

Supplementary Online Content

Wang DD, Li Y, Chuive SE, et al. Association of specific dietary fats with total and cause-specific mortality. *JAMA Intern Med*. Published online July 5, 2016.
doi:10.1001/jamainternmed.2016.2417.

eTable 1. Exclusion Criteria and Number of Participants Excluded

eTable 2. Categories for Causes of Death

eTable 3. Associations Between Total and Specific Types of Fat Intake and Total Mortality

eTable 4. Hazard Ratio for Substituting 1% of Energy From Carbohydrate by the Same Energy From Specific Types of Fat

eTable 5. Spearman Correlations Between Specific Total and Types of Fat Intakes in the Middle of Follow-up (1994)

eTable 6. Associations Between Dietary ω -6 and ω -3 PUFA Intake and Total Mortality

eTable 7. Associations Between Most Recent Total and Specific Types of Fat Intakes and Total and Cause-Specific Mortality

eTable 8. Associations Between Total and Specific Types of Fat Intakes and Total and Cause-Specific Mortality From the 4-Year Lag Analysis

eTable 9. Associations Between Total and Specific Types of Fat Intakes and Total and Cause-Specific Mortality From the Sensitivity Analysis Further Adjusting for the Alternate Healthy Eating Index–2010 Without Component Scores for Fatty Acids

eTable 10. Associations Between Total and Specific Types of Fat Intakes and Total and Cause-Specific Mortality From the Sensitivity Analysis Restricted to Participants Without History of Hypertension and/or Hypercholesterolemia at Baseline

eTable 11. Associations Between Total and Specific Types of Fat Intakes and Cardiovascular Disease Mortality

eTable 12. Associations Between Dietary ω -6 and ω -3 Polyunsaturated Fatty Acid Intake and Cardiovascular Disease Mortality

eTable 13. Associations Between Total and Specific Types of Fat Intakes and Cancer Mortality

eTable 14. Associations Between Dietary ω -6 and ω -3 Polyunsaturated Fatty Acid Intake and Cancer Mortality

eTable 15. Associations Between Total and Specific Types of Fat Intakes and Neurodegenerative Disease Mortality

eTable 16. Associations Between Total and Specific Types of Fat Intakes and Respiratory Disease Mortality

eTable 17. Associations Between Dietary ω -6 and ω -3 Polyunsaturated Fatty Acid Intake and Neurodegenerative Disease Mortality

eTable 18. Associations Between Dietary ω -6 and ω -3 Polyunsaturated Fatty Acid Intake and Respiratory Disease Mortality

eTable 19. Data Source of Figure 2

eTable 20. Major Food Sources of Specific Types of Dietary Fat

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Exclusion Criteria and Number of Participants Excluded

Exclusion reason	Nurses' Health Study (1980)	Health Professionals Follow-up Study (1986)
Original sample size for the cohort	92468	51529
Baseline diabetes	2954	1663
Baseline cardiovascular disease	427	3626
Baseline cancer	4007	1966
Baseline missing or implausible dietary information ^a	1731	1390
Total number of participants left for the current analysis	83349	42884

^a Participants who left too many blanks on the questionnaire, or implausible total energy intake (<800 or >4200 kcal/d for men and <600 or >3500 kcal/d for women).

eTable 2. Categories for Causes of Death

Causes of death	ICD-8 code	ICD-9 code
Cancer	140-207	140-208
Cardiovascular disease	390-458	390-459
Respiratory disease	460-519	460-519
Neurodegenerative disease	290, 340, 342, and 348	290, 332, 335, and 340

eTable 3. Associations Between Total and Specific Types of Fat Intake and Total Mortality

	Quintile of Dietary Fatty Acid Intake					P Value	HR (95% CI) ^a
	1	2	3	4	5		
Total fat intake							
NHS							
Median, % of energy	25.4	30.0	33.2	36.6	42.2	NA	NA
No. of deaths	5852	4625	4069	3386	2382	NA	NA
Age-adjusted model	1 [Reference]	1.04 (1.00-1.08)	1.14 (1.10-1.19)	1.20 (1.15-1.26)	1.36 (1.29-1.43)	<.001	1.10 (1.08-1.11)
MV-adjusted model ^b	1 [Reference]	0.95 (0.92-0.99)	0.95 (0.91-0.99)	0.88 (0.84-0.93)	0.80 (0.76-0.85)	<.001	0.94 (0.93-0.96)
HPFS							
Median, % of energy	23.8	28.3	31.3	34.2	38.4	NA	NA
No. of deaths	2698	2604	2647	2605	2436	NA	NA
Age-adjusted model	1 [Reference]	1.02 (0.97-1.08)	1.10 (1.04-1.16)	1.16 (1.10-1.23)	1.21 (1.15-1.28)	<.001	1.07 (1.05-1.09)
MV-adjusted model ^b	1 [Reference]	0.96 (0.91-1.01)	0.97 (0.91-1.02)	0.96 (0.91-1.02)	0.89 (0.84-0.95)	.002	0.97 (0.95-0.99)
Pooled^c							
Age-adjusted model	1 [Reference]	1.03 (1.00-1.07)	1.13 (1.09-1.16)	1.19 (1.15-1.23)	1.29 (1.24-1.34)	<.001	1.09 (1.08-1.10)
MV-adjusted model ^b	1 [Reference]	0.95 (0.92-0.99)	0.96 (0.92-0.99)	0.91 (0.88-0.95)	0.84 (0.81-0.88)	<.001	0.95 (0.94-0.96)
Saturated fat intake							
NHS							
Median, % of energy	8.2	10.2	11.8	13.5	16.5	NA	NA
No. of deaths	5660	4729	4217	3376	2332	NA	NA
Age-adjusted model	1 [Reference]	1.17 (1.13-1.22)	1.38 (1.32-1.43)	1.56 (1.50-1.63)	1.92 (1.82-2.02)	<.001	1.49 (1.45-1.54)
MV-adjusted model ^b	1 [Reference]	1.05 (1.00-1.09)	1.11 (1.06-1.17)	1.12 (1.06-1.18)	1.07 (1.00-1.15)	<.001	1.08 (1.04-1.12)
HPFS							
Median, % of energy	7.1	9.0	10.2	11.5	13.5	NA	NA
No. of deaths	2606	2662	2602	2548	2572	NA	NA
Age-adjusted model	1 [Reference]	1.13 (1.07-1.19)	1.21 (1.15-1.28)	1.29 (1.22-1.36)	1.50 (1.42-1.59)	<.001	1.36 (1.31-1.42)
MV-adjusted model ^b	1 [Reference]	1.03 (0.97-1.09)	1.05 (0.99-1.13)	1.04 (0.96-1.12)	1.09 (1.01-1.18)	.02	1.07 (1.01-1.14)
Pooled^c							
Age-adjusted model	1 [Reference]	1.16 (1.12-1.19)	1.32 (1.27-1.36)	1.45 (1.40-1.50)	1.71 (1.65-1.78)	<.001	1.45 (1.42-1.48)
MV-adjusted model ^b	1 [Reference]	1.04 (1.00-1.08)	1.09 (1.05-1.14)	1.09 (1.04-1.14)	1.08 (1.03-1.14)	<.001	1.08 (1.04-1.11)

Unsaturated fat intake							
NHS							
Median, % of energy	14.2	16.8	18.7	20.6	23.8	NA	NA
No. of deaths	6024	4589	3864	3285	2552	NA	NA
Age-adjusted model	1 [Reference]	0.98 (0.94-1.01)	1.00 (0.96-1.04)	1.01 (0.97-1.05)	1.03 (0.98-1.08)	.19	1.02 (0.99-1.04)
MV-adjusted model ^b	1 [Reference]	0.88 (0.84-0.91)	0.82 (0.79-0.86)	0.78 (0.74-0.82)	0.73 (0.69-0.77)	<.001	0.84 (0.81-0.86)
HPFS							
Median, % of energy	13.7	16.3	18.0	19.7	22.3	NA	NA
No. of deaths	2760	2666	2657	2488	2419	NA	NA
Age-adjusted model	1 [Reference]	0.99 (0.94-1.04)	1.04 (0.99-1.10)	1.04 (0.98-1.09)	1.04 (0.98-1.09)	.07	1.02 (0.99-1.06)
MV-adjusted model ^b	1 [Reference]	0.90 (0.85-0.96)	0.89 (0.84-0.95)	0.84 (0.79-0.90)	0.79 (0.74-0.85)	<.001	0.87 (0.84-0.91)
Pooled ^c							
Age-adjusted model	1 [Reference]	0.98 (0.95-1.01)	1.02 (0.98-1.05)	1.02 (0.99-1.05)	1.03 (0.99-1.07)	.03	1.02 (1.00-1.04)
MV-adjusted model ^b	1 [Reference]	0.89 (0.86-0.92)	0.85 (0.82-0.88)	0.80 (0.77-0.83)	0.76 (0.72-0.79)	<.001	0.85 (0.83-0.87)
Polyunsaturated fat intake							
NHS							
Median, % energy	4.2	5.0	5.6	6.3	7.5	NA	NA
No. of deaths	4423	4380	3997	3829	3685	NA	NA
Age-adjusted model	1 [Reference]	0.92 (0.88-0.96)	0.84 (0.80-0.87)	0.79 (0.76-0.83)	0.69 (0.66-0.72)	<.001	0.58 (0.54-0.62)
MV-adjusted model ^b	1 [Reference]	1.01 (0.97-1.05)	0.93 (0.88-0.97)	0.89 (0.85-0.94)	0.82 (0.78-0.86)	<.001	0.74 (0.69-0.79)
HPFS							
Median, % of energy	4.4	5.2	5.8	6.5	7.7	NA	NA
No. of deaths	2872	2633	2513	2545	2427	NA	NA
Age-adjusted model	1 [Reference]	0.90 (0.85-0.94)	0.87 (0.82-0.92)	0.84 (0.80-0.89)	0.78 (0.74-0.83)	<.001	0.69 (0.64-0.75)
MV-adjusted model ^b	1 [Reference]	0.91 (0.86-0.96)	0.87 (0.82-0.93)	0.84 (0.79-0.89)	0.80 (0.75-0.85)	<.001	0.71 (0.65-0.79)
Pooled ^c							
Age-adjusted model	1 [Reference]	0.91 (0.88-0.94)	0.85 (0.82-0.88)	0.81 (0.78-0.84)	0.73 (0.70-0.75)	<.001	0.62 (0.59-0.65)
MV-adjusted model ^b	1 [Reference]	0.97 (0.94-1.00)	0.91 (0.87-0.94)	0.87 (0.84-0.91)	0.81 (0.78-0.84)	<.001	0.73 (0.69-0.77)
Monounsaturated fat intake							

NHS							
Median, % of energy	9.4	11.4	12.8	14.4	17.2	NA	NA
No. of deaths	6241	4769	3789	3191	2324	NA	NA
Age-adjusted model	1 [Reference]	1.07 (1.03-1.12)	1.12 (1.07-1.16)	1.18 (1.13-1.24)	1.28 (1.22-1.35)	<.001	1.17 (1.14-1.21)
MV-adjusted model ^b	1 [Reference]	0.95 (0.91-0.99)	0.91 (0.87-0.96)	0.90 (0.85-0.96)	0.86 (0.80-0.92)	<.001	0.88 (0.84-0.92)
HPFS							
Median, % of energy	8.9	10.8	12.1	13.3	15.3	NA	NA
No. of deaths	2748	2637	2622	2598	2385	NA	NA
Age-adjusted model	1 [Reference]	1.00 (0.95-1.06)	1.07 (1.02-1.13)	1.15 (1.09-1.21)	1.15 (1.08-1.21)	<.001	1.14 (1.09-1.18)
MV-adjusted model ^b	1 [Reference]	0.95 (0.90-1.01)	0.97 (0.90-1.04)	0.99 (0.92-1.07)	0.93 (0.85-1.02)	.18	0.95 (0.89-1.02)
Pooled ^c							
Age-adjusted model	1 [Reference]	1.05 (1.02-1.08)	1.10 (1.06-1.14)	1.17 (1.13-1.21)	1.22 (1.17-1.26)	<.001	1.16 (1.13-1.19)
MV-adjusted model ^b	1 [Reference]	0.95 (0.92-0.99)	0.93 (0.89-0.97)	0.93 (0.89-0.98)	0.89 (0.84-0.94)	<.001	0.90 (0.87-0.94)
<i>Trans</i> -fat intake							
NHS							
Median, % of energy	0.9	1.2	1.5	1.9	2.5	NA	NA
No. of deaths	5747	5158	4268	3099	2042	NA	NA
Age-adjusted model	1 [Reference]	1.40 (1.35-1.45)	1.68 (1.61-1.75)	1.85 (1.76-1.94)	2.02 (1.91-2.14)	<.001	2.50 (2.35-2.66)
MV-adjusted model ^b	1 [Reference]	1.12 (1.08-1.17)	1.17 (1.11-1.22)	1.13 (1.06-1.19)	1.06 (0.99-1.14)	.06	1.08 (1.00-1.17)
HPFS							
Median, % of energy	0.7	1.0	1.2	1.4	1.9	NA	NA
No. of deaths	2511	2642	2683	2698	2456	NA	NA
Age-adjusted model	1 [Reference]	1.14 (1.08-1.20)	1.23 (1.16-1.30)	1.37 (1.30-1.45)	1.47 (1.39-1.56)	<.001	1.95 (1.78-2.13)
MV-adjusted model ^b	1 [Reference]	1.08 (1.02-1.15)	1.11 (1.04-1.18)	1.19 (1.11-1.27)	1.19 (1.11-1.28)	<.001	1.34 (1.20-1.50)
Pooled ^c							
Age-adjusted model	1 [Reference]	1.31 (1.27-1.35)	1.49 (1.44-1.54)	1.63 (1.57-1.69)	1.73 (1.66-1.80)	<.001	2.31 (2.20-2.43)
MV-adjusted model ^b	1 [Reference]	1.11 (1.07-1.15)	1.14 (1.10-1.19)	1.15 (1.10-1.20)	1.13 (1.07-1.18)	<.001	1.16 (1.09-1.24)

Abbreviations: HPFS, Health Professional Follow-up Study; HR, hazard ratio; MV, multivariable; NA, not applicable; NHS, Nurses' Health Study.

^aIndicates hazard for total mortality substituting 5% of energy intake from total fatty acids, saturated fatty acids, unsaturated fatty acids, polyunsaturated fatty acids, and monounsaturated fatty acids and 2% of energy from *trans*-fatty acids for the same energy from carbohydrates.

^bAdjusted for age (in months), white race (yes vs no), marital status (with spouse, yes or no), body mass index (<23.0, 23.0-24.9, 25.0-29.9, 30.0-34.9, or ≥35.0 [calculated as weight in kilograms divided by height in meters squared]), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, or ≥27.0 h of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, or current ≥25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, or ≥15.0 g/d; men: 0, 0.1-4.9, 5.0-29.9, or ≥30.0 g/d), multivitamin use (yes vs no), vitamin E supplement use (yes vs no), current aspirin use (yes vs no), family history of myocardial infarction (yes vs no), family history of diabetes (yes vs no), family history of cancer (yes vs no), history of hypertension (yes vs no), history of hypercholesterolemia (yes vs no), intakes of total energy and dietary cholesterol (quintiles), percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, or postmenopausal current users). All models, except total fat intake, also included percentages of energy intake from remaining fatty acids (saturated, polyunsaturated, and monounsaturated and *trans*-fatty acids, all in quintiles).

^cResults for NHS and HPFS from the multivariable model were combined using the fixed-effects model.

eTable 4. Hazard Ratio for Substituting 1% of Energy From Carbohydrate by the Same Energy From Specific Types of Fat

	HR (95% CI)	<i>P</i> value
Saturated fat	1.02 (1.01, 1.02)	<.001
Monounsaturated fat	0.98 (0.97, 0.99)	<.001
Polyunsaturated fat	0.95 (0.94, 0.96)	<.001
<i>trans</i> fat	1.10 (1.07, 1.13)	<.001

Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, ≥35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, ≥15 g/d; men: 0, 0.1-4.9, 5.0-29.9, ≥30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), intakes of total energy, dietary cholesterol and percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models also included percentages of energy intake from remaining fatty acids (saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, *trans* fatty acids, modeled as continuous variables).

^c Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 5. Spearman Correlations Between Specific Total and Types of Fat Intakes in the Middle of Follow-up (1994) (% of total energy)

	Total fat	SFA	MUFA	PUFA	TFA	ω -6 PUFA	LA	AA	ω -3 PUFA	ALA	Marine ω -3 PUFA	UFA
NHS												
Total fat	1.00	0.89	0.95	0.55	0.65	0.47	0.52	0.24	0.12	0.53	-0.23	0.93
SFA		1.00	0.80	0.22	0.57	0.15	0.19	0.17	-0.07	0.38	-0.28	0.70
MUFA			1.00	0.50	0.64	0.44	0.47	0.24	0.11	0.43	-0.21	0.95
PUFA				1.00	0.41	0.91	0.99	0.16	0.46	0.66	-0.01	0.74
TFA					1.00	0.38	0.41	-0.01	-0.01	0.25	-0.31	0.64
ω -6 PUFA						1.00	0.93	0.09	0.46	0.48	-0.07	0.66
LA							1.00	0.08	0.38	0.60	-0.09	0.72
AA								1.00	0.26	0.10	0.32	0.24
ω -3 PUFA									1.00	0.58	0.67	0.25
ALA										1.00	0.05	0.57
Marine ω -3 PUFA											1.00	-0.16
UFA												1.00
HPFS												
Total fat	1.00	0.89	0.96	0.58	0.61	0.56	0.59	0.20	0.02	0.47	-0.23	0.93
SFA		1.00	0.79	0.23	0.56	0.24	0.24	0.12	-0.16	0.33	-0.29	0.67
MUFA			1.00	0.55	0.62	0.54	0.56	0.17	0.00	0.37	-0.22	0.95
PUFA				1.00	0.26	0.91	0.99	0.16	0.41	0.63	0.00	0.78
TFA					1.00	0.30	0.30	-0.06	-0.11	0.14	-0.29	0.56
ω -6 PUFA						1.00	0.93	0.05	0.35	0.47	-0.13	0.74
LA							1.00	0.08	0.31	0.57	-0.1	0.79
AA								1.00	0.30	0.11	0.37	0.19
ω -3 PUFA									1.00	0.56	0.76	0.15
ALA										1.00	0.09	0.51
Marine ω -3 PUFA											1.00	-0.16
UFA												1.00

Abbreviations: LA, Linoleic acid; AA, Arachidonic acid; ALA, α -linolenic acid, UFA, unsaturated fatty acid, TFA, *trans* fatty acid.

eTable 6. Associations Between Dietary ω -6 and ω -3 PUFA Intake and Total Mortality

	Quintile of Dietary Fatty Acid Intake					P Value	HR (95% CI) ^a
	1	2	3	4	5		
ω-6 PUFA Intake							
Total ω-6 PUFA							
NHS							
Median, % of energy	3.4	4.3	4.9	5.5	6.7	NA	NA
No. of deaths	4124	4346	4158	3897	3789	NA	NA
Age-adjusted model	1 [Reference]	0.89 (0.85-0.92)	0.83 (0.79-0.87)	0.77 (0.74-0.81)	0.72 (0.69-0.76)	<.001	0.82 (0.80-0.84)
MV-adjusted model ^b	1 [Reference]	0.99 (0.95-1.04)	0.94 (0.90-0.99)	0.90 (0.85-0.95)	0.88 (0.83-0.93)	<.001	0.92 (0.89-0.95)
HPFS							
Median, % of energy	3.7	4.5	5.1	5.8	6.9	NA	NA
No. of deaths	2874	2679	2622	2477	2338	NA	NA
Age-adjusted model	1 [Reference]	0.90 (0.85-0.95)	0.89 (0.85-0.94)	0.84 (0.80-0.89)	0.80 (0.76-0.85)	<.001	0.88 (0.85-0.91)
MV-adjusted model ^b	1 [Reference]	0.91 (0.86-0.96)	0.92 (0.87-0.97)	0.85 (0.79-0.90)	0.81 (0.75-0.87)	<.001	0.88 (0.84-0.92)
Pooled^c							
Age-adjusted model	1 [Reference]	0.89 (0.86-0.92)	0.85 (0.83-0.88)	0.80 (0.77-0.83)	0.75 (0.73-0.78)	<.001	0.84 (0.82-0.86)
MV-adjusted model ^b	1 [Reference]	0.96 (0.93-0.99)	0.93 (0.90-0.97)	0.88 (0.84-0.92)	0.85 (0.81-0.89)	<.001	0.90 (0.88-0.93)
Linoleic acid							
NHS							
Median, % of energy	3.3	4.2	4.8	5.4	6.5	NA	NA
No. of deaths	4165	4358	4148	3896	3747	NA	NA
Age-adjusted model	1 [Reference]	0.89 (0.85-0.93)	0.83 (0.80-0.87)	0.78 (0.74-0.81)	0.70 (0.67-0.74)	<.001	0.80 (0.78-0.82)
MV-adjusted model ^b	1 [Reference]	0.98 (0.94-1.03)	0.93 (0.89-0.98)	0.89 (0.84-0.94)	0.84 (0.79-0.89)	<.001	0.89 (0.86-0.92)
HPFS							
Median, % of energy	3.6	4.4	5.0	5.6	6.7	NA	NA
No. of deaths	2910	2670	2569	2508	2333	NA	NA
Age-adjusted model	1 [Reference]	0.92 (0.88-0.97)	0.90 (0.85-0.95)	0.85 (0.81-0.90)	0.79 (0.75-0.83)	<.001	0.86 (0.83-0.89)
MV-adjusted model ^b	1 [Reference]	0.94 (0.89-1.00)	0.90 (0.85-0.96)	0.86 (0.81-0.92)	0.80 (0.74-0.86)	<.001	0.86 (0.82-0.90)
Pooled^c							
Age-adjusted model	1 [Reference]	0.90 (0.87-0.93)	0.86 (0.83-0.89)	0.81 (0.78-0.84)	0.74 (0.71-0.76)	<.001	0.82 (0.81-0.84)

MV-adjusted model ^b	1 [Reference]	0.97 (0.93-1.00)	0.92 (0.89-0.96)	0.88 (0.84-0.91)	0.82 (0.79-0.86)	<.001	0.88 (0.86-0.91)
Arachidonic acid							
NHS							
Median % energy	0.05	0.06	0.07	0.09	0.11	NA	NA
Deaths, No.	5809	4329	3648	3419	3109	NA	NA
Age-adjusted model	1 [Reference]	0.99 (0.95-1.03)	0.96 (0.92-1.00)	0.97 (0.93-1.02)	0.94 (0.90-0.99)	.01	0.77 (0.63-0.94)
MV-adjusted model	1 [Reference]	0.99 (0.95-1.03)	0.94 (0.89-0.98)	0.94 (0.89-0.99)	0.90 (0.85-0.96)	<.001	0.61 (0.46-0.81)
HPFS							
Median, % of energy	0.05	0.06	0.07	0.09	0.11	NA	NA
No. of deaths	2644	2595	2519	2546	2686	NA	NA
Age-adjusted model	1 [Reference]	1.03 (0.97-1.08)	1.01 (0.95-1.06)	1.04 (0.99-1.10)	1.02 (0.96-1.08)	.45	1.08 (0.85-1.38)
MV-adjusted model ^b	1 [Reference]	1.00 (0.94-1.06)	0.94 (0.88-1.00)	0.96 (0.90-1.03)	0.89 (0.82-0.96)	.005	0.55 (0.38-0.78)
Pooled ^c							
Age-adjusted model	1 [Reference]	1.00 (0.97-1.04)	0.98 (0.94-1.01)	1.00 (0.97-1.03)	0.97 (0.94-1.01)	.14	0.89 (0.76-1.03)
MV-adjusted model ^b	1 [Reference]	0.99 (0.96-1.03)	0.94 (0.90-0.97)	0.94 (0.91-0.98)	0.90 (0.85-0.94)	<.001	0.58 (0.47-0.73)
ω-3 PUFA Intake							
Total ω-3 PUFA							
NHS							
Median, % of energy	0.48	0.57	0.63	0.72	0.88	NA	NA
No. of deaths	4132	3786	3875	4090	4431	NA	NA
Age-adjusted model	1 [Reference]	0.90 (0.86-0.94)	0.87 (0.83-0.91)	0.82 (0.78-0.86)	0.63 (0.60-0.66)	<.001	0.71 (0.69-0.74)
MV-adjusted model ^b	1 [Reference]	1.00 (0.95-1.04)	1.01 (0.96-1.06)	1.03 (0.98-1.08)	0.95 (0.90-1.00)	.04	0.96 (0.93-1.00)
HPFS							
Median, % of energy	0.46	0.57	0.65	0.75	0.94	NA	NA
No. of deaths	2441	2548	2645	2644	2712	NA	NA
Age-adjusted model	1 [Reference]	0.87 (0.83-0.93)	0.85 (0.80-0.90)	0.82 (0.78-0.87)	0.72 (0.68-0.77)	<.001	0.83 (0.80-0.86)
MV-adjusted model ^b	1 [Reference]	0.98 (0.92-1.04)	0.99 (0.94-1.05)	1.00 (0.94-1.06)	0.96 (0.90-1.02)	.26	0.97 (0.94-1.01)
Pooled ^c							
Age-adjusted model	1 [Reference]	0.89 (0.86-0.92)	0.86 (0.83-0.89)	0.82 (0.79-0.85)	0.66 (0.64-0.69)	<.001	0.77 (0.75-0.78)
MV-adjusted model ^b	1 [Reference]	0.99 (0.96-1.03)	1.00 (0.97-1.04)	1.02 (0.98-1.06)	0.95 (0.91-0.99)	.03	0.97 (0.94-0.99)
α-linolenic acid							
NHS							

Median, % of energy	0.41	0.48	0.53	0.59	0.70	NA	NA
No. of deaths	4274	3800	3831	3839	4570	NA	NA
Age-adjusted model	1 [Reference]	0.95 (0.91-0.99)	0.97 (0.93-1.01)	0.91 (0.87-0.95)	0.75 (0.72-0.78)	<.001	0.75 (0.72-0.78)
MV-adjusted model ^b	1 [Reference]	1.00 (0.95-1.04)	1.05 (1.00-1.10)	1.02 (0.97-1.07)	0.98 (0.93-1.04)	.49	0.98 (0.93-1.04)
HPFS							
Median, % of energy	0.38	0.45	0.50	0.56	0.68	NA	NA
No. of deaths	2398	2431	2544	2700	2917	NA	NA
Age-adjusted model	1 [Reference]	0.97 (0.91-1.02)	0.95 (0.90-1.01)	0.95 (0.90-1.00)	0.85 (0.80-0.90)	<.001	0.86 (0.81-0.90)
MV-adjusted model ^b	1 [Reference]	1.00 (0.94-1.06)	1.02 (0.96-1.08)	1.04 (0.98-1.10)	1.01 (0.94-1.08)	.67	0.99 (0.93-1.05)
Pooled ^c							
Age-adjusted model	1 [Reference]	0.96 (0.92-0.99)	0.96 (0.93-1.00)	0.93 (0.90-0.96)	0.79 (0.76-0.81)	<.001	0.79 (0.77-0.82)
MV-adjusted model ^b	1 [Reference]	1.00 (0.96-1.03)	1.04 (1.00-1.08)	1.03 (0.99-1.07)	0.99 (0.95-1.03)	.80	0.98 (0.94-1.02)
Marine ω -3 fatty acids (DHA+EPA)							
NHS							
Median, % of energy	0.03	0.05	0.08	0.12	0.21	NA	NA
No. of deaths	3725	4123	4247	4019	4200	NA	NA
Age-adjusted model	1 [Reference]	0.98 (0.94-1.03)	0.93 (0.89-0.97)	0.83 (0.80-0.87)	0.68 (0.65-0.72)	<.001	0.52 (0.48-0.55)
MV-adjusted model ^b	1 [Reference]	1.06 (1.02-1.11)	1.05 (1.01-1.10)	1.03 (0.98-1.08)	0.96 (0.91-1.01)	<.001	0.87 (0.81-0.94)
HPFS							
Median, % of energy	0.04	0.08	0.12	0.18	0.31	NA	NA
No. of deaths	2558	2655	2635	2490	2652	NA	NA
Age-adjusted model	1 [Reference]	0.97 (0.91-1.02)	0.97 (0.91-1.02)	0.90 (0.85-0.95)	0.82 (0.78-0.87)	<.001	0.80 (0.76-0.85)
MV-adjusted model ^b	1 [Reference]	1.00 (0.95-1.06)	1.05 (1.00-1.12)	1.03 (0.97-1.09)	0.98 (0.92-1.04)	.28	0.97 (0.91-1.04)
Pooled ^c							
Age-adjusted model	1 [Reference]	0.98 (0.94-1.01)	0.94 (0.91-0.98)	0.86 (0.83-0.89)	0.74 (0.71-0.76)	<.001	0.67 (0.64-0.70)
MV-adjusted model ^b	1 [Reference]	1.04 (1.00-1.07)	1.05 (1.02-1.09)	1.03 (0.99-1.07)	0.96 (0.93-1.00)	.002	0.93 (0.89-0.98)
ω -6: ω -3 ratio ^d							
NHS							
Median, % of energy	5.5	6.7	7.6	8.4	9.9	NA	NA
No. of deaths	4070	4316	4275	4147	3506	NA	NA
Age-adjusted model	1 [Reference]	1.14 (1.09-1.19)	1.18 (1.13-1.23)	1.22 (1.16-1.27)	1.23 (1.18-1.29)	<.001	1.05 (1.04-1.06)

MV-adjusted model ^b	1 [Reference]	1.06 (1.02-1.11)	1.05 (1.01-1.10)	1.06 (1.01-1.11)	1.02 (0.97-1.07)	.55	1.00 (0.99-1.01)
HPFS							
Median, % of energy	5.5	6.9	7.9	8.9	10.8	NA	NA
No. of deaths	2968	2782	2642	2432	2166	NA	NA
Age-adjusted model	1 [Reference]	1.07 (1.02-1.13)	1.11 (1.05-1.17)	1.13 (1.07-1.19)	1.11 (1.05-1.18)	<.001	1.02 (1.01-1.03)
MV-adjusted model ^b	1 [Reference]	1.00 (0.95-1.06)	0.97 (0.92-1.03)	0.96 (0.90-1.02)	0.94 (0.88-1.00)	.03	0.99 (0.98-1.00)
Pooled ^c							
Age-adjusted model	1 [Reference]	1.11 (1.07-1.15)	1.15 (1.11-1.19)	1.18 (1.14-1.22)	1.18 (1.14-1.23)	<.001	1.03 (1.03-1.04)
MV-adjusted model ^b	1 [Reference]	1.04 (1.01-1.08)	1.02 (0.99-1.06)	1.02 (0.98-1.06)	0.99 (0.95-1.03)	.29	1.00 (0.99-1.00)

Abbreviations: DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; HPFS, Health Professional Follow-up Study; HR, hazard ratio; MV, multivariable; NA, not applicable; NHS, Nurses' Health Study; PUFA, polyunsaturated fatty acid.

^aIndicates hazard for total mortality substituting 2% of energy from total ω -6 PUFA and linoleic acid and 0.3% of energy from total ω -3 PUFA, arachidonic acid, α -linolenic acid, and marine ω -3 fatty acids, for the same energy from carbohydrates.

^bAdjusted for age (in months), white race (yes vs no), marital status (with spouse, yes or no), body mass index (<23.0, 23.0-24.9, 25.0-29.9, 30.0-34.9, or \geq 35.0 [calculated as weight in kilograms divided by height in meters squared]), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, or \geq 27.0 h of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, or current \geq 25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, or \geq 15.0 g/d; men: 0, 0.1-4.9, 5.0-29.9, or \geq 30.0 g/d), multivitamin use (yes vs no), vitamin E supplement use (yes vs no), current aspirin use (yes vs no), family history of myocardial infarction (yes vs no), family history of diabetes (yes vs no), family history of cancer (yes vs no), history of hypertension (yes vs no), history of hypercholesterolemia (yes vs no), intakes of total energy and dietary cholesterol (quintiles), percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, or postmenopausal current users). All models also included percentages of energy intake from remaining fatty acids (saturated fatty acids, PUFAs, monounsaturated fatty acids, *trans*-fatty acids, ω -6 PUFAs, ω -3 PUFAs, linoleic acid, arachidonic acid, α -linolenic acid, and marine ω -3 fatty acids, all in quintiles).

^cResults for NHS and HPFS from the multivariable model were combined using the fixed-effects model.

^dHazards of total mortality were calculated for 1-unit increments.

eTable 7. Associations Between Most Recent Total and Specific Types of Fat Intakes and Total and Cause-Specific Mortality (Comparison is Isocaloric Substitution for Carbohydrate)

	Quintile of dietary fatty acid intake					<i>P</i> _{trend}
	Q1	Q2	Q3	Q4	Q5	
Total mortality						
Total fat						
Age-adjusted model	Ref.	1.01 (0.98, 1.04)	1.06 (1.02, 1.09)	1.09 (1.05, 1.13)	1.20 (1.16, 1.24)	<.001
MV-adjusted model	Ref.	0.94 (0.91, 0.97)	0.92 (0.89, 0.95)	0.88 (0.85, 0.91)	0.86 (0.82, 0.89)	<.001
Saturated fat						
Age-adjusted model	Ref.	1.11 (1.07, 1.14)	1.23 (1.19, 1.27)	1.34 (1.30, 1.39)	1.59 (1.53, 1.65)	<.001
MV-adjusted model	Ref.	1.02 (0.98, 1.06)	1.07 (1.02, 1.11)	1.07 (1.02, 1.11)	1.07 (1.02, 1.13)	<.001
Unsaturated fat						
Age-adjusted model	Ref.	0.98 (0.95, 1.01)	0.97 (0.94, 1.01)	0.97 (0.94, 1.01)	0.95 (0.91, 0.98)	0.002
MV-adjusted model	Ref.	0.87 (0.85, 0.90)	0.81 (0.78, 0.84)	0.77 (0.74, 0.81)	0.74 (0.71, 0.77)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.91 (0.88, 0.94)	0.87 (0.84, 0.90)	0.81 (0.78, 0.83)	0.71 (0.69, 0.73)	<.001
MV-adjusted model	Ref.	0.93 (0.90, 0.96)	0.90 (0.87, 0.93)	0.85 (0.82, 0.89)	0.80 (0.77, 0.83)	<.001
Monounsaturated fat						
Age-adjusted model	Ref.	1.03 (1.00, 1.07)	1.06 (1.02, 1.09)	1.10 (1.07, 1.14)	1.13 (1.09, 1.17)	<.001
MV-adjusted model	Ref.	0.95 (0.91, 0.98)	0.91 (0.87, 0.95)	0.91 (0.87, 0.95)	0.88 (0.84, 0.93)	<.001
trans fat						
Age-adjusted model	Ref.	1.32 (1.28, 1.37)	1.54 (1.49, 1.59)	1.74 (1.67, 1.80)	1.84 (1.77, 1.92)	<.001
MV-adjusted model	Ref.	1.15 (1.11, 1.19)	1.20 (1.16, 1.25)	1.24 (1.19, 1.30)	1.21 (1.15, 1.27)	<.001
Total ω-6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.90 (0.87, 0.93)	0.86 (0.83, 0.89)	0.81 (0.78, 0.84)	0.74 (0.72, 0.77)	<.001
MV-adjusted model	Ref.	0.95 (0.92, 0.98)	0.92 (0.89, 0.95)	0.89 (0.85, 0.93)	0.85 (0.82, 0.89)	<.001

Linoleic acid						
Age-adjusted model	Ref.	0.92 (0.89, 0.95)	0.88 (0.85, 0.91)	0.81 (0.78, 0.84)	0.73 (0.71, 0.76)	<.001
MV-adjusted model	Ref.	0.96 (0.93, 1.00)	0.94 (0.90, 0.97)	0.88 (0.85, 0.92)	0.84 (0.80, 0.88)	<.001
Arachidonic acid						
Age-adjusted model	Ref.	0.95 (0.92, 0.98)	0.95 (0.92, 0.98)	0.93 (0.90, 0.96)	0.89 (0.86, 0.92)	<.001
MV-adjusted model	Ref.	0.92 (0.89, 0.96)	0.91 (0.88, 0.95)	0.89 (0.85, 0.92)	0.85 (0.81, 0.89)	<.001
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.88 (0.85, 0.91)	0.86 (0.83, 0.89)	0.80 (0.77, 0.83)	0.65 (0.63, 0.68)	<.001
MV-adjusted model	Ref.	0.94 (0.90, 0.97)	0.97 (0.93, 1.00)	0.95 (0.91, 0.99)	0.91 (0.87, 0.95)	<.001
α -linolenic acid						
Age-adjusted model	Ref.	0.98 (0.95, 1.01)	0.97 (0.94, 1.01)	0.92 (0.89, 0.95)	0.78 (0.75, 0.81)	<.001
MV-adjusted model	Ref.	1.00 (0.96, 1.03)	1.01 (0.97, 1.04)	1.00 (0.96, 1.04)	0.98 (0.94, 1.02)	0.29
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.96 (0.93, 0.99)	0.93 (0.90, 0.96)	0.85 (0.83, 0.88)	0.72 (0.70, 0.75)	<.001
MV-adjusted model	Ref.	0.97 (0.94, 1.01)	0.99 (0.96, 1.03)	0.97 (0.94, 1.01)	0.90 (0.87, 0.93)	<.001
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.17 (1.13, 1.20)	1.22 (1.18, 1.26)	1.27 (1.22, 1.31)	1.24 (1.20, 1.28)	<.001
MV-adjusted model	Ref.	1.07 (1.03, 1.11)	1.06 (1.02, 1.10)	1.07 (1.03, 1.11)	1.05 (1.01, 1.09)	0.09
Cardiovascular disease mortality						
Total fat						
Age-adjusted model	Ref.	0.99 (0.93, 1.06)	1.05 (0.98, 1.12)	1.08 (1.01, 1.15)	1.16 (1.08, 1.25)	<.001
MV-adjusted model	Ref.	0.93 (0.87, 0.99)	0.92 (0.86, 0.99)	0.87 (0.81, 0.94)	0.82 (0.76, 0.89)	<.001
Saturated fat						
Age-adjusted model	Ref.	1.11 (1.04, 1.18)	1.21 (1.13, 1.29)	1.30 (1.22, 1.40)	1.53 (1.42, 1.64)	<.001
MV-adjusted model	Ref.	1.02 (0.95, 1.10)	1.05 (0.97, 1.14)	1.04 (0.95, 1.13)	1.03 (0.93, 1.13)	0.19
Unsaturated fat						
Age-adjusted model	Ref.	1.01 (0.95, 1.08)	0.97 (0.90, 1.03)	1.00 (0.93, 1.07)	0.95 (0.89, 1.03)	0.24
MV-adjusted model	Ref.	0.92 (0.86, 0.98)	0.83 (0.77, 0.90)	0.81 (0.75, 0.88)	0.76 (0.70, 0.83)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.89 (0.83, 0.95)	0.86 (0.81, 0.92)	0.77 (0.72, 0.83)	0.74 (0.69, 0.79)	<.001
MV-adjusted model	Ref.	0.90 (0.84, 0.97)	0.88 (0.82, 0.95)	0.80 (0.74, 0.87)	0.82 (0.76, 0.89)	<.001

Monounsaturated fat						
Age-adjusted model	Ref.	1.02 (0.96, 1.09)	1.07 (1.01, 1.15)	1.07 (1.00, 1.15)	1.09 (1.01, 1.17)	0.004
MV-adjusted model	Ref.	0.95 (0.88, 1.02)	0.95 (0.87, 1.03)	0.90 (0.82, 0.98)	0.85 (0.77, 0.95)	<.001
trans fat						
Age-adjusted model	Ref.	1.20 (1.12, 1.28)	1.43 (1.33, 1.53)	1.59 (1.48, 1.71)	1.73 (1.59, 1.87)	<.001
MV-adjusted model	Ref.	1.06 (0.99, 1.14)	1.14 (1.05, 1.23)	1.18 (1.08, 1.28)	1.19 (1.08, 1.32)	<.001
Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.86 (0.80, 0.92)	0.84 (0.78, 0.90)	0.79 (0.74, 0.85)	0.76 (0.71, 0.82)	<.001
MV-adjusted model	Ref.	0.91 (0.84, 0.97)	0.90 (0.83, 0.97)	0.86 (0.79, 0.93)	0.85 (0.78, 0.93)	<.001
Linoleic acid						
Age-adjusted model	Ref.	0.89 (0.84, 0.96)	0.87 (0.81, 0.93)	0.79 (0.73, 0.84)	0.74 (0.69, 0.79)	<.001
MV-adjusted model	Ref.	0.93 (0.87, 1.00)	0.92 (0.85, 0.99)	0.84 (0.78, 0.91)	0.81 (0.74, 0.88)	<.001
Arachidonic acid						
Age-adjusted model	Ref.	0.96 (0.90, 1.03)	1.02 (0.95, 1.09)	0.98 (0.92, 1.05)	1.04 (0.97, 1.11)	0.24
MV-adjusted model	Ref.	0.93 (0.86, 1.00)	0.95 (0.88, 1.03)	0.89 (0.82, 0.97)	0.90 (0.82, 0.99)	0.03
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.85 (0.79, 0.91)	0.83 (0.77, 0.89)	0.81 (0.75, 0.86)	0.74 (0.69, 0.79)	<.001
MV-adjusted model	Ref.	0.89 (0.82, 0.95)	0.90 (0.84, 0.97)	0.93 (0.86, 1.00)	0.97 (0.89, 1.05)	0.62
α -linolenic acid						
Age-adjusted model	Ref.	0.98 (0.91, 1.05)	0.93 (0.86, 0.99)	0.89 (0.82, 0.95)	0.82 (0.76, 0.88)	<.001
MV-adjusted model	Ref.	0.99 (0.92, 1.07)	0.94 (0.87, 1.02)	0.95 (0.87, 1.02)	0.98 (0.90, 1.07)	0.54
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.98 (0.92, 1.05)	0.94 (0.88, 1.01)	0.91 (0.85, 0.97)	0.81 (0.76, 0.87)	<.001
MV-adjusted model	Ref.	0.98 (0.92, 1.05)	0.98 (0.91, 1.05)	1.01 (0.94, 1.09)	0.96 (0.89, 1.03)	0.64
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.10 (1.02, 1.17)	1.15 (1.07, 1.23)	1.11 (1.03, 1.19)	1.13 (1.05, 1.22)	0.003
MV-adjusted model	Ref.	1.02 (0.95, 1.09)	1.03 (0.96, 1.10)	0.97 (0.90, 1.04)	1.01 (0.93, 1.09)	0.58
Cancer mortality						
Total fat						
Age-adjusted model	Ref.	1.04 (0.98, 1.10)	1.11 (1.05, 1.17)	1.15 (1.09, 1.22)	1.24 (1.17, 1.32)	<.001
MV-adjusted model	Ref.	0.97 (0.92, 1.02)	0.98 (0.92, 1.04)	0.95 (0.89, 1.01)	0.93 (0.87, 0.99)	0.01

Saturated fat						
Age-adjusted model	Ref.	1.11 (1.05, 1.17)	1.22 (1.15, 1.29)	1.38 (1.30, 1.46)	1.51 (1.42, 1.61)	<.001
MV-adjusted model	Ref.	1.04 (0.98, 1.11)	1.09 (1.02, 1.16)	1.15 (1.07, 1.23)	1.12 (1.03, 1.21)	<.001
Unsaturated fat						
Age-adjusted model	Ref.	1.02 (0.97, 1.08)	1.05 (0.99, 1.10)	1.07 (1.01, 1.13)	1.04 (0.98, 1.10)	0.07
MV-adjusted model	Ref.	0.94 (0.89, 0.99)	0.92 (0.86, 0.97)	0.90 (0.85, 0.96)	0.86 (0.80, 0.92)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.96 (0.91, 1.02)	0.97 (0.92, 1.03)	0.95 (0.89, 1.00)	0.87 (0.82, 0.92)	<.001
MV-adjusted model	Ref.	0.99 (0.93, 1.05)	1.00 (0.94, 1.06)	0.98 (0.92, 1.04)	0.91 (0.85, 0.97)	0.005
Monounsaturated fat						
Age-adjusted model	Ref.	1.09 (1.03, 1.15)	1.06 (1.00, 1.12)	1.15 (1.09, 1.22)	1.18 (1.11, 1.25)	<.001
MV-adjusted model	Ref.	1.00 (0.94, 1.06)	0.92 (0.86, 0.98)	0.96 (0.89, 1.03)	0.94 (0.87, 1.02)	0.07
trans fat						
Age-adjusted model	Ref.	1.18 (1.12, 1.24)	1.29 (1.21, 1.36)	1.38 (1.30, 1.46)	1.40 (1.31, 1.49)	<.001
MV-adjusted model	Ref.	1.05 (0.99, 1.11)	1.04 (0.97, 1.11)	1.03 (0.96, 1.10)	0.95 (0.88, 1.03)	0.10
Total ω-6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.98 (0.92, 1.03)	0.95 (0.90, 1.00)	0.94 (0.89, 0.99)	0.87 (0.82, 0.92)	<.001
MV-adjusted model	Ref.	1.01 (0.96, 1.08)	0.99 (0.93, 1.05)	0.98 (0.92, 1.05)	0.92 (0.85, 0.99)	0.03
Linoleic acid						
Age-adjusted model	Ref.	0.99 (0.94, 1.05)	0.96 (0.91, 1.02)	0.95 (0.89, 1.00)	0.88 (0.83, 0.93)	<.001
MV-adjusted model	Ref.	1.03 (0.97, 1.09)	1.00 (0.94, 1.07)	0.99 (0.93, 1.06)	0.94 (0.88, 1.02)	0.08
Arachidonic acid						
Age-adjusted model	Ref.	0.98 (0.93, 1.03)	0.99 (0.94, 1.05)	0.98 (0.93, 1.04)	0.96 (0.91, 1.02)	0.22
MV-adjusted model	Ref.	0.95 (0.90, 1.01)	0.94 (0.89, 1.00)	0.92 (0.86, 0.99)	0.88 (0.81, 0.95)	0.002
Total ω-3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.93 (0.87, 0.98)	0.92 (0.87, 0.97)	0.92 (0.87, 0.97)	0.78 (0.74, 0.83)	<.001
MV-adjusted model	Ref.	0.97 (0.91, 1.03)	0.98 (0.93, 1.05)	1.01 (0.95, 1.08)	0.94 (0.88, 1.01)	0.15
α-linolenic acid						
Age-adjusted model	Ref.	1.02 (0.96, 1.08)	1.05 (0.99, 1.11)	1.02 (0.97, 1.08)	0.95 (0.89, 1.00)	0.03
MV-adjusted model	Ref.	1.01 (0.95, 1.07)	1.05 (0.98, 1.11)	1.04 (0.98, 1.11)	1.04 (0.97, 1.11)	0.25

Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.97 (0.92, 1.03)	0.95 (0.90, 1.00)	0.88 (0.84, 0.94)	0.81 (0.77, 0.86)	<.001
MV-adjusted model	Ref.	0.99 (0.94, 1.05)	1.01 (0.95, 1.07)	0.99 (0.93, 1.05)	0.95 (0.89, 1.01)	0.12
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.13 (1.07, 1.19)	1.16 (1.10, 1.23)	1.19 (1.13, 1.26)	1.13 (1.07, 1.20)	<.001
MV-adjusted model	Ref.	1.08 (1.02, 1.14)	1.07 (1.01, 1.13)	1.08 (1.02, 1.15)	1.02 (0.96, 1.09)	0.73
Neurodegenerative disease mortality						
Total fat						
Age-adjusted model	Ref.	0.86 (0.77, 0.95)	0.84 (0.76, 0.94)	0.79 (0.70, 0.89)	0.88 (0.77, 0.99)	<.001
MV-adjusted model	Ref.	0.86 (0.78, 0.96)	0.80 (0.72, 0.90)	0.72 (0.63, 0.81)	0.69 (0.60, 0.79)	<.001
Saturated fat						
Age-adjusted model	Ref.	0.92 (0.83, 1.03)	1.05 (0.94, 1.16)	1.09 (0.97, 1.21)	1.19 (1.05, 1.35)	0.002
MV-adjusted model	Ref.	0.88 (0.78, 0.98)	0.98 (0.86, 1.11)	0.97 (0.84, 1.11)	0.89 (0.76, 1.05)	0.87
Unsaturated fat						
Age-adjusted model	Ref.	0.89 (0.80, 0.98)	0.78 (0.70, 0.87)	0.73 (0.64, 0.82)	0.68 (0.60, 0.77)	<.001
MV-adjusted model	Ref.	0.83 (0.75, 0.92)	0.68 (0.61, 0.77)	0.61 (0.53, 0.69)	0.59 (0.52, 0.68)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.80 (0.72, 0.90)	0.66 (0.59, 0.74)	0.53 (0.47, 0.59)	0.44 (0.40, 0.50)	<.001
MV-adjusted model	Ref.	0.89 (0.80, 1.00)	0.83 (0.74, 0.93)	0.72 (0.64, 0.82)	0.73 (0.64, 0.83)	<.001
Monounsaturated fat						
Age-adjusted model	Ref.	0.96 (0.87, 1.06)	0.98 (0.88, 1.09)	0.99 (0.88, 1.12)	0.90 (0.79, 1.02)	0.14
MV-adjusted model	Ref.	0.93 (0.83, 1.04)	0.84 (0.73, 0.95)	0.82 (0.71, 0.96)	0.72 (0.60, 0.86)	<.001
trans fat						
Age-adjusted model	Ref.	1.66 (1.49, 1.85)	2.18 (1.95, 2.44)	2.91 (2.58, 3.28)	2.96 (2.56, 3.41)	<.001
MV-adjusted model	Ref.	1.27 (1.13, 1.41)	1.40 (1.24, 1.59)	1.66 (1.45, 1.90)	1.47 (1.24, 1.75)	<.001
Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.80 (0.72, 0.89)	0.69 (0.62, 0.77)	0.57 (0.50, 0.64)	0.51 (0.45, 0.57)	<.001
MV-adjusted model	Ref.	0.94 (0.84, 1.05)	0.92 (0.81, 1.04)	0.85 (0.74, 0.98)	0.91 (0.78, 1.06)	0.15
Linoleic acid						
Age-adjusted model	Ref.	0.79 (0.71, 0.88)	0.68 (0.61, 0.76)	0.57 (0.50, 0.64)	0.48 (0.43, 0.54)	<.001
MV-adjusted model	Ref.	0.92 (0.82, 1.03)	0.91 (0.81, 1.03)	0.84 (0.73, 0.96)	0.85 (0.73, 0.99)	0.03

Arachidonic acid						
Age-adjusted model	Ref.	0.83 (0.75, 0.92)	0.75 (0.67, 0.84)	0.76 (0.68, 0.85)	0.60 (0.54, 0.68)	<.001
MV-adjusted model	Ref.	0.85 (0.76, 0.95)	0.79 (0.69, 0.89)	0.85 (0.74, 0.97)	0.80 (0.69, 0.93)	0.004
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.75 (0.67, 0.84)	0.70 (0.62, 0.78)	0.57 (0.51, 0.64)	0.36 (0.32, 0.40)	<.001
MV-adjusted model	Ref.	0.84 (0.75, 0.95)	0.88 (0.78, 0.99)	0.82 (0.73, 0.93)	0.73 (0.63, 0.84)	<.001
α -linolenic acid						
Age-adjusted model	Ref.	0.85 (0.76, 0.94)	0.73 (0.65, 0.82)	0.61 (0.54, 0.68)	0.42 (0.37, 0.47)	<.001
MV-adjusted model	Ref.	0.95 (0.84, 1.06)	0.89 (0.79, 1.01)	0.85 (0.74, 0.96)	0.80 (0.69, 0.92)	0.001
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.97 (0.87, 1.07)	0.88 (0.79, 0.99)	0.86 (0.77, 0.96)	0.57 (0.51, 0.64)	<.001
MV-adjusted model	Ref.	1.00 (0.90, 1.12)	0.87 (0.78, 0.98)	0.95 (0.85, 1.07)	0.80 (0.71, 0.91)	<.001
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.27 (1.13, 1.42)	1.37 (1.22, 1.54)	1.54 (1.38, 1.73)	1.65 (1.47, 1.86)	<.001
MV-adjusted model	Ref.	1.08 (0.96, 1.22)	1.08 (0.96, 1.22)	1.14 (1.01, 1.29)	1.17 (1.03, 1.33)	0.01
Respiratory disease mortality						
Total fat						
Age-adjusted model	Ref.	1.22 (1.08, 1.37)	1.24 (1.10, 1.40)	1.56 (1.38, 1.76)	1.71 (1.51, 1.94)	<.001
MV-adjusted model	Ref.	1.05 (0.93, 1.18)	0.97 (0.86, 1.11)	1.08 (0.95, 1.24)	1.03 (0.90, 1.19)	0.39
Saturated fat						
Age-adjusted model	Ref.	1.29 (1.14, 1.46)	1.58 (1.40, 1.78)	1.80 (1.59, 2.04)	2.60 (2.30, 2.95)	<.001
MV-adjusted model	Ref.	1.10 (0.96, 1.26)	1.22 (1.05, 1.40)	1.21 (1.04, 1.41)	1.41 (1.19, 1.67)	<.001
Unsaturated fat						
Age-adjusted model	Ref.	0.94 (0.84, 1.06)	1.13 (1.00, 1.26)	1.20 (1.07, 1.35)	1.05 (0.93, 1.19)	0.009
MV-adjusted model	Ref.	0.74 (0.65, 0.84)	0.78 (0.68, 0.89)	0.75 (0.65, 0.86)	0.63 (0.55, 0.73)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.97 (0.86, 1.09)	0.92 (0.81, 1.04)	0.90 (0.80, 1.02)	0.74 (0.65, 0.84)	<.001
MV-adjusted model	Ref.	0.97 (0.85, 1.09)	0.92 (0.81, 1.04)	0.91 (0.79, 1.03)	0.80 (0.69, 0.92)	0.001
Monounsaturated fat						
Age-adjusted model	Ref.	1.04 (0.93, 1.17)	1.34 (1.20, 1.51)	1.41 (1.25, 1.59)	1.34 (1.17, 1.52)	<.001
MV-adjusted model	Ref.	0.83 (0.73, 0.95)	0.93 (0.80, 1.07)	0.88 (0.75, 1.03)	0.73 (0.61, 0.88)	0.002

trans fat						
Age-adjusted model	Ref.	1.51 (1.34, 1.70)	1.95 (1.72, 2.20)	2.31 (2.02, 2.63)	2.98 (2.59, 3.43)	<.001
MV-adjusted model	Ref.	1.18 (1.04, 1.34)	1.27 (1.10, 1.46)	1.29 (1.11, 1.50)	1.52 (1.29, 1.81)	<.001
Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.92 (0.82, 1.04)	0.90 (0.80, 1.02)	0.89 (0.79, 1.01)	0.77 (0.68, 0.88)	<.001
MV-adjusted model	Ref.	0.95 (0.83, 1.08)	0.93 (0.81, 1.07)	0.94 (0.81, 1.08)	0.87 (0.74, 1.03)	0.13
Linoleic acid						
Age-adjusted model	Ref.	0.94 (0.84, 1.06)	0.90 (0.79, 1.01)	0.89 (0.78, 1.00)	0.77 (0.68, 0.87)	<.001
MV-adjusted model	Ref.	0.96 (0.85, 1.09)	0.91 (0.80, 1.04)	0.92 (0.79, 1.06)	0.85 (0.72, 0.99)	0.04
Arachidonic acid						
Age-adjusted model	Ref.	0.91 (0.81, 1.02)	0.96 (0.85, 1.07)	0.85 (0.75, 0.96)	0.78 (0.69, 0.88)	<.001
MV-adjusted model	Ref.	0.89 (0.78, 1.00)	0.94 (0.83, 1.07)	0.88 (0.76, 1.02)	0.88 (0.75, 1.04)	0.15
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.88 (0.78, 0.99)	0.93 (0.83, 1.05)	0.77 (0.68, 0.87)	0.59 (0.52, 0.67)	<.001
MV-adjusted model	Ref.	0.93 (0.82, 1.06)	1.04 (0.91, 1.18)	0.90 (0.79, 1.04)	0.88 (0.76, 1.02)	0.07
α -linolenic acid						
Age-adjusted model	Ref.	1.00 (0.88, 1.14)	1.13 (1.00, 1.28)	1.02 (0.90, 1.16)	0.85 (0.75, 0.96)	0.003
MV-adjusted model	Ref.	0.98 (0.85, 1.12)	1.09 (0.95, 1.25)	1.02 (0.88, 1.17)	1.00 (0.85, 1.16)	0.95
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.99 (0.88, 1.11)	0.91 (0.81, 1.03)	0.76 (0.68, 0.86)	0.54 (0.48, 0.62)	<.001
MV-adjusted model	Ref.	1.04 (0.92, 1.16)	1.04 (0.92, 1.17)	0.99 (0.87, 1.12)	0.84 (0.73, 0.96)	0.001
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.36 (1.20, 1.55)	1.50 (1.32, 1.70)	1.60 (1.41, 1.81)	1.61 (1.42, 1.83)	<.001
MV-adjusted model	Ref.	1.16 (1.02, 1.32)	1.16 (1.02, 1.32)	1.16 (1.01, 1.32)	1.18 (1.03, 1.35)	0.05

Abbreviations: HR, hazard ratio; CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MV, multivariable; NHS, Nurses' Health Study; HPFS, Health Professional Follow-up Study.

Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, ≥ 35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥ 27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥ 25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, ≥ 15 g/d; men: 0, 0.1-4.9, 5.0-29.9, ≥ 30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), intakes of total energy, dietary cholesterol and

percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models also included percentages of energy intake from remaining fatty acids (saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, *trans* fatty acids, ω -6 polyunsaturated fatty acids, ω -3 polyunsaturated fatty acids, linoleic acid, arachidonic acid, α -linolenic acid and marine ω -3 fats, all in quintiles). Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 8. Associations Between Total and Specific Types of Fat Intakes and Total and Cause-Specific Mortality From the 4-Year Lag Analysis (Comparison is Isocaloric Substitution for Carbohydrate)

	Quintile of dietary fatty acid intake					<i>P</i> _{trend}
	Q1	Q2	Q3	Q4	Q5	
Total mortality						
Total fat						
Age-adjusted model	Ref.	1.04 (1.01, 1.08)	1.10 (1.06, 1.14)	1.16 (1.12, 1.21)	1.28 (1.24, 1.33)	<.001
MV-adjusted model	Ref.	0.97 (0.94, 1.00)	0.95 (0.92, 0.99)	0.92 (0.89, 0.96)	0.91 (0.87, 0.95)	<.001
Saturated fat						
Age-adjusted model	Ref.	1.14 (1.10, 1.18)	1.25 (1.21, 1.29)	1.37 (1.32, 1.42)	1.57 (1.51, 1.63)	<.001
MV-adjusted model	Ref.	1.09 (1.05, 1.13)	1.13 (1.09, 1.18)	1.16 (1.10, 1.21)	1.20 (1.14, 1.27)	<.001
Unsaturated fat						
Age-adjusted model	Ref.	1.00 (0.97, 1.03)	1.01 (0.98, 1.04)	1.02 (0.99, 1.06)	1.08 (1.04, 1.12)	<.001
MV-adjusted model	Ref.	0.91 (0.88, 0.94)	0.85 (0.82, 0.89)	0.81 (0.77, 0.84)	0.78 (0.75, 0.82)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.90 (0.87, 0.93)	0.88 (0.85, 0.91)	0.86 (0.83, 0.89)	0.84 (0.81, 0.87)	<.001
MV-adjusted model	Ref.	0.94 (0.91, 0.97)	0.90 (0.87, 0.94)	0.88 (0.85, 0.91)	0.85 (0.81, 0.88)	<.001
Monounsaturated fat						
Age-adjusted model	Ref.	1.04 (1.00, 1.07)	1.07 (1.04, 1.11)	1.14 (1.10, 1.18)	1.20 (1.15, 1.24)	<.001
MV-adjusted model	Ref.	0.96 (0.92, 0.99)	0.93 (0.89, 0.97)	0.92 (0.87, 0.97)	0.89 (0.84, 0.94)	<.001
trans fat						
Age-adjusted model	Ref.	1.13 (1.09, 1.16)	1.20 (1.16, 1.24)	1.31 (1.26, 1.36)	1.34 (1.28, 1.39)	<.001
MV-adjusted model	Ref.	1.00 (0.97, 1.04)	1.01 (0.97, 1.05)	1.05 (1.00, 1.10)	1.02 (0.97, 1.07)	0.14
Total ω-6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.92 (0.89, 0.95)	0.89 (0.86, 0.92)	0.86 (0.83, 0.89)	0.85 (0.82, 0.88)	<.001
MV-adjusted model	Ref.	0.97 (0.93, 1.00)	0.93 (0.90, 0.97)	0.90 (0.87, 0.94)	0.87 (0.83, 0.92)	<.001
Linoleic acid						
Age-adjusted model	Ref.	0.90 (0.87, 0.93)	0.86 (0.83, 0.89)	0.86 (0.83, 0.89)	0.83 (0.80, 0.85)	<.001
MV-adjusted model	Ref.	0.94 (0.90, 0.97)	0.89 (0.86, 0.93)	0.88 (0.85, 0.92)	0.83 (0.80, 0.87)	<.001
Arachidonic acid						
Age-adjusted model	Ref.	1.00 (0.96, 1.03)	0.98 (0.95, 1.02)	1.01 (0.97, 1.04)	1.07 (1.04, 1.11)	<.001
MV-adjusted model	Ref.	1.00 (0.96, 1.03)	0.98 (0.94, 1.02)	0.99 (0.95, 1.03)	1.01 (0.96, 1.07)	0.78

Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.91 (0.88, 0.94)	0.88 (0.85, 0.91)	0.86 (0.83, 0.89)	0.81 (0.78, 0.84)	<.001
MV-adjusted model	Ref.	0.98 (0.95, 1.02)	0.98 (0.94, 1.01)	0.98 (0.95, 1.02)	0.99 (0.95, 1.03)	0.82
α -linolenic acid						
Age-adjusted model	Ref.	0.97 (0.94, 1.01)	0.96 (0.93, 1.00)	0.97 (0.94, 1.01)	0.93 (0.90, 0.96)	<.001
MV-adjusted model	Ref.	0.99 (0.96, 1.03)	0.99 (0.95, 1.03)	1.00 (0.96, 1.04)	0.98 (0.94, 1.03)	0.52
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.93 (0.90, 0.96)	0.88 (0.85, 0.91)	0.85 (0.82, 0.89)	0.79 (0.77, 0.82)	<.001
MV-adjusted model	Ref.	0.98 (0.94, 1.01)	0.97 (0.93, 1.01)	0.99 (0.95, 1.03)	0.96 (0.92, 1.00)	0.25
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.00 (0.97, 1.04)	1.04 (1.01, 1.08)	1.05 (1.01, 1.08)	1.05 (1.01, 1.09)	<.001
MV-adjusted model	Ref.	0.98 (0.95, 1.02)	0.98 (0.95, 1.02)	0.97 (0.93, 1.01)	0.96 (0.92, 1.00)	0.03
Cardiovascular disease mortality						
Total fat						
Age-adjusted model	Ref.	1.04 (0.97, 1.11)	1.07 (1.00, 1.14)	1.13 (1.05, 1.22)	1.26 (1.17, 1.36)	<.001
MV-adjusted model	Ref.	0.96 (0.89, 1.02)	0.91 (0.84, 0.98)	0.88 (0.81, 0.95)	0.86 (0.79, 0.94)	<.001
Saturated fat						
Age-adjusted model	Ref.	1.10 (1.03, 1.18)	1.24 (1.16, 1.33)	1.29 (1.20, 1.38)	1.54 (1.42, 1.66)	<.001
MV-adjusted model	Ref.	1.03 (0.95, 1.11)	1.10 (1.01, 1.20)	1.05 (0.95, 1.15)	1.13 (1.01, 1.26)	0.05
Unsaturated fat						
Age-adjusted model	Ref.	1.01 (0.95, 1.08)	0.99 (0.93, 1.06)	1.01 (0.94, 1.09)	1.09 (1.01, 1.17)	0.06
MV-adjusted model	Ref.	0.93 (0.86, 1.00)	0.85 (0.78, 0.92)	0.82 (0.75, 0.89)	0.79 (0.72, 0.88)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.93 (0.87, 1.00)	0.85 (0.79, 0.91)	0.86 (0.80, 0.92)	0.85 (0.79, 0.91)	<.001
MV-adjusted model	Ref.	0.96 (0.89, 1.03)	0.86 (0.80, 0.93)	0.87 (0.80, 0.94)	0.85 (0.78, 0.92)	<.001
Monounsaturated fat						
Age-adjusted model	Ref.	1.04 (0.98, 1.11)	1.03 (0.96, 1.10)	1.11 (1.04, 1.20)	1.20 (1.11, 1.29)	<.001
MV-adjusted model	Ref.	0.98 (0.90, 1.06)	0.91 (0.83, 1.00)	0.93 (0.83, 1.03)	0.90 (0.79, 1.02)	0.09
trans fat						
Age-adjusted model	Ref.	1.12 (1.05, 1.20)	1.22 (1.14, 1.30)	1.26 (1.17, 1.36)	1.35 (1.25, 1.46)	<.001
MV-adjusted model	Ref.	1.00 (0.93, 1.08)	1.02 (0.94, 1.11)	1.03 (0.94, 1.12)	1.04 (0.94, 1.16)	0.31

Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.91 (0.85, 0.97)	0.85 (0.79, 0.91)	0.86 (0.80, 0.92)	0.84 (0.78, 0.90)	<.001
MV-adjusted model	Ref.	0.94 (0.88, 1.01)	0.88 (0.82, 0.95)	0.89 (0.81, 0.97)	0.86 (0.78, 0.94)	0.001
Linoleic acid						
Age-adjusted model	Ref.	0.92 (0.86, 0.98)	0.83 (0.77, 0.89)	0.87 (0.81, 0.93)	0.82 (0.76, 0.88)	<.001
MV-adjusted model	Ref.	0.95 (0.88, 1.02)	0.85 (0.78, 0.92)	0.88 (0.81, 0.96)	0.82 (0.75, 0.90)	<.001
Arachidonic acid						
Age-adjusted model	Ref.	1.06 (0.99, 1.13)	1.08 (1.00, 1.16)	1.11 (1.03, 1.19)	1.23 (1.14, 1.32)	<.001
MV-adjusted model	Ref.	1.06 (0.99, 1.14)	1.06 (0.98, 1.15)	1.06 (0.97, 1.16)	1.09 (0.98, 1.21)	0.18
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.91 (0.84, 0.97)	0.90 (0.84, 0.97)	0.87 (0.81, 0.93)	0.84 (0.79, 0.91)	<.001
MV-adjusted model	Ref.	0.97 (0.90, 1.05)	0.99 (0.92, 1.07)	0.98 (0.91, 1.06)	1.00 (0.92, 1.09)	0.71
α -linolenic acid						
Age-adjusted model	Ref.	0.93 (0.86, 0.99)	0.95 (0.89, 1.03)	0.91 (0.85, 0.98)	0.90 (0.84, 0.97)	0.007
MV-adjusted model	Ref.	0.93 (0.86, 1.00)	0.96 (0.89, 1.04)	0.92 (0.85, 1.00)	0.92 (0.85, 1.01)	0.10
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.96 (0.89, 1.03)	0.87 (0.81, 0.94)	0.92 (0.86, 0.99)	0.85 (0.79, 0.92)	0.004
MV-adjusted model	Ref.	1.01 (0.93, 1.08)	0.96 (0.89, 1.04)	1.07 (0.99, 1.16)	1.02 (0.93, 1.11)	0.25
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	0.98 (0.91, 1.04)	0.97 (0.90, 1.04)	0.97 (0.91, 1.05)	0.97 (0.91, 1.05)	0.44
MV-adjusted model	Ref.	0.96 (0.90, 1.03)	0.92 (0.85, 0.99)	0.91 (0.85, 0.99)	0.91 (0.84, 0.99)	0.02
Cancer mortality						
Total fat						
Age-adjusted model	Ref.	1.03 (0.97, 1.09)	1.12 (1.06, 1.19)	1.18 (1.12, 1.25)	1.25 (1.17, 1.33)	<.001
MV-adjusted model	Ref.	0.97 (0.92, 1.03)	1.01 (0.95, 1.07)	1.01 (0.95, 1.07)	0.98 (0.92, 1.06)	0.92
Saturated fat						
Age-adjusted model	Ref.	1.09 (1.03, 1.15)	1.19 (1.12, 1.26)	1.28 (1.21, 1.36)	1.38 (1.30, 1.48)	<.001
MV-adjusted model	Ref.	1.05 (0.99, 1.12)	1.10 (1.03, 1.18)	1.12 (1.04, 1.21)	1.12 (1.02, 1.22)	0.02
Unsaturated fat						
Age-adjusted model	Ref.	1.02 (0.96, 1.07)	1.03 (0.97, 1.09)	1.10 (1.04, 1.17)	1.12 (1.05, 1.19)	<.001
MV-adjusted model	Ref.	0.97 (0.91, 1.03)	0.94 (0.88, 1.00)	0.96 (0.89, 1.03)	0.92 (0.85, 1.00)	0.08

Polyunsaturated fat						
Age-adjusted model	Ref.	0.91 (0.86, 0.96)	0.92 (0.86, 0.97)	0.93 (0.88, 0.98)	0.92 (0.86, 0.97)	0.02
MV-adjusted model	Ref.	0.94 (0.88, 0.99)	0.93 (0.88, 0.99)	0.94 (0.88, 1.00)	0.90 (0.84, 0.97)	0.02
Monounsaturated fat						
Age-adjusted model	Ref.	1.03 (0.98, 1.09)	1.09 (1.03, 1.15)	1.16 (1.09, 1.23)	1.21 (1.14, 1.29)	<.001
MV-adjusted model	Ref.	0.99 (0.93, 1.06)	1.00 (0.93, 1.08)	1.02 (0.94, 1.11)	1.01 (0.91, 1.11)	0.64
trans fat						
Age-adjusted model	Ref.	1.03 (0.97, 1.08)	1.05 (0.99, 1.11)	1.16 (1.10, 1.23)	1.14 (1.07, 1.22)	<.001
MV-adjusted model	Ref.	0.93 (0.88, 0.99)	0.91 (0.85, 0.97)	0.97 (0.90, 1.04)	0.92 (0.85, 1.00)	0.21
Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.95 (0.89, 1.00)	0.93 (0.88, 0.98)	0.94 (0.88, 0.99)	0.92 (0.87, 0.98)	0.009
MV-adjusted model	Ref.	0.98 (0.92, 1.03)	0.95 (0.89, 1.02)	0.95 (0.89, 1.02)	0.90 (0.83, 0.97)	0.006
Linoleic acid						
Age-adjusted model	Ref.	0.93 (0.88, 0.98)	0.90 (0.85, 0.95)	0.92 (0.87, 0.97)	0.91 (0.85, 0.96)	0.002
MV-adjusted model	Ref.	0.95 (0.89, 1.00)	0.91 (0.85, 0.97)	0.91 (0.85, 0.98)	0.87 (0.80, 0.94)	<.001
Arachidonic acid						
Age-adjusted model	Ref.	1.01 (0.95, 1.07)	1.01 (0.95, 1.07)	1.06 (1.00, 1.13)	1.12 (1.05, 1.18)	<.001
MV-adjusted model	Ref.	1.00 (0.94, 1.06)	0.99 (0.93, 1.06)	1.04 (0.97, 1.12)	1.06 (0.97, 1.15)	0.16
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.96 (0.90, 1.02)	0.95 (0.89, 1.00)	0.93 (0.88, 0.99)	0.95 (0.89, 1.00)	0.07
MV-adjusted model	Ref.	1.00 (0.95, 1.07)	1.01 (0.95, 1.07)	1.01 (0.95, 1.08)	1.05 (0.98, 1.13)	0.11
α -linolenic acid						
Age-adjusted model	Ref.	1.04 (0.98, 1.10)	1.03 (0.97, 1.10)	1.06 (1.00, 1.13)	1.07 (1.01, 1.13)	0.02
MV-adjusted model	Ref.	1.05 (0.98, 1.11)	1.04 (0.98, 1.11)	1.06 (1.00, 1.14)	1.07 (1.00, 1.15)	0.07
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.92 (0.87, 0.98)	0.91 (0.85, 0.96)	0.91 (0.85, 0.96)	0.86 (0.81, 0.91)	<.001
MV-adjusted model	Ref.	0.94 (0.89, 1.00)	0.95 (0.89, 1.01)	0.98 (0.92, 1.05)	0.95 (0.88, 1.01)	0.64
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	0.97 (0.92, 1.03)	1.01 (0.95, 1.07)	1.01 (0.95, 1.06)	0.96 (0.91, 1.02)	0.47
MV-adjusted model	Ref.	0.96 (0.91, 1.02)	0.98 (0.92, 1.04)	0.96 (0.91, 1.03)	0.92 (0.86, 0.98)	0.01

Neurodegenerative disease mortality						
Total fat						
Age-adjusted model	Ref.	1.08 (0.98, 1.19)	1.05 (0.94, 1.17)	0.98 (0.87, 1.11)	1.09 (0.95, 1.26)	0.54
MV-adjusted model	Ref.	1.01 (0.92, 1.12)	0.91 (0.81, 1.02)	0.76 (0.66, 0.87)	0.74 (0.63, 0.87)	<.001
Saturated fat						
Age-adjusted model	Ref.	1.21 (1.10, 1.33)	1.25 (1.12, 1.39)	1.34 (1.19, 1.51)	1.41 (1.21, 1.63)	<.001
MV-adjusted model	Ref.	1.22 (1.09, 1.36)	1.18 (1.03, 1.35)	1.17 (1.00, 1.38)	1.05 (0.86, 1.28)	0.48
Unsaturated fat						
Age-adjusted model	Ref.	0.94 (0.85, 1.03)	0.91 (0.82, 1.02)	0.99 (0.88, 1.11)	0.88 (0.77, 1.01)	0.06
MV-adjusted model	Ref.	0.85 (0.76, 0.94)	0.75 (0.66, 0.85)	0.76 (0.66, 0.87)	0.64 (0.54, 0.75)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.91 (0.81, 1.01)	0.88 (0.79, 0.98)	0.77 (0.68, 0.87)	0.75 (0.67, 0.85)	<.001
MV-adjusted model	Ref.	1.00 (0.90, 1.12)	0.99 (0.88, 1.11)	0.89 (0.78, 1.01)	0.90 (0.78, 1.03)	0.07
Monounsaturated fat						
Age-adjusted model	Ref.	0.95 (0.86, 1.05)	1.07 (0.96, 1.19)	0.97 (0.86, 1.09)	0.97 (0.85, 1.12)	0.69
MV-adjusted model	Ref.	0.81 (0.72, 0.91)	0.83 (0.72, 0.95)	0.68 (0.57, 0.80)	0.63 (0.52, 0.78)	<.001
trans fat						
Age-adjusted model	Ref.	1.18 (1.07, 1.31)	1.28 (1.15, 1.43)	1.52 (1.35, 1.72)	1.65 (1.43, 1.91)	<.001
MV-adjusted model	Ref.	1.05 (0.94, 1.17)	1.04 (0.91, 1.18)	1.14 (0.99, 1.32)	1.09 (0.92, 1.31)	0.06
Total ω-6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.95 (0.85, 1.06)	0.89 (0.79, 0.99)	0.82 (0.72, 0.92)	0.80 (0.71, 0.90)	<.001
MV-adjusted model	Ref.	1.06 (0.95, 1.19)	1.04 (0.92, 1.18)	1.00 (0.87, 1.16)	1.01 (0.87, 1.19)	0.92
Linoleic acid						
Age-adjusted model	Ref.	0.89 (0.80, 1.00)	0.88 (0.79, 0.98)	0.77 (0.69, 0.87)	0.78 (0.69, 0.88)	<.001
MV-adjusted model	Ref.	1.00 (0.89, 1.12)	1.02 (0.90, 1.16)	0.94 (0.82, 1.08)	0.98 (0.84, 1.15)	0.69
Arachidonic acid						
Age-adjusted model	Ref.	0.90 (0.81, 1.00)	0.85 (0.76, 0.95)	0.83 (0.74, 0.93)	0.82 (0.73, 0.93)	<.001
MV-adjusted model	Ref.	0.92 (0.82, 1.02)	0.87 (0.77, 0.99)	0.88 (0.76, 1.01)	0.94 (0.79, 1.11)	0.32
Total ω-3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.90 (0.80, 1.01)	0.78 (0.70, 0.88)	0.73 (0.65, 0.82)	0.63 (0.56, 0.70)	<.001
MV-adjusted model	Ref.	0.99 (0.88, 1.12)	0.91 (0.81, 1.03)	0.90 (0.79, 1.02)	0.86 (0.75, 0.99)	0.006

α -linolenic acid						
Age-adjusted model	Ref.	0.95 (0.85, 1.06)	0.84 (0.75, 0.94)	0.80 (0.71, 0.90)	0.70 (0.63, 0.78)	<.001
MV-adjusted model	Ref.	1.01 (0.90, 1.14)	0.91 (0.81, 1.04)	0.90 (0.78, 1.02)	0.87 (0.76, 1.01)	0.02
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.99 (0.88, 1.12)	0.98 (0.87, 1.10)	0.87 (0.78, 0.99)	0.75 (0.67, 0.85)	<.001
MV-adjusted model	Ref.	1.08 (0.96, 1.22)	1.10 (0.97, 1.24)	1.04 (0.92, 1.19)	1.01 (0.88, 1.15)	0.41
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.13 (1.01, 1.27)	1.15 (1.03, 1.29)	1.22 (1.08, 1.37)	1.34 (1.19, 1.51)	<.001
MV-adjusted model	Ref.	1.11 (0.99, 1.25)	1.08 (0.96, 1.22)	1.12 (0.98, 1.27)	1.16 (1.02, 1.32)	0.04
Respiratory disease mortality						
Total fat						
Age-adjusted model	Ref.	1.11 (0.98, 1.25)	1.36 (1.20, 1.53)	1.62 (1.43, 1.83)	1.87 (1.64, 2.14)	<.001
MV-adjusted model	Ref.	0.96 (0.85, 1.08)	1.03 (0.91, 1.18)	1.04 (0.91, 1.19)	1.03 (0.89, 1.20)	0.43
Saturated fat						
Age-adjusted model	Ref.	1.29 (1.15, 1.46)	1.59 (1.40, 1.80)	2.22 (1.96, 2.51)	2.64 (2.31, 3.02)	<.001
MV-adjusted model	Ref.	1.15 (1.01, 1.32)	1.30 (1.12, 1.52)	1.61 (1.37, 1.89)	1.69 (1.40, 2.04)	<.001
Unsaturated fat						
Age-adjusted model	Ref.	1.10 (0.98, 1.24)	1.25 (1.11, 1.41)	1.22 (1.08, 1.39)	1.36 (1.19, 1.55)	<.001
MV-adjusted model	Ref.	0.88 (0.77, 0.99)	0.84 (0.73, 0.96)	0.68 (0.58, 0.79)	0.66 (0.55, 0.78)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.86 (0.76, 0.97)	0.91 (0.80, 1.02)	0.90 (0.80, 1.02)	0.88 (0.77, 0.99)	0.11
MV-adjusted model	Ref.	0.92 (0.81, 1.04)	0.94 (0.82, 1.07)	0.92 (0.80, 1.06)	0.87 (0.75, 1.01)	0.13
Monounsaturated fat						
Age-adjusted model	Ref.	1.21 (1.07, 1.35)	1.35 (1.20, 1.52)	1.56 (1.38, 1.76)	1.59 (1.39, 1.82)	<.001
MV-adjusted model	Ref.	0.94 (0.82, 1.08)	0.86 (0.74, 1.01)	0.81 (0.67, 0.97)	0.70 (0.56, 0.86)	<.001
trans fat						
Age-adjusted model	Ref.	1.38 (1.23, 1.56)	1.60 (1.42, 1.81)	1.84 (1.62, 2.09)	2.03 (1.76, 2.35)	<.001
MV-adjusted model	Ref.	1.09 (0.96, 1.24)	1.09 (0.94, 1.25)	1.15 (0.98, 1.35)	1.19 (0.99, 1.42)	0.08
Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.92 (0.81, 1.04)	0.94 (0.83, 1.07)	0.89 (0.78, 1.01)	0.94 (0.83, 1.07)	0.32
MV-adjusted model	Ref.	1.00 (0.88, 1.13)	1.02 (0.88, 1.17)	0.96 (0.83, 1.12)	0.97 (0.82, 1.15)	0.58

Linoleic acid						
Age-adjusted model	Ref.	0.87 (0.77, 0.98)	0.91 (0.81, 1.03)	0.90 (0.80, 1.02)	0.88 (0.78, 1.00)	0.11
MV-adjusted model	Ref.	0.93 (0.82, 1.05)	0.95 (0.83, 1.09)	0.93 (0.80, 1.08)	0.87 (0.74, 1.02)	0.11
Arachidonic acid						
Age-adjusted model	Ref.	1.01 (0.91, 1.14)	0.95 (0.85, 1.08)	0.99 (0.87, 1.12)	0.99 (0.87, 1.12)	0.63
MV-adjusted model	Ref.	1.08 (0.95, 1.22)	1.06 (0.92, 1.21)	1.13 (0.96, 1.31)	1.13 (0.94, 1.36)	0.21
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.84 (0.74, 0.95)	0.81 (0.72, 0.92)	0.76 (0.67, 0.86)	0.71 (0.63, 0.80)	<.001
MV-adjusted model	Ref.	0.93 (0.82, 1.06)	0.93 (0.81, 1.06)	0.92 (0.80, 1.06)	0.95 (0.82, 1.10)	0.50
α -linolenic acid						
Age-adjusted model	Ref.	0.93 (0.82, 1.06)	0.97 (0.85, 1.10)	1.03 (0.91, 1.17)	1.03 (0.92, 1.17)	0.24
MV-adjusted model	Ref.	0.92 (0.81, 1.05)	0.93 (0.81, 1.06)	0.94 (0.82, 1.08)	0.96 (0.83, 1.12)	0.86
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.85 (0.75, 0.96)	0.74 (0.66, 0.84)	0.63 (0.56, 0.72)	0.57 (0.51, 0.65)	<.001
MV-adjusted model	Ref.	0.96 (0.85, 1.09)	0.92 (0.81, 1.05)	0.88 (0.77, 1.01)	0.92 (0.79, 1.06)	0.19
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.07 (0.95, 1.21)	1.16 (1.03, 1.32)	1.23 (1.08, 1.39)	1.38 (1.21, 1.56)	<.001
MV-adjusted model	Ref.	1.00 (0.88, 1.13)	0.98 (0.86, 1.12)	1.00 (0.87, 1.14)	1.08 (0.94, 1.25)	0.23

Abbreviations: HR, hazard ratio; CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MV, multivariable; NHS, Nurses' Health Study; HPFS, Health Professional Follow-up Study.

Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, ≥ 35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥ 27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥ 25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, ≥ 15 g/d; men: 0, 0.1-4.9, 5.0-29.9, ≥ 30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), intakes of total energy, dietary cholesterol and percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models also included percentages of energy intake from remaining fatty acids (saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, *trans* fatty acids, ω -6 polyunsaturated fatty acids, ω -3 polyunsaturated fatty acids, linoleic acid, arachidonic acid, α -linolenic acid and marine ω -3 fats, all in quintiles).

Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 9. Associations Between Total and Specific Types of Fat Intakes and Total and Cause-Specific Mortality From the Sensitivity Analysis Further Adjusting for the Alternate Healthy Eating Index-2010 Without Component Scores for Fatty Acids (Comparison is Isocaloric Substitution for Carbohydrate)

	Quintile of dietary fatty acid intake					<i>P</i> _{trend}
	Q1	Q2	Q3	Q4	Q5	
Total mortality						
Total fat						
Age-adjusted model	Ref.	1.03 (1.00, 1.07)	1.13 (1.09, 1.16)	1.18 (1.15, 1.23)	1.29 (1.24, 1.33)	<.001
MV-adjusted model	Ref.	0.94 (0.91, 0.97)	0.93 (0.90, 0.96)	0.88 (0.85, 0.91)	0.82 (0.79, 0.86)	<.001
Saturated fat						
Age-adjusted model	Ref.	1.16 (1.12, 1.19)	1.32 (1.27, 1.36)	1.45 (1.40, 1.50)	1.71 (1.65, 1.78)	<.001
MV-adjusted model	Ref.	1.03 (0.99, 1.06)	1.07 (1.03, 1.12)	1.06 (1.02, 1.11)	1.07 (1.01, 1.13)	<.001
Unsaturated fat						
Age-adjusted model	Ref.	0.98 (0.95, 1.01)	1.02 (0.98, 1.05)	1.02 (0.98, 1.05)	1.03 (0.99, 1.07)	0.04
MV-adjusted model	Ref.	0.89 (0.86, 0.92)	0.85 (0.82, 0.88)	0.81 (0.77, 0.84)	0.77 (0.73, 0.80)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.91 (0.88, 0.94)	0.85 (0.82, 0.88)	0.81 (0.78, 0.84)	0.72 (0.70, 0.75)	<.001
MV-adjusted model	Ref.	0.97 (0.94, 1.00)	0.91 (0.87, 0.94)	0.88 (0.84, 0.91)	0.82 (0.78, 0.85)	<.001
Monounsaturated fat						
Age-adjusted model	Ref.	1.05 (1.02, 1.08)	1.10 (1.07, 1.14)	1.17 (1.13, 1.21)	1.22 (1.17, 1.26)	<.001
MV-adjusted model	Ref.	0.95 (0.92, 0.99)	0.94 (0.90, 0.98)	0.93 (0.89, 0.98)	0.90 (0.85, 0.95)	<.001
trans fat						
Age-adjusted model	Ref.	1.31 (1.27, 1.35)	1.49 (1.45, 1.55)	1.63 (1.57, 1.69)	1.73 (1.67, 1.80)	<.001
MV-adjusted model	Ref.	1.09 (1.05, 1.12)	1.11 (1.07, 1.16)	1.12 (1.07, 1.17)	1.09 (1.04, 1.15)	0.005
Total ω-6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.89 (0.86, 0.92)	0.86 (0.83, 0.88)	0.80 (0.77, 0.83)	0.75 (0.73, 0.78)	<.001
MV-adjusted model	Ref.	0.95 (0.92, 0.99)	0.92 (0.89, 0.96)	0.87 (0.84, 0.91)	0.85 (0.81, 0.89)	<.001
Linoleic acid						
Age-adjusted model	Ref.	0.90 (0.87, 0.93)	0.86 (0.83, 0.89)	0.81 (0.78, 0.83)	0.74 (0.71, 0.76)	<.001
MV-adjusted model	Ref.	0.96 (0.93, 0.99)	0.92 (0.88, 0.95)	0.87 (0.84, 0.91)	0.82 (0.79, 0.86)	<.001

Arachidonic acid						
Age-adjusted model	Ref.	1.00 (0.97, 1.04)	0.97 (0.94, 1.01)	1.00 (0.97, 1.03)	0.97 (0.94, 1.01)	0.13
MV-adjusted model	Ref.	0.98 (0.95, 1.02)	0.93 (0.90, 0.97)	0.93 (0.90, 0.97)	0.88 (0.84, 0.93)	<.001
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.89 (0.86, 0.92)	0.86 (0.83, 0.89)	0.82 (0.79, 0.85)	0.66 (0.64, 0.69)	<.001
MV-adjusted model	Ref.	0.99 (0.95, 1.02)	1.01 (0.97, 1.05)	1.02 (0.98, 1.06)	0.96 (0.92, 1.00)	0.07
α -linolenic acid						
Age-adjusted model	Ref.	0.96 (0.92, 0.99)	0.96 (0.93, 1.00)	0.93 (0.90, 0.96)	0.79 (0.76, 0.81)	<.001
MV-adjusted model	Ref.	1.00 (0.96, 1.04)	1.04 (1.00, 1.08)	1.03 (0.99, 1.07)	1.00 (0.96, 1.04)	0.91
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.98 (0.94, 1.01)	0.94 (0.91, 0.98)	0.86 (0.83, 0.89)	0.74 (0.71, 0.76)	<.001
MV-adjusted model	Ref.	1.04 (1.00, 1.07)	1.06 (1.02, 1.10)	1.03 (0.99, 1.07)	0.97 (0.93, 1.01)	0.007
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.11 (1.07, 1.15)	1.15 (1.11, 1.19)	1.18 (1.14, 1.22)	1.18 (1.14, 1.22)	<.001
MV-adjusted model	Ref.	1.03 (1.00, 1.07)	1.01 (0.97, 1.05)	1.01 (0.97, 1.04)	0.98 (0.94, 1.02)	0.09
Cardiovascular disease mortality						
Total fat						
Age-adjusted model	Ref.	1.05 (0.99, 1.12)	1.12 (1.05, 1.20)	1.16 (1.08, 1.24)	1.30 (1.21, 1.40)	<.001
MV-adjusted model	Ref.	0.96 (0.89, 1.02)	0.93 (0.86, 1.00)	0.87 (0.80, 0.94)	0.83 (0.76, 0.91)	<.001
Saturated fat						
Age-adjusted model	Ref.	1.18 (1.11, 1.26)	1.28 (1.19, 1.37)	1.41 (1.31, 1.51)	1.66 (1.54, 1.79)	<.001
MV-adjusted model	Ref.	1.05 (0.97, 1.13)	1.05 (0.97, 1.14)	1.04 (0.94, 1.14)	1.03 (0.93, 1.15)	0.40
Unsaturated fat						
Age-adjusted model	Ref.	1.01 (0.94, 1.07)	1.01 (0.94, 1.07)	1.02 (0.95, 1.09)	1.04 (0.97, 1.12)	0.22
MV-adjusted model	Ref.	0.92 (0.86, 0.99)	0.85 (0.79, 0.92)	0.82 (0.75, 0.89)	0.78 (0.71, 0.85)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.90 (0.84, 0.96)	0.86 (0.80, 0.92)	0.80 (0.74, 0.85)	0.75 (0.70, 0.81)	<.001
MV-adjusted model	Ref.	0.94 (0.88, 1.01)	0.89 (0.82, 0.95)	0.83 (0.77, 0.90)	0.82 (0.76, 0.89)	<.001
Monounsaturated fat						
Age-adjusted model	Ref.	1.06 (1.00, 1.13)	1.06 (0.99, 1.14)	1.14 (1.07, 1.23)	1.22 (1.13, 1.32)	<.001
MV-adjusted model	Ref.	0.98 (0.91, 1.05)	0.92 (0.85, 1.01)	0.93 (0.84, 1.03)	0.90 (0.80, 1.01)	0.03

trans fat						
Age-adjusted model	Ref.	1.25 (1.17, 1.33)	1.45 (1.35, 1.55)	1.52 (1.41, 1.64)	1.73 (1.60, 1.87)	<.001
MV-adjusted model	Ref.	1.05 (0.97, 1.12)	1.11 (1.02, 1.20)	1.09 (0.99, 1.19)	1.16 (1.04, 1.28)	0.02
Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.85 (0.79, 0.91)	0.82 (0.77, 0.88)	0.78 (0.72, 0.83)	0.76 (0.71, 0.82)	<.001
MV-adjusted model	Ref.	0.89 (0.83, 0.95)	0.86 (0.79, 0.92)	0.81 (0.74, 0.88)	0.81 (0.74, 0.89)	<.001
Linoleic acid						
Age-adjusted model	Ref.	0.89 (0.84, 0.96)	0.84 (0.78, 0.90)	0.79 (0.73, 0.84)	0.75 (0.69, 0.80)	<.001
MV-adjusted model	Ref.	0.92 (0.86, 0.99)	0.86 (0.80, 0.93)	0.81 (0.74, 0.88)	0.79 (0.72, 0.86)	<.001
Arachidonic acid						
Age-adjusted model	Ref.	1.07 (1.00, 1.14)	1.01 (0.94, 1.08)	1.10 (1.03, 1.18)	1.15 (1.08, 1.24)	<.001
MV-adjusted model	Ref.	1.04 (0.97, 1.11)	0.94 (0.87, 1.02)	0.99 (0.90, 1.07)	0.98 (0.89, 1.08)	0.54
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.89 (0.82, 0.95)	0.87 (0.81, 0.93)	0.86 (0.80, 0.92)	0.73 (0.68, 0.79)	<.001
MV-adjusted model	Ref.	0.97 (0.90, 1.05)	1.01 (0.94, 1.09)	1.04 (0.96, 1.13)	1.01 (0.93, 1.10)	0.32
α -linolenic acid						
Age-adjusted model	Ref.	0.92 (0.86, 0.99)	0.93 (0.86, 1.00)	0.89 (0.83, 0.96)	0.79 (0.74, 0.85)	<.001
MV-adjusted model	Ref.	0.95 (0.88, 1.02)	0.98 (0.91, 1.06)	0.96 (0.89, 1.04)	0.94 (0.87, 1.03)	0.26
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.98 (0.92, 1.06)	0.95 (0.89, 1.02)	0.91 (0.84, 0.97)	0.83 (0.77, 0.89)	<.001
MV-adjusted model	Ref.	1.03 (0.96, 1.11)	1.06 (0.98, 1.14)	1.07 (0.99, 1.16)	1.05 (0.97, 1.14)	0.13
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.07 (1.00, 1.14)	1.08 (1.01, 1.15)	1.06 (0.98, 1.13)	1.07 (0.99, 1.15)	0.18
MV-adjusted model	Ref.	1.00 (0.94, 1.07)	0.96 (0.89, 1.03)	0.92 (0.85, 0.99)	0.91 (0.84, 0.99)	0.003
Cancer mortality						
Total fat						
Age-adjusted model	Ref.	1.04 (0.98, 1.10)	1.20 (1.14, 1.27)	1.20 (1.14, 1.27)	1.27 (1.20, 1.35)	<.001
MV-adjusted model	Ref.	0.96 (0.91, 1.02)	1.04 (0.98, 1.10)	0.96 (0.90, 1.02)	0.90 (0.84, 0.97)	0.009
Saturated fat						
Age-adjusted model	Ref.	1.10 (1.04, 1.16)	1.29 (1.23, 1.37)	1.40 (1.32, 1.48)	1.52 (1.42, 1.61)	<.001
MV-adjusted model	Ref.	1.02 (0.96, 1.08)	1.12 (1.04, 1.20)	1.11 (1.03, 1.20)	1.06 (0.97, 1.16)	0.05

Unsaturated fat						
Age-adjusted model	Ref.	1.02 (0.96, 1.07)	1.05 (0.99, 1.10)	1.10 (1.05, 1.17)	1.08 (1.02, 1.15)	<.001
MV-adjusted model	Ref.	0.96 (0.90, 1.01)	0.93 (0.87, 0.99)	0.94 (0.88, 1.00)	0.89 (0.82, 0.96)	0.002
Polyunsaturated fat						
Age-adjusted model	Ref.	0.98 (0.93, 1.03)	0.91 (0.86, 0.97)	0.93 (0.88, 0.98)	0.87 (0.82, 0.92)	<.001
MV-adjusted model	Ref.	1.04 (0.98, 1.10)	0.97 (0.92, 1.04)	0.99 (0.93, 1.06)	0.93 (0.87, 1.00)	0.03
Monounsaturated fat						
Age-adjusted model	Ref.	1.02 (0.96, 1.07)	1.12 (1.06, 1.18)	1.16 (1.10, 1.23)	1.20 (1.13, 1.28)	<.001
MV-adjusted model	Ref.	0.93 (0.88, 0.99)	0.96 (0.90, 1.03)	0.95 (0.88, 1.03)	0.93 (0.85, 1.02)	0.18
trans fat						
Age-adjusted model	Ref.	1.15 (1.09, 1.21)	1.22 (1.16, 1.30)	1.36 (1.28, 1.44)	1.36 (1.27, 1.45)	<.001
MV-adjusted model	Ref.	1.00 (0.94, 1.06)	0.97 (0.90, 1.03)	0.99 (0.92, 1.06)	0.92 (0.84, 1.00)	0.05
Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.93 (0.88, 0.99)	0.93 (0.88, 0.99)	0.90 (0.85, 0.95)	0.86 (0.81, 0.91)	<.001
MV-adjusted model	Ref.	0.99 (0.94, 1.05)	1.00 (0.93, 1.06)	0.96 (0.90, 1.03)	0.92 (0.85, 0.99)	0.02
Linoleic acid						
Age-adjusted model	Ref.	0.95 (0.90, 1.01)	0.93 (0.88, 0.98)	0.93 (0.88, 0.98)	0.86 (0.81, 0.91)	<.001
MV-adjusted model	Ref.	1.01 (0.96, 1.08)	0.98 (0.92, 1.05)	0.99 (0.92, 1.06)	0.92 (0.85, 0.99)	0.02
Arachidonic acid						
Age-adjusted model	Ref.	1.02 (0.97, 1.08)	1.00 (0.95, 1.06)	1.05 (1.00, 1.11)	1.03 (0.97, 1.09)	0.16
MV-adjusted model	Ref.	1.01 (0.95, 1.07)	0.97 (0.91, 1.03)	0.99 (0.93, 1.06)	0.93 (0.86, 1.01)	0.13
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.92 (0.87, 0.98)	0.94 (0.89, 1.00)	0.89 (0.84, 0.95)	0.80 (0.76, 0.85)	<.001
MV-adjusted model	Ref.	0.99 (0.94, 1.06)	1.05 (0.99, 1.12)	1.03 (0.97, 1.10)	1.00 (0.94, 1.08)	0.89
α -linolenic acid						
Age-adjusted model	Ref.	1.04 (0.98, 1.10)	1.07 (1.01, 1.13)	1.05 (0.99, 1.12)	0.99 (0.93, 1.05)	0.51
MV-adjusted model	Ref.	1.07 (1.01, 1.14)	1.12 (1.05, 1.19)	1.12 (1.05, 1.19)	1.13 (1.05, 1.21)	0.002
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.97 (0.91, 1.03)	0.97 (0.91, 1.03)	0.90 (0.84, 0.95)	0.81 (0.76, 0.86)	<.001
MV-adjusted model	Ref.	1.02 (0.96, 1.08)	1.06 (1.00, 1.13)	1.03 (0.97, 1.10)	0.98 (0.92, 1.05)	0.34

ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.08 (1.02, 1.14)	1.06 (1.01, 1.12)	1.11 (1.05, 1.18)	1.06 (1.00, 1.12)	0.03
MV-adjusted model	Ref.	1.04 (0.98, 1.10)	0.99 (0.93, 1.05)	1.01 (0.95, 1.08)	0.94 (0.88, 1.00)	0.03
Neurodegenerative disease mortality						
Total fat						
Age-adjusted model	Ref.	0.98 (0.89, 1.08)	0.95 (0.85, 1.06)	1.01 (0.90, 1.14)	1.03 (0.90, 1.18)	0.88
MV-adjusted model	Ref.	0.91 (0.82, 1.01)	0.80 (0.71, 0.89)	0.75 (0.66, 0.86)	0.64 (0.55, 0.76)	<.001
Saturated fat						
Age-adjusted model	Ref.	1.12 (1.01, 1.23)	1.25 (1.12, 1.39)	1.31 (1.17, 1.48)	1.56 (1.36, 1.79)	<.001
MV-adjusted model	Ref.	0.98 (0.88, 1.10)	1.01 (0.88, 1.15)	0.96 (0.82, 1.12)	0.94 (0.78, 1.14)	0.76
Unsaturated fat						
Age-adjusted model	Ref.	0.91 (0.83, 1.01)	0.90 (0.81, 1.00)	0.90 (0.80, 1.01)	0.80 (0.70, 0.91)	<.001
MV-adjusted model	Ref.	0.84 (0.75, 0.93)	0.76 (0.67, 0.85)	0.71 (0.62, 0.82)	0.62 (0.53, 0.73)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.91 (0.82, 1.01)	0.77 (0.69, 0.86)	0.63 (0.56, 0.71)	0.52 (0.46, 0.58)	<.001
MV-adjusted model	Ref.	1.06 (0.95, 1.19)	0.96 (0.85, 1.08)	0.85 (0.75, 0.96)	0.82 (0.71, 0.94)	<.001
Monounsaturated fat						
Age-adjusted model	Ref.	0.98 (0.89, 1.08)	1.06 (0.96, 1.19)	1.11 (0.98, 1.24)	1.04 (0.90, 1.19)	0.18
MV-adjusted model	Ref.	0.84 (0.74, 0.94)	0.83 (0.72, 0.96)	0.78 (0.66, 0.92)	0.71 (0.58, 0.87)	<.001
trans fat						
Age-adjusted model	Ref.	1.61 (1.45, 1.78)	2.07 (1.86, 2.32)	2.61 (2.31, 2.94)	2.53 (2.19, 2.92)	<.001
MV-adjusted model	Ref.	1.21 (1.08, 1.35)	1.30 (1.14, 1.48)	1.43 (1.23, 1.65)	1.27 (1.05, 1.52)	<.001
Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.89 (0.79, 0.99)	0.81 (0.72, 0.90)	0.64 (0.57, 0.72)	0.59 (0.52, 0.66)	<.001
MV-adjusted model	Ref.	1.05 (0.93, 1.17)	1.05 (0.93, 1.19)	0.91 (0.79, 1.05)	0.97 (0.83, 1.14)	0.41
Linoleic acid						
Age-adjusted model	Ref.	0.85 (0.76, 0.95)	0.80 (0.72, 0.90)	0.65 (0.58, 0.73)	0.55 (0.49, 0.62)	<.001
MV-adjusted model	Ref.	0.99 (0.89, 1.11)	1.04 (0.92, 1.18)	0.91 (0.79, 1.04)	0.90 (0.77, 1.05)	0.13
Arachidonic acid						
Age-adjusted model	Ref.	0.87 (0.79, 0.96)	0.84 (0.75, 0.94)	0.79 (0.71, 0.89)	0.69 (0.61, 0.77)	<.001
MV-adjusted model	Ref.	0.83 (0.75, 0.93)	0.80 (0.71, 0.91)	0.80 (0.70, 0.92)	0.79 (0.67, 0.93)	0.01

Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.90 (0.80, 1.00)	0.70 (0.63, 0.79)	0.65 (0.58, 0.73)	0.41 (0.36, 0.46)	<.001
MV-adjusted model	Ref.	1.02 (0.91, 1.14)	0.87 (0.77, 0.99)	0.95 (0.83, 1.08)	0.81 (0.70, 0.93)	<.001
α -linolenic acid						
Age-adjusted model	Ref.	0.89 (0.79, 0.99)	0.80 (0.71, 0.89)	0.66 (0.59, 0.74)	0.46 (0.41, 0.51)	<.001
MV-adjusted model	Ref.	0.98 (0.87, 1.10)	0.95 (0.84, 1.08)	0.88 (0.77, 1.01)	0.84 (0.73, 0.97)	0.003
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	1.07 (0.96, 1.20)	1.07 (0.96, 1.20)	0.90 (0.80, 1.02)	0.65 (0.58, 0.73)	<.001
MV-adjusted model	Ref.	1.12 (1.00, 1.26)	1.13 (1.00, 1.27)	1.03 (0.91, 1.17)	0.94 (0.82, 1.08)	0.02
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.23 (1.10, 1.38)	1.33 (1.19, 1.50)	1.56 (1.39, 1.75)	1.64 (1.45, 1.84)	<.001
MV-adjusted model	Ref.	1.09 (0.97, 1.23)	1.10 (0.97, 1.24)	1.19 (1.05, 1.35)	1.19 (1.04, 1.36)	0.005
Respiratory disease mortality						
Total fat						
Age-adjusted model	Ref.	1.19 (1.06, 1.33)	1.40 (1.24, 1.57)	1.63 (1.45, 1.84)	1.92 (1.69, 2.19)	<.001
MV-adjusted model	Ref.	0.96 (0.85, 1.08)	0.96 (0.85, 1.09)	0.94 (0.82, 1.07)	0.93 (0.80, 1.08)	0.32
Saturated fat						
Age-adjusted model	Ref.	1.40 (1.25, 1.58)	1.67 (1.48, 1.88)	2.21 (1.95, 2.50)	3.05 (2.68, 3.47)	<.001
MV-adjusted model	Ref.	1.12 (0.98, 1.28)	1.16 (1.00, 1.35)	1.31 (1.11, 1.54)	1.45 (1.21, 1.75)	<.001
Unsaturated fat						
Age-adjusted model	Ref.	1.04 (0.93, 1.17)	1.26 (1.12, 1.41)	1.21 (1.07, 1.37)	1.30 (1.14, 1.47)	<.001
MV-adjusted model	Ref.	0.84 (0.74, 0.95)	0.86 (0.75, 0.98)	0.72 (0.62, 0.84)	0.70 (0.60, 0.82)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.91 (0.81, 1.03)	0.89 (0.79, 1.00)	0.88 (0.78, 1.00)	0.74 (0.66, 0.84)	<.001
MV-adjusted model	Ref.	0.99 (0.87, 1.12)	0.94 (0.83, 1.07)	0.93 (0.81, 1.06)	0.83 (0.71, 0.96)	0.01
Monounsaturated fat						
Age-adjusted model	Ref.	1.29 (1.15, 1.44)	1.37 (1.22, 1.55)	1.61 (1.42, 1.81)	1.66 (1.45, 1.89)	<.001
MV-adjusted model	Ref.	1.01 (0.88, 1.15)	0.92 (0.79, 1.07)	0.90 (0.76, 1.07)	0.80 (0.65, 0.98)	0.01
trans fat						
Age-adjusted model	Ref.	1.57 (1.39, 1.76)	2.01 (1.78, 2.27)	2.19 (1.92, 2.50)	2.79 (2.42, 3.21)	<.001
MV-adjusted model	Ref.	1.10 (0.96, 1.24)	1.13 (0.98, 1.31)	1.07 (0.91, 1.26)	1.20 (1.00, 1.45)	0.12

Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.89 (0.79, 1.00)	0.85 (0.75, 0.96)	0.87 (0.77, 0.98)	0.77 (0.68, 0.88)	<.001
MV-adjusted model	Ref.	0.96 (0.85, 1.09)	0.91 (0.79, 1.04)	0.92 (0.80, 1.07)	0.84 (0.71, 1.00)	0.06
Linoleic acid						
Age-adjusted model	Ref.	0.91 (0.80, 1.02)	0.88 (0.78, 0.99)	0.86 (0.76, 0.97)	0.76 (0.67, 0.86)	<.001
MV-adjusted model	Ref.	0.98 (0.86, 1.11)	0.93 (0.81, 1.06)	0.90 (0.78, 1.04)	0.82 (0.69, 0.97)	0.01
Arachidonic acid						
Age-adjusted model	Ref.	1.02 (0.91, 1.14)	1.01 (0.90, 1.14)	0.95 (0.84, 1.07)	0.87 (0.77, 0.99)	0.01
MV-adjusted model	Ref.	1.05 (0.93, 1.18)	1.07 (0.94, 1.22)	1.03 (0.88, 1.19)	1.01 (0.84, 1.20)	0.76
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.86 (0.76, 0.97)	0.81 (0.71, 0.91)	0.79 (0.70, 0.89)	0.56 (0.49, 0.63)	<.001
MV-adjusted model	Ref.	0.98 (0.86, 1.11)	0.97 (0.85, 1.10)	1.04 (0.91, 1.20)	0.92 (0.79, 1.07)	0.29
α -linolenic acid						
Age-adjusted model	Ref.	0.99 (0.87, 1.12)	1.08 (0.96, 1.23)	1.00 (0.88, 1.13)	0.89 (0.79, 1.01)	0.04
MV-adjusted model	Ref.	1.00 (0.87, 1.14)	1.11 (0.97, 1.27)	1.02 (0.88, 1.17)	1.07 (0.92, 1.25)	0.40
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.91 (0.81, 1.02)	0.83 (0.74, 0.94)	0.68 (0.60, 0.77)	0.52 (0.46, 0.59)	<.001
MV-adjusted model	Ref.	1.04 (0.92, 1.17)	1.06 (0.94, 1.20)	1.02 (0.89, 1.16)	0.91 (0.79, 1.05)	0.04
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.25 (1.11, 1.42)	1.39 (1.23, 1.58)	1.38 (1.22, 1.57)	1.66 (1.46, 1.89)	<.001
MV-adjusted model	Ref.	1.08 (0.95, 1.23)	1.07 (0.94, 1.22)	0.99 (0.87, 1.14)	1.14 (0.99, 1.32)	0.16

Abbreviations: HR, hazard ratio; CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MV, multivariable; NHS, Nurses' Health Study; HPFS, Health Professional Follow-up Study.

Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, ≥ 35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥ 27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥ 25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, ≥ 15 g/d; men: 0, 0.1-4.9, 5.0-29.9, ≥ 30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), intakes of total energy, dietary cholesterol and percentage of energy intake from dietary protein (quintiles), the Alternate Healthy Eating Index-2010 without component scores for fatty acids and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models also included percentages of energy intake from remaining fatty acids (saturated fatty acids, polyunsaturated fatty acids,

monounsaturated fatty acids, *trans* fatty acids, ω -6 polyunsaturated fatty acids, ω -3 polyunsaturated fatty acids, linoleic acid, arachidonic acid, α -linolenic acid and marine ω -3 fats, all in quintiles).

Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 10. Associations Between Total and Specific Types of Fat Intakes and Total and Cause-Specific Mortality From the Sensitivity Analysis Restricted to Participants Without History of Hypertension and/or Hypercholesterolemia at Baseline (Comparison is Isocaloric Substitution for Carbohydrate)

	Quintile of dietary fatty acid intake					<i>P</i> _{trend}
	Q1	Q2	Q3	Q4	Q5	
Total mortality						
Total fat						
Age-adjusted model	Ref.	1.03 (1.00, 1.07)	1.13 (1.09, 1.17)	1.21 (1.16, 1.26)	1.30 (1.24, 1.35)	<.001
MV-adjusted model	Ref.	0.96 (0.92, 0.99)	0.95 (0.91, 0.99)	0.91 (0.87, 0.96)	0.84 (0.79, 0.88)	<.001
Saturated fat						
Age-adjusted model	Ref.	1.14 (1.10, 1.19)	1.34 (1.29, 1.39)	1.49 (1.43, 1.55)	1.72 (1.64, 1.80)	<.001
MV-adjusted model	Ref.	1.02 (0.98, 1.07)	1.10 (1.05, 1.16)	1.08 (1.03, 1.14)	1.06 (1.00, 1.13)	<.001
Unsaturated fat						
Age-adjusted model	Ref.	0.98 (0.94, 1.02)	1.01 (0.97, 1.05)	1.05 (1.00, 1.09)	1.02 (0.97, 1.06)	0.11
MV-adjusted model	Ref.	0.87 (0.84, 0.91)	0.83 (0.79, 0.87)	0.80 (0.76, 0.84)	0.73 (0.69, 0.77)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.91 (0.87, 0.95)	0.85 (0.82, 0.89)	0.82 (0.79, 0.85)	0.72 (0.69, 0.75)	<.001
MV-adjusted model	Ref.	0.96 (0.93, 1.00)	0.91 (0.87, 0.95)	0.87 (0.83, 0.91)	0.81 (0.77, 0.85)	<.001
Monounsaturated fat						
Age-adjusted model	Ref.	1.05 (1.01, 1.09)	1.10 (1.06, 1.15)	1.20 (1.15, 1.25)	1.20 (1.15, 1.26)	<.001
MV-adjusted model	Ref.	0.94 (0.90, 0.99)	0.91 (0.87, 0.96)	0.92 (0.87, 0.98)	0.86 (0.80, 0.92)	<.001
trans fat						
Age-adjusted model	Ref.	1.30 (1.25, 1.35)	1.50 (1.44, 1.57)	1.68 (1.61, 1.76)	1.75 (1.67, 1.84)	<.001
MV-adjusted model	Ref.	1.11 (1.06, 1.16)	1.17 (1.11, 1.22)	1.20 (1.14, 1.27)	1.16 (1.09, 1.23)	<.001
Total ω-6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.89 (0.85, 0.93)	0.86 (0.83, 0.90)	0.80 (0.77, 0.84)	0.75 (0.72, 0.78)	<.001
MV-adjusted model	Ref.	0.95 (0.91, 1.00)	0.94 (0.89, 0.98)	0.87 (0.83, 0.92)	0.85 (0.80, 0.90)	<.001
Linoleic acid						
Age-adjusted model	Ref.	0.89 (0.86, 0.93)	0.87 (0.84, 0.91)	0.81 (0.77, 0.84)	0.74 (0.71, 0.77)	<.001
MV-adjusted model	Ref.	0.95 (0.91, 1.00)	0.94 (0.90, 0.98)	0.87 (0.83, 0.91)	0.83 (0.78, 0.87)	<.001

Arachidonic acid						
Age-adjusted model	Ref.	1.03 (0.99, 1.07)	0.97 (0.93, 1.01)	0.99 (0.95, 1.04)	0.97 (0.93, 1.01)	0.09
MV-adjusted model	Ref.	1.01 (0.97, 1.05)	0.94 (0.89, 0.98)	0.94 (0.90, 0.99)	0.91 (0.86, 0.96)	<.001
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.90 (0.86, 0.93)	0.88 (0.84, 0.91)	0.83 (0.79, 0.86)	0.65 (0.63, 0.68)	<.001
MV-adjusted model	Ref.	0.98 (0.94, 1.03)	1.01 (0.96, 1.05)	1.01 (0.97, 1.06)	0.93 (0.88, 0.98)	0.005
α -linolenic acid						
Age-adjusted model	Ref.	0.95 (0.91, 0.99)	0.97 (0.93, 1.01)	0.93 (0.90, 0.97)	0.79 (0.75, 0.82)	<.001
MV-adjusted model	Ref.	0.99 (0.94, 1.03)	1.04 (0.99, 1.08)	1.02 (0.97, 1.07)	0.98 (0.93, 1.03)	0.49
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.98 (0.94, 1.03)	0.95 (0.91, 0.99)	0.85 (0.82, 0.89)	0.73 (0.70, 0.76)	<.001
MV-adjusted model	Ref.	1.05 (1.00, 1.09)	1.06 (1.01, 1.10)	1.02 (0.97, 1.07)	0.96 (0.92, 1.01)	0.003
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.12 (1.08, 1.17)	1.15 (1.11, 1.20)	1.20 (1.15, 1.25)	1.21 (1.16, 1.26)	<.001
MV-adjusted model	Ref.	1.05 (1.00, 1.09)	1.03 (0.98, 1.07)	1.03 (0.99, 1.08)	1.01 (0.96, 1.06)	0.86
Cardiovascular disease mortality						
Total fat						
Age-adjusted model	Ref.	0.98 (0.90, 1.07)	1.15 (1.05, 1.25)	1.17 (1.07, 1.28)	1.36 (1.24, 1.50)	<.001
MV-adjusted model	Ref.	0.91 (0.83, 0.99)	0.96 (0.88, 1.06)	0.88 (0.80, 0.97)	0.88 (0.79, 0.98)	0.03
Saturated fat						
Age-adjusted model	Ref.	1.14 (1.05, 1.25)	1.31 (1.20, 1.43)	1.46 (1.33, 1.60)	1.75 (1.59, 1.93)	<.001
MV-adjusted model	Ref.	1.02 (0.93, 1.13)	1.09 (0.98, 1.21)	1.06 (0.94, 1.20)	1.08 (0.94, 1.24)	0.06
Unsaturated fat						
Age-adjusted model	Ref.	0.99 (0.91, 1.07)	1.00 (0.92, 1.09)	1.04 (0.95, 1.14)	1.08 (0.98, 1.19)	0.08
MV-adjusted model	Ref.	0.88 (0.80, 0.96)	0.82 (0.74, 0.91)	0.79 (0.71, 0.88)	0.76 (0.68, 0.86)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.92 (0.84, 1.01)	0.86 (0.79, 0.94)	0.81 (0.74, 0.89)	0.77 (0.70, 0.84)	<.001
MV-adjusted model	Ref.	0.95 (0.87, 1.04)	0.89 (0.81, 0.98)	0.83 (0.75, 0.92)	0.81 (0.73, 0.91)	<.001
Monounsaturated fat						
Age-adjusted model	Ref.	1.05 (0.97, 1.14)	1.06 (0.97, 1.16)	1.19 (1.08, 1.30)	1.24 (1.13, 1.37)	<.001
MV-adjusted model	Ref.	0.95 (0.86, 1.05)	0.90 (0.80, 1.01)	0.92 (0.81, 1.05)	0.88 (0.75, 1.02)	0.03

trans fat						
Age-adjusted model	Ref.	1.27 (1.17, 1.38)	1.44 (1.32, 1.57)	1.62 (1.47, 1.78)	1.74 (1.56, 1.93)	<.001
MV-adjusted model	Ref.	1.11 (1.01, 1.22)	1.16 (1.04, 1.28)	1.21 (1.08, 1.36)	1.20 (1.05, 1.37)	0.008
Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.84 (0.77, 0.92)	0.83 (0.76, 0.91)	0.78 (0.71, 0.86)	0.77 (0.70, 0.84)	<.001
MV-adjusted model	Ref.	0.88 (0.80, 0.97)	0.88 (0.80, 0.98)	0.82 (0.73, 0.91)	0.82 (0.73, 0.93)	0.002
Linoleic acid						
Age-adjusted model	Ref.	0.91 (0.83, 0.99)	0.84 (0.77, 0.92)	0.80 (0.73, 0.87)	0.76 (0.70, 0.84)	<.001
MV-adjusted model	Ref.	0.95 (0.86, 1.04)	0.88 (0.79, 0.97)	0.82 (0.74, 0.92)	0.80 (0.71, 0.90)	<.001
Arachidonic acid						
Age-adjusted model	Ref.	1.07 (0.98, 1.17)	1.00 (0.91, 1.09)	1.04 (0.95, 1.14)	1.12 (1.02, 1.23)	0.04
MV-adjusted model	Ref.	1.04 (0.94, 1.14)	0.94 (0.84, 1.04)	0.93 (0.83, 1.05)	0.95 (0.83, 1.08)	0.19
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.90 (0.81, 0.98)	0.87 (0.79, 0.96)	0.85 (0.77, 0.93)	0.73 (0.66, 0.80)	<.001
MV-adjusted model	Ref.	0.97 (0.88, 1.07)	0.98 (0.89, 1.08)	1.01 (0.91, 1.11)	0.98 (0.87, 1.09)	0.99
α -linolenic acid						
Age-adjusted model	Ref.	0.91 (0.83, 1.00)	0.92 (0.84, 1.01)	0.89 (0.82, 0.98)	0.80 (0.73, 0.88)	<.001
MV-adjusted model	Ref.	0.93 (0.84, 1.02)	0.94 (0.85, 1.04)	0.92 (0.83, 1.02)	0.92 (0.82, 1.03)	0.20
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	1.03 (0.94, 1.13)	0.99 (0.90, 1.09)	0.88 (0.80, 0.96)	0.82 (0.75, 0.90)	<.001
MV-adjusted model	Ref.	1.09 (1.00, 1.20)	1.11 (1.00, 1.22)	1.03 (0.93, 1.15)	1.06 (0.95, 1.18)	0.71
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.06 (0.97, 1.15)	1.01 (0.93, 1.11)	1.10 (1.00, 1.20)	1.12 (1.02, 1.23)	0.02
MV-adjusted model	Ref.	0.99 (0.91, 1.09)	0.91 (0.83, 1.01)	0.97 (0.88, 1.07)	0.97 (0.87, 1.08)	0.42
Cancer mortality						
Total fat						
Age-adjusted model	Ref.	1.05 (0.98, 1.11)	1.18 (1.11, 1.26)	1.25 (1.17, 1.33)	1.25 (1.16, 1.34)	<.001
MV-adjusted model	Ref.	0.98 (0.92, 1.05)	1.04 (0.97, 1.11)	1.01 (0.94, 1.08)	0.89 (0.82, 0.97)	0.02
Saturated fat						
Age-adjusted model	Ref.	1.08 (1.01, 1.15)	1.30 (1.22, 1.38)	1.41 (1.32, 1.51)	1.49 (1.39, 1.61)	<.001
MV-adjusted model	Ref.	1.00 (0.93, 1.07)	1.12 (1.04, 1.21)	1.11 (1.01, 1.21)	1.03 (0.93, 1.14)	0.17

Unsaturated fat						
Age-adjusted model	Ref.	1.02 (0.96, 1.08)	1.04 (0.98, 1.11)	1.14 (1.07, 1.22)	1.08 (1.01, 1.16)	0.001
MV-adjusted model	Ref.	0.95 (0.89, 1.02)	0.92 (0.85, 0.99)	0.96 (0.89, 1.03)	0.87 (0.80, 0.95)	0.003
Polyunsaturated fat						
Age-adjusted model	Ref.	0.98 (0.92, 1.04)	0.92 (0.86, 0.98)	0.95 (0.89, 1.01)	0.88 (0.82, 0.94)	<.001
MV-adjusted model	Ref.	1.03 (0.96, 1.10)	0.97 (0.91, 1.04)	1.00 (0.93, 1.08)	0.94 (0.87, 1.01)	0.13
Monounsaturated fat						
Age-adjusted model	Ref.	1.02 (0.95, 1.08)	1.11 (1.05, 1.19)	1.20 (1.12, 1.28)	1.19 (1.10, 1.27)	<.001
MV-adjusted model	Ref.	0.93 (0.87, 1.00)	0.95 (0.87, 1.03)	0.96 (0.88, 1.06)	0.90 (0.81, 1.00)	0.05
trans fat						
Age-adjusted model	Ref.	1.12 (1.05, 1.19)	1.23 (1.15, 1.31)	1.38 (1.28, 1.48)	1.38 (1.28, 1.50)	<.001
MV-adjusted model	Ref.	0.99 (0.93, 1.06)	1.00 (0.93, 1.08)	1.03 (0.95, 1.12)	0.97 (0.88, 1.07)	0.86
Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.94 (0.88, 1.00)	0.95 (0.89, 1.01)	0.91 (0.86, 0.98)	0.88 (0.82, 0.94)	<.001
MV-adjusted model	Ref.	1.00 (0.93, 1.07)	1.01 (0.94, 1.09)	0.97 (0.90, 1.05)	0.94 (0.86, 1.03)	0.21
Linoleic acid						
Age-adjusted model	Ref.	0.94 (0.88, 1.00)	0.95 (0.89, 1.01)	0.93 (0.87, 0.99)	0.87 (0.81, 0.93)	<.001
MV-adjusted model	Ref.	0.99 (0.93, 1.06)	1.00 (0.93, 1.08)	0.98 (0.91, 1.06)	0.93 (0.86, 1.02)	0.17
Arachidonic acid						
Age-adjusted model	Ref.	1.08 (1.01, 1.15)	1.01 (0.95, 1.08)	1.08 (1.01, 1.16)	1.05 (0.98, 1.12)	0.24
MV-adjusted model	Ref.	1.06 (0.99, 1.13)	0.97 (0.90, 1.05)	1.01 (0.94, 1.10)	0.95 (0.87, 1.05)	0.18
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.91 (0.85, 0.98)	0.96 (0.90, 1.03)	0.91 (0.86, 0.98)	0.79 (0.74, 0.85)	<.001
MV-adjusted model	Ref.	0.97 (0.91, 1.04)	1.05 (0.98, 1.13)	1.03 (0.96, 1.11)	0.97 (0.90, 1.05)	0.58
α -linolenic acid						
Age-adjusted model	Ref.	1.01 (0.94, 1.08)	1.05 (0.99, 1.13)	1.05 (0.98, 1.12)	0.98 (0.91, 1.04)	0.54
MV-adjusted model	Ref.	1.03 (0.96, 1.10)	1.09 (1.01, 1.17)	1.08 (1.01, 1.17)	1.09 (1.00, 1.18)	0.04
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.97 (0.91, 1.04)	0.95 (0.89, 1.02)	0.89 (0.84, 0.96)	0.81 (0.76, 0.87)	<.001
MV-adjusted model	Ref.	1.01 (0.95, 1.09)	1.03 (0.96, 1.10)	1.01 (0.94, 1.09)	0.97 (0.90, 1.05)	0.27

ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.09 (1.03, 1.17)	1.08 (1.01, 1.15)	1.12 (1.05, 1.20)	1.09 (1.02, 1.17)	0.009
MV-adjusted model	Ref.	1.05 (0.98, 1.12)	1.01 (0.94, 1.08)	1.03 (0.96, 1.10)	0.97 (0.90, 1.05)	0.32
Neurodegenerative disease mortality						
Total fat						
Age-adjusted model	Ref.	1.04 (0.92, 1.17)	1.00 (0.88, 1.14)	1.06 (0.92, 1.21)	1.10 (0.93, 1.29)	0.38
MV-adjusted model	Ref.	0.98 (0.86, 1.10)	0.86 (0.75, 0.99)	0.78 (0.67, 0.91)	0.66 (0.55, 0.80)	<.001
Saturated fat						
Age-adjusted model	Ref.	1.23 (1.09, 1.38)	1.35 (1.19, 1.53)	1.39 (1.21, 1.60)	1.65 (1.39, 1.94)	<.001
MV-adjusted model	Ref.	1.08 (0.95, 1.24)	1.12 (0.96, 1.31)	0.99 (0.83, 1.19)	0.94 (0.75, 1.18)	0.86
Unsaturated fat						
Age-adjusted model	Ref.	0.95 (0.85, 1.07)	0.94 (0.83, 1.07)	0.91 (0.79, 1.04)	0.82 (0.70, 0.96)	0.005
MV-adjusted model	Ref.	0.86 (0.76, 0.98)	0.77 (0.66, 0.88)	0.69 (0.59, 0.81)	0.61 (0.50, 0.73)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.90 (0.79, 1.02)	0.74 (0.65, 0.85)	0.62 (0.54, 0.71)	0.51 (0.44, 0.59)	<.001
MV-adjusted model	Ref.	1.04 (0.91, 1.18)	0.91 (0.79, 1.05)	0.79 (0.68, 0.92)	0.78 (0.67, 0.92)	<.001
Monounsaturated fat						
Age-adjusted model	Ref.	1.02 (0.91, 1.15)	1.14 (1.00, 1.30)	1.13 (0.98, 1.31)	1.08 (0.92, 1.27)	0.10
MV-adjusted model	Ref.	0.86 (0.75, 0.99)	0.88 (0.74, 1.03)	0.81 (0.66, 0.98)	0.76 (0.60, 0.96)	<.001
trans fat						
Age-adjusted model	Ref.	1.56 (1.38, 1.77)	2.11 (1.85, 2.41)	2.69 (2.33, 3.10)	2.55 (2.15, 3.03)	<.001
MV-adjusted model	Ref.	1.17 (1.02, 1.33)	1.30 (1.12, 1.51)	1.44 (1.22, 1.71)	1.21 (0.98, 1.50)	0.003
Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.91 (0.80, 1.04)	0.76 (0.66, 0.86)	0.62 (0.54, 0.72)	0.58 (0.51, 0.67)	<.001
MV-adjusted model	Ref.	1.09 (0.95, 1.25)	1.00 (0.86, 1.16)	0.86 (0.73, 1.02)	0.94 (0.78, 1.14)	0.18
Linoleic acid						
Age-adjusted model	Ref.	0.83 (0.73, 0.95)	0.78 (0.69, 0.89)	0.62 (0.54, 0.71)	0.55 (0.48, 0.63)	<.001
MV-adjusted model	Ref.	0.99 (0.86, 1.13)	1.00 (0.87, 1.16)	0.85 (0.72, 1.01)	0.86 (0.71, 1.04)	0.06
Arachidonic acid						
Age-adjusted model	Ref.	0.92 (0.81, 1.03)	0.87 (0.77, 1.00)	0.79 (0.69, 0.91)	0.69 (0.60, 0.80)	<.001
MV-adjusted model	Ref.	0.87 (0.76, 0.99)	0.84 (0.73, 0.98)	0.82 (0.70, 0.97)	0.82 (0.67, 0.99)	0.04

Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.88 (0.77, 1.00)	0.69 (0.61, 0.80)	0.62 (0.54, 0.71)	0.40 (0.35, 0.46)	<.001
MV-adjusted model	Ref.	1.01 (0.88, 1.16)	0.88 (0.76, 1.02)	0.91 (0.78, 1.06)	0.80 (0.68, 0.95)	0.001
α -linolenic acid						
Age-adjusted model	Ref.	0.88 (0.77, 1.01)	0.80 (0.70, 0.92)	0.66 (0.57, 0.76)	0.45 (0.40, 0.52)	<.001
MV-adjusted model	Ref.	0.96 (0.84, 1.10)	0.97 (0.84, 1.13)	0.87 (0.74, 1.02)	0.82 (0.69, 0.98)	0.007
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	1.03 (0.90, 1.18)	1.07 (0.94, 1.23)	0.91 (0.79, 1.04)	0.64 (0.56, 0.74)	<.001
MV-adjusted model	Ref.	1.09 (0.94, 1.25)	1.14 (0.99, 1.32)	1.06 (0.91, 1.23)	0.96 (0.82, 1.13)	0.19
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.25 (1.10, 1.43)	1.27 (1.11, 1.46)	1.59 (1.39, 1.82)	1.59 (1.38, 1.83)	<.001
MV-adjusted model	Ref.	1.11 (0.96, 1.27)	1.06 (0.91, 1.22)	1.20 (1.04, 1.39)	1.15 (0.98, 1.34)	0.05
Respiratory disease mortality						
Total fat						
Age-adjusted model	Ref.	1.31 (1.14, 1.51)	1.43 (1.24, 1.65)	1.86 (1.61, 2.14)	2.14 (1.83, 2.50)	<.001
MV-adjusted model	Ref.	1.12 (0.97, 1.29)	1.04 (0.89, 1.21)	1.10 (0.94, 1.29)	1.07 (0.89, 1.27)	0.52
Saturated fat						
Age-adjusted model	Ref.	1.45 (1.26, 1.68)	1.72 (1.49, 1.99)	2.42 (2.10, 2.80)	3.32 (2.84, 3.87)	<.001
MV-adjusted model	Ref.	1.16 (0.99, 1.36)	1.19 (1.00, 1.42)	1.38 (1.14, 1.67)	1.51 (1.22, 1.87)	<.001
Unsaturated fat						
Age-adjusted model	Ref.	1.06 (0.92, 1.21)	1.25 (1.09, 1.44)	1.33 (1.16, 1.54)	1.34 (1.15, 1.56)	<.001
MV-adjusted model	Ref.	0.81 (0.70, 0.94)	0.81 (0.69, 0.95)	0.73 (0.61, 0.86)	0.66 (0.55, 0.80)	<.001
Polyunsaturated fat						
Age-adjusted model	Ref.	0.90 (0.78, 1.04)	0.94 (0.82, 1.09)	0.89 (0.77, 1.03)	0.76 (0.66, 0.89)	<.001
MV-adjusted model	Ref.	0.94 (0.81, 1.09)	0.96 (0.83, 1.12)	0.88 (0.75, 1.03)	0.80 (0.68, 0.95)	0.01
Monounsaturated fat						
Age-adjusted model	Ref.	1.34 (1.17, 1.53)	1.34 (1.16, 1.55)	1.77 (1.53, 2.04)	1.70 (1.45, 2.00)	<.001
MV-adjusted model	Ref.	1.00 (0.86, 1.17)	0.83 (0.69, 1.00)	0.91 (0.74, 1.12)	0.76 (0.60, 0.97)	0.008
trans fat						
Age-adjusted model	Ref.	1.59 (1.38, 1.83)	2.20 (1.91, 2.54)	2.43 (2.08, 2.84)	2.95 (2.49, 3.50)	<.001
MV-adjusted model	Ref.	1.16 (0.99, 1.34)	1.33 (1.12, 1.57)	1.28 (1.06, 1.54)	1.40 (1.13, 1.73)	0.003

Total ω -6 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.90 (0.78, 1.04)	0.91 (0.79, 1.05)	0.91 (0.79, 1.05)	0.78 (0.67, 0.91)	0.003
MV-adjusted model	Ref.	0.96 (0.82, 1.12)	0.95 (0.81, 1.12)	0.92 (0.78, 1.10)	0.84 (0.68, 1.02)	0.10
Linoleic acid						
Age-adjusted model	Ref.	0.91 (0.79, 1.05)	0.96 (0.83, 1.10)	0.90 (0.78, 1.04)	0.78 (0.68, 0.91)	0.002
MV-adjusted model	Ref.	0.97 (0.84, 1.13)	0.99 (0.85, 1.17)	0.91 (0.76, 1.08)	0.83 (0.68, 1.01)	0.05
Arachidonic acid						
Age-adjusted model	Ref.	1.03 (0.91, 1.18)	1.01 (0.88, 1.16)	0.98 (0.85, 1.13)	0.92 (0.80, 1.07)	0.19
MV-adjusted model	Ref.	1.06 (0.92, 1.23)	1.07 (0.91, 1.25)	1.07 (0.90, 1.28)	1.09 (0.88, 1.35)	0.50
Total ω -3 polyunsaturated fatty acids						
Age-adjusted model	Ref.	0.89 (0.77, 1.03)	0.81 (0.70, 0.94)	0.83 (0.72, 0.96)	0.55 (0.47, 0.64)	<.001
MV-adjusted model	Ref.	0.98 (0.84, 1.14)	0.92 (0.78, 1.07)	1.04 (0.89, 1.23)	0.86 (0.72, 1.03)	0.11
α -linolenic acid						
Age-adjusted model	Ref.	0.99 (0.84, 1.15)	1.15 (0.99, 1.33)	1.06 (0.91, 1.23)	0.90 (0.78, 1.04)	0.13
MV-adjusted model	Ref.	0.96 (0.82, 1.13)	1.11 (0.94, 1.30)	1.01 (0.85, 1.19)	1.02 (0.85, 1.22)	0.78
Marine ω -3 fats (DHA+EPA)						
Age-adjusted model	Ref.	0.89 (0.77, 1.02)	0.80 (0.70, 0.92)	0.67 (0.58, 0.78)	0.51 (0.44, 0.59)	<.001
MV-adjusted model	Ref.	1.01 (0.88, 1.16)	0.99 (0.86, 1.15)	0.98 (0.84, 1.15)	0.89 (0.75, 1.05)	0.08
ω -6/ ω -3 ratio						
Age-adjusted model	Ref.	1.25 (1.08, 1.44)	1.45 (1.25, 1.67)	1.47 (1.27, 1.70)	1.64 (1.41, 1.91)	<.001
MV-adjusted model	Ref.	1.07 (0.92, 1.25)	1.10 (0.94, 1.28)	1.06 (0.90, 1.24)	1.12 (0.94, 1.32)	0.23

Abbreviations: HR, hazard ratio; CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MV, multivariable; NHS, Nurses' Health Study; HPFS, Health Professional Follow-up Study.

Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, ≥ 35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥ 27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥ 25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, ≥ 15 g/d; men: 0, 0.1-4.9, 5.0-29.9, ≥ 30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), intakes of total energy, dietary cholesterol and percentage of energy intake from dietary protein (quintiles and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models also included percentages of energy intake from remaining fatty acids (saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids,

trans fatty acids, ω -6 polyunsaturated fatty acids, ω -3 polyunsaturated fatty acids, linoleic acid, arachidonic acid, α -linolenic acid and marine ω -3 fats, all in quintiles).

Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 11. Associations Between Total and Specific Types of Fat Intakes and Cardiovascular Disease Mortality (comparison is isocaloric substitution for carbohydrate)

	Quintile of dietary fatty acid intake					<i>P</i> _{trend}	HR (95% CI) ^a
	Q1	Q2	Q3	Q4	Q5		
Total fat							
NHS							
Median (% energy)	25.4	30.0	33.2	36.6	42.2		
Deaths (n)	1169	944	773	630	484		
Age-adjusted model	Ref.	1.11 (1.02, 1.21)	1.17 (1.07, 1.28)	1.23 (1.11, 1.36)	1.55 (1.39, 1.73)	<.001	1.12 (1.09, 1.16)
MV-adjusted model ^b	Ref.	1.03 (0.94, 1.12)	0.99 (0.89, 1.09)	0.91 (0.81, 1.01)	0.89 (0.79, 1.01)	0.03	0.96 (0.93, 1.00)
HPFS							
Median (% energy)	23.8	28.3	31.3	34.2	38.4		
Deaths (n)	853	789	795	757	684		
Age-adjusted model	Ref.	1.00 (0.90, 1.10)	1.07 (0.97, 1.18)	1.10 (1.00, 1.21)	1.13 (1.02, 1.25)	0.003	1.05 (1.01, 1.08)
MV-adjusted model	Ref.	0.92 (0.84, 1.02)	0.93 (0.84, 1.03)	0.90 (0.81, 1.00)	0.82 (0.73, 0.93)	0.002	0.94 (0.91, 0.98)
Pooled ^c							
Age-adjusted model	Ref.	1.06 (0.99, 1.13)	1.12 (1.05, 1.20)	1.16 (1.08, 1.25)	1.31 (1.21, 1.41)	<.001	1.09 (1.06, 1.11)
MV-adjusted model	Ref.	0.98 (0.92, 1.05)	0.96 (0.89, 1.03)	0.90 (0.84, 0.97)	0.86 (0.79, 0.93)	<.001	0.95 (0.93, 0.98)

Saturated fat							
NHS							
Median (% energy)	8.2	10.2	11.8	13.5	16.5		
Deaths (n)	1104	968	805	638	485		
Age-adjusted model	Ref.	1.26 (1.15, 1.37)	1.40 (1.28, 1.53)	1.61 (1.45, 1.78)	2.19 (1.96, 2.45)	<.001	1.58 (1.48, 1.68)
MV-adjusted model	Ref.	1.15 (1.04, 1.26)	1.17 (1.04, 1.31)	1.18 (1.03, 1.34)	1.21 (1.03, 1.41)	0.02	1.11 (1.02, 1.22)
HPFS							
Median (% energy)	7.1	9.0	10.2	11.5	13.5		
Deaths (n)	825	810	773	765	705		
Age-adjusted model	Ref.	1.10 (1.00, 1.21)	1.15 (1.04, 1.27)	1.25 (1.13, 1.38)	1.33 (1.20, 1.47)	<.001	1.25 (1.16, 1.35)
MV-adjusted model	Ref.	0.97 (0.87, 1.08)	0.97 (0.86, 1.10)	0.96 (0.84, 1.10)	0.93 (0.80, 1.07)	0.50	0.96 (0.86, 1.07)
Pooled							
Age-adjusted model	Ref.	1.18 (1.11, 1.26)	1.28 (1.19, 1.37)	1.41 (1.32, 1.52)	1.66 (1.54, 1.79)	<.001	1.43 (1.37, 1.50)
MV-adjusted model	Ref.	1.06 (0.99, 1.14)	1.07 (0.99, 1.16)	1.06 (0.97, 1.17)	1.05 (0.94, 1.17)	0.17	1.05 (0.98, 1.12)
Unsaturated fat							
NHS							
Median (% energy)	14.2	16.8	18.7	20.6	23.8		
Deaths (n)	1220	926	755	616	483		
Age-adjusted model	Ref.	1.01 (0.93, 1.10)	1.03 (0.94, 1.13)	1.03 (0.93, 1.14)	1.09 (0.98, 1.21)	0.12	1.04 (0.99, 1.10)
MV-adjusted model	Ref.	0.91 (0.83, 1.00)	0.84 (0.75, 0.93)	0.76 (0.67, 0.85)	0.68 (0.60, 0.78)	<.001	0.82 (0.76, 0.87)

HPFS							
Median (% energy)	13.7	16.3	18.0	19.7	22.3		
Deaths (n)	864	828	763	728	695		
Age-adjusted model	Ref.	1.00 (0.91, 1.10)	0.97 (0.88, 1.07)	1.01 (0.92, 1.12)	1.01 (0.91, 1.11)	0.86	1.00 (0.95, 1.06)
MV-adjusted model	Ref.	0.93 (0.84, 1.03)	0.86 (0.77, 0.96)	0.87 (0.77, 0.98)	0.83 (0.73, 0.94)	0.002	0.90 (0.84, 0.96)
Pooled							
Age-adjusted model	Ref.	1.01 (0.94, 1.07)	1.01 (0.94, 1.08)	1.02 (0.95, 1.10)	1.04 (0.97, 1.12)	0.21	1.02 (0.99, 1.06)
MV-adjusted model	Ref.	0.92 (0.85, 0.98)	0.85 (0.78, 0.91)	0.81 (0.75, 0.88)	0.76 (0.69, 0.83)	<.001	0.85 (0.81, 0.90)
Polyunsaturated fat							
NHS							
Median (% energy)	4.2	5.0	5.6	6.3	7.5		
Deaths (n)	947	861	786	725	681		
Age-adjusted model	Ref.	0.88 (0.80, 0.96)	0.82 (0.75, 0.91)	0.78 (0.70, 0.86)	0.70 (0.63, 0.77)	<.001	0.59 (0.51, 0.68)
MV-adjusted model	Ref.	0.94 (0.86, 1.04)	0.89 (0.80, 0.98)	0.85 (0.76, 0.94)	0.80 (0.71, 0.89)	<.001	0.72 (0.62, 0.85)
HPFS							
Median (% energy)	4.4	5.2	5.8	6.5	7.7		
Deaths (n)	863	818	755	722	720		
Age-adjusted model	Ref.	0.93 (0.84, 1.02)	0.89 (0.81, 0.99)	0.82 (0.74, 0.91)	0.81 (0.74, 0.90)	<.001	0.71 (0.62, 0.82)
MV-adjusted model	Ref.	0.93 (0.84, 1.02)	0.88 (0.79, 0.98)	0.80 (0.72, 0.90)	0.83 (0.74, 0.94)	<.001	0.73 (0.61, 0.87)

Pooled							
Age-adjusted model	Ref.	0.90 (0.84, 0.96)	0.86 (0.80, 0.92)	0.80 (0.74, 0.86)	0.75 (0.70, 0.81)	<.001	0.65 (0.59, 0.72)
MV-adjusted model	Ref.	0.94 (0.87, 1.00)	0.88 (0.82, 0.95)	0.83 (0.76, 0.89)	0.81 (0.75, 0.88)	<.001	0.73 (0.65, 0.82)
Monounsaturated fat							
NHS							
Median (% energy)	9.4	11.4	12.8	14.4	17.2		
Deaths (n)	1263	966	719	588	464		
Age-adjusted model	Ref.	1.10 (1.01, 1.20)	1.10 (1.00, 1.20)	1.15 (1.04, 1.28)	1.39 (1.24, 1.55)	<.001	1.20 (1.13, 1.28)
MV-adjusted model	Ref.	0.97 (0.88, 1.07)	0.88 (0.78, 0.99)	0.82 (0.72, 0.95)	0.79 (0.67, 0.94)	0.001	0.84 (0.75, 0.93)
HPFS							
Median (% energy)	8.9	10.8	12.1	13.3	15.3		
Deaths (n)	853	815	761	775	674		
Age-adjusted model	Ref.	1.01 (0.92, 1.11)	1.02 (0.93, 1.13)	1.13 (1.03, 1.25)	1.10 (0.99, 1.22)	0.01	1.10 (1.02, 1.18)
MV-adjusted model	Ref.	0.99 (0.88, 1.10)	0.98 (0.86, 1.11)	1.06 (0.92, 1.23)	0.99 (0.84, 1.17)	0.98	1.01 (0.89, 1.14)
Pooled							
Age-adjusted model	Ref.	1.06 (1.00, 1.13)	1.06 (0.99, 1.13)	1.14 (1.07, 1.23)	1.22 (1.14, 1.32)	<.001	1.16 (1.10, 1.21)
MV-adjusted model	Ref.	0.98 (0.91, 1.05)	0.92 (0.84, 1.01)	0.93 (0.84, 1.03)	0.89 (0.79, 1.00)	0.01	0.90 (0.83, 0.98)

<i>trans</i> fat							
NHS							
Median (% energy)	0.9	1.2	1.5	1.9	2.5		
Deaths (n)	1072	987	868	615	458		
Age-adjusted model	Ref.	1.30 (1.19, 1.42)	1.63 (1.48, 1.79)	1.79 (1.61, 1.99)	2.32 (2.06, 2.62)	<.001	2.87 (2.50, 3.28)
MV-adjusted model	Ref.	1.02 (0.93, 1.13)	1.11 (1.00, 1.24)	1.08 (0.95, 1.23)	1.22 (1.05, 1.43)	0.007	1.29 (1.07, 1.54)
HPFS							
Median (% energy)	0.7	1.0	1.2	1.4	1.9		
Deaths (n)	740	817	836	789	696		
Age-adjusted model	Ref.	1.18 (1.07, 1.30)	1.26 (1.14, 1.39)	1.31 (1.18, 1.45)	1.37 (1.23, 1.53)	<.001	1.65 (1.40, 1.95)
MV-adjusted model	Ref.	1.13 (1.02, 1.26)	1.16 (1.04, 1.31)	1.17 (1.03, 1.32)	1.18 (1.03, 1.35)	0.05	1.24 (1.01, 1.54)
Pooled							
Age-adjusted model	Ref.	1.25 (1.17, 1.33)	1.44 (1.35, 1.55)	1.52 (1.41, 1.64)	1.73 (1.60, 1.87)	<.001	2.30 (2.07, 2.55)
MV-adjusted model	Ref.	1.07 (1.00, 1.15)	1.14 (1.05, 1.23)	1.13 (1.03, 1.23)	1.20 (1.08, 1.33)	<.001	1.27 (1.10, 1.46)

Abbreviations: HR, hazard ratio; CI, confidence interval; MV, multivariable; NHS, Nurses' Health Study; HPFS, Health Professional Follow-up Study.

^a Hazard ratios (95% confidence interval) of cardiovascular disease mortality for substituting 5% of energy from saturated fatty acids, unsaturated fatty acids, polyunsaturated fatty acids, and monounsaturated fatty acids, and 2% of energy from *trans* fatty acids, for the same energy from carbohydrate.

^b Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, ≥35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, ≥15 g/d; men: 0, 0.1-4.9, 5.0-29.9, ≥30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), intakes of total energy, dietary cholesterol and

percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models, except total fat, also included percentages of energy intake from remaining fatty acids (saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids and *trans* fatty acids, all in quintiles).^c Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 12. Associations Between Dietary ω -6 and ω -3 Polyunsaturated Fatty Acid Intake and Cardiovascular Disease Mortality (comparison is isocaloric substitution for carbohydrate)

n	Quintile of dietary fatty acid intake					<i>P</i> _{trend}	HR (95% CI) ^a
	Q1	Q2	Q3	Q4	Q5		
ω-6 polyunsaturated fatty acid							
Total ω-6 polyunsaturated fatty acids							
NHS							
Median (% energy)	3.4	4.3	4.9	5.5	6.7		
Deaths (n)	903	829	823	728	717		
Age-adjusted model	Ref.	0.80 (0.73, 0.88)	0.80 (0.72, 0.88)	0.72 (0.65, 0.80)	0.71 (0.64, 0.78)	<.001	0.82 (0.77, 0.87)
^b MV-adjusted model	Ref.	0.88 (0.80, 0.98)	0.88 (0.79, 0.98)	0.82 (0.73, 0.92)	0.84 (0.74, 0.96)	0.02	0.91 (0.84, 0.98)
HPFS							
Median (% energy)	3.7	4.5	5.1	5.8	6.9		
Deaths (n)	885	826	743	730	694		
Age-adjusted model	Ref.	0.90 (0.82, 0.99)	0.84 (0.77, 0.93)	0.83 (0.76, 0.92)	0.82 (0.74, 0.90)	<.001	0.88 (0.83, 0.94)
MV-adjusted model	Ref.	0.90 (0.81, 0.99)	0.84 (0.75, 0.94)	0.80 (0.71, 0.91)	0.78 (0.68, 0.89)	<.001	0.86 (0.79, 0.93)
Pooled ^c							
Age-adjusted model	Ref.	0.85 (0.79, 0.91)	0.82 (0.77, 0.88)	0.78 (0.72, 0.83)	0.76 (0.71, 0.82)	<.001	0.85 (0.81, 0.88)
MV-adjusted model	Ref.	0.89 (0.83, 0.95)	0.86 (0.80, 0.93)	0.81 (0.75, 0.88)	0.81 (0.74, 0.89)	<.001	0.88 (0.83, 0.93)
Linoleic acid							
NHS							
Median (% energy)	3.3	4.2	4.8	5.4	6.5		
Deaths (n)	896	868	795	746	695		
Age-adjusted model	Ref.	0.85 (0.78, 0.94)	0.79 (0.72, 0.87)	0.76 (0.69, 0.84)	0.70 (0.63, 0.77)	<.001	0.80 (0.75, 0.85)
MV-adjusted model	Ref.	0.93 (0.84, 1.03)	0.87 (0.78, 0.97)	0.85 (0.75, 0.95)	0.81 (0.71, 0.93)	0.002	0.88 (0.81, 0.96)
HPFS							
Median (% energy)	3.6	4.4	5.0	5.6	6.7		
Deaths (n)	893	831	759	709	686		
Age-adjusted model	Ref.	0.94 (0.86, 1.04)	0.89 (0.81, 0.98)	0.82 (0.74, 0.90)	0.80 (0.72, 0.88)	<.001	0.85 (0.80, 0.91)
MV-adjusted model	Ref.	0.92 (0.84, 1.02)	0.86 (0.77, 0.95)	0.78 (0.69, 0.87)	0.75 (0.66, 0.86)	<.001	0.82 (0.75, 0.89)
Pooled							

Age-adjusted model	Ref.	0.90 (0.84, 0.96)	0.84 (0.78, 0.90)	0.79 (0.73, 0.84)	0.74 (0.69, 0.80)	<.001	0.82 (0.79, 0.86)
MV-adjusted model	Ref.	0.93 (0.86, 0.99)	0.86 (0.80, 0.93)	0.81 (0.75, 0.88)	0.78 (0.71, 0.86)	<.001	0.85 (0.80, 0.90)
Arachidonic acid							
NHS							
Median (% energy)		0.05	0.06	0.07	0.09	0.11	
Deaths (n)	1156	880	699	654	611		
Age-adjusted model	Ref.	1.05 (0.96, 1.15)	0.98 (0.89, 1.08)	1.02 (0.93, 1.13)	1.07 (0.97, 1.18)	0.32	1.26 (0.80, 1.98)
MV-adjusted model	Ref.	1.04 (0.95, 1.14)	0.95 (0.85, 1.06)	0.95 (0.85, 1.07)	0.97 (0.84, 1.11)	0.35	0.73 (0.38, 1.40)
HPFS							
Median (% energy)	0.05	0.06	0.07	0.09	0.11		
Deaths (n)	735	767	715	781	880		
Age-adjusted model	Ref.	1.11 (1.00, 1.22)	1.06 (0.95, 1.17)	1.20 (1.08, 1.33)	1.26 (1.14, 1.39)	<.001	2.86 (1.85, 4.43)
MV-adjusted model	Ref.	1.05 (0.95, 1.17)	0.95 (0.84, 1.07)	1.05 (0.93, 1.19)	1.03 (0.89, 1.19)	0.57	1.12 (0.59, 2.12)
Pooled							
Age-adjusted model	Ref.	1.07 (1.01, 1.15)	1.01 (0.95, 1.09)	1.10 (1.03, 1.18)	1.16 (1.08, 1.24)	<.001	1.93 (1.41, 2.64)
MV-adjusted model	Ref.	1.05 (0.97, 1.12)	0.95 (0.88, 1.03)	1.00 (0.92, 1.09)	1.00 (0.90, 1.10)	0.79	0.91 (0.57, 1.43)
ω-3 polyunsaturated fatty acid							
Total ω-3 polyunsaturated fatty acids							
NHS							
Median (% energy)	0.48	0.57	0.63	0.72	0.88		
Deaths (n)	881	727	772	834	786		
Age-adjusted model	Ref.	0.84 (0.76, 0.92)	0.85 (0.77, 0.93)	0.84 (0.76, 0.92)	0.61 (0.55, 0.67)	<.001	0.72 (0.67, 0.77)
MV-adjusted model	Ref.	0.92 (0.83, 1.02)	0.99 (0.89, 1.10)	1.04 (0.94, 1.16)	0.90 (0.80, 1.01)	0.25	0.95 (0.87, 1.04)
HPFS							
Median (% energy)	0.46	0.57	0.65	0.75	0.94		
Deaths (n)	679	762	770	773	894		
Age-adjusted model	Ref.	0.95 (0.85, 1.05)	0.89 (0.81, 0.99)	0.88 (0.79, 0.98)	0.89 (0.80, 0.99)	0.03	0.94 (0.88, 0.99)
MV-adjusted model	Ref.	1.03 (0.92, 1.14)	1.02 (0.92, 1.14)	1.03 (0.92, 1.15)	1.12 (0.99, 1.26)	0.05	1.06 (0.99, 1.14)
Pooled							
Age-adjusted model	Ref.	0.89 (0.82, 0.95)	0.87 (0.81, 0.93)	0.86 (0.80, 0.92)	0.73 (0.68, 0.79)	<.001	0.84 (0.80, 0.87)
MV-adjusted model	Ref.	0.97 (0.90, 1.05)	1.00 (0.93, 1.08)	1.04 (0.96, 1.12)	1.00 (0.92, 1.09)	0.45	1.02 (0.96, 1.07)
α-linolenic acid							

NHS							
Median (% energy)	0.41	0.48	0.53	0.59	0.70		
Deaths (n)	936	741	744	730	849		
Age-adjusted model	Ref.	0.87 (0.79, 0.96)	0.91 (0.83, 1.00)	0.86 (0.78, 0.95)	0.74 (0.67, 0.81)	<.001	0.75 (0.69, 0.83)
MV-adjusted model	Ref.	0.89 (0.81, 0.99)	0.96 (0.86, 1.06)	0.92 (0.82, 1.03)	0.90 (0.80, 1.02)	0.20	0.92 (0.82, 1.04)
HPFS							
Median (% energy)	0.38	0.45	0.50	0.56	0.68		
Deaths (n)	727	740	754	788	869		
Age-adjusted model	Ref.	0.98 (0.89, 1.09)	0.94 (0.85, 1.04)	0.93 (0.84, 1.03)	0.86 (0.77, 0.95)	0.001	0.85 (0.77, 0.94)
MV-adjusted model	Ref.	0.99 (0.89, 1.11)	0.99 (0.89, 1.10)	1.00 (0.89, 1.12)	0.97 (0.86, 1.10)	0.62	0.94 (0.84, 1.06)
Pooled							
Age-adjusted model	Ref.	0.92 (0.86, 0.99)	0.93 (0.86, 0.99)	0.89 (0.83, 0.96)	0.79 (0.74, 0.85)	<.001	0.80 (0.75, 0.85)
MV-adjusted model	Ref.	0.94 (0.87, 1.01)	0.97 (0.90, 1.05)	0.96 (0.89, 1.04)	0.94 (0.86, 1.02)	0.21	0.93 (0.86, 1.02)
Marine ω-3 fats (DHA+EPA)							
NHS							
Median (% energy)	0.03	0.05	0.08	0.12	0.21		
Deaths (n)	777	814	837	785	787		
Age-adjusted model	Ref.	0.93 (0.84, 1.03)	0.88 (0.80, 0.97)	0.79 (0.71, 0.87)	0.66 (0.60, 0.73)	<.001	0.51 (0.44, 0.59)
MV-adjusted model	Ref.	1.00 (0.91, 1.11)	1.01 (0.91, 1.12)	1.00 (0.89, 1.11)	0.94 (0.84, 1.06)	0.19	0.89 (0.75, 1.06)
HPFS							
Median (% energy)	0.04	0.08	0.12	0.18	0.31		
Deaths (n)	686	773	763	775	881		
Age-adjusted model	Ref.	1.05 (0.94, 1.16)	1.05 (0.94, 1.16)	1.06 (0.95, 1.17)	1.03 (0.93, 1.14)	0.77	1.02 (0.92, 1.12)
MV-adjusted model	Ref.	1.06 (0.96, 1.18)	1.10 (0.99, 1.22)	1.15 (1.03, 1.28)	1.16 (1.03, 1.30)	0.01	1.16 (1.04, 1.31)
Pooled							
Age-adjusted model	Ref.	0.99 (0.92, 1.06)	0.95 (0.89, 1.02)	0.91 (0.84, 0.98)	0.83 (0.77, 0.89)	<.001	0.82 (0.76, 0.89)
MV-adjusted model	Ref.	1.03 (0.96, 1.11)	1.05 (0.98, 1.13)	1.07 (0.99, 1.15)	1.05 (0.96, 1.13)	0.19	1.07 (0.97, 1.18)

ω -6/ ω -3 ratio							
NHS							
Median	5.5	6.7	7.6	8.4	9.9		
Deaths (n)	793	853	847	808	699		
Age-adjusted model	Ref.	1.11 (1.01, 1.23)	1.15 (1.04, 1.26)	1.15 (1.04, 1.27)	1.18 (1.07, 1.31)	0.001	1.04 (1.01, 1.06)
MV-adjusted model	Ref.	1.04 (0.95, 1.15)	1.02 (0.92, 1.13)	1.00 (0.90, 1.12)	0.99 (0.88, 1.10)	0.61	0.99 (0.97, 1.02)
HPFS							
Median	5.5	6.9	7.9	8.9	10.8		
Deaths (n)	959	867	784	668	600		
Age-adjusted model	Ref.	1.04 (0.95, 1.14)	1.02 (0.93, 1.13)	0.97 (0.88, 1.07)	0.96 (0.87, 1.07)	0.31	0.99 (0.97, 1.01)
MV-adjusted model	Ref.	0.99 (0.90, 1.09)	0.92 (0.83, 1.02)	0.86 (0.77, 0.95)	0.87 (0.77, 0.97)	0.002	0.97 (0.95, 0.99)
Pooled							
Age-adjusted model	Ref.	1.07 (1.00, 1.15)	1.08 (1.01, 1.16)	1.06 (0.99, 1.13)	1.07 (0.99, 1.15)	0.18	1.01 (1.00, 1.02)
MV-adjusted model	Ref.	1.01 (0.95, 1.09)	0.97 (0.90, 1.05)	0.93 (0.86, 1.00)	0.93 (0.85, 1.00)	0.009	0.98 (0.96, 1.00)

Abbreviations: HR, hazard ratio; CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MV, multivariable; NHS, Nurses' Health Study; HPFS, Health Professional Follow-up Study.

^a Hazard ratios (95% confidence interval) of cardiovascular disease mortality for substituting 2% of energy from total ω -6 polyunsaturated fatty acids and linoleic acid, and 0.3% of energy from total ω -3 polyunsaturated fatty acids, arachidonic acid, and α -linolenic acid and marine ω -3 fats, for the same energy from carbohydrate. For ω -6/ ω -3 ration, the Hazard ratios (95% confidence interval) of total mortality were calculated for 1-unit increment.

^b Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, ≥ 35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥ 27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥ 25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, ≥ 15 g/d; men: 0, 0.1-4.9, 5.0-29.9, ≥ 30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), intakes of total energy, dietary cholesterol and percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models also included percentages of energy intake from remaining fatty acids (saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, *trans* fatty acids, ω -6 polyunsaturated fatty acids, ω -3 polyunsaturated fatty acids, linoleic acid, arachidonic acid, α -linolenic acid and marine ω -3 fats, all in quintiles).

^c Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 13. Associations Between Total and Specific Types of Fat Intakes and Cancer Mortality (comparison is isocaloric substitution for carbohydrate)

	Quintile of dietary fatty acid intake					<i>P</i> _{trend}	HR (95% CI) ^a
	Q1	Q2	Q3	Q4	Q5		
Total fat							
NHS							
Median (% energy)	25.4	30.0	33.2	36.6	42.2		
Deaths (n)	2039	1741	1708	1430	1001		
Age-adjusted model	Ref.	1.04 (0.98, 1.11)	1.20 (1.13, 1.28)	1.21 (1.13, 1.30)	1.27 (1.18, 1.38)	<.001	1.08 (1.06, 1.11)
^b MV-adjusted model	Ref.	0.97 (0.90, 1.03)	1.03 (0.96, 1.10)	0.94 (0.88, 1.02)	0.85 (0.78, 0.93)	0.001	0.96 (0.94, 0.98)
HPFS							
Median (% energy)	23.8	28.3	31.3	34.2	38.4		
Deaths (n)	822	805	894	843	828		
Age-adjusted model	Ref.	1.04 (0.94, 1.14)	1.20 (1.09, 1.32)	1.20 (1.09, 1.32)	1.28 (1.16, 1.41)	<.001	1.09 (1.06, 1.13)
MV-adjusted model	Ref.	0.99 (0.90, 1.10)	1.10 (0.99, 1.22)	1.04 (0.94, 1.16)	1.02 (0.91, 1.14)	0.59	1.01 (0.97, 1.04)
Pooled ^c							
Age-adjusted model	Ref.	1.04 (0.99, 1.10)	1.20 (1.14, 1.27)	1.21 (1.14, 1.28)	1.28 (1.20, 1.36)	<.001	1.09 (1.07, 1.11)
MV-adjusted model	Ref.	0.97 (0.92, 1.03)	1.05 (0.99, 1.11)	0.98 (0.92, 1.04)	0.91 (0.85, 0.98)	0.02	0.98 (0.96, 1.00)
Saturated fat							
NHS							
Median (% energy)	8.2	10.2	11.8	13.5	16.5		
Deaths (n)	2026	1776	1733	1452	932		
Age-adjusted model	Ref.	1.11 (1.04, 1.18)	1.33 (1.25, 1.42)	1.47 (1.37, 1.58)	1.55 (1.43, 1.69)	<.001	1.35 (1.29, 1.41)
MV-adjusted model	Ref.	1.03 (0.96, 1.11)	1.15 (1.06, 1.25)	1.15 (1.05, 1.26)	1.02 (0.91, 1.15)	0.18	1.04 (0.98, 1.11)
HPFS							
Median (% energy)	7.1	9.0	10.2	11.5	13.5		
Deaths (n)	824	823	857	832	856		
Age-adjusted model	Ref.	1.08 (0.98, 1.19)	1.22 (1.11, 1.34)	1.28 (1.16, 1.41)	1.48 (1.34, 1.63)	<.001	1.35 (1.26, 1.45)
MV-adjusted model	Ref.	1.01 (0.91, 1.13)	1.09 (0.97, 1.23)	1.07 (0.94, 1.22)	1.14 (0.99, 1.31)	0.03	1.12 (1.01, 1.24)

Pooled							
Age-adjusted model	Ref.	1.10 (1.04, 1.16)	1.30 (1.23, 1.37)	1.40 (1.32, 1.48)	1.52 (1.43, 1.62)	<.001	1.35 (1.30, 1.40)
MV-adjusted model	Ref.	1.02 (0.96, 1.09)	1.13 (1.06, 1.21)	1.12 (1.04, 1.21)	1.07 (0.98, 1.17)	0.02	1.06 (1.01, 1.12)
Unsaturated fat							
NHS							
Median (% energy)	14.2	16.8	18.7	20.6	23.8		
Deaths (n)	2087	1772	1533	1442	1085		
Age-adjusted model	Ref.	1.01 (0.95, 1.07)	1.00 (0.94, 1.07)	1.09 (1.01, 1.16)	1.07 (0.99, 1.15)	0.02	1.04 (1.01, 1.08)
MV-adjusted model	Ref.	0.94 (0.88, 1.01)	0.88 (0.82, 0.95)	0.91 (0.84, 0.99)	0.85 (0.78, 0.94)	0.001	0.93 (0.88, 0.97)
HPFS							
Median (% energy)	13.7	16.3	18.0	19.7	22.3		
Deaths (n)	824	833	873	845	817		
Age-adjusted model	Ref.	1.05 (0.95, 1.15)	1.14 (1.03, 1.25)	1.15 (1.04, 1.26)	1.13 (1.03, 1.25)	0.002	1.08 (1.02, 1.14)
MV-adjusted model	Ref.	0.99 (0.89, 1.10)	1.02 (0.91, 1.14)	0.98 (0.88, 1.10)	0.92 (0.82, 1.04)	0.15	0.95 (0.89, 1.01)
Pooled							
Age-adjusted model	Ref.	1.02 (0.97, 1.08)	1.05 (0.99, 1.11)	1.11 (1.05, 1.17)	1.09 (1.03, 1.16)	<.001	1.05 (1.02, 1.09)
MV-adjusted model	Ref.	0.96 (0.90, 1.01)	0.93 (0.87, 0.99)	0.93 (0.87, 1.00)	0.88 (0.82, 0.95)	<.001	0.93 (0.90, 0.97)
Polyunsaturated fat							
NHS							
Median (% energy)	4.2	5.0	5.6	6.3	7.5		
Deaths (n)	1601	1743	1579	1559	1437		
Age-adjusted model	Ref.	1.00 (0.94, 1.07)	0.92 (0.86, 0.99)	0.92 (0.86, 0.99)	0.84 (0.78, 0.90)	<.001	0.76 (0.69, 0.84)
MV-adjusted model	Ref.	1.08 (1.01, 1.16)	0.99 (0.92, 1.07)	1.00 (0.92, 1.08)	0.90 (0.83, 0.98)	0.007	0.86 (0.76, 0.96)
HPFS							
Median (% energy)	4.4	5.2	5.8	6.5	7.7		
Deaths (n)	887	832	793	844	836		
Age-adjusted model	Ref.	0.94 (0.85, 1.03)	0.90 (0.82, 1.00)	0.94 (0.86, 1.04)	0.93 (0.85, 1.03)	0.26	0.91 (0.79, 1.04)
MV-adjusted model	Ref.	0.97 (0.88, 1.07)	0.93 (0.84, 1.04)	0.98 (0.88, 1.09)	0.98 (0.87, 1.10)	0.85	0.97 (0.82, 1.14)
Pooled							
Age-adjusted model	Ref.	0.98 (0.93, 1.03)	0.91 (0.86, 0.97)	0.93 (0.88, 0.98)	0.87 (0.82, 0.92)	<.001	0.81 (0.75, 0.88)
MV-adjusted model	Ref.	1.04 (0.98, 1.10)	0.97 (0.92, 1.03)	0.99 (0.93, 1.05)	0.93 (0.87, 0.99)	0.02	0.89 (0.81, 0.98)
Monounsaturated fat							

NHS							
Median (% energy)	9.4	11.4	12.8	14.4	17.2		
Deaths (n)	2125	1771	1608	1410	1005		
Age-adjusted model	Ref.	1.03 (0.97, 1.10)	1.12 (1.05, 1.19)	1.17 (1.09, 1.26)	1.22 (1.13, 1.32)	<.001	1.15 (1.10, 1.21)
MV-adjusted model	Ref.	0.94 (0.88, 1.01)	0.96 (0.88, 1.05)	0.97 (0.88, 1.07)	0.96 (0.86, 1.08)	0.42	0.97 (0.90, 1.04)
HPFS							
Median (% energy)	8.9	10.8	12.1	13.3	15.3		
Deaths (n)	848	808	866	838	832		
Age-adjusted model	Ref.	0.99 (0.90, 1.09)	1.12 (1.01, 1.23)	1.14 (1.03, 1.25)	1.18 (1.07, 1.30)	<.001	1.16 (1.08, 1.24)
MV-adjusted model	Ref.	0.91 (0.82, 1.02)	0.95 (0.84, 1.08)	0.91 (0.79, 1.05)	0.87 (0.74, 1.02)	0.10	0.90 (0.80, 1.02)
Pooled							
Age-adjusted model	Ref.	1.02 (0.97, 1.07)	1.12 (1.06, 1.18)	1.16 (1.10, 1.23)	1.21 (1.14, 1.28)	<.001	1.15 (1.11, 1.20)
MV-adjusted model	Ref.	0.93 (0.88, 0.99)	0.96 (0.89, 1.03)	0.95 (0.88, 1.03)	0.93 (0.85, 1.02)	0.12	0.95 (0.89, 1.01)
trans fat							
NHS							
Median (% energy)	0.9	1.2	1.5	1.9	2.5		
Deaths (n)	2036	1973	1693	1334	883		
Age-adjusted model	Ref.	1.19 (1.11, 1.27)	1.29 (1.20, 1.38)	1.38 (1.28, 1.49)	1.42 (1.30, 1.55)	<.001	1.57 (1.43, 1.74)
MV-adjusted model	Ref.	1.02 (0.95, 1.09)	0.99 (0.91, 1.07)	0.95 (0.87, 1.05)	0.89 (0.80, 0.99)	0.04	0.87 (0.76, 0.99)
HPFS							
Median (% energy)	0.7	1.0	1.2	1.4	1.9		
Deaths (n)	809	834	826	923	800		
Age-adjusted model	Ref.	1.07 (0.97, 1.18)	1.10 (1.00, 1.22)	1.32 (1.20, 1.45)	1.28 (1.16, 1.41)	<.001	1.62 (1.38, 1.89)
MV-adjusted model	Ref.	1.01 (0.91, 1.12)	0.97 (0.87, 1.09)	1.10 (0.98, 1.24)	1.00 (0.88, 1.13)	0.60	1.08 (0.88, 1.32)
Pooled							
Age-adjusted model	Ref.	1.15 (1.09, 1.22)	1.23 (1.16, 1.30)	1.36 (1.28, 1.44)	1.36 (1.27, 1.45)	<.001	1.59 (1.46, 1.72)
MV-adjusted model	Ref.	1.01 (0.96, 1.07)	0.98 (0.92, 1.05)	1.01 (0.94, 1.08)	0.93 (0.86, 1.01)	0.14	0.93 (0.83, 1.03)

Abbreviations: HR, hazard ratio; CI, confidence interval; MV, multivariable; NHS, Nurses' Health Study; HPFS, Health Professional Follow-up Study.

^a Hazard ratios (95% confidence interval) of cancer mortality for substituting 5% of energy from saturated fatty acids, unsaturated fatty acids, polyunsaturated fatty acids, and monounsaturated fatty acids, and 2% of energy from *trans* fatty acids, for the same energy from carbohydrate.

^b Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, ≥35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, ≥15 g/d; men: 0, 0.1-4.9, 5.0-29.9, ≥30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), intakes of total energy, dietary cholesterol and percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models, except total fat, also included percentages of energy intake from remaining fatty acids (saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids and *trans* fatty acids, all in quintiles).

^c Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 14. Associations Between Dietary ω -6 and ω -3 Polyunsaturated Fatty Acid Intake and Cancer Mortality (comparison is isocaloric substitution for carbohydrate)

	Quintile of dietary fatty acid intake					<i>P</i> _{trend}	HR (95% CI) ^a
	Q1	Q2	Q3	Q4	Q5		
ω-6 polyunsaturated fatty acid							
Total ω-6 polyunsaturated fatty acids							
NHS							
Median (% energy)	3.4	4.3	4.9	5.5	6.7		
Deaths (n)	1526	1695	1653	1582	1463		
Age-adjusted model	Ref.	0.94 (0.88, 1.01)	0.92 (0.85, 0.98)	0.89 (0.83, 0.96)	0.83 (0.78, 0.90)	<.001	0.90 (0.86, 0.94)
MV-adjusted model ^b	Ref.	1.03 (0.96, 1.11)	1.00 (0.93, 1.09)	0.98 (0.90, 1.07)	0.91 (0.83, 1.00)	0.04	0.94 (0.89, 1.00)
HPFS							
Median (% energy)	3.7	4.5	5.1	5.8	6.9		
Deaths (n)	892	826	859	814	801		
Age-adjusted model	Ref.	0.92 (0.84, 1.01)	0.97 (0.88, 1.07)	0.92 (0.84, 1.02)	0.93 (0.84, 1.02)	0.18	0.95 (0.90, 1.01)
MV-adjusted model	Ref.	0.94 (0.85, 1.04)	1.00 (0.90, 1.11)	0.94 (0.83, 1.05)	0.93 (0.82, 1.06)	0.37	0.96 (0.89, 1.04)
Pooled ^c							
Age-adjusted model	Ref.	0.94 (0.88, 0.99)	0.93 (0.88, 0.99)	0.90 (0.85, 0.96)	0.87 (0.82, 0.92)	<.001	0.92 (0.89, 0.95)
MV-adjusted model	Ref.	1.00 (0.94, 1.06)	1.00 (0.94, 1.07)	0.97 (0.90, 1.03)	0.92 (0.85, 0.99)	0.03	0.95 (0.91, 0.99)
Linoleic acid							
NHS							
Median (% energy)	3.3	4.2	4.8	5.4	6.5		
Deaths (n)	1543	1699	1644	1580	1453		

Age-adjusted model	Ref.	0.94 (0.88, 1.01)	0.91 (0.85, 0.98)	0.89 (0.83, 0.96)	0.83 (0.77, 0.89)	<.001	0.89 (0.85, 0.93)
MV-adjusted model	Ref.	1.02 (0.95, 1.10)	0.99 (0.91, 1.07)	0.97 (0.89, 1.06)	0.89 (0.81, 0.98)	0.01	0.93 (0.88, 0.98)
HPFS							
Median (% energy)	3.6	4.4	5.0	5.6	6.7		
Deaths (n)	884	847	808	857	796		
Age-adjusted model	Ref.	0.98 (0.89, 1.07)	0.94 (0.86, 1.04)	1.00 (0.91, 1.09)	0.93 (0.84, 1.03)	0.23	0.96 (0.90, 1.02)
MV-adjusted model	Ref.	1.01 (0.92, 1.12)	0.97 (0.87, 1.08)	1.03 (0.92, 1.15)	0.96 (0.84, 1.09)	0.62	0.98 (0.90, 1.06)
Pooled							
Age-adjusted model	Ref.	0.95 (0.90, 1.01)	0.92 (0.87, 0.98)	0.93 (0.88, 0.98)	0.86 (0.81, 0.91)	<.001	0.91 (0.88, 0.95)
MV-adjusted model	Ref.	1.02 (0.96, 1.08)	0.98 (0.92, 1.05)	0.99 (0.93, 1.06)	0.92 (0.85, 0.99)	0.02	0.95 (0.90, 0.99)
Arachidonic acid							
NHS							
Median (% energy)	0.05	0.06	0.07	0.09	0.11		
Deaths (n)	2014	1711	1486	1427	1281		
Age-adjusted model	Ref.	1.02 (0.95, 1.09)	0.98 (0.91, 1.05)	1.02 (0.95, 1.09)	1.01 (0.94, 1.08)	0.76	1.05 (0.76, 1.45)
MV-adjusted model	Ref.	1.01 (0.94, 1.08)	0.95 (0.88, 1.02)	0.96 (0.88, 1.04)	0.91 (0.83, 1.01)	0.08	0.66 (0.42, 1.05)
HPFS							
Median (% energy)	0.05	0.06	0.07	0.09	0.11		
Deaths (n)	817	833	823	865	854		
Age-adjusted model	Ref.	1.05 (0.95, 1.15)	1.05 (0.96, 1.16)	1.14 (1.03, 1.25)	1.09 (0.99, 1.20)	0.03	1.52 (1.00, 2.33)
MV-adjusted	Ref.	1.05 (0.94, 1.16)	1.03 (0.92, 1.15)	1.10 (0.97, 1.24)	1.01 (0.87, 1.16)	0.81	1.00 (0.53, 1.86)

model							
Pooled							
Age-adjusted model	Ref.	1.03 (0.97, 1.08)	1.00 (0.95, 1.06)	1.06 (1.00, 1.12)	1.04 (0.98, 1.10)	0.12	1.20 (0.93, 1.56)
MV-adjusted model	Ref.	1.02 (0.96, 1.08)	0.97 (0.91, 1.04)	1.00 (0.94, 1.08)	0.94 (0.87, 1.02)	0.20	0.76 (0.53, 1.11)
ω-3 polyunsaturated fatty acid							
Total ω-3 polyunsaturated fatty acids							
NHS							
Median (% energy)	0.48	0.57	0.63	0.72	0.88		
Deaths (n)	1542	1479	1581	1599	1718		
Age-adjusted model	Ref.	0.93 (0.87, 1.00)	0.95 (0.89, 1.02)	0.88 (0.82, 0.95)	0.79 (0.74, 0.85)	<.001	0.84 (0.80, 0.88)
MV-adjusted model	Ref.	1.00 (0.93, 1.07)	1.05 (0.98, 1.14)	1.02 (0.94, 1.10)	0.99 (0.91, 1.08)	0.81	0.99 (0.93, 1.05)
HPFS							
Median (% energy)	0.46	0.57	0.65	0.75	0.94		
Deaths (n)	782	810	859	873	868		
Age-adjusted model	Ref.	0.91 (0.82, 1.00)	0.93 (0.84, 1.02)	0.91 (0.83, 1.01)	0.83 (0.75, 0.92)	<.001	0.90 (0.85, 0.95)
MV-adjusted model	Ref.	0.99 (0.90, 1.10)	1.04 (0.94, 1.16)	1.05 (0.95, 1.17)	1.01 (0.90, 1.13)	0.80	1.00 (0.94, 1.07)
Pooled							
Age-adjusted model	Ref.	0.92 (0.87, 0.98)	0.94 (0.89, 1.00)	0.89 (0.84, 0.95)	0.80 (0.76, 0.85)	<.001	0.87 (0.83, 0.90)
MV-adjusted model	Ref.	1.00 (0.94, 1.06)	1.05 (0.99, 1.12)	1.03 (0.97, 1.10)	1.00 (0.93, 1.07)	0.99	1.00 (0.95, 1.04)

α-linolenic acid							
NHS							
Median (% energy)	0.41	0.48	0.53	0.59	0.70		
Deaths (n)	1558	1517	1559	1556	1729		
Age-adjusted model	Ref.	1.01 (0.94, 1.09)	1.07 (1.00, 1.15)	1.05 (0.97, 1.12)	0.95 (0.89, 1.02)	0.20	0.96 (0.89, 1.02)
MV-adjusted model	Ref.	1.05 (0.97, 1.13)	1.12 (1.04, 1.21)	1.11 (1.03, 1.20)	1.10 (1.01, 1.20)	0.03	1.10 (1.01, 1.20)
HPFS							
Median (% energy)	0.38	0.45	0.50	0.56	0.68		
Deaths (n)	723	821	830	864	954		
Age-adjusted model	Ref.	1.09 (0.98, 1.20)	1.06 (0.96, 1.17)	1.07 (0.97, 1.18)	1.06 (0.96, 1.18)	0.42	1.03 (0.94, 1.13)
MV-adjusted model	Ref.	1.11 (1.00, 1.23)	1.10 (0.99, 1.22)	1.11 (0.99, 1.24)	1.15 (1.02, 1.29)	0.06	1.10 (0.98, 1.22)
Pooled							
Age-adjusted model	Ref.	1.04 (0.98, 1.10)	1.07 (1.01, 1.13)	1.05 (0.99, 1.12)	0.99 (0.93, 1.05)	0.60	0.98 (0.93, 1.04)
MV-adjusted model	Ref.	1.07 (1.01, 1.13)	1.11 (1.05, 1.19)	1.11 (1.04, 1.18)	1.12 (1.04, 1.20)	0.004	1.10 (1.03, 1.18)
Marine ω-3 fats (DHA+EPA)							
NHS							
Median (% energy)	0.03	0.05	0.08	0.12	0.21		
Deaths (n)	1320	1562	1685	1640	1712		
Age-adjusted model	Ref.	0.99 (0.92, 1.06)	0.95 (0.88, 1.02)	0.87 (0.80, 0.93)	0.79 (0.73, 0.85)	<.001	0.66 (0.59, 0.73)
MV-adjusted model	Ref.	1.04 (0.97, 1.12)	1.04 (0.96, 1.12)	1.00 (0.92, 1.08)	0.96 (0.89, 1.05)	0.09	0.90 (0.80, 1.02)
HPFS							
Median (% energy)	0.04	0.08	0.12	0.18	0.31		

energy)							
Deaths (n)	806	822	880	838	846		
Age-adjusted model	Ref.	0.94 (0.86, 1.04)	1.01 (0.92, 1.11)	0.94 (0.86, 1.04)	0.85 (0.77, 0.94)	<.001	0.85 (0.77, 0.93)
MV-adjusted model	Ref.	0.99 (0.90, 1.09)	1.10 (1.00, 1.22)	1.08 (0.97, 1.20)	1.00 (0.89, 1.12)	0.92	1.00 (0.90, 1.12)
Pooled							
Age-adjusted model	Ref.	0.97 (0.92, 1.03)	0.97 (0.91, 1.03)	0.89 (0.84, 0.95)	0.81 (0.76, 0.86)	<.001	0.76 (0.70, 0.81)
MV-adjusted model	Ref.	1.02 (0.96, 1.09)	1.06 (1.00, 1.13)	1.03 (0.97, 1.10)	0.98 (0.91, 1.04)	0.22	0.95 (0.88, 1.04)
ω-6/ω-3 ratio							
NHS							
Median	5.5	6.7	7.6	8.4	9.9		
Deaths (n)	1564	1740	1630	1617	1368		
Age-adjusted model	Ref.	1.11 (1.04, 1.19)	1.07 (0.99, 1.14)	1.10 (1.03, 1.19)	1.08 (1.00, 1.16)	0.06	1.01 (1.00, 1.03)
MV-adjusted model	Ref.	1.08 (1.01, 1.16)	1.02 (0.95, 1.10)	1.04 (0.97, 1.12)	0.98 (0.91, 1.07)	0.41	0.99 (0.98, 1.01)
HPFS							
Median	5.5	6.9	7.9	8.9	10.8		
Deaths (n)	946	872	839	835	700		
Age-adjusted model	Ref.	1.02 (0.93, 1.12)	1.05 (0.96, 1.16)	1.13 (1.03, 1.24)	1.02 (0.92, 1.12)	0.27	1.01 (0.99, 1.03)
MV-adjusted model	Ref.	0.97 (0.88, 1.07)	0.94 (0.85, 1.04)	0.98 (0.88, 1.09)	0.87 (0.78, 0.97)	0.03	0.98 (0.96, 1.00)
Pooled							
Age-adjusted model	Ref.	1.08 (1.02, 1.14)	1.06 (1.00, 1.12)	1.11 (1.05, 1.18)	1.06 (1.00, 1.12)	0.03	1.01 (1.00, 1.02)
MV-adjusted model	Ref.	1.04 (0.98, 1.10)	0.99 (0.93, 1.05)	1.02 (0.96, 1.08)	0.94 (0.88, 1.01)	0.04	0.99 (0.97, 1.00)

Abbreviations: HR, hazard ratio; CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MV, multivariable; NHS, Nurses' Health Study; HPFS, Health Professional Follow-up Study.

^a Hazard ratios (95% confidence interval) of cancer mortality for substituting 2% of energy from total ω -6 polyunsaturated fatty acids and linoleic acid, and 0.3% of energy from total ω -3 polyunsaturated fatty acids, arachidonic acid, and α -linolenic acid and marine ω -3 fats, for the same energy from carbohydrate. For ω -6/ ω -3 ration, the Hazard ratios (95% confidence interval) of total mortality were calculated for 1-unit increment.

^b Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, \geq 35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, \geq 27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current \geq 25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, \geq 15 g/d; men: 0, 0.1-4.9, 5.0-29.9, \geq 30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), intakes of total energy, dietary cholesterol and percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models also included percentages of energy intake from remaining fatty acids (saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, *trans* fatty acids, ω -6 polyunsaturated fatty acids, ω -3 polyunsaturated fatty acids, linoleic acid, arachidonic acid, α -linolenic acid and marine ω -3 fats, all in quintiles).

^c Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 15. Associations Between Total and Specific Types of Fat Intakes and Neurodegenerative Disease Mortality (comparison is isocaloric substitution for carbohydrate)

	Quintile of dietary fatty acid intake					<i>P</i> _{trend}	HR (95% CI) ^a
	Q1	Q2	Q3	Q4	Q5		
Total fat							
NHS							
Median (% energy)	25.4	30.0	33.2	36.6	42.2		
Deaths (n)	776	525	355	267	156		
Age-adjusted model	Ref.	0.99 (0.89, 1.11)	0.92 (0.81, 1.04)	0.96 (0.83, 1.10)	1.05 (0.88, 1.25)	0.79	0.99 (0.95, 1.04)
^b MV-adjusted model	Ref.	0.95 (0.85, 1.07)	0.80 (0.70, 0.91)	0.73 (0.62, 0.85)	0.60 (0.50, 0.73)	<.001	0.86 (0.82, 0.90)
HPFS							
Median (% energy)	23.8	28.3	31.3	34.2	38.4		
Deaths (n)	193	168	174	173	132		
Age-adjusted model	Ref.	0.94 (0.77, 1.16)	1.04 (0.84, 1.27)	1.14 (0.93, 1.40)	1.01 (0.81, 1.27)	0.42	1.03 (0.96, 1.10)
MV-adjusted model	Ref.	0.89 (0.72, 1.10)	0.91 (0.73, 1.14)	0.93 (0.74, 1.17)	0.76 (0.59, 0.98)	0.07	0.92 (0.85, 1.00)
Pooled ^c							
Age-adjusted model	Ref.	0.98 (0.89, 1.08)	0.95 (0.85, 1.06)	1.01 (0.90, 1.14)	1.04 (0.90, 1.19)	0.83	1.00 (0.97, 1.04)
MV-adjusted model	Ref.	0.94 (0.85, 1.04)	0.83 (0.74, 0.93)	0.78 (0.69, 0.89)	0.66 (0.56, 0.77)	<.001	0.88 (0.84, 0.92)
Saturated fat							
NHS							
Median (% energy)	8.2	10.2	11.8	13.5	16.5		
Deaths (n)	746	509	404	264	156		
Age-adjusted model	Ref.	1.09 (0.98, 1.22)	1.25 (1.11, 1.41)	1.31 (1.13, 1.51)	1.65 (1.39, 1.97)	<.001	1.34 (1.22, 1.46)
MV-adjusted model	Ref.	0.97 (0.85, 1.10)	1.01 (0.87, 1.17)	0.95 (0.79, 1.14)	0.86 (0.68, 1.09)	0.60	0.97 (0.85, 1.10)
HPFS							
Median (% energy)	7.1	9.0	10.2	11.5	13.5		
Deaths (n)	175	185	170	165	145		
Age-adjusted model	Ref.	1.20 (0.98, 1.48)	1.25 (1.01, 1.54)	1.33 (1.07, 1.64)	1.43 (1.15, 1.78)	<.001	1.30 (1.11, 1.52)
MV-adjusted model	Ref.	1.08 (0.85, 1.36)	1.07 (0.82, 1.38)	1.03 (0.78, 1.37)	1.03 (0.76, 1.41)	0.76	1.03 (0.82, 1.29)

Pooled							
Age-adjusted model	Ref.	1.12 (1.01, 1.23)	1.25 (1.12, 1.39)	1.31 (1.17, 1.48)	1.56 (1.36, 1.79)	<.001	1.33 (1.23, 1.43)
MV-adjusted model	Ref.	0.99 (0.89, 1.11)	1.02 (0.90, 1.17)	0.97 (0.83, 1.13)	0.92 (0.76, 1.11)	0.76	0.98 (0.88, 1.10)
Unsaturated fat							
NHS							
Median (% energy)	14.2	16.8	18.7	20.6	23.8		
Deaths (n)	790	485	349	265	190		
Age-adjusted model	Ref.	0.88 (0.79, 0.99)	0.85 (0.75, 0.97)	0.82 (0.71, 0.94)	0.79 (0.68, 0.93)	<.001	0.87 (0.81, 0.94)
MV-adjusted model	Ref.	0.82 (0.73, 0.93)	0.72 (0.63, 0.83)	0.66 (0.56, 0.78)	0.62 (0.51, 0.75)	<.001	0.74 (0.67, 0.81)
HPFS							
Median (% energy)	13.7	16.3	18.0	19.7	22.3		
Deaths (n)	188	182	174	173	123		
Age-adjusted model	Ref.	1.01 (0.82, 1.23)	1.03 (0.84, 1.27)	1.12 (0.91, 1.37)	0.81 (0.65, 1.02)	0.28	0.93 (0.83, 1.05)
MV-adjusted model	Ref.	0.89 (0.71, 1.11)	0.84 (0.66, 1.07)	0.86 (0.67, 1.10)	0.62 (0.47, 0.81)	<.001	0.77 (0.67, 0.90)
Pooled							
Age-adjusted model	Ref.	0.91 (0.82, 1.00)	0.90 (0.80, 1.00)	0.90 (0.80, 1.01)	0.80 (0.70, 0.91)	<.001	0.89 (0.84, 0.95)
MV-adjusted model	Ref.	0.84 (0.75, 0.93)	0.75 (0.67, 0.85)	0.71 (0.62, 0.82)	0.62 (0.53, 0.72)	<.001	0.75 (0.69, 0.81)
Polyunsaturated fat							
NHS							
Median (% energy)	4.2	5.0	5.6	6.3	7.5		
Deaths (n)	507	495	399	329	349		
Age-adjusted model	Ref.	0.91 (0.80, 1.03)	0.71 (0.62, 0.81)	0.56 (0.48, 0.64)	0.48 (0.42, 0.56)	<.001	0.31 (0.25, 0.37)
MV-adjusted model	Ref.	1.13 (1.00, 1.29)	0.99 (0.86, 1.14)	0.88 (0.76, 1.03)	0.92 (0.78, 1.07)	0.04	0.80 (0.64, 0.99)
HPFS							
Median (% energy)	4.4	5.2	5.8	6.5	7.7		
Deaths (n)	188	176	174	170	132		
Age-adjusted model	Ref.	0.91 (0.74, 1.12)	0.91 (0.74, 1.13)	0.84 (0.68, 1.03)	0.62 (0.49, 0.78)	<.001	0.51 (0.37, 0.69)
MV-adjusted model	Ref.	0.92 (0.74, 1.14)	0.90 (0.72, 1.13)	0.80 (0.63, 1.01)	0.62 (0.48, 0.81)	<.001	0.50 (0.35, 0.73)
Pooled							
Age-adjusted model	Ref.	0.91 (0.82, 1.01)	0.76 (0.68, 0.85)	0.63 (0.56, 0.71)	0.52 (0.46, 0.58)	<.001	0.35 (0.30, 0.42)
MV-adjusted model	Ref.	1.07 (0.96, 1.20)	0.96 (0.86, 1.08)	0.86 (0.76, 0.97)	0.83 (0.73, 0.95)	<.001	0.71 (0.59, 0.86)
Monounsaturated fat							

NHS							
Median (% energy)	9.4	11.4	12.8	14.4	17.2		
Deaths (n)	836	494	340	251	158		
Age-adjusted model	Ref.	0.99 (0.88, 1.10)	1.04 (0.92, 1.19)	1.08 (0.94, 1.25)	1.07 (0.90, 1.27)	0.23	1.06 (0.96, 1.16)
MV-adjusted model	Ref.	0.81 (0.71, 0.92)	0.76 (0.64, 0.89)	0.69 (0.57, 0.84)	0.59 (0.46, 0.76)	<.001	0.68 (0.58, 0.79)
HPFS							
Median (% energy)	8.9	10.8	12.1	13.3	15.3		
Deaths (n)	191	172	182	167	128		
Age-adjusted model	Ref.	0.96 (0.78, 1.19)	1.12 (0.92, 1.38)	1.14 (0.93, 1.41)	1.00 (0.79, 1.25)	0.49	1.05 (0.90, 1.23)
MV-adjusted model	Ref.	0.92 (0.73, 1.17)	1.05 (0.80, 1.38)	1.04 (0.76, 1.41)	0.96 (0.67, 1.36)	0.87	0.98 (0.75, 1.28)
Pooled							
Age-adjusted model	Ref.	0.98 (0.89, 1.08)	1.07 (0.96, 1.19)	1.10 (0.98, 1.24)	1.04 (0.91, 1.19)	0.17	1.06 (0.98, 1.15)
MV-adjusted model	Ref.	0.83 (0.74, 0.94)	0.83 (0.72, 0.95)	0.78 (0.66, 0.91)	0.69 (0.57, 0.85)	<.001	0.74 (0.65, 0.84)
trans fat							
NHS							
Median (% energy)	0.9	1.2	1.5	1.9	2.5		
Deaths (n)	637	572	430	294	146		
Age-adjusted model	Ref.	1.79 (1.59, 2.01)	2.42 (2.13, 2.75)	3.19 (2.76, 3.69)	3.25 (2.70, 3.92)	<.001	5.39 (4.49, 6.47)
MV-adjusted model	Ref.	1.28 (1.13, 1.45)	1.37 (1.19, 1.59)	1.45 (1.22, 1.73)	1.15 (0.92, 1.45)	0.02	1.37 (1.06, 1.76)
HPFS							
Median (% energy)	0.7	1.0	1.2	1.4	1.9		
Deaths (n)	161	162	176	188	153		
Age-adjusted model	Ref.	1.13 (0.91, 1.40)	1.35 (1.08, 1.67)	1.68 (1.35, 2.09)	1.73 (1.38, 2.18)	<.001	2.83 (1.98, 4.05)
MV-adjusted model	Ref.	1.10 (0.87, 1.39)	1.24 (0.97, 1.59)	1.47 (1.13, 1.91)	1.43 (1.07, 1.90)	0.002	2.07 (1.33, 3.25)
Pooled							
Age-adjusted model	Ref.	1.62 (1.46, 1.79)	2.08 (1.86, 2.32)	2.62 (2.32, 2.95)	2.54 (2.20, 2.93)	<.001	4.72 (4.01, 5.55)
MV-adjusted model	Ref.	1.24 (1.11, 1.38)	1.34 (1.18, 1.52)	1.46 (1.26, 1.69)	1.25 (1.05, 1.50)	<.001	1.51 (1.21, 1.88)

Abbreviations: HR, hazard ratio; CI, confidence interval; MV, multivariable; NHS, Nurses' Health Study; HPFS, Health Professional Follow-up Study.

^a Hazard ratios (95% confidence interval) of neurodegenerative disease mortality for substituting 5% of energy from saturated fatty acids, unsaturated fatty acids, polyunsaturated fatty acids, and monounsaturated fatty acids, and 2% of energy from *trans* fatty acids, for the same energy from carbohydrate.

^b Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, ≥35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, ≥15 g/d; men: 0, 0.1-4.9, 5.0-29.9, ≥30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), intakes of total energy, dietary cholesterol and percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models, except total fat, also included percentages of energy intake from remaining fatty acids (saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids and *trans* fatty acids, all in quintiles).

^c Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 16. Associations Between Total and Specific Types of Fat Intakes and Respiratory Disease Mortality (comparison is isocaloric substitution for carbohydrate)

	Quintile of dietary fatty acid intake					<i>P</i> _{trend}	HR (95% CI) ^a
	Q1	Q2	Q3	Q4	Q5		
Total fat							
NHS							
Median (% energy)	25.4	30.0	33.2	36.6	42.2		
Deaths (n)	398	344	325	309	208		
Age-adjusted model	Ref.	1.22 (1.05, 1.41)	1.51 (1.30, 1.75)	1.91 (1.64, 2.22)	2.29 (1.93, 2.71)	<.001	1.30 (1.24, 1.36)
MV-adjusted model ^b	Ref.	1.00 (0.86, 1.16)	1.05 (0.90, 1.23)	1.08 (0.91, 1.27)	1.01 (0.83, 1.23)	0.63	1.01 (0.96, 1.07)
HPFS							
Median (% energy)	23.8	28.3	31.3	34.2	38.4		
Deaths (n)	190	200	203	189	206		
Age-adjusted model	Ref.	1.13 (0.93, 1.38)	1.22 (1.00, 1.49)	1.23 (1.01, 1.51)	1.53 (1.25, 1.87)	<.001	1.14 (1.07, 1.22)
MV-adjusted model	Ref.	1.00 (0.81, 1.23)	0.97 (0.78, 1.20)	0.90 (0.72, 1.12)	0.98 (0.78, 1.23)	0.63	0.98 (0.91, 1.06)
Pooled ^c							
Age-adjusted model	Ref.	1.19 (1.06, 1.33)	1.40 (1.24, 1.57)	1.63 (1.45, 1.84)	1.93 (1.69, 2.19)	<.001	1.24 (1.20, 1.29)
MV-adjusted model	Ref.	1.00 (0.88, 1.13)	1.02 (0.90, 1.16)	1.01 (0.88, 1.15)	1.00 (0.86, 1.15)	0.92	1.00 (0.96, 1.05)
Saturated fat							
NHS							
Median (% energy)	8.2	10.2	11.8	13.5	16.5		
Deaths (n)	360	350	331	315	228		
Age-adjusted model	Ref.	1.45 (1.25, 1.68)	1.91 (1.64, 2.22)	2.78 (2.39, 3.24)	4.03 (3.40, 4.78)	<.001	2.36 (2.15, 2.59)
MV-adjusted model	Ref.	1.17 (0.99, 1.37)	1.33 (1.11, 1.60)	1.63 (1.33, 1.99)	1.75 (1.38, 2.22)	<.001	1.46 (1.28, 1.67)
HPFS							
Median (% energy)	7.1	9.0	10.2	11.5	13.5		
Deaths (n)	178	208	184	189	229		
Age-adjusted model	Ref.	1.32 (1.08, 1.62)	1.29 (1.05, 1.59)	1.47 (1.20, 1.81)	2.11 (1.73, 2.57)	<.001	1.71 (1.48, 1.97)
MV-adjusted model	Ref.	1.14 (0.91, 1.43)	1.04 (0.80, 1.33)	1.07 (0.82, 1.40)	1.32 (0.99, 1.75)	0.11	1.18 (0.96, 1.45)
Pooled							
Age-adjusted model	Ref.	1.40 (1.25, 1.58)	1.67 (1.48, 1.88)	2.21 (1.96, 2.50)	3.06 (2.69, 3.48)	<.001	2.15 (1.99, 2.32)
MV-adjusted model	Ref.	1.16 (1.01, 1.32)	1.22 (1.05, 1.41)	1.40 (1.19, 1.64)	1.56 (1.30, 1.87)	<.001	1.37 (1.23, 1.54)

Unsaturated fat							
NHS							
Median (% energy)	14.2	16.8	18.7	20.6	23.8		
Deaths (n)	433	347	322	274	208		
Age-adjusted model	Ref.	1.09 (0.95, 1.26)	1.29 (1.12, 1.49)	1.36 (1.16, 1.58)	1.42 (1.20, 1.68)	<.001	1.23 (1.13, 1.33)
MV-adjusted model	Ref.	0.83 (0.71, 0.96)	0.80 (0.68, 0.94)	0.71 (0.59, 0.85)	0.64 (0.52, 0.79)	<.001	0.79 (0.71, 0.87)
HPFS							
Median (% energy)	13.7	16.3	18.0	19.7	22.3		
Deaths (n)	207	189	225	175	192		
Age-adjusted model	Ref.	0.94 (0.77, 1.14)	1.20 (0.99, 1.45)	1.00 (0.81, 1.22)	1.13 (0.93, 1.38)	0.17	1.08 (0.97, 1.20)
MV-adjusted model	Ref.	0.81 (0.65, 1.00)	0.92 (0.74, 1.14)	0.68 (0.54, 0.87)	0.70 (0.55, 0.90)	0.003	0.81 (0.71, 0.93)
Pooled							
Age-adjusted model	Ref.	1.04 (0.92, 1.16)	1.26 (1.12, 1.41)	1.21 (1.07, 1.37)	1.29 (1.14, 1.47)	<.001	1.17 (1.10, 1.25)
MV-adjusted model	Ref.	0.82 (0.73, 0.93)	0.84 (0.74, 0.96)	0.70 (0.60, 0.81)	0.67 (0.57, 0.78)	<.001	0.80 (0.73, 0.86)
Polyunsaturated fat							
NHS							
Median (% energy)	4.2	5.0	5.6	6.3	7.5		
Deaths (n)	332	343	312	309	288		
Age-adjusted model	Ref.	0.98 (0.84, 1.14)	0.92 (0.78, 1.07)	0.91 (0.78, 1.06)	0.77 (0.65, 0.91)	<.001	0.69 (0.55, 0.86)
MV-adjusted model	Ref.	1.05 (0.90, 1.23)	0.95 (0.81, 1.12)	0.93 (0.79, 1.10)	0.82 (0.68, 0.98)	0.03	0.75 (0.59, 0.97)
HPFS							
Median (% energy)	4.4	5.2	5.8	6.5	7.7		
Deaths (n)	224	190	191	204	179		
Age-adjusted model	Ref.	0.82 (0.67, 0.99)	0.85 (0.70, 1.03)	0.85 (0.70, 1.03)	0.71 (0.58, 0.86)	0.003	0.64 (0.48, 0.85)
MV-adjusted model	Ref.	0.85 (0.69, 1.03)	0.87 (0.70, 1.07)	0.86 (0.69, 1.06)	0.75 (0.59, 0.95)	0.03	0.67 (0.47, 0.94)
Pooled							
Age-adjusted model	Ref.	0.91 (0.81, 1.03)	0.89 (0.79, 1.00)	0.88 (0.78, 1.00)	0.74 (0.66, 0.84)	<.001	0.67 (0.56, 0.80)
MV-adjusted model	Ref.	0.97 (0.86, 1.10)	0.92 (0.81, 1.05)	0.90 (0.79, 1.03)	0.79 (0.68, 0.92)	0.002	0.72 (0.59, 0.88)
Monounsaturated fat							
NHS							
Median (% energy)	9.4	11.4	12.8	14.4	17.2		
Deaths (n)	414	397	310	277	186		

Age-adjusted model	Ref.	1.43 (1.24, 1.64)	1.55 (1.33, 1.80)	1.84 (1.58, 2.15)	1.97 (1.65, 2.35)	<.001	1.58 (1.43, 1.75)
MV-adjusted model	Ref.	1.05 (0.89, 1.23)	0.94 (0.77, 1.14)	0.89 (0.72, 1.11)	0.77 (0.59, 1.00)	0.01	0.81 (0.69, 0.96)
HPFS							
Median (% energy)	8.9	10.8	12.1	13.3	15.3		
Deaths (n)	202	197	196	206	187		
Age-adjusted model	Ref.	1.03 (0.85, 1.25)	1.12 (0.92, 1.36)	1.29 (1.07, 1.57)	1.32 (1.08, 1.61)	<.001	1.28 (1.11, 1.48)
MV-adjusted model	Ref.	0.91 (0.73, 1.14)	0.86 (0.67, 1.12)	0.89 (0.66, 1.18)	0.81 (0.59, 1.13)	0.24	0.88 (0.68, 1.12)
Pooled							
Age-adjusted model	Ref.	1.28 (1.15, 1.44)	1.37 (1.22, 1.55)	1.61 (1.42, 1.81)	1.65 (1.45, 1.89)	<.001	1.48 (1.36, 1.61)
MV-adjusted model	Ref.	1.00 (0.88, 1.14)	0.91 (0.78, 1.06)	0.89 (0.75, 1.06)	0.78 (0.64, 0.96)	0.006	0.83 (0.73, 0.95)
trans fat							
NHS							
Median (% energy)	0.9	1.2	1.5	1.9	2.5		
Deaths (n)	375	416	373	255	165		
Age-adjusted model	Ref.	1.79 (1.55, 2.07)	2.47 (2.12, 2.87)	2.84 (2.40, 3.37)	3.54 (2.91, 4.31)	<.001	4.85 (3.94, 5.96)
MV-adjusted model	Ref.	1.19 (1.02, 1.39)	1.27 (1.07, 1.52)	1.20 (0.98, 1.48)	1.22 (0.95, 1.57)	0.15	1.23 (0.93, 1.64)
HPFS							
Median (% energy)	0.7	1.0	1.2	1.4	1.9		
Deaths (n)	180	192	204	189	223		
Age-adjusted model	Ref.	1.20 (0.98, 1.47)	1.39 (1.13, 1.70)	1.46 (1.18, 1.80)	2.14 (1.75, 2.63)	<.001	3.51 (2.54, 4.87)
MV-adjusted model	Ref.	1.08 (0.87, 1.35)	1.13 (0.89, 1.42)	1.12 (0.87, 1.43)	1.47 (1.13, 1.90)	0.005	1.82 (1.20, 2.76)
Pooled							
Age-adjusted model	Ref.	1.57 (1.39, 1.76)	2.01 (1.78, 2.27)	2.18 (1.91, 2.49)	2.79 (2.42, 3.21)	<.001	4.42 (3.71, 5.26)
MV-adjusted model	Ref.	1.15 (1.02, 1.31)	1.22 (1.06, 1.40)	1.17 (1.00, 1.37)	1.33 (1.11, 1.59)	0.005	1.40 (1.11, 1.77)

Abbreviations: HR, hazard ratio; CI, confidence interval; MV, multivariable; NHS, Nurses' Health Study; HPFS, Health Professional Follow-up Study.

^a Hazard ratios (95% confidence interval) of respiratory disease mortality for substituting 5% of energy from saturated fatty acids, unsaturated fatty acids, polyunsaturated fatty acids, and monounsaturated fatty acids, and 2% of energy from *trans* fatty acids, for the same energy from carbohydrate.

^b Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, ≥35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥25 cigarettes/d), alcohol consumption (women: 0, 0.1-

4.9, 5.0-14.9, ≥ 15 g/d; men: 0, 0.1-4.9, 5.0-29.9, ≥ 30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), intakes of total energy, dietary cholesterol and percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models, except total fat, also included percentages of energy intake from remaining fatty acids (saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids and *trans* fatty acids, all in quintiles).^c Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 17. Associations Between Dietary ω -6 and ω -3 Polyunsaturated Fatty Acid Intake and Neurodegenerative Disease Mortality (comparison is isocaloric substitution for carbohydrate)

	Quintile of dietary fatty acid intake					<i>P</i> _{trend}	HR (95% CI) ^a
	Q1	Q2	Q3	Q4	Q5		
ω-6 polyunsaturated fatty acid							
Total ω-6 polyunsaturated fatty acids							
NHS							
Median (% energy)	3.4	4.3	4.9	5.5	6.7		
Deaths (n)	446	491	430	351	361		
Age-adjusted model	Ref.	0.89 (0.79, 1.02)	0.75 (0.65, 0.85)	0.59 (0.51, 0.68)	0.54 (0.47, 0.63)	<.001	0.66 (0.61, 0.72)
MV-adjusted model ^b	Ref.	1.13 (0.98, 1.29)	1.08 (0.93, 1.25)	0.95 (0.80, 1.12)	1.04 (0.86, 1.26)	0.81	0.99 (0.88, 1.10)
HPFS							
Median (% energy)	3.7	4.5	5.1	5.8	6.9		
Deaths (n)	188	172	186	155	139		
Age-adjusted model	Ref.	0.86 (0.70, 1.06)	0.95 (0.78, 1.17)	0.79 (0.64, 0.98)	0.71 (0.57, 0.89)	0.002	0.82 (0.72, 0.93)
MV-adjusted model	Ref.	0.90 (0.73, 1.12)	1.05 (0.84, 1.32)	0.89 (0.69, 1.15)	0.87 (0.65, 1.17)	0.42	0.93 (0.78, 1.10)
Pooled ^c							
Age-adjusted model	Ref.	0.88 (0.79, 0.99)	0.80 (0.72, 0.90)	0.64 (0.57, 0.72)	0.59 (0.52, 0.66)	<.001	0.70 (0.66, 0.75)
MV-adjusted model	Ref.	1.06 (0.95, 1.19)	1.07 (0.94, 1.21)	0.93 (0.81, 1.07)	0.99 (0.84, 1.16)	0.52	0.97 (0.88, 1.06)
Linoleic acid							
NHS							
Median (% energy)	3.3	4.2	4.8	5.4	6.5		
Deaths (n)	461	470	439	350	359		
Age-adjusted model	Ref.	0.84 (0.74, 0.96)	0.76 (0.66, 0.86)	0.58 (0.50, 0.66)	0.51 (0.45, 0.59)	<.001	0.64 (0.59, 0.70)
MV-adjusted model	Ref.	1.04 (0.91, 1.19)	1.08 (0.93, 1.25)	0.93 (0.79, 1.09)	0.97 (0.80, 1.16)	0.51	0.96 (0.86, 1.08)
HPFS							
Median (% energy)	3.6	4.4	5.0	5.6	6.7		
Deaths (n)	195	170	177	165	133		
Age-adjusted model	Ref.	0.87 (0.71, 1.07)	0.92 (0.75, 1.13)	0.83 (0.68, 1.03)	0.66 (0.53, 0.82)	<.001	0.78 (0.68, 0.89)
MV-adjusted model	Ref.	0.93 (0.75, 1.15)	1.00 (0.79, 1.25)	0.92 (0.72, 1.18)	0.78 (0.58, 1.04)	0.13	0.86 (0.72, 1.03)
Pooled							
Age-adjusted model	Ref.	0.85 (0.76, 0.95)	0.80 (0.72, 0.90)	0.65 (0.57, 0.73)	0.55 (0.49, 0.62)	<.001	0.68 (0.63, 0.73)

MV-adjusted model	Ref.	1.01 (0.90, 1.13)	1.05 (0.93, 1.19)	0.92 (0.81, 1.06)	0.91 (0.77, 1.06)	0.17	0.93 (0.85, 1.03)
Arachidonic acid							
NHS							
Median (% energy)	0.05	0.06	0.07	0.09	0.11		
Deaths (n)	767	430	340	290	252		
Age-adjusted model	Ref.	0.89 (0.79, 1.00)	0.85 (0.75, 0.96)	0.78 (0.68, 0.90)	0.69 (0.60, 0.80)	<.001	0.17 (0.09, 0.33)
MV-adjusted model	Ref.	0.84 (0.74, 0.96)	0.82 (0.71, 0.95)	0.83 (0.70, 0.98)	0.87 (0.71, 1.05)	0.20	0.55 (0.22, 1.36)
HPFS							
Median (% energy)	0.05	0.06	0.07	0.09	0.11		
Deaths (n)	211	162	165	157	145		
Age-adjusted model	Ref.	0.82 (0.66, 1.00)	0.83 (0.68, 1.02)	0.82 (0.67, 1.01)	0.67 (0.54, 0.82)	0.001	0.19 (0.07, 0.51)
MV-adjusted model	Ref.	0.79 (0.64, 0.99)	0.77 (0.61, 0.97)	0.76 (0.58, 0.98)	0.65 (0.48, 0.88)	0.02	0.14 (0.03, 0.57)
Pooled							
Age-adjusted model	Ref.	0.87 (0.78, 0.96)	0.84 (0.76, 0.94)	0.79 (0.71, 0.89)	0.69 (0.61, 0.77)	<.001	0.18 (0.10, 0.31)
MV-adjusted model	Ref.	0.83 (0.74, 0.93)	0.80 (0.71, 0.91)	0.81 (0.70, 0.93)	0.80 (0.68, 0.94)	0.02	0.37 (0.17, 0.79)
ω-3 polyunsaturated fatty acid							
Total ω-3 polyunsaturated fatty acids							
NHS							
Median (% energy)	0.48	0.57	0.63	0.72	0.88		
Deaths (n)	486	420	364	392	417		
Age-adjusted model	Ref.	0.88 (0.77, 1.00)	0.69 (0.60, 0.79)	0.63 (0.55, 0.72)	0.39 (0.34, 0.45)	<.001	0.50 (0.45, 0.54)
MV-adjusted model	Ref.	1.02 (0.89, 1.17)	0.90 (0.77, 1.04)	1.00 (0.86, 1.17)	0.91 (0.77, 1.07)	0.22	0.93 (0.82, 1.05)
HPFS							
Median (% energy)	0.46	0.57	0.65	0.75	0.94		
Deaths (n)	159	196	171	173	141		
Age-adjusted model	Ref.	0.94 (0.76, 1.16)	0.75 (0.60, 0.93)	0.71 (0.57, 0.89)	0.47 (0.37, 0.59)	<.001	0.61 (0.54, 0.70)
MV-adjusted model	Ref.	1.08 (0.87, 1.34)	0.89 (0.71, 1.12)	0.92 (0.72, 1.16)	0.66 (0.51, 0.86)	<.001	0.72 (0.62, 0.85)
Pooled							
Age-adjusted model	Ref.	0.90 (0.80, 1.00)	0.71 (0.63, 0.79)	0.65 (0.58, 0.73)	0.41 (0.36, 0.46)	<.001	0.53 (0.49, 0.58)
MV-adjusted model	Ref.	1.04 (0.92, 1.16)	0.89 (0.79, 1.01)	0.98 (0.86, 1.11)	0.83 (0.72, 0.96)	0.002	0.85 (0.77, 0.93)
α-linolenic acid							
NHS							

Median (% energy)	0.41	0.48	0.53	0.59	0.70		
Deaths (n)	537	408	371	335	428		
Age-adjusted model	Ref.	0.85 (0.75, 0.96)	0.75 (0.66, 0.86)	0.59 (0.52, 0.68)	0.42 (0.37, 0.48)	<.001	0.40 (0.36, 0.46)
MV-adjusted model	Ref.	0.96 (0.84, 1.10)	0.95 (0.82, 1.09)	0.87 (0.74, 1.02)	0.90 (0.76, 1.06)	0.10	0.87 (0.73, 1.03)
HPFS							
Median (% energy)	0.38	0.45	0.50	0.56	0.68		
Deaths (n)	157	173	173	176	161		
Age-adjusted model	Ref.	1.01 (0.81, 1.25)	0.92 (0.74, 1.15)	0.86 (0.69, 1.07)	0.60 (0.47, 0.75)	<.001	0.58 (0.47, 0.71)
MV-adjusted model	Ref.	1.08 (0.86, 1.35)	1.03 (0.81, 1.30)	0.99 (0.77, 1.26)	0.79 (0.60, 1.03)	0.04	0.70 (0.55, 0.91)
Pooled							
Age-adjusted model	Ref.	0.89 (0.79, 0.99)	0.80 (0.71, 0.89)	0.66 (0.59, 0.74)	0.46 (0.41, 0.51)	<.001	0.45 (0.40, 0.50)
MV-adjusted model	Ref.	0.99 (0.88, 1.11)	0.97 (0.86, 1.09)	0.90 (0.79, 1.03)	0.87 (0.75, 1.00)	0.01	0.81 (0.70, 0.94)
Marine ω-3 fats (DHA+EPA)							
NHS							
Median (% energy)	0.03	0.05	0.08	0.12	0.21		
Deaths (n)	379	445	451	405	399		
Age-adjusted model	Ref.	1.16 (1.01, 1.33)	1.15 (1.00, 1.32)	1.00 (0.87, 1.15)	0.66 (0.57, 0.76)	<.001	0.44 (0.36, 0.53)
MV-adjusted model	Ref.	1.22 (1.06, 1.40)	1.19 (1.03, 1.37)	1.14 (0.98, 1.33)	1.03 (0.88, 1.21)	0.32	0.89 (0.70, 1.12)
HPFS							
Median (% energy)	0.04	0.08	0.12	0.18	0.31		
Deaths (n)	183	178	182	142	155		
Age-adjusted model	Ref.	0.90 (0.73, 1.10)	0.94 (0.76, 1.15)	0.72 (0.58, 0.89)	0.63 (0.51, 0.79)	<.001	0.58 (0.47, 0.72)
MV-adjusted model	Ref.	0.94 (0.76, 1.16)	1.03 (0.83, 1.28)	0.83 (0.66, 1.05)	0.80 (0.62, 1.02)	0.04	0.75 (0.58, 0.97)
Pooled							
Age-adjusted model	Ref.	1.07 (0.96, 1.20)	1.08 (0.96, 1.21)	0.91 (0.80, 1.02)	0.65 (0.58, 0.73)	<.001	0.50 (0.43, 0.58)
MV-adjusted model	Ref.	1.12 (1.00, 1.26)	1.14 (1.01, 1.28)	1.04 (0.92, 1.18)	0.95 (0.83, 1.09)	0.03	0.82 (0.69, 0.98)

ω-6/ω-3 ratio							
NHS							
Median		5.5	6.7	7.6	8.4	9.9	
Deaths (n)		395	408	435	469	372	
Age-adjusted model	Ref.	1.22 (1.06, 1.40)	1.38 (1.20, 1.58)	1.62 (1.42, 1.85)	1.65 (1.43, 1.91)	<.001	1.13 (1.09, 1.16)
MV-adjusted model	Ref.	1.06 (0.92, 1.22)	1.12 (0.97, 1.30)	1.21 (1.05, 1.40)	1.15 (0.98, 1.34)	0.03	1.04 (1.00, 1.07)
HPFS							
Median		5.5	6.9	7.9	8.9	10.8	
Deaths (n)		175	190	162	161	152	
Age-adjusted model	Ref.	1.30 (1.06, 1.60)	1.24 (1.00, 1.53)	1.41 (1.14, 1.75)	1.58 (1.27, 1.97)	<.001	1.09 (1.05, 1.13)
MV-adjusted model	Ref.	1.21 (0.98, 1.50)	1.07 (0.85, 1.35)	1.18 (0.93, 1.49)	1.25 (0.98, 1.61)	0.12	1.05 (1.00, 1.09)
Pooled							
Age-adjusted model	Ref.	1.24 (1.11, 1.39)	1.34 (1.19, 1.50)	1.56 (1.39, 1.75)	1.63 (1.45, 1.84)	<.001	1.11 (1.09, 1.14)
MV-adjusted model	Ref.	1.11 (0.98, 1.24)	1.11 (0.98, 1.25)	1.20 (1.06, 1.36)	1.18 (1.03, 1.34)	0.008	1.04 (1.01, 1.07)

Abbreviations: HR, hazard ratio; CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MV, multivariable; NHS, Nurses' Health Study; HPFS, Health Professional Follow-up Study.

^a Hazard ratios (95% confidence interval) of neurodegenerative disease mortality for substituting 2% of energy from total ω -6 polyunsaturated fatty acids and linoleic acid, and 0.3% of energy from total ω -3 polyunsaturated fatty acids, arachidonic acid, and α -linolenic acid and marine ω -3 fats, for the same energy from carbohydrate. For ω -6/ ω -3 ratio, the Hazard ratios (95% confidence interval) of total mortality were calculated for 1-unit increment.

^b Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, \geq 35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, \geq 27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current \geq 25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, \geq 15 g/d; men: 0, 0.1-4.9, 5.0-29.9, \geq 30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), intakes of total energy, dietary cholesterol and percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models also included percentages of energy intake from remaining fatty acids (saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, *trans* fatty acids, ω -6 polyunsaturated fatty acids, ω -3 polyunsaturated fatty acids, linoleic acid, arachidonic acid, α -linolenic acid and marine ω -3 fats, all in quintiles).

^c Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 18. Associations Between Dietary ω -6 and ω -3 Polyunsaturated Fatty Acid Intake and Respiratory Disease Mortality (comparison is isocaloric substitution for carbohydrate)

	Quintile of dietary fatty acid intake					<i>P</i> _{trend}	HR (95% CI) ^a
	Q1	Q2	Q3	Q4	Q5		
ω-6 polyunsaturated fatty acid							
Total ω-6 polyunsaturated fatty acids							
NHS							
Median (% energy)	3.4	4.3	4.9	5.5	6.7		
Deaths (n)	307	342	322	308	305		
Age-adjusted model	Ref.	0.94 (0.81, 1.10)	0.89 (0.76, 1.04)	0.86 (0.73, 1.00)	0.82 (0.70, 0.96)	0.008	0.88 (0.80, 0.97)
MV-adjusted model ^b	Ref.	1.02 (0.87, 1.20)	0.93 (0.78, 1.11)	0.89 (0.73, 1.08)	0.86 (0.70, 1.07)	0.13	0.91 (0.80, 1.03)
HPFS							
Median (% energy)	3.7	4.5	5.1	5.8	6.9		
Deaths (n)	229	193	189	210	167		
Age-adjusted model	Ref.	0.80 (0.66, 0.97)	0.81 (0.67, 0.98)	0.89 (0.73, 1.07)	0.71 (0.58, 0.87)	0.008	0.85 (0.75, 0.95)
MV-adjusted model	Ref.	0.83 (0.68, 1.02)	0.88 (0.71, 1.10)	0.98 (0.77, 1.23)	0.81 (0.62, 1.06)	0.31	0.90 (0.77, 1.06)
Pooled ^c							
Age-adjusted model	Ref.	0.88 (0.78, 1.00)	0.85 (0.76, 0.96)	0.87 (0.77, 0.98)	0.77 (0.68, 0.88)	<.001	0.87 (0.81, 0.93)
MV-adjusted model	Ref.	0.94 (0.83, 1.07)	0.91 (0.79, 1.05)	0.92 (0.80, 1.07)	0.84 (0.71, 1.00)	0.07	0.90 (0.82, 1.00)
Linoleic acid							
NHS							
Median (% energy)	3.3	4.2	4.8	5.4	6.5		
Deaths (n)	316	341	320	307	300		
Age-adjusted model	Ref.	0.92 (0.79, 1.08)	0.87 (0.75, 1.02)	0.85 (0.72, 0.99)	0.78 (0.67, 0.92)	0.002	0.86 (0.78, 0.94)

MV-adjusted model	Ref.	0.99 (0.84, 1.17)	0.90 (0.75, 1.07)	0.84 (0.70, 1.02)	0.80 (0.64, 0.98)	0.02	0.86 (0.75, 0.97)
HPFS							
Median (% energy)	3.6	4.4	5.0	5.6	6.7		
Deaths (n)	224	198	193	203	170		
Age-adjusted model	Ref.	0.88 (0.73, 1.07)	0.88 (0.73, 1.07)	0.89 (0.74, 1.08)	0.73 (0.60, 0.90)	0.006	0.84 (0.74, 0.95)
MV-adjusted model	Ref.	0.96 (0.78, 1.18)	0.96 (0.78, 1.20)	1.01 (0.80, 1.27)	0.85 (0.65, 1.11)	0.28	0.89 (0.76, 1.05)
Pooled							
Age-adjusted model	Ref.	0.91 (0.81, 1.02)	0.88 (0.78, 0.99)	0.86 (0.76, 0.98)	0.76 (0.67, 0.87)	<.001	0.85 (0.79, 0.92)
MV-adjusted model	Ref.	0.98 (0.86, 1.11)	0.92 (0.81, 1.06)	0.91 (0.78, 1.05)	0.82 (0.69, 0.96)	0.01	0.87 (0.79, 0.96)
Arachidonic acid							
NHS							
Median (% energy)	0.05	0.06	0.07	0.09	0.11		
Deaths (n)	486	346	281	257	214		
Age-adjusted model	Ref.	1.01 (0.88, 1.16)	0.97 (0.83, 1.12)	0.99 (0.85, 1.15)	0.89 (0.76, 1.05)	0.20	0.62 (0.30, 1.29)
MV-adjusted model	Ref.	1.07 (0.92, 1.24)	1.09 (0.92, 1.28)	1.14 (0.94, 1.37)	1.15 (0.91, 1.44)	0.24	1.87 (0.66, 5.29)
HPFS							
Median (% energy)	0.05	0.06	0.07	0.09	0.11		
Deaths (n)	212	203	216	172	185		
Age-adjusted model	Ref.	1.03 (0.85, 1.24)	1.09 (0.90, 1.31)	0.88 (0.72, 1.08)	0.84 (0.69, 1.03)	0.02	0.33 (0.14, 0.80)
MV-adjusted model	Ref.	1.04 (0.85, 1.27)	1.07 (0.86, 1.33)	0.92 (0.72, 1.17)	0.92 (0.69, 1.23)	0.31	0.40 (0.11, 1.45)
Pooled							
Age-adjusted model	Ref.	1.01 (0.91, 1.13)	1.01 (0.90, 1.14)	0.95 (0.84, 1.07)	0.87 (0.77, 0.99)	0.01	0.48 (0.27, 0.84)
MV-adjusted	Ref.	1.06 (0.94, 1.19)	1.08 (0.94, 1.23)	1.05 (0.90, 1.22)	1.05 (0.88, 1.26)	0.78	1.02 (0.45, 2.28)

model							
ω-3 polyunsaturated fatty acid							
Total ω-3 polyunsaturated fatty acids							
NHS							
Median (% energy)	0.48	0.57	0.63	0.72	0.88		
Deaths (n)	322	308	290	344	320		
Age-adjusted model	Ref.	0.97 (0.83, 1.13)	0.86 (0.73, 1.01)	0.91 (0.78, 1.06)	0.59 (0.50, 0.69)	<.001	0.69 (0.62, 0.77)
MV-adjusted model	Ref.	1.07 (0.91, 1.26)	0.99 (0.83, 1.17)	1.17 (0.98, 1.39)	0.97 (0.80, 1.18)	0.84	0.99 (0.86, 1.13)
HPFS							
Median (% energy)	0.46	0.57	0.65	0.75	0.94		
Deaths (n)	212	189	213	185	189		
Age-adjusted model	Ref.	0.71 (0.58, 0.86)	0.74 (0.61, 0.89)	0.61 (0.50, 0.74)	0.51 (0.42, 0.62)	<.001	0.68 (0.60, 0.76)
MV-adjusted model	Ref.	0.84 (0.68, 1.03)	0.89 (0.72, 1.10)	0.80 (0.64, 1.00)	0.76 (0.60, 0.97)	0.04	0.85 (0.74, 0.98)
Pooled							
Age-adjusted model	Ref.	0.86 (0.76, 0.97)	0.81 (0.71, 0.91)	0.78 (0.69, 0.89)	0.56 (0.49, 0.63)	<.001	0.68 (0.63, 0.74)
MV-adjusted model	Ref.	0.97 (0.86, 1.11)	0.95 (0.83, 1.08)	1.01 (0.88, 1.16)	0.88 (0.76, 1.02)	0.11	0.92 (0.83, 1.02)
α-linolenic acid							
NHS							
Median (% energy)	0.41	0.48	0.53	0.59	0.7		
Deaths (n)	303	285	309	309	378		
Age-adjusted model	Ref.	1.04 (0.89, 1.23)	1.17 (1.00, 1.37)	1.10 (0.94, 1.30)	0.92 (0.79, 1.07)	0.21	0.91 (0.79, 1.05)
MV-adjusted model	Ref.	1.00 (0.85, 1.19)	1.11 (0.94, 1.32)	1.04 (0.87, 1.25)	1.02 (0.84, 1.24)	0.94	1.01 (0.83, 1.22)

HPFS							
Median (% energy)	0.38	0.45	0.50	0.56	0.68		
Deaths (n)	181	174	199	192	242		
Age-adjusted model	Ref.	0.90 (0.73, 1.11)	0.96 (0.78, 1.18)	0.84 (0.68, 1.03)	0.84 (0.69, 1.03)	0.08	0.85 (0.71, 1.03)
MV-adjusted model	Ref.	0.95 (0.77, 1.18)	1.06 (0.85, 1.32)	0.93 (0.74, 1.17)	1.06 (0.83, 1.34)	0.58	1.05 (0.84, 1.33)
Pooled							
Age-adjusted model	Ref.	0.99 (0.87, 1.12)	1.08 (0.96, 1.23)	1.00 (0.88, 1.13)	0.89 (0.79, 1.01)	0.04	0.89 (0.79, 1.00)
MV-adjusted model	Ref.	0.98 (0.86, 1.12)	1.09 (0.95, 1.25)	0.99 (0.86, 1.15)	1.03 (0.89, 1.20)	0.68	1.03 (0.89, 1.19)
Marine ω-3 fats (DHA+EPA)							
NHS							
Median (% energy)	0.03	0.05	0.08	0.12	0.21		
Deaths (n)	340	330	338	296	280		
Age-adjusted model	Ref.	0.86 (0.74, 1.00)	0.81 (0.70, 0.94)	0.67 (0.57, 0.79)	0.49 (0.42, 0.58)	<.001	0.32 (0.25, 0.41)
MV-adjusted model	Ref.	1.01 (0.87, 1.18)	1.06 (0.91, 1.25)	1.04 (0.88, 1.24)	0.95 (0.79, 1.14)	0.54	0.92 (0.70, 1.21)
HPFS							
Median (% energy)	0.04	0.08	0.12	0.18	0.31		
Deaths (n)	222	235	201	166	164		
Age-adjusted model	Ref.	0.98 (0.82, 1.18)	0.86 (0.71, 1.04)	0.70 (0.57, 0.85)	0.56 (0.46, 0.69)	<.001	0.50 (0.41, 0.61)
MV-adjusted model	Ref.	1.04 (0.87, 1.26)	0.98 (0.80, 1.20)	0.90 (0.73, 1.12)	0.77 (0.61, 0.97)	0.007	0.71 (0.56, 0.91)
Pooled							
Age-adjusted model	Ref.	0.91 (0.81, 1.02)	0.83 (0.74, 0.93)	0.68 (0.60, 0.77)	0.52 (0.46, 0.59)	<.001	0.41 (0.35, 0.48)
MV-adjusted model	Ref.	1.03 (0.91, 1.16)	1.03 (0.91, 1.17)	0.99 (0.86, 1.13)	0.88 (0.76, 1.01)	0.01	0.80 (0.66, 0.95)
ω-6/ω-3 ratio							

NHS							
Median	5.5	6.7	7.6	8.4	9.9		
Deaths (n)	275	332	353	314	310		
Age-adjusted model	Ref.	1.30 (1.11, 1.53)	1.46 (1.25, 1.71)	1.38 (1.17, 1.62)	1.67 (1.41, 1.96)	<.001	1.11 (1.07, 1.14)
MV-adjusted model	Ref.	1.10 (0.94, 1.30)	1.11 (0.94, 1.31)	0.98 (0.83, 1.17)	1.11 (0.93, 1.33)	0.56	1.01 (0.97, 1.05)
HPFS							
Median	5.5	6.9	7.9	8.9	10.8		
Deaths (n)	201	203	200	188	196		
Age-adjusted model	Ref.	1.18 (0.97, 1.43)	1.31 (1.07, 1.59)	1.39 (1.14, 1.70)	1.66 (1.36, 2.03)	<.001	1.10 (1.06, 1.14)
MV-adjusted model	Ref.	1.09 (0.89, 1.33)	1.06 (0.86, 1.30)	1.07 (0.86, 1.34)	1.30 (1.03, 1.63)	0.04	1.05 (1.00, 1.09)
Pooled							
Age-adjusted model	Ref.	1.25 (1.11, 1.42)	1.40 (1.24, 1.58)	1.38 (1.22, 1.57)	1.66 (1.47, 1.89)	<.001	1.10 (1.08, 1.13)
MV-adjusted model	Ref.	1.10 (0.97, 1.25)	1.09 (0.96, 1.24)	1.02 (0.89, 1.16)	1.18 (1.03, 1.36)	0.06	1.03 (1.00, 1.06)

Abbreviations: HR, hazard ratio; CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MV, multivariable; NHS, Nurses' Health Study; HPFS, Health Professional Follow-up Study.

^a Hazard ratios (95% confidence interval) of respiratory disease mortality for substituting 2% of energy from total ω -6 polyunsaturated fatty acids and linoleic acid, and 0.3% of energy from total ω -3 polyunsaturated fatty acids, arachidonic acid, and α -linolenic acid and marine ω -3 fats, for the same energy from carbohydrate. For ω -6/ ω -3 ration, the Hazard ratios (95% confidence interval) of total mortality were calculated for 1-unit increment.

^b Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, ≥ 35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥ 27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥ 25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, ≥ 15 g/d; men: 0, 0.1-4.9, 5.0-29.9, ≥ 30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), intakes of total energy, dietary cholesterol and percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models also included percentages of energy intake from remaining

fatty acids (saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, *trans* fatty acids, ω -6 polyunsaturated fatty acids, ω -3 polyunsaturated fatty acids, linoleic acid, arachidonic acid, α -linolenic acid and marine ω -3 fats, all in quintiles).

^c Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 19. Data Source of Figure 2

Hazard ratio (95% confidence interval) for substituting energy from saturated fat by the same energy from specific types of fat.

	total mortality		CVD mortality		Cancer mortality		Neurodegenerative disease mortality	
	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Unsaturated fat (5%)	0.78 (0.75, 0.82)	<.001	0.80 (0.73, 0.88)	<.001	0.88 (0.82, 0.94)	<.001	0.76 (0.65, 0.88)	<.001
Monounsaturated fat (5%)	0.87 (0.82, 0.93)	<.001	0.96 (0.84, 1.09)	0.53	0.91 (0.82, 1.01)	0.07	0.71 (0.57, 0.88)	0.002
Polyunsaturated fat (5%)	0.73 (0.70, 0.77)	<.001	0.72 (0.65, 0.80)	<.001	0.86 (0.79, 0.94)	<.001	0.79 (0.66, 0.94)	0.007
<i>trans</i> fat (2%)	1.16 (1.09, 1.24)	<.001	1.16 (1.01, 1.33)	0.03	0.94 (0.84, 1.05)	0.25	1.41 (1.13, 1.76)	0.002
total ω -6 PUFA (2%)	0.93 (0.91, 0.96)	<.001	0.89 (0.85, 0.94)	<.001	0.96 (0.92, 1.00)	0.04	1.07 (0.98, 1.16)	0.14
Total ω -3 PUFA (0.3%)	0.95 (0.93, 0.96)	<.001	1.01 (0.97, 1.05)	0.68	0.98 (0.95, 1.01)	0.26	0.82 (0.76, 0.88)	<.001

Multivariable-adjusted model adjusted for age (in month), Caucasian (yes vs. no), marital status (with spouse, yes or no), body-mass index (<23, 23-24.9, 25-29.9, 30-34.9, ≥ 35 kg/m²), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥ 27.0 hours of metabolic equivalent tasks per week), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥ 25 cigarettes/d), alcohol consumption (women: 0, 0.1-4.9, 5.0-14.9, ≥ 15 g/d; men: 0, 0.1-4.9, 5.0-29.9, ≥ 30 g/d), multivitamin use (yes vs. no), vitamin E supplementation use (yes vs. no), current aspirin use (yes vs. no), family history of myocardial infarction (yes vs. no), family history of diabetes (yes vs. no), family history of cancer (yes vs. no), history of hypertension (yes vs. no), history of hypercholesterolemia (yes vs. no), intakes of total energy, dietary cholesterol and percentage of energy intake from dietary protein (quintiles), and menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users). All models also included percentages of energy intake from remaining fatty acids (saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, *trans* fatty acids, ω -6 polyunsaturated fatty acids, ω -3 polyunsaturated fatty acids, linoleic acid, arachidonic acid, α -linolenic acid and marine ω -3 fats, all modeled as continuous variables).

^c Results for NHS and HPFS from the multivariate model were combined using the fixed-effects model.

eTable 20. Major Food Sources of Specific Types of Dietary Fat.

Nurses' Health Study						
1986			1994		2010	
	Food item	Contribution (%)	Food item	Contribution (%)	Food item	Contribution (%)
Saturated fat	Beef or lamb as a main dish, e.g. steak, roast	12.5	Beef or lamb as a main dish, e.g. steak, roast	7.9	Other cheese, e.g. American, cheddar, etc.	9.9
	Other cheese, e.g. American, cheddar, etc.	11.5	Other cheese, e.g. American, cheddar, etc.	7.1	Ice cream	6.1
	Skim milk	5.3	Milk with 1-2% fat	4.9	Pure butter	5.0
	Beef, pork, or lam as sandwich or mixed dish	4.8	Beef, pork, or lam as sandwich or mixed dish	4.7	Milk with 1-2% fat	4.1
	Regular hamberg	4.7	Chicken or turkey, without skin	4.7	Milk chocolate (bar or pack)	3.9
Polyunsaturated fat	Mayonnaise	13.9	Chicken or turkey, without skin	7.3	Walnuts	10.9
	Salad Dressing	9.8	Mayonnaise	6.6	Salad Dressing	6.3
	Margarine	9.0	Margarine	6.5	Mayonnaise	5.2
	Pure butter	4.0	Salad Dressing	6.1	Peanut butter	4.7
	Peanuts	3.7	Pure butter	3.6	Other nuts	4.3
Monounsaturated fat	Beef or lamb as a main dish, e.g. steak, roast	13.0	Olive oil	7.8	Olive oil	11.4
	Margarine	5.9	Beef or lamb as a main dish, e.g. steak, roast	7.2	Other nuts	6.2
	Regular hamberg	5.0	Chicken or turkey, without skin	5.1	Salad Dressing	6.1
	Beef, pork, or lam as sandwich or mixed dish	5.0	Beef, pork, or lam as sandwich or mixed dish	4.3	Peanut butter	5.2
	Other cheese, e.g. American, cheddar, etc.	4.8	Pork as main dish, e.g., ham or chops	3.6	Other cheese, e.g. American, cheddar, etc.	3.8
	trans fat	Beef or lamb as a main dish, e.g. steak, roast	12.3	Fried foods away from home	12.8	Olive oil
	Salad Dressing	7.9	Crackers	9.1	Salad Dressing	7.1
	Margarine	6.0	Sweet roll, coffee cake or other pastry	8.2	Other cheese, e.g. American, cheddar, etc.	6.3

	French Fries	5.8	Margarine	7.9	Beef or lamb as a main dish, e.g. steak, roast	4.6
	Mayonnaise	5.1	Potato or corn chips, chocolate and cookies	6.6	Sweet roll, coffee cake or other pastry	3.8
Marine ω -3 fats (DHA+EPA)	Dark meat fish, e.g., tuna steak, mackerel, salmon, sardines, bluefish, swordfish	28.6	Dark meat fish, e.g., tuna steak, mackerel, salmon, sardines, bluefish, swordfish	25.1	Fish oil	55.8
	Breaded fish cakes, pieces or fish sticks	27.1	Canned tuna fish	23.3	Dark meat fish, e.g., tuna steak, mackerel, salmon, sardines, bluefish, swordfish	20.2
	Other fish, e.g., cod, haddock, halibut	24.1	Other fish, e.g., cod, haddock, halibut	19.9	Canned tuna fish	7.1
	Chicken or turkey, without skin	7.4	Chicken or turkey, without skin	10.9	Other fish, e.g., cod, haddock, halibut	3.5
	Shrimp, lobster, scallops	5.2	Fish oil	6.0	Shrimp, lobster, scallops	2.7
α -linolenic acid	Mayonnaise	15.4	Mayonnaise	7.5	Walnuts	18.1
	Salad Dressing	12.6	Salad Dressing	7.3	Salad Dressing	6.6
	Beef or lamb as a main dish, e.g. steak, roast	6.5	Margarine	4.3	Mayonnaise	5.5
	Margarine	4.8	Beef or lamb as a main dish, e.g. steak, roast	4.0	Flaxseed	5.3
	Other cheese, e.g. American, cheddar, etc.	4.1	Low-fat or fat-free mayonnaise	3.6	Fried foods away from home	3.5
Linoleic acid	Mayonnaise	14.4	Margarine	7.0	Walnuts	10.5
	Salad Dressing	9.9	Chicken or turkey, without skin	6.9	Salad Dressing	6.7
	Margarine	9.9	Mayonnaise	6.9	Peanut butter	5.6
	Pure butter	4.6	Salad Dressing	6.3	Mayonnaise	5.5
	Peanuts	4.2	Pure butter	4.1	Other nuts	5.1
Arachidonic acid	Chicken or turkey, without skin	23.1	Chicken or turkey, without skin	37.0	Dark meat fish, e.g., tuna steak, mackerel, salmon, sardines, bluefish, swordfish	21.0
	Regular eggs including yolk	13.7	Regular eggs including yolk	9.8	Regular eggs including yolk	16.3
	Chicken or turkey, with skin	11.5	Chicken or turkey, with skin	9.1	Chicken or turkey, without skin	14.6
	Regular hamberg	7.2	Lean or extra lean hamberg	4.5	Chicken/turkey sandwich or frozen dinner	9.4

	Beef or lamb as a main dish, e.g. steak, roast	7.0	Pork as main dish, e.g., ham or chops	4.3	Fish oil	4.5
Health Professionals Follow-Up Study						
Saturated fat	Beef or lamb as a main dish, e.g. steak, roast	11.7	Beef or lamb as a main dish, e.g. steak, roast	8.5	Other cheese, e.g. American, cheddar, etc.	9.2
	Other cheese, e.g. American, cheddar, etc.	9.8	Other cheese, e.g. American, cheddar, etc.	6.9	Pizza	5.7
	Regular hamburger	5.4	Beef, pork, or lam as sandwich or mixed dish	4.9	Ice cream	5.3
	Skim milk	5.0	Skim milk	4.4	Dark chocolate	4.3
	Beef, pork, or lam as sandwich or mixed dish	4.8	Chicken or turkey, without skin	3.6	Milk chocolate (bar or pack)	3.8
Polyunsaturated fat	Mayonnaise	10.8	Mayonnaise	6.4	Walnuts	9.6
	Salad Dressing	7.7	Salad Dressing	5.9	Other nuts	5.5
	Margarine	6.0	Chicken or turkey, without skin	5.5	Peanuts	5.0
	Peanuts	5.5	Margarine	4.9	Salad Dressing	4.9
	Chicken or turkey, with skin	4.3	Peanuts	4.5	Mayonnaise	4.3
Monounsaturated fat	Beef or lamb as a main dish, e.g. steak, roast	11.1	Beef or lamb as a main dish, e.g. steak, roast	7.6	Olive oil	10.3
	Regular hamburger	5.3	Olive oil	5.4	Other nuts	7.6
	Beef, pork, or lam as sandwich or mixed dish	4.6	Beef, pork, or lam as sandwich or mixed dish	4.3	Peanuts	5.2
	Peanuts	4.1	Fried foods away from home	4.3	Salad Dressing	5.0
	Margarine	3.8	Chicken or turkey, without skin	3.9	Peanut butter	3.9
trans fat	Beef or lamb as a main dish, e.g. steak, roast	10.9	Fried foods away from home	23.3	Olive oil	7.4
	French fried potatoes	9.0	Crackers	11.9	Other cheese, e.g. American, cheddar, etc.	5.9
	Salad Dressing	6.5	Sweet roll, coffee cake or other pastry	8.0	Salad Dressing	5.7
	Regular hamburger	4.9	Margarine	7.3	Beef or lamb as a main dish, e.g. steak, roast	5.6
	Beef, pork, or lam as sandwich or mixed dish	4.5	Potato or corn chips, chocolate and cookies	6.5	Pizza	4.3

Marine ω -3 fats (DHA+EPA)	Dark meat fish, e.g., tuna steak, mackerel, salmon, sardines, bluefish, swordfish	40.7	Dark meat fish, e.g., tuna steak, mackerel, salmon, sardines, bluefish, swordfish	34.6	Fish oil	45.3
	Other fish, e.g., cod, haddock, halibut	22.0	Other fish, e.g., cod, haddock, halibut	19.7	Dark meat fish, e.g., tuna steak, mackerel, salmon, sardines, bluefish, swordfish	30.8
	Breaded fish cakes, pieces or fish sticks	18.8	Canned tuna fish	16.3	Canned tuna fish	6.0
	Chicken or turkey, without skin	5.7	Fish oil	10.2	Other fish, e.g., cod, haddock, halibut	3.8
	Shrimp, lobster, scallops	5.0	Chicken or turkey, without skin	6.4	Shrimp, lobster, scallops	3.3
α -linolenic acid	Mayonnaise	13.5	Salad Dressing	8.1	Walnuts	16.9
	Salad Dressing	11.1	Mayonnaise	7.6	Flaxseed	5.4
	Beef or lamb as a main dish, e.g. steak, roast	6.3	Beef or lamb as a main dish, e.g. steak, roast	4.6	Salad Dressing	5.4
	Margarine	3.6	Margarine	3.7	Mayonnaise	4.8
	Other cheese, e.g. American, cheddar, etc.	3.5	Chicken or turkey, without skin	2.7	French Fries	4.7
Linoleic acid	Mayonnaise	11.2	Mayonnaise	6.8	Walnuts	9.3
	Salad Dressing	7.8	Salad Dressing	6.1	Other nuts	6.5
	Margarine	6.5	Margarine	5.3	Peanuts	5.9
	Peanuts	6.3	Peanuts	5.3	Salad Dressing	5.1
	Pure butter	4.4	Chicken or turkey, without skin	5.2	Mayonnaise	4.5
Arachidonic acid	Chicken or turkey, without skin	19.9	Chicken or turkey, without skin	30.2	Dark meat fish, e.g., tuna steak, mackerel, salmon, sardines, bluefish, swordfish	29.9
	Regular eggs including yolk	13.4	Chicken or turkey, with skin	11.7	Regular eggs including yolk	13.8
	Chicken or turkey, with skin	12.5	Regular eggs including yolk	10.7	Chicken or turkey, without skin	9.6
	Regular hamberg	7.6	Dark meat fish, e.g., tuna	6.0	Chicken/turkey sandwich	9.0

			steak, mackerel, salmon, sardines, bluefish, swordfish		or frozen dinner	
	Home-made soup without bouillon cube	6.0	Regular hamberg	5.3	Chicken or turkey, with skin	4.6