

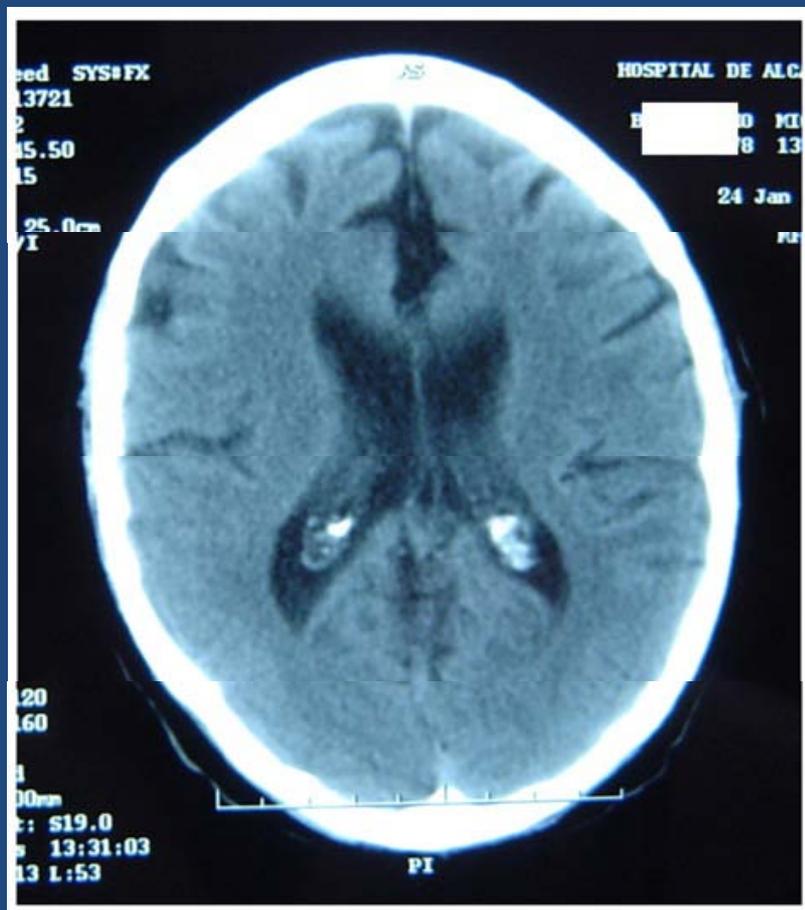
# Ασθενής με αγγειακό εγκεφαλικό επεισόδιο & δυσλιπιδαιμία

Σαββόπουλος Χρήστος  
Επίκουρος Καθηγητής Παθολογίας ΑΠΘ

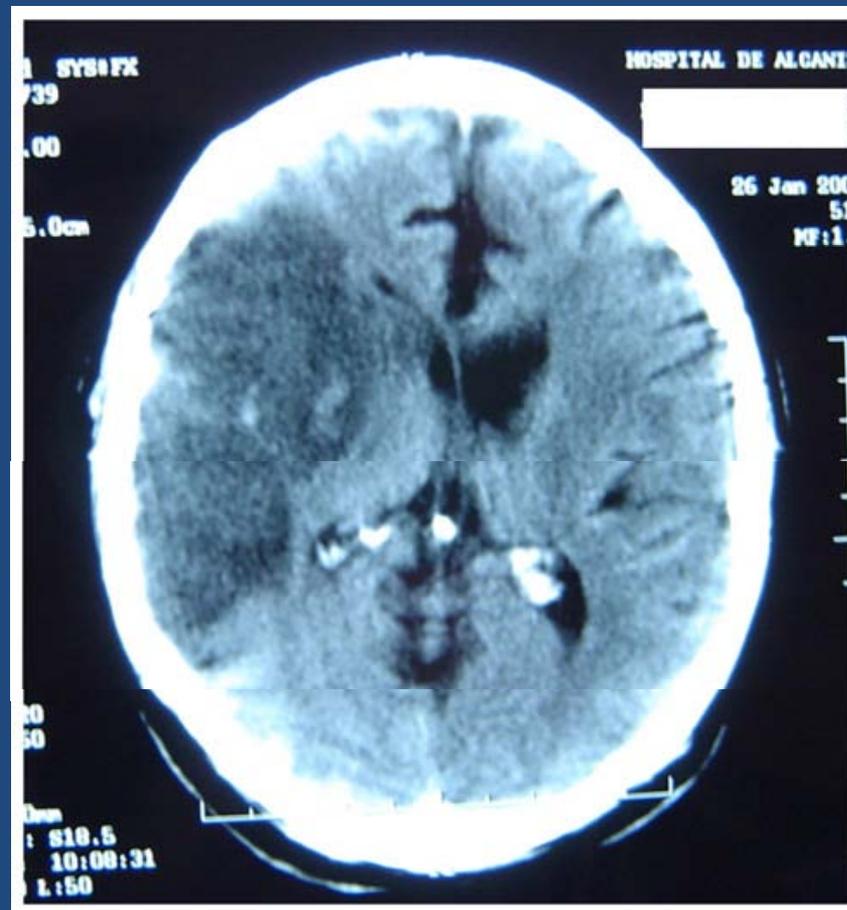


68χρονος ασθενής με ιστορικό κολπικής μαρμαρυγής & ΑΥ εισάγεται με ΑΡ ημιπληγία από 2ώρου, κεφαλαλγία, ΑΠ 210/110 mmHg.

Επείγουσα CT χωρίς σημεία αιμορραγίας, πρώϊμα σημεία ισχαιμικού εμφράκτου στην κατανομή της ΔΕ μέσης εγκεφαλικής αρτηρίας



CT εισαγωγής



Μεγάλο έμφρακτο με πιεστικά φαινόμενα στην κατανομή της ΔΕ μέσης εγκεφαλικής 48h μετά

# Εργαστηριακός Έλεγχος



- Ολ. Χοληστερόλη: 245 mg/dl
- LDL: 147 mg/dl
- Τριγλυκερίδια: 260 mg/dl
- HDL: 46 mg/dl
- Λοιπός βιοχημικός έλεγχος :κφ
- Κάπνισμα: όχι
- BMI: 33 (παχύσαρκος)
- ΑΠ: 150/85 mmHg
- Age: 68
- Gender: male
- Total Cholesterol: 245 mg/dL
- HDL Cholesterol: 47 mg/dL
- Smoker: No
- SBP: 150 mm/Hg
- On medication for HBP: Yes
- **Risk Score\* 23%**  
Means 23 of 100 people with this level of risk will have an attack in the next 10 years.

# Διαστρωμάτωση Καρδιαγγειακού κινδύνου

- Χαμηλός, μέτριος, **υψηλός** και πολύ υψηλός επιπρόσθετος καρδιαγγειακός κίνδυνος (ΕΚΚ)
- Απόλυτος 10ετής κίνδυνος για καρδιαγγειακό νόσημα (ΚΚ)

Κατά Framingham <15%, 15 έως 20%, **20 έως 30%** και > 30% αντίστοιχα

Κατά SCORE <4%, 4 έως 5%, 5 έως 8% και > 8% αντίστοιχα





## Αντιμετώπιση έπειτα από ΑΕΕ

- 1) Αρτηριακή υπέρταση
- 2) **Υπερλιπιδαιμία**
- 3) Σακχαρώδης Διαβήτης
- 4) Αντιαμοπεταλιακή-αντιθρομβωτική αγωγή
- 5) Επαναγγείωση
- 6) Κάπνισμα
- 7) Παχυσαρκία
- 8) Κατάχρηση αλκοόλης
- 9) Λοιποί παράγοντες



## Κίνδυνος εμφάνισης ΑΕΕ

(σε επίπεδο πρωτογενούς ή δευτερογενούς πρόληψης)  
ανάλογα με την ύπαρξη ενός εκ των παρακάτω μεμονωμένων ΠΚ

- ΑΥ 49 %
- Χοληστερόλη 20 %
- Κάπνισμα 12 %
- ΚΜ 9.4 %
- Λήψη Αλκοόλ 4.7 %



# FRAMINGHAM RISK SCORE to predict 10 year ABSOLUTE RISK of CHD EVENT

ST ALBANS & HEMEL HEMPSTEAD NHS TRUST : CARDIOLOGY DEPARTMENT



This risk assessment only applies to assessment for PRIMARY PREVENTION of CHD, in people who do not have evidence of established vascular disease. Patients who already have evidence of vascular disease usually have a >20% risk of further events of over 10 years, and require vigorous SECONDARY PREVENTION. People with a Family History of premature vascular disease are at higher risk than predicted; Southern Europeans and some Asians may have a lower risk in relation to standard risk factors.

**STEP 1: Add scores by sex for Age, Total Cholesterol, HDL-Cholesterol, BP, Diabetes and Smoking.** (If HDL unknown, assume 1.1 in Males, 1.4 in Females)

Age	M		F	
	M	F	M	F
30-34	-1	-1	-9	-9
35-39	0	0	-4	-4
40-44	1	1	0	0
45-49	2	2	3	3
50-54	3	3	6	6
55-59	4	4	7	7
60-64	5	5	8	8
65-69	6	6	8	8
70-74	7	7	8	8

Total Cholesterol	M		F	
	M	F	M	F
< 4.1	-3	-3	-2	-2
4.1 - 5.1	0	0	0	0
5.2 - 6.2	1	1	1	1
6.3 - 7.1	2	2	1	1
7.2	3	3	3	3

HDL Cholesterol	M		F	
	M	F	M	F
< 0.9	2	5	2	5
0.9 - 1.16	1	2	1	2
1.17 - 1.29	0	1	0	1
1.30 - 1.55	0	0	0	0
≥ 1.56	-2	-3	-2	-3

Systolic BP	Diastolic BP					
	<80	80-84	85-89	90-99	≥100	
Male	<120	0	0	1	2	3
120-129	0	0	1	2	3	
130-139	1	1	1	2	3	
140-159	2	2	2	2	3	
≥160	3	3	3	3	3	
Female	<120	-3	0	0	2	3
120-129	0	0	0	2	3	
130-139	0	0	0	2	3	
140-159	2	2	2	2	3	
≥160	3	3	3	3	3	

If Systolic and Diastolic BP fall into different categories, use score from higher category

Diabetes	M	F
	No	0
Yes	2	4

Smoking	M	F
	No	0
Yes	2	2

Categorisation of 10 year Risk of CHD Event	
Very Low risk	< 10%
Low risk	< 16%
Moderate risk	15-20%
High risk	> 20%

**STEP 2: Use total score to determine Predicted 10 year Absolute Risk of CHD Event (Coronary Death, Myocardial Infarction, Angina) by sex**

Total Score	≤-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	≥17
10 year Risk: Male		<2%	3%	3%	4%	5%	7%	8%	10%	13%	16%	20%	25%	31%	37%	45%	53%	53%	53%	53%
10 year Risk: Female	<1%	2%	2%	2%	3%	3%	4%	4%	5%	6%	7%	8%	10%	11%	13%	15%	18%	20%	24%	27%

**STEP 3: Compare Predicted 10 year Absolute Risk with "Average" and "Ideal" 10 year Risks, to give Relative Risks**

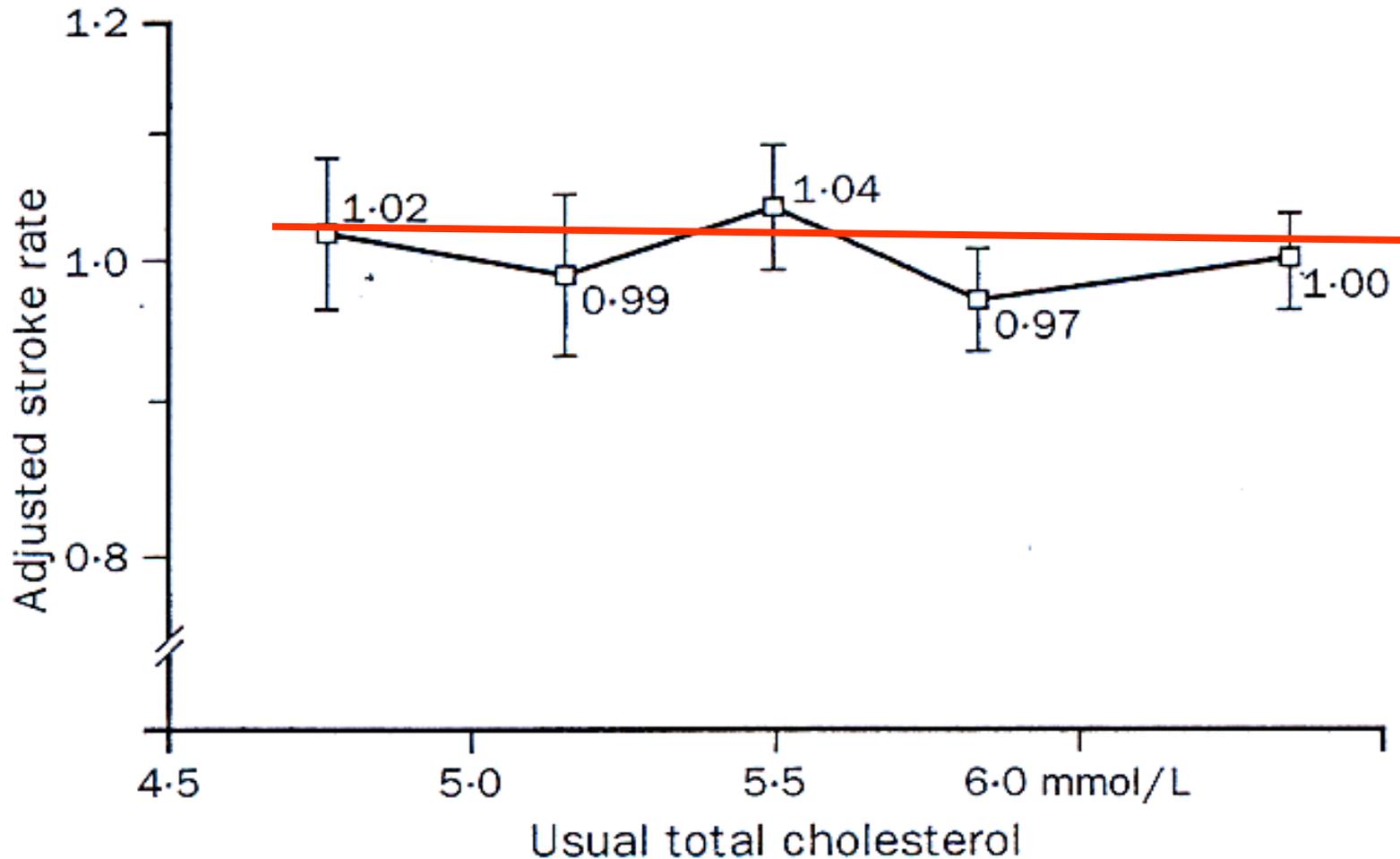
Age	30 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 - 59	60 - 64	65 - 69	70 - 74
"Average" Male	3%	5%	7%	11%	14%	16%	21%	25%	30%
"Ideal" Male	2%	3%	4%	4%	6%	7%	9%	11%	14%
"Average" Female	< 1%	< 1%	2%	5%	8%	12%	12%	13%	14%
"Ideal" Female	< 1%	< 1%	2%	3%	5%	7%	8%	8%	8%

"Ideal" risk represents
Total Cholesterol = 4.1 - 5.1
HDL = 1.2 (Male), 1.4 (Female)
BP < 120/80
No Diabetes, Non Smoker

People with an absolute risk of ≥20% should be considered for treatment: with a Statin to achieve a Total Cholesterol <5 and/or LDL cholesterol <3.2 with anti-hypertensives to achieve a BP ≤160/90 (ideally ≤140/80)

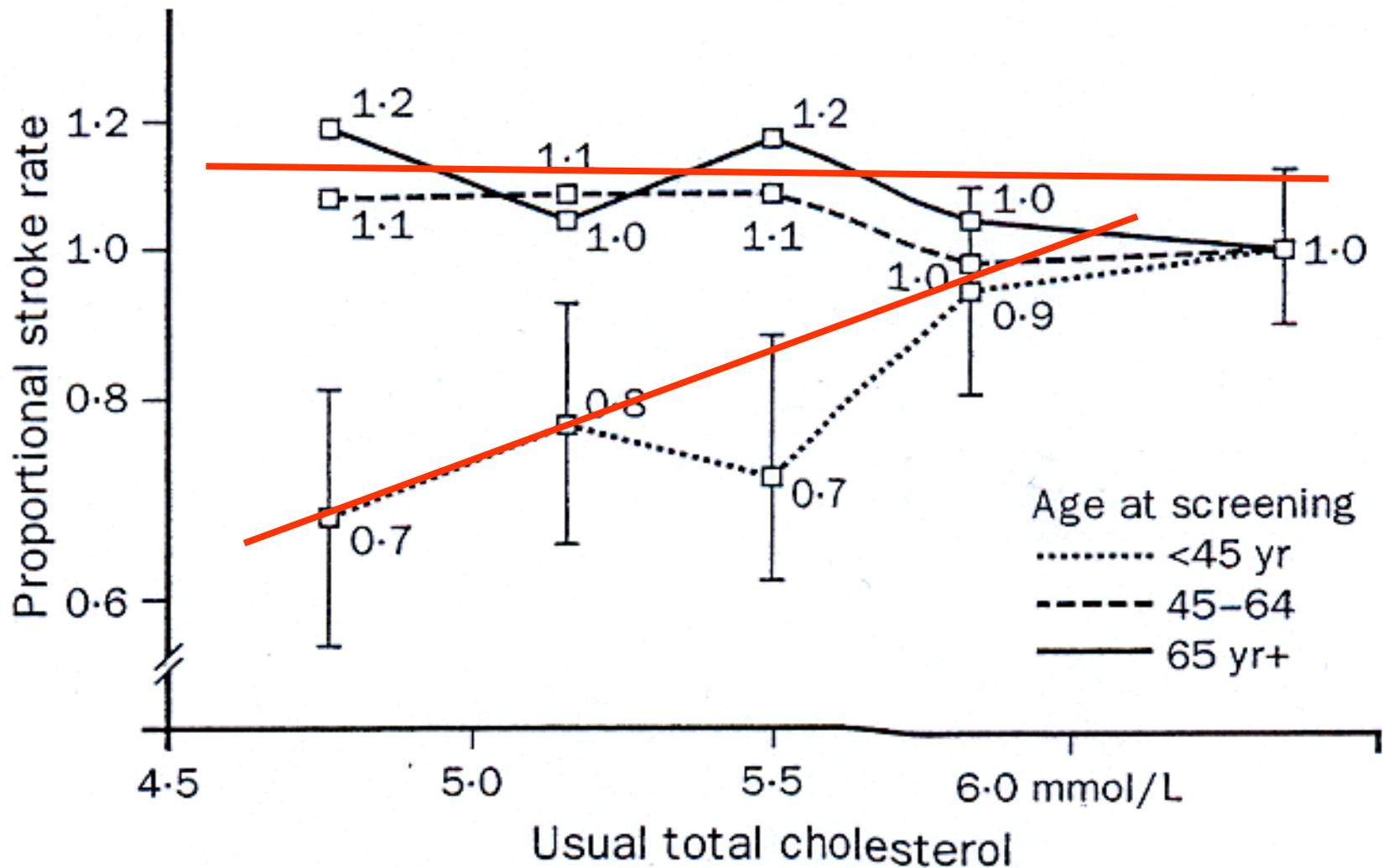
# Stroke risk by usual total cholesterol

Prospective **observational** studies collaboration  
450,000 people, 45 prospective cohorts, 13,000 strokes



Adjusted for age, sex, DBP, history of CHD and ethnicity

# Proportional stroke risk, by age and usual total cholesterol



# Προβλήματα

- Most observational studies not representative of whole population at risk for stroke
- No studies have assessed relationship between cholesterol and stroke in high risk cohort
- Only mortality recorded but not the incidence of stroke in the majority of studies
- Not available type of stroke, so possible positive relation in ischemic strokes and negative in haemorrhagic

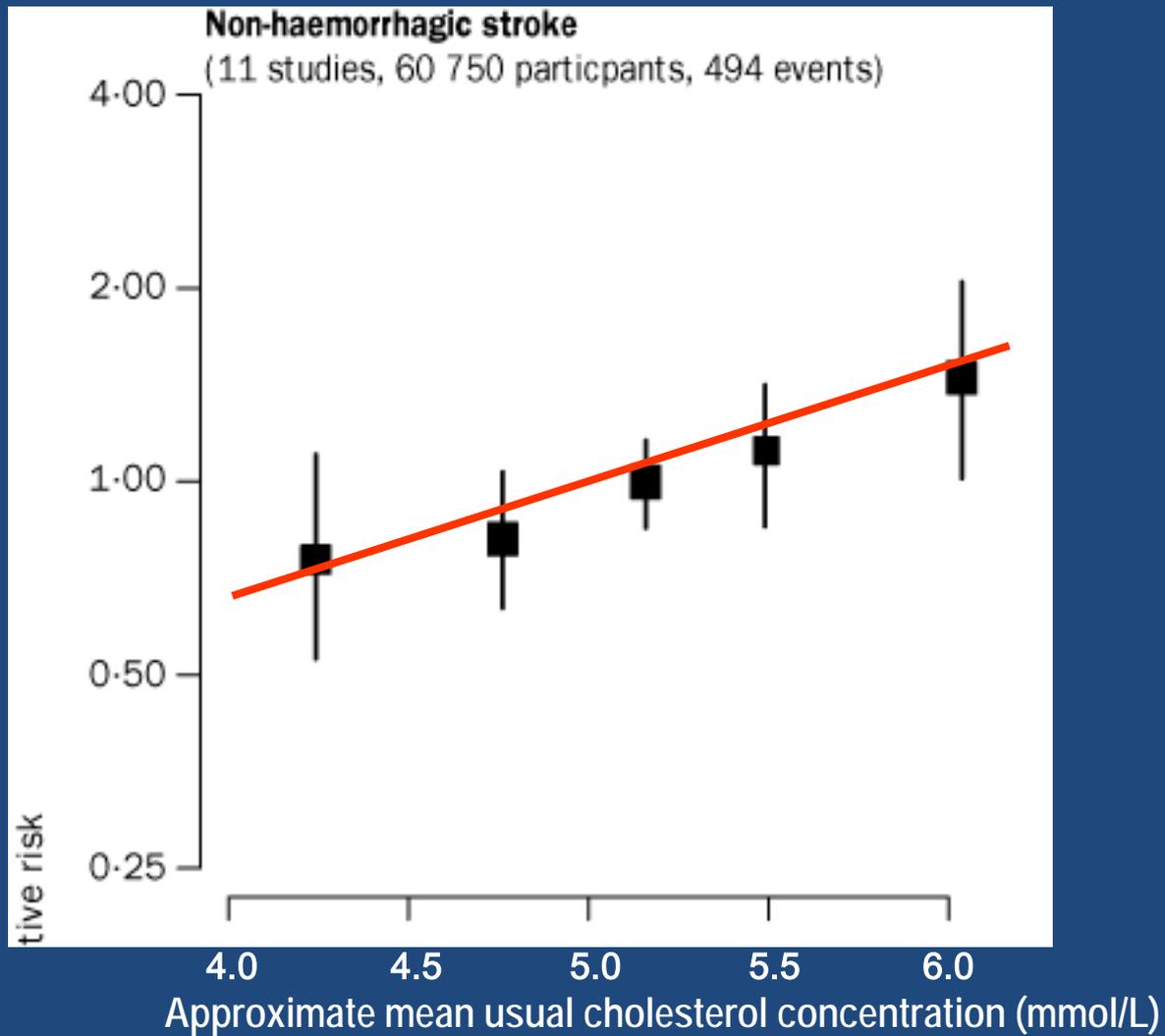


# Προβλήματα

- Cohorts primarily selected to study CHD
- Included middle aged people at risk of MI
- Higher risk of fatal MI before stroke
- Aggressive risk factor management?



# Association between cholesterol and ischemic stroke



# Lipid-lowering trials and stroke prevention

# Δευτερογενής πρόληψη ΣΝ & ΑΕΕ

<b>4-S</b>	<b>CARE</b>	<b>LIPID</b>
T.C >6.8 mmol/L	T.C <6.0 mmol/L	T.C 4- 6.8 mmol/L
Simva 10-40mg	Prava 40 mg	Prava 40 mg
CHD ↓ 34%	CHD ↓ 24%	CHD ↓ 24%
Stroke ↓ 30% p=0.02	Stroke ↓ 31% p=0.03	Ischemic stroke ↓ 19% p=0.05
Mainly TIAs		

## PROSPER: Baseline demographics

<b>Variable</b>	<b>Placebo n = 2913</b>	<b>Pravastatin n = 2891</b>
<b>Age (yrs)</b>	<b>75.3</b>	<b>75.4</b>
<b>Male (%)</b>	<b>48.3</b>	<b>48.3</b>
<b>Smoker (%)</b>	<b>27.6</b>	<b>26.0</b>
<b>Diabetes (%)</b>	<b>11.0</b>	<b>10.5</b>
<b>Hypertension (%)</b>	<b>61.6</b>	<b>62.2</b>
<b>Vascular dis* (%)</b>	<b>43.2</b>	<b>45.2</b>

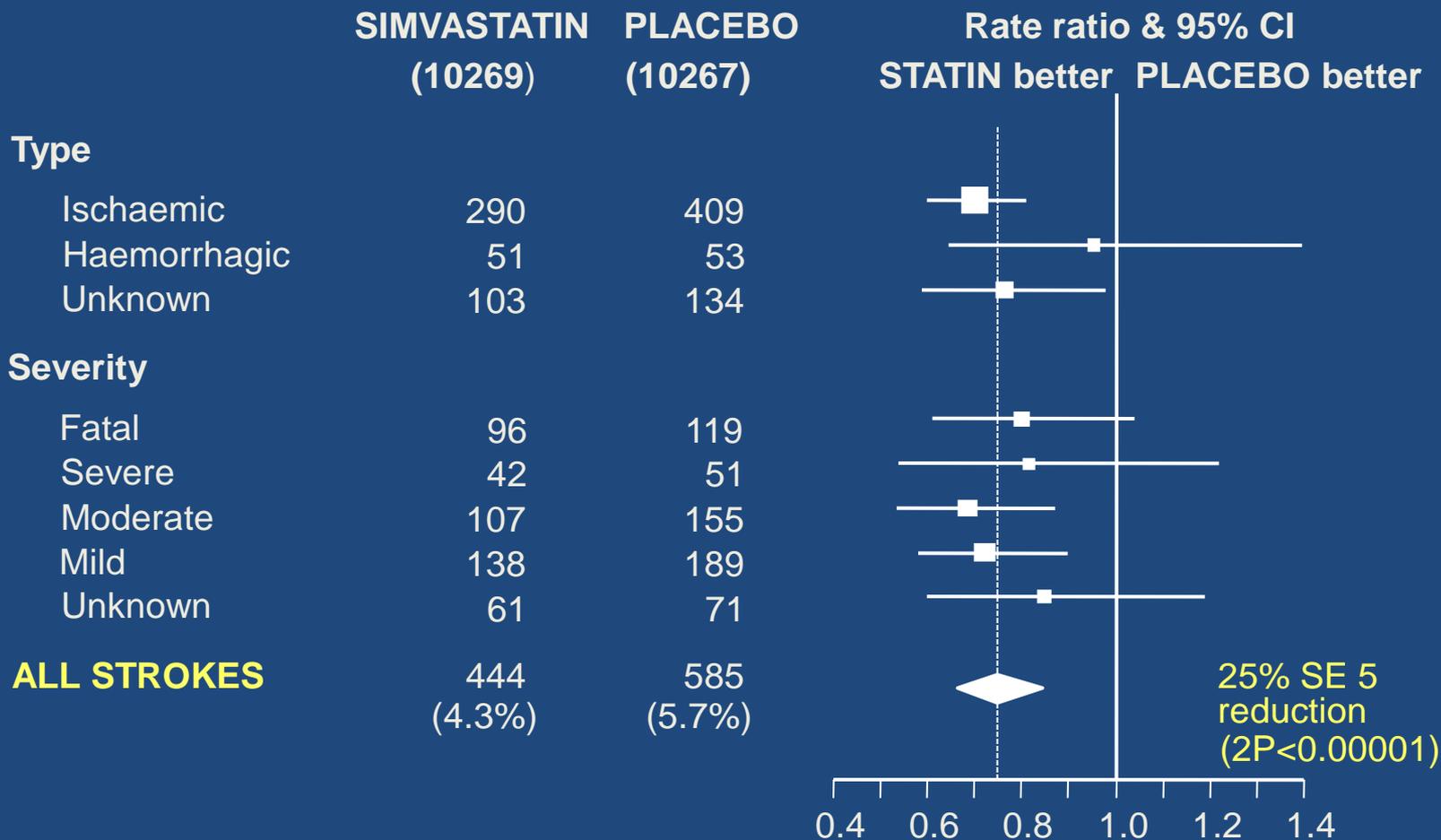
\* AP, IC, CVA, TIA, MI, PAD

## PROSPER: Results

Endpoint	HR	p
1° (fatal CHD/NF AMI or fatal/NF stroke)	0.85 (0.74-0.97)	0.014
Fatal CHD/NF AMI	0.81 (0.69-0.94)	0.006
Fatal/NF stroke	1.03 (0.81-1.31)	0.81
Cancer diagnoses	1.25 (1.04-1.51)	0.02

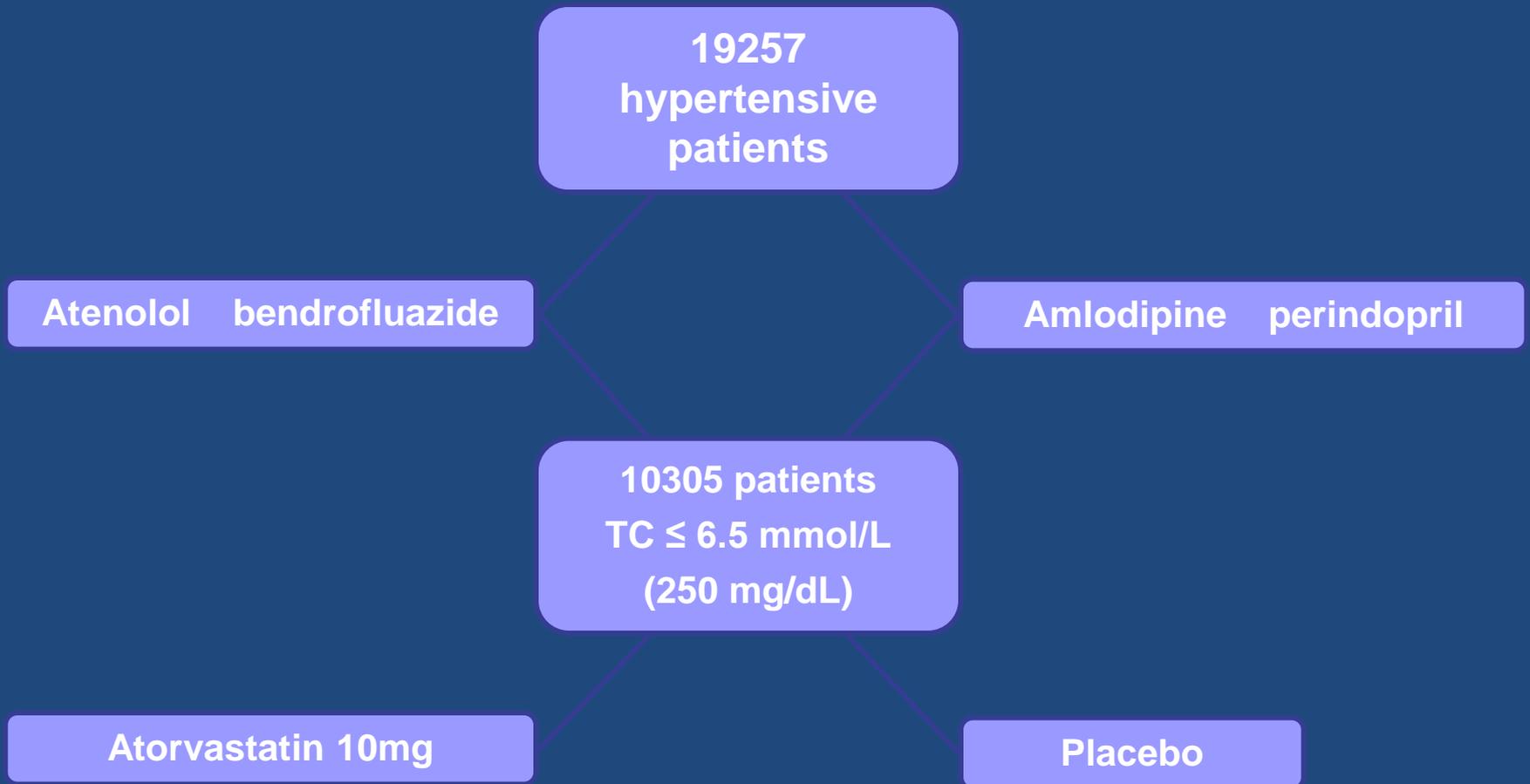
# Heart Protection study

## SIMVASTATIN: STROKE INCIDENCE

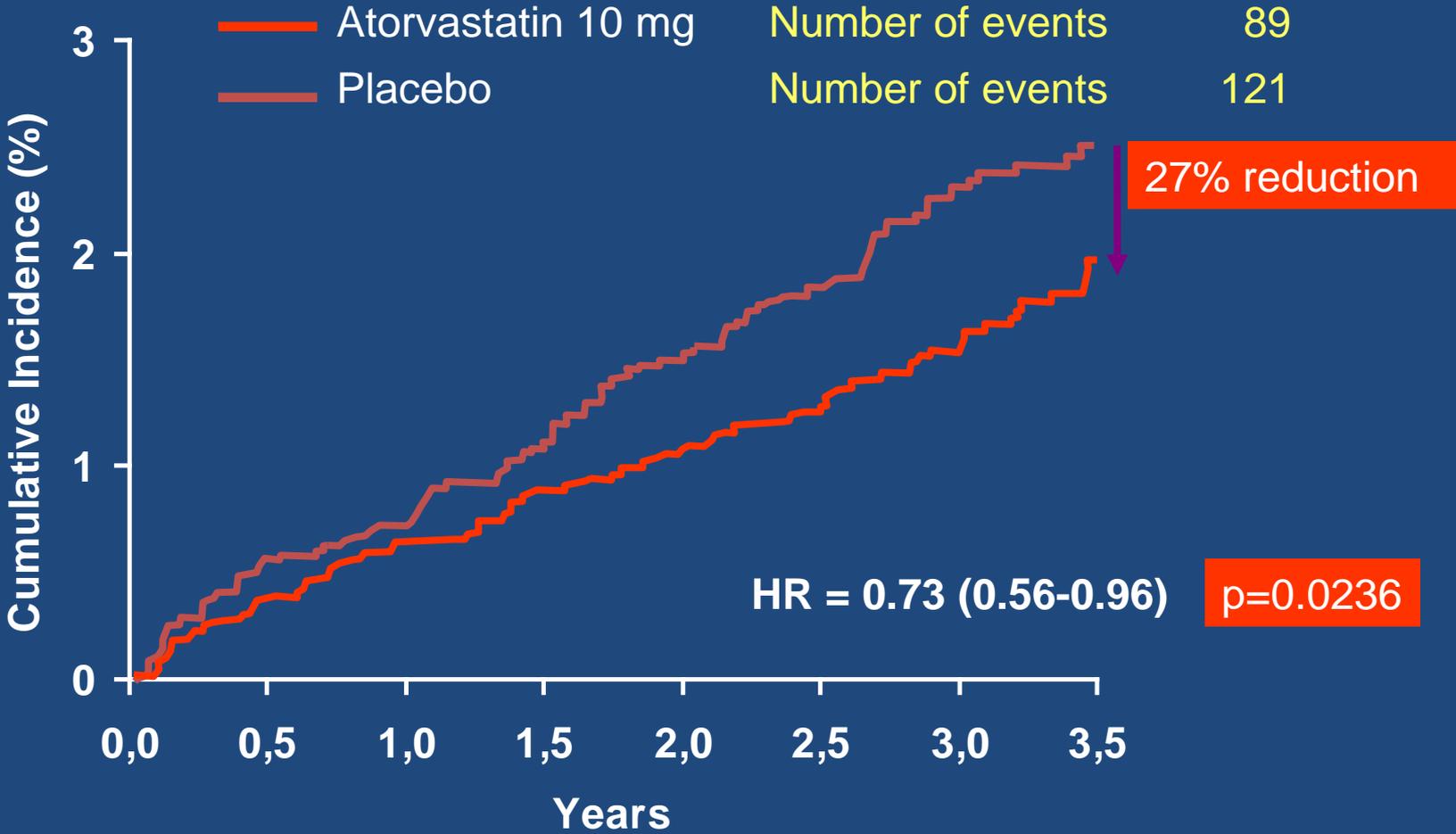




# ASCOT LLA



# Secondary End Point: Fatal and Nonfatal Stroke

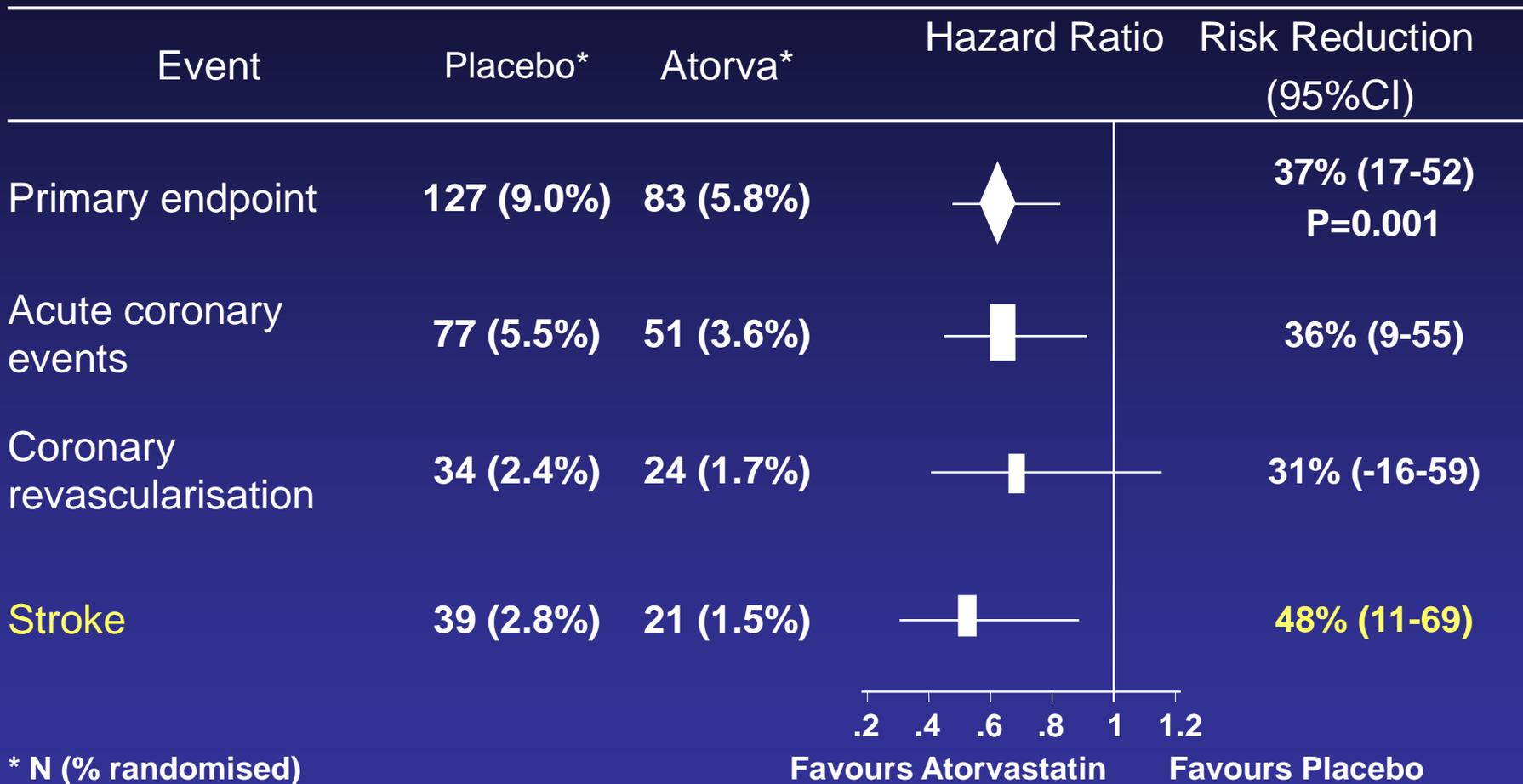


# Stroke benefits associated with atorvastatin in ASCOT-LLA

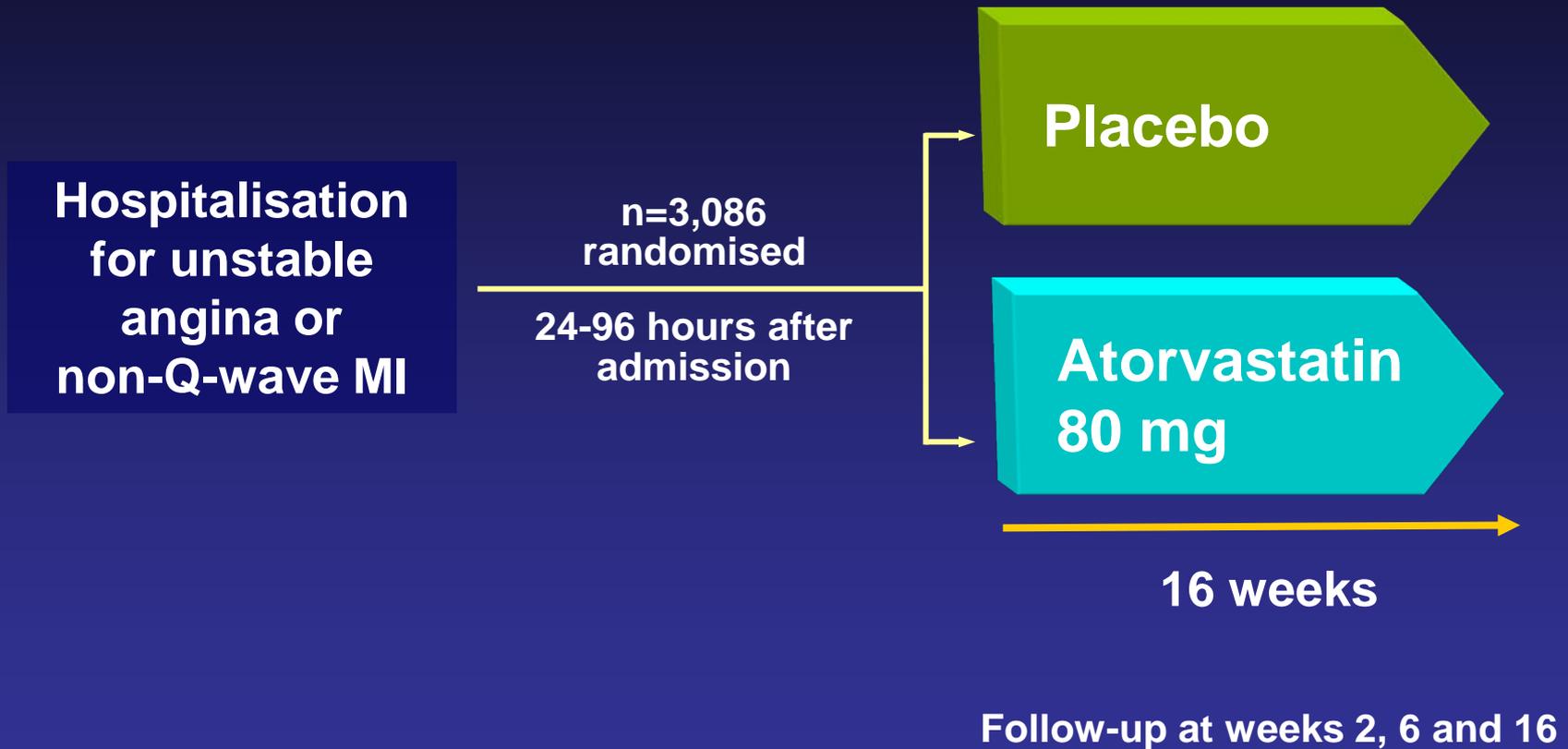
↓ 23-35%

Stroke type	Number of strokes		Hazard ratios (95%CI)
	Atorva	Placebo	
Fatal & non-fatal	89	121	0.73 (0.56-0.96)
Fatal	15	22	0.68 (0.35-1.31)
Non-fatal	78	100	0.77 (0.58-1.04)
Ischaemic	74	95	0.77 (0.57-1.05)
Haemorrhagic	13	20	0.65 (0.32-1.30)

# CARDS : Lipid lowering diabetes



# MIRACL Study design



# Secondary endpoints

	Placebo (n=1,548) n (%)	Atorvastatin (n=1,538) n (%)	RR (95% CI)*
<b>Stroke</b>			
Fatal and non-fatal	24 (1.6)	12 (0.8)	0.50 (0.26-0.99)
Non-fatal	22 (1.4)	9 (0.6)	0.41 (0.20-0.87)
<b>Coronary revascularisation</b>	250 (16.1)	254 (16.5)	1.02 (0.87-1.20)
Percutaneous coronary intervention	143 (9.2)	150 (9.8)	1.06 (0.85-1.32)
Surgical	110 (7.1)	106 (6.9)	0.97 (0.75-1.25)
<b>Worsening angina</b>	106 (6.8)	91 (5.9)	0.86 (0.66-1.13)
<b>New or worsening CHF</b>	43 (2.8)	40 (2.6)	0.94 (0.62-1.43)
<b>Any outcome</b>	344 (22.2)	344 (22.4)	1.01 (0.88-1.15)

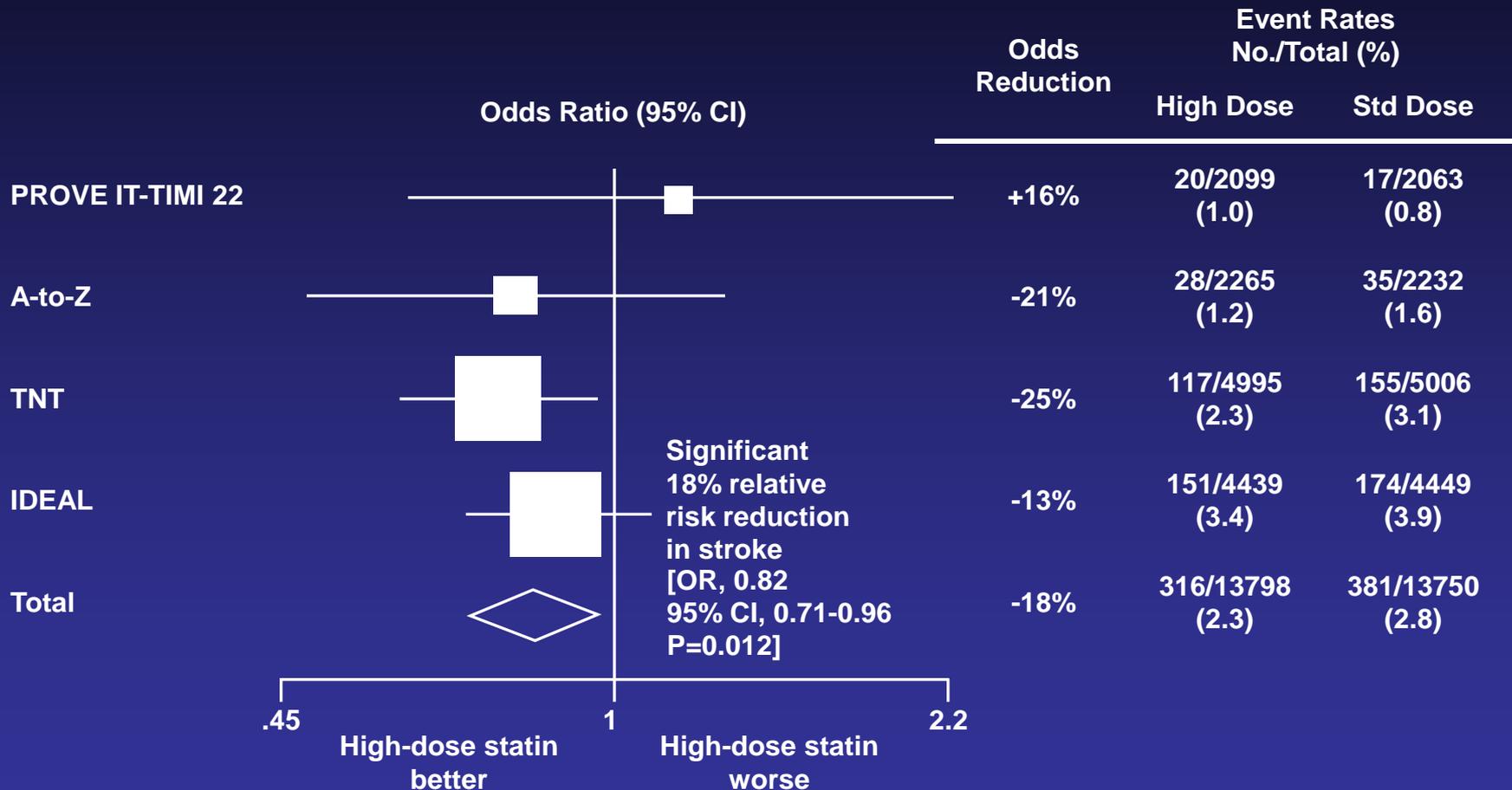
\* Based on Cox Mantel-Haenszel analysis

Adapted from Schwartz GG et al. JAMA 2001; 285 (13): 1711-1718

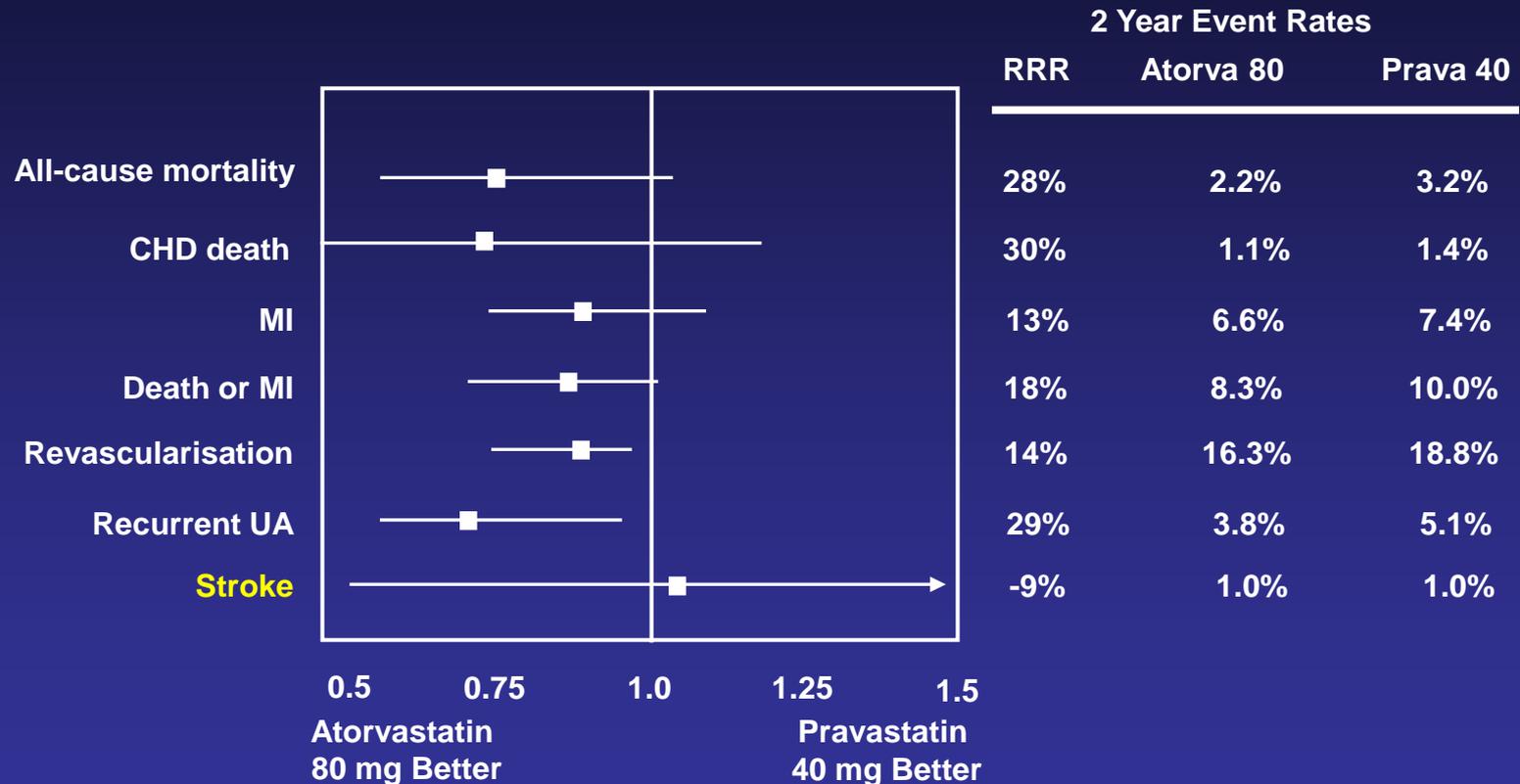
# Intensive vs Moderate Statin Therapy: Meta-Analysis



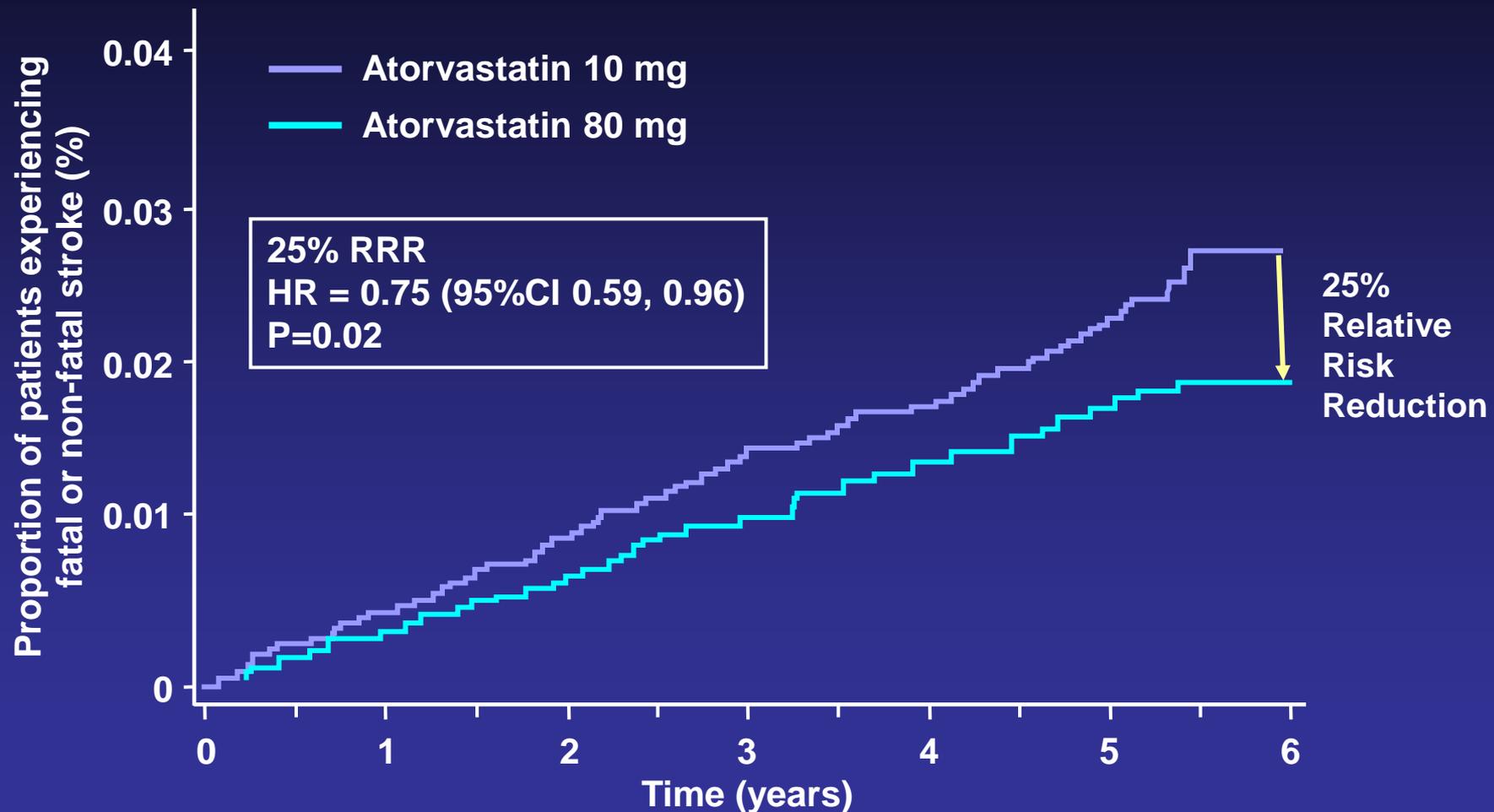
# Risk of stroke – individual trials & pooled analysis



# PROVE-IT, TIMI 2 Benefits of intensive lipid-lowering on individual endpoints at 2 years



# TNT Fatal or non-fatal stroke



# Μετα-ανάλυση 2004

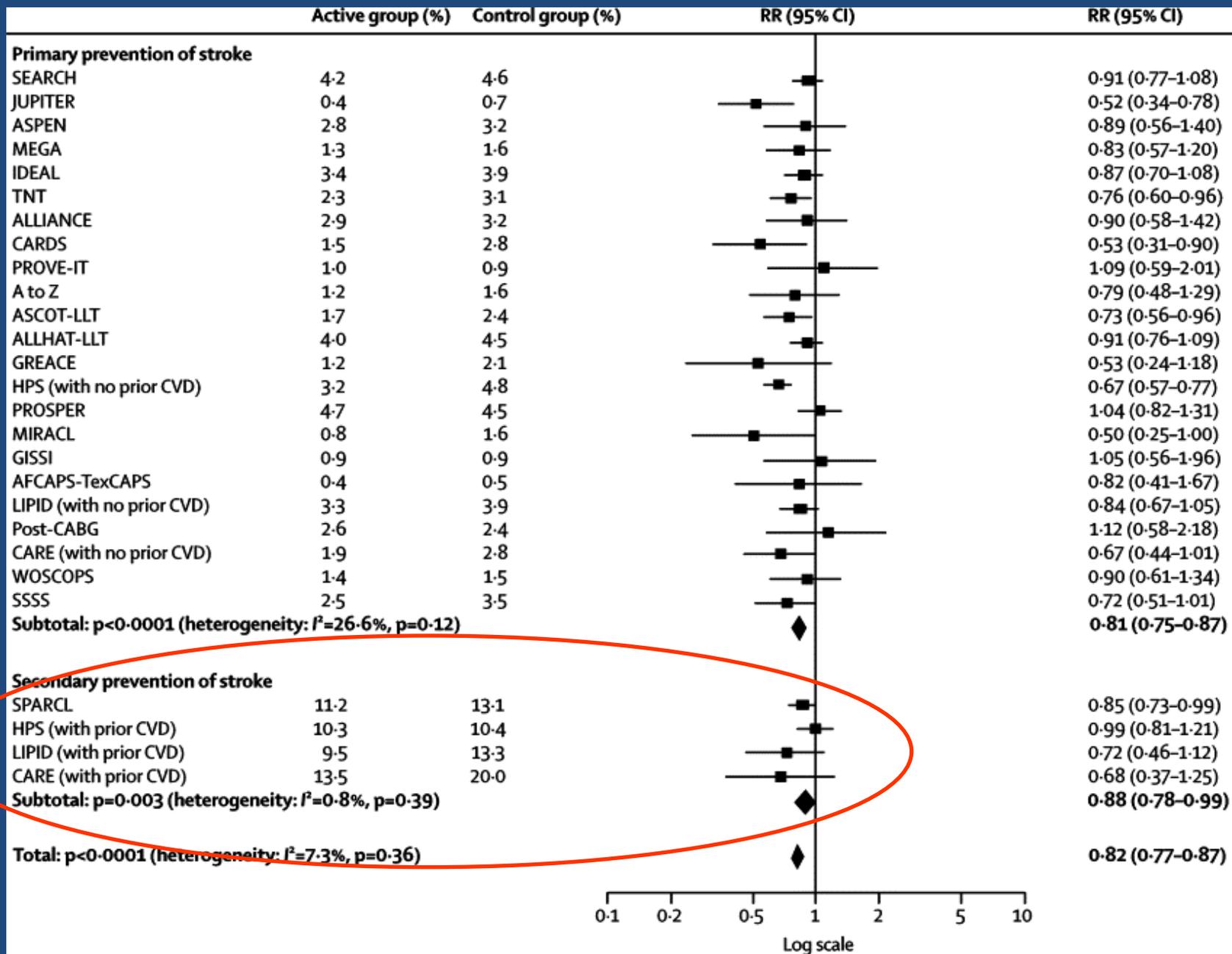
## Statins in Stroke Prevention and Carotid Atherosclerosis Systematic Review and Up-to-Date Meta-Analysis

Pierre Amarenco, MD; Julien Labreuche, Bst; Philippa Lavallée, MD; Pierre-Jean Touboul, MD

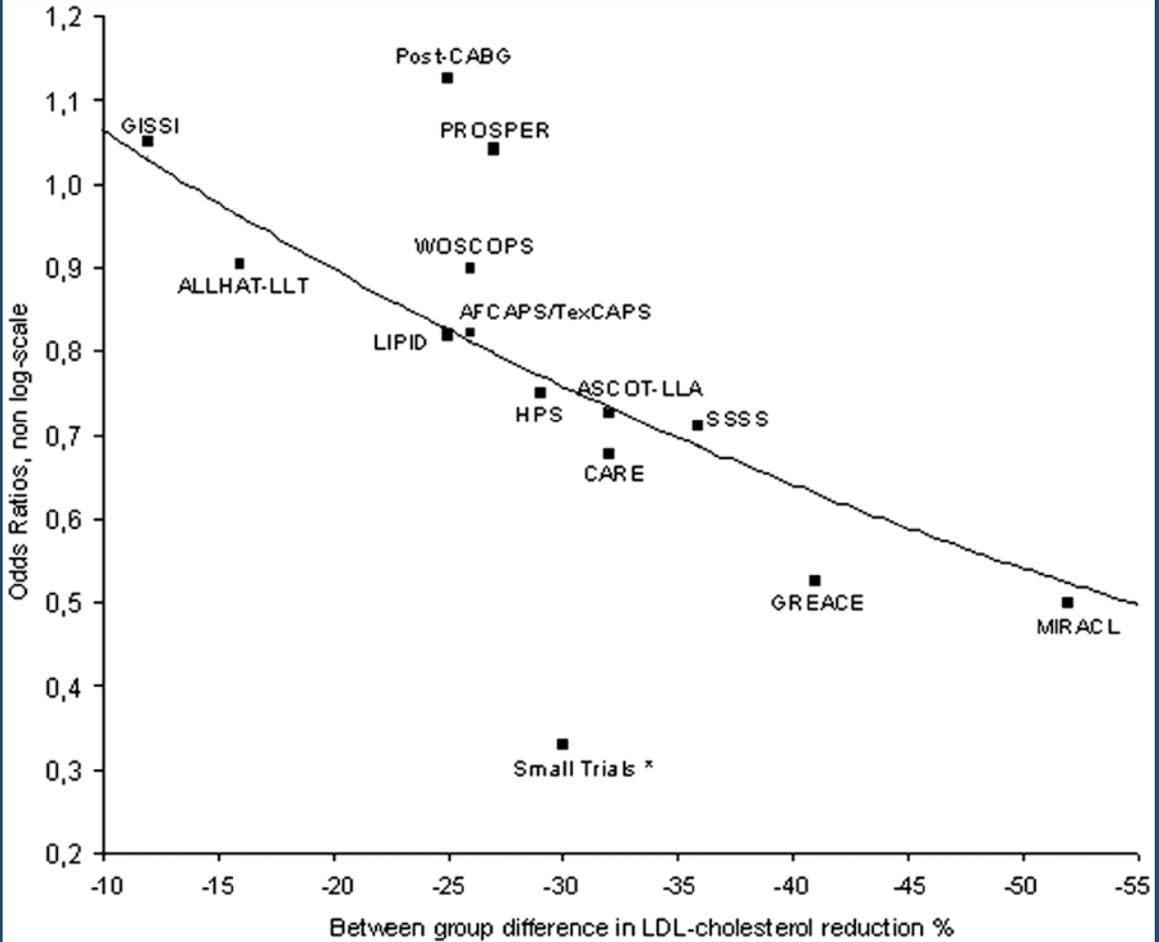
**Background and Purpose**—Previously published meta-analyses exploring the effect of statins on stroke incidence included 20 000 patients and found a 2% to 30% risk reduction. It is not clear whether this is attributable to low-density lipoprotein-cholesterol (LDL-C) reduction. Statin trials have now included >90 000 patients. We have determined the effect of statins and LDL-C reduction on stroke prevention

**Summary of Review**—We performed a systematic review and meta-analysis of all randomized trials testing statin drugs published before August 2003. The trials were identified using a computerized PubMed search. We analyzed separately statin effect on incident strokes and on carotid intima-media thickness (IMT) according to LDL-C reduction. The relative risk reduction for stroke was 21% (odds ratio [OR], 0.79 [0.73 to 0.85]), with no heterogeneity between trials. Fatal strokes were reduced but not significantly: by 9% (OR, 0.91 [0.76 to 1.10]). There was no increase in hemorrhagic strokes (OR, 0.90 [0.65 to 1.22]). Statin size effect was closely associated with LDL-C reduction. Each 10% reduction in LDL-C was estimated to reduce the risk of all strokes by 15.6% (95% CI, 6.7 to 23.6) and carotid IMT by 0.73% per year (95% CI, 0.27 to 1.19).

**Conclusions**—Statins may reduce the incidence of all strokes without any increase in hemorrhagic strokes, and this effect is mainly driven by the extent of between-group LDL-C reduction. Carotid IMT progression also strongly correlated with LDL-C reduction. (*Stroke*. 2004;35:2902-2909.)



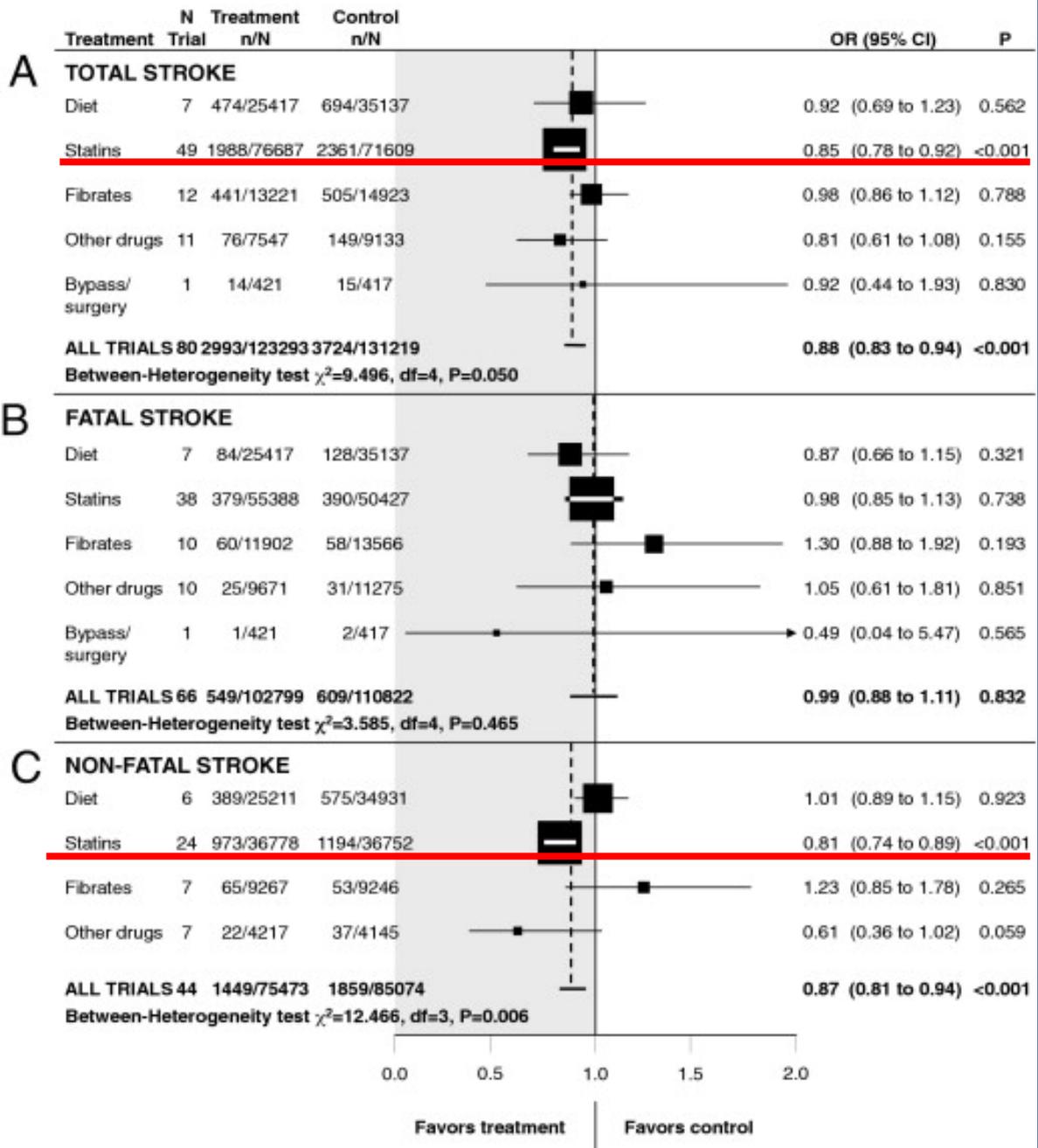
# Relationship between ORs for stroke events and corresponding LDL-C reduction



## Major statin trials with stroke end point

Trials	Statin, dose	LDL reduction, mean between-group difference	Number of patients (follow up length [years])	Number of strokes		Relative risk reduction (95%CI)	Absolute risk reduction	Strokes prevented per 1000 people
				Control	Statin			
4S	Simvastatin, 10–40 mg	35%, 68 mg	4444 (5.4)	95 in 2223 (4.3%)†	61 in 2221 (2.7%)	30% (4–48%)	1.6%	16
CARE	Pravastatin, 40 mg	32%, 38 mg	4159 (5.0)	76 in 2078 (3.7%)†	52 in 2081 (2.5%)	32% (4–52%)	1.2%	12
LIPID	Pravastatin, 40 mg	23%, 39 mg	9014 (6.0)	204 in 4502 (4.5%)†	169 in 4512 (3.7%)	19% (0–34%)	0.8%	8
HPS	Pravastatin, 40 mg	·, 39 mg	20 536 (5.3)	585 in 10 267 (5.7%)†	444 in 10 269 (4.3%)	25% (15–34%)	1.4%	14
PROSPER	Pravastatin, 40 mg	27%, 40 mg§	5804 (3.2)	131 in 2913 (4.5%)†	135 in 2891 (4.7%)	3% (–31–19%)	·	·
ALLHAT-LLT	Pravastatin, 20–40 mg	27.7%, 24 mg	10 355 (48)	231 in 5185 (4.5%)‡	209 in 5170 (4.1%)	9% (–14–21)	0.4%	4
KLIS	Pravastatin, 10–20 mg	20%, 11 mg	3853 (5.0)	41 in 1634 (2.5%)‡	47 in 2219 (2.1%)	22% (–13–49%)	0.4%	4
GREACE	Atorvastatin, 10–80 mg	46%, 70 mg	1600 (3.0)	17 in 800 (2.1%)‡	9 in 800 (1.1%)	47% (·)	1.0%	10
ASCOT	Atorvastatin	35%, 37 mg	10 305 (3.3)	121 in 5137 (2.4)†	89 in 5168 (1.7%)	27% (4–44%)	0.7%	7
Combined total*			70 070	1501 (4.3%)	1215 (3.4%)	21% (15–27%)	0.9%	9

SUMMARY - ALL TRIALS

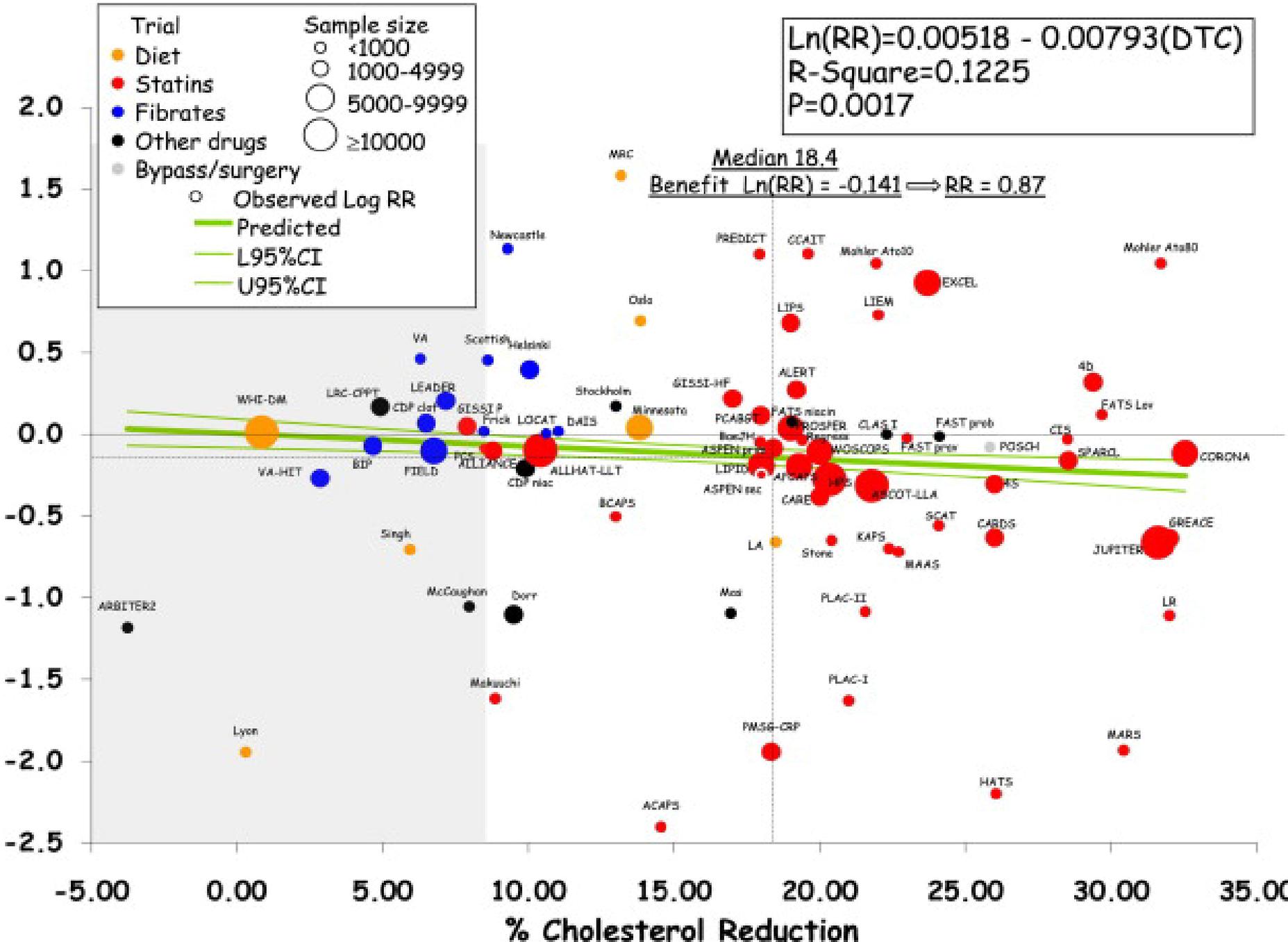


Among cholesterol-lowering treatments, **statins** are the **most effective** at decreasing the risk of total stroke, but their benefit is proportional to the **percent reduction of total CHO & LDL**.

No lipid-lowering intervention was associated with a reduction of fatal stroke.

# Percent cholesterol reduction and total stroke

Log Relative Risk of Total Stroke



**Guidelines for the Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack. A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association**

Karen L. Furie, Scott E. Kasner, Robert J. Adams, Gregory W. Albers, Ruth L. Bush, Susan C. Fagan, Jonathan L. Halperin, S. Claiborne Johnston, Irene Katzan, Walter N. Kernan, Pamela H. Mitchell, Bruce Ovbiagele, Yuko Y. Palesch, Ralph L. Sacco, Lee H. Schwamm, Sylvia Wassertheil-Smoller, Tanya N. Turan, Deidre Wentworth and on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Clinical Cardiology, and Interdisciplinary Council on Quality of Care and Outcomes Research

*Stroke* published online Oct 21, 2010;

DOI: 10.1161/STR.0b013e3181f7d043

## *Recommendations*

1. Statin therapy with intensive lipid-lowering effects is recommended to reduce risk of stroke and cardiovascular events among patients with ischemic stroke or TIA who have evidence of atherosclerosis, an LDL-C level  $\geq 100$  mg/dL, and who are without known CHD (*Class I; Level of Evidence B*).
2. For patients with atherosclerotic ischemic stroke or TIA and without known CHD, it is reasonable to target a reduction of at least 50% in LDL-C or a target LDL-C level of <70 mg/dL to obtain maximum benefit<sup>51,57</sup> (*Class IIa; Level of Evidence B*). (New recommendation)
3. Patients with ischemic stroke or TIA with elevated cholesterol or comorbid coronary artery disease should be otherwise managed according to the NCEP III guidelines, which include lifestyle modification, dietary guidelines, and medication recommendations<sup>59,60</sup> (*Class I; Level of Evidence A*).
4. Patients with ischemic stroke or TIA with low HDL-C may be considered for treatment with niacin or gemfibrozil<sup>61,62</sup> (*Class IIb; Level of Evidence B*) (Table 3).



- Cholesterol IS a risk factor for ischemic stroke.
- Lipid-lowering with statins reduces incidence of ischemic stroke by on average 20 – 25%.
- Benefit related to magnitude of cholesterol reduction and achieved cholesterol levels.
- Benefits of blood pressure reduction and lipid lowering additive or synergistic? From trial evidence at least 60% reduction in incidence.

