

# Lipids-JBS-2?

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# Outline

- SMH
  - **GP lectures**
  - **RACPC**
  - **Cons in your surgery**
  - **Arrhythmia Rx**



# Risk factors for CVD

## MODIFIABLE

High LDL cholesterol

Low HDL cholesterol

High blood pressure

Smoking

Left ventricular hypertrophy

Lack of exercise

Central obesity

Diabetes & glucose intolerance

## NON-MODIFIABLE

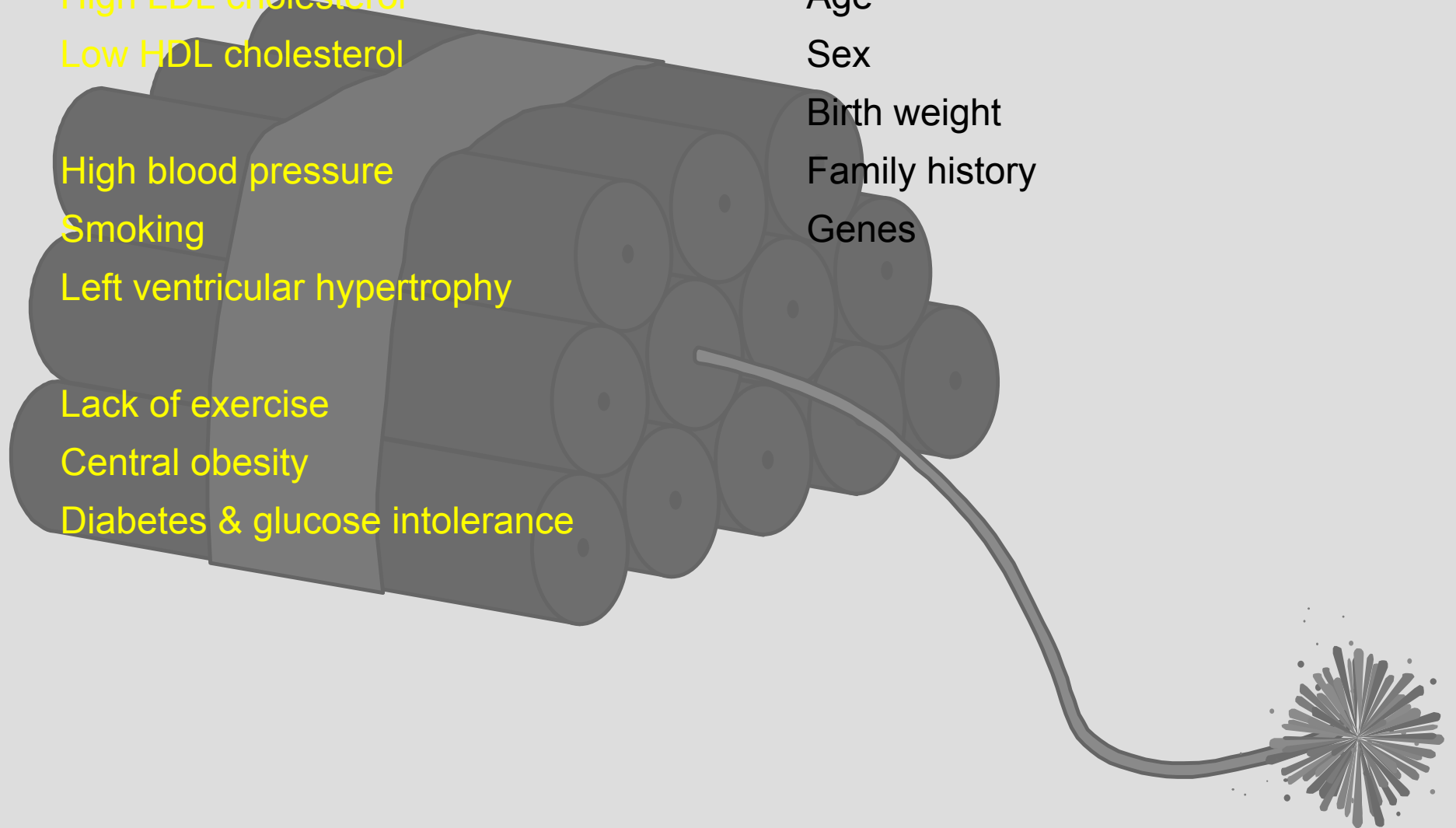
Age

Sex

Birth weight

Family history

Genes



# What are Lipids?

**Total Cholesterol**

**LDL cholesterol**

**HDL cholesterol**

**Triglycerides**

**TC/HDL ratio**

# JS guidelines 2005

**Focus on those :**

- with CVD
- With DM
- At  $>20\%$  10 yr risk CVD
- Single elevated risk factor
  - BP $>160/100$ , TC/HDL $>6$ , FH lipids

# JS Guidelines

How to assess risk?

Use chart+

- Asian x1.4
- FH x1.3
- Abdom obesity, TG>1.7

# JS targets

## BP

- non-high risk 140/85 (150/90)
- High risk 130/80 (145/85)

## Chol

- TC 4, LDL <2 or 30% dec LDL (TC<5)

## Glucose fasting <6

(HbA1c <7.4%)

- FG > 7 on two occasions =DM
- OGTT >11.1 =DM
- FG 6.1-7, then impaired fasting glycaemia
- OGTT 7.8-11.1 then IGT

## How do we do it?

### Titration upwards with a statin?

- Time consuming
- Costly
- Wastes time?

**ME?    Atorvastatin 20mg/simvastatin 40mg**

### Difficulty

- Higher dose
- Add fibrate
- Try Ezetrol (ezetimibe)

# Trials of primary prevention of CHD with lipid lowering

- Early trials\*
  - few strokes, underpowered
- WOSCOPS (hypercholesterolaemia)
  - CHD reduced by 31%
  - stroke outcome no benefit (46 vs 51 strokes)
- AFCAPS/TEXCAPS
  - strokes not reported

\* e.g. Lipid Research Clinics Coronary 1<sup>o</sup> Prevention Trial/ Helsinki Heart Study

# Trials of 2<sup>o</sup> prevention of CHD with statins

Trial	4-S	CARE	LIPID
Population	CHD	Post-MI	CHD
Total Cholesterol	5.5 - 8.0 mmol/L	< 6.2 mmol/L	4 - 7 mmol/L
Statin	Simva 10-40mg	Prava 40 mg	Prava 40 mg
Effect on CHD	Major coronary events ↓ 34%	Fatal / non-fatal coronary event ↓ 24%	CHD mortality ↓ 24%
Effect on stroke	↓ 30% [inc. TIA] (p=0.02)	↓ 32% (p=0.03)	↓ 19% (p=0.048)



## Randomized Design

High-risk  
hypertensives  
(n=42,418)

Randomised

Chlorthalidone  
Amlodipine  
Doxazosin  
Lisinopril

Eligible for lipid-lowering (n=10355)  
(LCL 3.1 - 4.9 mmol/L)

Not eligible for lipid-lowering

Randomised

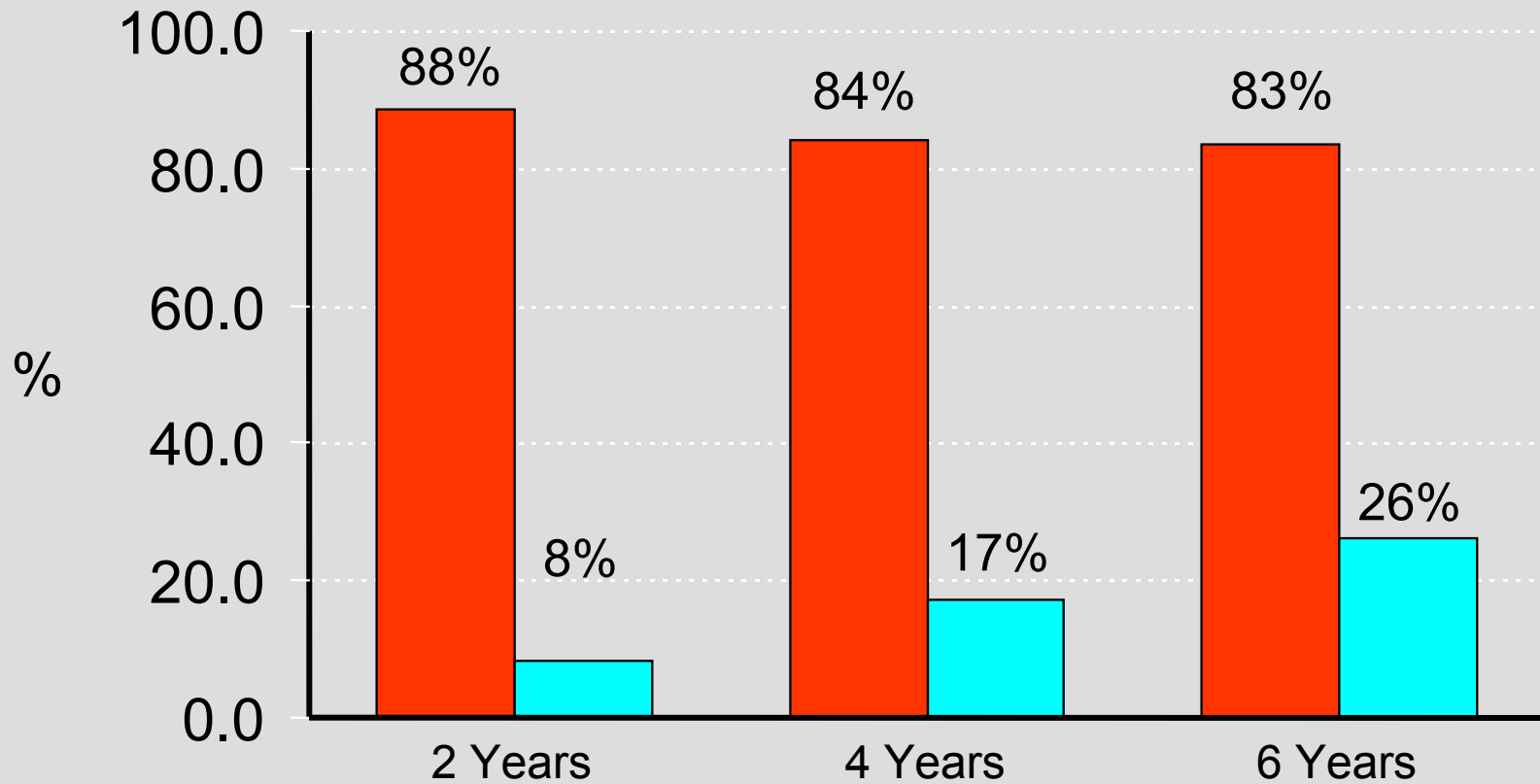
Pravastatin (20-40mg)

Usual care

Follow until death or end of study (max 7.8 yr, average 4.8 yr).



# Percent on Statin



■ Pravastatin, N\*

4353

■ Usual Care, N

4295

3063

2996

848

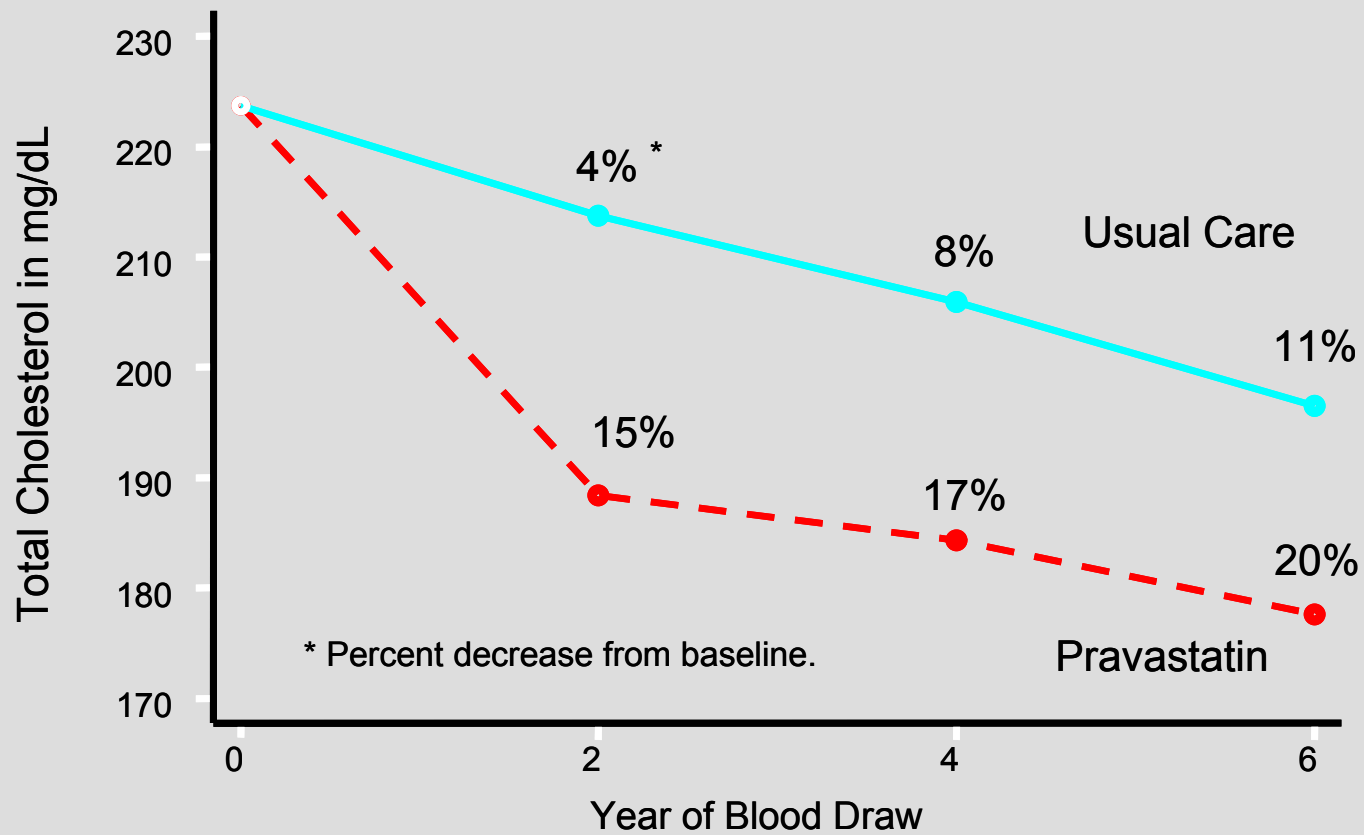
824

\* N gives the total number of participants at the visit.

JAMA 2002

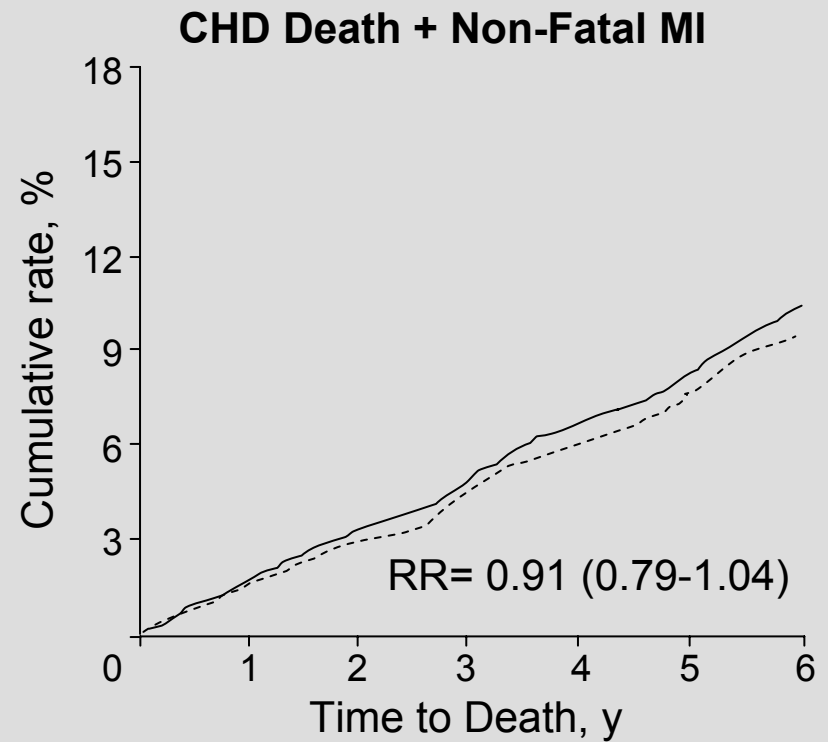
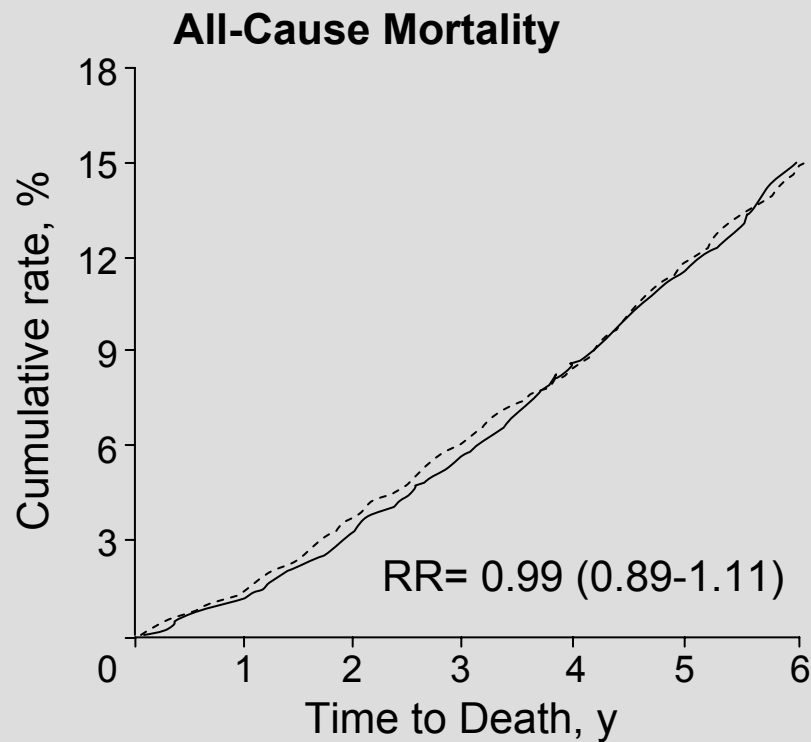


## Effects on total cholesterol





# Effects on total mortality & CHD



----- Pravastatin  
—— Usual care

# The Anglo-Scandinavian Cardiac Outcomes Trial

Randomised controlled trial of prevention of CHD and other vascular events by blood pressure lowering and by cholesterol lowering (factorial design)

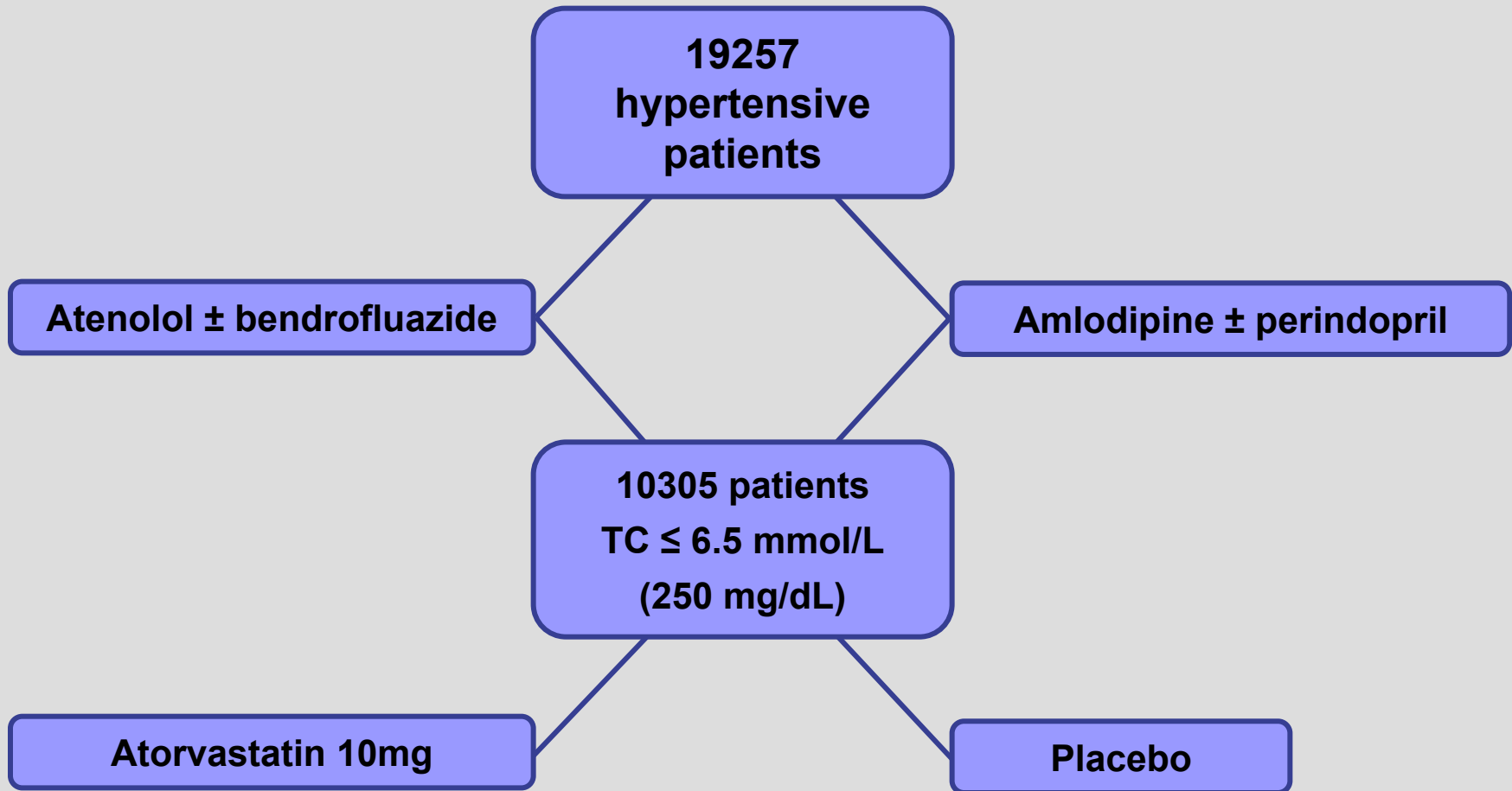


## Study population / eligibility criteria

- Hypertension
  - SBP  $\geq$ 160 mm Hg +/- DBP  $\geq$ 100 mm Hg (untreated); or
  - SBP  $\geq$ 140 mm Hg +/- DBP  $\geq$ 90 mm Hg (treated)
- No prior myocardial infarction
- 40-79 years of age
- $\geq$  3 CVD risk factors, including:
  - Smoking, LVH, diabetes, PVD, history of cerebrovascular event, male, age ( $\geq$ 55 years), microalbuminuria/proteinuria, TC:HDL-C  $\geq$ 6, history of early CHD in first-degree relative

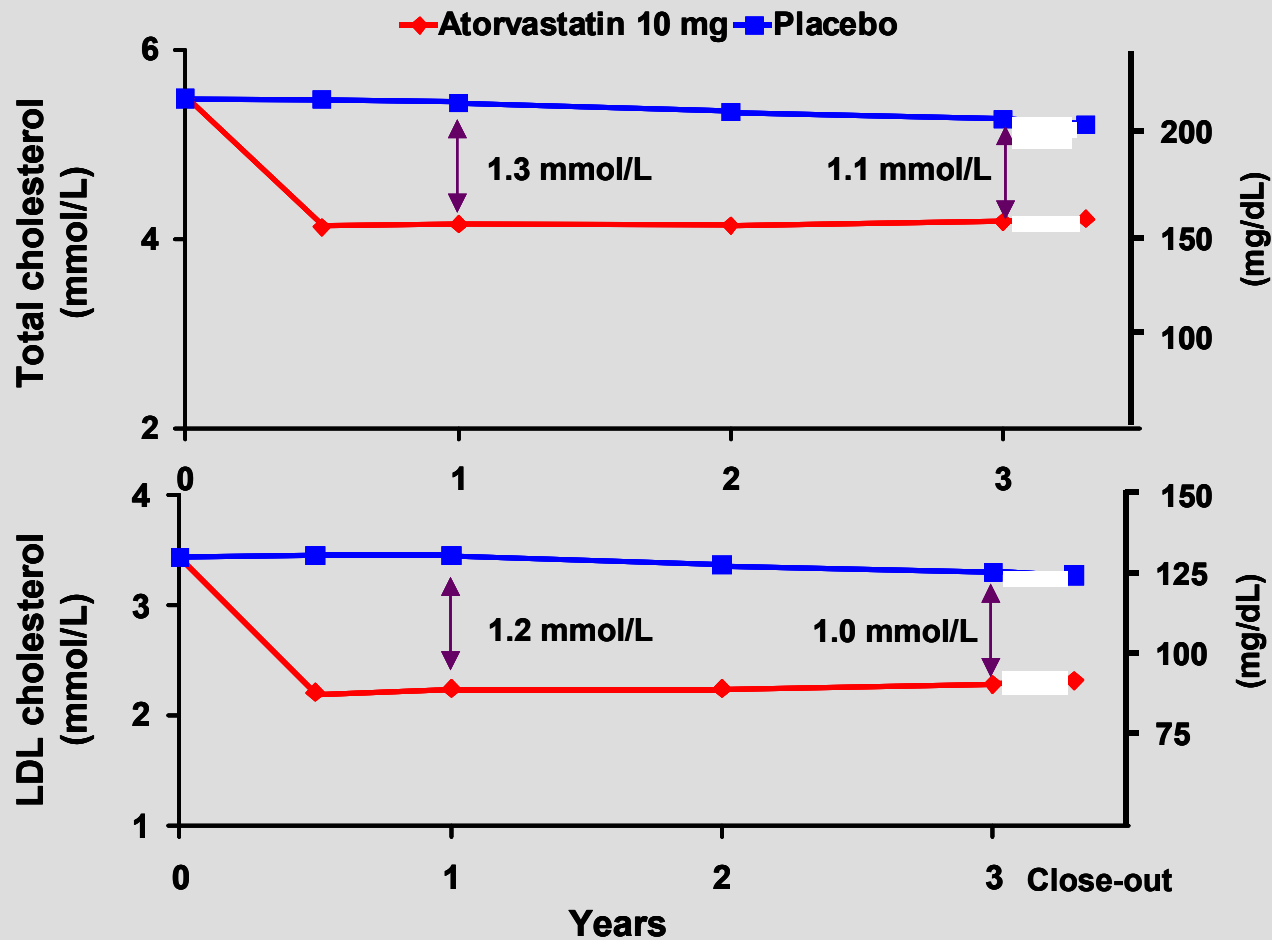


# Study Design



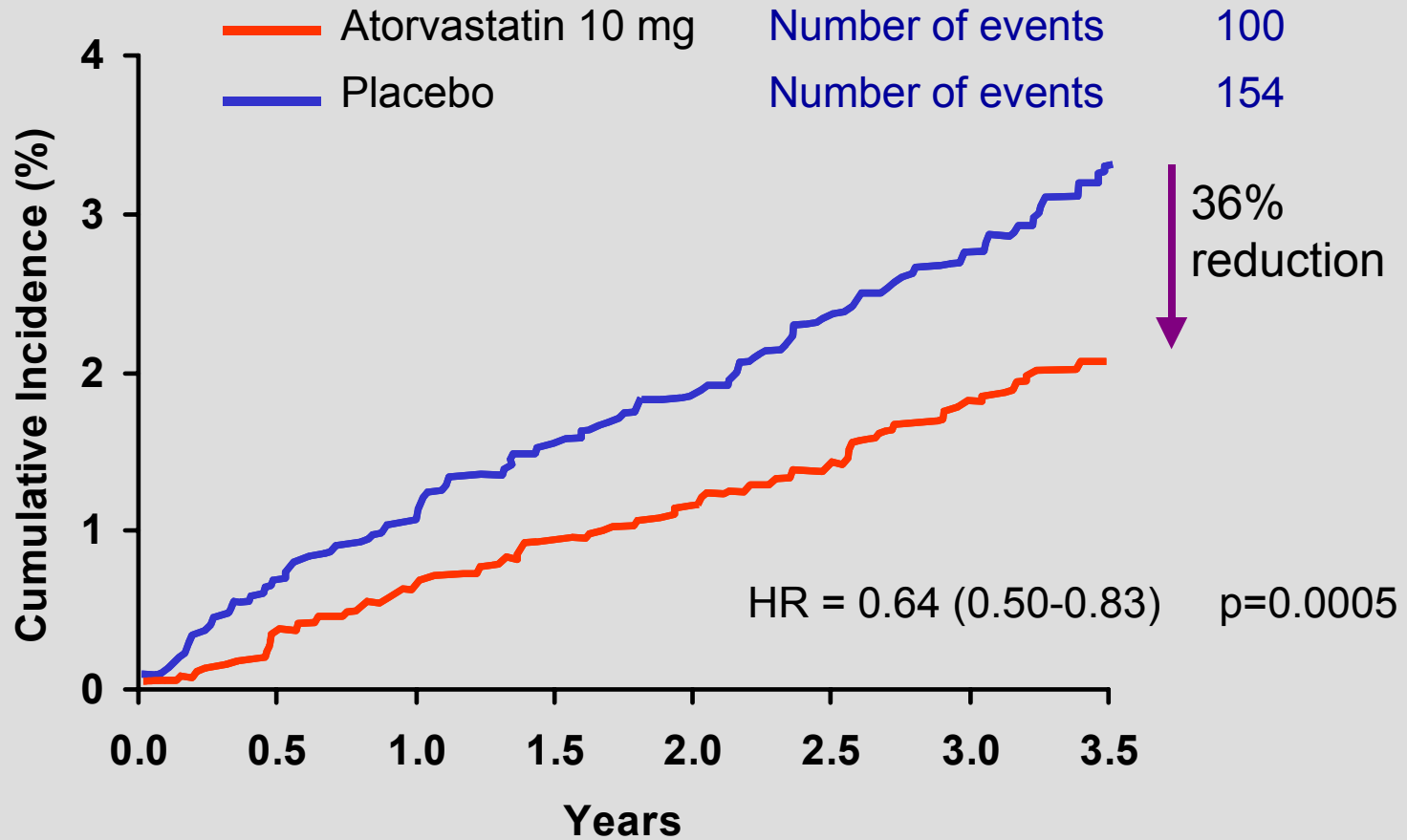


# Reductions in Total and LDL-C



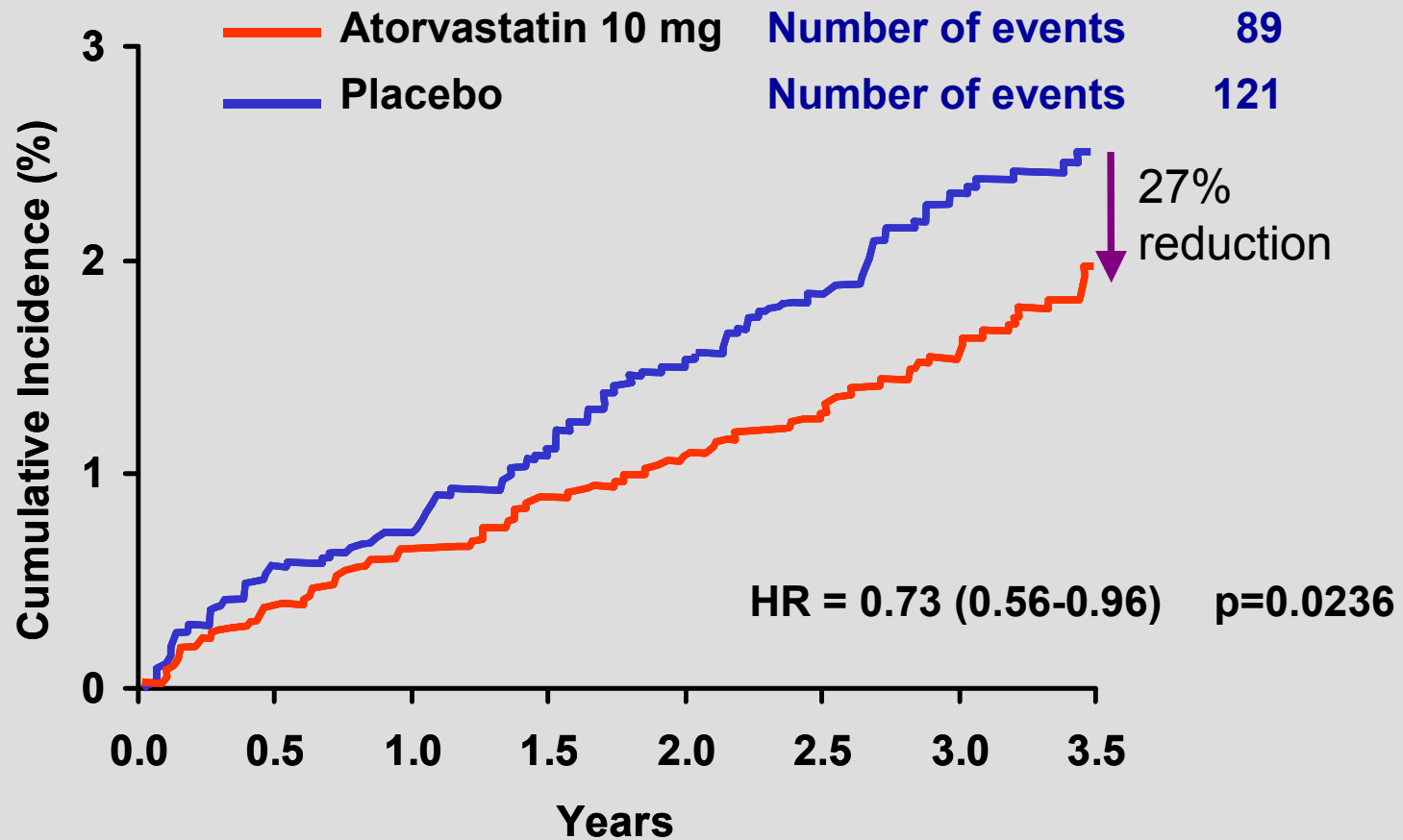


# 1° end point: Nonfatal MI & fatal CHD



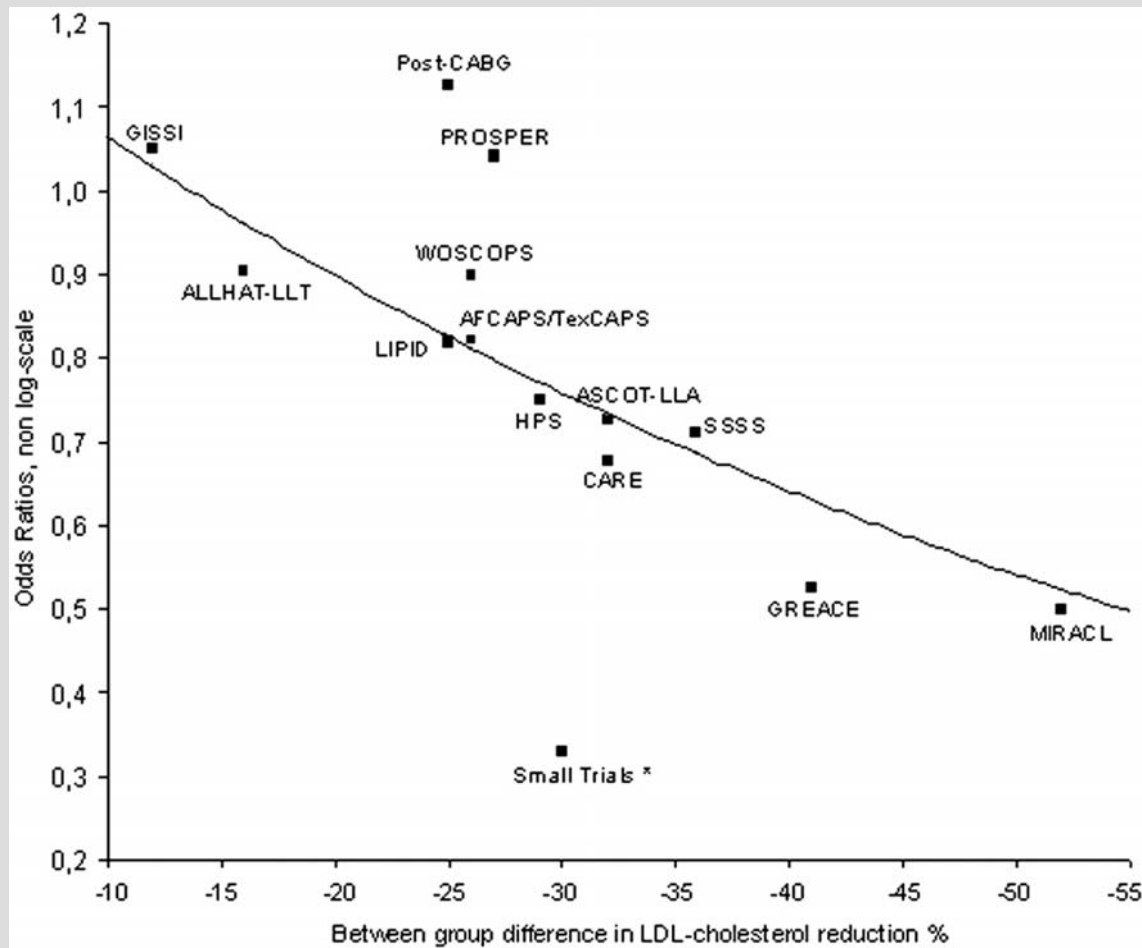


## 2° end point: Fatal & non-fatal stroke

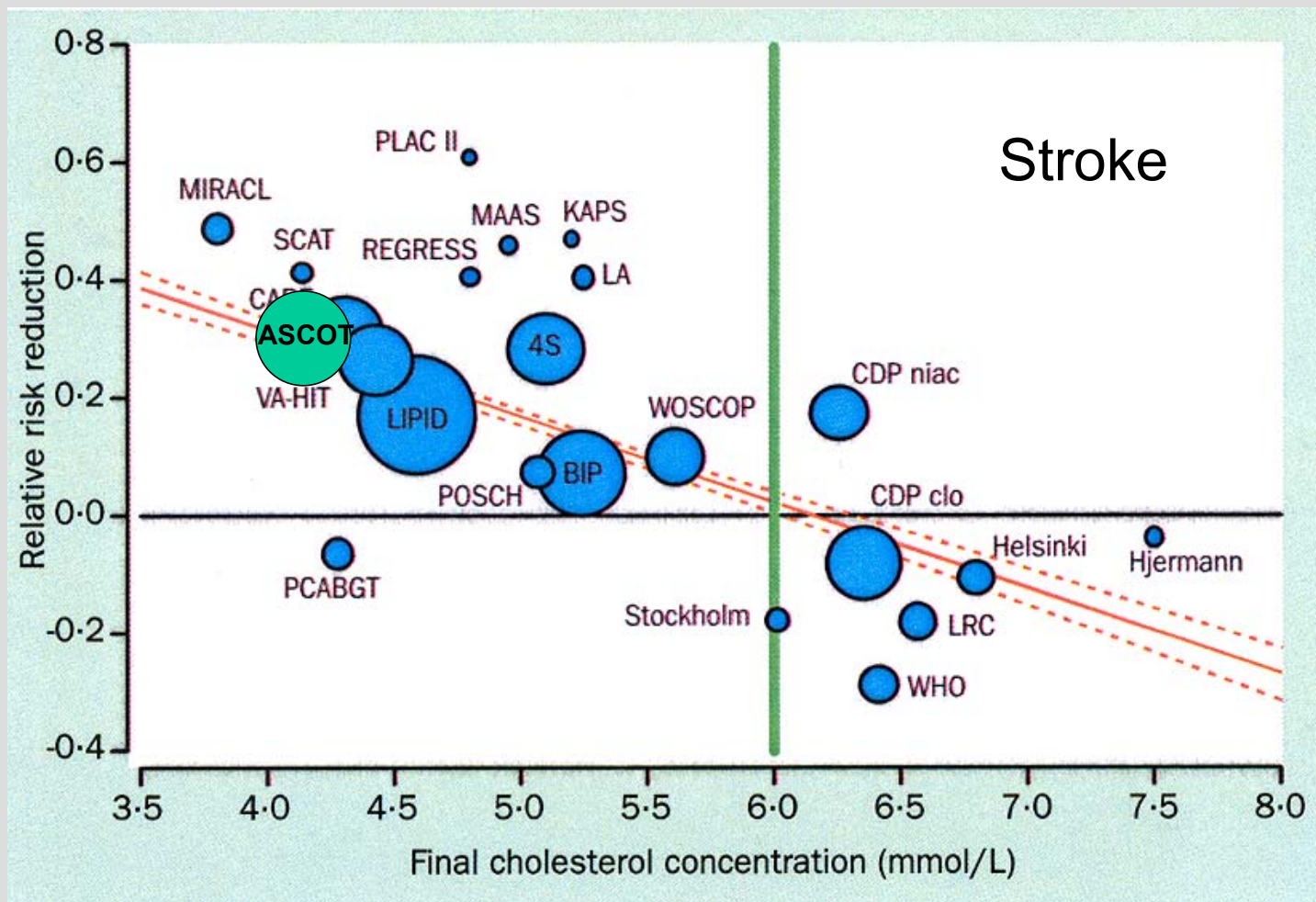


# Benefits of lipid-lowering $\propto$ to LDL-C reduction

Each 10%  $\downarrow$  LDL-C estimated to  $\downarrow$  stroke risk by 15.6% (95% CI, 6.7 to 23.6)



# Benefits $\propto$ to final cholesterol concentration



# Lipid-lowering and secondary stroke prevention

# Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL)

- Entry criteria
  - Prior stroke (ischaemic or haemorrhagic) or TIA, 1-6/12 pre-randomization
  - LDL-cholesterol  $\geq 2.6$  mmol/L and  $\leq 4.9$  mmol/L
  - Modified Rankin score  $\leq 3$  (e.g. functionally independent)
- Participants randomised to:
  - atorvastatin 80mg (n=2365) or
  - placebo (n=2366)
- Mean LDL-C at baseline 3.4 mmol/L
- Mean follow-up 4.9 years
- Mean difference in LDL-C 1.45 mmol/L

# SPARCL - results

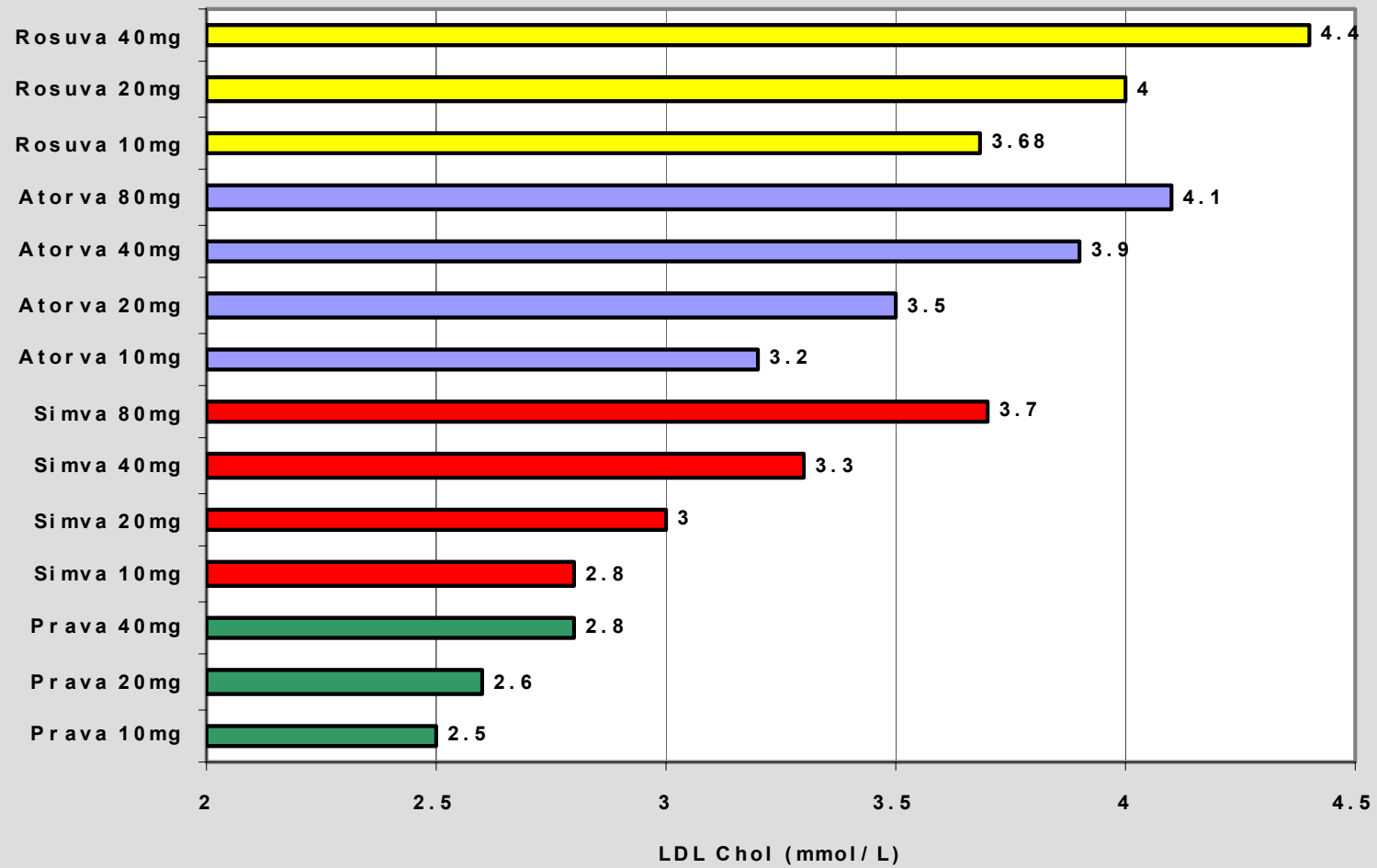
	Atorvastatin N events (%)	Placebo N events (%)	HR (95% CI)	p
Fatal/non-fatal stroke*	285 (11.2)	311 (13.1)	0.84 (0.71-0.99)	0.03
Fatal stroke	24 (1.0)	41 (1.7)	0.57 (0.35-0.95)	0.03
Non-fatal stroke	247 (1.4)	280 (11.8)	0.87 (0.73-1.03)	0.11
Post-hoc analyses				
Ischaemic stroke	218 (9.2)	274 (11.6)	0.78 (0.66-0.94)	0.01
Haemorrhagic stroke	55 (2.3)	33 (1.4)	1.66 (1.08-2.55)	0.02

\*Primary endpoint

# Lipid-lowering guidelines

- Treat all with established vascular disease
- In primary prevention (those without established vascular disease) prescribe statins for those with:
  - total cholesterol  $>3.5$ mmol/L; and
  - 10 yr CVD risk  $> 20\%$
- Titrate treatment to:
  - total cholesterol  $< 4$  mmol/L ( LDL  $< 2$  mmol/L ); or
  - 25% reduction - whichever is the greater

### Efficacy of Statins in LDL-C Reduction from baseline to a target of 2mmol/L

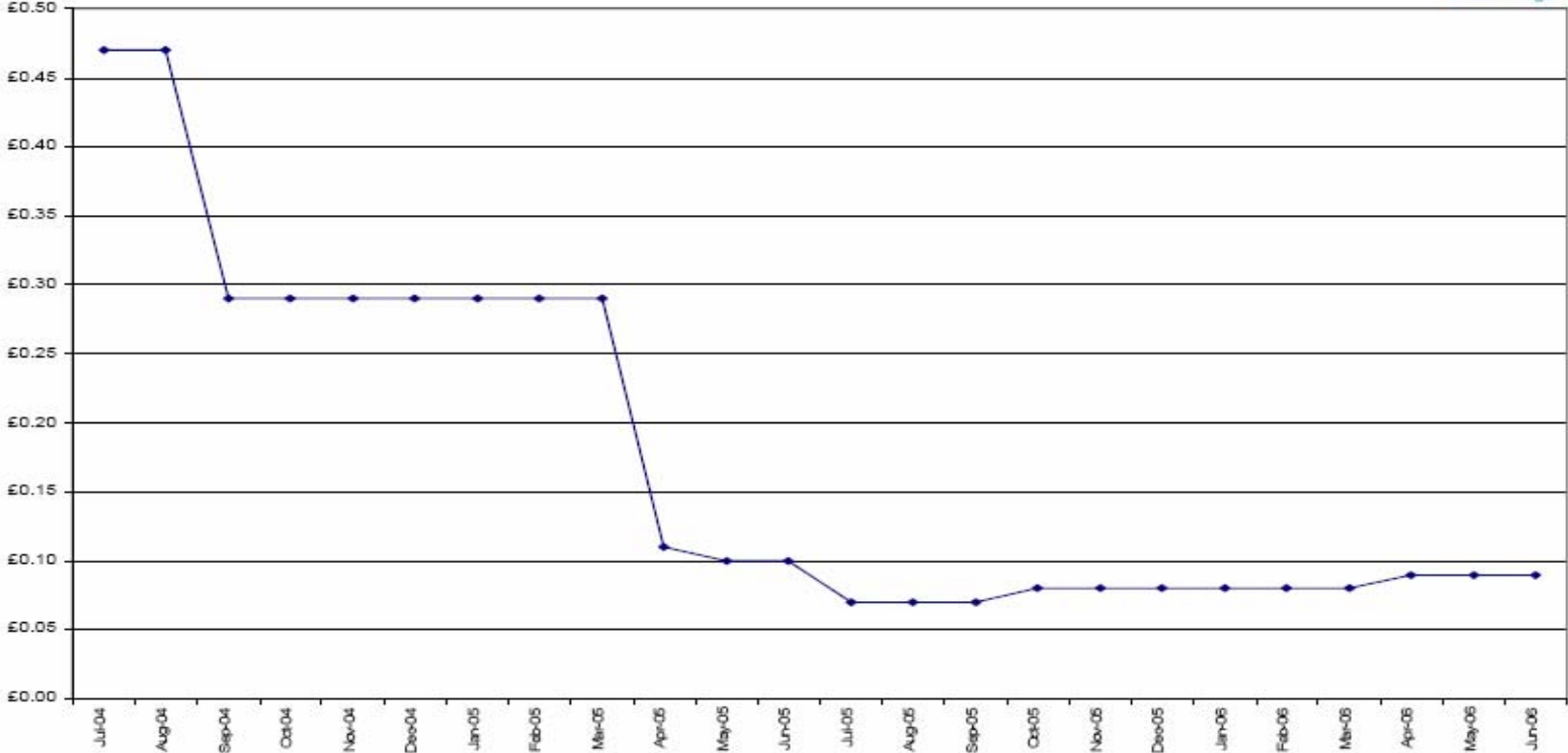


# Simvastatin use

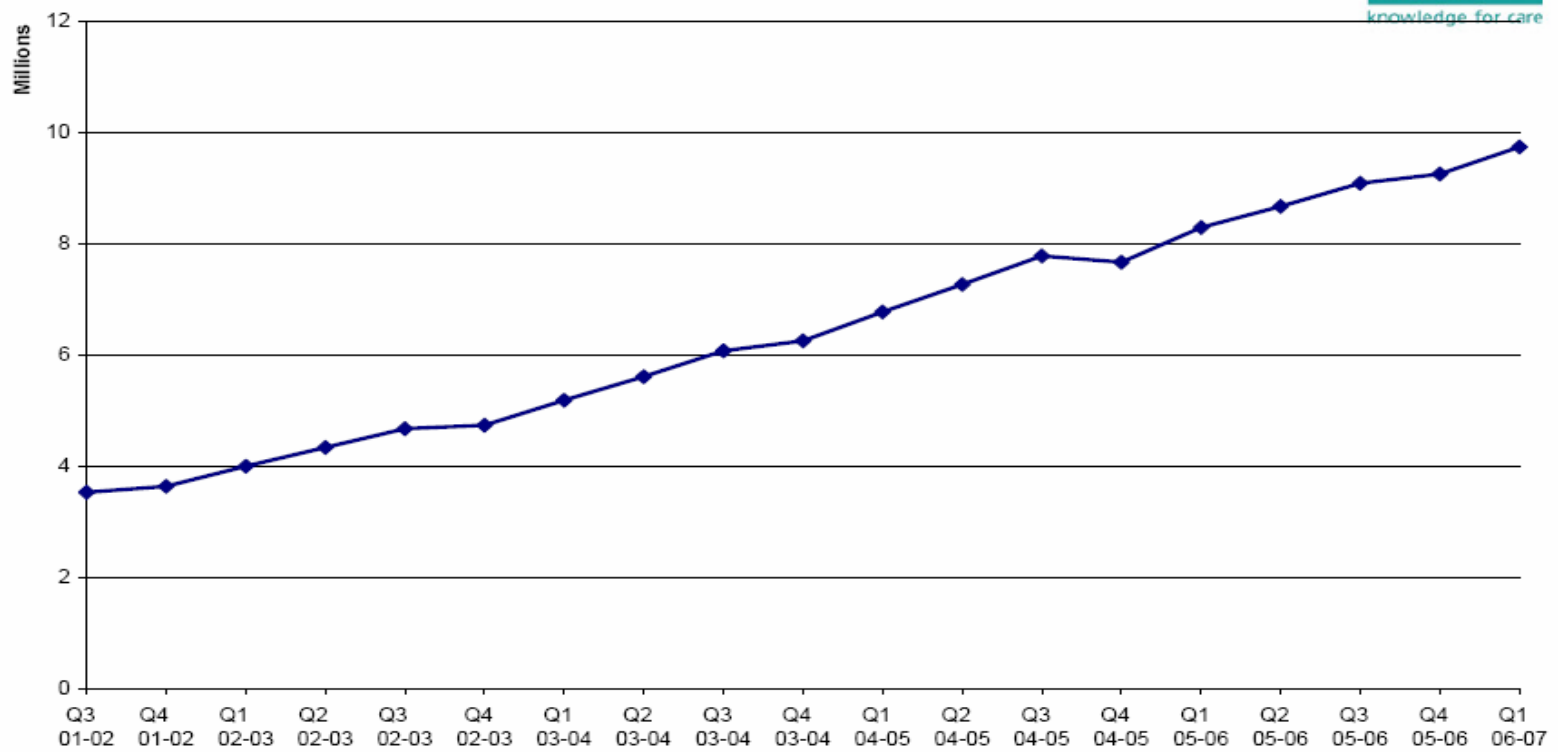
NIC per ADQ: Simvastatin



knowledge for care



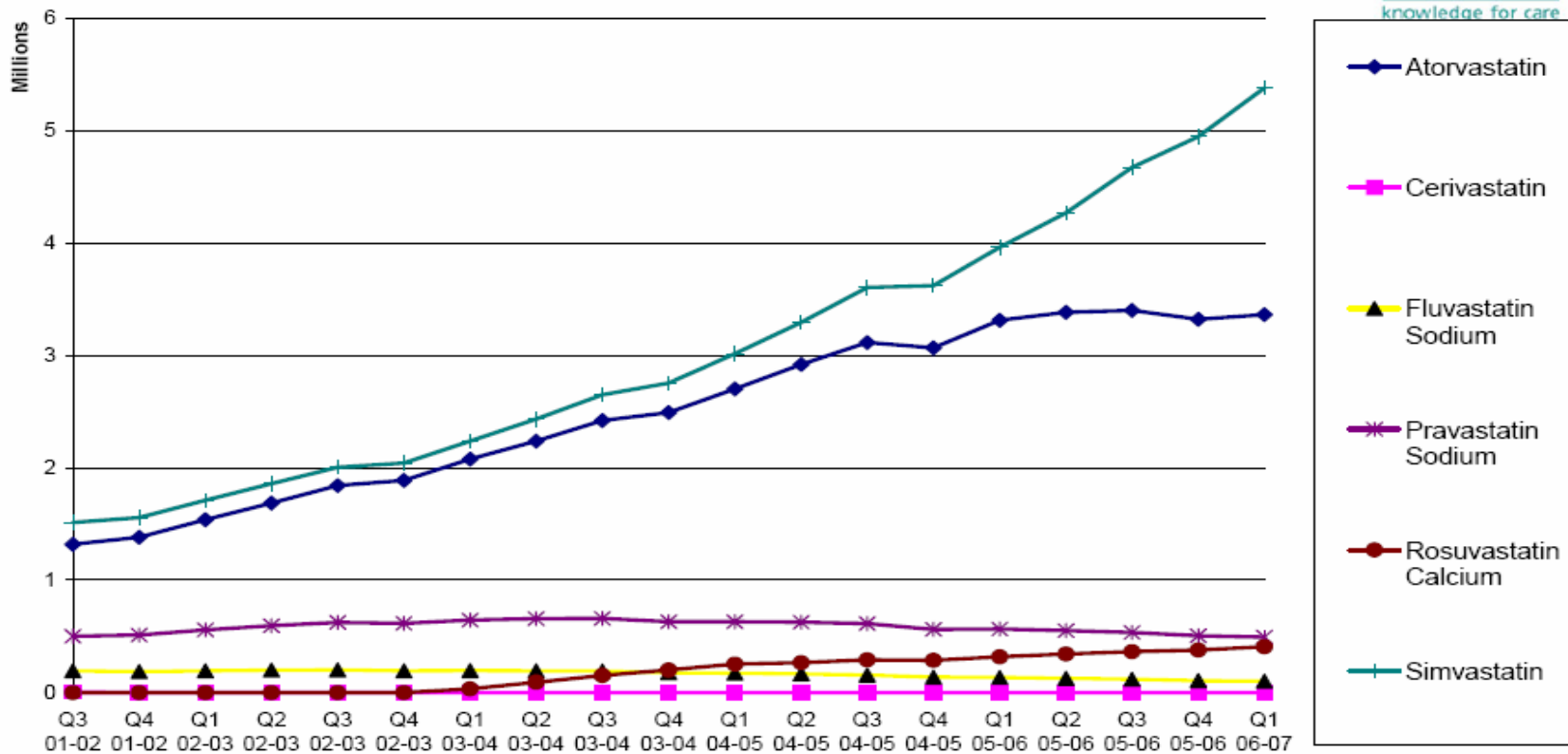
England. All Statins, items prescribed by quarter



# Comparing statins



England. Statins, items prescribed by quarter



# Growth of costs



## National top 5 BNF sections by cost (NIC), first quarter 2005/06

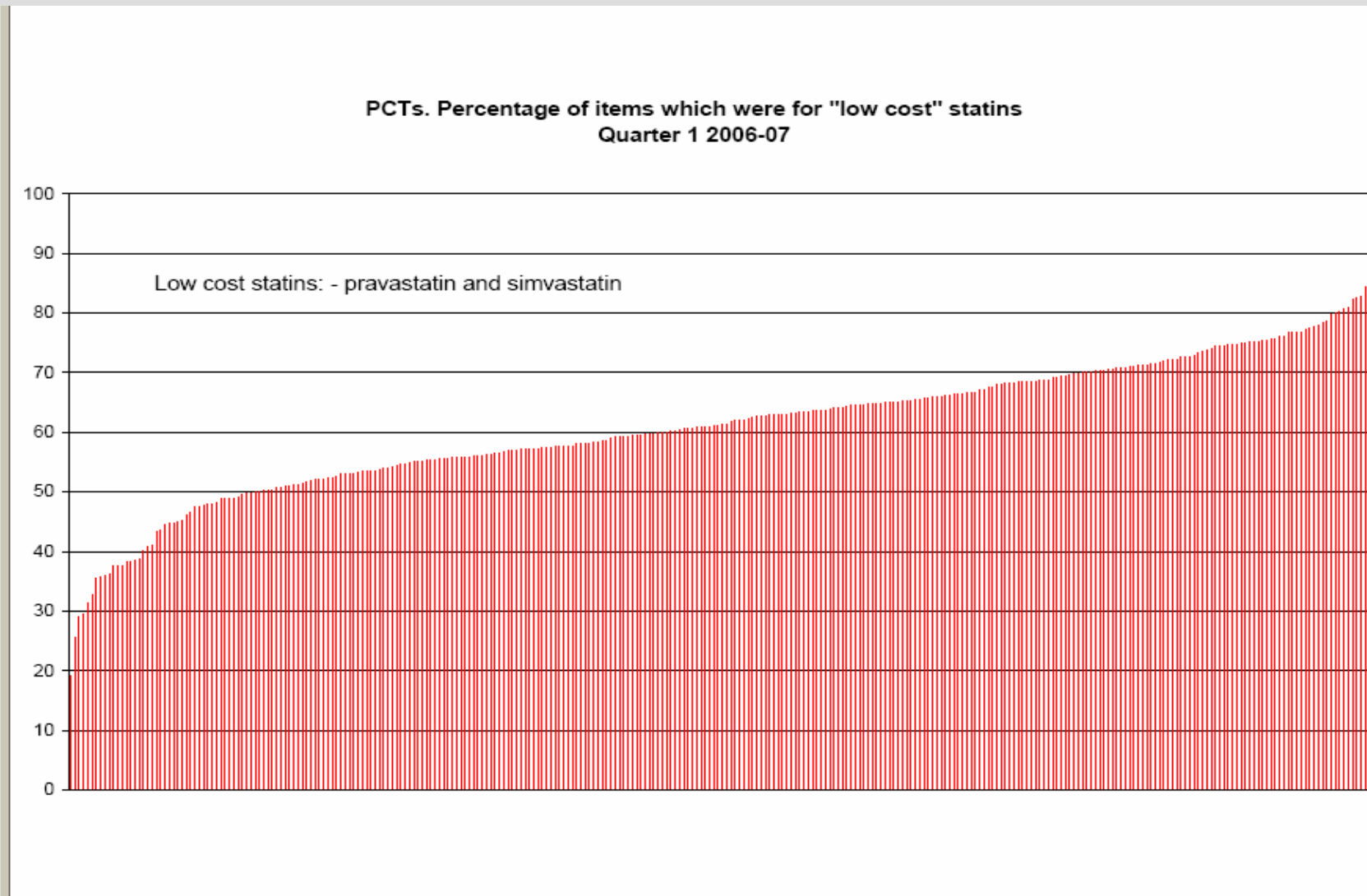
BNF Name	Total Nic	% nat total	% NIC growth	Total Items	% item growth
Lipid-Regulating Drugs	145,707,098	8	-25	8,724,520	23
Antihypertensive Therapy	113,361,942	6	-26	10,651,684	13
Ulcer-Healing Drugs	121,196,776	7	7	6,655,353	12
Drugs Used In Diabetes	121,033,846	7	11	6,608,025	10
Nit,Calc Blockers & Potassium Activators	94,352,758	5	-9	8,056,131	6

**NIC: Net Ingredient Cost**

**% nat total: % of national drug costs (NIC)**

**% growth: growth over the same quarter last year**

# Comparing PCTs



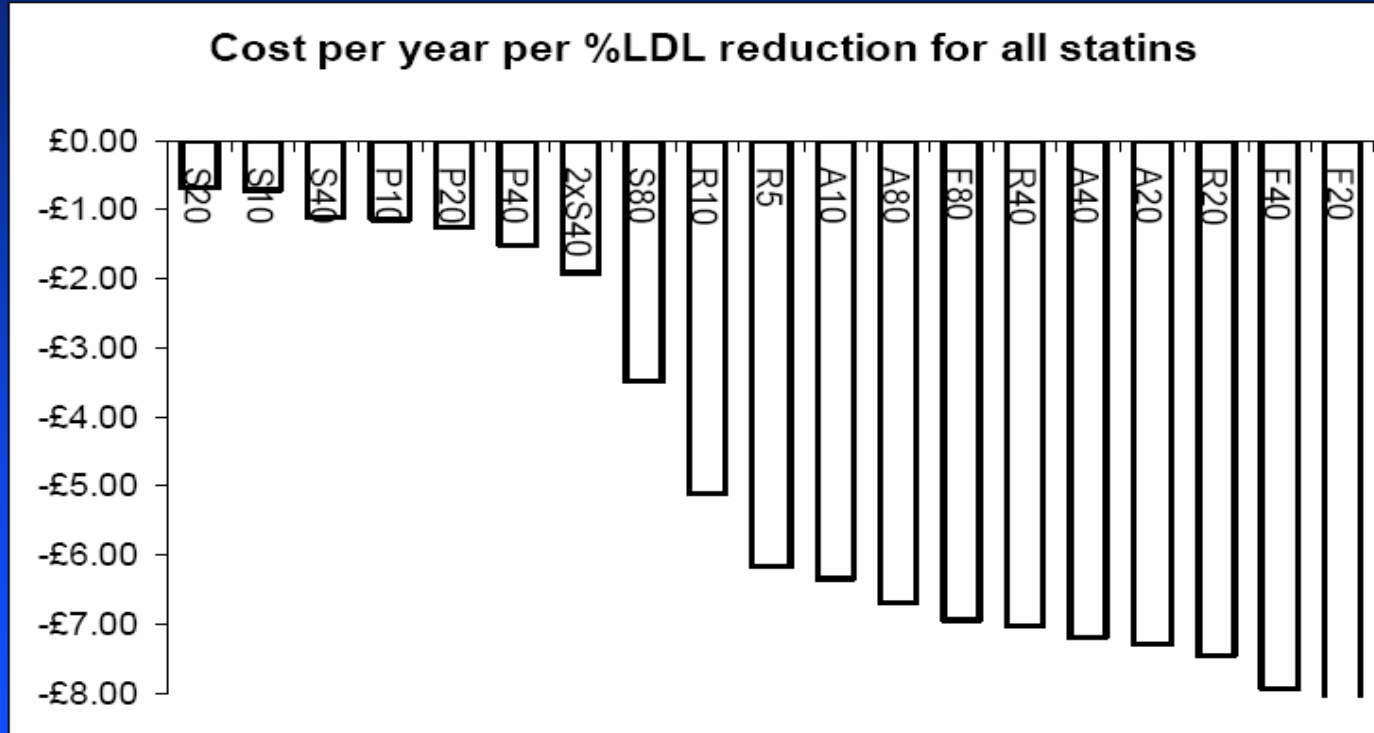
# In your pocket?

## Quality points – Secondary prevention of CHD

▪ register	6
▪ patients with newly diagnosed angina who are referred	7
▪ patients with record of smoking	7
▪ patients who have been offered smoking cessation advice	4
▪ patients with record of BP	7
▪ patients with BP < 150/90	19
▪ patients with record of cholesterol	7
▪ patients with total cholesterol < 5	16
▪ patients on anti-platelet therapy or anti-coagulant	7
▪ patients on beta blocker	7
▪ patients on ACE inhibitor	7
▪ patients with influenza immunisation	7

# Cost per LDL reduction

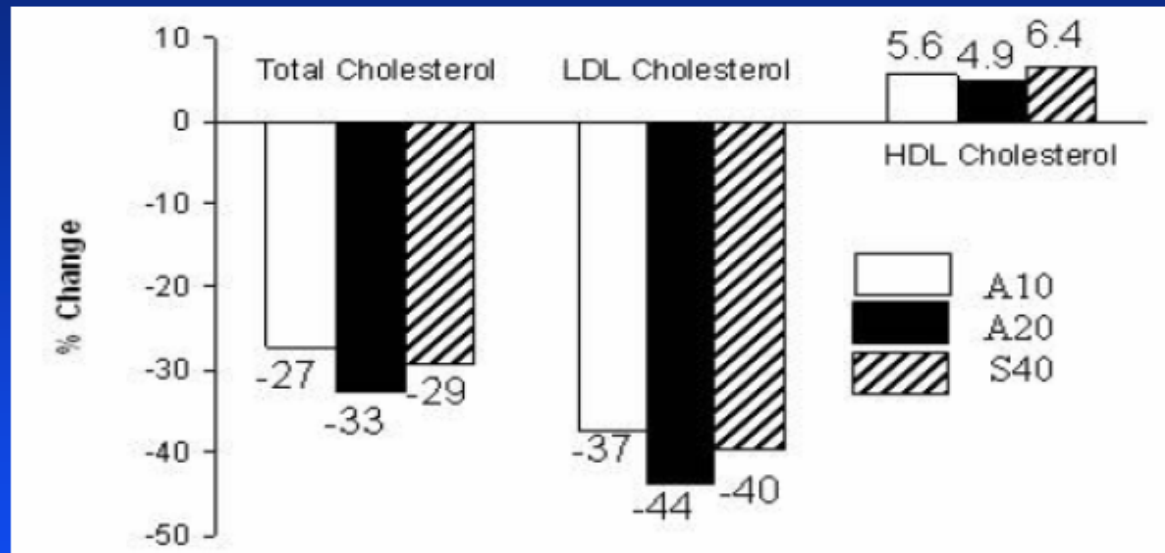
LDL/cost lowering – left is better



Prices as per October 2006

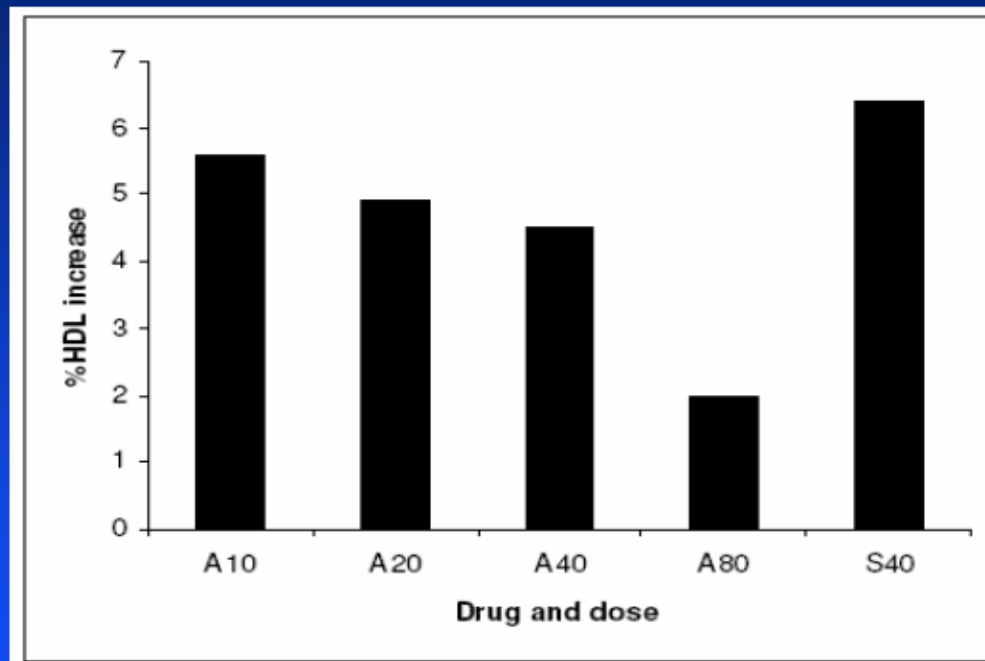
# S vs A

## A10/20 vs S40



Simvastatin 40mg *slightly* more effective than atorvastatin 10mg and *slightly* less effective than atorvastatin 20mg at lowering LDL

## Atorvastatin: negative HDL dose response curve



# switching

## Statin switching - it can work

### Recommendations

#### First line therapy:

1. Simvastatin 40mg is the first choice.
2. Patients admitted on atorvastatin 10mg and 20mg will receive and be discharged on simvastatin 40mg
3. In patients intolerant\* of simvastatin 20mg or 40mg:  
Pravastatin up to 40mg is the first alternative  
Simvastatin 10mg is the second alternative
4. Atorvastatin 10mg and 20mg will not be available from pharmacy.

#### Intensive lipid lowering therapy:

1. Caution is required to avoid drug interactions and side-effects
2. Simvastatin 80mg (prescribed as 2x40mg tablets) is first line
3. Alternative monotherapy strategies are atorvastatin 40mg or 80mg
4. Combination therapies (ezetimibe/fish oils/fibrates + statins) may be considered on a case by case basis.

\*intolerance is typically muscle or liver related: myalgia, CK or LFTs >3x normal

# Switching

**Never go backwards!**

**IF atorvastatin 10, the simvastatin 40 will do. (bit better)**

**IF atorvastatin 20, then I worry about switch**

**IF atorvastatin 40, then don't.**

# Starting

**ACS/ PTCA/ CABG/ PVD/ CVA**

**Atorvastatin 40mg**

**target 4, 2**

**Primary prevention**

**Simvastatin 40**

**target 5,3**

**Recheck**

**if fail**

**Atorvastatin 40mg**

**Or**

**Rosuvastatin 10-20 mg**

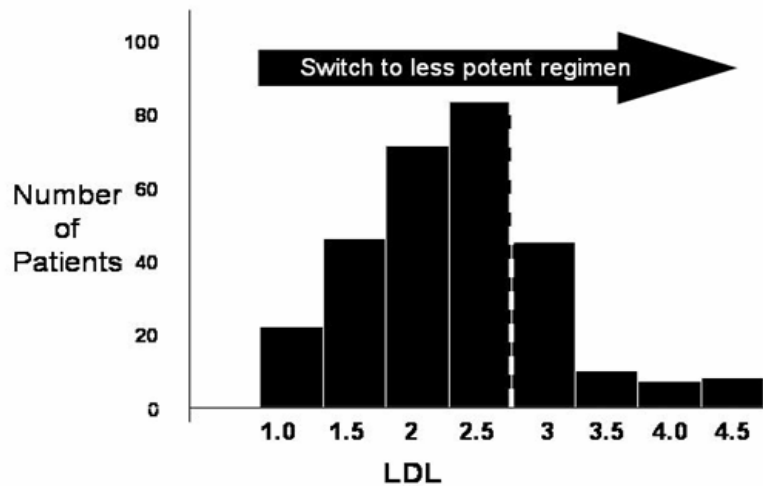
**Ezetimibe- no**

## 4 trials- mod vs high dose statin n=27,000

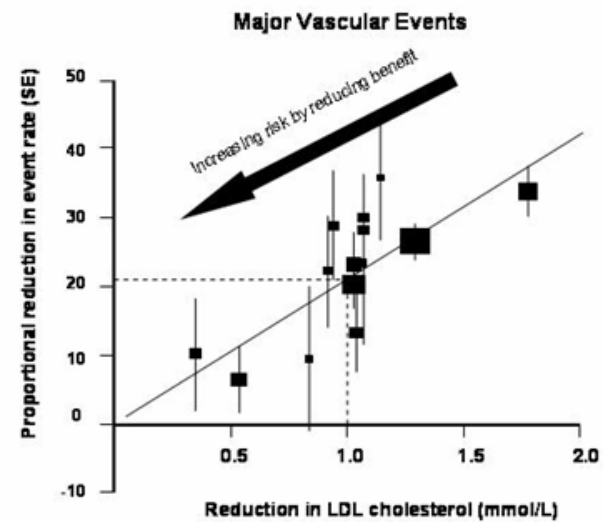
<b>Coronary Death or non- fatal MI</b>	0.84	0.77-0.91	0.00003
<b>Coronary Death or any Cardiovascular event</b>	0.84	0.80-0.89	<0.0001
<b>Stroke</b>	0.82	0.71-0.96	0.012
<b>Heart Failure</b>	0.73	0.63-0.84	<0.001

# Any risk?

Switching statins to less a potent regimen in CHD patients



Per population a 0.5 mmol increase in LDL after statin switching will increase risk by 10.5%



# PRIMARY PREVENTION



# SECONDARY PREVENTION



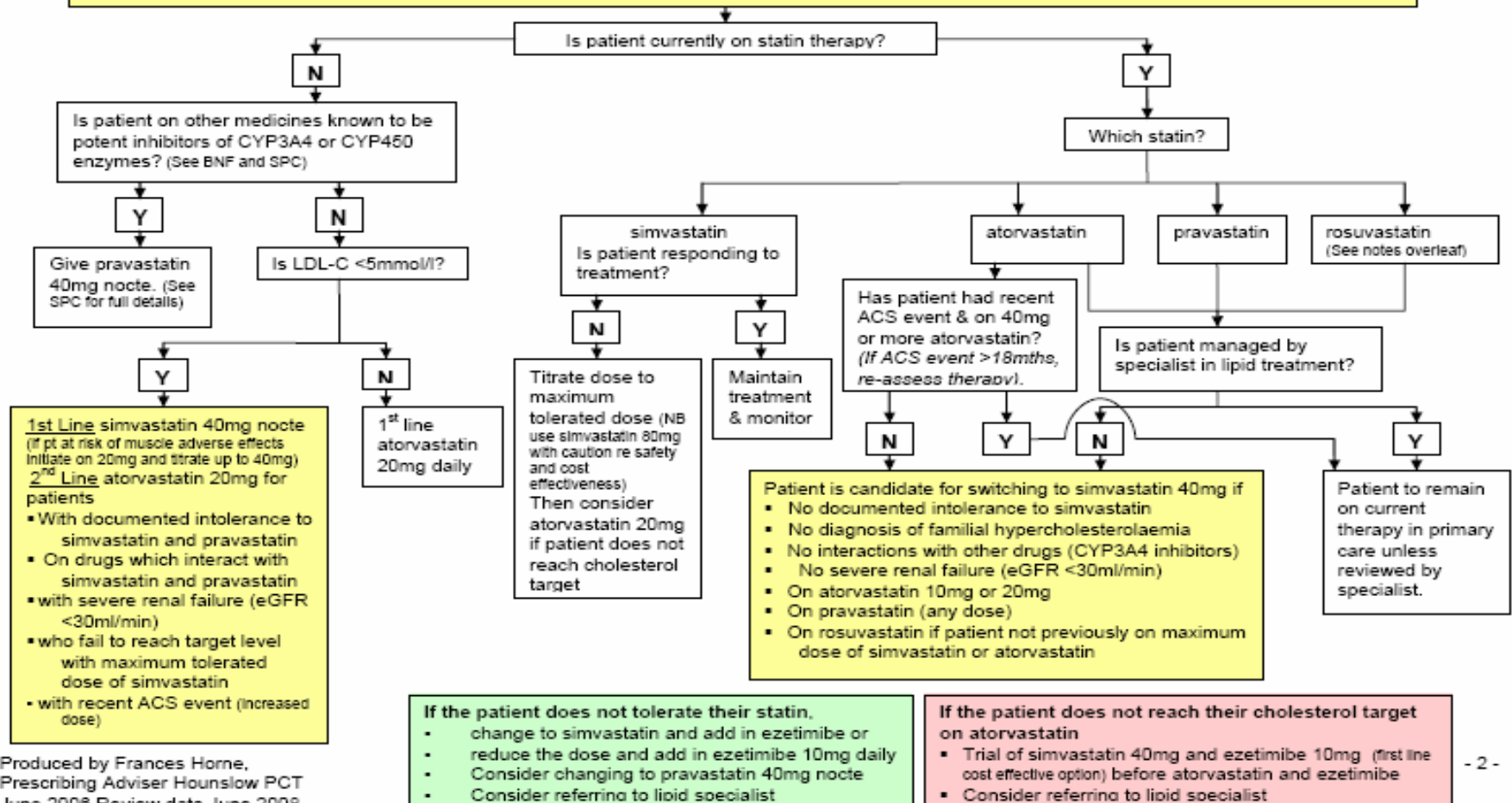


## Guidance on Prescribing of Statins in Primary and Secondary Care across NW London

### Patient identified as requiring treatment with a statin

**Primary Prevention** All patients with 20% or more CVD risk over the next 10 years and all diabetic patients aged >40 years

**Secondary Prevention** All patients with confirmed diagnosis of coronary heart disease or other atherosclerotic vascular disease



# NWLCN

## Guideline Targets

**NSF** National minimum targets, equivalent to the JBS audit standard  
**JBS Guidelines** Not national targets, but aspirational targets  
**nGMSc** This should be treated as an audit target below which to aim for all eligible diabetes, CHD and stroke patients

Target	NSF Guidelines March 2000	nGMSc updated for 2006-2007	Joint British Societies Guidelines <sup>1</sup>	
	Primary and secondary Prevention	The practice can provide a register of all patients with diabetes, CHD and stroke	Secondary & Primary Prevention, Diabetes	
			Optimal Standard	Audit Standard
Total Cholesterol	<5mmol/l or reduced by 30% (whichever is greater)	40-70% of patients on register have total cholesterol <5mmol/l	<4.0 mmol/l or 20% reduction	<5.0 mmol/l
LDL-C	<3mmol/l or reduced by 30% (whichever is greater)		<2.0 mmol/l	<3.0 mmol/l

### References

<sup>1</sup> Joint British Societies' guidelines on prevention of cardiovascular disease in clinical practice. published December 2005 [www.heartjnl.com](http://www.heartjnl.com)

### Risk Calculators

Cardiovascular Risk Prediction Charts are included in the back of the BNF.  
 Online risk calculators should be available from Summer 2006 at:

<http://www.access2information.org/health/cvra/>

**High Risk Patients <sup>1</sup>**  
 The following patients are likely to derive significant benefit from statin therapy

- BP>160/100 with target organ damage
- TC:HDL ratio >6
- Familial Hypercholesterolaemia
- Diabetics aged 18-39 with one or more of the following retinopathy, nephropathy, HbA1c >9%, Elevated BP requiring treatment, TC >6mmol/l, features of metabolic syndrome or FH of CVD in a first degree relative

# League tables

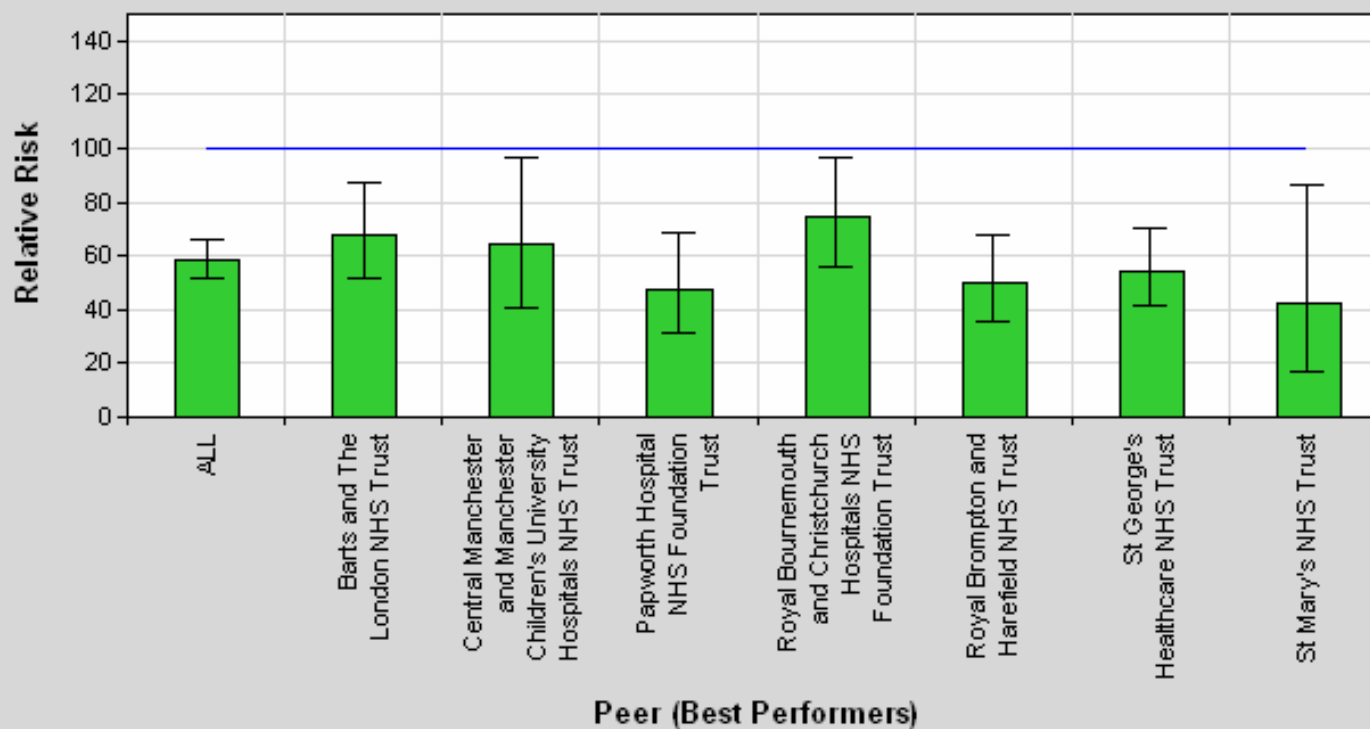
National position		Percentage of low cost statins	Productivity opportunity	Change from last period
62	Bromley PCT	70.42%	£0	*
74	Southwark PCT	69.13%	£0	*
NATIONAL TOP QUARTILE: Trusts above this line performed in the top 25% [68.69%]				
79	Sutton and Merton PCT	68.53%	£10,000	*
88	Croydon PCT	67.52%	£56,000	*
103	Bexley Care Trust	65.77%	£111,000	*
106	Kingston PCT	65.45%	£85,000	*
108	Lewisham PCT	65.30%	£134,000	*
109	Hammersmith and Fulham PCT	65.21%	£76,000	*
118	Lambeth PCT	64.67%	£132,000	*
121	Haringey Teaching PCT	64.48%	£144,000	*
123	Islington PCT	64.06%	£111,000	*
124	City and Hackney Teaching PCT	64.06%	£139,000	*
143	Camden PCT	62.61%	£155,000	*
144	Hounslow PCT	62.48%	£232,000	*
149	Richmond and Twickenham PCT	61.84%	£164,000	*
160	Hillingdon PCT	60.52%	£379,000	*
167	Wandsworth Teaching PCT	59.81%	£314,000	*
169	Harrow PCT	59.62%	£343,000	*
NATIONAL AVERAGE Grey shading indicates poorer than average performance [58.8%]				
198	Greenwich Teaching PCT	57.09%	£356,000	*
202	Tower Hamlets PCT	56.67%	£332,000	*
213	Havering PCT	55.74%	£652,000	*
221	Kensington and Chelsea PCT	55.22%	£311,000	*
233	Enfield PCT	53.47%	£709,000	*
237	Merton PCT	52.82%	£181,000	*

# Real league tables

Mortality (in-hospital) | Diagnoses | Acute myocardial infarction



Mortality (in-hospital) | Diagnoses | Acute myocardial infarction



**Thanks**

**To Maria**

**For not vetoing the talk!**