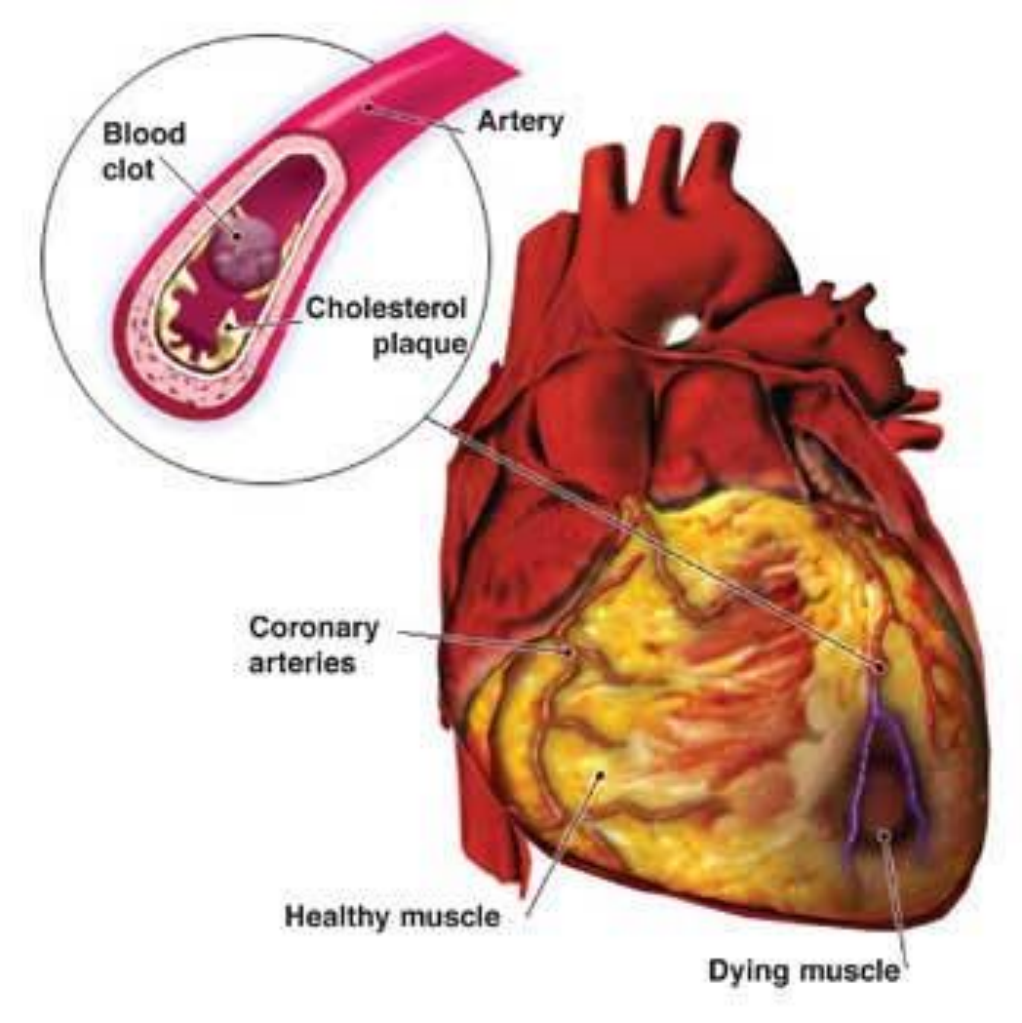
Should You Be On A Statin Drug?

Making Sense Of The New Cholesterol Guidelines

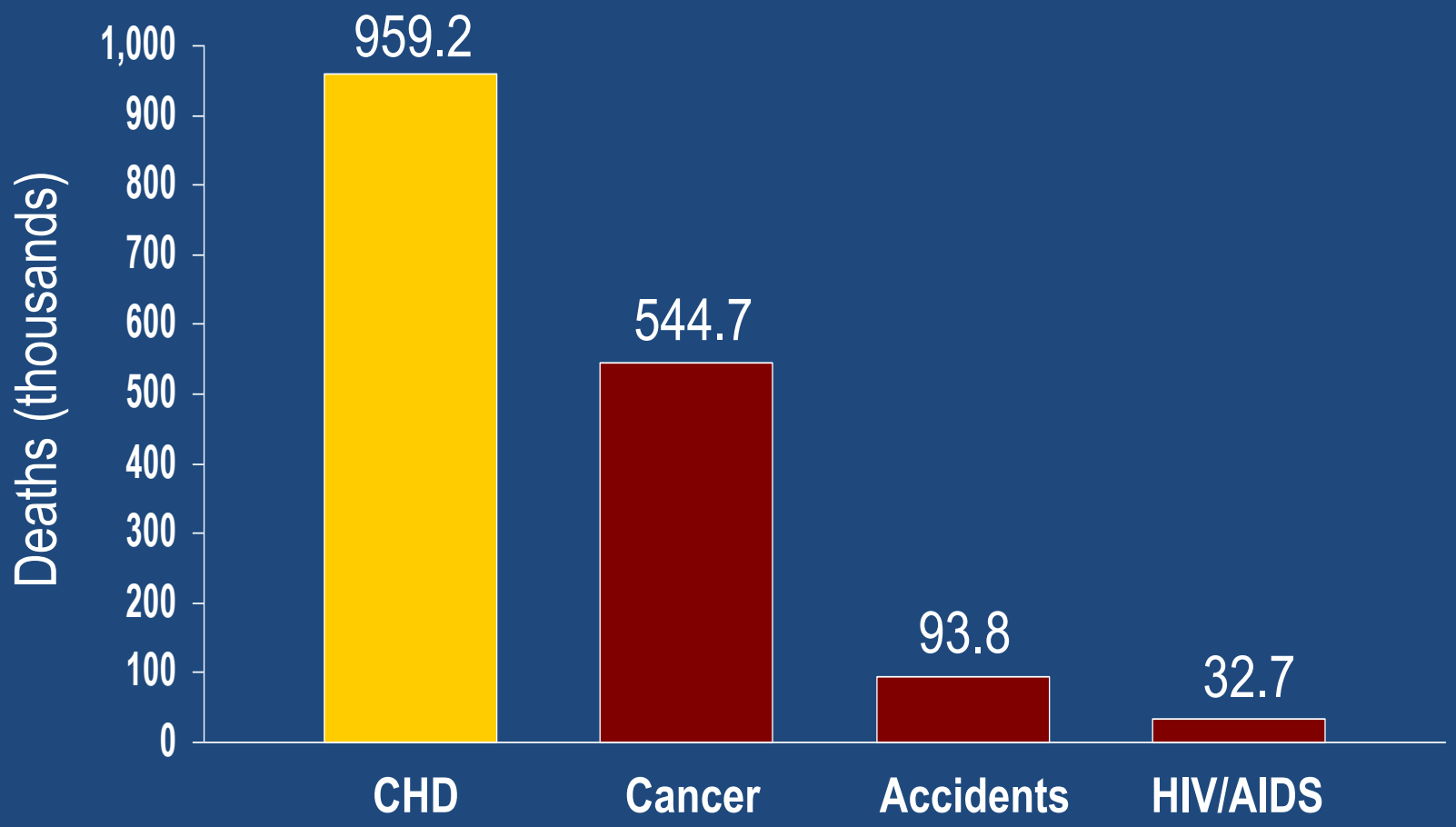
Robert DuBroff (no financial disclosures)

Don’t shoot the messenger

Atherothrombosis Causes Heart Attacks

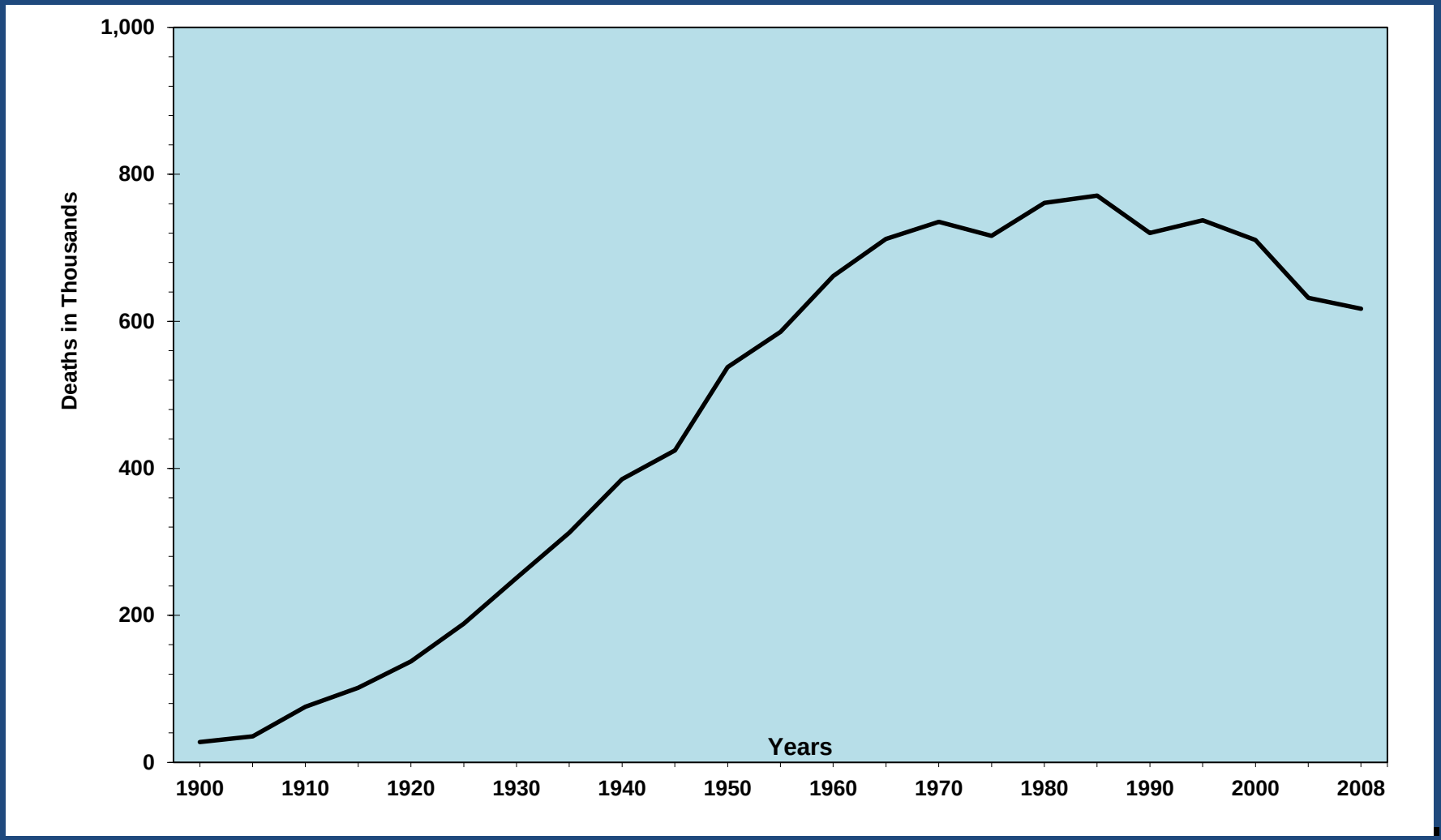


Causes of Death in the United States



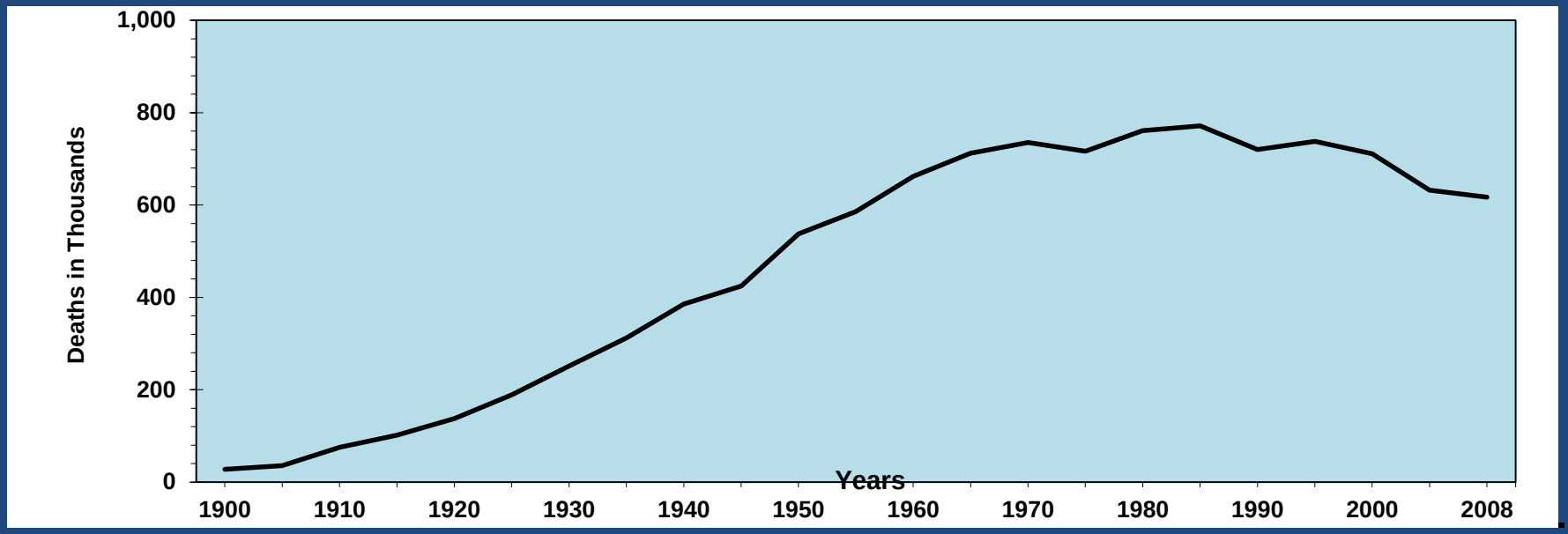
American Heart Association. *Heart and Stroke Statistical Update.*

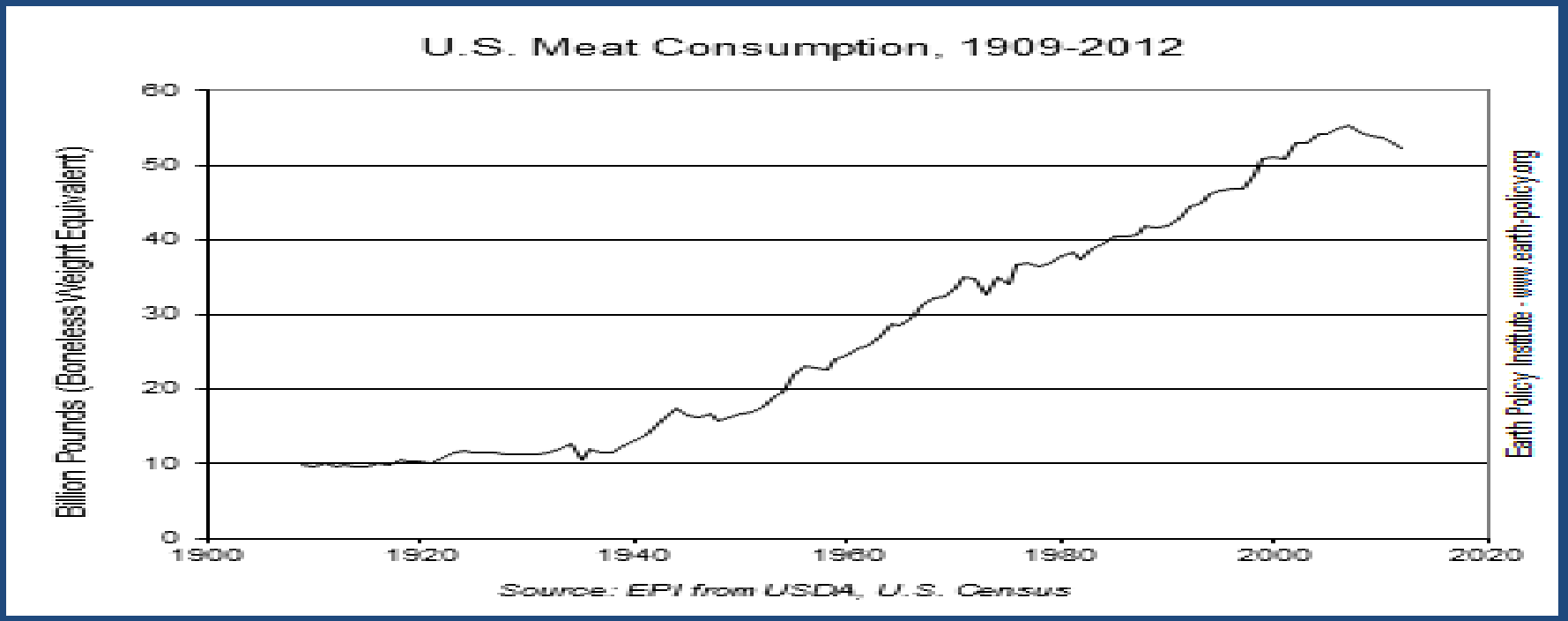
Deaths due to diseases of the heart (United States: 1900–2008)

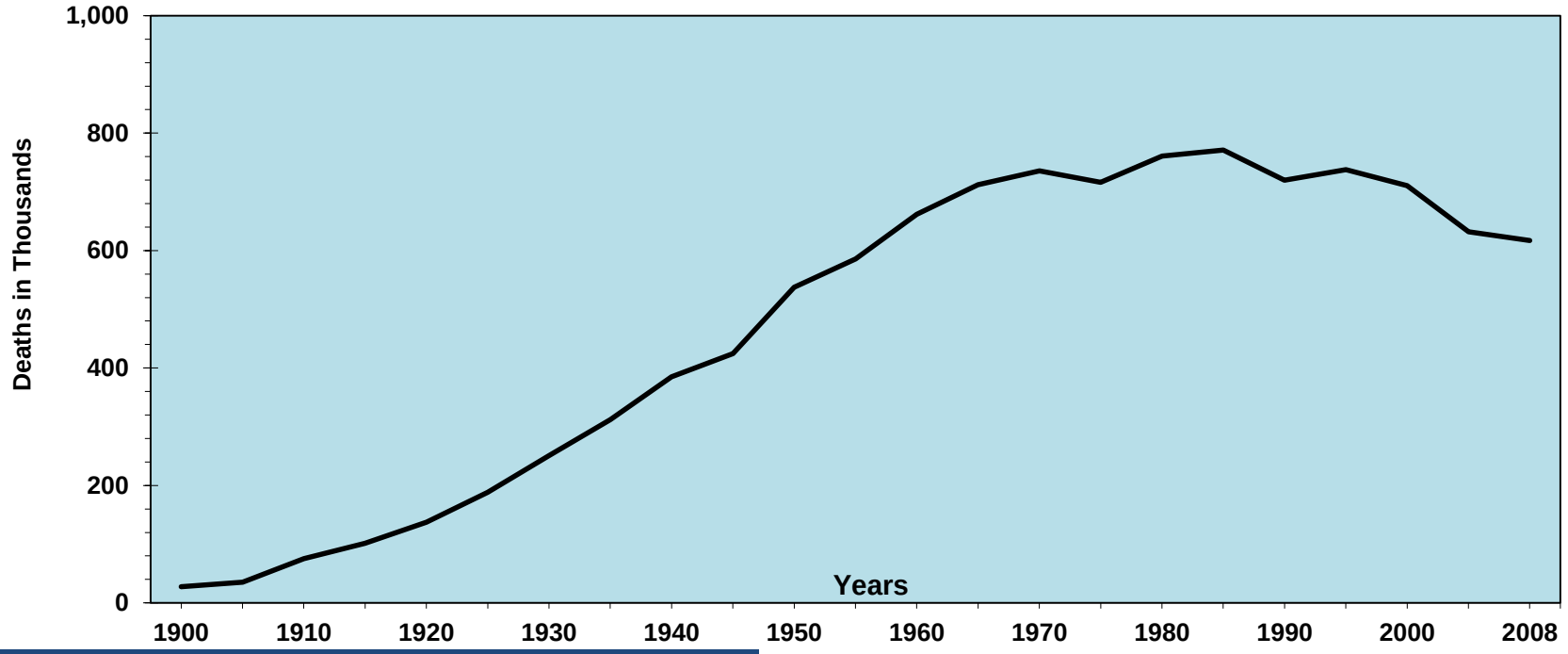


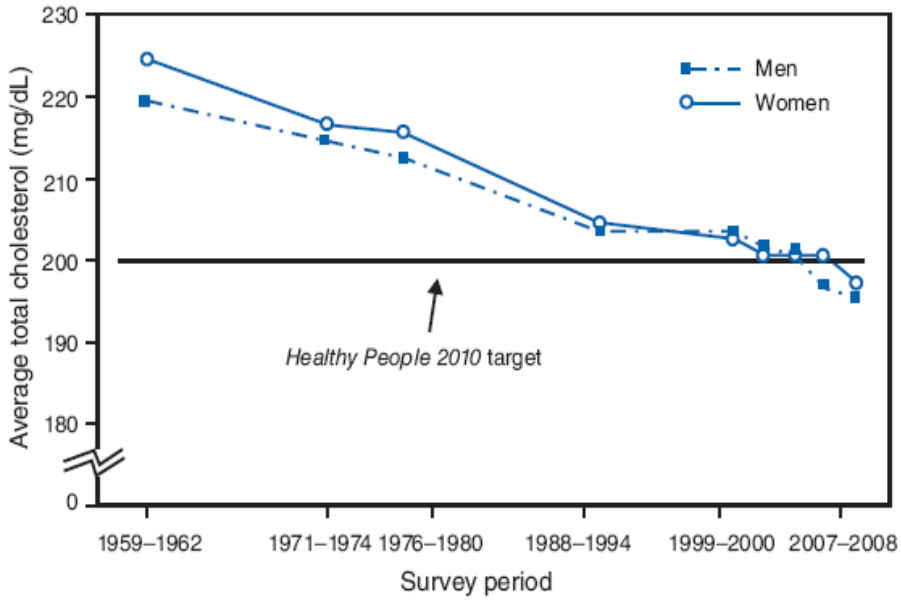
Source: National Center for Health Statistics.

Roger VL et al. Published online in *Circulation* Dec. 15, 2011

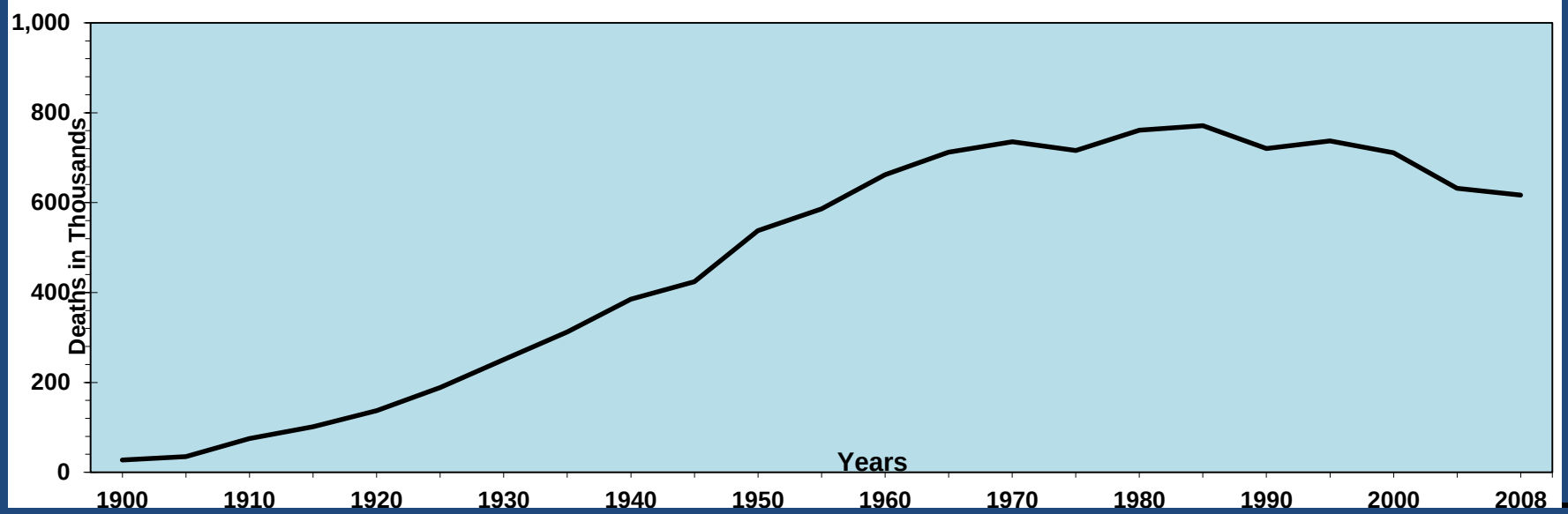

Deaths in Thousands
1,000
800
600
400
200
0
Years
1900
1910
1920
1930
1940
1950
1960
1970
1980
1990
2000
2008


U.S. Meat Consumption, 1909-2012
Billion Pounds (Boneless Weight Equivalent)
60
50
40
30
20
10
0
1900
1920
1940
1960
1980
2000
2020
Source: EPI from USDA, U.S. Census
Earth Policy Institute - www.earth-policy.org





MMWR September 25, 2009 / 58(37);1045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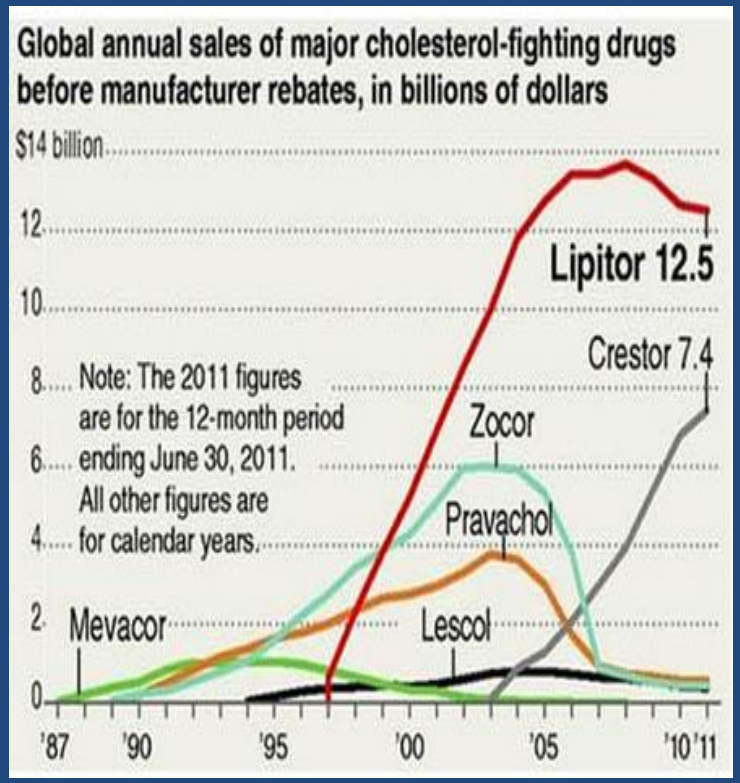
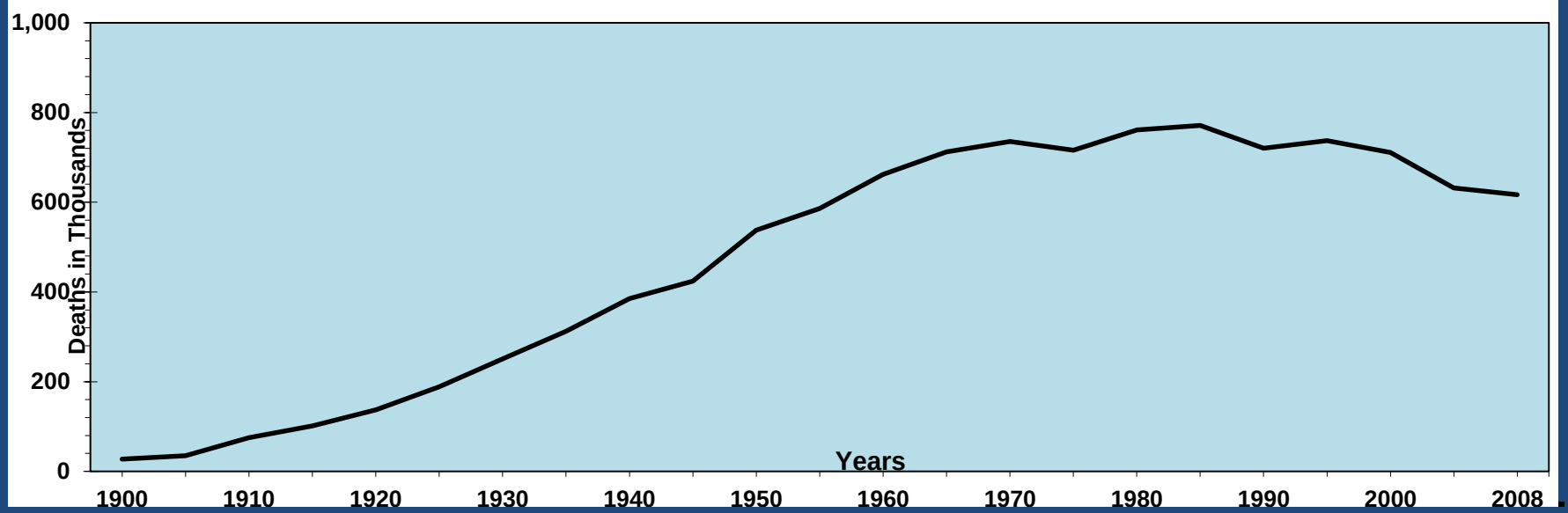

Global annual sales of major cholesterol-fighting drugs before manufacturer rebates, in billions of dollars
$14 billion
12
10
8
6
4
2
0
Note: The 2011 figures are for the 12-month period ending June 30, 2011. All other figures are for calendar years.
Lipitor 12.5
Crestor 7.4
Zocor
Pravachol
Mevacor
Lescol
'87
'90
'95
'00
'05
'10
'11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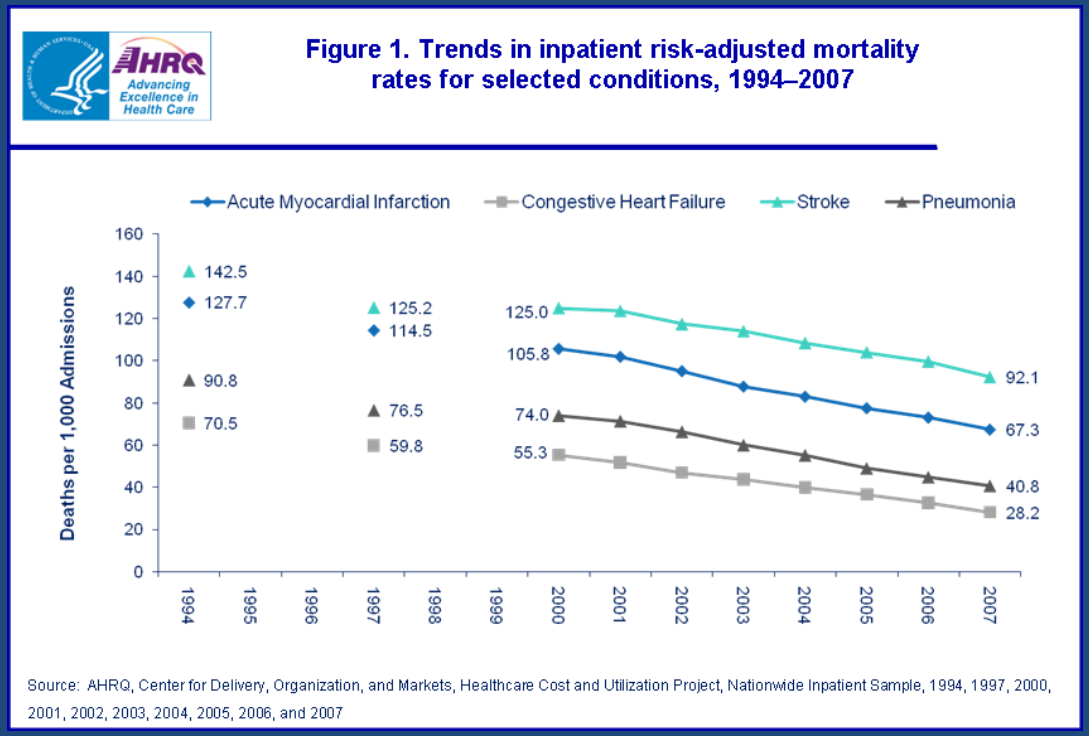
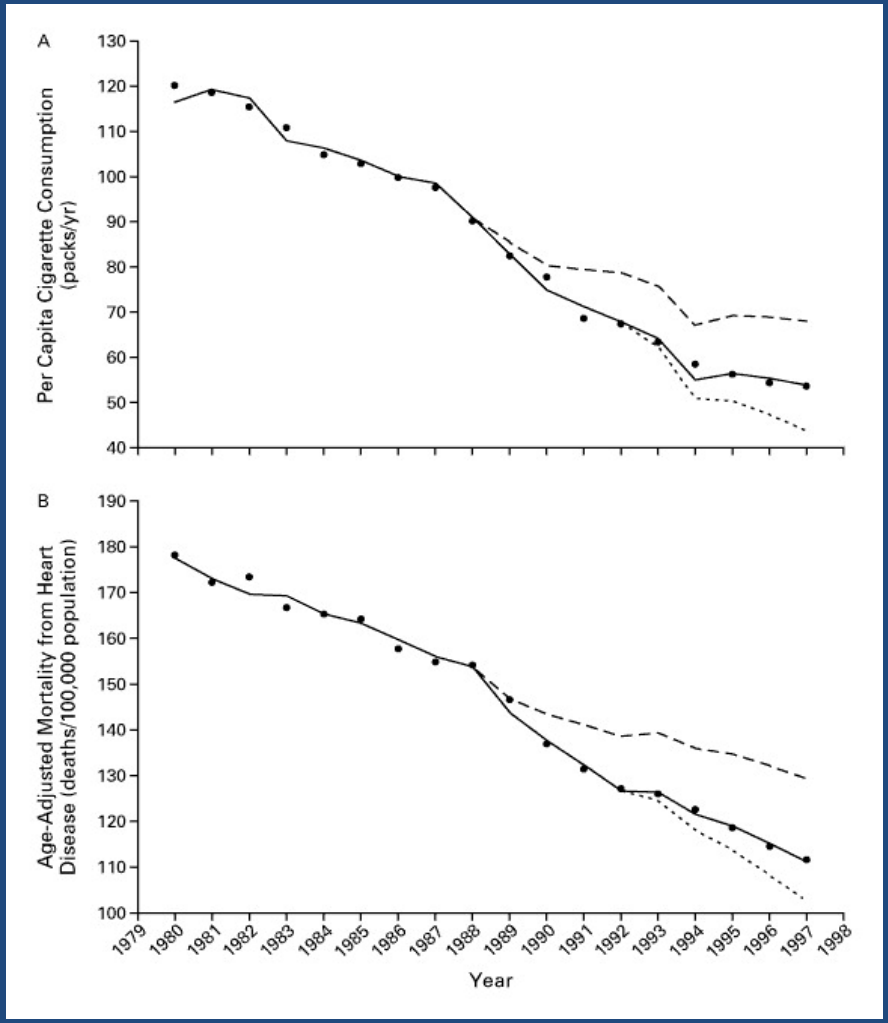

AHRQ
Advancing Excellence in Health Care
Figure 1. Trends in inpatient risk-adjusted mortality rates for selected conditions, 1994–2007
Acute Myocardial Infarction
Congestive Heart Failure
Stroke
Pneumonia
Deaths per 1,000 Admissions
160
140
120
100
80
60
40
20
0
142.5
127.7
90.8
70.5
125.2
114.5
76.5
59.8
125.0
105.8
74.0
55.3
92.1
67.3
40.8
28.2
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
Source: AHRQ, Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project, Nationwide Inpatient Sample, 1994, 1997, 2000, 2001, 2002, 2003, 2004, 2005, 2006, and 2007

Rates of per Capita Cigarette Consumption and Age-Adjusted Rates of Death from Heart Disease in California Relative to Rates in the Rest of the United States and Predicted Rates If the Tobacco-Control Program Had Not Been Instituted in 1989 and If It Had Not Been Cut Back in 1992.



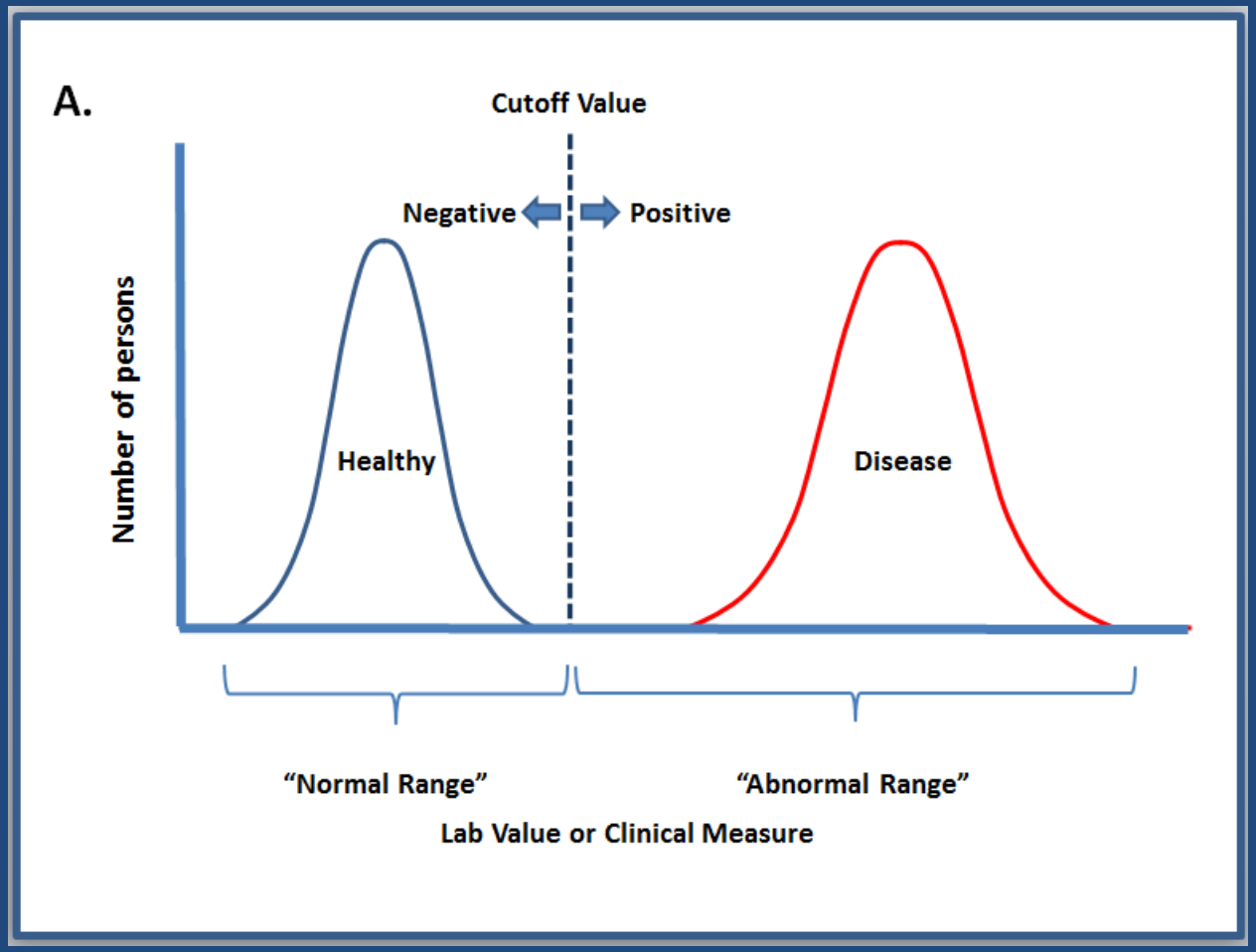
Fichtenberg CM, Glantz SA. N Engl J Med 2000;343:1772-1777.

The NEW ENGLAND JOURNAL of MEDICINE

Is Cholesterol The Right Target?

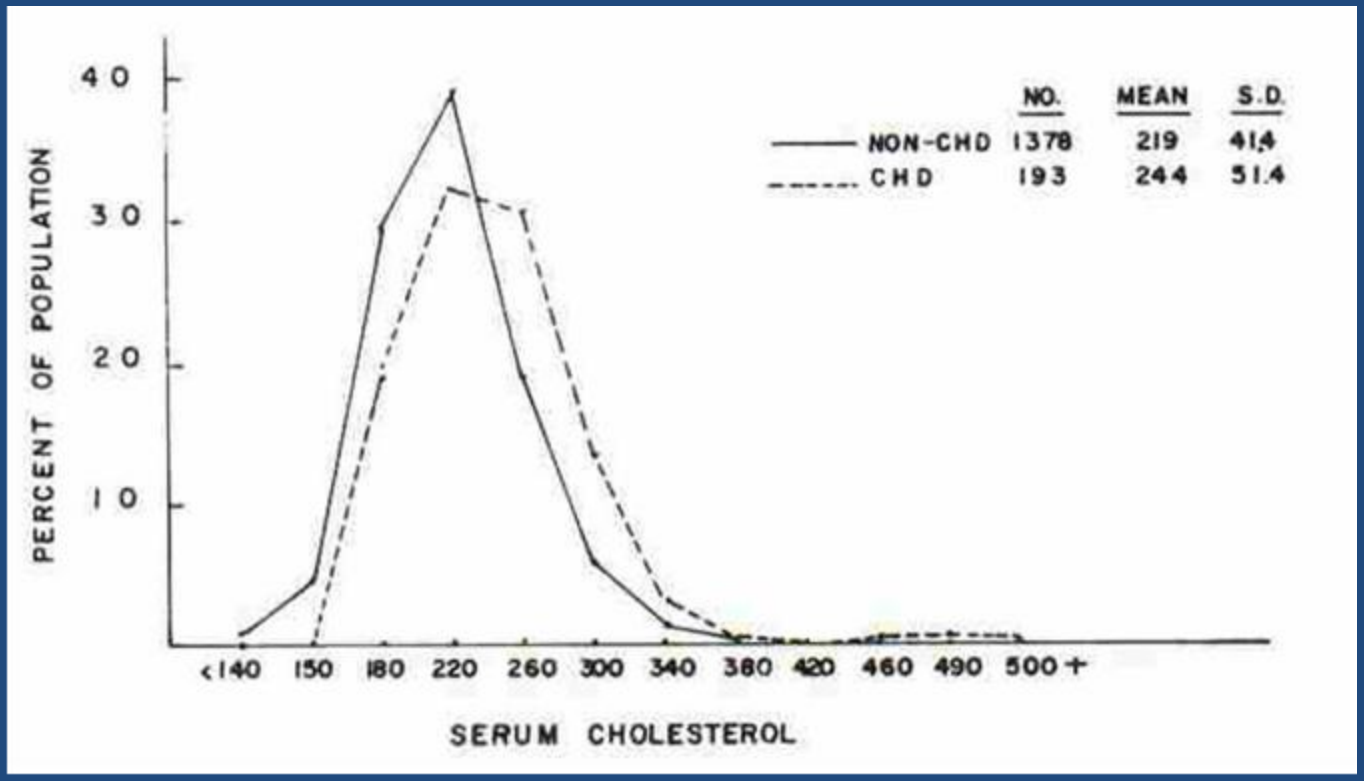
- Is cholesterol a good risk factor?
- Does lowering cholesterol by diet reduce CV mortality rates?
- Does lowering LDL cholesterol by non-statin drugs reduce CV mortality rates?
- Does lowering LDL cholesterol by statin drugs reduce CV mortality?

Ideal Risk Factor



Framingham Heart Study

WILLIAM B. KANNEL, M.D., M.P.H.; WILLIAM P. CASTELLI, M.D.; TAVIA GORDON, Cholesterol in the Prediction of Atherosclerotic Disease: New Perspectives Based on the Framingham Study. Ann Intern Med. 1979; 90



The Women's Health Initiative Randomized Controlled Dietary Modification Trial

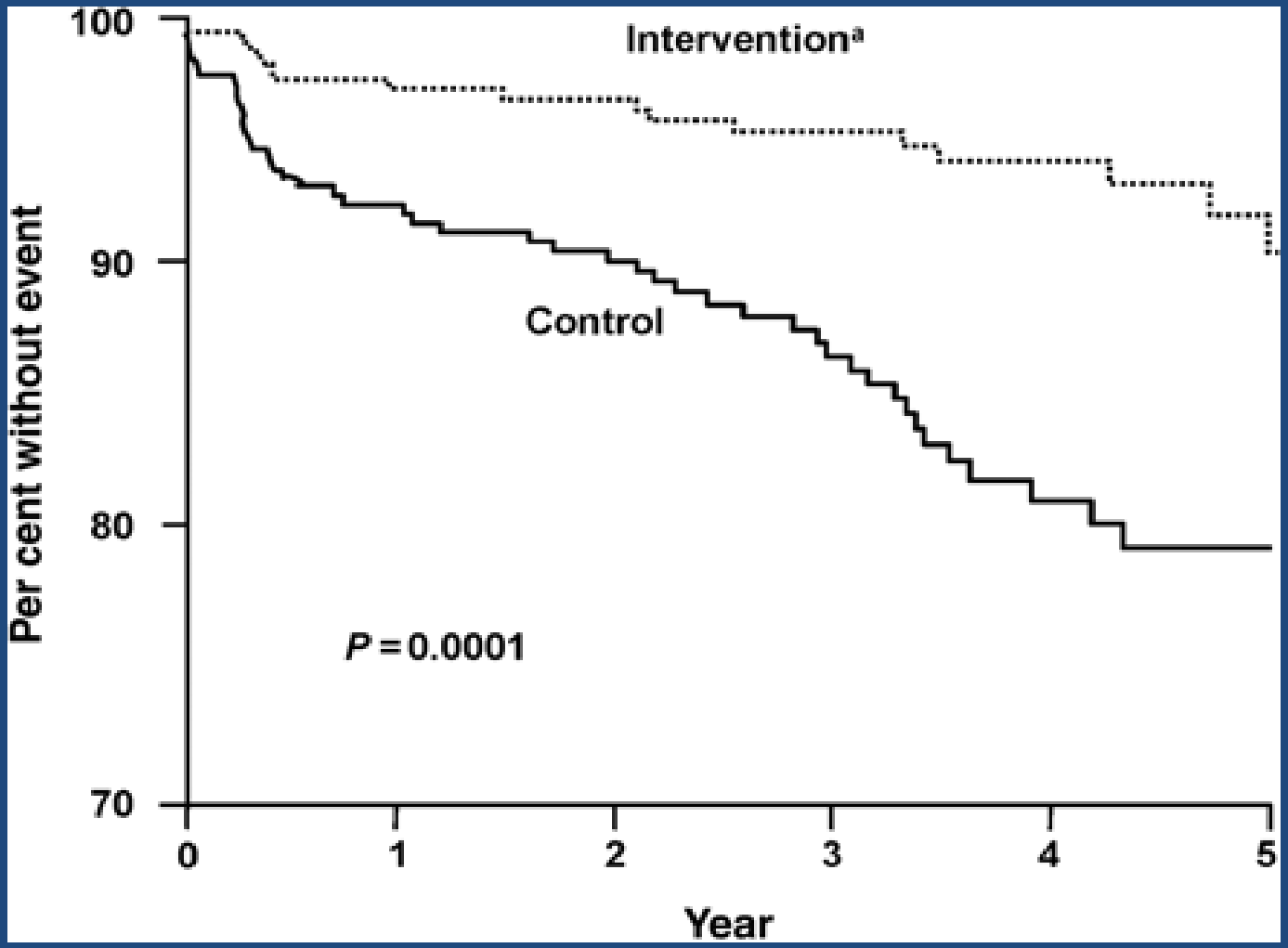
- 48,835 women age 50-79 years
- Intervention - low fat diet (<20% of calories from fat), fruits & vegetables 5 servings/day, grains 6 servings/day
- Control group
- After 8.1 years no reduction in stroke, CHD, or CVD
- LDL cholesterol decreased 133 to 123 mg/dl

JAMA 2006, vol 295, no 6, 655-666

Association of Dietary, Circulating, and Supplement Fatty Acids With Coronary Risk: A Systematic Review and Meta-analysis

Ann Intern Med 2014; 160: 398-406

- Meta-analysis of 72 studies of reduced dietary saturated fat and CV outcomes
- **Conclusion:** Current evidence does not clearly support cardiovascular guidelines that encourage high consumption of polyunsaturated fatty acids and low consumption of total saturated fats.



Lyon Diet Heart Study: Cumulative Survival
de Lorgeril M et al. Lancet. 1994;343:1454-1459.

OLDWAYS
HEALTH THROUGH HERITAGE

Mediterranean Diet Pyramid

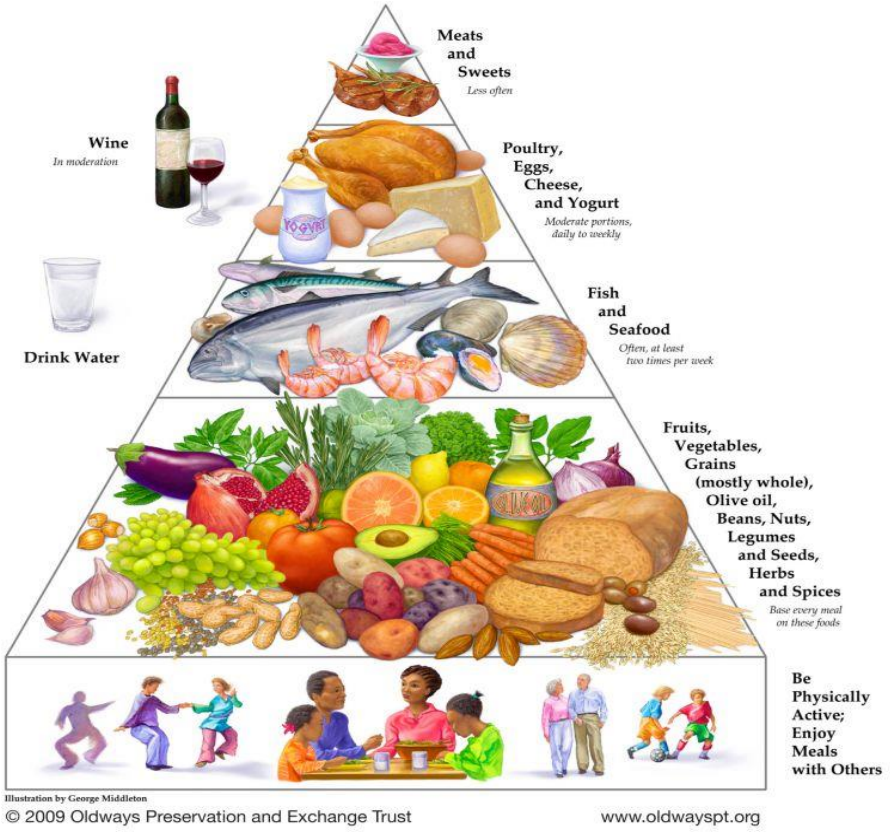


Illustration by George Middleton

www.oldwayspt.org

MEDITERRANEAN FOODS ALLIANCE
AN OLDWAYS PROGRAM

www.oldwayspt.org

Dietary Prevention of Coronary Heart Disease: The Lyon Diet Heart Study

Circulation. 1999;99:733-735

- Simple dietary changes achieved greater reductions in all cause mortality than any statin trial.
- Unprecedented reductions in CHD was not associated with any change in cholesterol levels.
- Patient adherence was outstanding and no adverse side effects reported.
- Promotion of the Mediterranean diet would lead to dramatic cost savings over traditionally employed drugs, devices, and surgery.

Comparing Diets

DASH (Dietary Approaches to Stop Hypertension)

- Fruits, vegetables, nuts, legumes, whole grains
- Low sodium
- Low fat (<27% calories)
- Some red meat
- No wine
- Lowers BP and cholesterol at 8 weeks
- No RCT mortality studies

Mediterranean

- Fruits, vegetables, nuts, legumes, whole grains
- No sodium restriction
- Higher fat – fish, olive oil
- Replace red meat with seafood
- Red wine
- Minor effect on BP and cholesterol but dramatic reduction in DM
- Dramatic mortality reduction in RCTs at up to 10 years

The Mediterranean diet revisited: evidence of its effectiveness grows

Francesco Sofi[a,b,c]

[a]Department of Medical and Surgical Critical Care, Thrombosis Centre, University of Florence, [b]Regional Agency for Nutrition, Azienda Ospedaliero – Universitaria Careggi and [c]Don Carlo Gnocchi Foundation, Onlus IRCCS, Impruneta, Florence, Italy

Correspondence to Francesco Sofi, MD, PhD, Department of Medical and Surgical Critical Care, Thrombosis Centre, University of Florence, Viale Morgagni 85, Florence 50134, Italy
Tel: +39 055 7949420; fax: +39 055 7949418; e-mail: francescosofi@gmail.com

Current Opinion in Cardiology 2009, 24:442–446

Purpose of review

The optimal dietary strategy for the prevention of chronic degenerative diseases remains a challenging and a highly relevant preventive health issue. In recent years, there have been ongoing investigations of the effectiveness of the Mediterranean diet in preventing the development of cardiovascular and other chronic diseases. Initial research suggested that the consumption of diets high in vegetable oil, fish, and complex grains and carbohydrates conferred a benefit in reducing the prevalence of cardiovascular disease. The purpose of this review is to examine the evidence in support of the effectiveness of the Mediterranean diet in reducing the prevalence of cardiovascular and chronic disease and their associated risk factors.

Over a dozen studies involving > 1.5 million participants consistently show adherence to a Mediterranean diet protects again premature cardiovascular and neoplastic diseases

Drugs Which Reduce Cholesterol

- Bile acid sequestrants
- Niacin
- Fibrates
- Cholesterol absorption inhibitors
- Statins

Problems with Statin Trials

1. Combined clinical endpoints instead of mortality
2. Premature trial terminations
3. Oversight by the pharmaceutical company sponsor
4. Post-2005 studies don’t show mortality benefit

Statin Trials in High Risk Populations

- Elderly – PROSPER
- Heart failure – CORONA, GISSI-HF
- Renal failure – 4D, AURORA, SHARP
- PVD – Cochrane meta-analysis (18 studies)
- ACS – Cochrane meta-analysis (18 studies)
- High CCS – St. Francis Heart
- Diabetes – CARDS, 4D, ASPEN

Cholesterol Guidelines

The European Atherosclerosis Society

Common Elements of All Cholesterol Guidelines

1. Lifestyle management
   a) Smoking cessation
   b) Regular exercise
   c) Healthy diet
2. Primary prevention statin use
3. Secondary prevention statin use
4. Intensity of treatment
5. Non-statin medications

Bumps in the Road to New Cholesterol Guidelines

The New York Times

November 25, 2013

Dr. Steven Nissen, a Cleveland Clinic cardiologist, said of a medical committee's guidelines, "There will be a large backlash."

Criticism of the new guidelines

- **The risk calculator may overestimate risk.**
- **Out of 46 recommendations, 20 were based only on expert opinion.**
- **Too many people will be put on statins.**
- **Numerous professional organizations do not endorse the new guidelines.**
- **Conflict of interest: six out of the 15 authors reported having recent or current ties to manufacturers of statin drugs.**
- **Lack of LDL targets may discourage desired patient behavior**

Four Statin Eligible Patient Groups

- **Individuals with clinical ASCVD**
- **Individuals with primary elevations of LDL–C ≥190 mg/dL.**
- **Individuals 40 to 75 years of age with diabetes and LDL–C 70 to 189 mg/dL without clinical ASCVD**
- **Individuals without clinical ASCVD or diabetes who are 40 to 75 years of age with LDL–C 70 to 189 mg/dL and have an estimated 10-year ASCVD risk of 7.5% or higher.**

Statin Intensity

HIGH

- DM, age 40-75 years with ASCVD
- ASCVD, age < 75 years
- LDL > 190, age > 21 years

MODERATE

- DM, age 40-75 years, no ASCVD
- ASCVD, age > 75 years
- LDL 70-189, risk > 7.5%/10 years

Non-Statin Drug Therapy

Bile acid sequestrants
Niacin
Fibrates
Cholesterol absorption inhibitors

Not recommended, use is optional

High- and Moderate-Intensity Statin Therapy

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy
Lowers LDL-C by ~≥50%	Lowers LDL-C by ~30% to <50%
Atorvastatin 40*-80 mg Rosuvastatin 20 mg (*40 mg*)	Atorvastatin 10 mg (*20 mg*) Rosuvastatin (*5 mg*) 10 mg Simvastatin 20-40 mg† Pravastatin 40 mg (*80 mg*) Lovastatin 40 mg *Fluvastatin XL 80 mg* Fluvastatin 40 mg bid *Pitavastatin 2-4 mg*

*Down titrate if unable to tolerate atorvastatin 80 mg;
†Initiation of or titration to simvastatin is not recommended by the FDA due to increased myopathy risk
Italics denotes FDA-approved doses that were not tested in trials reviewed for guideline development
Once-daily doses unless otherwise specified. Avg LDL-C–lowering potential listed expected to vary in clinical practice.

Stone NJ, et al. *J Am Coll Cardiol*. 2013. doi:10.1016/j.jacc.2013.11.002.

American Heart Association.

AMERICAN COLLEGE of CARDIOLOGY

2013 Prevention Guidelines Tools

CV RISK CALCULATOR

Age
Gender
Total Cholesterol
HDL Cholesterol
Smoking
Systolic BP
Hypertensive meds

http://my.americanheart.org/cvriskcalculator

Estimating Risk of ASCVD

For Intermediate Risk < 7.5%/10 yr
Optional use of tools to refine risk

- Family history of premature ASCVD
- High-sensitivity CRP
- Coronary artery calcium score
- Ankle brachial index

Primary Prevention
How to Predict Cardiovascular Events

Use Risk Factors

- Framingham Risk Score
- Pooled Cohort Equations

Look for atherosclerosis

Paradigm Shift in Risk Prediction
Atherosclerosis Versus Risk Factors

Don't Rely on Risk Factors!

Jim Fixx
Famous US Marathoner

- Not Overweight
- Very Fit
- Non-Smoker

DIED OF A MASSIVE HEART ATTACK AT AGE 52

Winston Churchill
Prime Minister during WWII

- Overweight
- Not Fit
- Heavy Smoker

LIVED TO AGE 89

Screening for Atherosclerosis

Risk Factors vs Disease

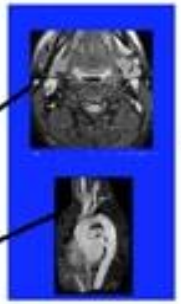
Numerous Risk Factors

- High LDL
- Low HDL
- High BP
- Diabetes
- Smoking
- CRP
- Metabolic Syn
- Lp(a)
- Homocysteine
- Dense LDL
- Lp-PLA2
- ApoB/ApoA
- Family History
- Sedentary Life
- Obesity
- Stress
- ...
- ?

Over 200 risk factors have been reported.

Carotid IMT and Plaque Measured by Ultrasound

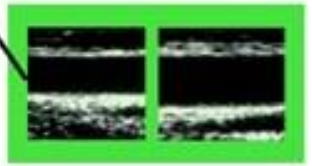
Examples of Arterial Structure Tests



Aortic and Carotid Plaque Detected by MRI

Coronary Calcium Score Measured by CT

Ankle Brachial Index



Brachial Vasoreactivity Measured by Ultrasound

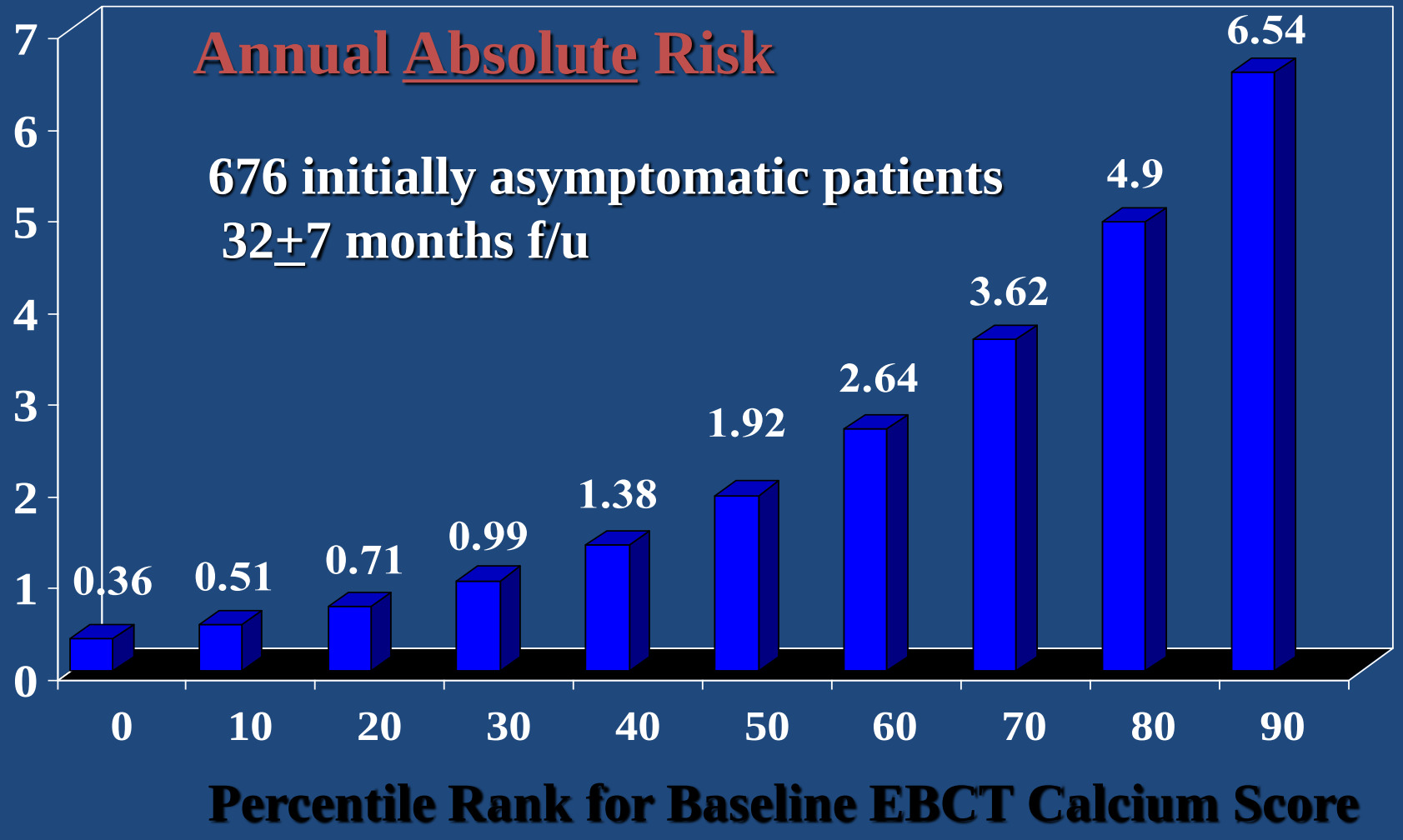
Vascular Compliance Measured by Radial Tonometry

Examples of Arterial Function Tests

Microvascular Reactivity Measured by Fingertip Tonometry

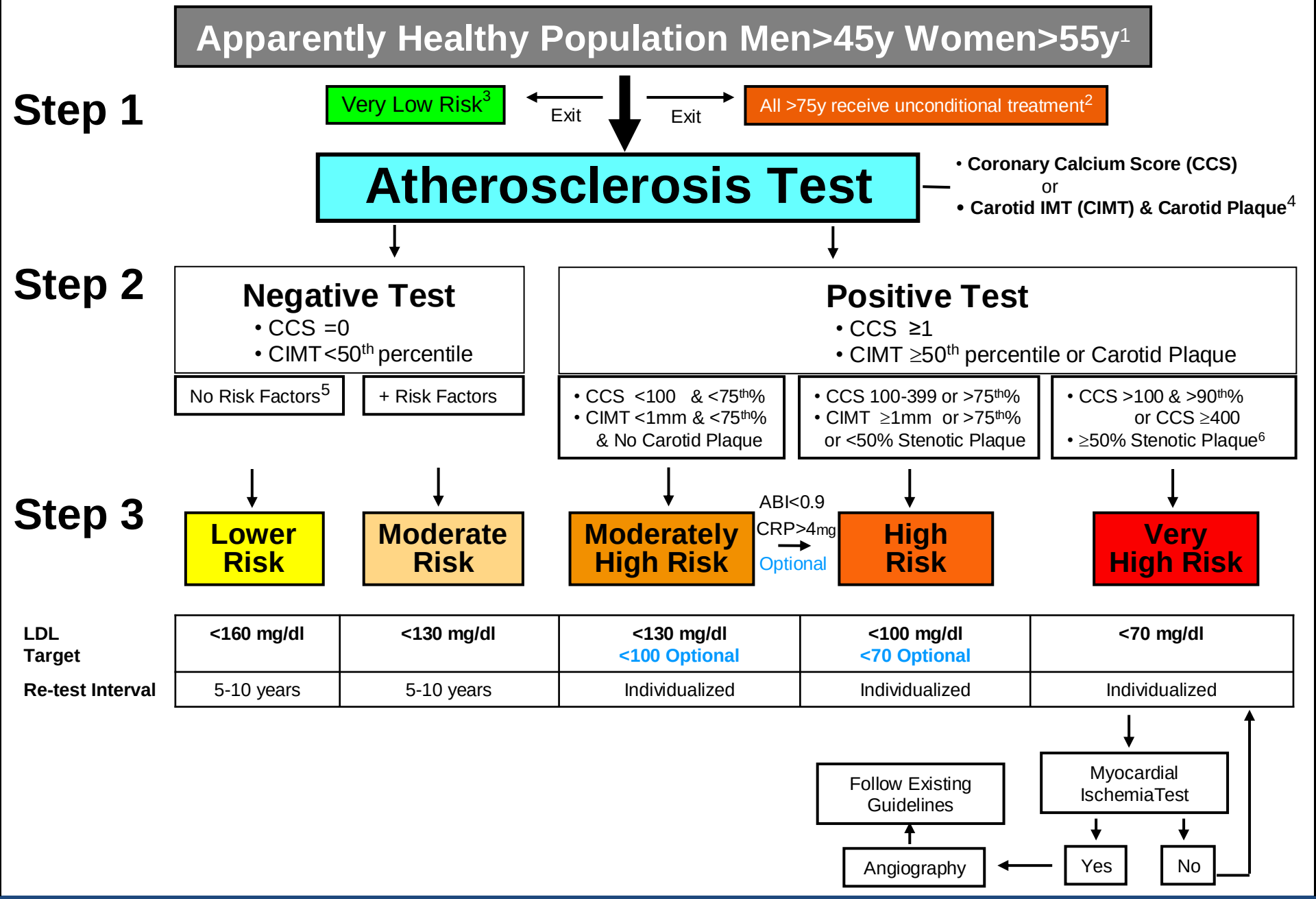
Prediction of MI/SCD in Asymptomatic Patients: EBT

Raggi et al AHJ 2001;141:193-199



The 1st S.H.A.P.E. Guideline

Towards the National Screening for Heart Attack Prevention and Education (SHAPE) Program



A statin a day keeps the doctor away: comparative proverb assessment modelling study

9400 lives saved if every UK citizen over age 50 took a daily statin

8500 lives saved if every UK citizen over age 50 ate an apple a day

BMJ 2013;347:f7267 (Published 17 December 2013)

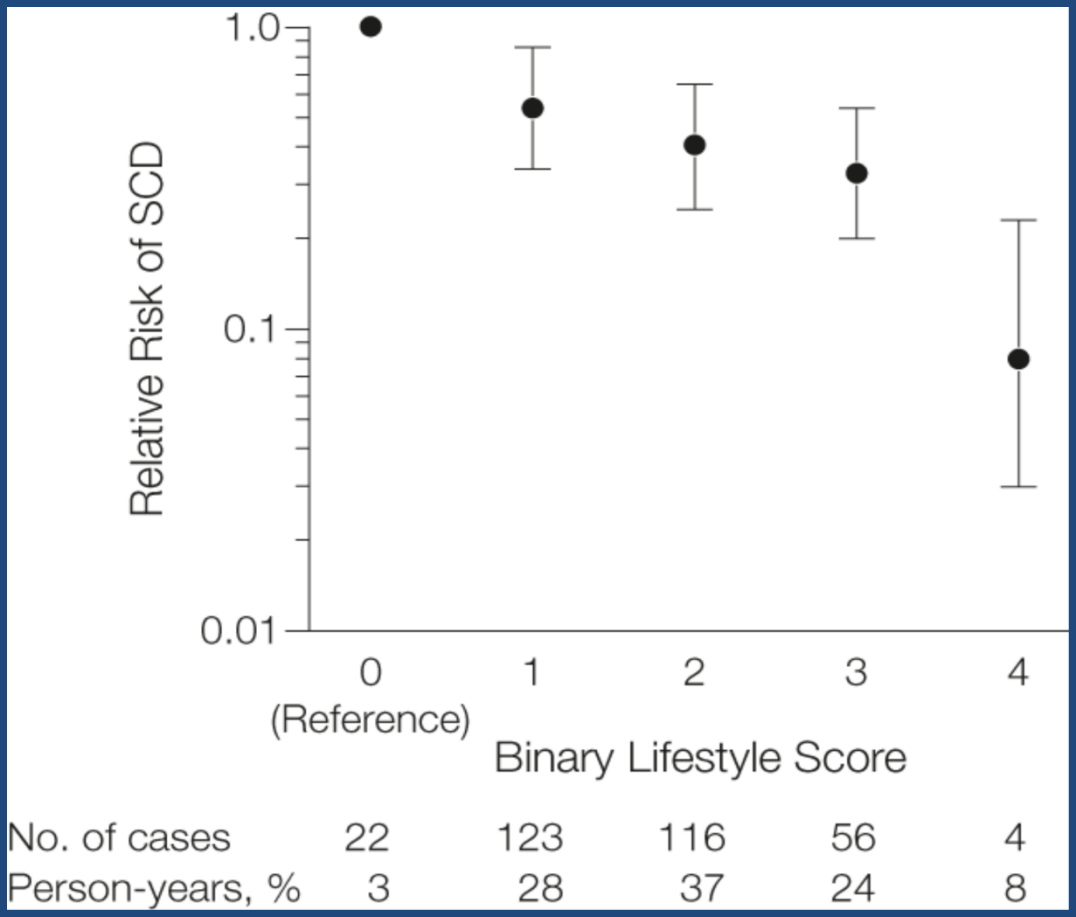
Final Exam

By following a healthy lifestyle and diet one may potentially reduce the risk of sudden cardiac death by:

a. 20%
b. 44%
c. 68%
d. 92%

Adherence to a Low-Risk, Healthy Lifestyle and Risk of Sudden Cardiac Death Among Women

JAMA 2011;306(1):62-69



Final Thoughts

- Will the new guidelines result in too many people taking a statin drug?
- What is the best way to identify high risk patients for primary prevention?
- What intensity of statin should I use?
- Should I take patients off of non-statin lipid therapies?
- Is there a better option than statins for CVD prevention?

“Heads you take a statin drug, tails you become a pescatarian.”