

Population Intake of Omega-3 Fatty Acids in the United States

The major source of omega-3 fatty acids is dietary intake of fish, fish oil, vegetable oils (principally canola and soybean), some nuts including walnuts, and dietary supplements. Two population-based surveys, the Continuing Food Survey of Intakes by Individuals 1994-98 (CSFII) and the third National Health and Nutrition Examination (NHANES III) 1988-94 surveys, are the main source of dietary intake data for the U.S. population. NHANES III collected information on the U.S. population aged =2 months. Mexican Americans and non-Hispanic African-Americans, children =5 years old, and adults = 60 years old were over-sampled to produce more precise estimates for these population groups. There were no imputations for missing 24-hour dietary recall data. A total of 29,105 participants had complete and reliable dietary recall. Complete descriptions of the methods used and fuller analyses are later described in this report, under “Methods: Method to Assess the Dietary Intake of Omega-3 Fatty Acids in the US population” and “Results: Population Intake of Omega-3 Fatty Acids in the United States”. CSFII 1994-96, popularly known as the What We Eat in America survey, addressed the requirements of the National Nutrition Monitoring and Related Research Act of 1990 (Public Law 101-445) for continuous monitoring of the dietary status of the American population. In CSFII 1994-96, an improved data-collection method known as the multiple-pass approach for the 24-hour recall was used. Given the large variation in intake from day-to-day, multiple 24-hours recalls are considered to be the best suited for most nutrition monitoring and will produce stable estimates of mean nutrient intakes from groups of individuals⁹. In 1998, the Supplemental Children’s Survey, a survey of food and nutrient intake by children under age of 10, was conducted as the supplement to the CSFII 1994-96. The CSFII 1994-96, 1998 surveyed 20,607 people of all ages with over-sampling of low-income population (<130% of the poverty threshold). Dietary intake data by individuals of all ages were collected over 2 nonconsecutive days by use of two 1-day dietary recalls.

Table 1.1 reports the NHANES III survey mean intake ± the standard error of the mean (SEM), as well as, the median and range for each omega-3 fatty acid. Distributions of EPA, DPA, and DHA were very skewed; therefore, the means and standard errors of the means should be used and interpreted with caution. Table 1.2 reports the CSFII survey mean and median intakes for each omega-3 fatty acid, along with SEMs, as reported in Dietary Reference Intakes by the Institute of Medicine².

Table 1.1 Estimates of the mean±standard error of the mean (SEM) intake of linoleic acid (LA), alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) in the US population, based on analyses of a single 24-hour dietary recall of NHANES III data

	Grams/day		% Kcal/day	
	Mean±SEM	Median (range) ^a	Mean±SEM	Median (range) ^a
LA (18:2 n-6)	14.1±0.2	9.9 (0 - 168)	5.79±0.05	5.30 (0 - 39.4)
ALA (18:3 n-3)	1.33±0.02	0.90 (0 - 17)	0.55±0.004	0.48 (0 - 4.98)
EPA (20:5 n-3)	0.04±0.003	0.00 (0 - 4.1)	0.02±0.001	0.00 (0 - 0.61)
DHA (22:6 n-3)	0.07±0.004	0.00 (0 - 7.8)	0.03±0.002	0.00 (0 - 2.86)

^a The distributions are not adjusted for the over-sampling of Mexican Americans, non-Hispanic African-Americans, children =5 years old, and adults = 60 years old in the NHANES III dataset.

Table 1.2 Mean, range, and median usual daily intakes of linoleic acid (LA), total omega-3 fatty acids (n-3 FA), alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA) in the US population, based on CSFII data (1994-1996, 1998)

	<u>Grams/day</u>	
	<u>Mean±SEM</u>	<u>Median±SEM</u>
LA (18:2 n-6)	13.0±0.1	12.0±0.1
Total n-3 FA	1.40±0.01	1.30±0.01
ALA (18:3 n-3)	1.30±0.01	1.21±0.01
EPA (20:5 n-3)	0.028	0.004
DPA (22:5 n-3)	0.013	0.005
DHA (22:6 n-3)	0.057±0.018	0.046±0.013

Dietary Sources of Omega-3 Fatty Acids

Omega-3 fatty acids can be found in many different sources of food, including fish, shellfish, some nuts, and various plant oils. Table 1.3 lists the amount of omega-3 fatty acids in some commonly consumed fish, shellfish, nuts, and edible oils, selected from the USDA website (accessed November 3, 2003) <http://www.nal.usda.gov/fnic/foodcomp> (Finfish and Shellfish Products, sr16fg15.pdf; Fats and Oils, sr16fg04.pdf; and Nut and Seed Products, sr16fg12.pdf)

¹⁰.

Table 1.3 The omega-3 fatty acid content, in grams per 100 g food serving, of a representative sample of commonly consumed fish, shellfish, and fish oils, and nuts and seeds, and plant oils that contain at least 5 g omega-3 fatty acids per 100 g (<http://www.nal.usda.gov/fnic/foodcomp>) .

Food item	EPA	DHA	ALA	Food item	EPA	DHA	ALA
Fish (Raw^a)				Fish, continued			
Anchovy, European	0.6	0.9	-	Tuna, Fresh, Yellowfin	trace	0.2	trace
Bass, Freshwater, Mixed Sp.	0.2	0.4	0.1	Tuna, Light, Canned in Oil ^e	trace	0.1	trace
Bass, Striped	0.2	0.6	trace	Tuna, Light, Canned in Water ^e	trace	0.2	trace
Bluefish	0.2	0.5	-	Tuna, White, Canned in Oil ^e	trace	0.2	0.2
Carp	0.2	0.1	0.3	Tuna, White, Canned in Water ^e	0.2	0.6	trace
Catfish, Channel	trace	0.2	0.1	Whitefish, Mixed Sp.	0.3	0.9	0.2
Cod, Atlantic	trace	0.1	trace	Whitefish, Mixed Sp., Smoked	trace	0.2	-
Cod, Pacific	trace	0.1	trace	Wolfish, Atlantic	0.4	0.3	trace
Eel, Mixed Sp.	trace	trace	0.4				
Flounder & Sole Sp.	trace	0.1	trace	Shellfish (Raw)			
Grouper, Mixed Sp.	trace	0.2	trace	Abalone, Mixed Sp.	trace	-	-
Haddock	trace	0.1	trace	Clam, Mixed Sp.	trace	trace	trace
Halibut, Atlantic and Pacific	trace	0.3	trace	Crab, Blue	0.2	0.2	-
Halibut, Greenland	0.5	0.4	trace	Crayfish, Mixed Sp., Farmed	trace	0.1	trace
Herring, Atlantic	0.7	0.9	0.1	Lobster, Northern	-	-	-
Herring, Pacific	1.0	0.7	trace	Mussel, Blue	0.2	0.3	trace
Mackerel, Atlantic	0.9	1.4	0.2	Oyster, Eastern, Farmed	0.2	0.2	trace
Mackerel, Pacific and Jack	0.6	0.9	trace	Oyster, Eastern, Wild	0.3	0.3	trace
Mullet, Striped	0.2	0.1	trace	Oyster, Pacific	0.4	0.3	trace
Ocean Perch, Atlantic	trace	0.2	trace	Scallop, Mixed Sp.	trace	0.1	-
Pike, Northern	trace	trace	trace	Shrimp, Mixed Sp.	0.3	0.2	trace
Pike, Walleye	trace	0.2	trace	Squid, Mixed Sp.	0.1	0.3	trace
Pollock, Atlantic	trace	0.4	-				
Pompano, Florida	0.2	0.4	-	Fish Oils			
Roughy, Orange	trace	-	trace	Cod Liver Oil	6.9	11.0	0.9
Salmon, Atlantic, Farmed	0.6	1.3	trace	Herring Oil	6.3	4.2	0.8
Salmon, Atlantic, Wild	0.3	1.1	0.3	Menhaden Oil	13.2	8.6	1.5
Salmon, Chinook	1.0	0.9	trace	Salmon Oil	13.0	18.2	1.1
Salmon, Chinook, Smoked ^b	0.2	0.3	-	Sardine Oil	10.1	10.7	1.3
Salmon, Chum	0.2	0.4	trace				
Salmon, Coho, Farmed	0.4	0.8	trace	Nuts and Seeds			
Salmon, Coho, Wild	0.4	0.7	0.2	Butternuts, Dried	-	-	8.7
Salmon, Pink	0.4	0.6	trace	Flaxseed			18.1
Salmon, Pink, Canned ^c	0.9	0.8	trace	Walnuts, English	-	-	9.1
Salmon, Sockeye	0.6	0.7	trace				
Sardine, Atlantic, Canned in Oil ^d	0.5	0.5	0.5	Plant Oils			
Seabass, Mixed Sp.	0.2	0.4	-	Canola (Rapeseed)	-	-	9.3
Seatrout, Mixed Sp.	0.2	0.2	trace	Flaxseed Oil	-	-	53.3
Shad, American	1.1	1.3	0.2	Soybean Lecithin Oil	-	-	5.1
Shark, Mixed Sp.	0.3	0.5	trace	Soybean Oil	-	-	6.8
Snapper, Mixed Sp.	trace	0.3	trace	Walnut Oil	-	-	10.4
Swordfish	0.1	0.5	0.2	Wheatgerm Oil	-	-	6.9
Trout, Mixed Sp.	0.2	0.5	0.2				
Trout, Rainbow, Farmed	0.3	0.7	trace				
Trout, Rainbow, Wild	0.2	0.4	0.1				
Tuna, Fresh, Bluefin	0.3	0.9	-				
Tuna, Fresh, Skipjack	trace	0.2	-				

trace = <0.1; - = 0 or no data; Sp. = species.

a Except as indicated.

b Lox.

c Solids with bone and liquid.

d Drained solids with bone.

e Drained solids.

Chapter 3. Results

In this chapter, we present the results of our review of the effects of omega-3 fatty acids on cardiovascular disease (CVD) outcomes. The chapter is divided into 3 major sections. The first section reports on the dietary intake of omega-3 fatty acids in the US population. The second section reports on the effect of omega-3 fatty acid supplements or fish consumption on all cause mortality and CVD outcomes. The last section describes adverse events and drug interactions in human clinical studies of omega-3 fatty acids. Relevant tables are embedded within, or appear at the end, of each section.

Population Intake of Omega-3 Fatty Acids in the United States

A total of 33,994 persons were interviewed between 1988 and 1994 in the third National Health and Nutrition Examination Survey (NHANES III). The sociodemographic characteristics of the NHANES III sample population are shown in Table 3.1. Because a large number of participants (6%) refused to report their income or income category during the interview, all the analyses on the poverty income ratio (PIR) should be used carefully. In Tables 3.2 to 3.9, results of the mean daily intakes with a standard error of the mean (SEM) are tabulated for linoleic acid (LA, 18:2 n-6), alpha linolenic acid (ALA, 18:3 n-3), eicosapentaenoic acid (EPA, 20:5 n-3), and docosahexaenoic acid (DHA, 22:6 n-3) by gender, race/ethnicity, and age groups. Two tables were created for each fatty acid. The first table presents the means and SEMs for the fatty acid from the NHANES III (1988-94) database and the Continuing Survey of Food Intakes by Individuals (CSFII, 1994-96, 1998) database. No statistical test was performed to compare the NHANES III (1988-94) and CSFII (1994-96, 1998) data due to the differences in the dietary survey designs. The second table for each fatty acid shows the means and SEMs for the fatty acid by race/ethnicity groups using NHANES

Table 3.1. The Sociodemographic Characteristics of the Participants in the Third National Health and Nutrition Survey, 1988-94

Sub-populations	Number of participants	Percent
Gender		
- Male	16,295	48%
- Female	17,699	52%
Race/ethnicity		
- Non-Hispanic white	13,085	38%
- Non-Hispanic black	9,627	28%
- Mexican-American	9,751	29%
- Other	1,531	5%
Age groups *		
- 2-6 months	1,076	3%
- 7-12 months	1,129	3%
- 1-3 years	3,189	9%
- 4-8 years	4,271	13%
- 9-13 years	2,744	8%
- 14-18 years	2,183	6%
- 19-30 years	4,550	13%
- 31-50 years	6,307	19%
- 51-70 years	4,678	14%
- 71+ years	3,848	11%
Urbanization of living areas		
- Metro areas	17,183	51%
- Non-metro areas	16,811	49%
Poverty Income Ratio †		
- = 1.3	13,335	39%
- > 1.3	18,509	54%

* Contain small number of missing data.

† 6% (2,150) participants refused to report their income or income category.

Table 3.2. Means and the Standard Error of the Mean (SEMs) for Usual Daily Intake of Linoleic Acid (LA, 18:2 n-6), United States, NHANES III (1988-94) and CSFII (1994-1996, 1998) Data[§]

Age/Gender Groups	NHANES III (1988-94)			CSFII (1994-1996, 1998)		
	Sample Size	Population Size	Mean Intake (g/day)	Mean Intake (%kcal/day)	Sample Size	Mean Intake (g/day)
Both sexes, 0-6 months [¶]	793	1,323,807	6.90	8.32	596	6.70
SEM			0.15	0.14		0.10
Both sexes, 7-12 months	915	1,625,559	5.91	5.28	530	6.90
SEM			0.14	0.12		0.20
Both sexes, 1-3 y	2,734	8,724,437	7.27	4.69	3,949	7.30
SEM			0.14	0.07		0.10
Both sexes, 4-8 y	3,673	17,409,438	10.31	5.16	3,935	10.10
SEM			0.28	0.11		0.10
M, 9-13 y	1,251	9,113,670	13.79	5.09	595	13.40
SEM			0.48	0.11		0.40
M, 14-18 y	925	8,908,287	18.12	5.37	474	16.60
SEM			0.92	0.17		0.50
M, 19-30 y	1,902	21,918,936	19.34	5.60	920	17.60
SEM			0.59	0.13		0.50
M, 31-50 y	2,579	35,368,777	18.90	5.95	1,806	17.00
SEM			0.50	0.09		0.30
M, 51-70 y	1,934	18,623,500	15.37	5.86	1,680	15.30
SEM			0.34	0.09		0.30
M, 71+ y	1,296	6,723,233	12.42	5.69	722	12.20
SEM			0.29	0.09		0.40
F, 9-13 y	1,261	8,888,987	12.23	5.56	606	11.00
SEM			0.41	0.14		0.30
F, 14-18 y	1,062	8,962,331	13.61	5.98	449	11.70
SEM			0.54	0.19		0.50
F, 19-30 y	2,181	22,809,351	13.59	6.13	808	11.80
SEM			0.36	0.11		0.30
F, 31-50 y	3,097	37,172,408	13.44	6.24	1,690	11.70
SEM			0.26	0.10		0.20
F, 51-70 y	2,075	20,961,630	10.62	5.82	1,605	11.00
SEM			0.29	0.13		0.20
F, 71+ y	1,421	9,687,597	9.54	5.92	670	9.30
SEM			0.21	0.10		0.30
All individuals	29,099	238,221,947	14.13	5.79	21,159	13.00
SEM			0.20	0.05		0.10

[§] All NHANES III variance estimates were based on Taylor Series (WR) method.

[¶] NHANES III data consisted of individuals = 2 months and excluded nursing infants and children.

Table 3.3. Means and the Standard Error of the Mean (SEMs) for Usual Daily Intake of Linoleic Acid (LA, 18:2 n-6) (g/d), United States, NHANES III (1988-94) by Race/Ethnicity Groups

Age/Gender Groups	Non-Hispanic White			Non-Hispanic Black			Mexican-American			Other		
	Sample Size	Mean	SEM	Sample Size	Mean	SEM	Sample Size	Mean	SEM	Sample Size	Mean	SEM
Both Sexes, Total	10,634	14.27	0.24	8,510	14.23	0.20	8,626	14.07	0.20	1,329	12.77	0.48
Both sexes, 2-6 months	444	6.45	0.18	156	7.50	0.40	124	8.03	0.44	69	8.03	0.44
Both sexes, 7-12 months	488	5.36	0.14	156	7.53	0.47	181	6.58	0.38	90	6.58	0.38
Both sexes, 1-3 y	854	7.08	0.20	784	8.78	0.19	962	7.78	0.18	134	7.78	0.18
Both sexes, 4-8 y	989	10.19	0.45	1,179	11.54	0.25	1,322	10.38	0.29	183	10.38	0.29
Both sexes, 9-13 y	646	13.14	0.40	886	13.23	0.39	881	13.21	0.55	99	13.21	0.55
Both sexes, 14-18 y	517	15.58	0.81	714	17.07	0.54	646	14.87	0.56	110	14.87	0.56
Both sexes, 19-30 y	1,065	16.31	0.47	1,314	17.68	0.44	1,533	16.75	0.34	171	16.75	0.34
Both sexes, 31-50 y	1,894	16.45	0.39	1,869	15.54	0.32	1,669	16.07	0.32	244	16.07	0.32
Both sexes, 51-70 y	1,836	13.19	0.29	1,024	11.05	0.35	985	12.18	0.39	164	12.18	0.39
Both sexes, 71+ y	1,901	10.91	0.21	428	9.44	0.51	323	9.79	0.55	65	9.79	0.55
M, Total	5,028	16.70	0.34	4,001	15.87	0.25	4,264	15.84	0.25	628	14.40	0.66
M, 2-6 months	229	6.52	0.23	81	7.57	0.41	66	8.64	0.55	32	8.64	0.55
M, 7-12 months	239	5.38	0.19	78	7.55	0.71	96	6.09	0.44	37	6.09	0.44
M, 1-3 y	421	7.55	0.25	396	9.23	0.27	478	8.04	0.29	81	8.04	0.29
M, 4-8 y	491	11.10	0.72	580	11.71	0.36	627	10.78	0.45	102	10.78	0.45
M, 9-13 y	320	14.07	0.64	440	13.08	0.49	440	13.11	0.65	51	13.11	0.65
M, 14-18 y	228	18.14	1.13	333	18.82	0.74	320	16.13	0.74	44	16.13	0.74
M, 19-30 y	460	19.85	0.76	583	20.33	0.73	776	19.27	0.55	83	19.27	0.55
M, 31-50 y	853	19.22	0.61	826	18.14	0.49	800	18.57	0.38	100	18.57	0.38
M, 51-70 y	895	15.70	0.41	483	12.46	0.61	488	14.72	0.51	68	14.72	0.51
M, 71+	892	12.75	0.29	201	10.35	0.69	173	10.99	0.84	30	10.99	0.84
F, Total	5,606	11.96	0.19	4,509	12.82	0.21	4,362	12.20	0.21	701	11.23	0.61
F, 2-6 months	215	6.37	0.27	75	7.41	0.52	58	7.28	0.46	37	7.28	0.46
F, 7-12 months	249	5.33	0.24	78	7.52	0.42	85	7.16	0.60	53	7.16	0.60
F, 1-3 y	433	6.60	0.25	388	8.34	0.27	484	7.50	0.23	53	7.50	0.23
F, 4-8 y	498	9.15	0.32	599	11.36	0.35	695	10.01	0.37	81	10.01	0.37
F, 9-13 y	326	12.17	0.55	446	13.39	0.55	441	13.32	0.72	48	13.32	0.72
F, 14-18 y	289	12.88	0.70	381	15.32	0.67	326	13.58	0.74	66	13.58	0.74
F, 19-30 y	605	13.03	0.43	731	15.48	0.51	757	13.63	0.35	88	13.63	0.35
F, 31-50 y	1,041	13.71	0.30	1,043	13.38	0.35	869	13.50	0.38	144	13.50	0.38
F, 51-70 y	941	10.93	0.37	541	10.00	0.38	497	9.99	0.51	96	9.99	0.51
F, 71+	1,009	9.65	0.22	227	8.84	0.66	150	8.61	0.75	35	8.61	0.75

Table 3.4. Means and the Standard Error of the Mean (SEMs) for Usual Daily Intake of Alpha Linolenic Acid (ALA, 18:3 n-3), United States, NHANES III (1988-94) and CSFII (1994-1996, 1998) Data §

Age/Gender Groups	NHANES III (1988-94)			CSFII (1994-1996, 1998)		
	Sample Size	Population Size	Mean Intake (g/day)	Sample Size	Mean Intake (g/day)	
Both sexes, 0-6 months ¶	793	1,323,807	0.62	0.74	596	0.72
SEM			0.02	0.021		0.02
Both sexes, 7-12 months	915	1,625,559	0.60	0.54	530	0.77
SEM			0.02	0.013		0.02
Both sexes, 1-3 y	2,734	8,724,437	0.73	0.48	3,949	0.77
SEM			0.01	0.005		0.01
Both sexes, 4-8 y	3,673	17,409,438	0.98	0.49	3,935	0.97
SEM			0.03	0.010		0.01
M, 9-13 y	1,251	9,113,670	1.29	0.49	595	1.26
SEM			0.05	0.009		0.04
M, 14-18 y	925	8,908,287	1.73	0.52	474	1.65
SEM			0.08	0.018		0.05
M, 19-30 y	1,902	21,918,936	1.80	0.52	920	1.66
SEM			0.05	0.011		0.05
M, 31-50 y	2,579	35,368,777	1.76	0.57	1,806	1.73
SEM			0.04	0.009		0.04
M, 51-70 y	1,934	18,623,500	1.46	0.57	1,680	1.55
SEM			0.03	0.010		0.03
M, 71+ y	1,296	6,723,233	1.18	0.55	722	1.26
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F, 19-30 y	2,181	22,809,351	1.25	0.56	808	1.18
SEM			0.04	0.012		0.03
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F, 71+ y	1,421	9,687,597	0.92	0.58	670	0.97
SEM			0.02	0.011		0.03
All individuals	29,099	238,221,947	1.33	0.55	21,159	1.30
SEM			0.02	0.004		0.01

§ All NHANES III variance estimates were based on Taylor Series (WR) method.

¶ NHANES III data consisted of individuals = 2 months and excluded nursing infants and children.

Table 3.5. Means and the Standard Error of the Mean (SEMs) for Usual Daily Intake of Alpha Linolenic Acid (ALA, 18:3 n-3) (g/d), United States, NHANES III (1988-94) by Race/Ethnicity Groups

Age/Gender Groups	Non-Hispanic White			Non-Hispanic Black			Mexican-American			Other		
	Sample Size	Mean	SEM	Sample Size	Mean	SEM	Sample Size	Mean	SEM	Sample Size	Mean	SEM
Both Sexes, Total	10,634	1.37	0.02	8,510	1.27	0.02	8,626	1.20	0.02	1,329	1.12	0.04
Both sexes, 2-6 months	444	0.55	0.02	156	0.71	0.06	124	0.81	0.07	69	0.76	0.08
Both sexes, 7-12 months	488	0.54	0.02	156	0.76	0.04	181	0.65	0.05	90	0.60	0.04
Both sexes, 1-3 y	854	0.73	0.02	784	0.82	0.02	962	0.73	0.01	134	0.64	0.03
Both sexes, 4-8 y	989	0.98	0.04	1,179	1.04	0.02	1,322	0.97	0.03	183	0.87	0.04
Both sexes, 9-13 y	646	1.28	0.05	886	1.18	0.03	881	1.19	0.04	99	1.06	0.08
Both sexes, 14-18 y	517	1.48	0.07	714	1.53	0.06	646	1.30	0.06	110	1.42	0.19
Both sexes, 19-30 y	1,065	1.56	0.04	1,314	1.56	0.04	1,533	1.41	0.03	171	1.27	0.08
Both sexes, 31-50 y	1,894	1.57	0.04	1,869	1.38	0.03	1,669	1.30	0.03	244	1.17	0.08
Both sexes, 51-70 y	1,836	1.28	0.03	1,024	1.02	0.03	985	1.06	0.04	164	1.06	0.08
Both sexes, 71+ y	1,901	1.05	0.02	428	0.87	0.05	323	0.83	0.04	65	0.88	0.15
M, Total	5,028	1.60	0.03	4,001	1.43	0.02	4,264	1.36	0.02	628	1.29	0.06
M, 2-6 months	229	0.56	0.03	81	0.73	0.02	66	0.91	0.08	32	0.77	0.09
M, 7-12 months	239	0.55	0.02	78	0.79	0.06	96	0.63	0.06	37	0.66	0.06
M, 1-3 y	421	0.75	0.02	396	0.85	0.07	478	0.74	0.02	81	0.69	0.03
M, 4-8 y	491	1.08	0.07	580	1.08	0.02	627	0.98	0.03	102	0.87	0.06
M, 9-13 y	320	1.35	0.07	440	1.21	0.03	440	1.21	0.07	51	1.12	0.08
M, 14-18 y	228	1.73	0.09	333	1.70	0.04	320	1.50	0.07	44	2.00	0.46
M, 19-30 y	460	1.89	0.07	583	1.80	0.07	776	1.62	0.06	83	1.35	0.09
M, 31-50 y	853	1.84	0.05	826	1.63	0.06	800	1.49	0.04	100	1.38	0.15
M, 51-70 y	895	1.51	0.04	483	1.11	0.05	488	1.26	0.04	68	1.34	0.11
M, 71+	892	1.22	0.04	201	0.97	0.07	173	0.92	0.07	30	0.94	0.23
F, Total	5,606	1.15	0.02	4,509	1.14	0.02	4,326	1.05	0.02	701	0.97	0.04
F, 2-6 months	215	0.54	0.03	75	0.69	0.08	58	0.68	0.07	37	0.75	0.10
F, 7-12 months	249	0.54	0.03	78	0.72	0.05	85	0.68	0.05	53	0.56	0.05
F, 1-3 y	433	0.71	0.02	388	0.78	0.03	484	0.72	0.02	53	0.58	0.05
F, 4-8 y	498	0.86	0.02	599	1.00	0.02	695	0.96	0.04	81	0.87	0.07
F, 9-13 y	326	1.22	0.06	446	1.15	0.04	441	1.16	0.05	48	0.99	0.17
F, 14-18 y	289	1.22	0.07	381	1.36	0.08	326	1.10	0.05	66	1.03	0.09
F, 19-30 y	605	1.25	0.04	731	1.35	0.05	757	1.15	0.03	88	1.16	0.16
F, 31-50 y	1,041	1.30	0.03	1,043	1.18	0.03	869	1.10	0.03	144	1.01	0.08
F, 51-70 y	941	1.07	0.04	541	0.95	0.03	497	0.90	0.04	96	0.79	0.08
F, 71+	1,009	0.94	0.02	227	0.80	0.05	150	0.75	0.06	35	0.81	0.12

Table 3.6. Means and the Standard Error of the Mean (SEMs) for Usual Daily Intake of Eicosapentaenoic Acid (EPA, 20:5 n-3), United States, NHANES III (1988-94) and CSFII (1994-1996, 1998) Data §

Age/Gender Groups	NHANES III (1988-94)			CSFII (1994-1996, 1998)‡		
	Sample Size	Population Size	Mean Intake (g/day)	Mean Intake (%kcal/day)	Sample Size	Mean Intake (g/day)
Both sexes, 0-6 months [§]	793	1,323,807	-	-	578	<0.0005
SEM						
Both sexes, 7-12 months	915	1,625,559	†	†	487	0.002
SEM						
Both sexes, 1-3 y	2,734	8,724,437	†	†	3,777	0.008
SEM						
Both sexes, 4-8 y	3,673	17,409,438	0.010	0.010	3,769	0.012
SEM			0.002	0.002		
M, 9-13 y	1,251	9,113,670	†	†	569	0.016
SEM						
M, 14-18 y	925	8,908,287	†	†	446	0.018
SEM						
M, 19-30 y	1,902	21,918,936	0.040	†	854	0.030
SEM			0.005			
M, 31-50 y	2,579	35,368,777	0.060	0.02	1,684	0.038
SEM			0.007	0.003		
M, 51-70 y	1,934	18,623,500	0.050	0.02	1,606	0.046
SEM			0.005	0.002		
M, 71+ y	1,296	6,723,233	0.050	0.02	674	0.049
SEM			0.006	0.003		
F, 9-13 y	1,261	8,888,987	†	†	580	0.012
SEM						
F, 14-18 y	1,062	8,962,331	0.020	†	436	0.016
SEM			0.003			
F, 19-30 y	2,181	22,809,351	0.030	0.01	760	0.024
SEM			0.005	0.002		
F, 31-50 y	3,097	37,172,408	0.040	0.01	1,614	0.027
SEM			0.005	0.002		
F, 51-70 y	2,075	20,961,630	0.040	0.03	1,539	0.035
SEM			0.005	0.003		
F, 71+ y	1,421	9,687,597	0.030	†	623	0.029
SEM			0.006			
All individuals	29,099	238,221,947	0.040	0.02	20,108	0.03
SEM			0.003	0.001		

§ All NHANES III variance estimates were based on Taylor Series (WR) method.

‡ EPA estimates of CSFII (1994-96, 98) in the IOM report were calculated using SAS PROC UNIVARIATE, not via JACKKNIFE replication method. SEM data was not available in IOM report.

[§] NHANES III data consisted of individuals ≥ 2 months and excluded nursing infants and children. Distribution of EPA is very skewed; means and standard errors of the means should be used and interpreted with caution.

- estimate = 0; † Indicates a statistic that is potentially unreliable because the ratio of the SEM to the estimate times 100 > 20%.

Table 3.7. Means and the Standard Error of the Mean (SEMs) for Usual Daily Intake of Eicosapentaenoic Acid (EPA, 20:5 n-3) (g/d), United States, NHANES III (1988-94) by Race/Ethnicity Groups

Age/Gender Groups	Non-Hispanic White			Non-Hispanic Black			Mexican-American			Other		
	Sample Size	Mean	SEM	Sample Size	Mean	SEM	Sample Size	Mean	SEM	Sample Size	Mean	SEM
Both Sexes, Total	10,634	0.03	0.003	8,510	0.05	0.002	8,626	0.02	0.003	1,329	0.06	0.012
Both sexes, 2-6 months	444	-		156	-		124	-		69	†	
Both sexes, 7-12 months	488	†		156	†	0.001	181	†		90	†	
Both sexes, 1-3 y	854	0.01	0.001	784	0.01	0.001	962	†		134	†	
Both sexes, 4-8 y	989	†		1,179	0.01	0.002	1,322	0.01	0.002	183	†	
Both sexes, 9-13 y	646	†		886	0.02	0.004	881	†		99	†	
Both sexes, 14-18 years	517	†		714	†		646	†		110	†	
Both sexes, 19-30 y	1,065	0.03	0.005	1,314	0.05	0.004	1,533	0.03	0.004	171	†	
Both sexes, 31-50 y	1,894	0.04	0.005	1,869	0.07	0.008	1,669	0.04	0.007	244	†	
Both sexes, 51-70 y	1,836	0.04	0.004	1,024	0.06	0.006	985	0.03	0.004	164	†	
Both sexes, 71+ y	1,901	0.03	0.003	428	†		323	†		65	†	
M, Total	5,028	0.04	0.004	4,001	0.05	0.005	4,264	0.03	0.004	628	0.06	0.010
M, 2-6 months	229	-		81	-		66	-		32	†	
M, 7-12 months	239	†		78	†		96	†		37	†	
M, 1-3 y	421	0.01	0.002	396	0.01	0.001	478	†	0.001	81	†	
M, 4-8 y	491	†		580	0.02	0.003	627	0.01	0.002	102	†	
M, 9-13 y	320	†		440	0.02	0.004	440	†		51	†	
M, 14-18 y	228	†		333	†		320	†		44	†	
M, 19-30 y	460	0.04	0.008	583	0.05	0.008	776	0.03	0.006	83	0.06	0.011
M, 31-50 y	853	0.06	0.009	826	0.09	0.015	800	†		100	†	
M, 51-70 y	895	0.05	0.006	483	0.07	0.013	488	†		68	†	
M, 71+	892	0.05	0.006	201	†		173	†		30	†	
F, Total	5,606	0.03	0.003	4,509	0.04	0.002	4,362	0.02	0.003	701	†	
F, 2-6 months	215	-		75	-		58	-		37	-	
F, 7-12 months	249	†		78	-		85	-		53	†	
F, 1-3 y	433	†		388	†		484	†		53	†	
F, 4-8 y	498	†		599	†		695	†		81	†	
F, 9-13 y	326	†		446	†		441	†		48	†	
F, 14-18 y	289	†		381	†		326	†		66	†	
F, 19-30 y	605	0.03	0.005	731	0.04	0.005	757	†		88	†	
F, 31-50 y	1,041	0.03	0.004	1,043	0.06	0.006	869	†		144	†	
F, 51-70 y	941	0.04	0.005	541	0.05	0.007	497	†		96	†	
F, 71+	1,009	0.02	0.003	227	†		150	†		35	†	

- estimate = 0; † Indicates a statistic that is potentially unreliable because the ratio of the SEM to the estimate times 100 > 20%.

Table 3.8. Means and the Standard Error of the Mean (SEMs) for Usual Daily Intake of Docosahexaenoic Acid (DHA, 22:6 n-3), United States, NHANES III (1988-94) and CSFII (1994-1996, 1998) Data §

Age/Gender Groups	NHANES III (1988-94)			CSFII (1994-1996, 1998)	
	Sample Size	Population Size	Mean Intake (g/day)	Sample Size	Mean Intake (g/day)
Both sexes, 0-6 months ¶	793	1,323,807	-	596	<0.0005
SEM					0.001
Both sexes, 7-12 months	915	1,625,559	†	530	0.030
SEM					0.008
Both sexes, 1-3 y	2,734	8,724,437	0.020	3,949	0.032
SEM			0.002		0.001
Both sexes, 4-8 y	3,673	17,409,438	0.030	3,935	0.050
SEM			0.003		0.005
M, 9-13 y	1,251	9,113,670	0.030	595	0.063
SEM			0.005		0.010
M, 14-18 y	925	8,908,287	†	474	0.072
SEM					0.012
M, 19-30 y	1,902	21,918,936	0.090	920	0.079
SEM			0.008		0.006
M, 31-50 y	2,579	35,368,777	0.120	1,806	0.094
SEM			0.012		0.006
M, 51-70 y	1,934	18,623,500	0.100	1,680	0.111
SEM			0.008		0.007
M, 71+ y	1,296	6,723,233	0.080	722	0.128
SEM			0.008		0.019
F, 9-13 y	1,261	8,888,987	0.030	606	0.055
SEM			0.006		0.009
F, 14-18 y	1,062	8,962,331	0.030	449	0.062
SEM			0.004		0.009
F, 19-30 y	2,181	22,809,351	0.060	808	0.067
SEM			0.010		0.006
F, 31-50 y	3,097	37,172,408	0.080	1,690	0.071
SEM			0.009		0.009
F, 51-70 y	2,075	20,961,630	0.080	1,605	0.089
SEM			0.007		0.006
F, 71+ y	1,421	9,687,597	0.050	670	0.077
SEM			0.008		0.010
All individuals	29,099	238,221,947	0.070	21,159	0.057
SEM			0.004		0.018

§ All NHANES III variance estimates were based on Taylor Series (WR) method.

¶ NHANES III data consisted of individuals = 2 months and excluded nursing infants and children. Distribution of EPA is very skewed; means and standard errors of the means should be used and interpreted with caution.

- estimate = 0

† Indicates a statistic that is potentially unreliable because the ratio of the SEM to the estimate times 100 > 20%.

‡ EPA estimates of CSFII (1994-96, 98) in the IOM report were calculated using SAS PROC UNIVARIATE, not via JACKKNIFE replication method. SEM data was not available in IOM report.

Table 3.9. Means and the Standard Error of the Mean (SEMs) for Usual Daily Intake of Docosahexaenoic Acid (DHA, 22:6n-3) (g/d), United States, NHANES III (1988-94) by Race/Ethnicity Groups

Age/Gender Groups	Non-Hispanic White			Non-Hispanic Black			Mexican-American			Other		
	Sample Size	Mean	SEM	Sample Size	Mean	SEM	Sample Size	Mean	SEM	Sample Size	Mean	SEM
Both Sexes, Total	10,634	0.07	0.005	8,510	0.09	0.004	8,626	0.05	0.003	1,329	0.10	0.015
Both sexes, 2-6 months	444	†	-	156	-	-	124	-	-	69	-	-
Both sexes, 7-12 months	488	†	-	156	*	0.002	181	*	0.002	90	†	-
Both sexes, 1-3 y	854	†	-	784	0.02	0.004	962	0.01	0.002	134	†	-
Both sexes, 4-8 y	989	0.02	0.004	1,179	0.03	0.003	1,322	0.03	0.004	183	†	-
Both sexes, 9-13 y	646	0.03	0.004	886	0.04	0.005	881	0.03	0.003	99	†	-
Both sexes, 14-18 years	517	†	-	714	0.07	0.012	646	0.03	0.004	110	†	-
Both sexes, 19-30 y	1,065	0.07	0.010	1,314	0.10	0.007	1,533	0.06	0.006	171	†	-
Both sexes, 31-50 y	1,894	0.09	0.009	1,869	0.13	0.013	1,669	0.07	0.010	244	†	-
Both sexes, 51-70 y	1,836	0.08	0.006	1,024	0.10	0.008	985	0.06	0.007	164	0.13	0.024
Both sexes, 71+ y	1,901	0.06	0.004	428	†	-	323	0.04	0.008	65	†	-
M, Total	5,028	0.08	0.006	4,001	0.11	0.008	4,264	0.06	0.004	628	0.10	0.012
M, 2-6 months	229	†	-	81	-	-	66	-	-	32	-	-
M, 7-12 months	239	†	-	78	†	-	96	*	0.003	37	†	-
M, 1-3 y	421	0.02	0.004	396	0.02	0.003	478	0.01	0.002	81	†	-
M, 4-8 y	491	0.02	0.004	580	0.03	0.004	627	0.03	0.002	102	†	-
M, 9-13 y	320	0.03	0.006	440	0.05	0.006	440	0.03	0.005	51	†	-
M, 14-18 y	228	†	-	333	0.08	0.017	320	0.03	0.004	44	†	-
M, 19-30 y	460	0.08	0.012	583	0.13	0.014	776	0.07	0.007	83	0.10	0.011
M, 31-50 y	853	0.11	0.013	826	0.18	0.025	800	0.08	0.015	100	0.14	0.028
M, 51-70 y	895	0.09	0.010	483	0.12	0.015	488	0.08	0.013	68	†	-
M, 71+	892	0.08	0.009	201	†	-	173	0.06	0.016	30	†	-
F, Total	5,606	0.05	0.005	4,509	0.07	0.003	4,326	0.04	0.004	701	†	-
F, 2-6 months	215	-	-	75	-	-	58	-	-	37	-	-
F, 7-12 months	249	†	-	78	*	0.001	85	*	0.002	53	†	-
F, 1-3 y	433	†	-	388	†	-	484	†	-	53	†	-
F, 4-8 y	498	0.03	0.006	599	0.03	0.005	695	†	-	81	†	-
F, 9-13 y	326	0.03	0.006	446	0.04	0.007	441	†	-	48	†	-
F, 14-18 y	289	0.03	0.005	381	0.06	0.011	326	0.03	0.005	66	†	-
F, 19-30 y	605	0.06	0.012	731	0.08	0.007	757	0.04	0.006	88	†	-
F, 31-50 y	1,041	0.07	0.009	1,043	0.09	0.008	869	0.06	0.009	144	†	-
F, 51-70 y	941	0.07	0.008	541	0.08	0.011	497	0.04	0.006	96	†	-
F, 71+	1,009	0.04	0.006	227	†	-	150	†	0.010	35	†	-

- estimate = 0; * Value < 0.001 but greater than 0.

† Indicates a statistic that is potentially unreliable because the ratio of the SEM to the estimate times 100 > 20%.

Table 3.10. Means and the Standard Error of the Mean (SEMs) for Usual Daily Intake of Linoleic Acid (LA, 18:2 n-6) and Omega-3 PUFAs, United States, NHANES III (1988-94), Adults vs. Youths (Age < 18 y)

PUFAs	Sample Size	Population Size	Mean	SEM	Design Effect
LA (18:2 n-6) (g/d) †					
Total	29,099	238,221,947	14.13	0.1962	9.48
Adults	16,683	175,098,828	14.94	0.2298	7.02
Youths	12,416	63,123,119	11.88	0.2215	6.65
ALA (18:3 n-3) (g/d) †					
Total	29,099	238,221,947	1.33	0.0154	6.81
Adults	16,683	175,098,828	1.40	0.0191	5.59
Youths	12,416	63,123,119	1.13	0.0191	5.97
¶ EPA (20:5 n-3) (g/d)					
Total	29,099	238,221,947	0.04	0.0026	8.57
Adults	16,683	175,098,828	0.04	0.0035	6.99
Youths	12,416	63,123,119	0.01	0.0014	3.90
¶ DHA (22:6 n-3) (g/d)					
Total	29,099	238,221,947	0.07	0.0044	8.69
Adults	16,683	175,098,828	0.08	0.0058	7.40
Youths	12,416	63,123,119	0.03	0.0031	4.18
LA (18:2 n-6) (%kcal/d) †					
Total	29,097	238,218,723	5.79	0.0458	7.29
Adults	16,683	175,098,828	5.95	0.0512	5.06
Youths	12,414	63,119,895	5.36	0.0603	6.19
ALA (18:3 n-3) (%kcal/d) †					
Total	29,097	238,218,723	0.55	0.0041	5.78
Adults	16,683	175,098,828	0.56	0.0049	4.33
Youths	12,414	63,119,895	0.51	0.0047	4.12
¶ EPA (20:5 n-3) (%kcal/d)					
Total	29,097	238,218,723	0.02	0.0011	8.47
Adults	16,683	175,098,828	0.02	0.0014	6.89
Youths	12,414	63,119,895	0.01	0.0006	3.56
¶ DHA (22:6 n-3) (%kcal/d)					
Total	29,097	238,218,723	0.03	0.0019	10.67
Adults	16,683	175,098,828	0.04	0.0025	8.52
Youths	12,414	63,119,895	0.01	0.0010	3.97

† $P < .001$ between groups

¶ Distribution of EPA and DHA were very skewed; means and standard errors of the means should be used and interpreted with caution. No test of differences in the mean intakes of EPA, DPA, and DHA between groups was performed.

Table 3.11. Means and the Standard Error of the Mean (SEMs) for Usual Daily Intake of Linoleic Acid (LA, 18:2 n-6) & Omega-3 PUFAs, United States, NHANES III (1988-94), Males vs. Females

PUFAs	Sample Size	Population Size	Mean	SEM	Design Effect
LA (18:2 n-6) (g/d) †					
Total	29,105	238,245,897	14.13	0.1962	9.48
Male	13,923	115,778,180	16.36	0.2841	7.48
Female	15,182	122,467,717	12.02	0.1618	5.04
ALA (18:3 n-3) (g/d) †					
Total	29,105	238,245,897	1.33	0.0154	6.81
Male	13,923	115,778,180	1.54	0.0233	6.05
Female	15,182	122,467,717	1.13	0.0134	3.84
¶ EPA (20:5 n-3) (g/d)					
Total	29,105	238,245,897	0.04	0.0026	8.57
Male	13,923	115,778,180	0.04	0.0032	4.89
Female	15,182	122,467,717	0.03	0.0031	8.34
¶ DHA (22:6 n-3) (g/d)					
Total	29,105	238,245,897	0.07	0.0044	8.69
Male	13,923	115,778,180	0.08	0.0050	4.36
Female	15,182	122,467,717	0.06	0.0051	8.11
LA (18:2 n-6) (%kcal/d) †					
Total	29,103	238,242,673	5.79	0.0458	7.29
Male	13,922	115,776,672	5.65	0.0526	5.02
Female	15,181	122,466,001	5.93	0.0606	6.22
ALA (18:3 n-3) (%kcal/d) †					
Total	29,103	238,242,673	0.55	0.0041	5.78
Male	13,922	115,776,672	0.54	0.0047	4.05
Female	15,181	122,466,001	0.56	0.0054	4.81
¶ EPA (20:5 n-3) (%kcal/d)					
Total	29,103	238,242,673	0.02	0.0011	8.47
Male	13,922	115,776,672	0.02	0.0011	4.67
Female	15,181	122,466,001	0.02	0.0014	7.40
¶ DHA (22:6 n-3) (%kcal/d)					
Total	29,103	238,242,673	0.03	0.0019	10.67
Male	13,922	115,776,672	0.03	0.0020	5.19
Female	15,181	122,466,001	0.03	0.0023	9.00

† $P < .001$ between groups

¶ Distribution of EPA and DHA were very skewed; means and standard errors of the means should be used and interpreted with caution. No test of differences in the mean intakes of EPA, DPA, and DHA between groups was performed.

Table 3.12. Means and the Standard Error of the Mean (SEMs) for Usual Daily Intake of Linoleic Acid (LA, 18:2n-6) & Omega-3 PUFAs, United States, NHANES III (1988-94), by Race/Ethnicity groups

PUFAs	Sample Size	Population Size	Mean	SEM	Design Effect
LA (18:2 n-6) (g/d)					
Total	29,105	238,245,897	14.13	0.1962	9.48
* Non-Hispanic white	10,634	174,119,805	14.27	0.2354	5.05
* Non-Hispanic black	8,513	29,355,656	14.23	0.1956	2.55
* Mexican-American	8,627	14,878,866	14.07	0.2025	2.82
Other	1,331	19,891,569	12.77	0.4797	2.78
ALA (18:3 n-3) (g/d)					
Total	29,105	238,245,897	1.33	0.0154	6.81
† Non-Hispanic white	10,634	174,119,805	1.37	0.0192	3.78
* Non-Hispanic black	8,513	29,355,656	1.27	0.0166	2.16
* Mexican-American	8,627	14,878,866	1.20	0.0168	3.04
Other	1,331	19,891,569	1.12	0.0379	2.32
EPA (20:5 n-3) (g/d)					
Total	29,105	238,245,897	0.04	0.0026	8.56
Non-Hispanic white	10,634	174,119,805	0.03	0.0026	3.79
Non-Hispanic black	8,513	29,355,656	0.05	0.0024	1.37
Mexican-American	8,627	14,878,866	0.02	0.0026	4.35
Other	1,331	19,891,569	0.06	0.0120	4.60
DHA (22:6 n-3) (%kcal/d)					
Total	29,105	238,245,897	0.07	0.0044	8.69
Non-Hispanic white	10,634	174,119,805	0.07	0.0048	3.93
Non-Hispanic black	8,513	29,355,656	0.09	0.0040	1.58
Mexican-American	8,627	14,878,866	0.05	0.0033	4.27
Other	1,331	19,891,569	0.10	0.0153	4.21

(continued to the next page)

PUFAs	Sample Size	Population Size	Mean	SEM	Design Effect
LA (18:2 n-6) (%kcal/d)					
Total	29,103	238,242,673	5.79	0.0458	7.29
* Non-Hispanic white	10,634	174,119,805	5.79	0.0579	4.38
† Non-Hispanic black	8,512	29,353,940	5.98	0.0592	3.42
† Mexican-American	8,626	14,877,359	5.93	0.0476	2.11
Other	1,331	19,891,569	5.37	0.1279	2.48
ALA (18:3 n-3) (%kcal/d)					
Total	29,103	238,242,673	0.55	0.0041	5.78
† Non-Hispanic white	10,634	174,119,805	0.56	0.0054	3.55
† Non-Hispanic black	8,512	29,353,940	0.54	0.0051	2.77
† Mexican-American	8,626	14,877,359	0.52	0.0063	5.20
Other	1,331	19,891,569	0.48	0.0106	2.23
EPA (20:5 n-3) (%kcal/d)					
Total	29,103	238,242,673	0.02	0.0011	8.47
Non-Hispanic white	10,634	174,119,805	0.01	0.0010	3.26
Non-Hispanic black	8,512	29,353,940	0.02	0.0009	1.18
Mexican-American	8,626	14,877,359	0.01	0.0009	3.39
Other	1,331	19,891,569	0.03	0.0057	4.72
DHA (22:6 n-3) (%kcal/d)					
Total	29,103	238,242,673	0.03	0.0019	10.67
Non-Hispanic white	10,634	174,119,805	0.03	0.0019	4.20
Non-Hispanic black	8,512	29,353,940	0.04	0.0016	1.63
Mexican-American	8,626	14,877,359	0.02	0.0013	3.60
Other	1,331	19,891,569	0.05	0.0079	4.67

Other race/ethnicity group was the reference group.

* $P < .05$ compared to the reference group.

† $P < .001$ compared to the reference group.

* Distribution of EPA and DHA were very skewed; means and standard errors of the means should be used and interpreted with caution. No test of differences in the mean intakes of EPA, DPA, and DHA between groups was performed.

Table 3.13. Means and the Standard Error of the Mean (SEMs) for Usual Daily Intake of Linoleic Acid (LA, 18:2 n-6) and Omega-3 PUFAs, United States, NHANES III (1988-94), Metro vs. Non-metro Areas

PUFAs	Sample Size	Population Size	Mean	Design SEM	Effect
LA (18:2 n-6) (g/d)					
Total	29,105	238,245,897	14.13	0.1962	9.48
Metro	14,374	114,581,912	14.28	0.2701	8.23
Non-metro	14,731	123,663,985	13.99	0.2479	8.25
ALA (18:3 n-3) (g/d)					
Total	29,105	238,245,897	1.33	0.0154	6.81
Metro	14,374	114,581,912	1.34	0.0250	8.28
Non-metro	14,731	123,663,985	1.32	0.0203	6.39
EPA (20:5 n-3) (g/d)					
Total	29,105	238,245,897	0.04	0.0026	8.56
Metro	14,374	114,581,912	0.04	0.0032	6.45
Non-metro	14,731	123,663,985	0.03	0.0040	10.49
DHA (22:6 n-3) (g/d)					
Total	29,105	238,245,897	0.07	0.0044	8.69
Metro	14,374	114,581,912	0.08	0.0056	5.81
Non-metro	14,731	123,663,985	0.06	0.0069	13.43
LA (18:2 n-6) (%kcal/d)					
Total	29,103	238,242,673	5.79	0.0458	7.29
Metro	14,373	114,580,196	5.79	0.0554	5.06
Non-metro	14,730	123,662,477	5.79	0.0629	7.28
ALA (18:3 n-3) (%kcal/d)					
Total	29,103	238,242,673	0.55	0.0041	5.78
Metro	14,373	114,580,196	0.55	0.0066	6.97
Non-metro	14,730	123,662,477	0.55	0.0059	6.29
EPA (20:5 n-3) (%kcal/d)					
Total	29,103	238,242,673	0.02	0.0011	8.47
Metro	14,373	114,580,196	0.02	0.0014	6.39
Non-metro	14,730	123,662,477	0.01	0.0017	10.44
DHA (22:6 n-3) (%kcal/d)					
Total	29,103	238,242,673	0.03	0.0019	10.67
Metro	14,373	114,580,196	0.03	0.0021	5.95
Non-metro	14,730	123,662,477	0.03	0.0032	16.57

^aDistribution of EPA and DHA were very skewed; means and standard errors of the means should be used and interpreted with caution. No test of differences in the mean intakes of EPA, DPA, and DHA between groups was performed.

Table 3.14. Means and the Standard Error of the Mean (SEMs) for Usual Daily Intake of Linoleic Acid (LA, 18:2 n-6) & Omega-3 PUFAs, United States, NHANES III (1988-94)^{*}, PIR = 1.3 vs. PIR > 1.3

Poverty Index Ratio (PIR)	Sample Size	Population Size	Mean	SEM	Design Effect
LA (18:2 n-6) (g/d)					
Total	27,482	226,488,050	14.15	0.2015	9.48
PIR <= 1.3	11,711	53,365,381	12.85	0.2258	5.50
PIR > 1.3	15,771	173,122,669	14.55	0.2289	6.89
ALA (18:3 n-3) (g/d)					
Total	27,482	226,488,050	1.33	0.0160	6.88
PIR <= 1.3	11,711	53,365,381	1.19	0.0191	4.67
PIR > 1.3	15,771	173,122,669	1.38	0.0186	5.22
¶ EPA (20:5 n-3) (g/d)					
Total	27,482	226,488,050	0.04	0.0026	8.03
PIR <= 1.3	11,711	53,365,381	0.03	0.0027	4.67
PIR > 1.3	15,771	173,122,669	0.04	0.0031	6.45
¶ DHA (22:6 n-3) (g/d)					
Total	27,482	226,488,050	0.07	0.0042	7.77
PIR <= 1.3	11,711	53,365,381	0.06	0.0056	5.65
PIR > 1.3	15,771	173,122,669	0.07	0.0050	6.15
LA (18:2 n-6) (%kcal/d)					
Total	27,480	226,484,827	5.79	0.0470	7.27
PIR <= 1.3	11,710	53,363,665	5.58	0.0562	4.35
PIR > 1.3	15,770	173,121,162	5.86	0.0527	5.27
ALA (18:3 n-3) (%kcal/d)					
Total	27,480	226,484,827	0.55	0.0042	5.83
PIR <= 1.3	11,710	53,363,665	0.52	0.0056	4.83
PIR > 1.3	15,770	173,121,162	0.56	0.0047	4.00
¶ EPA (20:5 n-3) (%kcal/d)					
Total	27,480	226,484,827	0.01	0.0011	7.98
PIR <= 1.3	11,710	53,363,665	0.01	0.0009	3.09
PIR > 1.3	15,770	173,121,162	0.02	0.0013	6.68
¶ DHA (22:6 n-3) (%kcal/d)					
Total	27,480	226,484,827	0.03	0.0019	9.97
PIR <= 1.3	11,710	53,363,665	0.02	0.0015	3.41
PIR > 1.3	15,770	173,121,162	0.03	0.0023	7.97

* 6% participants refused to report their income or income category.

¶ Distribution of EPA and DHA were very skewed; means and standard errors of the means should be used and interpreted with caution. No test of differences in the mean intakes of EPA, DPA, and DHA between groups was performed.

Table 3.15. The Demographic Characteristics of Adult Participants With and Without a History of Cardiovascular Diseases, United States, NHANES III (1988-94)[§]

Gender and Race/Ethnicity Groups	People With a History of CVD		People Without a History of CVD	
	Sample Size	Population Size	Sample Size	Population Size
Total	2,121	14,964,332	14,562	160,134,496
Male	1,136	8,036,546	6,664	75,438,001
Female	985	6,927,787	7,898	84,696,495
Non-Hispanic White				
Total	973	10,966,582	5,771	121,941,462
Male	554	6,165,912	2,567	57,378,183
Female	419	4,800,670	3,204	64,563,276
Non-Hispanic Black				
Total	686	2,445,381	4,033	17,057,068
Male	353	1,175,699	1,777	7,493,735
Female	333	1,269,682	2,256	9,563,333
Mexican-American				
Total	391	502,292	4,176	8,673,940
Male	205	261,129	2,060	4,507,199
Female	186	241,163	2,116	4,166,741
Other				
Total	71	1,050,078	582	12,462,026
Male	24	433,807	260	6,058,884
Female	47	616,271	322	6,403,141

§ All NHANES III variance estimates were based on Taylor Series (WR) method.

Table 3.16. The Mean Intakes ± SEMs of Linoleic Acid (LA, 18:2n-6), Respondents With a History of CVD Compared to Those Without CVD, NHANES III (1988-94)

	Linoleic acid (LA, 18:2n-6)							
	CVD		Non-CVD		CVD		Non-CVD	
	Mean (g/d)	SEM	Mean (g/d)	SEM	Mean (%kcal/d)	SEM	Mean (%kcal/d)	SEM
Total	12.58	0.4753	15.16	0.2355	5.80	0.0954	5.96	0.0536
Male	15.12	0.8243	17.96	0.3390	5.87	0.1263	5.80	0.0598
Female	9.64	0.2815	12.67	0.1980	5.73	0.1343	6.10	0.0729
Non-Hispanic White								
Total	13.06	0.6196	15.20	0.2798	5.98	0.1178	5.96	0.0663
Male	15.62	1.0596	18.17	0.4158	6.06	0.1699	5.82	0.0739
Female	9.76	0.3733	12.57	0.2245	5.88	0.1803	6.08	0.0844
Non-Hispanic Black								
Total	11.71	0.5201	15.42	0.2521	5.60	0.1378	6.09	0.0687
Male	13.96	0.7583	17.85	0.3712	5.62	0.1692	5.79	0.0613
Female	9.62	0.4955	13.52	0.2714	5.57	0.1811	6.33	0.0999
Mexican-American								
Total	11.36	0.4970	15.92	0.2814	5.79	0.1469	6.16	0.0706
Male	11.28	0.6263	18.57	0.3443	5.17	0.2655	6.06	0.0874
Female	11.44	0.7056	13.05	0.3075	6.46	0.2943	6.26	0.0819
Other								
Total	10.27	1.3049	13.88	0.5446	4.43	0.4121	5.67	0.1486
Male	13.47	2.9402	15.65	0.6688	4.16	0.7905	5.44	0.2131
Female	8.02	0.7190	12.21	0.7737	4.62	0.4265	5.88	0.2396

Table 3.17. The Mean Intakes ± SEMs of Alpha Linolenic Acid (ALA, 18:3 n-3), Respondents With a History of CVD Compared to Those Without CVD, NHANES III (1988-94)

	Alpha Linolenic Acid (ALA, 18:3 n-3)							
	CVD		Non-CVD		CVD		Non-CVD	
	Mean (g/d)	SEM	Mean (g/d)	SEM	Mean (%kcal/d)	SEM	Mean (%kcal/d)	SEM
Total	1.16	0.0349	1.42	0.0201	0.55 *†	0.0093	0.57 *†	0.0051
Male	1.38	0.0600	1.69	0.0298	0.55	0.0132	0.55	0.0059
Female	0.90	0.0238	1.19	0.0181	0.54	0.0108	0.58	0.0066
Non-Hispanic White								
Total	1.20	0.0399	1.46	0.0253	0.56	0.0105	0.58	0.0069
Male	1.40	0.0651	1.75	0.0368	0.57	0.0148	0.57	0.0075
Female	0.93	0.0305	1.21	0.0224	0.56	0.0132	0.59	0.0089
Non-Hispanic Black								
Total	1.08	0.0456	1.37	0.0222	0.52	0.0115	0.54	0.0057
Male	1.25	0.0684	1.60	0.0389	0.51	0.0141	0.52	0.0067
Female	0.92	0.0552	1.19	0.0224	0.54	0.0192	0.56	0.0079
Mexican-American								
Total	0.96	0.0453	1.32	0.0221	0.49	0.0161	0.52	0.0078
Male	1.04	0.0600	1.53	0.0332	0.47	0.0252	0.50	0.0099
Female	0.87	0.0627	1.09	0.0248	0.52	0.0234	0.53	0.0095
Other								
Total	1.07	0.1754	1.18	0.0453	0.44	0.0370	0.48	0.0167
Male	1.57	0.3688	1.13	0.0701	0.46	0.0820	0.46	0.0244
Female	0.72	0.0584	1.03	0.0724	0.42	0.0314	0.50	0.0233

* Univariate analysis showed significant differences between the CVD groups ($P=.04$)

† Multivariate analysis (adjusted for sex, age, and race/ethnicity) showed significant differences between the CVD groups. The results are shown in Appendix C in detail.

Table 3.18. The Mean Intakes ± SEMs of Eicosapentaenoic Acid (EPA, 20:5 n-3), Respondents with a History of CVD Compared to Those Without CVD, NHANES III (1988-94) §

	Eicosapentaenoic acid (EPA, 20:5 n-3)							
	CVD		Non-CVD		CVD		Non-CVD	
	Mean (g/d)	SEM	Mean (g/d)	SEM	Mean (%kcal/d)	SEM	Mean (%kcal/d)	SEM
Total	0.04	0.0042	0.04	0.0037	0.02	0.0023	0.02	0.0015
Male	0.05	0.0071	0.05	0.0045	0.02	0.0034	0.02	0.0017
Female	0.04	0.0061	0.04	0.0041	0.03	0.0043	0.02	0.0019
Non-Hispanic White								
Total	0.04	0.0044	0.04	0.0036	0.02	0.0028	0.02	0.0013
Male	0.04	0.0067	0.05	0.0056	0.02	0.0033	0.02	0.0018
Female	0.04	0.0082	0.03	0.0034	0.03	0.0061	0.02	0.0014
Non-Hispanic Black								
Total	0.07	0.0131	0.06	0.0039	0.03	0.0057	0.02	0.0013
Male	0.09	0.0261	0.07	0.0082	0.04	0.0103	0.02	0.0025
Female	0.05	0.0113	0.05	0.0027	0.03	0.0061	0.02	0.0013
Mexican-American								
Total	0.02	0.0064	0.03	0.0039	0.01	0.0030	0.01	0.0014
Male	0.04	0.0117	0.04	0.0058	0.02	0.0053	0.01	0.0019
Female	0.01	0.0040	0.02	0.0039	0.00	0.0014	0.01	0.0017
Other								
Total	0.07	0.0240	0.08	0.0188	0.03	0.0110	0.04	0.0088
Male	0.11	0.0530	0.07	0.0138	0.05	0.0224	0.03	0.0066
Female	0.04	0.0184	0.09	0.0290	0.02	0.0097	0.04	0.0137

§ Distribution of this nutrient is very skewed; means and standard errors of the means should be used and interpreted with caution.

Table 3.19. The Mean Intakes \pm SEMs of Docosahexaenoic Acid (DHA, 22:6 n-3), Respondents With a History of CVD Compared to Those Without CVD, NHANES III (1988-94) \S

	Docosahexaenoic acid (DHA, 22:6 n-3)							
	CVD		Non-CVD		CVD		Non-CVD	
	Mean (g/d)	SEM	Mean (g/d)	SEM	Mean (%kcal/d)	SEM	Mean (%kcal/d)	SEM
Total	0.08	0.0050	0.09	0.0062	0.04	0.0032	0.04	0.0026
Male	0.08	0.0085	0.10	0.0074	0.04	0.0042	0.04	0.0031
Female	0.07	0.0103	0.07	0.0067	0.04	0.0066	0.03	0.0029
Non-Hispanic White								
Total	0.07	0.0060	0.08	0.0066	0.04	0.0040	0.03	0.0025
Male	0.07	0.0096	0.10	0.0088	0.03	0.0045	0.03	0.0033
Female	0.06	0.0132	0.06	0.0065	0.04	0.0091	0.03	0.0024
Non-Hispanic Black								
Total	0.12	0.0167	0.12	0.0063	0.06	0.0078	0.05	0.0023
Male	0.14	0.0280	0.15	0.0129	0.06	0.0104	0.05	0.0040
Female	0.09	0.0205	0.09	0.0041	0.06	0.0104	0.04	0.0020
Mexican-American								
Total	0.05	0.0093	0.06	0.0049	0.03	0.0047	0.03	0.0018
Male	0.08	0.0158	0.08	0.0069	0.04	0.0082	0.03	0.0023
Female	0.03	0.0053	0.05	0.0051	0.02	0.0025	0.03	0.0023
Other								
Total	0.11	0.0300	0.13	0.0234	0.05	0.0138	0.06	0.0119
Male	0.14	0.0580	0.13	0.0142	0.06	0.0249	0.05	0.0086
Female	0.08	0.0358	0.14	0.0385	0.04	0.0151	0.07	0.0194

\S Distribution of this nutrient is very skewed; means and standard errors of the means should be used and interpreted with caution.

Effects of Consumption of Omega-3 Fatty Acid from Fish or Overall Diet, or from Supplements of Fish Oil or ALA, on Cardiovascular Disease Outcomes

In this section, we present results from our review of studies that examined the effect of omega-3 fatty acid supplements or fish consumption on all-cause mortality and CVD outcomes. An overview of our literature search is presented first, followed by findings from secondary and primary prevention studies. Specific key questions relating to the efficacy of omega-3 fatty acids on CVD outcomes are also discussed. Relevant summary tables appear at the end of this section.

Summary of Studies Analyzed

We screened over 7,464 abstracts that were indexed as English language articles concerning humans. Based on this initial review, we retrieved and screened 768 full text articles for potentially relevant human data. We subsequently examined 118 articles that passed a screen for studies that might have CVD clinical outcome data. We rejected 80 articles. Thirty of the rejected articles were reviews or commentaries that did not provide primary data. The reasons for rejecting the remaining 50 articles are listed in the section, Excluded Studies.

Thirty-nine unique studies fulfilled our inclusion criteria for reporting mortality or CVD clinical outcomes with a follow-up duration of 1 year or longer (interim reports or articles reporting different outcomes from the same overall study were counted as a single study). The 39

Table 3.20 Randomized controlled trials of omega-3 fatty acid supplements on cardiovascular disease outcomes: all cause mortality, CVD death, cardiac death, sudden death (secondary prevention)

Author Year Country	N	Type Dose	Control	Duration (year)		All cause mortality Control Group Event Rate (%)	CVD death Control Group Event Rate (%)	Cardiac death Control Group Event Rate (%)	Sudden death Control Group Event Rate (%)	Quality RR 95% CI	Applicability								
											RR 95% CI	RR 95% CI	RR 95% CI						
EPA + DHA																			
Marchioli 2002	Italy	5665	EPA + DHA (1:2) 0.85 g/d±Vit E	5658	Control ±Vit E	3.5	9.8	0.79 ¹ 0.66-0.93	6.5	0.70 ¹ 0.56-0.86	5.4	0.65 ¹ 0.51-0.82	2.7	0.55 ¹ 0.39-0.77	B	3	A	CVD I	
Nilsen 2001	Norway	150	EPA + DHA (1:2) 1.7 g/d	150	Corn oil 1.7 g/d	1.5	7.3	1.0 0.45-2.2	-	nd	5.3	1.0 0.39-2.6	-	nd.	B	4	U	CVD II	
Singh 1997 India		122	EPA + DHA (1:1) g/d	118	Non-oil placebo	1	-	nd	-	nd	22	0.52 0.29-0.95	6.6	0.24 0.05-1.1	C	4	I	CVD II	
Leng 1998	Scotland	60	EPA 0.27g/d	60	Sun flower seed oil 3 g/d	2	5.0	1.0 0.21-4.8	3.3	1.0 0.15-6.9	-	nd	-	nd.	A	5	A	CVD II	
Sacks 1995 US		31	EPA + DHA (3:2) 4.8 g/d	28	Olive Oil	2.4	3.6	0.3 0.01-7.1	3.6	0.3 0.01-7.1	3.6	0.3 0.01-7.1	0	nd	B	3	U	CVD II	
ALA																			
Singh 1997 India		120	Mustard Oil ALA 2.9 g/d	118	Non-oil placebo	1	-	nd	-	nd	22	0.61 0.34-1.1	6.6	0.25 0.05-1.1	C	4	I	CVD II	

¹ RR adjusted for main confounders as reported in article.

Alloc. conceal. – allocation concealment; g/d – grams per day; nd – no data

Applicability is derived from a combination of the target population (GEN or CVD) and the three-level grades (I, II, III). CVD-II represents a relevant subgroup of US subjects with history or risk of CVD. Most studies in this table are graded CVD-II because they are foreign mixed-gender populations with different background diets at risk for CVD.

Table 3.21 Randomized controlled trials of omega-3 fatty acid supplements on cardiovascular disease outcomes: myocardial infarction, stroke, all CVD events (secondary prevention)

Author Year Country	Omega -3 Fatty acid		Control		Fatal MI		Non-fatal MI		All strokes		All CVD events		Quality		Applicability						
	N	Type Dose	N	Type Dose	Duration (year)		Control group event rate (%)	RR 95% CI	Control group event rate (%)	RR 95% CI	Control group event rate (%)	RR 95% CI	Alloc. conceal. Jadad score Summary	CVD I							
EPA + DHA																					
Marchioli 2002 Italy	5665	EPA + DHA (1:2) 0.85 g/d±Vit E	5658	Control Or Vit E	3.5	4.6	0.68 ¹ 0.53-0.88	4.1	0.91 ¹ 0.70-1.2	1.4	1.2 ¹ 1.9	0.81- 1.9	11	0.80 ¹ 0.68-0.94	B	3	A	CVD I			
Nilsen 2001 Norway	150	EPA + DHA (1:2) g/d	150	Corn oil 1.7 g/d	1.5	-	nd	10	1.4 0.75-2.6	-	nd	47	1.1 0.84-1.3	B	4	U	CVD II				
Singh 1997 India	122	EPA + DHA (1:1) 1.8 g/d	118	Non-oil placebo	1	-	nd	25	0.52 0.3-0.9	-	nd	35	0.71 1.1	0.48- C	4	I	CVD II				
Leng 1998 Scotland	60	EPA 0.27g/d	60	Sunflower seed oil 3 g/d	2	-	nd	6.7	0.75 3.2	0.18- 1.7	Non-fatal stroke 3.0 0.32- 28	3.0 0.32- 28	0.86 ² 1.7	0.43- A	5	A	CVD II				
Sacks 1995 US	31	EPA + DHA (3:2) g/d	48	Olive Oil	2.4	3.6	0.3 0.01-7.1	7.1	0.45 0.04-4.7	0 2.7	0.12- 64	-	nd	B	3	U	CVD II				
ALA																					
Singh 1997 India	120	Mustard Oil ALA 2.9 g/d	118	Non-oil placebo	1	-	nd	25	0.59 0.35-1.0	-	nd	35	0.82 1.2	0.56- C	4	I	CVD II				

¹RR adjusted for main confounders as reported in article. ² Includes critical ischemia/amputation, angioplasty and bypass surgery.

Alloc. conceal. – allocation concealment; g/d – grams per day; nd – no data

Applicability is derived from a combination of the target population (GEN or CVD) and the three-level grades (I, II, III). CVD-II represents a relevant subgroup of US subjects with history or risk of CVD. Most studies in this table are graded CVD-II because they are foreign mixed-gender populations with different background diets at risk for CVD

Table 3.22 Randomized controlled trials of omega-3 fatty acid diet or dietary advice on cardiovascular disease outcomes: all cause mortality, CVD death, cardiac death, sudden death (secondary prevention)

Author Year Country	N	Diet / Fish advice	No Diet / No fish advice	All cause mortality				CVD death				Cardiac death				Sudden death				Quality				
				RR Control group event rate (%)	95% CI	Control group event rate (%)		RR Control group event rate (%)	95% CI	Control group event rate (%)		RR Control group event rate (%)	95% CI	Control group event rate (%)		RR Control group event rate (%)	95% CI	Control group event rate (%)		RR Control group event rate (%)	95% CI	Alloc. conceal. Jadad score Summary		
						EPA	g/wk			EPA	g/wk			EPA	g/wk			EPA	g/wk					
EPA estimate																								
Burr 2003 UK	1571	EPA 2.11-2.65 g/wk	1543	EPA 0.12-0.17 g/wk	5	16	HR 1.15 1.36	0.86	-	-	9	HR 1.26 (1.00-1.58)	3	HR 1.54 (1.06-2.23)	C	2	A	CVD II						
Burr 1989 UK	1015	EPA 2.4 g/wk (SD 1.4)	1018	EPA 0.06 g/wk (0.7)	2	13	0.73 0.56-0.93	-	nd	11	0.67 0.51-0.89	-	nd	C	1	U	CVD II							
ALA estimate																								
Singh 2002 India	499	Indo Mediterranean diet ALA 1.8 g/d	501	ALA 0.8 g/d	2	8	0.63 0.38-1.04	-	nd	-	nd	-	nd	3.2	0.38 0.15-0.95	C	3	U	CVD II					
Leren Norway 1966	406	Cholesterolowering diet ¹ ALA 1.1-1.9 g/d (soybean oil)	406	Usual diet	5	27	0.75 0.52-1.06	25	0.73 0.50-1.06	-	nd	13	1.00 1.64	0.61-	C	2	I	CVD II						
DeLongeril 1999 France	302	Cretan Mediterranean diet ¹ ALA 1.9 g/d	303	Prudent diet ² 0.67 g/d	ALA 2.3	7.9	0.44 ³ 0.94	0.21-	-	nd	6.3	0.35 ³ 0.15-0.83	2.6	0.06 1.02	0.003-	C	4	A	CVD II					
Bemelmans 2002 Netherlands	109	ALA 6.3 g/d	157	ALA 1.0 g/d	2	6	4.3 0.46-4.1	0.6	1.44 0.09-23	-	nd	-	nd	B	3	A	CVD I							

¹ ALA=0.84 % energy = calculated from daily nutrient recorded on the final visit in 144 unselected consecutive experimental patients

² ALA=0.29% energy = calculated from daily nutrient recorded on the final visit in 83 unselected consecutive control patients

³ RR adjusted for main confounders as reported in article.

Alloc. conceal. – allocation concealment; g/d – grams per day; nd – no data

Table 3.23 Randomized controlled trials of omega-3 fatty acid diet or dietary advice on cardiovascular disease outcomes: myocardial infarction, stroke, all CVD events (secondary prevention)

Author Year Country	N	Diet / Fish advice	No Diet / No fish advice		Fatal MI		Non-fatal MI		All strokes		All CVD events		Quality	Applicability		
			Estimated omega-3 fatty acid intake	N	Estimated omega-3 fatty acid intake		Duration (year)		RR 95% CI		RR 95% CI					
					Control group event rate (%)		Control group event rate (%)		Control group event rate (%)		Control group event rate (%)					
					EPA estimate											
Burr 2003 UK	1571	EPA 2.11-2.65 g/wk	1543		EPA 0.12-0.17 g/wk	5	-	nd	-	nd	-	nd	C 1	CVD II		
Burr 1989 UK	1015	EPA 2.4 g/wk	1018		EPA 0.6g/wk (SD 0.7)	2	-	0.7 0.5-0.9	3.2 0.97-2.3	-	nd	-	C 1	CVD II		
ALA estimate																
Singh 2002 India	499	Indo Mediterranean ALA 1.8 g/d	501		ALA 0.8 g/d	2	3.4	0.71 0.34-1.5	8.6 0.30-0.81	2.6	0.54 0.22- 1.3	-	nd	C 3	CVD II	
Leren 1966 Norway	406	Cholesterol- lowering diet ALA 1.1-1.9 g/d (soybean oil)	406		Usual diet	5	11	0.43 0.89	15 0.77-1.27	-	nd	-	nd	C 2	CVD II	
Delorgeril 1999 France	302	Cretan Mediterranean diet ¹ ALA 1.9 g/d	303	Prudent diet ² 0.67 g/d	ALA 2.3	-	nd	8.3 0.32- 0.70	1.3 0.01-2.1	0.11 59	0.53 ³ 0.38-0.74	C 4	A	CVD II		
Bemelmans 2002 Netherlands	109	ALA 6.3 g/d	157		ALA 1.0 g/d	2	-	nd	2.5 0.16- 2.9	1.3 0.01-5.9	0.29 5.7	0.16 0.02-1.3	B 3	A	CVD I	

¹ALA = 0.84% daily energy = calculated from daily nutrient recorded on the final visit in 144 unselected consecutive experimental patients

²ALA = 0.29% daily energy = calculated from daily nutrient recorded on the final visit in 83 unselected consecutive control patients

³ Total major and minor endpoints.

Alloc. conceal. – allocation concealment; g/d – grams per day; nd – no data

Characteristics of the diet and dietary advice trials. (Tables 3.22-3.23) Evidence for the effects of diet or dietary advice on CVD outcomes in populations known to have CVD was derived from 6 RCTs. About 4,000 patients were studied in the trials, and trial duration ranged from 2 to 5 years.

Two of the trials of diet and dietary advice were conducted among males from the ^{40,41}. The amount of omega-3 fatty acid consumption in these 2 trials can only be estimated. The methodological quality of the trials was poor (grade C) and the study populations were rated as CVD-II (relevant subgroups). Two other trials reported estimates of EPA intake. The weekly EPA consumption in the first of these trials was 0.6 g in the control group and 2.4 g in the intervention group. Weekly EPA consumption in the second trial was 0.12g in the control group and 2.7 g in the intervention group.

Four trials provided estimates of daily ALA consumption. In the control groups of these trials, estimated ALA consumption ranged from 0.67 g/d to 1 g/d. Estimated ALA intake of the intervention groups was at least double that of the control groups (range 1.8 g/d to 6.3 g/d⁴²⁻⁴⁵). The methodological quality of 3 of the 4 trials was poor (Grade C). The applicability of the trials ranged from CVD-I (highly applicable) to CVD-III (limited applicability). The subjects were mostly MI survivors or those at significant CVD risk. The study by Bemelmans et al. randomized patients in a factorial design to consume a margarine rich in ALA or LA, and to receive nutritional education or not ⁴⁵. The amount of margarine prescribed was not fixed, but instead was based on the participants' usual consumption patterns. The study by ⁴⁴ was conducted among patients in India. Two-thirds of the participants were vegetarians, which limits the applicability of the study results to the US population.

Table 3.24 Association of estimates of fish consumption with all cause mortality, cardiovascular death, and myocardial infarction in prospective cohort studies (secondary prevention)

Author Year Location	N	Duration (year)	Dietary Assessment	Results			Trend P-value	Overall effect	Quality	Applicability
				Fish consumption (amount or frequency) Relative risk (unless stated otherwise)						
Erkkila 2003 Finland	415	5	4-day food record	0	1.57	>57 g/d	0.06	+	B	CVD II
				All cause mortality	1.0	0.50	0.37*	NS		
				CV Death	1.0	0.64	0.45	NS		
				CAD death or MI	1.0	1.0	0.49	NS	0	

There was 1 prospective cohort study⁴⁶ (Table 3.24) in a CVD population that associated estimates of daily fish consumption with CVD outcomes. The methodological quality of this study was good (grade B). The study populations were rated as CVD-II (relevant subgroups). This study lasted 5 years and included 415 subjects with known coronary artery disease. A 4-day food record was used to assess the daily fish intake. Fish intake was divided into 3 categories: no intake, below medium consumption (57 g/d), and above medium consumption.

Table 3.25 Randomized controlled trials of omega-3 fatty acid supplements on cardiovascular disease outcomes: all cause mortality, CVD death, cardiac death, sudden death (Primary intervention)

Author Year Country	Omega -3 Fatty acid		Control		All cause mortality		CVD death		Cardiac death		Sudden death		Quality	Applicability					
	N	Type Dose	N	Type Dose	RR 95% CI		RR 95% CI		RR 95% CI		RR 95% CI			Alloc. conceal.	Jadad score	Summary			
					Control group event rate (%)		Control group event rate (%)		Control group event rate (%)		Control group event rate (%)								
ALA																			
Natvig 1968 Norway	6716	Linseed oil 5.5 g/d	ALA 6690	Sunflower seed oil ALA 0.14 g/d	1	0.6	1.1	1.6	0.7	-	nd	0.4	1.0 0.58-1.7	-	nd	C 4	A II GEN		

Table 3.26 Randomized controlled trials of omega-3 fatty acid supplements on cardiovascular disease outcomes: myocardial infarction, stroke, all CVD events (Primary intervention)

Author Year Country	Omega -3 Fatty acid		Control		Fatal MI		Non-fatal MI		All strokes		All CVD events		Quality	Applicability					
	N	Type Dose	N	Type Dose	RR 95% CI		RR 95% CI		RR 95% CI		RR 95% CI			Alloc. conceal.	Jadad score	Summary			
					Control group event rate (%)		Control group event rate (%)		Control group event rate (%)		Control group event rate (%)								
ALA																			
Natvig 1968 Norway	6716	Linseed oil 5.5 g/d	ALA 6690	Sunflower seed oil ALA 0.14 g/d	1	All MI 1.2 (0.84-1.7)	All MI 0.8	All MI 1	0.13	1.4 0.62-3.4	-	nd	C 4	A II GEN					

Table 3.27 Association of estimates of omega-3 fatty acid consumption with all cause mortality in prospective cohort studies

Author Year Location	N	Duration (year)	Dietary Assessment	Results ¹					Trend P-value ²	Overall effect	Quality	Applicability
				Estimated omega-3 fatty acid consumption Relative risk (unless stated otherwise)								
Nagata 2002 Japan	29079	7	FFQ	EPA+DHA Men 0.41 0.6 0.79 1.1 1.6 g/d Hazard ratio 1.0 0.82* 0.87 0.88 0.87 Women 0.33 0.49 0.64 0.83 1.3 g/d Hazard ratio 1.0 0.92 0.84 0.90 0.77*					NS 0.01	++	A	GEN II
Yuan 2001 China	18244	12	FFQ	EPA+DHA 0.15 0.38 0.65 0.91 1.7 g/wk 1.0 0.79* 0.76* 0.86* 0.79*					0.01	++	A	GEN II
Dolecek 1992 US MRFIT	6250	10.5	Multiple 24-hr recall	ALA 0.87 1.3 1.6 1.9 2.8 g/d 1.0 0.96 0.69 0.89 0.69 EPA+DHA 0.0 0.009 0.046 0.15 0.66 g/d 1.0 1.1 1.0 0.85 0.76					0.014 0.01	++	A	GEN II

The footnotes and abbreviations below apply to summary tables 3.27– 3.39 in this section.

¹ Adjusted results are presented here when reported in original study. See evidence tables for details.

² Trend for inverse association. Up arrow indicates a statistically significant positive association (worse outcome).

* Statistically significant p<0.05; numerical p-value reported for p<0.1.

Study acronyms:

ABCC = Alpha-Tocopherol Beta-Carotene Cancer Prevention

ADVENTIST = Adventist Health Study

CHS = Cardiovascular Health Study

HPS = Health Professionals Study

MRFIT = Multiple Risk Factor Intervention Study

NHANES = National Health and Nutrition Examination Study

NHS = Nurses' Health Study

PHS = Physicians' Health Study

WES = Western Electric Company Study

Table 3.28 Association of estimates of fish consumption with all cause mortality in prospective cohort studies

Author Year Location	N	Duration (year)	Dietary Assessment	Results					Trend P-value	Overall effect	Quality	Applicability		
				Fish consumption (amount or frequency) Relative risk (unless stated otherwise)										
Nagata 2002 Japan	29079	7	FFQ	Men Hazard ratio Women Hazard ratio	46 1.0 37 1.0	68 0.92 54 0.93	87 0.91 69 0.96	112 0.90 88 0.93	158 0.94 122 0.86	g/d	NS	0	A	GEN II
Albert 1998 US PHS	20551	12	FFQ	$\leq 1/\text{mo}$ 1.0	$1\text{-}3/\text{mo}$ 0.79	$1\text{-}2/\text{wk}$ 0.71*	$2\text{-}5/\text{wk}$ 0.70*	$=5/\text{wk}$ 0.73*			0.045	++	A	GEN II
Yuan 2001 China	18244	12	FFQ	≤ 50 1.0	50-100 0.79*	100-150 0.76*	150-200 0.86*	=200 0.79*		g/wk	0.01	++	A	GEN II
Mann 1997 UK	10802	13.3	FFQ	Death rate ratio	0 100	<1 97	=1/wk 96				NS	0	B	GEN II
Gillum 2000 US NHANES	8825	18.8	FFQ + 24-hr recall	Never White Men Black Men White Women Black Women	1.0 1.0 1.0 1.0	0.88 1.0 1.0 0.77	0.76* 1.0 1.0 0.79	0.85 1.1 0.90 0.82		/wk	0.01 NS nd nd	+	B	GEN I
Osler 2003 Denmark	8497	18	FFQ	Hazard ratio	$\leq 1/\text{mo}$ 0.88	$2/\text{mo}$ 0.84*	$1/\text{wk}$ 1.0 (ref)	$>2/\text{wk}$ 1.1			0.02-	-	B	GEN I
Daviglus 1997 US WES	1822	30	FFQ	$\leq 1/\text{mo}$ 1.0	$1\text{-}17$ 1.02	$18\text{-}34$ 0.98	$=35$ 0.85			g/d	NS	0	A	GEN II
Fraser 1997 US Adventist	603	12	FFQ	>84 years old subset of Adventist Health Study							NS	0	B	GEN III
Kromhout 1995 Holland	272	17	CCD	Non-fish eaters 1.0		Fish Eaters (24 g/d) 0.96					NS	0	C	GEN II

Table 3.29 Association of estimates of omega-3 fatty acid consumption with cardiovascular death in prospective cohort studies

Author Year Location	N	Duration (year)	Dietary Assessment	Results							Trend P-value	Overall effect	Quality	Applicability
				Estimated omega-3 fatty acid consumption Relative risk (unless stated otherwise)										
Nagata 2002 Japan	29079	7	FFQ	Men	1.0	0.74	0.71	0.82	0.76	Hazard ratio	NS	+	A	GEN II
Dolecek 1992 US MRFIT	6250	10.5	Multiple 24-hr recall	ALA	0.87	1.3	1.6	1.9	2.8	g/d	0.067	++	A	GEN II
					1.0	0.89	0.64	0.83	0.6					
				EPA+DHA	0.0	0.009	0.046	0.15	0.66	g/d	0.004			
					1.0	1.06	0.92	0.92	0.59					

Table 3.30 Association of estimates of fish consumption with cardiovascular death in prospective cohort studies

Author Year Location	N	Duration (year)	Dietary Assessment	Results					Trend P-value	Overall effect	Quality	Applicability	
				Fish consumption (amount or frequency) Relative risk (unless stated otherwise)									
Albert 1998 US PHS	20551	11	FFQ	<1/mo	1-3/mo	1-<2/wk	2-<5/wk	=5/wk		NS	+	A	GEN II
				1.0	0.96	0.79	0.84	0.81					
Gillum 2000 US NHANES	8825	18.8	FFQ + 24-hr recall	Never	<1	1	>1	/wk		NS	0	B	GEN II
				White men	1.0	0.98	0.87	0.95					
				Black men	1.0	0.96	0.99	1.1					
				White women	1.0	1.1	1.1	1.1					
				Black women	1.0	0.85	0.94	0.99					
Daviglus 1997 US WES	1822	30	FFQ	0	1-17	18-34	=35	g/d		0.01	++	A	GEN II
				1.0	0.94	0.89	0.74						

Table 3.31 Association of estimates of omega-3 fatty acids with cardiac death in prospective cohort studies

Author Year Location	N	Duration (year)	Dietary Assessment	Results					Trend P-value	Overall effect	Quality	Applicability		
				Estimated omega-3 fatty acid consumption Relative risk (unless stated otherwise)										
Pietinen 1997 Finland ABCC	21930	6.1	FFQ	ALA	0.9 1.0	1.2 0.94	1.5 0.98	1.9 1.03	2.5 0.99	g/d	NS	0	A	GEN II
Dolecek 1992 US MRFIT	6250	10.5	Multiple 24-hr recall	EPA+DHA	0.2 1.0	0.3 0.94	0.4 1.0	0.5 1.1	0.8 1.3	g/d	NS 0.01	++	A	GEN II
				ALA	0.87 1.0	1.3 0.98	1.6 0.57	1.9 0.98	2.8 0.68	g/d				
				EPA+DHA	0 1.0	0.009 1.1	0.046 0.91	0.15 0.88	0.66 0.60	g/d				

Table 3.32 Association of estimates of fish consumption with cardiac death in prospective cohort studies

Author Year Location	N	Duration (year)	Dietary Assessment	Results					Trend P-value	Overall effect	Quality	Applicability	
				Fish consumption (amount or frequency) Relative risk (unless stated otherwise)									
Hu 2002, US NHS	84688	16	FFQ	<1/mo 1.0	1-3/mo 0.80	1/wk 0.65*	2-4/wk 0.72	>5/wk 0.55*	0.01	++	A	GEN II	
Ascherio 1995, US HPS	44895	6	FFQ	1-3/mo 0.74	1/wk 0.86	2-3/wk 0.71	4-5/wk 0.54*	>6/wk 0.77	NS	+	A	GEN II	
Egeland 2001 Norway	42612	7	Dietary quest-ionnaire	None Never smoker	Cod liver oil Hazard ratio 1.0	1.0 0.7	1.0 0.8	1.0 0.8	NS	+	C	GEN II	
Fraser 1997, US Adventist	26743	6	FFQ	0 Hazard ratio 1.0	<1/wk 1.1	>1/wk 0.74			nd	0	B	GEN II	
Albert 1998, US PHS	20551	11	FFQ	<1/mo 1.0	1-3/mo 1.18	1-2/wk 0.82	2-5/wk 0.91	=5/wk 0.81	NS	+	A	GEN II	
Mann 1997 UK	10802	13.3	FFQ	0 Death Rate Ratio 100	<1 121	=1 /wk 123			NS	-	B	GEN II	
Rodriguez 1996 US Honolulu	8006	23	Dietary quest-ionnaire	Cigarettes/d <20 20-30 >30	<2/wk 0.30 0.38 1.0	=2/wk 0.42 0.45 0.50*	Fish consumption		NS NS nd	+	C	GEN II	
Osler 2003 Denmark	8497	18	FFQ	=1/mo Hazard ratio 1.1	2/mo 0.98	1/wk 1.0 (ref)	>2/wk 0.98		NS	0	B	GEN I	
Mozaffarian 2003 US CHS	3910	9.3	FFQ	Tuna/other fish Total IHD death Fried fish/sand. Total IHD death	<1/mo 1.0 <1/mo 1.0	1-3/mo 0.78 1-3/mo 1.2	1/wk 0.77 1/wk 1.6	2/wk 0.53* 2/wk 1.1	0.47* 0.47 1.4	0.002 NS	++ -	A	GEN II
Oomen 2000 Finland Italy Holland	2738	20	CCD	1-19 Total fish Fatty fish	20-39 0.93 0.57*	>40 g/d 1.1 0.87(=20 g/d)			NS	+	A	GEN II	
Daviglus 1997, US WES	1822	30	FFQ	0 1.0	1-17 0.88	18-34 0.84	=35 0.62*	g/d	0.04	++	A	GEN II	
Kromhout 1985 Holland	852	20	CCD	0 1.0	1-14 0.64	5-29 0.56	30-44 0.36*	45 g/d 0.39	nd	+	B	GEN II	
Kromhout 1995 Holland	272	17	CCD	No fish 1.0	Fish eater 0.51*				nd	+	C	GEN I	

Table 3.33 Association of estimates of omega-3 fatty acids with sudden death in prospective cohort and case-control studies

Author Year Location	N	Duration (year)	Dietary Assessment	Results					Trend P-value	Overall effect	Quality	Applicability			
				Estimated omega-3 fatty acid consumption Relative risk (unless stated otherwise)											
Prospective cohort															
Albert 1998 US PHS	20551	12	FFQ	EPA+DHA	<0.3 1.0	0.3-2.7 0.58	2.7-4.9 0.34*	4.9-7.4 0.60	>7.4 g/mo 0.43*	NS	++	A	GEN II		
Case control															
Siscovick 1995 US	827	na	FFQ	EPA+DHA Odds ratio	0 1.0	0.96 0.9*	2.9 0.7*	5.5 0.5*	13.7 g/mo 0.4*	ND	++	A	GEN I		

Table 3.34 Association of estimates of fish consumption with sudden death in prospective cohort studies

Author Year Location	N	Duration (year)	Dietary Assessment	Results					Trend P-value	Overall effect	Quality	Applicability	
				Fish consumption (amount or frequency) Relative risk									
Albert 1998 US PHS	20551	12	FFQ	<1/mo 1.0	1-3/mo 0.64	1-2/wk 0.47*	2-5/wk 0.51	=5/wk 0.39*		NS	++	A	GEN II
Daviglus 1997 US WES	1822	30	FFQ	0 1.0	1-17 0.78	18-34 0.80	=35 0.68	g/d		NS	+	A	GEN II

Table 3.35 Association of estimates of omega-3 fatty acids consumption with myocardial infarction in prospective cohort and case-control studies

Author Year Location	N	Duration (year)	Dietary Assessment	Results					Trend P-value	Overall effect	Quality	Applicability					
				Estimated omega-3 fatty acid consumption													
Prospective cohort																	
Hu 2002		16		EPA+DHA													
Hu 1999	84688		FFQ	Median intake (% energy) 0.03 0.05 0.08 0.14 0.24					<0.001	++	A	GEN II					
US NHS		10		Nonfatal MI 1.0 0.92 0.83 0.75* 0.69*													
ALA																	
Ascherio 1995	44895	6	FFQ	Median intake g/d 0.71 0.86 0.98 1.12 1.36					0.001	++							
US HPS				Fatal IHD 1.0 0.99 0.90 0.67 0.55*					0.05								
Non-fatal MI 1.0 0.92 0.94 1.02 0.85																	
Morris 1995	21185	4	FFQ	EPA+DHA <0.05 0.5-<1.0 1.0-<1.7 1.7-<2.3 >2.3 g/wk													
US PHS				Total MI 1.0 1.6 1.4 1.2 1.2					NS	-	A	GEN II					
Nonfatal MI 1.0 1.5 1.3 1.2 1.1																	
Yuan 2001	18244	12	FFQ	EPA+DHA <0.27 0.27-0.43 0.44-0.72 0.73-1.1 >1.1 g/wk					0.02	++	A	GEN II					
China				Fatal MI 1.0 0.39* 0.67 0.53* 0.43*													
Oomen 2001	67	0	CD	ALA (% energy) <0.45 0.45-0.58 >0.58													
Holland				Fatal and nonfatal CAD 1.0 1.5 1.7					NS	-	B	GEN III					
Fatal CAD 1.0 0.99 1.6																	
Case control																	
Tavani 2001	975	na	FFQ	EPA+DHA <0.81 0.81-1.28 >1.28 g/wk					0.03	++	B	GEN II					
Italy				Nonfatal MI odds ratio 1.0 0.71* 0.67*													

Table 3.36 Association of estimates of fish consumption with myocardial infarction in prospective cohort and case control studies

Author Year Location	N	Duration (year)	Dietary Assessment	Results					Trend P-value	Overall effect	Quality	Applicability			
				Fish consumption (amount or frequency) Relative risk (unless stated otherwise)											
Prospective cohort															
Hu 2002 NHS	84688	16	FFQ	1-3/mo Nonfatal MI	0.78*	0.74*	0.68*	0.73	0.03	++	A	GEN II			
Ascherio 1995 US HPS	44895	6	FFQ	<1/mo MI Nonfatal MI	0 1.0 1.0	7 0.66* 0.62*	18 0.82 0.80	37 0.69* 0.67*	69 0.65* 0.69	119 g/d 0.90 0.96	NS NS	++	A	GEN II	
Fraser 1992a US Adventist	26743	6	FFQ	0 Nonfatal MI	1.0	<1 1.0	>1/wk 1.04				NS	0	B	GEN II	
Albert 1998 US PHS	20551	11	FFQ	<1/mo All MI	1.0	1-3/mo 0.91	1-2/wk 0.99	2-5/wk 1.0	>5/wk 1.0		NS	0	A	GEN II	
Yuan 2001 China	18244	12	FFQ	<50 Fatal MI	1.0	50-100 0.55*	100-150 0.65	150-200 0.66	=200 0.41*	g/wk	0.03	++	A	GEN II	
Mozaffarian 2003 US CHS	3910	9.3	FFQ	Tuna/other fish Nonfatal MI Fried fish/sandwich Nonfatal MI	1-3/m 0.81 1-3/m 1.3	1/wk 0.71 1/wk 1.6	2/wk 0.75 2/wk 1.2	>3/wk 0.67 >3/wk 1.9		Hazard ratio	0.10 NS	+	A	GEN II	
Davilglus 1997 US WES	1822	30	FFQ	0 All MI	1.0	1-17 0.88	18-34 0.76	=35 0.56*	g/d		0.017	++	A	GEN II	
Case control															
Tavani, 2001 Italy	975	na	FFQ	≤1 Nonfatal MI odds ratio	1.0	1-2 0.79	≥2 0.67*	/wk			0.02	++	B	GEN II	
Sasazuki 2001 Japan	1846	na	FFQ	≤2 Nonfatal MI odds ratio Men Women	1.0 1.0	2-3 0.6*	>4 /wk 0.7*				NS 0.09	+	B	GEN II	

Table 3.37 Association of estimates of omega-3 fatty acid consumption with stroke in prospective cohort and case-control studies

Author Year Location	N	Duration (year)	Assessment	Results						Trend P-value	Overall effect	Quality	Applicability			
				Estimated omega-3 fatty acid consumption Relative risk (unless stated otherwise)												
Prospective cohort																
Iso 2001 US NHS	79839	14	FQ	EPA+DHA	0.077	0.12	0.17	0.22	0.48 g/d	NS	+	A	GEN II			
				Ischemic	1.0	0.83	0.67*	0.82	0.71	NS						
				Hemorrhagic	1.0	0.94	0.66	0.93	0.76	NS						
He 2002 US HPS	43671	12	FQ	EPA+DHA	<0.05	0.05-<0.2	0.2-0.4	0.4-<0.6	>0.6 g/d	NS	++	A	GEN II			
				Ischemic	1.0	0.56*	0.63*	0.54*	0.73	NS						
				Hemorrhagic	1.0	1.3	1.0	0.89	1.1	NS						
Morris 1995 US PHS	21185	4	FQ	EPA+DHA	<0.5	0.5-<1.0	1.0-<1.7	1.7-<2.3	>2.3 g/wk	NS	0	A	GEN II			
				All strokes	1.0	0.9	1.1	0.7	1.0	NS						
Yuan 2001 China	18244	9	FFQ	EPA+DHA	<0.26	0.27-0.43	0.44-0.72	0.73-1.1	≥1.1 g/wk	NS	+	A	GEN II			
				Fatal strokes	1.0	0.76	0.76*	0.93	1.0	NS						
Seino 1997 Japan	2283	15.5	FFQ	n-3 fatty acid	1.8	2.3	2.7	3.2	g/d	NS	-	B	GEN II			
				Ischemic stroke	1.0	0.99	1.6	1.4		NS						
Case control																
Caicoya 2002 Spain	913	na	FQ	EPA+DHA	<0.12	0.12-0.32	0.32-0.66	>0.66	g/d	0.01-	-	A	GEN II			
				All strokes odds ratio	1.0	1.1	1.4	1.8								

Table 3.38 Association of estimates of fish consumption with stroke in prospective cohort and case-control studies

Author Year Location	N	Duration (year)	Dietary Assessment	Results					Trend P-value	Overall effect	Quality	Applicability			
				Fish consumption (amount or frequency) Relative risk (unless stated otherwise)											
Prospective cohort															
Kinjo 1999 Japan	223170	15	1-page questionnaire	>1 Ischemic deaths Hemorrhagic deaths	1.0 1.0	1-3 0.83 1.0	0.99 0.69 1.1	>4 0.38 0.93	/wk	nd nd	0	C	GEN II		
Iso 2001 US NHS	79839	14	FQ	<1/m Ischemic Hemorrhagic	1.0 1.0	1-3/m 0.83 1.4	1/wk 0.69 1.1	2-4/wk 0.63 0.93	>5/wk 0.38 1.0	0.09 NS	+	A	GEN II		
He 2002 US HPS	43671	12	FQ	<1/mo Ischemic Hemorrhagic	1.0 1.0	1-3/mo 0.57* 1.8	1/wk 0.56* 1.4	2-4/wk 0.55* 0.96	>5/wk 0.54* 1.6	NS NS	++	A	GEN II		
Morris 1995 US PHS	21185	4	FFQ	<1 Non-fatal strokes	1.0	1 1.3*	2-4 1.1	>5 0.9	/wk	NS	-	A	GEN II		
Yuan 2001 China	18244	9	FQ	<50 Fatal strokes	1.0	50-100 0.93	100-150 0.79	150-200 1.01	=200 g/wk 1.11	NS	0	A	GEN II		
Gillum 1996 US NHANES	5192	12	FFQ	Ischemic stroke Women aged 45-74 Men aged 45-74	0 1.0	<1 0.78	1 0.77	>1 0.55*	/wk	nd na	+	B	GEN I		
Orencia 1996 USA WES	1847	30	FFQ / 24-hr recall	Black men+women Stroke incidence Stroke death	Never fish 1.0	some fish 0.51*				NS	0	A	GEN II		
Keli 1994 Holland	872	15	CCD	All strokes	0 1.0	1-17 0.94	18-34 0.89	>35 1.3	g/d Hazard ratio	0.06	+	B	GEN II		
Case control															
Caicoya 2002 Spain	913	na	FFQ	Total Odds ratio Ischemic Odds ratio	0 1.0	1-22.5 0.30*	23-45 0.44	46-90 0.59	>91 g/d 0.76	nd 0.08-	+	A	GEN II		
											-				

Table 3.39 Association of estimates of omega-3 fatty acid consumption with all CVD events in cross-sectional study

Author Year Location	N	Duration (year)	Dietary Assessment	Results						Trend P-value	Overall effect	Quality	Applicability
				Estimated omega-3 fatty acid consumption Prevalence odds ratio for all CVD events									
Djousse 2001 US	40 6	n.a	FQ	ALA 0.53 0.67 0.78 0.90 1.1 g/d men 1.0 0.77 0.61* 0.58* 0.60*						0.012	++	B	GEN I
				ALA 0.46 0.58 0.65 0.76 0.96 g/d women 1.0 0.57 0.52 0.30* 0.42*						0.014			

Primary Prevention Studies (Tables 3.25-3.39)

Evidence for the effects of the consumption of omega-3 fatty acids, omega-3 fatty acid supplements, or fish on CVD outcomes in the general population is derived from 22 prospective cohort studies, 4 case-control studies, 1 cross-sectional study, and 1 RCT. The methodological quality of most of the studies within their study design category was good (grades A or B); 4 prospective cohort studies were graded as poor (grade C).

We found only 1 RCT that examined omega-3 fatty acid supplements in the general population. (Tables 3.25-3.26) The methodological quality of this study was poor (grade C). The study, which compares linseed oil (5.5 g/d of ALA) with sunflower seed oil (0.14 g/d ALA), was conducted in Norway more than 30 years ago⁴⁹ and lasted 1 year. It is the largest of all ALA supplement trials, with over 13,000 subjects. Presumably, subjects had high background omega-3 fatty acid levels because of characteristically large consumption of fish. There were too few all-cause mortality or CVD events in the control group, and it reported no benefit on any of the CVD outcomes. This trial does not contribute substantively to the assessment of the effect of omega-3 fatty acid supplements on CVD outcomes. The major conclusion one can draw from this study is that ALA, given at a dose of 0.14 g/d for 1 year, has no effect on CVD outcomes in the general population with a high fish consumption background diet.

The 22 prospective cohort studies were conducted in many parts of the world, including the US, China, Japan, and countries in the Mediterranean and Northern Europe. Most of the cohorts had several thousand subjects. The majority of the studies received an applicability grade of GEN-II, reflecting either relevant subgroups or differences in the background diet of the study population when compared with the US population. Several of the large population studies conducted in the US were graded as GEN-II because of single sex (male or female) cohorts. If viewed together, however, these studies would provide evidence that is highly applicable to the US population (GEN-I). Study duration in the cohort studies ranged from 4 to 30 years. The number of subjects followed in the cohorts ranged from 272 to as many as 223,170; many of the cohorts had tens of thousands of study subjects.

Most of the studies used the food frequency questionnaire to estimate the dietary fish intake. Most studies provided quantitative estimates of the amount of fish consumed (many also quantified the amount of EPA+DHA intake) and categorized them into various quantiles (e.g.,

Table 3.40 Association of estimates of omega-3 fatty acid consumption with all cause mortality in prospective cohort studies of general population (based on data in Table 3.27)

Applicability	Methodological Quality			
		A	B	C
	I			
II	<u>Study</u> <u>Year</u> <u>N</u> <u>Effect</u>			
	Nagata 2002 29079 ++			
III	Yuan 2001 18244 ++			
	MRFIT 1992 6250 ++			

Table 3.41 Association of estimates of fish consumption with all cause mortality in prospective cohort studies of general population (based on data in Table 3.28)

Applicability	Methodological Quality			
		A	B	C
	I		<u>Study</u> <u>Year</u> <u>N</u> <u>Effect</u>	
II	<u>Study</u> <u>Year</u> <u>N</u> <u>Effect</u>		<u>Study</u> <u>Year</u> <u>N</u> <u>Effect</u>	<u>Study</u> <u>Year</u> <u>N</u> <u>Effect</u>
	Nagata 2002 29079 0		Mann 1997 10802 0	Kromhout 1995 272 0
III	PHS 1998 20551 ++			
	Yuan 2001 18244 ++			
WES	WES 1997 1822 0		<u>Study</u> <u>Year</u> <u>N</u> <u>Effect</u>	
	Adventist 1997 603 0			

Study acronyms (apply to tables 3.40-3.51):

ABCC = Alpha-Tocopherol Beta-Carotene Cancer Prevention

ADVENTIST = Adventist Health Study

CHS = Cardiovascular Health Study

HPS = Health Professionals Study

MRFIT = Multiple Risk Factor Intervention Study

NHANES = National Health and Nutrition Examination Study

NHS = Nurses' Health Study

PHS = Physicians' Health Study

WES = Western Electric Company Study

Table 3.42 Association of estimates of omega-3 fatty acid consumption with cardiovascular death in prospective cohort studies of general population (based on data in Table 3.29)

	Methodological Quality			
		A	B	C
I				
II	Study Year N Effect Nagata 2002 29079 + MRFIT 1992 6250 ++			
III				

Table 3.43 Association of estimates of fish consumption with cardiovascular death in prospective cohort studies of general population (based on data in Table 3.30)

	Methodological Quality			
		A	B	C
I				
II	Study Year N Effect PHS 1998 20551 + WES 1997 1822 ++	Study Year N Effect NHANES 2000 8825 0		
III				

Table 3.44 Association of estimates of omega-3 fatty acid consumption with cardiac death in prospective cohort studies of general population (based on data in Table 3.31)

	Methodological Quality			
		A	B	C
Applicability	I			
	II	<u>Study</u> <u>Year</u> <u>N</u> <u>Effect</u> ABCC 1997 21930 0 MRFIT 1992 6250 ++		
	III			

Table 3.45 Association of estimates of fish consumption with cardiac death in prospective cohort studies of general population (based on data in Table 3.32)

	Methodological Quality			
		A	B	C
Applicability	I		<u>Study</u> <u>Year</u> <u>N</u> <u>Effect</u> Osler 2003 8497 0	<u>Study</u> <u>Year</u> <u>N</u> <u>Effect</u> Kromhout 1985 272 +
	II	<u>Study</u> <u>Year</u> <u>N</u> <u>Effect</u> NHS 2002 84688 ++ HPS 1995 44895 + PHS 1998 20551 + CHS 2003 3910 ++ Oomen 2000 2738 + WES 1997 1822 ++	<u>Study</u> <u>Year</u> <u>N</u> <u>Effect</u> Adventist 1997 26743 0 Mann 1997 10802 - Kromhout 1985 852 +	<u>Study</u> <u>Year</u> <u>N</u> <u>Effect</u> Egeland 2001 42612 + Honolulu 1996 8006 +
	III			

Table 3.46 Association of estimates of omega-3 fatty acid consumption with sudden death in prospective cohort studies of general population (based on data in Table 3.33)

	Methodological Quality			
		A	B	C
Applicability	I			
	II	Study Year N Effect PHS 1998 20551 ++ CHS 2003 3910 +		
	III			

Table 3.47 Association of estimates of fish consumption with sudden death in prospective cohort studies of general population (based on data in Table 3.34)

	Methodological Quality			
		A	B	C
Applicability	I			
	II	Study Year N Effect PHS 1998 20551 ++ CHS 2003 3910 +		
	III			

Table 3.48 Association of estimates of omega-3 fatty acid consumption with myocardial infarction in prospective cohort studies of general population (based on data in Table 3.35)

	Methodological Quality			
		A	B	C
Applicability	I			
	II	Study Year N Effect NHS 2002 84688 ++ HPS 1995 44895 + PHS 1995 21185 - Yuan 2001 18244 ++		
	III		Study Year N Effect Oomen 2001 667 -	

¹ Nurses' Health Study analysis using fish oil (EPA+DHA) published in 2002 and analysis using ALA published in 1999 both reported significant beneficial effect on myocardial infarction.

Table 3.49 Association of estimates of fish consumption with myocardial infarction in prospective cohort studies of general population (based on data in Table 3.36)

	Methodological Quality			
		A	B	C
Applicability	I			
	II	Study Year N Effect NHS 2002 84688 ++ HPS 1995 44895 ++ PHS 1998 20551 0 Yuan 2001 18244 ++ CHS 2003 3910 + WES 1997 1822 ++	Study Year N Effect Adventist 1992 26743 0	
	III			

Table 3.50 Association of estimates of omega-3 fatty acid consumption with stroke in prospective cohort studies of general population (based on data in Table 3.37)

Applicability	Methodological Quality							
		A			B			C
	I							
II	Study	Year	N	Effect	Study	Year	N	Effect
	NHS	2001	79839	+	Seino	1997	2283	-
	HPS	2002	43671	++				
	PHS	1995	21185	0				
III	Yuan	2001	18244	+				

Table 3.51 Association of estimates of fish consumption with stroke in prospective cohort studies of general population (based on data in Table 3.38)

Applicability	Methodological Quality							
		A			B			C
	I							
II	Study	Year	N	Effect	Study	Year	N	Effect
	NHS	2001	79839	+	NHANES	1996	5192	+
	HPS	2002	43671	++	Keli	1994	872	+
	PHS	1995	21185	-				
III	Yuan	2001	18244	+				
	WES	1996	1847	0				

Answers to Specific Key Questions

Many of the questions noted below ask about the efficacy of omega-3 fatty acids on CVD outcomes. Efficacy has been defined in an Institute of Medicine report as “what a method can accomplish in expert hands when correctly applied to an appropriate patient.”⁶⁵ This is generally interpreted as treatment effect assessed in controlled trial settings. Comparative efficacy among different omega-3 fatty acids can only be assessed reliably within the same or across similarly designed RCTs. Similarly, the comparative effects of omega-3 fatty acids on different subpopulations or different CVD outcomes should be assessed with subgroups within the same trial or across similarly designed RCTs. However, due to the limited availability of RCTs, we

Table 3.52. Randomized Controlled Trials That Reported Adverse Events with Consumption of Omega-3 Fatty Acid Supplements

Author Year	Omega-3 Fatty Acids		Control		Duration (weeks)	Clinical Bleeding		GI Complaints		Withdraw Due to AE		Comments
	n	Type Dose (g/d)	n	Type Dose (g/d)		N-3	C	N-3	C	N-3	C	
General population												
Wander 1996	24	EPA+DHA 4.3	24	Soybean oil 4 capsules	36			1	0			Post- menopausal women
Hamazaki 1996	13	DHA 1.5-1.8	11	Soybean oil ND	13			2	3			1 weight gain in each group
Kaminski 1993	7	EPA+DHA 5.8	7	ND	6			"some"				
Allard 1997	35	EPA+DHA 5.4	37	Olive oil 6.3	6			3	0	3	0	
Hawkes 2002	40	EPA+DHA 0.74	40	Placebo oil 2.0	4			4				1 skin rash in n-3 FA
	40	EPA+DHA 0.37										
Stark 2000	18	EPA+DHA 4.0	17	Primrose oil 8 capsules	4			2				Post- menopausal women
Harris 1993	4	EPA+DHA 0.64	4	Olive oil ND	4			1				1 headache in n- 3 FA
Mueller 1991	6	n-3 FA 8.0 + EPA 3.5	6	Olive oil 8 capsules	3			3	3			1 constipation, 1 weight gain, 1 headache in n-3 FA 1 diarrhea in olive oil
Total	187		146					16	6	3	0	
Cardiovascular disease population												
GISSI-P 2001	5665	EPA+DHA 0.85±VitE	5658	Vit E or Control	182			179	93	215	119	
Sacks 1995	31	EPA+DHA 4.8	28	Olive oil ND	112			3		3	0	≥93% in both groups took antiplatelet agents
Von Schacky 1999	111	EPA+DHA 3.5 to 1.7	112	Blend of fish oil	104			4	3	4	3	1 rash in n-3 FA
Leng 1998	60	GLA 1.7 + EPA 0.27	60	Sunflower seed oil 3.0	104			30	19			47 vs 40% on aspirin
Kaul 1992	58	EPA+DHA 3.0	49	Calcium blocker	48	0	0	2	0			All on aspirin
Borchgre- vink 1966	100	Linseed oil 10 ml	100	Corn oil 10 ml	40			7	7	3	0	All taking anticoagulants
Eritsland 1995	119	EPA+DHA ² and Aspirin	106	Aspirin	36	10	8	34		5	4	See footnote 2

Table 3.52. Randomized Controlled Trials That Reported Adverse Events with Consumption of Omega-3 Fatty Acid Supplements

Author Year	Omega-3 Fatty Acids		Control		Duration (weeks)	Clinical Bleeding		GI Complaints		Withdraw Due to AE		Comments
	n	Type Dose (g/d)	n	Type Dose (g/d)		N-3	C	N-3	C	N-3	C	
General population												
	132	EPA+DHA ² and Warfarin	154	Warfarin		17	14					
Maresta 2002	125	EPA+DHA 5.1	132	Olive oil	26	0	0	2	2			All on aspirin
Leaf 1994	226	EPA+DHA 6.9	221	Corn oil	24	8	8	19	22	3	8	All on aspirin, 4% (11) infections in each group
Johansen 1999	196	EPA+DHA 5.1	192	Corn oil 5.1	24			3	2			71 vs 67 % on Aspirin 18 % vs 16 on Warfarin
Reis 1989	124	n-3 FA 6.0 + aspirin	62	Olive oil	24	4 ³	0	59	11		46	n-3 vs olive Weight gain: 6 vs 3 (5% in each group) Diarrhea: 15 vs 4
Milner 1989	95	EPA+DHA 4.5	99	Olive oil	24	1 ⁴	0	24				1 insomnia, 1 headache in n-3 FA
Bairati 1992	59	EPA+DHA 4.5	60	Olive oil 15	24			29	30			All on aspirin
Bellamy 1992	60	EPA+DHA 3.0	53	ND	24			4	0			1 diarrhea with n-3 FA, 96% of all on aspirin
Dehmer 1988	43	EPA+DHA 5.4	39	ND	24	0	0	7	3			All on aspirin + dipyridamole
Cairns 1996	325	EPA+DHA 5.4	328	Corn oil	18	17	38	122	101	3	3	All on aspirin See footnote 5
Franzen 1993	92	n-3 FA 3.2	83	Olive oil 9 capsules	16	0	0	13	5		13	All on aspirin
Berrettini 1996	20	EPA+DHA 2.6	19	Corn oil 3.0	16				1	0	1	> 2/3 on aspirin
Berg 1965	42	Linseed oil 10 - 30 ml	37	Corn oil 10 - 30 ml	12			5		0	0	Diarrhea: 5 in n- 3 FA, all on anticoagulants
Berg 1988	14	EPA+DHA 4.5	16	Vegetable oil 15 capsules	12			0	1	0	1	
Davidson 1989	15	EPA+DHA 3.6	15	Olive oil 20 capsules	4							1 diarrhea in olive oil
		EPA+DHA 2.4										
Total	7712		7623			57	68	512	300	236	139	
Hyperlipidemia population												

Table 3.52. Randomized Controlled Trials That Reported Adverse Events with Consumption of Omega-3 Fatty Acid Supplements

Author Year	Omega-3 Fatty Acids		Control		Duration (weeks)	Clinical Bleeding		GI Complaints		Withdraw Due to AE		Comments
	n	Type Dose (g/d)	n	Type Dose (g/d)		N-3	C	N-3	C	N-3	C	
General population												
Sirtori 1997	470	EPA+DHA 2.5 to 1.7	465	Olive oil ND	24			18	21			
Harris 1997	22	EPA+DHA 3.4	20	Corn oil ND	16			4	3	0	0	
Boberg 1986	7	EPA+DHA 3.0	7	Olive oil ND	16			"some"				1 skin rash in n-3 FA
Grundt 1995	28	EPA+DHA 3.4	29	Corn oil 4.0	12			"some"				
Alaswad 1999	11	EPA+DHA 3.4	42	Placebo	12	1 nose	0					
Bonaa 1992	72	EPA+DHA 5.1	74	Corn oil 6.0	10			10	7			
Wilt 1989	19	EPA+DHA 6.0	19	Placebo	12			8	8			
Silva, 1996	20	EPA+DHA 3.6	15	Soya oil 12 capsules	8			4		4		
Mori 1999a	36	EPA+DHA 4.0	20	Olive oil 4.0	6			1		1		
Mori 2000a	26	EPA+DHA 4.0	14	Olive oil 4.0	6			1		1		
Davidson 1997	18	DHA 1.25 or 2.5	8	Corn and soybean oil 12 capsules	6			"some"				
Contacos 1993	10	EPA+DHA 3.0	11	Placebo	6			1				
Brox 1983	7	Cod liver oil 30 ml	11	ND	6			2	0			
Demke 1988	13	EPA+DHA 1.7	18	Safflower oil 5.0	4			"some"				Some diarrhea and headache
Subtotal	759		753			1	0	34	31			
Diabetes population												
Myrup 2001	14	EPA+DHA 4.6	15	Olive oil 21 ml	52			3	1	3	0	
Rossing 1996	14	EPA+DHA 4.6	15	Olive oil 21 ml	52			2	0	2	0	
Scheet- man 1988	13	EPA+DHA 4.0	13	Safflower oil 12	24			1	0	1	0	
Vessby 1990	5	EPA+DHA 3.0	9	Olive oil 10	8			"some"		0	1	
Hendra 1990	40	EPA+DHA 3.0	40	Olive oil 5 capsules	6			1	0	1	0	
Mori 1991	9	EPA+DHA 5.2	9	Olive oil ND	3			"some"				

Table 3.52. Randomized Controlled Trials That Reported Adverse Events with Consumption of Omega-3 Fatty Acid Supplements

Author Year	Omega-3 Fatty Acids		Control		Duration (weeks)	Clinical Bleeding		GI Complaints		Withdraw Due to AE		Comments
	n	Type Dose (g/d)	n	Type Dose (g/d)		N-3	C	N-3	C	N-3	C	
General population												
Fasching 1996	5	EPA+DHA 4.7	5	Gemfibrozil (0.9)	2			2	0			
Subtotal	100		106					9	1	7	1	
Hypertension population												
Margolin 1991	22	n-3 FA 4.7	24	Corn oil 9.0	8	1		4				1.8% dizziness 5.1% diarrhea, 1 skin rash in n-3 FA
Gray 1996	9	EPA+DHA 3.4	10	Corn oil 1 capsule	8			0	3	0	0	4 headaches in n-3 FA
Levinson 1990	8	EPA+DHA 15	8	Vegetable oil 50	6			2	1	1	0	
Landmark 1993	8	EPA+DHA 4.6	10	Olive oil 5 capsules	4			2	1	0	0	No diarrhea
Subtotal	47		52					4	5	1	0	
All Studies												
Total	8805		8680			58	68	575	373	247	140	

AE= Adverse Events; C=Control; ND= No data

[1] Serious adverse events defined by Scotia Pharmaceuticals based on a WHO scale, including death, life-threatening illness, significant disability or handicap and in-patient hospitalization for any reason.

[2] Only bleeding episodes detected clinically were recorded. One bleeding episode required transfusion and operation, the other episodes were minor. In addition, a bleeding complication was the reason for withdrawal in 9 out of the 66 patients.

[3] Important bleeding occurred in 4 patients on fish oil and none on placebo. Two patients had severe bleeding at the site of femoral puncture.

[4] one patient with chronic lower GI bleeding + and a known diagnosis of diverticulosis required partial colectomy.

[5] Most bleeding was mild, leading to permanent discontinuation of study medication in 6 patients.

Table 3.53. Adverse Events Reported in Non-randomized Studies of Omega-3 Fatty Acid Supplements

Author Year	n	Omega-3 fatty acids (g/d)	Duration (weeks)	Clinical bleeding	GI complaints	Withdrawal due to AE	Comments
General population							
Schmidt 1992a	24	EPA+DHA 3.2	36		"some"		
Berg 1990	10	n-3 FA 1.3 - 9	18		"some"		
Brown 1991	12	n-3 FA 5.0	6			5	1 weight gain after 2 wk
Mortensen 1983	20	n-3 FA 4.0	4		1		
Wojenski 1991	9	EPA+DHA 3.0	4		4		
<i>Subtotal</i>	75				4	5	
Cardiovascular disease population							
Bowles 1991	85	EPA 2.8	24		28		"Considerable symptoms" and some diarrhea
Verheugt 1986	5	n-3 FA 3.0	24		1		
Smith 1989	22	EPA+DHA 3.4	4	1 nose	3		
Kahl 1987	16	n-3 FA 8.1	2		10		4 increased appetite
<i>Subtotal</i>	128			1	42		
Hyperlipidemia population							
Dallongeville 1991	18	EPA+DHA 4.8	12		6	0	
Schectman 1989	16	EPA+DHA 6.0	12		18	1	3 diarrhea
Pichter 1992	12	EPA+DHA 3.6	12				Inverse in blood glucose from 97-249 mg/dl, HbA from 5.5 to 7.1%, after removal of n-3 fatty acids, blood glucose normalized.
Otto 1996	23	EPA+DHA 1.5 to 3.0	8		1		
Schmidt 1989a	17	EPA+DHA 5.1	6		"some"		
<i>Subtotal</i>	86				25	1	
Diabetes population							
Tamura 1987	62	EPA 1.8 to 2.7	16		1 or 2		
Mori 1989	10	EPA+DHA 4.3	3		2		
Fasching 1991	8	EPA+DHA 6.3	2		2		

Author Year	n	Omega-3 fatty acids (g/d)	Duration (weeks)	Clinical bleeding	GI complaints	Withdrawal due to AE	Comments
Subtotal	80				5 - 6		

GI = Gastrointestinal (not including liver inflammation). AE= Adverse Events

Table 3.54. Randomized Trials of Omega-3 Fatty Acid Supplements that Reported No Adverse Events

Author, Year	N	Omega-3 Fatty Acids (g/d)	Duration (Weeks)
Nilsen, 2001	150	EPA+DHA 1.7	104
Brox, 2001	36	EPA+DHA 2.6	56
Eritsland, 1994	260	EPA+DHA 3.4	36
Satterfield, 1991	175	n-3 FA 3.0	24
Hamazaki 1996	16	EPA 1.8	24
Radack, 1990	17	n-3 FA 1.1 - 2.2	20
Toft, 1997	38	EPA+DHA 3.4	16
Gans, 1990	16	EPA+DHA 3.0	16
Goodfellow, 2000	15	EPA+DHA 3.4	16
Prisco, 1994	10	EPA+DHA 3.4	16
Prisco, 1995	10	EPA+DHA 3.4	16
Prisco, 1998	8	EPA+DHA 3.4	16
Schmidt, 1988	18	n-3 FA 4.5	12
Radack, 1991	16	n-3 FA 2.0	12
Vandongen, 1993	17	EPA 1.3 – 2.6	12
Nenseter, 2000	34	Fish powder 10	12
Yam, 2002	34	n-3 FA 7.0	12
Adler, 1997	10	n-3 FA 3.6	12
Morris, 1993	12	n-3 FA 3.0 – 6.0	12
Salanchas, 1994	20	EPA+DHA 4.0	12
Warner, 1989	7	Max EPA 50ml	12
Solomon, 1990	5	EPA+DHA 4.6	12
Mehta, 1988	8	EPA+DHA 5.4	12
Calabresi, 2000	14	EPA+DHA 3.4	8
Schmidt, 1992	11	n-3 FA 2.0 – 9.0	8
Steiner, 1989	3	EPA+DHA 1.6	8
Wing, 1990	20	EPA+DHA 4.5	8
Luo , 1998	6	EPA+DHA 1.8	8
Grimsaard, 1998	147	EPA+DHA 4.0	7
Hansen, 1993	11	EPA+DHA 3.4 to 3.6	7
Grimsaard 1997	147	EPA 4, DHA 4	7
Honstra, 1990	40	n-3 FA 1.7	6
Van Houwelingen, 1988	40	EPA+DHA 4.7	6
Howe, 1994	28	n-3 FA 5.0	6
Chan, 2003a	25	EPA+DHA 3.4	6
Pirich, 1999	13	EPA+DHA 0.4	6
Chan, 2002	12	EPA+DHA 3.4	6
Conquer, 1999	10	EPA+DHA 3.0	6
Vericel, 1999	10	EPA+DHA 0.2	6
Axelrod, 1994	9	EPA+DHA 2.6	6
Brox, 1981	6	Cod liver oil 25 ml	6
Chan 2002b	25	EPA+DHA 3.4	6
Balestieri, 1996	8	n-3 FA 5.1	4
Baumann, 1999	7	EPA+DHA 4.6	4
Freese, 1997	24	EPA+DHA 5.2	4

Author, Year	N	Omega-3 Fatty Acids (g/d)	Duration (Weeks)
Mori, 1992	15	EPA+DHA 4.6	4
Nozaki, 1991	12	EPA+DHA 8.0	4
Davi, 1990	10	EPA 1.8	4
Harris, 1991	16	EPA+DHA 2.2	4
Villa, 2002	10	n-3 FA 3.0 – 6.0	4
Swails, 1993	7	EPA+DHA 1.6	1
Total	1,618		

Table: 3.55. Non-Randomized Studies of Omega-3 Fatty Acid Supplements that Reported No Adverse Events

Author, Year	N	Omega-3 Fatty Acid (g/d)	Duration (week)
Saynor, 1992	365	EPA+DHA 1.1 – 1.8	4-364
Shinozaki, 1996	16	EPA 1.8	96
Blok, 1997	44	EPA+DHA 1.0 – 2.9	52
Rhodes, 1994	15	EPA+DHA 3.0	24
Von Schacky, 1985	6	Cod liver oil 10 - 40 ml	20
Nelson, 1997	10	DHA 6.0	17
Russo, 1995	24	EPA+DHA 2.6	16
Meydani, 1991	25	EPA+DHA 2.4	12
Bagdade, 1990	8	EPA+DHA 6.0	12
Nau, 1991	14	EPA+DHA 1.0	8
Toth, 1995	10	n-3 FA 0.2	8
Bonanome, 1996	12	n-3 FA 2.5	8
Bagdade, 1996	9	EPA+DHA 4.6	8
Berg, 1989	10	EPA+DHA 0.7	6
Schmidt, 1991	10	EPA+DHA 0.7	6
Schmidt, 1990	10	EPA+DHA 2.1	6
Schmidt, 1989	10	n-3 FA 4.0	6
Berg, 1989	17	EPA+DHA 5.1	6
Haglund, 1990	13	EPA 2.7 – 5.4	4
Glauber, 1988	6	EPA+DHA 5.5	4
Suehiro, 1994	27	EPA 1.8	4
Harris , 1983	12	n-3 FA 20 - 29	4
Owens, 1990	6	EPA+DHA 4.5	4
Kasim-Karakas, 1995	14	EPA+DHA 3.3	4
Terano, 1983	8	EPA+DHA 0.3	4
Nordoy, 1994	6	EPA+DHA 4.8	3
Total	707		