The Food & Drink Innovation Network

FATS and SYNDROME X

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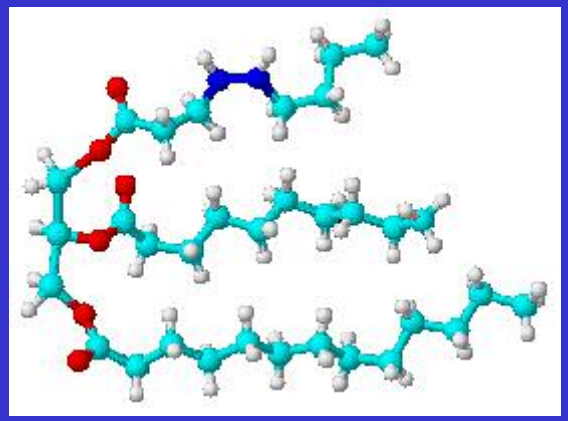
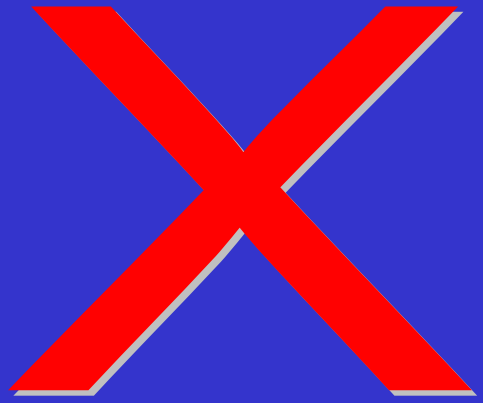
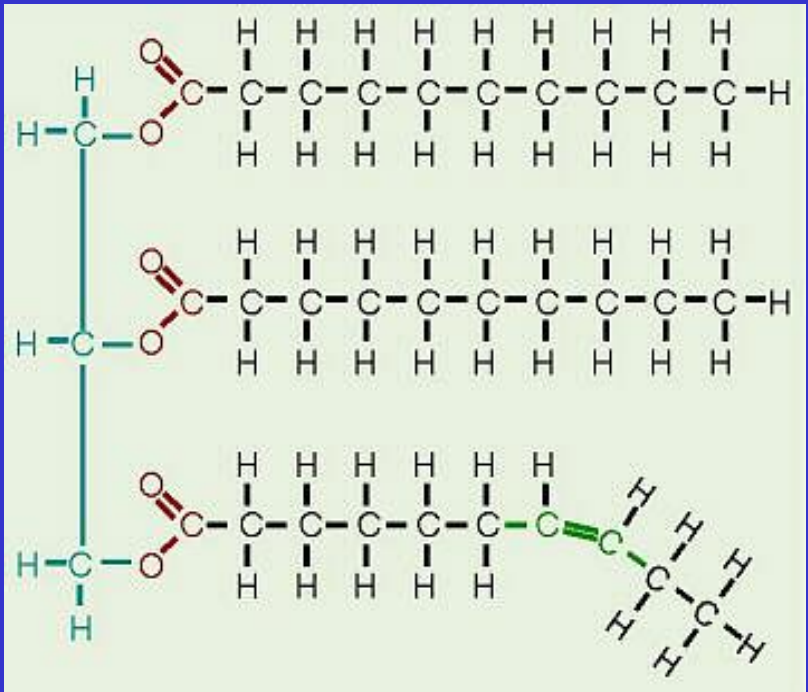




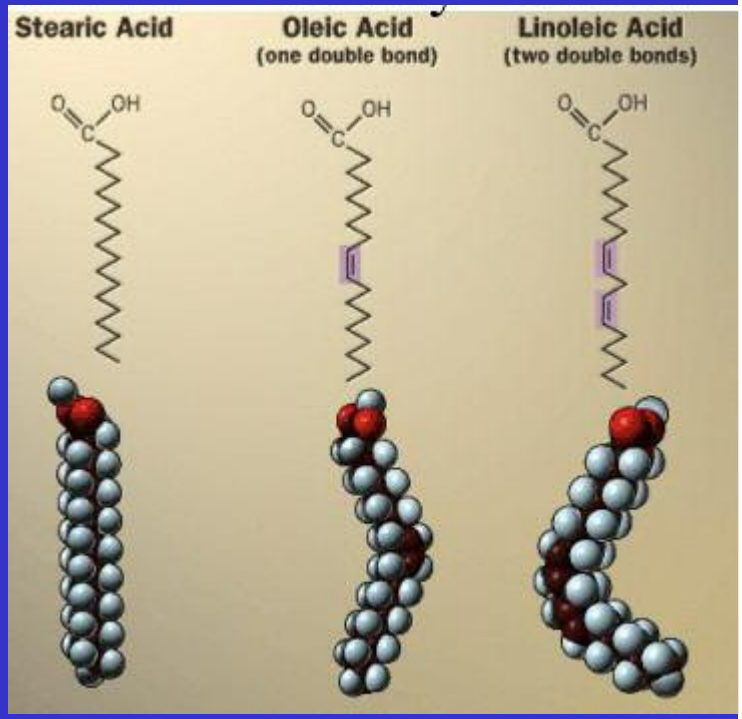
Fats in food

- 95% as triglycerides
- remainder as cholesterol, phospholipids & minor fats

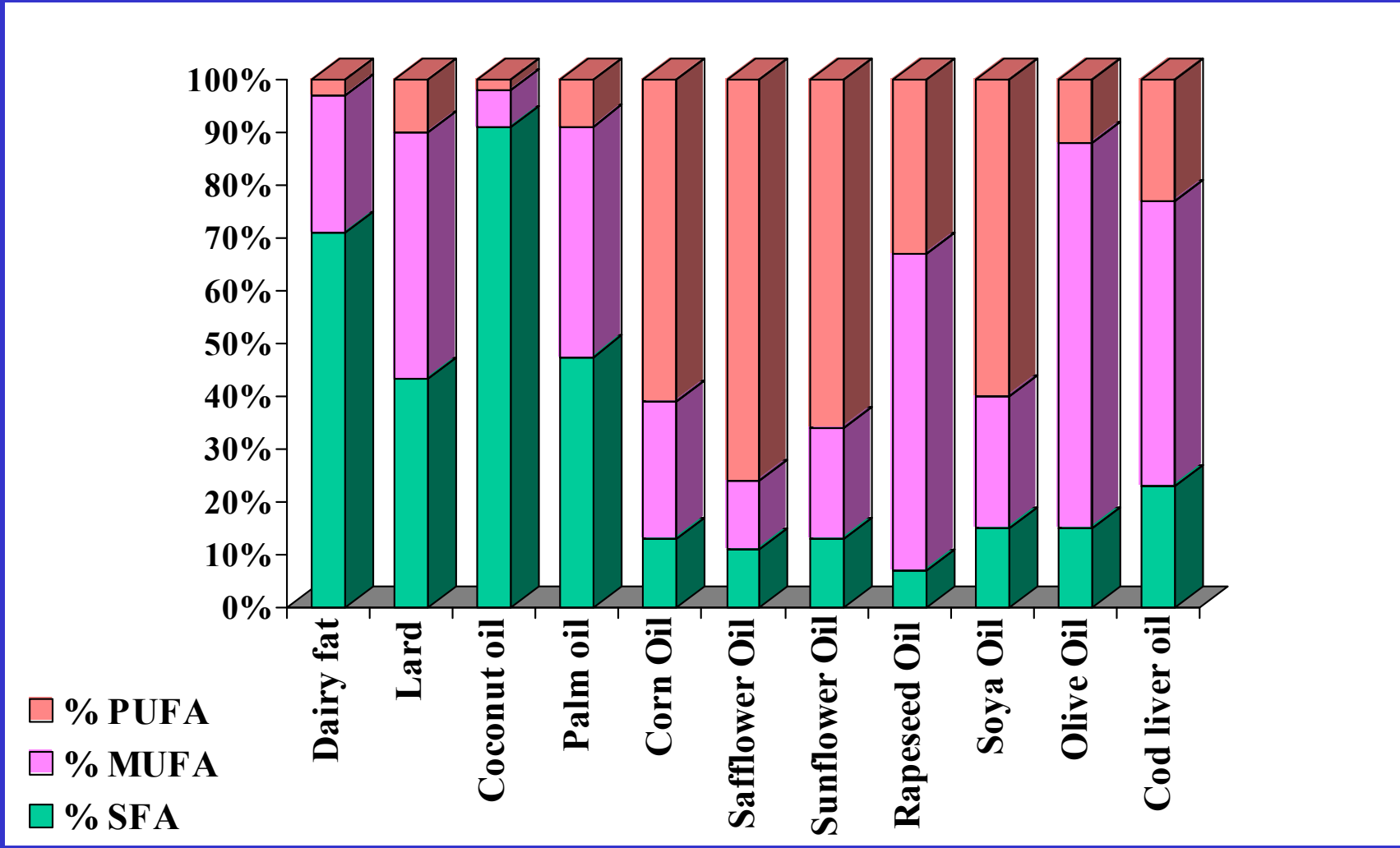


Type of fatty acids

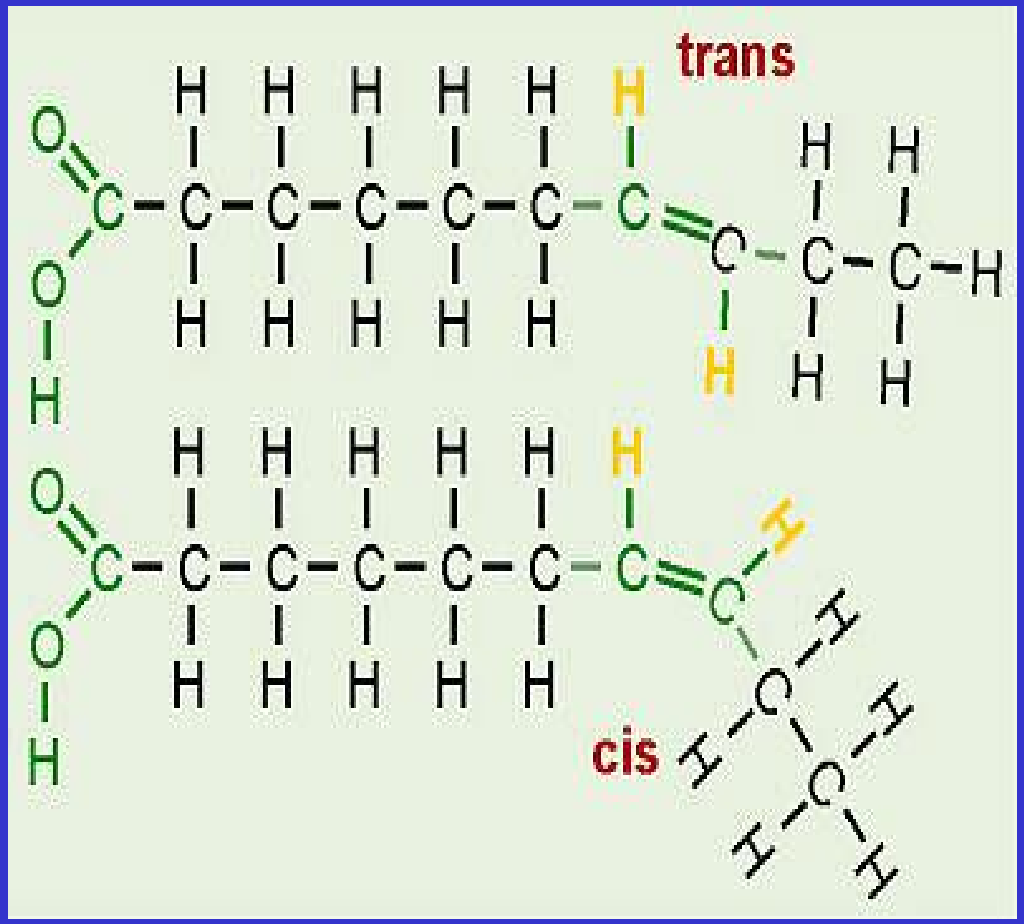
Fatty acid	Structural title	Commonly used abbreviation
Saturated		SFA
Lauric	C12:0	
Myristic	C14:0	
Palmitic	C16:0	
Stearic	C18:0	
Monounsaturated		MUFA
Oleic	C18:1-*cis* (n-9)	OA
Elaidic	C18:1-*trans* (n-9)	
Vaccenic	C18:1-*trans* (n-11)	
Polyunsaturated		PUFA
Linoleic	C18:2-*cis* (n-6)	LA
α-linolenic	C18:3-*cis* (n-3)	ALNA
Eicosapentaenoic acid	C20:5-*cis* (n-3)	EPA
Docosahexaenoic acid	C22:6-cis (n-3)	DHA



Fat composition of common fat sources

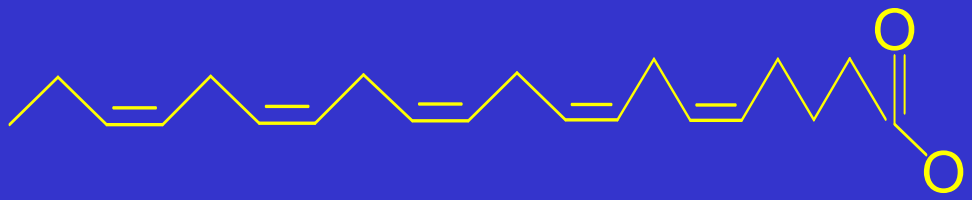


Cis vs trans fatty acids

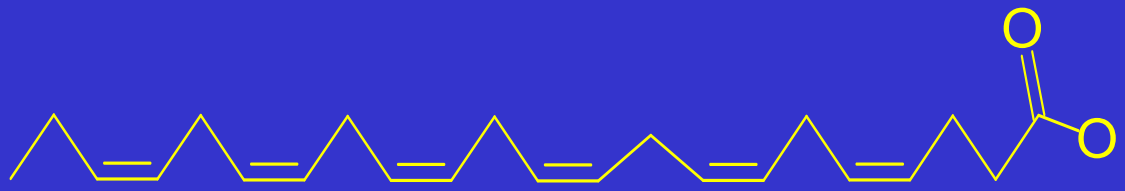


n-3 PUFA in foods

α-linolenic acid (ALNA) C18:3, n-3

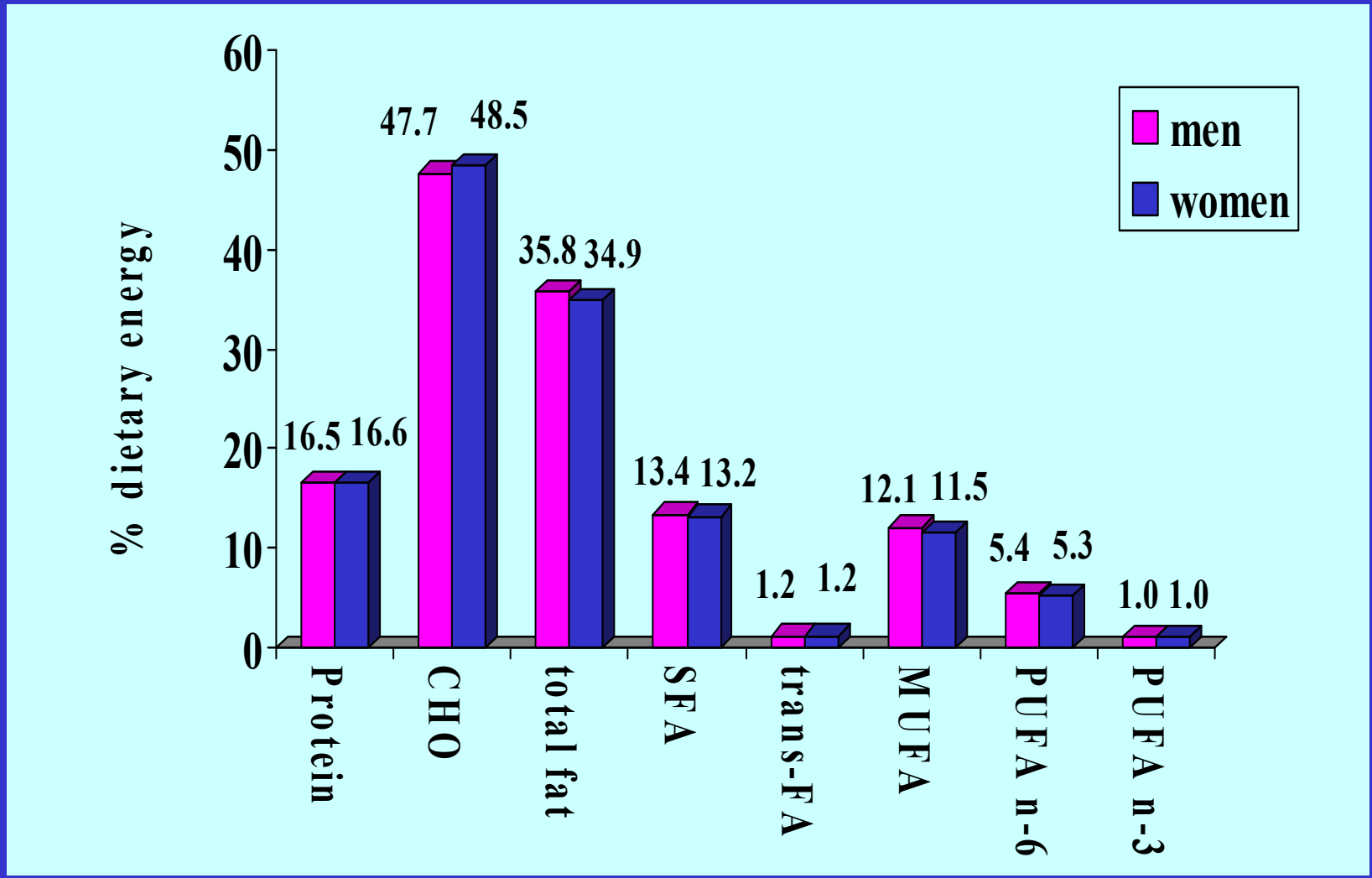


Eicosapentaenoic acid (EPA, C20:5, n-3)



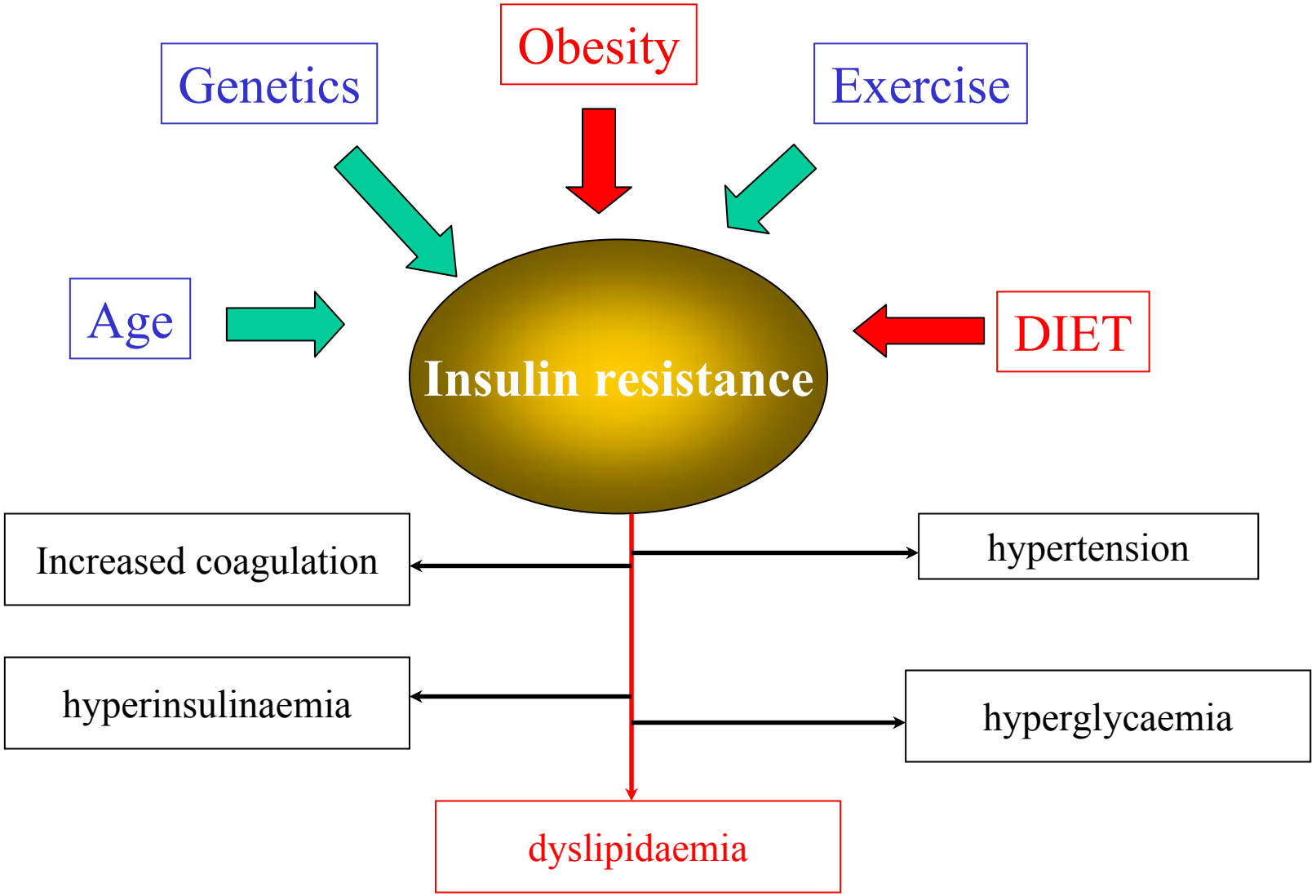
Docosahexaenoic acid (DHA, C22:6, n-3)

Macronutrient composition of UK diet



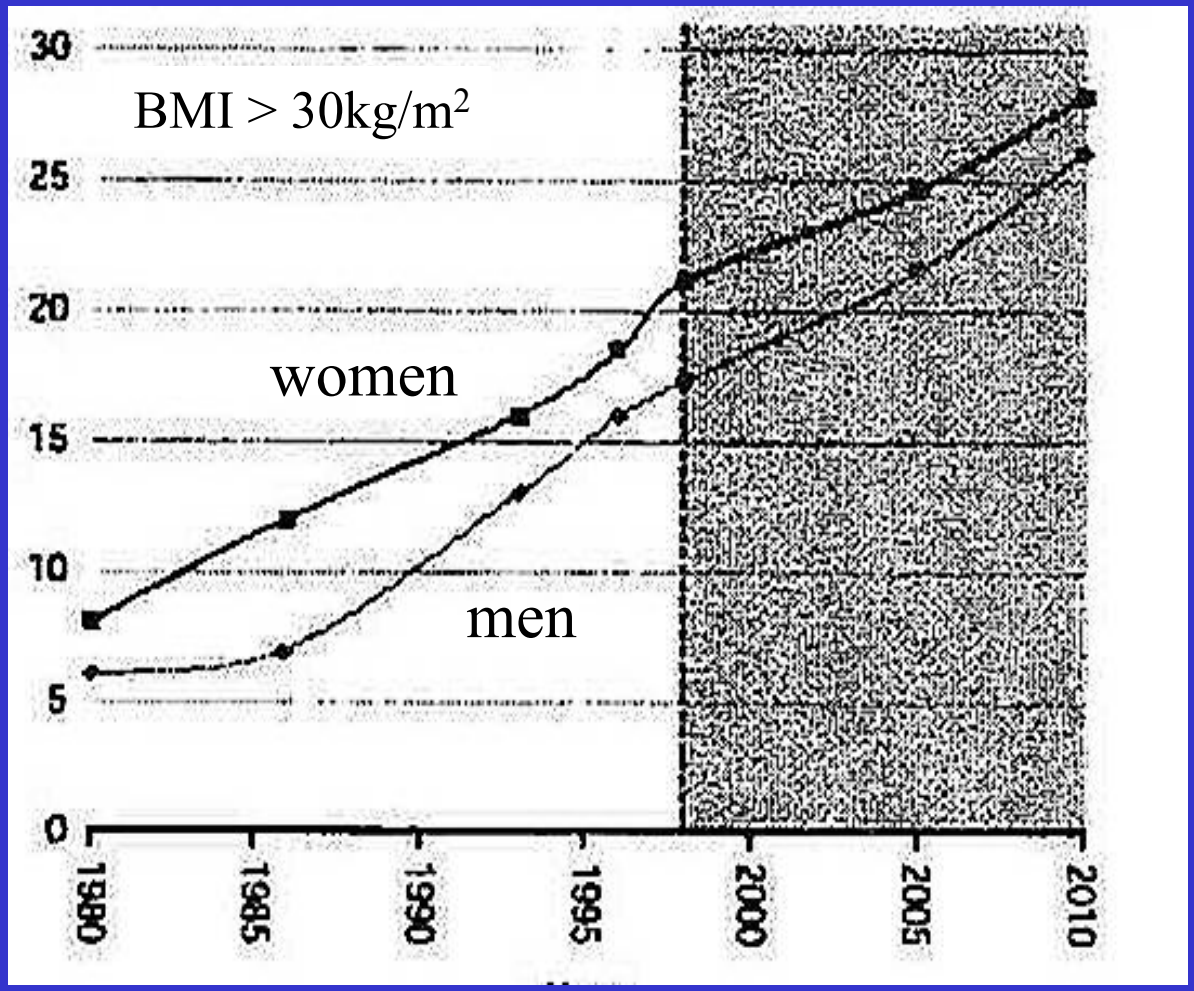
National Diet & Nutrition Survey 2003

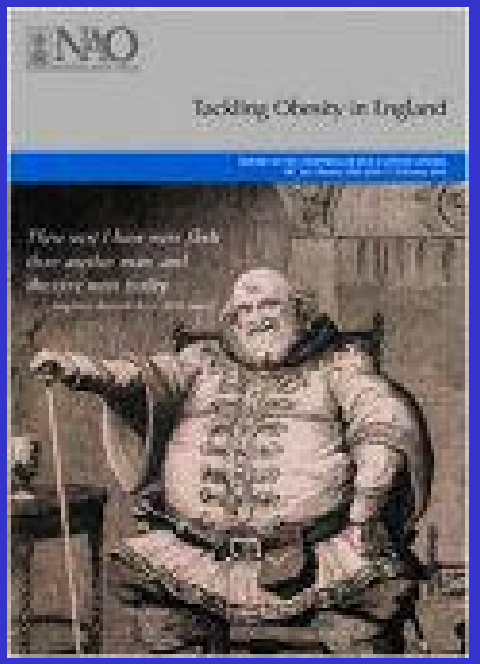
Causes and consequences of insulin resistance



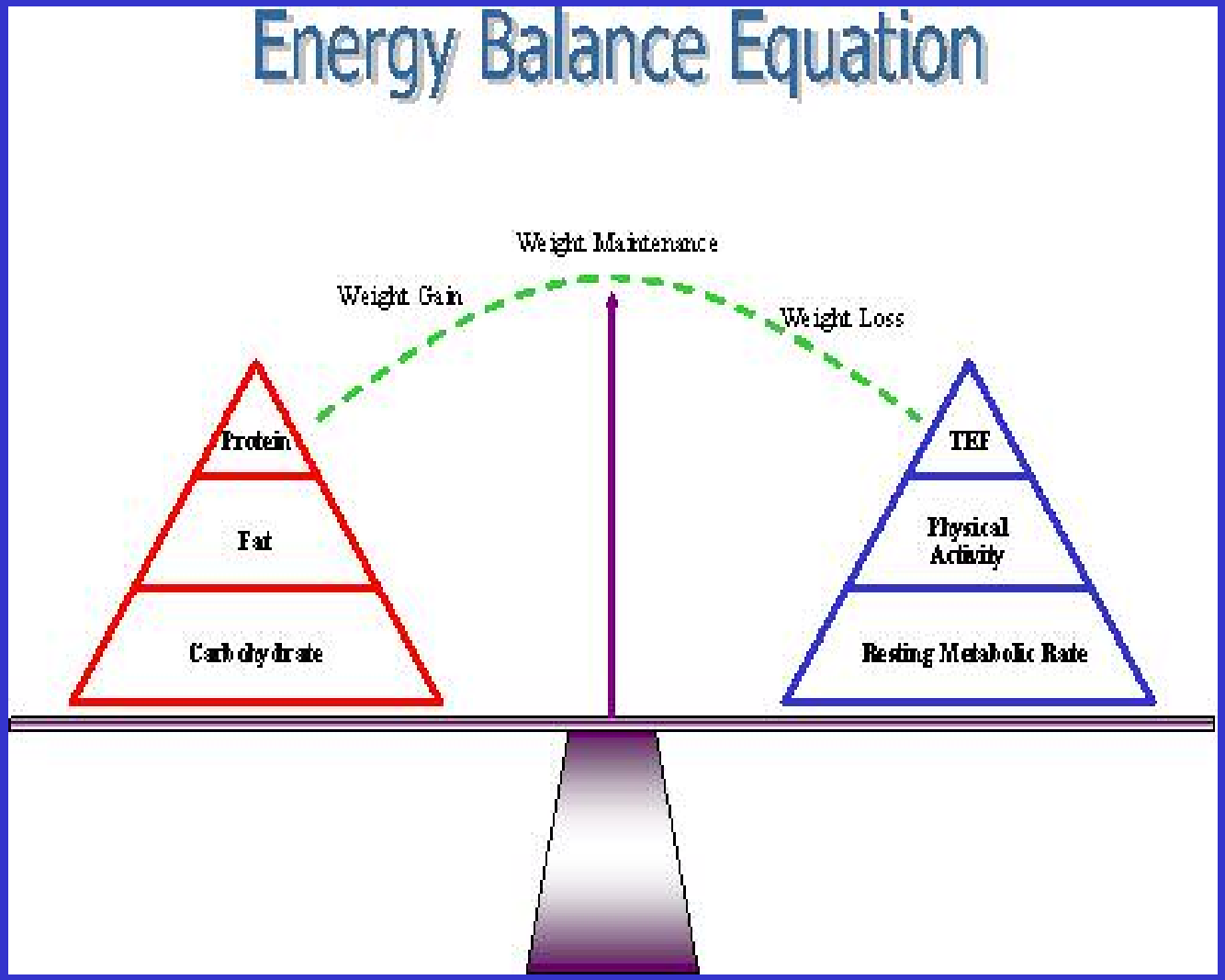
Dietary fat & obesity

Obesity trends in UK





Key components of energy balance
intake> expenditure= weight gain



Dietary fat and body weight

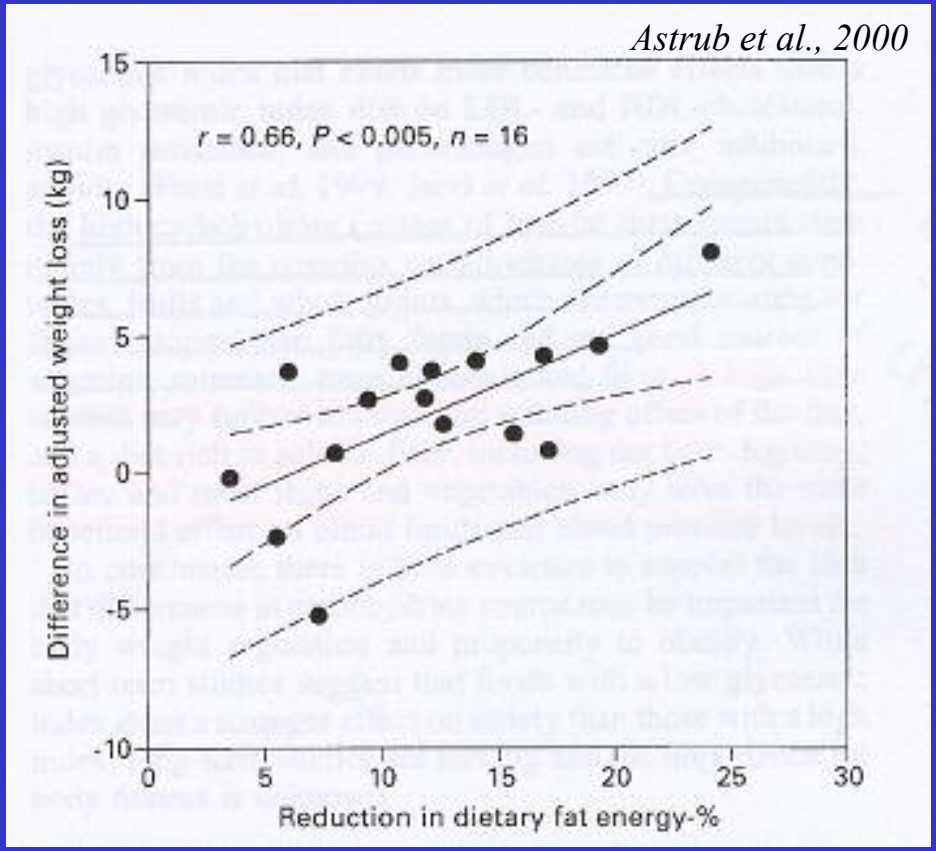
- The role of dietary fat in the aetiology of obesity remains controversial (Willett et al., 1998; Seidell, 1998)
- Dietary fat induces 'passive over consumption'
  - more palatable
  - fat/calorie is less satiating than CHO or protein
  - fat high energy density
- Diet induced thermogenesis
- '.. In the longer term, fat consumption within the range 18-40% appears to have little if any effect on body fatness'

  (Willett et al., 1998, Katan et al., 1997)
- <u>Is a high fat diet a risk factor for obesity independent of energy??</u>

Medium term dietary intervention with low fat diet and weight loss

- > 2-12m
- Low fat ad libitum versus control
- No restriction in dietary energy

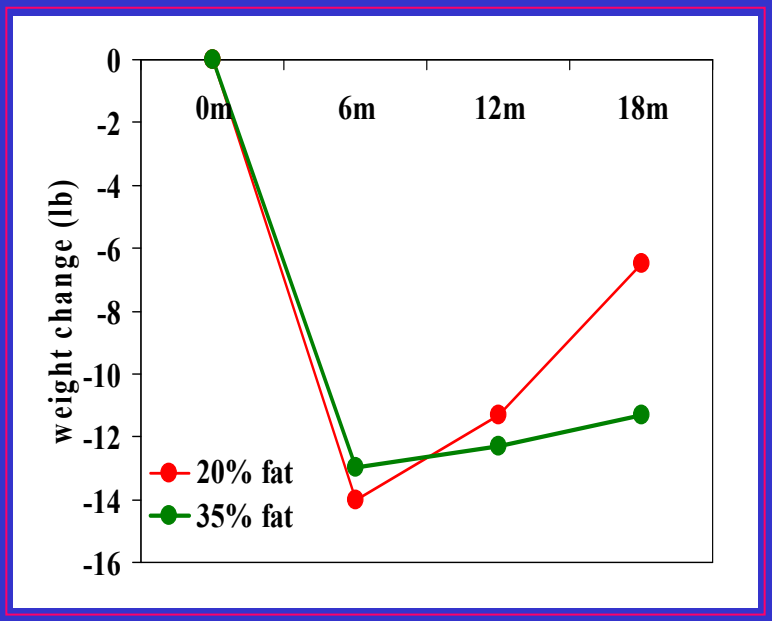
- 1% ↓ energy as fat = 0.37kg ↓ wt

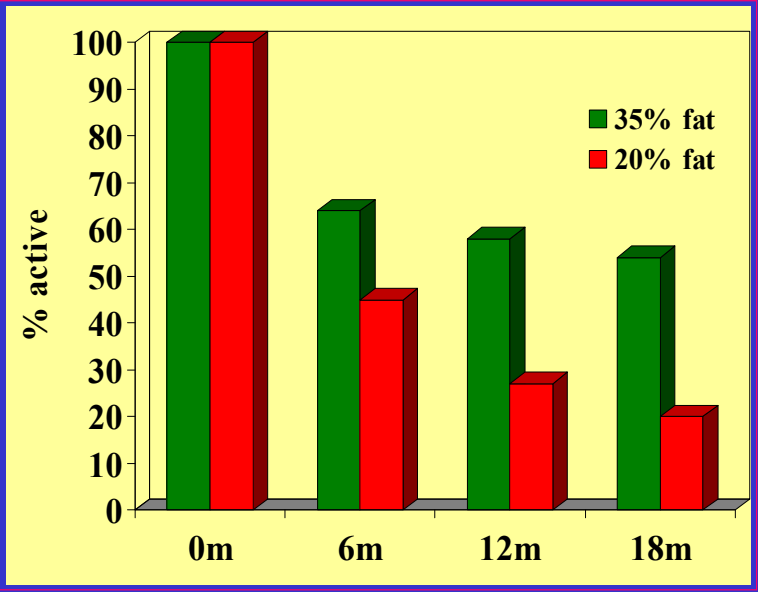


Long term intervention low fat diet and weight loss

101

20% fat diet vs 35% fat Mediterranean type diet-isocaloric

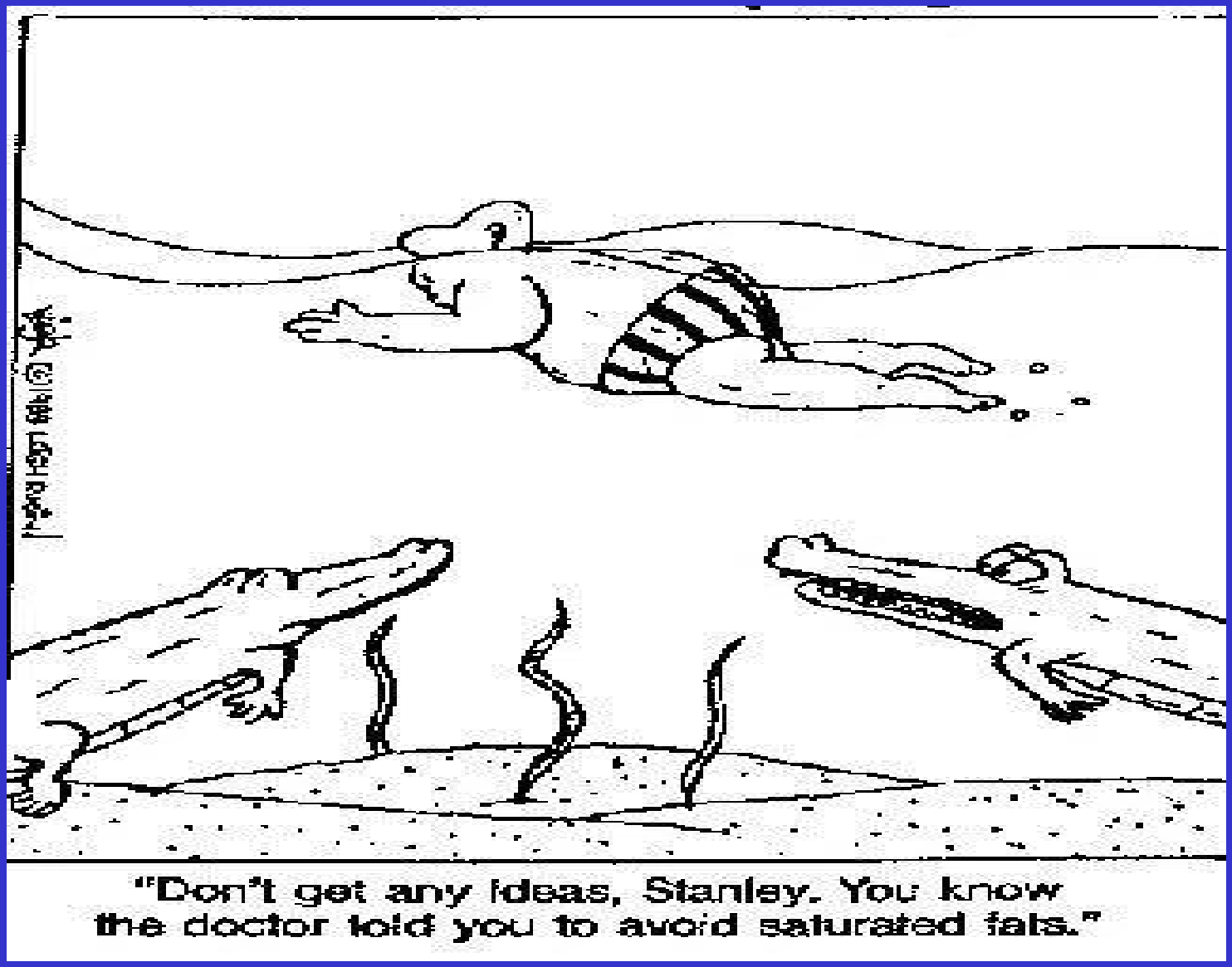




Long term weight reduction/maintenance may be most effectively by following a moderate fat restricted calorie diet rather than a low fat diet

Dietary fat & insulin sensitivity

- High fat diet is associated with insulin insensitivity and an increased risk of diabetes (Vessby et al., 2001; Lovejoy and DiGirolamo, 1992)


"Don't get any ideas, Stanley. You know
the doctor told you to avoid saturated fats."

Plasma fatty acid composition and insulin sensitivity
Saturated fat is associated with insulin insensitivity

n=579

70y old men

Fatty acid	Plasma- fatty acid insulin sensitivity correlation
C16:0	-0.24 (P<0.001)
C16:1	-0.28 (P<0.001)
C18:2	+0.26 (P<0.001)

Vessby et al., 1994

Membrane fatty acid composition and insulin sensitivity

- SFA in muscle and insulin insensitivity (Vessby et al., 1994)
- n-6:n-3 ratio muscle and insulin insensitivity (Pan et al., 1995; Storlein et al., 1996)
- C20-C22 fatty acids and insulin action (Borkman et al., 1993; Pan et al., 1995)
- Consistent body of animal evidence suggests that enrichment of membranes with EPA & DHA improves insulin action (Behme, 1996; D'Alssandro et al., 2002)

Studies on the impact of dietary fatty acid composition on insulin action in human have proved disappointing!!

Study	Dietary change	time (wk)	Outcome
Fasching, (1996)	SFA v MUFA v n-6 PUFA	1	NS
Louheranta, (1998)	Stearic acid v oleic acid	4	NS
Vessby (2001)	SFA vs rapeseed oil	3	NS
Borkman (1989)	fish oil vs safflower oil	3	NS
Lou (1998)	fish oil vs sunflower oil	8	NS

Dietary n-6:n-3 ratio in UK Asians: relevance to cardiovascular risk factors and modification by dietary means FSA 1999-2003

Background

->x3 incidence of diabetes

-high dietary n-6 PUFA

-high tissue n-6:n-3 ratio

Overall objective

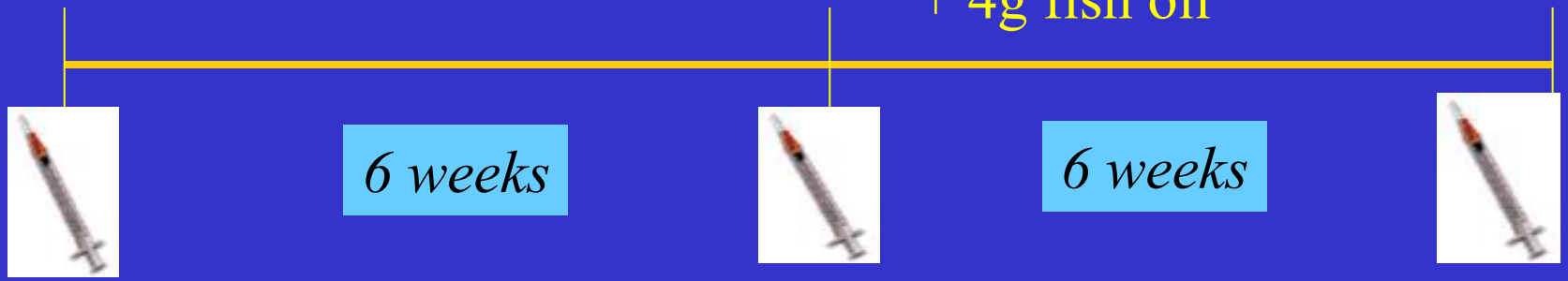
To determine the impact of dietary n-6:n-3 ratio and fish oil intake on tissue fatty acid levels, blood lipids and insulin sensitivity in Sikhs

n=29

n-6:n-3=16
n-6:n-3=9

n-6:n-3=16
n-6:n-3=9

+ 4g fish oil



No overall impact of treatments on any measures of insulin sensitivity

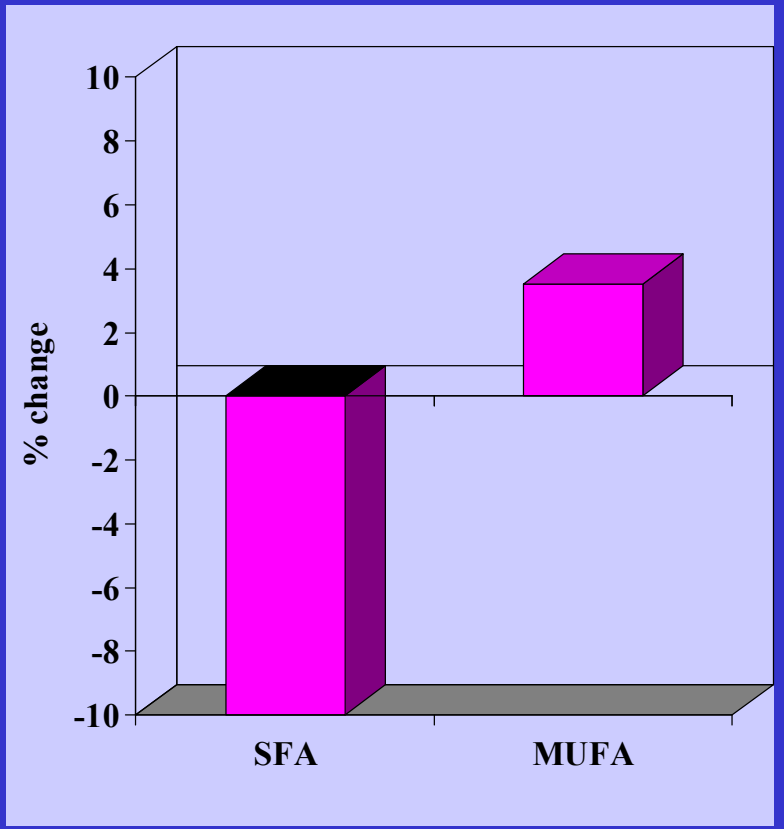
Minihane, Brady, Lovegrove et al., EJN 2003 in press
Brady, Minihane, Lovegrove et al., AJCN 2003 in press

KANWU study
Vessby et al., 2001

- 162 healthy men and women
- 3 months
- SFA v MUFA rich diet

- 37% fat, 17% SFA, 14% MUFA
- 37% fat, 8% SFA, 23% MUFA
- +/- 3.6g EPA+DHA per day

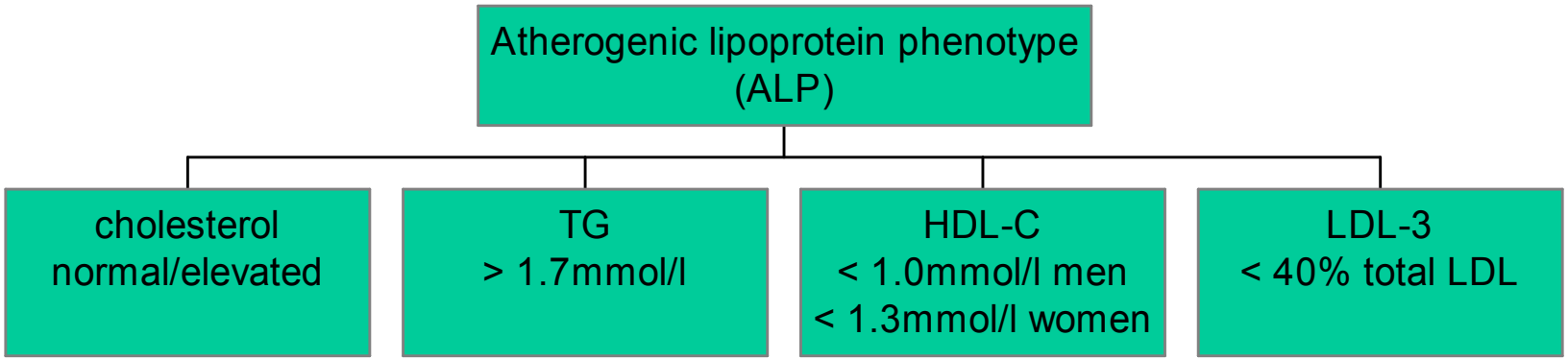
- **MUFA increased insulin sensitivity compared to SFA diet**
- **No evident in those with total fat > 37% energy**
- **No effect of fish oil**



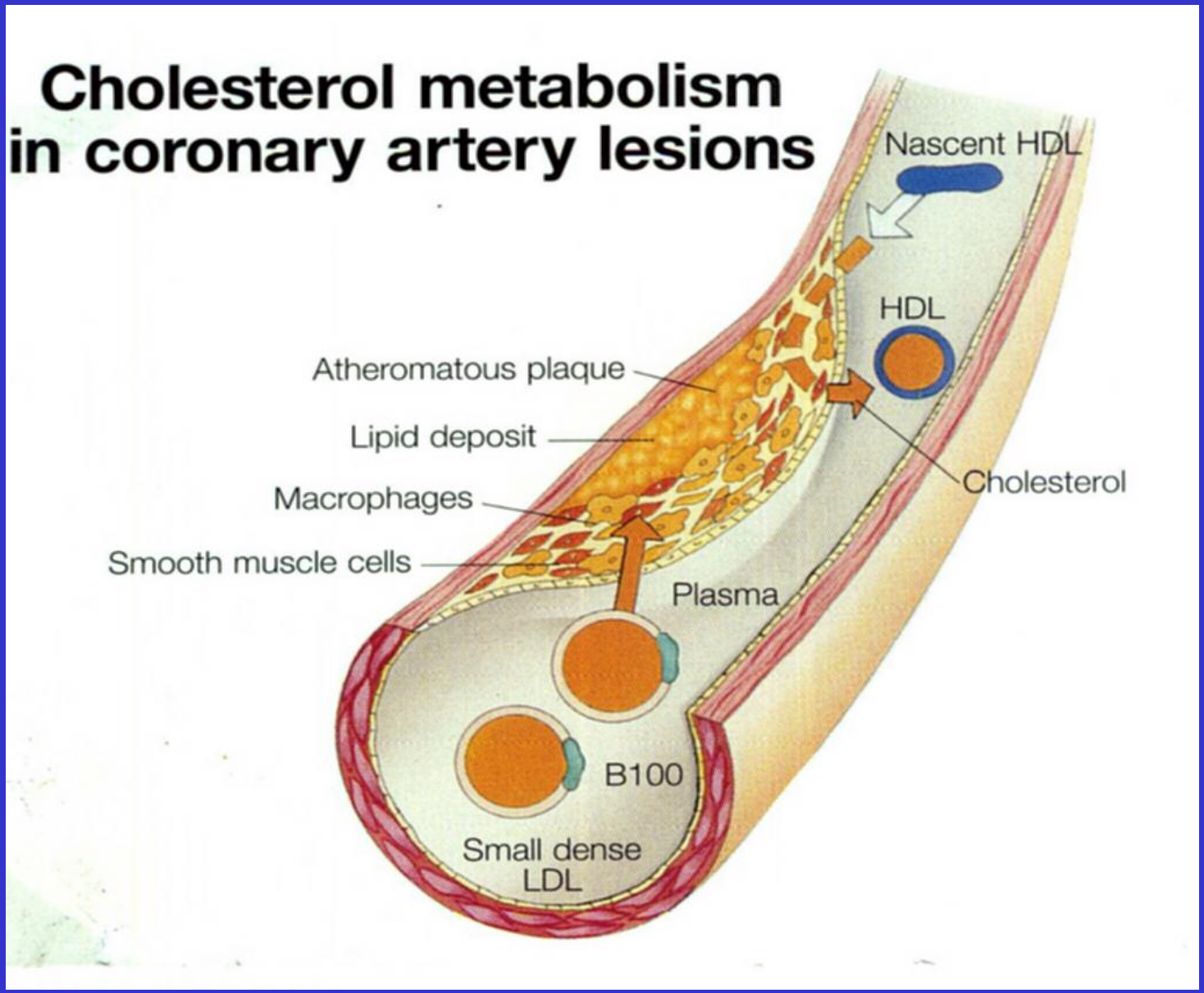
High total fat intake is associated with insulin insensitivity. Although observational studies have observed associations between the membrane fatty acid profile and insulin action, intervention studies have proved disappointing. Thus, there a great need for properly powered long term intervention studies to examine the potential of dietary fatty composition as a determinant of insulin sensitivity

Dietary fat & lipid metabolism

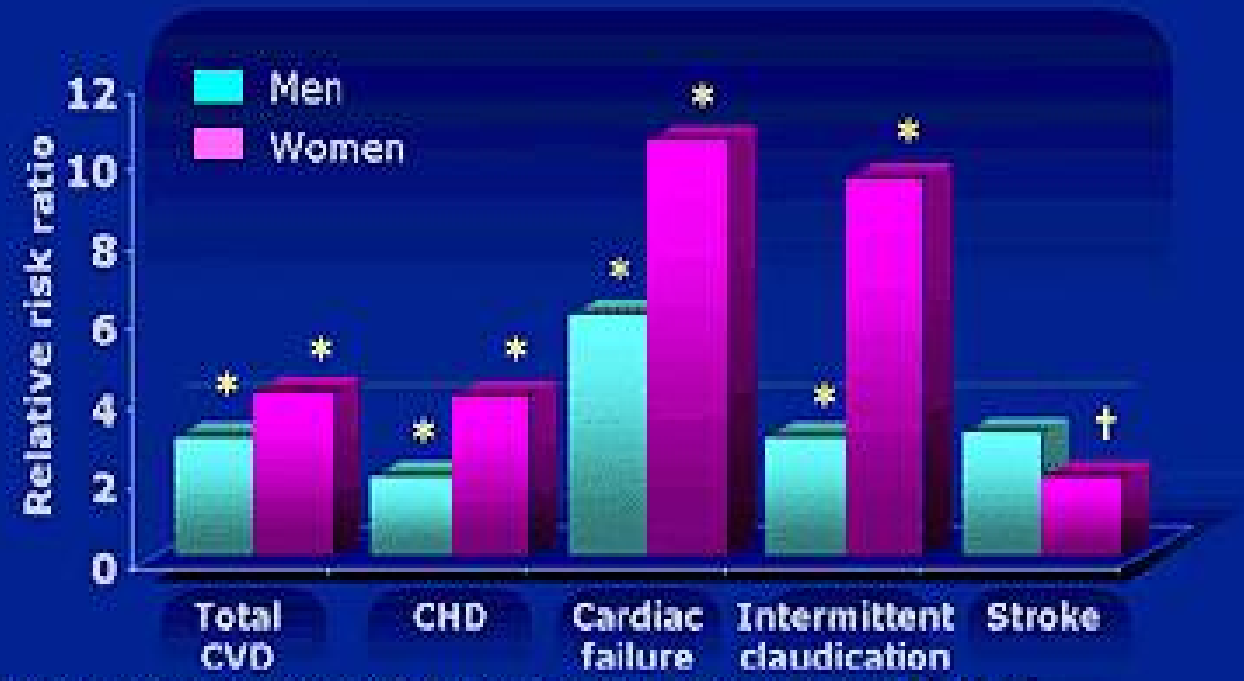
Dyslipidaemia of the metabolic syndrome



CJ Packard & J Shepherd 1996



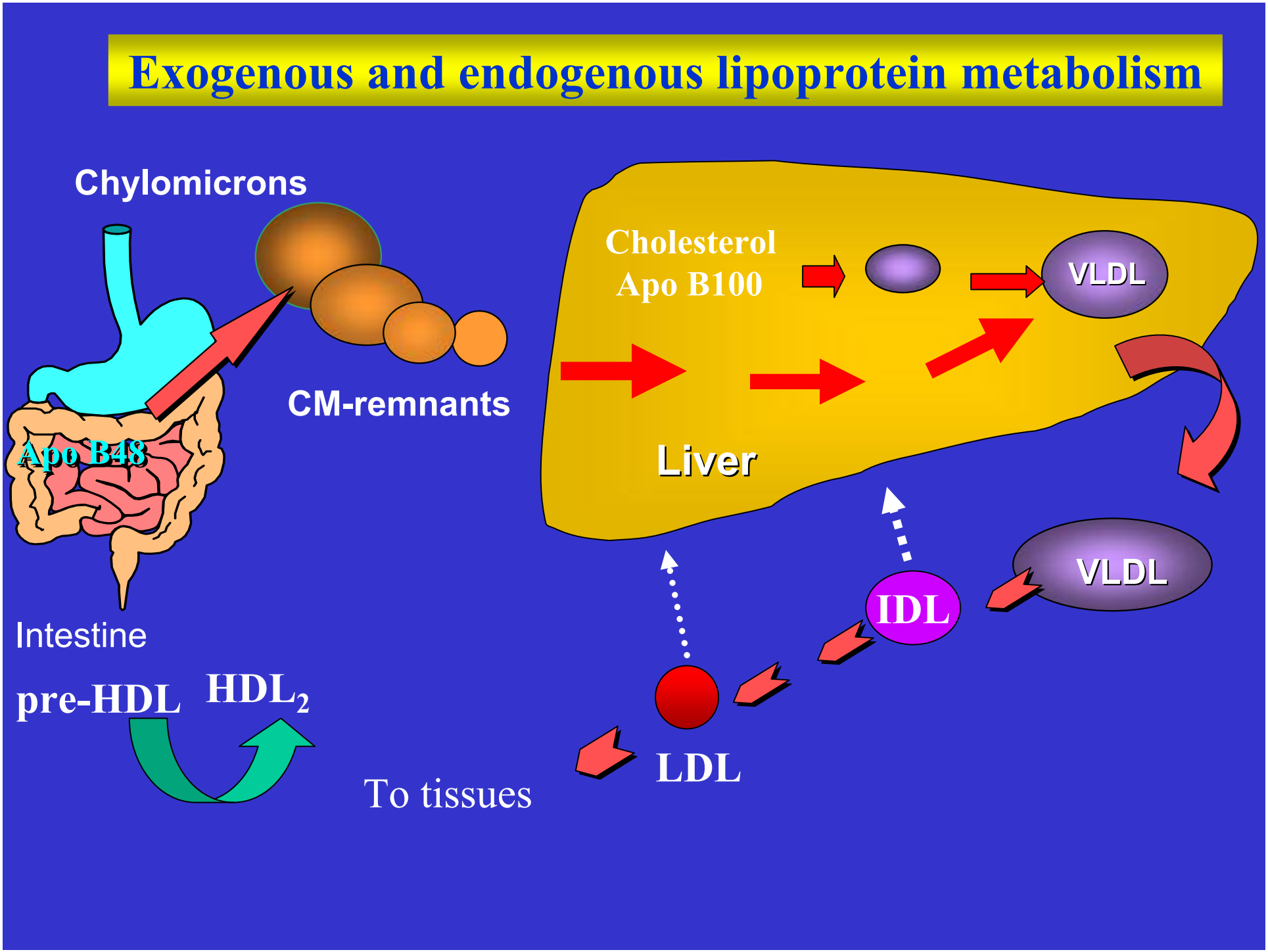
Framingham Heart Study
CVD Events in Diabetics



CVD=cardiovascular disease CHD=coronary heart disease *P<0.01 †P<0.05

Wilson PWF, Kannel WB. In: Hyperglycemia, Diabetes and Vascular Disease. Ruderman N, et al. eds. Oxford;1992. ©Copyright 1992, American Physiological Society. Used by permission of Oxford University Press, Inc.

Exogenous and endogenous lipoprotein metabolism



Predicted changes in lipids following dietary macronutrient change

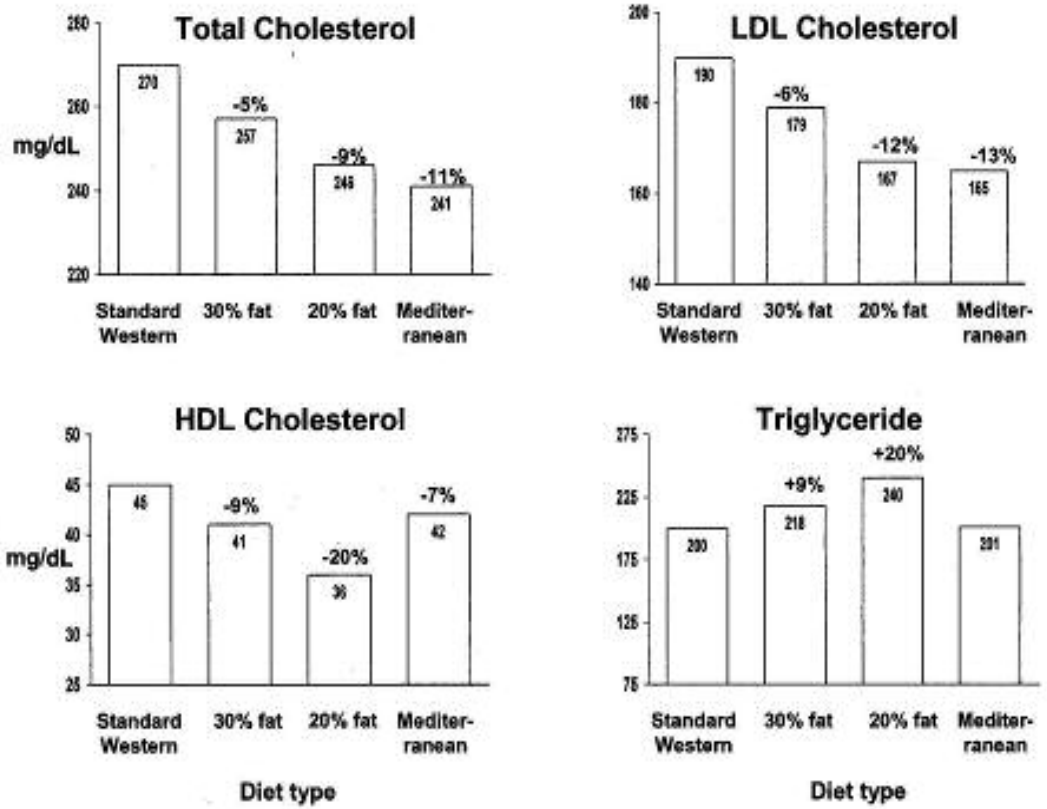


Figure 1. Predicted changes in plasma cholesterol and triglyceride concentrations caused by 3 types of diet treatment: 30% fat (step 1), 20% low-fat, and Mediterranean. The standard Western and Mediterranean diets have 38% fat. The dietary changes are described more fully in the text. The meta-analysis of Mensink and Katan[15] was used for changes in dietary fatty acids and that of Clarke et al[17] for changes in dietary cholesterol. Note that the effects of carbohydrate on triglycerides are less if the carbohydrate comes from low-glycemic-index foods, as described in the text. HDL = high-density lipoprotein; LDL = low-density lipoprotein.

Are PUFA or MUFA a more efficacious replacement for SFA in lowering cholesterol?

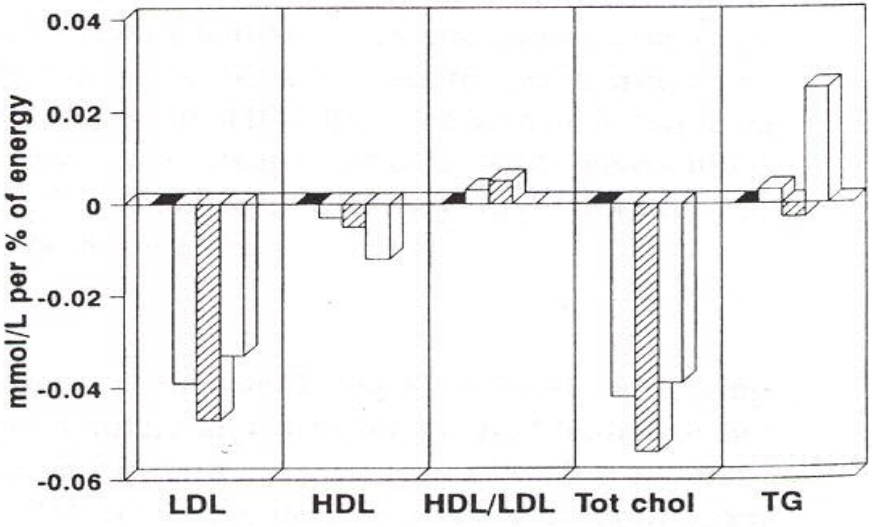


FIG 2. Predicted changes in serum lipids and lipoproteins when 1% of dietary saturated fatty acids is replaced by fatty acids of a particular class or by carbohydrates under isoenergetic metabolic-ward or equivalent conditions. ■, saturated; ▩, monounsaturated; ▨, polyunsaturated; □, carbohydrate. Chol, cholesterol; TG, triglyceride.

Katan et al., 1994

However high intakes of n-6 PUFA significantly decrease HDL-C relative to MUFA

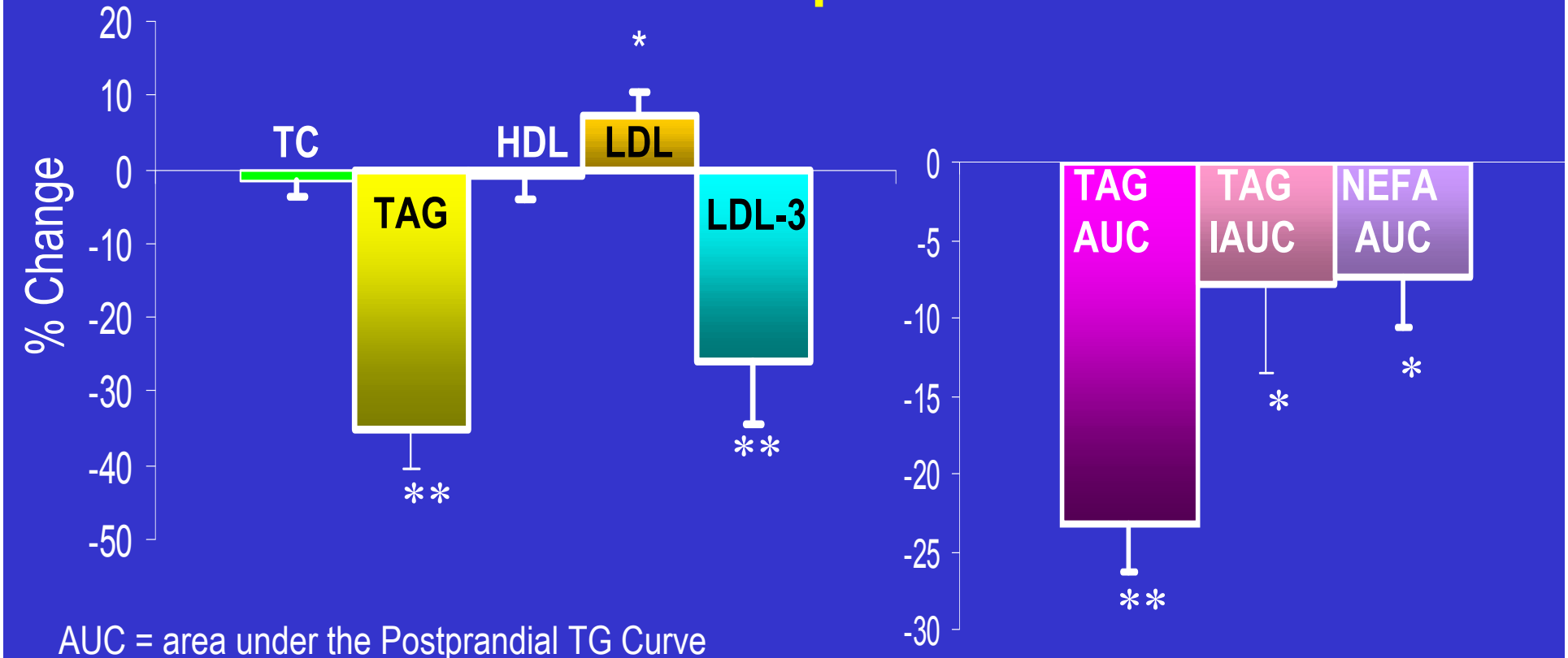
Is fish oil beneficial in counteracting the dyslipidaeima of the metabolic syndrome?

Double-blind placebo-controlled cross over study- n=55

6 x 1g capsules (50% EPA / DHA) / day or 6g olive oil/day for 6 weeks with a 12 week washout

Griffin,Minihane et al., 1999

Effect of Fish Oil on Fasting and Postprandial Lipids



AUC = area under the Postprandial TG Curve

IAUC = Incremental area under the PP TG curve

* p< 0.05 ** p< 0.001

Minihane et al., 2000a

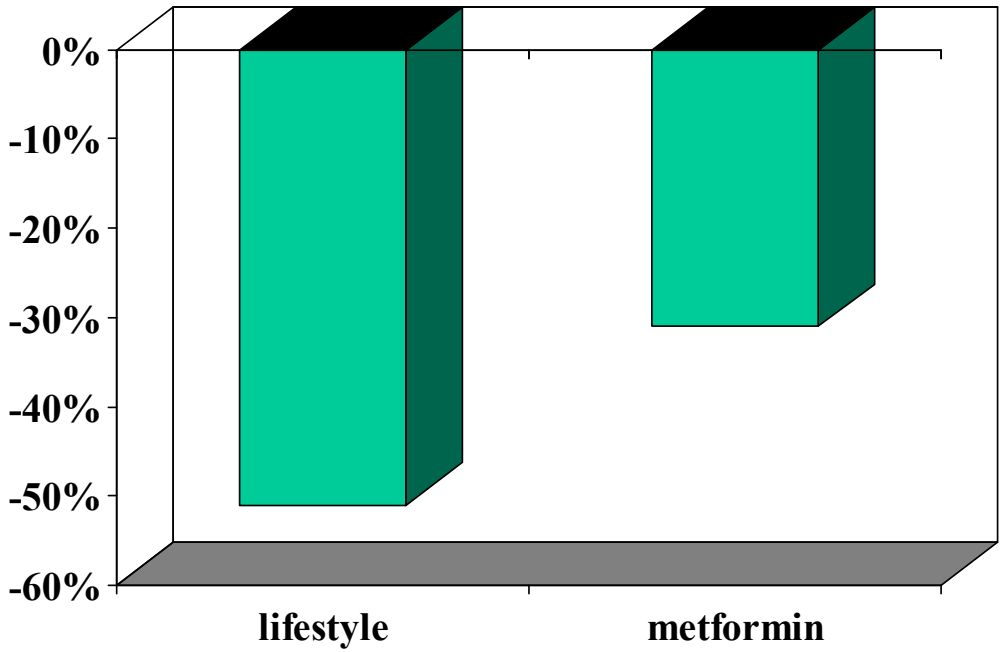
SFA is associated with high circulating total-, LDL- and HDL-cholesterol levels. The replacement of SFA with MUFA, PUFA and CHO results in marked decreases in total and LDL-cholesterol. However increased dietary n-6 PUFA and refined CHO may be associated with lower HDL-C and higher triglycerides respectively. The consumption of a modest fat, high MUFA diet, with increased consumption of long chain n-3 PUFA appears optimal with respect to the dyslipidaemia of the metabolic syndrome

Key points

- World-wide incidence of MS is reaching epidemic proportions
- A change in the macronutrient composition of the diet, specifically a reduction in SFA would undoubtedly contribute to reduced incidence and progression of diabetes
- The need to provide the consumer with accessible, and affordable products with an improved fat quality (lower in SFA, higher MUFA/PUFA, rich in EPA/DHA) is an essential component of a multi-discipline approach to reducing the public health burden of diabetes/MS

Will dietary and other lifestyle changes be as efficacious as commonly available drug therapies in combating the metabolic syndrome epidemic?

Diabetes Prevention Programme-US
(The Diabetes Prevention Program Research Group, 1999

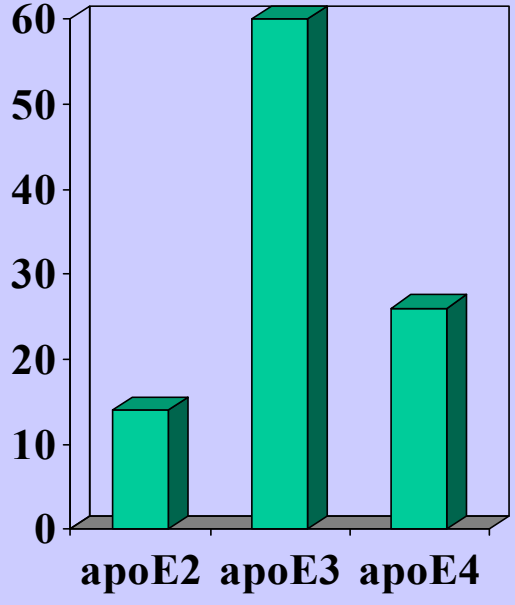


n=3000

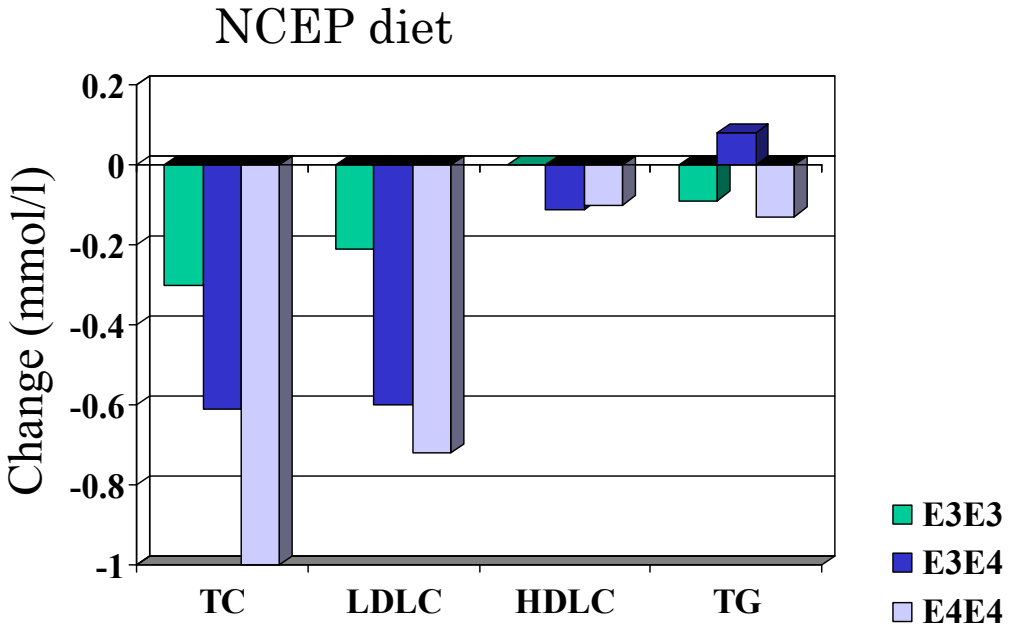
Should dietary advice be personalised depending on an individuals genetic background?

Apolipoprotein E

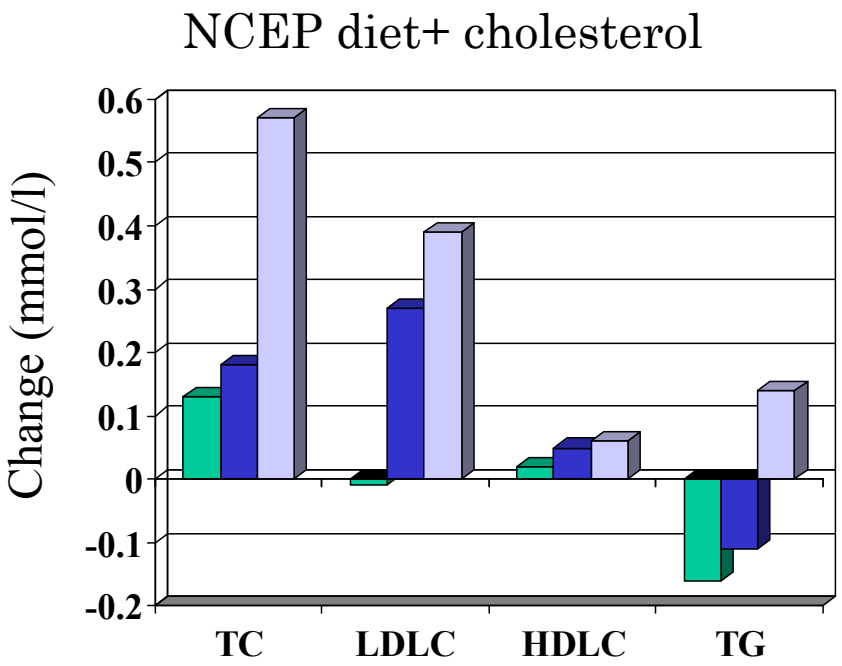
- Involved in all stages of lipoprotein metabolism
- Polymorphic- 3 alleles
- E2, E3, E4



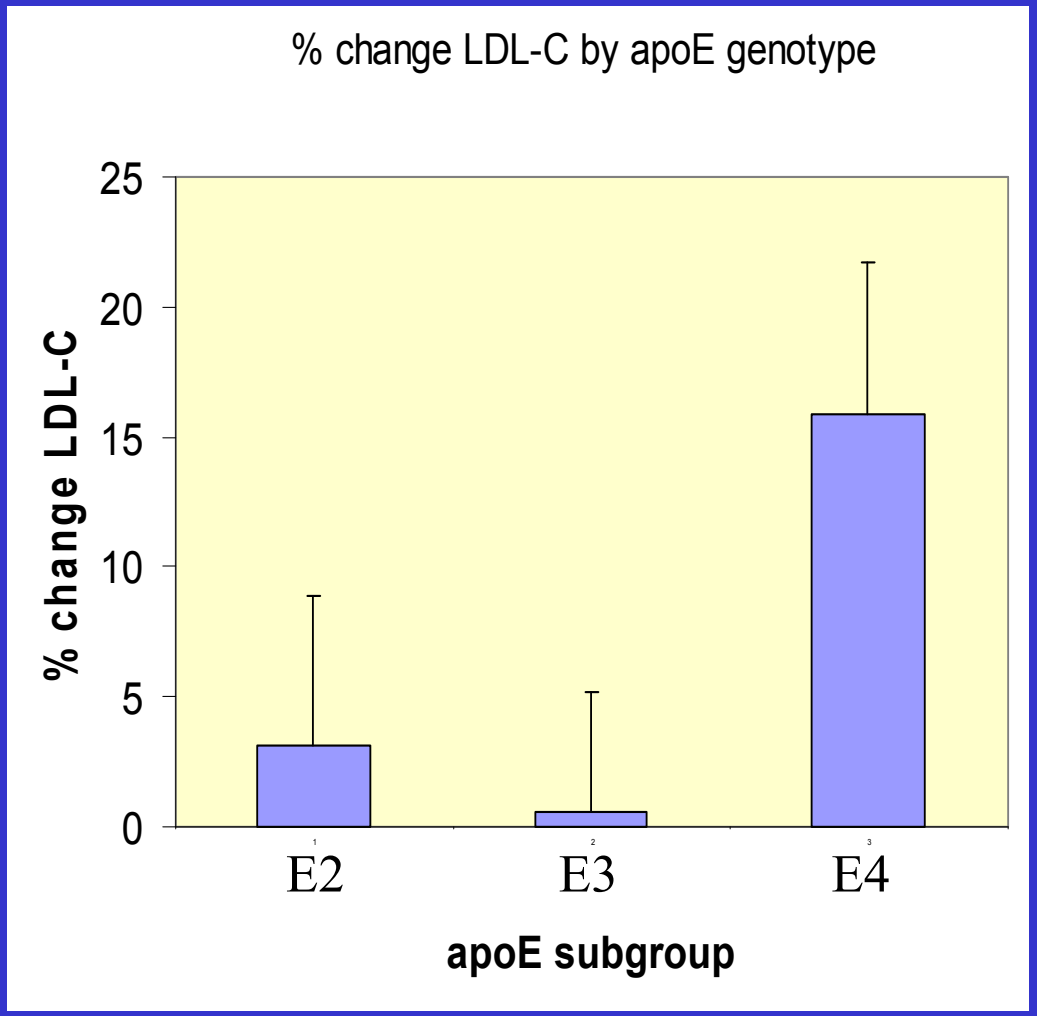
Sarkkinen et al., 1998



The impact of apoE genotype on cholesterol levels/CHD risk depends on the total fat and cholesterol content of the background diet



Minihane et al., 2000



Fat composition and apoE genotype-cholesterol-CHD associations

* Fingen study- Minihane et al., 2003-2005

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