# Eat Fat Get Thin?

## Do fat calories behave differently?

*Or might fat make all calories behave differently?*

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# No Disclosures

- *Unless a dark chocolate habit clouds my thinking about saturated fat*

# Learning Objectives

- De-demonize fat
- Upgrade dietary fats
- Understand the roles of fatty acids for a healthy metabolism

# Undoing half a century of misguided science

"Keep everything as simple as possible....
but not one bit simpler" Einstein


1994 Fat Activism march on the Capitol

# The Original Case Against Fat

- Ancel Keys "7-Country Study" in fact listed 6, studied 22
- Started in 1958, continued for 15 yr

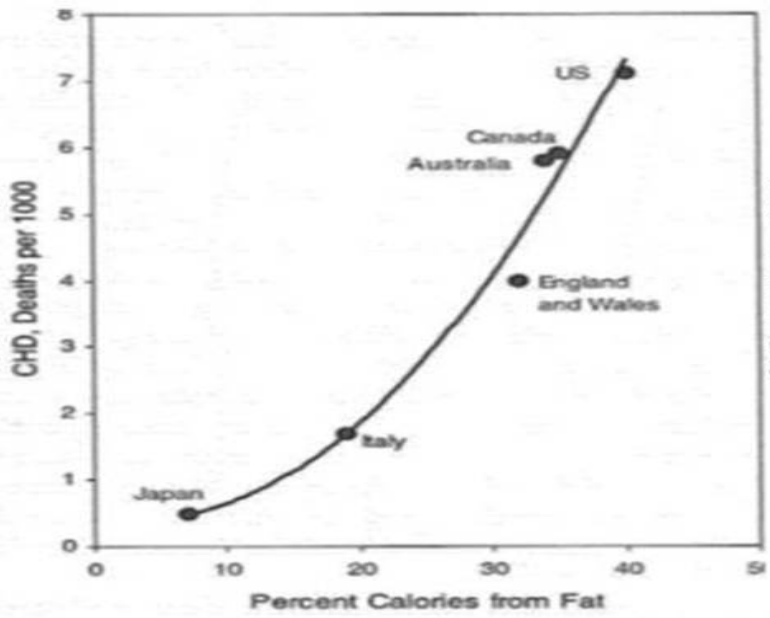



**Figure 1A.** Correlation between the total fat consumption as a percent of total calorie consumption, and mortality from coronary heart disease in six countries. Data from Keys.[1]

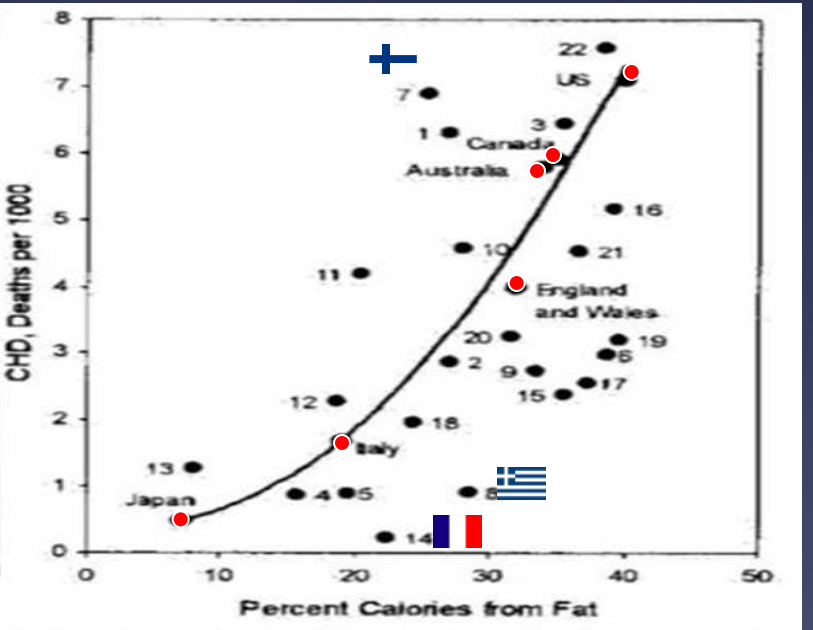
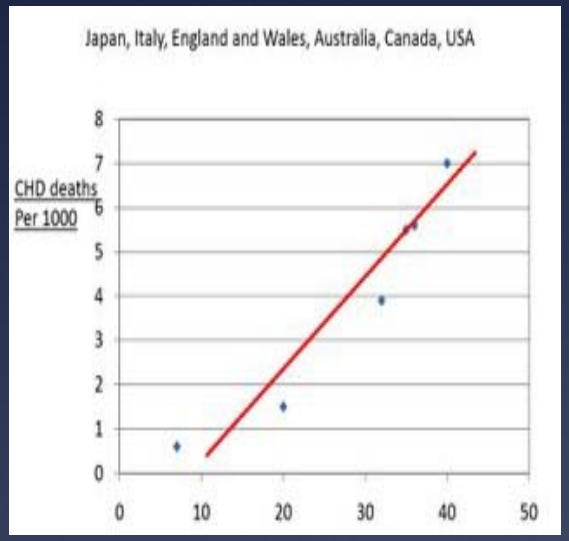
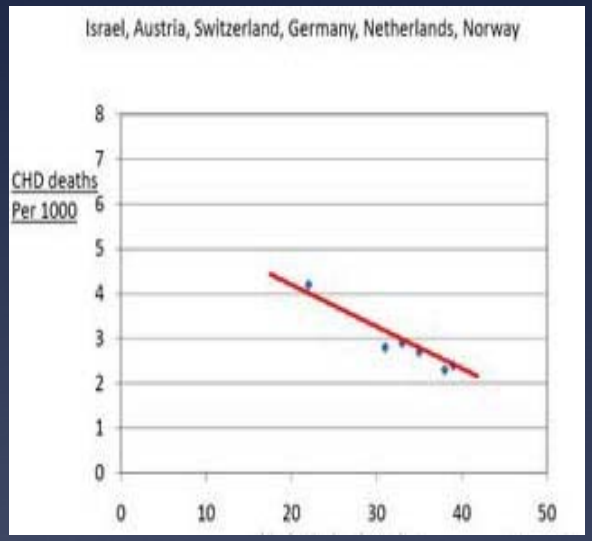
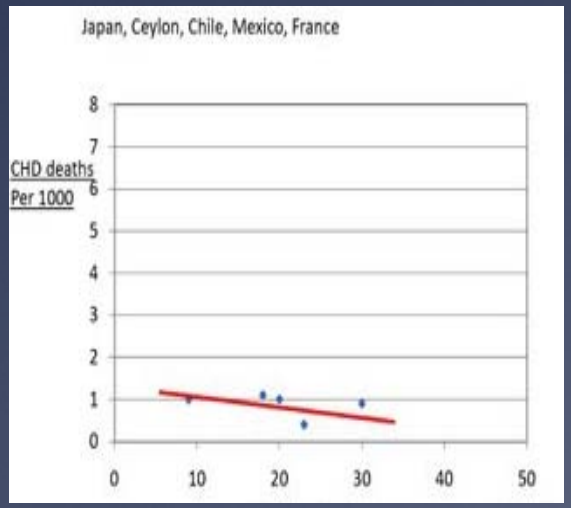


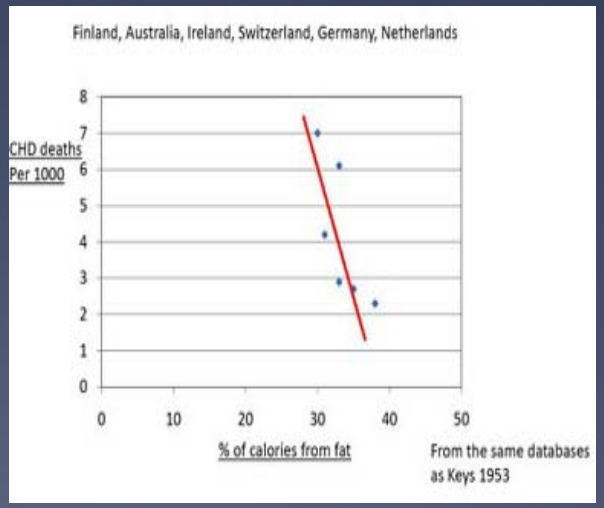

Figure 1B – as 1A but with all countries where data were available when Keys published. 1 Australia 2 Italy 3 Canada 4 Ceylon 5 Chile 6 Denmark 7 Finland 8 France 9 W Germany 10 Ireland 11 Israel 12 Italy 13 Japan 14 Mexico 15 Holland 16 New Zealand 17 Norway 18 Portugal 19 Sweden 20 Switzerland 21 Great Britain 22 USA
Data from Yerushalamy and Hilleboe

# Pick your favorite series?



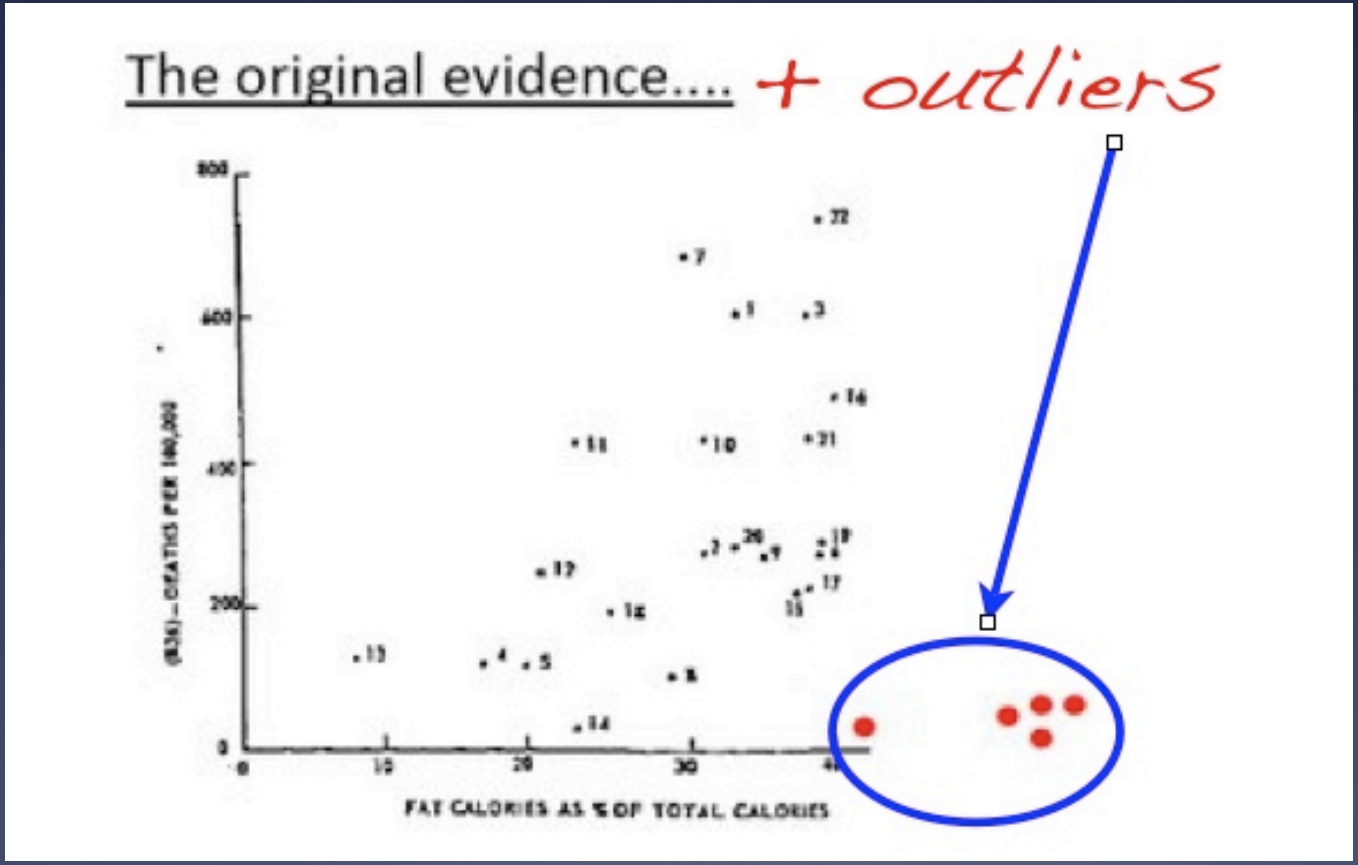



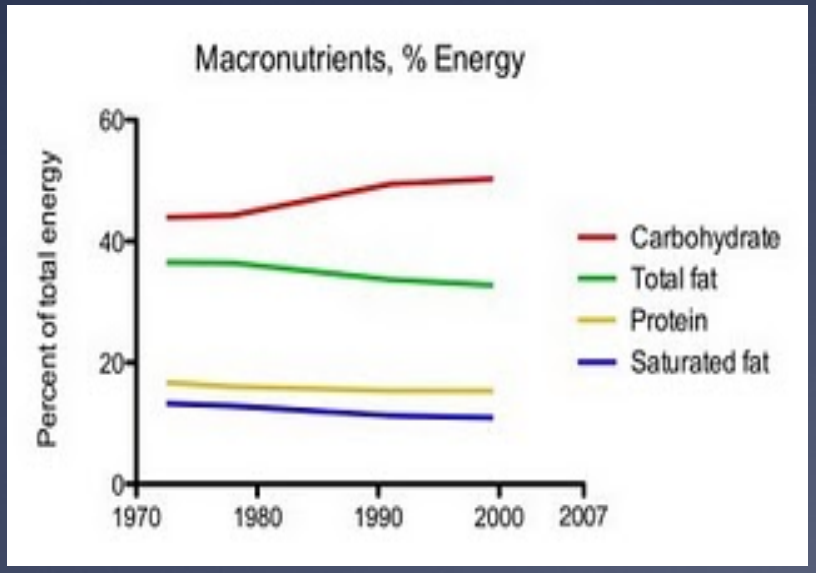

*From Chris Masterjohn, The Daily Lipid; cholesterol-and-health.com*

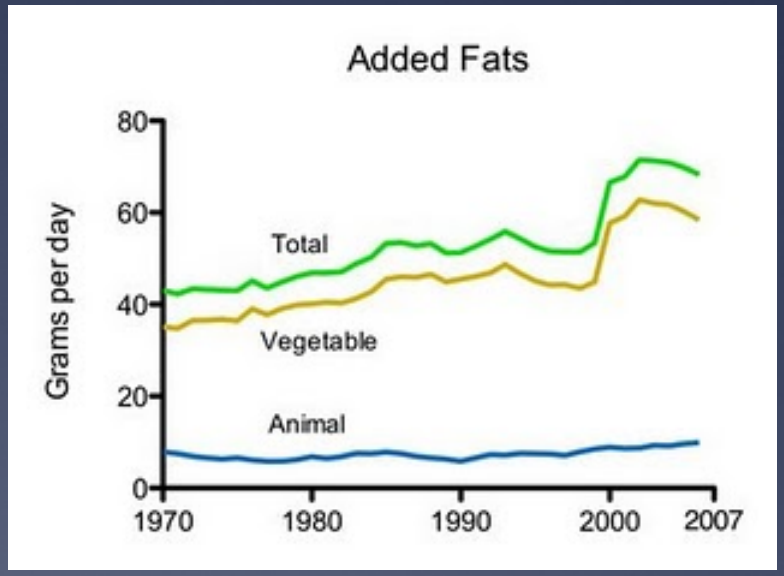
# Add in the Masai, Inuit, Rendile, and Tokelau indiginous tribes



# Keys' Legacy

- Total and saturated fat intake- *as a % of total kcal*- has fallen since ~1970
- Compensatory doubling of *added* vegetable oils- especially linoleic (ω6) - ramping up the ω6:ω3 ratio
- Trans fat was created to replace butter & lard

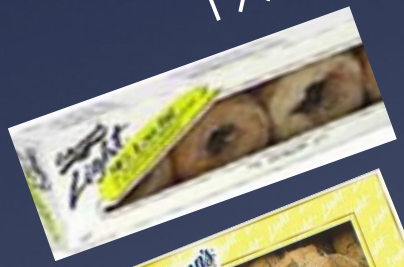



*Adapted from USDA food records by Stephan Guyenet;wholehealthsource.com*

# From Entenmann's® to Olestra

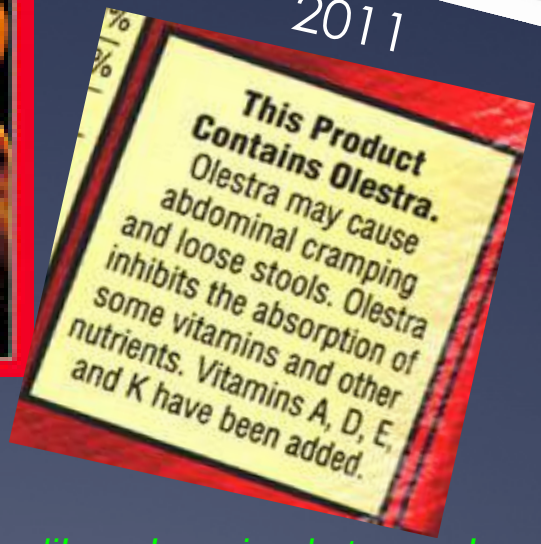

1990's






Jan 08, 1996


2011

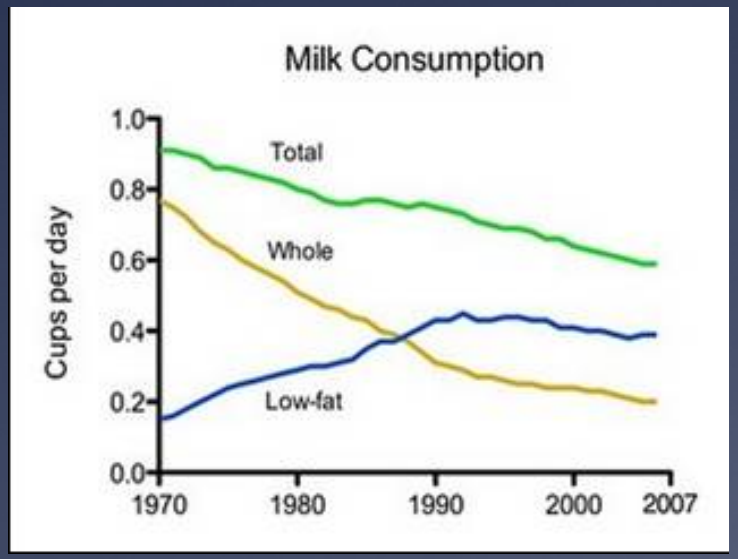


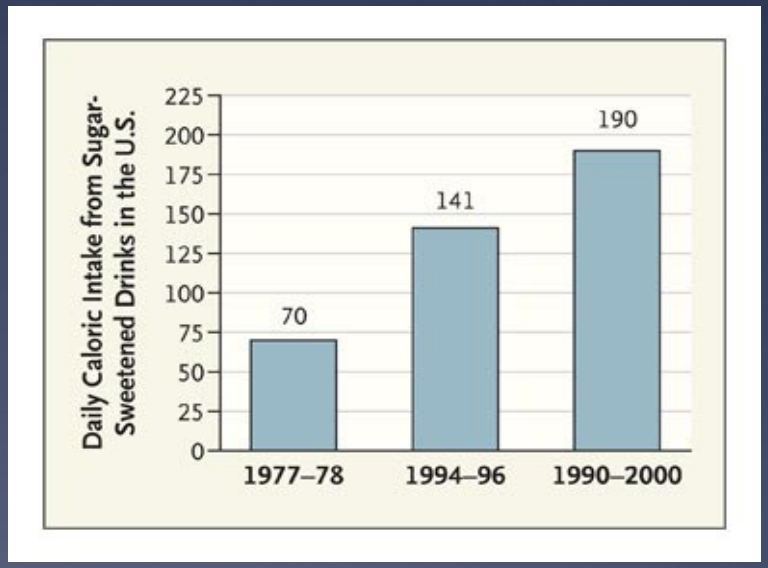

*Procter & Gamble is also using olestra-like chemicals to make eco-friendly paints and lubricants!*

*The new product line is called Sefose (you didn't think they would call it Olestra?)*

# Both total & whole milk intake fell

- With decline in full fat dairy, came prevalent deficiencies in Ca++, fat soluble vitamins A & D
  - Major decline in Conjugated Linoleic Acid
- *Liquid sugars picked up the slack*

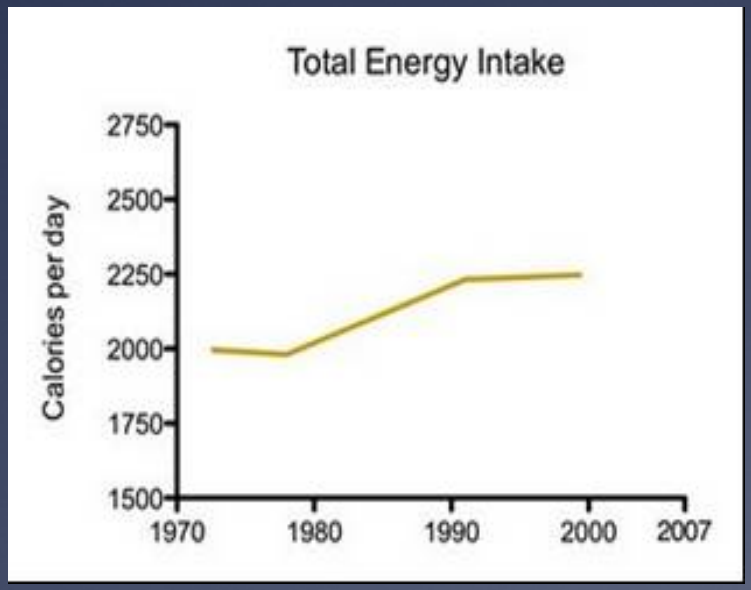


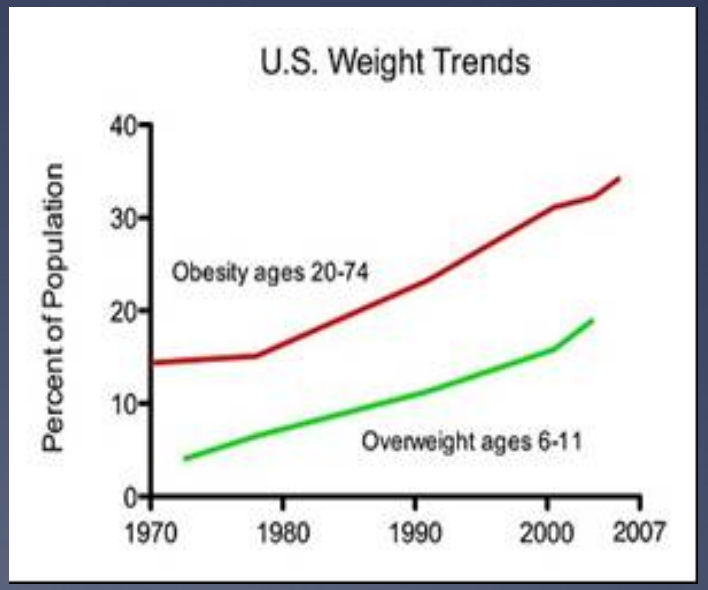




*Brownell & Frieden, NEJM 2009;360:1805*

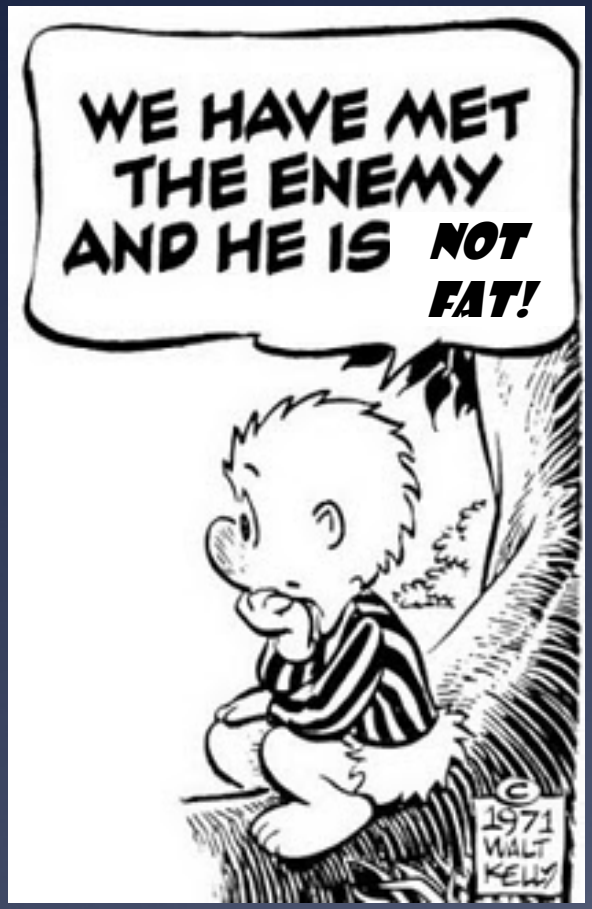
# Caloric intake & weight climbing

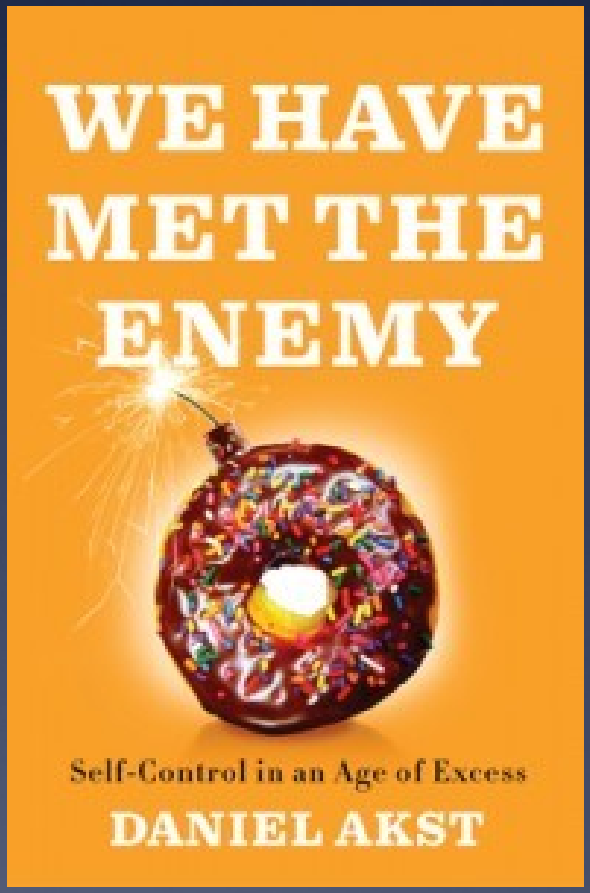
- Notwithstanding reduction in our most calorie dense food energy
- Does less dietary fat make us hungrier?
  - *May depend on sugar*
- Does the lack of essential fatty acids undermine energy regulation?



# Is Fat + Sugar & Salt our Timebomb?




*With sweet & savory fats → salience and reward trump satiety*

# Saturated Fats (SFA)

- Raise both LDL and HDL cholesterol- but large, buoyant phenotypes
- Lower lipoprotein(a)
- Protect the liver from toxins
- Serve as an energy reserve around heart muscle
- Enhance immunity
- Exert antimicrobial properties in the digestive tract
- Comprise 50% of cell membranes

*recall Keys country #14:*

*The French consume 4x more butter, 60% more cheese & 3x more pork than American counterparts, but experience ~ ½ as much heart disease…*

*The French Paradox?*

"If you're afraid of butter, use cream."
— Julia Child

# Monounsaturates (MUFA)

- Lower LDL cholesterol but favor HDL
- Rich in phytochemicals that boost immunity
- Naturally high in mixed VitE tocopherols and tocotrienols
- Associated with less visceral adipose storage
  - Increased adiponectin
  - Decreased hsCRP
- Credited with many of Mediterranean diet's benefits

*recall Keys country #6:*

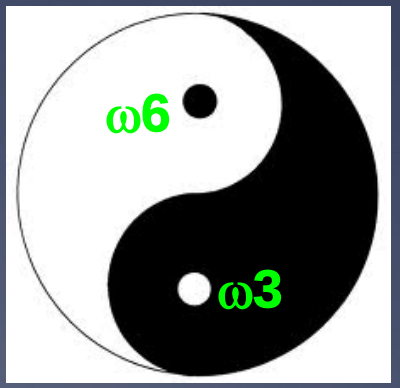
*Continued 25 yr follow-up in 7 countries from Keys' original cohort- including Greece (Crete)- showed 10-fold less CVD mortality vs northern Europe; attributed to greater balance of MUFA in o/w high total fat intake*

# Polyunsaturates (PUFA)

- Lower Total to HDL cholesterol ratio
  - Each 1 unit lowering associated with 44% less CVD
- Improve insulin sensitivity
- Reduce inflammation
- Efficacy however across trials vary
  - As a function of SFA replacement

    *Mozzaffarian, PLoS Med, 2010;7:e1000252*
  - Quality-Quantity issues are key

*Only PUFA trials with both ω6 & ω3 PUFA show benefit-*
*ω6 only, effect null*

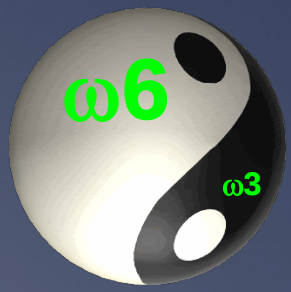



*Ramsden, Meta-analysis of PUFA trials, Br J Nutr, 2010;104:1586*

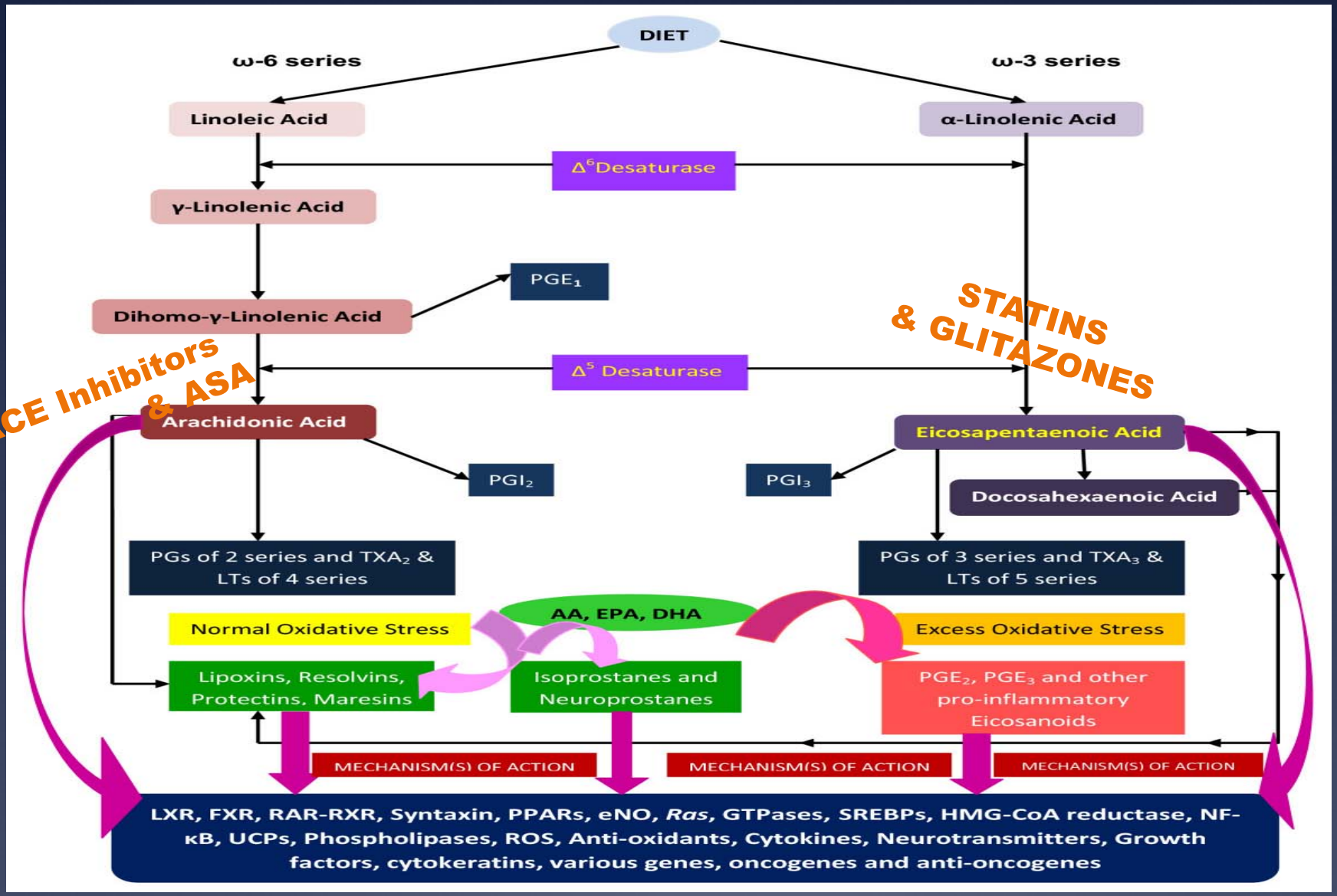
# *Essential* Fatty Acids (EFA)

- Are – well – essential for survival & not synthesized by human bodies
- All EFA are PUFA but not visa versa
- ω-6 series from linoleic acid (LA)
  - converted to arachidonic acid
- ω-3 series from alpha-linolenic acid (ALA)
  - conversion to DHA and EPA requires Vit B6, Zn, Mg *and normal insulin sensitivity*

*Frank deficiency rare but ancestral ratio of ~1:1 ω-6 :ω-3 shifted in modern diet to ~16 to 20:1*



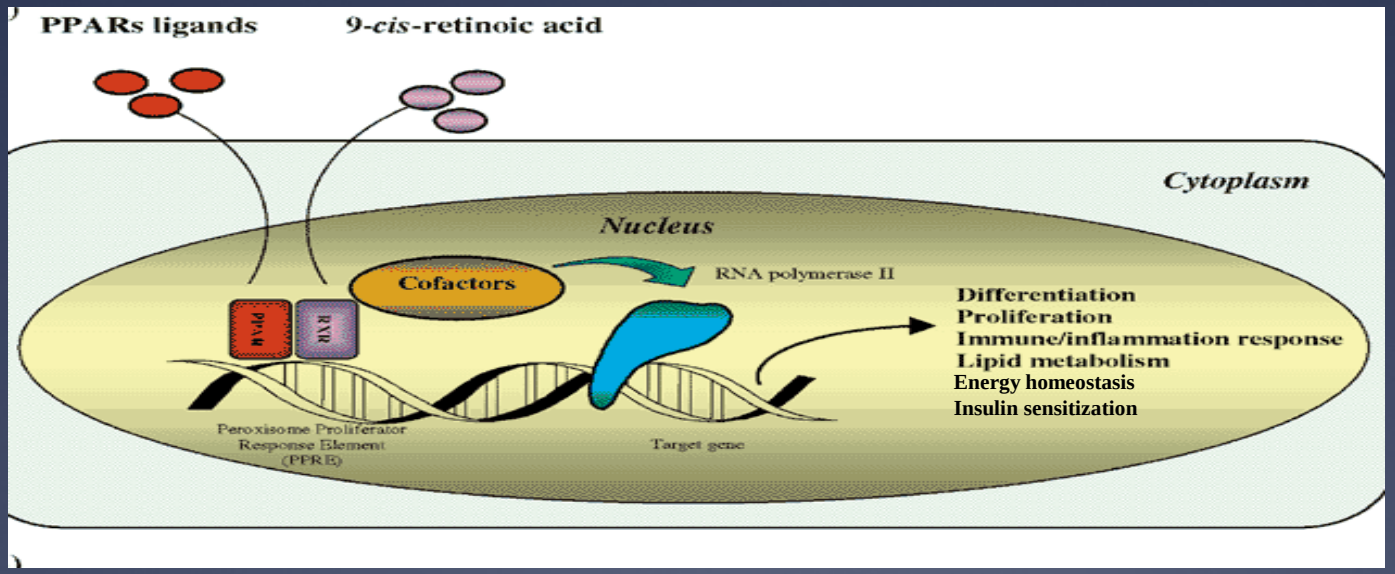
# EFA better than a polypill?



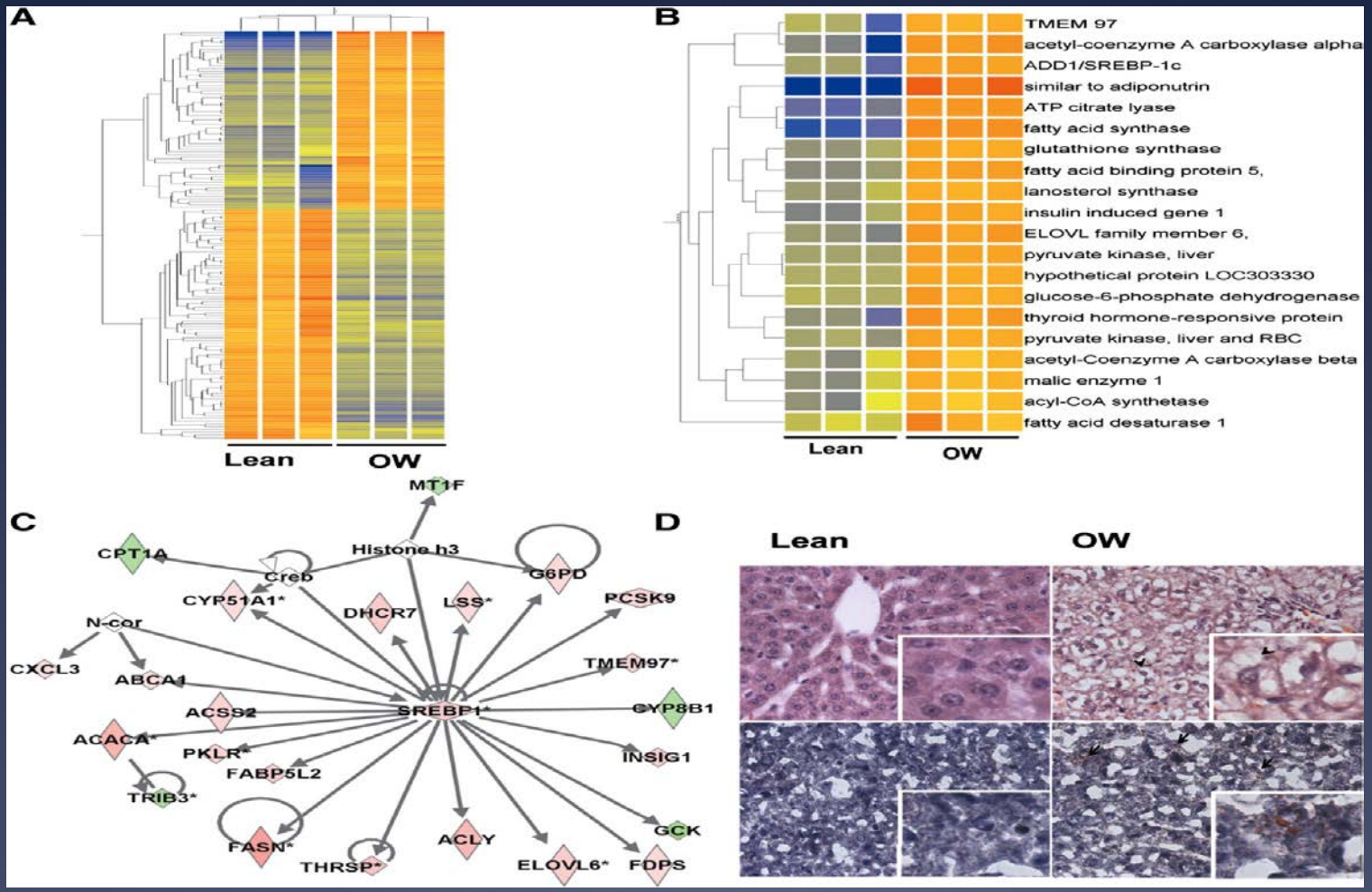

Das, Lipids in Health and Disease, 2008;7:37

# How fatty acids achieve metabolic activity

- Cell membrane fluidity & receptor function
- Endogenous ligands (MUFA & PUFA, esp ω3 PUFA, some SFA) for global transcriptional regulators called PPARs



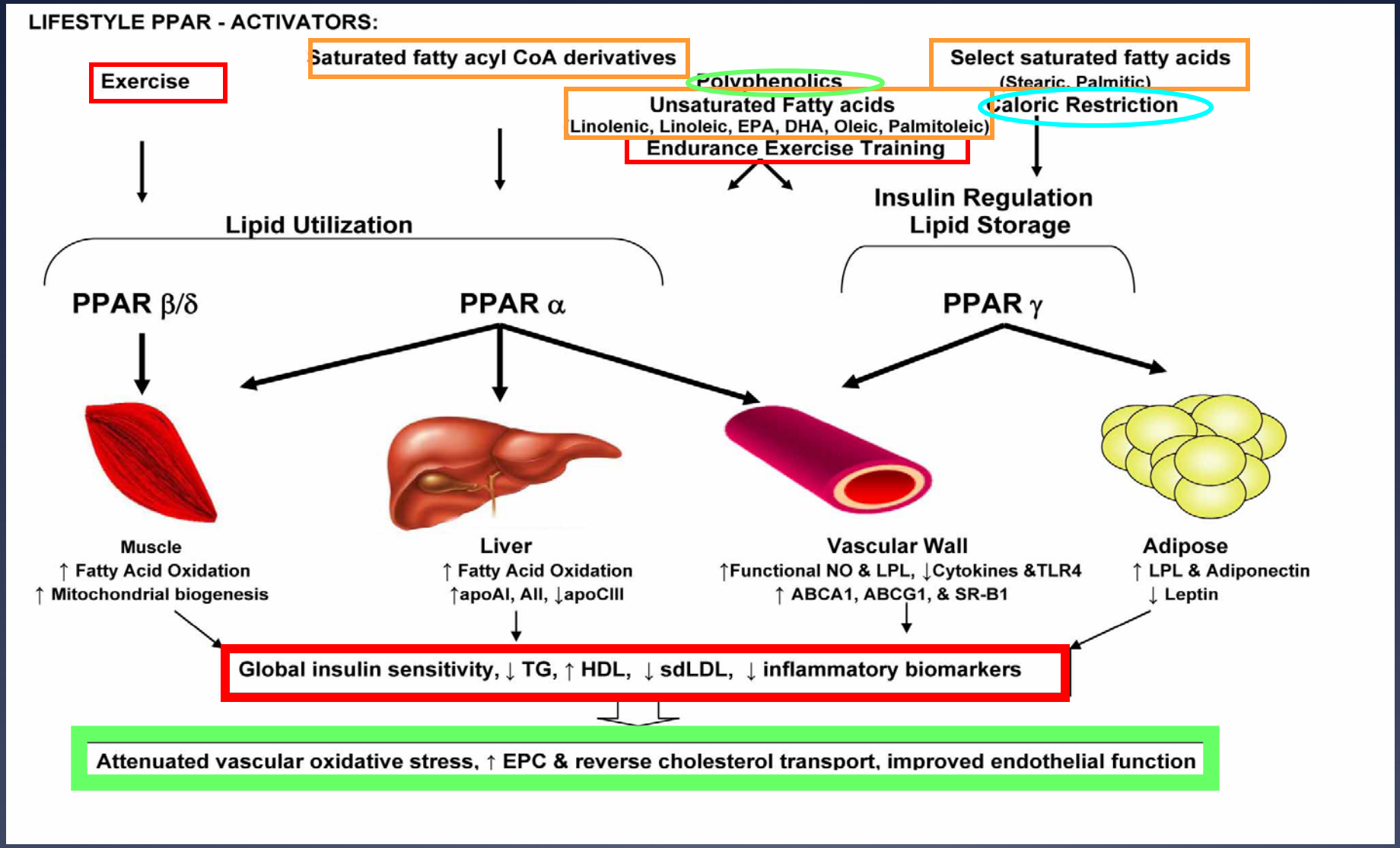
# PPAR gene network activation differs in offspring of lean vs o/w mothers




*SREBP-1, at the hub, itself downstream from PPAR gamma*

Shankar K et al. Endocrinology 2010;151:2577-2589

# Lifestyle PPAR Activators




Mietus-Snyder & Krauss, JCL, 2008;2:127

# In nature fats are never delivered in a vacuum


INGREDIENTS: partially hydrogenated soybean and cottonseed oil, mono- and diglycerides

*Increasing evidence documents synergy among nutrients for optimal fatty acid metabolism - notably polyphenolics, fiber, minerals, antiox vits and B vit methyl donors*

# PPARs Promote Mitochondria (Build a Hybrid Engine)

## LIMITED ANAEROBIC ACCESS TO ENERGY

* We have ~ 10 seconds worth of ATP ready on hand; another 10-15 minutes stored in glycogen

## AEROBIC POTENTIAL VIA MITOCHONDRIAL COMBUSTION

* Gas guzzling engine burns glucose; 36-38 ATP/molecule glucose
  * Good for about 90 min moderate activity
* Electric engine burns fat; 460 ATP/fatty acid
  * Moves endurance athletes through 'the wall'
* The more fat burned, the more energy for robust immunity, healthy lipid metabolism, weight & vitality

# When PPAR Function Fails

- Insulin resistance
- Ectopic fat deposition
  - Visceral adiposity & the metabolic syndrome
  - Also fatty pancreas, heart, liver, kidney & vasculature
  - Resultant diabetes, congestive heart failure, nonalcoholic fatty liver disease, renal failure, atherosclerosis
- Impaired immunity
- Mitochondrial dysfunction; energy ebbs
- Accelerated aging and chronic disease

# In Summary

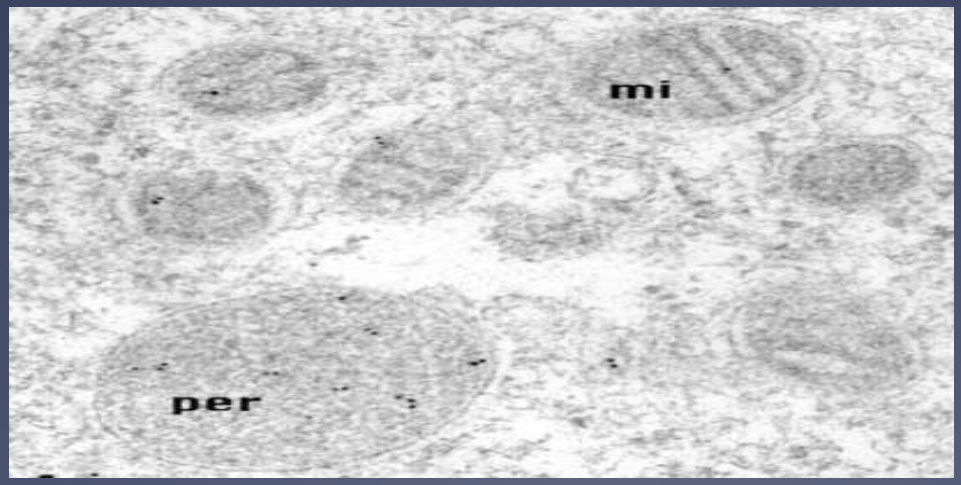
- Fatty acids are our highest octane fuel
  - Adipose tissue is a good place to store energy
  - Ectopic fat is a problem
- Useful fat storage requires a good mechanism for retrieval and disposition
  - Fat revs its own engine
- Foods that contain fat are essential in the context of other key micro and macronutrients for optimal lipid metabolism, immunity and weight regulation
- Fat calories do make all calories behave differently

# PPARs = Peroxisome Proliferator-Activated Receptors

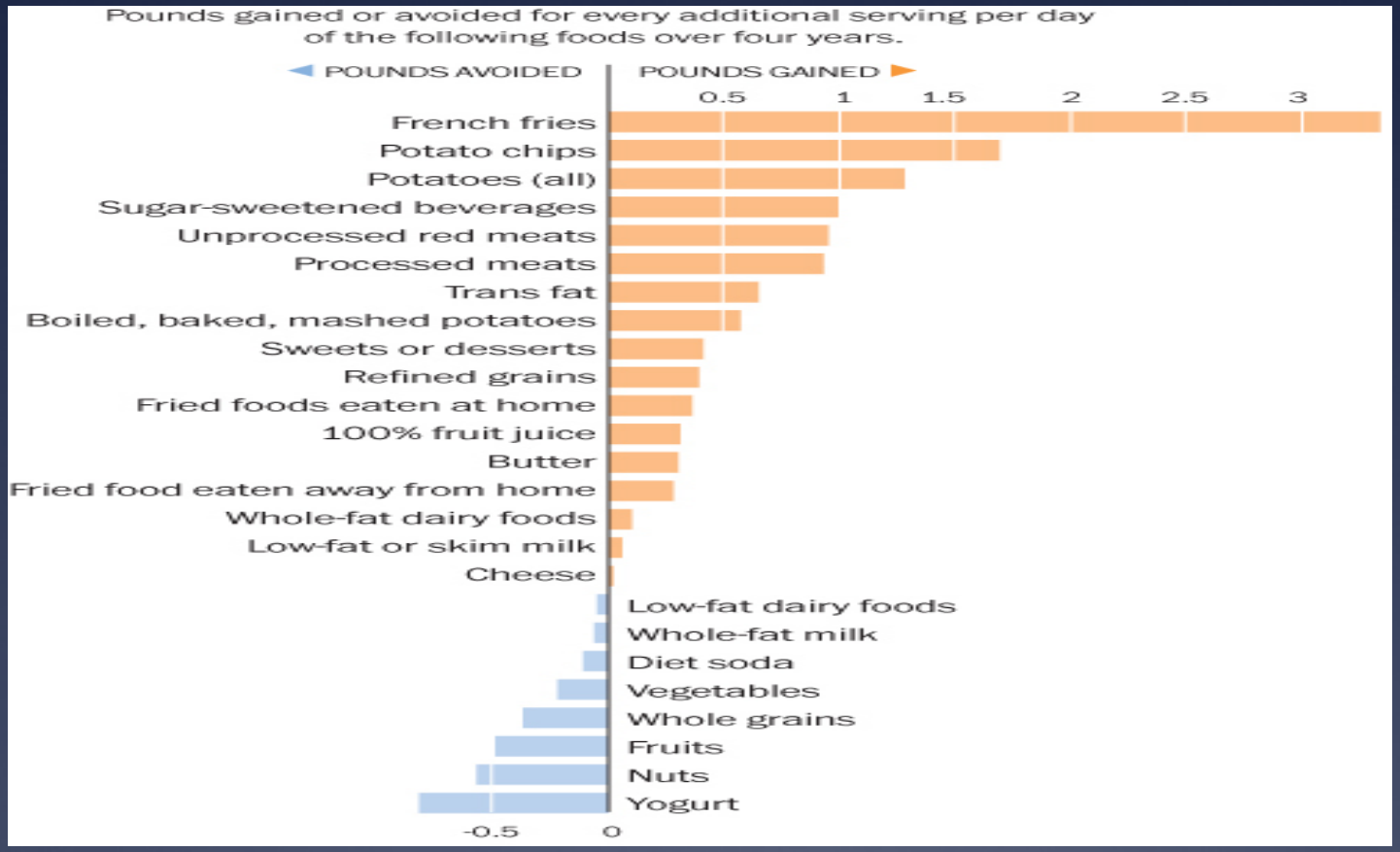
- Family of interrelated gene regulators
- Part of the body's quick-response mechanism to respond to the environment- diet, activity level, infection, stress
- Coordinated on and off switch for 100's of downstream genes
- Dependent on a complex of regulatory cofactors
- ***But what are peroxisomes?***

# Peroxisomes
## Metabolic links with Mitochondria

- Self-replicating organelles (like mitochodria) sans genome
- Evolutionary predecessors of mitochodria
  - Now critical support for mitochondrial biogenesis
- Essential functions for fat metabolism
  - Catalytic: fatty acid beta oxidation (generates ATP)
  - Anabolic: bile acid & neurolipid myelin synthesis
  - Detox: converts $H_2O_2$ to water; renders ETOH inert



# Dietary Quality and Long Term Weight Changes




*Mozzaffarian, NEJM, 2011;364:2392-404*