The Diet/Heart Disease Relationship
Sixty years of Ambiguity, Two Competing Paradigms

Gary Taubes
The Context
Context: the obesity epidemic

U.S. prevalence of obesity
Millions of people

31 million
15% of U.S. pop.

111 million
34% of U.S. pop.

Source: Center for Disease Control and Prevention.
And the diabetes epidemic

U.S. prevalence of diabetes

Milliseconds of people

4.2 million

2% of U.S. pop.

8% of U.S. pop.

21.1 million

Source: Center for Disease Control and Prevention.
Fat and Saturated Fat? Guidelines
“Intakes of dietary fatty acids and cholesterol are major determinants of cardiovascular disease (CVD) and T2D, two major causes of morbidity and mortality in Americans.... In order to reduce the population’s burden from CVD and T2D and their risk factors, the preponderance of the evidence indicates beneficial health effects are associated with several changes in consumption of dietary fats and cholesterol. These include limiting saturated fatty acid intake to less than 7 percent of total calories...”

Dietary Guidelines Advisory Committee, 2010
2010 Dietary Guidelines

“Consume less than 10 percent of calories from saturated fatty acids by replacing them with monounsaturated and polyunsaturated fatty acids

“Reduce the intake of calories from solid fats...”
Fat and Saturated Fat?
The Evidence
“The available evidence from cohort and randomized controlled trials is unsatisfactory and unreliable to make judgment about and substantiate the effects of dietary fat on risk of CHD.”
FAO/WHO Expert Consultation background paper, 2009

“A meta-analysis of prospective epidemiologic studies showed that there is no significant evidence for concluding that dietary saturated fat is associated with an increased risk of CHD or CVD.”

A History Lesson
1951-1961
Ancel Keys and his wife Margaret visit Naples, Italy. They assess the cholesterol and fat content of the diet among workers (no heart disease) and the wealthy (heart disease). Margaret Keys measures cholesterol levels.
Keys presents his hypothesis at a WHO meeting in Amsterdam: “fatty diet, raised serum cholesterol, atherosclerosis, myocardial infarction.”
1957

The American Heart Association, part 1

A 15-page AHA report by Irving Page and a committee of cardiologists criticizes Keys for taking “uncompromising stands based on evidence that does not stand up under critical examination.”
A 4-page AHA report from an ad-hoc committee that now includes Keys concludes that “the best scientific evidence of the time” strongly suggests that Americans would reduce their risk of heart disease by reducing the fat in their diets, and replacing saturated fats with polyunsaturated fats.
Keys tells Time that the ideal heart-healthy diet should be almost 70% carbohydrate and only 15% fat.
The competing philosophies

Proponents
We don’t have time to wait for “definitive scientific evidence” because people are dying out there.
The competing philosophies

Opponents/skeptics
Without definitive evidence, we don’t know if we’re right
Selection bias
1957-1970

Each new research adds detail, reduces areas of uncertainty, and, so far, provides further reason to believe.
Ancel Keys, 1957

Selection bias
1957-1970

“Bing Crosby Epidemiology”
Accentuate the positive, eliminate the negative

Framingham Heart Study

Positive data:
Framingham links cholesterol to heart disease.

Negative data:
In women over 50 “cholesterol had no predictive value.”

Framingham Heart Study

(Unpublished) negative data

Framingham compares the diets of men with cholesterol over 300 to those of men with cholesterol under 170 and finds no association with the amount or type of fat consumed.

“There is considerable range of serum cholesterol within the Framingham Study Group. Something explains this interindividual variation, but it is not diet (as measured here).”

More negative evidence

Studies of Benedictine and Trappist monks, Navajo Indians, Irish immigrants to Boston, Swiss Alpine farmers and Masai and other African pastoralists report no association of saturated fat to heart disease.

Keys rejects them as having “no relevance to diet-cholesterol-CHD relationships in other populations.”

CONFIRMATION BIAS
AN EXTENDED LESSON
Oglesby Paul and colleagues study 5400 male employees of the Western Electric Company. They compare the 15 percent of men who reported eating the fattest diets to the 15 percent who reported eating the leanest. “Worthy of comment, is the fact that of the 88 coronary cases, 14 have appeared in the high-fat intake group and 16 in the low-fat group.”
1981

Shekelle, Stamler et al return to Western Electric

They compare heart disease morbidity and mortality to the fat content of the diet in 1957.

“The amount of saturated fatty acids in the diet was not significantly associated with the risk of death from CHD.”
Shekelle, Stamler et al rationalize:

“Although most attempts to document the relation of dietary cholesterol, saturated fatty acids, and polyunsaturated fatty acids to serum cholesterol concentration in persons who are eating freely have been unsuccessful, positive results have been obtained in [four] investigations besides the Western Electric Study.”
Shekelle, Stamler et al rationalize further:

“If viewed in isolation, the conclusions that can be drawn from a single epidemiologic study are limited. Within the context of the total literature, however, the present observations support the conclusion that the [fat] composition of the diet affects the level of serum cholesterol and the long-term risk of death from CHD in middle-aged American men.”
1981

Enter the media...

*Washington Post*

“The new report strongly reinforces the view that a high-fat, high-cholesterol diet can clog arteries and cause heart disease.”

Shekelle in the *New York Times*

“The message of these findings is that it is prudent to decrease the amount of saturated fats and cholesterol in your diet.”
The denouement...

The AHA and NHLBI co-author a report called “The Cholesterol Facts.”

The Western Electric study is included as one of seven “epidemiologic studies showing the link between diet and CHD [that] have produced particularly impressive results” and “showing a correlation between saturated fatty acids and CHD” -- precisely what it did not do.
Paradoxical State of the Evidence

The 1970s
1970

An American Heart Association committee recommends low-saturated-fat diets (less than 10% of calories) for every American, including “infants, children, adolescents, lactating and pregnant women, and older persons.”

1975

“Two strikingly polar attitudes persist on this subject, with much talk from each and little listening between.”

Henry Blackburn, New England Journal of Medicine

1978

“It must still be admitted that the diet-heart relation is an unproved hypothesis that needs much more investigation.”

Thomas Dawber, New England Journal of Medicine

Blackburn, 1975. NEJM. Jan 9; 105-7.
Clinical Trials
Pre-1977
Low-fat diets?

1963
Hungarian researchers report a benefit of consuming a maximum of 1.5 ounce of fat per day.

1965
British researchers report no benefit of consuming a maximum of 1.5 ounces of fat per day: “A low-fat diet has no place in the treatment of myocardial infarction.”

Korányi, 1963. Ther Hung. 11:17
Cholesterol-lowering diets?

**1966**

The Anti-Coronary Club

Heart disease reduced among the intervention group.

*Caveat:* total mortality increased

(8 deaths in intervention group; 0 among controls)

**1969**

Los Angeles VA Hospital

Cholesterol reduced among interventions; heart disease mortality reduced.

*Caveat:* cancer mortality increased.

Cholesterol-lowering diets?

1972

Helsinki Mental Hospital Study
Heart disease rates reduced by half. Longevity increased among men.

Caveat: no effect on longevity in women.

Cholesterol-lowering diets?

1973*

Minnesota Coronary Study
9000 men and women.
269 deaths in intervention group. 248 in controls

Cholesterol-lowering diets?

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*Results go unpublished for 16 years. Why? “We were disappointed in the way they turned out.” (Frantz)

The Tipping Point

January, 1977
“The first comprehensive statement by any branch of the Federal Government on risk factors in the American diet.”

1. Increase carbohydrate consumption to 55 to 60 percent of calories

2. Reduce fat consumption to 30 percent of calories
“The question to be asked is not why should we change our diet but why not? There are [no risks] that can be identified and important benefits can be expected.”

Mark Hegsted, Harvard, at the press conference
The Tipping Point, revised

December, 1977
“Important questions, which are currently being investigated:

1. Does lowering the plasma cholesterol level through dietary modification prevent or delay heart disease in man?”
Cohort Studies
1977-1984
1977

First reports on LDL and HDL from Framingham, San Francisco, Puerto Rico, Albany and Honolulu cohorts.

Total cholesterol does not predict future heart disease

LDL is a “marginal risk factor”

HDL is a 4-fold better predictor of risk than LDL and the only reliable predictor of risk for men or women over 50

Caveats: Saturated fat raises HDL. Carbohydrates lower it.

1981

Honolulu, Framingham and Puerto Rico

Saturated fat and total fat negatively associated w/ risk of heart attack

Saturated fat and total fat positively associated w/ longevity

Feinleib, 1983. Cancer Res. May;2503s-2507s.
1981-3

Low serum cholesterol (<160 mg/dl) associated with a higher risk of cancer.

Observed in every cohort study with 3 exceptions (all Chicago cohorts studied by Jeremiah Stamler)

Clinical Trials
1977-1984
1982

The Multiple Risk Factor Intervention Trial
Cost: $115,000,000

7 year mortality:
41.2/1000 (intervention) vs. 40.4/1000 (controls)

Wall Street Journal
“Heart attacks, a test collapses.”

MRFIT, 1982. JAMA. Sep 24;1465-77.
January, 1984

The Lipid Research Clinics Primary Prevention Trial
Cost: $150,000,000

10 year mortality
35.8/1000 (intervention) vs. 37.3/1000 (controls)

Time Magazine
“Sorry, it’s true. Cholesterol really is a killer.”

"It is now indisputable that lowering cholesterol with diet and drugs can actually cut the risk of developing heart disease and having a heart attack."

The LRC results “strongly indicate that the more you lower cholesterol and fat in your diet, the more you reduce your risk of heart disease.”

Basil Rifkin, NIH director of the LRCCPT, in *Time*

Why’d they exaggerate?

"It's an imperfect world. The data that would be definitive is ungettable, so you do your best with what is available."

Basil Rifkin, 2002
Consensus Building
1987 -1989

“In sciences that are based on supposition and opinion, the object is to command assent, not master the thing itself.”

Francis Bacon, Novum Organum, 1620
There is “no doubt” that a low-fat diet “will afford significant protection against coronary heart disease” to every American over the age of two.
December, 1984

The NIH consensus conference

Caveat

If there had been a true consensus, says Dan Steinberg (chair of the consensus panel, co-PI of LRCPPT), “you wouldn’t have had to have a consensus conference.”

National Cholesterol Education Program

“The guidelines urge that all Americans, starting at age 20, have their cholesterol levels tested as part of a general medical examination. Those whose levels are high, generally over 240 milligrams per deciliter of blood, would be put on strict diets and, if necessary, drugs they might have to take all their lives.”

The New York Times

1988

Surgeon General’s Report on Nutrition and Health (700 pages)

The “disproportionate consumption of food high in fats” is held responsible for two-thirds of the 2.1 million deaths in the U.S. that year.

“The depth of the science base,” says C. Everett Koop, “is even more impressive than that for tobacco and health in 1964.”

1989

National Academy of Sciences *Diet and Health: Implications for Reducing Chronic Disease Risk* (1300 pages)

“Highest priority is given to reducing fat intake, because the scientific evidence concerning dietary fats and other lipids and human health is strongest and the likely impact on public health the greatest.”

Evidence Post-consensus

1990 - today
Total mortality vs. CHD mortality (1990)

Meta-Analyses (2001)

Cochrane Collaboration: “Reduced or Modified dietary fat for preventing cardiovascular disease”

27 well-controlled randomized trials
10,000 subjects followed for an average of three years each.

“The answers are not definitive, the data being too sparse to be convincing.”

Meta-Analyses (2006)

Cochrane Collaboration: “Multiple risk factor interventions for primary prevention for coronary heart disease”

Multiple interventions include lowering blood pressure and cholesterol
10 well-controlled trials
900,000 patient years of observation

“The pooled effects suggest multiple risk factor intervention has no effect on mortality.”

Women’s Health Initiative (2006)

48,835 post-menopausal women randomized to a low-fat diet or a control diet

After six years, total fat consumption is reduced by 8.2%; saturated fat is reduced by 2.9%.

“Modest” increases in fruits, vegetables and whole grains
Women’s Health Initiative (2006)

“The intervention did not reduce risk of CHD or stroke.”

“A low-fat dietary pattern did not result in a statistically significant reduction in the risk of invasive breast cancer...”

“There is no evidence that a low-fat dietary pattern intervention reduces colorectal cancer risk...”

“A low-fat dietary pattern among generally healthy postmenopausal women showed no evidence of reducing diabetes risk...”

Diet trials

N obese men and women

Conventional LOW-FAT, HIGH-CARB, CALORIE-RESTRICTED diet instruction

HIGH-FAT, LOW-CARB, CALORIE UNRESTRICTED diet instruction

Foster et al. 2003. NEJM. May 22;2082-90
Summary

A systematic review and meta-analysis were carried out to study the effects of low-carbohydrate diet (LCD) on weight loss and cardiovascular risk factors (search performed on PubMed, Cochrane Central Register of Controlled Trials and Scopus databases). A total of 23 reports, corresponding to 17 clinical investigations, were identified as meeting the pre-specified criteria. Meta-analysis carried out on data obtained in 1,141 obese patients, showed the LCD to be associated with significant decreases in body weight (−7.04 kg [95% CI −7.20/−6.88]), body mass index (−2.09 kg m\(^{-2}\) [95% CI −2.15/−2.04]), abdominal circumference (−5.74 cm [95% CI −6.07/−5.41]), systolic blood pressure (−4.81 mm Hg [95% CI −5.33/−4.29]), diastolic blood pressure (−3.10 mm Hg [95% CI −3.45/−2.74]), plasma triglycerides (−29.71 mg dL\(^{-1}\) [95% CI −31.99/−27.44]), fasting plasma glucose (−1.05 mg dL\(^{-1}\) [95% CI −1.67/−0.44]), glycated haemoglobin (−0.21% [95% CI −0.24/−0.18]), plasma insulin (−2.24 micro IU mL\(^{-1}\) [95% CI −2.65/−1.82]) and plasma C-reactive protein, as well as an increase in high-density lipoprotein cholesterol (1.73 mg dL\(^{-1}\) [95% CI 1.44/2.01]). Low-density lipoprotein cholesterol and creatinine did not change significantly, whereas limited data exist concerning plasma uric acid.

LCD was shown to have favourable effects on body weight and major cardiovascular risk factors; however the effects on long-term health are unknown.
Why the confidence?

Pre-1984

Populations with very low cholesterol levels have a low incidence of heart disease
Why the confidence?

Post-1984

Cholesterol-lowering drugs work (statins, in particular)
Caveat

Drugs and diets are not comparable.

Drugs have multiple actions as do diets.

Saying that statins reduce heart disease risk by lowering cholesterol, is like “saying that aspirin reduces heart disease risk by reducing headaches.” (Kronmal)
Counter-arguments?
The obesity epidemic

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The Alternative Paradigm
Metabolic Syndrome
Metabolic syndrome history

1950 (Gofman in Science)
Lipoproteins, not their cholesterol, are atherogenic

1951 (Barr and Eder)
Low HDL predicts high CHD risk

Late 1950s (Ahrens and Gofman)
Carbohydrates elevate VLDL/triglycerides
Metabolic syndrome history

“Neglect of [the carbohydrate] factor can lead to rather serious consequences. First, in the failure to correct the diet in some individuals who are very sensitive to the carbohydrate action; and second, by allowing certain individuals sensitive to the carbohydrate action to take too much carbohydrate as a replacement for some of their animal fats.”

Gofman, 1958
Metabolic syndrome history

Early 1960s (Albrink, then Kuo): High triglycerides predict high CHD risk

1965 onward (Reaven and Farquhar, DeFronzo): The Causal Pathway

Carbohydrates drive insulin hyperinsulinemia/insulin resistance hypertriglyceridemia, low HDL
Cognitive dissonance?

NIH Consensus Panel on NIDDM -- December 1986

“The data speak for themselves.”
George Cahill, chair of the consensus panel

“High protein levels can be bad for the kidneys. High fat is bad for your heart. Now Reaven is saying not to eat high carbohydrates. We have to eat something… Sometimes we wish it would go away because nobody knows how to deal with it.”
Robert Silverman, NIDDK

Reaven Introduces MetSyn (aka Syndrome X) 1988

Syndrome X = insulin resistance, hyperinsulinemia, high triglycerides, low HDL cholesterol, and high blood pressure

Common in obesity and NIDDM; caused by carbohydrate-rich diets, mediated via insulin

increases risk of CHD

MetSyn Today

CDC estimates 75 million Americans with MetSyn

NCEP ATP III (2002, the last one): An “emerging risk factor for heart disease.”

Official treatment: a low-fat, high carbohydrate diet

Why a low-fat diet?

Because LDL cholesterol is still considered the “driving force behind coronary atherogenesis”

Why?

Because statins work
The Clinical Evidence
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LCD was shown to have favourable effects on body weight and major cardiovascular risk factors; however the effects on long-term health are unknown.
Conclusions

1. The evidence that saturated fat causes CHD is at best poor

2. The evidence that low-fat diets are healthy diets has always been contradicted by the evidence that high-carb diets increase CHD risk and weight

3. Low-carbohydrate, high-fat diets have the far longer pedigree

4. Low-carbohydrate diets address most if not all of the metabolic/hormonal derangements of metabolic syndrome