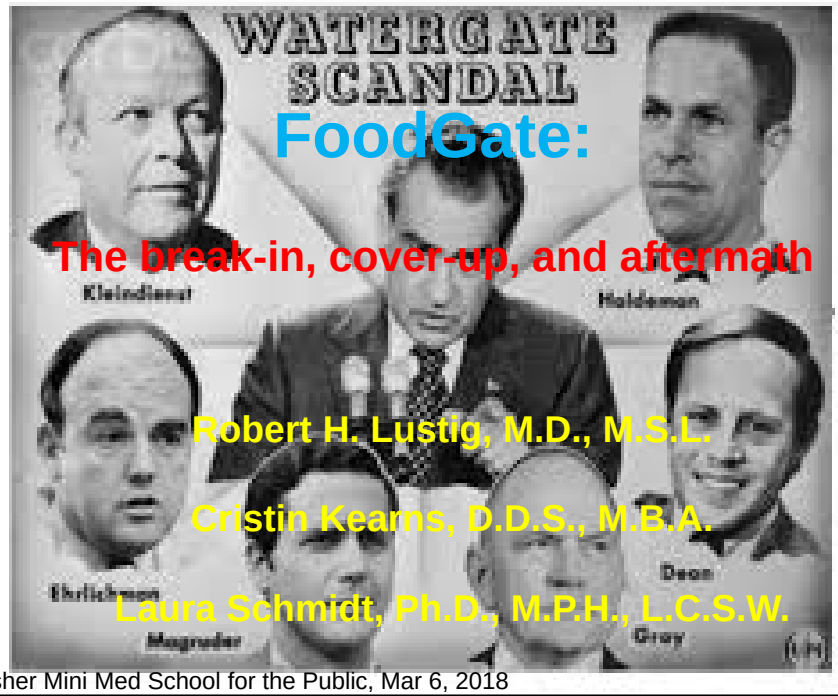


FoodGate:

The break-in, cover-up, and aftermath

Robert H. Lustig, M.D., M.S.L.

Cristin Kearns, D.D.S., M.B.A.

Laura Schmidt, Ph.D., M.P.H., L.C.S.W.

Osher Mini Med School for the Public, Mar 6, 2018

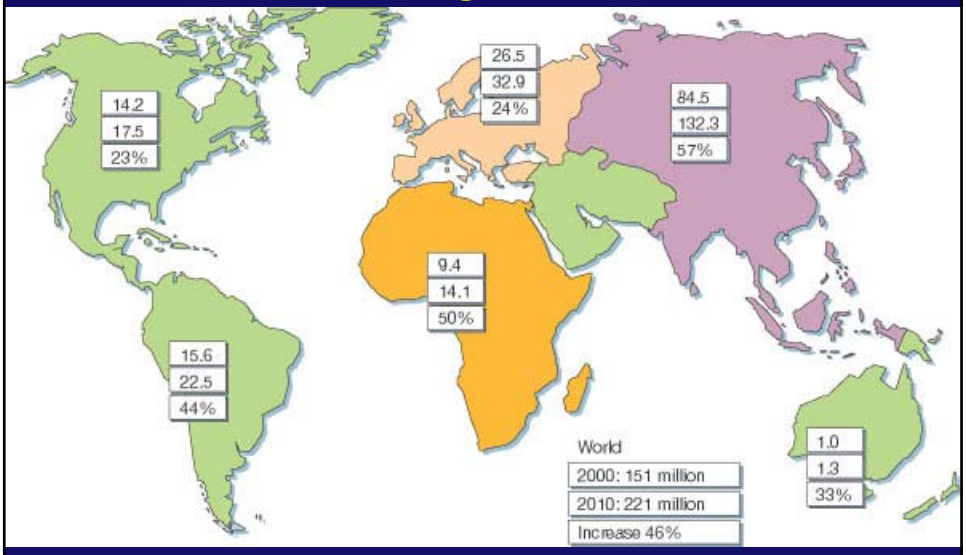
Decrease in U.S. Deaths from Heart Disease 1980–2000 offset by Type 2 Diabetes — and they're not dying!

Ford et al, NEJM 356:2388, 2007

Table 2. Deaths from Coronary Heart Disease That Were Prevented or Postponed as a Result of Changes in Population Risk Factors in the United States, 1980 to 2000.*

Risk Factor†	Absolute Level of Risk Factor‡		Change in Risk Factor		Beta Regression Coefficient for Change in Mortality Rate§	Relative Risk	Deaths Prevented or Postponed					
	1980	2000	Absolute Change	Relative Change (%)			Best Estimate	Minimum Estimate	Maximum Estimate	Best Estimate	Minimum Estimate	Maximum Estimate
							no. of deaths			*percent of total reduction*		
Smoking prevalence (%)	36.3	24.6	−11.7	−32.2			39,925	34,955	52,435	11.7	10.2	15.3
Men						2.52						
Women						2.14						
Systolic blood pressure (mm Hg)	129.0	123.9	−5.1	−4.0			68,800	53,730	105,060	20.1	15.7	30.7
Men					−0.0334							
Women					−0.0413							
Total cholesterol (mmol/liter)	5.67	5.33	−0.34	−6.1			82,830	58,455	95,570	24.2	17.1	28.0
Men					−0.9458							
Women					−0.9121							
Physical inactivity (%)	29.6	27.3	−2.3	−7.8	—		17,445	8,340	29,035	5.1	2.4	8.5
Men						1.27						
Women						1.33						
BMI	25.6	28.2	+2.6	10.1			−25,905	−14,430	−40,405	−7.6	−4.2	−11.8
Men					0.0297							
Women					0.0297							
Diabetes prevalence (%)	6.5	9.4	+2.9	44.2	—		−33,465	−23,885	−43,330	−9.8	−7.0	−12.7
Men						1.93						
Women						2.59						
Total risk factors							149,635	117,165	198,360	43.8	34.3	58.0

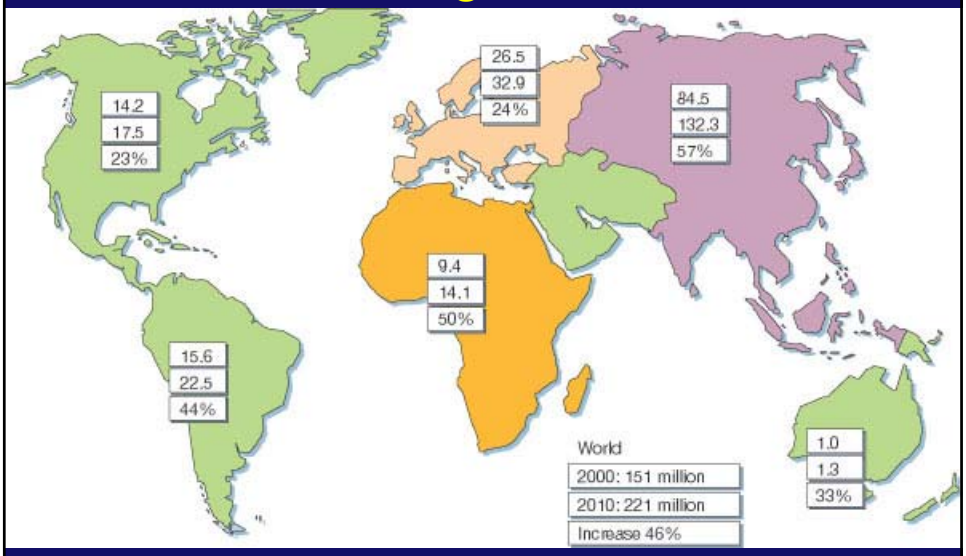
T2DM increasing around the world



People with DM (in millions) for 2000, projection for 2010, and % increase

Zimmet et al. Nature 414: 782, 2001

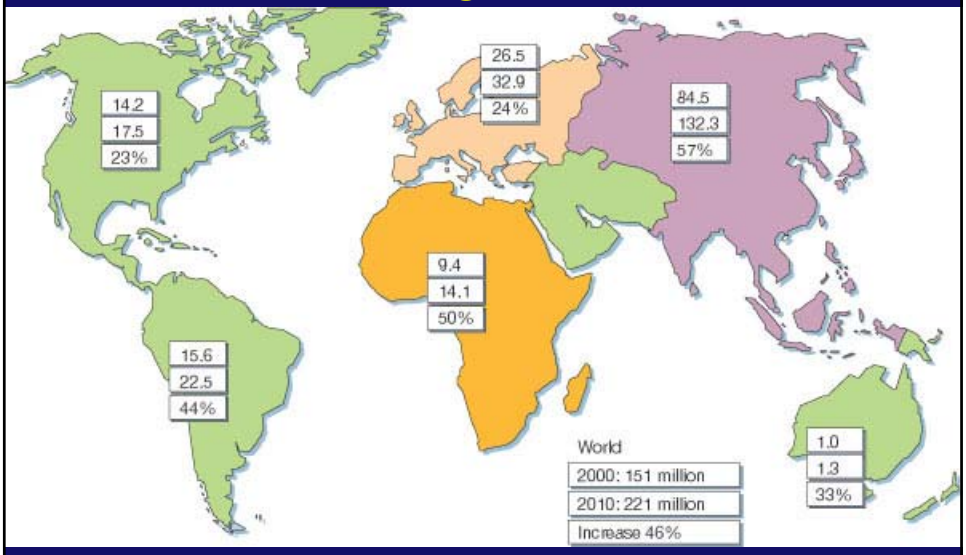
T2DM increasing around the world



People with DM (in millions) for 2000, projection for 2010, and % increase

Zimmet et al. Nature 414: 782, 2001 **285 MILLION IN 2010, up 8.9% per yr**

T2DM increasing around the world

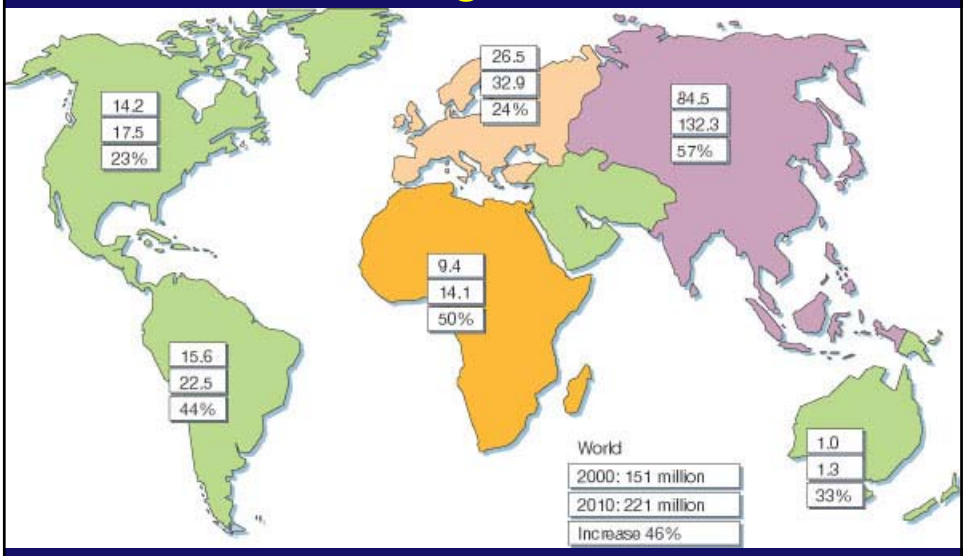


People with DM (in millions) for 2000, projection for 2010, and % increase

Zimmet et al. Nature 414: 782, 2001

412 MILLION IN 2014, up 11.7% per yr

T2DM increasing around the world

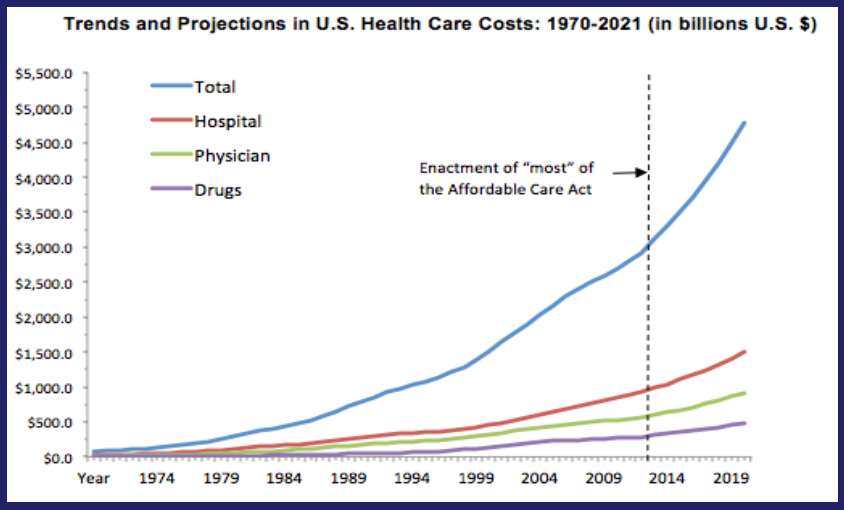


People with DM (in millions) for 2000, projection for 2010, and % increase

Zimmet et al. Nature 414: 782, 2001

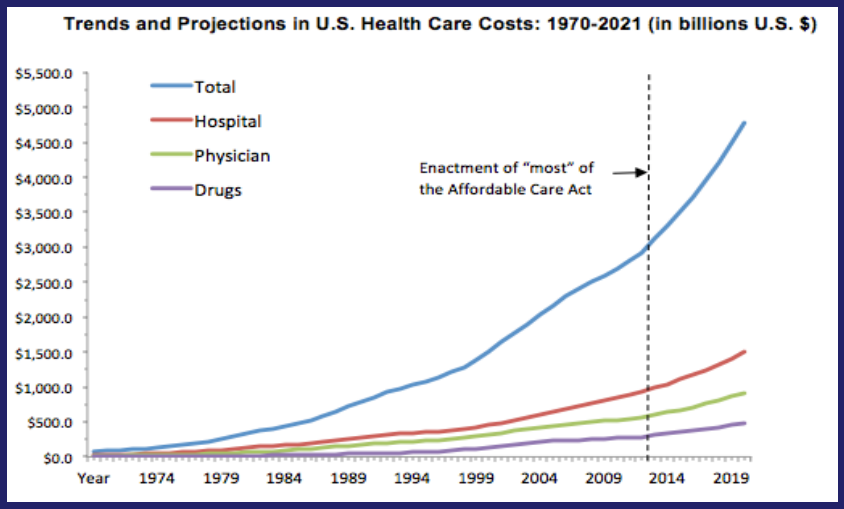
WTF??

The money is not going to hospitals, physicians, or Big Pharma



The money is not going to hospitals, physicians, or Big Pharma

It's going to chronic metabolic disease



Two inconvenient truths

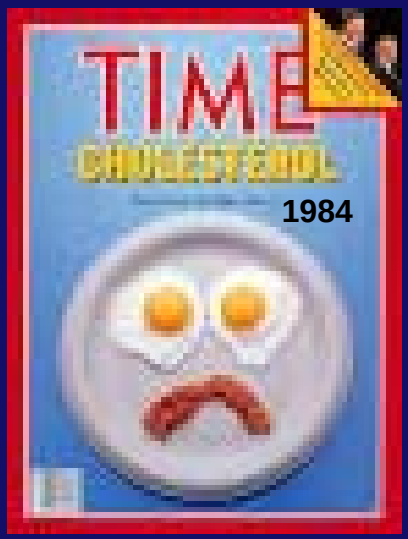
Two inconvenient truths

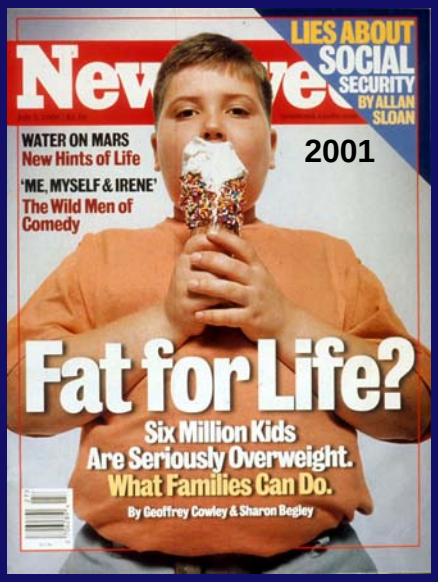
- There is no medicalized prevention for chronic metabolic disease
- There's just long-term treatment

Two inconvenient truths

- There is no medicalized prevention for chronic metabolic disease
- There's just long-term treatment

- You can't fix healthcare until you fix health
- You can't fix health until you fix the diet
- And you can't fix the diet until you know what is wrong





2001

Epidemiology

12

U.S. DIETARY GOALS 1977

1. Increase carbohydrate consumption to account for 55 to 60 percent of the energy (caloric) intake.
2. Reduce overall fat consumption from approximately 40 to 30 percent energy intake.
3. Reduce saturated fat consumption to account for about 10 percent of total energy intake; and balance that with poly-unsaturated and mono-unsaturated fats, which should account for about 10 percent of energy intake each.
4. Reduce cholesterol consumption to about 300 mg. a day.
5. Reduce sugar consumption by about 40 percent to account for about 15 percent of total energy intake.
6. Reduce salt consumption by about 50 to 85 percent to approximately 3 grams a day.

12

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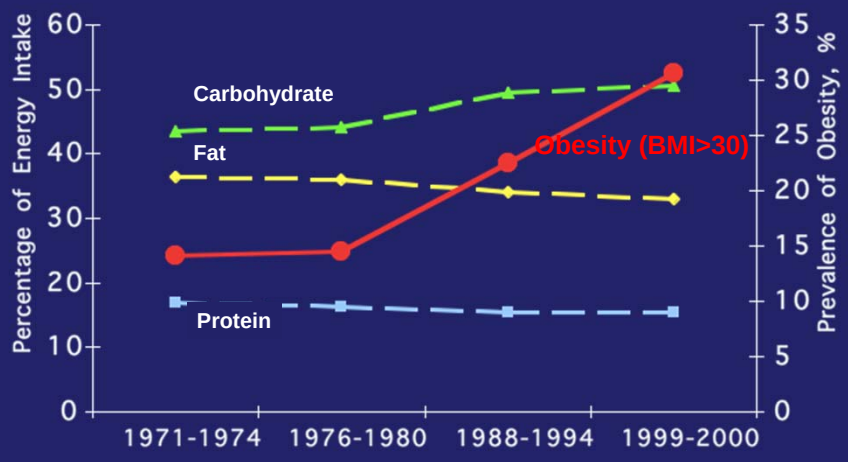
5. Reduce sugar consumption by about 40 percent to account for about 15 percent of total energy intake.
6. Reduce salt consumption by about 50 to 85 percent to approximately 3 grams a day.

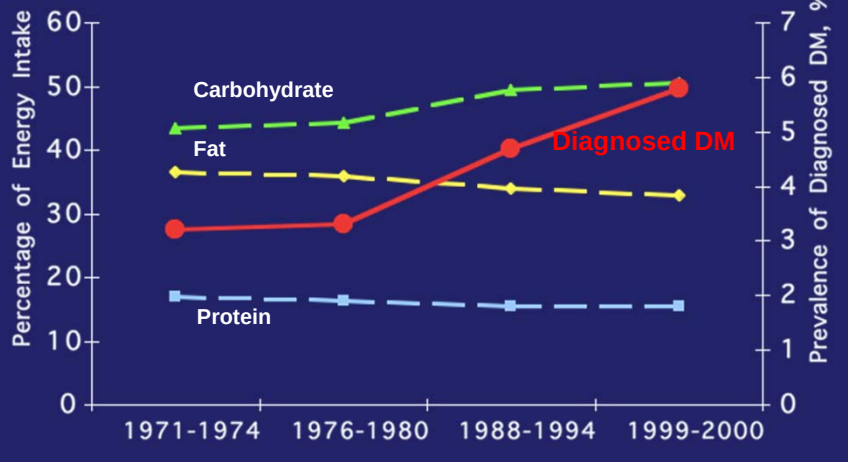
Nothing about fruit, vegetable, or fiber consumption

Trends in macronutrient intake and obesity



Based on NHANES data. Int J Obes 1998;22:39-47. JAMA 2002;288:1723. MMWR 2004;53:80-82.

Trends in macronutrient intake and diabetes



Based on NHANES data. MMWR 2004;53:80-82. Diabetes Care 2004;27:2806.

Prospective Urban and Rural Epidemiology (PURE)

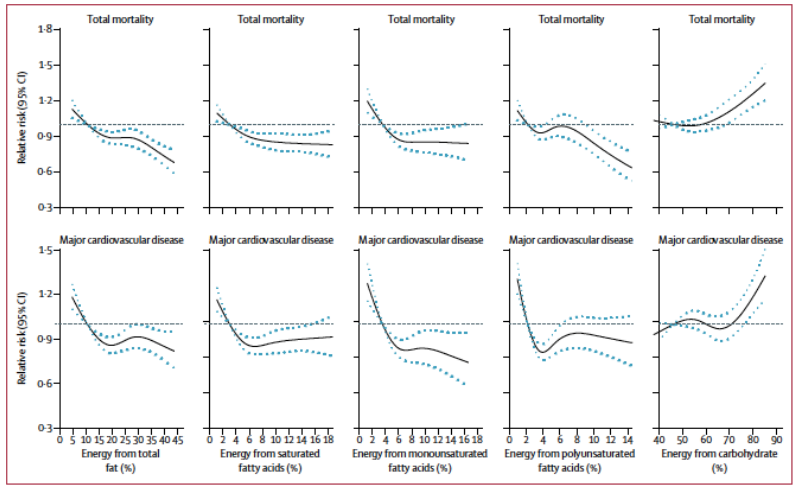


Figure 1: **Association between estimated percentage energy from nutrients and total mortality and major cardiovascular disease (n=135 335)**
Adjusted for age, sex, education, waist-to-hip ratio, smoking, physical activity, diabetes, urban or rural location, centre, geographical regions, and energy intake.
Major cardiovascular disease=fatal cardiovascular disease+myocardial infarction+stroke+heart failure.

Dehghan et al. Lancet epub Aug 29, 2017

The animal-based food effect on T2DM goes away after you control for iron/heme intake

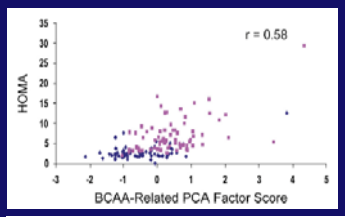
Table 2. Hazard Ratios for Incident Type 2 Diabetes According to Intakes of Different Meat Types, the Singapore Chinese Health Study, 1993–2010

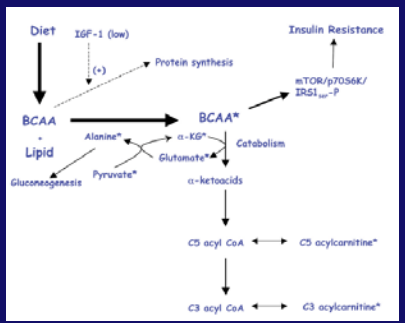
Meat Type and Model	Quartile of Meat Intake									
	1					4				
	No. of Cases	No. of Person Years	Median	HR	95% CI	No. of Cases	No. of Person Years	Median	HR	95% CI	*P* for Trend[a]
Red meat	1,240	127,885	12.3			1,462	121,692	48.8			
Model 1[b]				1.00	Referent				1.24	1.15, 1.34	<0.001
Model 2[c]				1.00	Referent				1.23	1.14, 1.33	<0.001
Model 3[d]				1.00	Referent				1.13	1.01, 1.25	0.017
Poultry	1,224	123,045	5.8			1,408	127,377	35.9			
Model 1[b]				1.00	Referent				1.14	1.06, 1.23	0.001
Model 2[c]				1.00	Referent				1.15	1.06, 1.24	0.001
Model 3[d]				1.00	Referent				1.01	0.91, 1.12	0.973
Fish/shellfish	1,239	122,515	27.9			1,417	124,823	82.7			
Model 1[b]				1.00	Referent				1.12	1.04, 1.21	0.003
Model 2[c]				1.00	Referent				1.07	0.99, 1.16	0.116
Model 3[d]				1.00	Referent				1.00	0.92, 1.09	0.983

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a] Linear trend was tested by treating the median intake values of quartiles as continuous variables using Cox proportional hazards models.
[b] Adjusted for age, sex, dialect, year of interview, and educational level.
[c] Adjusted for the variables in model 1 and body mass index, physical activity level, smoking status, alcohol use, baseline history of self-reported hypertension, adherence to the vegetable-, fruit-, and soy-rich dietary pattern, and total energy intake.
[d] Adjusted for the variables in model 2 and heme iron intake.

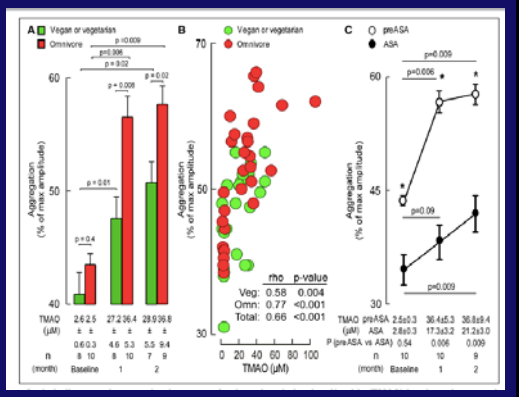
Talaei et al. Am J Epidemiol DOI: 10.1093/aje/kwx156, 2017

Branched chain amino-acids or choline in red meat may contribute to insulin resistance and inflammation





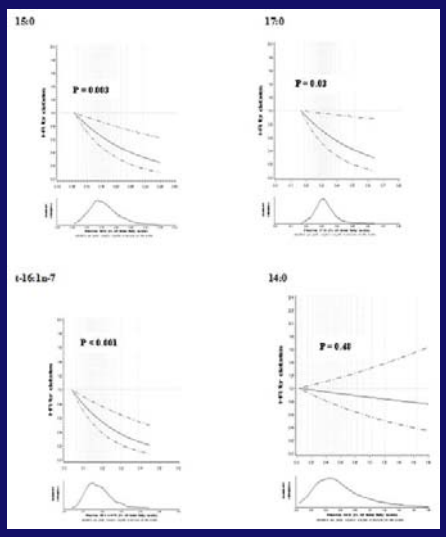
Newgard et al. Cell Metab 9:311, 2009



Trimethylamine Oxide (TMAO), a bacterial metabolite of dietary choline, appears to be pro-inflammatory

Zhu et al. Circulation 135:1671, 2017

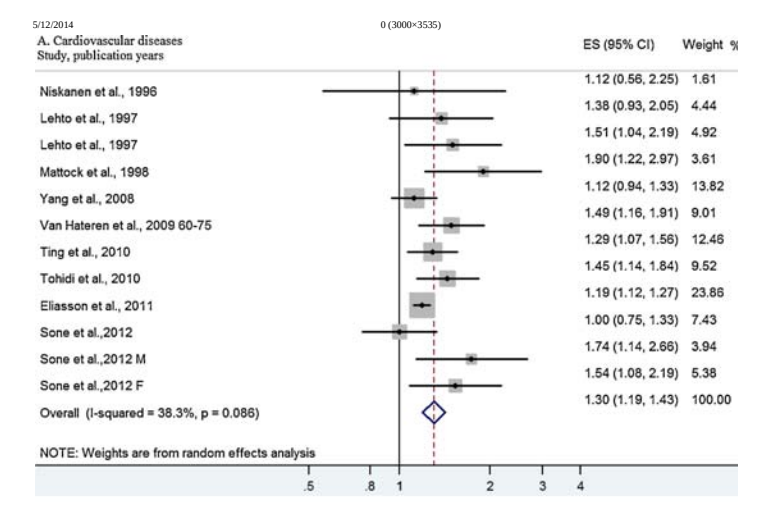
Blood levels of dairy saturated fatty acids correlate with protection from T2DM



Yakoob et al. Circulation 133:1645, 2016

Surrogate markers

LDL correlates with CVD, but not all that well



Open Access Research

BMJ Open

Lack of an association or an inverse association between low-density-lipoprotein cholesterol and mortality in the elderly: a systematic review

Uffe Ravnskov,[1] David M Diamond,[2] Rokura Hama,[3] Tomohito Hamazaki,[4] Björn Hammarskjöld,[5] Niamh Hynes,[6] Malcolm Kendrick,[7] Peter H Langsjoen,[8] Aseem Malhotra,[9] Luca Mascitelli,[10] Kilmer S McCully,[11] Yoichi Ogushi,[12] Harumi Okuyama,[13] Paul J Rosch,[14] Tore Schersten,[15] Sherif Sultan,[6] Ralf Sundberg[16]

Ravnskov et al. BMJ Open 6:e010401, 2016

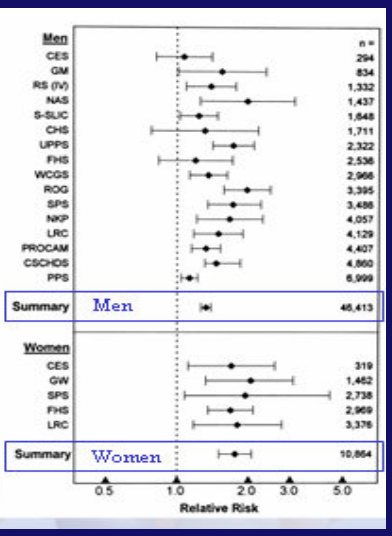
Hypertriglyceridemia is a better CVD risk factor

In Meta-Analysis (univariate risk)

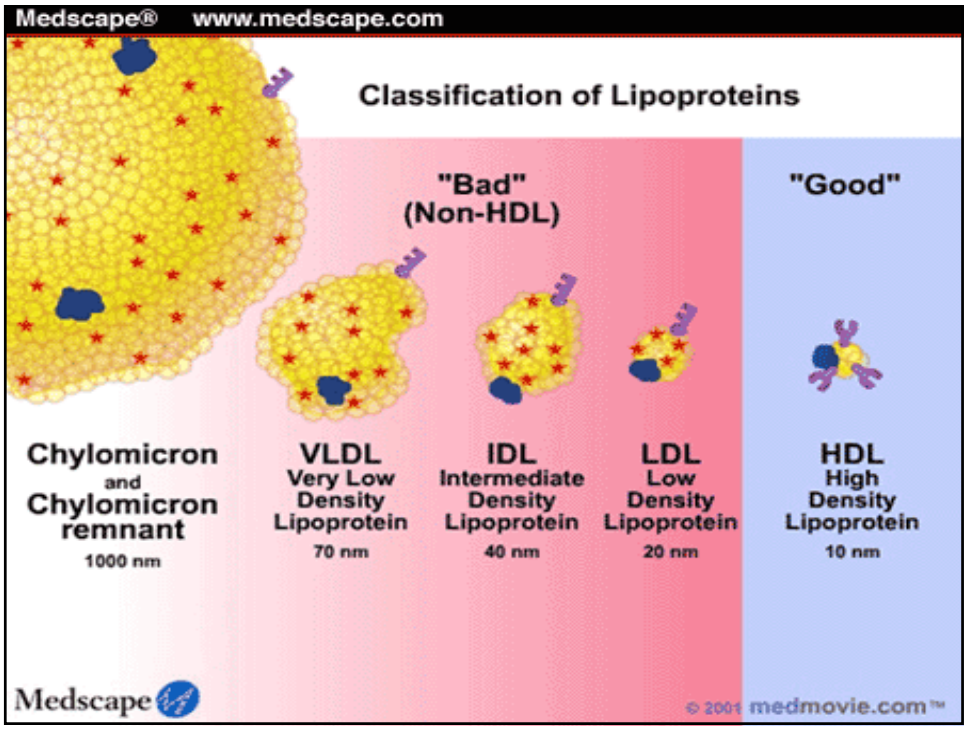
46,413 Men (16 studies)
2445 Events
8.4 yr f/u

10,864 women (5 studies)
439 events
11.4 yr f/u

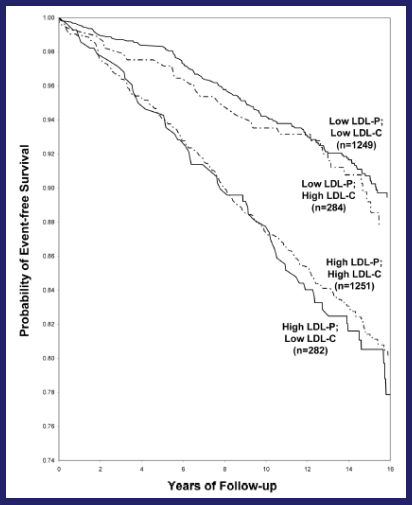
holds up in mutltivariate analysis



Austin et al, Am J Cardiol 81:7B, 1998

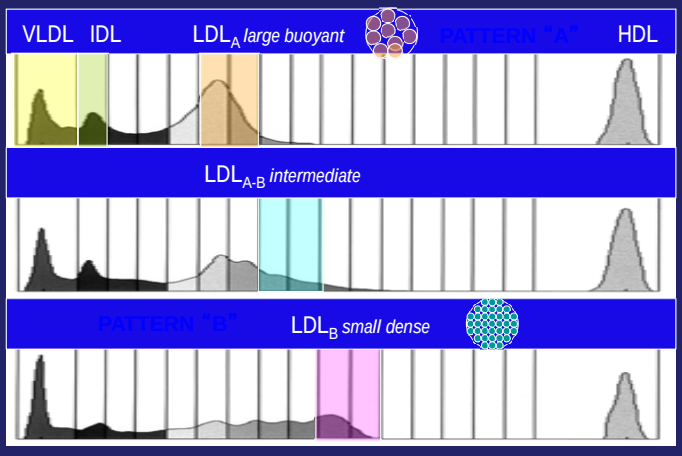


Atherogenic dyslipidemia— It's not about LDL cholesterol, it's about LDL particle number



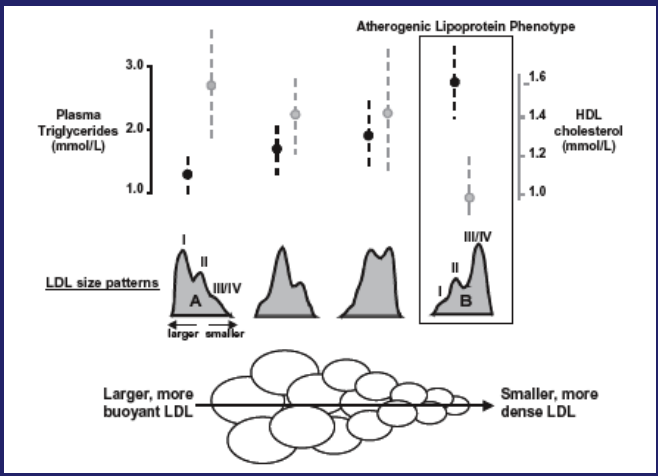
Cromwell et al. J Clin Lipidol 1:583, 2007

The lipoprotein continuum



"Total LDL" won't tell you particle number -
There's more LDL$_B$ than LDL$_A$ at the same total concentration

TG and HDL change with LDL sizing

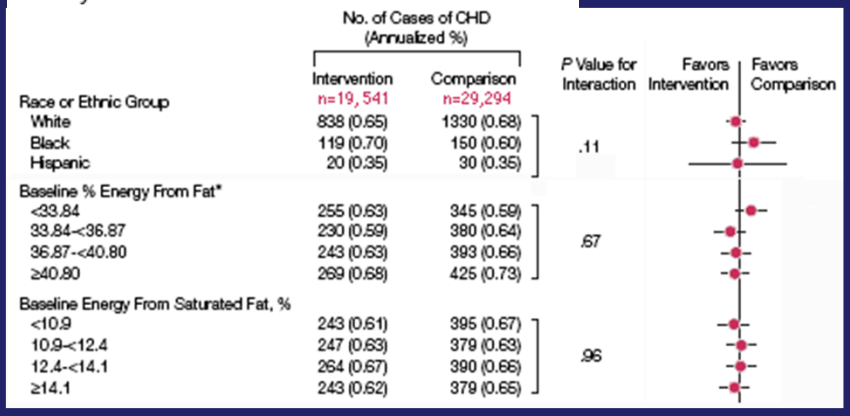


Rizzo and Berneis, Quart J Med 99:1, 2006

Randomized Clinical Trials

Low-Fat Dietary Pattern and Risk of Cardiovascular Disease

The Women's Health Initiative Randomized Controlled Dietary Modification Trial



	No. of Cases of CHD (Annualized %)		P Value for Interaction
	Intervention	Comparison	
Race or Ethnic Group	n=19,541	n=29,294	
White	838 (0.65)	1330 (0.68)	.11
Black	119 (0.70)	150 (0.60)	
Hispanic	20 (0.35)	30 (0.35)	
Baseline % Energy From Fat*			
<33.84	255 (0.63)	345 (0.59)	.67
33.84-<36.87	230 (0.59)	380 (0.64)	
36.87-<40.80	243 (0.63)	393 (0.66)	
≥40.80	269 (0.68)	425 (0.73)	
Baseline Energy From Saturated Fat, %			
<10.9	243 (0.61)	395 (0.67)	.96
10.9-<12.4	247 (0.63)	379 (0.63)	
12.4-<14.1	264 (0.67)	390 (0.66)	
≥14.1	243 (0.62)	379 (0.65)	

Favors Intervention | Favors Comparison

Conclusions: A dietary intervention that reduced total fat intake and increased intakes of vegetables, fruits, and grains did not significantly reduce the risk of CHD or stroke.

Howard et al. JAMA 295:655, 2006

LDL-C lowering as primary or secondary prevention of CVD

Randomized controlled trials (RCTs) of drug (41) or dietary (3) interventions

- No overall benefit on mortality
- Most of these trials did not reduce CVD events
- Some of the drug studies reported harm

DuBroff, Evidence-Based Medicine.;22:15, 2017

CREDIT SUISSE

September 2015

Research **Institute**

Thought leadership from Credit Suisse Research and the world's foremost experts

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September 2015

A high intake of omega-6 fats (vegetable oils) has not been proven as beneficial for our health and trans-fats have been shown to have negative health effects. The higher intake of vegetable oils and the increase in carbohydrate consumption in the last 30-40 years are the two leading factors behind the high rates of obesity and metabolic syndrome in the U.S. Saturated and monounsaturated fats are not.

Saturated fat does not clog the arteries: coronary heart disease is a chronic inflammatory condition, the risk of which can be effectively reduced from healthy lifestyle interventions

Aseem Malhotra,[1] Rita F Redberg,[2,3] Pascal Meier[4,5]

AM National Health Trust, UK
RR Editor-in-Chief, JAMA Int Med
PM Editor-in-Chief, BMJ Open Heart

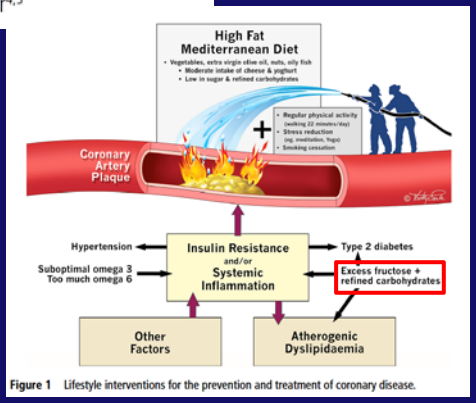


Figure 1 Lifestyle interventions for the prevention and treatment of coronary disease.

Malhotra et al. Br J Sports Med April 26, 2017 doi: 10.1136/bjsports-2016-097285

Is saturated fat really 'back?' In short, no, argue experts at ICVN 2018

By Elaine Watson
01-Mar-2018 - Last updated on 02-Mar-2018 at 00:28 GMT

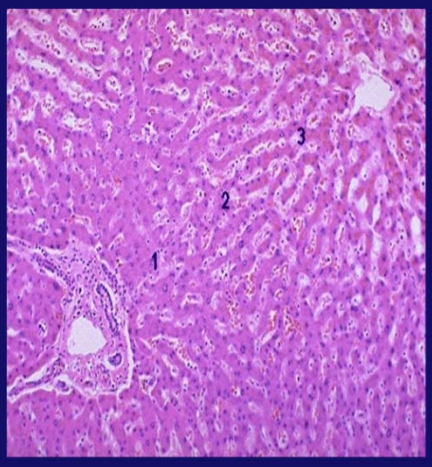
132 POST A COMMENT

"So the ketogenic diet, sure, it will cause you to lose weight in the short term. So would cholera, or a cocaine binge, but that doesn't mean it's a good idea," observed Dr David Katz at the 7th International Congress on Vegetarian Nutrition (ICVN) this week. "There is more than one way to eat badly and the American public is committed to exploring them all."

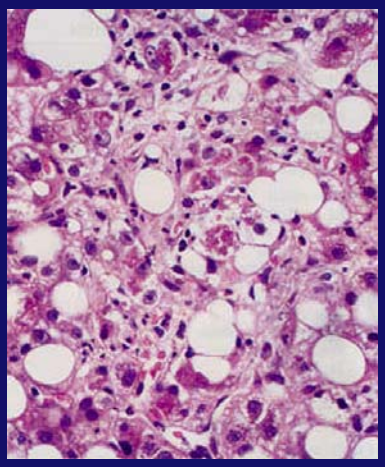
New York Times, April 17, 2011

Nature 487:27-29, Feb 1, 2012

Histology of (N)AFLD



Normal



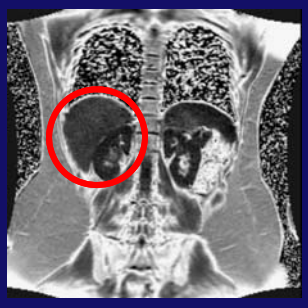
(N)AFLD

MRI Fat Fraction Maps

Obese

Low Liver Fat = 2.6%

MRI Fat Fraction Maps

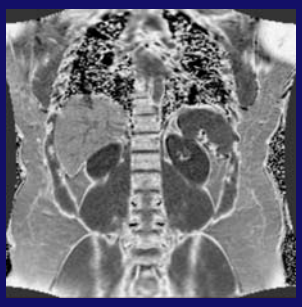


Obese

Low Liver Fat = 2.6%

MRI Fat Fraction Maps

Obese
Low Liver Fat = 2.6%



Obese
High Liver Fat = 24%

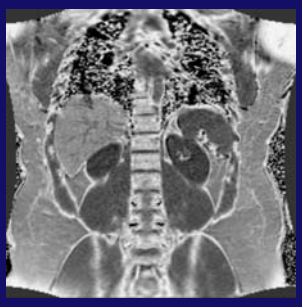
MRI Fat Fraction Maps

Obese
Low Liver Fat = 2.6%

Obese
High Liver Fat = 24%

MRI Fat Fraction Maps

Obese
Low Liver Fat = 2.6%

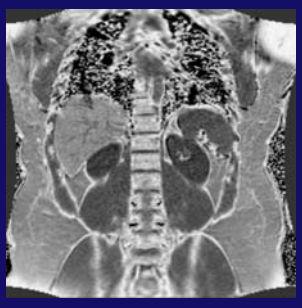


Obese
High Liver Fat = 24%

Thin
High Liver Fat = 23%

MRI Fat Fraction Maps

Fat Healthy
Low Liver Fat = 2.6%



Fat Sick
High Liver Fat = 24%

Thin Sick
High Liver Fat = 23%

Sugar and Diabetes

(Causation)

Sugar is toxic unrelated to calories


Original Article
PEDIATRIC OBESITY

Obesity

Isocaloric Fructose Restriction and Metabolic Improvement in Children with Obesity and Metabolic Syndrome

Robert H. Lustig[1], Kathleen Mulligan[2,3], Susan M. Noworolski[4], Viva W. Tai[2], Michael J. Wen[2], Ayca Erkin-Cakmak[1], Alejandro Gugliucci[3], and Jean-Marc Schwarz[5]

Lustig et al. Obesity 24:453, 2016


Short-term isocaloric fructose restriction lowers apoC-III levels and yields less atherogenic lipoprotein profiles in children with obesity and metabolic syndrome

Alejandro Gugliucci [a,*], Robert H. Lustig [b], Russell Caccavello [a], Ayca Erkin-Cakmak [b], Susan M. Noworolski [d], Viva W. Tai [c], Michael J. Wen [c], Kathleen Mulligan [a,c], Jean-Marc Schwarz [e]

Gugliucci et al. Atherosclerosis 253:171, 2016


Effects of Dietary Fructose Restriction on Liver Fat, De Novo Lipogenesis, and Insulin Kinetics in Children With Obesity

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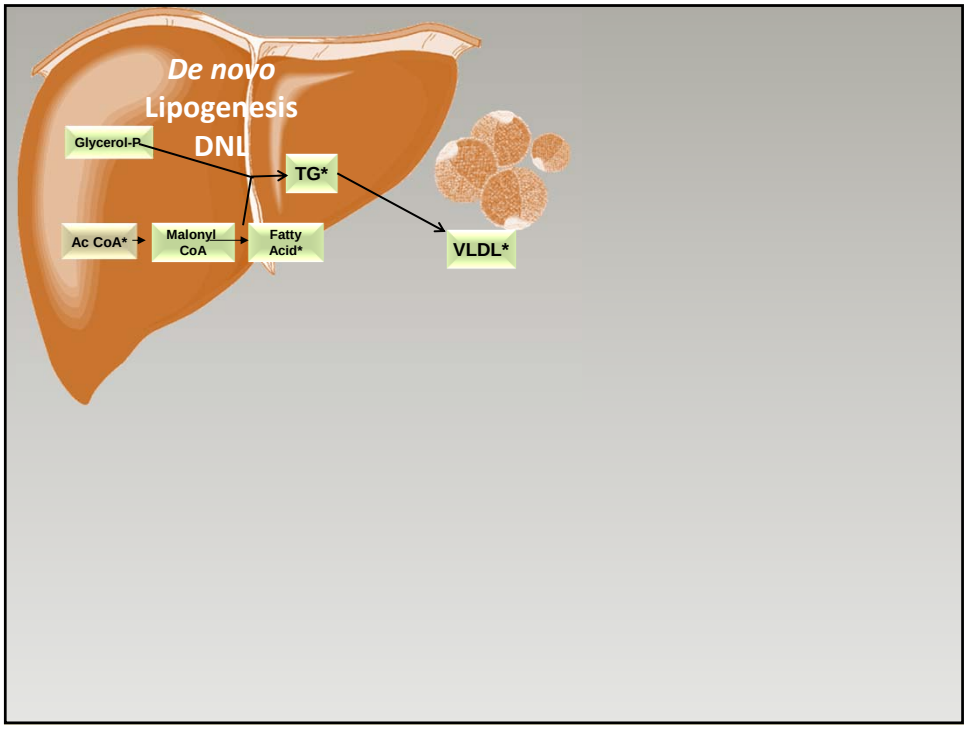
Schwarz et al. Gastroenterology 153:743, 2017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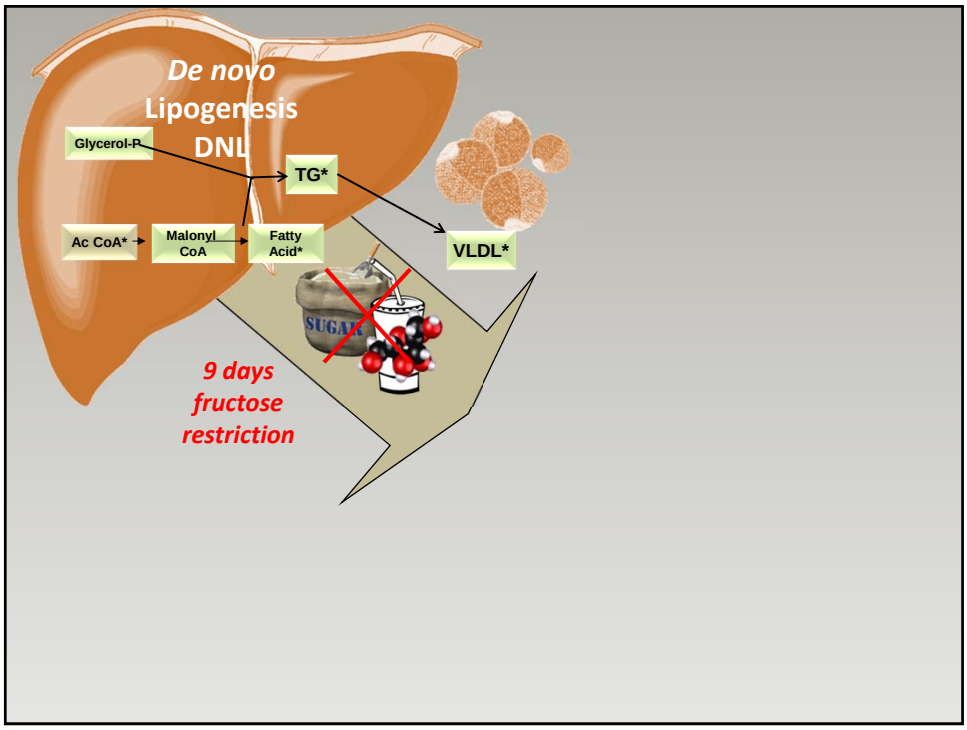
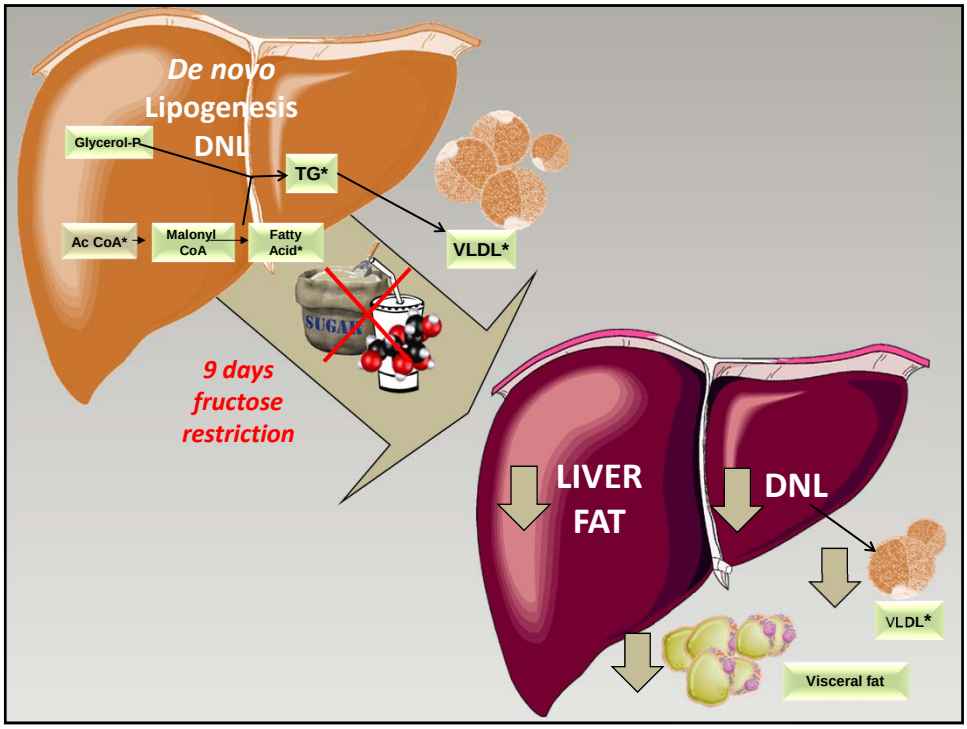
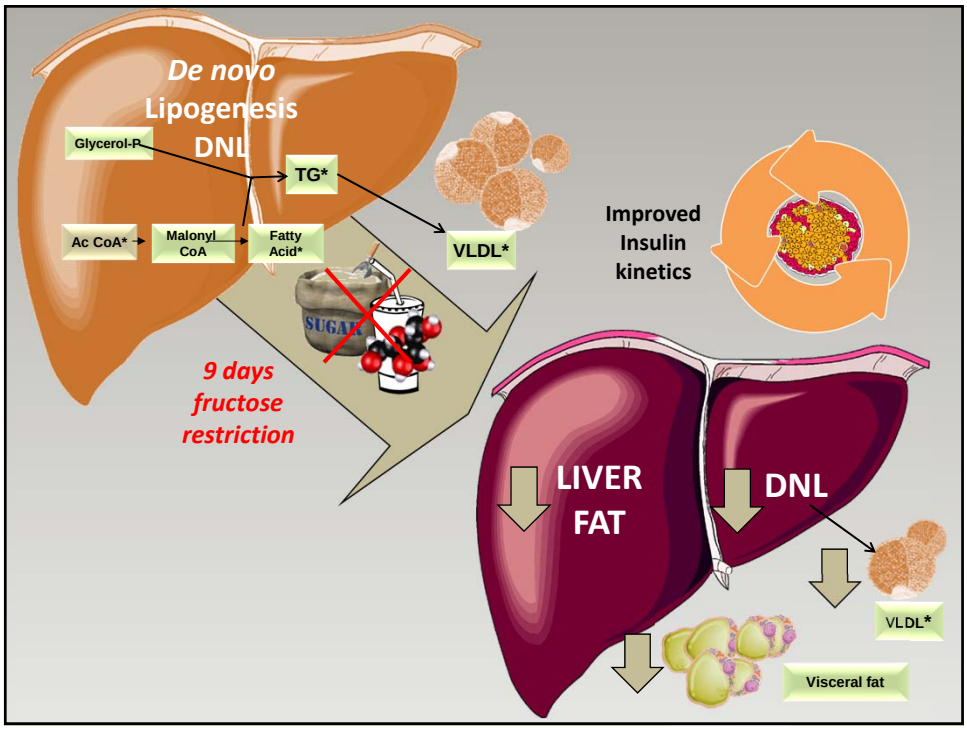
Lipogenesis
DNL
Glycerol-P
TG*
Ac CoA*
Malonyl CoA
Fatty Acid*
VLDL*


De novo
Lipogenesis
DNL
Glycerol-P
TG*
Ac CoA*
Malonyl CoA
Fatty Acid*
VLDL*
SUGAR
9 days
fructose
restriction


De novo
Lipogenesis
DNL
Glycerol-P
TG*
Ac CoA*
Malonyl CoA
Fatty Acid*
VLDL*
SUGAR
9 days
fructose
restriction
LIVER
FAT
DNL
VLDL*
Visceral fat


De novo
Lipogenesis
DNL
Glycerol-P
TG*
Ac CoA*
Malonyl CoA
Fatty Acid*
VLDL*
SUGAR
9 days
fructose
restriction
Improved
Insulin
kinetics
LIVER
FAT
DNL
VLDL*
Visceral fat

Sugar and disease

- **Causation**
  - Diabetes
  - Heart Disease
  - Fatty Liver Disease
  - Tooth Decay
- **Correlation**
  - Cancer
  - Dementia

Opinion

VIEWPOINT

Processed Food—An Experiment That Failed

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Those of us who have participated in science know that 9 of every 10 experiments are failures. Now imagine that the last 50 years has been a grand clinical research experiment, with the American population as unwitting participants, conducted by 10 principal investigators—Coca-Cola, Pepsico, Kraft, Unilever, General Mills, Nestlé, Mars, Kellogg, Proctor & Gamble, and Johnson & Johnson. In 1965, these corporations posed the hypothesis that processed food is better than real food. To determine if the experiment was a success or a failure, we have

nitrates. Nitrates (cured meat) can be metabolized into nitrosoureas, which can predispose individuals to colon cancer. (9) Too much salt. Approximately 15% of the population is salt sensitive and can manifest with hypertension and cardiac disease. (10) Too much ethanol. Ethanol is converted into liver fat and drives oxidative stress. While clearly a concern in adults, it is less likely that ethanol poses a metabolic risk in most children, as their access is limited. (11) Too much fructose. Children consume fructose instead. In fact, fructose is metabolized

Lustig, JAMA Pediatrics 171:212, 2017

PROCESSED food is high-sugar, low fiber

PROCESSED food is high-sugar, low fiber

REAL food is low-sugar, high-fiber

PROCESSED food is high-sugar, low fiber

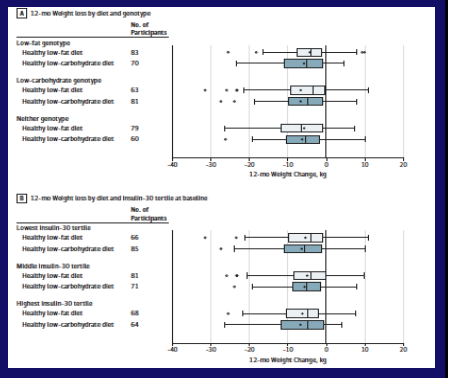
REAL food is low-sugar, high-fiber

All diets that work are REAL food

High fat or high carb doesn't matter; it's processed food that matters (DIETFITS)

Table 3. 12-Month Change Estimates for Anthropometric Variables by Diet

	12-mo Change Estimate (95% CI)[a]		
	Healthy Low-Fat Diet (n = 305)	Healthy Low-Carbohydrate Diet (n = 304)	Between-Group Difference (95% CI)[b]
Weight, kg	−5.29 (−5.93 to −4.65)	−5.99 (−6.63 to −5.35)	0.70 (−0.21 to 1.60)
Body mass index[c]	−1.75 (−1.97 to −1.52)	−2.07 (−2.30 to −1.85)	0.33 (0.01 to 0.64)
Body fat %[d]	−1.97 (−2.38 to −1.56)	−2.15 (−2.54 to −1.75)	0.18 (−0.40 to 0.75)
Waist circumference, cm	−3.74 (−4.64 to −2.84)	−4.41 (−5.31 to −3.51)	0.67 (−0.60 to 1.94)
Lipid level, mmol/L			
High-density lipoprotein cholesterol	0.40 (−0.37 to 1.18)	2.64 (1.87 to 3.41)	−2.24 (−3.33 to −1.15)
Low-density lipoprotein cholesterol	−2.12 (−4.70 to 0.47)	3.62 (1.04 to 6.19)	−5.74 (−9.38 to −2.09)
Triglycerides	−9.95 (−17.46 to −2.44)	−28.20 (−35.67 to −20.72)	18.25 (7.65 to 28.84)
Blood pressure, mm Hg			
Systolic	−3.18 (−4.33 to −2.03)	−3.72 (−4.86 to −2.58)	0.54 (−1.07 to 2.16)
Diastolic	−1.94 (−2.65 to −1.22)	−2.64 (−3.34 to −1.93)	0.70 (−0.31 to 1.71)
Fasting glucose, mg/dL	−3.67 (−4.90 to −2.44)	−2.10 (−3.32 to −0.87)	−1.58 (−3.31 to 0.16)
Fasting insulin, μIU/mL	−2.64 (−3.79 to −1.49)	−2.33 (−3.48 to −1.19)	−0.31 (−1.93 to 1.31)
Insulin-30, μIU/mL*	−15.38 (−21.13 to −9.62)	−11.48 (−17.18 to −5.78)	−3.90 (−12.00 to 4.20)
Metabolic syndrome, No. (%)[f]			
Had metabolic syndrome at baseline but not at 12 mo	36 (11.8)	36 (11.8)	
Had metabolic syndrome at baseline and 12 mo	39 (12.8)	36 (11.8)	
Did not have metabolic syndrome at baseline or 12 mo	128 (42.0)	137 (45.1)	
Did not have metabolic syndrome at baseline but had metabolic syndrome at 12 mo	13 (4.3)	11 (3.6)	
Respiratory exchange ratio[g]	−0.008 (−0.018 to 0.002)	−0.027 (−0.037 to −0.018)	0.020 (0.006 to 0.033)
Resting energy expenditure, kcal[g]	−66.45 (−96.65 to −36.26)	−76.93 (−106.68 to −47.19)	10.48 (−31.91 to 52.87)
Energy expenditure, kcal/kg/d	0.55 (0.20 to 0.90)	0.49 (0.13 to 0.84)	0.06 (−0.44 to 0.56)



Conclusions: Real food led to weight loss, in either a high-fat or high-carb diet. Processed food doesn't.

Gardner et al. JAMA 319:667, 2018