Mediterranean Diet and inflammatory markers

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Diet Score and inflammation-coagulation: the ATTICA Study

Results from multiple regression analysis (b-coefficient ± standard error) regarding the association between the Mediterranean diet score (per 10-unit increase) and inflammation and coagulation markers, in sub-groups of the participants

	All subjects	Hypertensive subjects	Diabetic subjects	Hypercholesterolemic subjects	Smokers
Amyloid A (per 1 mg / dL)	-0.08±0.28	-0.12±0.78	-0.12±0.34	-0.07±0.51	-0.09±0.11
C-reactive protein (per 1 mg/L)	-0.22±0.11*	-0.20±0.32*	-0.17±0.18*	-0.19±0.16*	-0.17±0.23*
Fibrinogen (per 1 mg / dL)	-12.5±1.15*	-11.5±1.54*	-10.5±1.01*	-11.8±1.23*	-12.1±1.26*
Homocysteine (per 1 μmol/L)	-0.87±0.25*	-0.88±0.23*	-0.79±0.87	-0.64±0.37*	-0.79±0.21*
Interleukin – 6 (per 1 pg/ml)	-0.21±0.34*	-0.17±0.58*	-0.15±0.44*	-0.17±0.81	-0.19±0.21*
TNF – a (per 1 pg / mL)	-0.28±1.18	-0.19±1.78	-0.22±1.34	-0.19±0.91	-0.19±0.31
White blood cell (x 1000 counts)	-0.23±0.09*	-0.20±0.08*	-0.18±0.19*	-0.19±0.22*	-0.18±0.12*

*** P values < 0.05, after adjusting for age, sex, smoking, physical activity, education status, presence of hypertension, diabetes, hypercholesterolemia, family history of CHD, as well as BMI.**

Chrysohoou C et al J Am Coll Cardiol 2004

The Nurses' Health Study I

- Cross-sectional study of 732 women aged 43-69 y
- A prudent pattern (high intake of fruits and vegetables, legumes, fish poultry, and whole grains) was inversely associated with CRP and E-selectin
- A western pattern (high intake of red and processed meats, sweets, desserts, french fries and refined grains) was positively associated with CRP, IL-6, E-selectin, sICAM-1 and sVCAM-1

Lopez-Garcia E et al Am J Clin Nutr 2004;80:1029-35

Evening Standard

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METRO LIFE
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Live Aid II
Joss set to play Hyde Park PAGE THREE

G.I. DIET CUTS RISK OF HEART DISEASE

BY REBECCA SMITH
Health Correspondent

DOCTORS today hailed the latest diet as being good for your heart as well as your waistline.

The glycaemic index (GI) distinguishes between "good" and "bad" carbohydrates and gives foods a score based on how long they take to digest.

Foods with a low GI release their sugar in a slow, controlled way which helps you to feel fuller for longer.

It also avoids the sugar highs and then subsequent lows which can lead to cravings and overeating.

The GI diet has been used for some time by diabetics to help control their sugar intake and avoid dangerous highs and lows in their blood glucose.

New low-sugar regime wins doctors' praise

Now researchers at Hammersmith Hospitals NHS Trust have shown that people who choose foods with a low GI have lower blood sugar levels than those who do not.

This puts them at less risk of heart disease and diabetes in later life. The team published their findings in the British Journal of Nutrition, which reveals that by simply replacing one item per meal with a lower-GI alternative lowers blood glucose levels for the whole day.

The good news on the glycaemic index diet comes after health scares over crazes such as the Atkins Diet.

Dr Gary Frost, head of nutrition and dietetics and lead researcher, said even small changes using the GI diet can create real health benefits.

He said: "The scientific benefits of low GI diets are becoming increasingly clear, and this new research is a further indicator of the potential that including these foods in a balanced diet has.

"What is interesting is that replacing just one item per meal has this

Continued on Page 4 ▶

GI diet

▶ Continued from Page 1

beneficial effect on blood sugar levels, putting people at lower risk of metabolic syndrome, a condition which can increase the risk of heart disease and diabetes.

"Any dietary intervention that is going to be successful needs to be realistic and manageable.

"The positive effects we see from a slight modification in diet, for example replacing white bread with its lower GI alternative, wholemeal bread, is very good news."

GI scores for common foods:

Low (up to 55): Apples, oranges, pears, peaches, beans and lentils, pasta (all types made from durum wheat), barley, porridge, custard.

Medium (between 55 and 70): basmati rice, honey, jam, Weetabix, ice cream, new potatoes.

High (above 70): glucose, white and wholemeal bread, brown rice, cornflakes, baked potato, mashed potato.

Soul girl: Joss Stone could be joined by Robbie Williams and Annie Lennox at free concert organised by Bob Geldof to highlight poverty

"The health benefits of a low GI diet are becoming increasingly clear….putting people at lower risk of metabolic syndrome and cardiovascular risk"

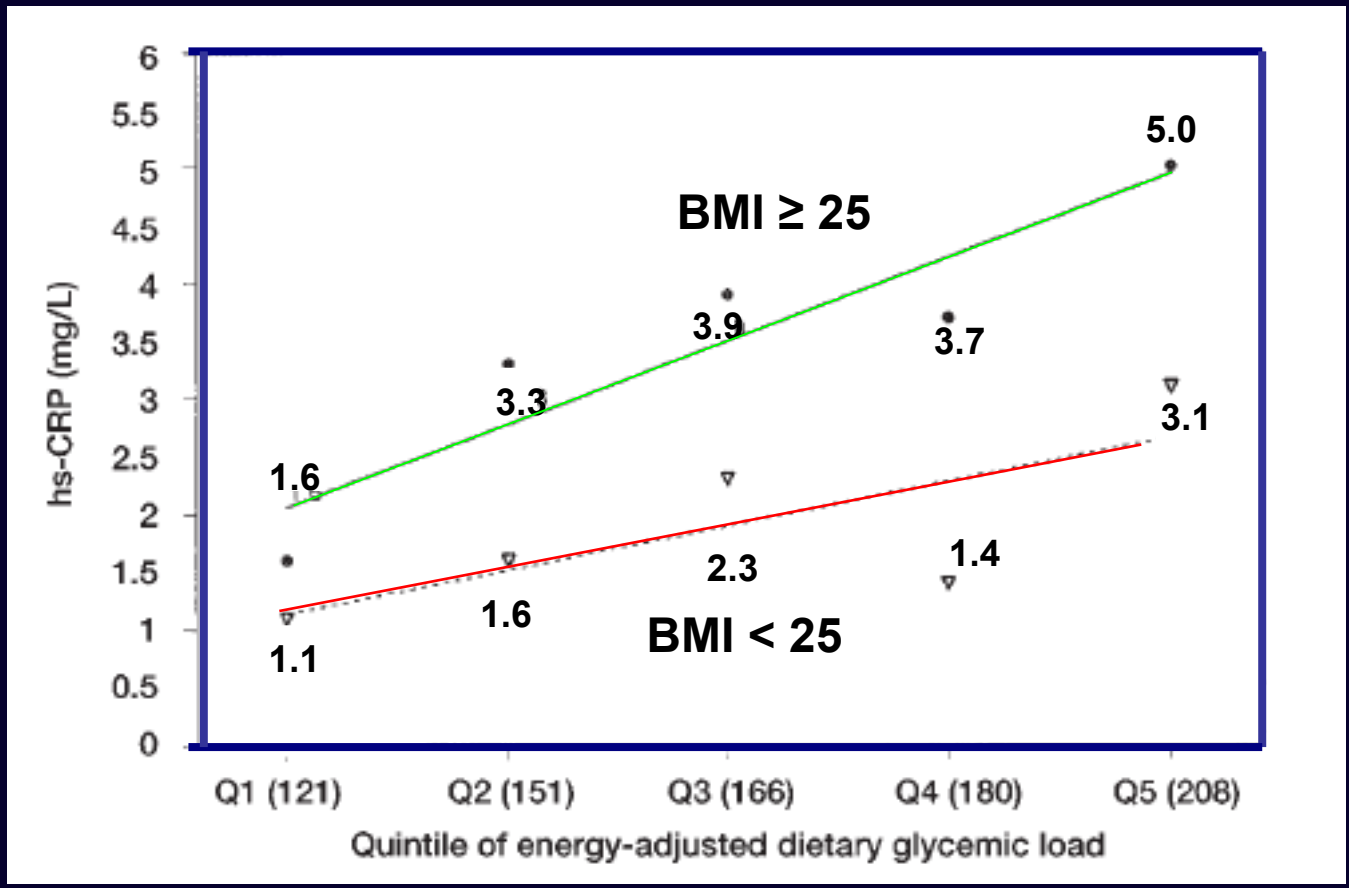
Professor Gary Frost 2005

What is Glycaemic Index

$$\frac{\text{Incremental area under the blood glucose response curve for 50g of available carbohydrate from test food}}{\text{Corresponding area after equi-carbohydrate portion of glucose}} \times 100$$

GLYCAEMIC INDEX & GLYCAEMIC LOAD

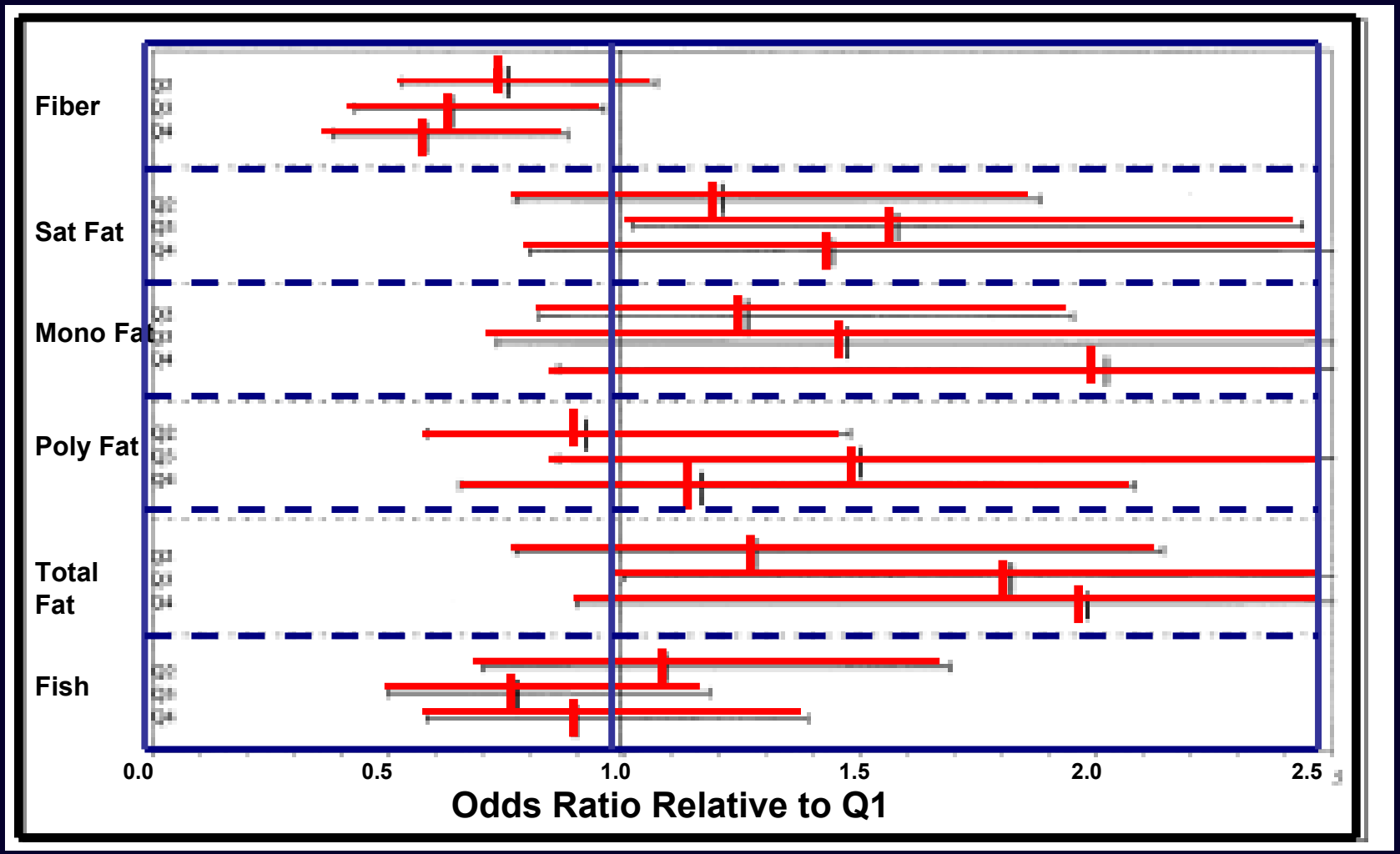
- **Glycaemic Index [GI]** - area under blood glucose curve following 50g CHO portion of food compared to 50g standard
- **Glycaemic Load [GL]** - GI x g carbohydrate per portion/meal/day [must be defined]



Dietary glycemic load is significantly and positively associated with plasma hs-CRP in healthy middle aged women, independent of conventional risk factors for ischaemic heart disease

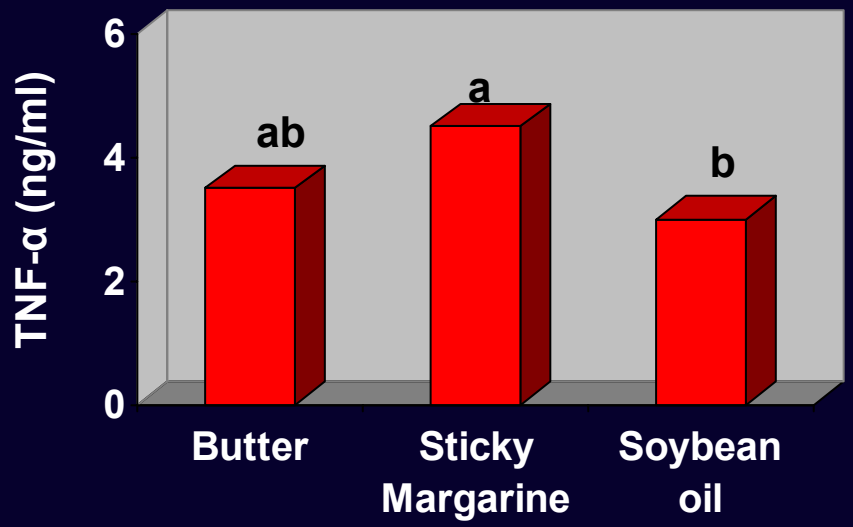
Liu S et al Am J Clin Nutr 2002;75:492-8

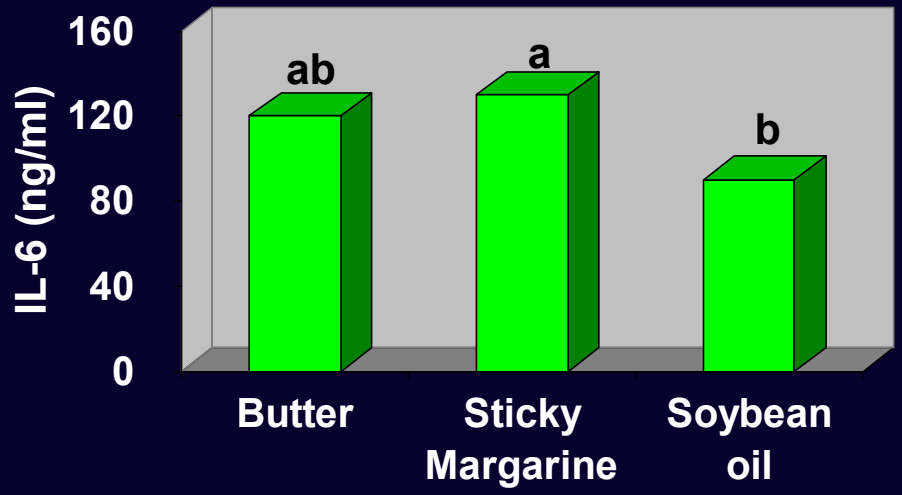
Adjusted ORs of elevated highly sCRP (>3.0 mg/L) risk for each quartile of nutrient consumption relative to the lowest quartile for each nutrient. The NHANES



King DE et al Am J Cardiol 2003;92:1335-9

Effect of different dietary fats on production of TNF-α and IL-6 by peripheral blood mononuclear cells





- Double blind cross over study
- 19 subjects, 32 day intervention
- 30% total fat (2/3 of it from the fat under investigation
- Means not sharing the same letters are significantly different

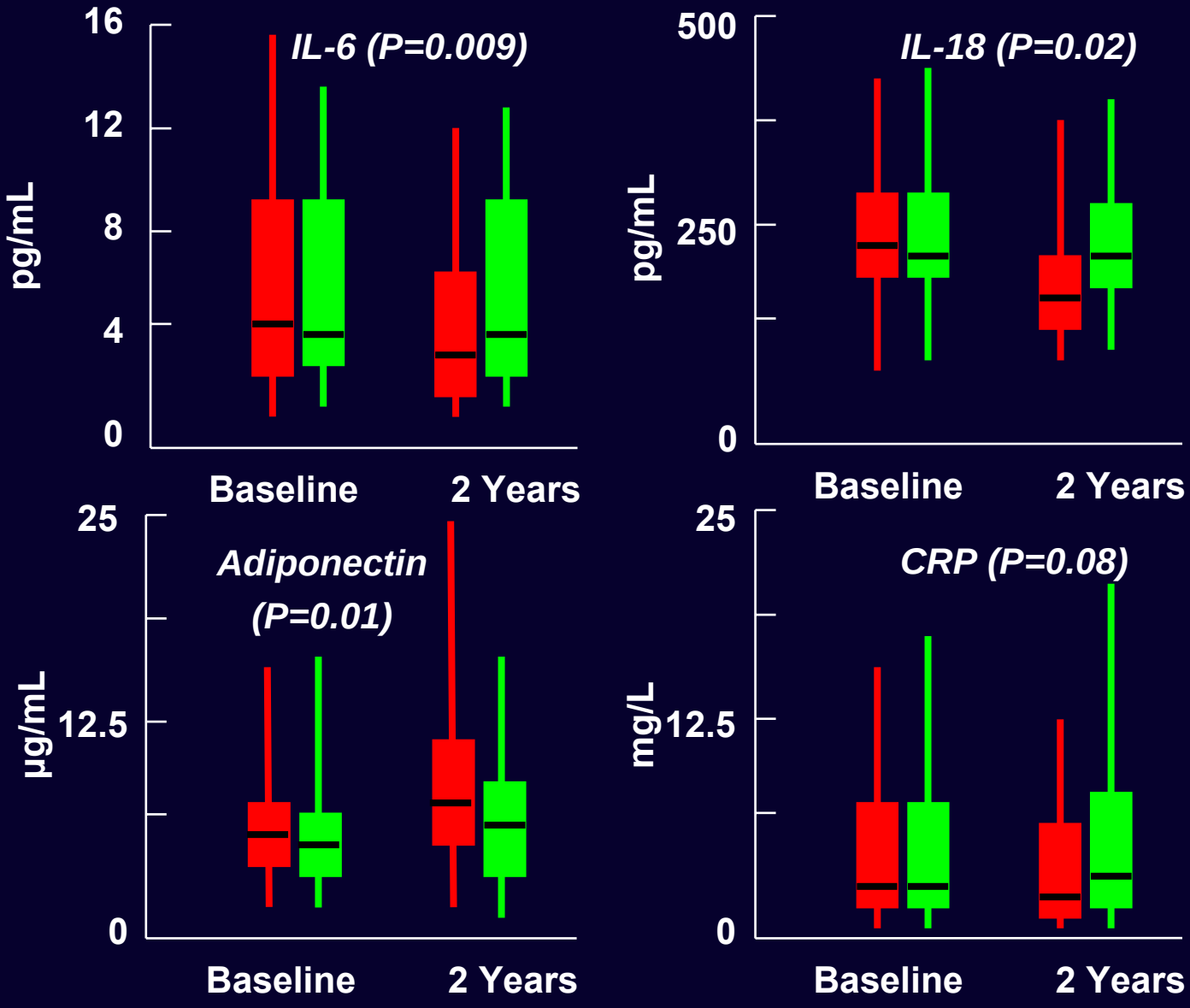
Nim Han S et al J Lipid Res 2002;43:445-52

Age-adjusted geometric means (95% CI) of plasma concentrations of biomarkers of inflammation and endothelial dysfunction by quintiles of trans fatty acid intake in the Nurses Health Study

Quintile	*n*	CRP *mg/L*	IL-6 *ng/L*	sTNFR-2 *μg/L*	E-selectin *ng/L*	sICAM-1 *μg/L*	sVCAM-1 *μg/L*
Trans fatty acids, (*range: g/d*)							
Q1 (0.61–1.87)	147	1.1 (0.9, 1.3)	1.8 (1.6, 2.0)	2339 (2176, 2515)	41.8 (39.0, 44.9)	238 (229, 247)	504 (484, 525)
Q2 (1.88–2.26)	145	1.3 (1.1, 1.6)	1.7 (1.5, 2.0)	2136 (1986, 2298)	41.9 (39.0, 45.0)	246 (236, 256)	520 (499, 542)
Q3 (2.27–2.64)	146	1.5 (1.3, 1.8)	1.8 (1.6, 2.0)	2259 (2102, 2429)	41.9 (39.0, 45.0)	242 (232, 252)	537 (515, 559)
Q4 (2.65–3.13)	146	1.7 (1.4, 2.0)	1.9 (1.7, 2.2)	2338 (2175, 2514)	45.1 (42.0, 48.4)	253 (243, 263)	523 (502, 545)
Q5 (3.14–7.58)	146	1.9 (1.6, 2.3)	2.1 (1.8, 2.3)	2466 (2294, 2651)	50.3 (46.8, 54.0)	261 (251, 272)	556 (533, 579)
P for trend[2]		<0.001	0.02	0.04	<0.001	<0.001	0.004

Lopez-Garcia E et al J Nutr 2005;135:562-6

Serum concentrations of cytokines and CRP at baseline and 2 Years



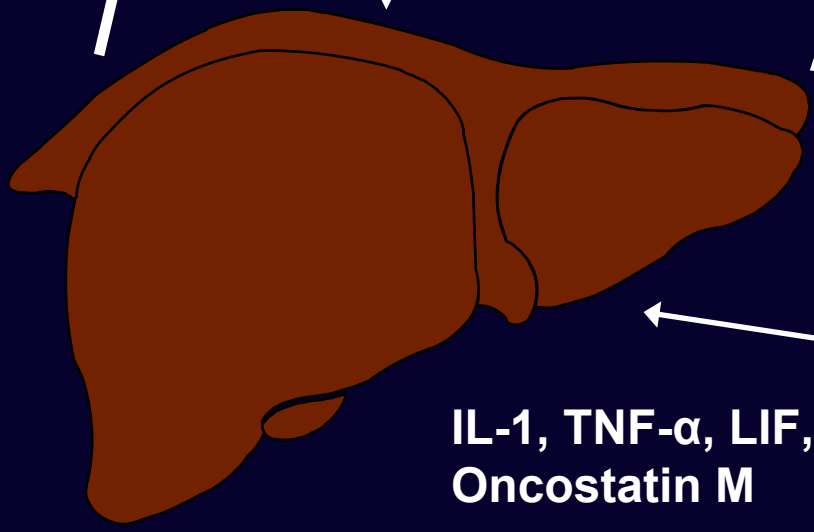
Esposito K et al JAMA 2003;289:1799-1804

Tissue factor, activated complement, LDL uptake

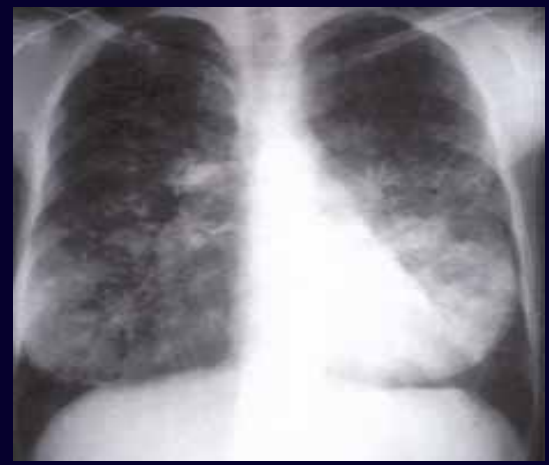
CRP

IL-6, IL-1

IL-6, TNF-α



IL-1, TNF-α, LIF, LPS, Oncostatin M



Infection

Clinical trials

Study	Design	Intervention	Absolute risk reduction (%)	Relative risk reduction (%)
DART	Randomized controlled, 2 year follow-up, 2033 men after MI	Fish meal twice weekly or fish oil capsules if unable to tolerate fish (1.5 g/d)	3.7	32.5
Indian Experiment of Infarct Survival	Randomized double-blind placebo-controlled, 1 year follow-up, 360 patients after MI	Fish oil (EPA + DHA 1.8 g/d) or mustard seed oil (ALA 2.9 g/d)	10.6	48.2
GISSI	Randomized, controlled, 3.5 year follow-up, 11324 patients after MI	Fish oil (EPA + DHA 0.85 g/d)	2	29.7

Inflammatory markers and fish consumption: the ATTICA Study

	Fish consumption				
	No	< 150 g/w	150–300 g/w	> 300 g/w	P ⊥
N (%)	319 (11%)	1719 (56%)	745 (24%)	259 (9%)	-
CRP (mg/L)	2.7±1.2	2.0±1.1**	2.0±2.1**	1.8±1.1**	0.004
IL – 6 (ng/ml)	1.5±0.5	1.3±0.6*	1.2±1.1**	1.0±0.3**	0.03
TNF–α (mg/dl)	5.3±3	5.1±2	4.7±3**	4.2±2**	< 0.001
Amyloid A (mg/dl)	6.4±4	5.9±4	5.1±4*	4.6±3**	0.004

No gender differences were observed.

* P < 0.05 and ** P < 0.01 (Bonferroni corrected) for the differences between fish consumption groups vs. no consumption. Probability values derived from the ANOVA test.

⊥ P – values derived from ANOVA test that evaluated the associations between inflammatory markers (dependent) and fish intake (independent factor).

Zampelas A et al J Am Coll Cardiol 2005

Linoleic acid **(18:2 ω-6)**

(vegetable oils, seeds)

Δ_6 Desaturase

γ-linolenic acid (18:3 ω-6)

arachidonic acid (20:4 ω-6)

(meat)

Eicosanoids from ω-6

Thromboxane A_2 (pro-aggregatory)

Leukotriene B_4 (promotes aggregation of leukocytes)

α-linolenic acid (18:3 ω-3)

(legumes, leafy vegetables, flaxseed oil)

Δ_6 Desaturase

eicosapentaenoic acid (20:5 ω-3)

(fish oils)

docosahexaenoic acid (22:6 ω-3)

(fish oils)

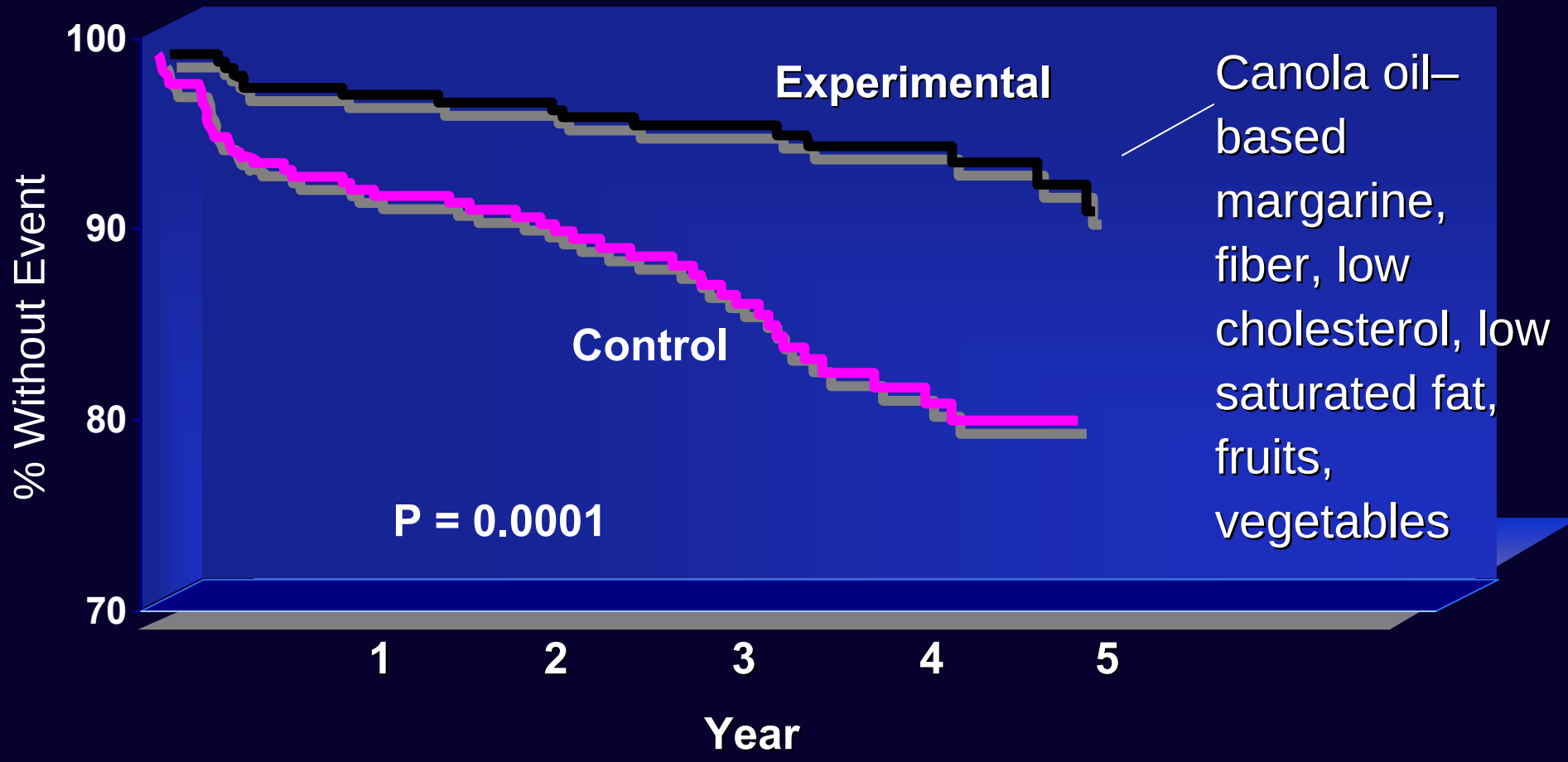
Eicosanoids from ω-3

Prostacycline (anti-aggregatory)

Thromboxane A_3 (less active)

Leukotriene B_5 (< 5-10% active compared to B_4)

Lyon Diet Heart Study: Cumulative Survival without Cardiac Death and Nonfatal MI



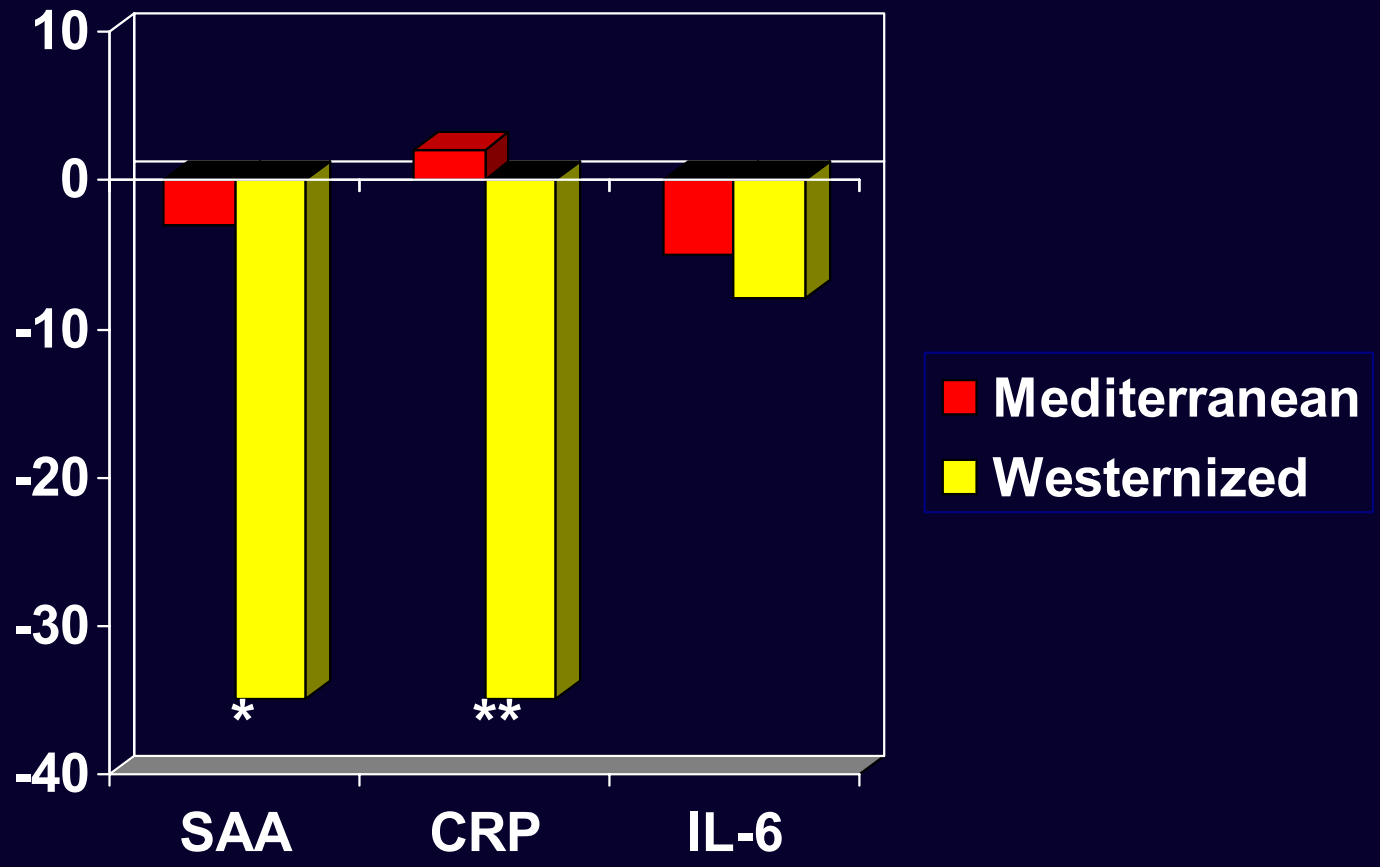
de Lorgeril M et al Circulation 1999;99:779-85

Inflammatory markers before and after the intervention in the ALA and LA groups (values of inflammatory markers are expressed as median and 25th and 75th percentile)

Variables	At the beginning of the intervention	At the end of the intervention	P value
ALA group (n=50)			
CRP (mg/L)	1.24 (0.72-3.70)	0.93 (0.56-1.80)	0.0008
SAA (mg/L)	3.24 (2.30-5.30)	2.39 (1.70-3.90)	0.0001
IL-6 (pg/ml)	2.18 (1.35-3.90)	1.70 (1.30-2.80)	0.01
LA group (n=26)			
CRP (mg/L)	1.54 (0.62-3.10)	1.25 (0.64-1.70)	0.35
SAA (mg/L)	3.52 (2.10-4.90)	3.34 (2.15-4.40)	0.58
IL-6 (pg/ml	1.77 (1.30-2.70)	2.20 (1.10-2.70)	0.69

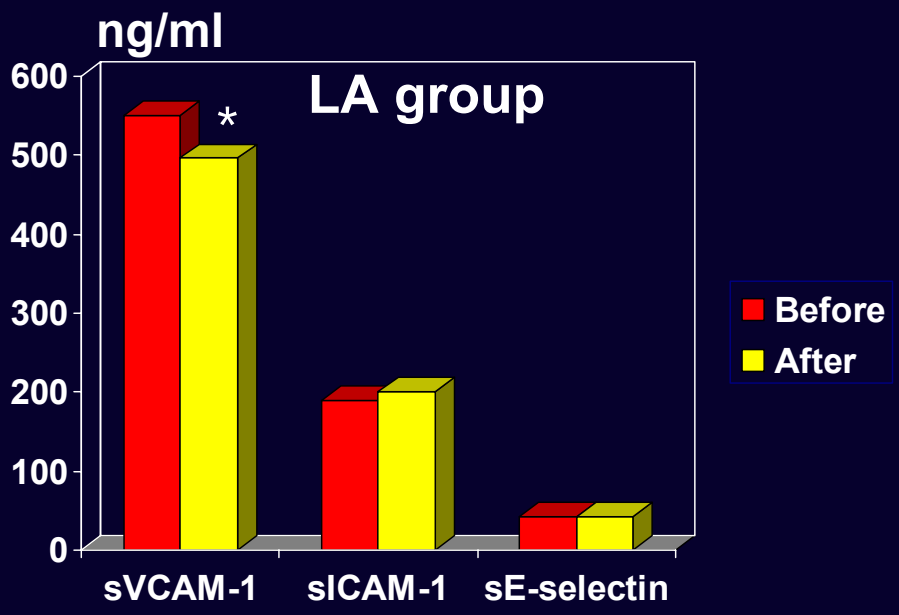
Rallidis L et al Atherosclerosis 2003;167:237-42

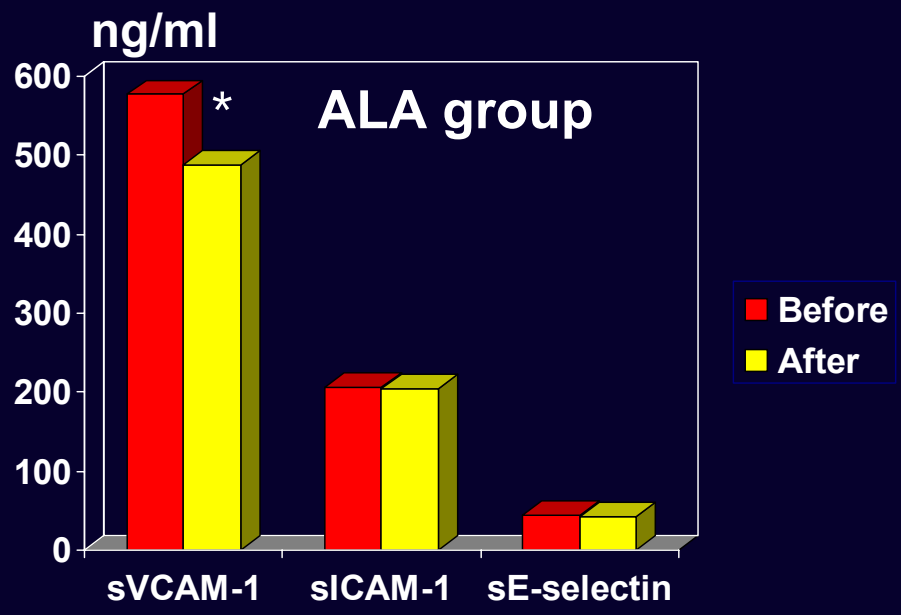
Percentage differences of concentrations of inflammatory markers after α-linolenic acid supplementation of subjects with two different background diets



Paschos G et al Br J Nutr 2004;92:649-55

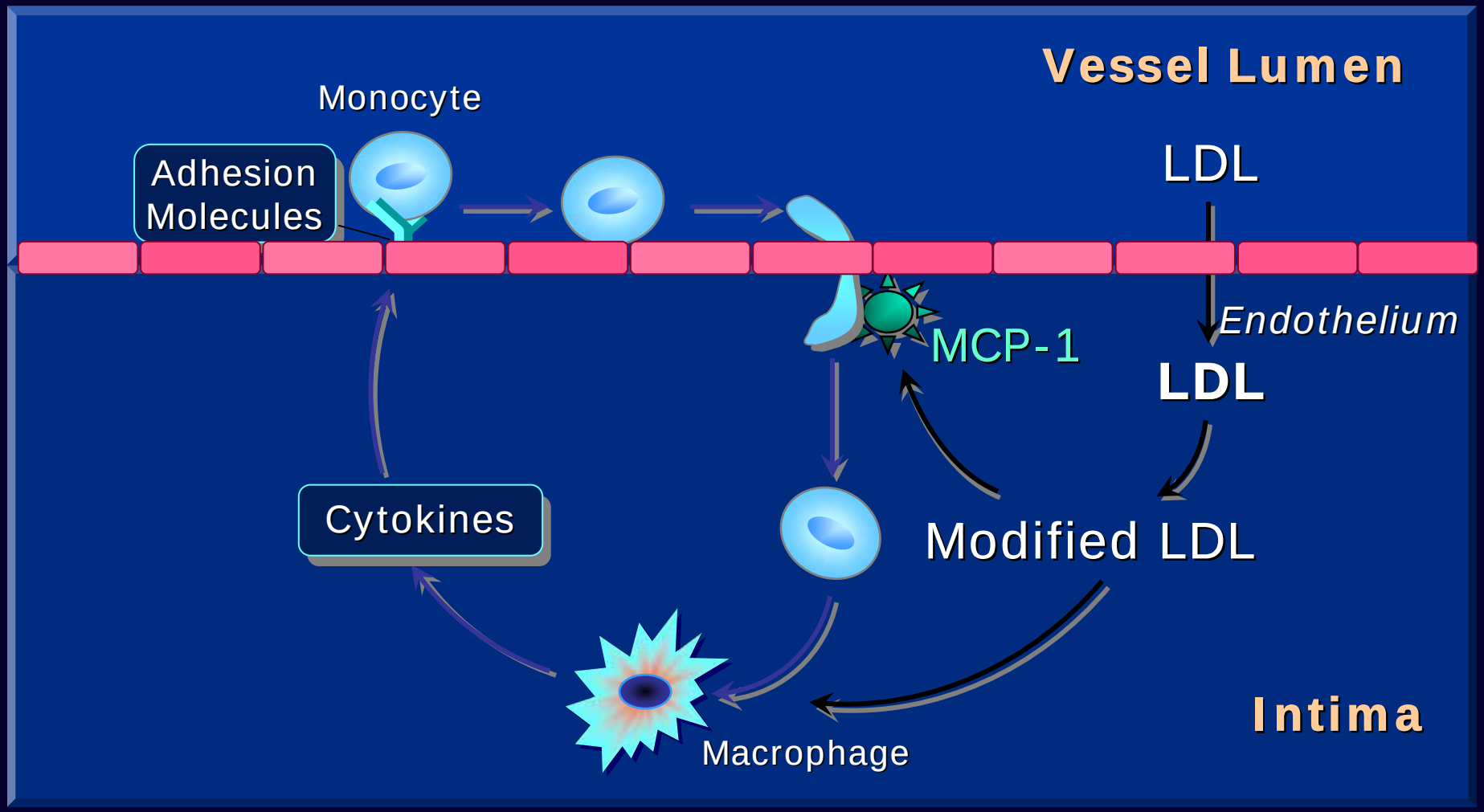
Soluble cellular adhesion molecules before and after 3 month dietary intervention with LA and ALA





Rallidis L et al Atherosclerosis 2004;174:127-32

Modified LDL Induces Macrophages to Release Cytokines That Stimulate Adhesion Molecule Expression in Endothelial Cells



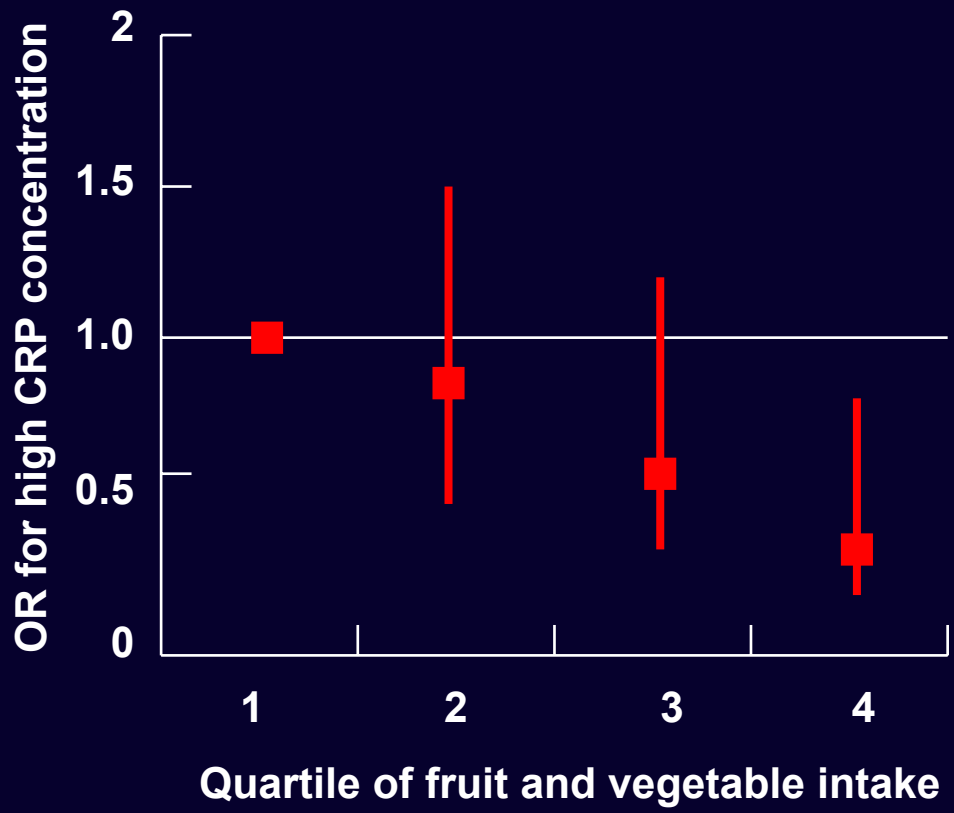
Nathan CF J Clin Invest 1987;79:319-26

Plasma CRP and HCy concentrations of elderly Hispanic and non-Hispanic men and women by quartile of fruit and vegetable intake

	1	2	3	4	*P* for trend
n	149	150	151	149	
CRP (mg/L)	4.8 (1.1)	4.8 (1.0)	4.5 (1.1)	3.9 (1.1)	0.01
Hcy (µmol/L)	11.6 (1.0)	10.8 (1.0)	11.0 (1.0)	10.5 (1.0)	0.03

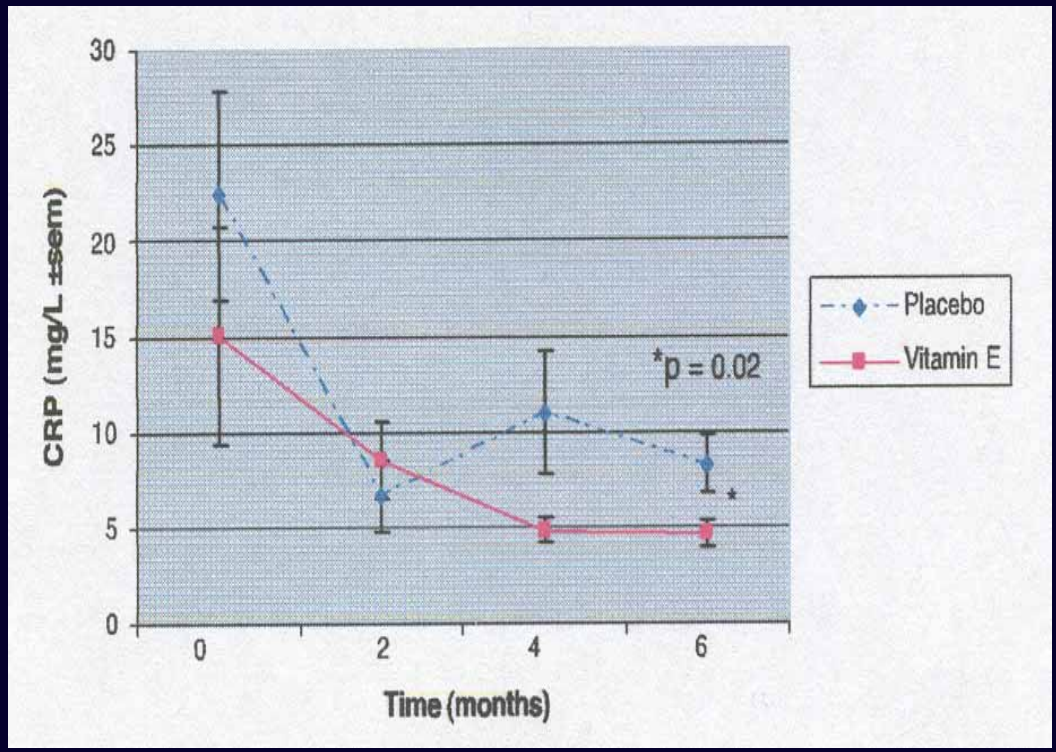
Gao X et al J Nutr 2004;134:913-8

ORs for high plasma CRP (> 10 mg/L) by fruit and vegetable intake



Gao X et al J Nutr 2004;134:913-8

Vitamin E vs placebo: effect on mean CRP levels in smokers at 2, 4 and 6 months



- Randomized, double blind, placebo controlled trial
- 110 patients with ACS
- 400 IU vitamin E for 6 months
- CRP, IL-6, sVCAM-1, sICAM-1, sE-selectin, sP-selectin

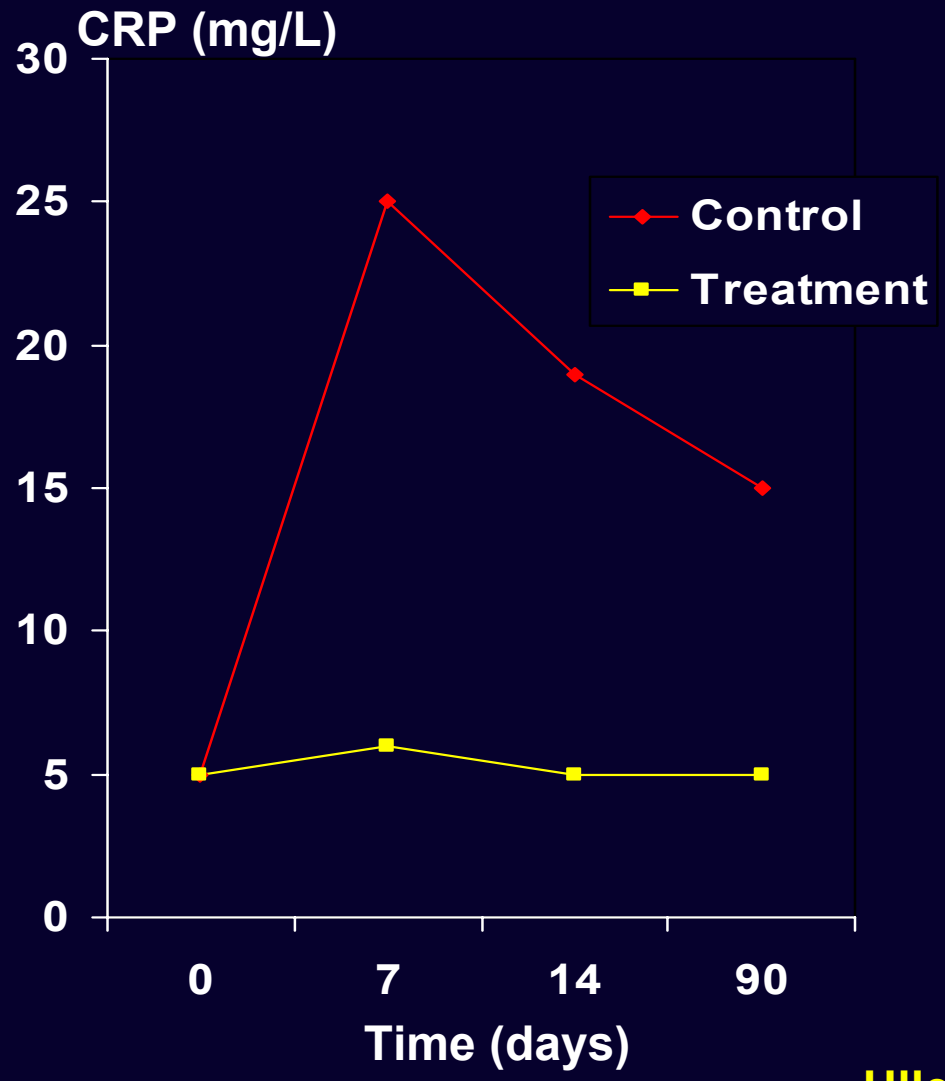
Murphy RT et al Free Rad Biol Med 2004;36:959-65

Plasma TNF-α, IL-6 and CRP in healthy men before and after 3 year of antioxidant supplementation (91 mg (136 IU) α-tocopherol + 250 mg vitamin C) or placebo: The ASAP Study

	n	Intervention	Baseline	After 3 y
TNF-α (ng/L)	54	Vitamin E + C	1.6 (1.0-2.5)	1.4 (0.8-2.0)
	51	Placebo	1.3 (0.8-2.2)	1.1 (0.8-1.8)
IL-6 (ng/L)	54	Vitamin E + C	1.8 (1.2-2.6)	1.5 (1.1-2.8)
	51	Placebo	1.6 (1.1-2.5)	1.5 (1.0-2.3)
CRP (mg/L)	50	Vitamin E + C	1.0 (0.4-2.7)	1.2 (0.3-2.9)
	52	Placebo	1.5 (0.4-3.3)	1.7 (0.5-3.6)

Bruunsgaard H et al J Nutr 2003;133:1170-3

Median CRP concentration over 3 months in the treatment and control groups



- 48 patients with acute ischaemic stroke
- 14 days intervention
- 5 mg folate, 5 mg B2, 50 mg B6, 0.4 mg B12

Ullegaddi R et al Cli Sci 2004;107:477-84

The Supplementation et Vitamines et Mineraux Antioxidants (SU.VI.MAX) Study

- Randomized, double-blind, placebo-controlled primary prevention trial.
- 13017 French adults were included and followed for 7.5 years.
- 120 mg ascorbic acid, 30 mg vitamin E, 6 mg beta carotene, 100 µg selenium and 20 mg zinc.
- No differences between the groups in total cancer incidence, ischaemic cardiovascular disease incidence or all-cause mortality.
- Significant differences in cancer incidence and all cause mortality in men (gender-group interaction)

Hercberg S et al Arch Intern Med 2004;164:2335-42

Effect of a Mediterranean-Style Diet on Endothelial Dysfunction and markers of Vascular Inflammation in the Metabolic Syndrome.

A Randomized Trial

- 24 month randomized, single-blind trial
- Advise to increase grain, fruits, vegetables, nuts and olive oil consumption.
- Significant decreases in CRP, IL-6, IL-8 and IL-18 levels

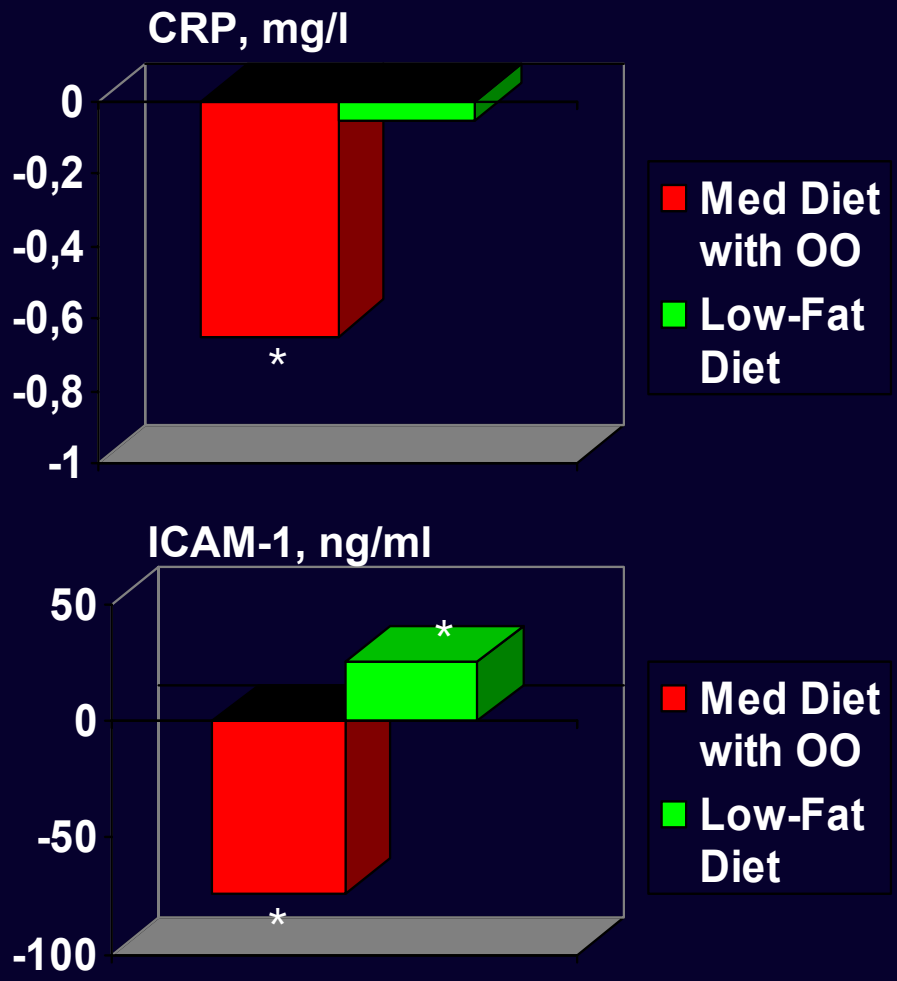
Esposito K et al JAMA 2004;292:1440-6

Changes in Energy and Nutrient Intakes (Substudy of the PREDIMED Study, n=515)

Nutrients	Mediterranean Diet with Olive Oil vs Low-Fat Diet	
	Mean (95% CI) Between-Group Difference	P Value
Energy, kcal	4.5 (-139.0 to 148.0)	0.95
Protein, %	-0.47 (-1.07 to 0.13)	0.122
CHO, %	0.22 (-1.30 to 1.70)	0.84
Fiber, g/d	0.49 (-1.90 to 2.90)	0.69
Total fat, %	0.45 (-1.00 to 1.90)	0.55
SFA, %	-0.09 (-0.55 to 0.36)	0.69
MUFA, %	0.58 (-0.30 to 1.45)	0.198
PUFA, %	0.03 (-0.53 to 0.58)	0.93
LA, g/d	-0.27 (-0.85 to 0.31)	0.76
ALA, g/d	0.03 (-0.32 to 0.25)	0.82
EPA, DHA, g/d	0.11 (-0.26 to 0.04)	0.143
Energy from Olive Oil, %	1.9 (0.55 to 3.20)	0.006
Cholesterol, mg/d	-38 (-152 to 76)	0.27

Estruch R et al Ann Intern Med 2006;145:1-11

Changes from baseline in plasma concentrations of the inflammatory biomarkers



Estruch R et al Ann Intern Med 2006;145:1-11

Conclusions

- Epidemiological studies and one clinical trial indicate that the Mediterranean Dietary Pattern may be anti-inflammatory and Westernized-type or high glycemic load diets are pro-inflammatory
- There is some evidence that total fat intake, saturated fat and trans fatty acids may increase some inflammatory markers
- ω-3 fatty acids are considered to be anti-inflammatory
- There is some evidence to suggest that increased intake of fruits and vegetables is inversely associated with some inflammatory markers
- There is no clear role of vitamins