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

David Diamond, Ph.D.

Departments of Psychology, Molecular Pharmacology and Physiology
USF Neuroscience Collaborative
University of South Florida
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

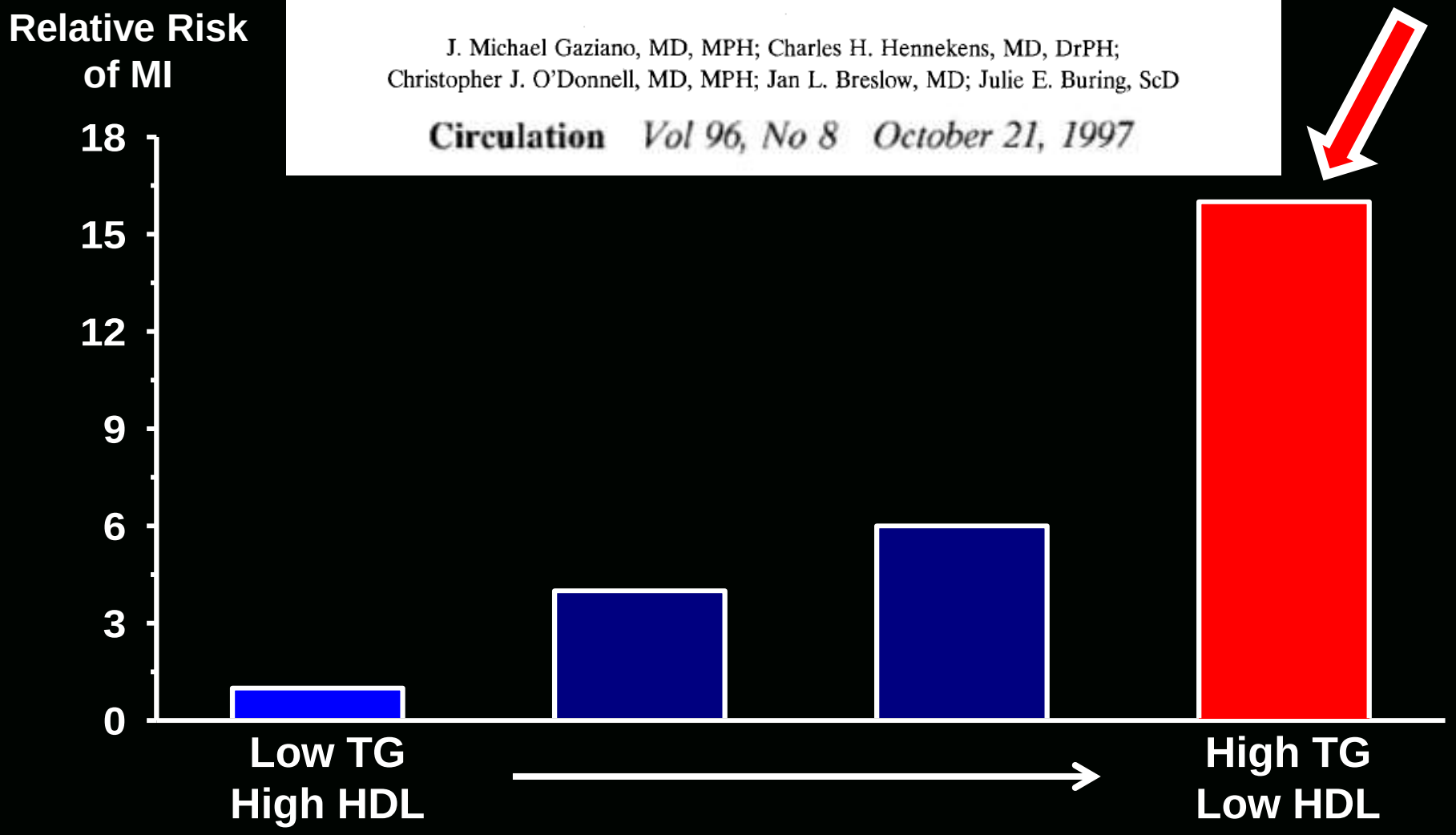
Departments o… …d Physiology

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*



Diet Doctor | Low carb & keto | Recipes | Health | Lose weight

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*
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Barry Groves*
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Carbohydrate Restriction as the FIRST approach in Diabetes Management

Critical Review

Nutrition 31 (2015) 1–13

Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base

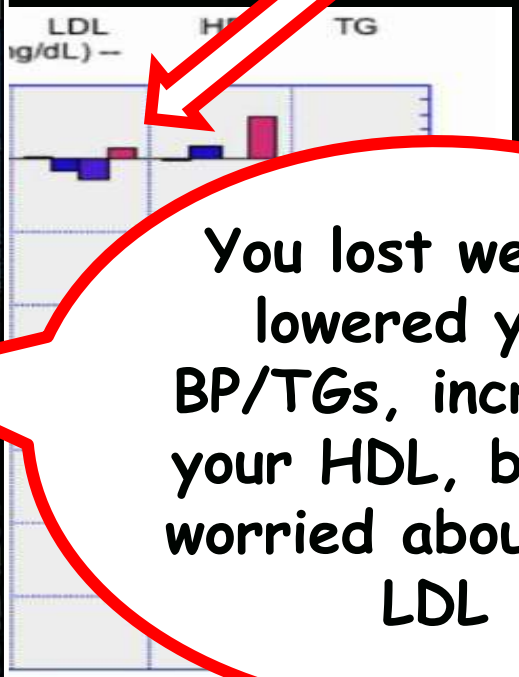
Richard D. Feinman Ph.D. [a,*], Wendy K. Pogozelski Ph.D. [b], Arne Astrup M.D. [c], Richard K. Bernstein M.D. [d], Eugene J. Fine M.S., M.D. [e], Eric C. Westman M.D., M.H.S. [f], Anthony Accurso M.D. [g], Lynda Frassetto M.D. [h], Barbara A. Gower Ph.D. [i], Samy I. McFarlane M.D. [j], Jörgen Vesti Nielsen M.D. [k], Thure Krarup M.D. [l], Laura Saslow Ph.D. [m], Karl S. Roth M.D. [n], Mary C. Vernon M.D. [o], Jeff S. Volek R.D., Ph.D. [p], Gilbert B. Wilshire M.D. [q], Annika Dahlqvist M.D. [r], Ralf Sundberg M.D., Ph.D. [s], Ann Childers M.D. [t], Katharine Morrison M.R.C.G.P. [u], Anssi H. Manninen M.H.S. [v], Hussain M. Dashti M.D., Ph.D., F.A.C.S., F.I.C.S. [w], Richard J. Wood Ph.D. [x], Jay Wortman M.D. [y], Nicolai Worm Ph.D. [z]

The Elephant in the Conference Room: Even a Small Increase in LDL (Bad Cholesterol) Increases One's Risk of a Heart Attack

Critical Review Nutrition 31 (2015) 1–13

Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base

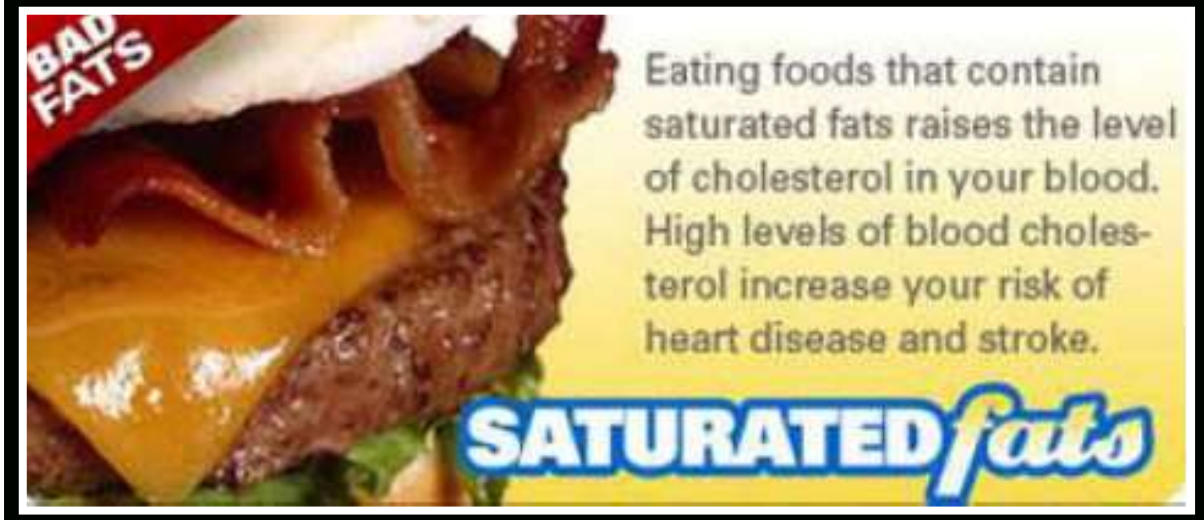
Richard D. Feinman Ph.D. [a,*], Wendy K. Pogozelski Ph.D. [b], Arne Astrup M.D. [c], Richard K. Bernstein M.D. [d], Eugene J. Fine M.S., M.D. [e], Eric C. Westman M.D., M.H.S. [f], Anthony Accurso M.D. [g], Lynda Frassetto M.D. [h], Barbara A. Gower Ph.D. [i], Samy I. McFarlane M.D. [j], Jörgen Vesti Nielsen M.D. [k], Thure Krarup M.D. [l], Laura Saslow Ph.D. [m], Karl S. Roth M.D. [n], Mary C. Vernon M.D. [o], Jeff S. Volek R.D., Ph.D. [p], Gilbert B. Wilshire M.D. [q], Annika Dahlqvist M.D. [r], Ralf Sundberg M.D., Ph.D. [s], Ann Childers M.D. [t], Katharine Morrison M.R.C.G.P. [u], Anssi H. Manninen M.H.S. [v], Hussain M. Dashti M.D., Ph.D., F.A.C.S., F.I.C.S. [w], Richard J. Wood Ph.D. [x], Jay Wortman M.D. [y], Nicolai Worm Ph.D. [z]



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

American Heart Association.



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

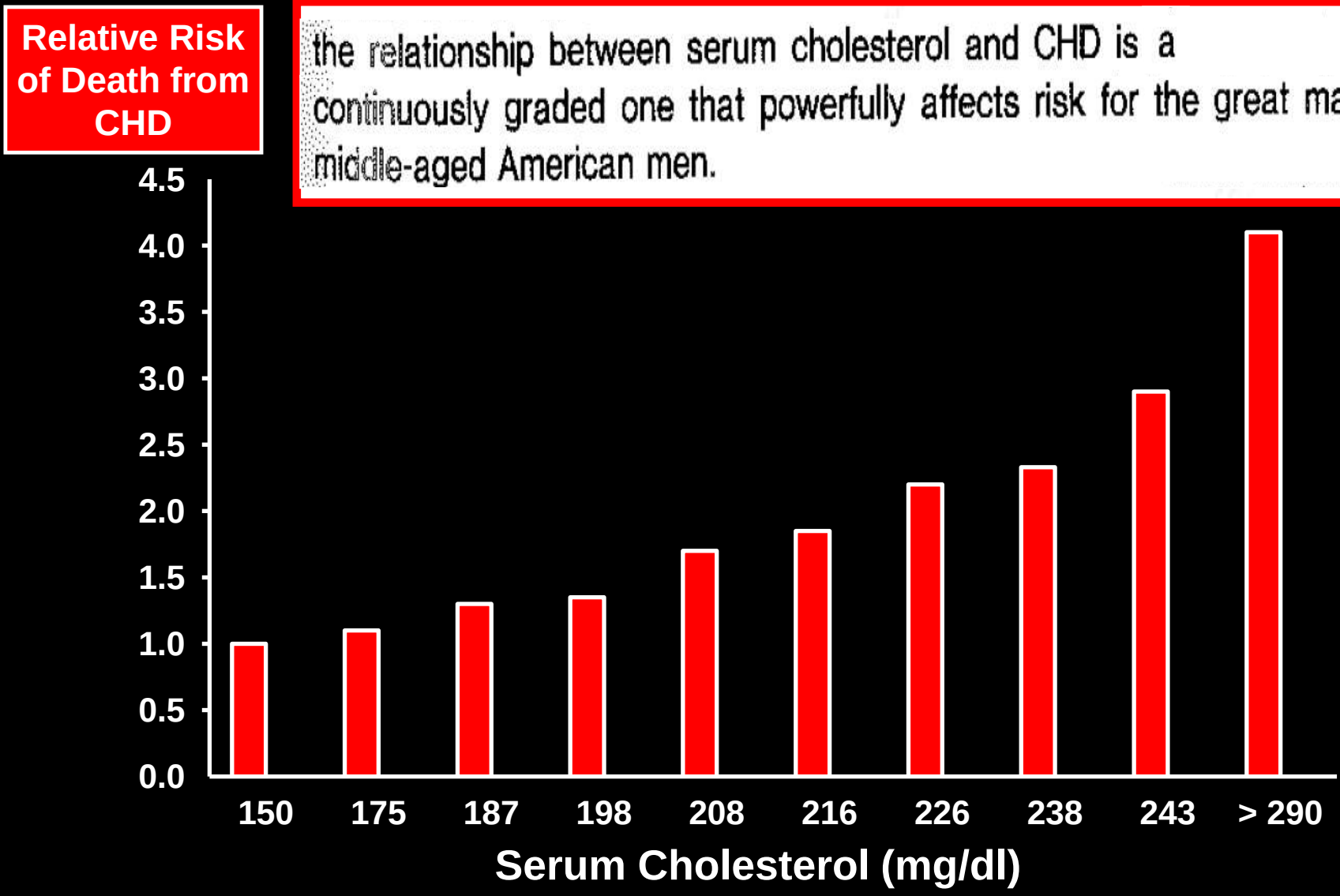
demonstrates unequivocally the causal relation between an elevated circulating LDL level and atherosclerosis.

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

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.



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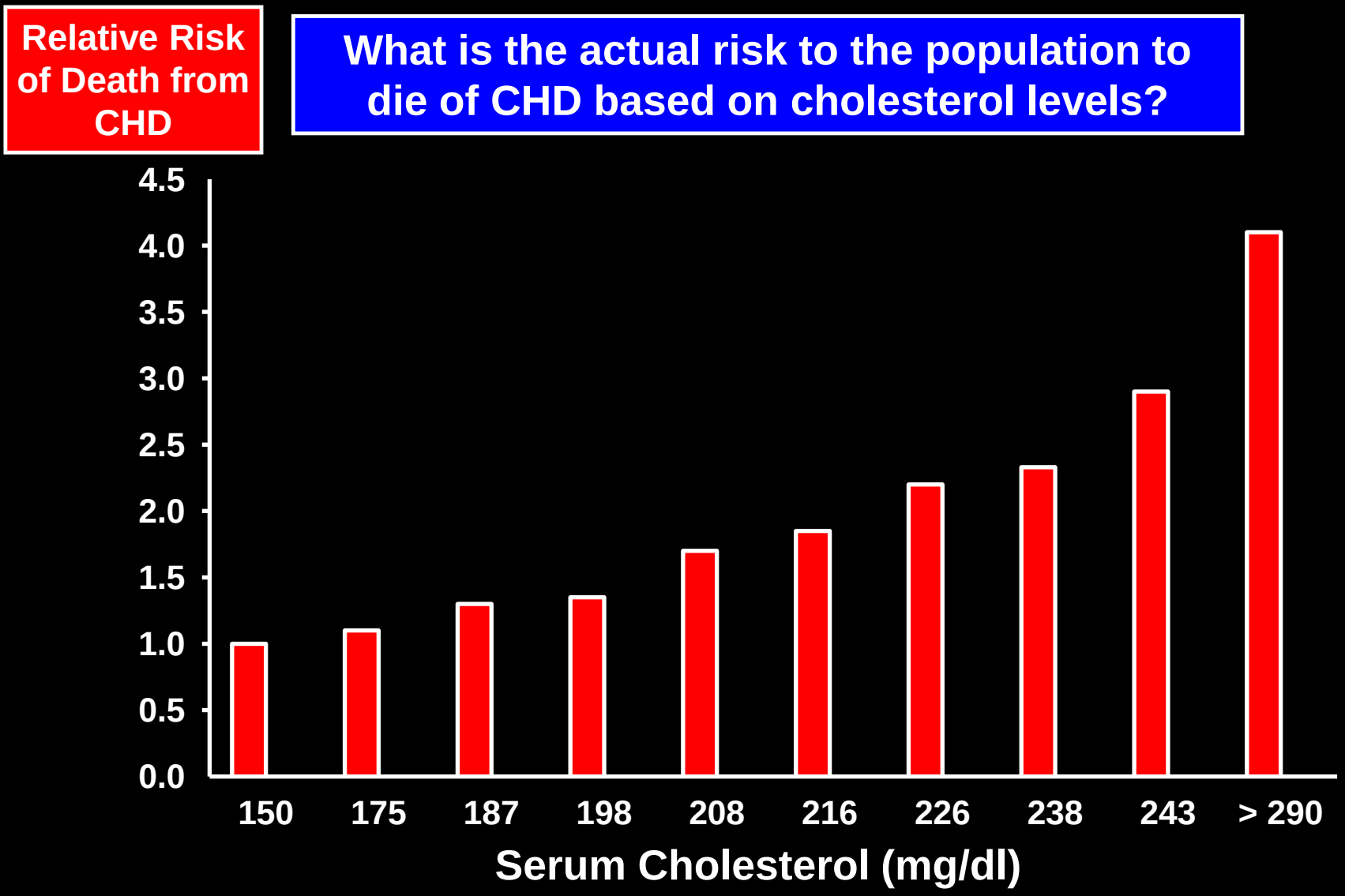
What is the actual risk to the population to die of CHD based on cholesterol levels?



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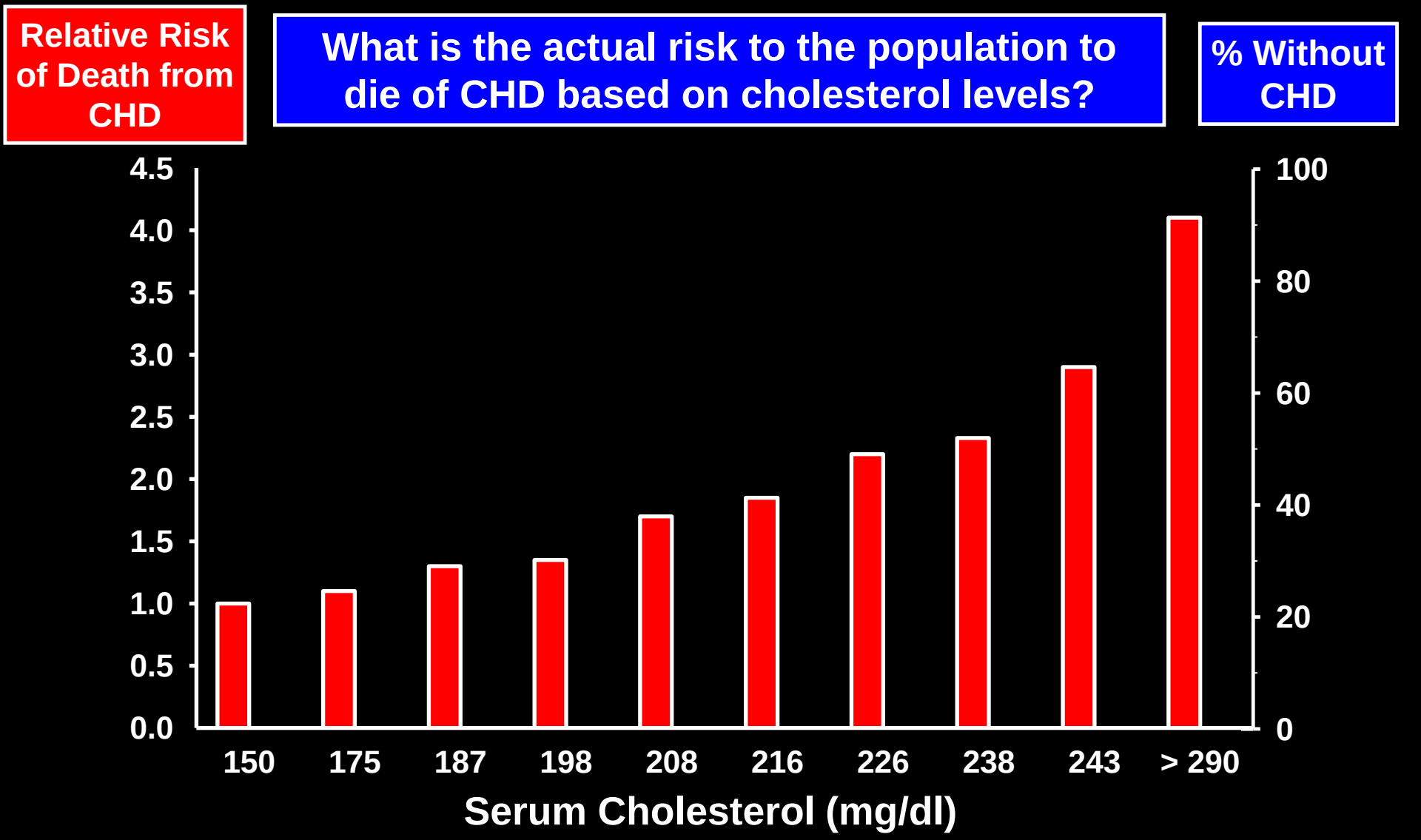

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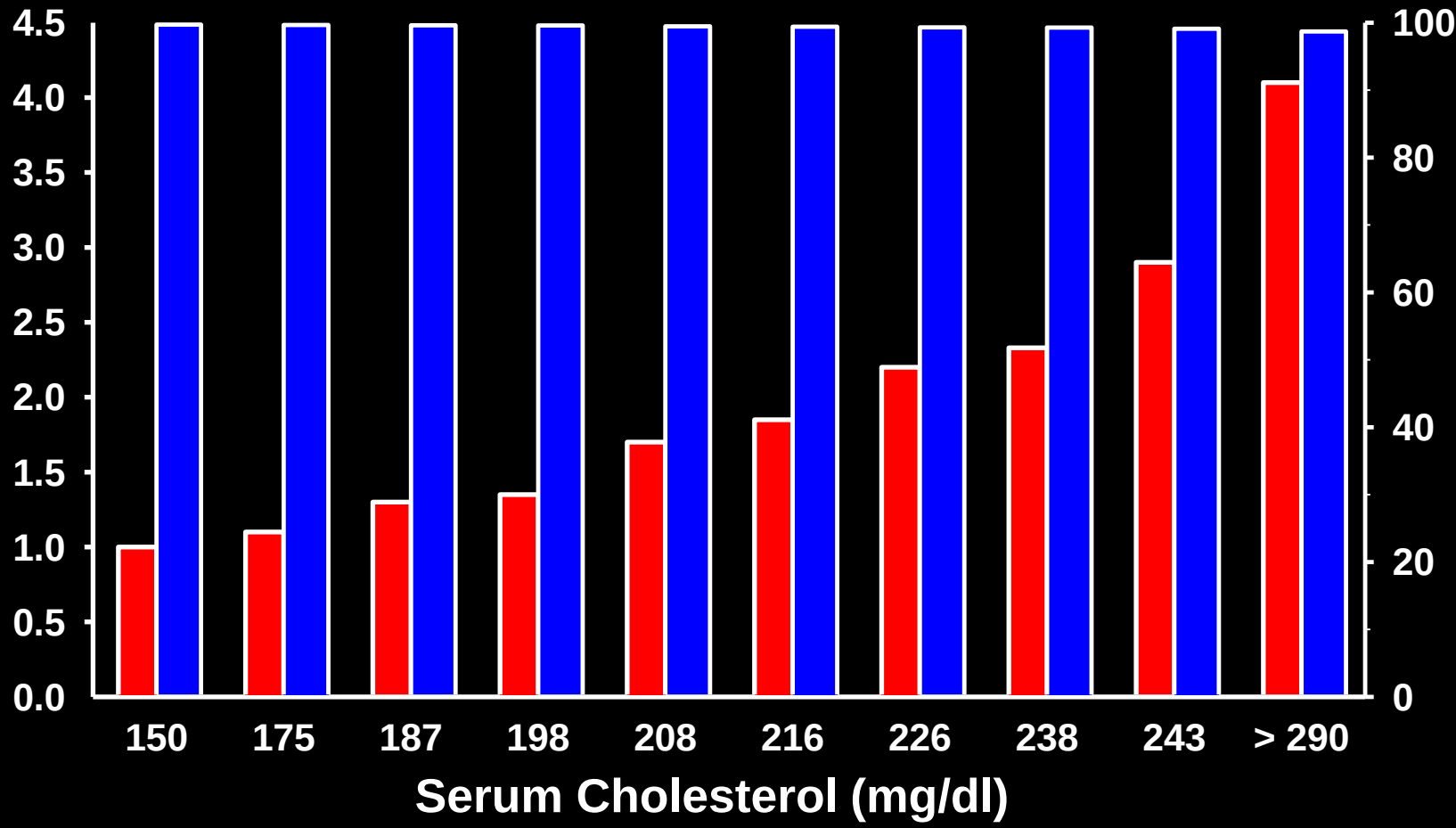
Relative Risk of Death from CHD

What is the actual risk to the population to die of CHD based on cholesterol levels?

% Without CHD



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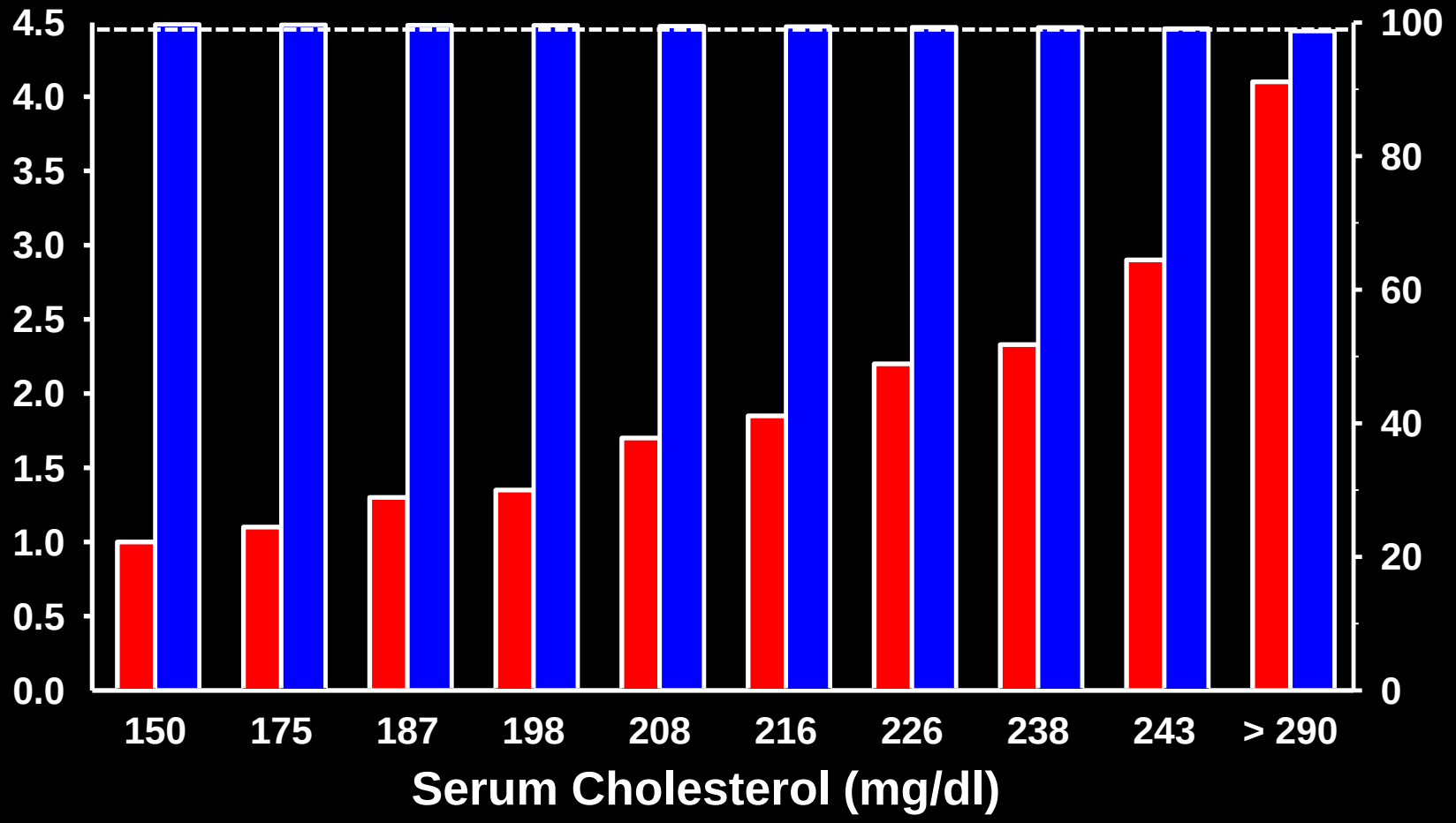

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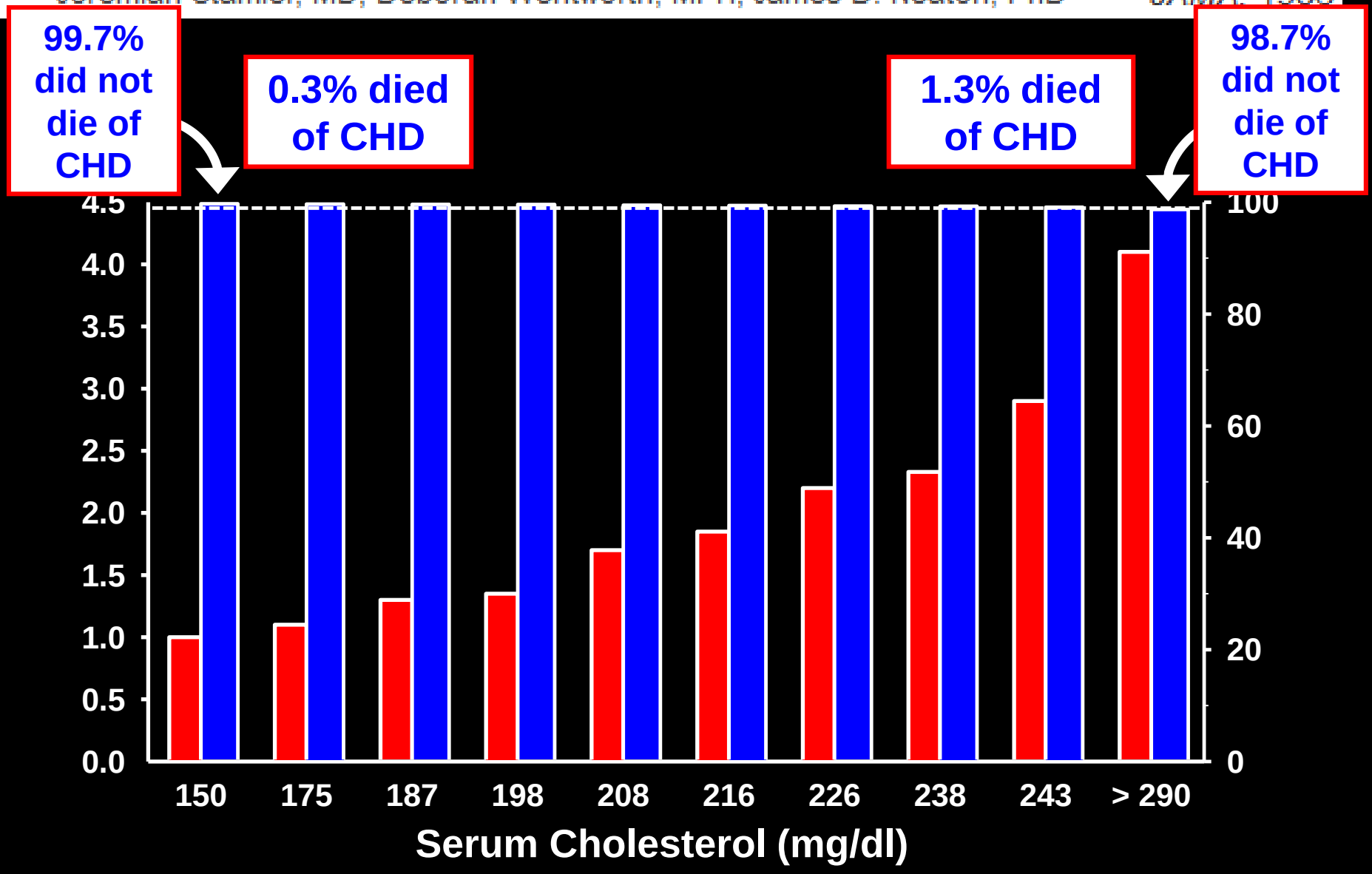

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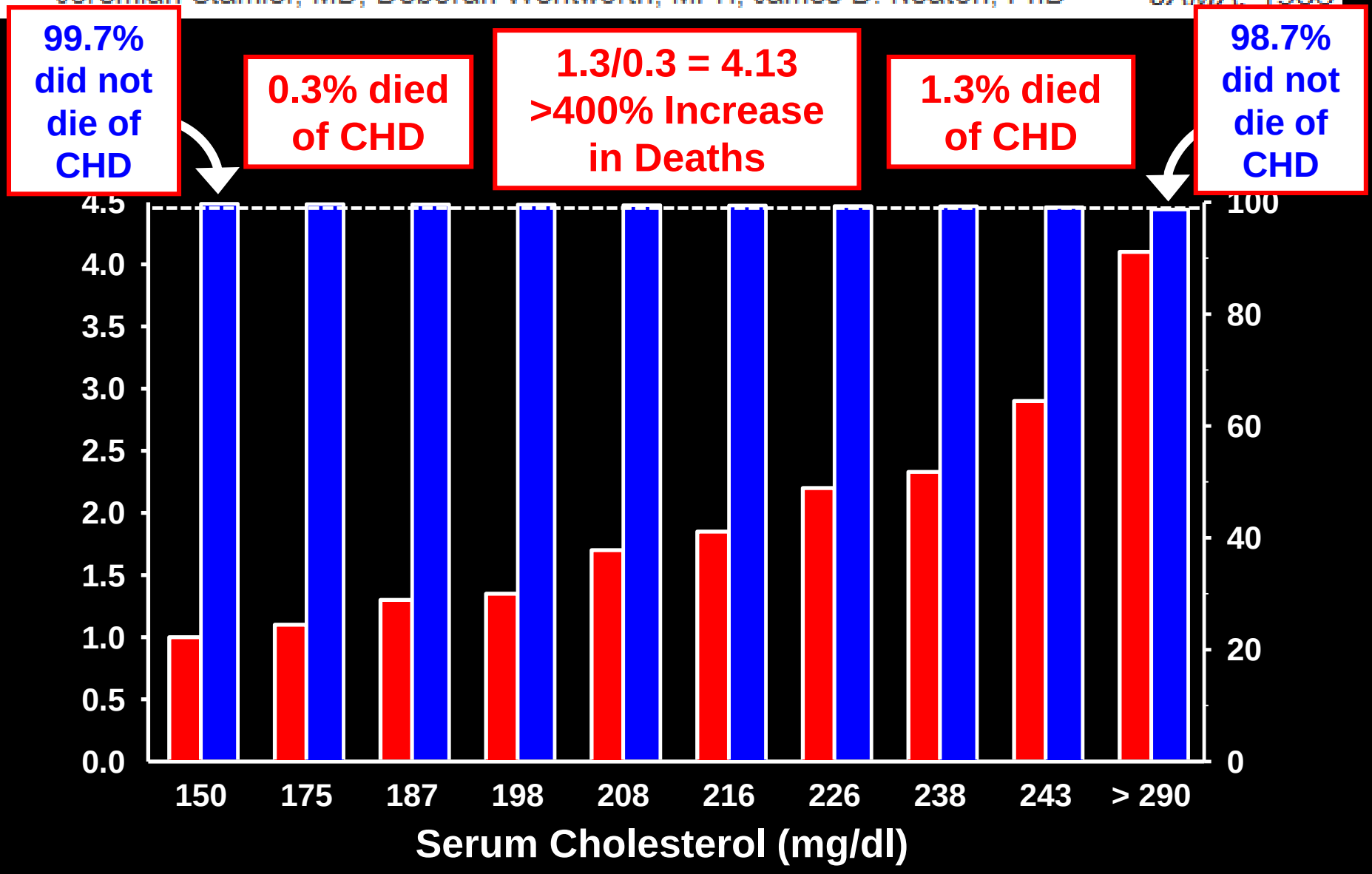
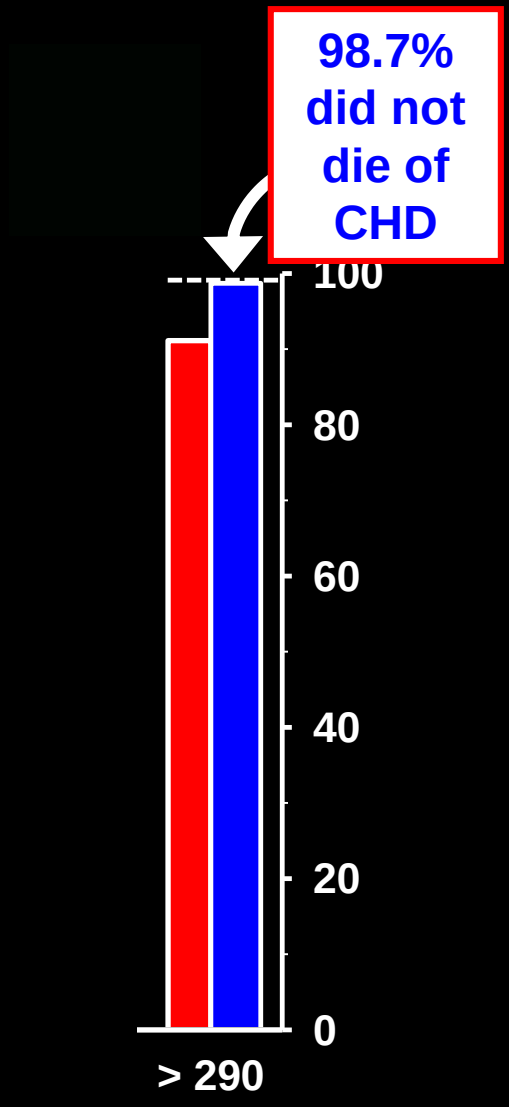


Fear of the Highest Cholesterol – Justified?



Familial Hypercholesterolemia: An Inevitable Early Coronary Death Sentence?

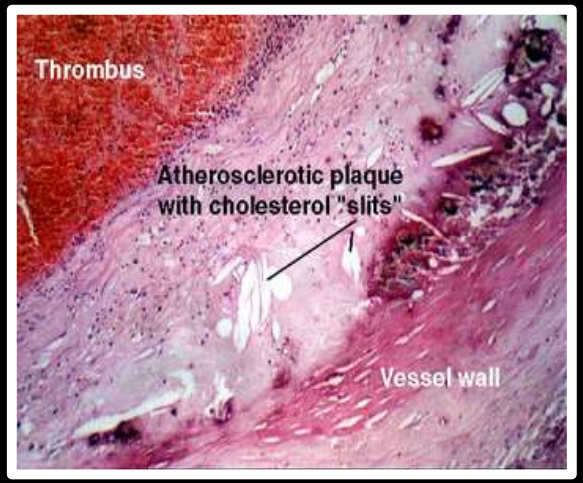
Hypercholesteremia with Predisposition to Atherosclerosis*

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

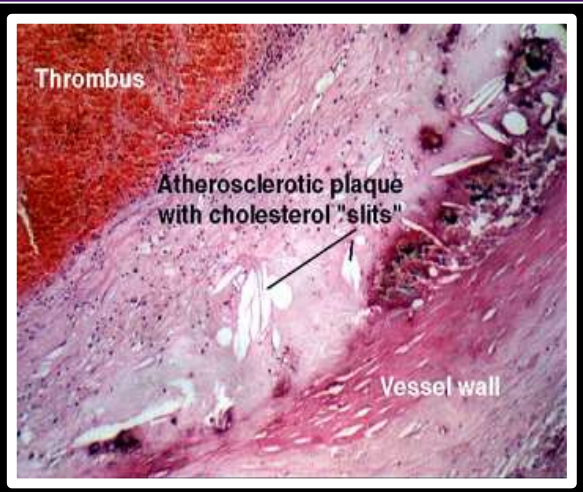
Hypercholesteremia with Predisposition to Atherosclerosis*

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



No Overall Adverse Effect of High Cholesterol on Longevity
Normal Lifespan In People With Familial Hypercholesterolemia

FAMILIAL HYPERCHOLESTEROLEMIA: A GENETIC AND METABOLIC STUDY[1]

WILLIAM R. HARLAN, JR.,[2] JOHN B. GRAHAM,[3] AND E. HARVEY ESTES[4]

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.

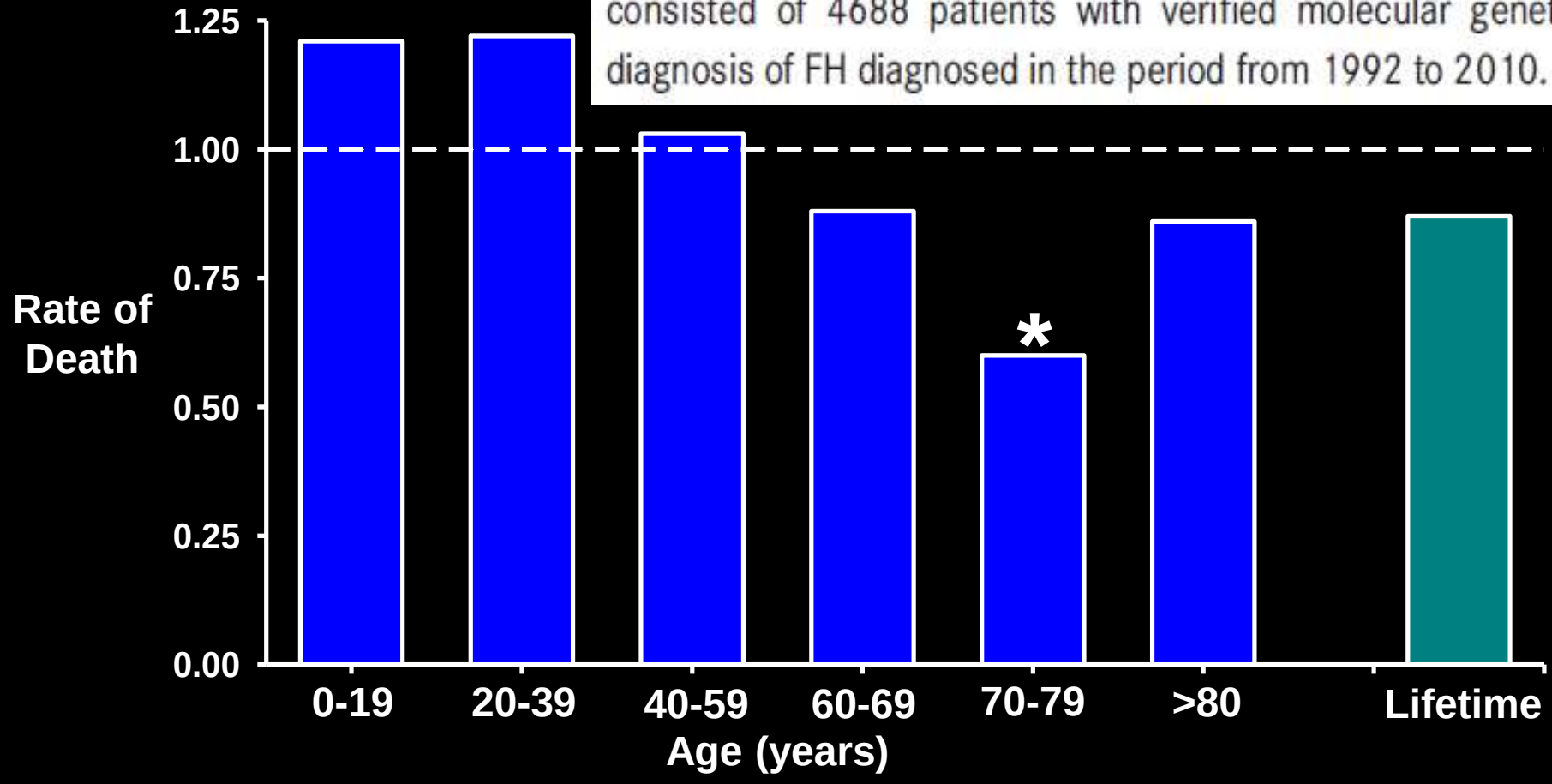
No Overall Adverse Effect of High Cholesterol on Longevity
Normal Lifespan In People With Familial Hypercholesterolemia

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

J Am Heart Assoc. 2014

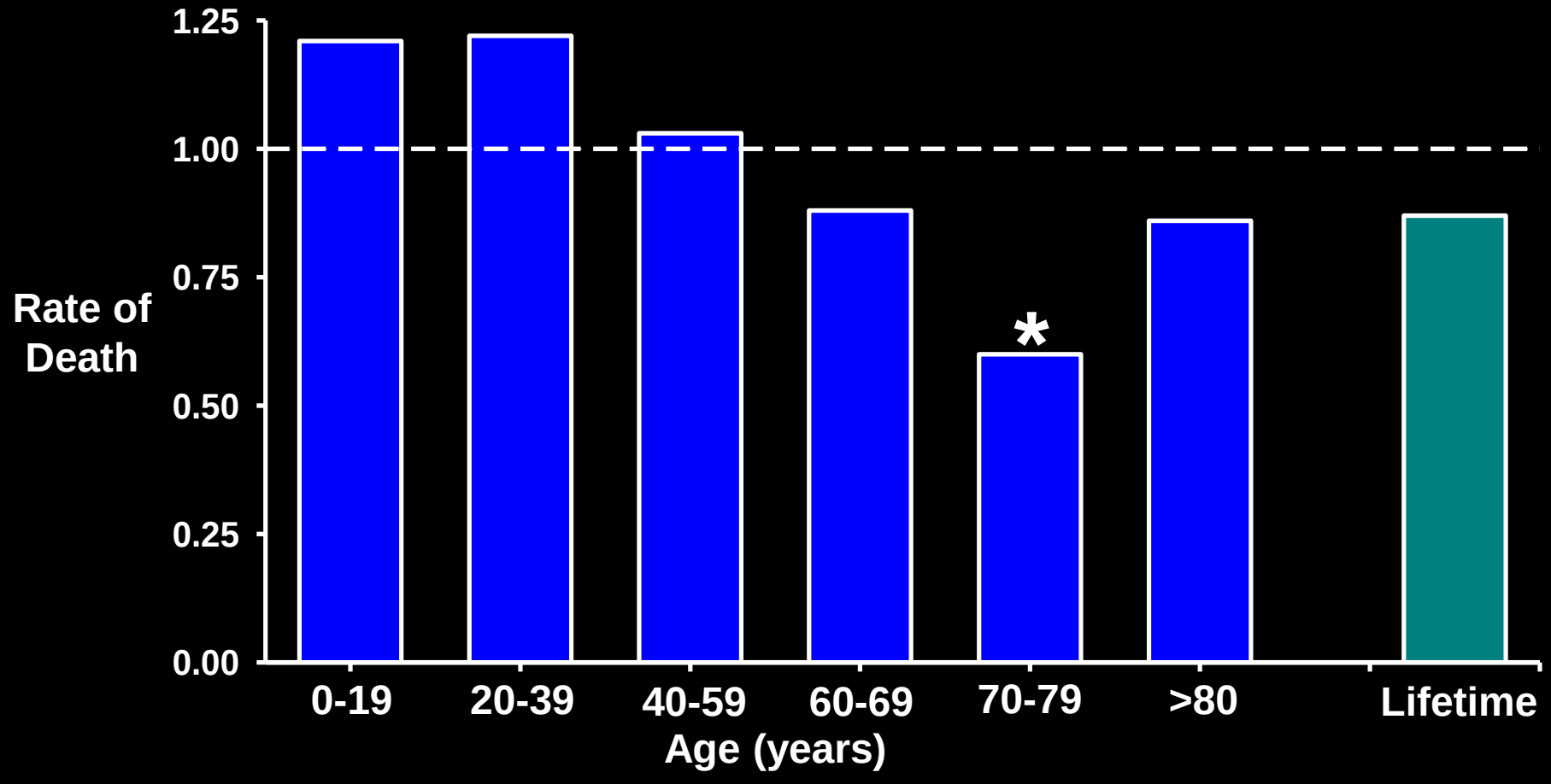
Liv Mundal, MD; Mirza Sarancic, MSc; Leiv Ose, MD, PhD; Per Ole Iversen, MD, PhD; Jens-Kristian Borgan, MSc; Marit B. Veierød, PhD; Trond P. Leren, MD, PhD; Kjetil Retterstøl, MD, PhD

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

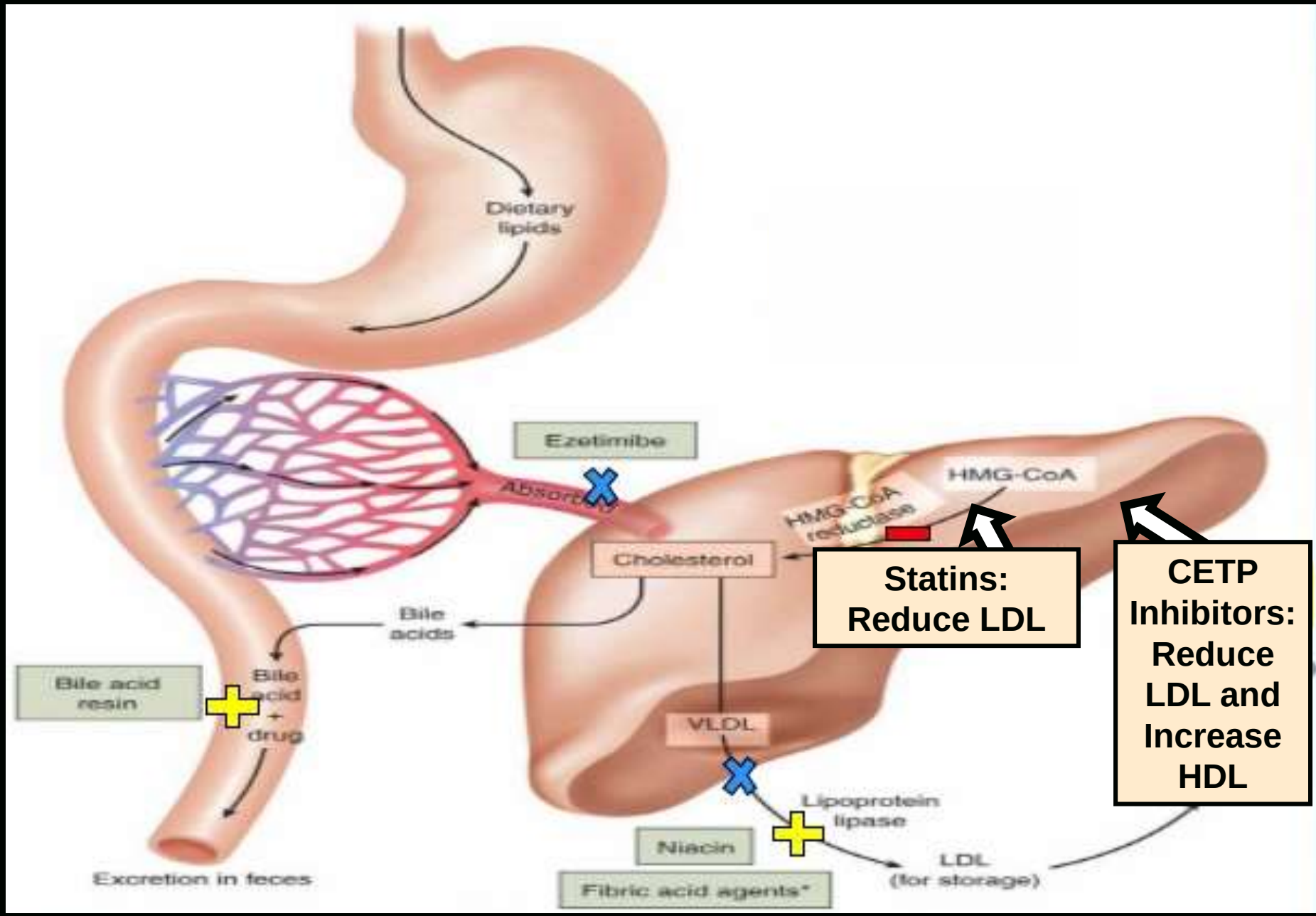
Lack of an association or an inverse association between low-density-lipoprotein cholesterol and mortality in the elderly: a systematic review

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 Sundberg[16]

BMJ Open 2016

. 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?



2 Decades of Failure: No CVD Benefit to Pharmacological Increase of HDL and Reduction of LDL with CETP Inhibitors

Dashing Hopes, Study Shows a Cholesterol Drug Had No Effect on Heart Health

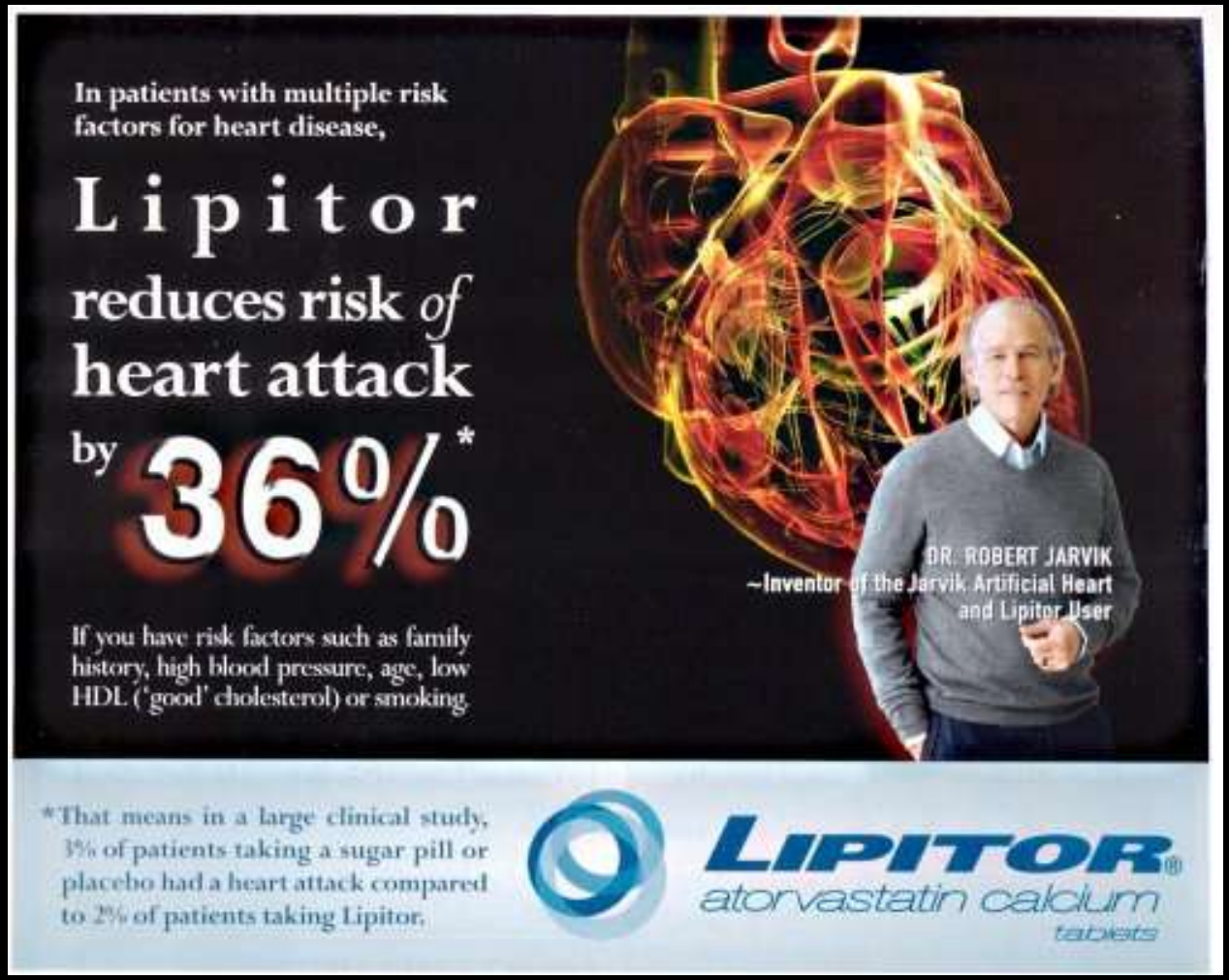
APRIL 3, 2016

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!



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

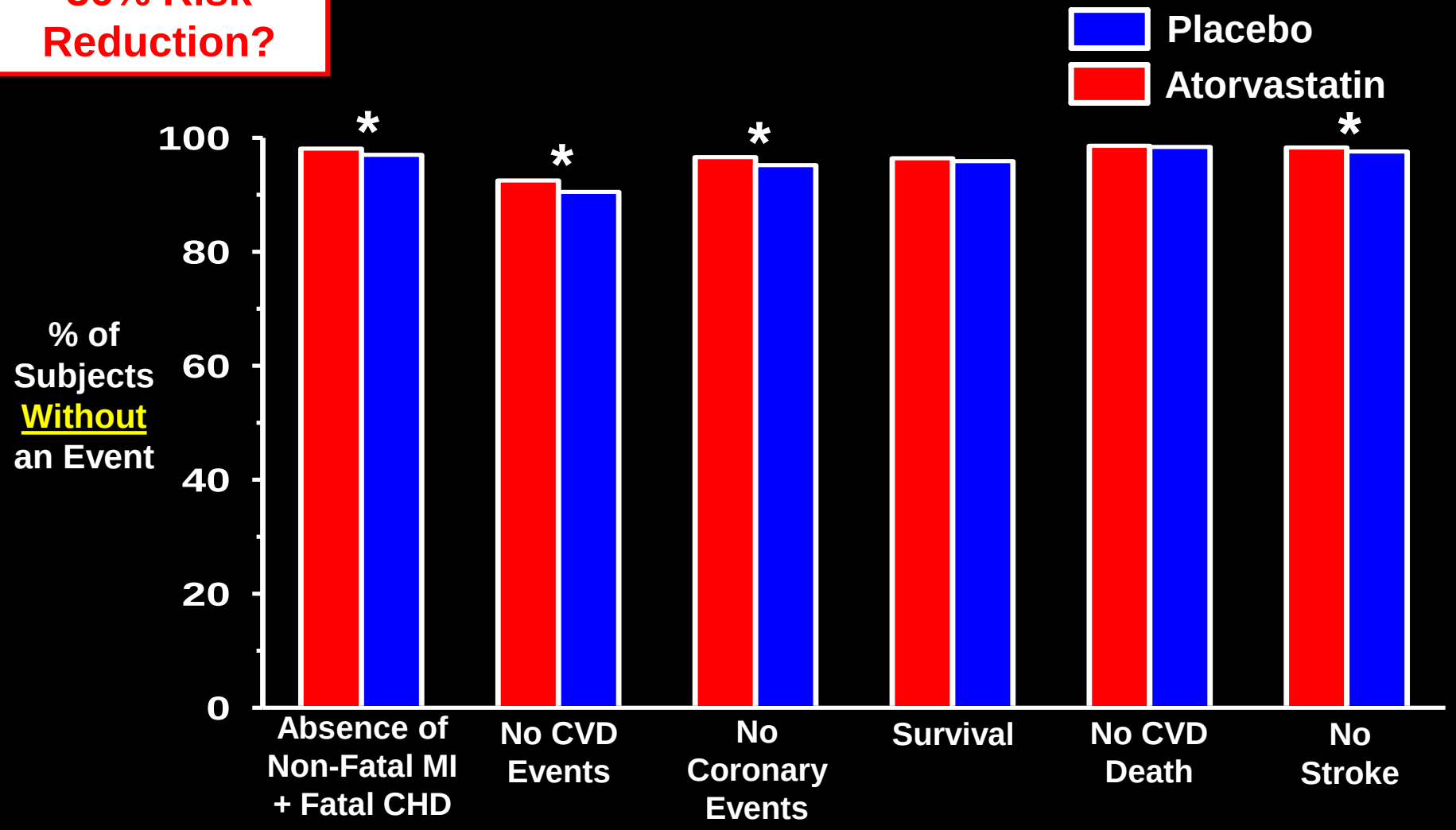
Discussion

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?



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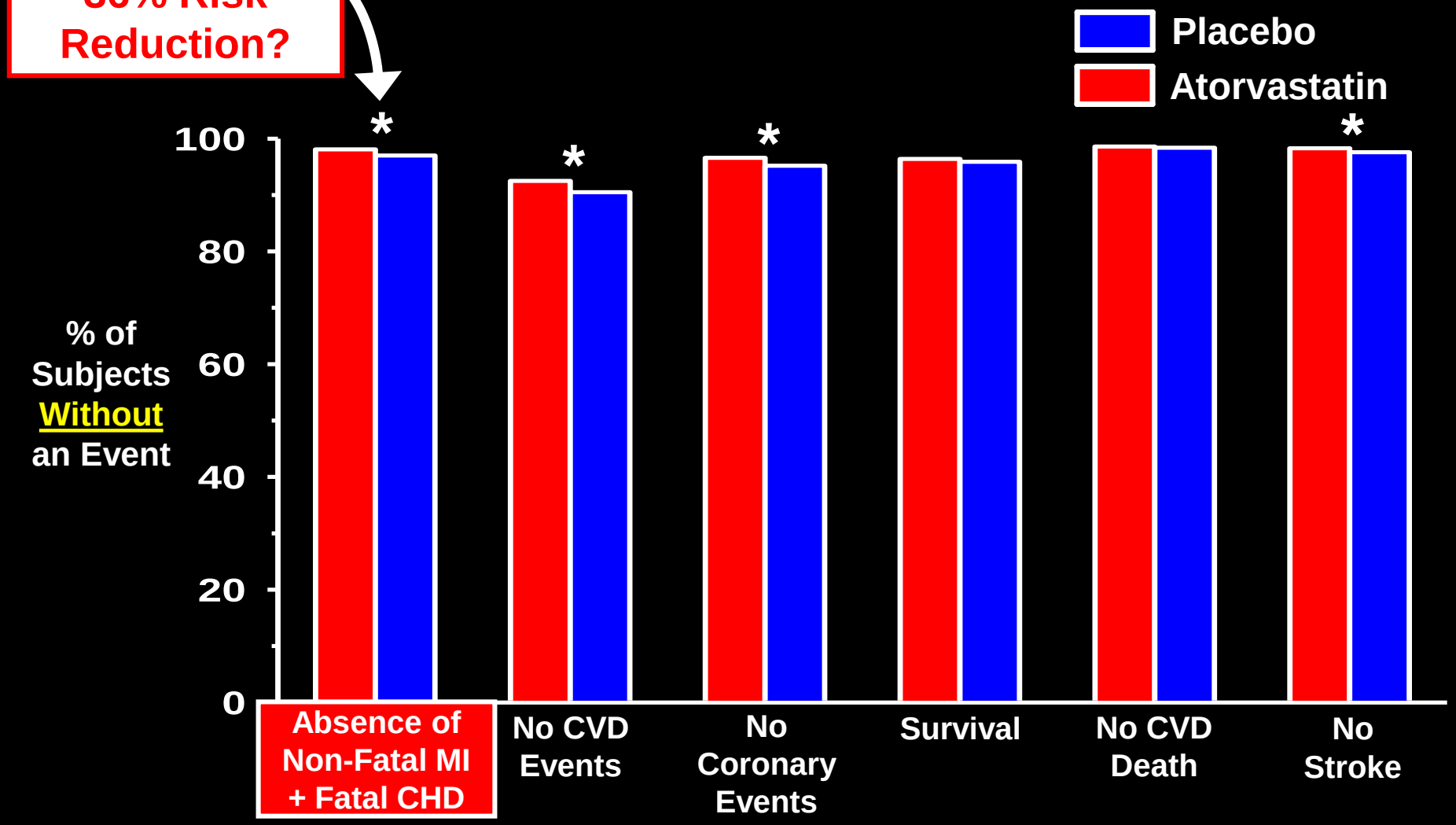
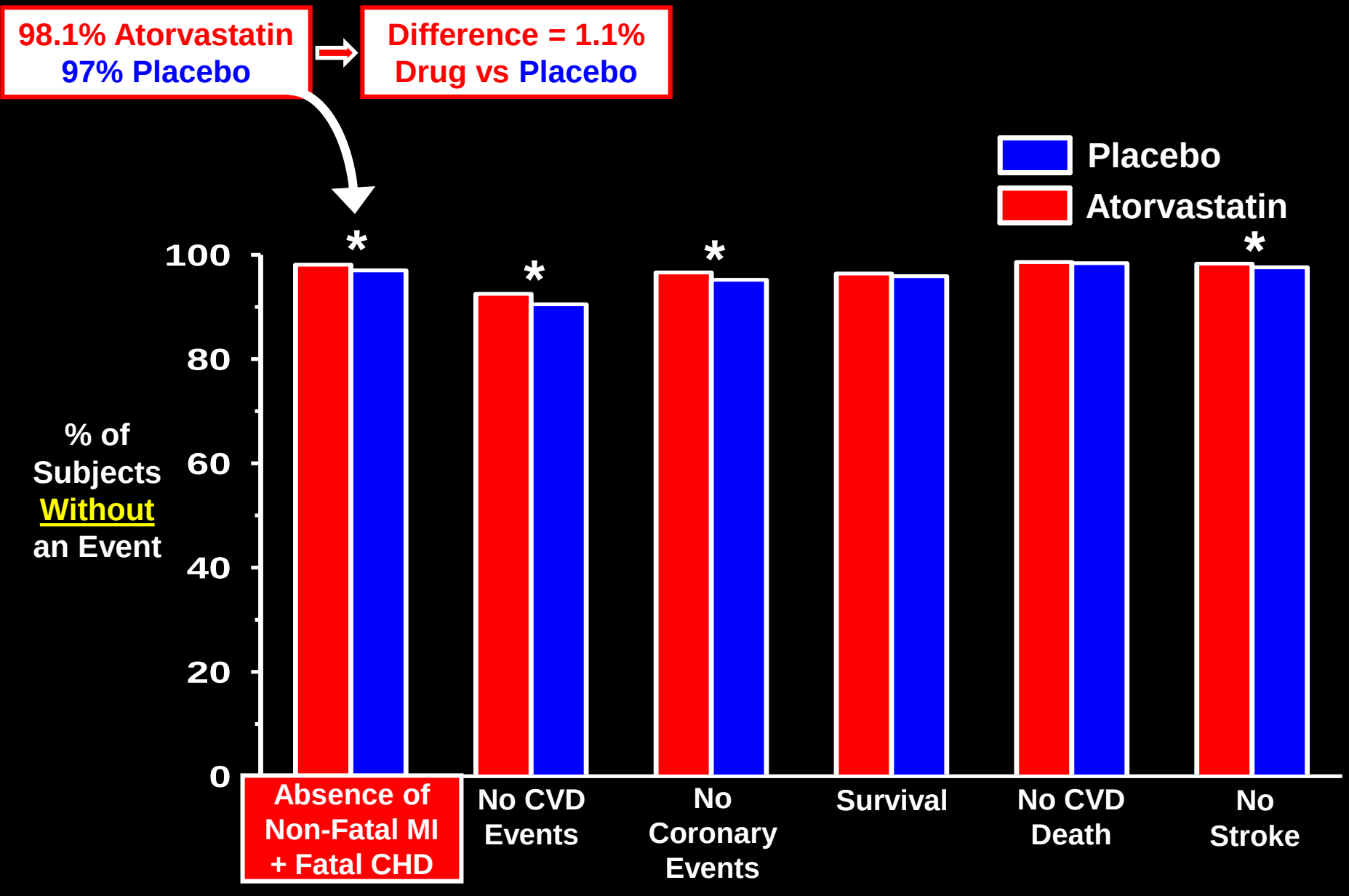
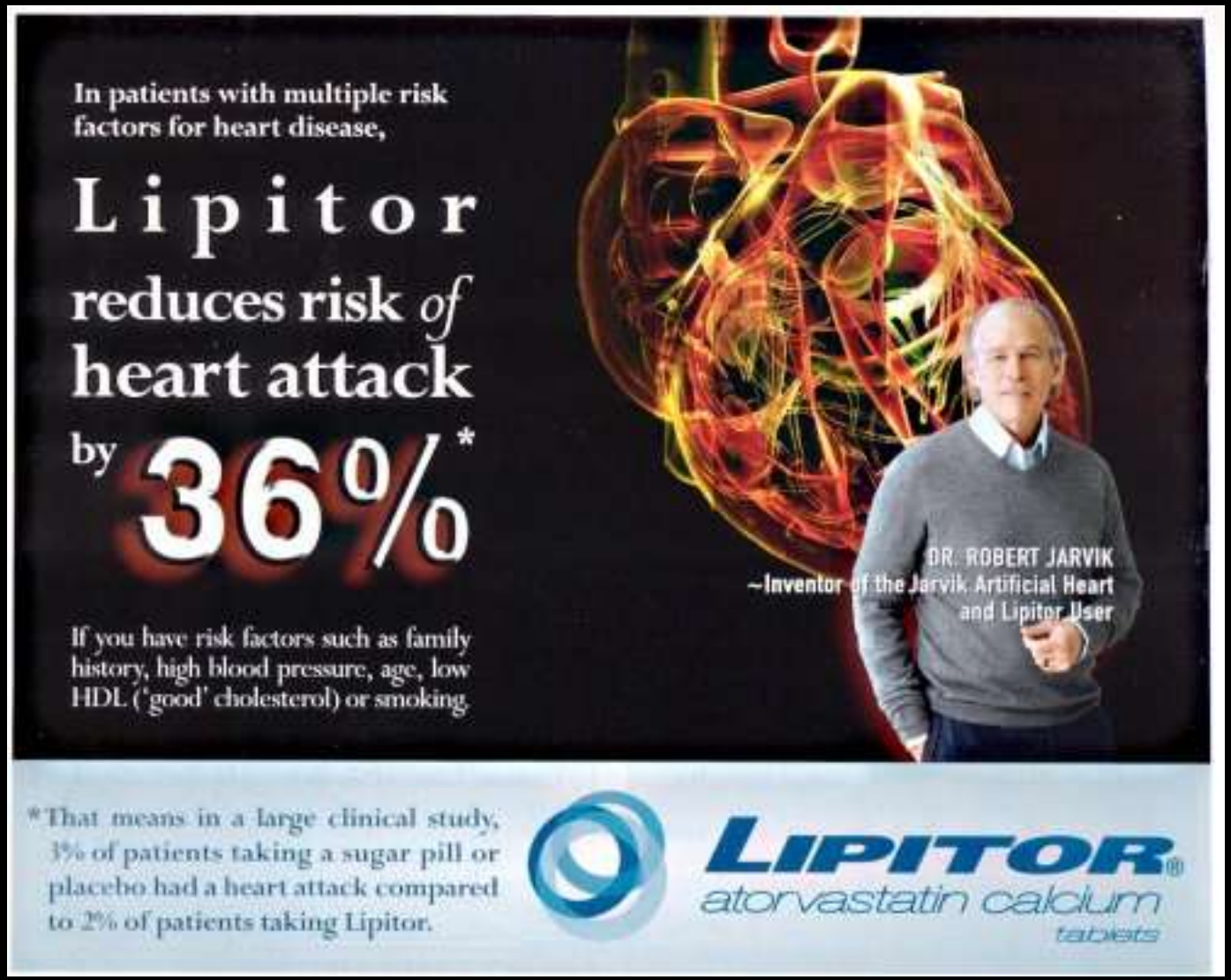


The Actual Difference in Treated (Atorvastatin) versus Untreated (Placebo) Groups is About 1%



How Can the Effect be 1.1% as well as 36%?

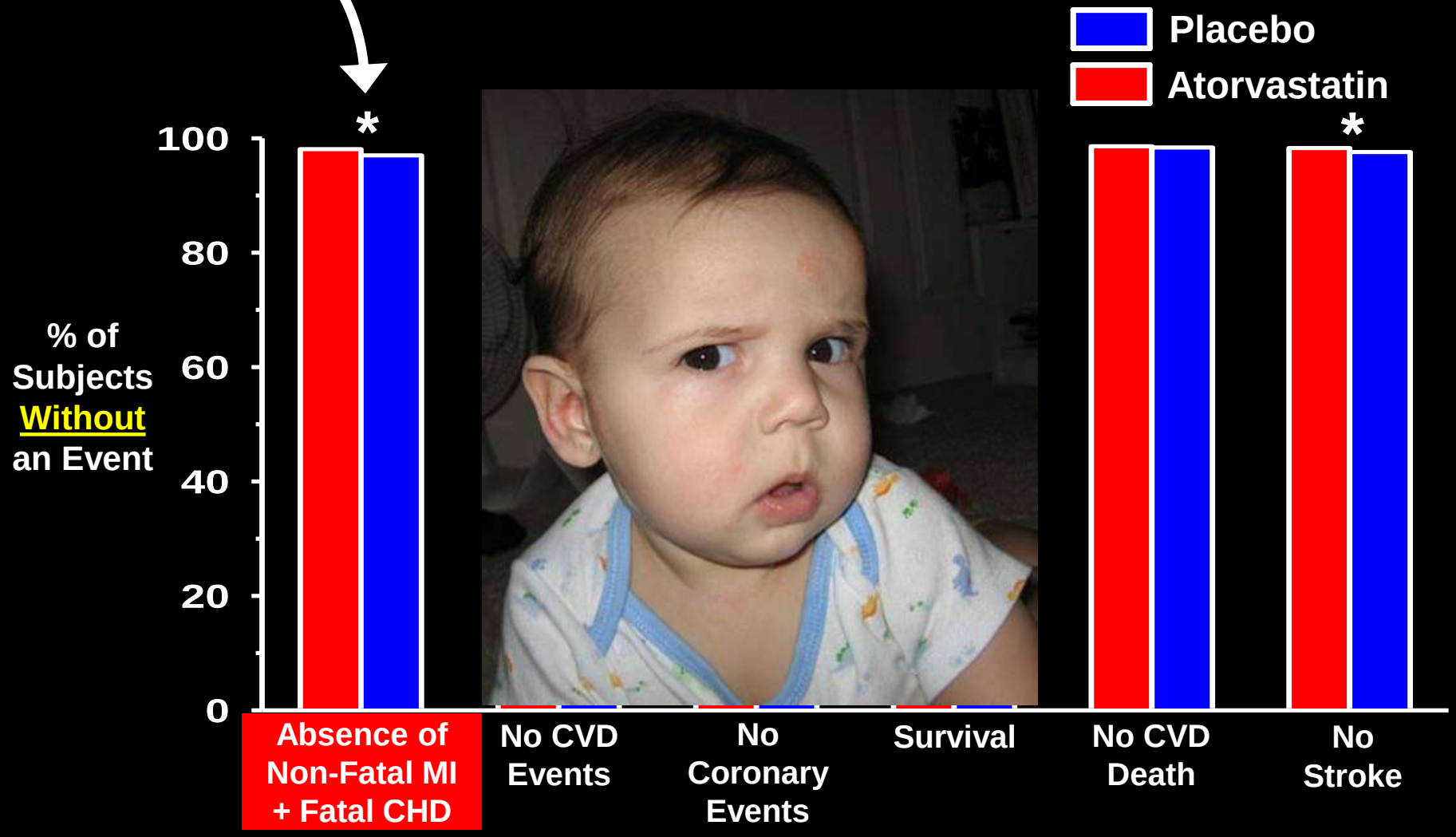
(read the fine print)



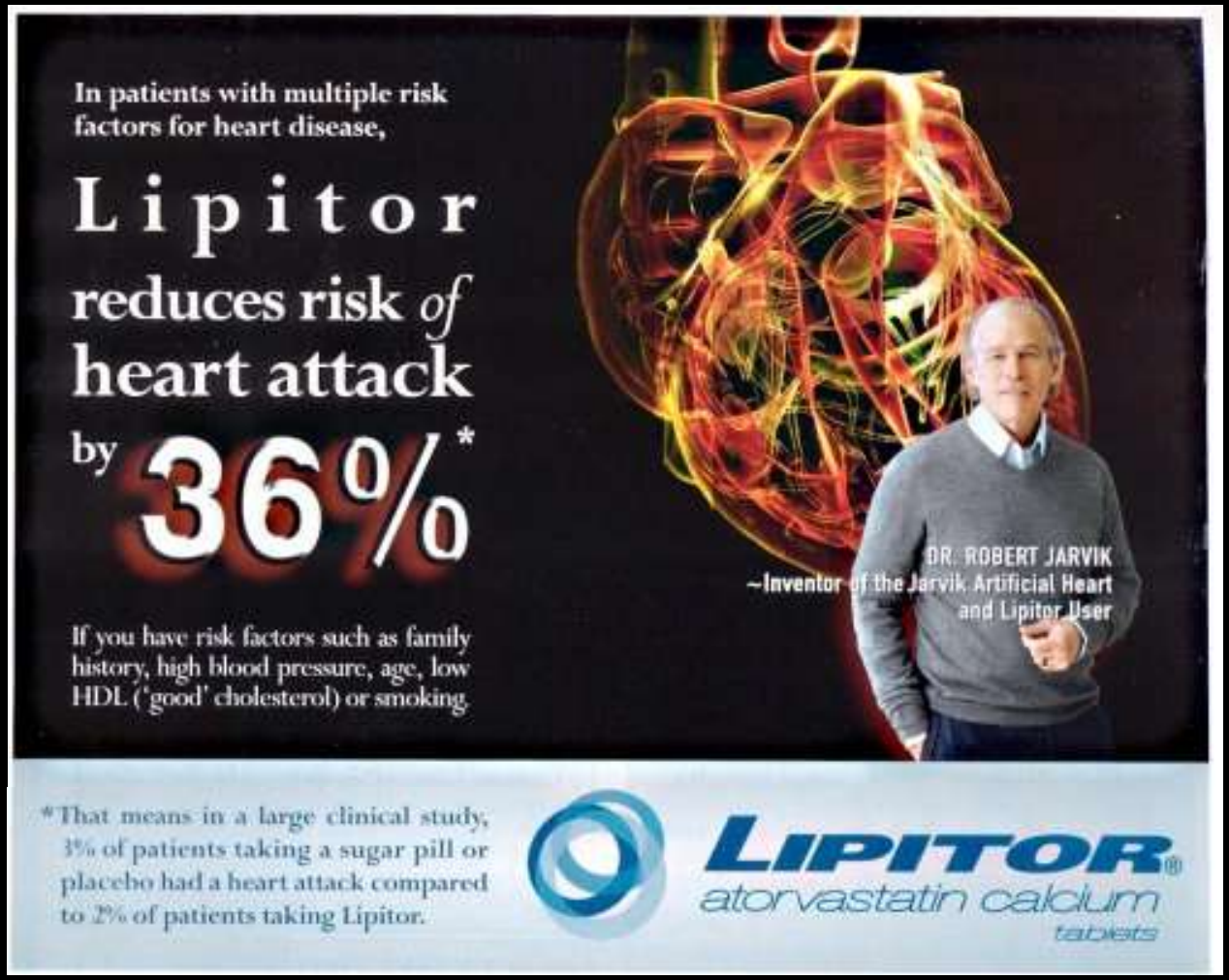
98.1% Atorvastatin
97% Placebo

Difference = 1.1%
Drug vs Placebo

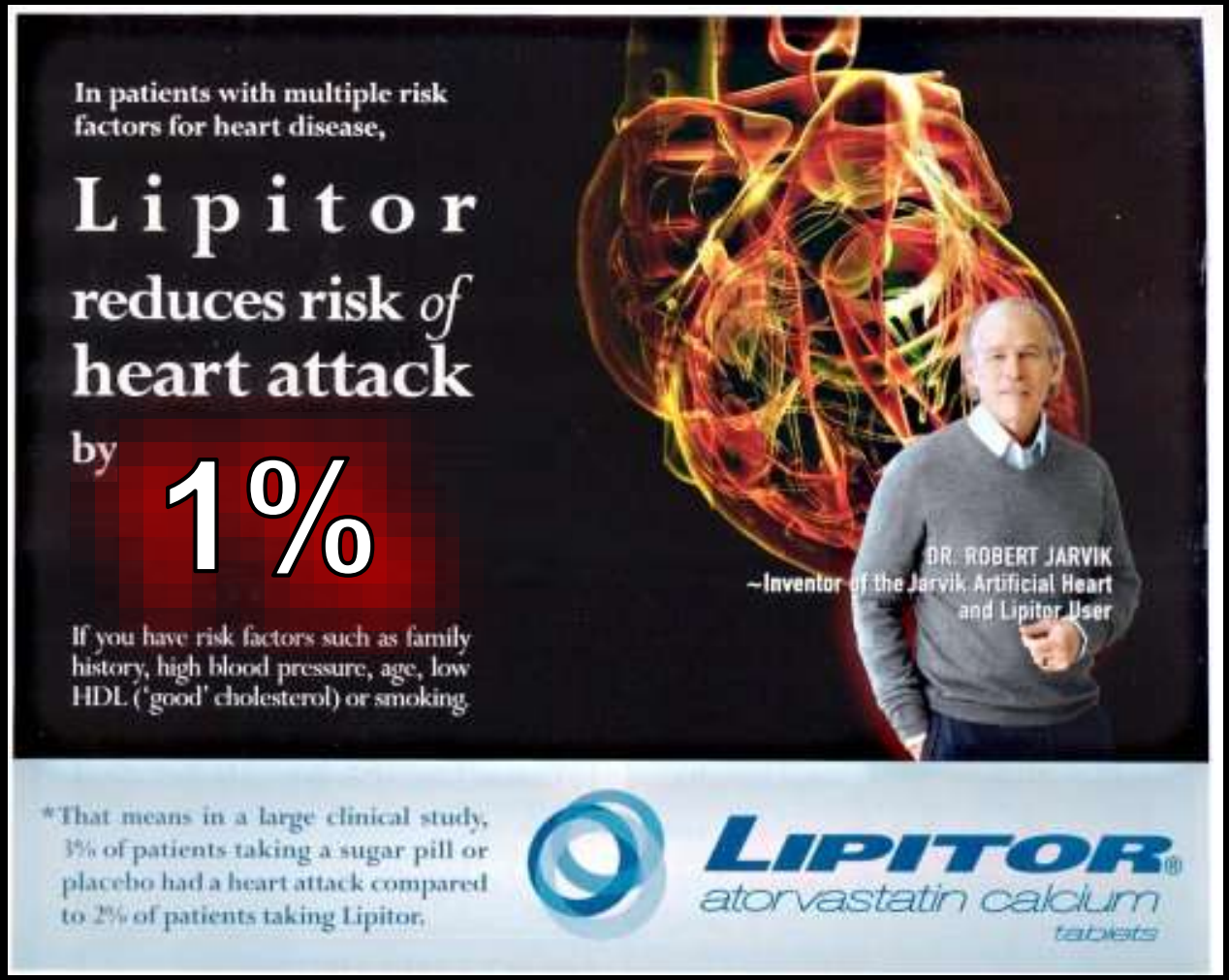
1.1% : 3% = 36%



Under ideal Conditions only 1/100 patients will Benefit



Statins Lose Their Appeal When the Real Effectiveness Data is Shown



JUPITER Study – Crestor

Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein

Paul M Ridker, M.D., Eleanor Danielson, M.I.A., Francisco A.H. Fonseca, M.D., Jacques Genest, M.D., Antonio M. Gotto, Jr., M.D., John J.P. Kastelein, M.D., Wolfgang Koenig, M.D., Peter Libby, M.D., Alberto J. Lorenzatti, M.D., Jean G. MacFadyen, B.A., Børge G. Nordestgaard, M.D., James Shepherd, M.D., James T. Willerson, M.D., and Robert J. Glynn, Sc.D., for the JUPITER Study Group*

N Engl J Med 2008;359:2195-207.

Special Issue
Forbes

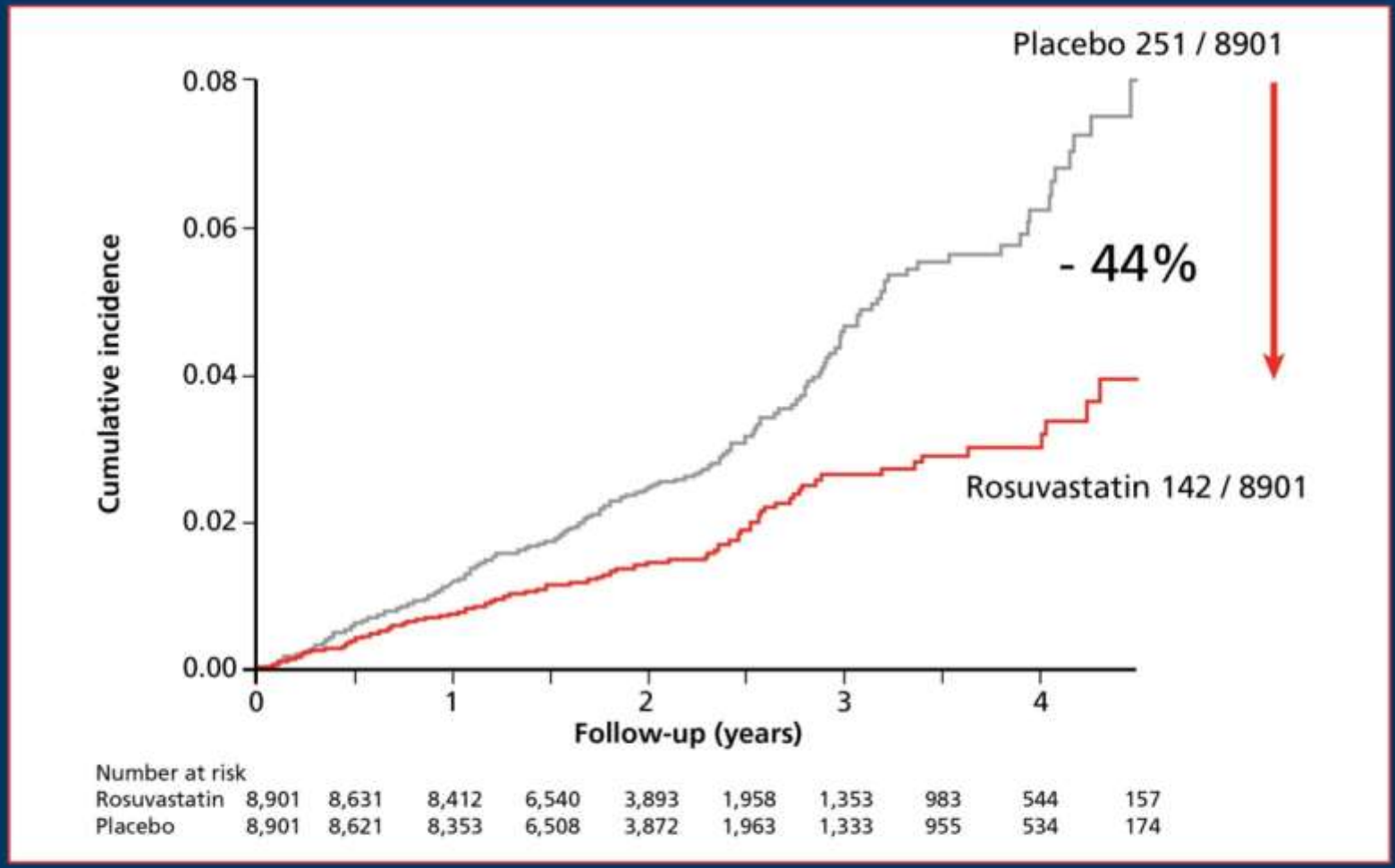
Eat Your Statins

"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

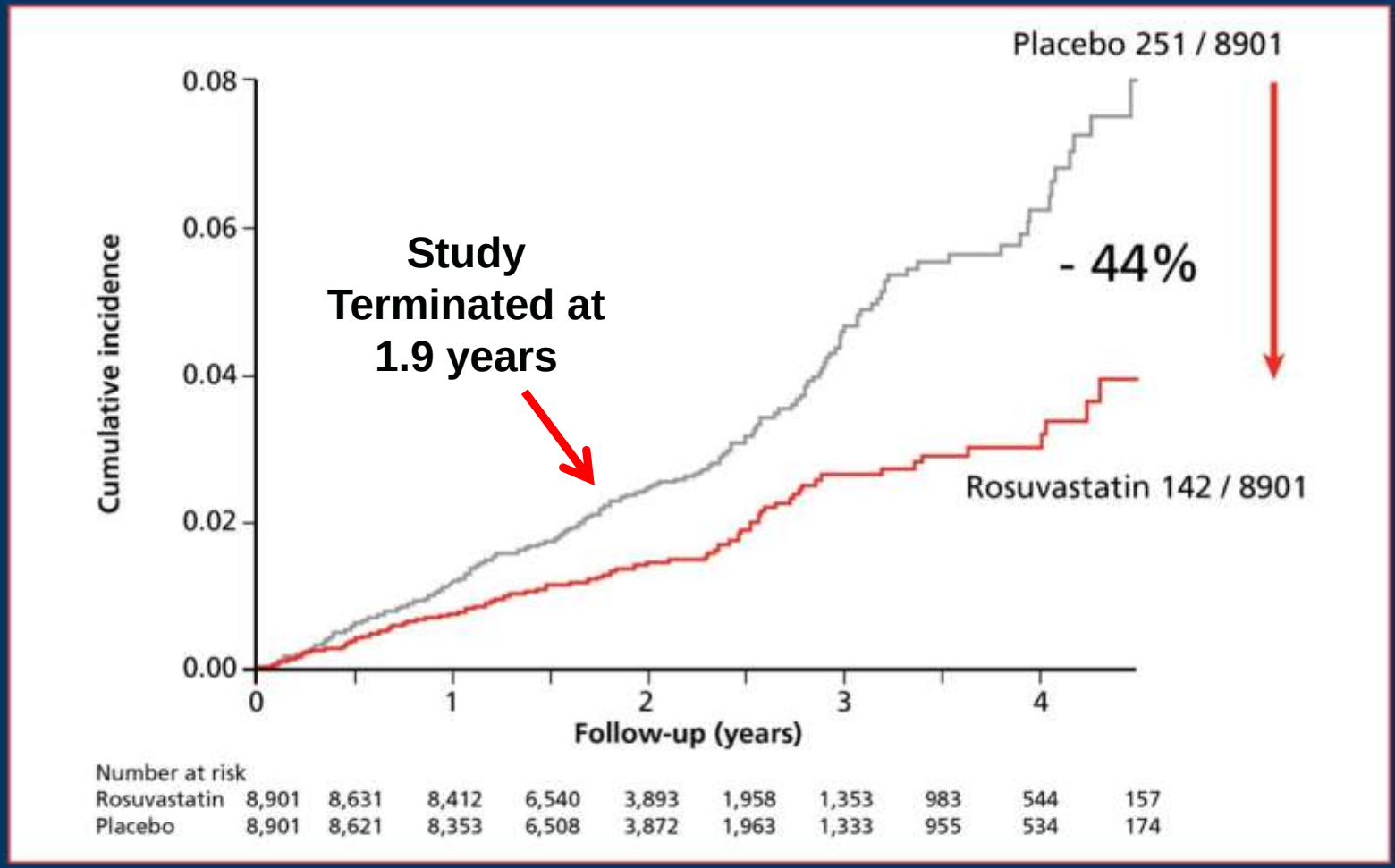
"It's a breathtaking study. It's a blockbuster. It's absolutely paradigm-shifting,

A Clinical Conference Presentation of the JUPITER Study: "Impressive" 44% Reduction in Coronary Events



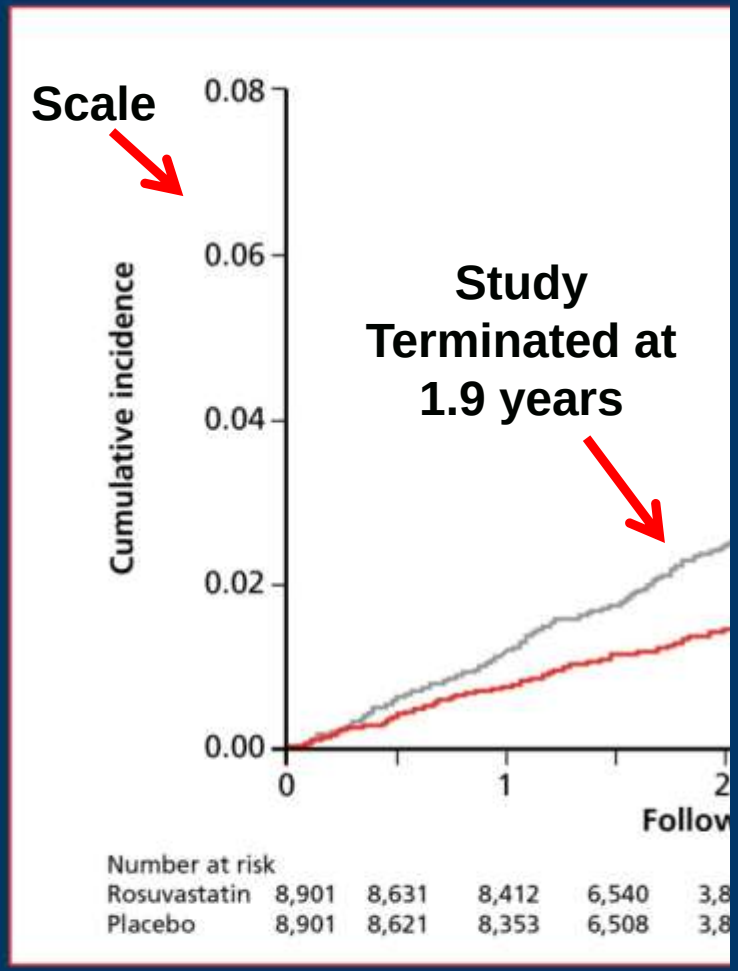
Adapted from Ridker et al. *NEJM* 2008.

A Sobering Closer Look at JUPITER



Adapted from Ridker et al. *NEJM* 2008.

The Study was Terminated Prematurely at 1.9 Years on an "Ethical Basis"



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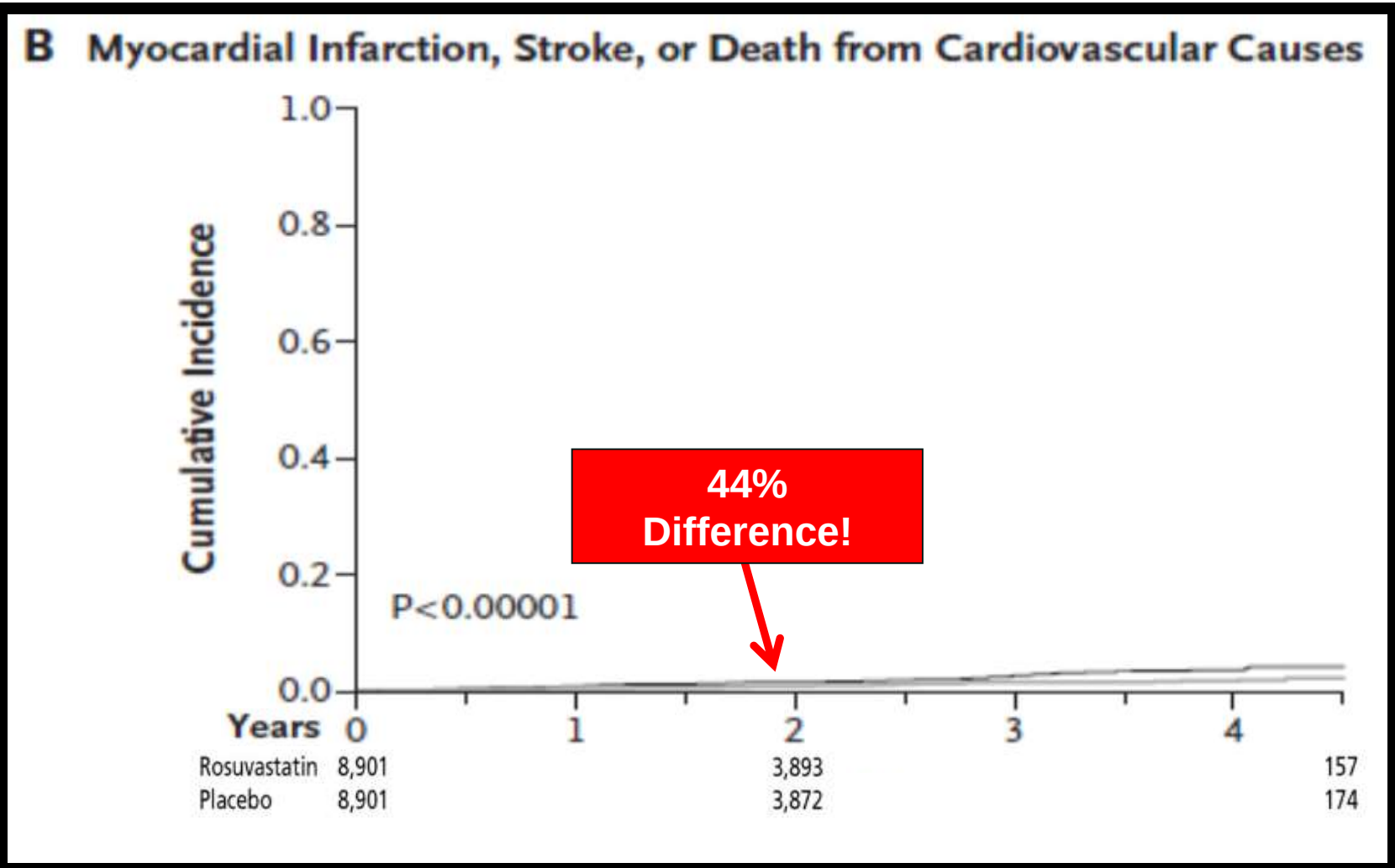
Published Data

Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein

N Engl J Med 2008;359:2195-207.



Published Data

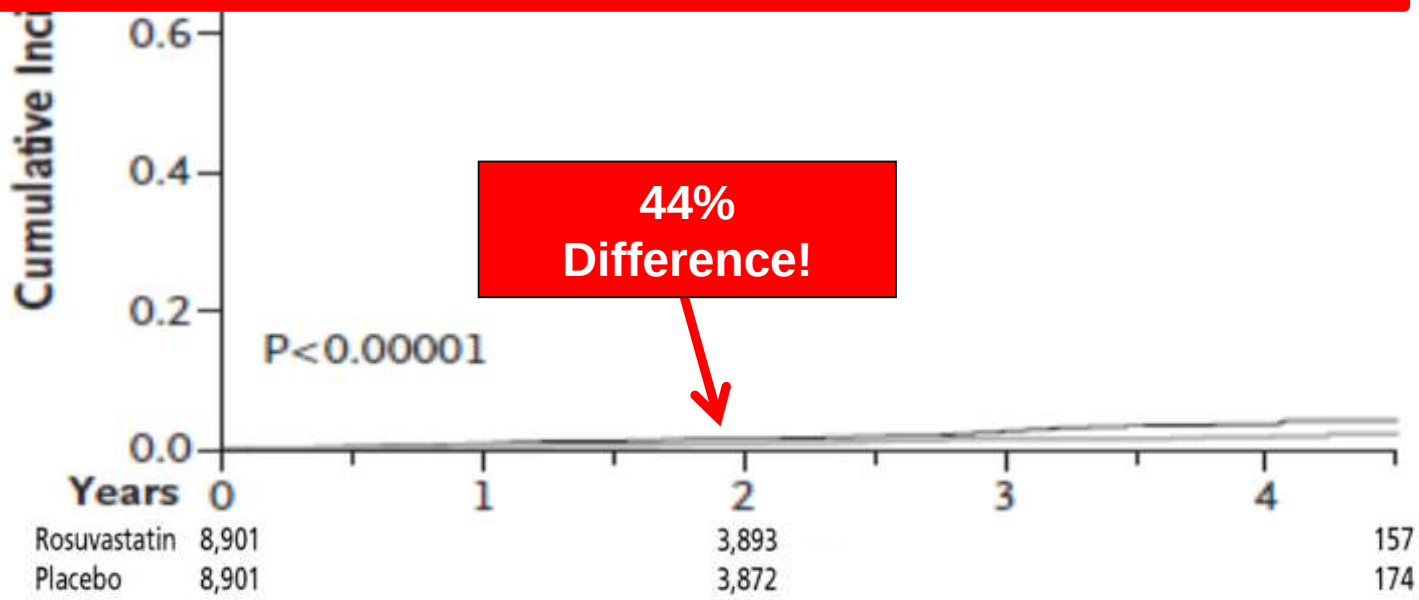
Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein

N Engl J Med 2008;359:2195-207.

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,

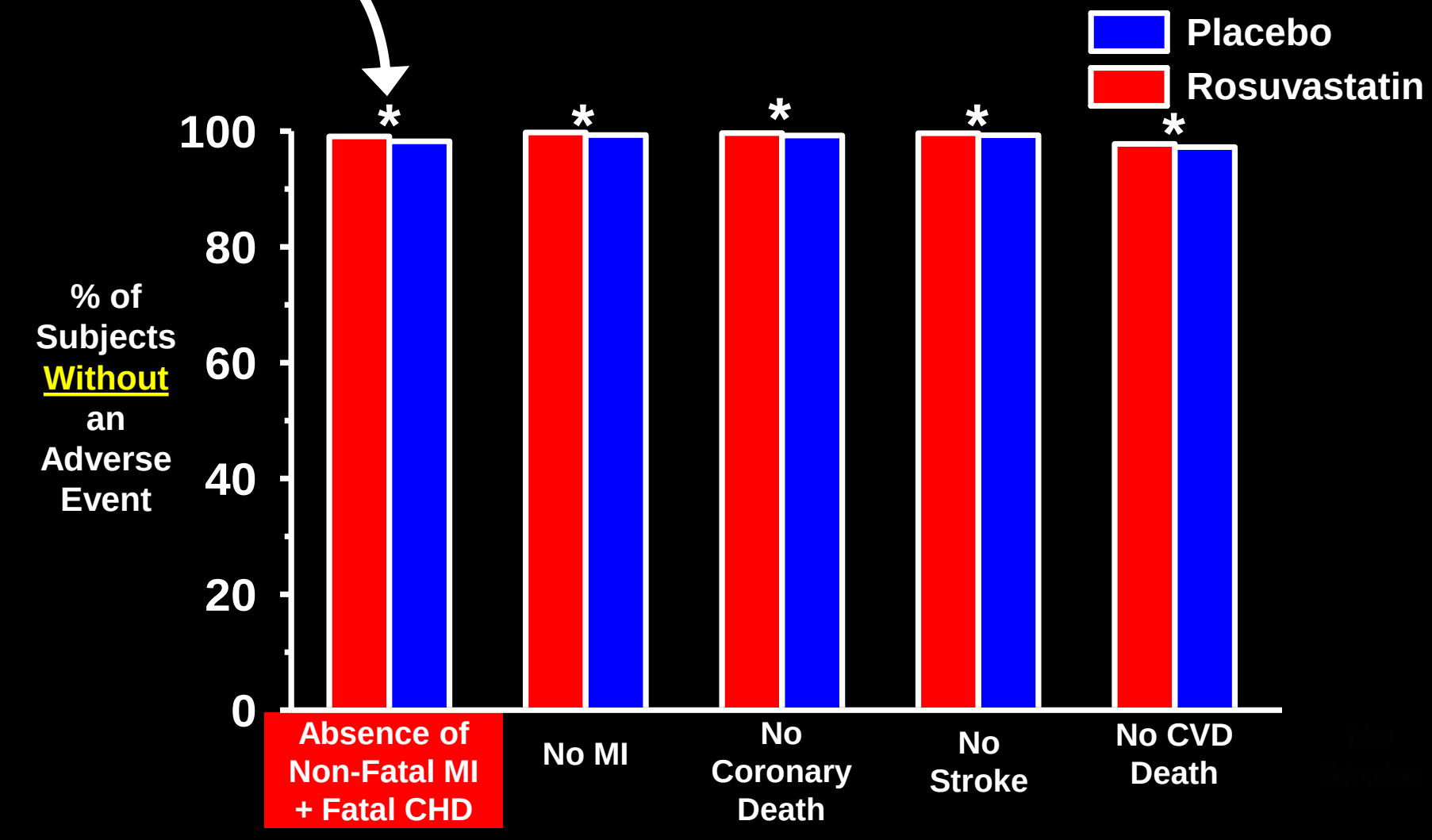


JUPITER Study – Statistical Alchemy
How to Turn a Miniscule 1.2% Effect into a Spectacular 44% Effect

98.4% Rosuvastatin
97.2% Placebo

→ Difference = 1.2%
Drug vs Placebo

→ 1.2% : 2.8% = 44%



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

Journal of Clinical Pharmacy and Therapeutics (1996) **21**, 89–94

Effect of Statins on Total Testosterone Levels in Male Veterans

SEPTEMBER 2012 • FEDERAL PRACTITIONER •

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, MD[a], Jian Huang, MD[b,c], Steven Tringali, DO[c], Christopher R. Frei, PharmD, MSc[d,e], Eric M. Mortensen, MD, MSc[f,g,h], and Ishak A. Mansi, MD[f,g,h,*]

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

Statin Therapy and Risk of Developing Type 2 Diabetes: A Meta-Analysis

SWAPNIL N. RAJPATHAK, MD, DRPH[1]
DHARAM J. KUMBHANI, MD, SM[2]
JILL CRANDALL, MD[1]
NIR BARZILAI, MD[1]
MICHAEL ALDERMAN, MD[1]
PAUL M. RIDKER, MD[3]

DIABETES CARE, VOLUME 32, NUMBER 10, OCTOBER 2009

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

(*J Clin Endocrinol Metab* 103: 75–84, 2018)

BMJ

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

BMJ 2010;340:c2197

Julia Hippisley-Cox, professor of clinical epidemiology and general practice, Carol Coupland, associate professor in medical statistics

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

Insights From Large Randomized Statin Trials

Alawi A. Alsheikh-Ali, MD, Prasad V. Maddukuri, MD, Hui Han, MD, Richard H. Karas, MD, PHD
Boston, Massachusetts

Journal of the American College of Cardiology Vol. 50, No. 5, 2007

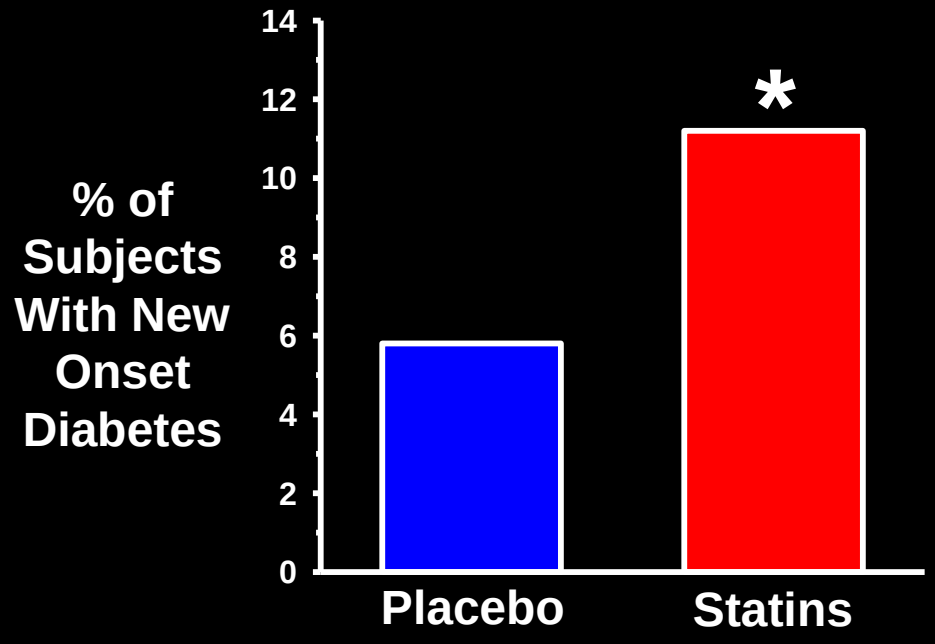
44% Increased Risk of Diabetes in People on Statins

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

Diabetologia 10 March 2015

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



Little if Any Evidence of an All-Cause Mortality Benefit

REVIEW ARTICLE

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, FRCPath

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

Data were available on 65 229 participants followed for approximately 244 000 person-years, during which 2793 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.

EXPERT REVIEWS

David M Diamond*[1–3] and Uffe Ravnskov[4]

[1]Medical Research Service, Veterans Hospital, Tampa, 33612 FL, USA
[2]Department of Psychology, Center for Preclinical and Clinical Research on PTSD, University of South Florida, Tampa, 33620 FL, USA
[3]Department of Molecular Pharmacology and Physiology, Center for Preclinical and Clinical Research on PTSD, University of South Florida, Tampa, 33620 FL, USA

How statistical deception created the appearance that statins are safe and effective in primary and secondary prevention of cardiovascular disease

Expert Rev. Clin. Pharmacol. 8(2), 201–210 (2015)

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"

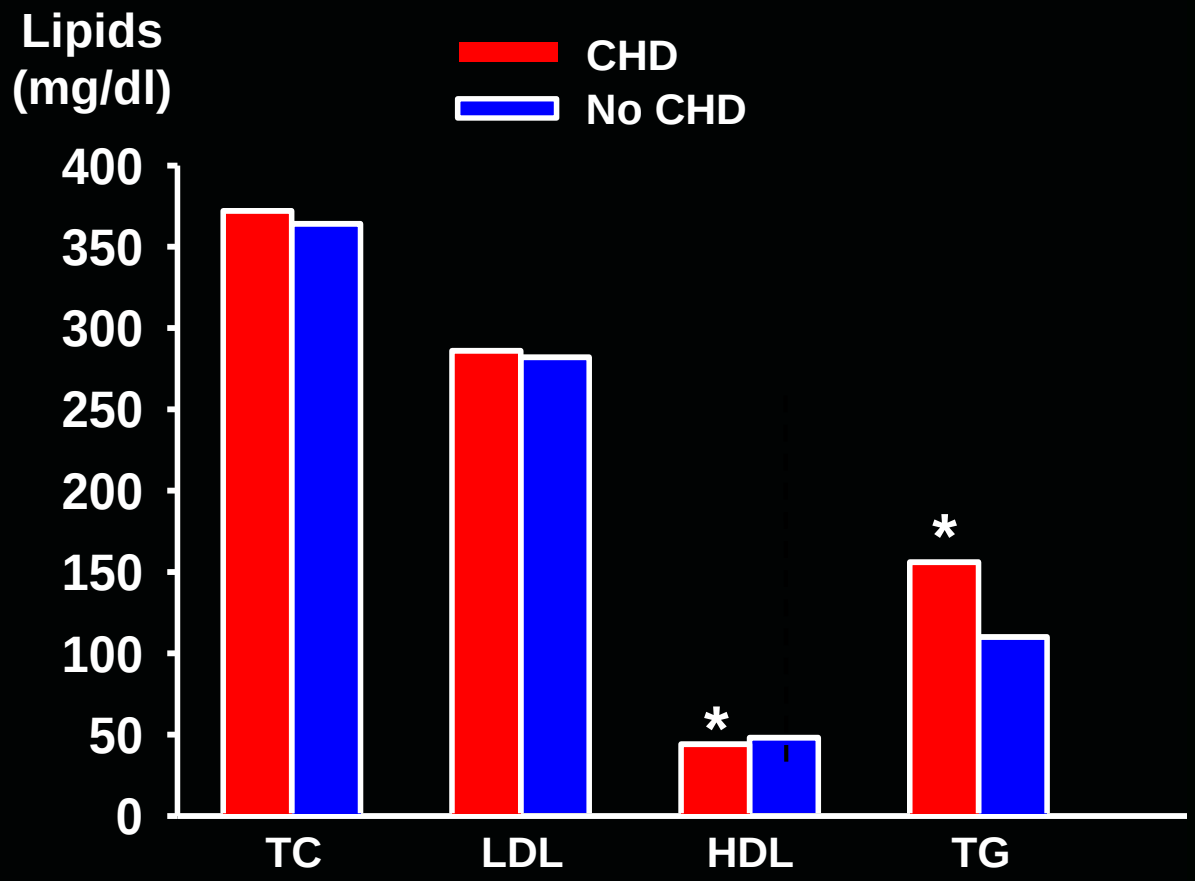
3. The small benefits of statins are Offset by their Adverse Effects

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

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

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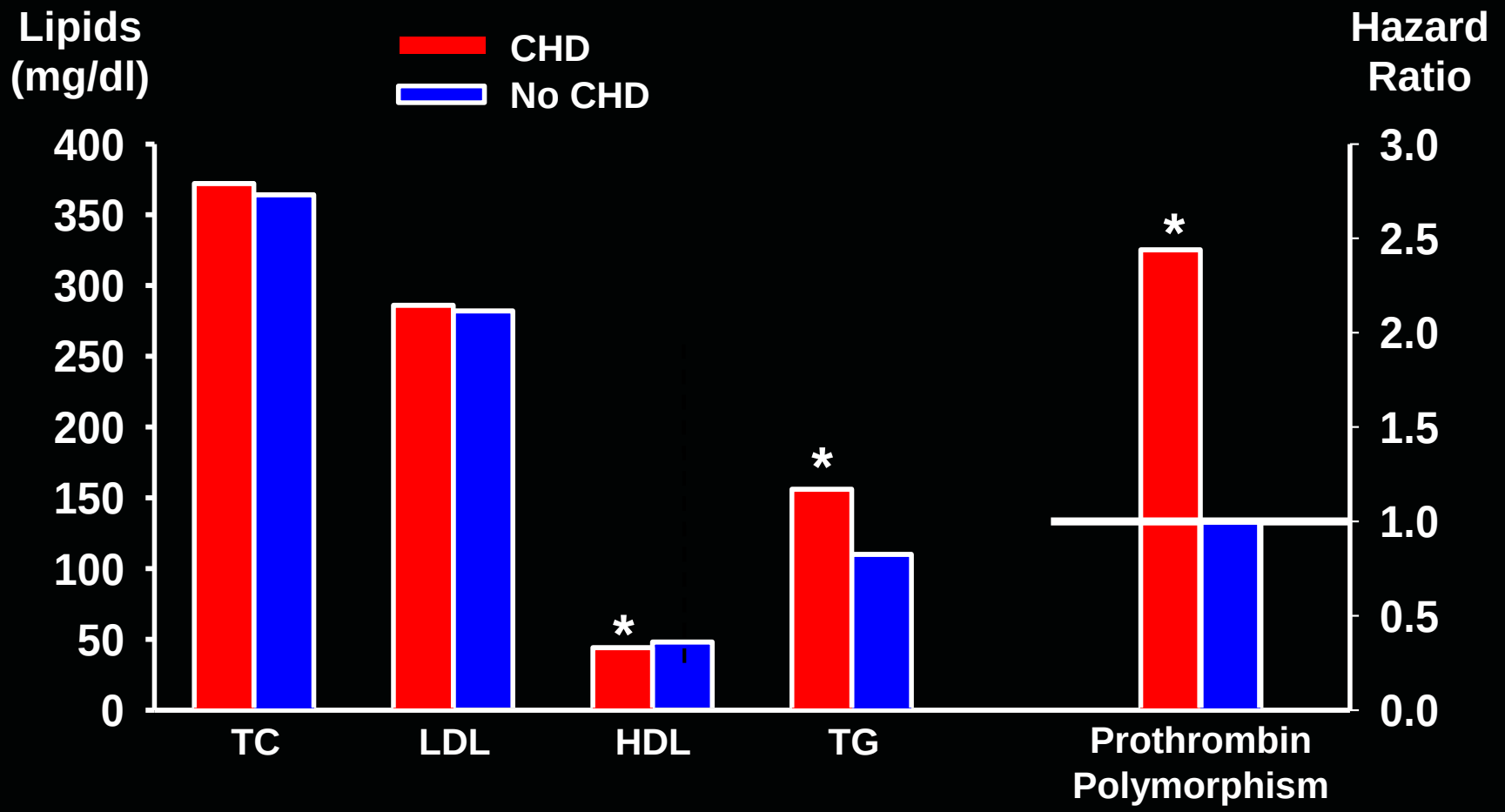
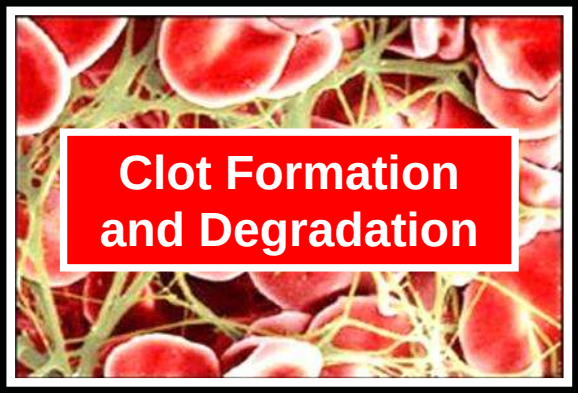


Activation of Coagulation Factors and/or Reduced Fibrinolysis Linked to Risk Factors for CVD



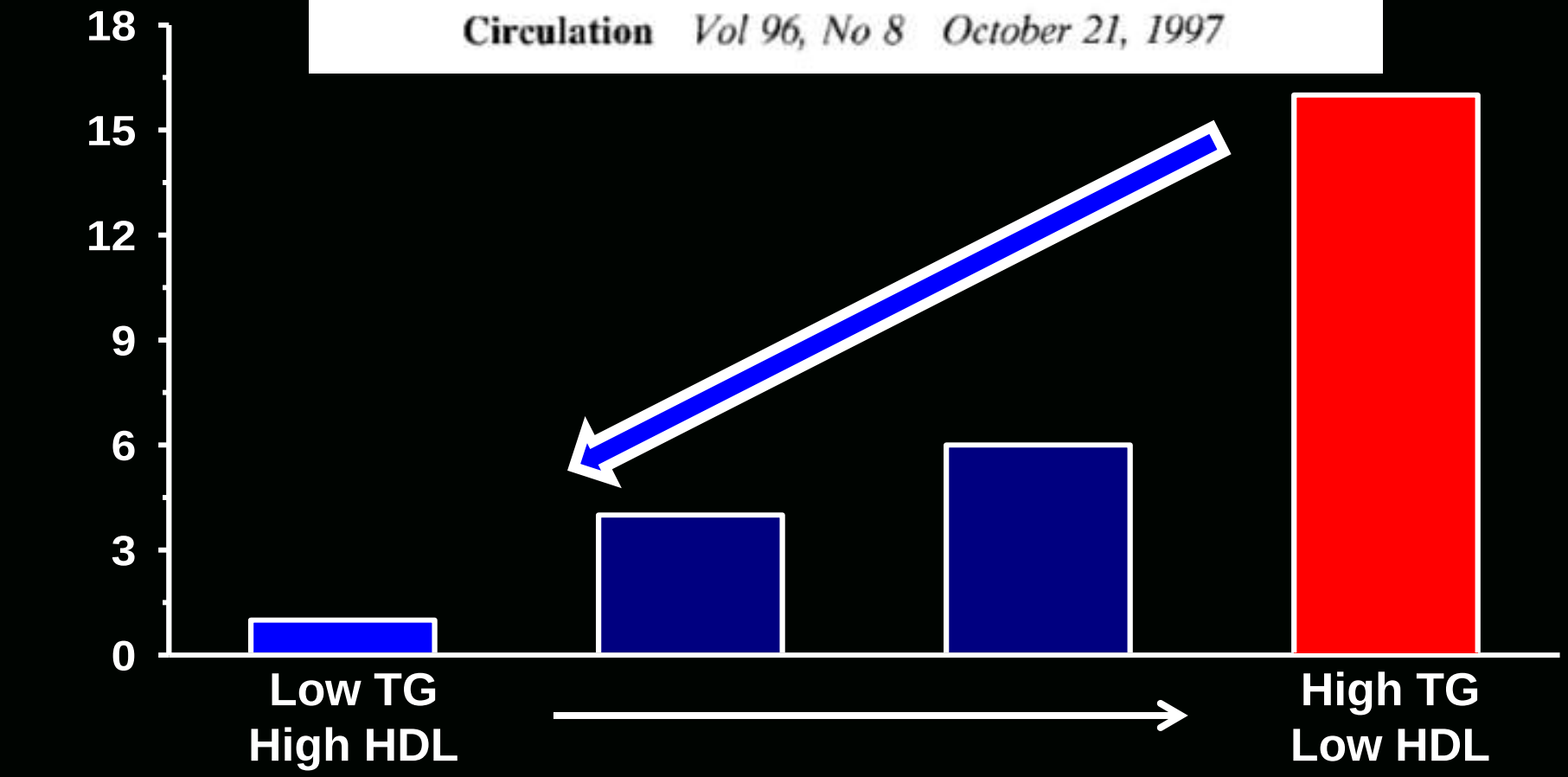
- Obesity/Metabolic Syndrome
- High Blood Glucose T2 Diabetes
- Smoking
- Inflammation
- Advanced Age
- Hypertension
- Psychological Stress
- Bacterial Infection
- Subset of Familial Hypercholesterolemia

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*



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

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Supported by key opinion leaders sponsored by food and drug companies

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The primary target for CVD protection should be hypercoagulation, preferably through optimizing diet and lifestyle

THANK YOU
for your
ATTENTION!