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Dietary fat composition, health and disease

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Outline…….

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- Background: Dietary fat, current recommendations, chronic disease incidence
- Dietary fat & cardiovascular disease
- Dietary fat & diabetes
- The ongoing *Trans* fatty acid saga
- Omega-3 (n-3) fatty acids metabolism
- Genetic variation and response to dietary change, personalised nutrition

Dietary fat……needs a new PR agent!

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- Fat is an essential nutrient

Provides 30-40% dietary energy

Component of cell membranes

Regulator of cell signalling/gene expression

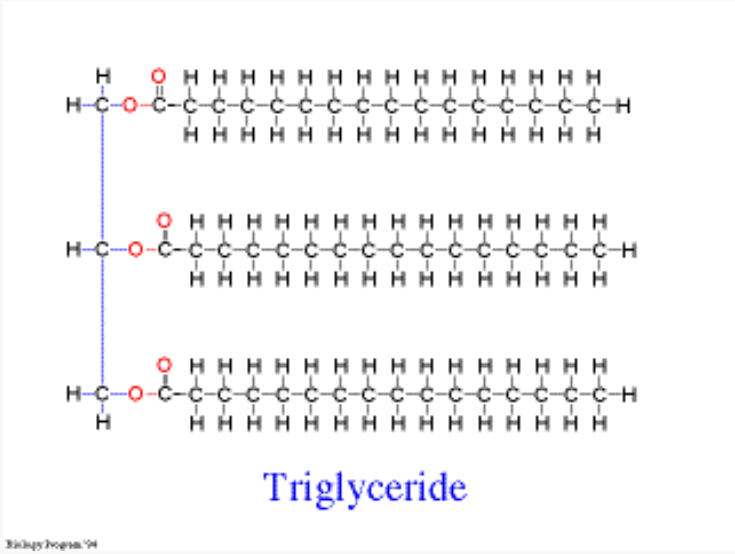
Vehicle for absorption of fat soluble vitamins

Precursors for bioactives e.g eicosanoids

- Total dietary fat content and dietary fat composition mediator chronic disease risk

Fats (lipids) in the diet

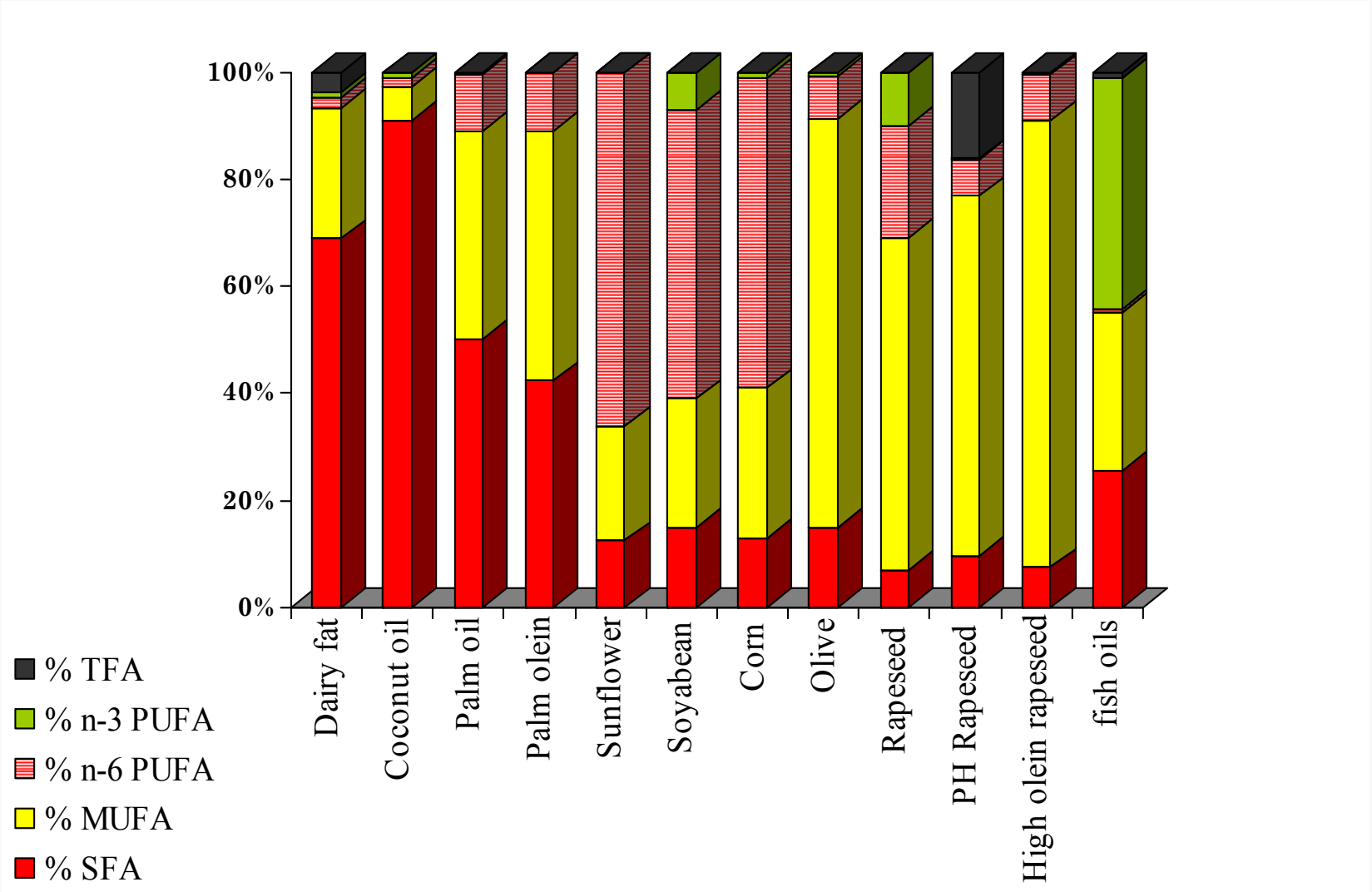
- Consume 50-100g/day
- Triglycerides, cholesterol, phospholipids, minor fats
- 90-95% as trigylcerides



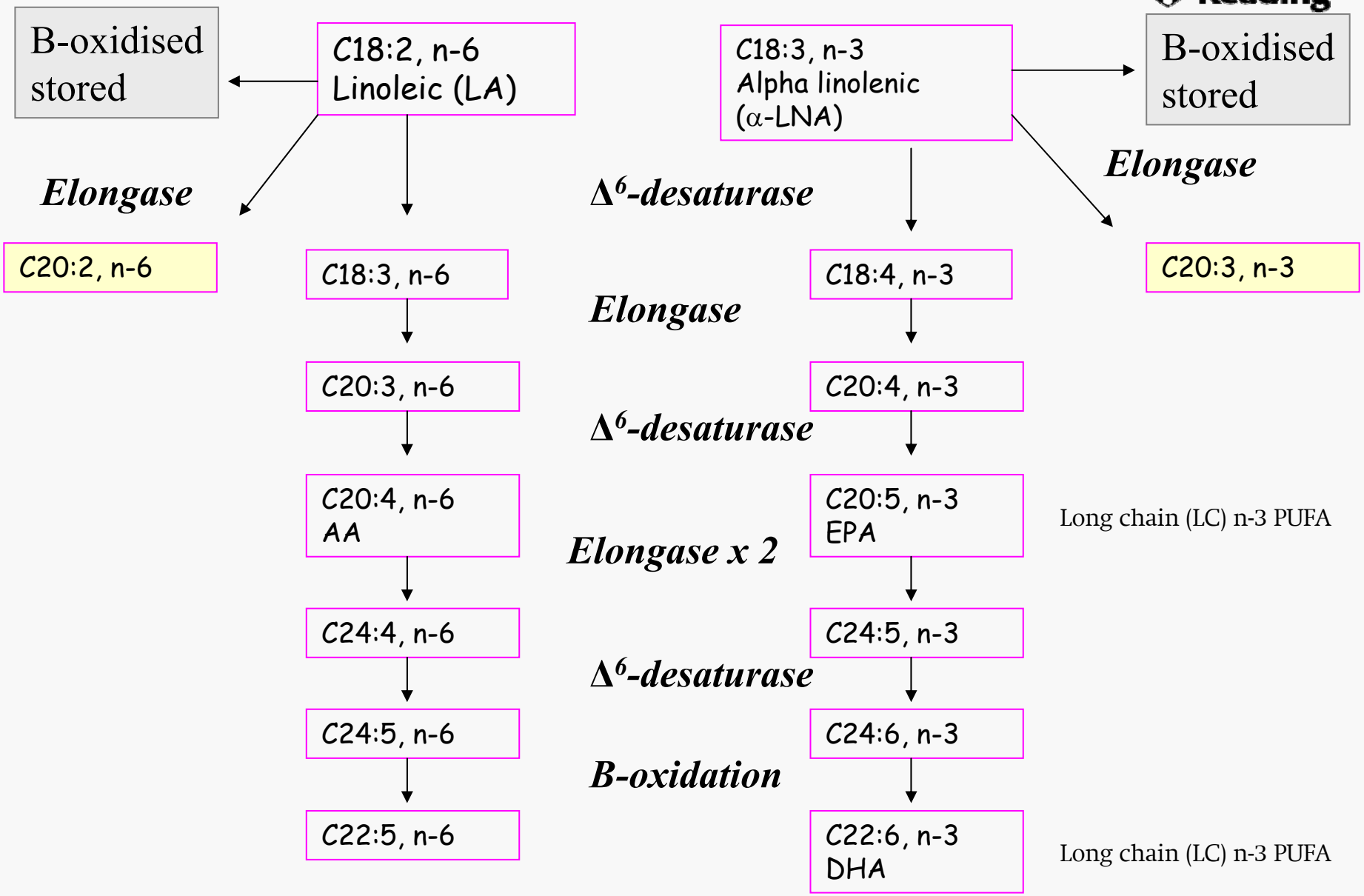
Important fatty acids in foods

Butyric acid	C4:0	Saturated fat (SFA)
Caproic acid	C6:0	
Caprylic acid	C8:0	
Capric acid	C10:0	
Lauric acid	C12:0	
Myristic acid	C14:0	
Palmitic acid	C16:0	
Stearic acid	C18:0	
Oleic acid	C18:1 (n-9) cis	Monounsaturared fat (MUFA)
Eladic acid	C18:1 (n-9) trans	
Erucic	C22:1 (n-9)	
Linoleic	C18:2 (n-6)	Polyunsaturated fat (PUFA)
α-linolenic acid	C18:3 (n-3)	
Arachadonic acid	C20:4 (n-6)	
Eicosapentaenoic acid	C20:5 (n-3)	
Docosahexaenoic acid	C22:6 (n-3)	

Fat composition of common fat sources



Biosynthesis of long chain PUFA from essential fatty acids



Mortality statistics from cardiovascular disease

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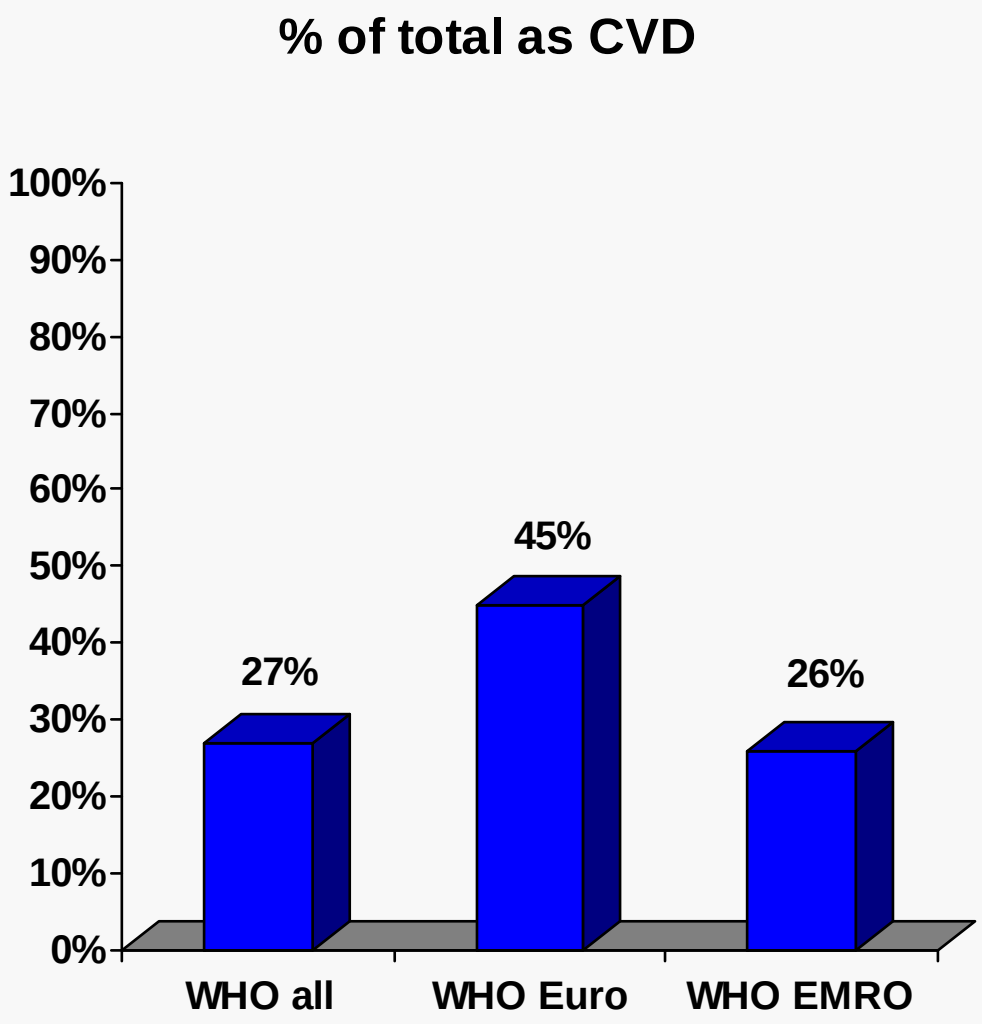

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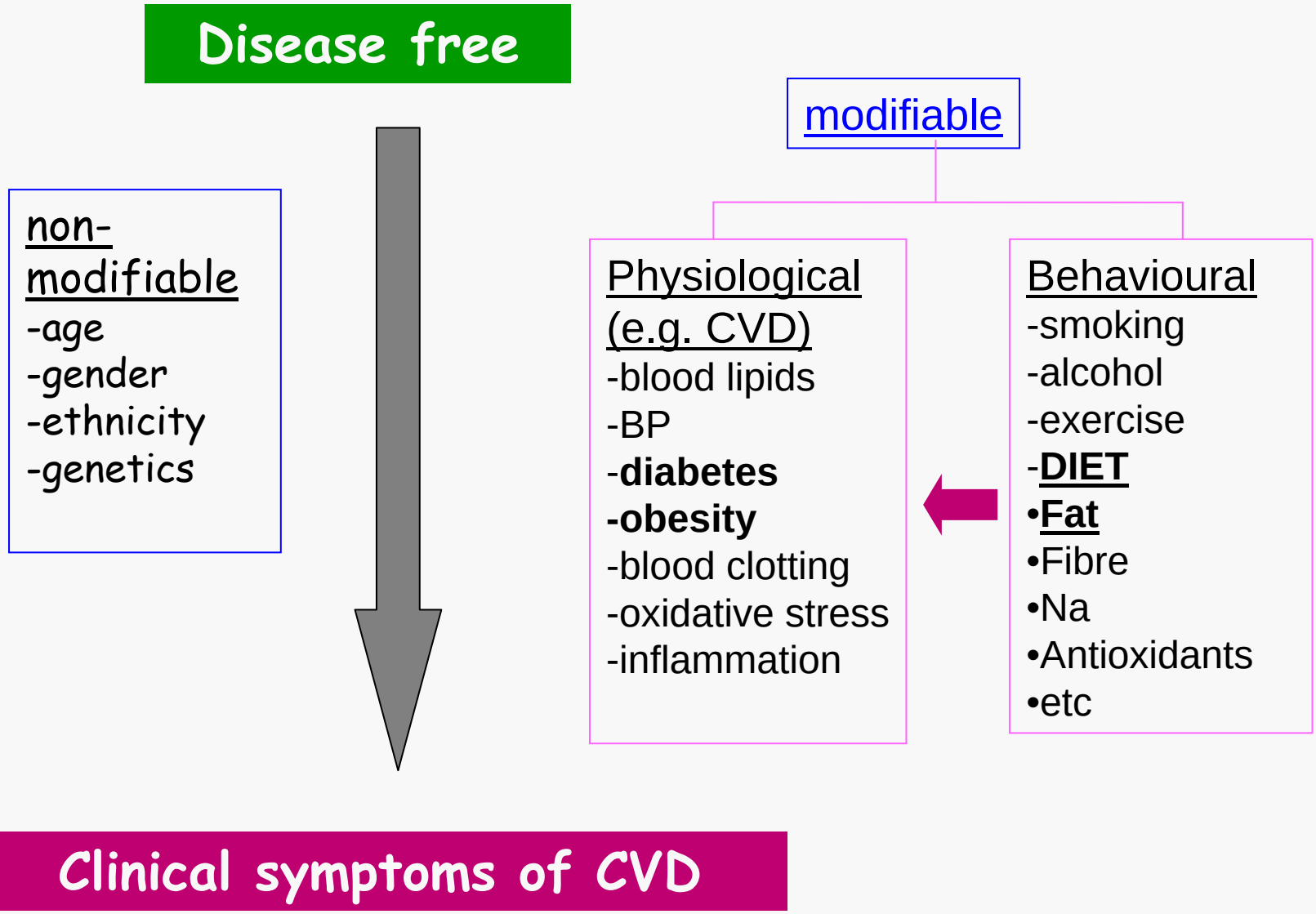

Impact of diabetes on cardiovascular risk

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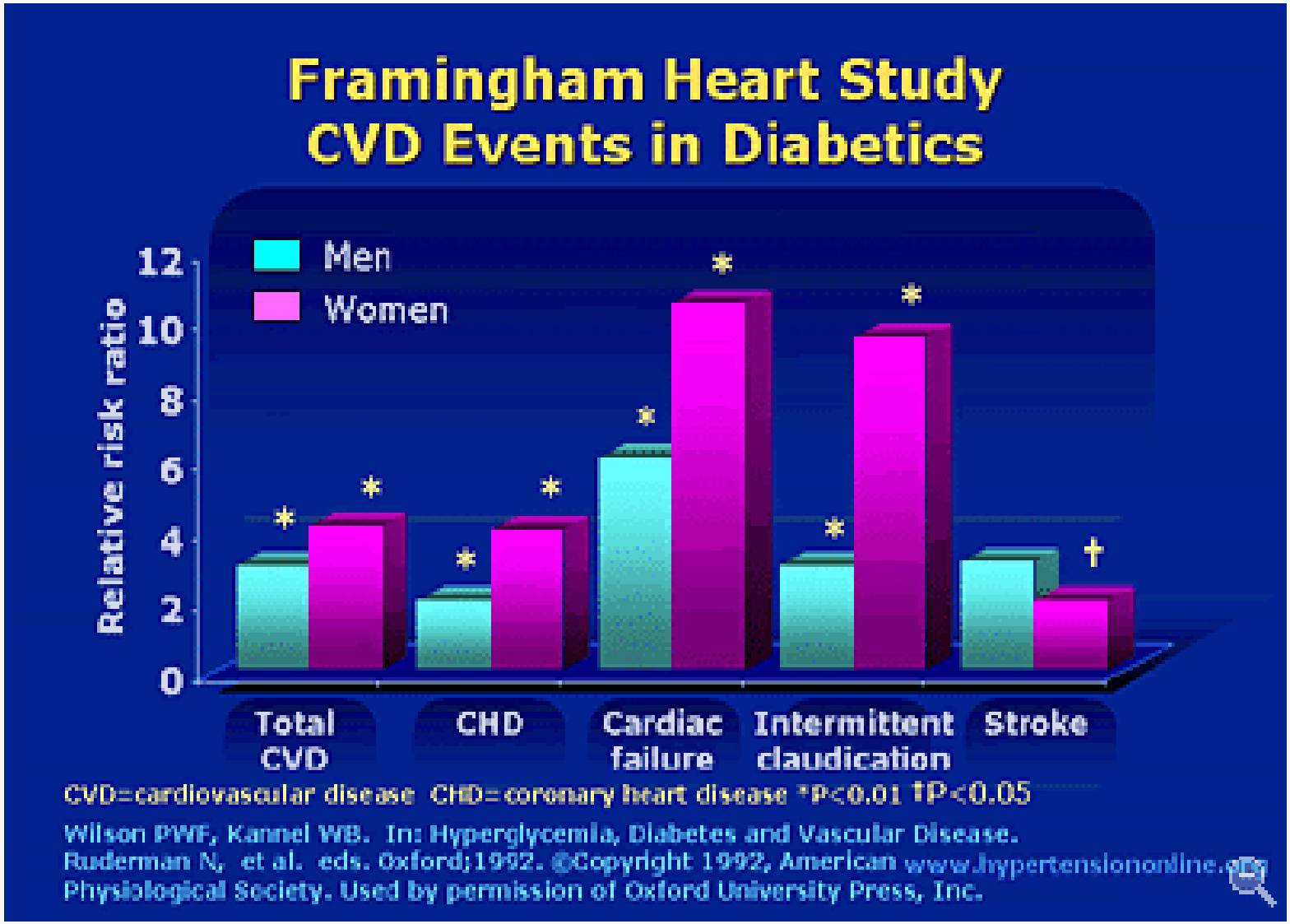

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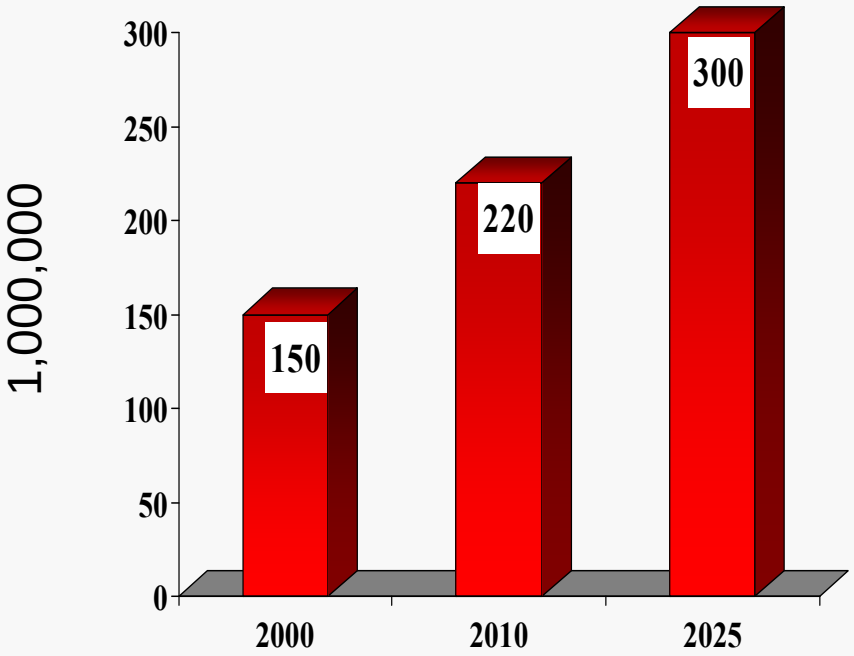
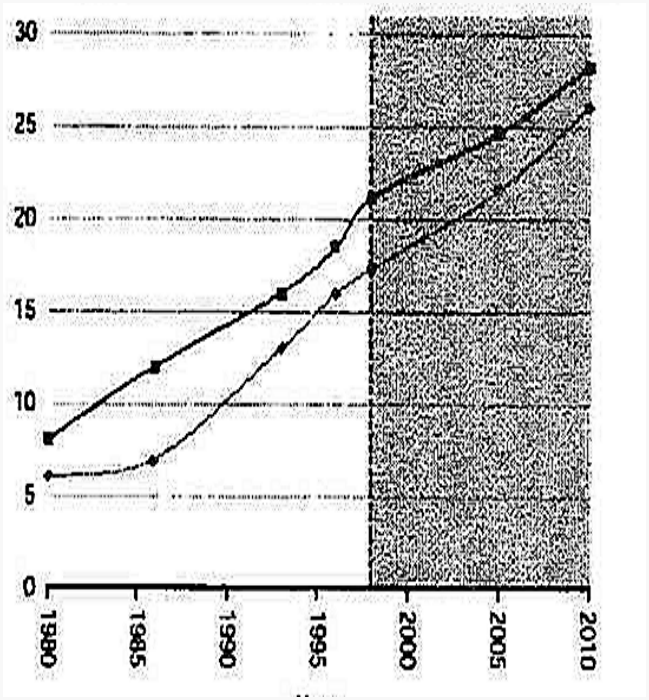
Obesity and diabetes 'the epidemic of the 21st century'



Diabetes worldwide



Obesity UK

- Obese x 12.7 RR diabetes women, x 5.2 men

STRENGTH OF EVIDENCE ON DIETARY FAT AND RISK OF HRONIC DISEASE (WHO/FAO, 2003)

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Evidence	Decreased risk	No relationship	Increased risk
CVD			
Convincing	**LC n-3 PUFA** **Linoleic acid**		**C14:0, C16:0** **Trans FA**
Probable	**α-linolenic acid** **Oleic acid**	**C18:0**	
Possible			**C12:0**
T 2 Diabetes			
Probable			**SFA**
Possible	**LC n-3 PUFA**		**Total fat intake**

FAO/WHO dietary fat guidelines 2003

Fat	% energy
Total fat	no specific recommendation but up to < 35% in highly active group, with high F&V…….. Otherwise much lower
SFA	<10% food energy, < 7% high risk individuals
PUFA	6-10% energy
n-6:n-3 PUFA	2.5:1-8:1
MUFA	no specific recommendation
Trans	<1%
Long chain n-3 PUFA	eat fish once or twice a week

Macronutrient composition of UK diet

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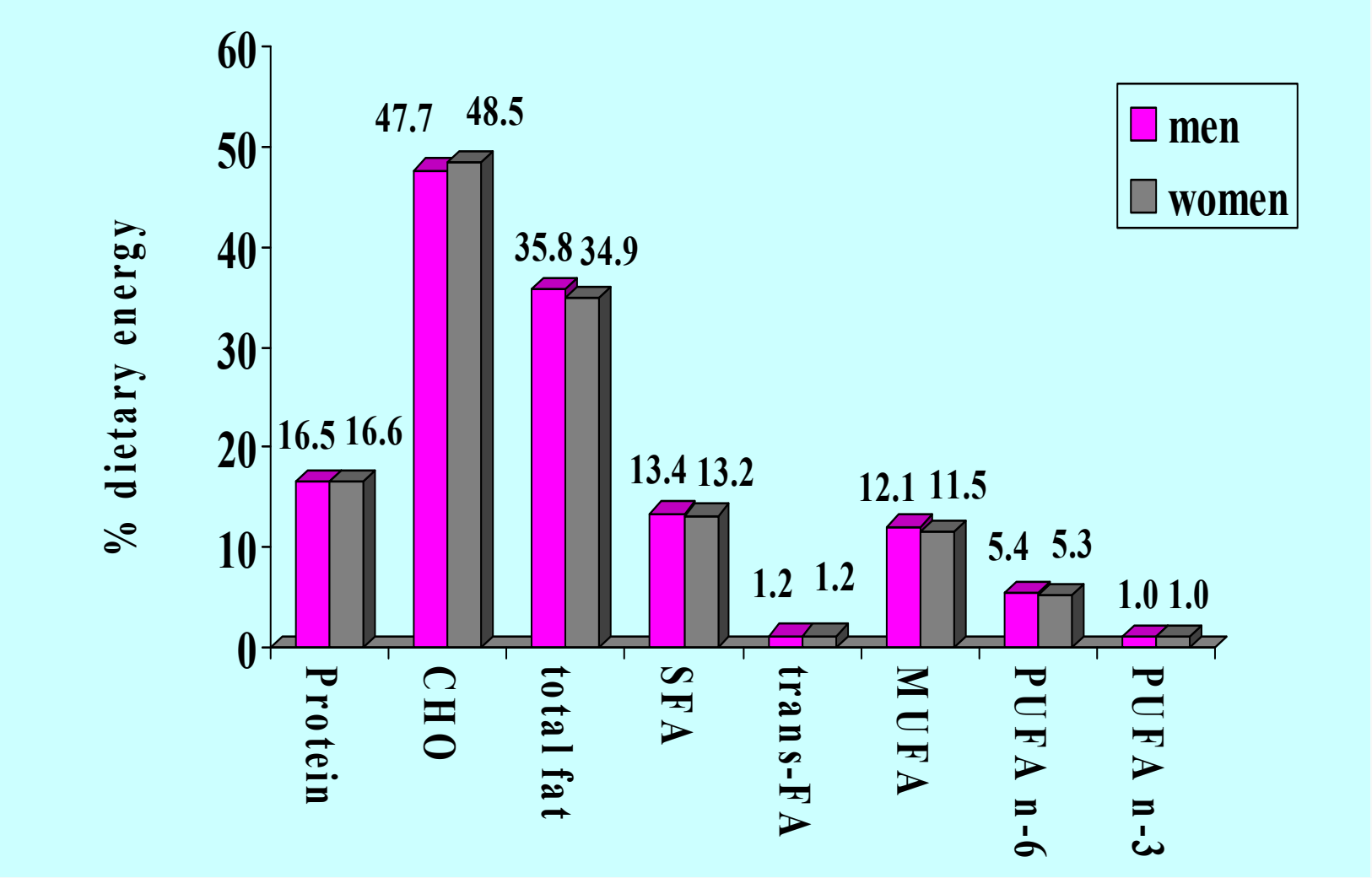

National Diet & Nutrition Survey 2003

Physiological impact of dietary fat

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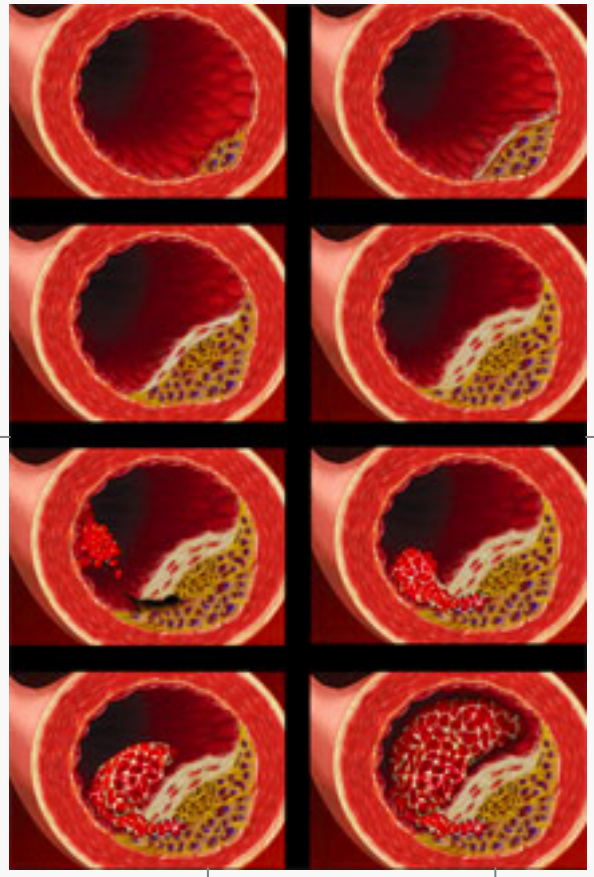
Lipoprotein Metabolism

Blood pressure

Thrombosis & fibrinolysis



Inflammation/ endothelial function/ vascular tone

Plaque structure

homocysteine

obesity

Diabetes/ insulin resistance

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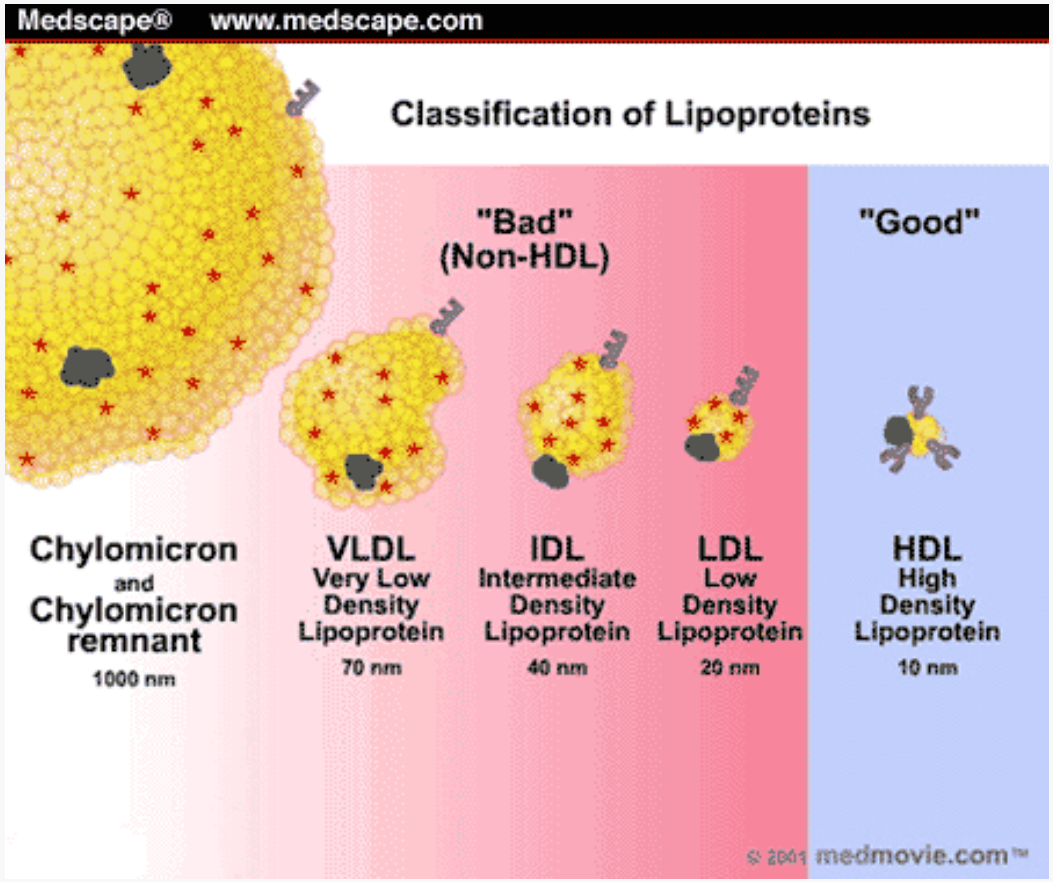

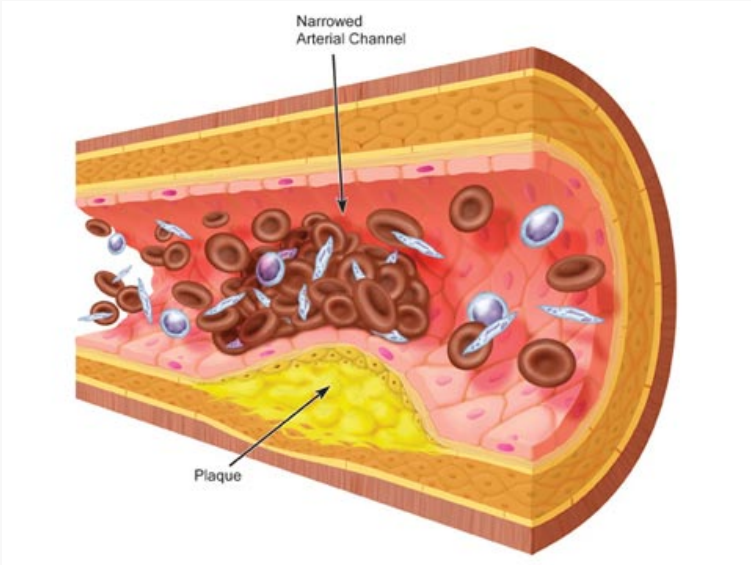

Diabetes/obese: ↑ TG, ↑ LDL-3, ↓ HDL

Fat replacement strategies and impact on blood lipids

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A Symposium: Effects of Dietary Fat and Carbohydrate on Plasma Lipoproteins and CVD/Sacks and Katan

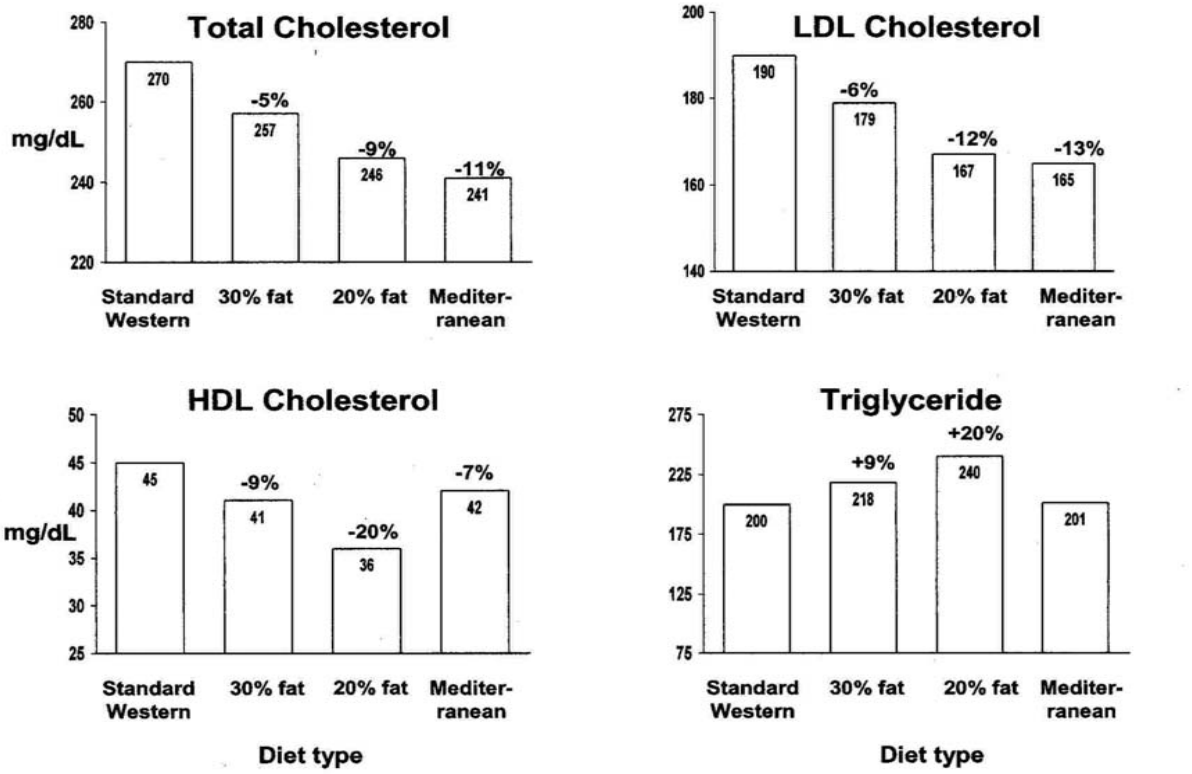

Figure 1. Predicted changes in plasma cholesterol and triglyceride concentrations caused by 3 types of diet treatment: 30% fat (step 1), 20% low-fat, and Mediterranean. The standard Western and Mediterranean diets have 38% fat. The dietary changes are described more fully in the text. The meta-analysis of Mensink and Katan[13] 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?

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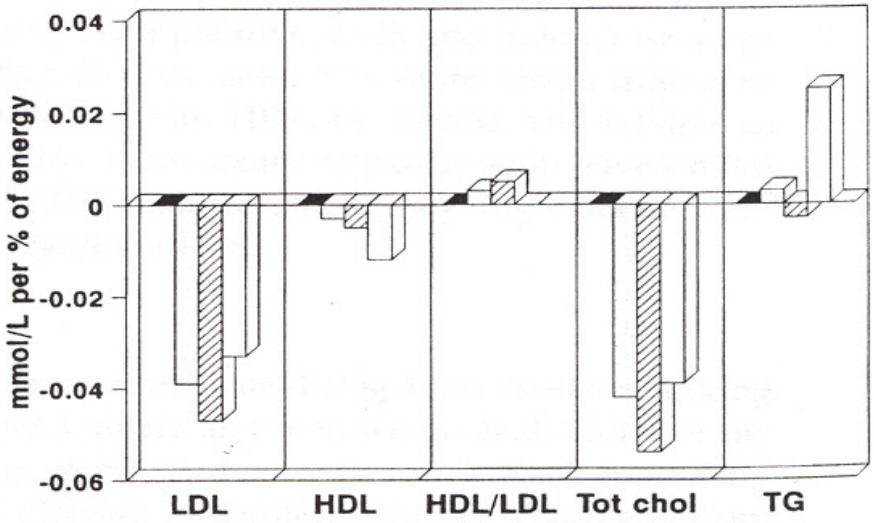

FIG 2. Predicted changes in serum lipids and lipoproteins when 1% of dietary saturated fatty acids is replaced by fatty acids of a particular class or by carbohydrates under isoenergetic metabolic-ward or equivalent conditions. ■, saturated; ▩, monounsaturated; ▨, polyunsaturated; □, carbohydrate. Chol,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

Katan et al., 1994

Are all saturated fats 'equal' with respect to their cholesterol lowering effects

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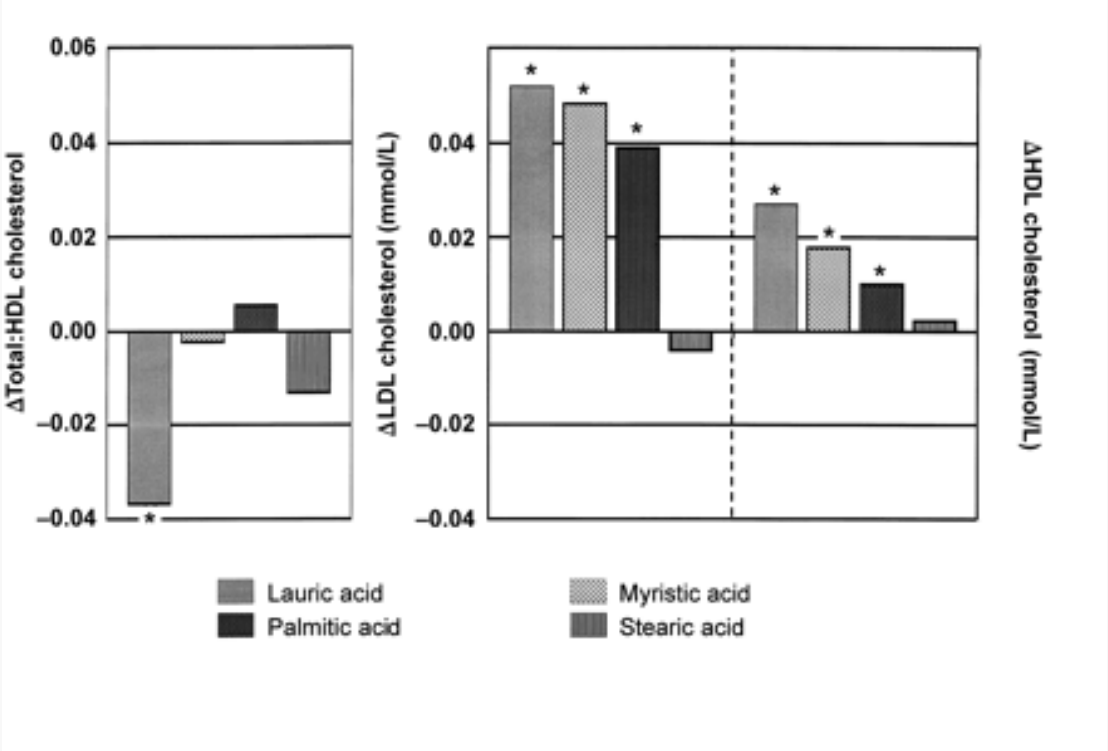
- Katan et al., 1994; Mensink et al., 2003
- Lauric (C12:0), Myristic (C14:0), Palmitic (16:0)
- No as different as originally thought



New focus on cholesterol ratio!
Dietary fat & total:HDL-cholesterol ratio

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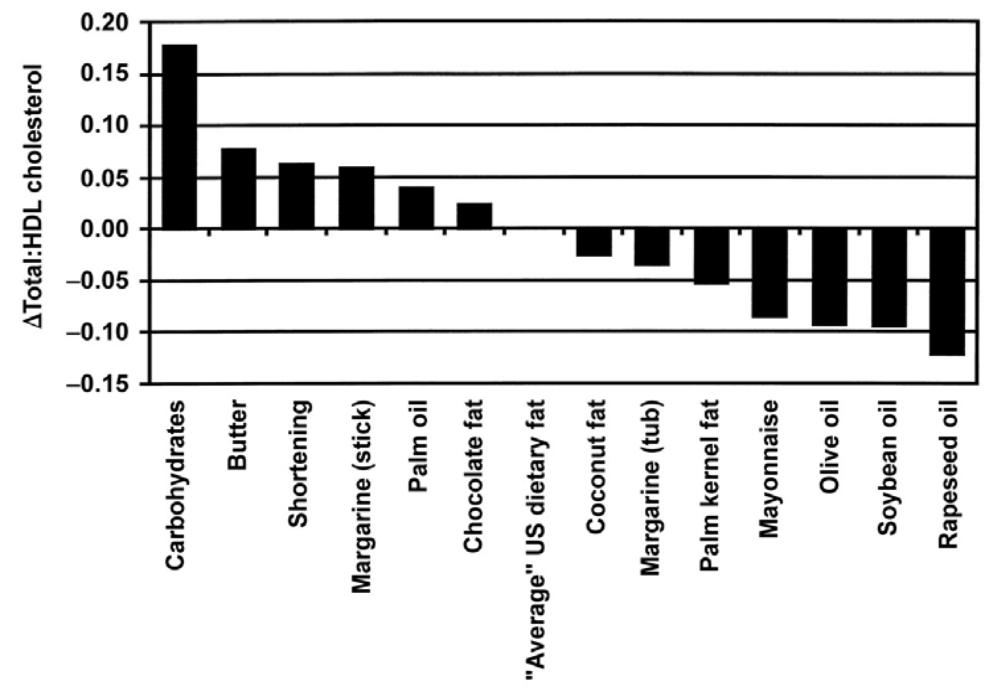
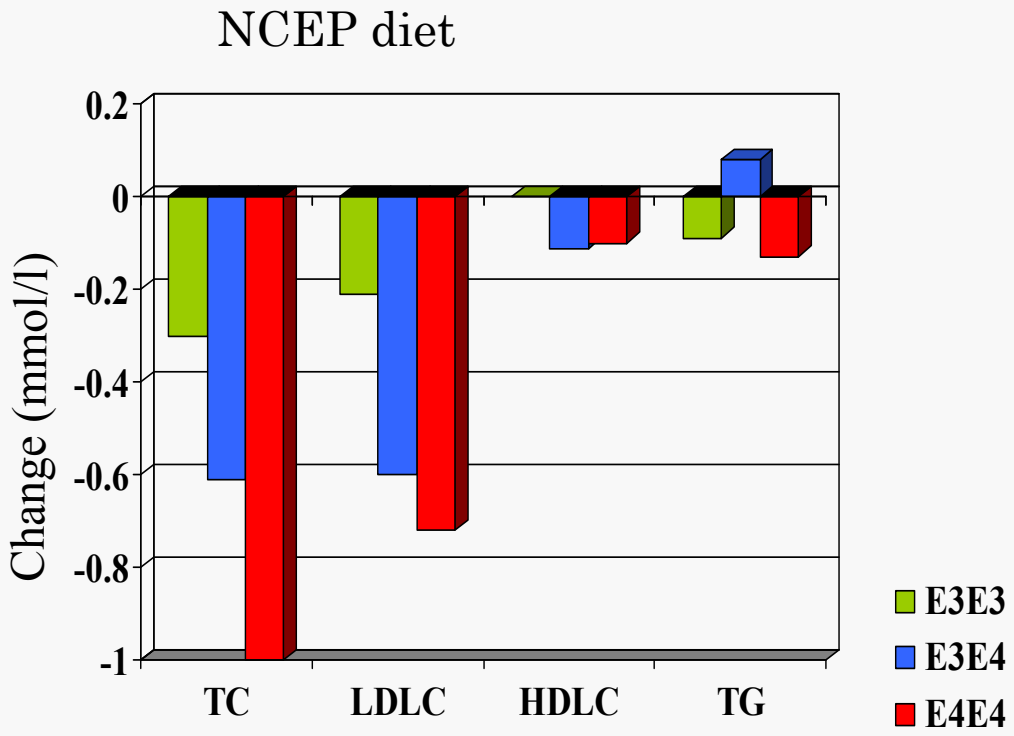
- meta-analysis of n=60 trials
- n=1672



Mensink *et al.*, 2003

Benefits gained from dietary fat manipulation are highly variable and dependant on your genetic make-up/gender/medication use etc

Move towards more personalised approach to the prevision of dietary advice



Sarkkinen et al., 1998

Cardiovascular benefits of fish oil fatty acids consistently demonstrated Physicians Health Study: n=22,000, 17y follow-up, Albert *et al.*, NEJM, 2002)

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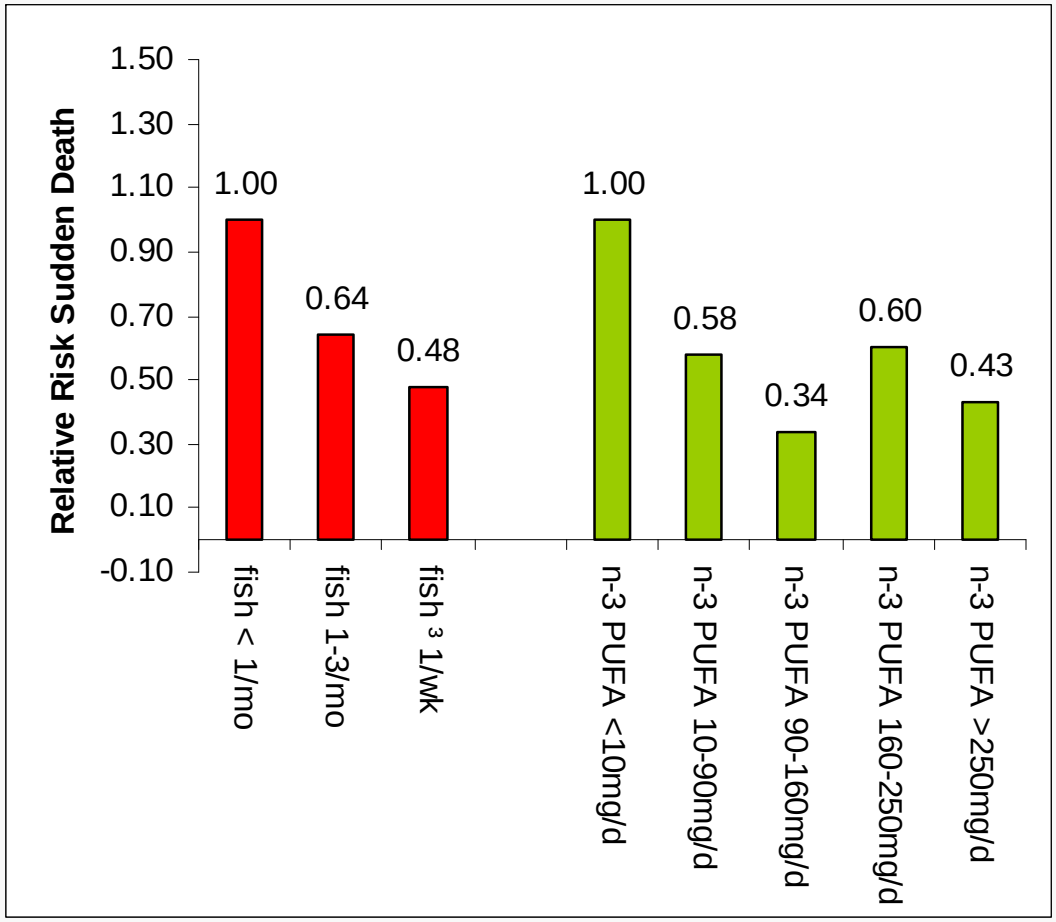

No evidence for benefit for CVD incidence or MI incidence

Why are EPA/DHA cardioprotective?

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Improve lipoprotein profile

↓ blood clotting

plaque structure

↓ blood pressure

improves endothelial function

anti-inflammatory

anti-arrhythmic

Buckley R, Shewring B, Turner R, Yaqoob P, Minihane AM. *British Journal of Nutrition* 2004:92:477-483.

Dolores Mesa, M, Buckley R, Minihane AM, Yaqoob P *Atherosclerosis* 2004;175:333-343.

Finnegan YE, Minihane AM, Leigh-Firbank EC, Kew S, Meijer GW, Muggli R, Calder PC, Williams CM. *American Journal of Clinical Nutrition* 2003:77:783-95.. (3.3)

Finnegan YE, Howarth D, Minihane AM, Kew S, Miller GJ, Calder PC, Williams CM. Plant and marine derived (n-3) polyunsaturated fatty acids do not affect blood coagulation and fibrinolytic factors in moderately hyperlipidemic humans. *J Nutrition* 2003;133:2210-2213. (3.3)

Khan S, Minihane AM, Talmud P, Wright JW, Murphy MC, Williams CM, Griffin BA. *Journal of Lipid Research* 2002;43:979-985. (3.9)

Minihane AM, Khan S, Leigh-Firbank EC, Talmud PJ, Wright JW , Murphy MC, Griffin BA, Williams CM. *Arteriosclerosis, Thrombosis and Vascular Biology* 2000;20:1990-7.

Fish oil fatty acids & blood lipids

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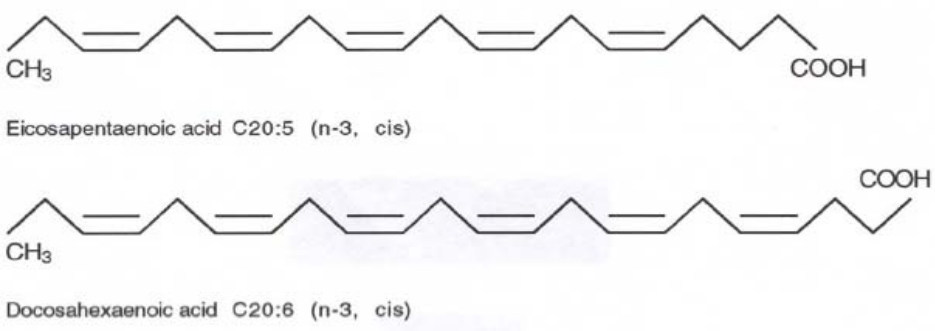
Double-blind placebo-controlled cross over study- n=55

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

Fish oil fatty acids & blood lipids

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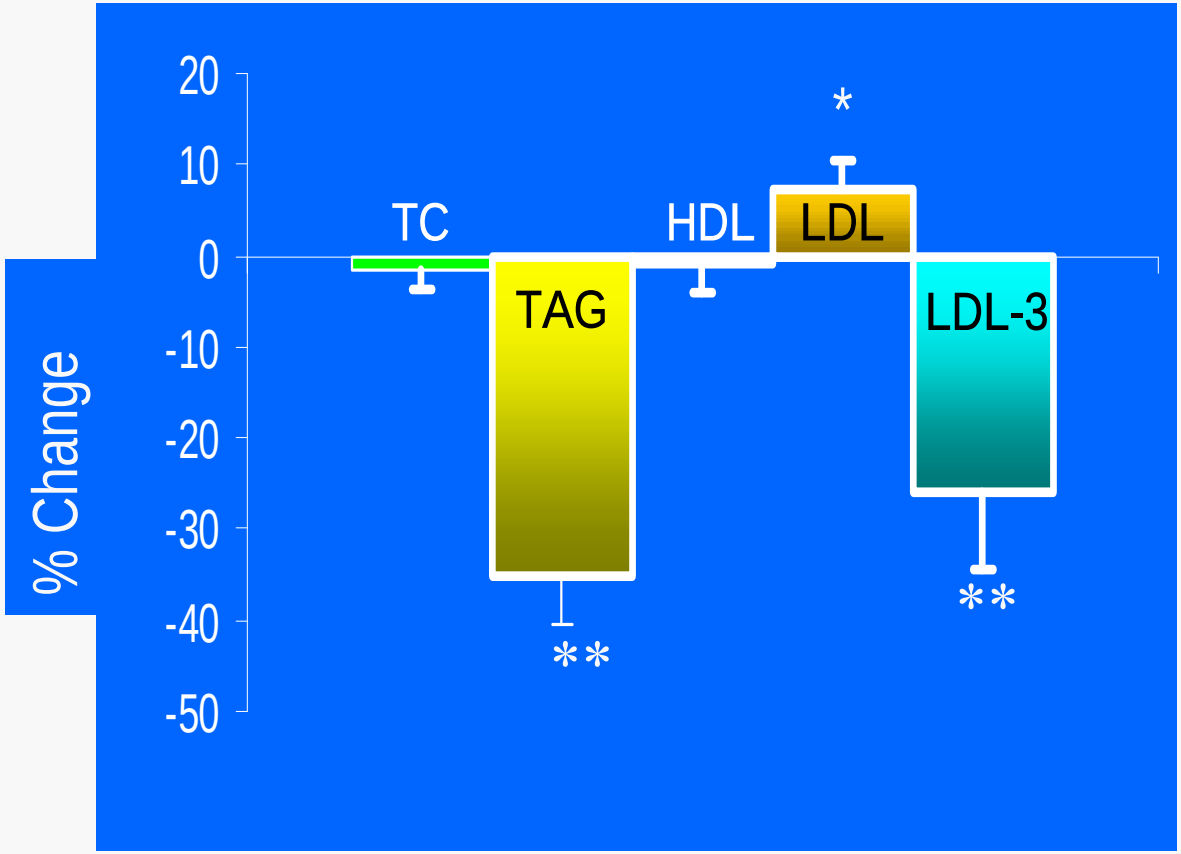
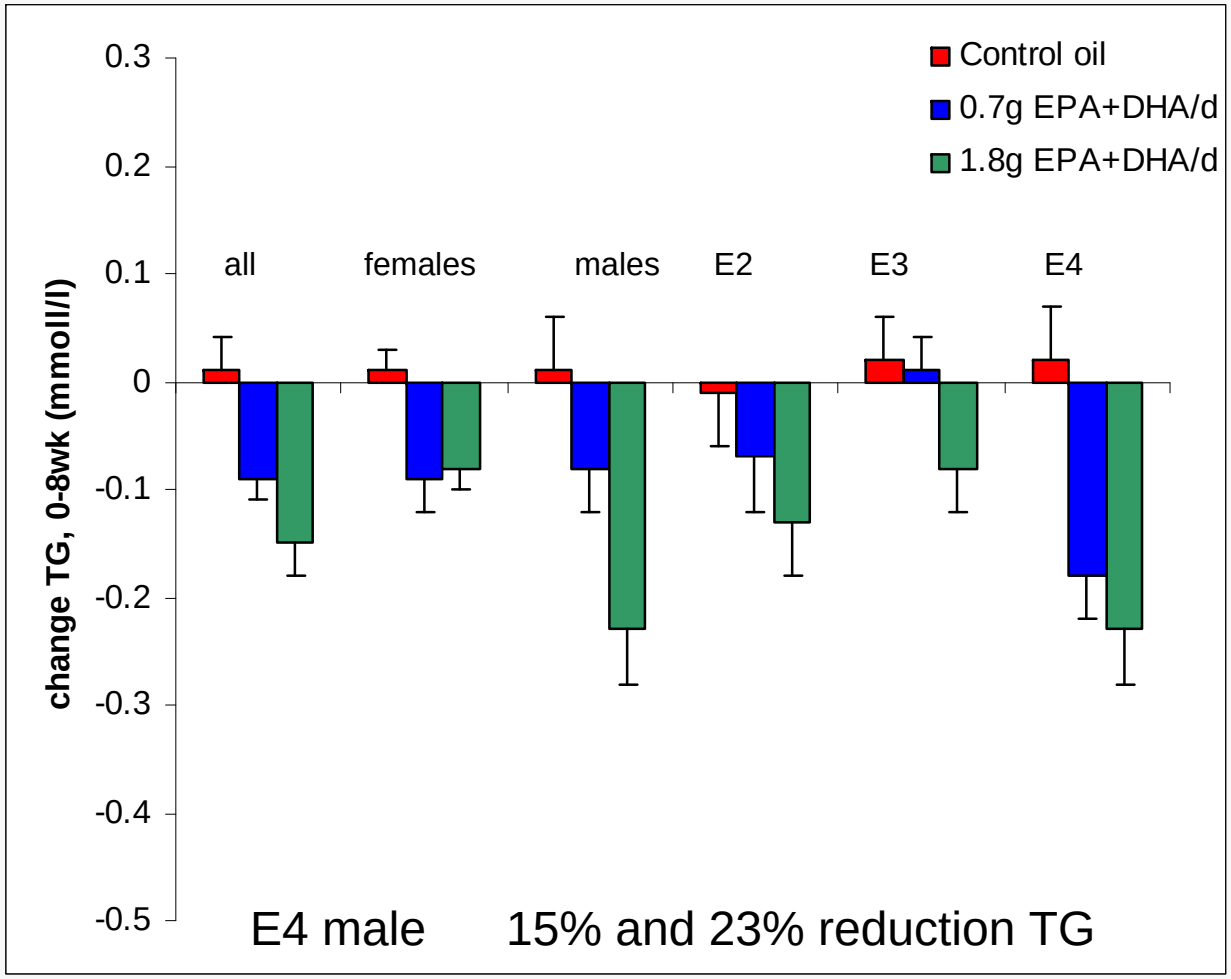


Minihane *et al.*, 2000

* p< 0.05 ** p< 0.001

TG lowering was dependant on gender and apoE genotype



Minihane *et al., AJCN submitted*

Fish oils improve vascular reactivity

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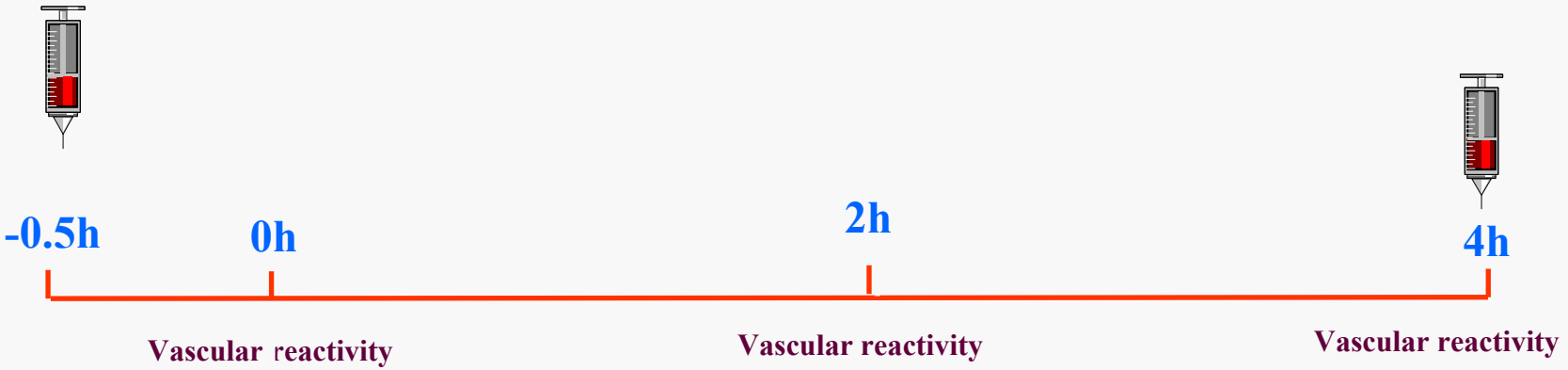
- 25 healthy men - mean age 46 (SD 18) years
  BMI 25.5 (SD 3.8) kg/m^2
- test meals:
  - placebo oil meal (40 g mixed oil; 80:20, palm olein:soybean oil)
  - fish oil meal (31 g mixed oil and 9 g fish oil; **5.4 g EPA/DHA**)



Plasma – TAG (automated enzyme based assay)
– total nitrite (colorimetric assay)

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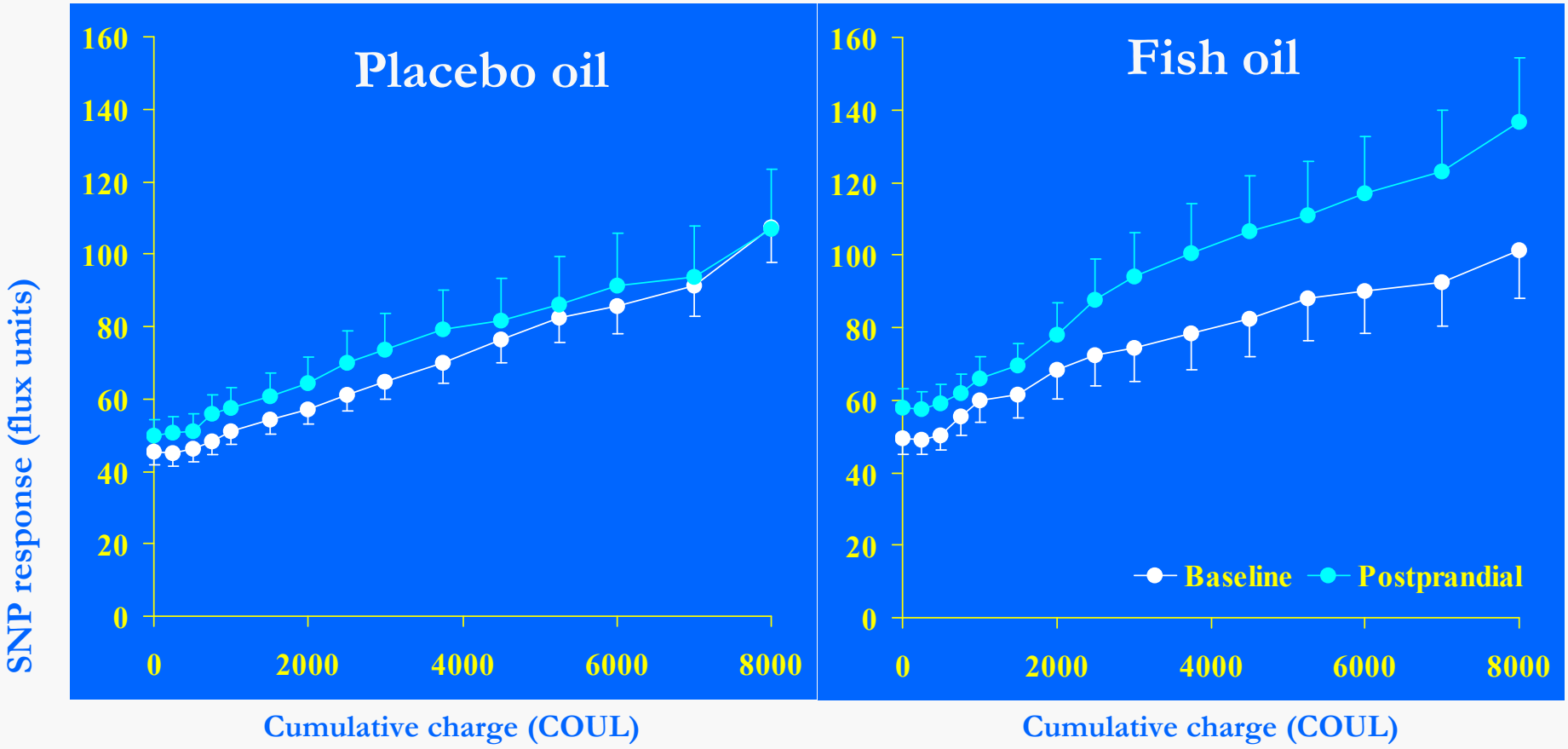

Armah *et al.*, 2007; Jackson *et al.*, 2007

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Recent estimated daily intakes of EPA + DHA in various countries

Country	Details	Intake of EPA+ DHA (mg/person/d)	Reference
UK	Adults, 19-64 years mean	244	Givens and Gibbs (2006)
UK	Females, 19-24 years, mean	109	Gibbs *et al*. (2007)
Belgium	Females, 18-39 years, mean	209	Sioen *et al*. (2006)
Belgium	Females, 18-39 years, median	50	Sioen *et al*. (2006)
Belgium	Children 4-6.5 years, mean	75	Sioen *et al*. (2007)
France	Women 45-63 years	344	Astorg *et al*. (2004)
Australia	Adults	143	Howe *et al*. (2006)
N. America	Adults	200	Vermunt and Zock (2007)
Mid-Europe	Adults	250	Vermunt and Zock (2007)
Northern Europe	Adults	590	Vermunt and Zock (2007)
Japan	Adults	950	Vermunt and Zock (2007)

Alpha-linolenic acid (αLNA) as a substitute for EPA/DHA
Linseed/Rapeseed/Soybean as a substitute for fish oils?

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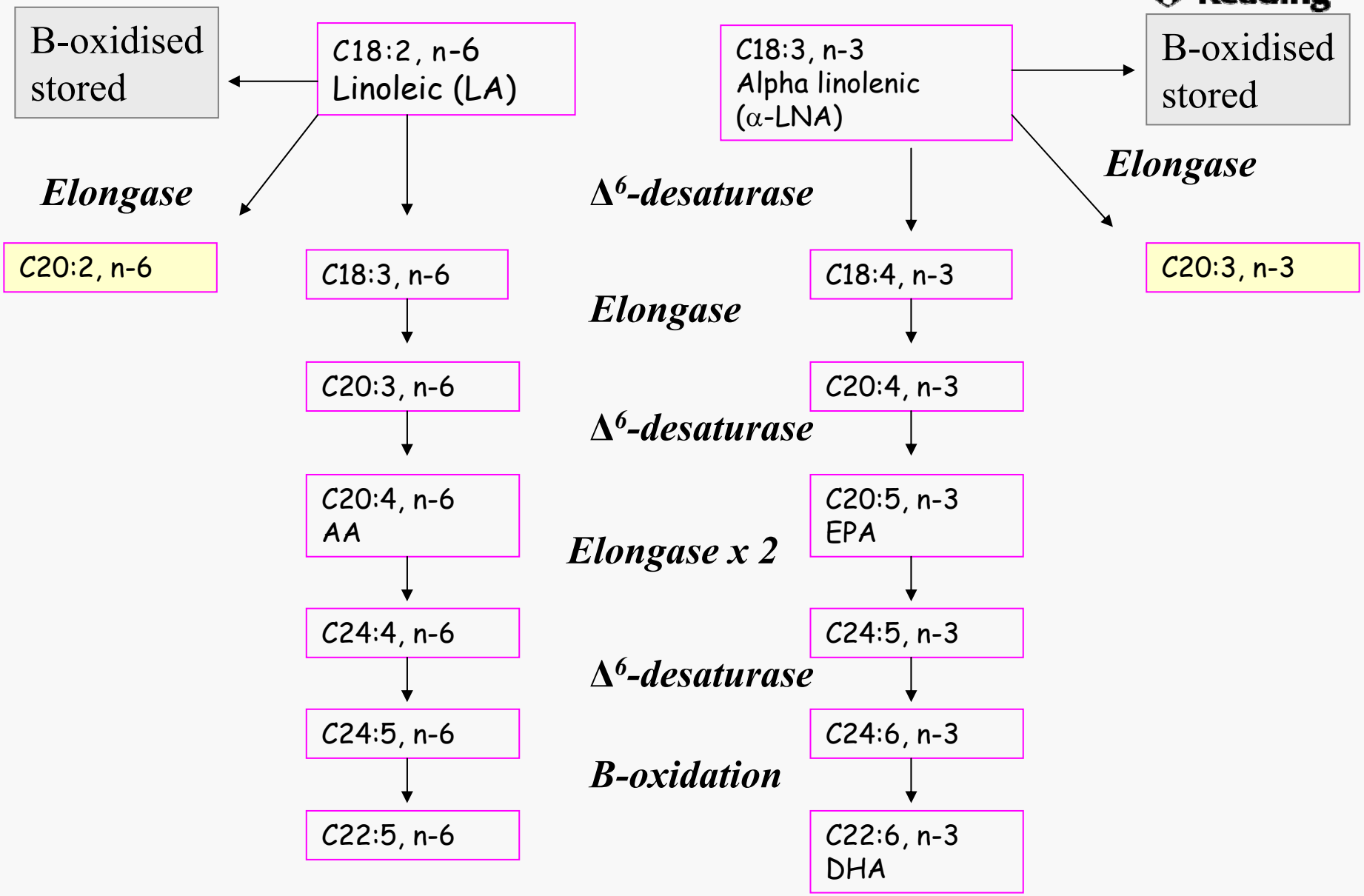
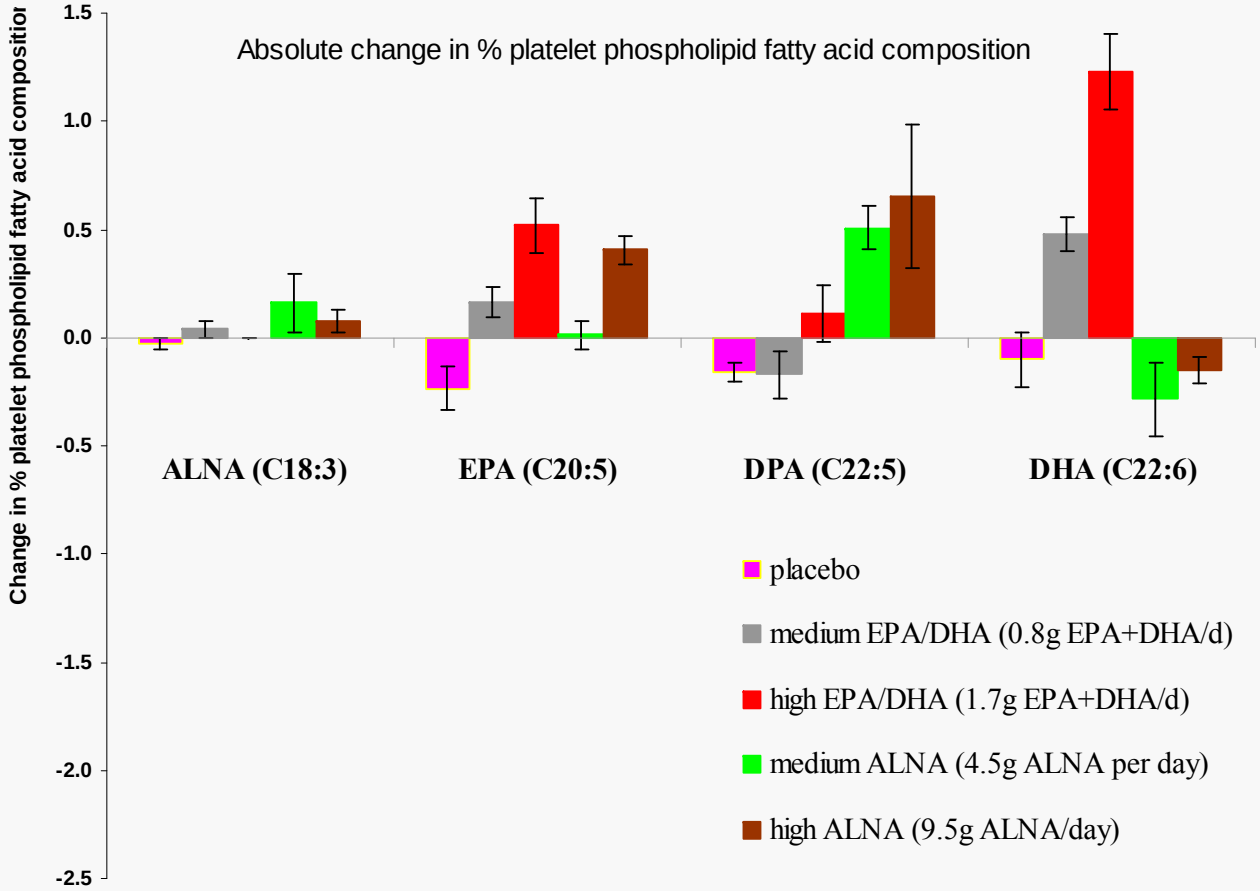
- not independently?
- Burdge & Calder, Nutrition Research Reviews, 2006
- 'Overall the limited capacity for conversion to the longer-chain n-3 fatty acids, and the lack of efficacy in ameliorating CVD risk factors and inflammatory markers in man suggests than increased consumption of ALNA may be of little benefit in altering EPA+DHA status or in improving health outcomes compared with other dietary interventions'

Wang C, Harris *et al.*, **n-3 Fatty acids from fish or fish-oil supplements, but not alpha-linolenic acid, benefit cardiovascular disease outcomes in primary- and secondary-prevention studies: a systematic review.**
Am J Clin Nutr. 2006 Jul;84(1):5-17.

Biosynthesis of long chain PUFA from essential fatty acids



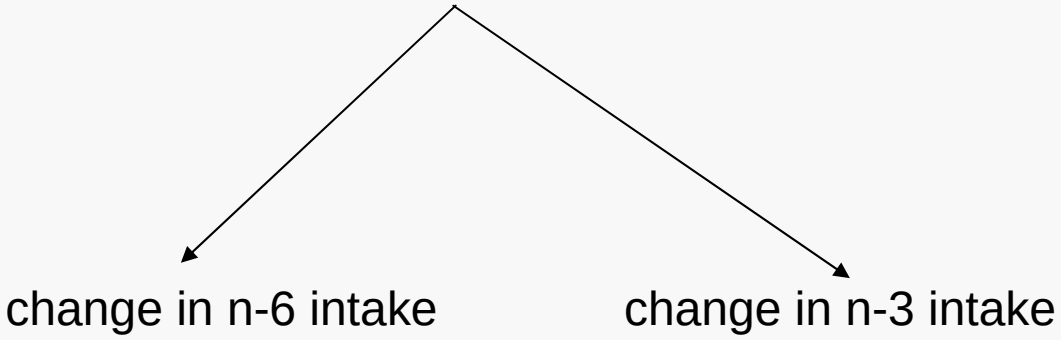
αLNA as a source of EPA/DHA: Bioconversion efficiency is poor



Burdge et al., 2003; Funnegan et al., 2003a ; Finnegan et al., 2003b; Kew et al.,2003a; Kew et al., 2003b

What are the main factors which influence the efficiency of conversion of α-LNA to EPA/DHA

1. Gender
2. Physiological status: Pre vs postmenopausal, pregnant vs non-pregnant??
3. αLNA intake, LA intake, LA:αLNA (n-6:n-3 PUFA) ratio; altered by



αLNA metabolism: men vs women

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Conversion of αLNA to:-	Men	Women
EPA	4%	21%
DPA	8%	6%
DHA	<0.02%	9%
β-oxidation	33%	22%

Burdge et al. 2002; Burdge & Wootton 2002, 2003

Compromised vegan EPA/DHA status
(Davis & Kris-Etherton2003)

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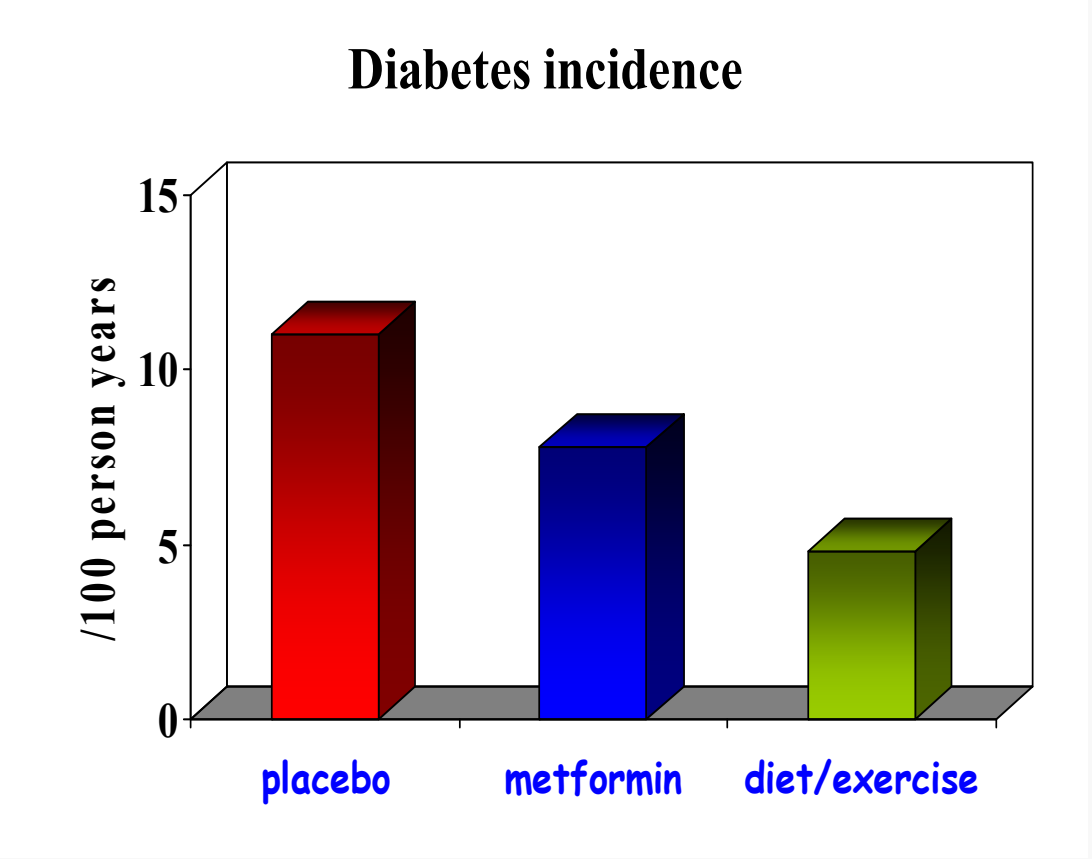
- Associated with compromised EPA/DHA status
- Sanders et al., 1978: EPA and DHA levels in vegans of 12-15% and 32-35% those in omnivores
- Sanders et al., 1992: Vegan infants < 30% of EPA/DHA relative to omnivores
- More compromised in vegans than vegetarians as eggs (~50mg DHA/egg) and milk a source
- n-6: n-3 PUFA ratio: < 10:1, 10:1-16:1 and 14:1-20:1 in omnivores, vegetarians and vegans
- αLNA rich oils suggested as oil source in vegetarians and vegans
  -Linseed (flaxseed) n-6:n-3 PUFA- 0.28:1
  -Rapeseed oil (canola): n-6:n-3 PUFA- 2:1
  -Soybean: n-6:n-3 PUFA- 2:1

Strong emerging evidence to indicate lifestyle has large impact on diabetes risk

- n= 3234 subjects with high fasting and post-load glucose
- Follow up 2.3 years



Knowler et al. (2002) *New Engl. J Med*, 346, 393-403

Observation studies in humans and animal invention trials have shown that saturated fat is associated with a loss of insulin sensitivity…..

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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

Human intervention trials to date disappointing!

KANWU study
Vessby et al., 2001

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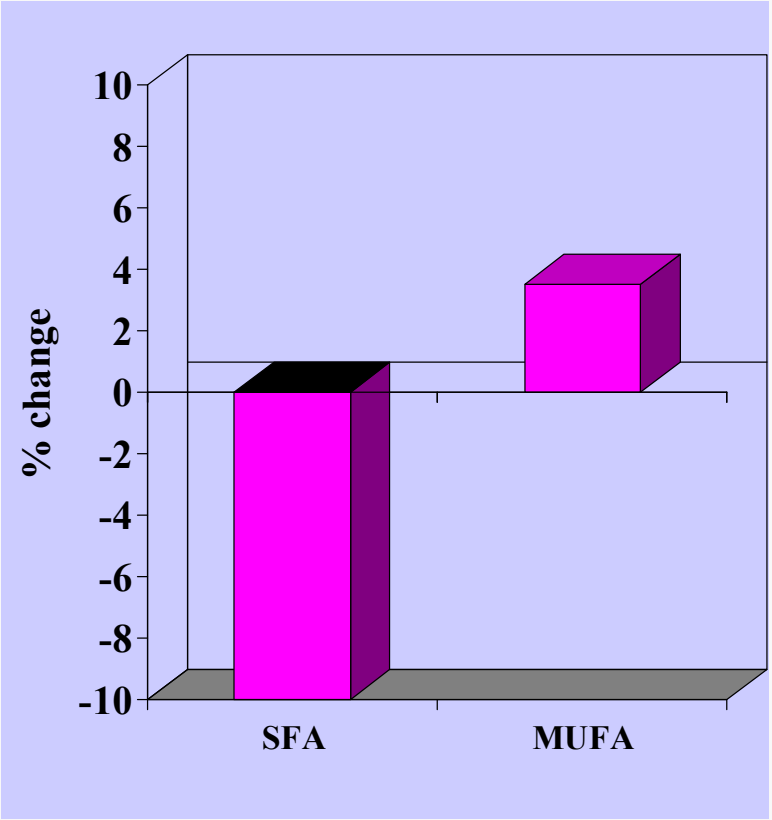
- 162 healthy men and women
- 3 months
- SFA v MUFA rich diet

- 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**



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Research needs in dietary fat composition and insulin action/MS/diabetes

Intervention studies with following study attributes

- Compare impact of realistic alterations in total fat intake or fat composition (SFA, MUFA, PUFA ratios) on insulin action
- Use of robust measurements of insulin action
- Adequately power
- Longer intervention periods
- Healthy or early disease cohorts

RISCK
READING/IMPERIAL/SURREY/CAMBRIDGE/KINGS

www.risck.org.uk

-n=650
-6 months intervention

-5 diets
Diet A: 38% fat, 18% SFA, 12% MUFA
Diet B: 38% fat, 10% SFA, 20% MUFA
Diet C: Diet B with low GI
Diet D: 28% fat
Diet E: Diet D with low GI

Lipgene

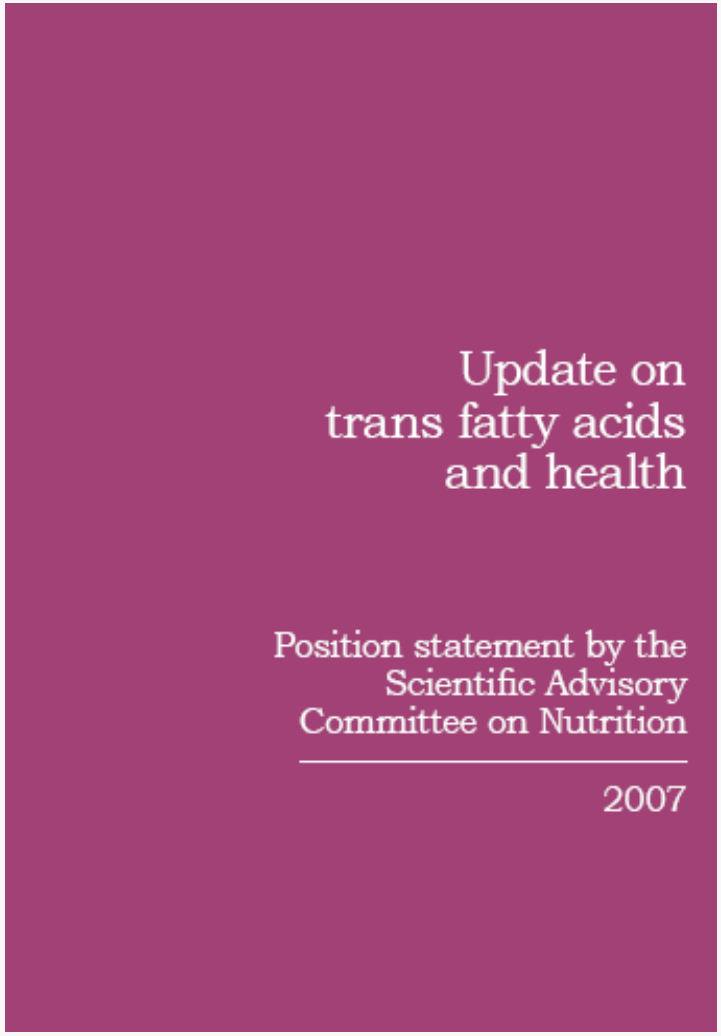
SIXTH FRAMEWORK PROGRAMME

www.lipgene.tcd.ie

-n=480
-3 months intervention

-4 diets
Diet A: 38% fat, 18% SFA, 12% MUFA
Diet B: 38% fat, 10% SFA, 20% MUFA
Diet C: 28% fat
Diet D: Diet C + 1g EPA/DHA

Reading: Lovegrove, Williams, et al.,



Main conclusions of report

- Consistent evidence TFA ↑ CHD risk
- Largely due to effects on LDLC and HDLC
- Other mechanisms also likely
- Most evidence derived from epidemiological studies where range of intakes several fold higher than current intakes
- Some suggestion TFA associated with diabetes & obesity. However evidence limited
- Distinct lack of information on 1-3% of dietary energy range

- Great care is needed that reformulation of fat currently underway to minimise TFA intakes do not inadvertently increase SFA intakes

Zupthen Elderly Study
1985, 10y follow up

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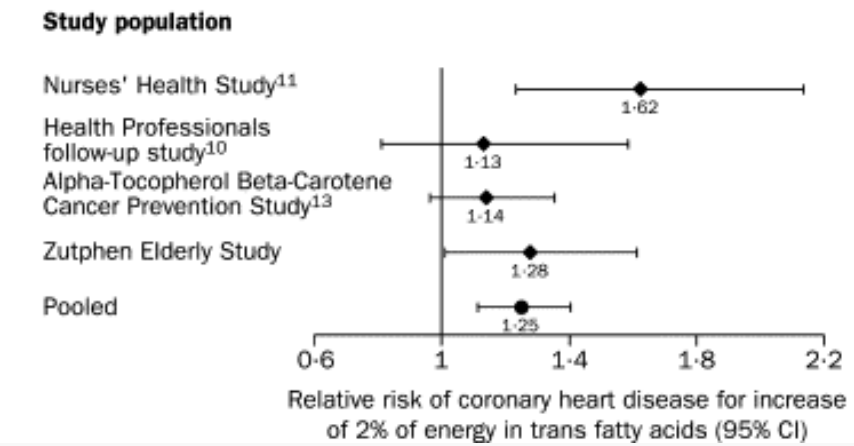
Risk of CHD

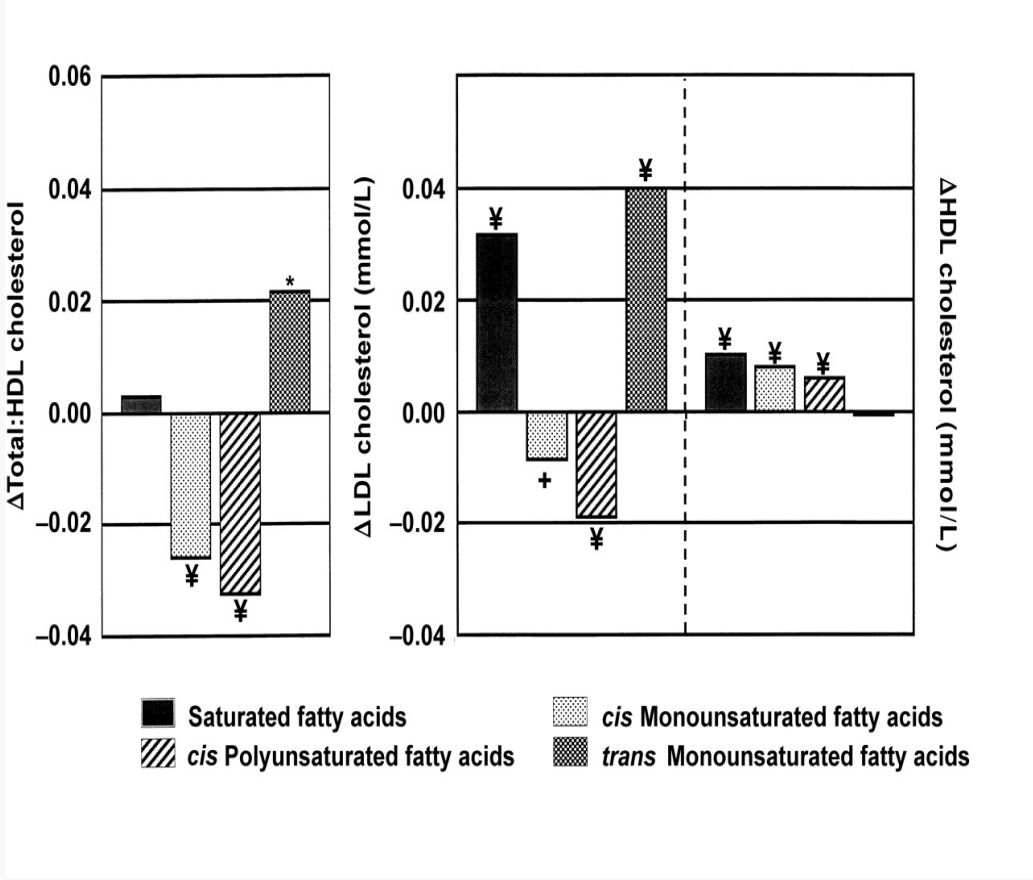
	Trans fatty acid tertile (% of energy)			p value*
	<3·11 (n=222)	3·11–4·86 (n=223)	>4·86 (n=222)	
Median intake (% of energy)	2·36	3·87	6·38	..
Cases	24 (11%)	33 (14%)	44 (20%)	..
Relative risks (95% CI)				
Crude	1	1·26 (0·74–2·15)	2·09 (1·24–3·34)	0·009
Age+energy adjusted	1	1·36 (0·79–2·34)	2·19 (1·32–3·62)	0·002
Fully adjusted	1	1·34 (0·75–2·37)	2·00 (1·07–3·75)	0·03

*Values were obtained by modelling the median value of each category as a continuous variable.

n=~150,000



Impact of *Trans Fatty* acids on CHD risk largely due to blood lipid effects



Emerging evidence for effect of *trans* fatty acids on inflammation and endothelial function

Closing remarks….

- Current dietary SFA intake too high- replacement with MUFA/PUFA not (refined) carbohydrates
- 'Over' focus on *trans* fats. Care must be taken did current efforts to reduce *trans* intake does not inadvertently increase SFA content of foods
- Evidence from human intervention trials to demonstrate the impact of dietary fat composition on insulin sensitivity and diabetes risk is as yet limited
- Cardioprotective effect EPA/DHA attributable to multiple mechanisms
- Further studies to investigate dose-effect relationships needs
- αLNA levels evidence of independent health benefit
- αLNA source of EPA/DHA but bioconversion poor
- Great need for better understanding of individual response to dietary fat change

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