
Omega-3 Fatty Acids and Health Across the Life Cycle

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Outline

- Dietary recommendations for omega-3 fatty acids
 - Alpha-linolenic acid (ALA)
 - Eicosapentaenoic acid (EPA) & Docosahexaenoic Acid (DHA)
 - Fish recommendations
- Scientific justification for dietary recommendations
 - Achieve nutrient adequacy
 - Chronic disease risk reduction – CVD, neurodegenerative diseases, colorectal cancer
 - Other – pregnancy, infant development
- Meeting dietary recommendations for omega-3 fatty acids –
 - Special considerations – (n-6 recommendations, environmental contaminants)
- Summary

Essential Fatty Acid Families

ω -6 family



C18:2 ω -6 **Linoleic**

- Soybean Oil
- Corn Oil
- Safflower Oil
- Sunflower Oil



C20:4 ω -6 **Arachidonic**

*More thrombotic
and inflammatory
metabolites*

ω -3 family



C18:3 ω -3 **α -Linolenic**

- Flaxseed Oil
- Canola Oil
- Soybean Oil
- Walnuts



C20:5 ω -3 **Eicosapentaenoic (EPA)**



C22:6 ω -3 **Docosahexaenoic (DHA)**

*Less thrombotic
and inflammatory
metabolites*

- Oily Fish
- Fish Oil Capsules

**DRIs for Fatty Acids and
Total Fat (for infants only) are based on a
Nutrient Requirement Model**

AI is defined for:

- Linoleic acid
- α -linolenic acid
- Total fat (for infants only, 0-12 mos)

AI for α -Linolenic Acid

- AI is based on the median intakes of α -linolenic acid in the United States where the presence of n-3 polyunsaturated fatty acid deficiency is nonexistent
- AI for ALA is 1.6 g/d for men and 1.1 g/d for women

Criteria and AIs* for n-3 or α -Linolenic Acid (g/day)

<u>Life Stage</u>	<u>Criterion</u>	<u>Male</u>	<u>Female</u>
0-6 m	Milk intake	0.5	0.5
7-12 m	Milk + other foods	0.5	0.5
1-3 y	Median intake	0.7	0.7
4-8 y	Median intake	0.9	0.9
9-13 y	Median intake	1.2	1.0
14-18 y	Median intake	1.6	1.1
19 +	Median intake	1.6	1.1
Pregnancy	Median intake		1.4
Lactation	Median intake		1.3

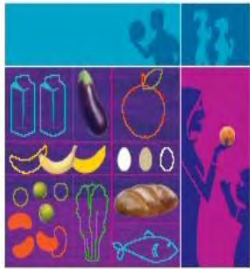
*Assumed adequate to prevent EFA deficiency (rare in the U.S. and Canada)

AMDR for α -Linolenic Acid

- AMDR set at 0.6 to 1.2 % of energy intake
 - Lower boundary of the range meets the AI for α -linolenic acid
 - Up to 10% of the range can be consumed as EPA and/or DHA
 - Growing body of literature suggests that diets higher in α -linolenic acid, EPA and DHA may afford some degree of protection against CHD

Acceptable Macronutrient Distribution Ranges

	Range (percent of energy)		
<u>Macronutrient</u>	<u>1-3 yrs</u>	<u>4-18 yrs</u>	<u>Adults</u>
Fat	30-40	25-35	20-35
<i>n</i>-6 linoleic acid	5-10	5-10	5-10
<i>n</i>-3* <i>α</i>-linolenic acid	0.6-1.2	0.6-1.2	0.6-1.2
Carbohydrate	45-65	45-65	45-65
Protein	5-20	10-30	10-35
<p>*Approximately 10% of the total can come from longer-chain <i>n</i>-3 fatty acids. The lower boundary of the range meets the AI</p>			



Dietary Guidelines
for Americans
2005

Recommendation for Fish Consumption

- Evidence suggests that consuming approximately two servings of fish per week (approximately 8 oz. total) may reduce the risk of mortality from coronary heart disease and that consuming EPA and DHA may reduce the risk of mortality from cardiovascular disease in people who have already experienced a cardiac event.

– Dietary Guidelines for Americans, 2005

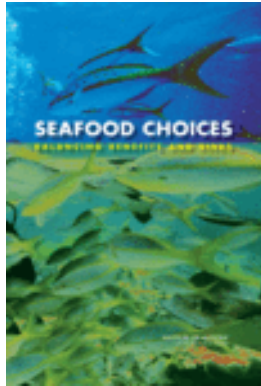


U.S. and Canadian Dietary Recommendations for LC n-3 Fatty Acids and Fish Intake

1. NCEP: fish is recommended as a food item for people to choose more often, 2002
2. AHA: 2 servings of fish (preferably fatty) per week, 2002, 2006
3. National Academies: seafood is part of a healthy diet and can be substituted for other protein sources that are higher in saturated fat, 2006
4. The ADA and Dietitians of Canada recommend two servings of fish per week, preferably fatty fish, to provide 500 mg/day of EPA & DHA, 2007
5. Am. Diabetes Assoc. : 2 or more servings of fish per week (except commercially fried fish filets) provide omega-3 PUFAs and are recommended, 2008
6. Mozaffarian & Rimm (2006), and Deckelbaum et al. (2008): 250 mg/d
7. Harris et al. (2008): 500 mg/d

AHA Recommendations for Omega-3 FA Intake

Population	Recommendation
Patients without documented CHD	Eat a variety of (preferably oily) fish at least twice a week. Include oils and foods rich in α -linolenic acid (flaxseed, canola, and soybean oils; flaxseeds; and walnuts)
Patients with documented CHD	Consume ~1 g of EPA+DHA per day, preferably from oily fish. EPA+DHA supplements could be considered in consultation with the physician
Patients needing triglyceride lowering	2–4 grams of EPA+DHA per day provided as capsules under a physician's care



Seafood Choices – Balancing Benefits and Risk

Summary of Appropriate Guidance for Population Groups

- Females who are or may become pregnant or who are breast feeding, and children up to 12 yrs of age:
 - may benefit from consuming seafood.....
- Healthy adolescent and adult males and females (who will not become pregnant), and adult males and females at risk of CVD:
 - may reduce their risk for CVD.....

Fish Guidelines

- The consumption of two servings (~ 8 oz) per week of fish high in EPA and DHA is associated with reduced risk of both sudden death and CHD death in adults. (2005 Dietary Guidelines Advisory Committee)
- Women and young children should include fish in their diets and can safely consume up to 12 ounces per week of cooked fish. (FDA/EPA Advisory)

Consensus Recommendations for LC-PUFA in Pregnancy, Lactation and Infancy *

- Pregnant and lactating women should aim to achieve an average daily intake of at least 200 mg DHA
- Use of infant formula providing DHA at levels between 0.2 and 0.5 weight percent of total fat, and with the minimum amount of ARA equivalent to the contents of DHA. The American Dietetic Association and Dietitians of Canada recommend that DHA should be at least 0.2% of total fatty acids and the level of ARA should not be lower than DHA
- Dietary LC-PUFA supply should continue after the first 6 months of life

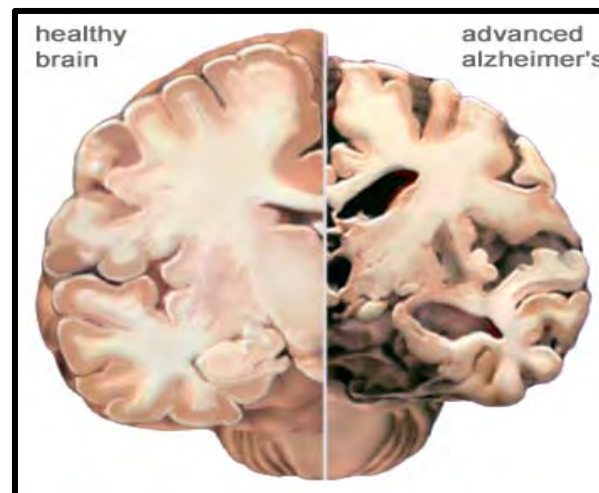
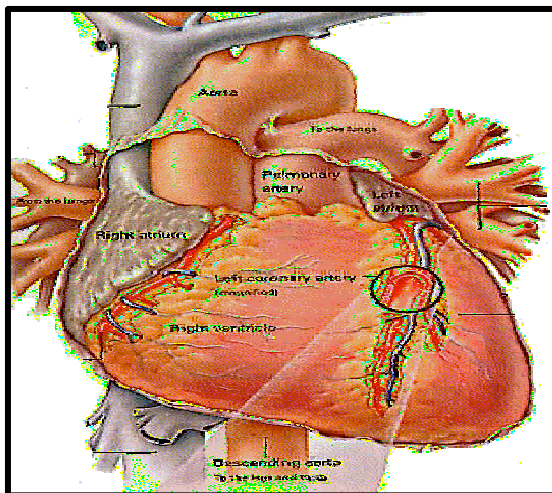
* World Assoc. of Perinatal Medicine, the Early Nutrition Academy and the Child Health Foundation

Koletzko et al., J Perinat Med. 36: 5-14, 2008

Kris-Etherton and Innis, JADA. 107:1599-1611, 2007

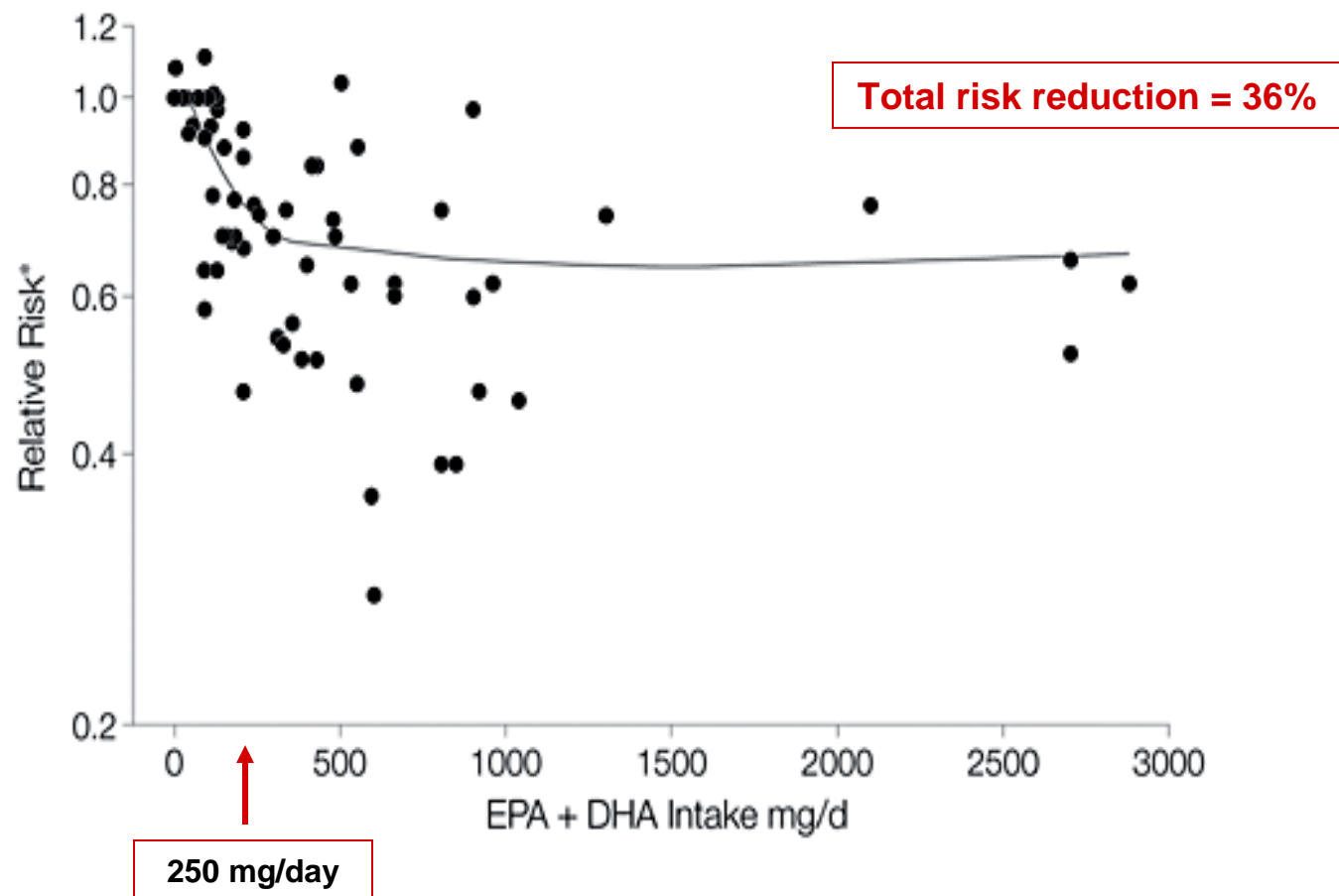
Omega-3 Fatty Acids and Major Chronic Diseases

- Cardiovascular Diseases
- Alzheimer's Disease
- Colorectal Cancer



Fish or Fish Oil Intake and Relative Risk of *CHD Death* in Prospective Cohort Studies and RCTs

Total of 16 prospective cohort studies (**n = 326,572**) and 4 RCTs (**n = 35,115**) from U.S., Europe, and Asia

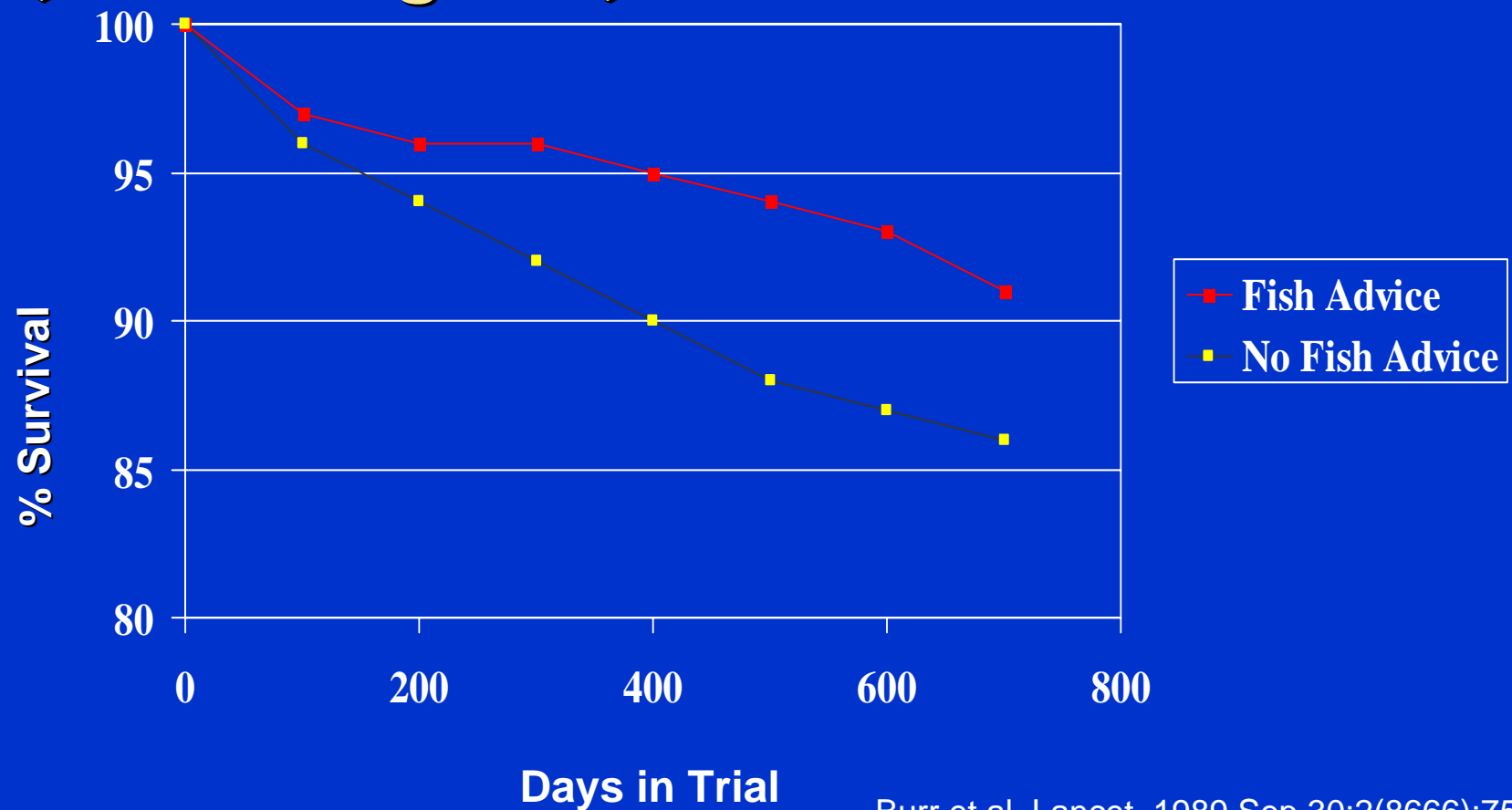


Diet And Reinfarction Trial

■ Recommended Intake

- 2 meals of fatty fish per week
- 200 to 400 g per week of fish
- Assume 300 g of fatty fish per week
- At 1.2g EPA+DHA/100gm = 510 mg/day

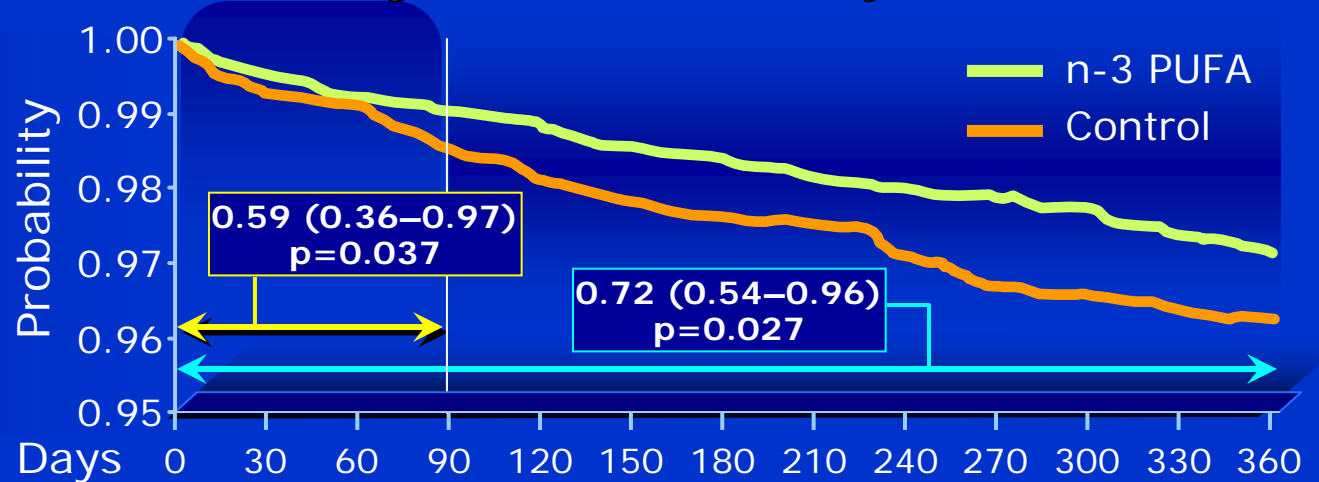
DART Study - 29% Reduction in All-Cause Mortality with High n-3 Fish Consumption (200-400 g/wk)



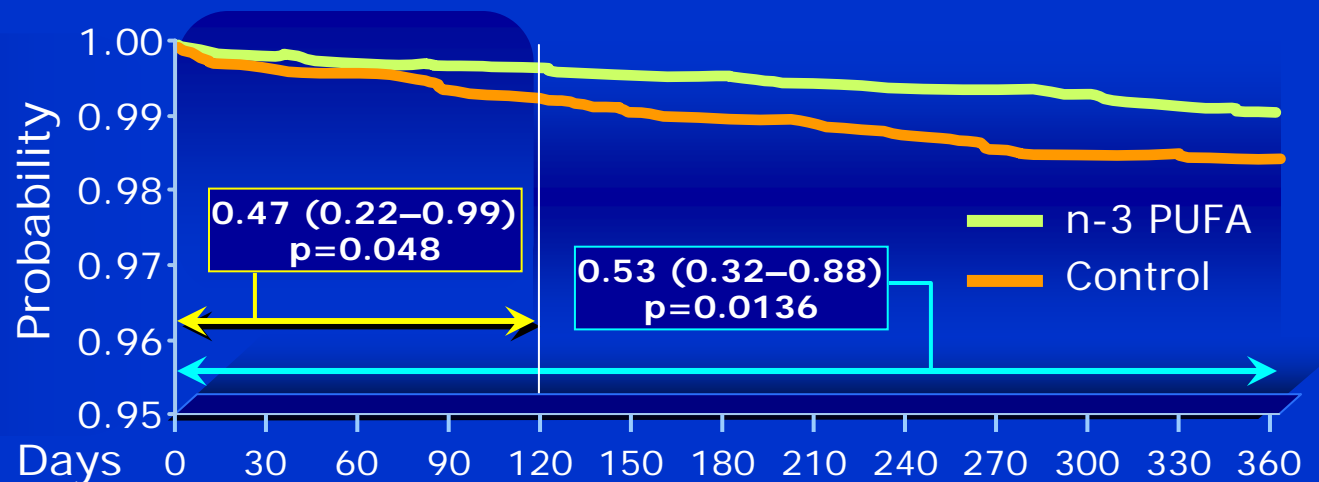
GISSI-Prevenzione: *Time Course of Clinical Events*

>11,300 post-MI patients were given usual care with or without **850 mg EPA+DHA** for 3.5 years

Total mortality reduced by 28% (p=0.027)



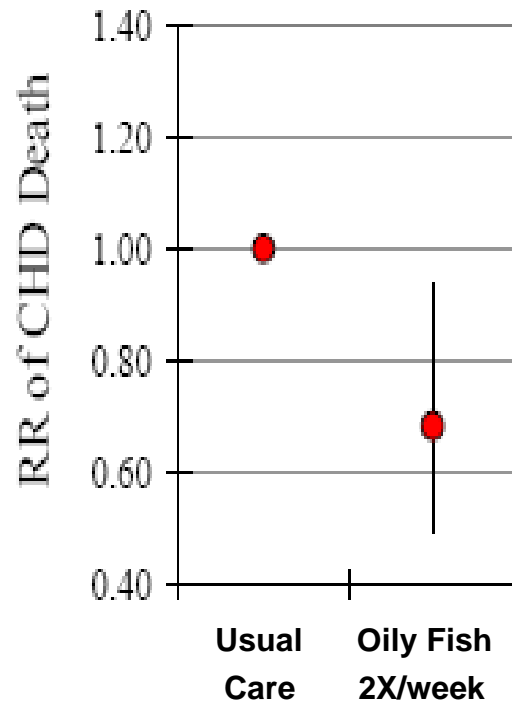
Sudden death reduced by 47% (p=0.0136)



Randomized Controlled Trials of Fish or Fish Oil

DART Trial

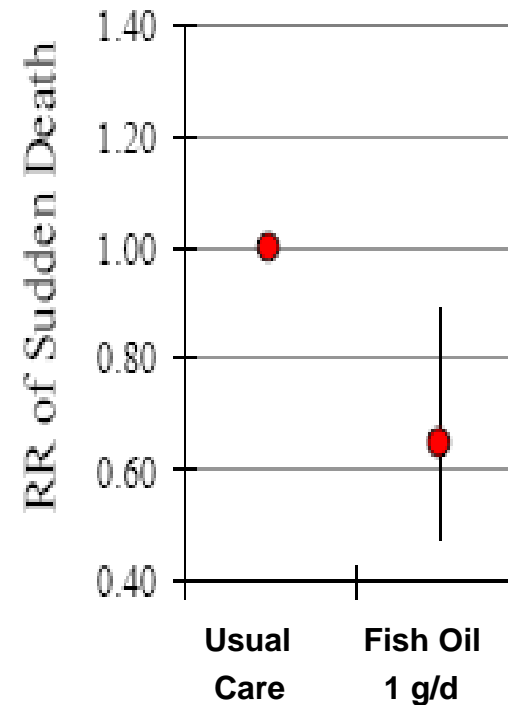
2,033 English men with prior MI



Burr et al. Lancet 1989

GISSI-P Trial

11,323 Italian men with prior MI

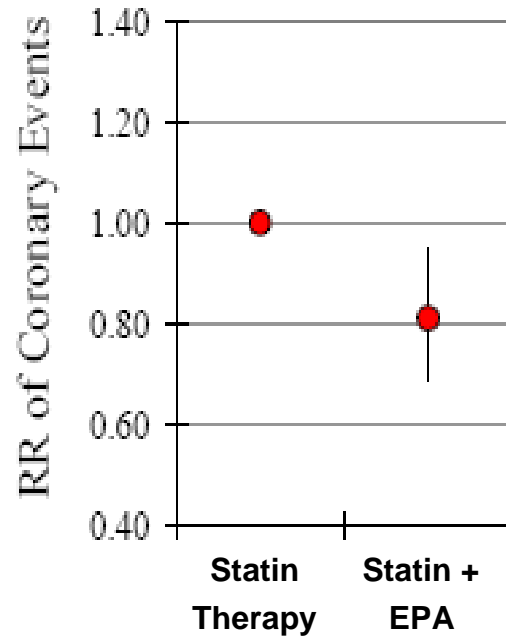


GISSI Investigators. Lancet, 1999

Randomized Controlled Trials of EPA or Fish Oil

JELIS Trial

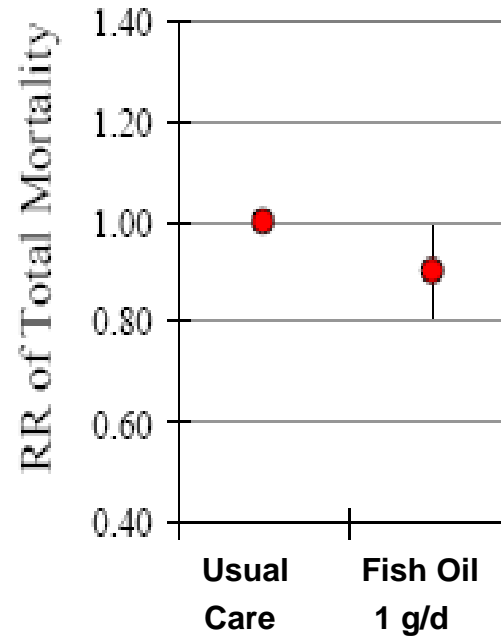
18,645 Japanese M&F with high cholesterol



Yokoyama et al. Lancet 2007

GISSI-HF Trial

6,975 Italians with heart failure



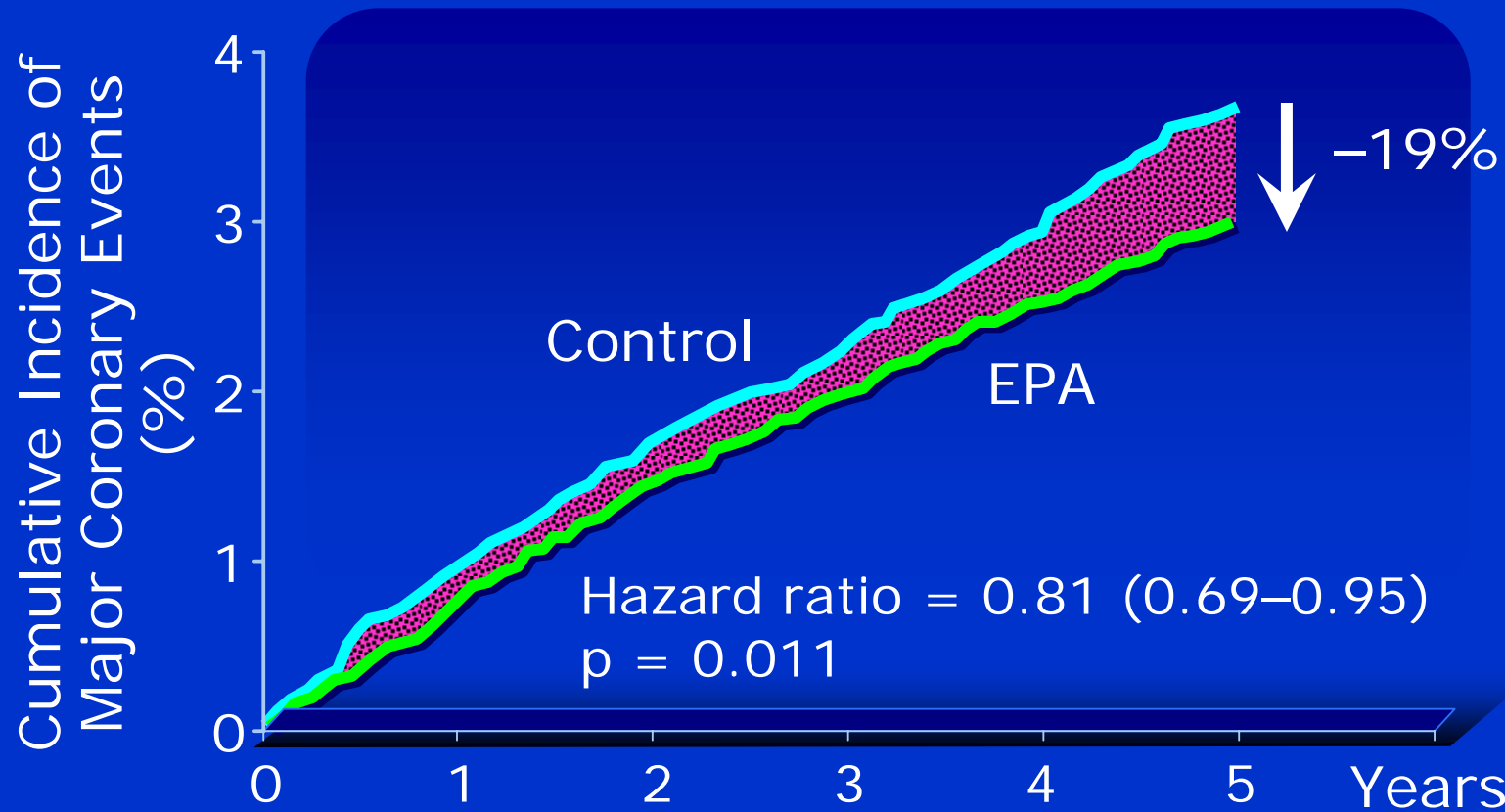
GISSI Investigators. Lancet, 2008

Fish Intake & CHD Death: Randomized Controlled Trials

<u>Study</u>	<u># Participants</u>	<u># CHD Deaths</u>
DART - 1989	2,033	194
DART 2 - 2003	3,114	319
GISSI – Prevenzione – 1999	5,664	273
JELIS Primary Prevention – 2007	14,981	21
JELIS Secondary Prevention – 2007	3,664	39
GISSI – Heart Failure – 2008	<u>6,975</u>	<u>632</u>
TOTALS	36,431	1,478

*Total of 36,431 individuals (1,478 cardiac deaths)
in U.S., Europe, and Asia*

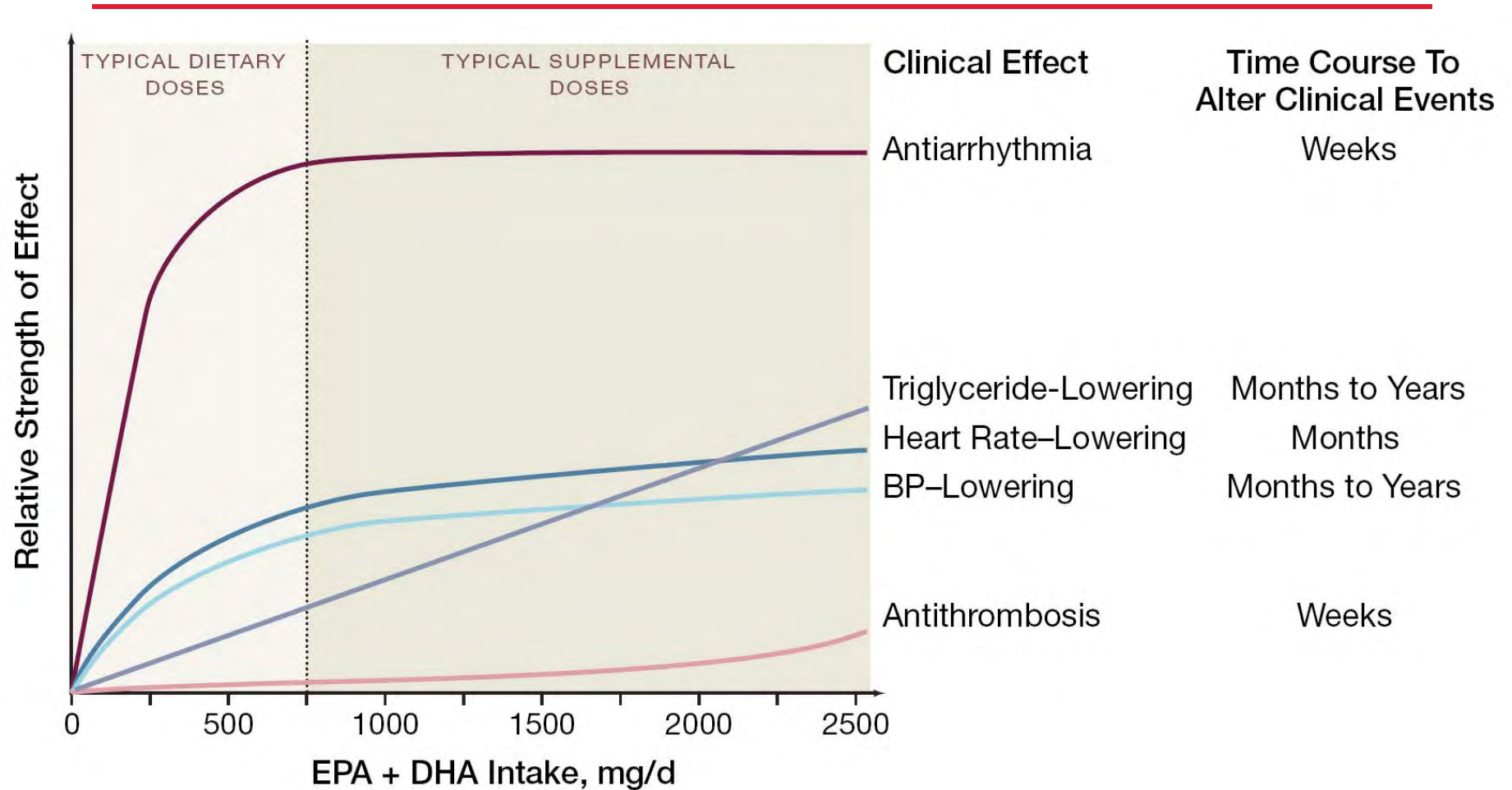
Japan EPA Lipid Intervention Study (JELIS)



18,645 Japanese (70% women, mean age 61 years) randomized to statin alone or statin + EPA (1.8 g/d) and followed for 5 years

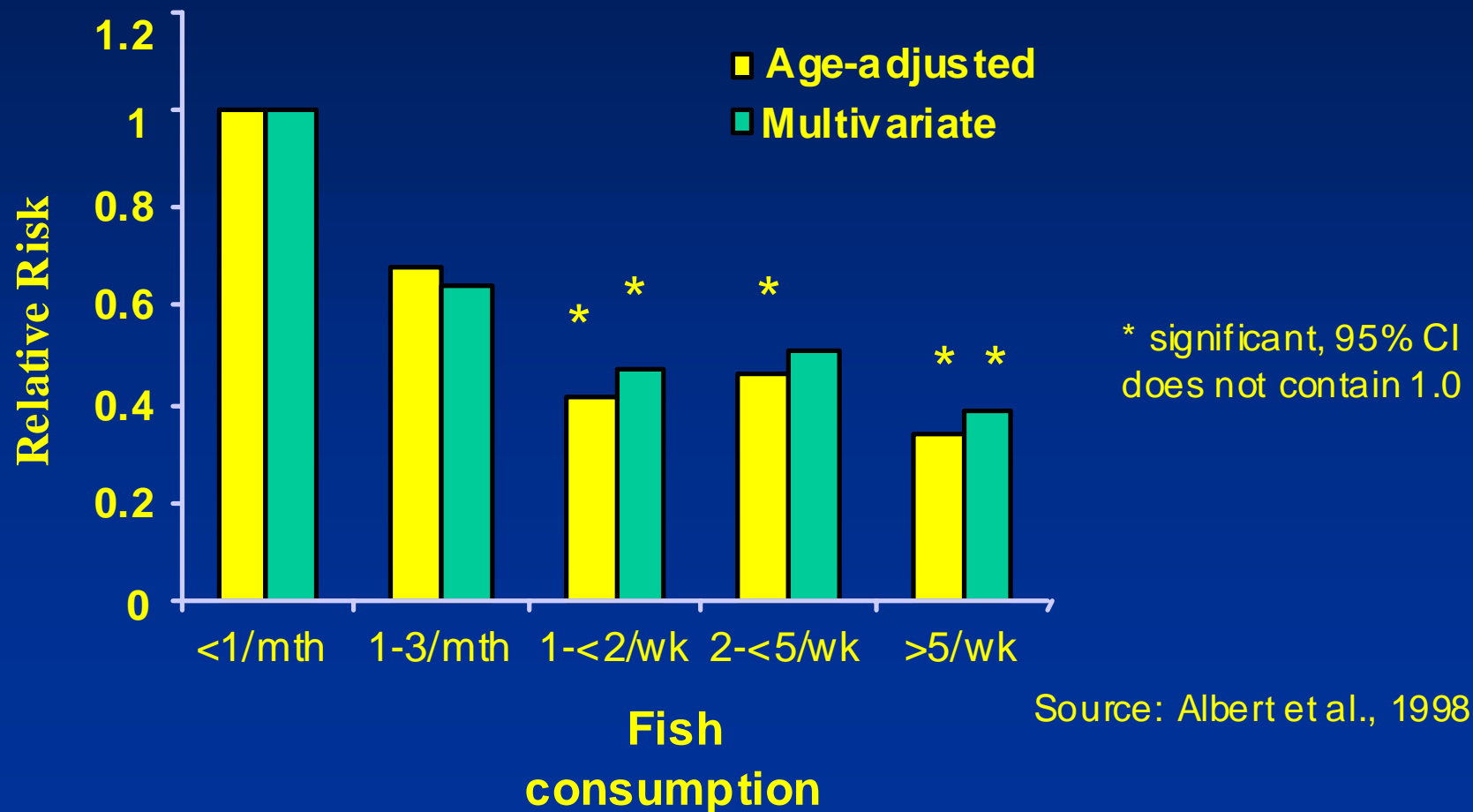
Yokoyama et al. Lancet 369:1090-1098, 2007

Potential Dose Responses and Time Courses of Clinical Events in Response to Fish or Fish Oil Intake

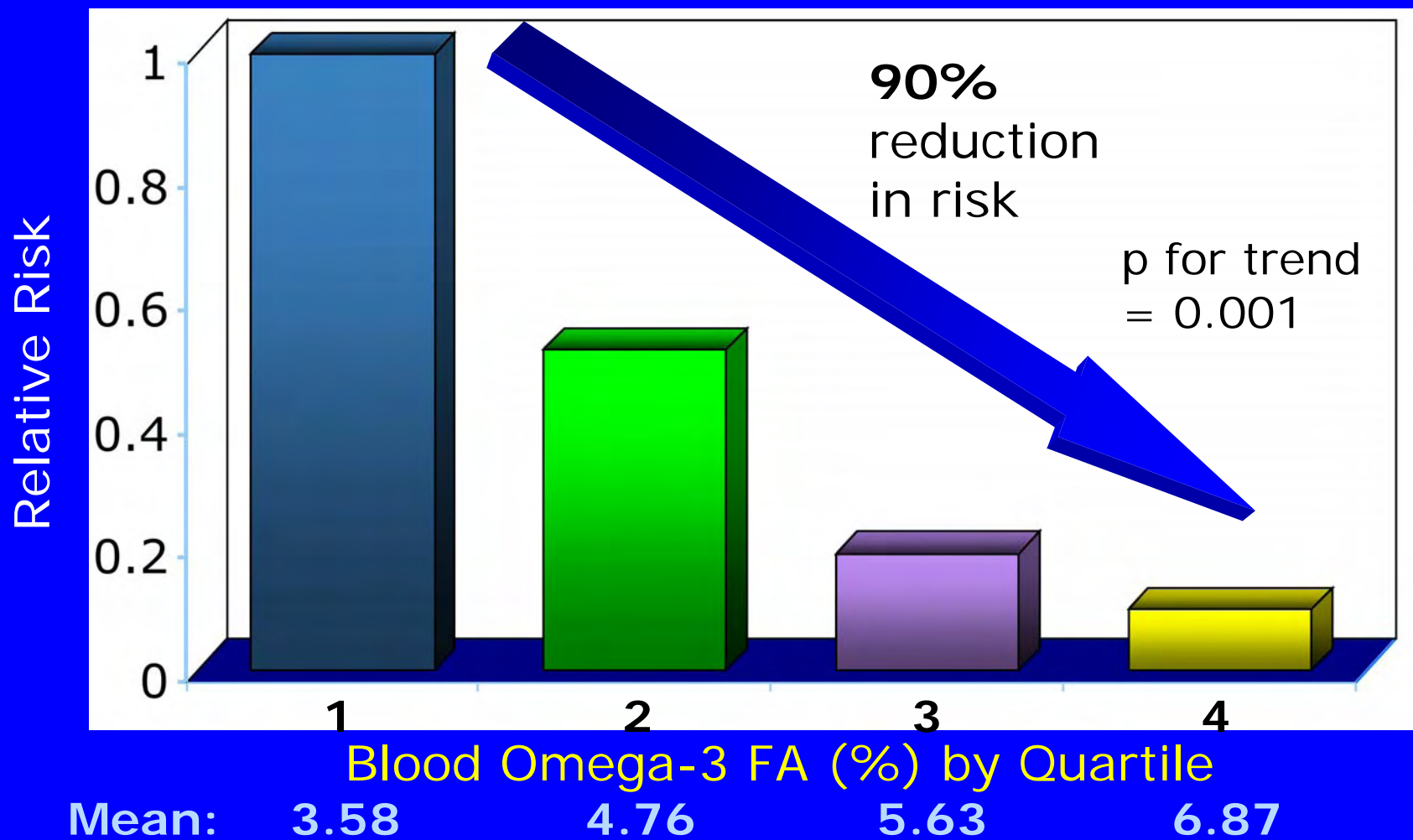


Mozaffarian D, Rimm EB. JAMA. 2006;296:1885-1899.

Risk of Sudden Death According to Dietary Fish Intake in 20,551 Male Physicians Followed for 11 Years

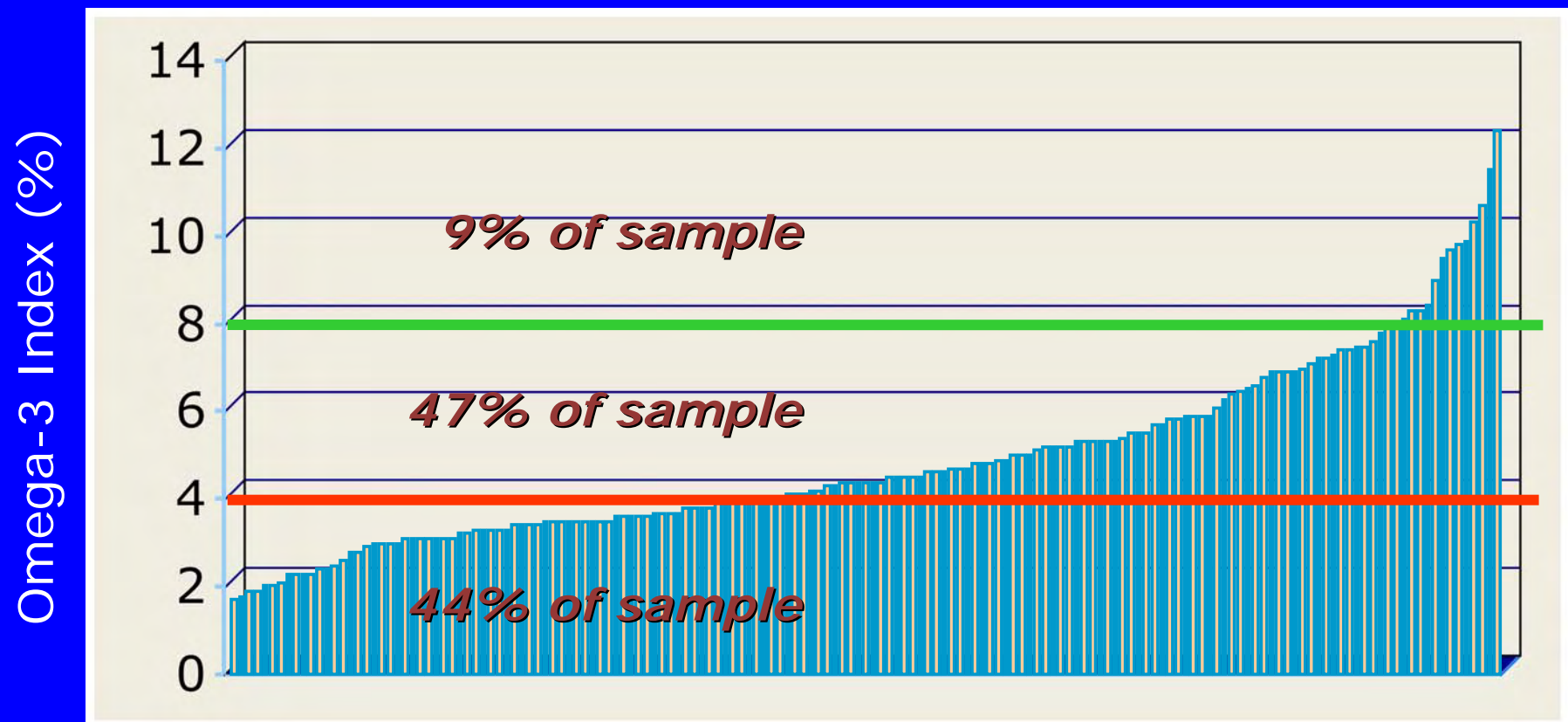


Relative Risk of Sudden Cardiac Death and Blood Omega-3 Levels: *Physicians' Health Study*

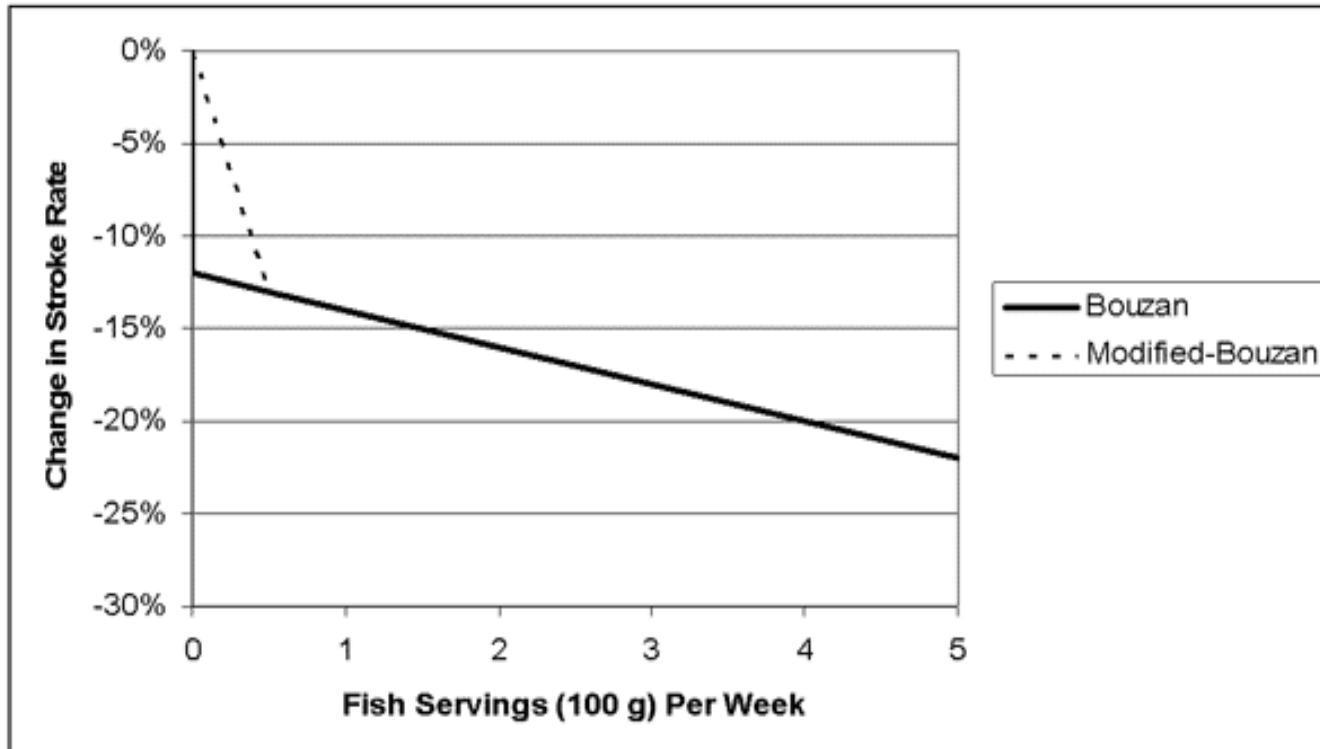


Albert CM et al. *N Engl J Med* 2002;346:1113-1118.

Distribution of Omega-3 Index (% n-3 HUFA in RBC) in 163 Adults Not Taking Omega-3 Supplements

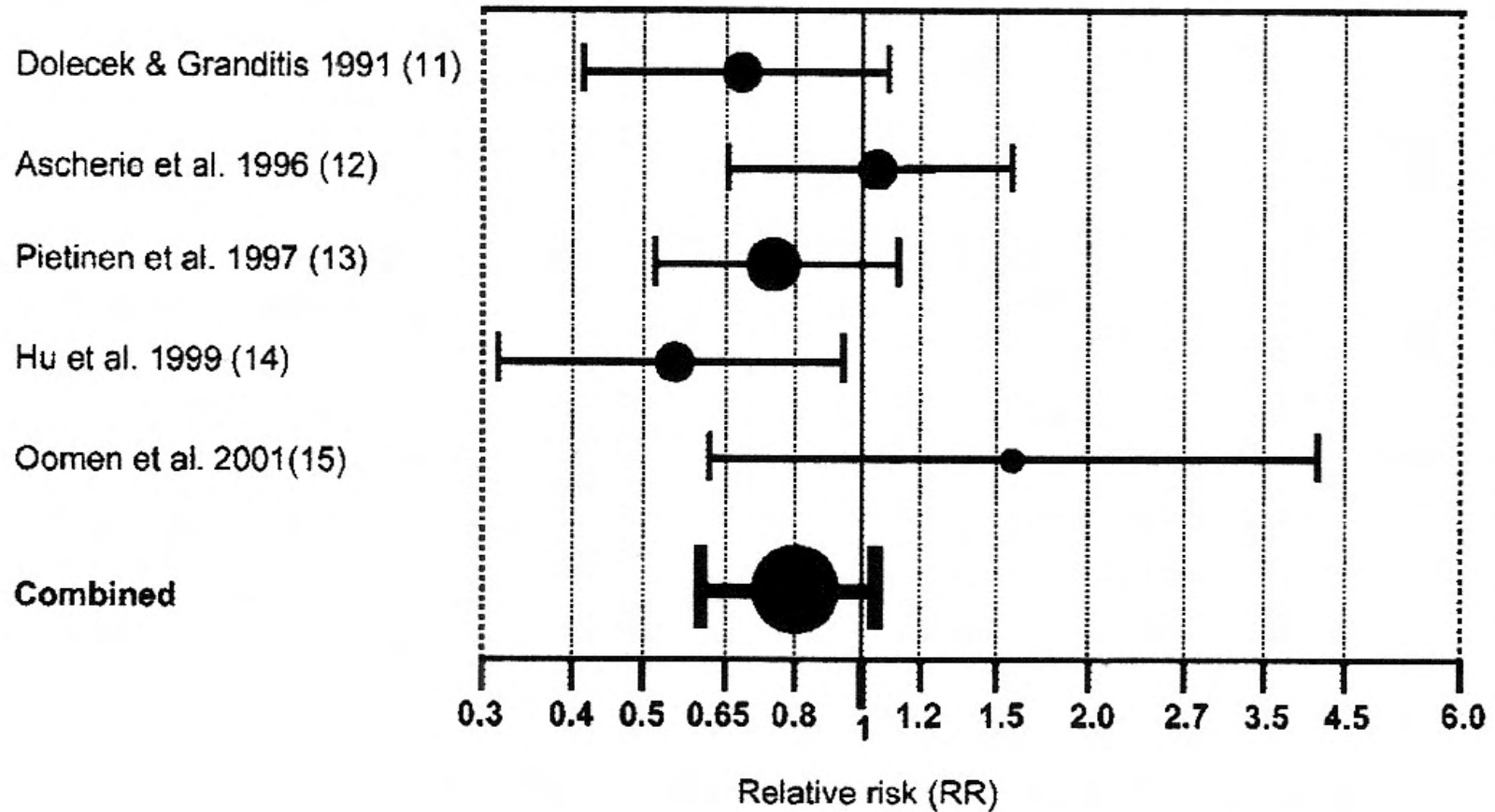


The Effect of Fish Consumption on Risk of Fatal Strokes



Dose-response function for Stroke. The intersection of the dotted line and the straight line represents the lowest dose that Bouzan et al. (2005) modeled.

Cardioprotective Benefits of ALA Epidemiologic Studies



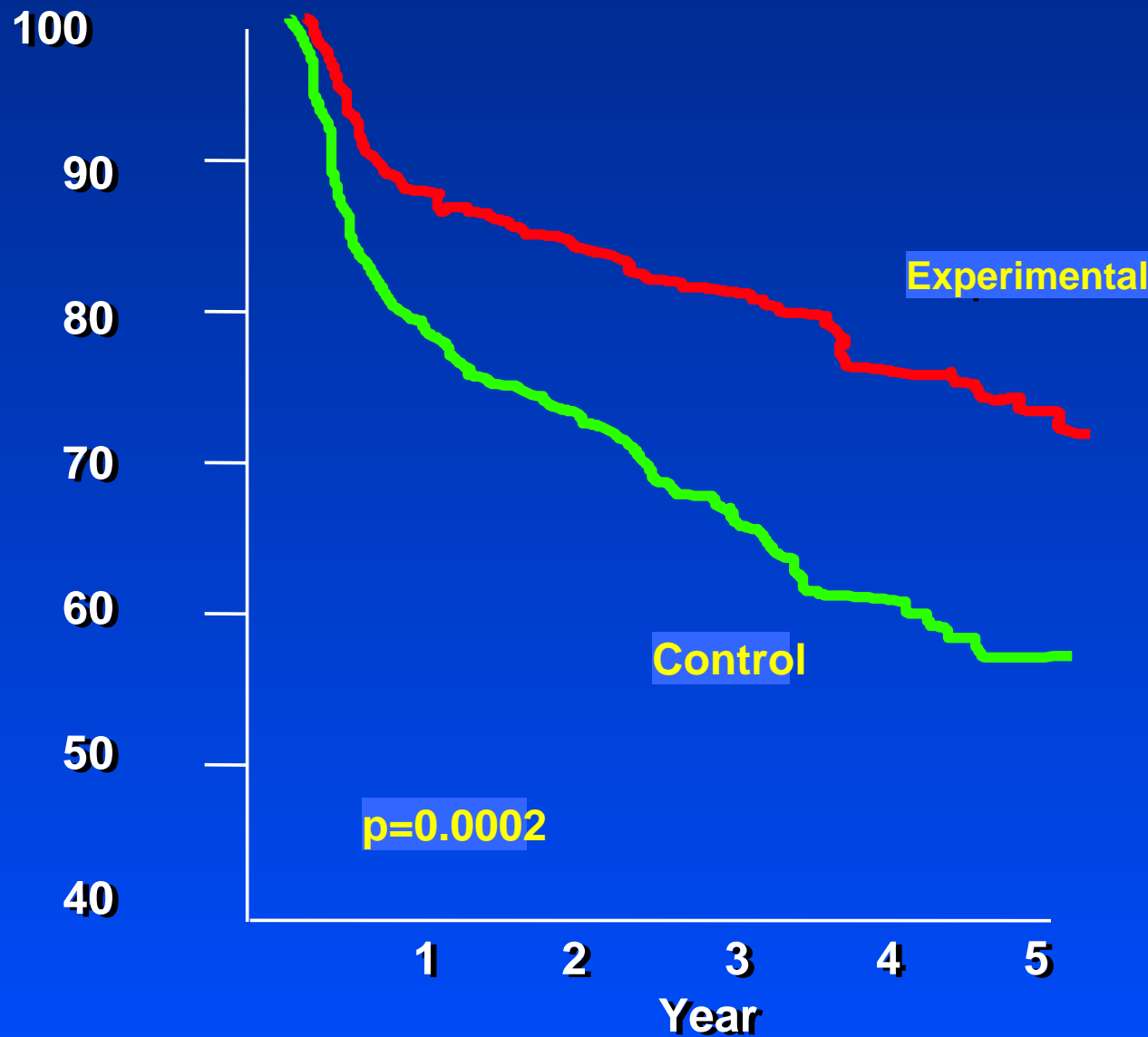
Lyon Diet Heart Study: Nutrient Intake at Final Visit

(Mean Follow-up = 46 months)

Nutrient (% cal)	Control (n=83)	Experimental (n=144)	P value
Total Lipids	33.6	30.4	0.002
Saturated Fat	11.7	8.0	0.0001
18:1, oleic	10.8	12.9	0.0001
18:2, linoleic	5.3	3.6	0.0001
18:3, linolenic	0.3	0.8	0.0001
Alcohol	6.0	5.8	0.8
Cholesterol	312	203	0.0001

Cumulative Survival Without Nonfatal Infarction, Without Major Secondary End Points, and Without Minor Secondary End Points

Lyon Diet Heart Study



de Lorgeril et al, 1999;99:779-785.

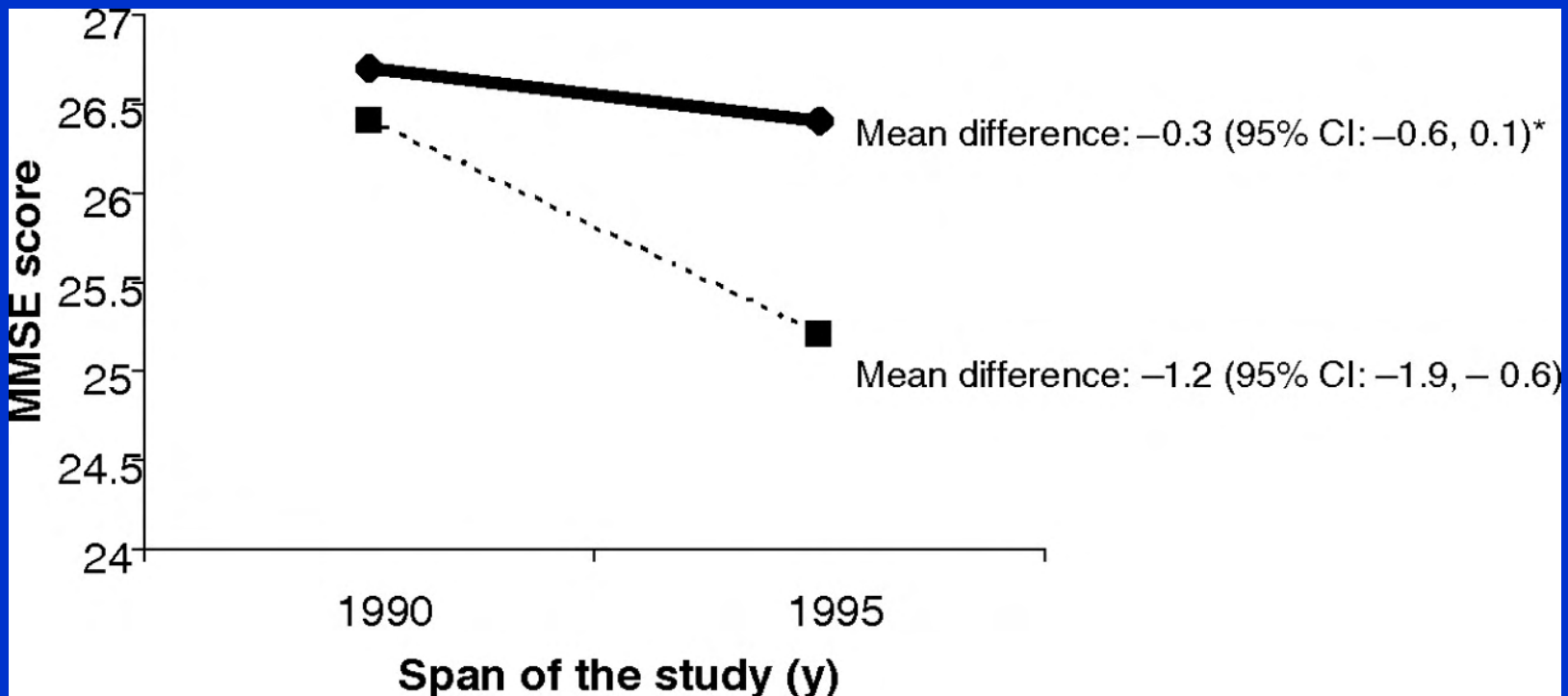
Prospective Studies Demonstrate a Benefit of Fish Consumption on Dementia and Alzheimer Disease (ALZ)

Author	Study	Subject #/Age	Follow-up	Results
Huang et al, 2005	CV Health Cognition Study	2, 233 ≥ 65 yrs	X = 5.4 yrs	Fatty Fish > 2/wk – ↓ dementia 28%
Morris et al, 2003	Chicago Health & Aging Project	815 ≥ 65 yrs	X = 3.9 yrs	Fish ≥ 1/wk – ↓ ALZ 60%
Barberger- Gateau et al, 2002	PAQUID Epidemiologic Study	1674 ≥ 68 yrs	7 yrs	Fish ≥ 1/wk – ↓ dementia 34% ↓ ALZ 31%
Kalmijn et al., 1997	Rotterdam Study	5,386 X = 68 yrs	X = 2.1 yrs	≤ 3 g/day vs 18.5 g/day – ↓ dementia 30% ↓ ALZ 70%

Cohort Studies Demonstrate a Benefit of Higher HUFA Intake Against Age-Related Cognitive Decline

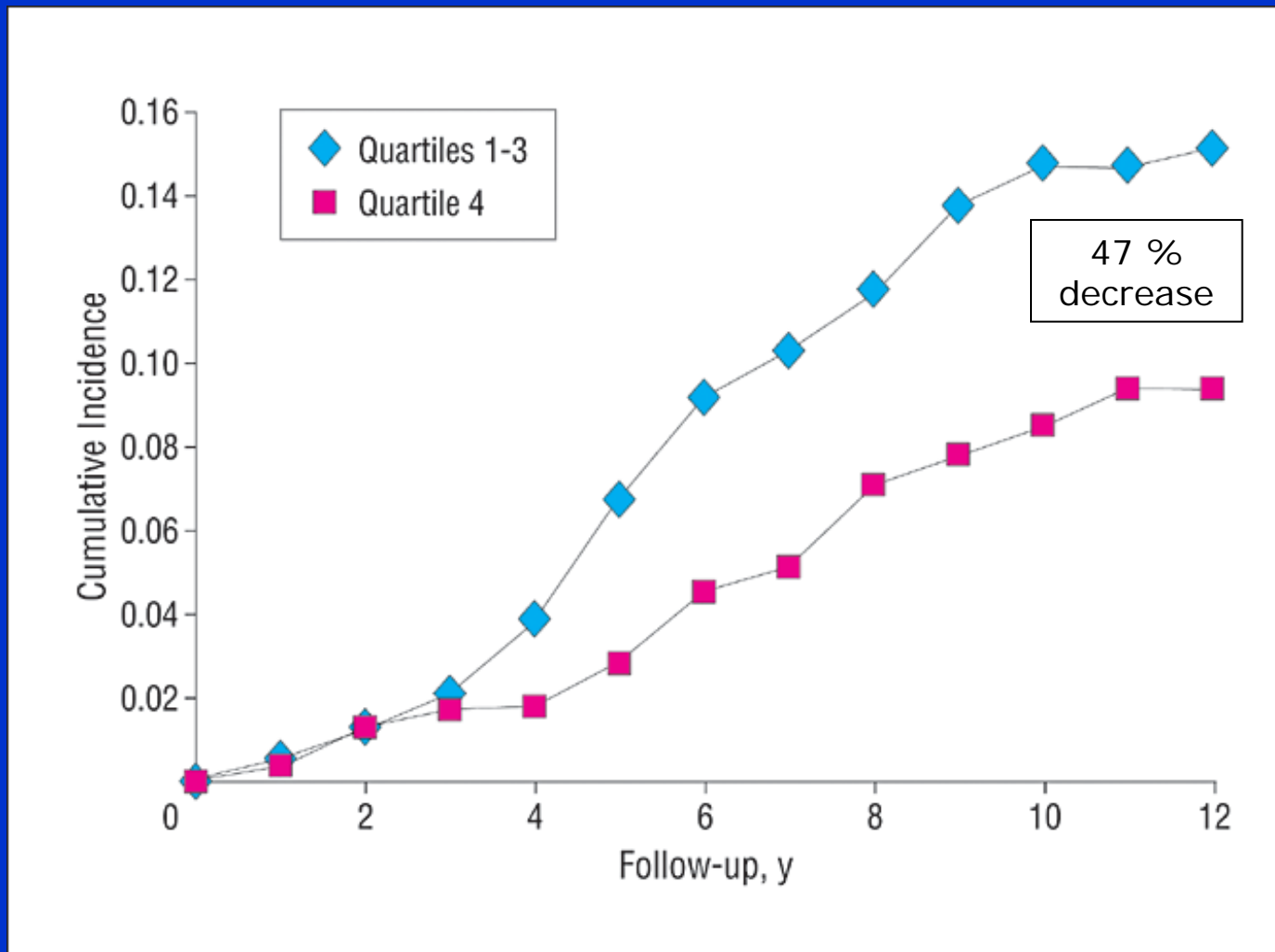
Author	Study	Subject #/Age	Follow-up	Results
Beydoun et al, 2007	ARIC Study	11, 557 ≥ 50 yrs	6 yrs	Increase in %en HUFA (1 SD) ↓risk of cognitive decline 21%
Van Gelder et al, 2007	Zutphen Elderly Study	210 70 to 89 yrs	5 yrs	Fish Consumption vs no fish ↓ cognitive decline
Morris et al, 2002	Chicago Health & Aging Project	3,718 ≥ 65 yrs	7 yrs	10% slower rate w/ 1 fish meal/wk; 13% slower w/ 2/wk
Heude et al., 2003	EVA Study Cohort	246 63 to 74 yrs	4 yrs	Higher RBC HUFAs vs lower- ↓ risk cognitive decline 59%

Multivariate Linear Regression Analysis of 5-y Cognitive Decline in 210 Elderly Men in Relation to Fish Consumption in 1990, Showing the Mean Change in Cognitive Functioning Between 1990 and 1995

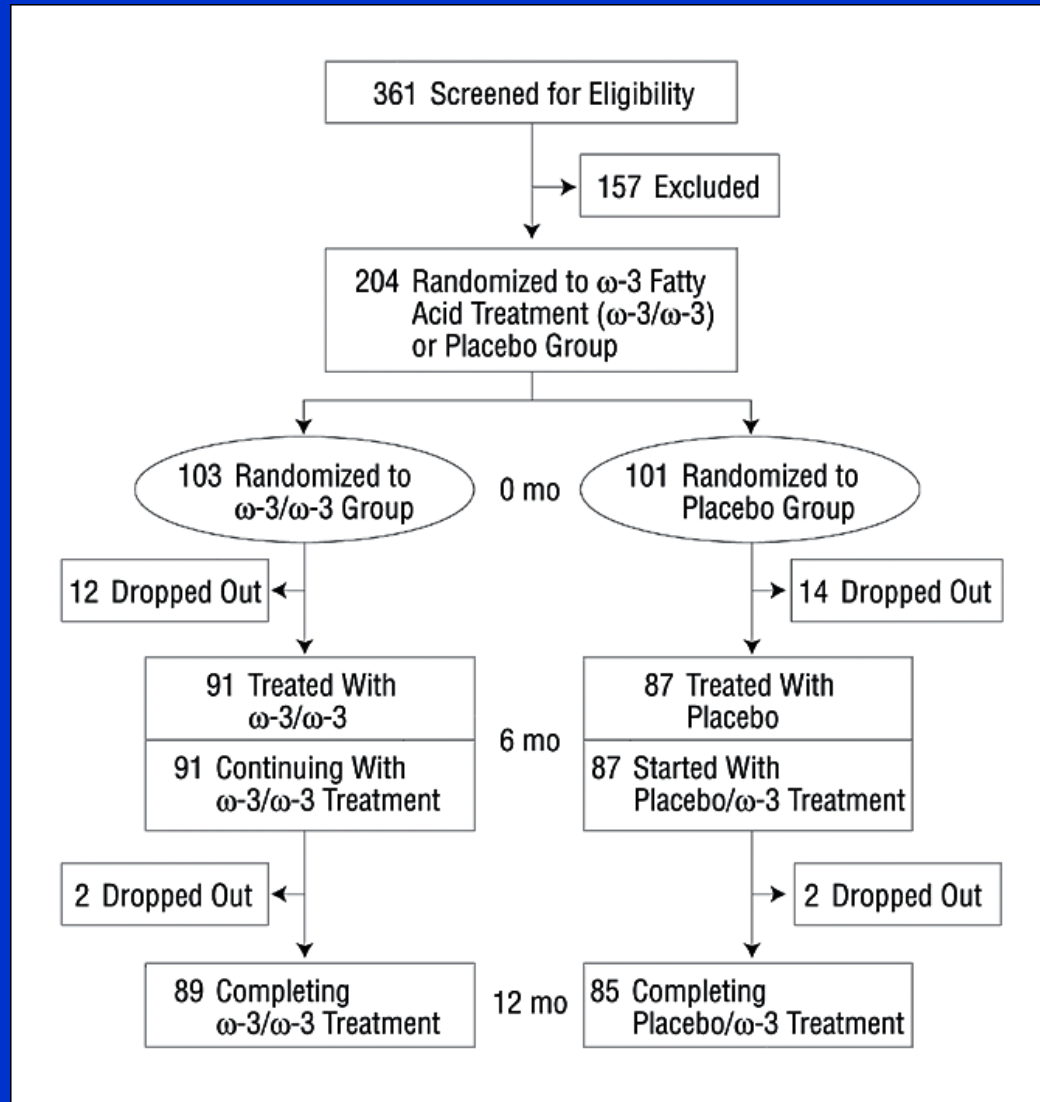


Data adjusted for age, education, alcohol consumption, smoking status, physical activity, energy intake, and baseline cognitive functioning

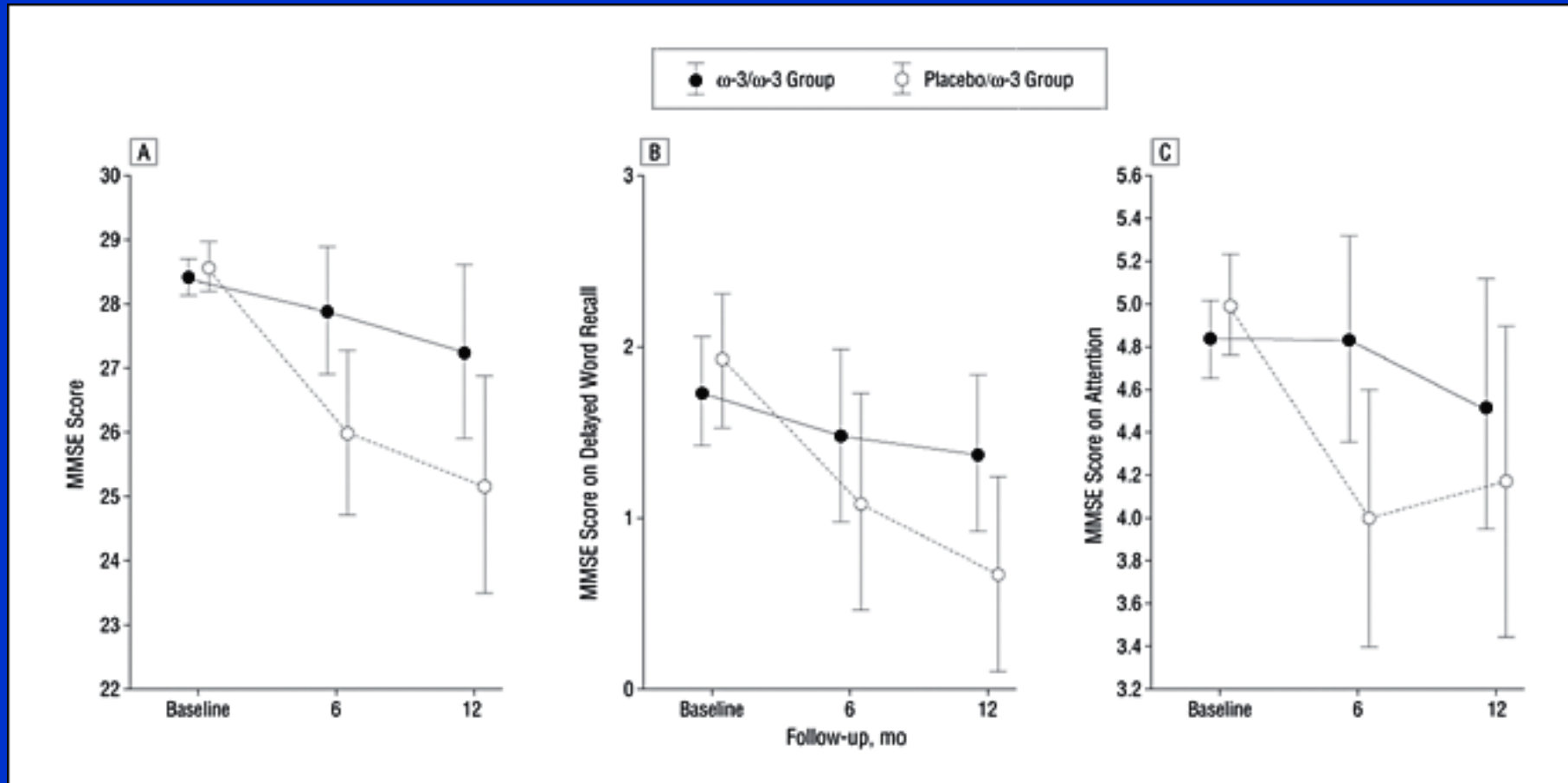
Cumulative Incidence of Dementia in Subjects with Baseline Plasma Phosphatidylcholine Docosahexaenoic Acid (PC DHA) Levels in the Upper Quartile Versus the Lower 3 Quartiles (Framingham Study)



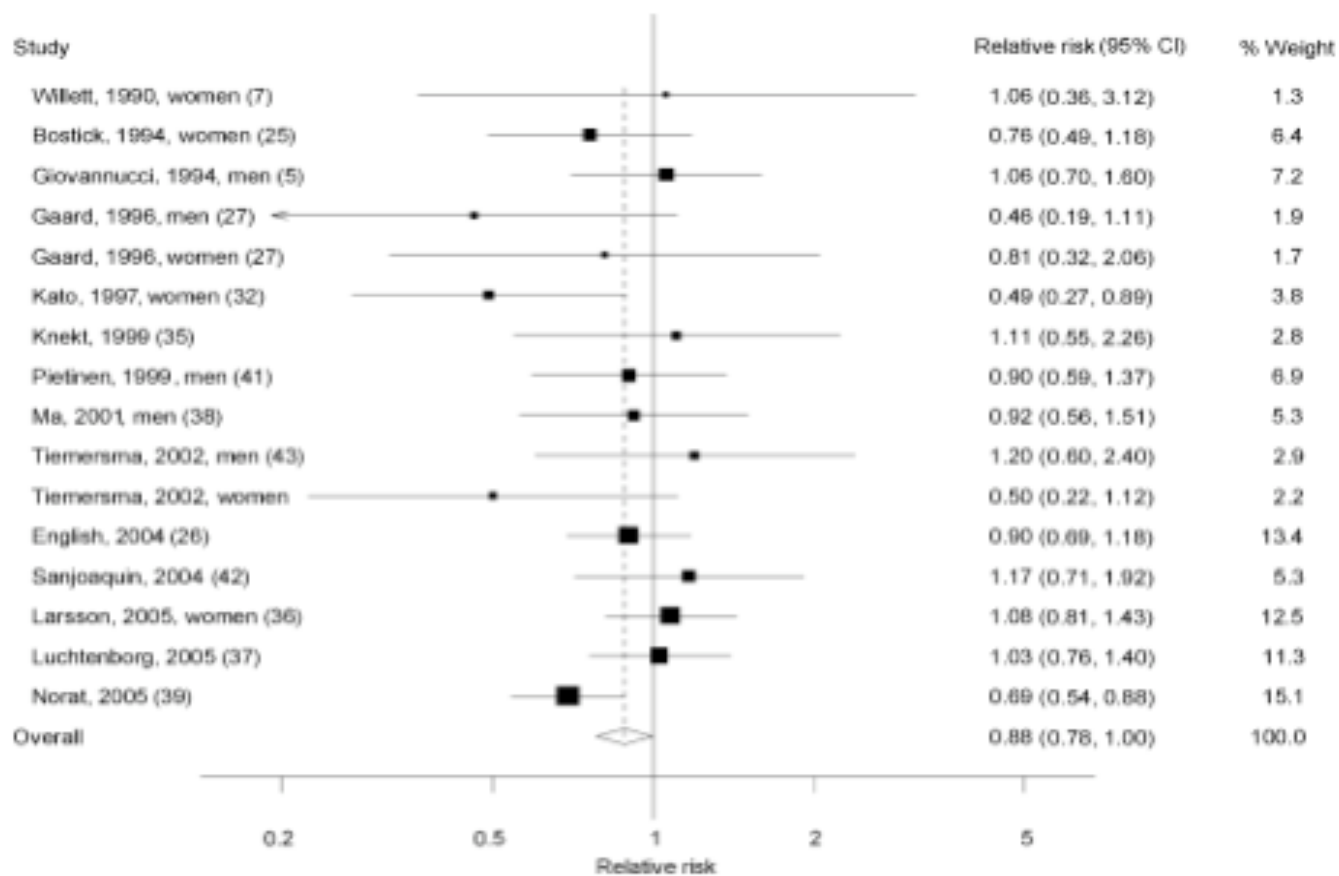
Omega AD Study: Design of Study and Trial Profile



Cognitive Tests In Patients With Very Mild Alzheimer Disease (Mini-mental State Examination [MMSE] Score >27 Points)



Relative Risks of Colorectal Cancer Incidence and Fish Consumption*

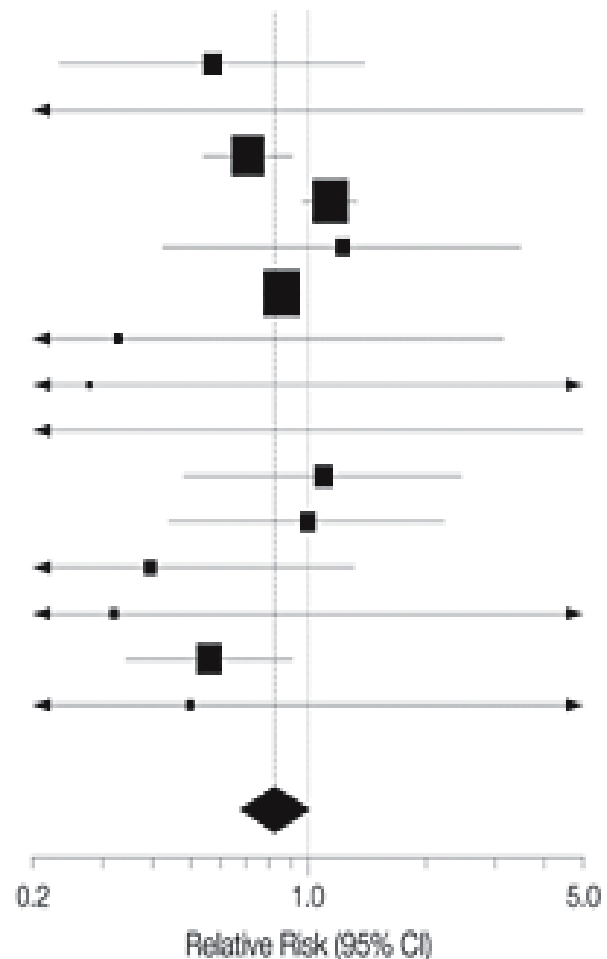


*Highest versus lowest intake category.

Geelen et al., Am J Epidemiol. 2007;166:1116-1125

Fish or Fish Oil Intake Reduces Risk of Total Mortality - Randomized Clinical Trials

Source	% Weight	Relative Risk (95% CI)
Brouwer et al, ⁶² 2006	3.9	0.57 (0.24-1.38)
Brox et al, ⁶⁷ 2001	0.3	0.17 (0.01-4.05)
Burr et al, ³ 1989	18.7	0.71 (0.55-0.92)
Burr et al, ⁵¹ 2003	24.4	1.15 (0.99-1.34)
Eritsland et al, ⁶⁸ 1998	2.9	1.23 (0.43-3.51)
Gruppo Italiano, ⁹ 1999	26.0	0.86 (0.76-0.97)
Johansen et al, ⁶⁹ 1999	0.7	0.33 (0.03-3.18)
Kaul et al, ⁶⁰ 1992	0.3	0.28 (0.01-6.78)
Leaf et al, ⁶¹ 1994	0.4	0.20 (0.01-4.18)
Leaf et al, ⁶¹ 2005	4.6	1.09 (0.49-2.46)
Nilsen et al, ⁶² 2001	4.6	1.00 (0.45-2.24)
Raitt et al, ⁶⁰ 2005	2.3	0.40 (0.12-1.32)
Sacks et al, ⁶⁶ 1995	0.3	0.32 (0.01-7.57)
Singh et al, ⁶³ 1997	9.9	0.58 (0.34-0.91)
von Schacky et al, ⁶⁷ 1999	0.6	0.50 (0.05-5.39)
Overall	100.0	0.83 (0.68-1.00)





U.S. Food and Drug Administration
Center for food safety and applied nutrition



January 15, 2009

**Draft Risk and Benefit Assessment Report and
Draft Summary of Published Research**

**Report of Quantitative Risk and Benefit
Assessment of Consumption of Commercial Fish,
Focusing on Fetal Neurodevelopment Effects
(Measured by Verbal Development in Children)
and on Coronary Heart Disease and Stroke in the
General Population**

and

**Summary of Published Research on the Beneficial
Effects of Fish Consumption and Omega-3 Fatty
Acids for Certain Neurodevelopmental and
Cardiovascular Endpoints**

The effect of increased fish consumption on total blood mercury, in women aged 16-49 participating in NHANES 1999-2002

Fish Consumption (frequency in past 30 days)	Total Blood Hg (mg/l)	
	Mean	SE
0	0.6	0.05
1-4 times	1.6	0.1
5-8 times	2.2	0.3
≤ 9 times	4.2	0.7

I.Q. Loss in Children from Maternal Mercury Exposure (modeled estimates)

Percentile of exposure (Hg in hair): U. S. women of child-bearing age	Change in IQ (central estimates)
10 th	0.00 of an IQ point*
50 th	0.02 of an IQ point
90 th	0.13 of an IQ point
95 th	0.20 of an IQ point
99 th	0.43 of an IQ point
99.9 th	0.87 of an IQ point

*** This number is actually higher than zero, but is low enough to "round" to zero when only two digits to the right of the decimal point are shown.**

FDA Risk & Benefit Assessment:
<http://www.cfsan.fda.gov/~dms/mehg109.html>

The Net Effect on Fetal Neurodevelopment from Eating Commercial Fish that, Collectively, Contain an Average Amount of Mercury and an Average Amount of Beneficial Nutrients

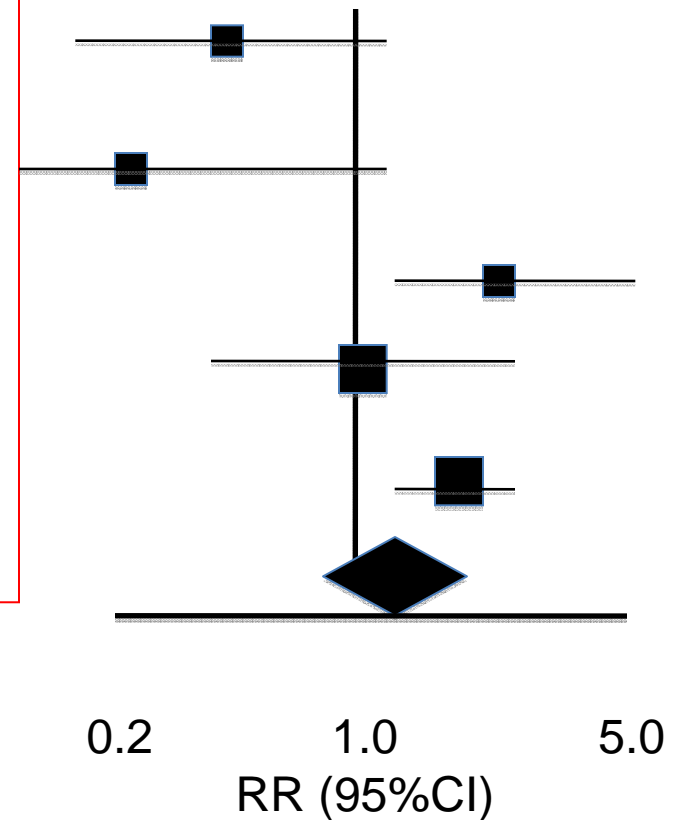
Hg Dose (ppm in maternal hair)	Amount of Fish Consumed (g/day)	Change in Z-Score	Change in IQse
0.02	0.8	0.008 (0.0001, 0.0018)	0.0126 (0.0018, 0.0268)
0.04	2.0	0.0021 (0.0003, 0.0044)	0.0310 (0.0043, 0.0660)
0.12	5.5	0.0057 (0.0008, 0.0121)	0.0851 (0.0115, 0.1813)
0.30	13.3	0.0137 (0.0018, 0.0293)	0.2054 (0.0276, 0.4389)
0.63	28.6	0.0292 (0.0037, 0.0627)	0.4373 (0.0561, 0.9405)
0.98	44.2	0.0448 (0.0058, 0.0969)	0.6714 (0.0866, 1.4531)
2.16	97.5	0.0985 (0.0121, 0.2139)	1.4778 (0.1816, 3.2090)
2.83	127.8	0.1291 (0.0156, 0.2803)	1.9361 (0.2345, 4.2044)
4.37	205.7	0.2078 (0.0253, 0.4526)	3.1177 (0.3788, 6.7895)

Annual Frequency of Death from CHD Based on Amounts of Fish Consumed Using "CHD Meta-Analysis Model"

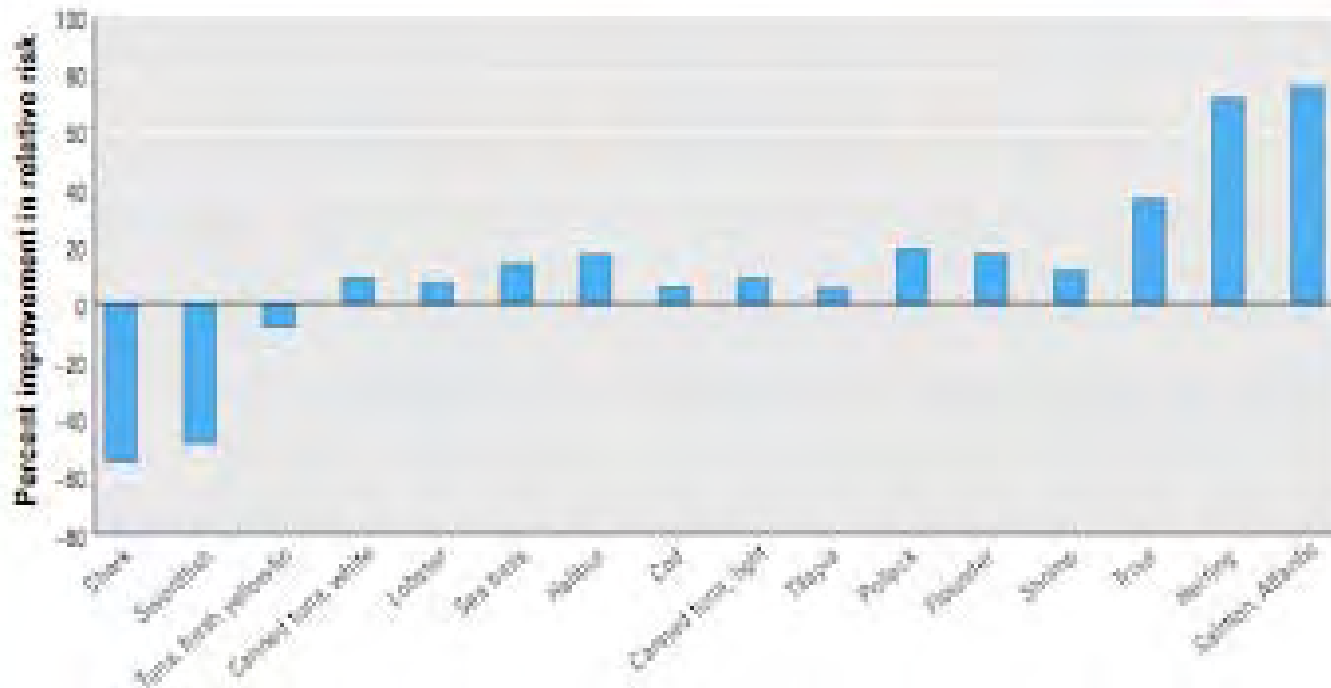
Fish Consumption Percentile	Women 16-45	Women 46+	Men 16-45	Men 46+
10 th	0.142 in 10,000	40.2 in 10,000	1.350 in 10,000	54.4 in 10,000
25 th	0.141 in 10,000	39.7 in 10,000	1.33 in 10,000	53.6 in 10,000
50 th	0.139 in 10,000	39.0 in 10,000	1.30 in 10,000	52.4 in 10,000
75 th	0.134 in 10,000	37.6 in 10,000	1.25 in 10,000	50.2 in 10,000
90 th	0.126 in 10,000	35.1 in 10,000	1.14 in 10,000	46.0 in 10,000
95 th	0.119 in 10,000	32.6 in 10,000	1.04 in 10,000	42.1 in 10,000
99 th	0.098 in 10,000	25.9 in 10,000	0.71 in 10,000	29.4 in 10,000

Risk of Incident CHD with Higher Levels of Mercury Exposure

Source	Study Design	# Events	RR (95% CI)
Ahlqwist et al., 1999	Prospective	87	0.71(0.4-1.3)
Hallgren et al., 2001	Prospective	78	0.51(0.2-1.2)
Guallar et al., 2002	Retrospective	684	2.16(1.1-4.3)
Yoshizawa et al., 2002	Prospective	470	1.03(0.7-1.7)
Virtanen et al., 2005	Prospective	282	1.66(1.2-2.3)
Overall			1.12(0.7-1.8)



Estimated Net Effect of MeHg and Fish Oils on CVD Risk, one 6-oz Fish Meal Per Week



Grading the Evidence Base for Omega-3 Fatty Acids, Fish Oil, ALA

Key to Grades:

- A: Strong scientific evidence for this use**
- B: Good scientific evidence for this use**
- C: Unclear scientific evidence for this use**
- D: Fair scientific evidence **against** this use**
- F: Strong scientific evidence **against** this use**

Grading the Evidence Base for Omega-3 Fatty Acids, Fish Oil, ALA

CVD Risk Factors and Outcomes

Grade

High Blood Pressure	A
HyperTG (fish oil/EPA + DHA)	
A	
Secondary CVD Prevention (fish oil/EPA + DHA)	A
Primary CVD Prevention (fish intake)	B
Angina Pectoris	C
Atherosclerosis	C
Cardiac arrhythmias (abnormal heart rhythms)	C
Acute coronary syndrome	C
Peripheral vascular disease/ Claudication	C
Prevention of graft failure after bypass surgery	C
Prevention of restenosis after PTCA	C
Primary CVD prevention (ALA)	C
Secondary CVD prevention (ALA)	C
Stroke prevention	C
Hypercholesterolemia	D
Transplant rejection (kidney and heart)	D

Grading the Evidence Base for Omega-3 Fatty Acids, Fish Oil, ALA

Pregnancy and Infancy Outcomes

Grade

Infant eye/brain development

B

Pregnancy nutritional supplement

B

Preeclampsia

C

Growth rates

C

Immune function (infant)

C

Grading the Evidence Base for Omega-3 Fatty Acids, Fish Oil, ALA

Mental Health Outcomes

Grade

Attention deficit hyperactivity disorder
Bipolar disorder
Dementia
Depression
Impulse problems
Schizophrenia

C
C
C
C
C
C

Grading the Evidence Base for Omega-3 Fatty Acids, Fish Oil, ALA

Other Selected Health Outcomes

Grade

Inflammation	B
Nutrition & GI disorders	B
Rheumatoid arthritis (fish oil)	B
Cancer prevention	C
Colon cancer	C
Dysmenorrhea (painful menstruation)	C
Eczema	C
Inflammatory bowel disease	C
Osteoporosis	C
Prostate problems	C
Psoriasis	C
Diabetes	D

Benefits of n-3 LC PUFA In Pregnancy



- Prolongs Gestation by 1.6 to 2.6 days

Szajewska et al., Am J Clin Nutr. 2006;83:1337-1344

Makrides et al. Cochrane Database Syst. Rev.2006. #3;
CD003402

-Reduced Risk Preterm Birth (< 34 wks)

31% for all pregnancies & 61% for high risk

Makrides et al. Cochrane Database Syst. Rev.2006. #3;
CD003402

Horvath et al., Br J Nutr. 2007;98:253-259.

Benefits of n-3 LC PUFA In Infancy



- Slight Increase in Birth Weight (47-54 g)

Szajewska et al., Am J Clin Nutr. 2006;83:1337-1344

Makrides et al. Cochrane Database Syst. Rev.2006. #3;
CD003402

- Supplementing preterm infants with n-3 LC PUFA shows mixed results for visual development at < 6 months of age

Eilander et al., Prostaglandins Leukot Essent Fatty Acids. 2007;76:189-203.

SanGiovanni et al., Pediatrics 2000;105:1292-1298.

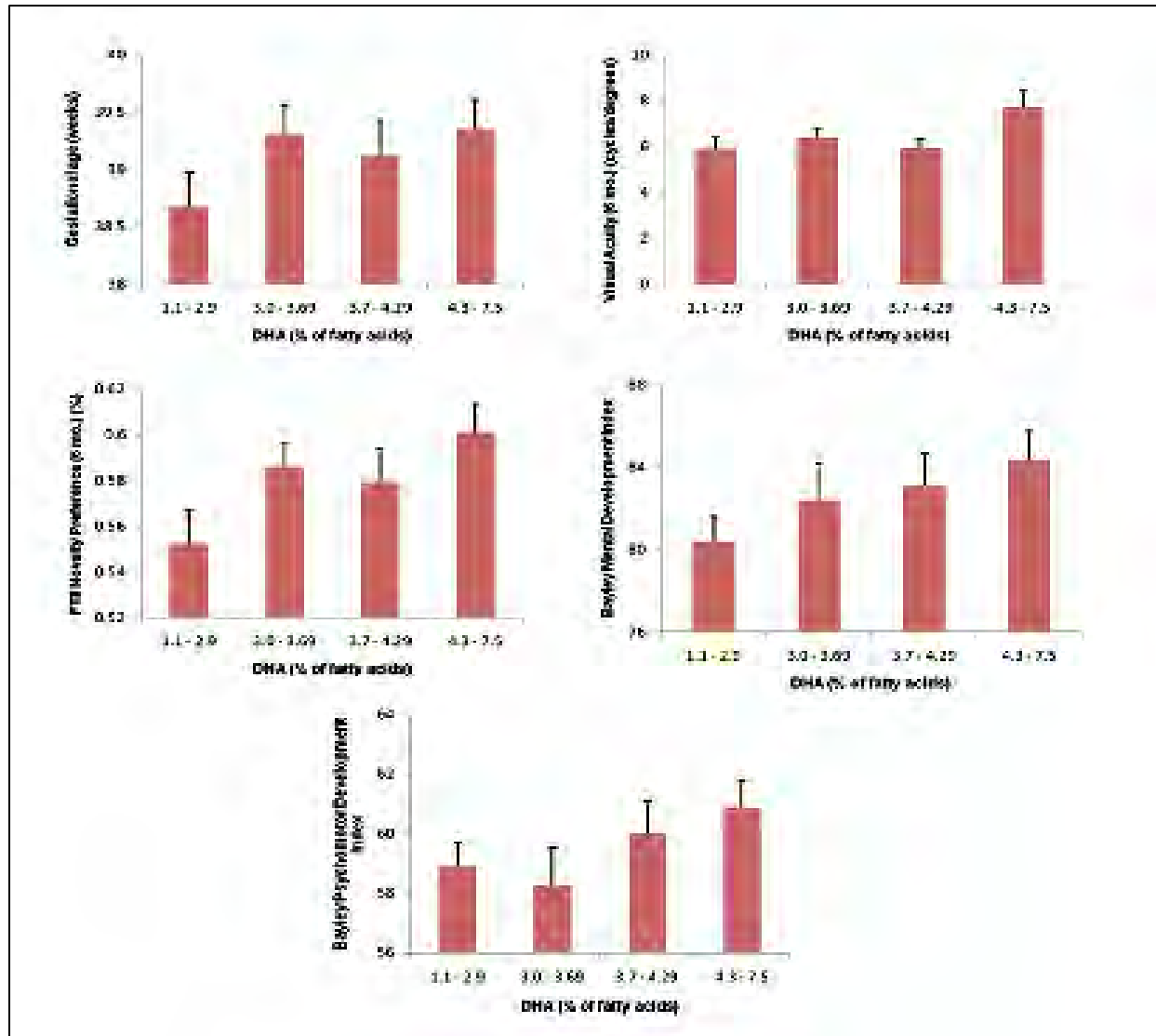
- Supplementing term infants with n-3 LC PUFA (100 mg DHA & 200 mg AA) beneficially affects visual development during the first year of life.

Eilander et al., Prostaglandins Leukot Essent Fatty Acids. 2007;76:189-203.

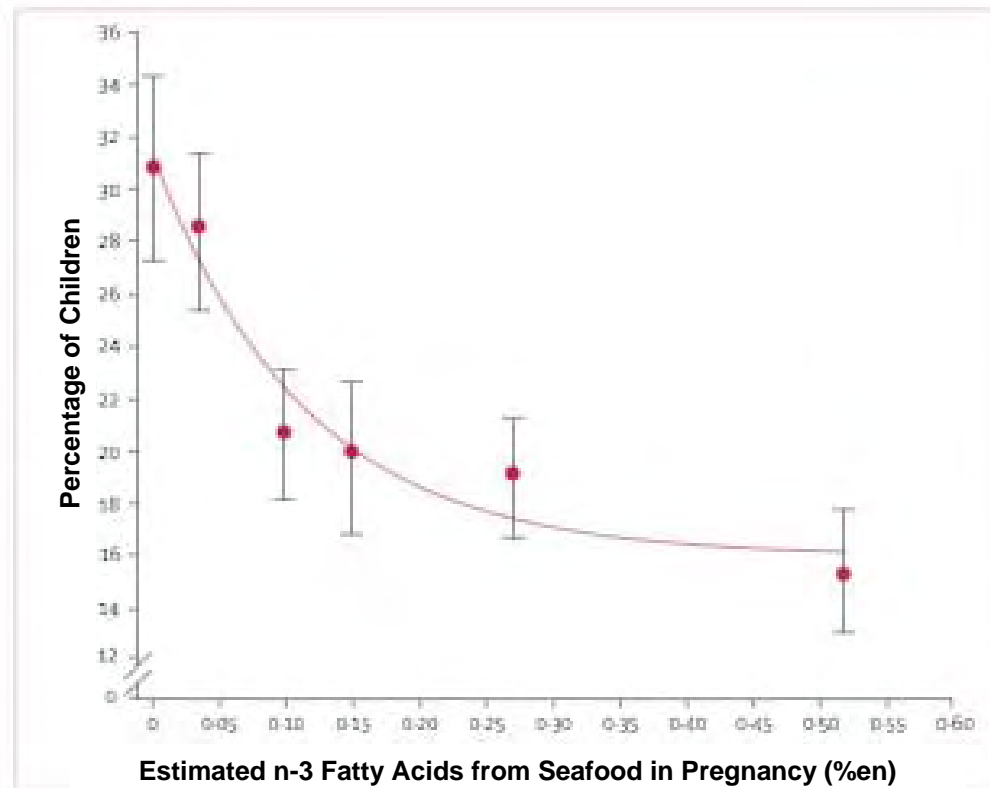
- Supplementation with n-3 LC PUFA shows benefits on cognition in preterm but not full term and young children

-Eilander et al., Prostaglandins Leukot Essent Fatty Acids. 2007;76:189-203.

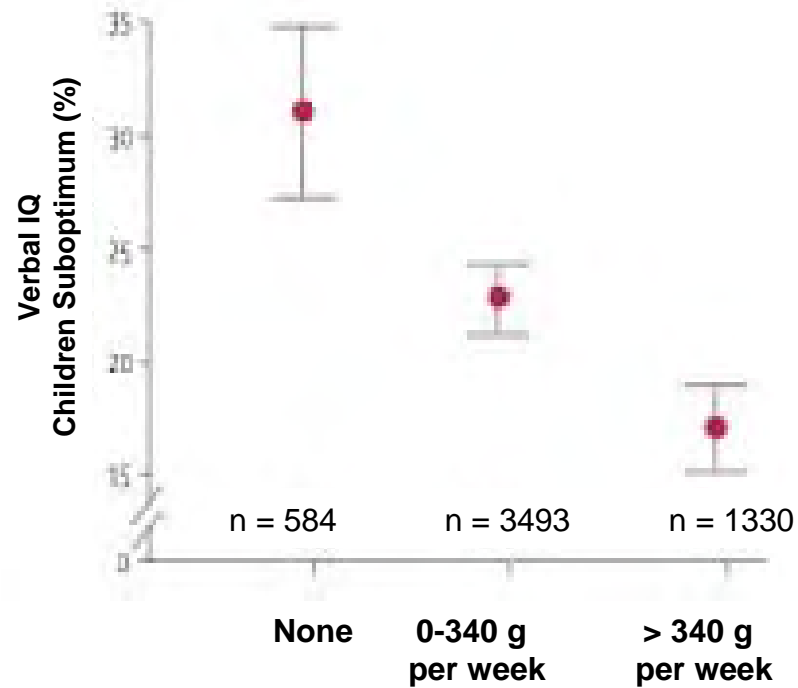
Relationship of Cord Plasma PL DHA and Inuit Infant Developmental Outcome



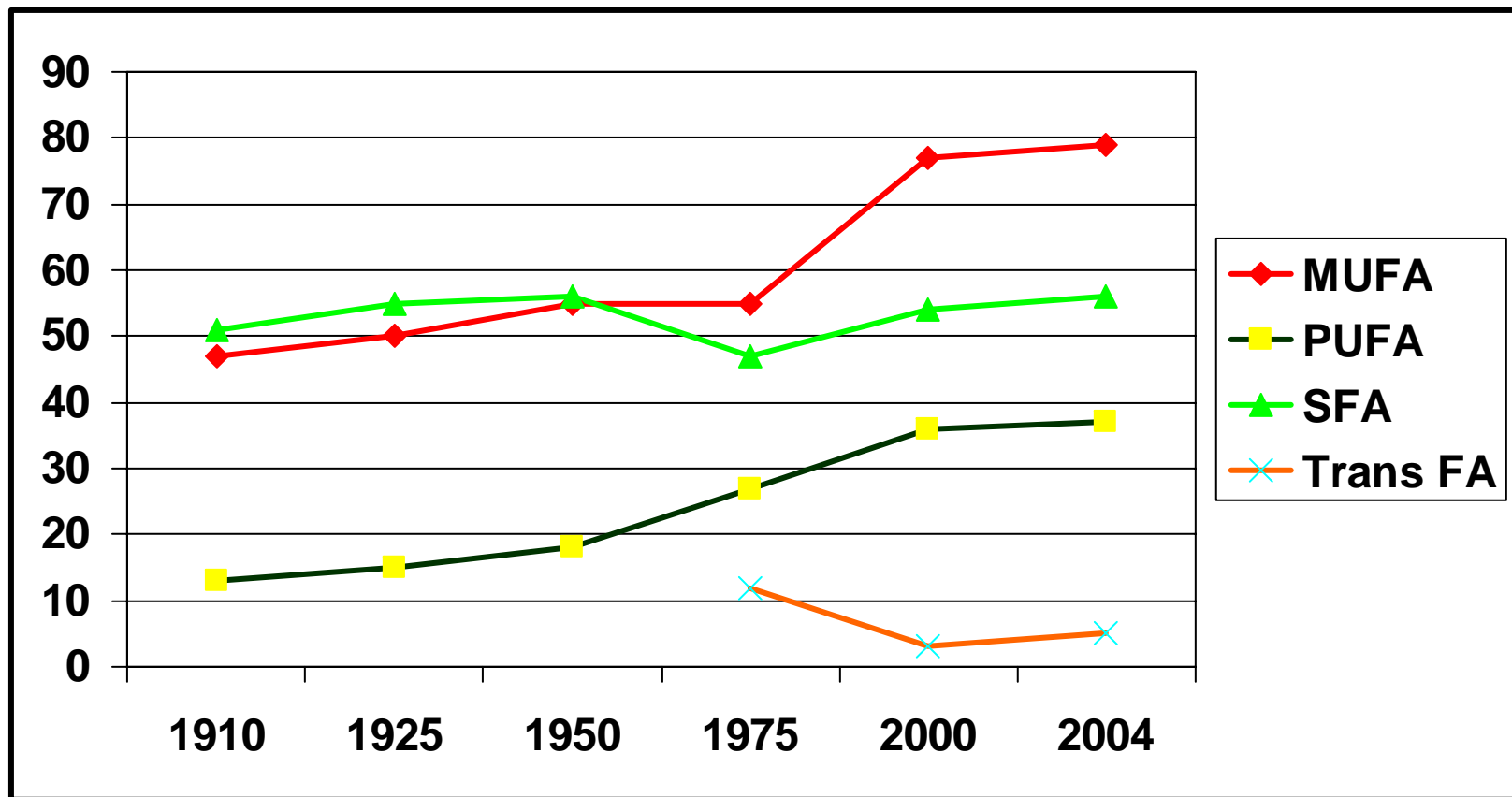
Prevalence of Children with Low Verbal IQ According to Mother's n-3 Fatty Acids from Seafood



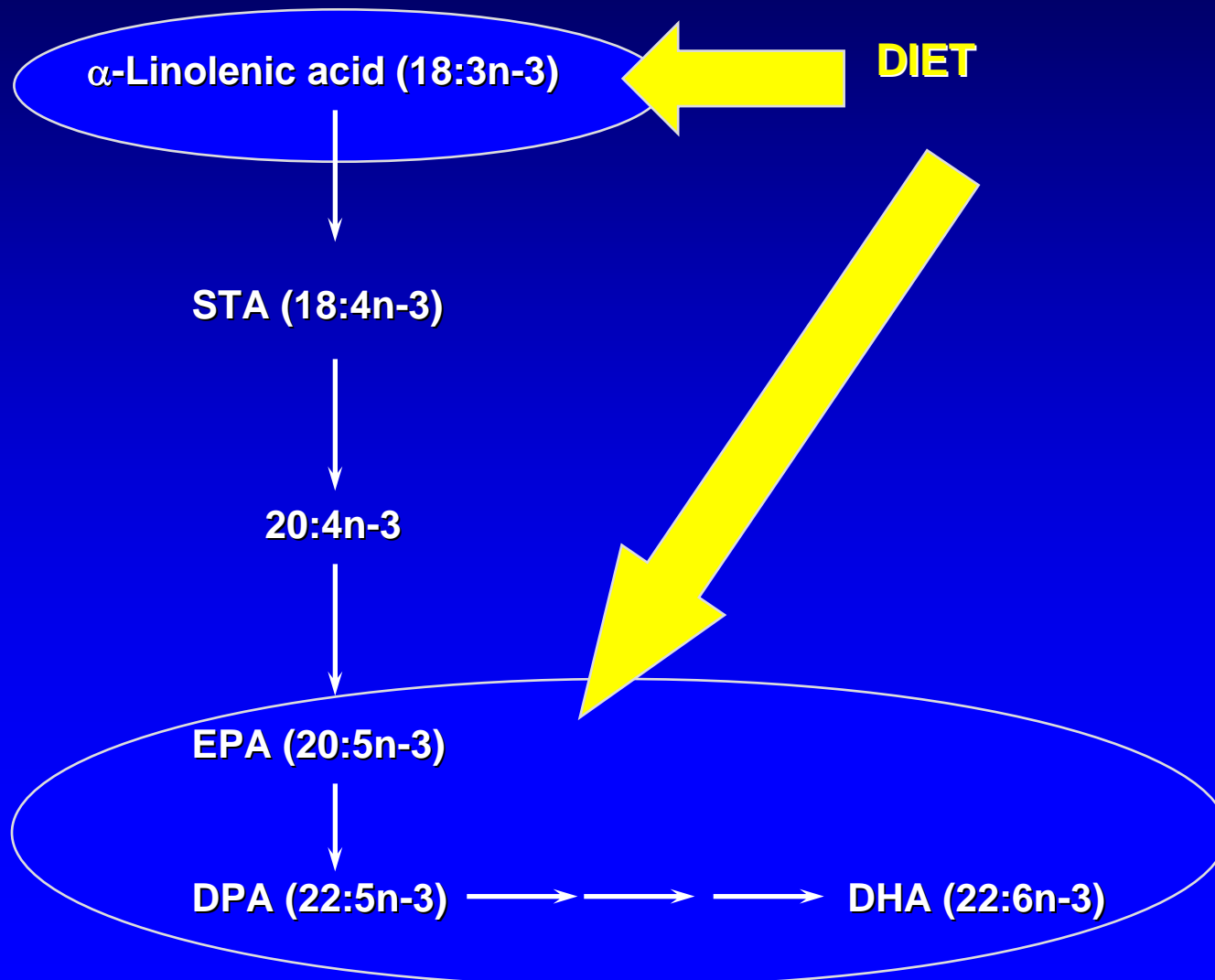
Suboptimum Outcomes (Verbal IQ) in Children According to Mothers' Seafood Consumption



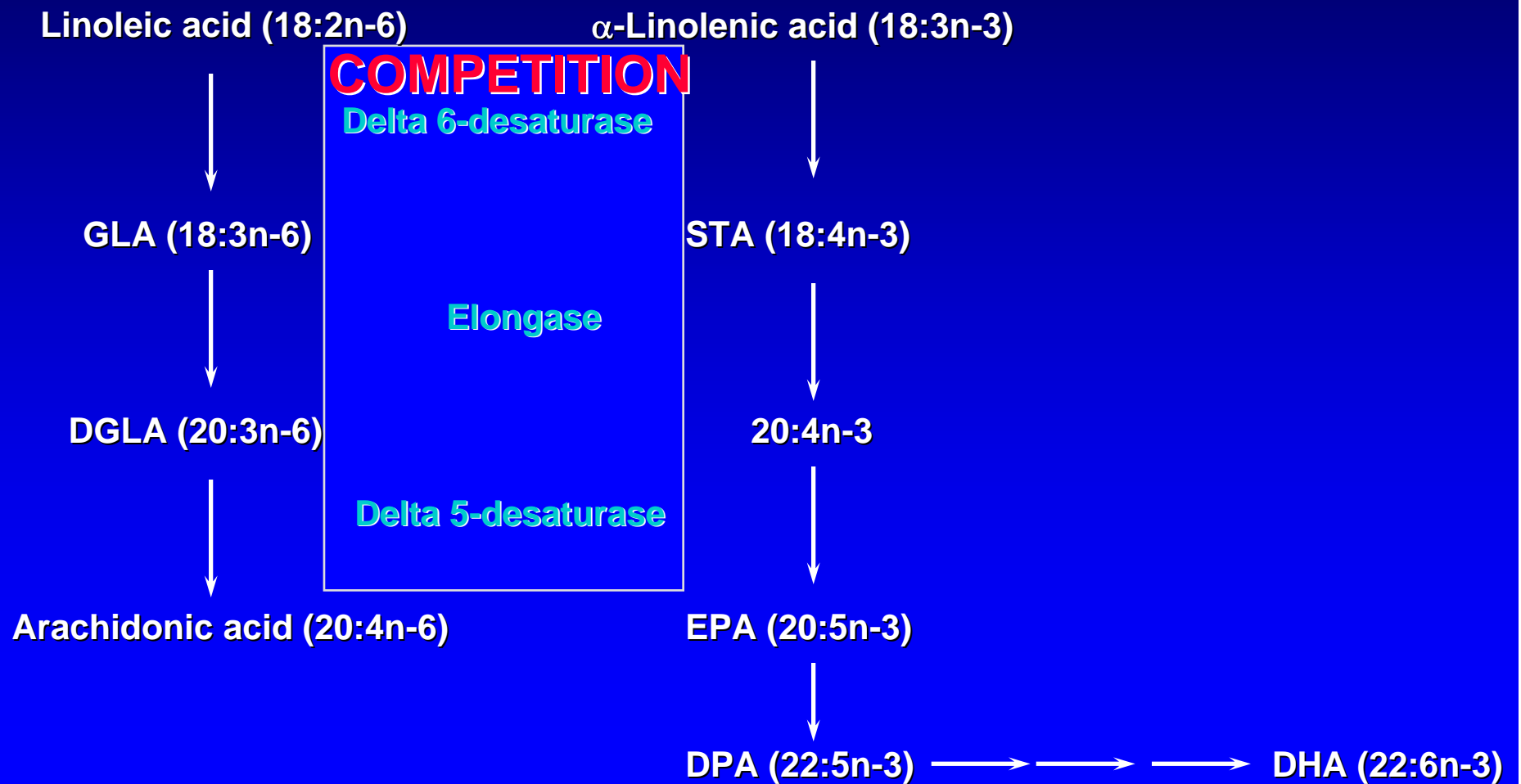
U.S. Food Supply, 1900-2004 grams per capita per day



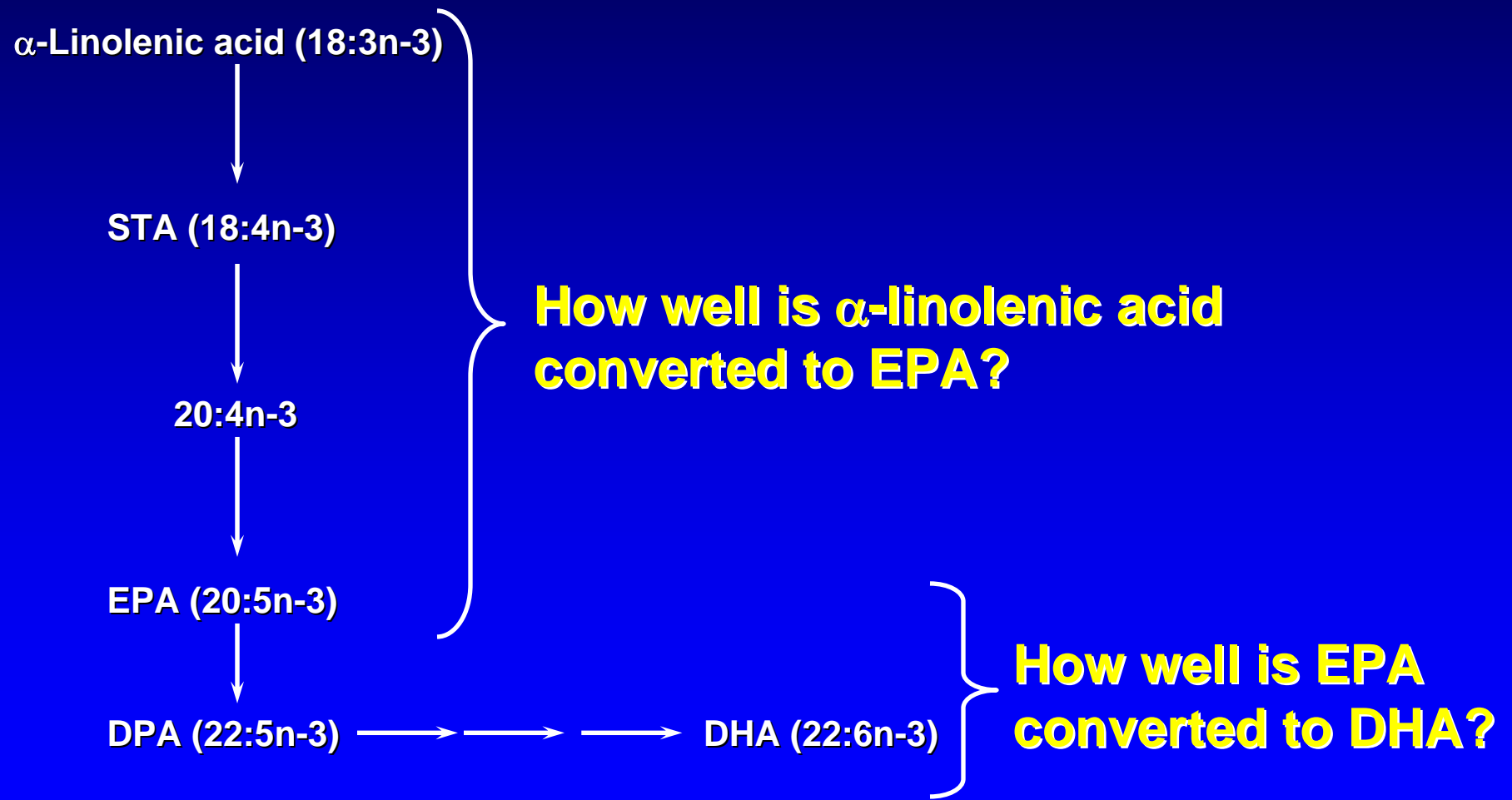
Sources of Omega-3 Fatty Acids – Diet and Conversion



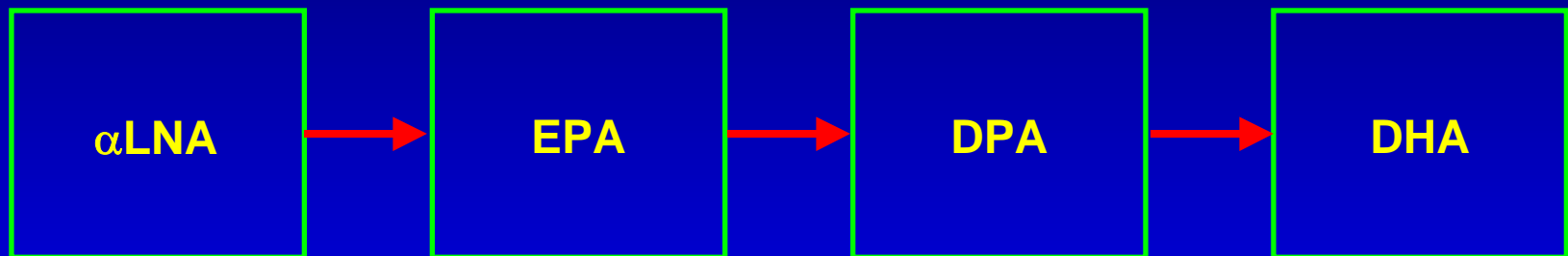
Metabolism of n-6 and n-3 PUFA



Is α -linolenic acid an adequate precursor for EPA and DHA in humans?



Estimated conversion rates of ALA based on stable isotope modeling



**Overall
conversion**



0.3% to 7%



0.01%

Goyens et al., Am J Clin Nutr. 2006;84:44-53
Hussein et al., J Lipid Res. 2005;46:269280

AHA Science Advisory

Omega-6 Fatty Acids and Risk for Cardiovascular Disease

A Science Advisory From the American Heart Association Nutrition Subcommittee of the Council on Nutrition, Physical Activity, and Metabolism; Council on Cardiovascular Nursing; and Council on Epidemiology and Prevention

William S. Harris, PhD, FAHA, Chair; Dariush Mozaffarian, MD, DrPH, FAHA; Eric Rimm, ScD, FAHA; Penny Kris-Etherton, PhD, FAHA; Lawrence L. Rudel, PhD, FAHA; Lawrence J. Appel, MD, MPH, FAHA; Marguerite M. Engler, PhD, FAHA; Mary B. Engler, PhD, FAHA; Frank Sacks, MD, FAHA

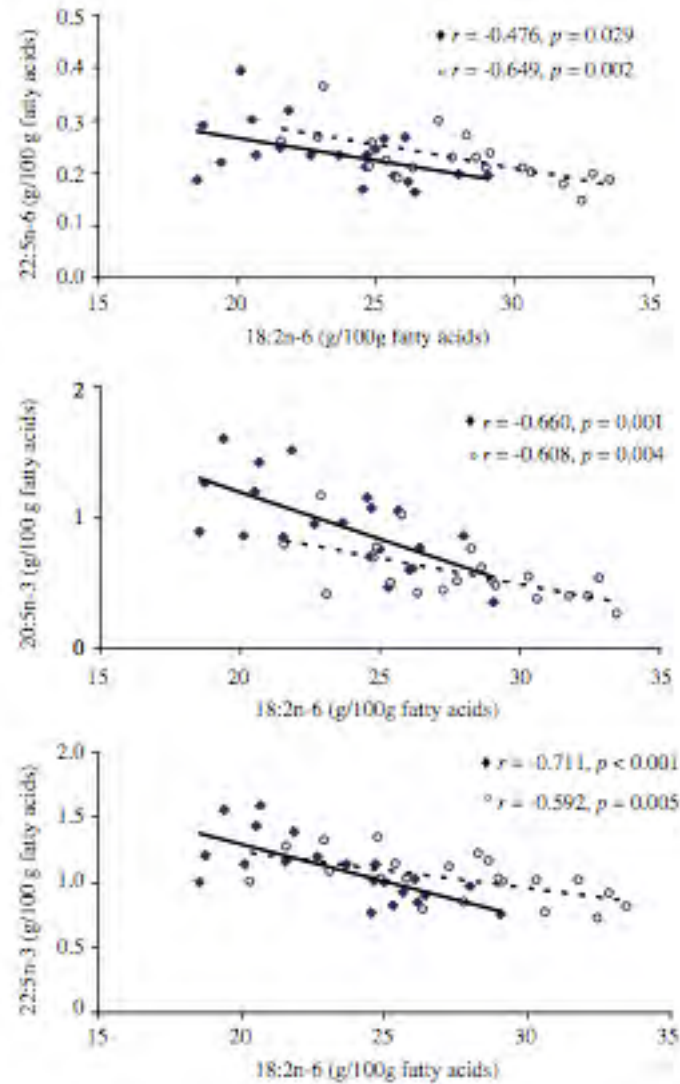
“In summary, the AHA supports an omega-6 PUFA intake of at least 5% to 10% of energy in the context of other AHA lifestyle and dietary recommendations. To reduce omega-6 PUFA intakes from their current levels would be more likely to increase than to decrease risk for CHD.”

Circulation 2009;119:902-907

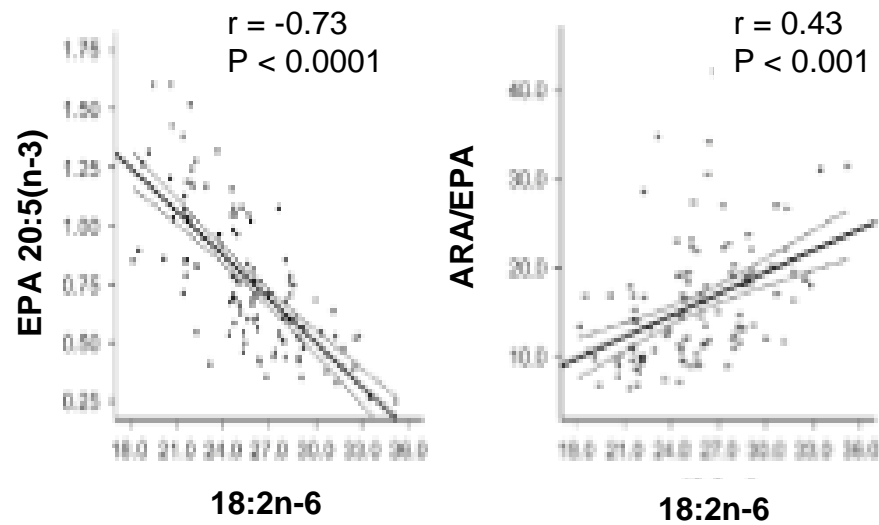
Clinical Trials : Substitution of PUFA for SFA to Reduce Coronary Events

	N	Dietary Fat (%)	Duration (yr)	PUFA Intake (%)	Δ Cholesterol (%)	Δ CVD (%)
Finnish Mental Hospital	676	34	6	14	-15	-43
Oslo	412	39	5	21	-14	-25
MRC Soy Oil	393	46	4	9.4 from soy oil added to diet	-15	-12
Los Angeles	846	40	8	17	-13	-34

Long Chain Omega-3 Fatty Acids and Plasma PL in Adult Men After Consuming 10.5% (high) or 3.8% (low) Linoleic Acid



**Associations between Phospholipid LA and EPA (Left)
and ARA:EPA Ratio (right) in Men who Consumed
Low and High LA Diets**



“Because omega-6 and omega-3 fatty acids compete with each other to be converted to active metabolites in the body, benefits can be reached either by decreasing intake of omega-6 fatty acids or by increasing omega-3 fatty acids.”

U.S. Intake of Omega-3 Fatty Acids for all Individuals, n=8,604

Fatty Acid	Mean	SE
α -linolenic acid	1.4 g	0.02
EPA	0.03 g	0.002
DHA	0.07 g	0.003

Average Daily Fish Consumption, 2003-2004 NHANES

Population Statistic	Women 16-45	Women 46+	Men 16-45	Men 46+
Average	13.4 (12.7, 13.9)	15.1 (14.3, 16.1)	18.3 (17.1, 19.2)	19.0 (18.0, 20.6)
10th %tile	0.1 (0.0, 0.9)	0.2 (0.0, 1.3)	0.2 (0.0, 1.2)	0.3 (0.0, 1.7)
25th %tile	2.8 (2.0, 3.6)	3.4 (2.7, 4.3)	3.7 (2.7, 4.6)	4.6 (3.5, 5.8)
50th %tile	7.2 (6.4, 7.9)	8.4 (7.4, 9.1)	9.6 (8.3, 10.6)	10.8 (9.5, 11.9)
75th %tile	16.3 (14.9, 17.7)	18.4 (16.9, 19.6)	21.9 (19.6, 23.1)	22.7 (21.0, 24.5)
90th %tile	32.3 (29.3, 34.4)	36.4 (33.7, 39.5)	43.7 (40.1, 47.6)	44.4 (40.5, 49.5)
95th %tile	46.4 (42.1, 50.7)	53.7 (47.4, 60.5)	65.5 (58.5, 74.7)	65.1 (58.2, 75.3)
99th %tile	88.3 (74.4, 114.3)	101.5 (85.0, 128.3)	136.0 (106.8, 179.3)	131.8 (108.3, 178.4)
NHANES average for comparison	10.3	14.2	16.8	20.8

Daily Fish Consumption (g/day); Median (5th percentile, 95th percentile)

Total Fish & Other Seafood Consumption

- Measured in terms of ounce equivalents per day
- 8 ounces per week = 1.41 ounces/day
- 12 ounces per week = 1.71 ounces/day
- Up through the 75th percentile, adult intakes are below 8 ounces per week
- None of the women or young children showed intakes greater than 12 ounces per week, at the 95th percentile.

Compliments of Dr. Sue Krebs-Smith, NCI

Fish (oz.) Required per Day to Provide ~ 500mg of EPA+DHA

	<u>Ounces</u>
Tuna	
Light, canned in water	6
White, canned in water	2
Fresh	1-6
Sardines	1-1.5
Salmon	
Sockeye or Pink	1.5
Chinook	1
Atlantic, farmed	1
Atlantic, wild	1-1.5
Trout, rainbow	
Farmed	1.5
Wild	1.5
Cod	
Atlantic	11.5
Pacific	6.0
Catfish	
Farmed	10
Wild	7.5
Flounder/Sole	3.5

Ways to Get 500 mg/d EPA+DHA

- **Fish**
 - 1 to 1.5 oz salmon, sardines, mackerel per day
- **Dietary Supplements**
 - *Low Potency*: 300 mg EPA+DHA per capsule
(Typical drug store capsules; about 1.5 capsules/day)
 - *Mid Potency*: 500–700 mg EPA+DHA per capsule
 - (Mail-order, online, etc; 1 capsule/day)
- **Drugs**
 - *High Potency*: 850 mg EPA+DHA/g
(Omega-3 acid ethyl esters; 1 capsule every other day)
- **Cod Liver Oil**
 - 0.5 tsp gives 0.4 g of EPA + DHA

DHA and EPA Content of Supplements

(per capsule)

	Calories	DHA, mg	EPA, mg
ABC Vitamin Life	10	240	360
Max EPA	10	120	180
Herbal Remedies	5	150	200
Omega Max	10	240	360
Nordic Naturals (Ultimate Omega)	10	225	325
nutraOrigin	10	240	420

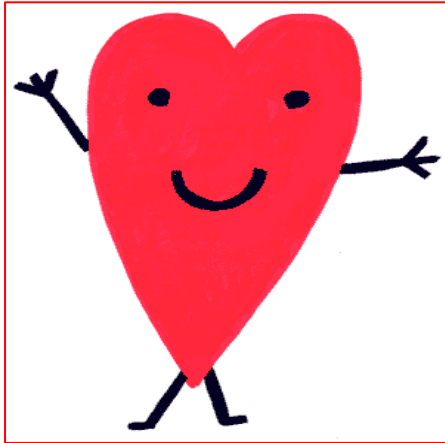


Analysis finds fish oil supplements safe (12/15/2004)

- ConsumerLab.com found that of 41 fish oil supplements tested, none were contaminated with mercury or PCBs.
- Testing did find some product-integrity issues with two brands not containing as much omega-3's as claimed.
- A listing of products is at www.consumerlab.com

Summary





Conclusions

Dietary omega-3 fatty acids confer important health benefits for heart health, good mental status throughout the life cycle, and infant neurodevelopment.

