaenoic acid; FAs, fatty acids; MI, myocardial infarction; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids; Q, quintile; SFAs, saturated fatty acids; TFAs, *trans*-fatty acids.
Values are shown as mean ±SD, median (IQR) or *n* (%) unless stated otherwise. [*]*P* value for linear trend, through median values across categories of intake using a linear regression model, or obtained from chi-square test for categorical variables; [†]<1% of patients had missing values for body mass index, time since MI, smoking status, physical activity, educational level and blood pressure; [‡] part of the cohort had missing values for total cholesterol, HDL cholesterol and triglycerides (n=61), LDL cholesterol (n=252) and plasma glucose (n=33); [§]to convert to mg/dL, divide by 0.02586 for total, LDL, HDL cholesterol and by 0.01129 for triglycerides; [‖]values for dietary TFAs, fiber and cholesterol were non-energy adjusted.

Supplemental Table 3. Baseline characteristics of the Alpha Omega Cohort in categories of dietary ALA intake

	Dietary ALA intake, adjusted for energy					P^*
	≤0.5 g/d (n=222)	>0.5 to 1.0 g/d (n=1902)	>1.0 to 1.5 g/d (n=1285)	>1.5 to 2.0 g/d (n=412)	>2.0 g/d (n=246)	
Age, y	69.3±5.4	69.2±5.6	68.9±5.6	68.3±5.6	68.6±5.4	0.002
Men	198 (89.2)	1477 (77.7)	976 (76.0)	351 (85.2)	219 (89.0)	<0.001
Body mass index, kg/m^{2†}	27.0±3.3	27.8±3.8	27.8±3.9	27.8±3.9	27.7±3.4	0.27
Obese (≥30 kg/m^2)	33 (14.9)	467 (24.6)	311 (24.2)	93 (22.6)	49 (19.9)	0.013
Time since MI, y†	3.9 (1.5-6.9)	3.7 (1.7-6.3)	3.8 (1.7-6.4)	3.5 (1.6-6.1)	2.9 (1.2-6.2)	0.10
Smoking status†						<0.001
Never	20 (9.0)	343 (18.0)	224 (17.4)	50 (12.1)	26 (10.6)	
Former	163 (73.4)	1253 (65.9)	840 (65.4)	306 (74.3)	168 (68.3)	
Current	39 (17.6)	305 (16.0)	221 (17.2)	56 (13.6)	52 (21.1)	
Physical activity†						0.30
Low	91 (41.2)	780 (41.3)	538 (42.1)	149 (36.3)	94 (38.4)	
Middle	79 (35.8)	707 (37.4)	468 (36.7)	181 (44.0)	93 (38.0)	
High	51 (23.1)	404 (21.4)	271 (21.2)	81 (19.7)	58 (23.7)	
Highest level of education†						0.15
Primary	47 (21.2)	376 (19.9)	251 (19.6)	74 (18.1)	55 (22.6)	
Lower secondary	81 (36.5)	648 (34.3)	473 (37.0)	162 (39.6)	98 (40.3)	
Higher secondary or lower tertiary	63 (28.4)	627 (33.1)	386 (30.2)	126 (30.8)	73 (30.0)	
Higher tertiary	31 (14.0)	241 (12.7)	170 (13.3)	47 (11.5)	17 (7.0)	
Alcohol intake						<0.001
No	5 (2.3)	95 (5.0)	71 (5.5)	23 (5.6)	9 (3.7)	
Low	94 (42.3)	980 (51.5)	730 (56.8)	218 (52.9)	133 (54.1)	
Moderate	58 (26.1)	497 (26.1)	331 (25.8)	108 (26.2)	73 (29.7)	
High	65 (29.3)	330 (17.4)	153 (11.9)	63 (15.3)	31 (12.6)	
Medication use						
Statins	192 (86.5)	1631 (85.8)	1098 (85.5)	355 (86.2)	218 (88.6)	0.76
Antithrombotic drugs	216 (97.3)	1855 (97.5)	1256 (97.7)	408 (99.0)	243 (98.8)	0.29

	Dietary ALA intake, adjusted for energy					P^*
	≤0.5 g/d (n=222)	>0.5 to 1.0 g/d (n=1902)	>1.0 to 1.5 g/d (n=1285)	>1.5 to 2.0 g/d (n=412)	>2.0 g/d (n=246)	
Antihypertensive drugs	195 (87.8)	1718 (90.3)	1150 (89.5)	373 (90.5)	214 (87.0)	0.41
Serum lipids, mmol/L[‡,§]						
Total cholesterol	4.72±0.92	4.75±0.95	4.71±0.95	4.67±0.93	4.51±0.93	<0.001
LDL cholesterol	2.59±0.85	2.60±0.81	2.56±0.81	2.55±0.78	2.43±0.83	0.007
HDL cholesterol	1.30±0.33	1.30±0.35	1.28±0.34	1.28±0.34	1.23±0.30	0.004
Triglycerides	1.59 (1.24-2.09)	1.65 (1.19-2.31)	1.66 (1.22-2.35)	1.67 (1.21-2.34)	1.66 (1.21-2.32)	0.98
Plasma glucose, mmol/L[‡]	5.50 (5.08-6.18)	5.62 (5.04-6.68)	5.61 (5.07-6.58)	5.62 (5.08-6.58)	5.61 (5.00-6.40)	0.95
Blood pressure (mmHg)[†]						
Systolic	142±23	142±22	142±21	142±22	141±20	0.59
Diastolic	81±11	80±11	80±11	81±11	80±11	0.76
Prevalent diabetes	26 (11.7)	380 (20.0)	282 (22.0)	84 (20.4)	41 (16.7)	0.006
Family history of MI	27 (12.2)	227 (11.9)	142 (11.1)	50 (12.1)	21 (8.5)	0.56
Family history of diabetes	47 (21.2)	369 (19.4)	292 (22.7)	77 (18.7)	49 (19.9)	0.18
Dietary factors						
Energy, kcal/d	2539±466	1879±467	1793±499	2027±524	2186±516	0.17
Protein, en%	13.1±2.6	15.1±2.8	15.4±2.8	14.6±2.6	13.9±2.4	0.028
Total fat, en%	33.6±7.1	32.2±6.3	33.9±5.4	37.1±4.8	39.7±4.9	<0.001
SFAs, en%	13.4±3.5	12.4±3.2	12.3±2.8	12.8±2.9	12.6±3.1	0.93
cis MUFAs, en%	9.0±2.3	9.1±2.3	9.5±2.1	10.3±1.7	11.0±1.5	<0.001
PUFAs, en%	6.5±2.1	6.2±2.3	7.4±1.6	9.3±1.6	11.4±1.7	<0.001
Total n-3 FAs, en%	0.63±0.28	0.61±0.22	0.72±0.19	0.93±0.19	1.16±0.19	<0.001
ALA, g/d	0.37±0.13	0.79±0.13	1.21±0.14	1.72±0.14	2.40±0.38	<0.001
EPA+DHA, mg/d	72 (17-142)	109 (46-188)	115 (53-194)	107 (47-179)	97 (32-162)	0.98
Total n-6 FAs, en%	4.8±2.0	4.5±1.5	5.6±1.6	7.5±1.6	9.4±1.7	<0.001
trans-FAs, g/d[‖]	2.1±0.7	1.5±0.6	1.5±0.6	1.7±0.6	1.8±0.6	<0.001
Carbohydrates, en%	47.5±7.7	47.7±6.9	46.7±6.5	44.1±5.8	42.7±5.2	<0.001
Fiber, g/d[‖]	24.0±8.0	21.4±6.7	21.0±6.4	22.0±7.3	22.5±6.2	0.80
Cholesterol, mg/d[‖]	218±83	181±66	177±69	194±66	192±70	0.94

	Dietary ALA intake, adjusted for energy					P^*
	≤0.5 g/d (n=222)	>0.5 to 1.0 g/d (n=1902)	>1.0 to 1.5 g/d (n=1285)	>1.5 to 2.0 g/d (n=412)	>2.0 g/d (n=246)	
Total fish (g/d)	9.2 (1.1-15.3)	14.0 (5.2-19.6)	14.5 (6.2-20.8)	13.2 (5.0-19.8)	11.5 (3.5-17.6)	0.80
Oily fish (g/d)	3.6 (0-8.2)	5.5 (1.3-11.0)	5.8 (1.6-11.4)	5.3 (1.1-10.2)	5.0 (0.6-9.4)	0.52
DHD-15 score	74.0±13.4	79.1±13.5	80.5±13.5	78.6±13.6	79.5±13.4	0.014
Circulating FAs, % total FAs						
SFAs	13.4±1.8	13.2±1.1	13.1±1.0	13.0±1.1	13.0±1.0	<0.001
MUFAs	23.3±3.3	22.8±3.2	22.2±3.2	22.1±3.4	21.6±2.8	<0.001
PUFAs	61.8±4.6	62.6±4.0	63.4±4.0	63.6±4.1	64.1±3.5	<0.001
Total n-3 PUFAs	2.40 (1.93-3.09)	2.37 (1.95-3.03)	2.36 (1.93-2.98)	2.30 (1.90-2.82)	2.26 (1.88-2.78)	<0.001
ALA	0.53±0.15	0.51±0.15	0.50±0.14	0.50±0.14	0.49±0.14	0.035
EPA	1.06 (0.77-1.67)	1.07 (0.80-1.58)	1.08 (0.80-1.51)	1.01 (0.78-1.38)	1.00 (0.78-1.41)	0.001
DHA	0.66 (0.50-0.83)	0.67 (0.53-0.84)	0.67 (0.54-0.84)	0.66 (0.53-0.82)	0.64 (0.50-0.82)	0.13
Total n-6 PUFAs	58.9±4.9	59.7±4.4	60.6±4.3	60.9±4.4	61.4±3.9	<0.001
Linoleic acid, 18:2 n-6	48.9±5.5	49.6±4.9	50.3±5.0	50.8±5.0	51.0±4.5	<0.001
Arachidonic acid, 20:4 n-6	8.2±1.9	8.3±2.0	8.5±2.1	8.3±2.0	8.6±2.1	0.007

ALA, alpha-linolenic acid; DHA, docosahexaenoic acid; DHD-15, 2015 Dutch Healthy Diet score; EPA, eicosapentaenoic acid; FAs, fatty acids; MI, myocardial infarction; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids; Q, quintile; SFAs, saturated fatty acids; TFAs, *trans*-fatty acids.
Values are shown as mean ±SD, median (IQR) or *n* (%) unless stated otherwise. [*]*P* value for linear trend, through median values across categories of intake using a linear regression model, or obtained from chi-square test for categorical variables; [†]<1% of patients had missing values for body mass index, time since MI, smoking status, physical activity, educational level and blood pressure; [‡] part of the cohort had missing values for total cholesterol, HDL cholesterol and triglycerides (n=61), LDL cholesterol (n=252) and plasma glucose (n=33); [§]to convert to mg/dL, divide by 0.02586 for total, LDL, HDL cholesterol and by 0.01129 for triglycerides; [‖]values for dietary TFAs, fiber and cholesterol were non-energy adjusted.

Supplemental Table 4. Baseline characteristics of the Alpha Omega Cohort in quintiles of circulating ALA

	Circulating ALA, in quintiles					P^*
	Q1 (n=799)	Q2 (n=806)	Q3 (n=826)	Q4 (n=823)	Q5 (n=813)	
Circulating ALA, % total FAs (range)	0-0.39	0.39-0.46	0.46-0.53	0.53-0.61	0.61-1.66	
Age, y	68.2±5.5	68.9±5.7	68.9±5.5	69.3±5.6	69.5±5.5	<0.001
Men	665 (83.2)	667 (82.8)	654 (79.2)	629 (76.4)	606 (74.5)	<0.001
Body mass index, kg/m^{2†}	27.6±3.6	28.2±3.8	27.9±3.8	27.8±4.0	27.1±3.6	<0.001
Obese (≥30 kg/m^2)	184 (23.1)	208 (25.8)	204 (24.7)	192 (23.4)	165 (20.3)	0.10
Time since MI, y†	3.4 (1.5-6.2)	3.9 (1.8-6.3)	3.7 (1.6-6.4)	3.8 (1.6-6.3)	3.7 (1.7-6.3)	0.37
Smoking status†						0.06
Never	106 (13.3)	124 (15.4)	141 (17.1)	133 (16.2)	159 (19.6)	
Former	551 (69.0)	546 (67.8)	564 (68.3)	548 (66.6)	521 (64.1)	
Current	142 (17.8)	135 (16.8)	121 (14.7)	142 (17.3)	133 (16.4)	
Physical activity†						0.31
Low	341 (43.0)	325 (40.5)	325 (39.6)	321 (39.3)	340 (41.9)	
Middle	268 (33.8)	301 (37.5)	326 (39.8)	323 (39.5)	310 (38.2)	
High	185 (23.3)	176 (22.0)	169 (20.6)	173 (21.2)	162 (20.0)	
Highest level of education†						0.08
Primary	151 (19.0)	152 (19.0)	155 (18.9)	178 (21.7)	167 (20.6)	
Lower secondary	281 (35.4)	266 (33.2)	304 (37.1)	298 (36.3)	313 (38.7)	
Higher secondary or lower tertiary	243 (30.6)	279 (34.8)	252 (30.8)	253 (30.8)	248 (30.7)	
Higher tertiary	120 (15.1)	104 (13.0)	108 (13.2)	93 (11.3)	81 (10.0)	
Alcohol intake						0.32
No	50 (6.3)	34 (4.2)	41 (5.0)	37 (4.5)	41 (5.0)	
Low	421 (52.7)	459 (57.0)	430 (52.1)	425 (51.6)	420 (51.7)	
Moderate	217 (27.2)	189 (23.5)	216 (26.2)	230 (28.0)	215 (26.5)	
High	111 (13.9)	124 (15.4)	139 (16.8)	131 (15.9)	137 (16.9)	
Medication use						
Statins	751 (94.0)	732 (90.8)	732 (88.6)	677 (82.3)	602 (74.1)	<0.001
Antithrombotic drugs	782 (97.9)	791 (98.1)	807 (97.7)	804 (97.7)	794 (97.7)	0.96
Antihypertensive drugs	717 (89.7)	731 (90.7)	722 (87.4)	741 (90.0)	739 (90.9)	0.14

	Circulating ALA, in quintiles					P^*
	Q1 (n=799)	Q2 (n=806)	Q3 (n=826)	Q4 (n=823)	Q5 (n=813)	
Serum lipids, mmol/L[‡,§]						
Total cholesterol	4.45±0.84	4.53±0.90	4.72±0.96	4.85±0.95	5.00±0.99	<0.001
LDL cholesterol	2.37±0.75	2.43±0.72	2.58±0.83	2.70±0.84	2.78±0.84	<0.001
HDL cholesterol	1.29±0.34	1.27± 0.32	1.29±0.35	1.28±0.33	1.30±0.37	0.52
Triglycerides	1.54 (1.11-2.20)	1.59 (1.18-2.20)	1.67 (1.23-2.31)	1.71 (1.28-2.41)	1.79 (1.30-2.52)	<0.001
Plasma glucose, mmol/L[‡]	5.59 (5.05-6.54)	5.68 (5.07-6.88)	5.60 (5.03-6.50)	5.65 (5.12-6.66)	5.48 (5.00-6.38)	0.29
Blood pressure (mmHg)[†]						
Systolic	141±21	143±21	143±21	142±23	142±21	0.47
Diastolic	80±11	80±11	81±11	80±12	80±11	0.31
Prevalent diabetes	159 (19.9)	194 (24.1)	140 (17.0)	175 (21.3)	145 (17.8)	0.003
Family history of MI	94 (11.8)	92 (11.4)	95 (11.5)	89 (10.8)	97 (11.9)	0.96
Family history of diabetes	177 (22.2)	173 (21.5)	156 (18.9)	180 (21.9)	148 (18.2)	0.15
Dietary factors						
Energy, kcal/d	1908±527	1899±497	1909±492	1919±507	1971±563	0.006
Protein, en%	14.9±2.7	15.2±2.8	14.9±2.8	15.0±2.7	14.9±2.9	0.32
Total fat, en%	33.6±6.3	33.7±5.8	33.6±6.3	34.1±6.3	33.9±6.2	0.26
SFAs, en%	12.2±3.0	12.4±2.8	12.5±3.1	12.7±3.2	12.6±3.2	0.002
cis MUFAs, en%	9.7±2.2	9.5±2.1	9.4± 2.2	9.5±2.2	9.4±2.2	0.025
PUFAs, en%	7.3±2.3	7.3±2.2	7.1±2.2	7.2±2.2	7.2±2.3	0.59
Total n-3 FAs, en%	0.71±0.26	0.72±0.25	0.70±0.25	0.71±0.25	0.72±0.26	0.34
ALA, g/d[‖]	1.11±0.52	1.12±0.49	1.06±0.45	1.09±0.51	1.07±0.51	0.06
EPA+DHA, mg/d[‖]	104 (46-178)	112 (46-189)	111 (48-186)	106 (46-189)	108 (45-189)	0.21
Total n-6 FAs, en%	5.7±2.1	5.6±2.1	5.3±2.0	5.5±2.0	5.4±2.1	0.022
trans-FAs, g/d[‖]	1.5±0.7	1.5±0.6	1.6±0.6	1.6±0.6	1.6±0.7	0.018
Carbohydrates, en%	47.1±6.8	46.8±6.6	46.8±6.8	46.4±6.8	46.6±6.9	0.12
Fiber, g/d[‖]	21.3±6.6	21.6±6.6	21.6±6.8	21.5±6.8	21.8±7.0	0.18
Cholesterol, mg/d[‖]	179±66	183±67	182±69	187±71	188±71	0.004
Total fish (g/d)	13.5 (5.3-19.0)	14.0 (5.5-20.5)	13.7 (5.4-20.3)	13.7 (5.8-19.7)	13.0 (4.6-19.0)	0.84
Oily fish (g/d)	5.3 (1.3-9.8)	5.4 (1.2-10.8)	5.5 (1.2-11.4)	5.7 (1.2-11.1)	5.2 (1.2-10.8)	0.64

	Circulating ALA, in quintiles					P^*
	Q1 (n=799)	Q2 (n=806)	Q3 (n=826)	Q4 (n=823)	Q5 (n=813)	
DHD-15 score	79.9±14.2	79.5±13.3	79.6±14.0	78.0±12.9	79.2±13.4	0.09
Circulating FAs, % total FAs						
SFAs	13.1±1.2	13.2±1.0	13.2±1.1	13.1±1.0	13.1±1.2	0.39
MUFAs	22.1±3.3	22.5±2.9	22.6±3.1	22.6±3.2	22.7±3.4	<0.001
PUFAs	63.5±4.2	63.0±3.7	62.8±3.9	62.8±4.0	62.7±4.2	<0.001
Total n-3 PUFAs	1.98 (1.63-2.55)	2.26 (1.88-2.84)	2.39 (2.01-2.99)	2.44 (2.04-3.05)	2.62 (2.20-3.30)	<0.001
EPA	0.87 (0.64-1.28)	1.02 (0.78-1.45)	1.10 (0.87-1.56)	1.13 (0.84-1.60)	1.17 (0.86-1.69)	<0.001
DHA	0.68 (0.56-0.84)	0.70 (0.57-0.86)	0.68 (0.55-0.85)	0.64 (0.52-0.82)	0.62 (0.48-0.80)	<0.001
Total n-6 PUFAs	61.1±4.5	60.3±4.0	59.9±4.3	60.0±4.3	59.6±4.6	<0.001
Linoleic acid, 18:2n-6	49.7±5.3	49.5±4.7	49.7±4.9	50.2±4.8	50.7±5.0	<0.001
Arachidonic acid, 20:4n-6	9.6±2.1	9.0±2.0	8.3±1.8	7.9±1.8	7.1±1.6	<0.001

ALA, alpha-linolenic acid; DHA, docosahexaenoic acid; DHD-15, 2015 Dutch Healthy Diet score; EPA, eicosapentaenoic acid; FAs, fatty acids; MI, myocardial infarction; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids; Q, quintile; SFAs, saturated fatty acids; TFAs, *trans*-fatty acids.
Values are shown as mean ±SD, median (IQR) or *n* (%) unless stated otherwise. [*]*P* value for linear trend, through median values across categories of intake using a linear regression model, or obtained from chi-square test for categorical variables; [†]<1% of patients had missing values for body mass index, time since MI, smoking status, physical activity, educational level and blood pressure; [‡] part of the cohort had missing values for total cholesterol, HDL cholesterol and triglycerides (n=61), LDL cholesterol (n=252) and plasma glucose (n=33); [§]to convert to mg/dL, divide by 0.02586 for total, LDL, HDL cholesterol and by 0.01129 for triglycerides; [‖]values for dietary TFAs, fiber and cholesterol were non-energy adjusted.

Supplemental Table 5. Associations of circulating EPA+DHA in categories based on converted Omega-3 index cut-offs with CHD, CVD and all-cause mortality in the Alpha Omega Cohort

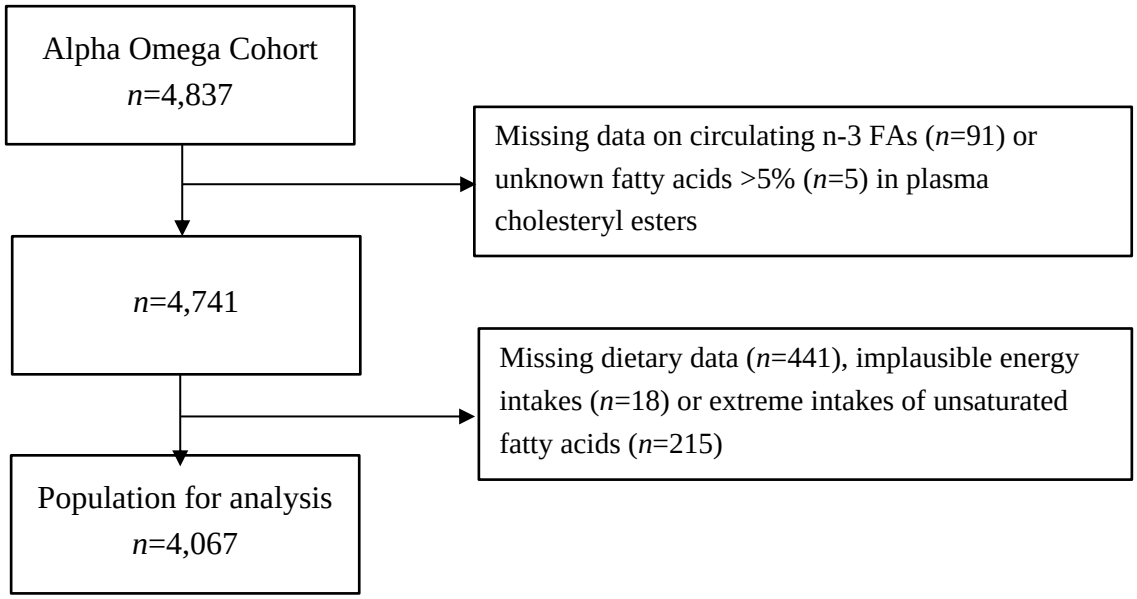
	Categories of circulating n-3 fatty acids				*P* trend*
	≤1.3% (n=844)	>1.3 to ≤2.2 (n=2058)	>2.2 to ≤3.1 (n=739)	>3.1 (n=426)	
Median circulating EPA+DHA, % total FA	1.12	1.66	2.54	3.73	
Person-years	9169	22,779	8460	4821	
CHD mortality					
Cases, *n*	127	250	90	48	
Age- and sex-adjusted HR	1.00	0.82 (0.66-1.01)	0.80 (0.61-1.05)	0.71 (0.51-0.98)	0.06
Multivariable HR†	1.00	0.80 (0.64-1.01)	0.80 (0.60-1.07)	0.63 (0.44-0.90)	0.026
CVD mortality					
Cases, *n*	189	411	155	79	
Age- and sex-adjusted HR	1.00	0.89 (0.75-1.06)	0.91 (0.73-1.12)	0.77 (0.59-1.00)	0.09
Multivariable HR	1.00	0.87 (0.73-1.05)	0.90 (0.71-1.13)	0.70 (0.53-0.93)	0.038
All-cause mortality					
Cases, *n*	436	945	313	183	
Age- and sex-adjusted HR	1.00	0.89 (0.80-0.99)	0.80 (0.69-0.92)	0.77 (0.65-0.94)	0.001
Multivariable HR	1.00	0.90 (0.80-1.01)	0.81 (0.69-0.94)	0.73 (0.60-0.87)	<0.001

CHD, coronary heart disease; CVD, cardiovascular disease; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; FA, fatty acid; Q, quintile; ref., reference; values in Table represent hazard ratios (HRs) with 95% confidence intervals, estimated from multivariable Cox models; **P* for linear trend, through median values across categories of circulating EPA+DHA, using a linear regression model; †HRs were adjusted for age, sex, educational level, physical activity, smoking status, alcohol intake, obesity, prevalent diabetes, cardiovascular drugs, serum cholesterol, circulating 18:2 n-6 (linoleic acid), and circulating 20:4 n-6 (arachidonic acid).

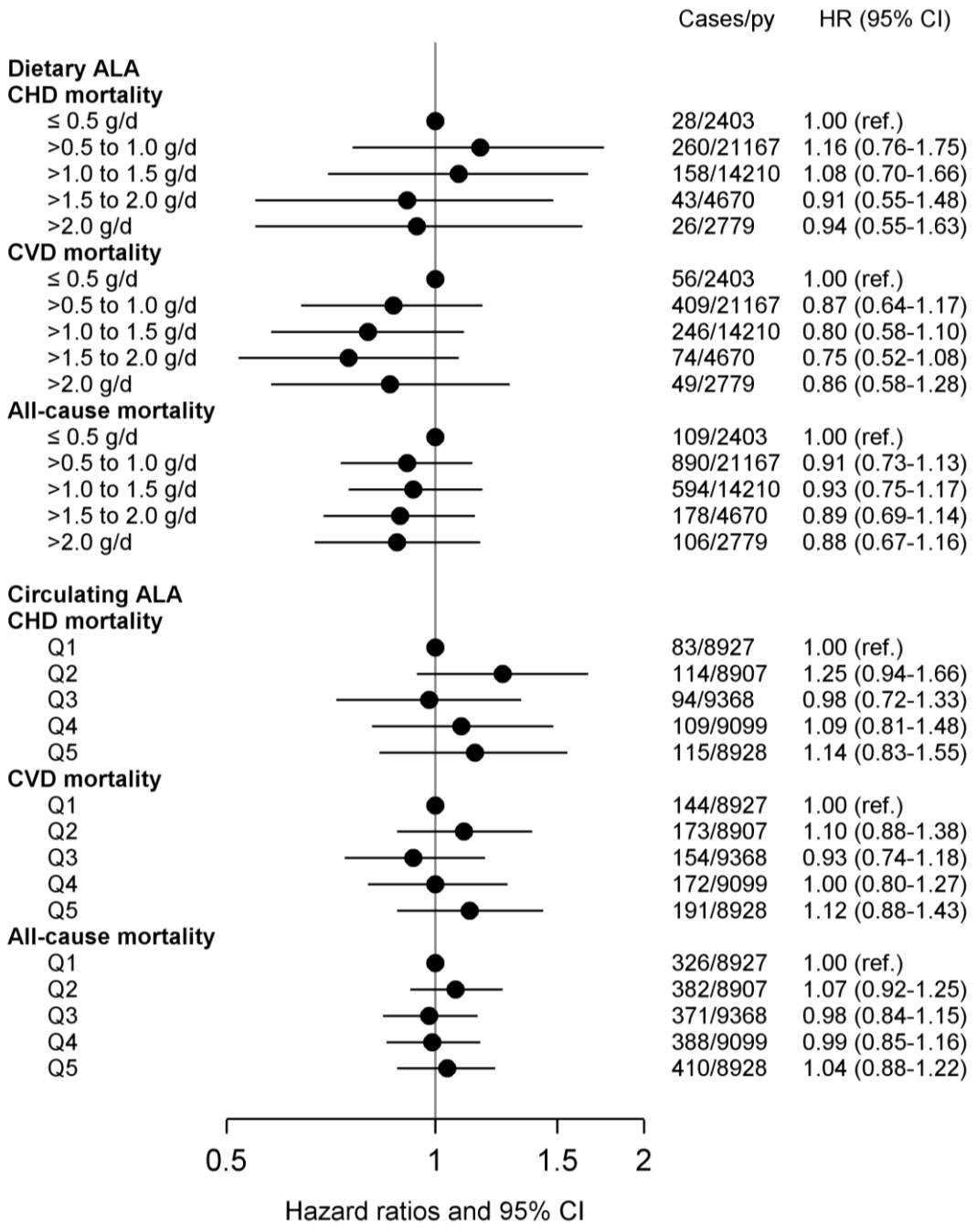
Supplemental Table 6. Sensitivity analyses for continuous associations of dietary and circulating n-3 FAs with all-cause, CVD and CHD mortality in the Alpha Omega Cohort

	EPA+DHA			ALA		
	CHD mortality	CVD mortality	All-cause mortality	CHD mortality	CVD mortality	All-cause mortality
Dietary intake						
Main analysis (*n*=4067)	0.92 (0.86-0.98)	0.96 (0.92-1.01)	0.97 (0.94- 1.00)	0.87 (0.72-1.05)	0.91 (0.79-1.05)	0.98 (0.89- 1.07)
Excluding ≤2 y follow-up (*n*=3921)	0.95 (0.89-1.01)	0.98 (0.93-1.03)	0.98 (0.95- 1.01)	0.89 (0.73-1.08)	0.93 (0.80-1.08)	1.00 (0.90- 1.10)
Excluding fish oil supplement users (*n*=3880)	0.92 (0.86-0.98)	0.96 (0.92-1.01)	0.97 (0.94, 1.00)	0.88 (0.73-1.06)	0.91 (0.79-1.06)	0.97 (0.88- 1.07)
Circulating levels						
Main analysis (*n*=4067)	0.85 (0.77-0.95)	0.88 (0.82-0.96)	0.90 (0.85, 0.94)	1.01 (0.92-1.11)	1.02 (0.95-1.10)	1.01 (0.96- 1.06)
Excluding ≤2 y follow-up (*n*=3921)	0.86 (0.77-0.97)	0.89 (0.82-0.97)	0.90 (0.85- 0.95)	0.98 (0.89-1.09)	1.00 (0.93-1.08)	1.01 (0.96- 1.06)
Excluding fish oil supplement users (*n*=3880)	0.85 (0.76-0.94)	0.88 (0.81-0.96)	0.90 (0.86-0.95)	1.02 (0.92-1.11)	1.02 (0.95-1.10)	1.02 (0.97- 1.07)

ALA, alpha-linoleic acid; CHD, coronary heart disease; CVD, cardiovascular disease; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid, FAs, fatty acids, MI, myocardial infarction; values in Table represent hazard ratios (HRs) with 95% confidence intervals, estimated from multivariable Cox models (see Methods); HRs are expressed per 100 mg/d of dietary EPA+DHA, per 1 g/d of dietary ALA or per 1-SD of circulating EPA+DHA or ALA; numbers (*n*) refer to patients included in the analysis.



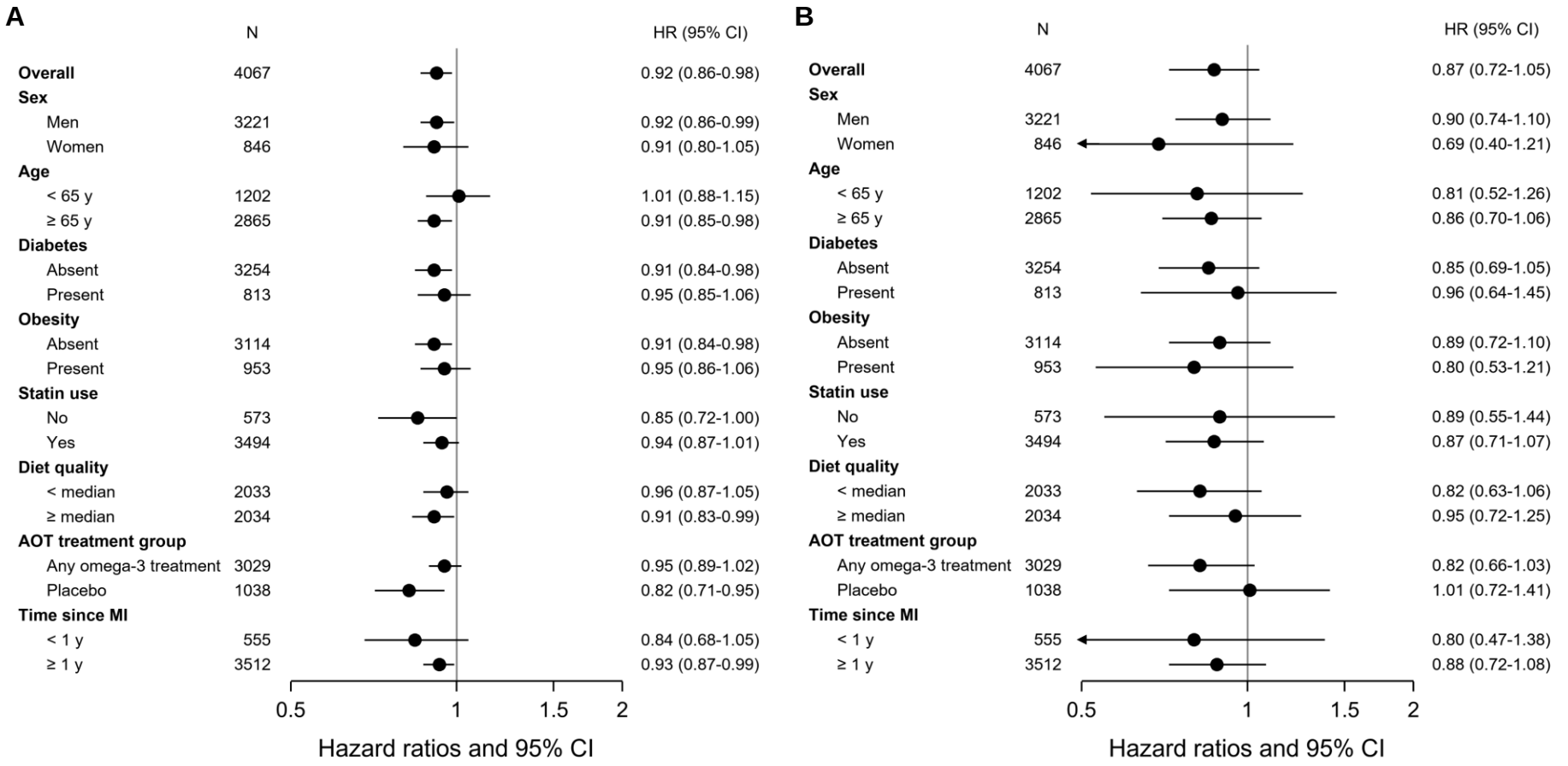
Supplemental Figure 1. Flow diagram for selecting the population for analysis from the Alpha Omega Cohort.



Supplemental Figure 2. Associations of dietary ALA (in categories) and circulating ALA (in quintiles) with CHD, CVD and all-cause mortality.

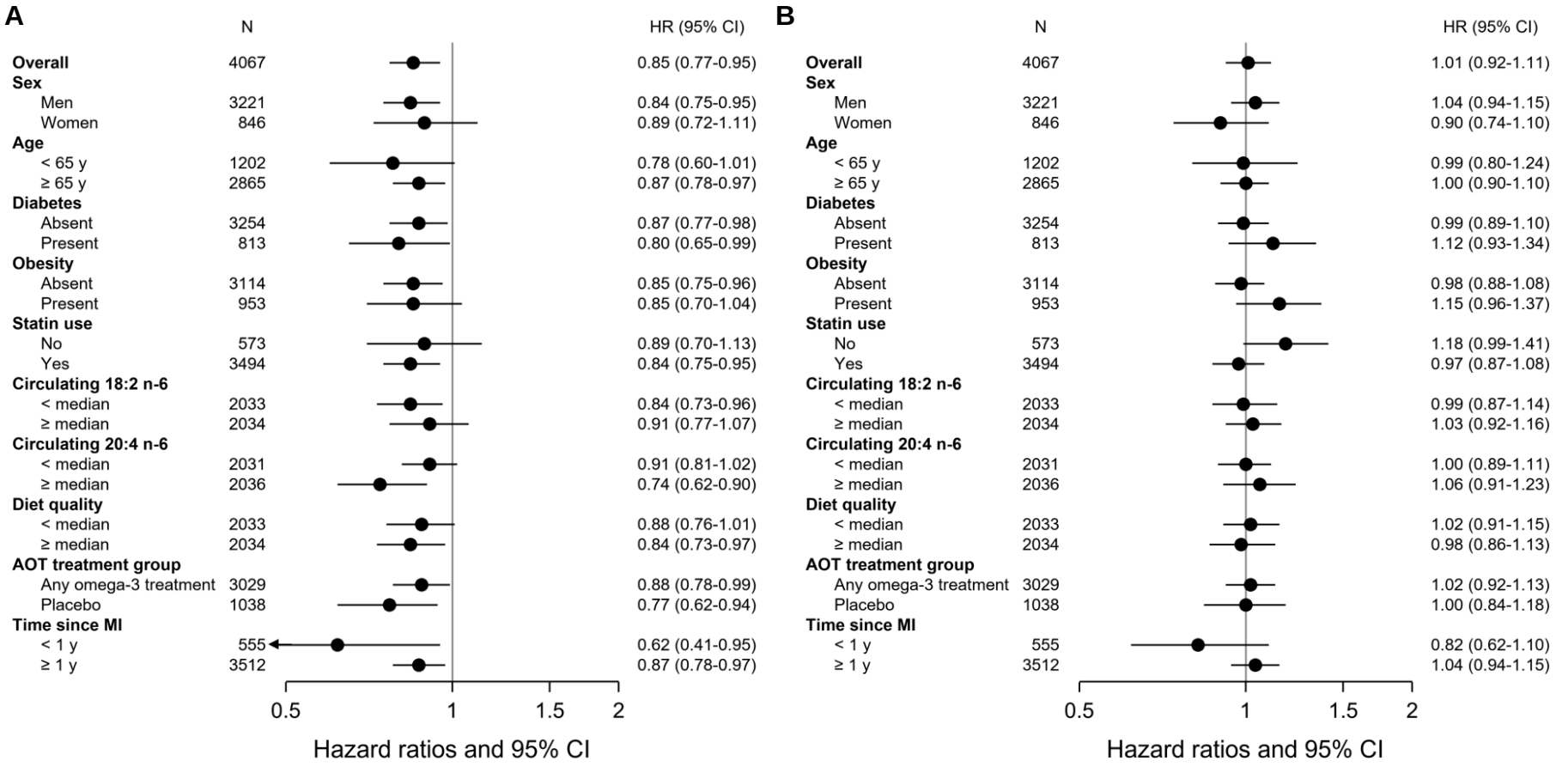
ALA, alpha-linoleic acid; CHD, coronary heart disease; CVD, cardiovascular disease; py, person-years; Q, quintile; ref., reference.

Hazard ratios (HRs) and 95% confidence intervals (CIs) were obtained from multivariable Cox models, using the lowest category as reference; HRs for dietary ALA were adjusted for age, sex, education level, physical activity, smoking status, alcohol intake, obesity, prevalent diabetes, cardiovascular drugs, time since MI, and intake of total energy, cholesterol, fiber and *trans* fatty acids; HRs for circulating ALA were adjusted for the same covariates except dietary factors, plus serum total cholesterol, circulating 18:2 n-6 and circulating 20:4 n-6; All *P* values for linear trend >0.05.



Supplemental Figure 3. Associations of dietary (A) EPA+DHA (per 100 mg/d) and (B) ALA (per 1 g/d) with CHD mortality in subgroups of the Alpha Omega Cohort.

ALA, alpha-linoleic acid; AOT, Alpha Omega Trial; CHD, coronary heart disease; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; hazard ratios (HRs) and 95% confidence intervals (CIs) were obtained from multivariable Cox models (see Methods); dietary quality was based on the 2015 Dutch Healthy Diet score (DHD-15; median: 79, range: 33-125); $P = 0.07$ for interaction between EPA+DHA and AOT treatment group; $P > 0.10$ for other interactions.



Supplemental Figure 4. Associations of circulating (A) EPA+DHA (per 1-SD) and (B) ALA (per 1-SD) with CHD mortality in subgroups of the Alpha Omega Cohort.

ALA, alpha-linoleic acid; AOT, Alpha Omega Trial; CHD, coronary heart disease; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; hazard ratios (HRs) and 95% confidence intervals (CIs) were obtained from multivariable Cox models (see Methods); median circulating 18:2 n-6 (linoleic acid) was 49.96 % total FAs; median circulating 20:4 n-6 (arachidonic acid) was 8.26 % total FAs; dietary quality was based on the 2015 Dutch Healthy Diet score (DHD-15;

median: 79, range: 33-125); $P = 0.07$ for interaction between EPA+DHA and circulating 20:4 n-6 (arachidonic acid); $P = 0.06$ for interaction between ALA and statin use; $P > 0.10$ for other interactions.