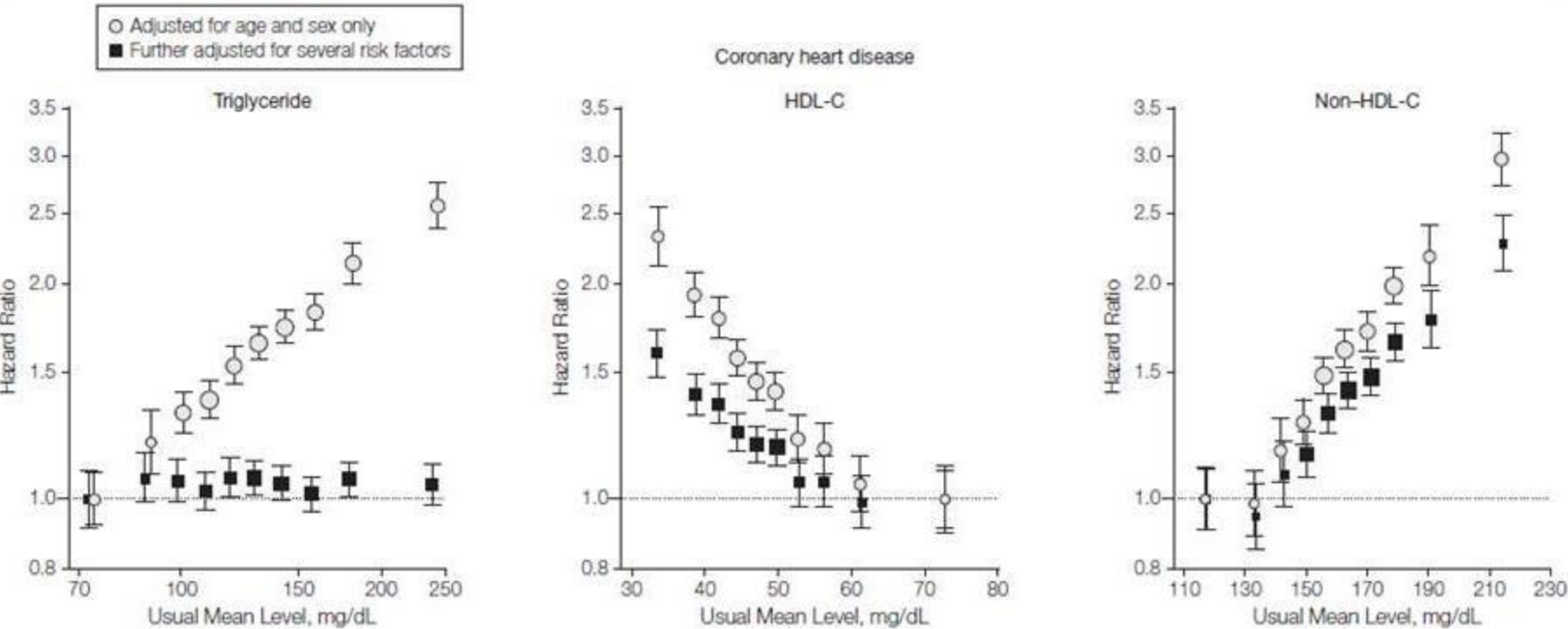


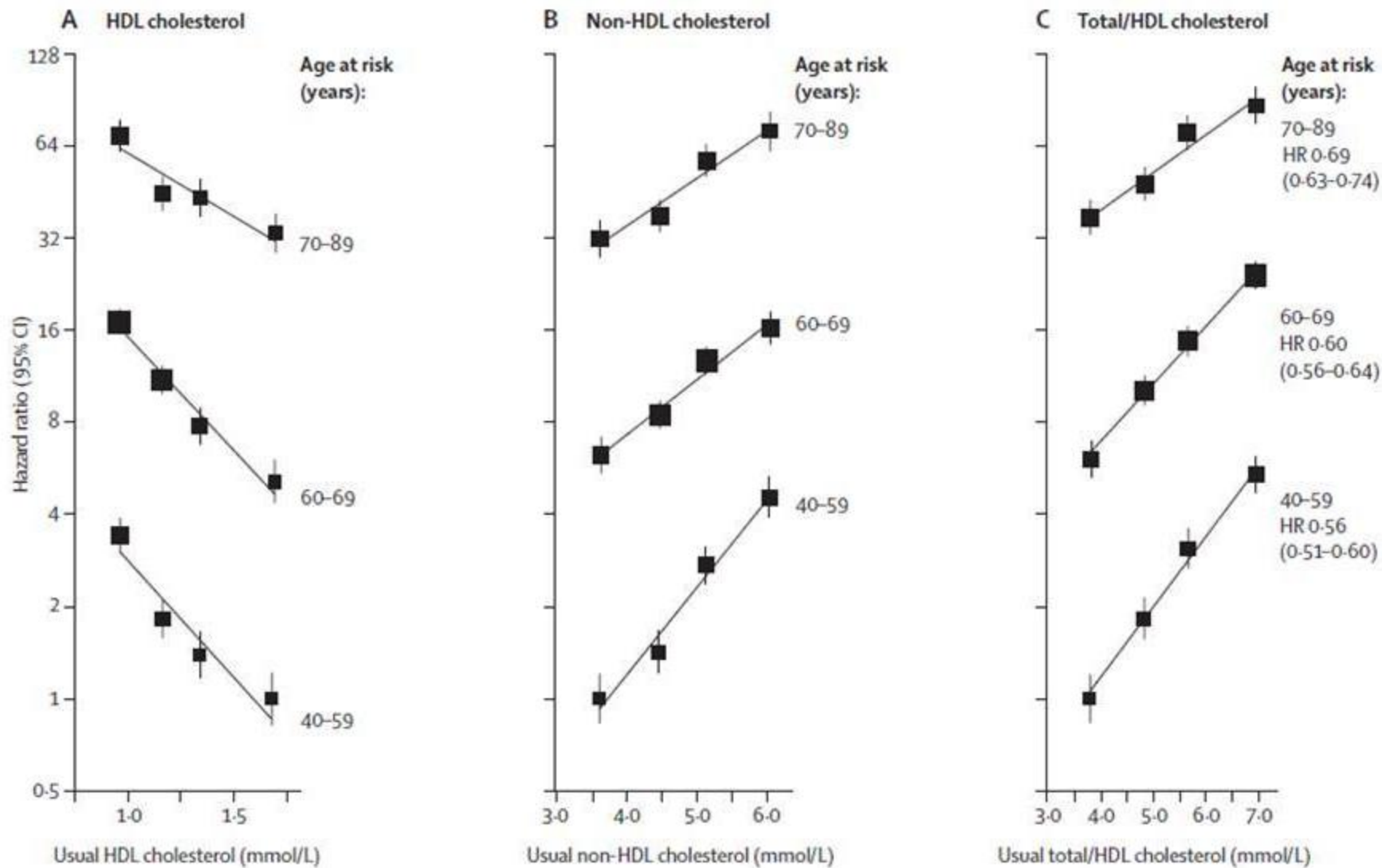
# Saturated fat- how long can you go/how low should you go?

Peter Clifton

Baker IDI Heart and Diabetes  
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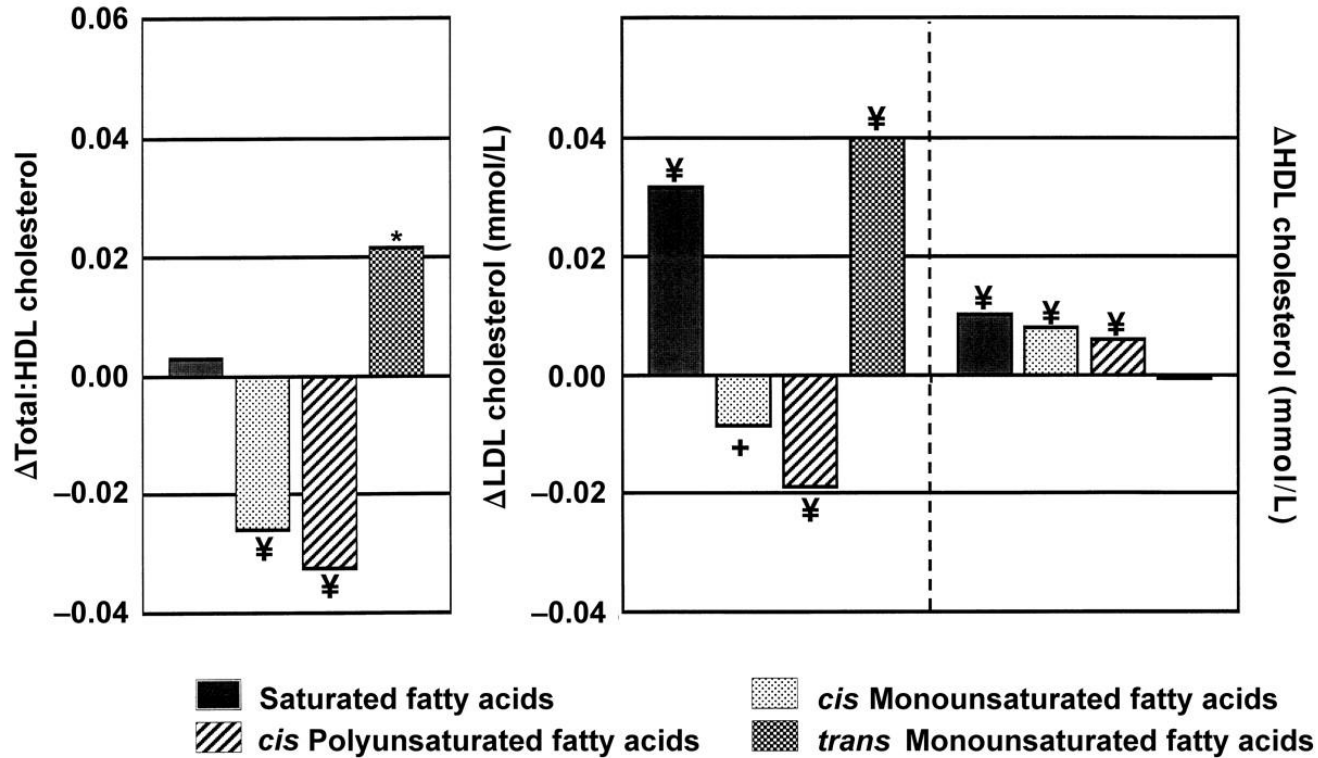
**Figure 1. Hazard Ratios for Coronary Heart Disease or Ischemic Stroke Across Quantiles of Usual Triglyceride, HDL-C, and Non-HDL-C Levels**





**Figure 3: IHD mortality (3020 deaths) versus usual (A) HDL cholesterol; (B) non-HDL cholesterol; and (C) total/HDL cholesterol**  
 Age-specific associations. Conventions as in figure 1. HR denotes the hazard ratio (95% CI) per 1.33 lower total/HDL cholesterol (see also webfigure 5).

**FIGURE 1.** Predicted changes ( $\Delta$ ) in the ratio of serum total to HDL cholesterol and in LDL- and HDL-cholesterol concentrations when carbohydrates constituting 1% of energy are replaced isoenergetically with saturated, cis monounsaturated, cis polyunsaturated, or trans monounsaturated fatty acids



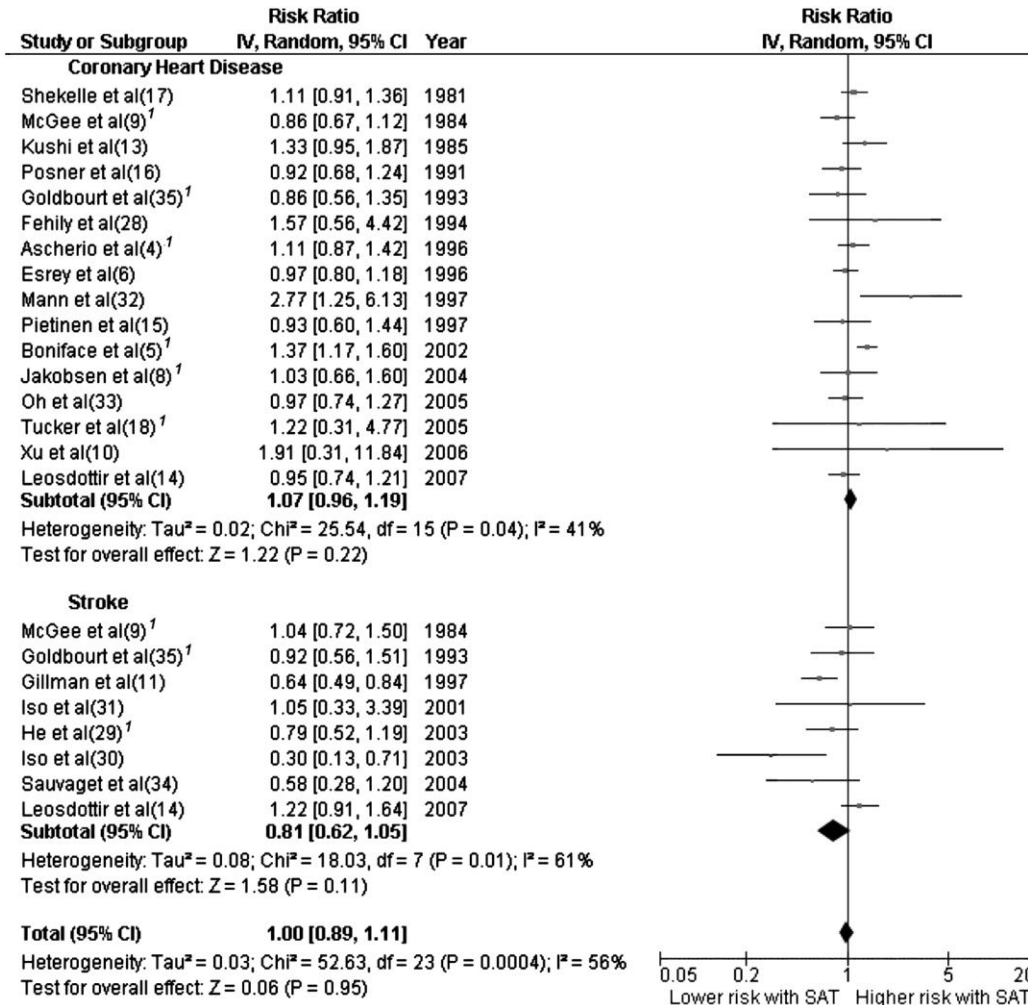
Mensink, R. P et al. Am J Clin Nutr 2003;77:1146-1155



# Saturated fat

- *Meta analysis: Siri-Tarino 2010*
- 16 cohorts for CHD, 8 cohorts for stroke
- The RRs (95% CIs) were 1.07 (0.96, 1.19) for risk of CHD.
- 5–23 y follow-up 347,747 subjects. 11,006 developed CHD or stroke.
- *Meta analysis: Jakobsen 2009*
- 11 cohorts 4-10 y of follow-up, 5249 coronary events and 2155 coronary deaths , 344,696 persons.
- 5% lower SFAs with higher PUFAs, 0.87; 95% CI: 0.77, 0.97 coronary events; coronary deaths was 0.74 (95% CI: 0.61, 0.89).
- 5% lower SFAs higher carbohydrates, 1.07; 95% CI: 1.01, 1.14); coronary deaths was 0.96 (95% CI: 0.82, 1.13)

**FIGURE 2 Risk ratios and 95% CIs for fully adjusted random-effects models examining associations between saturated fat intake in relation to coronary heart disease and stroke**



Siri-Tarino, P. W et al. Am J Clin Nutr 2010;91:535-546

# Saturated fat-unexpected?

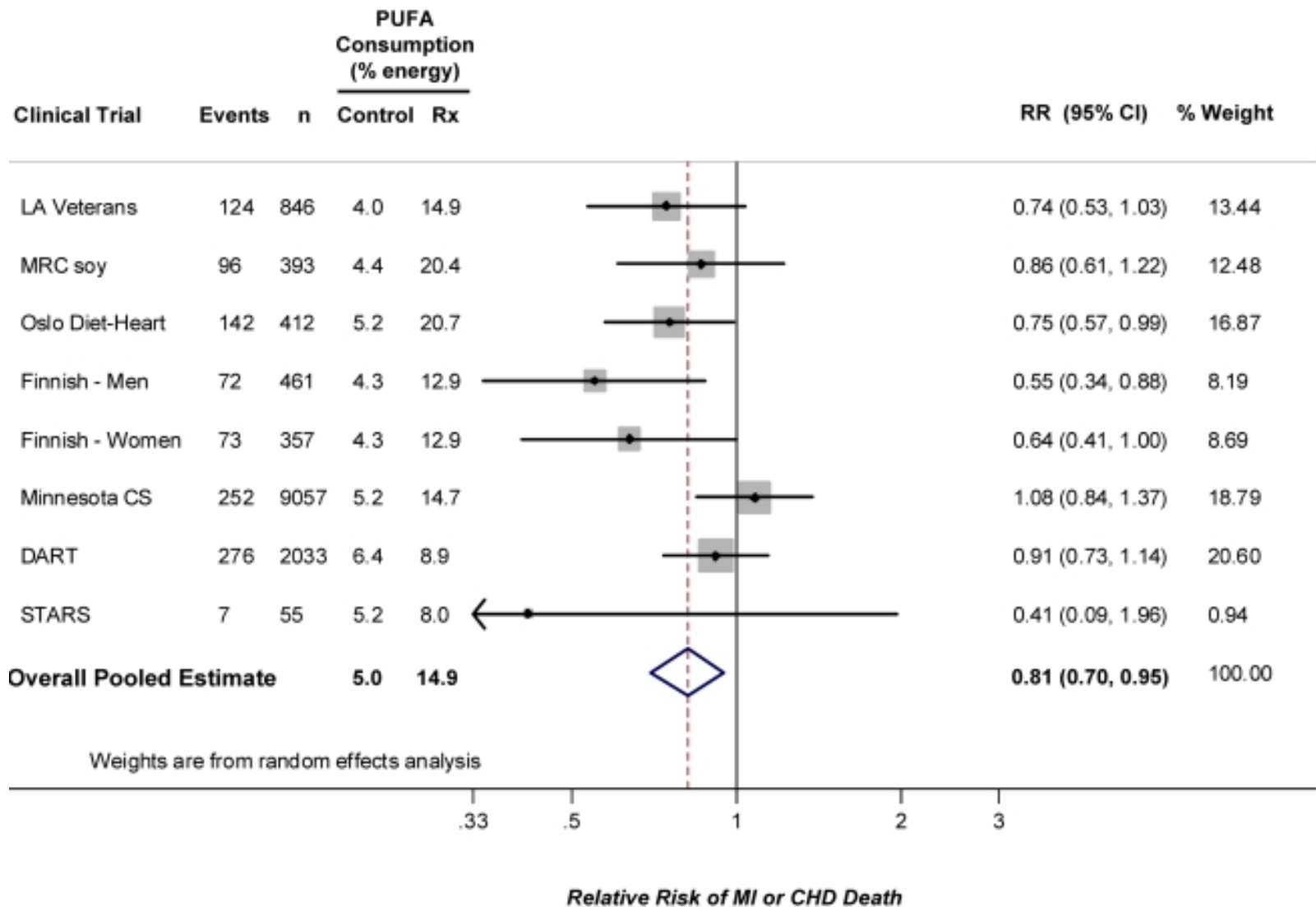
- Siri-Tarino: the changes are what is expected. If the change in saturated fat from first to 5th quintile is 7% to 17% then the expected LDL change for this change in fat is 0.33 mmol/L.
- Statin pooling project 1 mmol LDL lowering, 22% reduction in CHD. Thus a 0.33 mmol/L difference should produce about a 7% difference in events.
- The meta analysis showed a 7% difference ( $p=0.22$ ) but epidemiology is very noisy and you would never expect a 7% increase to be significant-you need at least 15%.
- Saturated fat is a weak LDL elevator -so it did what was expected. These are all healthy people without disease.
- The impact in those with CHD or diabetes may be greater

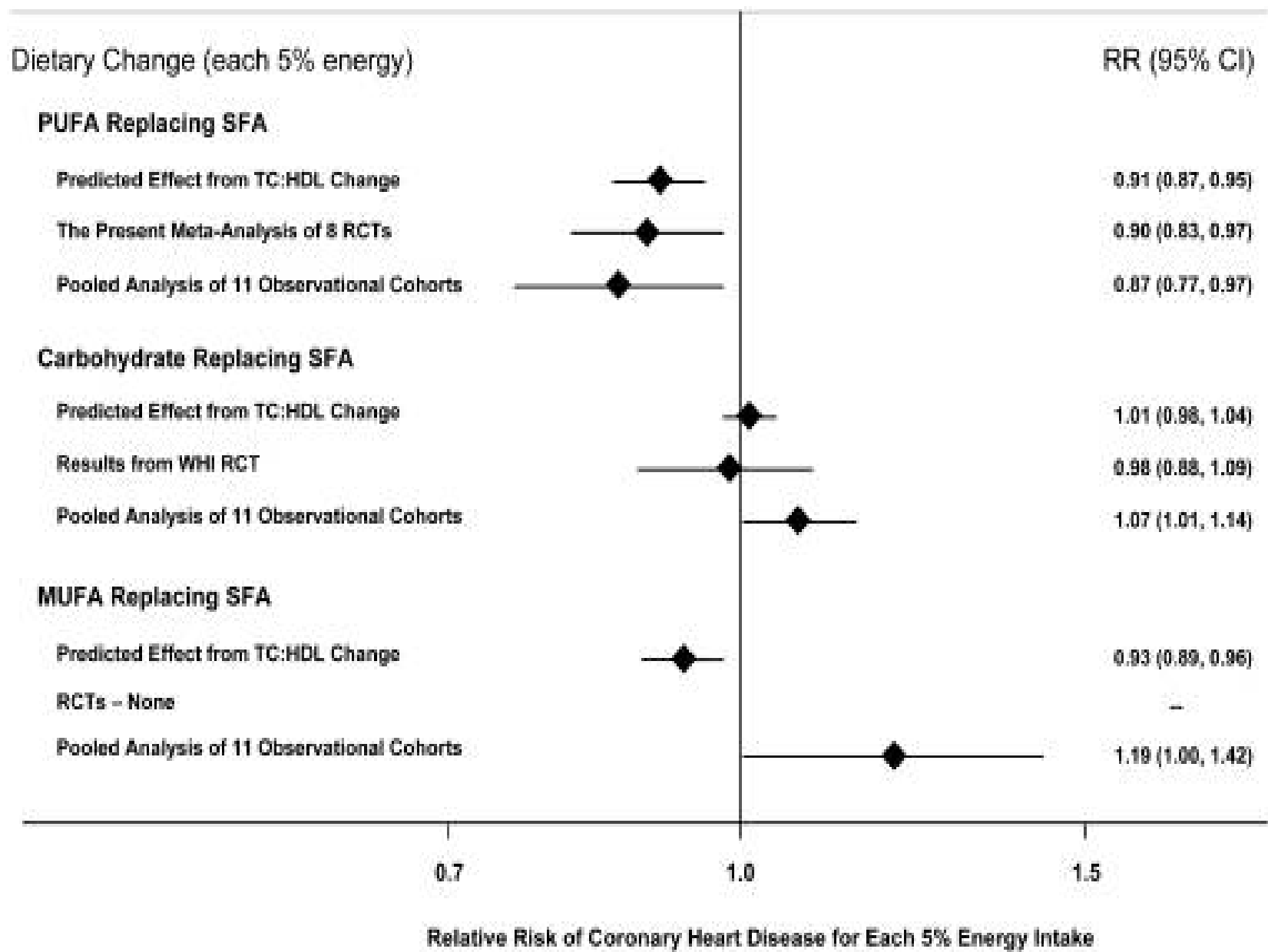
# Fat, CHO and atherosclerosis

- 235 post menopausal women, 3.1 year follow up , 2243 coronary segments (Mozzafarian 2004)
- In multivariate analyses, a higher saturated fat intake was associated with a smaller decline in mean minimal coronary diameter ( $P = 0.001$ ) and less progression of coronary stenosis ( $P = 0.002$ ) during follow-up.
- Carbohydrate intake was positively associated with atherosclerotic progression ( $P = 0.001$ ), particularly when the glycemic index was high

# Interventions-meta analysis

- Eight trials met inclusion criteria, totalling 13,614 participants with 1,042 CHD events.
- Average weighted PUFA consumption was 14.9% energy (range 8.0%-20.7%) in intervention groups versus 5.0% energy (range 4.0%-6.4%) in controls.
- The overall pooled risk reduction was 19% (RR = 0.81, 95% confidence interval [CI] 0.70-0.95,  $p = 0.008$ ), ie 10% reduced CHD risk (RR = 0.90, 95% CI = 0.83-0.97) for each 5% energy of increased PUFA. (*Mozzafarian et al 2010*)
- New hypothesis that it is just N3 fats (ALA) responsible for this not n6 fats (*Ramsden et al 2010*)

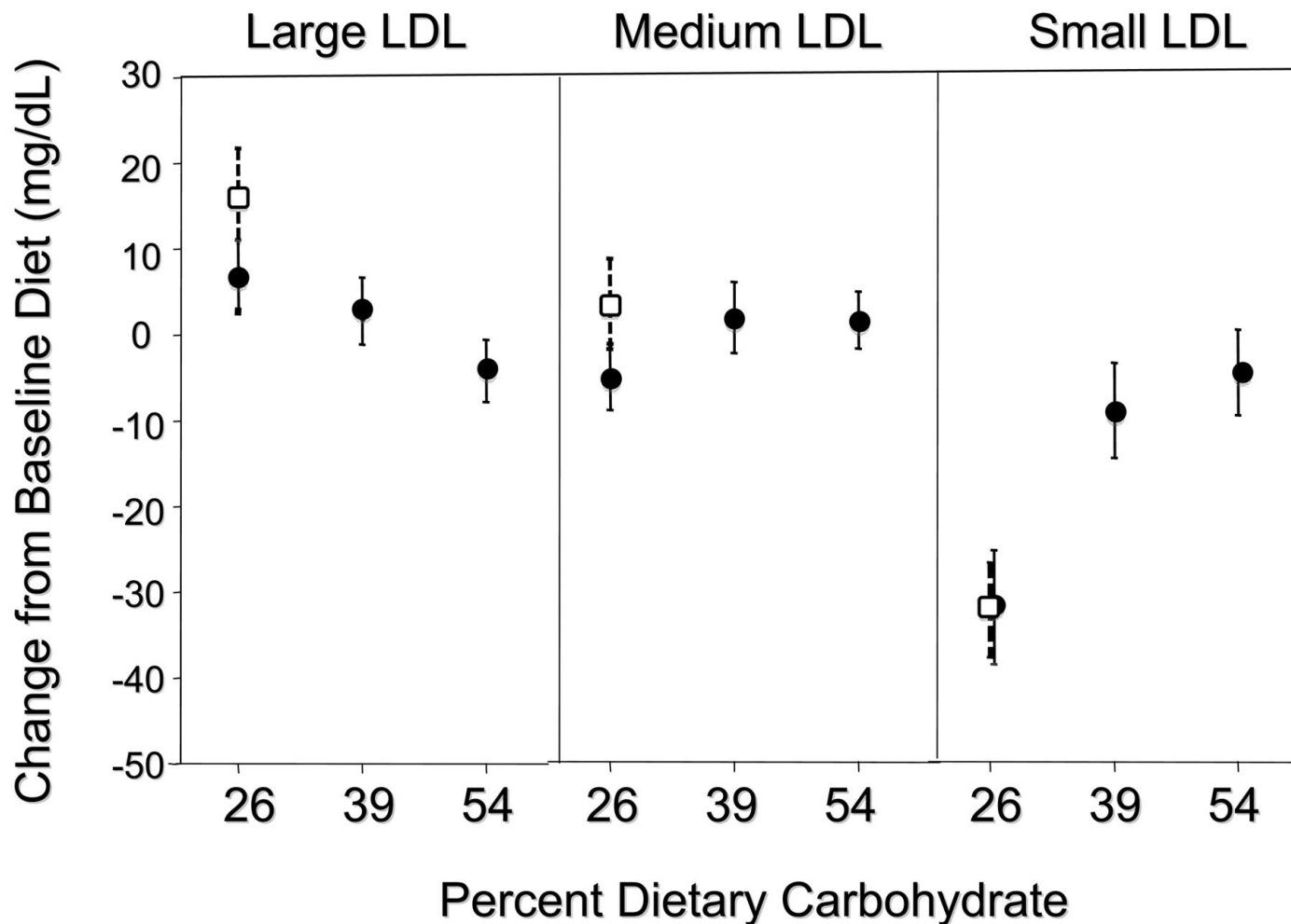




# CHO replacement-no effects

- Ball, KP, Hanington, E, McAllen, P, *et al.*. Low fat diet in myocardial infarction: a controlled trial. *Lancet* 1965;286:501–4
- Burr, ML, Fehily, AM, Gilbert, JF, *et al.*. Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: diet and reinfarction trial (DART). *Lancet* 1989;2:757–61
- WHI:>48,000 postmenopausal women low-fat or control Saturated fat intake was significantly lower in the intervention group than in the comparison group (means: 9.5% and 12.4%, respectively). Polyunsaturated fat was also lower (difference = 1.5%), and dietary carbohydrate was higher (difference = 8.1%)
- After 6 y of follow-up, there were no differences between the groups in incidence of fatal and nonfatal coronary heart disease (CHD) and total CVD, including stroke. The hazard ratio for the intervention group was 0.94 (95% CI: 0.86–1.02). LDL reduced by <0.1mmol/L (expect 0.06 mmol/L and 2.2% lowering of CVD). Howard 2006

**FIGURE 1 Mean ( $\pm$ SEM) effects of variation in dietary carbohydrate and saturated fat on LDL subclasses**



Siri-Tarino, P. W et al. Am J Clin Nutr 2010;91:502-509



# Type 2 diabetes

- 5672 women with type 2 diabetes from the Nurses' Health Study,
- **Results:** 619 new cases of CVD.
- Each 5% of energy intake from saturated fat, as compared with equivalent energy from carbohydrates, was associated with a 29% greater risk of CVD (RR: 1.29,  $P = 0.04$ ).
- The ratio of polyunsaturated to saturated fat (P:S) was inversely associated with the risk of fatal CVD.
- The replacement of 5% of energy from saturated fat with equivalent energy from monounsaturated fat was associated with a 37% lower risk of CVD, respectively.
- Tanasescu, M, Cho, E, Manson, JE & Hu, FB. Dietary fat and cholesterol and the risk of cardiovascular disease among women with type 2 diabetes. Am J Clin Nutr 2004;79:999–1005..

# CHO: Glycemic index

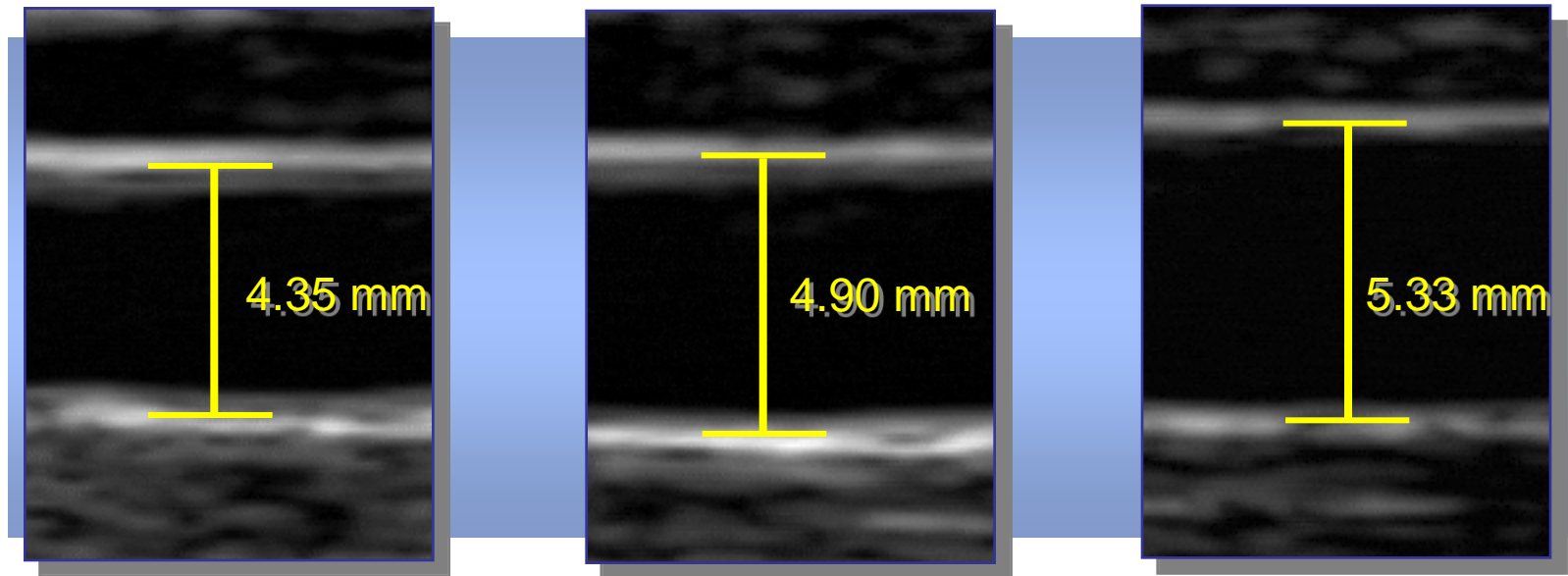
- **Positive:** Beulens, JW, de Bruijne, LM, Stolk, RP, *et al.*. High dietary glycemic load and glycemic index increase risk of cardiovascular disease among middle-aged women: a population-based follow-up study. *J Am Coll Cardiol* 2007;50:14–21 Dutch women
- Liu, S, Willett, WC, Stampfer, MJ, *et al.*. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. *Am J Clin Nutr* 2000;71:1455–61
- **Negative:** Levitan, EB, Mittleman, MA, Hakansson, N & Wolk, A. Dietary glycemic index, dietary glycemic load, and cardiovascular disease in middle-aged and older Swedish men. *Am J Clin Nutr* 2007;85:1521–6
- van Dam, RM, Visscher, AW, Feskens, EJ, Verhoef, P & Kromhout, D. Dietary glycemic index in relation to metabolic risk factors and incidence of coronary heart disease: the Zutphen Elderly Study. *Eur J Clin Nutr* 2000;54:726–31
- **Meta analysis:** 37 studies: coronary heart disease (GI RR = 1.25, 95% CI: 1.00, 1.56) Barclay 2008

# Other effects of sat fat

- Vessby, B, Unsitupa, M, Hermansen, K, *et al.* Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: the KANWU Study. *Diabetologia* 2001;44:312–9 (and elevates BP)
- Saturated fats, but not unsaturated fats, can induce the activation of nuclear factor- kappa B and the expression of Cox2 and other inflammatory markers, including IL6 and TNF- alpha ? via Toll-like receptor 4 (Kennedy et al 2009)
- HDL collected from individuals after a coconut meal compared with a safflower or unsaturated fat meal was associated with a 50–70% increase in ICAM and VCAM expression on ECs (Nicholls 2006)

# Brachial Artery Ultrasound

## Ultrasound images of the brachial artery

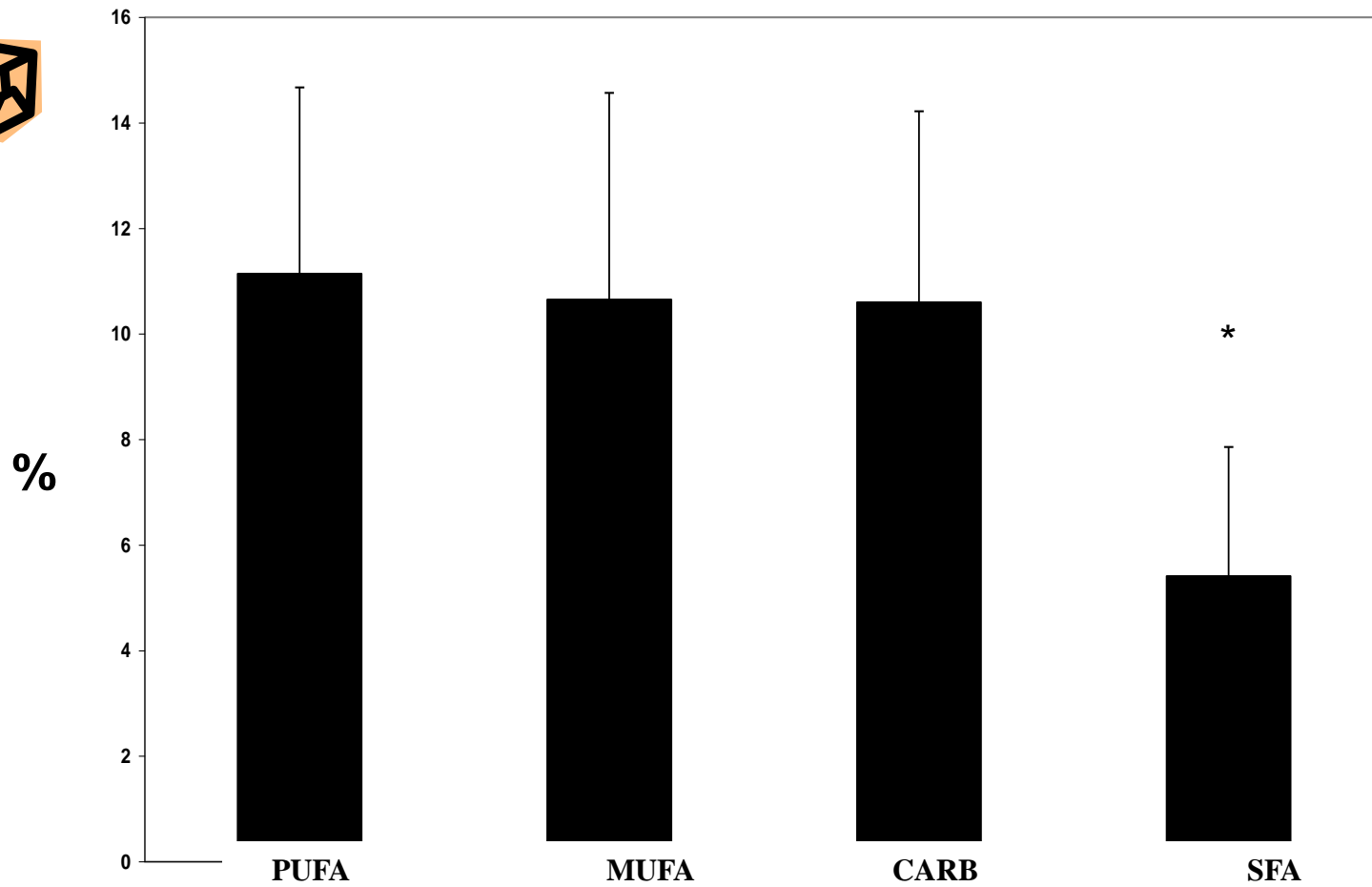
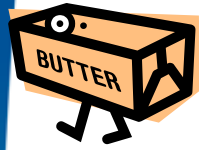


**Baseline**

**Flow-mediated  
Vasodilation**

**NTG-induced  
Vasodilation**

# FMD

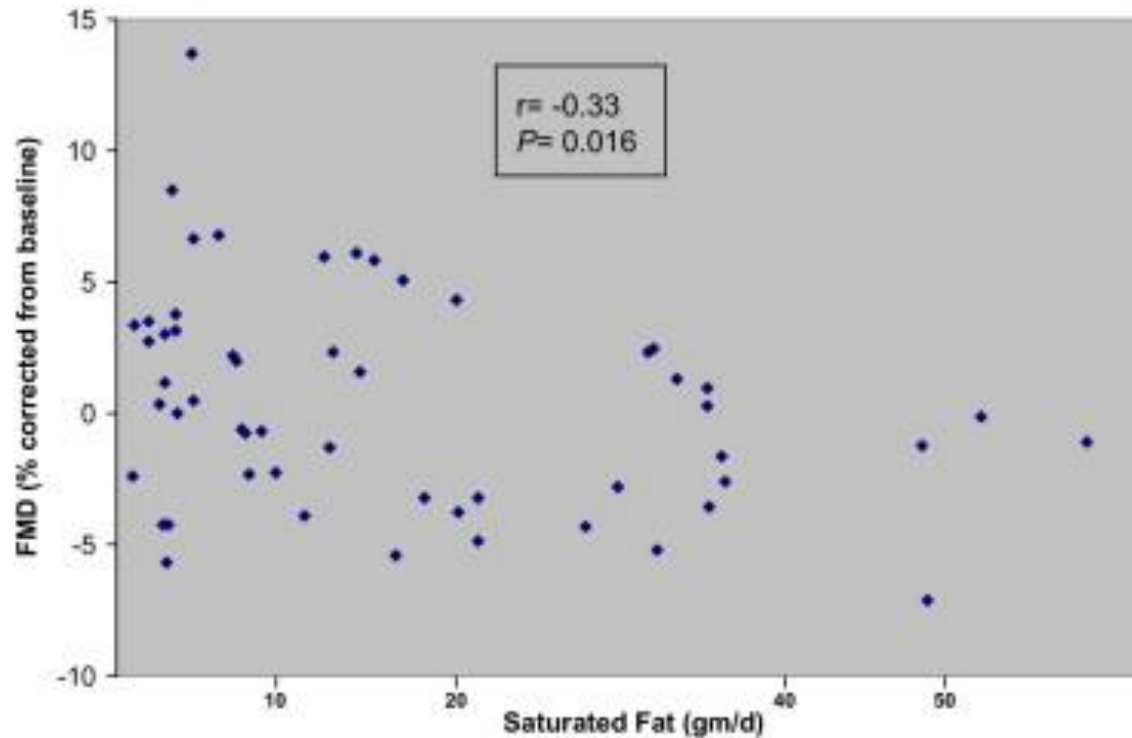


\*P<0.05

# Results 12 months FMD

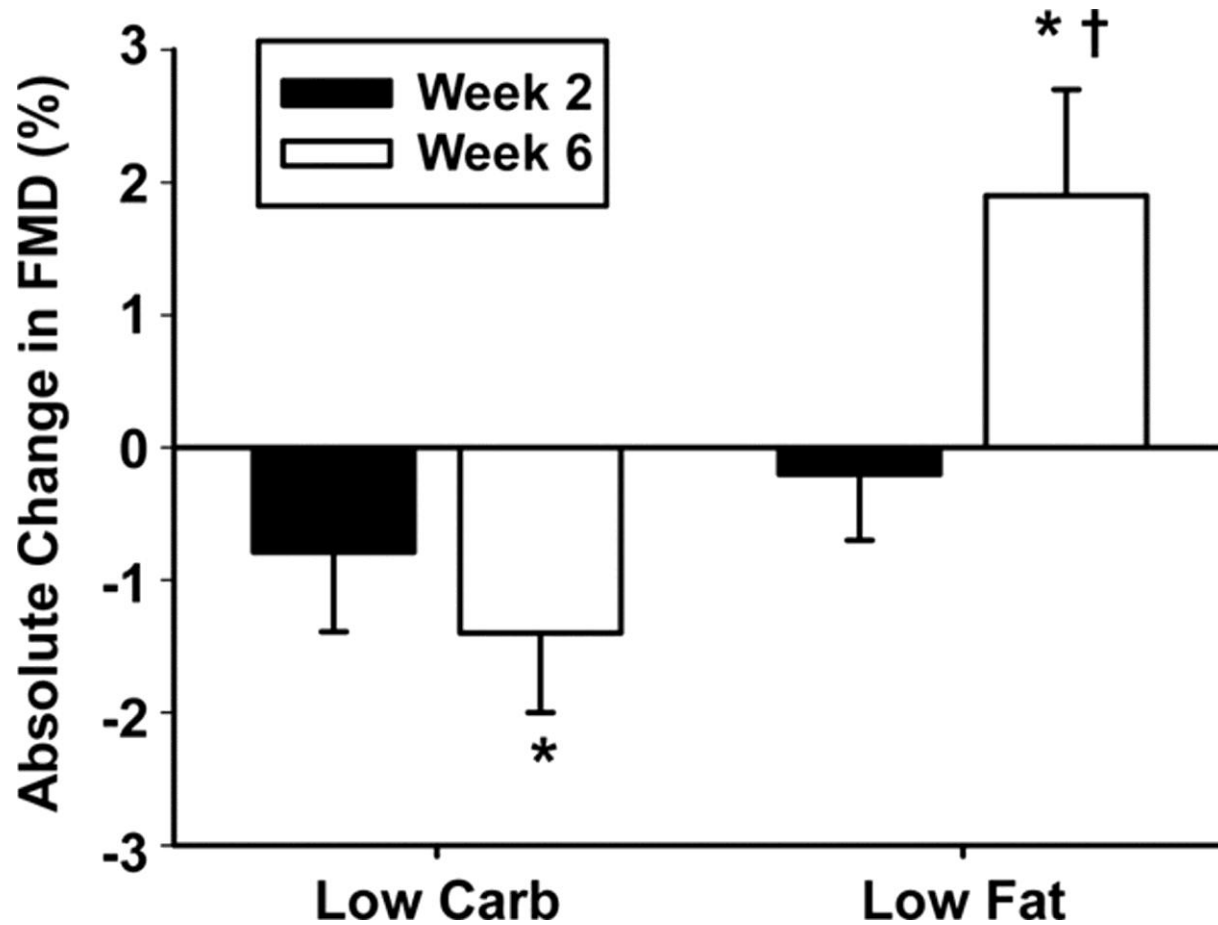
- 49 (26 LC, 23 HC) subjects
- Weight loss LC  $-14.9 \pm 10.5$  kg, HC  $-11.5 \pm 7.4$  kg;  $P=0.20$ .
- Fall in BP, glucose, TG, rise in HDL
- FMD decreased on LC diet ( $P < 0.05$  for diet interaction)
  - $5.70 \pm 3.59\%$  to  $3.65 \pm 2.65\%$ ,  $P=0.001$
- No change on HC diet
  - HC  $5.86 \pm 2.54\%$  to  $5.51 \pm 3.52\%$ ;  $P=0.60$

# Inverse correlation between saturated fat and FMD



- South Beach vs. Ornish vs. Atkins n=18. weight stable

# Change in FMD at 2 & 6 weeks



# Conclusions

- Saturated fat-still a weak contributor to risk. Needs large changes in intake to see an effect on lipids. May be more important in some individuals eg diabetics.
- May operate beside mechanisms other than LDL cholesterol.
- Replace with polyunsaturated fat- effects beyond cholesterol-lowering (?or low GI CHO-less evidence)