Discussing Today :
The role of fat and LDL cholesterol on heart disease.

Anthony Grise   &   Matthew Nagra

Each presenting 12 studies for our case.
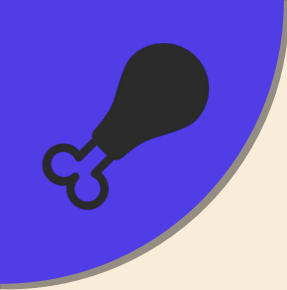
About Me – Anthony Grisé

i

- I greatly value my **health** and **wellbeing** & aim to live a **simple**, **happy**, **stress free** life.

- I enjoy **problem solving**, **critical thinking** and challenging the **status quo**.

- Being a curious guy, I've spent + 2 years **reading**, **researching** and **learning** about nutrition and health.

- It's my opinion that an **Animal-Based / Low-Carb, High-Fat diet** is optimal for human health.

- I've been following a **Low-Carb diet** for + 2 years & have been following an **Animal-Based diet** for + 1 year (*and feel great!*).

- **No professional accreditation** in the field of health or nutrition – but you don't need a degree to do independent research.

- **Critical thinking isn't taught in school.**

ii **About Me**

- Disclosure :
  - I am **not affiliated** with the meat or dairy industry.
  - I **do not receive money** from any organization.

- **My opinions are my own** and based on my independent research.

- I do have a **website** where I share my view on health + large collection of studies and resources.
  - *fndmntl.ca*

- I don't discredit a Plant-Based diet. It's clear that **many people see improvements** in health from it.

- Plant-Based advocates are **well intentioned**, and I **respect their efforts** to want to improve peoples' health.

- … But I **don't agree** that **eliminating animal foods and animal fats** from the diet is optimal for health and may even be harmful.
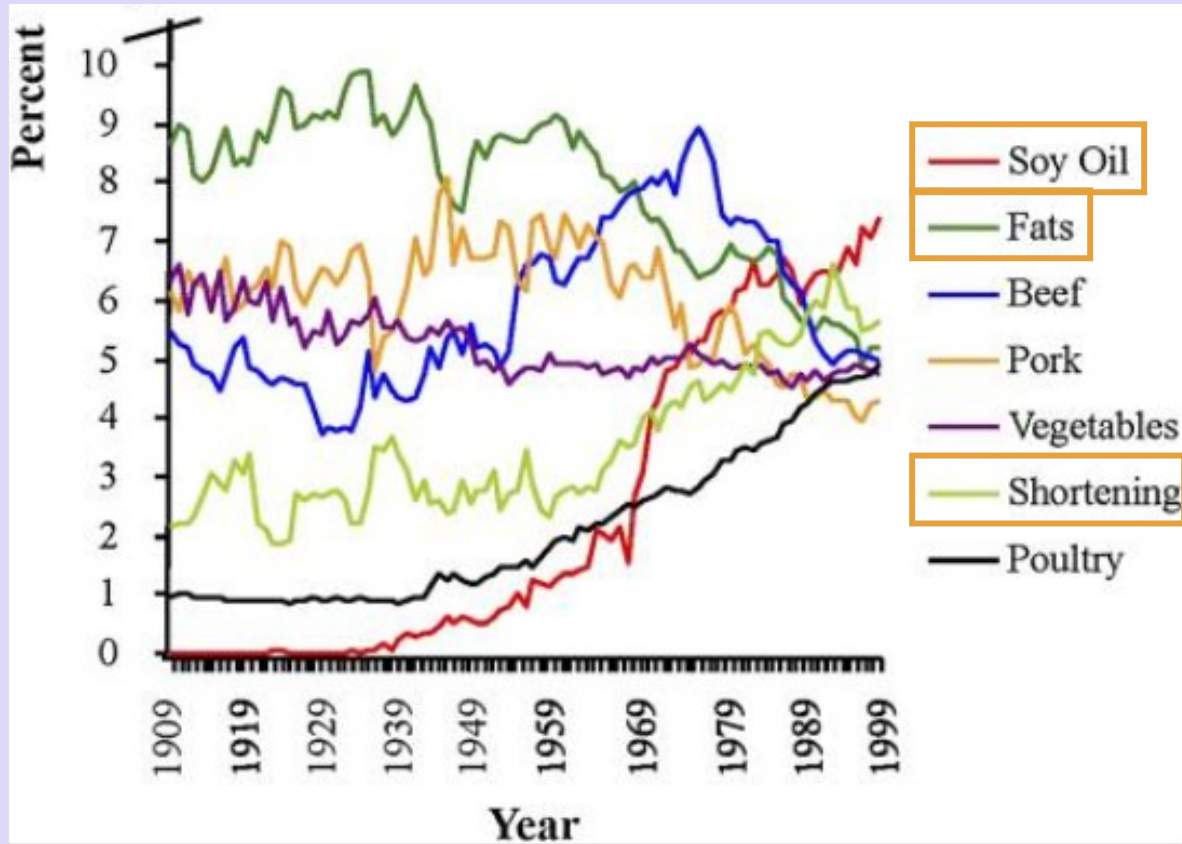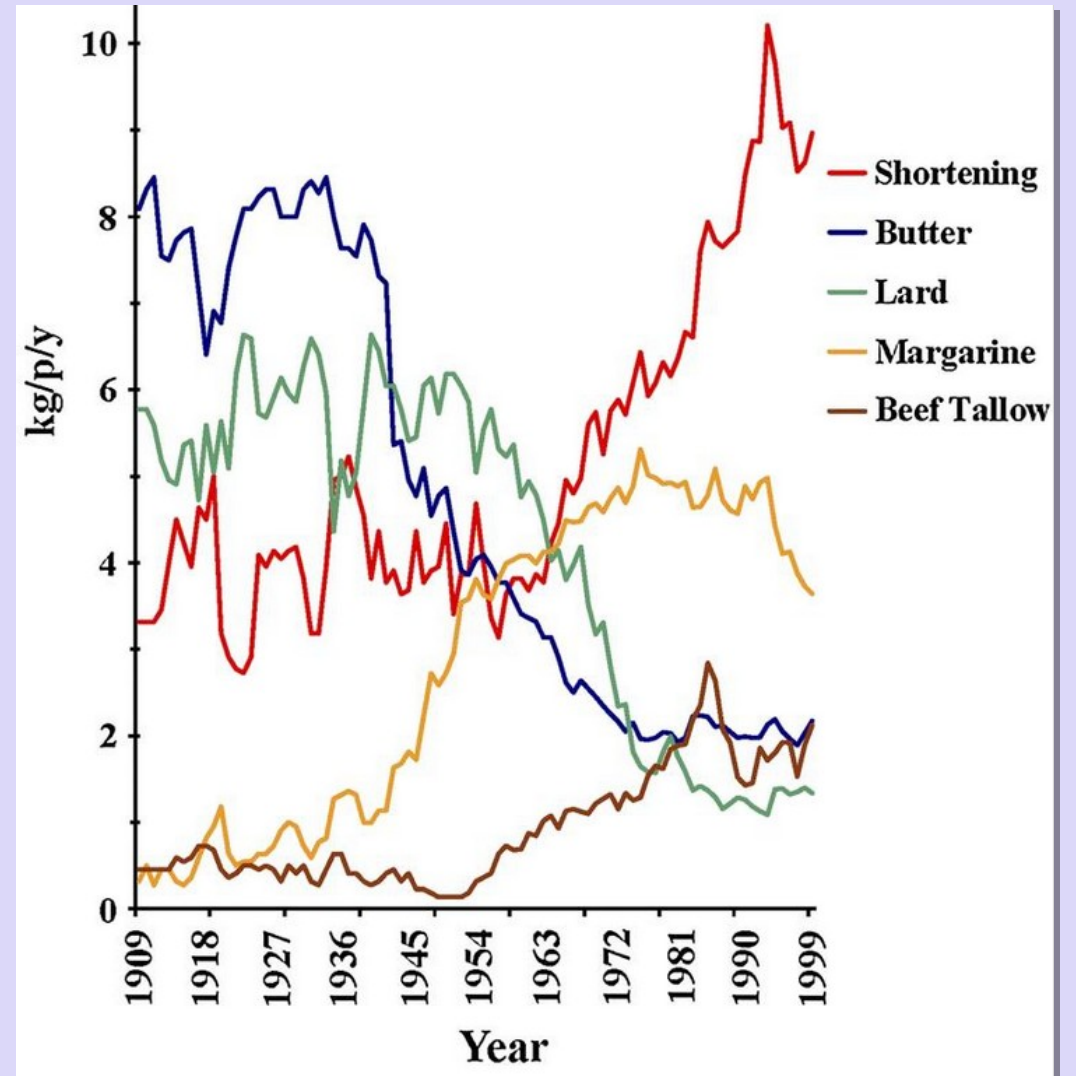
Anthony's Studies
High-fat / Animal-Based

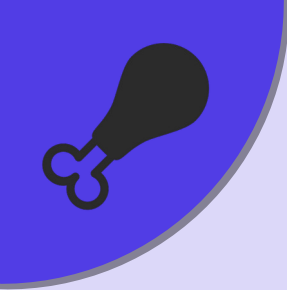# Matthew's Studies
Low-fat / Plant-Based

Changes in consumption of omega-3 and omega-6 fatty acids in the United States during the 20th century

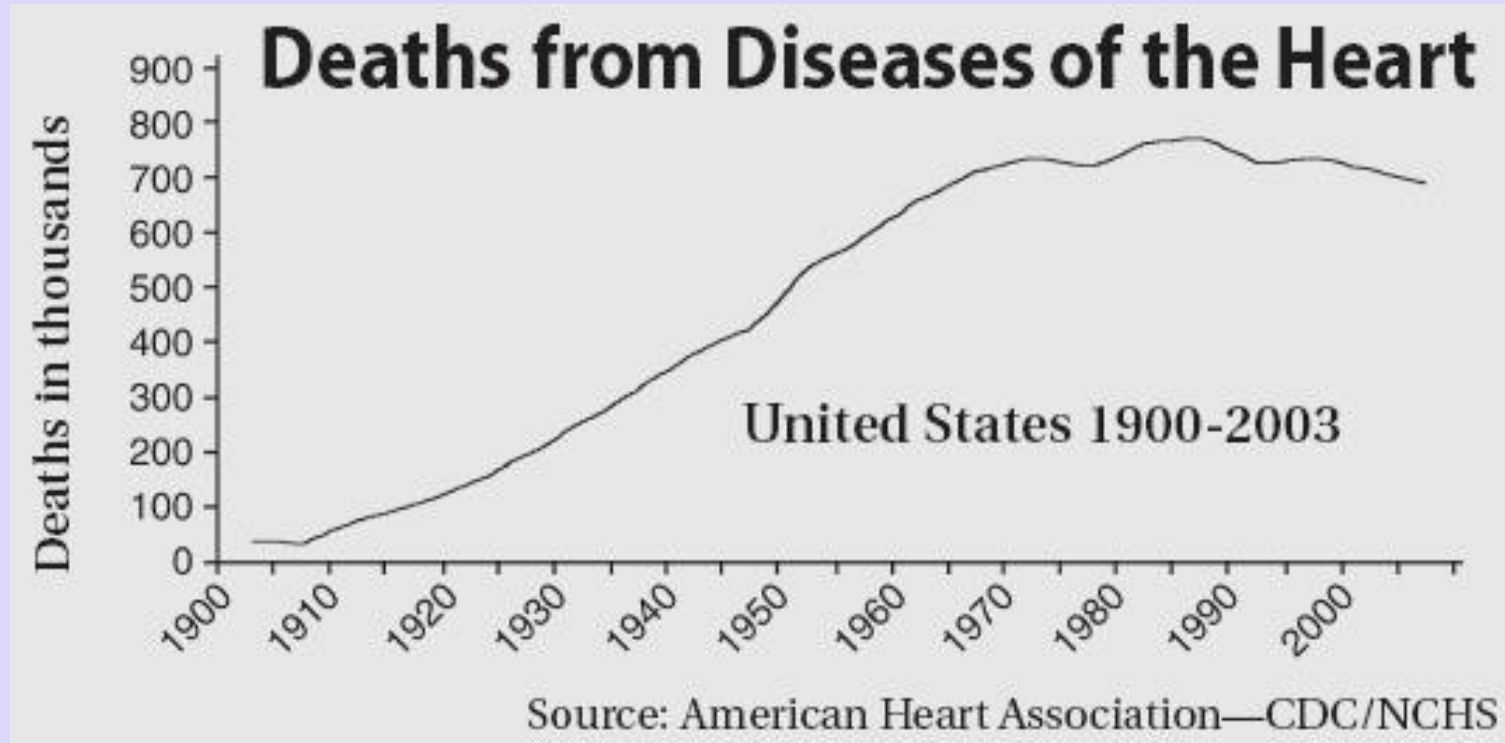

Percent / Year

Legend:
- Soy Oil
- Fats
- Beef
- Pork
- Vegetables
- Shortening
- Poultry

* Fats include shortening, butter, lard, margarine, and beef tallow.

kg/p/y / Year

Legend:
- Shortening
- Butter
- Lard
- Margarine
- Beef Tallow

And yet...

Deaths from Diseases of the Heart

United States 1900-2003

Deaths in thousands — 0, 100, 200, 300, 400, 500, 600, 700, 800, 900

Years: 1900, 1910, 1920, 1930, 1940, 1950, 1960, 1970, 1980, 1990, 2000

Source: American Heart Association—CDC/NCHS

2 Dietary cholesterol and cardiovascular disease: a systematic review and meta-analysis

- **40 studies** (17 cohorts with 361,923 subjects and 19 trials [of which 16 RCTs] with 632 subjects).

- Dietary **cholesterol** statistically significantly **increased** both serum **total cholesterol** and **LDL** cholesterol [and] **HDL** cholesterol.

- *But...* Dietary cholesterol was **not statistically significantly associated** with any **coronary artery disease** (no summary RR), **ischemic stroke** (RR: 1.13), or **hemorrhagic stroke** (RR: 1.09).

- Reviewed studies ... **lacked the methodologic rigor to draw any conclusions** regarding the effects of dietary cholesterol on CVD risk.

3. Re-evaluation of the traditional diet-heart hypothesis: analysis of recovered data from Minnesota Coronary Experiment (1968-73)

- A **double-blind randomized cohort of 9423** women and men aged 20-97 [all living in state **mental hospitals** or a **nursing home**].

- Compared the effects of a 39% fat [as energy] **control diet** (**18% saturated fat**, 5% polyunsaturated fat, 16% monounsaturated fat) with a 38% fat **treatment diet** (**9% saturated fat**, 15% polyunsaturated fat, 14% monounsaturated fat).

- The intervention group had significant **reduction** in serum **cholesterol** compared with controls (−13.8%).

- *But...* There was **no evidence of benefit** in the intervention group for **coronary atherosclerosis or myocardial infarcts**.

- *In fact...* There was a **22% higher risk of death** for each 30 mg/dL (0.78 mmol/L) reduction in serum cholesterol.
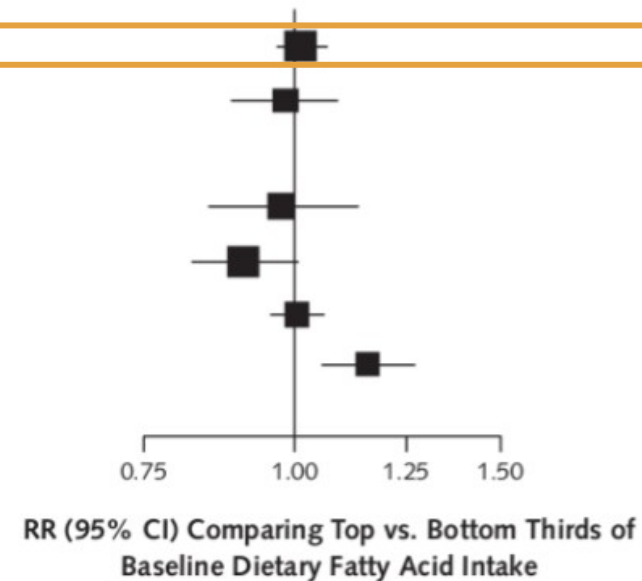
Association of Dietary, Circulating, and Supplement Fatty Acids With Coronary Risk

- **32 observational studies** (512 420 participants) of fatty acids from dietary intake; **17 observational studies** (25 721 participants) of fatty acid biomarkers; and **27 randomized, controlled trials** (105 085 participants) of fatty acid supplementation.

- In observational studies (*FFQ's...*), relative risks for coronary disease were :
  - **1.03** (95% CI, 0.98 to 1.07) for saturated,
  - **1.00** (CI, 0.91 to 1.10) for monounsaturated,
  - **0.87** (CI, 0.78 to 0.97) for long-chain ω-3 polyunsaturated,
  - **0.98** (CI, 0.90 to 1.06) for ω-6 polyunsaturated, and
  - **1.16** (CI, 1.06 to 1.27) for trans fatty acids

- In randomized, controlled trials, relative risks for coronary disease were
  - **0.97** (CI, 0.69 to 1.36) for α-linolenic,
  - **0.94** (CI, 0.86 to 1.03) for long-chain ω-3 polyunsaturated, and
  - **0.86** (CI, 0.69 to 1.07) for ω-6 polyunsaturated fatty acid supplementations.

Figure 1. RRs for coronary outcomes in prospective cohort studies of dietary fatty acid intake.

Dietary Fatty Acid Intake	Studies, n	Participants, n	Events, n		RR (95% CI)*
Total saturated fatty acids	20	283 963	10 518		1.02 (0.97–1.07)
Total monounsaturated fatty acids	9	143 985	6020		0.99 (0.89–1.09)
Total ϖ-3 fatty acids					
α-Linolenic	7	154 338	6615		0.99 (0.86–1.14)
Total long-chain ϖ-3	16	422 071	8313		0.93 (0.84–1.02)
Total ϖ-6 fatty acids	6	169 935	5884		1.01 (0.96–1.07)
Total trans fatty acids	5	155 270	4662		1.16 (1.06–1.27)

0.75   1.00   1.25   1.50

RR (95% CI) Comparing Top vs. Bottom Thirds of
Baseline Dietary Fatty Acid Intake

Current evidence **does not support** cardiovascular guidelines that encourage **high consumption of polyunsaturated fatty acids and low consumption of total saturated fats.**

5 **Milk and dairy consumption and risk of cardiovascular diseases and all-cause mortality: dose-response meta-analysis of prospective cohort studies**

- A total of 29 cohort studies were available for meta-analysis, with **938,465 participants** and 93,158 mortality, 28,419 CHD and 25,416 CVD cases.

- **No associations were found** for total (high-fat/low-fat) **dairy**, and milk with the health outcomes of **mortality, CHD or CVD**.

- …funding from the Global Dairy Platform, Dairy Research Institute and Dairy Australia.

Epidemiology of ischemic heart disease in India with special reference to causation

- **1.15 million railway workers** between the ages of 18-55 years [studied over 5 years] in different parts of India.

- The **highest mortality** was in the southern zone (135 per 100,000) in the **south of India**, and the **lowest** in the northern, western, and north-eastern zones (20, 25, and 33 per 100,000 respectively) in the **north of India**.

TABLE I

FIVE-YEAR MORTALITY FROM ARTERIOSCLEROTIC AND CORONARY HEART DISEASE ON VARIOUS INDIAN ZONAL RAILWAYS DURING 1958–1962, BASED ON THE TOTAL NUMBER OF EMPLOYEES ON PAY-ROLLS

| Railway zones	No. of deaths	Total no. of employees (18–55 years)	Mortality rate per 100,000 employees during quinquennium	Total in-patient admissions for all diseases	Percentage of deaths to total admissions
Northern	36	178,311	20	23,313	0·15
Western	41	162,264	25	17,771	0·23
North-eastern	28	84,964	33	27,148	0·10
Eastern	88	176,633	50	43,027	0·20
North-east frontier	36	63,120	57	12,330	0·29
Central	126	200,308	63	25,504	0·49
South-eastern	105	123,497	85	15,660	0·67
Southern	219	161,719	135	28,528	0·77
Total	679	1,150,816	59	193,281	0·35
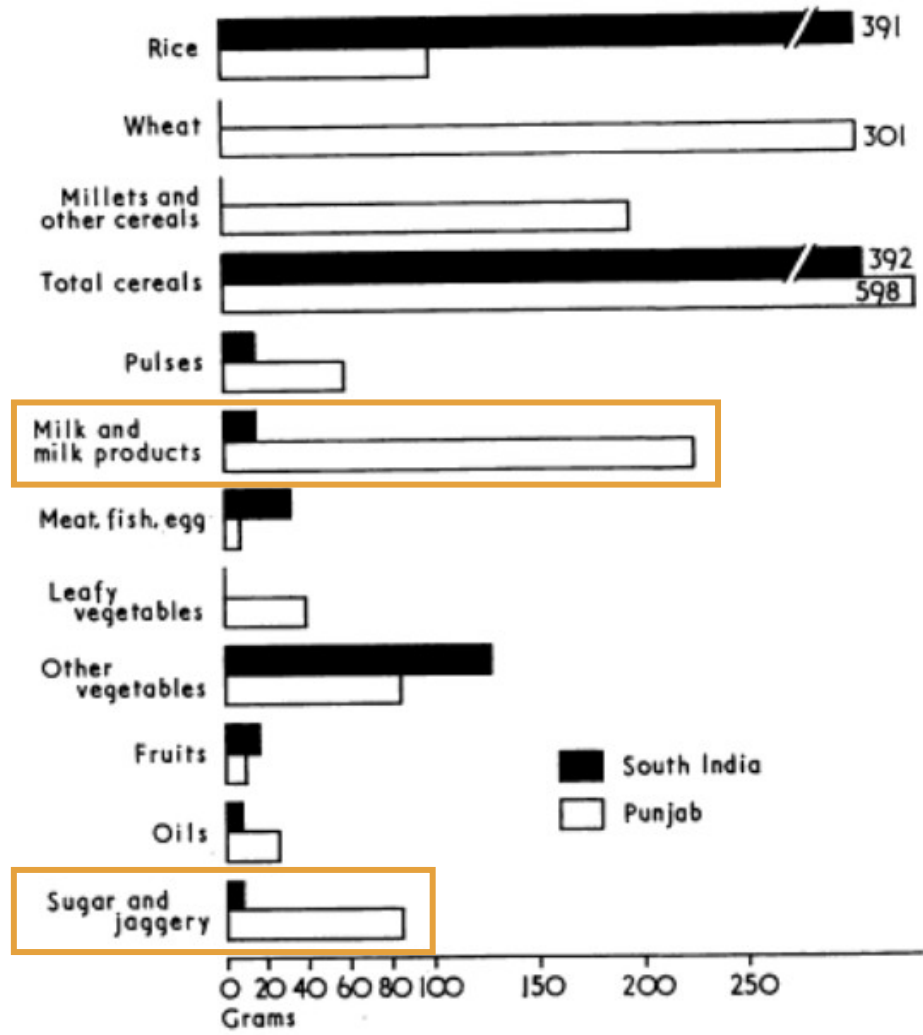
FIG. 2.—Food consumption pattern in south India and the Punjab. (From Diet Atlas of India, *Indian Coun. med. Res. Sp. Rep. Ser.* No. 48)

Epidemiology of ischemic heart disease in India with special reference to causation (cont.)

- The **consumption of fats** – [most of which are **animal fats**] – **is 8-19 times higher** in the Punjab (**north India**) as compared with Madras in the **south.**

- *Despite that...* **[heart] disease** is [almost] **<u>7 times less [prevalent]</u>** in the **north** than in the **south**.

- Moreover, while the **milk fats eaten in the north** have a preponderance of **saturated fatty acids**, the **seed oils** used in the **south** are mainly composed of **unsaturated fatty acids**.

- Neither **smoking**, nor **socio-economic** factors, nor **physical activity** of work, nor even **stress** and strain have provided any tenable associations with the immunity from or a liability to develop ischemic heart disease.
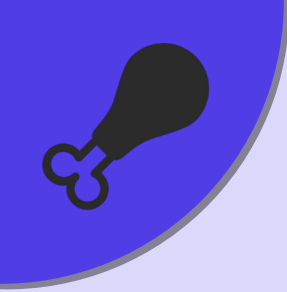
LDL
Low-density Lipoprotein
("bad" cholesterol)

HDL
High-density Lipoprotein
("good" cholesterol)

The liver sends off LDL to deliver its "fat" cargo to various parts of the body.
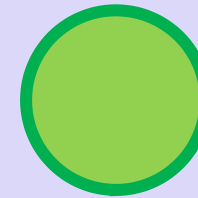
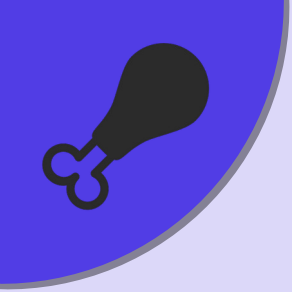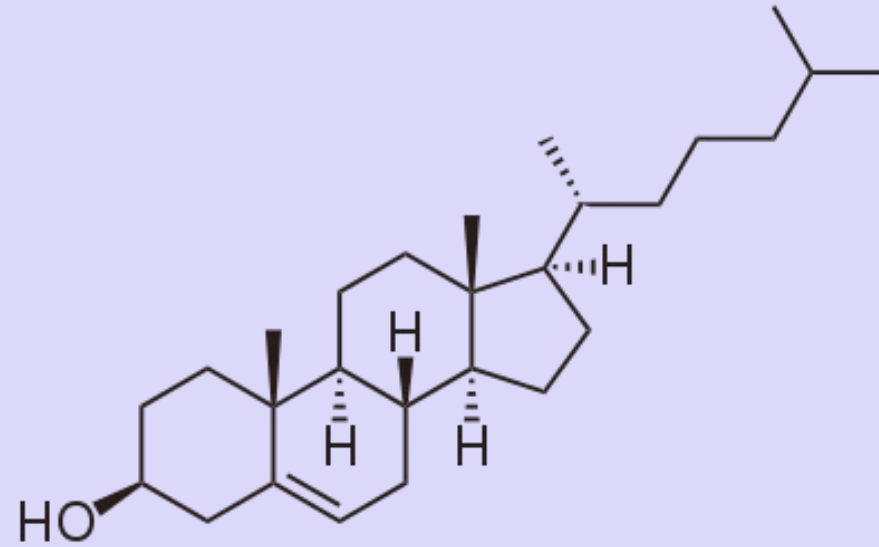HDL collects "fatty waste" from around the body and returns it to the liver to be processed.

Cholesterol ester

**Vital** for life
+ Serves a **multitude** of functions
+ The **liver produces** what you don't consume

Lipid levels in patients hospitalized with coronary artery disease: An analysis of 136,905 hospitalizations in Get With The Guidelines

- 541 hospitals, admission lipid levels [among **136,905 patients hospitalized with coronary artery disease**] were documented.

- Mean lipid levels were :
  - **LDL = 104.9** mg/dl (2.71 mmol/L), = **average / good**
  - **HDL = 39.7** mg/dl (1.03 mmol\L), and = **LOW**
  - **Triglyceride = 161** mg/dL (1.82 mmol/L). = **moderately elevated**

- LDL cholesterol **<70 mg/dL** was observed in **17.6%** & almost **half** had admission LDL levels **<100 mg/dL**.

- ❖ *So why did these people with low LDL **still get heart disease**?*
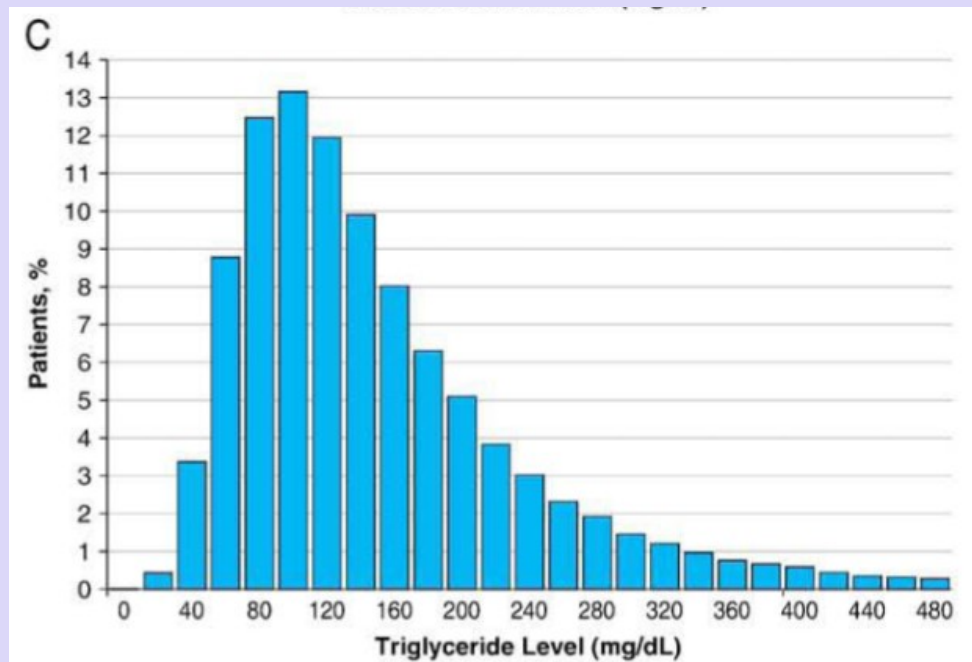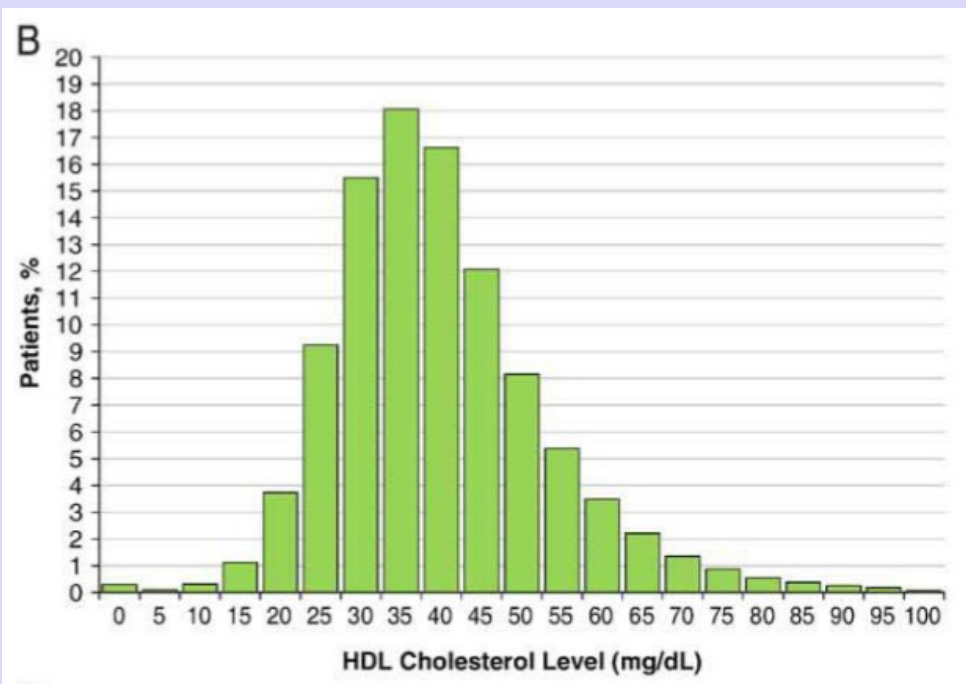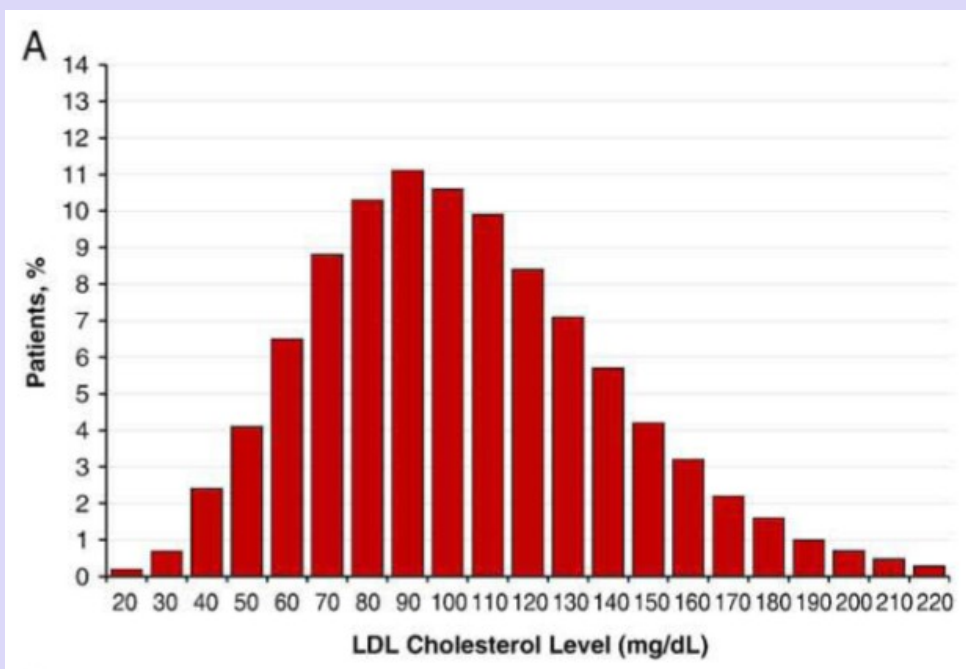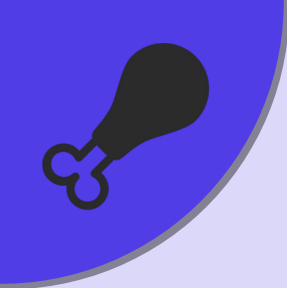
Distribution of admission LDL, HDL, and triglyceride levels. (**A**) Histogram of admission LDL levels in 10 mg/dL increments. (**B**) Histogram of admission HDL levels in 5 mg/dL increments. (**C**) Histogram of admission triglyceride levels in 20 mg/dL increments (truncated at 480 mg/dL).
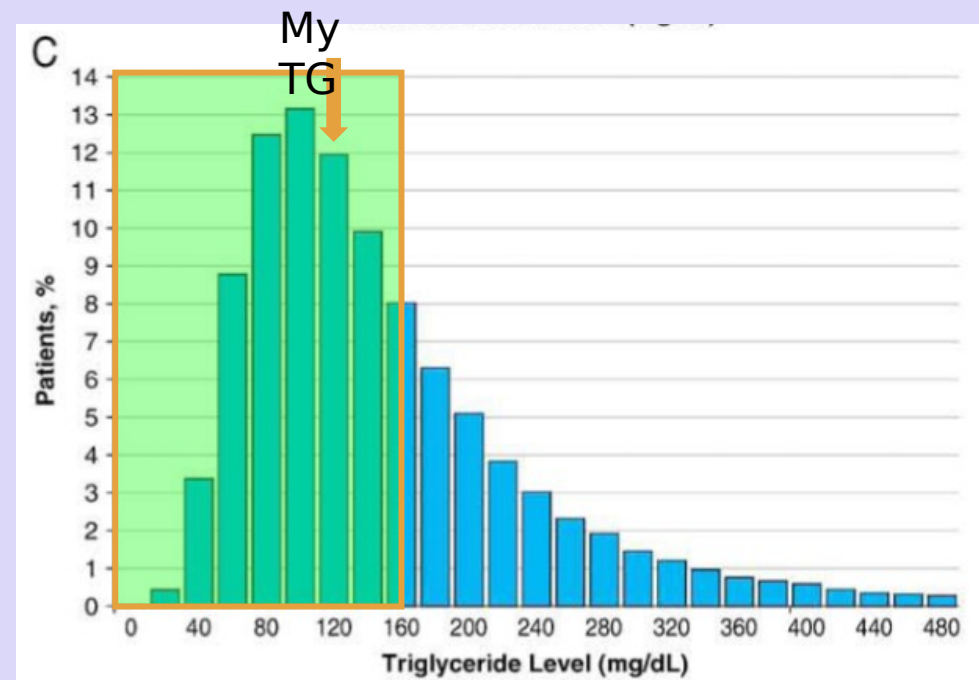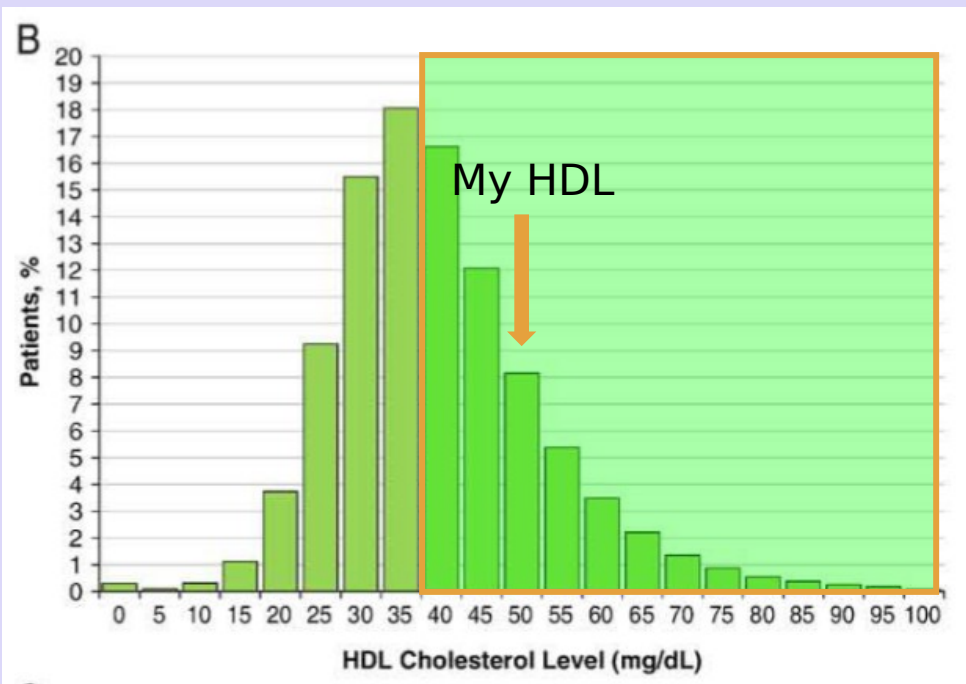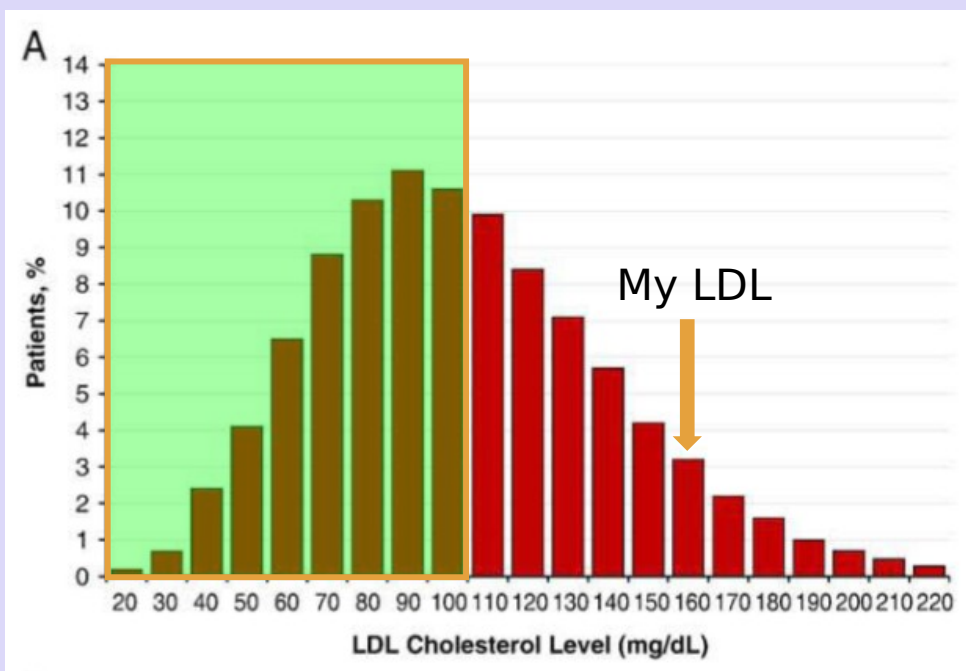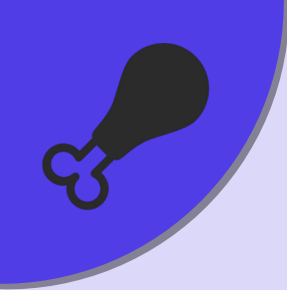
Distribution of admission LDL, HDL, and triglyceride levels. (A) Histogram of admission LDL levels in 10 mg/dL increments. (B) Histogram of admission HDL levels in 5 mg/dL increments. (C) Histogram of admission triglyceride levels in 20 mg/dL increments (truncated at 480 mg/dL).
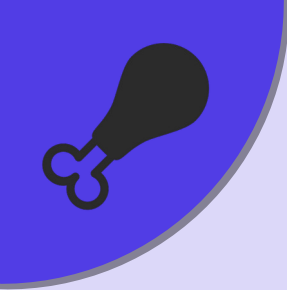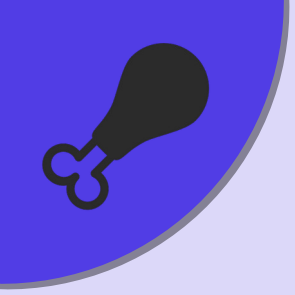
8 **Increased risk of coronary heart disease death in men with low total and low-density lipoprotein cholesterol in the Russian Lipid Research Clinics Prevalence Follow-up Study**

- **12-year** coronary heart disease mortality among 40 to 59 year-old men was analyzed [in] 6431 men [...] free of prevalent coronary heart disease.

- A **J-shaped cholesterol-coronary heart disease risk** function was present for both **total** and **LDL cholesterol**.

- Further examination showed **hypocholesterolemic men** (low cholesterol) to have **lower LDL** and **HDL** cholesterol, higher **alcohol** consumption, **leaner** body mass, and **less education** than men with normal or high cholesterol levels. (... potential confounding factors)

Figure showing RATE PER 1000 P/Y versus LDL-C QUINTILES. Data points: 4.10, 3.41, 2.98, 4.86, 6.15.
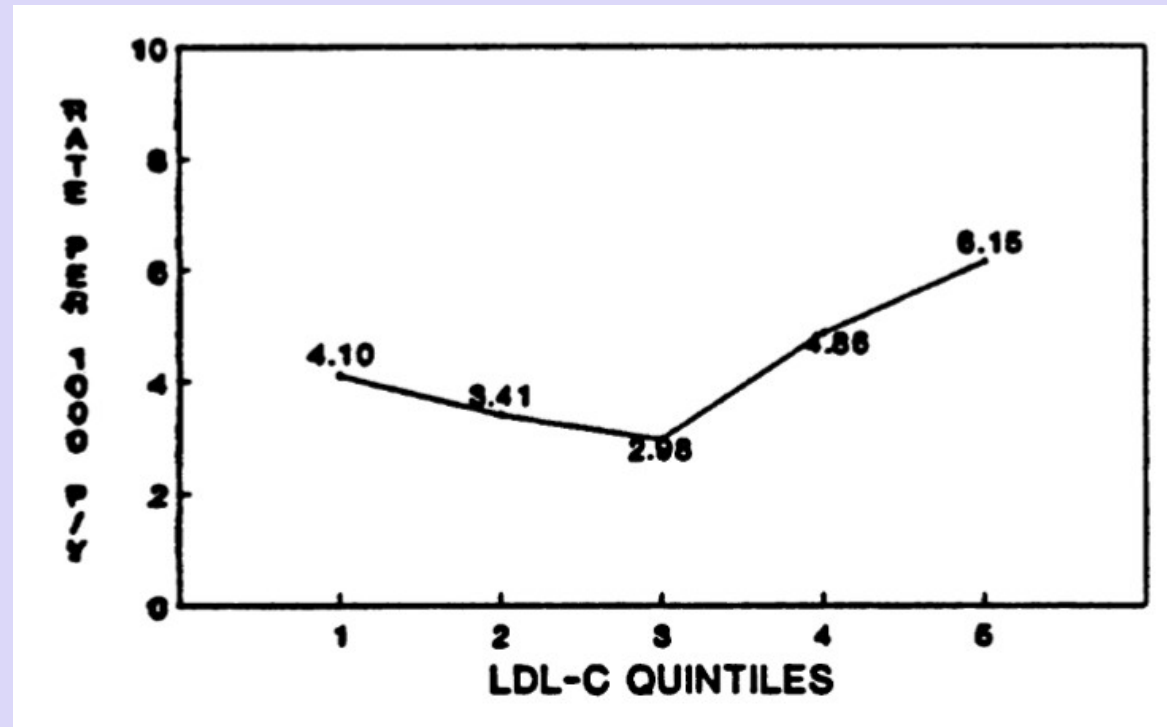
TABLE 2. Quintile Cut-Points of Selected Risk Factors

			Quintile		
	1	2	3	4	5
Cholesterol	<188	188-207	208-226	227-250	251+
LDL-C	<112	112-132	133-150	151-172	173+

Why do some populations that consume **lots of saturated fat** have relatively **little heart disease?** (French, Masai, Polynesians)

Why do people with **low LDL** still develop **heart disease?**

There are **inconsistencies** and **logical fallacies** in the traditional **Lipid Heart Hypothesis**.
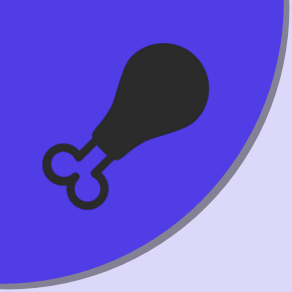
Not all LDL is the same.

"Saturated fat makes LDL high, but sugar makes LDL bad."

- Dr. Paul Mason, a low-carb / animal-based diet advocate
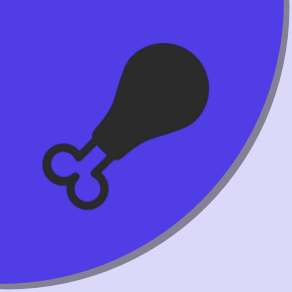
Large Buoyant LDL
Pattern A
(less atherogenic)

Small Dense LDL
Pattern B
(more atherogenic)
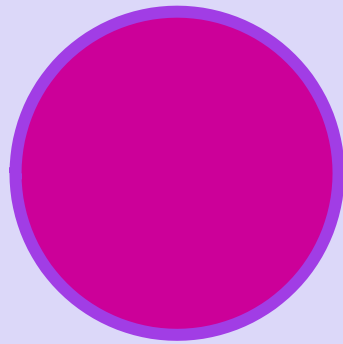
Caused by a high fat diet.
(More fat to transport)
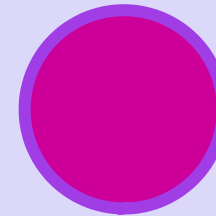
Caused by glycation or
oxidation of large, healthy
LDL.
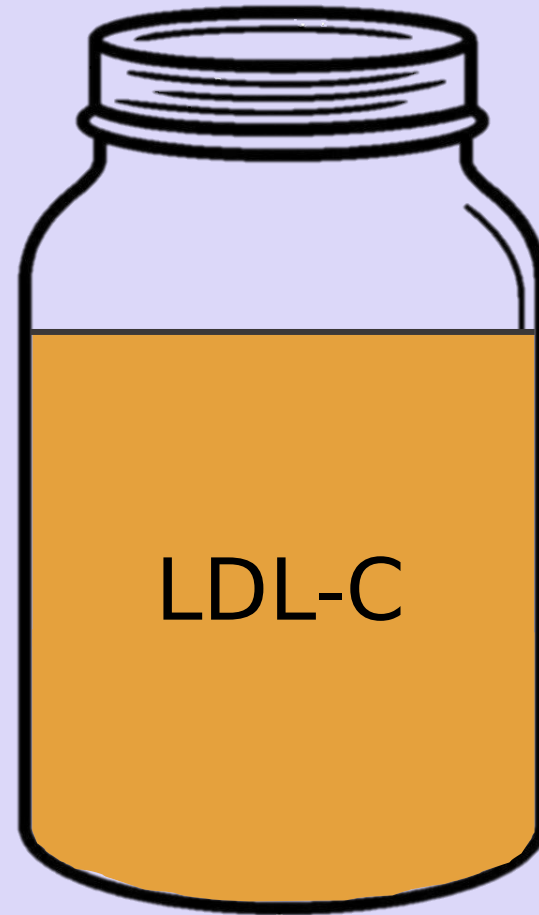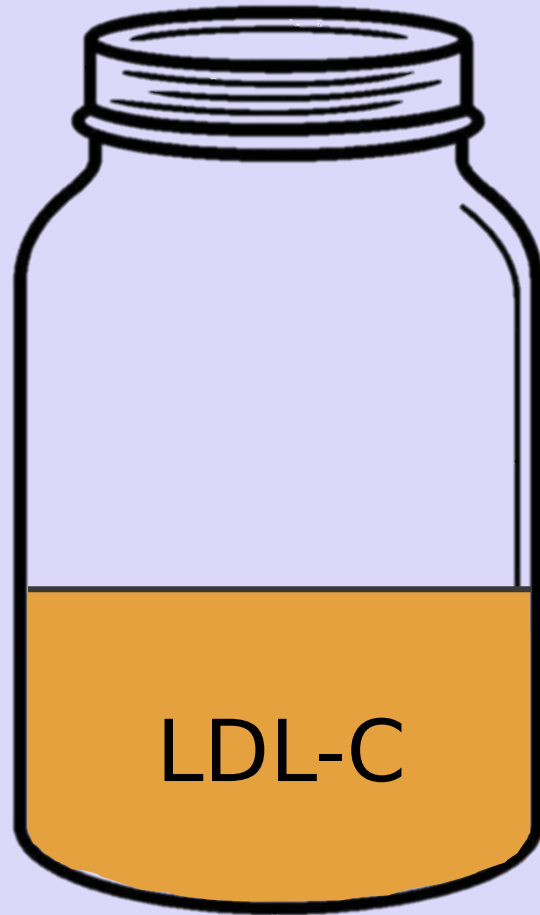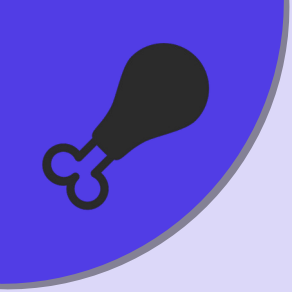
* LDL-C = Total Cholesterol - HDL – Triglycerides / 2.17 (mmol/L).
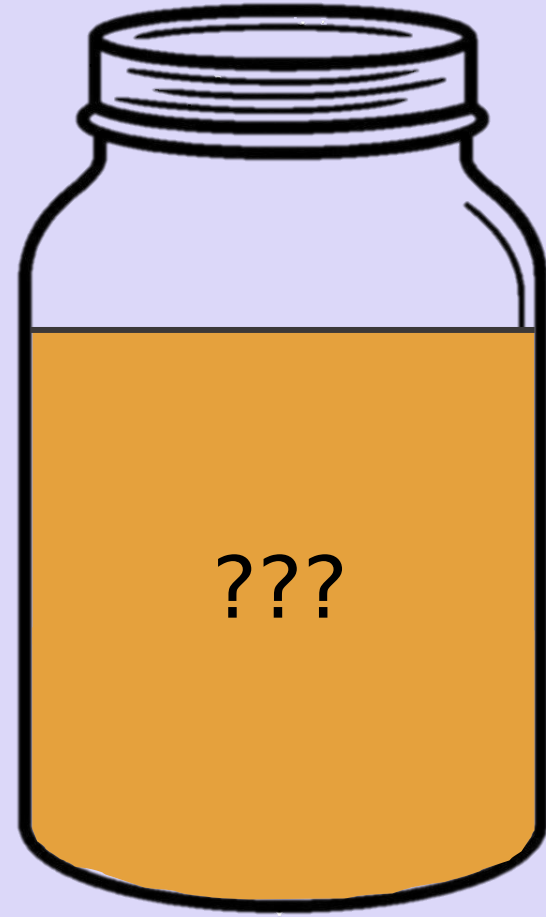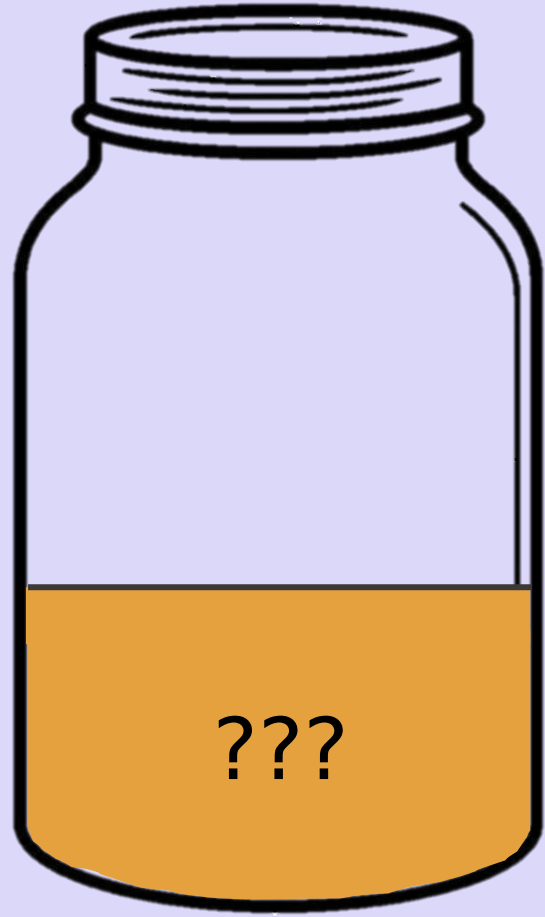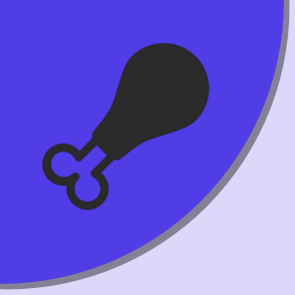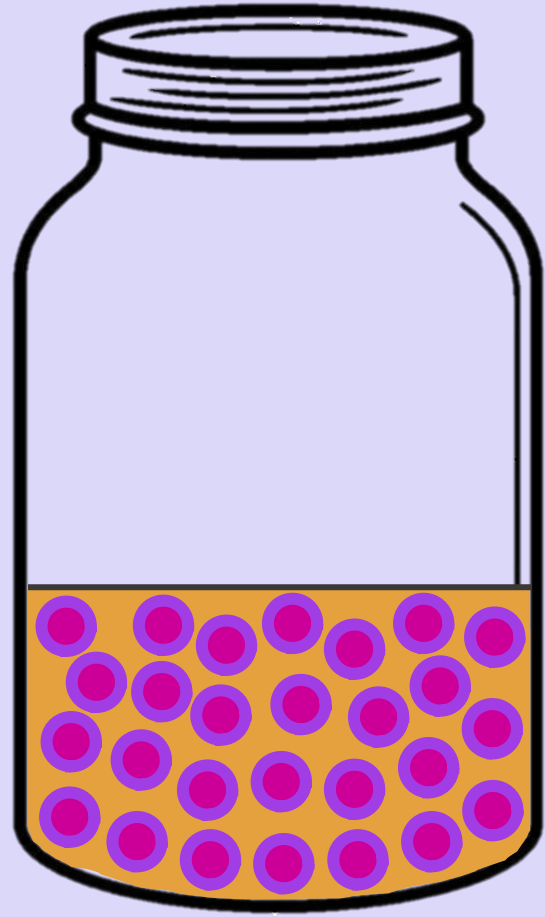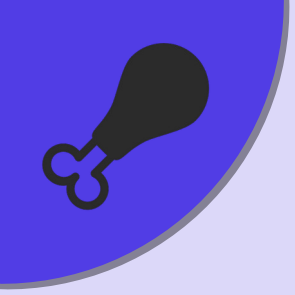
Small Dense LDL
(Pattern B)
particles
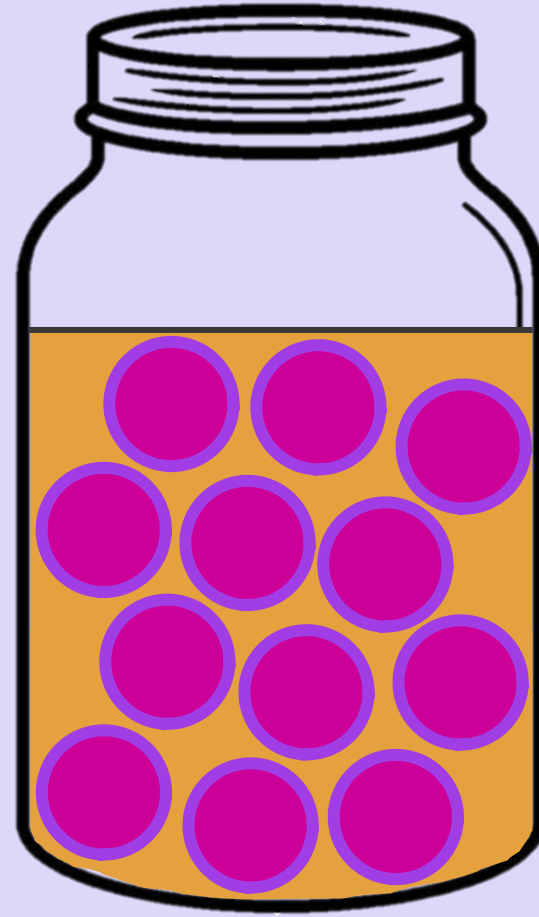
Large Buoyant
LDL
(Pattern A)
particles
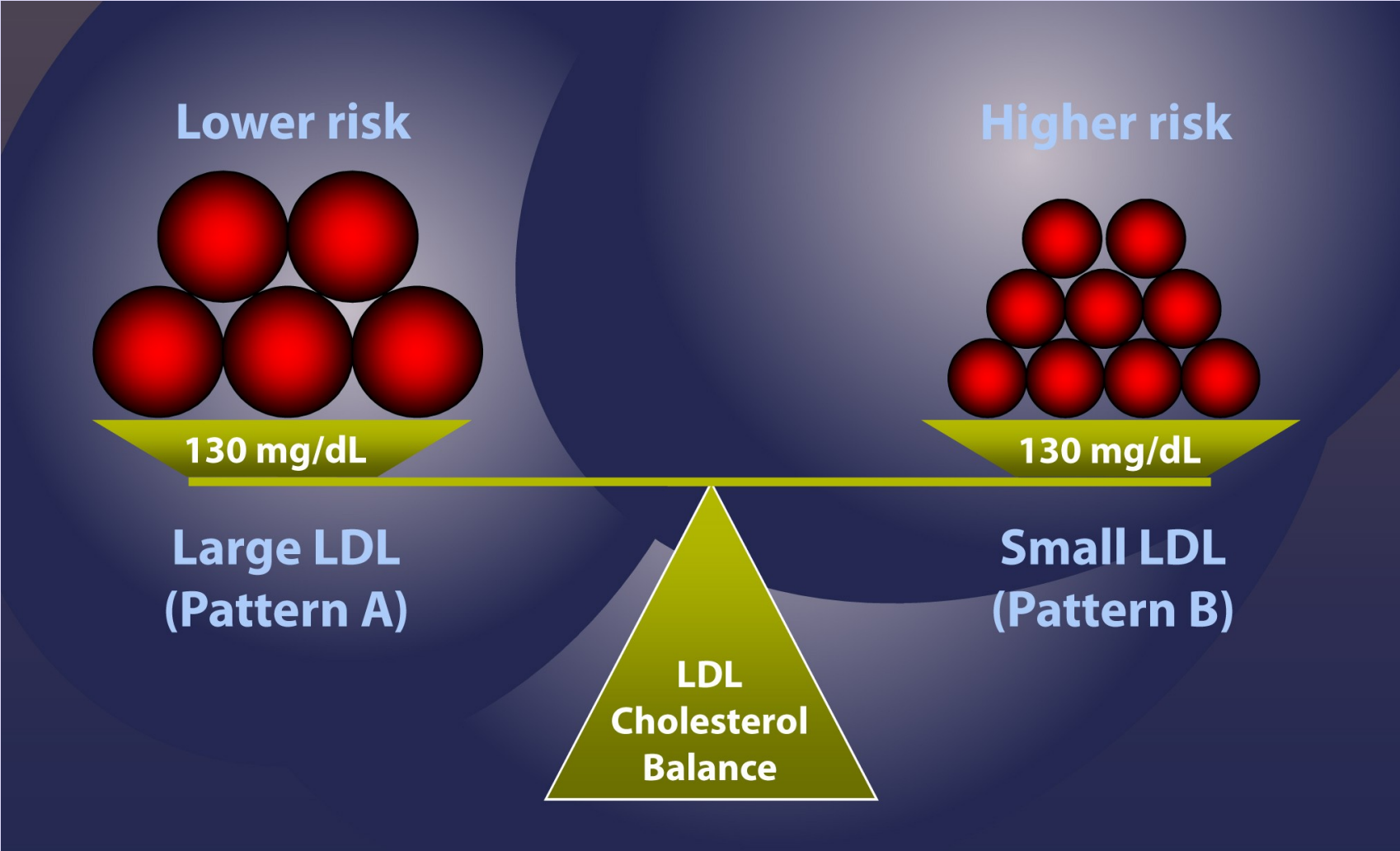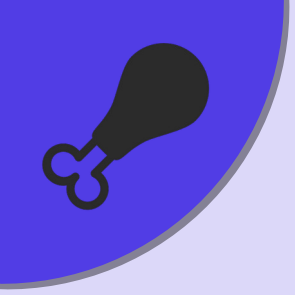
Association Between Circulating Oxidized LDL and Atherosclerotic Cardiovascular Disease: A Meta-analysis of Observational Studies

- 12 included studies consisted of 3 nested case-control studies, 1 case-cohort study, 5 hospital-based cohort studies, and 3 community-based cohort studies.

- The summary effect size of increased circulating **ox-LDL** was **1.79 [+80%] for ASCVD**.

❖ *Many factors can oxidize LDL :*
   ❖ *a high-carbohydrate diet,*
   ❖ *trans-fats,*
   ❖ *smoking,*
   ❖ *diabetes,*
   ❖ *environmental toxins, and*
   ❖ *even stress.*

Study ID	ES (95% CI)	Weight %	Events/Total
Shimada,K. (2004)	3.15 (1.47, 6.76)	3.22	76/246
Meisinger,C. (2005)	2.79 (1.21, 6.42)	2.69	88/346
Johnston,N. (2006)	1.71 (0.84, 3.46)	3.74	57/433
Wu,T.(female) (2006)	1.53 (0.65, 3.57)	2.58	235/705
Wu,T.(male) (2006)	1.64 (0.83, 3.25)	4.02	266/798
Kiechl,S. (2007)	2.40 (1.30, 4.30)	5.24	82/765
Gomez,M. (2009)	1.66 (1.07, 2.57)	9.77	270/1371
Drogan,D. (2010)	1.31 (0.56, 3.05)	2.61	116/958
Tsimikas,S. (2010)	1.67 (1.32, 2.12)	33.41	763/2160
Finckh,A. (2012)	1.90 (0.69, 5.29)	1.81	19/118
Zuliani,G. (2013)	1.17 (0.79, 1.73)	12.20	166/1025
Gomez,M. (2014)	1.70 (1.02, 2.84)	7.15	103/2793
Zhang,Y.C. (2014)	2.88 (1.93, 4.32)	11.55	124/425
Overall (I-squared = 21.2%, p = 0.230)	1.79 (1.56, 2.05)	100.00	2365/12143

Low-Density Lipoprotein Subfractions and the Long-Term Risk of Ischemic Heart Disease in Men

- 2072 men ... free of [heart disease] at the baseline examination and followed-up for a period of **13 years**.

- Our results support the notion that the **small dense LDL** phenotype confers an **increased risk of IHD**, particularly over a short period of follow-up, and that levels of **large LDL** are **not associated** with an increased risk of IHD.

- Men with **elevated** cholesterol levels within **large LDL** subfraction ... had a **50% lower IHD risk** over the first 7 years of follow-up.

- **Total LDL cholesterol** levels is only a **crude marker** of the overall atherogenicity of LDL because different LDL subclasses show very different associations with the risk of IHD.

large LDL

Survival probabilities

Tertiles of LDL-C$_{\geq 260\text{Å}}$
—— <1.03 mmol/l
······ 1.03-1.68 mmol/l
—— ≥1.68 mmol/l

Time*LDL-C$_{\geq 260\text{Å}}$
interaction, P=0.17

P=0.09

Follow-up (years)

small LDL

Survival probabilities

Tertiles of LDL-C$_{<255\text{Å}}$
—— <1.07 mmol/l
······ 1.07-1.86 mmol/l
—— ≥1.86 mmol/l

Time*LDL-C$_{<255\text{Å}}$
interaction, P=0.001

P<0.001

Follow-up (years)
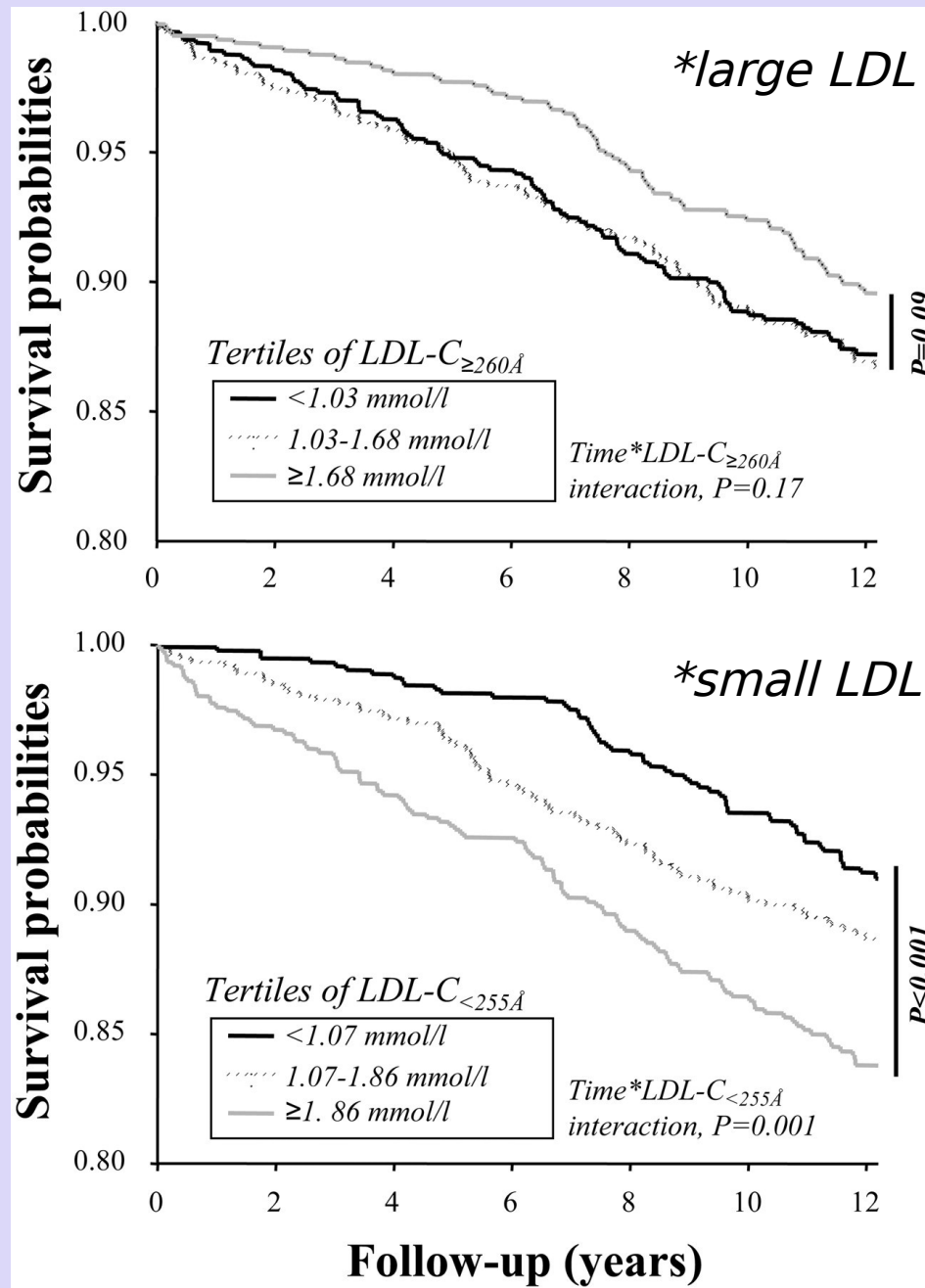
Change in dietary saturated fat intake is correlated with change in mass of large low-density-lipoprotein particles in men

- 103 men were **randomly** assigned to a **low-fat** (24% fat) and a **high-fat** (46% fat) diet for **6 weeks** each in a crossover design.

- A **high saturated fat intake** is associated with **increased** concentrations of **larger, cholesterol-enriched LDL** [and] was **inversely** correlated with concentrations of **small, dense LDL.**

❖ *This doesn't directly translate to heart disease risk…*

❖ *It could be that what damages LDL (making it a small dense particle) also damages the arterial wall. So maybe it's not the small dense LDL itself that is atherogenic, but is a marker for cardiovascular damage.*
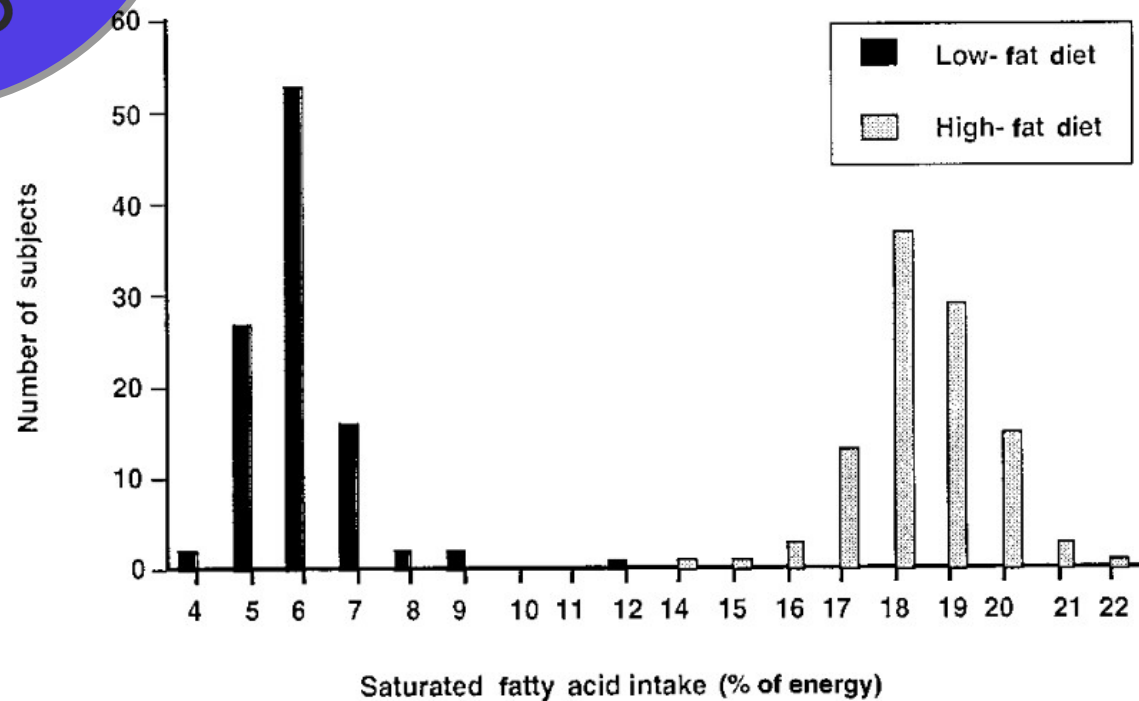
TABLE 2

Plasma lipoprotein concentrations in all subjects[1]

	Low-fat diet	High-fat diet
Triacylglycerol (mmol/L)	1.59 ± 0.09	1.12 ± 0.05^2
LDL cholesterol (mmol/L)	3.26 ± 0.08	3.70 ± 0.09^2
HDL cholesterol (mmol/L)	1.08 ± 0.02	1.27 ± 0.03^2
Apolipoprotein A-I (mmol/L)	40.87 ± 0.53	44.84 ± 0.60^2
Apolipoprotein B (mmol/L)	1.98 ± 0.04	2.00 ± 0.05
Lipoprotein mass (g/L)		
VLDL	127.30 ± 8.84	75.91 ± 6.10^2
IDL	33.49 ± 1.66	32.86 ± 1.64
LDL		
LDL-I (S_f° 7–12)	92.44 ± 3.91	131.83 ± 4.56^2
LDL-II (S_f° 5–7)	106.70 ± 3.48	122.57 ± 3.81^2
LDL-III (S_f° 3–5)	81.26 ± 3.98	59.82 ± 3.76^2
LDL-IV (S_f° 0–3)	17.99 ± 1.52	10.95 ± 1.02^2

TABLE 1

Reported (4-d food record) mean daily nutrient intake for 103 middle-aged men consuming low-fat and high-fat diets[1]

Nutrient	Low-fat diet	High-fat diet
Protein (% of energy)	16.6 ± 1.9	16.3 ± 0.9
Carbohydrate (% of energy)	59.0 ± 2.9	38.8 ± 2.3
Fat (% of energy)	24.2 ± 3.0	45.5 ± 2.3
Polyunsaturated fat (% of energy)	4.2 ± 0.9	11.8 ± 1.6

Atherogenic Lipoprotein Phenotype : A Proposed Genetic Marker for Coronary Heart Disease Risk

❖ *Measuring LDL particle size isn't a widely conducted test. However, other lipid markers can give you a good idea of your LDL pattern.*

- Two distinct phenotypes (denoted A and B) were identified of **LDL subclasses** [in] 301 subjects.

- **Phenotype B** was associated with :
  - **increases** in plasma levels of **triglyceride** and with
  - **decreases** in **HDL**.

C Cumulative Distribution of Adjusted Triglyceride Levels by ALP Phenotype
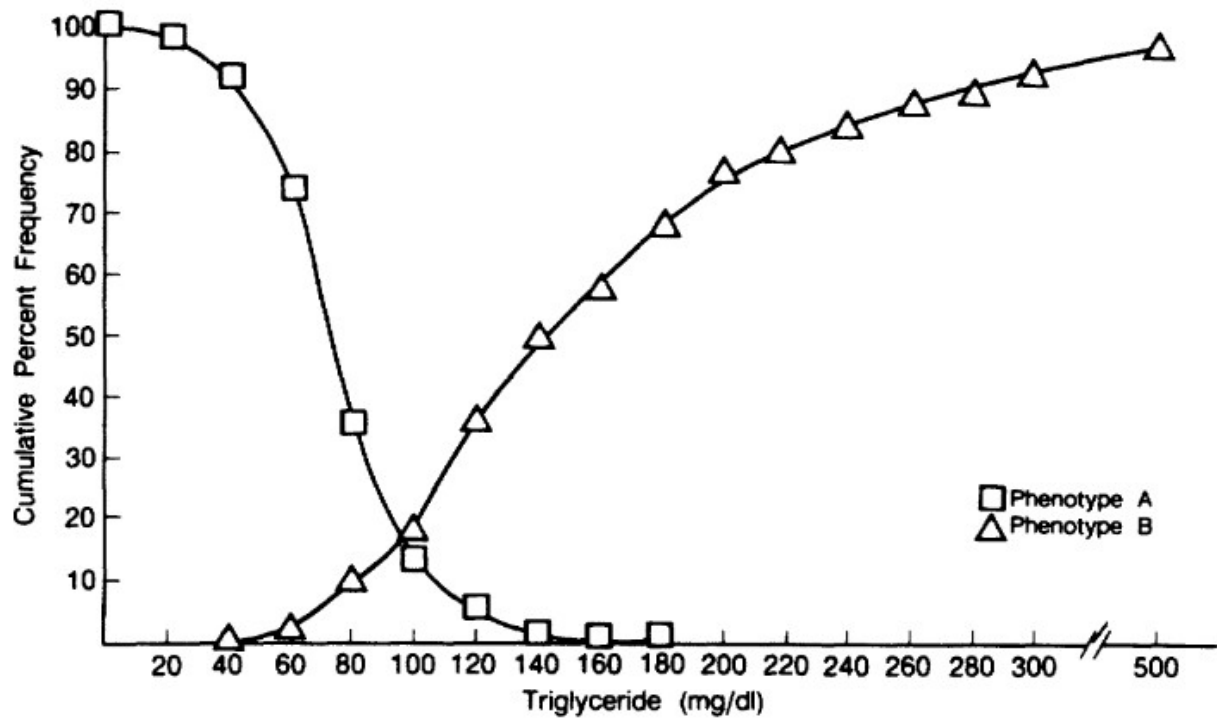
□ Phenotype A
△ Phenotype B

Cumulative Percent Frequency

Triglyceride (mg/dl)

C Cumulative Distribution of Adjusted HDL Cholesterol Levels by ALP Phenotype

□ Phenotype A
△ Phenotype B

Percent Cumulative Frequency

HDL Cholesterol

C Cumulative Distribution of Adjusted Triglyceride Levels by ALP Phenotype

□ Phenotype A
△ Phenotype B

Cumulative Percent Frequency

Triglyceride (mg/dl)

C Cumulative Distribution of Adjusted HDL Cholesterol Levels by ALP Phenotype

□ Phenotype A
△ Phenotype B

Percent Cumulative Frequency
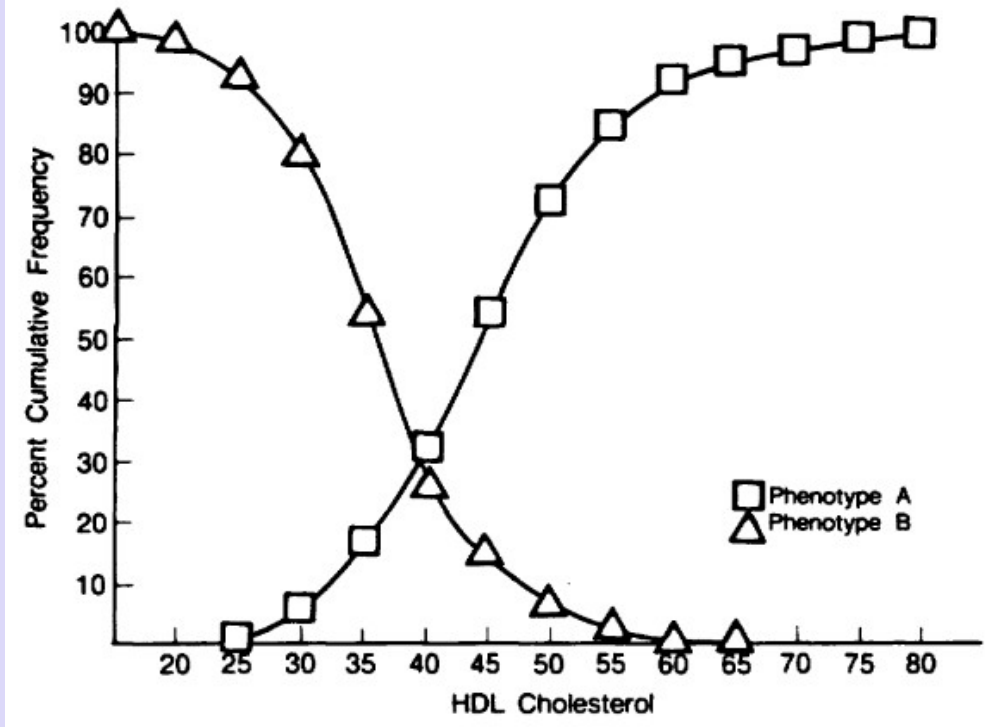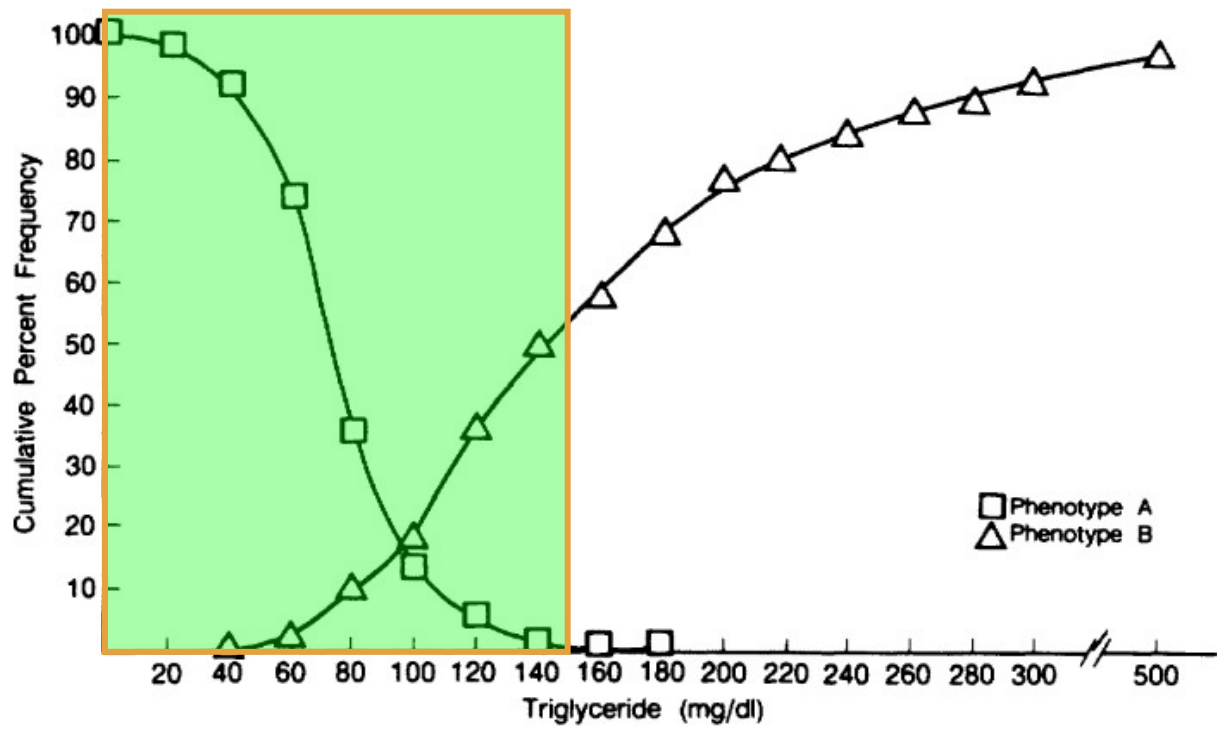
HDL Cholesterol
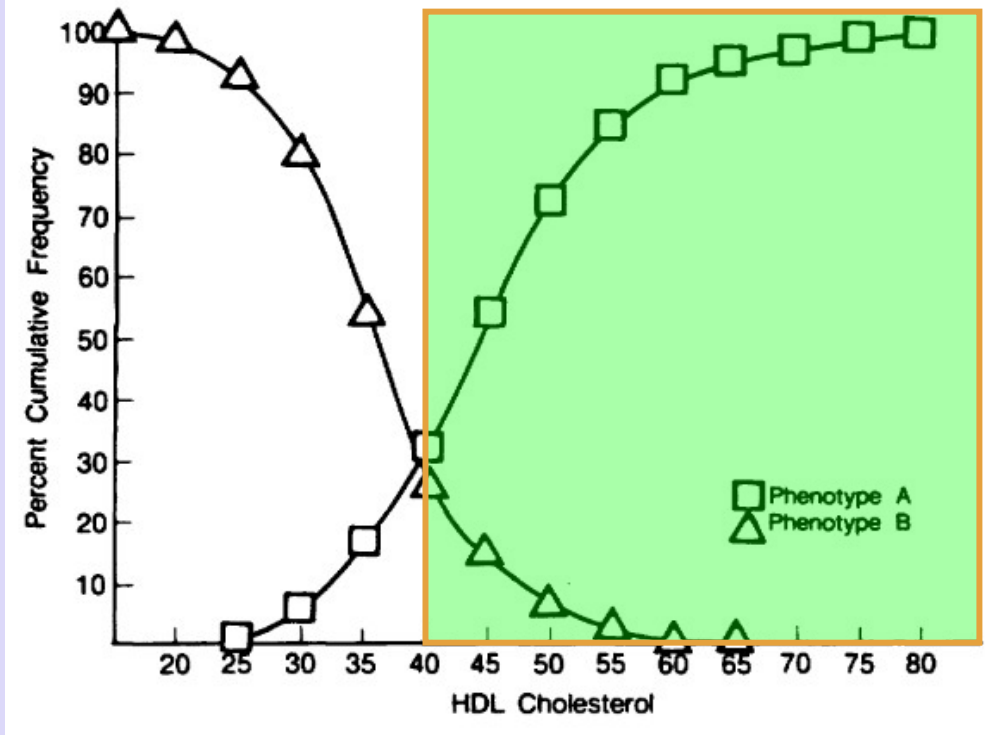
13 Fasting triglycerides, high-density lipoprotein, and risk of myocardial infarction

- 340 cases [of] men or women of <76 years of age with no prior history of coronary disease.

- Significant association of **elevated fasting triglycerides** with risk of **myocardial infarction** (RR Q1 vs. Q4 = **6.8**).

- The **ratio** of **triglycerides to HDL** was a **strong predictor** of **myocardial infarction** (RR Q1 vs. Q4 = **16.0!!!**)

- ❖ *Those with the **Highest Triglycerides** & **Lowest HDL** had **16x the risk of heart attacks** compare to those with the **Lowest Triglycerides** & **Highest HDL** .*

Kelly Hogan
Carnivore for 11 years

Dr. Paul Saladino
Carnivore for 2 years

A **perfect** CAC score = **0**
(one of the best indicators of
atherosclerosis)

A **perfect** CAC score = **0**
(one of the best indicators of
atherosclerosis)

To Conclude

❖ **Fat** and **Saturated Fat** intake **does not** appear to have a significant impact on **heart disease**.

❖ Patients with **low LDL** still develop **heart disease**.

❖ **Not all LDL is the same. Pattern B** (small dense) **LDL** – caused by glycated or oxidized LDL – seems to be **more atherogenic** than Pattern A (large buoyant) LDL.

❖ **Saturated Fat** seems to raise **Pattern A LDL** more than **Pattern B LDL**.

❖ The **ratio** of **triglycerides to HDL** seems to be a **strong predictor** of **heart attacks** (much more than simply LDL-C).

To Conclude

ii

❖ I think there is **some truth** that LDL has an effect on heart disease ... but it **doesn't** explain the **whole truth**.

❖ You **cannot generalize** that anything that **raises LDL** therefore **increase** your risk of **heart disease** if not measured directly.

❖ Many **non-LDL factors** play a role in **heart disease**, which **can be difficultly explained** with the current Lipid Heart Hypothesis.

❖ **Lowering LDL** for those following an unhealthy lifestyle full of refined carbs and processed food **may be beneficial for heart disease prevention**.

❖ However, I **don't** think this can be **generalized** to those following a **low-carb diet** (and hasn't specifically been studied to my knowledge).

❖ I think that you are very well intentioned and I respect what you do. But your belief that **fat causes heart disease** has many logical fallacies and doesn't explain the *whole* truth.

Anthony's Studies
High-fat / Animal-Based

Matthew's Studies
Low-fat / Plant-Based

Reprint of: Impact of Lipids on Cardiovascular Health: JACC Health Promotion Series

- A diet that is **low** in **saturated fats**, **low** in **refined carbohydrates** … can potentially **reduce** plasma **LDL** levels by up to 30 to 40 mg/d.

❖ But *how* does this directly **translate** to **heart disease**?

- The American Heart Association recently introduced the concept of ideal cardiovascular health [defined by 7 behavior / factors].
  - **not smoking**,
  - eating a diet low in saturated fats and refined carbohydrates,
  - **engaging in regular physical exercise,**
  - total cholesterol level <200 mg/dl
  - **blood pressure <120/80 mm Hg**,
  - **serum glucose concentration <100 mg/dl, and**
  - **a body mass index <25 kg/m2**

❖ *Of which 5 have* **little** *to* **no relationship** *to* **LDL cholesterol**.

Reprint of: Impact of Lipids on Cardiovascular Health: JACC Health Promotion Series (cont.)

- LDL particles … are **not measured directly**. Instead, plasma LDL cholesterol (LDL-C) concentration, an **estimate** of the total cholesterol **mass** carried by LDL particles.

- ❖ *LDL-C does not measure LDL particles themselves.*

- Circulating LDL … **freely flux** across the endothelial barrier, where they can … become retained in the [cell wall].

- ❖ ***What is it*** *specifically about* **LDL** *(and* **not HDL** *– a smaller particle) that makes it* **atherogenic***?*

Low LDL Cholesterol by PCSK9 Variation Reduces Cardiovascular Mortality

- PCSK9 alleles were associated with stepwise **lower LDL cholesterol** of up to 0.61 mmol/l and with **lower cardiovascular mortality** (**0.79**) [about 20%],

- **... but not with lower all-cause mortality**.

❖ *Drugs =/= Diet*

❖ *Good news : you won't die from heart disease. Bad News : you're not going to live any longer.*

3 **Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies**

- Any mechanism of **lowering** plasma **LDL** particle concentration should **reduce** the risk of **ASCVD** events proportional to the absolute reduction in LDL-C.

- ❖ *In the context of an **unhealthy**, **refined carb**, **processed food diet** – yes, possibly. But this can't be generalized to those following a **whole food low-carb / high-fat diet.***

- ❖ *To my knowledge, there are **no quality studies** specifically looking at **LDL** levels and **heart disease** risk in the context of a **low-carb diet**.*

- ❖ *Many of the authors of this study have received **funding** from the **pharmaceutical industry**.*

Normal LDL-Cholesterol Levels Are Associated With Subclinical Atherosclerosis in the Absence of Risk Factors

- Subclinical atherosclerosis (plaque or coronary artery calcification) was present in 49.7% of cardiovascular risk factors-free participants.

❖ *Why did **half** of people with **low cardiovascular risk factors** still have atherosclerosis?*

- **LDL-C** was **independently** associated with atherosclerosis (odds ratio 1.14 to 1.18).

❖ *What about atherosclerosis relative to **blood sugar**? Or t**riglycerides**? I think the same sort of trends would appear.*

5   A systematic review of LDL apheresis in the treatment of cardiovascular disease

- We conclude that **LDL apheresis** (removing LDL from the blood) reduces cardiovascular events in **hypercholesterolemic** patients.

❖ *High LDL from Familial Hypercholesterolemia (a **genetic condition**) =/= high LDL from **diet** or lifestyle factors. (Fewer Liver Receptors vs. More Fat Cargo)*

❖ *How did this intervention affect cardiovascular mortality?*

The role of lipoprotein subfractions in coronary artery disease: A Mendelian randomization study

- The concentration of **medium HDL particles** may have a protective effect on coronary artery disease.

- ❖ *How does diet affect medium HDL particles?*

- Our study **did not adjust** for other important risk factors such as **body mass index**, **blood pressure**, and **smoking**.

Dietary lipids and blood cholesterol: quantitative meta-analysis of metabolic ward studies

- Replacing 60% of saturated fats by other fats and avoiding 60% of dietary cholesterol would **reduce blood total cholesterol** by about 0.8 mmol/l (that is, by 10-15%), with four fifths of this reduction being in LDL cholesterol.

❖ *Again, **how** does this directly **translate** to **heart disease**?*

Effects of saturated fatty acids on serum lipids and lipoproteins: a systematic review and regression analysis

- Modifiable risk factors such as **poor diet**, **physical inactivity**, **tobacco** use and harmful use of **alcohol** are major **causes of CVD**.

❖ *Again, there are **more factors** that **play a role in CVD** than just LDL.*

- Replacing saturated fatty acids with other macronutrients, particularly polyunsaturated fatty acids, has a **favourable effect** on the blood lipid profile, including **lowering of LDL** cholesterol levels.

❖ *Again, **how** does this directly **translate** to **heart disease**?*

9 **Reduction in saturated fat intake for cardiovascular disease**

- Systematic review funded by the WHO.

- **Reducing** dietary **saturated fat** reduced the risk of combined **cardiovascular events by 21%** (risk ratio (RR) 0.79.

❖ *In the context of an* ***unhealthy, refined carb, processed food diet*** *– yes, possibly. But this can't be generalized to those following a* ***whole food low-carb / high-fat diet.***

- We found **little or no effect** of reducing saturated fat on :
  - **all-cause mortality** (RR 0.96),
  - **cardiovascular mortality** (RR 0.95),
  - **non-fatal myocardial infarction** (RR 0.97) or
  - **CHD mortality** (RR 0.97).

❖ ***Good news*** *: you won't have as many heart attacks.* ***Bad News*** *: you're still going to die from heart disease.*

Saturated fats and health: SACN report

- There were significant relationships between intake of **saturated fats** and **CVD and CHD events**, but **not CVD and CHD mortality**.

❖ ***Good news*** *: you won't have as many heart attacks.* ***Bad News*** *: you're still going to die from heart disease.*

11 **Association of types of dietary fats and all-cause and cause-specific mortality: A prospective cohort study and meta-analysis of prospective studies with 1,164,029 participants**

- We found a significant **inverse association** between **total fat** (0.89) [-11%] consumption and **all-cause mortality**.

- ❖ *So fat isn't the enemy?*

- A significant association between **saturated fat** intake and **CHD mortality** (1.10) [+10%] was observed.

- ❖ *In the context of an **unhealthy, refined carb, processed food diet** – yes, possibly. But this can't be generalized to those following a **whole food low-carb / high-fat diet.***

Effects on coronary heart disease of increasing polyunsaturated fat in place of saturated fat: a systematic review and meta-analysis of randomized controlled trials

- Average weighted **PUFA consumption** was **14.9%** energy in intervention groups versus **5.0%** energy in controls.

- The overall pooled **risk reduction was 19%** (RR = 0.81).

❖ *In the context of an **unhealthy, refined carb, processed food diet** – yes, possibly. But this can't be generalized to those following a **whole food low-carb / high-fat diet.***

❖ *Unless you are **fat adapted** and are following a **low-carb / high-fat diet**, I think that it **may be beneficial** to keep LDL lower.*