An Assessment of Cardiovascular Risks of a Low Carbohydrate, High Fat Diet

David Diamond, Ph.D.
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Tampa, Florida, USA
An Assessment of Cardiovascular Risks of a Low Carbohydrate, High Fat Diet

Low Carb Diet-Induced Increase in LDL
The Ultimate Bogeyman
Disclosure #1: 1997 – 2007
My High TG and Low HDL Carried the Highest Risk for a Heart Attack

Fasting Triglycerides, High-Density Lipoprotein, and Risk of Myocardial Infarction

J. Michael Gaziano, MD, MPH; Charles H. Hennekens, MD, DrPH; Christopher J. O’Donnell, MD, MPH; Jan L. Breslow, MD; Julie E. Buring, ScD

Circulation  Vol 96, No 8  October 21, 1997
"My Doctor Urged Me to Take Statins!"

Dr. David Diamond, Neuroscientist
Disclosure 2: My sources of information on diet, cholesterol and cardiovascular disease

Gary Taubes*  
Ivor Cummins*  
Uffe Ravnskov*  
Stephanie Seneff*  
Luca Mascitelli*  
Malcolm Kendrick*  
Sherif Sultan*  
Douglas Schocken*  
Barry Groves*  
Zoe Harcombe*  
Tim Noakes*  
Kilmer McCully*  
Robert Lustig*  
William Davis  
Nicolai Worm*  
Colin Champ  
John Abramson  
Beatrice Golomb  
Rita Redberg  
George Mann  
Robert Atkins  
Dwight Lundell  
Mark Hyman  
Michael Eades  
Nina Teicholz*, Ann Childers  
Paul Rosch*  
Carlos Monteiro*  
Richard Feinman*  
Kevin Kip*  
David Brownstein*  
Paul Leaverton*  
James DiNicolantonio*  
Eric Westman*  
Tom Naughton*  
David Ludwig*  
Robert DuBroff*  
Bruce Fife  
Edward H. Ahrens  
Alana/Peter Langsjoen*  
John Yudkin  
Marcia Angell  
Jason Fung  
Verner Wheelock  
Jay Wortman  
David Perlmutter  
Dave Feldman*  
Ted Naiman  
Jimmy Moore*  
Cate Shanahan*  
Jeff Volek*  
Barry Groves*  
Michel De Lorgeril*  
Aseem Malhotra*  
Harumi Okuyama*  
Joel Kauffman*  
Abdullah Alabdulgader*  
Gary/Belinda Fettke*  
Andreas Eenfeldt*  
Sarah Hallberg*  
Anthony Colpo*  
Fred Kummerow  
Mark Cucuzella*  
Maryanne Demasi*  
Steve Phinney  
Sally Fallon/Mary Enig  
Hussein Dashti  
Maria Luz Fernandez  
Georgia Ede*  
Marika Sboros  
Jeff Gerber*  
Amber O’Hearn
Disclosure 3: My Neuroscience Research Program (1978 – Present)
Support: Dept. of Veterans Affairs, Navy, NIH, DoD, NSF, Drug Companies

Diet/Cardiovascular Disease Research: Unfunded

Gary Taubes*
Ivor Cummins*
Uffe Ravnskov*
Stephanie Seneff*
Luca Mascitelli*
Malcolm Kendrick*
Sherif Sultan*
Douglas Schocken*
Barry Groves*
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Hussein Dashti
Maria Luz Fernandez
Georgia Ede*
Marika Sboros
Jeff Gerber*
Amber O’Hearn
Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base

Richard D. Feinman Ph.D.,* Wendy K. Pogozelski Ph.D., Arne Astrup M.D.,
Richard K. Bernstein M.D., Eugene J. Fine M.S., M.D.,
Eric C. Westman M.D., M.H.S., Anthony Accurso M.D.,
Lynda Frassetto M.D., Barbara A. Gower Ph.D., Samy I. McFarlane M.D.,
Jörgen Vest Nielsen M.D., Thure Krarup M.D., Laura Saslow Ph.D.,
Karl S. Roth M.D., Mary C. Vernon M.D.,
Jeff S. Volek R.D., Ph.D., Gilbert B. Wilshire M.D.,
Annika Dahlqvist M.D., Ralf Sundberg M.D., Ph.D.,
Ann Childers M.D., Katharine Morrison M.R.C.G.P.,
Anssi H. Manninen M.H.S., Hussain M. Dashti M.D., Ph.D., F.A.C.S.,
Richard J. Wood Ph.D., Jay Wortman M.D., and Nicolai Worm Ph.D.
You lost weight, lowered your BP/TGs, increased your HDL, but I'm worried about your LDL.
“saturated fat … increases blood cholesterol, damages arteries and leads to coronary disease.”
Ancel Keys, 1961

The American Heart Association recommends aiming for a dietary pattern that achieves 5% to 6% of calories from saturated fat.
Use soft margarine as a substitute for butter.
Nobel Prize Winners Declare LDL Guilty of Causing Heart Disease

How LDL Receptors Influence Cholesterol and Atherosclerosis

Michael S. Brown and Joseph L. Goldstein

1984 SCIENTIFIC AMERICAN

demonstrates unequivocally the causal relation between an elevated circulating LDL level and atherosclerosis.
the relationship between serum cholesterol and CHD is a continuously graded one that powerfully affects risk for the great majority of middle-aged American men.
What is the actual risk to the population to die of CHD based on cholesterol levels?
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What is the actual risk to the population to die of CHD based on cholesterol levels?
Is Relationship Between Serum Cholesterol and Risk of Premature Death From Coronary Heart Disease Continuous and Graded?
Findings in 356222 Primary Screenees of the Multiple Risk Factor Intervention Trial (MRFIT)
Jeremiah Stamler, MD; Deborah Wentworth, MPH; James D. Neaton, PhD
JAMA. 1986

What is the actual risk to the population to die of CHD based on cholesterol levels?
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Jeremiah Stamler, MD; Deborah Wentworth, MPH; James D. Neaton, PhD

99.7% did not die of CHD
0.3% died of CHD
1.3% died of CHD
98.7% did not die of CHD

Serum Cholesterol (mg/dl)
Is Relationship Between Serum Cholesterol and Risk of Premature Death From Coronary Heart Disease Continuous and Graded?

Findings in 356,222 Primary Screenees of the Multiple Risk Factor Intervention Trial (MRFIT)

Jeremiah Stamler, MD; Deborah Wentworth, MPH; James D. Neaton, PhD

JAMA, 1986

99.7% did not die of CHD
0.3% died of CHD
1.3/0.3 = 4.13 >400% Increase in Deaths
1.3% died of CHD
98.7% did not die of CHD
Fear of the Highest Cholesterol – Justified?

98.7% did not die of CHD
Familial Hypercholesterolemia: An Inevitable Early Coronary Death Sentence?

Hypercholesteremia with Predisposition to Atherosclerosis*

An Inborn Error of Lipid Metabolism

DAVID ADLERSBERG, M.D.

AMERICAN JOURNAL OF MEDICINE NOVEMBER, 1951

The common factor among most patients of young age with coronary atherosclerosis appears to be a hereditary disorder of lipid metabolism manifested by hypercholesteremia.
Tests of the Hypothesis That Cholesterol Causes Atherosclerosis

Hypercholesteremia with Predisposition to Atherosclerosis*

An Inborn Error of Lipid Metabolism

David Adlersberg, M.D.

1 – There should be a high rate of premature death in people with Familial Hypercholesterolemia

2 – Pharmacological reduction of cholesterol should reduce the rate of coronary events and mortality
FAMILIAL HYPERCHOLESTEROLEMIA: A GENETIC AND METABOLIC STUDY

WILLIAM R. HARLAN, JR., JOHN B. GRAHAM, AND E. HARVEY ESTES

MEDICINE 1966 Vol. 45, No. 2

Our studies provide no evidence that familial hypercholesterolemia appreciably shortens the life of affected individuals, either male or female. On the contrary, they show that high levels of serum cholesterol are clearly compatible with survival into the seventh and eighth decades.
No Overall Adverse Effect of High Cholesterol on Longevity
Normal Lifespan In People With Familial Hypercholesterolemia

Mortality Among Patients With Familial Hypercholesterolemia:
A Registry-Based Study in Norway, 1992–2010

Liv Mundal, MD; Mirza Sarancic, MSc; Leiv Ose, MD, PhD; Per Ole Iversen, MD, PhD; Jens-Kristian Borgan, MSc; Marit B. Veierød, PhD; Trond P. Leren, MD, PhD; Kjetil Retterstøl, MD, PhD

The UCCG Registry consisted of 4688 patients with verified molecular genetic diagnosis of FH diagnosed in the period from 1992 to 2010.
Discussion

No significant differences were noted in all-cause mortality between the FH patients and the general Norwegian population except for a significantly lower SMR in the age group 70 to 79 years.
Higher LDL is Associated with Equal or Greater Longevity

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 Sundberg16

Since elderly people with high LDL-C live as long or longer than those with low LDL-C, our analysis provides reason to question the validity of the cholesterol hypothesis.
Does Pharmacological Reduction of LDL Improve CVD Outcomes?

Statins:
- Reduce LDL

CETP Inhibitors:
- Reduce LDL and Increase HDL
It is a drug that reduces levels of LDL cholesterol, the dangerous kind, as much as statins do. And it more than doubles levels of HDL cholesterol, the good kind.

But these specialists were stunned by the results of a study of 12,000 patients, announced on Sunday at the American College of Cardiology’s annual meeting: There was no benefit from taking the drug, evacetrapib.

“We had an agent that seemed to do all the right things,” said Dr. Stephen J. Nicholls, the study’s principal investigator and the deputy director of the South Australian Health and Medical Research Institute in Adelaide. “It’s the most mind-boggling question.”
Statins as “Wonder Drugs”
36% Reduced Risk of a Heart Attack!

In patients with multiple risk factors for heart disease,

Lipitor reduces risk of heart attack by 36%*

If you have risk factors such as family history, high blood pressure, age, low HDL (‘good’ cholesterol) or smoking.

*That means in a large clinical study, 3% of patients taking a sugar pill or placebo had a heart attack compared to 2% of patients taking Lipitor.
Discussion

Our findings in the lipid-lowering arm of ASCOT show that in hypertensive patients, who on average were at moderate risk of developing cardiovascular events, cholesterol lowering with atorvastatin 10 mg conferred a 36% reduction in fatal CHD and non-fatal myocardial infarction compared with placebo.
Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial

THE LANCET • Vol 361 • April 5, 2003

36% Risk Reduction?

% of Subjects Without an Event

- Absence of Non-Fatal MI + Fatal CHD
- No CVD Events
- No Coronary Events
- Survival
- No CVD Death
- No Stroke

Placebo
Atorvastatin

* Indicates significant difference.
36% Risk Reduction?

% of Subjects Without an Event

- Absence of Non-Fatal MI + Fatal CHD
- No CVD Events
- No Coronary Events
- Survival
- No CVD Death
- No Stroke

Placebo
Atorvastatin

Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial

THE LANCET • Vol 361 • April 5, 2003
The Actual Difference in Treated (Atorvastatin) versus Untreated (Placebo) Groups is About 1%

98.1% Atorvastatin
97% Placebo

Difference = 1.1%
Drug vs Placebo

% of Subjects Without an Event

Absence of Non-Fatal MI + Fatal CHD
No CVD Events
No Coronary Events
Survival
No CVD Death
No Stroke

Placebo
Atorvastatin
How Can the Effect be 1.1% as well as 36%?
(read the fine print)
98.1% Atorvastatin
97% Placebo

Difference = 1.1%
Drug vs Placebo

1.1% : 3% = 36%

% of Subjects Without an Event

Absence of Non-Fatal MI + Fatal CHD

No CVD Events
No Coronary Events
Survival
No CVD Death
No Stroke

Placebo
Atorvastatin

*
Statins Lose Their Appeal When the Real Effectiveness Data is Shown
Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein


“It’s spectacular,” says John J.P. Kastelein of Academic Medical Center in Amsterdam, a co-author of the Crestor study. “We finally have strong data” that a statin prevents a first heart attack.

Dr. Steven Nissen of the famous Cleveland Clinic

“It’s a breathtaking study. It’s a blockbuster. It’s absolutely paradigm-shifting,
A Clinical Conference Presentation of the JUPITER Study: “Impressive” 44% Reduction in Coronary Events

Adapted from Ridker et al. NEJM 2008.
A Sobering Closer Look at JUPITER

Study Terminated at 1.9 years

Adapted from Ridker et al. NEJM 2008.
The Study was Terminated Prematurely at 1.9 Years on an “Ethical Basis”

Adapted from Ridker et al. NEJM 2008.
Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein


B  Myocardial Infarction, Stroke, or Death from Cardiovascular Causes

<table>
<thead>
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<th>Years</th>
<th>Cumulative Incidence</th>
<th>Rosuvastatin</th>
<th>Placebo</th>
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</tr>
</tbody>
</table>

P<0.000001

44% Difference!
Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein

Published Data


B Myocardial Infarction, Stroke, or Death from Cardiovascular Causes

Dr. Steven Nissen of the famous Cleveland Clinic
“It’s a breathtaking study. It’s a blockbuster. It’s absolutely paradigm-shifting,

44% Difference!
**JUPITER Study – Statistical Alchemy**

**How to Turn a Miniscule 1.2% Effect into a Spectacular 44% Effect**

98.4% Rosuvastatin  
97.2% Placebo  

**Difference = 1.2%**  
**Drug vs Placebo**  

1.2% : 2.8% = 44%

---

Absence of Non-Fatal MI + Fatal CHD

No MI  
No Coronary Death  
No Stroke  
No CVD Death

% of Subjects Without an Adverse Event

**Placebo**  
**Rosuvastatin**
1% is better than nothing – right?
Numerous Adverse Side Effects of Statins: Erectile Dysfunction/Low Testosterone, Kidney Disease, Muscle Atrophy

Men treated with hypolipidaemic drugs complain more frequently of erectile dysfunction

E. Bruckert MD, P. Giral MD, H. M. Heshmati MD and G. Turpin MD
Service d’Endocrinologie-Métabolisme, Hôpital de la Pitié-Salpêtrière, Paris, France

Effect of Statins on Total Testosterone Levels in Male Veterans

Muhammad Jawad Sethi, MD; and William P. Newman, MD

Statin Use and the Risk of Kidney Disease With Long-Term Follow-Up (8.4-Year Study)

Tushar Acharya, MDa, Jian Huang, MDb,cd, Steven Tringali, DOe, Christopher R. Frei, PharmD, MScd,e, Eric M. Mortensen, MD, MScfg,h, and Ishak A. Mansi, MDfg,h,i
Am J Cardiol 2015

Statins and Musculoskeletal Conditions, Arthropathies, and Injuries
Ishak Mansi, MD; Christopher R. Frei, PharmD, MSc; Mary Jo Pugh, PhD; Una Makris, MD; Eric M. Mortensen, MD, MSc
JAMA Internal Medicine 2013
Side Effects: Type 2 Diabetes, Impaired Motor Performance, Mitochondrial Dysfunction, Cataracts, Acute Renal Failure, Cancer and Liver Dysfunction

Statins Affect Skeletal Muscle Performance: Evidence for Disturbances in Energy Metabolism

Unintended effects of statins in men and women in England and Wales: population based cohort study using the QResearch database

Effect of the Magnitude of Lipid Lowering on Risk of Elevated Liver Enzymes, Rhabdomyolysis, and Cancer

Insights From Large Randomized Statin Trials
Increased risk of diabetes with statin treatment is associated with impaired insulin sensitivity and insulin secretion: a 6 year follow-up study of the METSIM cohort

Henna Cederberg · Alena Stančáková · Nagendra Yaluri · Shalem Modi · Johanna Kuusisto · Markku Laakso

Conclusions/interpretation Statin treatment increased the risk of type 2 diabetes by 46%, attributable to decreases in insulin sensitivity and insulin secretion.

44% Increased Risk of Diabetes in People on Statins
Little if Any Evidence of an All-Cause Mortality Benefit

Statins and All-Cause Mortality in High-Risk Primary Prevention

A Meta-analysis of 11 Randomized Controlled Trials Involving 65 229 Participants

Kausik K. Ray, MD, MPhil, FACC, FESC; Sreenivasa Rao Kondapally Seshasai, MD, MPhil; Sebhat Erqou, MD, MPhil, PhD; Peter Sever, PhD, FRCP, FESC; J. Wouter Jukema, MD, PhD; Ian Ford, PhD; Naveed Sattar, FRCPa

Arch Intern Med. 2010;170(12):1024-1031

Data were available on 65 229 participants followed for approximately 244 000 person-years, during which 27 933 deaths occurred. The use of statins in this high-risk primary prevention setting was not associated with a statistically significant reduction (risk ratio, 0.91; 95% confidence interval, 0.83-1.01) in the risk of all-cause mortality.

**Conclusion:** This literature-based meta-analysis did not find evidence for the benefit of statin therapy on all-cause mortality in a high-risk primary prevention set-up.
1. Elevated Levels of Cholesterol, per se, are NOT Inherently Atherogenic (e.g., elderly with high cholesterol live longer)

2. Deceptive Practices (Use of Relative Risk) Have Created the Appearance of Statins as “Wonder Drugs”

3. The small benefits of statins are Offset by their Adverse Effects
If Not Cholesterol What Causes CVD?

Genetic Determinants of Cardiovascular Disease Risk in Familial Hypercholesterolemia

Angelique C.M. Jansen, Emily S. van Aalst-Cohen, Michael W.T. Tanck, Suzanne Cheng, Marcel R. Fontecha, Jia Li, Joep C. Defesche, John J.P. Kastelein

*Arterioscler Thromb Vasc Biol. 2005*
Link of FH to CVD Through Gene Polymorphism that Increases Coagulation

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Arterioscler Thromb Vasc Biol. 2005
Activation of Coagulation Factors and/or Reduced Fibrinolysis Linked to Risk Factors for CVD

- Smoking
- Advanced Age
- Psychological Stress
- Bacterial Infection
- Inflammation
- Hypertension
- Obesity/Metabolic Syndrome
- High Blood Glucose
  T2 Diabetes
- Subset of Familial Hypercholesterolemia

Clot Formation and Degradation
My Decade-Long Journey To Treat My “Dyslipidemia” With LCD
A Tale of Deception and Enlightenment

Fasting Triglycerides, High-Density Lipoprotein, and Risk of Myocardial Infarction

J. Michael Gaziano, MD, MPH; Charles H. Hennekens, MD, DrPH; Christopher J. O’Donnell, MD, MPH; Jan L. Breslow, MD; Julie E. Buring, ScD

Circulation Vol 96, No 8 October 21, 1997

Relative Risk of MI

Low HDL

High HDL

Low TG

High TG
The Diet-Heart Hypothesis:
Dietary Saturated Fat → Increase in Serum Cholesterol → Cardiovascular Disease

There has been a continuing offensive against saturated fat and cholesterol
Supported by key opinion leaders sponsored by food and drug companies
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Dietary Saturated Fat → Increase in Serum Cholesterol → Cardiovascular Disease

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High levels of cholesterol (LDL-C) do not promote premature death, and are beneficial toward a reduced rate of morbidity and death from infection and cancer
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Despite praise from pharma-supported researchers, cholesterol reduction produces miniscule benefits with offsetting adverse side effects
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Despite praise from pharma-supported researchers, cholesterol reduction produces miniscule benefits with offsetting adverse side effects

The primary target for CVD protection should be hypercoagulation, preferably through optimizing diet and lifestyle
THANK YOU for your ATTENTION!