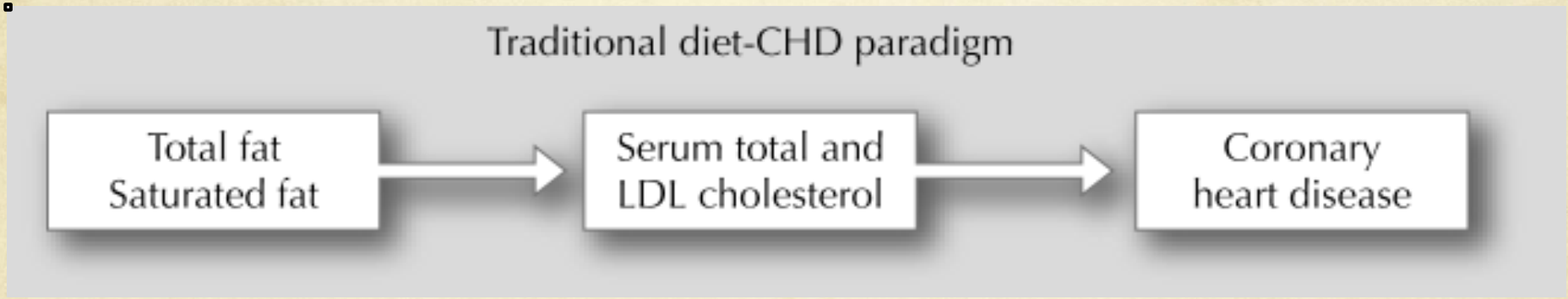
Saturated Fat & CVD: Wrongfully Accused?

Background

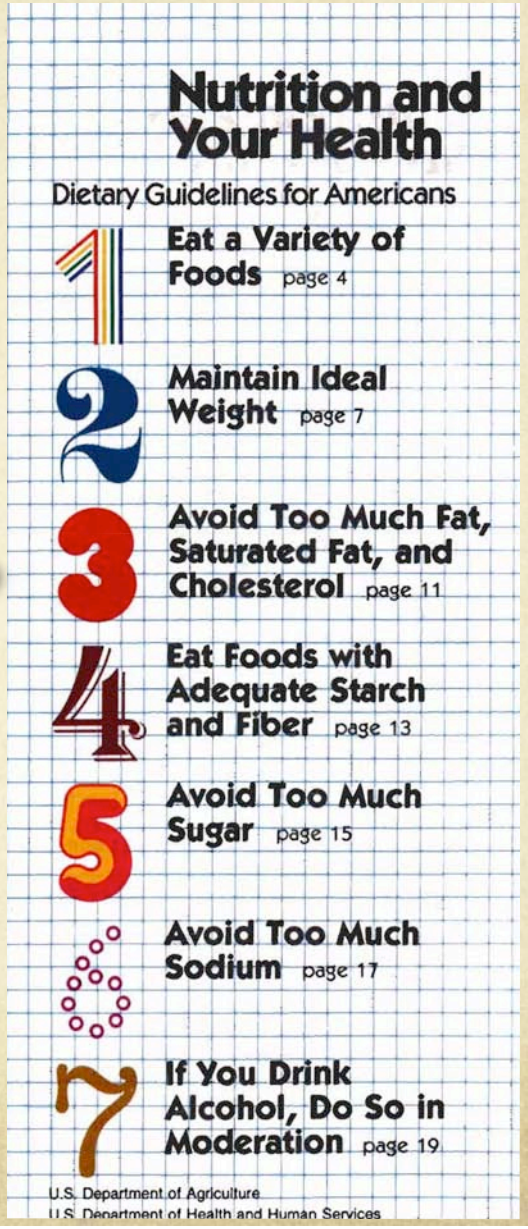
- Over the past 40 years, healthful diets have been synonymous with avoiding fat
  - Particularly saturated fat



Mozaffarian, 2005

Dietary Guidelines

- First published in 1980
- Nutritional & dietary guidance for the U.S. general public
- Foundation for:
  - Federal nutrition education/promotion programs
  - Food assistance programs
  - Food labeling



USDA.gov

Dietary Guidelines

- Current Recommendations:
  - "Consume less than 10% of calories from saturated fatty acids"

American Heart Association®

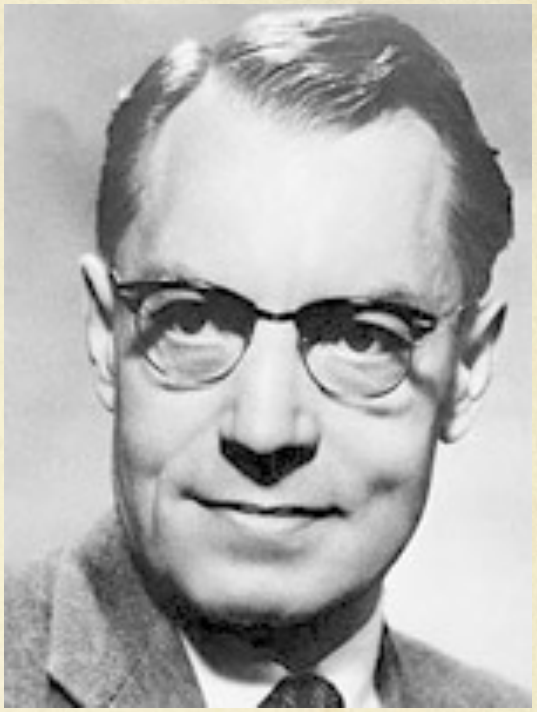
  - "Limit your intake of saturated fat to less than 7% of energy"

Lichenstein et al, 2006
Dietary Guidelines for Americans, 2005, USDA

So where did this recommendation come from?

Ancel Keys

- Professor at the University of Minnesota
- Seminal epidemiological study
  - Looked at several countries around the world relating fat intake and death
  - Conclusion: high-fat diet is correlated with mortality



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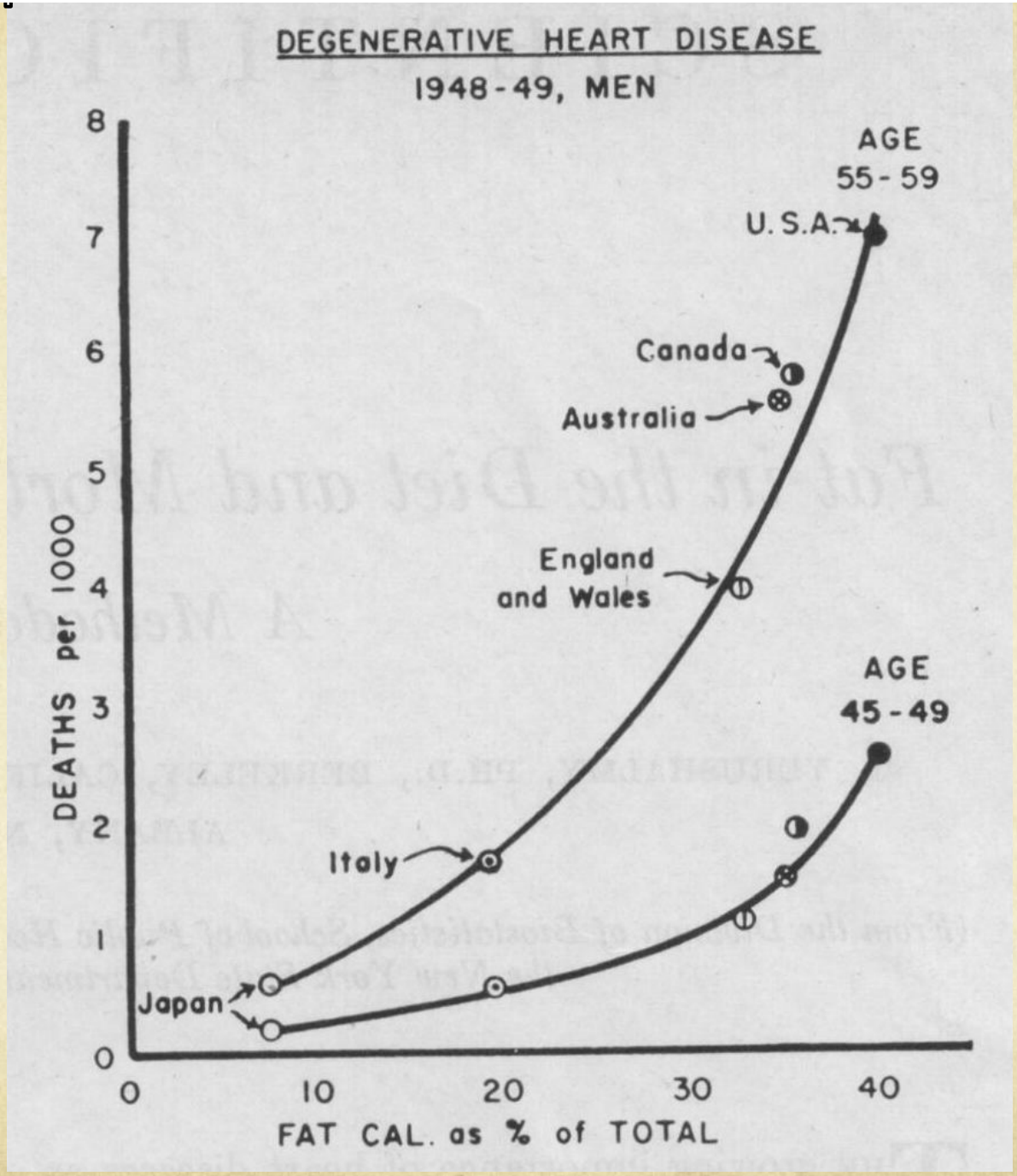
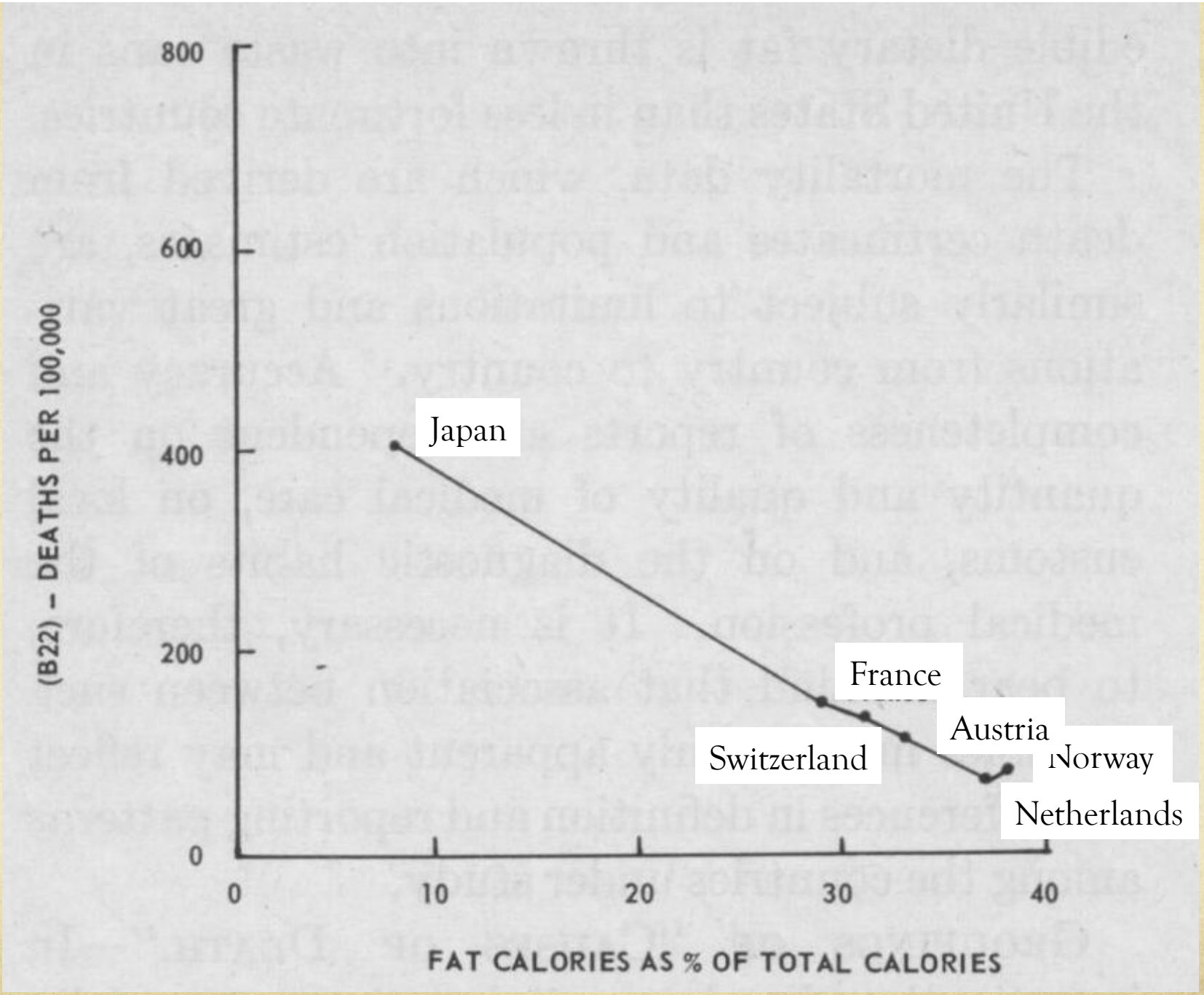


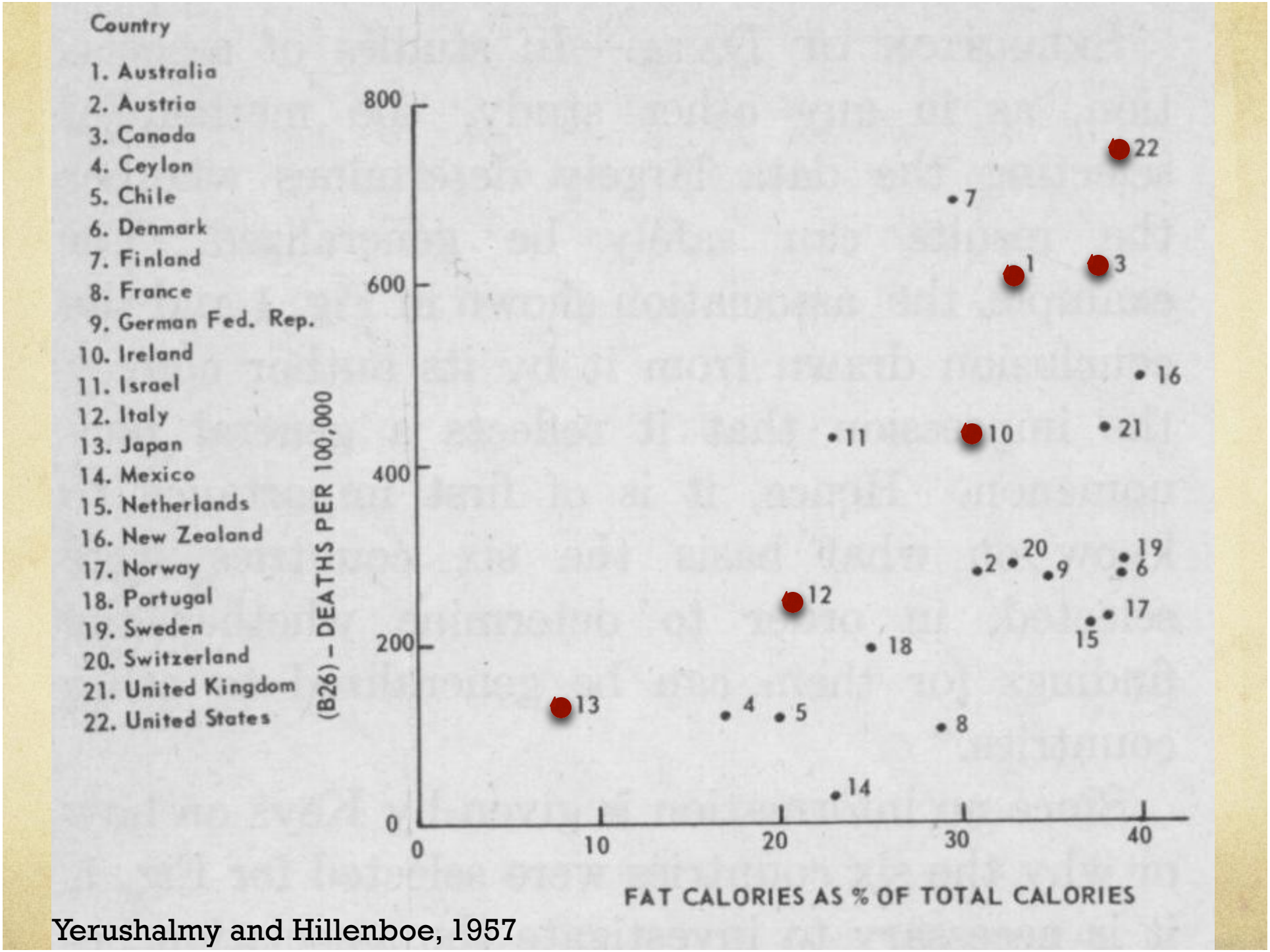
Keys, A. Atherosclerosis: a problem in newer public health. *J Mt Sinai Hosp NY*. 1953;20:134.

A clear link, or not?

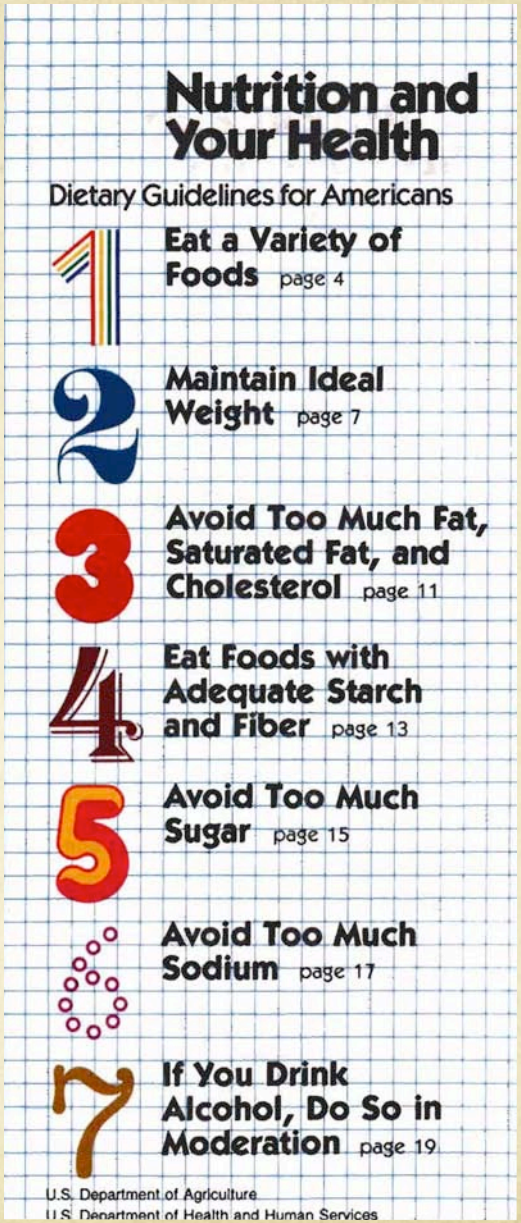
- Keys looked at 6 different countries using national food balance data
  - **But data for 22 countries were available**



Yerushalmy and Hillenboe, 1957



Yerushalmy and Hillenboe, 1957



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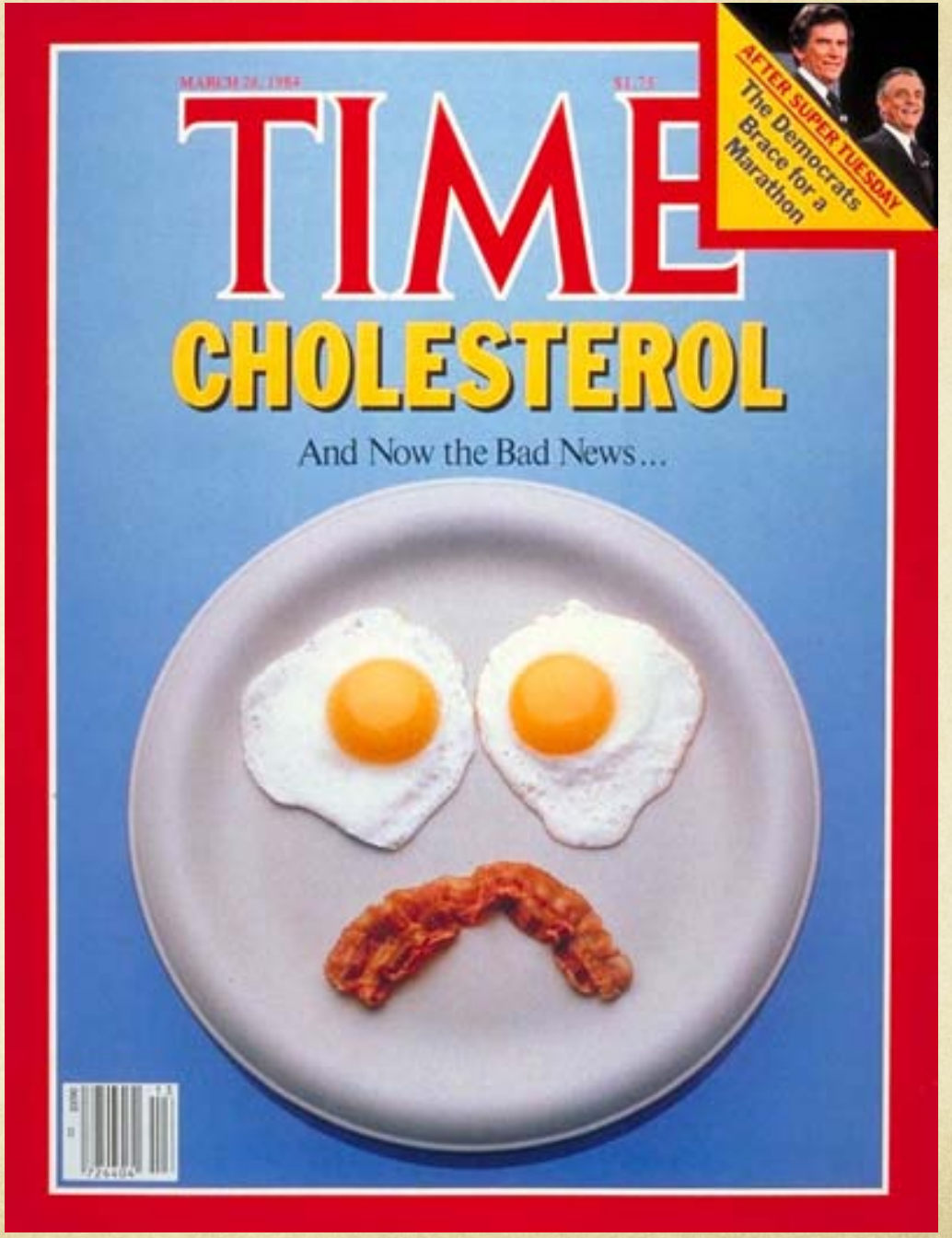
http://www.time.com/time/covers/0,16641,19610113,00.html

The Popular Press embraces idea



http://www.time.com/time/covers/0,16641,19840326,00.html

Conflicting Studies

- Framington heart study (5209 subjects)
- MRFIT (Multiple Risk Factor Intervention Trial) (12,866 men)
- Women's Health Initiative Dietary Modification Trial (48,835 women)
  - Largest randomized dietary intervention to date

- **All three studies found no significant association with either lowering Total Fat/SFA and CHD**

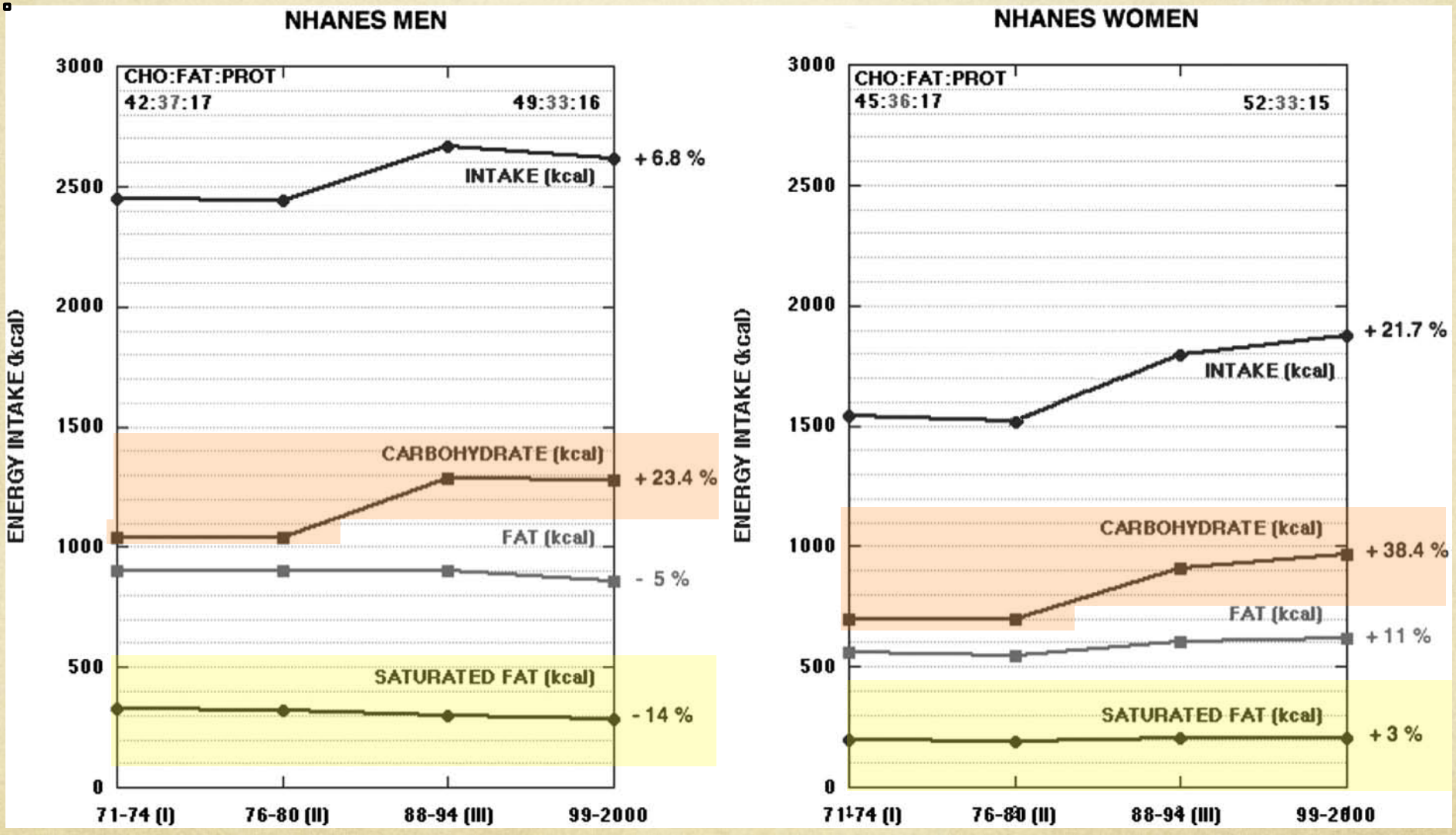
Posner et al, 1990
MRFIT Research Group, 1982
Howard et al, 2006

- "Despite decades of effort and many thousands of people randomized**, there is still only limited and inconclusive evidence of the effects of modification of total, saturated, monounsaturated, or polyunsaturated fats on cardiovascular morbidity and mortality.**"

-Lee Hooper

Hooper L, et al. Dietary fat intake and prevention of cardiovascular disease: systematic review. British Medical Journal. 2001 Mar 31;322(7289):757-63.

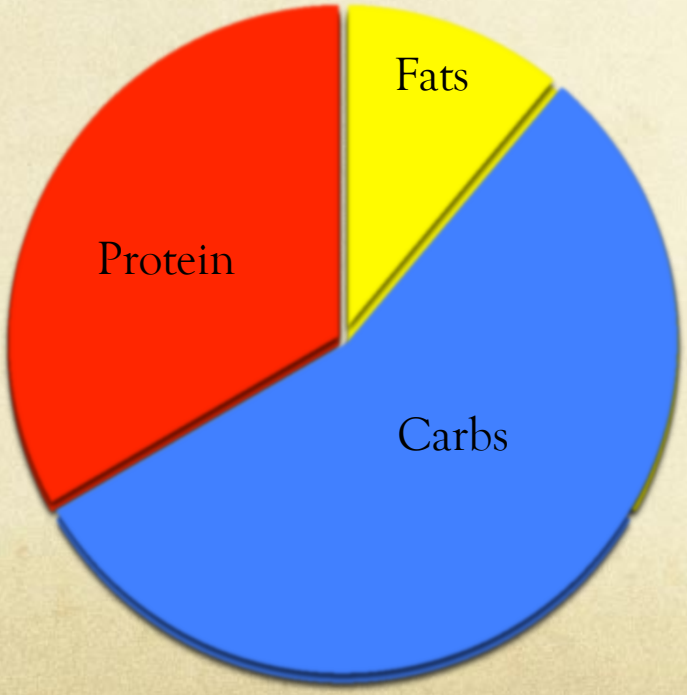
Nevertheless, the public changed their habits



Center for Disease Control, 2004

Diets are a trade-off

- Carbs, Protein, & Fat
- It's very hard to add pure protein alone in a diet
- By definition, a low-fat diet is generally a high-CHO diet



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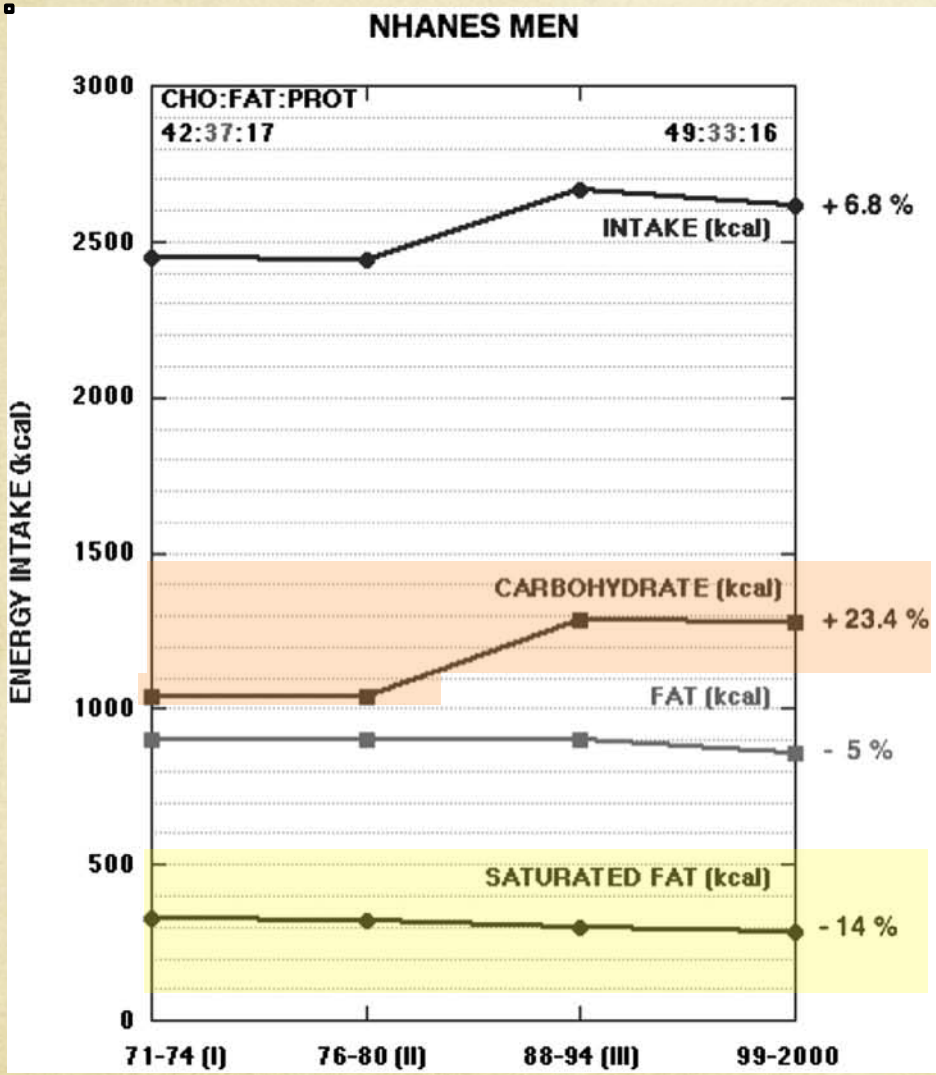
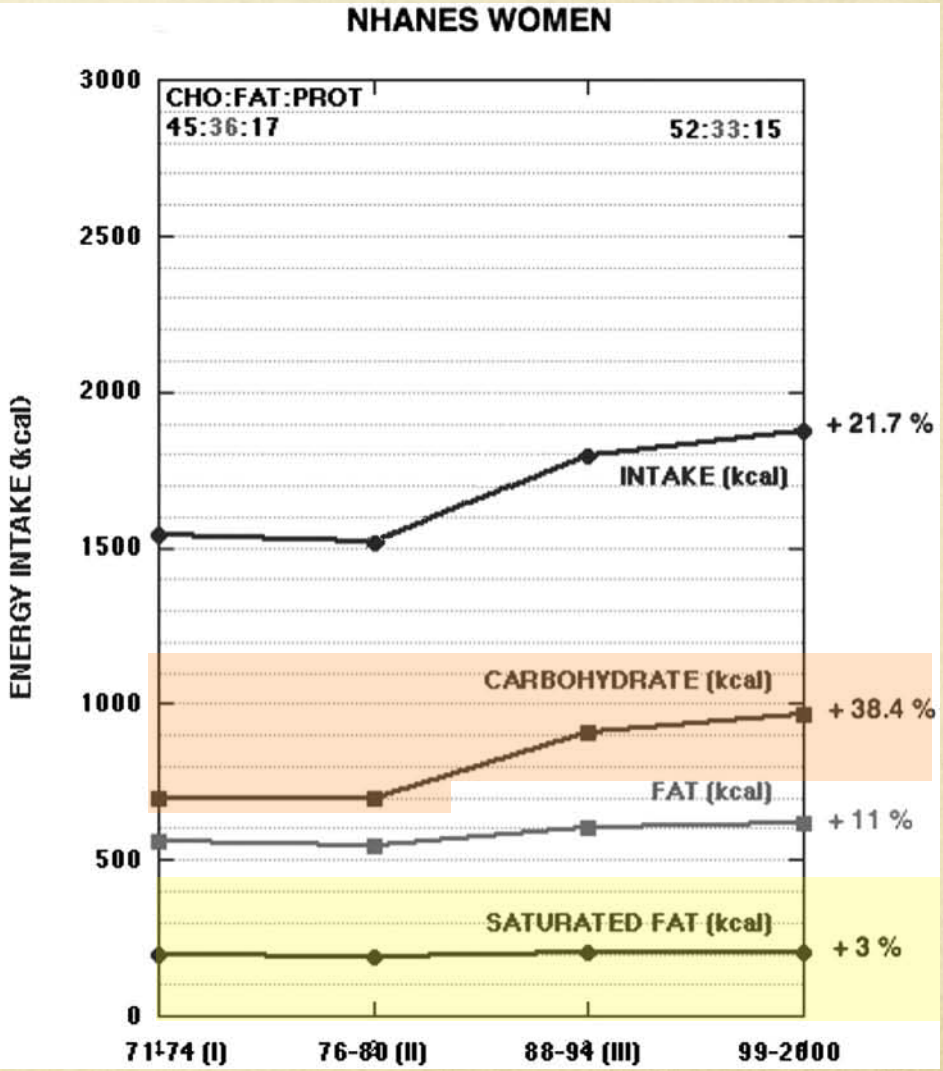




Center for Disease Control, 2004

Statement of Importance

- Dietary guidelines continue to advocate reducing dietary saturated fat to reduce CVD risk.
- However saturated fat may not be as atherogenic as believed, and high carbohydrate intake may pose equal or greater risk for CVD.
  - New insights from LDL particle size

Purpose

- Describe recent evidence that show recommending lower saturated fat intake may be counterproductive to lowering CVD risk
- Show that the diet-heart hypothesis may no longer be the whole truth

Now to the “heart” of the matter...

The American Journal of CLINICAL NUTRITION

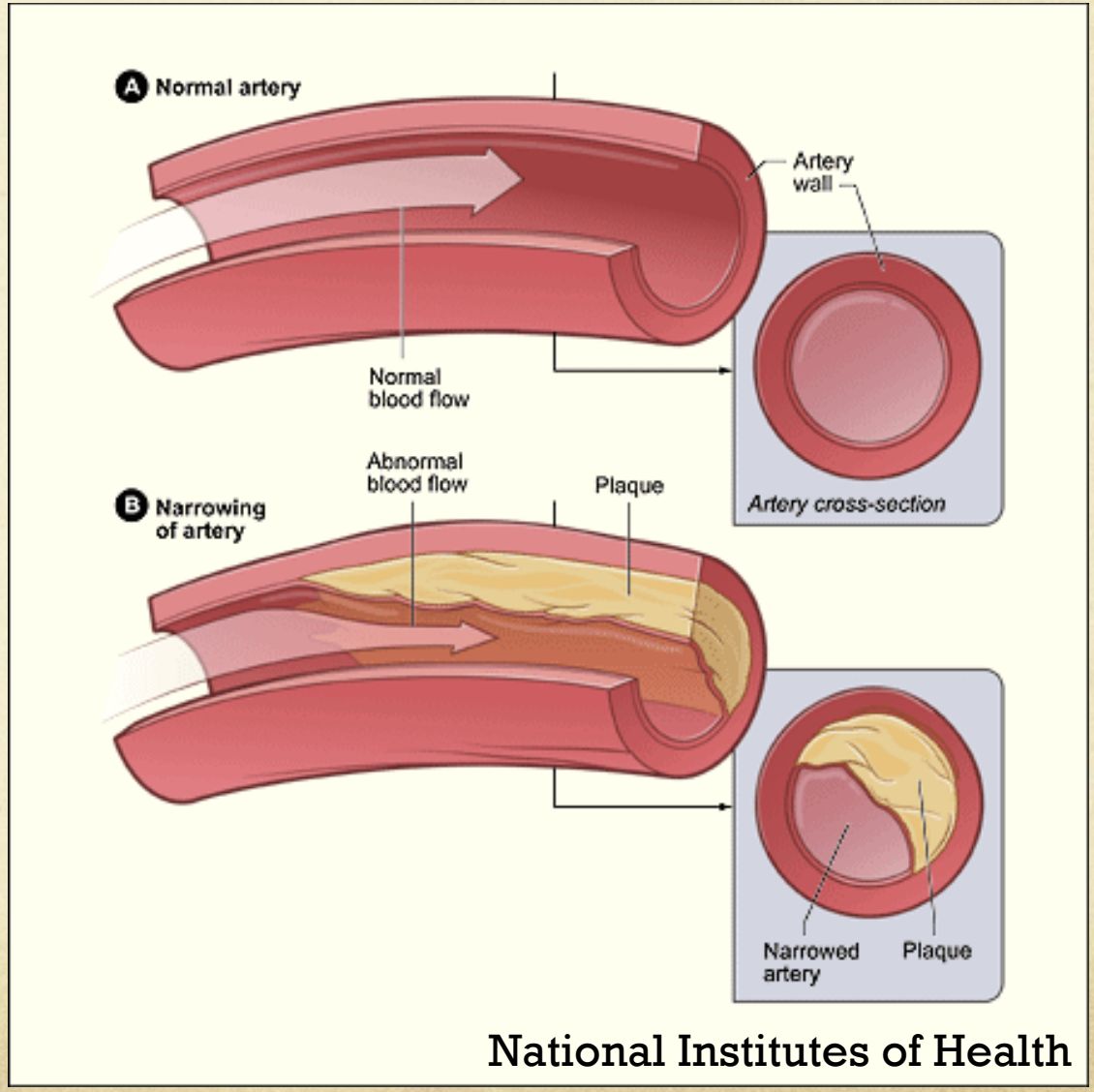
Dietary fats, carbohydrate, and progression of coronary atherosclerosis in postmenopausal women

D. Mozaffarian, E.B. Rimm, and D.M. Herrington

American Journal of Nutrition, 2004, Vol. 80: 1175-1184

Atherosclerosis

- Narrowing of the arteries
- Linked with heart disease



National Institutes of Health

Study Design/Methods

- Subjects taken from the Estrogen Replacement and Atherosclerosis (ERA) trial
  - 309 post-menopausal women with established coronary heart disease
  - Excluded if there was cancer, previous or planned coronary bypass surgery, uncontrolled hypertension or diabetes, among others
  - 235 women with 2243 evaluable coronary segments
- Dietary Assessment
  - Usual dietary intake assessed at beginning of study
    - Validated, semi-quantitative FFQ
- Angiogram

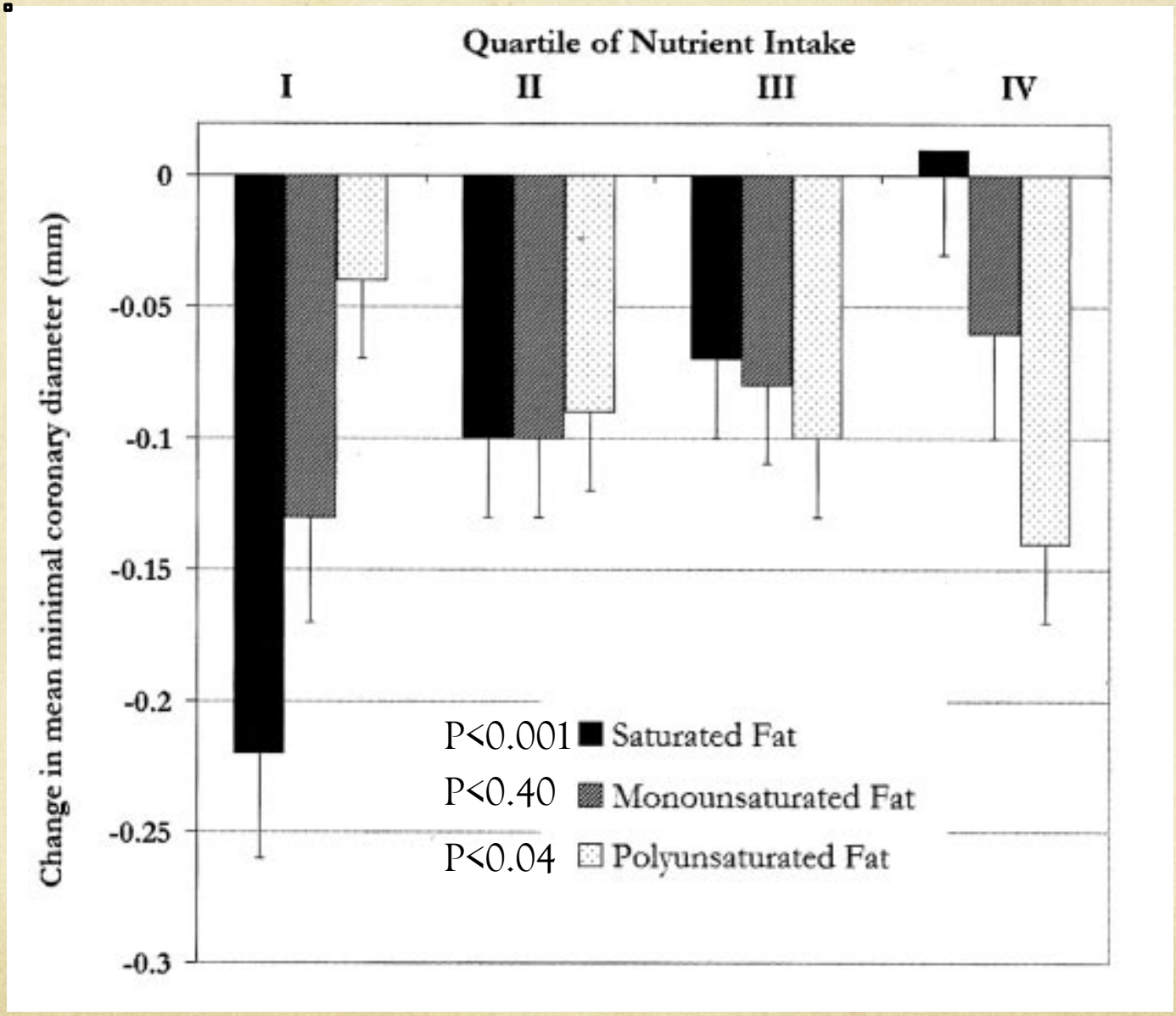
Results

- Follow-up after avg 3.1 years

Quartile of saturated fat intake (range of intake, % of energy)				
1 (3.5–7.0)	2 (7.1–8.6)	3 (8.7–10.5)	4 (10.6–16.0)	*P* for trend
1.86 ± 0.04[2]	1.91 ± 0.04	1.90 ± 0.04	2.02 ± 0.04[3]	0.01
1.71 ± 0.05	1.82 ± 0.05	1.81 ± 0.05	1.95 ± 0.05[4]	0.002

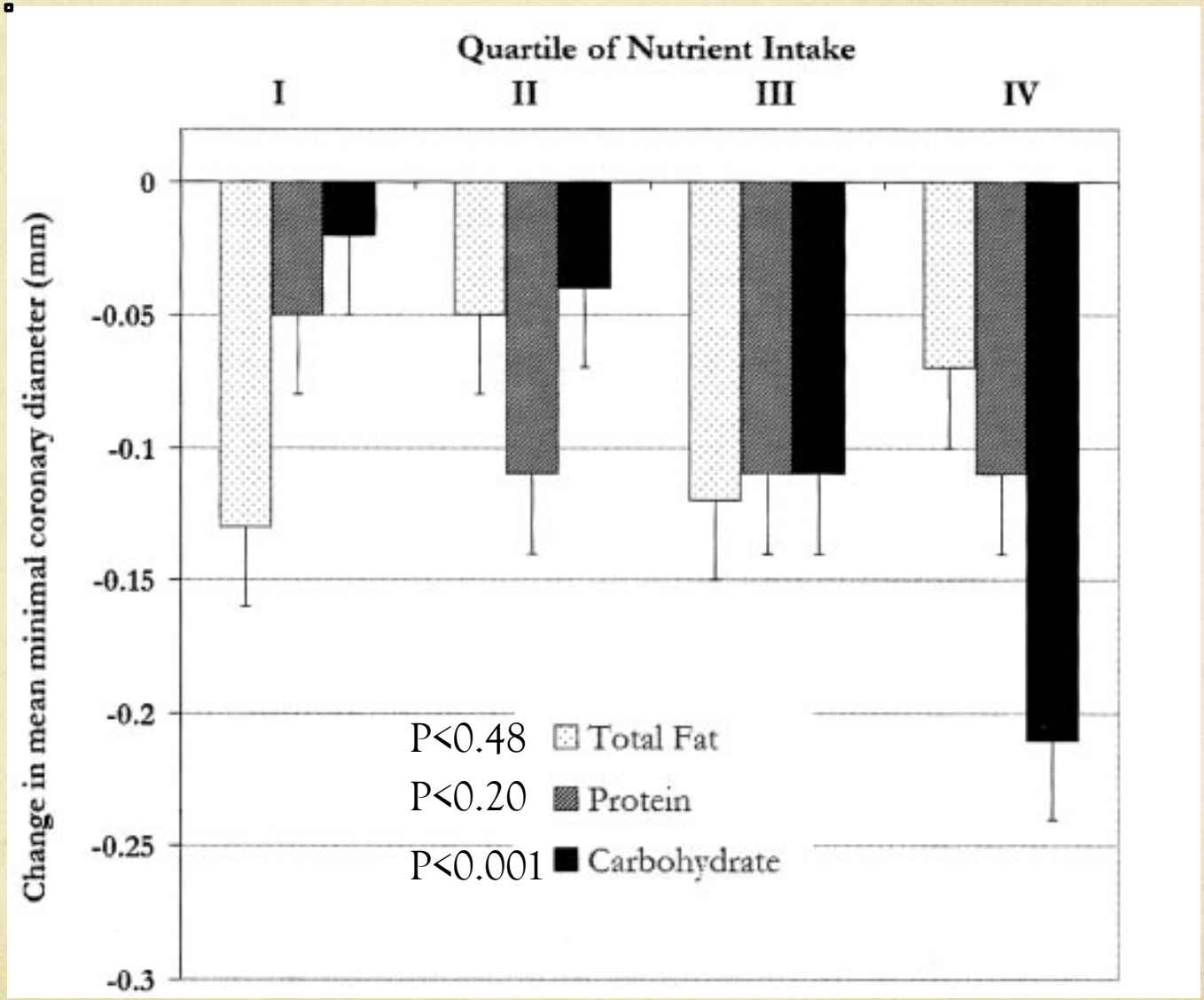
Minimal coronary artery diameter (mm)

Results



Mozaffarian, 2004

Results



Mozaffarian, 2004

Discussion

- This was noted as the first study to date evaluating association between macronutrients and atherosclerosis
- After 3 yr average follow-up:
- Greater saturated fat intake was associated with less progression of coronary atherosclerosis
- Greater carbohydrate intake was associated with greater progression of atherosclerosis

Strengths

- Prospective study
- Angiographs were evaluated through an independent party
- Directly examined progression of atherosclerosis rather than lipid risk factors
- Regression used to examine possible confounders

Limitations

- Food frequency questionnaire
- Looked at women with existing atherosclerosis
- Possible confounding with concurrent hormone therapy & lipid-lowering drugs

	Difference in change (95% CI)[2]	*P* for interaction[3]
	mm	
Lipid-lowering medication		
No ($n = 103$)	0.22 (0.11 to 0.33)	0.008
Yes ($n = 132$)	0.09 (−0.02 to 0.20)	
Hormone replacement therapy		
None ($n = 80$)	0.20 (0.08 to 0.32)	
Estrogen ($n = 74$)	0.12 (0.00 to 0.24)	0.42
Estrogen + progestin ($n = 81$)	0.16 (0.04 to 0.27)	

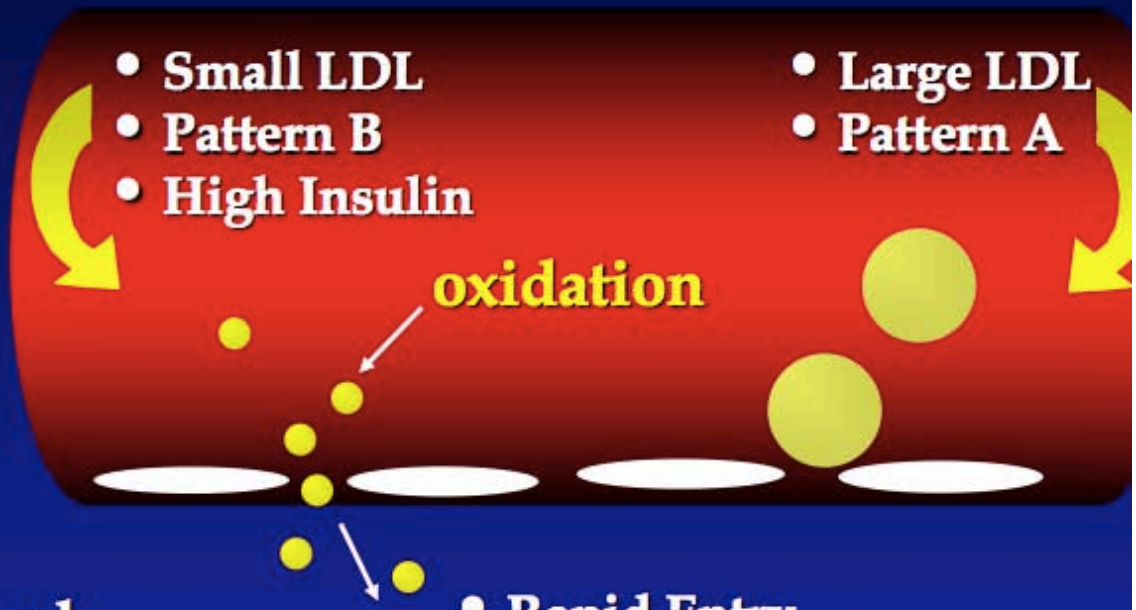
Mozaffarian, 2004

Related Evidence

- Effects of Drugs vs Diet
  - Statins have secondary anti-inflammatory and immunomodulatory effects independent of LDL levels
- Replacing saturated fat with PUFA and MUFA is better at reducing CHD than reducing total fat intake (Hu et al, 1997)
  - Anti-inflammatory effects of PUFA?
- Are all LDL's equal
  - Small, dense LDL vs Large, buoyant LDL

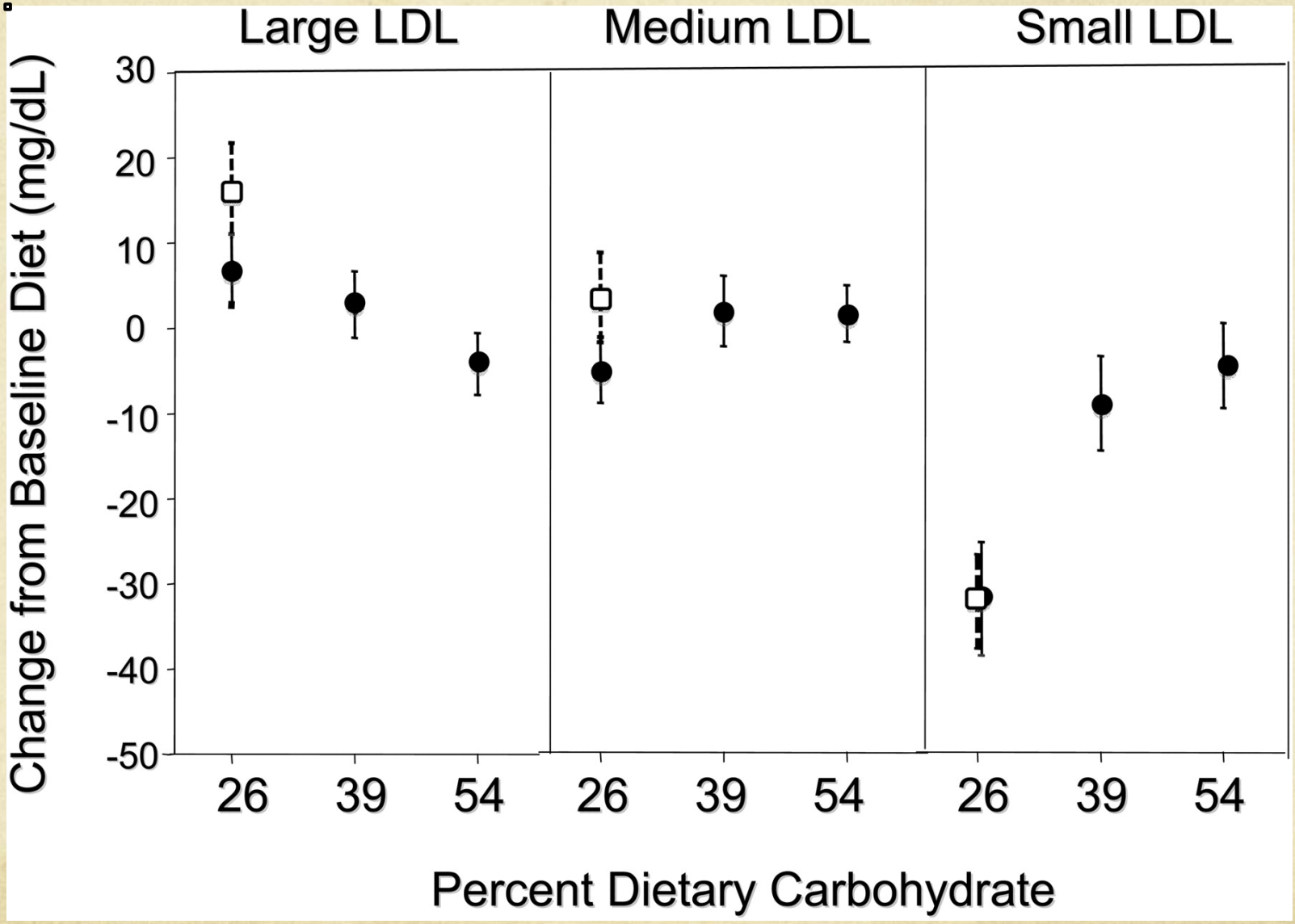
ALP (LDL Pattern B)
Why is it *Dangerous?*

- Rapid **entry** into arterial wall.
- Low **vitamin E** in lipoproteins.
- More susceptible to **oxidative** damage.
- High blood **insulin**.
- After a **meal**, blood fat level doubles in pattern B versus A.
- Poor blood vessel **relaxation**.



Issacson, Heart Hospital of North Dakota

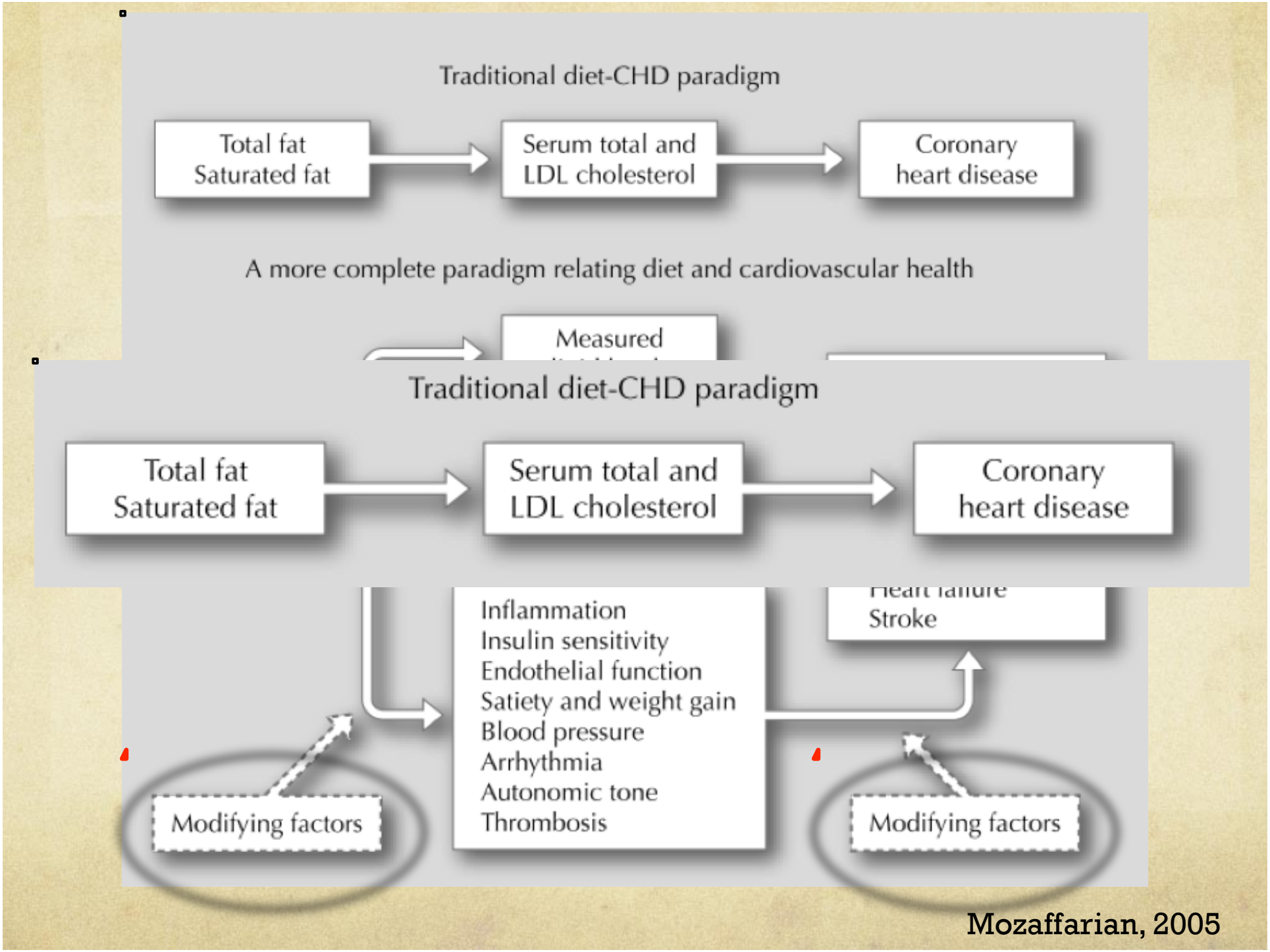
Mean (±SEM) effects of variation in dietary carbohydrate and saturated fat on LDL subclasses.



Siri-Tarino PW et al. *Am J Clin Nutr* 2010;91:502-509

Related Evidence

- LDL particle size (Siri-Tarino et al, 2010)
  - Saturated Fat increases LDL, but mainly the Large type
    - Saturated Fat also raises HDL (Mensink and Katan, 1992)
  - Carbohydrate increases appearance of small dense LDL
- Large LDL is not associated with CHD, while small dense LDL is (St. Pierre et al, 2005)



Mozaffarian, 2005

Closing Remarks

- Revise dietary guidelines?
  - Difficulty of Public Health Policy
- Future Research
  - Clinical trials
- Rethink the Diet-Heart Hypothesis
- Complexity of the Nutrition field

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