

A review of recent evidence on dietary factors in Coronary Heart Disease Prevention

Antonis Zampelas

Associate Professor in Human Nutrition

Member of the Executive Committee of the European Atherosclerosis Society

**Unit of Human Nutrition, Department of Food Science and Technology,
Agricultural University of Athens, Greece**

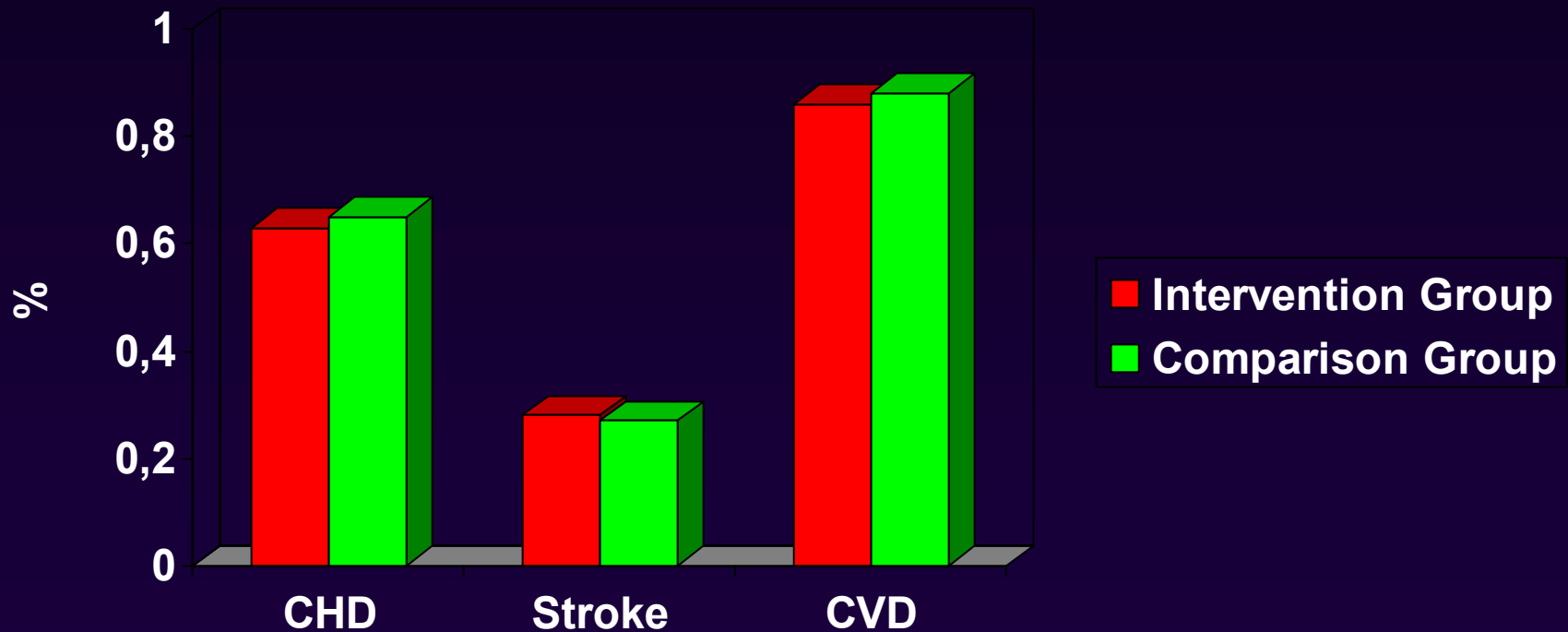
Low fat dietary pattern and risk of CVD: the Women's Health Initiative Randomized Controlled Modification Trial (n=48835)

	Intervention Year 1	Comparison Year 1	Difference between groups Year 6
Fat			
<i>% Energy</i>	24.3	35.1	-8.1
<i>SFA %</i>	8.1	11.8	-2.9
<i>PUFA %</i>	5.2	7.2	-1.4
<i>MUFA %</i>	8.9	13.3	-3.3
Cholesterol (mg/d)	172	229	-50
Dietary Fiber (g/d)	18	15	2.4
Energy (kcal/d)	1500	1593	-119
Consumption per day			
<i>Fruits and vegetables</i>	5.1	3.9	1.1
<i>Grains</i>	5.1	4.2	0.4
<i>Fiber</i>	18.1	14.9	2.4

Differences between the mean changes in cardiovascular disease risk factors from baseline to year 3 in the Intervention vs the Comparison Group (n=5.8% of the sample)

Risk Factor	Baseline Mean (SD)		Year 3, Mean (SD)	
	Intervention	Comparison	Intervention	Comparison
<i>Clinical Values</i>				
Weight, kg	76.8	76.7	75.7*	76.7
BMI	29.1	29.1	28.8*	29.2
Systolic BP	127.5	127.9	125.1	125.7
Diastolic BP	75.9	76.0	73.1*	73.6
<i>Lab Values</i>				
Total chol	224	224	214*	216
LDL-C	133	134	123*	127
HDL-C	60	58	60	58
TG	138	141	142	144

Percentage of subjects who developed CHD, stroke and CVD after 6 years of dietary intervention



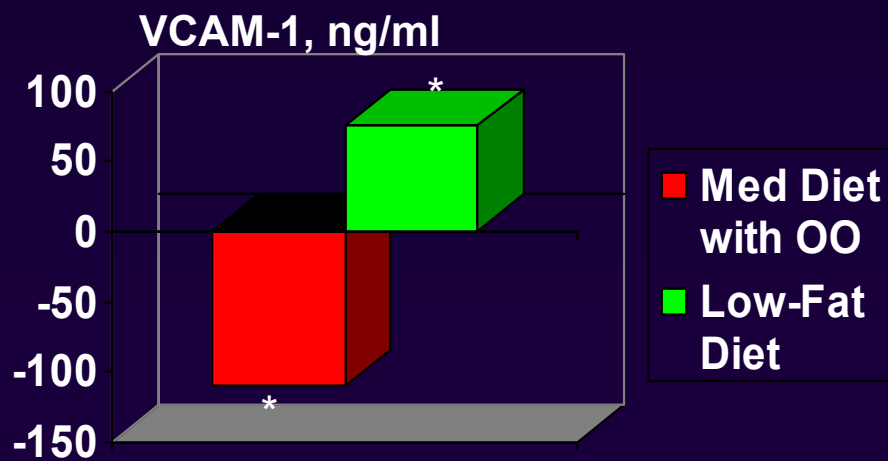
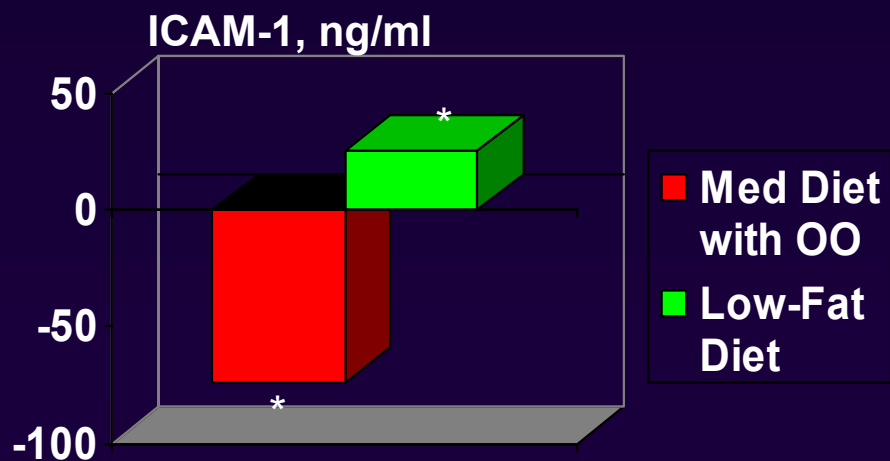
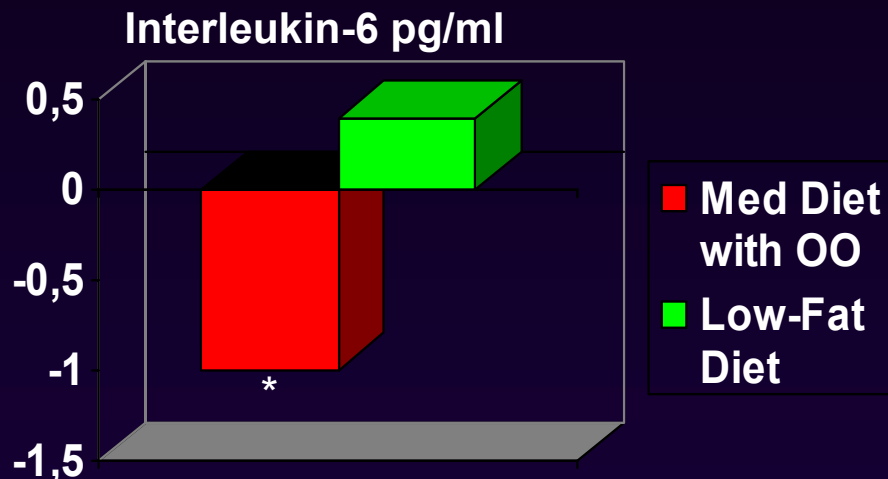
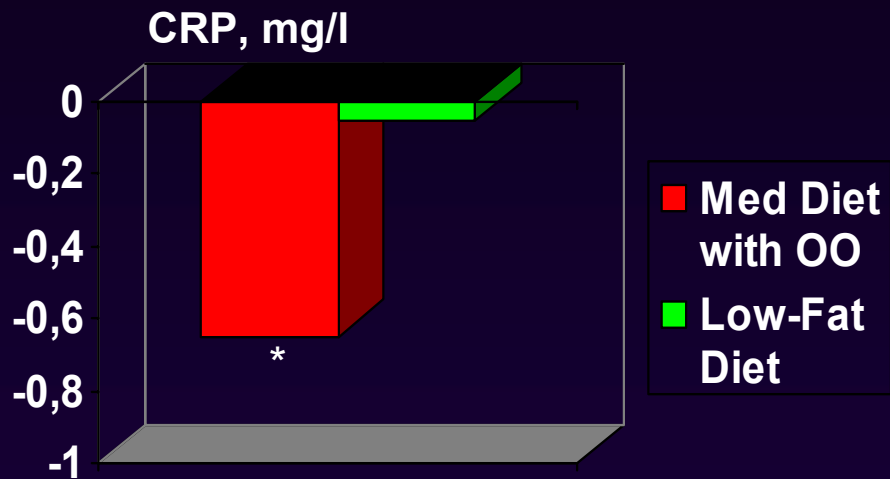
Changes in Energy and Nutrient Intakes (Substudy of the PREDIMED Study, n=515)

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

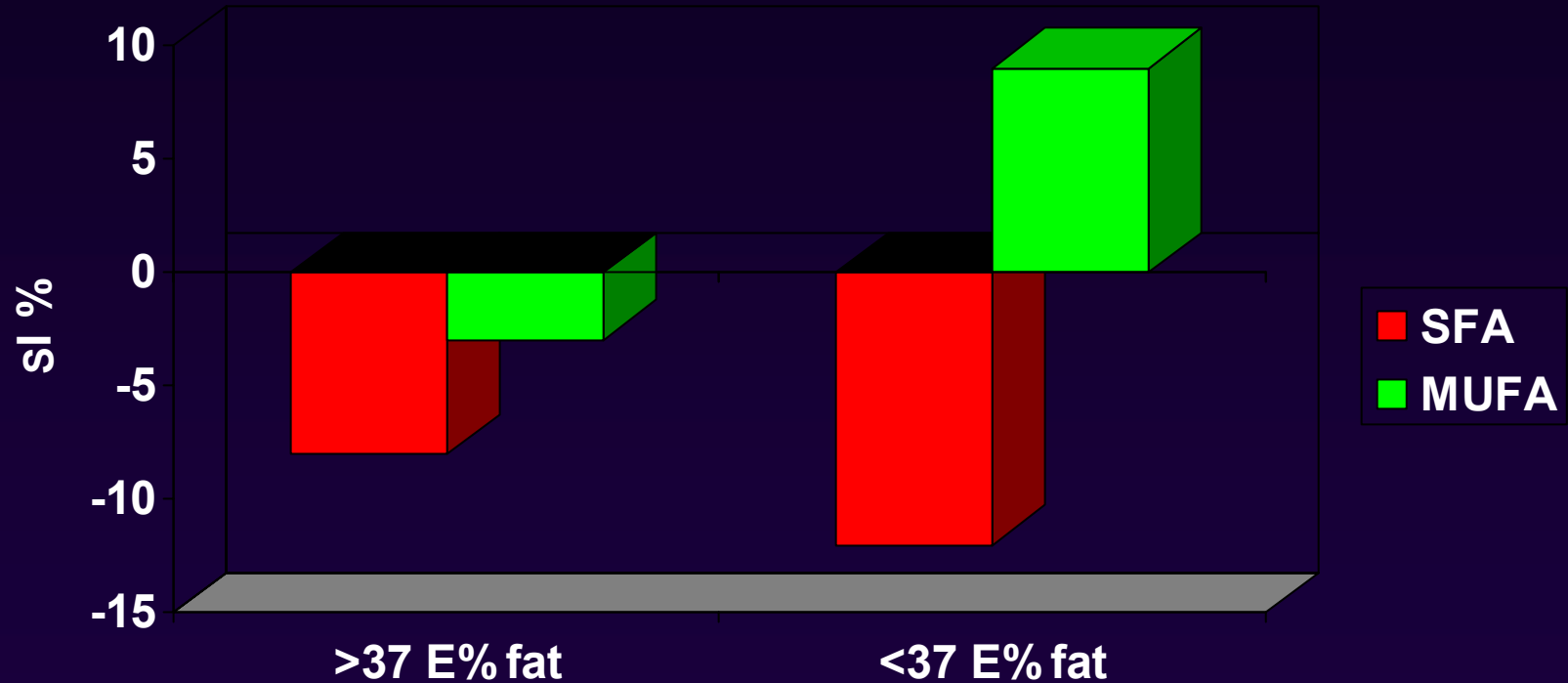
Changes in Adiposity, Blood Pressure, and Cardiovascular Risk Factors

Variable	Mediterranean Diet with Olive Oil vs Low-Fat Diet	
	Mean (95% CI) Between-Group Difference	P Value
Weight, kg	0.01 (-0.39 to 0.42)	0.96
BMI, kg/m ²	0.09 (-0.12 to 0.29)	0.40
Systolic BP	-5.9 (-8.7 to -3.1)	< 0.001
Diastolic BP	-1.60 (-3.00 to -0.01)	0.048
Glucose, mg/dl	-7.0 (-13.0 to -1.3)	0.017
Insulin, pmol/l	-16.7 (-27.1 to -0.4)	0.001
Cholesterol, mg/dl	-3.5 (-9.5 to 2.6)	0.26
LDL-C, mg/dl	-3.9 (-9.5 to 1.7)	0.177
HDL-C, mg/dl	2.9 (1.7 to 4.0)	< 0.001
Triglycerides, mg/dl	-7.1 (-18.0 to 3.9)	0.21
Cholesterol-HDLC ratio	-0.38 (-0.55 to -0.22)	<0.001

Changes from baseline in plasma concentrations of the inflammatory biomarkers



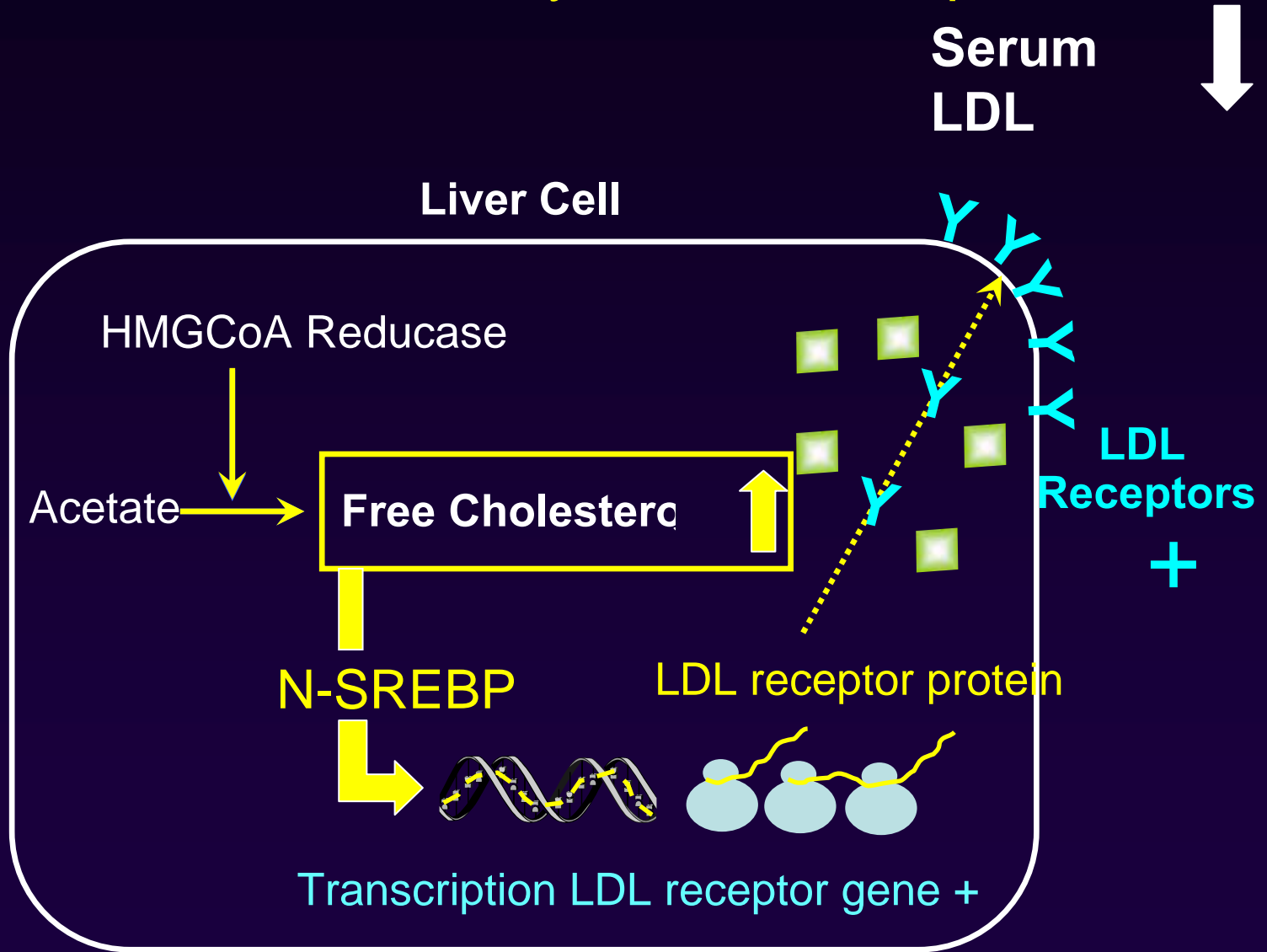
Effects of a change of dietary fat quality on insulin sensitivity when related to total dietary fat intake during treatment



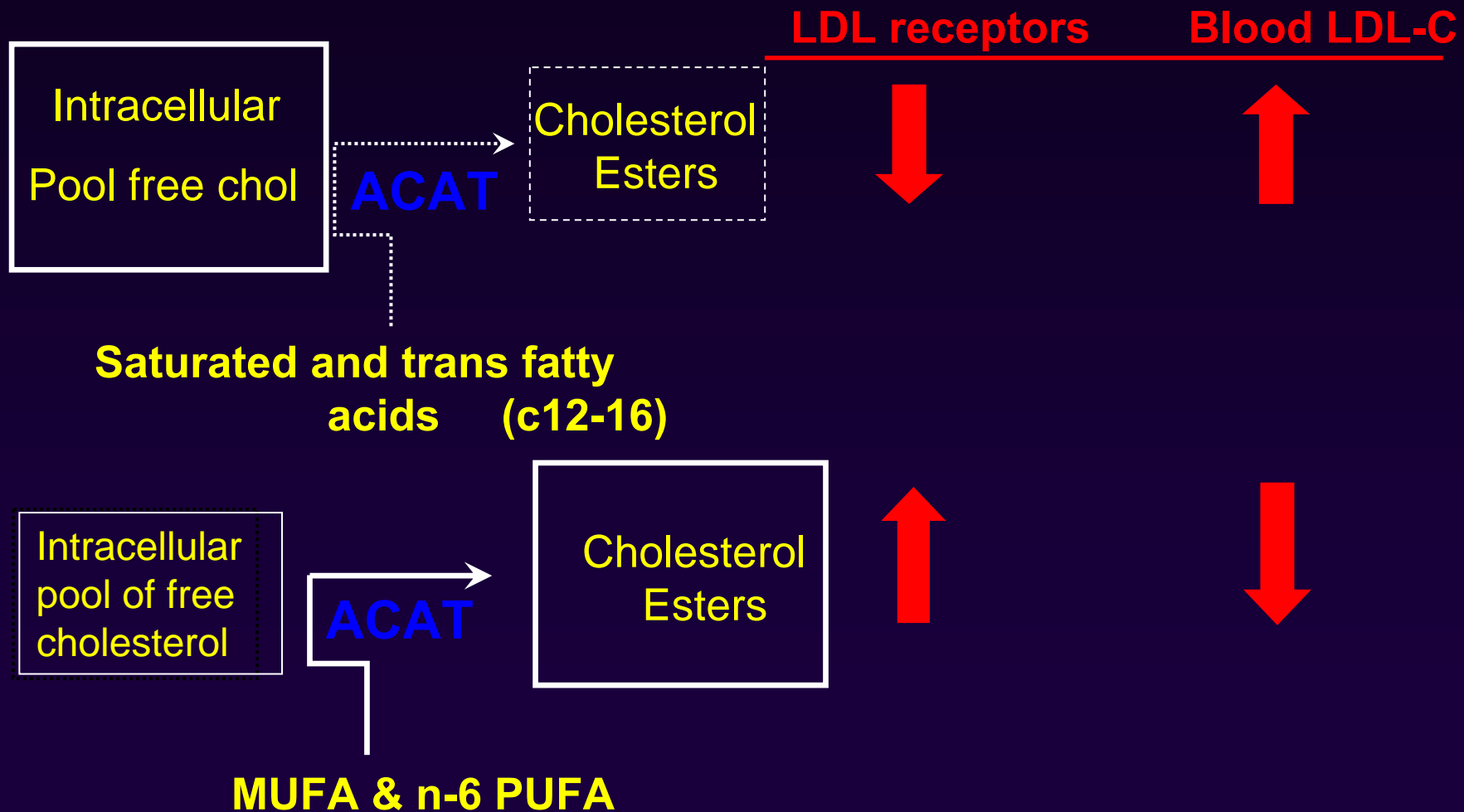
Trial	Subjects in the intervention group	Dietary intervention	Dietary fat (% energy) in the treatment group	P:S ratio in the treatment group	Duration (yrs)	Changes in TC	Changes in CHD
Finish Mental Hospital	424 M most had no evidence of existing heart disease	PUFA	35%	1.5	6	-15%	-43%
Los Angeles Veteran	206 MI M patients	PUFA	40%	NR	8	-13%	-31%
Oslo Diet Heart Study	199 MI M patients	PUFA	39%	2.4	5	-14%	-25%
MRC soy oil	4,393 M, 4,664 F	PUFA	46%	2.0	4	-16%	-12%
Minnesota Coronary Survey	204 MI primarily males	PUFA	38%	1.6	4.5	-14%	No change

Hu FB et al J Am Coll Nutr 2001;20:5-19

Serum Cholesterol Regulated by Intracellular Free Cholesterol & Activity of LDL Receptors



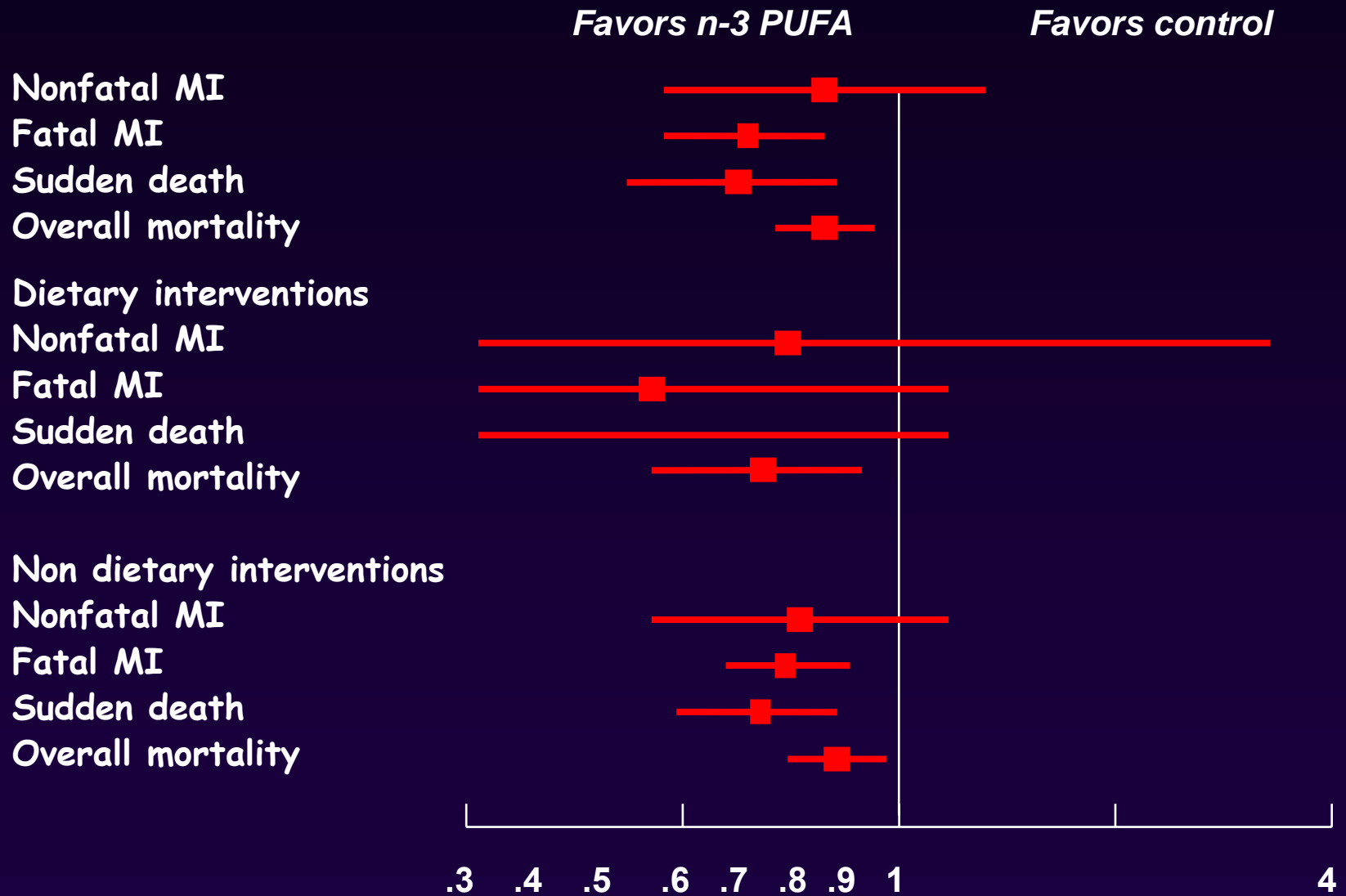
Dietary Fatty Acids Influence Serum Cholesterol through Differential Effects on Free Cholesterol & LDL Receptor Activity



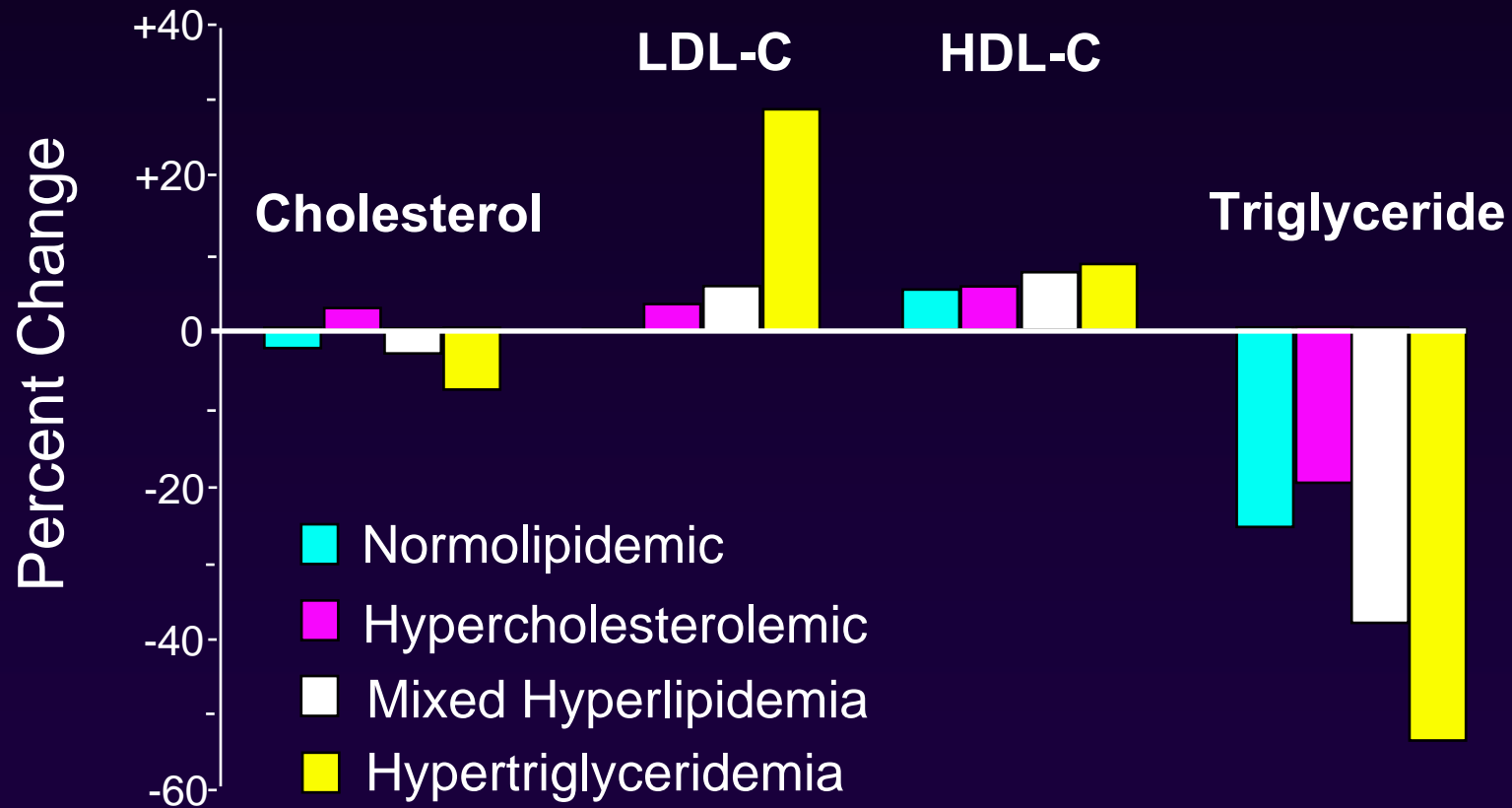
Overall relative risk (RR) of Coronary Heart Disease (CHD) Associated With Fish Consumption Categorized by Level

Portions of Fish/week	Fatal CHD			Total CHD		
	No. Study	RR (95% CI)	P value	No. Study	RR (95% CI)	P value
Any	13	0.83(0.76-0.90)	< 0.005	12	0.86(0.81-0.92)	< 0.005
< 2	9	0.83(0.75-0.92)	<0.005	7	0.85(0.80-0.91)	< 0.005
2-<4	11	0.75(0.62-0.92)	< 0.01	9	0.83(0.69-0.99)	< 0.05
≥ 4	5	0.84(0.63-1.10)	<0.15	7	0.84(0.70-1.01)	< 0.10

Pooled risk ratios and 95% confidence intervals for the different endpoints in randomized controlled trials of dietary and non dietary supplementation with n-3 fatty acids versus control or placebo



Effects of Fish-Oil on Blood Lipids & Lipoproteins



Adapted from Harris, J Lipid Res 1989;30:785-807

Inflammatory markers and fish consumption: the ATTICA Study

	Fish consumption				P [⊥]
	No	< 150 g/w	150–300 g/w	> 300 g/w	
N	319	1719	745	259	-
(%)	(11%)	(56%)	(24%)	(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

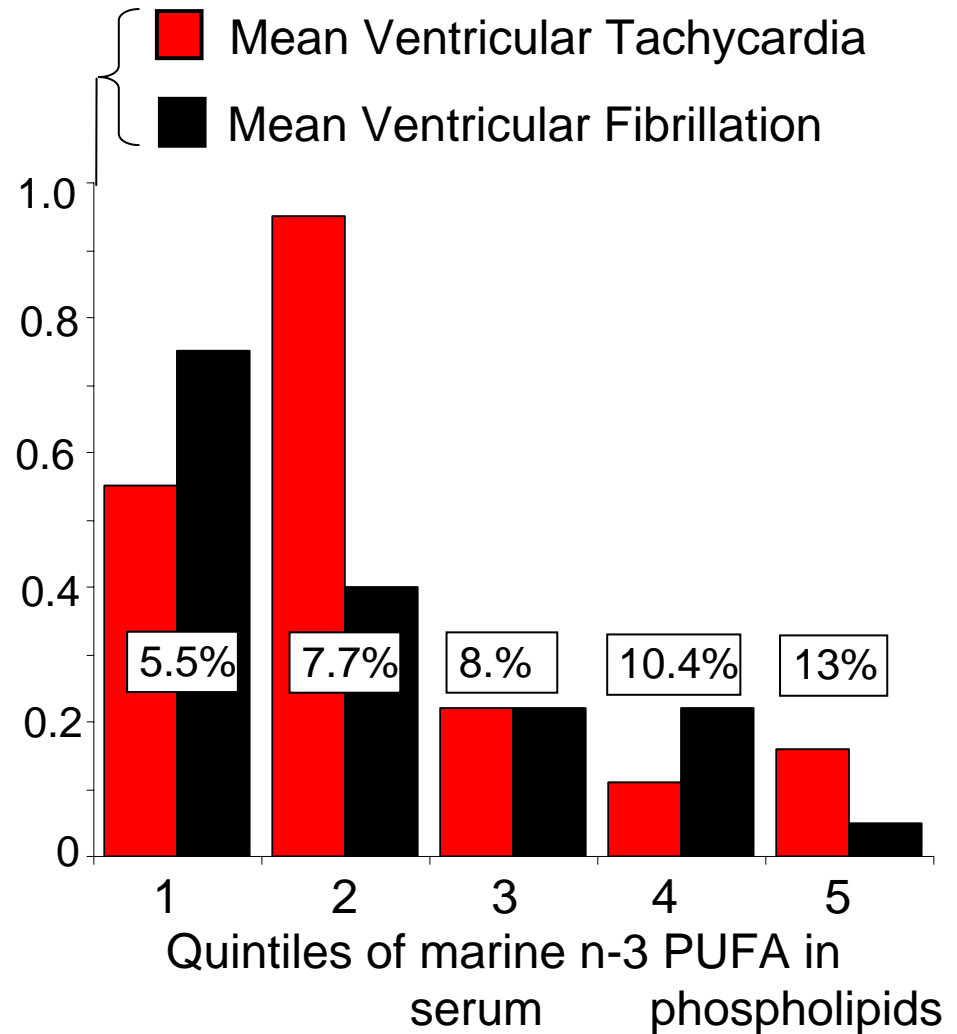
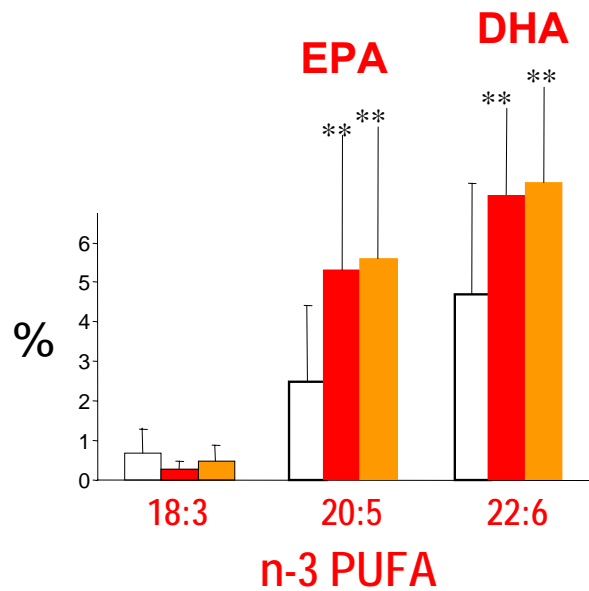
No gender differences were observed.

* 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.

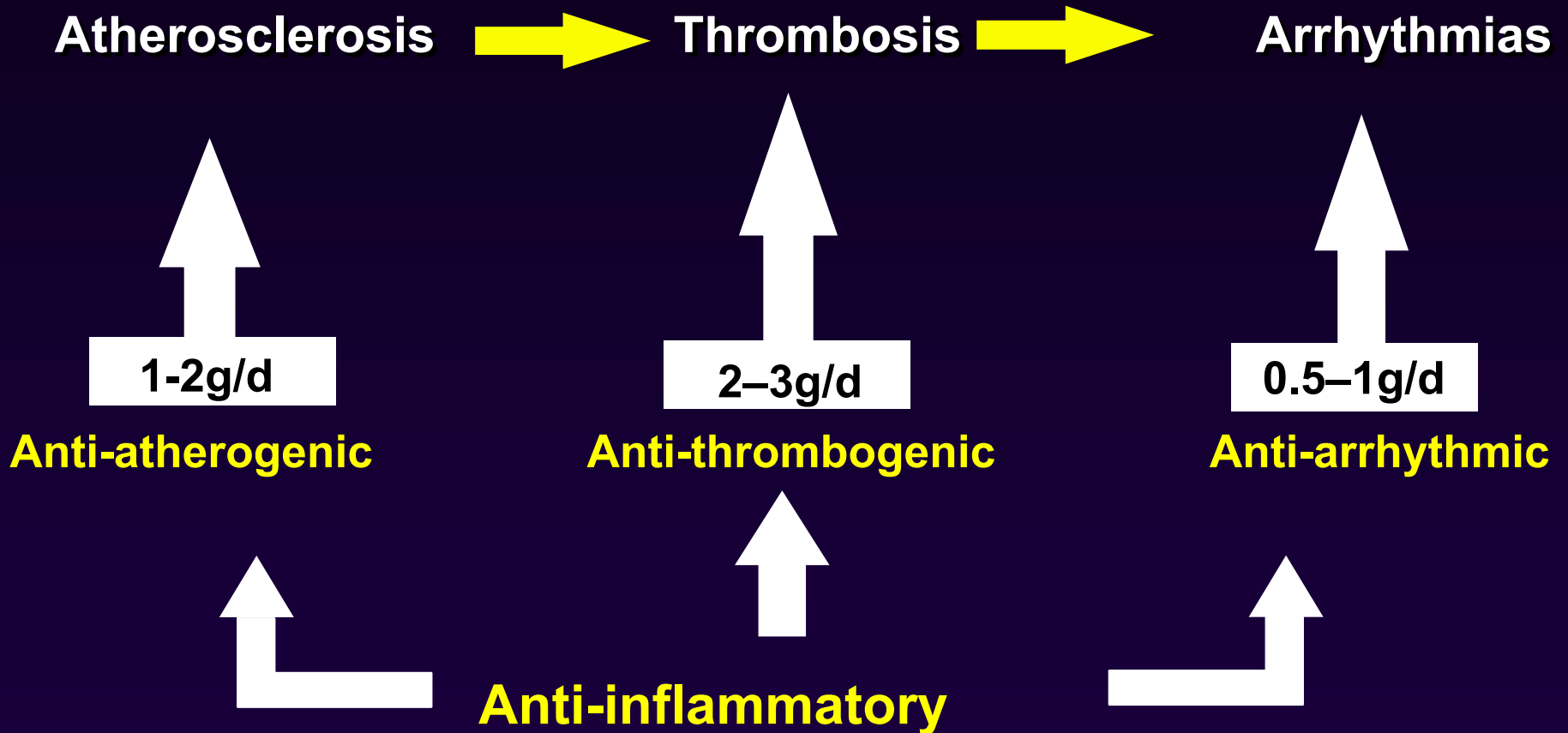
⊥ P – values derived from ANOVA test that evaluated the associations between inflammatory markers (dependent) and fish intake (independent factor).

Dietary and Erythrocyte Membrane EPA /DHA and Anti-arrhythmic Actions of Fish Oil in Humans

Erythrocyte membrane EPA & DHA after 6 ■ and 12 ■ weeks of fish-oil supplementation 3g/d



Manifestations of Cardiovascular Disease (CVD)



Effects of n-3 fatty acids are dose dependent

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

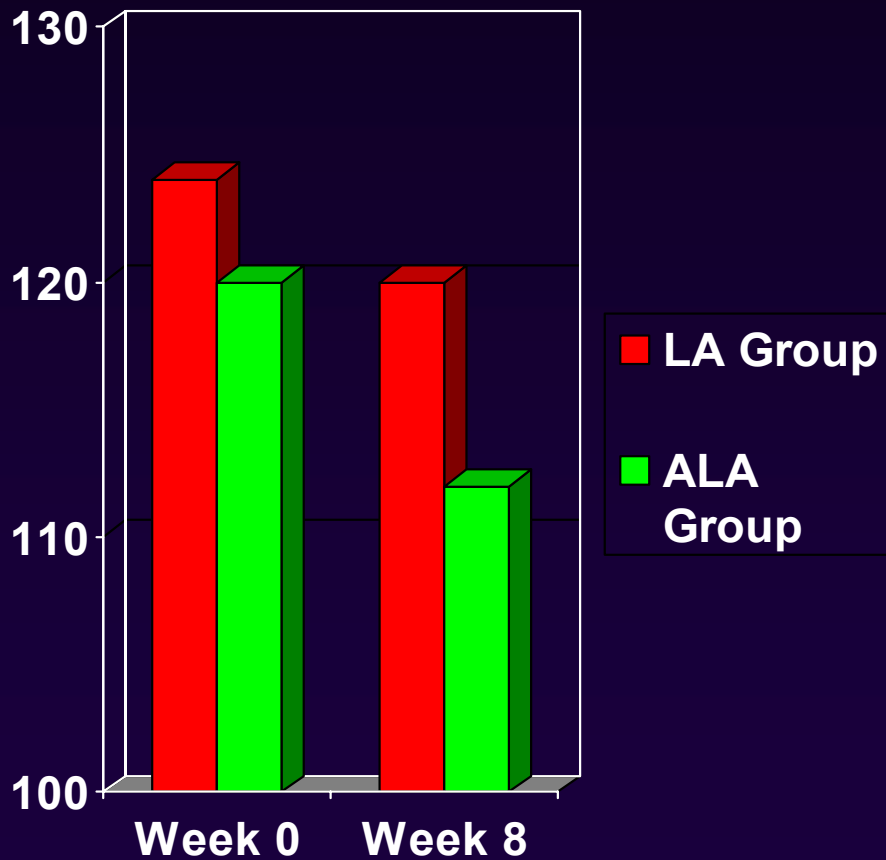
Prostacycline (anti-aggregatory)
Thromboxane A_3 (less active)
Leukotriene B_5 (< 5-10% active compared to B_4)

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)

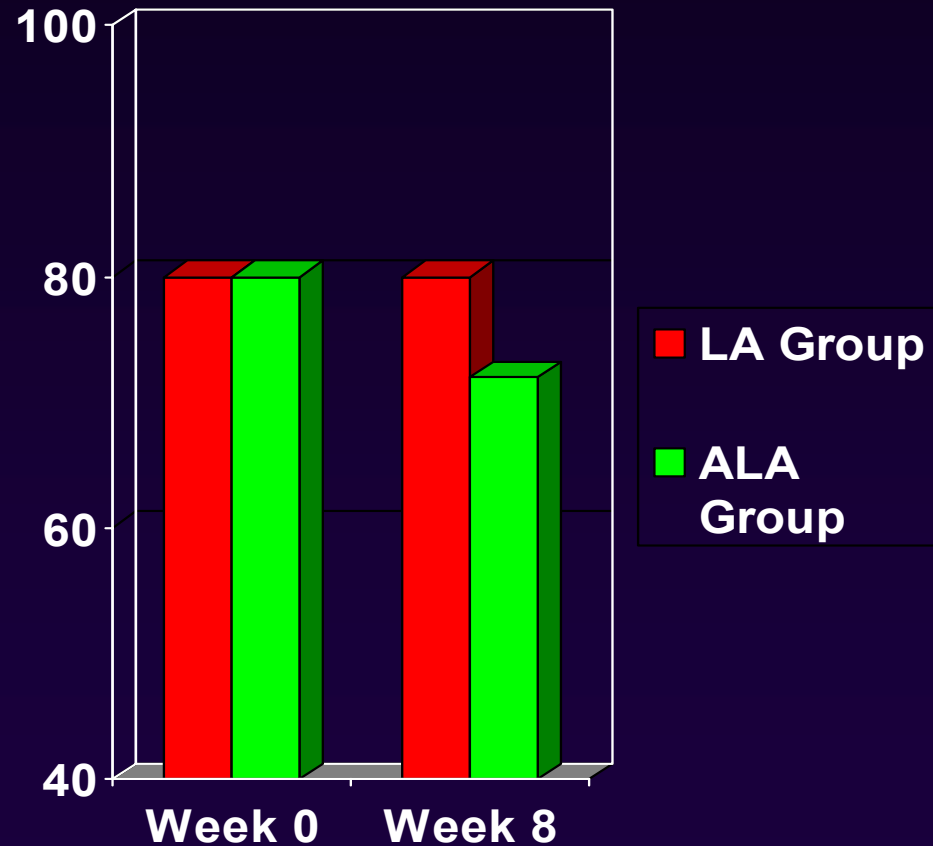
Variables	At the beginning of the intervention	At the end of the intervention	P value
ALA group (n=50)			
CRP (mg/L)	1.24 (0.72-3.70)	0.93 (0.56-1.80)	0.0008
SAA (mg/L)	3.24 (2.30-5.30)	2.39 (1.70-3.90)	0.0001
IL-6 (pg/ml)	2.18 (1.35-3.90)	1.70 (1.30-2.80)	0.01
LA group (n=26)			
CRP (mg/L)	1.54 (0.62-3.10)	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

Effects of flaxseed supplementation on blood pressure in dyslipidemic patients

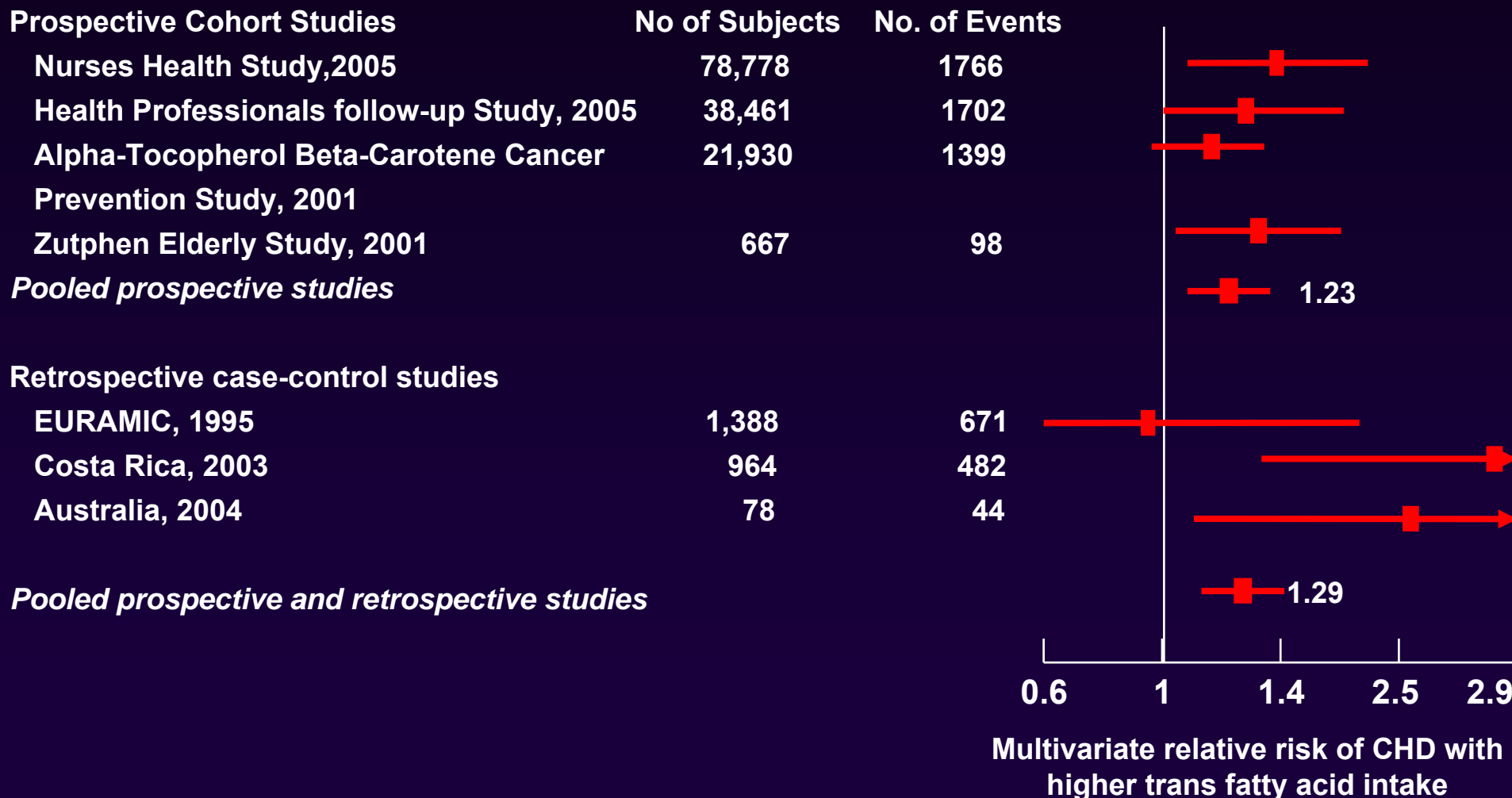
Systolic (mm Hg)



Diastolic (mm Hg)



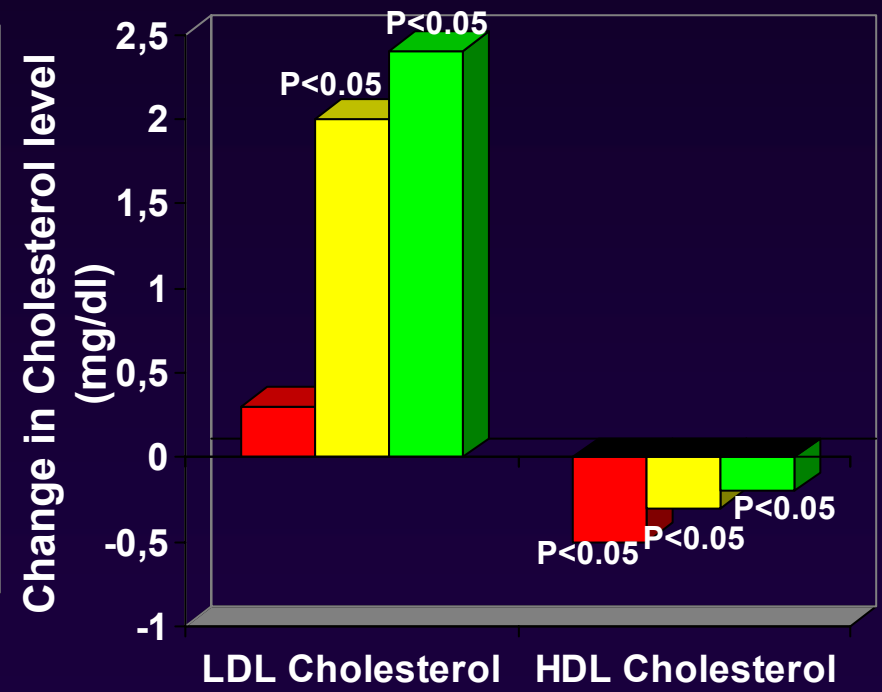
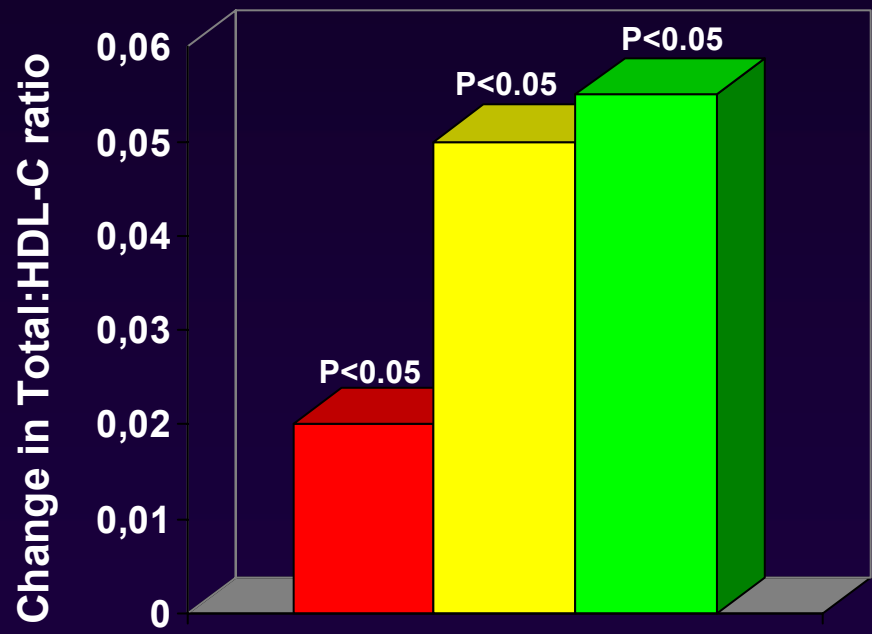
Multivariate adjusted relative risk of CHD associated with trans fatty acid intake



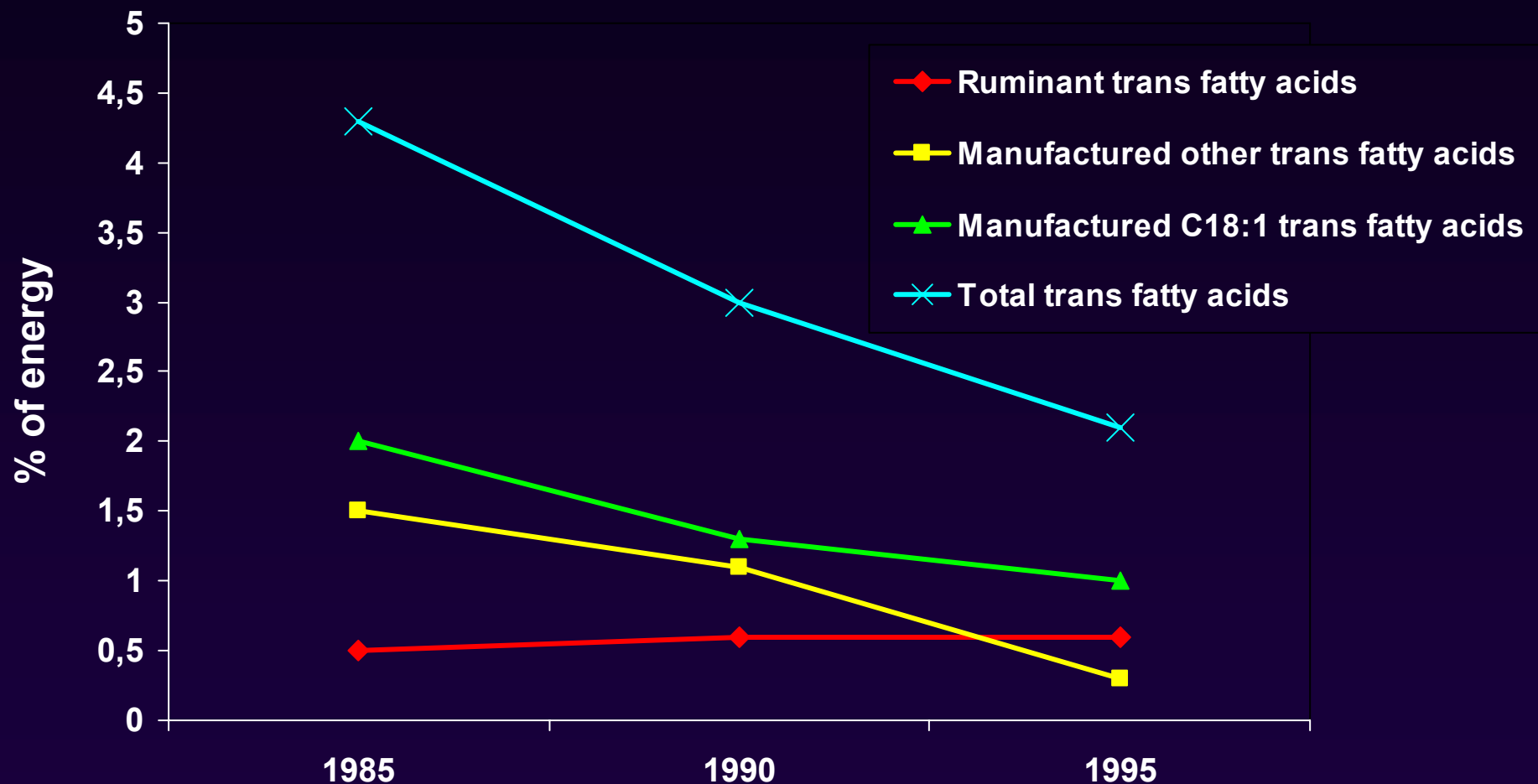
Changes in Total:HDL-C and levels of LDL and HDL cholesterol resulting from the replacement of saturated (1% of total energy intake) or cis unsaturated fatty acids with Trans Fatty Acids

- Replacing SFA with trans
- Replacing cis MUFA with trans
- Replacing cis PUFA with trans

- Replacing SFA with trans
- Replacing cis MUFA with trans
- Replacing cis PUFA with trans

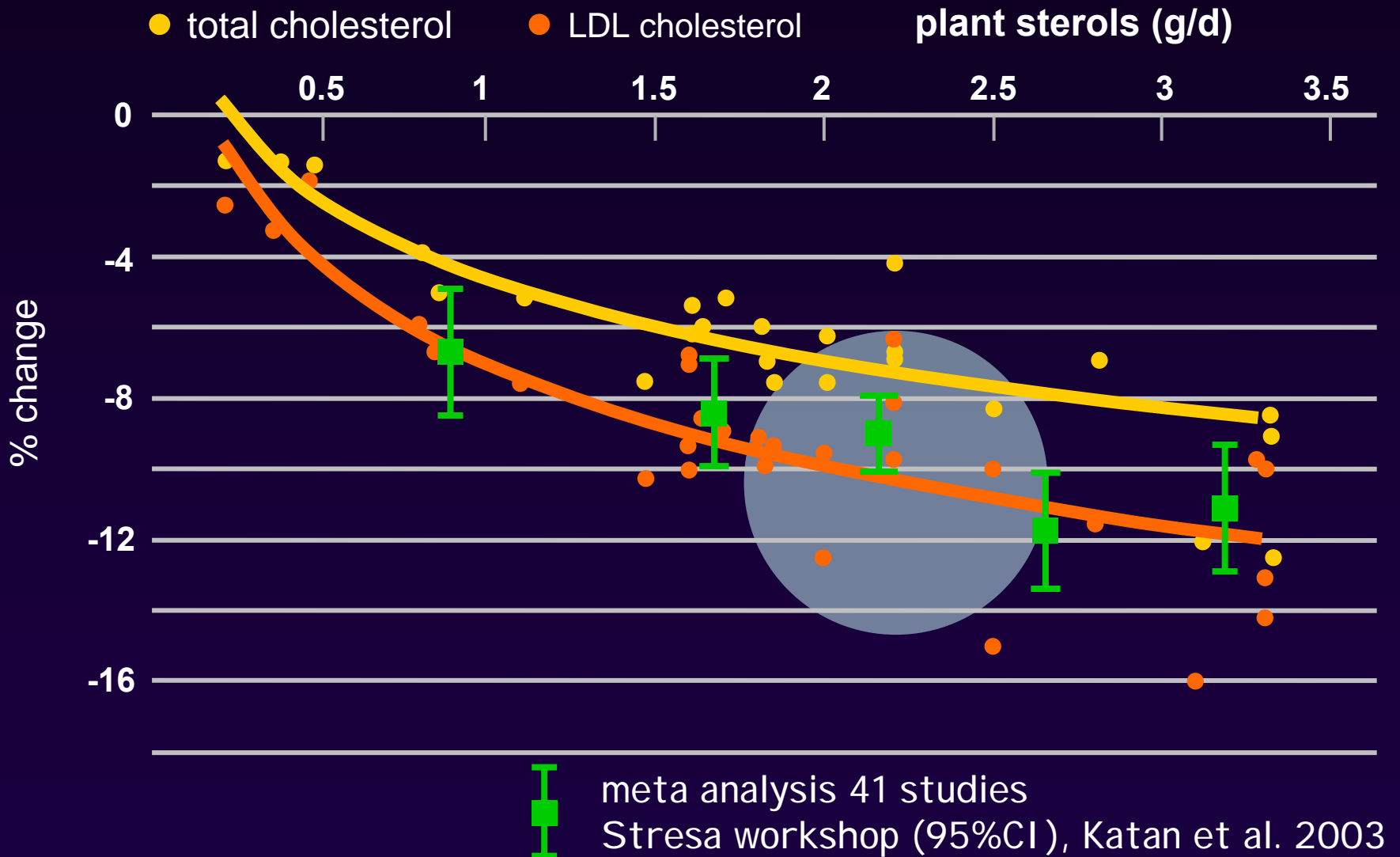


Daily intake of trans fatty acids in the Zutphen Elderly Study (n=667, 64-84 y)



Quote: 'The decrease in trans fatty acid intake of 2.4% of energy ... could have contributed to about 23% less coronary deaths (i.e. about 4600 of 20,000 deaths) in the Netherlands per year

Overview of cholesterol lowering trials with plant sterols



The cholesterol-lowering effect of plant sterols is additive to healthy diet



*low in saturated fat and cholesterol

**2-3 g/d of plant sterols in the form of enriched foods

A PORTFOLIO diet* effectively reduces LDL cholesterol

*dietary portfolio =

plant sterols, soy protein, viscous dietary fibre, nuts (almonds)



Plant sterols and blood fat soluble vitamin levels

Mean Change (95% CI) in Serum Concentrations of Vitamins in Randomized Placebo-Controlled Trials of Stanols/Sterols*

Vitamin	No. of trials	Mean change (%)	Mean change, adjusted for change in total serum cholesterol (%)
α -Tocopherol	15	-5.9 (-8.0 to -3.8) ($P < .001$)	2.1 (-0.3 to +4.5) ($P = \text{NS}$)
Alpha carotene	13	-8.7 (-13.8 to -3.5) ($P < .001$)	-0.3 (-5.7 to +5.2) ($P = \text{NS}$)
Beta carotene	15	-19.9 (-24.9 to -15.0) ($P < .001$)	-12.1 (-17.4 to -6.8) ($P < .001$)
Lycopene	13	-7.3 (-13.1 to -1.4) ($P = .01$)	-0.1 (-6.1 to +5.9) ($P = \text{NS}$)
Retinol	14	-0.1 (-1.6 to +1.5)	NA
Vitamin D	10	+0.5 (-2.6 to +3.6)	NA

*Only trials testing doses ≥ 1.5 g/d are included. CI = confidence interval; NA = not applicable; NS = not significant.

Katan *et al.*, Mayo Clin Proc 2003

Prospective cohort studies of CVD and consumption of nuts, fruits and vegetables, or whole grains

Nuts

Albert et al

Ellsworth et al

Brown et al

Hu et al

Fraser and Shavlik

Fraser et al

Fruits and vegetables

Bazzano et al

Liu et al

Joshiपुरa et al

Gaziano et al

Gillman et al

Knekt et al

Whole grains

Liu et al

Liu et al

Jacobs et al

Fraser et al



Cardiovascular Disease

- Whole grains may lower cholesterol levels in part because of high level of soluble (viscous) fiber
- Magnitude of risk reduction 27-37%
- Larger cholesterol level reductions than from reduced cholesterol intake alone

Rimm et al., 1996
Jacobs et al., 1999
Liu et al., 1999
Liu et al. *AJPH*, Sept 2000

Diabetes

- Consumption of whole grains included in recommendations for diabetes prevention
- 21 - 27% risk reduction by eating 3 servings of whole grain daily
- Whole grain intakes associated with improved insulin sensitivity

Meyer, et al., *AJCN*, Apr. 2000
Liu, et al., *AJPH*, Sept. 2000
Pereira et al., *AJCN* 2002

Cancer

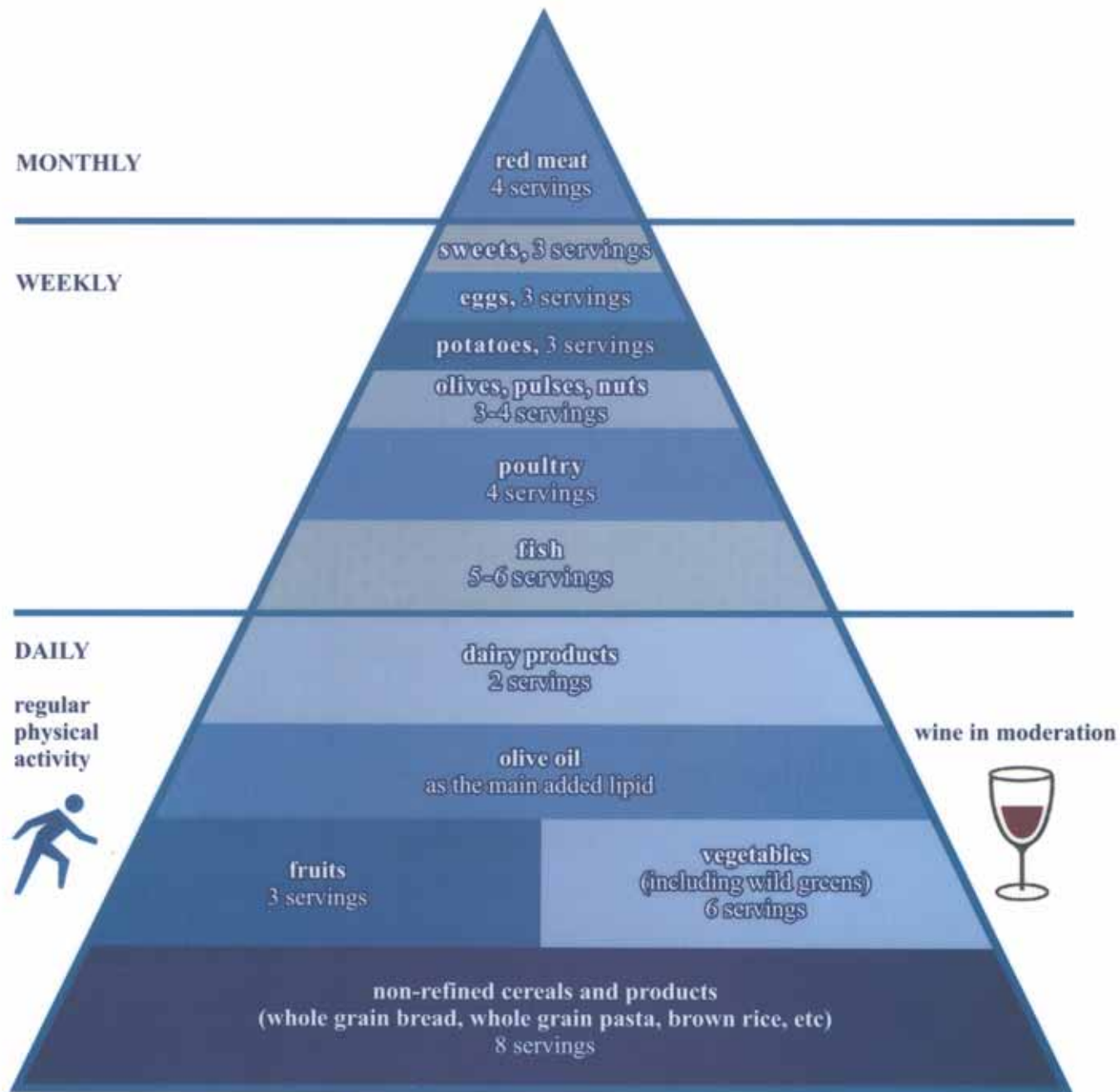
- Meta-analysis of GI cancers = 21 - 43% lower risk
- Meta-analysis of hormone dependent cancers = 10 - 40% risk reduction

Jacobs et. al., 1998
Chatenoud et. al., 1998

Obesity

- Higher intakes of whole grains
 - lower Body Mass Index
 - lower risk of major weight gain

Koh-Banerjee P. et.al. 2004
Liu et al. 2003



One serving equals approximately one half of the portions as defined in the Greek market regulations (portions served in restaurants)

Food consumption in men and women: the Attica Study

Food	Dietary Guidelines	Men (n=1514)	Women (n=1528)
Red meat	1 serving/week	4,8 ± 2,7*	4,0 ± 2,2*
Poultry	4 servings/week	1,4 ± 0,1*	1,5 ± 0,2*
Fish	5-6 servings/week	2,1 ± 1,1*	2,0 ± 1,2*
Eggs	3-4/week	1,1 ± 0,7*	1,2 ± 1*
Nuts	1 serving/week	1,3 ± 2,0	1,4 ± 2,1
Legumes	3-4 servings/week	5,4 ± 3,0	4,7 ± 2,2
Dairy	14 servings/week	11,5 ± 5*	12,9 ± 5*
Fruits	21 servings/week	26 ± 3*	28 ± 4*
Vegetables	42 servings/week	34 ± 15*	35 ± 13*
Potatoes	21 servings/week	13 ± 4*	14 ± 3*
Grains	56 servings/week	52 ± 18*	53 ± 18*
Olive oil	Daily use	88%	87%
Alcohol	15-30 g/day	12,5 ± 4	5,5 ± 3
Sweets	3 servings/week	4,9 ± 4*	4,8 ± 4*

**P* < 0.05 compared to the recommended dietary intake





AHA Pediatric Dietary Strategies for individuals Aged > 2 Years: Recommendations to All Patients and Families

- Balance dietary calories with physical activity to maintain normal growth**
- 60 min of moderate to vigorous play or physical activity daily**
- Eat vegetables and fruits daily, limit juice intake**
- Use vegetable oils and soft margarines low in saturated fat and trans fatty acids instead of butter or most other animal fats in the diet**
- Eat whole grain breads and cereals rather than refined grain products**
- Reduce the intake of sugar-sweetened beverages and foods**
- Use nonfat (skim) or low-fat milk and dairy products daily**
- Eat more fish, especially oily fish, broiled or baked**
- Reduce salt intake, including salt from processed foods**

NCEP ATP III dietary guidelines for a heart healthy diet

Main features of the NCEP ATP III:

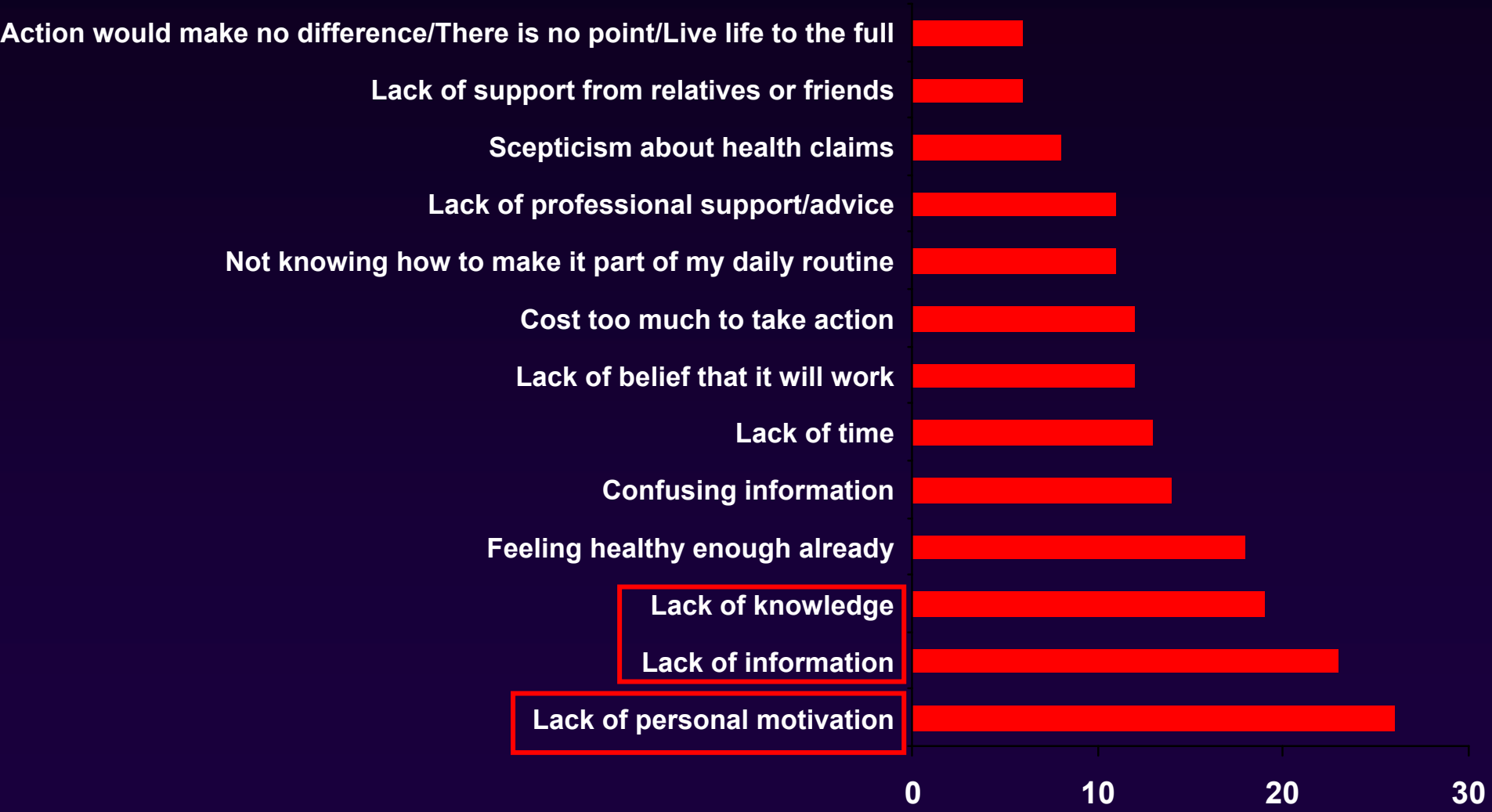
Therapeutic lifestyle Changes (TLC) Diet

- Weight reduction
- Increase physical activity
- Limit total fat intake to 25-35% of total calories
- Reduce intakes of saturated fatty acids and cholesterol
 - SAFA <7% of total calories
 - Cholesterol <200 mg/day
- Additional therapeutic options for enhancing LDL lowering
 - plant sterols/stanols 2 g/day
 - increased viscous (soluble) fibre intake 10-25 g/day

Most effective actions in reducing personal risk of type 2 diabetes or heart disease (%). Each respondent could give more than one answer (n=5967)



Self-reported barriers to take actions to reduce personal risk of type 2 diabetes or heart disease (%). Each respondent could give more than one answer (n=5967)



Thank you very much for
your attention