

# **“Lipids in 2007”**

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## **DISCLOSURE:**

**Advisory board, consultancy and speakers' bureau:**

**Merck-Schering, AstraZeneca, Pfizer, Fournier, Oryx**

# Case report: 1997

46 yr old male, truck driver

+smoker; +family history; +hypertension (unRx'd)

acute retrosternal chest discomfort

OE: BP 150/95; TC 6.4; LDL-C 4.5; HDL-C 1.3; TG 2

EKG: anterior STEMI

Rx: balloon angioplasty

ASA

pindolol

pravachol 20 mg: LDL-C 3.5 mmol/L (CARE)

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OE: BP 150/95; TC 6.4; LDL-C 4.5; HDL-C 1.3; TG 2

EKG: anterior STEMI

Rx: balloon angioplasty; drug-eluting stent

ASA 325; plavix 75 mg

ramipril 10 mg

metoprolol 50 mg

atorvastatin 80 mg: LDL-C 1.9 mmol/l

# Statin end point studies

## 2° prevention

## statin

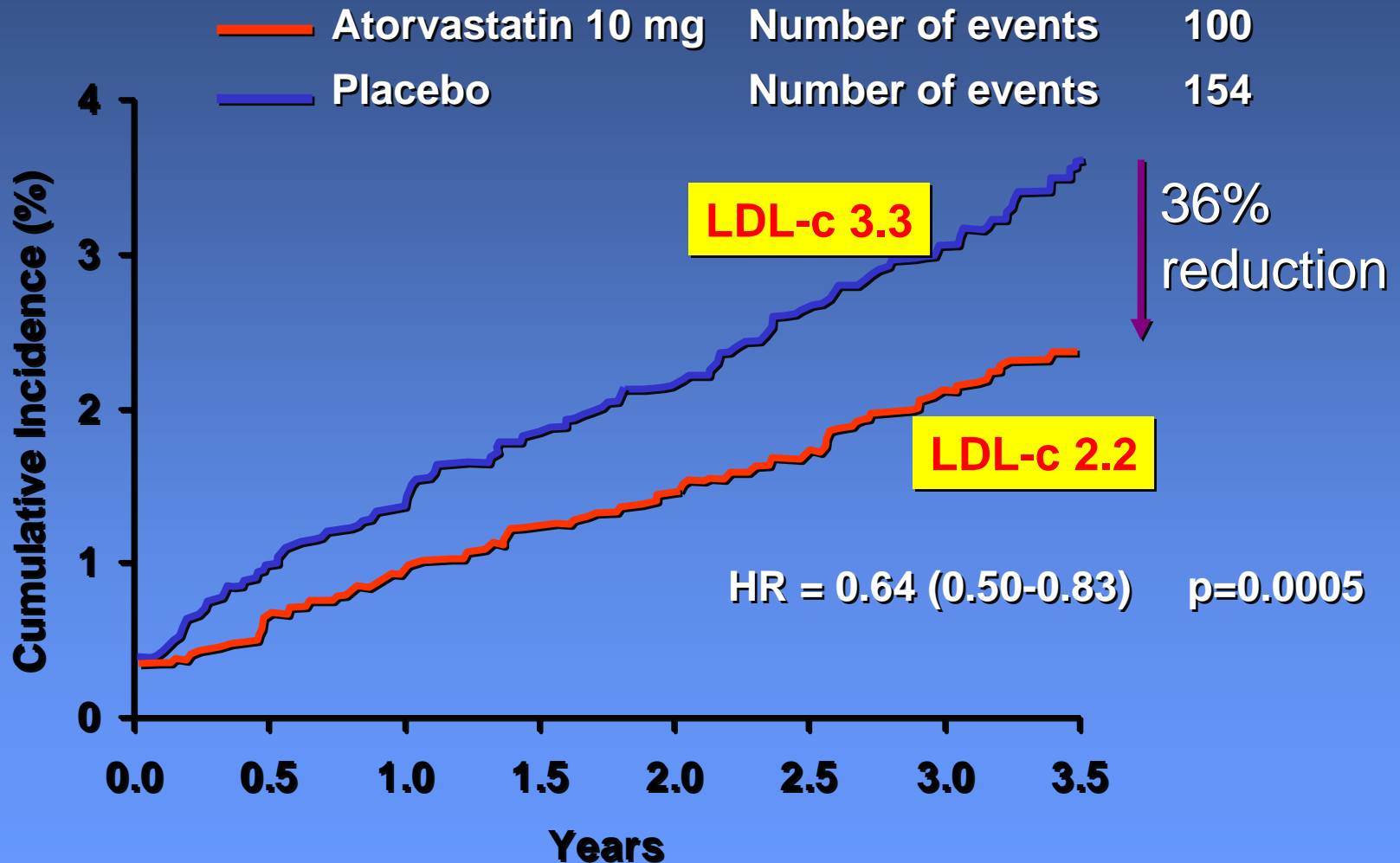
4S	simva
CARE	prava
LIPID	prava
<b>MIRACL</b>	<b>atorva</b>
<b>AVERT</b>	<b>atorva</b>
LCAS	fluva
LIPS	fluva
HPS	simva
<b>PROVEIT</b>	<b>atorva</b>
<b>TNT</b>	<b>atorva</b>
<b>IDEAL</b>	<b>atorva</b>
<b>SPRACL</b>	<b>atorva</b>

## 1° prevention

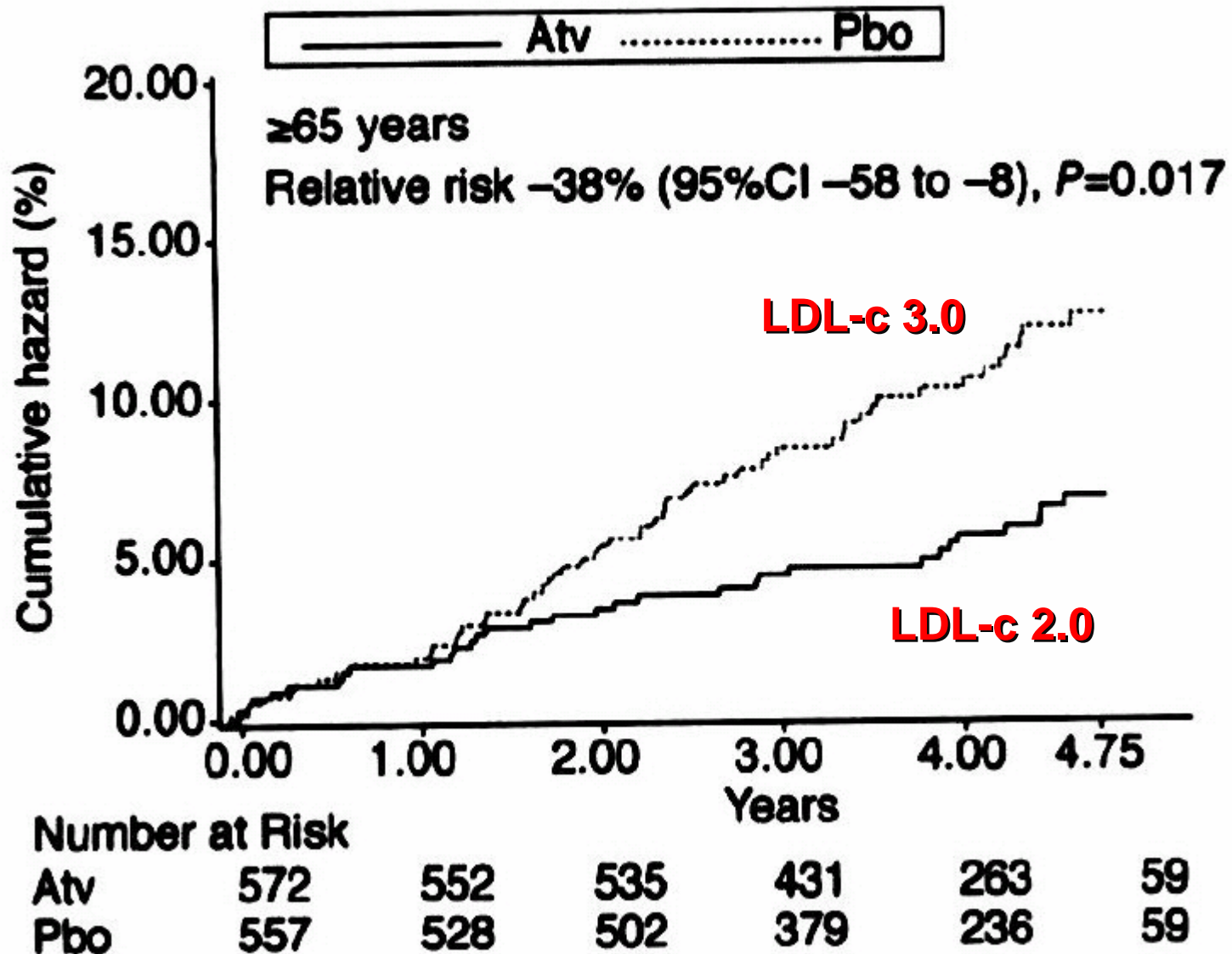
## statin

WOSCOPS	prava
AFCAPS	lova
<b>CARDS</b>	<b>atorva</b>
<b>ASCOT</b>	<b>atorva</b>
<b>ASPEN</b>	<b>atrova</b>

# ASCOT: Nonfatal MI and Fatal CHD

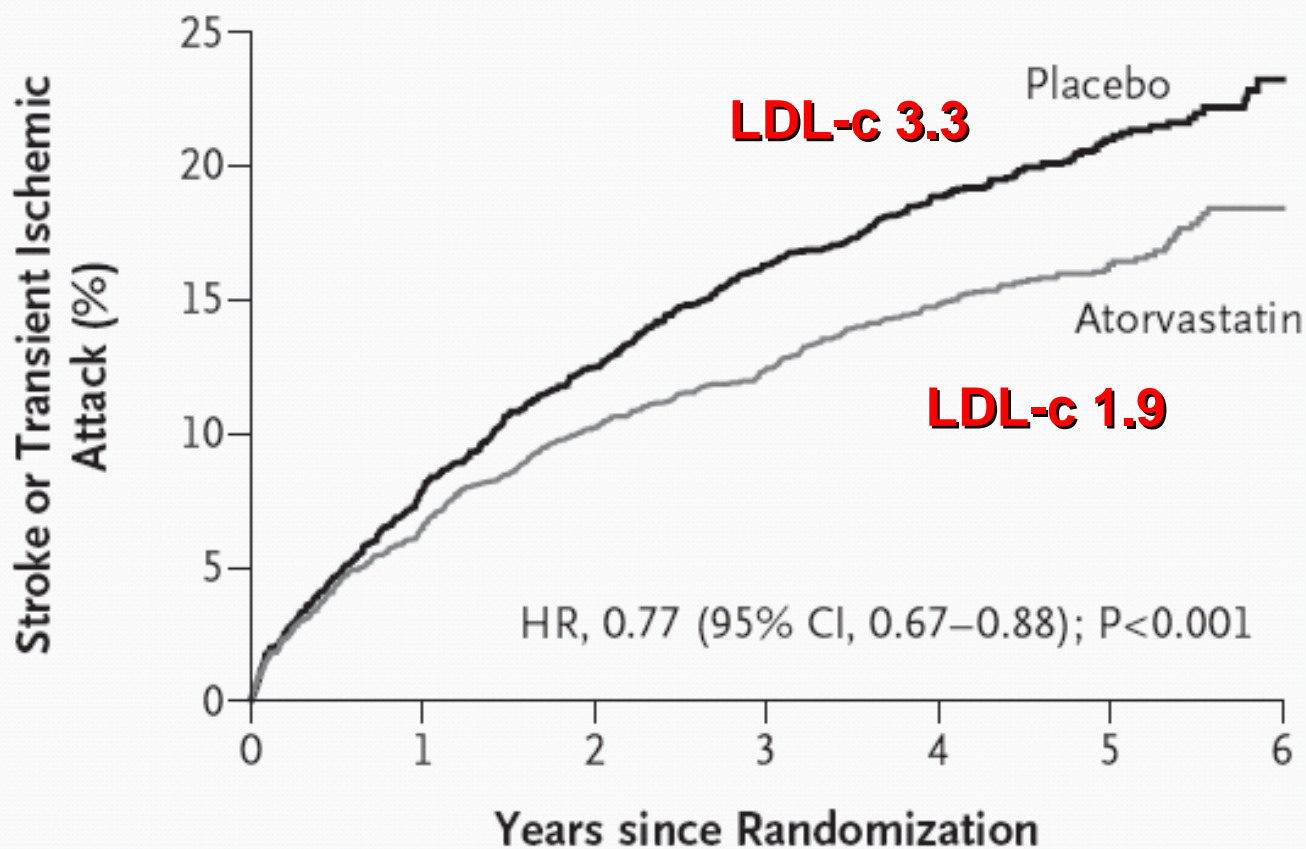


# CARDS: 1° endpoint $\geq 65$ yrs



# SPARCL: stroke prevention

D

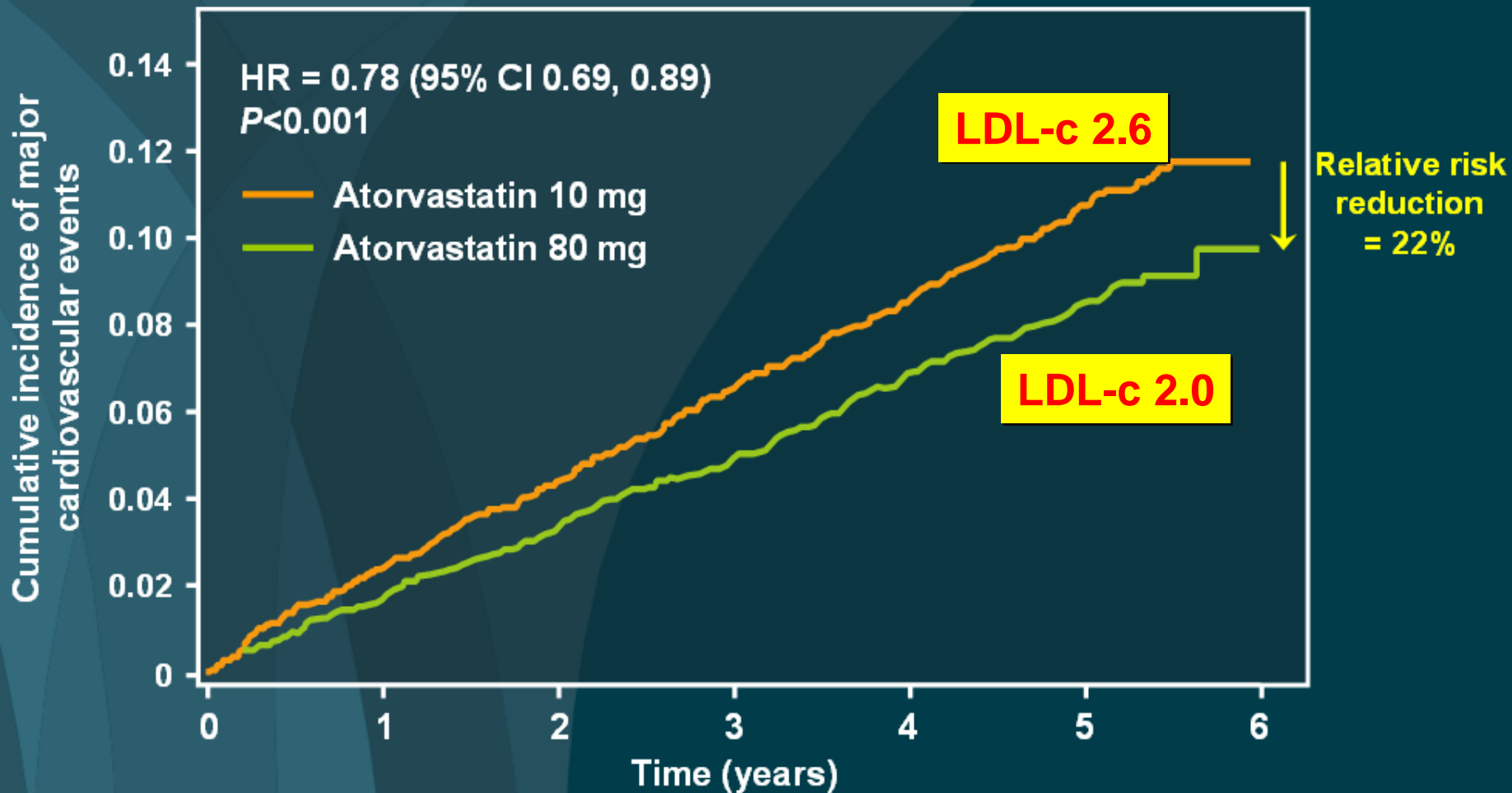


## No. at Risk

Atorvastatin	2365	2148	2023	1933	1837	871	119
Placebo	2366	2132	1998	1871	1780	803	126



# Primary Efficacy Outcome Measure: Major Cardiovascular Events\*



\*CHD death, nonfatal non-procedure-related MI, resuscitated cardiac arrest, fatal or nonfatal stroke

# The 2006 Lipid Guidelines

## Canadian Cardiovascular Society position statement – Recommendations for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease

R McPherson, J Frohlich, G Fodor, J Genest. Canadian Cardiovascular Society position statement – Recommendations for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease. *Can J Cardiol* 2006;22(11):913-927.

**ACKNOWLEDGEMENTS:** Primary review panel members: Steven Grover, Rafik Habib, Stewart Harris, Heather Arthur. Secondary review panel members: Peter Bogaty, Dominic Ng, André Carpentier, Robert A Hegele, Ehud Ur, John Mancini, Glen J Pearson, Milan Gupta.

# The 2006 Lipid Guidelines

## HIGHLIGHTS OF THE 2006 LIPID GUIDELINES

### Process

- Collaboration with the Canadian Cardiovascular Society;
- Primary and secondary review panels;
- Adherence to the Appraisal of Guidelines Research and Evaluation principles of guideline formation; and
- Grading of evidence for each recommendation.

### Content

- LDL-C treatment target of lower than 2.0 mmol/L for high-risk patients;
- Intervention point for initiation of lipid-lowering therapy in most low-risk individuals changed to an LDL-C of 5.0 mmol/L or a total cholesterol (TC) to high-density lipoprotein cholesterol (HDL-C) ratio of 6.0; and
- Recommendations regarding potential additional investigations for the further evaluation of CAD risk in subjects in the moderate-risk category.

# The 2006 Lipid Guidelines

## Screening (Class 2a, level C)

- Men > 40 y; Post-menopausal women (>50 y)
- Diabetes, Hypertension, MetS (visc obese)
- Family of premature CAD
- Dyspnea, erectile dysfunction, renal disease, SLE or atherosclerosis.

# The 2006 Lipid Guidelines

**TABLE 4**  
**Risk categories and treatment recommendations**

<b>Risk level</b>	<b>10-year CAD risk</b>	<b>Recommendations</b>	<b>Grade, level of evidence</b>
High*	≥20%	<i>Treatment targets</i> <sup>†</sup> : Primary: LDL-C <2.0 mmol/L Secondary: TC/HDL-C <4.0	Class I, level A Class IIa, level A
Moderate <sup>‡§</sup>	10% – 19%	<i>Treat when</i> : LDL-C ≥3.5 mmol/L or TC/HDL-C ≥5.0	Class I, level A Class I, level A
Low <sup>‡§</sup>	<10%	<i>Treat when</i> : LDL-C ≥5.0 mmol/L or TC/HDL-C ≥6.0	Class IIa, level A Class IIa, level A

***Question: “If a patient comes back from the hospital after an MI on a high dose statin (i.e. 80mg Lipitor) how long should this patient stay on this dose?”***

# The 2006 Lipid Guidelines

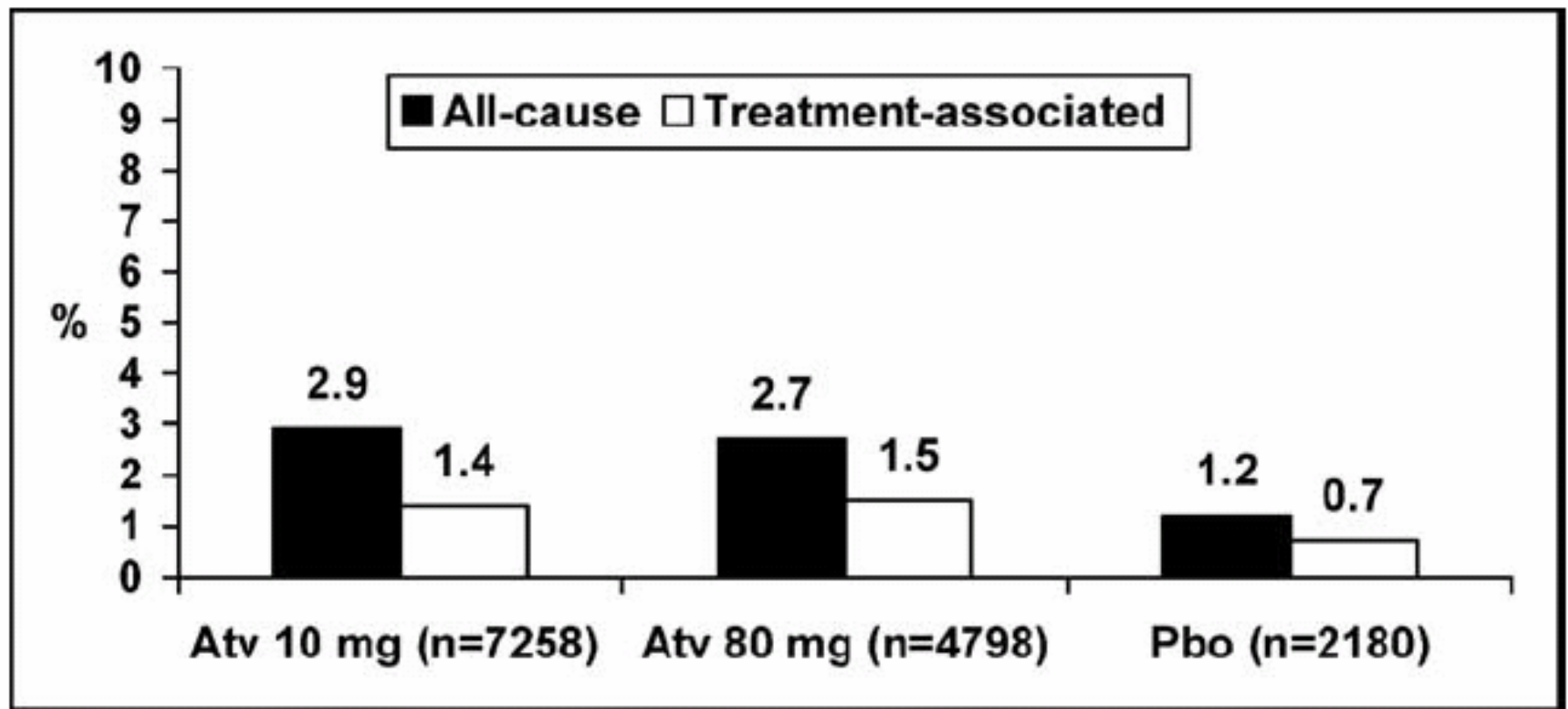
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***Question: “Can you comment on the safety of high dose statins?”***

# Comparative Safety of *Atorvastatin* 80 mg Versus 10 mg Derived from Analysis of 49 Completed Trials in 14,236 Patients

Connie Newman, MD\*, John Tsai, MD, Michael Szarek, MS, Don Luo, PhD, and Eric Gibson, PhD



***Question: “If a patient is not at target on a lower dose statin, what warning signs should I look for when increasing the dose to reach target?”***

# The 2006 Lipid Guidelines

## ADDITIONAL INVESTIGATIONS OF POTENTIAL USE IN RISK ASSESSMENT

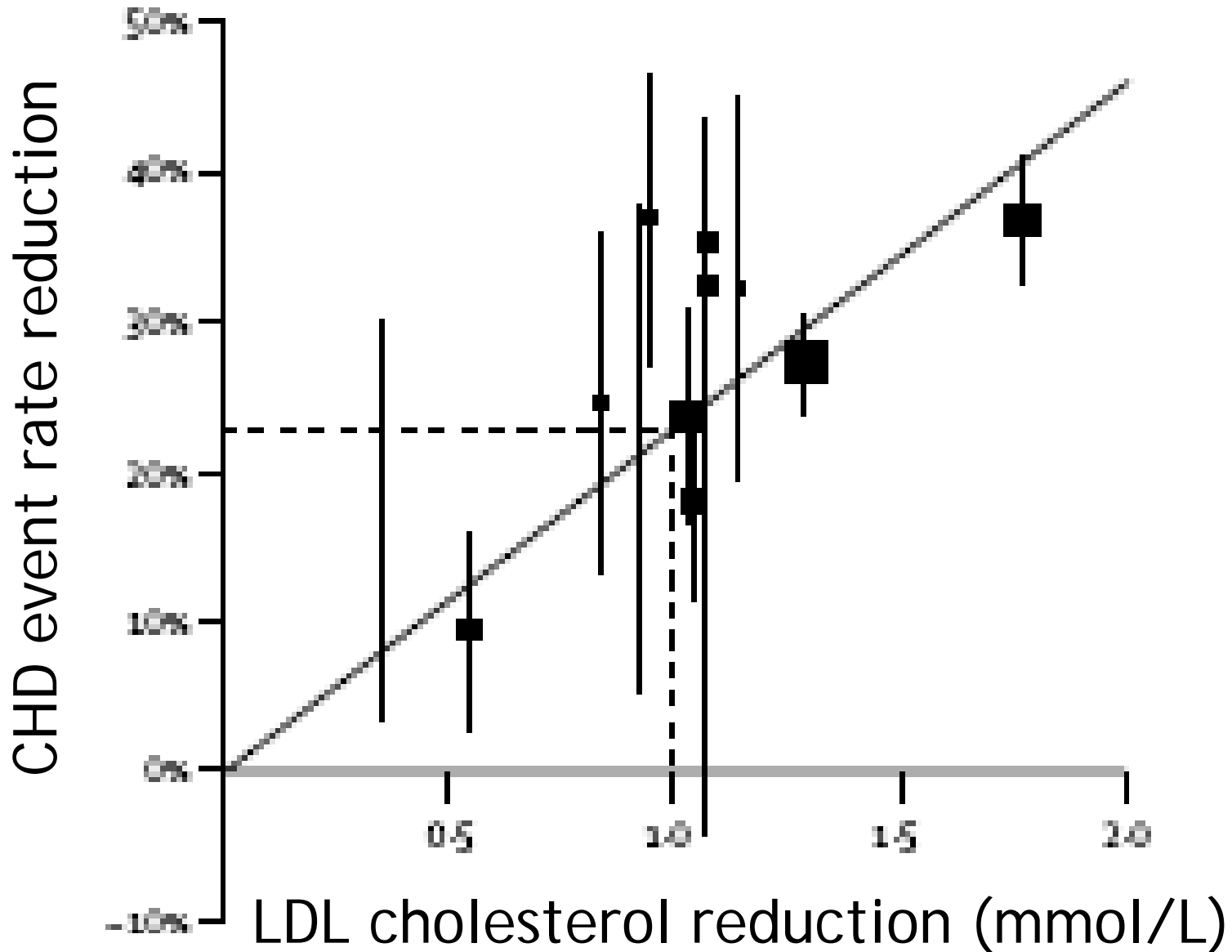
For patients with a low FRS (10-year risk less than 10%), no indicators of possible subclinical atherosclerosis and no family history of early CAD, additional investigations are not usually indicated. Individuals in the intermediate-risk category (FRS between 10% and 20%) may be moved to a higher or lower risk category based on additional investigations. Investigations of possible clinical use include:

- laboratory measurements such as apo B, hsCRP, Lp(a) and, for individuals with elevated plasma glucose, glycated hemoglobin (HbA1c);
- assessment of exercise capacity (metabolic equivalent [MET] level achieved) by graded exercise stress testing (61-64); and
- noninvasive assessment of atherosclerosis such as determination of ankle-brachial index (ABI) (65) and carotid imaging (66,67).



***Question: As physicians should we be more worried about the amount of LDL we lower in a patient versus the actual target level the patient reaches? For example, some patients will not get to their LDL goal of 2.0 mmol/L. However if we have achieved >50% LDL reduction in that patient is that sufficient?***

# CHD rate in LDL-C lowering trials



# Prospective meta-analysis: 90,056 participants in 14 randomized statin trials

- **For each 1 mmol/L LDL-C lowering**
  - 12% reduction in all cause mortality ( $p < 0.0001$ )
  - 19% reduction in coronary mortality ( $p < 0.0001$ )
  - 23% reduction in MI and coronary death ( $p < 0.0001$ )
  - 24% reduction in revascularizations ( $p < 0.0001$ )
  - 17% reduction in fatal or non-fatal stroke ( $p < 0.0001$ )
  - 21% reduction in any major vascular event ( $p < 0.0001$ )
  - no increase in non-vascular mortality or cancers



***Question: Combination therapy -  
Lipitor with niacin, fibrates and  
Ezetrol. What is the safety of  
this? Should it be done in the  
office or should these patients be  
referred to a specialist?***

# FIELD: conclusions

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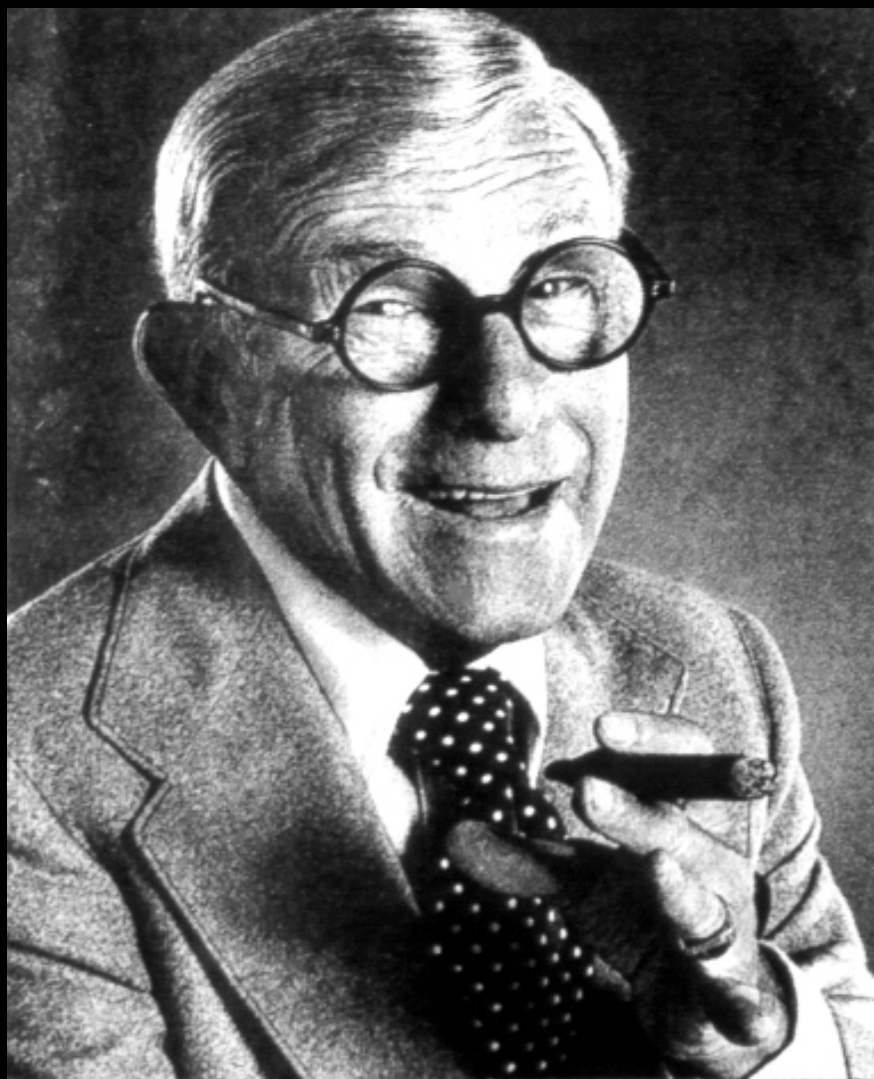
- **fenofibrate-statin combination in >2500 patients apparently well-tolerated**
- **Does adding fenofibrate to statin increase benefit? (ACCORD)**

# The 2006 Lipid Guidelines

For patients who do not tolerate or are not candidates for niacin and exhibit significant hypertriglyceridemia despite statin monotherapy, a combination of a statin with a fibrate may be used with close patient follow-up. Fibrates may increase serum creatinine and homocysteine levels. It should be noted that the recent Fenofibrate Intervention and Event Lowering in Diabetes (FIELD [127]) study demonstrated that fenofibrate monotherapy did not significantly reduce nonfatal MI or CAD death in patients with diabetes and mild hypertriglyceridemia. Statin and fibrate combination therapy should not be used in patients with renal impairment, but fibrates alone may be used with caution at low doses in cases of mild renal impairment. Available data suggest that fenofibrate is reasonably safe in combination with a statin (127,128). Studies are underway to determine whether addition of fenofibrate to a statin regimen alters CAD risk.

# The 2006 Lipid Guidelines

*Combination therapy:* In patients with combined dyslipidemia and low HDL-C levels, the combination of a statin with niacin is very effective, and was reported to significantly reduce CAD events in the HDL-Atherosclerosis Treatment Study (HATS) (123) and to halt progression of carotid atherosclerosis in the ARterial Biology for the Investigation of the Treatment Effects of Reducing cholesterol 2 (ARBITER-2) study (124). Niacin is more effective than fibrates in increasing HDL-C concentrations. Side effects are most manifest with crystalline niacin, and include flushing, dry skin and gastrointestinal irritation.



"Let me tell you my philosophy of life:  
I smoke 6 cigars a day,  
I eat all the salt I want,  
I have 4 martinis a day,  
I eat steak and french fries whenever I like.

What does my doctor think about this?

My doctor is dead."

*George Burns 1896-1996*