The New NCEP III Guideline

A Clinical Challenge to Interventional Cardiologists for Wider Utilization of Statins

Angioplasty Summit 2004

CVRF

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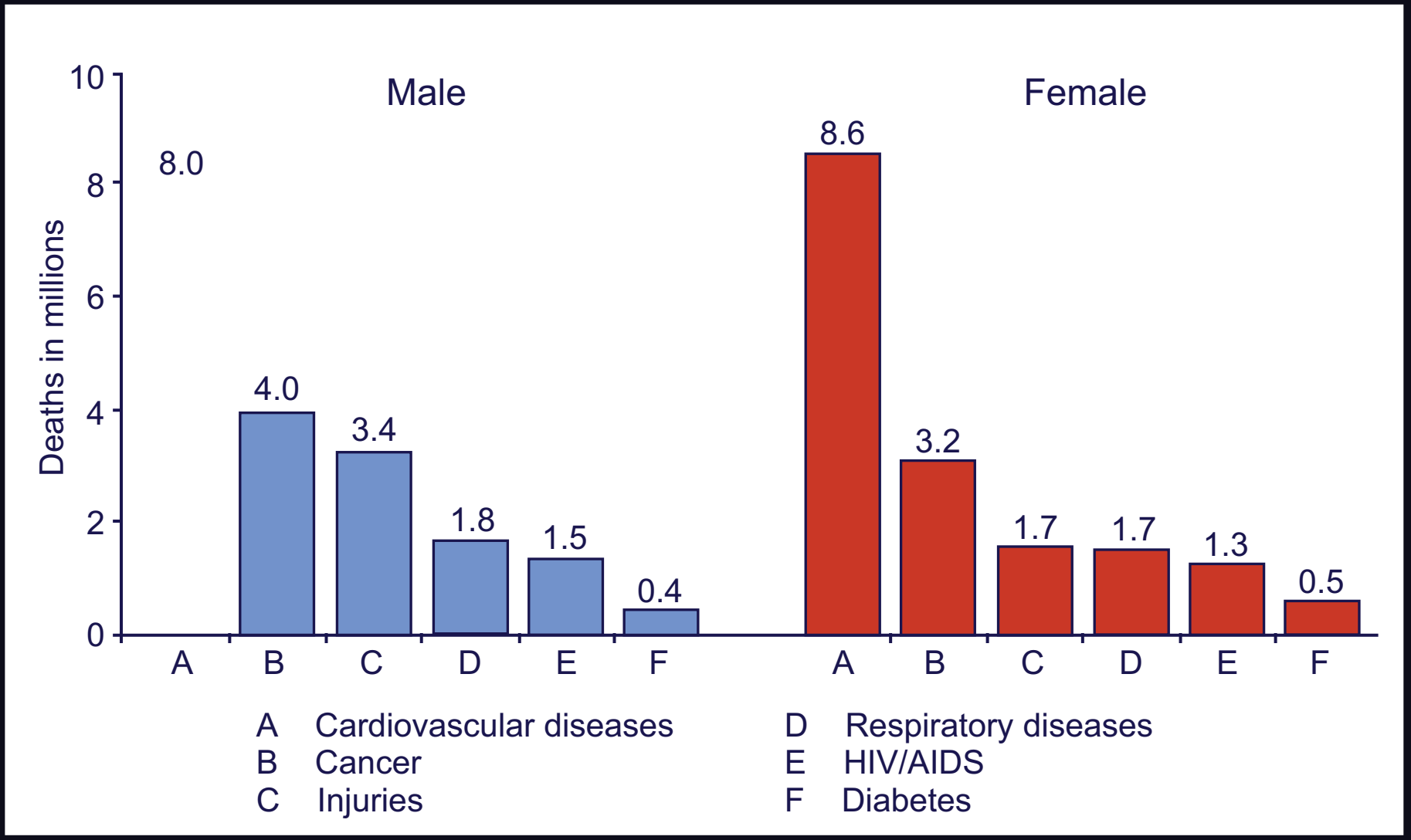
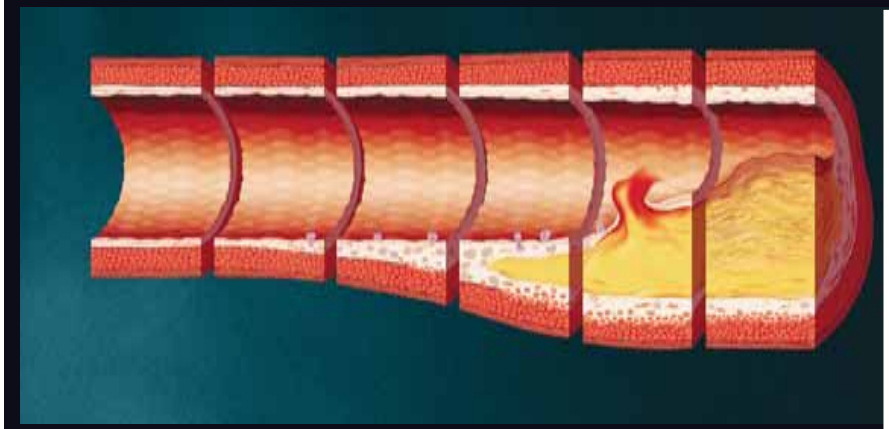
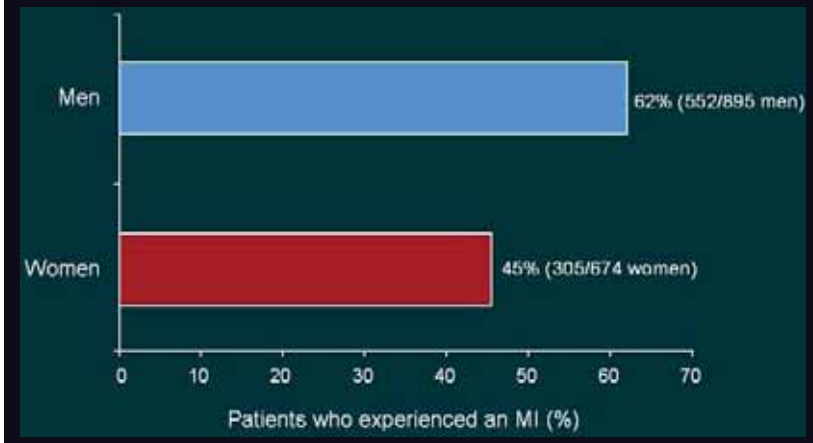
Causes of Death Worldwide, 2001



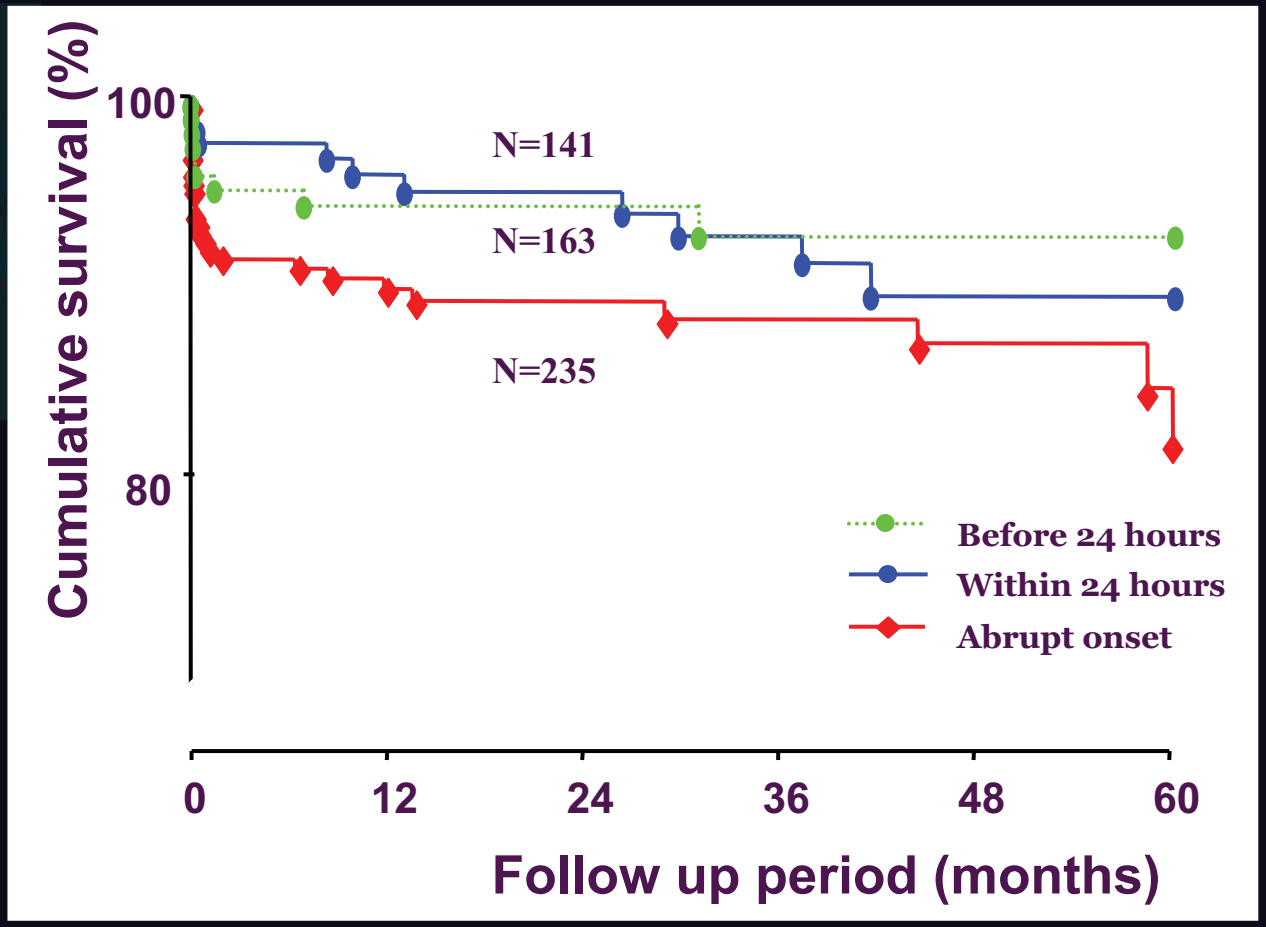
WHO. Global Burden of Disease Estimate 2001.

Atherosclerosis: Time Line



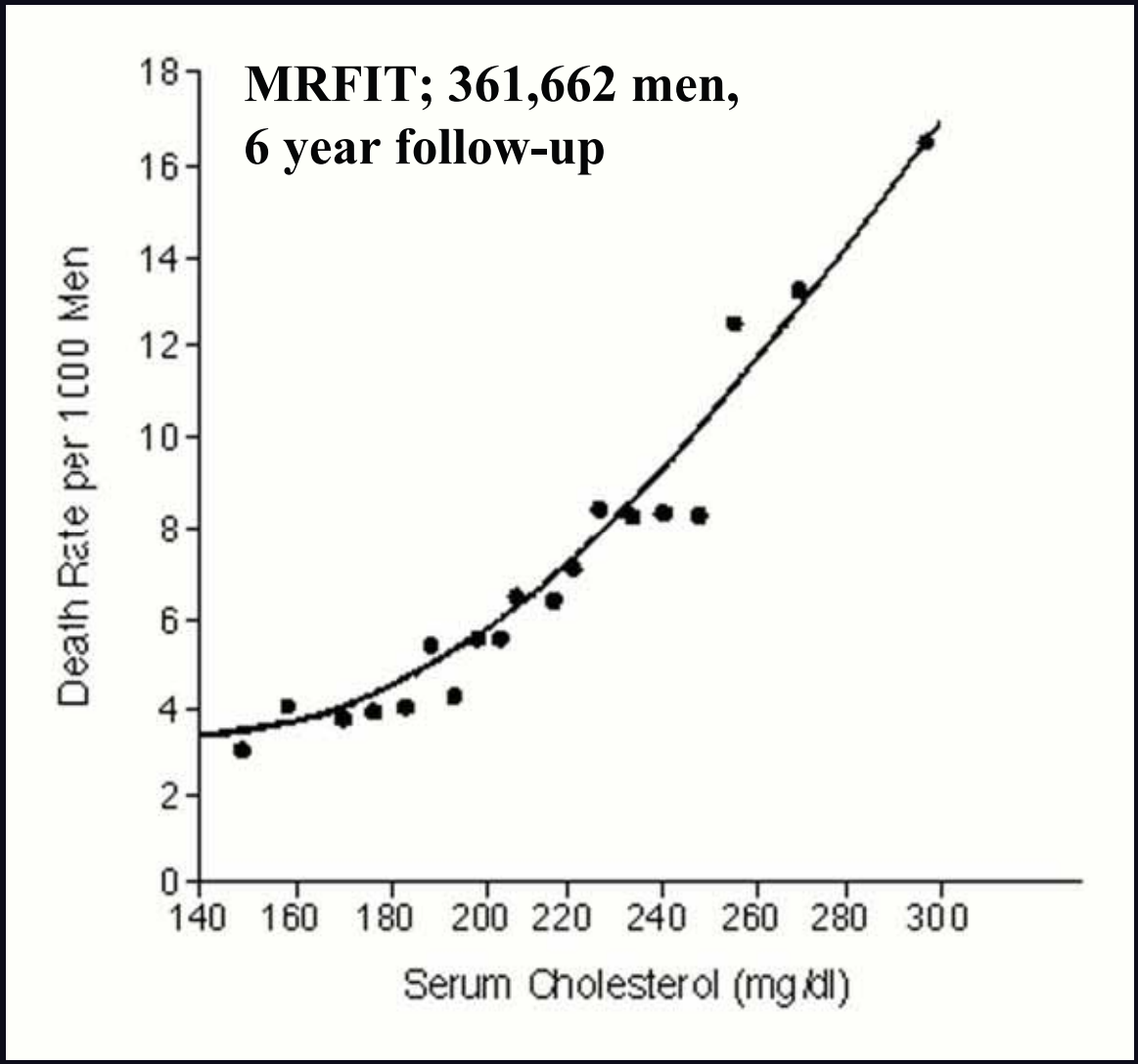


1st sign of CHD: SCD or AMI



AMC Data: AMI patients treated with primary angioplasty

No Clear Threshold



- **ATP III Classification**

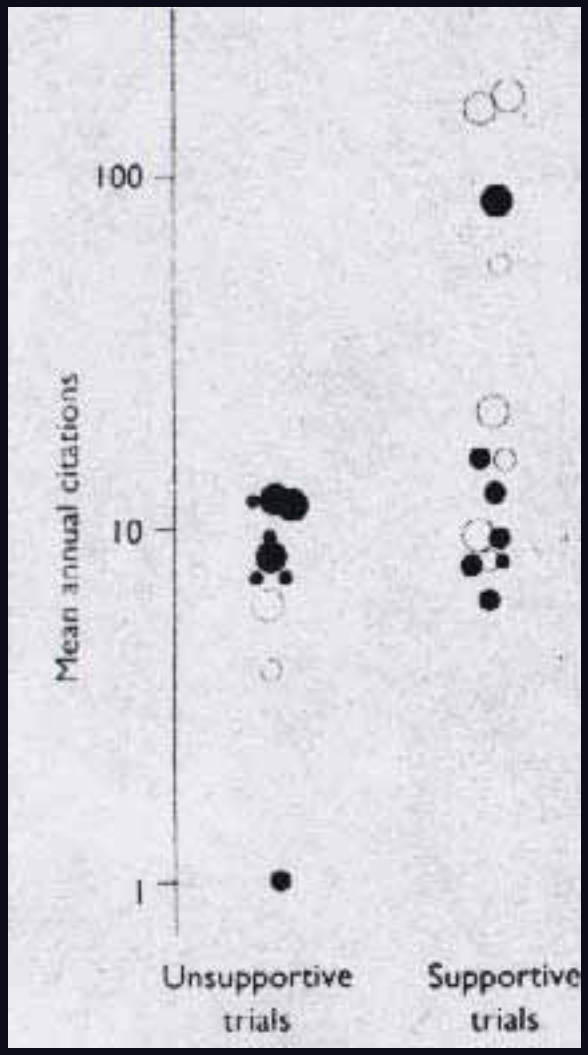
  LDL-C < 100mg/dl optimal

  T-Chol < 200mg/dl desirable

  HDL-C < 40mg/dl low

- **The relation between LDL-C levels and CHD risk is continuous over a broad range of LDL levels from low to high**

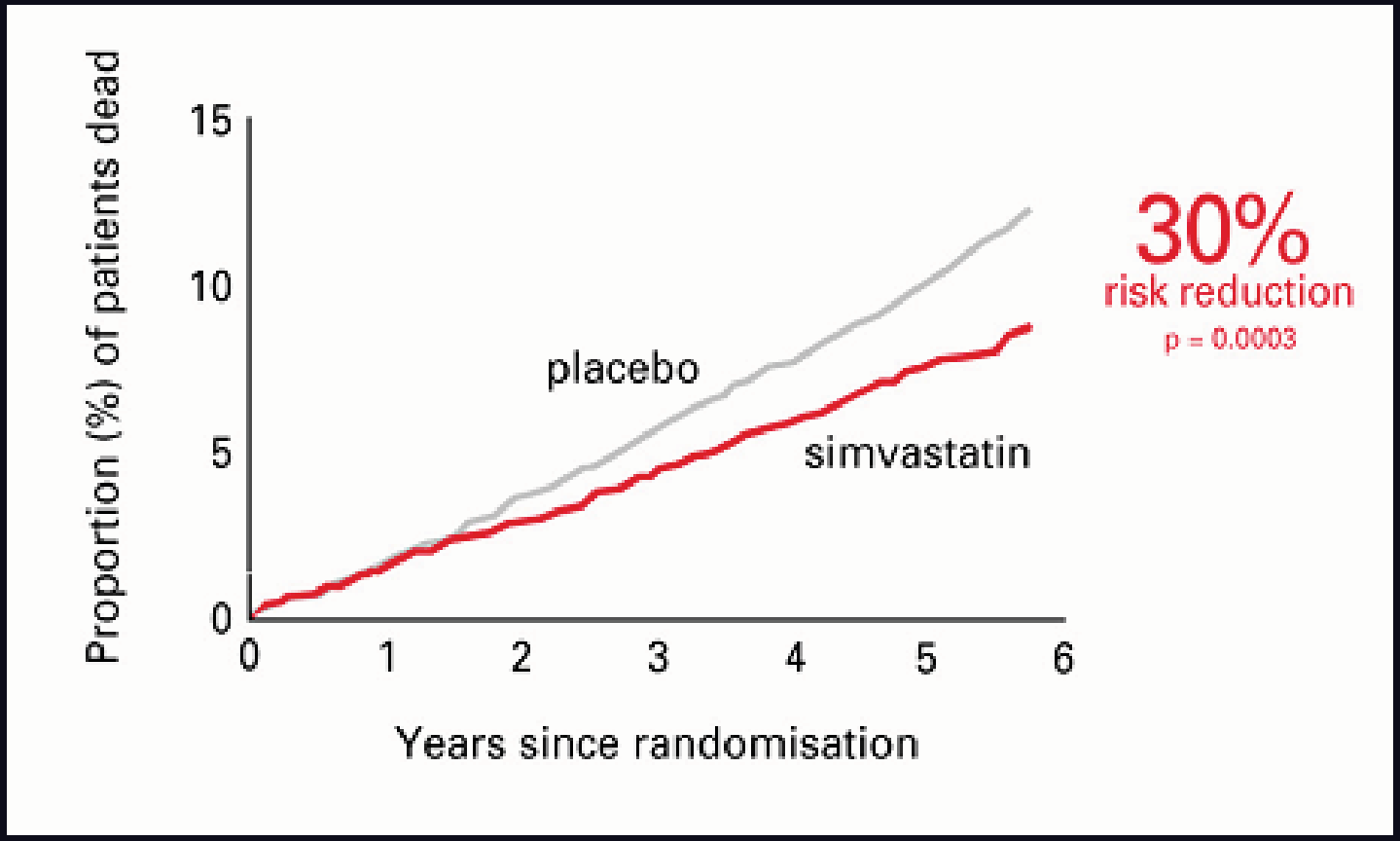
Cholesterol Lowering Trials



Lowering serum cholesterol concentrations does not reduce mortality and is unlikely to prevent coronary heart disease.

BMJ 1992;305:15-19

Scandinavian Simvastatin Survival Study (4S)



Long-term treatment with simvastatin is safe and improves survival in CHD patients.

Lancet 1994;344:1383

Landmark Clinical Event Trials: Relevance to Clinical Practice

High-risk CHD patients

Majority of CHD patients at risk

Patients at high risk for CHD

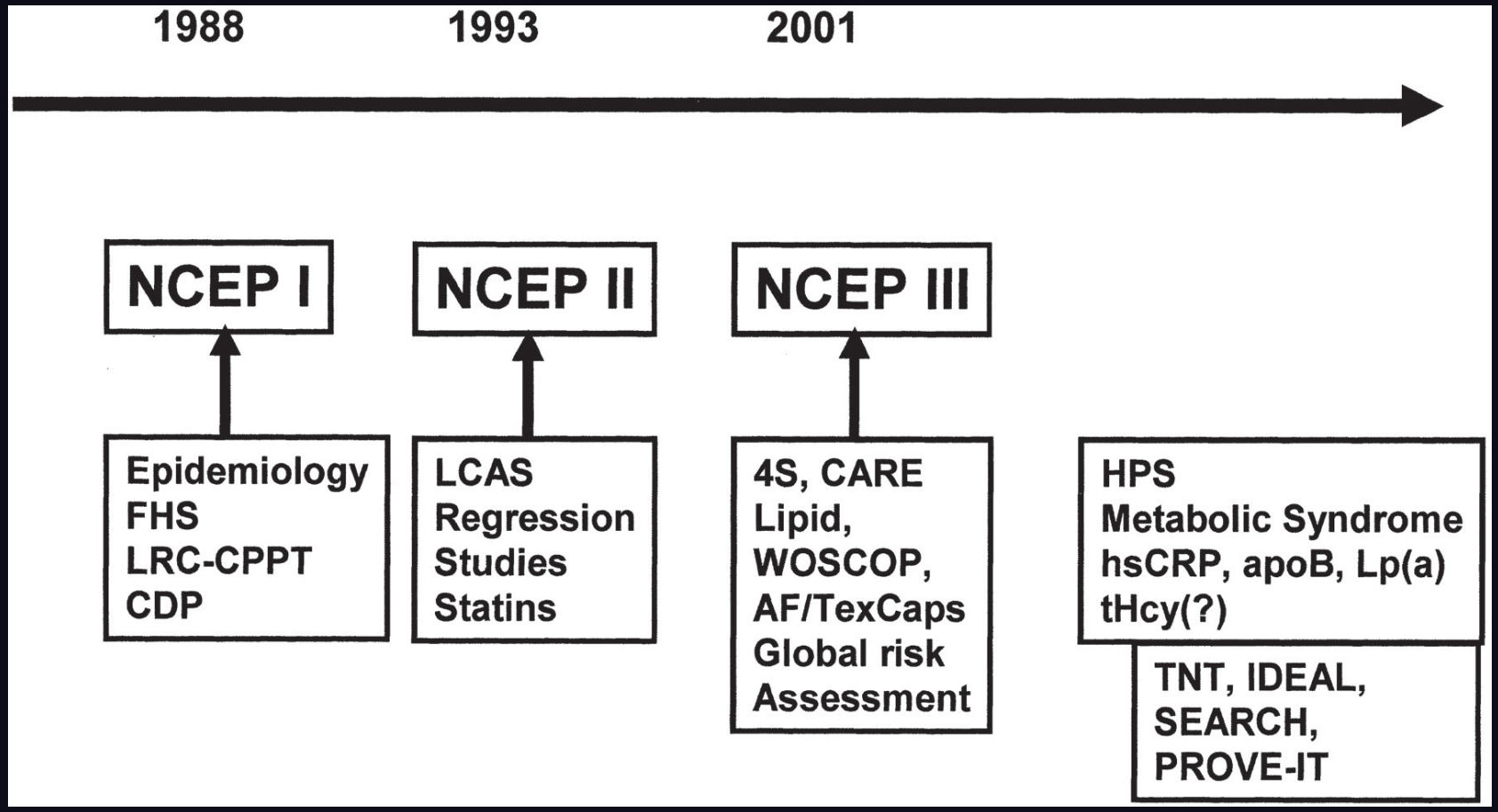
Patients at low risk for CHD

"The statins are to atherosclerosis what penicillin was to infectious disease"

Heart 2001;85:259-264

NCEP

Evidence-based guidelines on the management of patients with elevated blood cholesterol



Through all reports, 2 fundamental principles have been maintained:

1) LDL-C as the primary target of cholesterol-lowering therapy

2) The intensity of LDL-C lowering therapy adjusted as the absolute risk of the patients

Circulation 2003;107:2059

What's New in ATP III?

Pre-ATP III	ATP III
Primary Prevention Secondary Prevention Counting Risk Factors Relative Risk Reduction	Global Risk Assessment (low,mod,high) CHD Risk Equivalent Absolute Risk Reduction The Metabolic Syndrome

What Is High-Risk Status?

- Presence of CHD
- Other clinical forms of atherosclerotic disease (PAD, abd aortic aneurysm symptomatic CAD)
- Diabetes
- Multiple risk factors (10-y risk for CHD > 20%)

* Major risk factors to define the core risk status:
age (M>45, F>55), hypertension, smoking, low HDL(<40mg/dl),
family history of premature CHD

How to Assess Risk Status

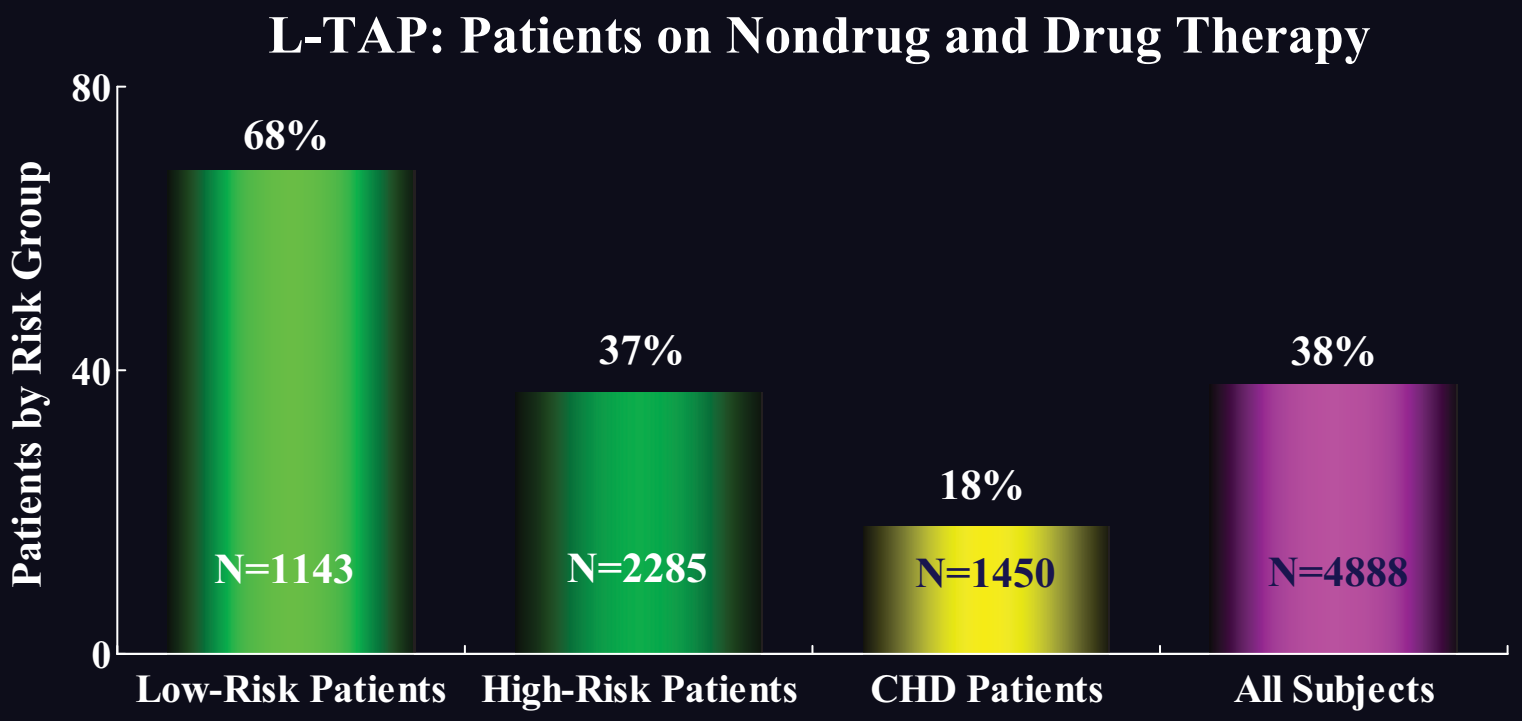
The number of risk factors is counted.
For persons with multiple(2+) risk factor,
10-year risk assessment with Framingham scoring

<10%	10-19%	≥20%
Lifestyle Therapy	Clinical Judgment	Drug Therapy

3 Categories of Risk That Modify LDL Goals

Risk Category	LDL Goal (mg/dl)	Initial TLC (mg/dl)	Consider Drug Therapy (mg/dl)
CHD or CHD Risk Equivalent (10-y risk > 20%)	< 100	≥ 100	≥ 130 (100-129: optional)
2+ Risk Factors (10-y risk ≤ 20%)	< 130	≥ 130	10-y 10-20%: ≥ 130 10-y <10%: ≥ 160
0-1 Risk Factor	< 160	≥ 160	≥ 190 160-189:optional

Few Treated Patients Achieve NCEP LDL-C Goals



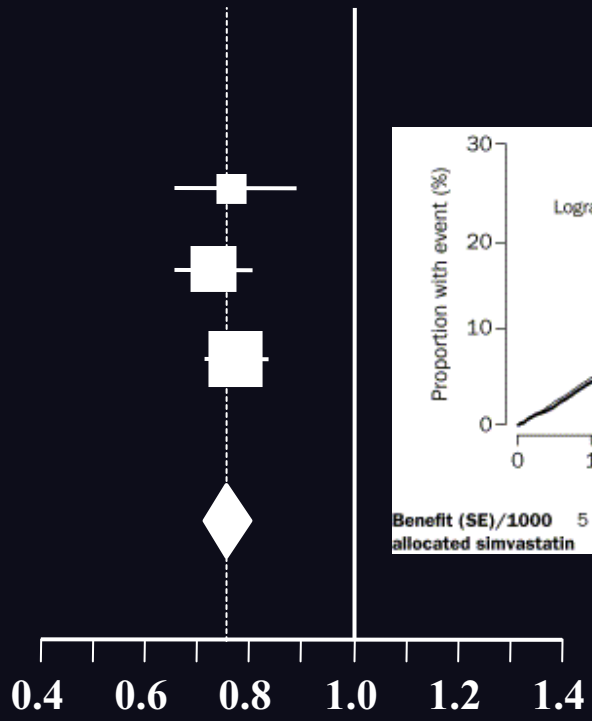
- Elevated cholesterol remains as one of the most prevalent and undertreated medical conditions in the world today.
- Patients, caregivers, and the health care system need to work together to improve effectiveness of treatments.

Arch Intern Med 2000;160:459

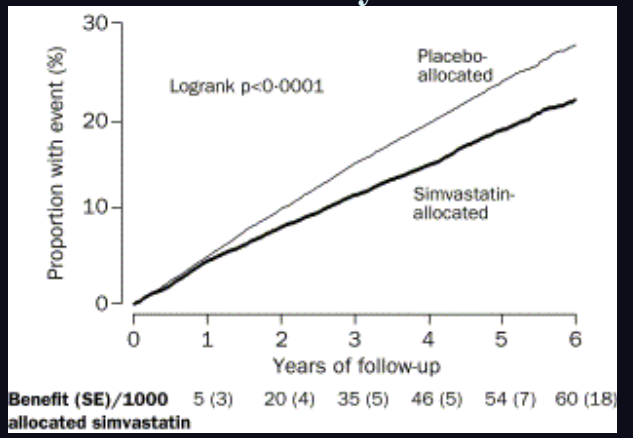
Heart Protection Study

Statins are the new aspirin.

Baseline Feature	STATIN (10269)	PLACEBO (10267)
LDL (mg/dl)		
< 100 (2.6 mmol/l)	285	360
≥ 100 < 130	670	881
≤ 130 (3.4 mmol/l)	1087	1365
ALL PATIENTS	2042 (19.9%)	2606 (25.4%)



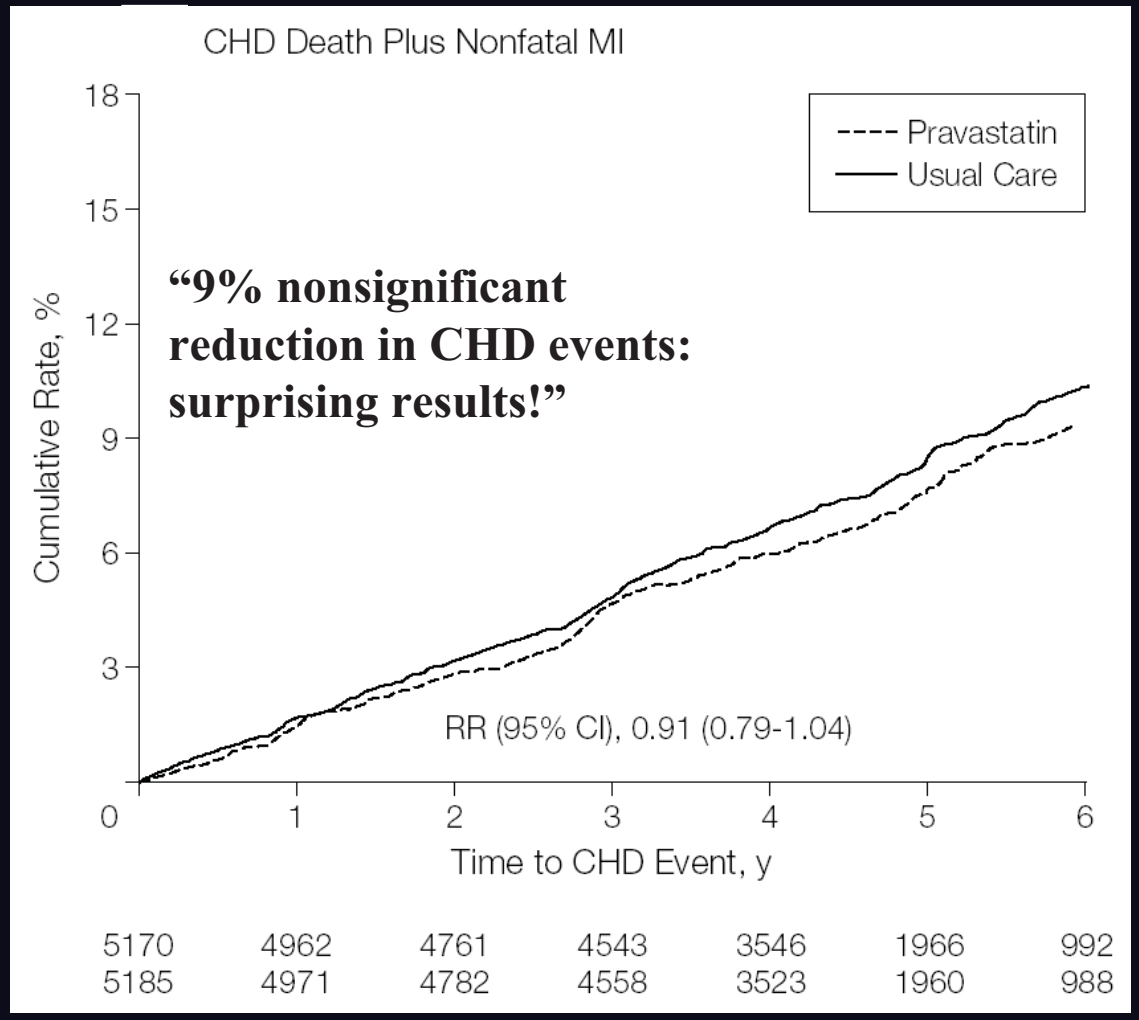
n=20,536
40-80 y



Lancet 2002:360:7

The second-largest lipid-lowering trial yet reported.

The ALLHAT Lipid Lowering Trial—Statins Do Not Work?



N = 10 355, ≥ aged 55 y
LDL-C: 120-189 mg/dL
(100 to 129 mg/dL if known CHD)
Pravastatin 40mg vs usual care

LDL-C levels: reduced by 28% with pravastatin vs 11% with usual care

Pravastatin did not reduce either all-cause mortality or CHD significantly when compared with usual care in older participants with well-controlled hypertension and moderately elevated LDL-C.

JAMA 2002;288:2998

What Are The Lessons of ALLHAT-LLT ?

- Usual care group had 26.1% statin use, but this is not much different from HPS placebo group

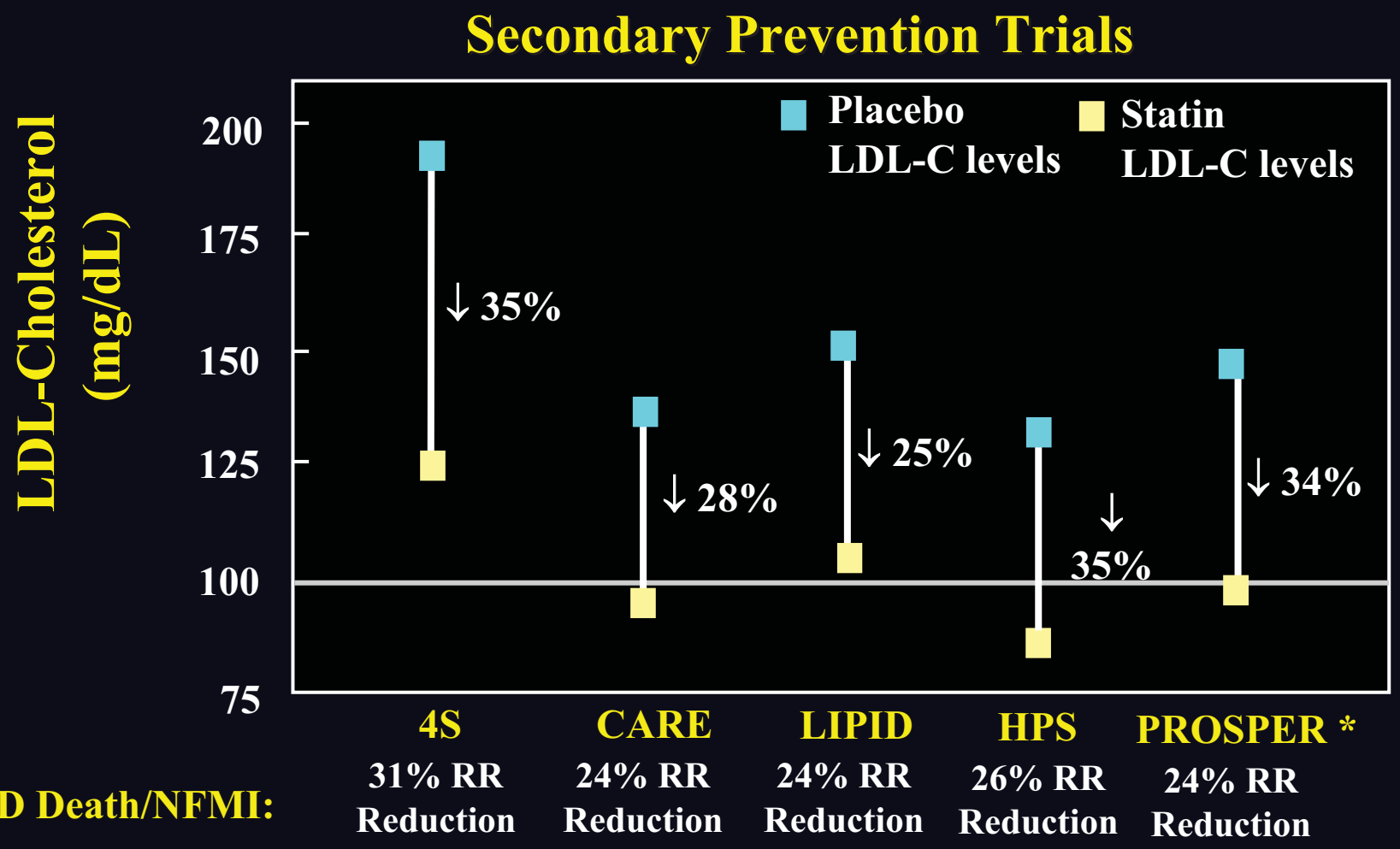
- ALLHAT-LLT should not be viewed as a negative trial for pravastatin.

  → Less cholesterol lowering produces less benefit in clinical outcomes.

- If less is less, is it necessarily true that more is more?

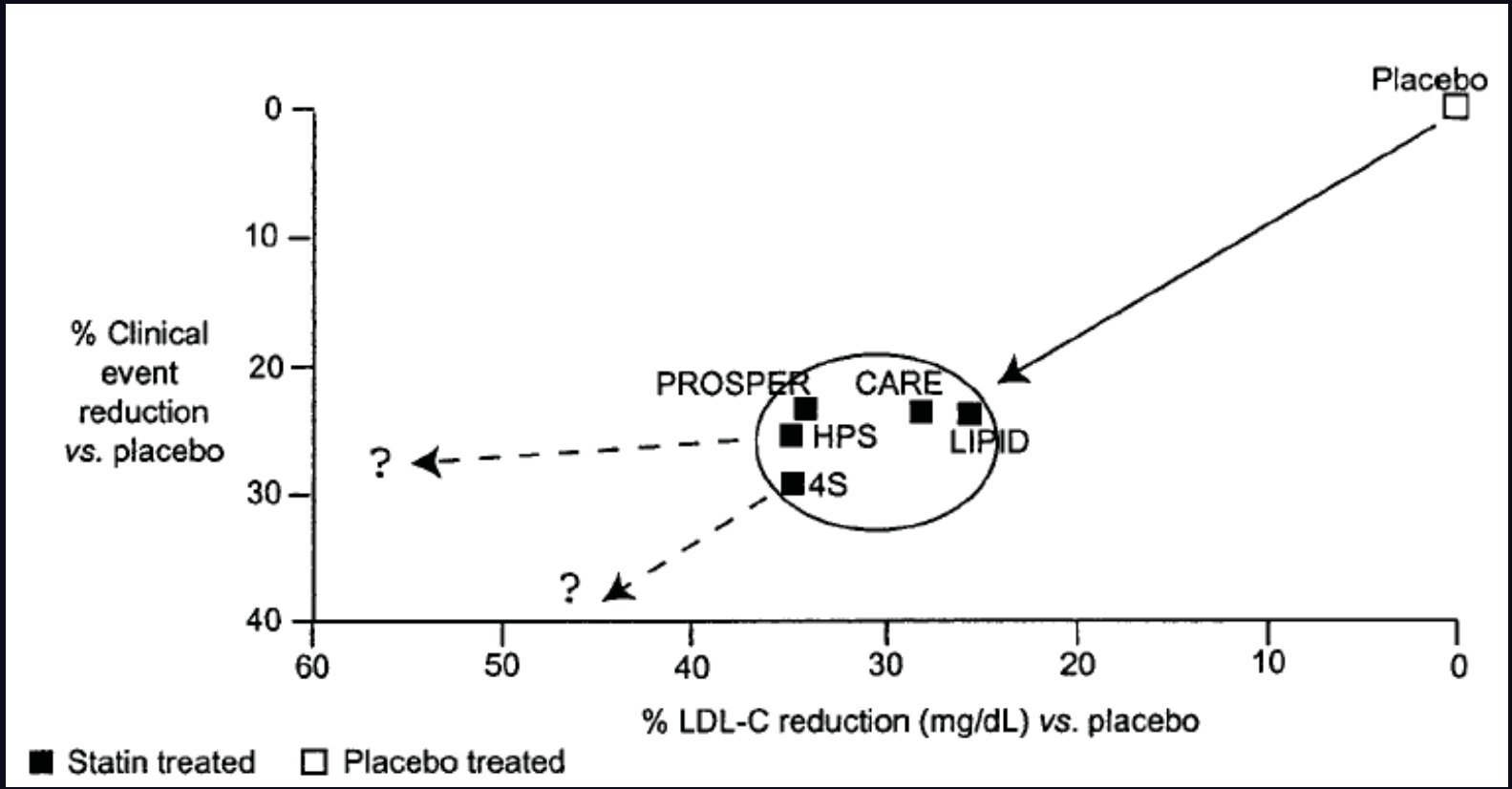
  Thus far, not for certain.

Despite Varying Degrees of LDL-C Lowering and Achieved LDL-C Levels; Statins Demonstrate Similar Reduction in Clinical Events



"No significant differences in clinical event rates when lowering LDL-C between 25% and 35%."

How Far Will the Benefits Go?



- It is not unclear whether lowering lipid levels further would increase the clinical benefit.
- HPS is not designed to answer the question of whether a lower LDL-C is better:
  The comparison (statin vs placebo) can only address the question of whether treatment better than no treatment. → We must consider treatment vs treatment.

Is Aggressive LDL-C Lowering More Effective in Reducing Clinical Events?

Trials in ACS

- PROVE-IT
- A-to-Z

Evaluate the effects of plaque stabilization and intermediate term clinical outcomes in ACS patients (2 years)

Trials in Chronic Stable Angina

- TNT
- SEARCH
- IDEAL

Evaluate the long term effects on clinical outcomes in patients with chronic stable atherosclerosis (5 years)

It's the LDL, stupid.
It is the drug as well ?

- **Statins as a class reduce mortality and morbidity.**

  → All members of a drug class are interchangeable.

- **PROVE-IT and REVERSAL**

  → **Lower is better ?**

  → **Statin differences: The statins do not have like effect?**

  LDL-C reduction alone does not explain all of the differences in efficacy.

A Sea Change in CV Medicine

- To Open or Not To Open ?
  - drug-eluting stents

    PTCA is like going to the dentist

    not cure, but control
- Beyond angioplasty (the event rate to towards zero)
  - Intensive statin therapy ?

    The future guidelines will help make treatment more effective, more widespread and more specific.