
**International Task Force for Prevention
Of Coronary Heart Disease**



*Coronary heart disease and stroke:
Risk factors and global risk*

Slide Kit 1

Stroke

Primary prevention of stroke

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Slide 1:

Stroke:

Primary prevention of ischemic stroke. Recommendations for risk factor management



**Primary Prevention of Ischemic Stroke
Recommendations for Risk Factor Management**



Risk factor	Goal / Recommendation
Hypertension	Systolic blood pressure < 140 mm Hg Diastolic blood pressure < 90 mm Hg
Smoking	Quitting
Diabetes	Improved glucose control; treatment of hypertension
Asymptomatic carotid stenosis	Endarterectomy may be considered in selected patients
Atrial fibrillation	Antithrombotic therapy (choice depends on age and risk factors)
Serum lipids	Treatment of dyslipidemia (choice depends on lipid profile and CHD risk factors)
Physical inactivity	≥ 30 mh of moderate- intensity activity daily (consider individual risk profile)
Poor diet / nutrition	≥ 5 servings of fruits and vegetables per day
Alcohol	Moderate intake (max. 2 drinks/day for men and 1 drink/day for women)
Drug abuse	Quitting

Source: Goldstein et al.; Stroke 2001, 32:280-299

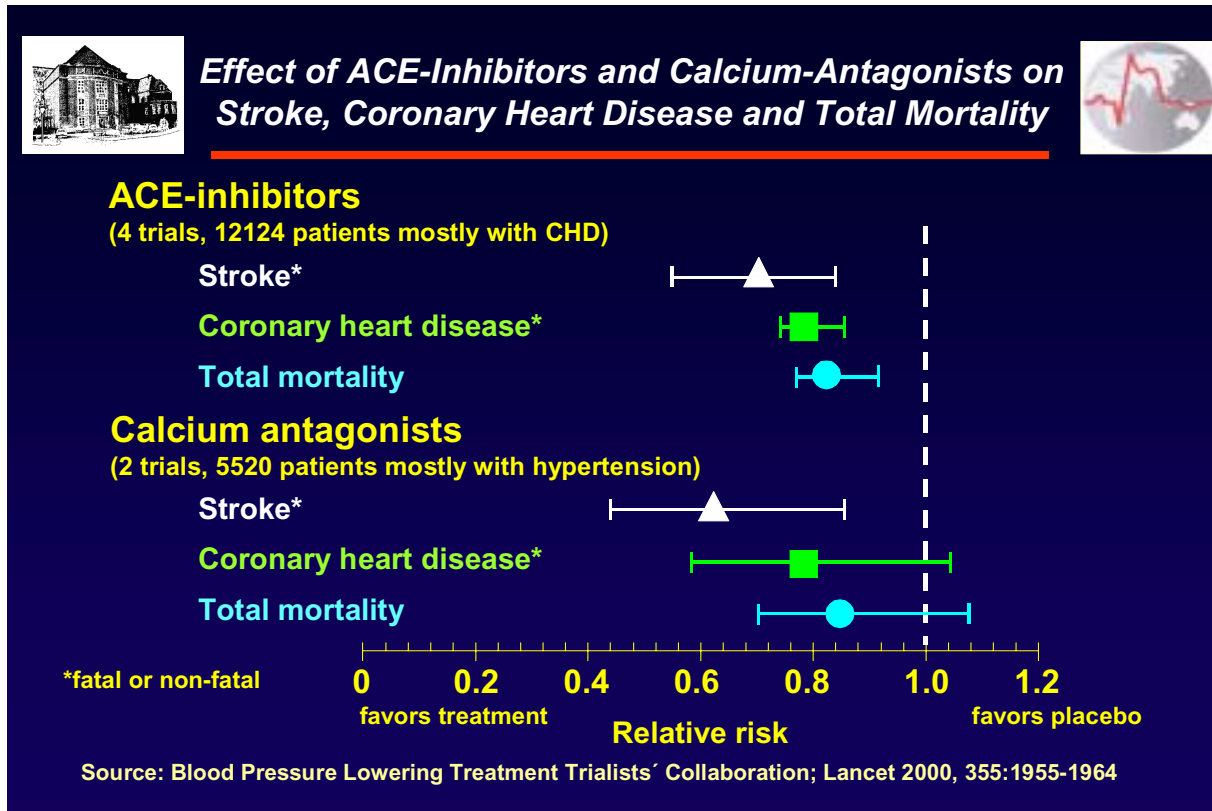
Primary prevention of ischemic stroke. Recommendations for risk factor management

This slide summarizes the guidelines of the Stroke Council of the American Heart Association for the management of modifiable risk factors for stroke.

Slide 2:

Stroke:

Effects of ACE-inhibitors and calcium-antagonists on stroke, coronary heart disease and total mortality

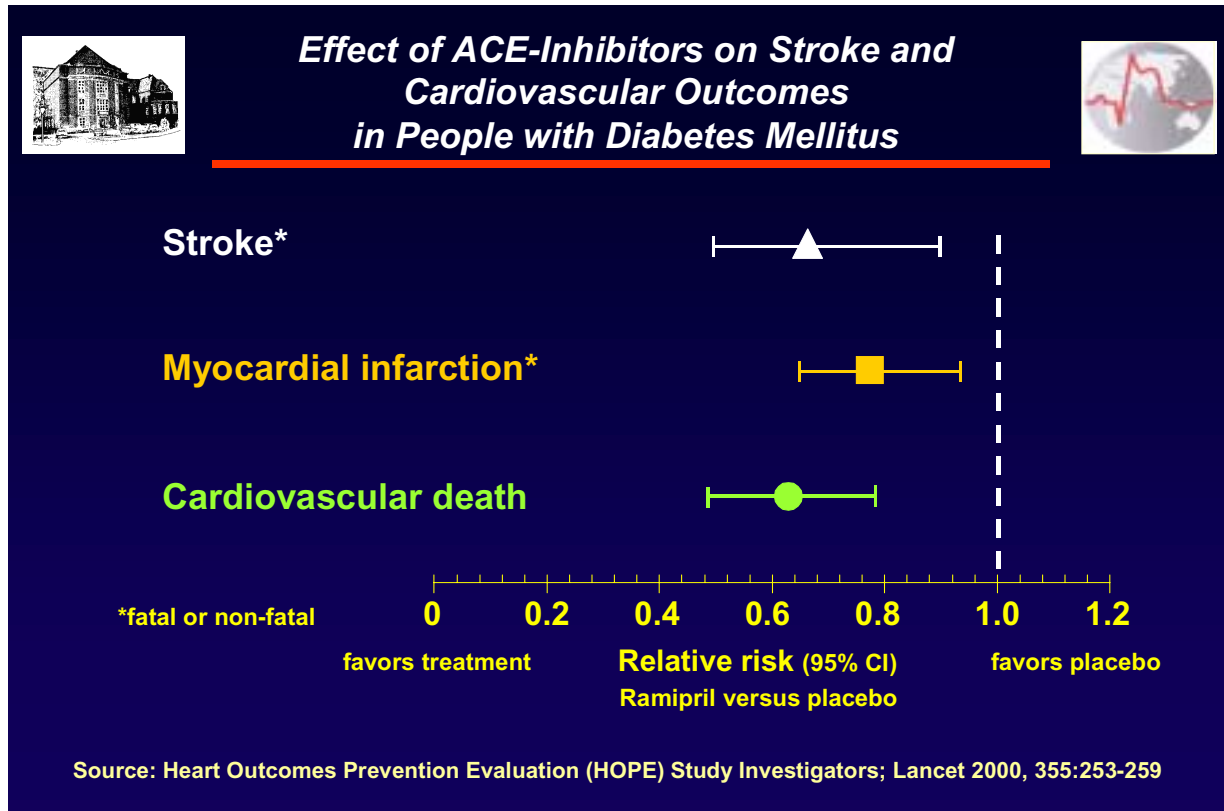


Effects of ACE-inhibitors and calcium-antagonists on stroke, coronary heart disease and total mortality

Effective treatment of hypertension reduces the incidence of fatal and nonfatal stroke by about 40%. By the mid 1990s, meta-analyses proved that both beta-blocker therapy and treatment with high-dose diuretics can prevent stroke. In 1995 the Blood Pressure Lowering Treatment Trialists' Collaboration was initiated under the aegis of the WHO-International Society of Hypertension Liaison Committee to investigate the effects of angiotensin-converting enzyme (ACE) inhibitors, calcium antagonists and other blood-pressure-lowering drugs on mortality and major cardiovascular morbidity in several patient populations. This slide shows the benefits of ACE inhibitors and calcium-antagonists for prevention of stroke and coronary heart disease.

Slide 3:

Stroke:
Effects of ACE-inhibitors on stroke and cardiovascular outcomes in people with diabetes




Effects of ACE-inhibitors on stroke and cardiovascular outcomes in people with diabetes

People with diabetes mellitus are at high risk of cardiovascular disease. The Heart Outcome Prevention Evaluation (HOPE) Study showed the particular benefits of ramipril (ACE-inhibitor) on cardiovascular outcomes in people with diabetes. The risk reduction for cardiovascular events was greater than would be expected from the observed mean difference in blood pressures (systolic blood pressure -2.4 mmHg, diastolic blood pressure -1.0 mmHg), suggesting additional protective effects of ACE inhibitors on the arterial wall.


Slide 4:

Stroke:

Primary prevention of ischemic stroke in patients with atrial fibrillation



Primary Prevention of Ischemic Stroke in Patients with Atrial Fibrillation



Antithrombotic therapy		
Age	Risk factors*	Recommendation
<65 years	- +	Aspirin Warfarin**
65-75 years	- +	Aspirin or Warfarin** Warfarin**
>75 years	-/+	Warfarin**

* Risk factors: hypertension, diabetes mellitus, poor left ventricular function, rheumatic mitral valve disease, prior TIA/stroke, systemic embolism or stroke, prosthetic heart valve

** Target International Normalized Ratio (INR) 2.5; range (2.0-3.0)


Sources: W. Hacke et al.; Eur J Neurology 2000, 7:607-623; L.B. Goldstein et al.; Stroke 2001, 32:280-299

Primary prevention of ischemic stroke in patients with atrial fibrillation


Atrial fibrillation is a common arrhythmia and is responsible for about half of all thromboembolic strokes. There are a limited number of predictors of high stroke risk within the population of patients with atrial fibrillation. Anticoagulation therapy with warfarin in patients with high-risk features reduces the risk of ischemic stroke by almost 70%. The slides shows the age- and risk-feature-specific recommendations for antithrombotic treatment of patients with atrial fibrillation currently adopted by the European Stroke Initiative (EUS) and the Stroke Council of the American Heart Association.

Slide 5:

**Stroke:
 Aspirin for primary prevention of stroke and other major vascular events**



Aspirin for Primary Prevention of Stroke and Other Major Vascular Events



Estimated effects (meta-analysis)

Population	Number of annual events per 1,000 given Aspirin			
	Stroke	Myocardial infarction	Death	Major Extracranial Bleeds
Middle-aged persons				
No vascular risk factors	↑ 0.5 (?)	↓ 1	0	↑ 1
vascular risk factors	0	↓ 3	↓ 1	↑ 2
Healthy elderly persons	↑ 1 (?)	↓ 3	↓ 1.5	↑ 3

parenthetical question mark: non-significant trend
 upward arrow: increased; downward arrow: decreased

Sources: Hart et al.; Arch Neurol 2000, 57:326-332



Aspirin for primary prevention of stroke and other major vascular events

This slide summarizes data from a meta-analysis of randomized clinical trials and large prospective observational cohort studies examining the relation between aspirin use and stroke in healthy male physicians and persons with diabetes mellitus, hypertension or with coronary risk factors. There is no scientific support for prescribing aspirin to reduce the risk of stroke. However, available data favor aspirin use for middle-aged persons at special risk for myocardial infarction.

Slide 6:

Stroke:

Primary prevention of ischemic stroke: recommendations for management of serum lipids



Primary Prevention of Ischemic Stroke Recommendations for Management of Serum Lipids

Goal / Recommendation

Initial lipid evaluation (no CHD)

- TC < 200 mg/dl and HDL ≥ 35 mg/dl	General education, re-evaluation within 5 years
- TC 200-239 mg/dl and HDL ≥ 35 mg/dl and < 2 CHD risk factors*	Dietary modification, re-evaluation in 1-2 years
- TC ≥ 240 mg/dl or HDL < 35 mg/dl or ≥ 2 CHD risk factors*	Lipoprotein analysis

LDL-evaluation

- No CHD and < 2 CHD risk factors*	LDL < 160 mg/dl
- No CHD but ≥ 2 CHD risk factors*	LDL < 130 mg/dl
- Definite CHD or other atherosclerotic disease	LDL < 100 mg/dl

* CHD risk factors: men ≥ 45 years, women ≥ 55 years or early menopause without hormone replacement therapy, family history of premature CHD, smoking, hypertension, HDL < 35 mg/dl, diabetes mellitus,


Source: Goldstein et al.; Stroke 2001, 32:280-299

Primary prevention of ischemic stroke: recommendations for management of serum lipids


This slide summarizes the recommendations for the management of serum lipids as part of the therapeutic approach to prevent an ischemic stroke. The recommendations given by the Stroke Council of the American Heart Association base on management guidelines for patients with elevated cholesterol levels.

Slide 7:

Stroke:
Genetic susceptibility and LDL-cholesterol in lacunar stroke



Genetic Susceptibility and LDL-Cholesterol in Lacunar Stroke



GG Genotype*	LDL-Tertile (mg/dl)	Controls n	Cases n	Odds ratio (95% CI)** for lacunar stroke
-	1st (< 102)	27	9	1.0 (reference)
-	2nd (102-132)	15	15	2.8 (0.7-11.5)
-	3rd (>132)	21	23	3.7 (1.2-11.7)
<hr/>				
+	1st	16	7	1.6 (0.3-6.9)
+	2nd	12	17	8.5 (1.9-38.9)
+	3rd	4	22	22.2 (4.1-120.1)

* The GG Genotype of the Glu298Asp polymorphism in the eNOS gene was more frequent in patients with lacunar stroke

** adjusted for cardiovascular history, lipid lowering drugs and blood sample delay

Sources: Elbaz et al.; Stroke 2000, 31:1634-1639

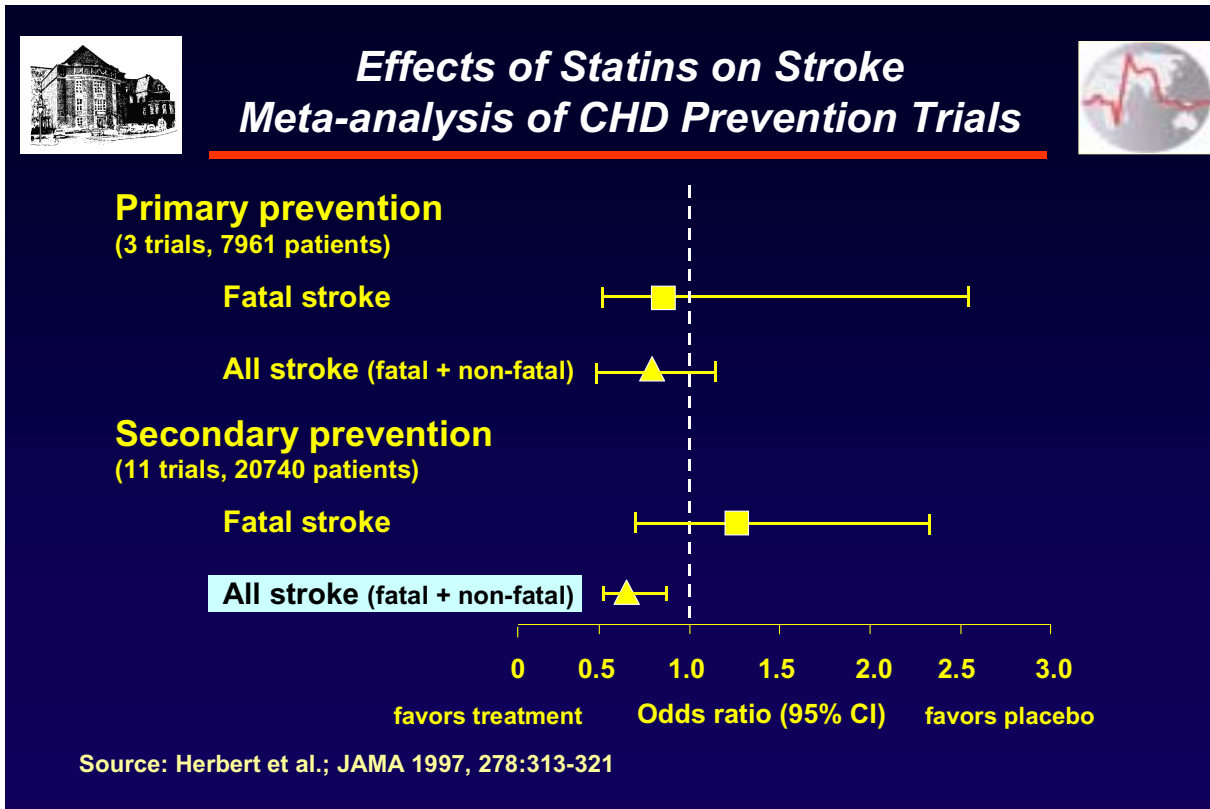
Genetic susceptibility and LDL-cholesterol in lacunar stroke

This slide provides an example of a potential synergistic relation between the genetic susceptibility and LDL-cholesterol levels for the risk of a lacunar stroke (small, deep infarct measuring <15mm – subtype of an ischemic stroke). In a case-control study homozygosity for the G allele of the Glu298Asp polymorphism in the endothelial constitutive nitric oxide synthase as well as elevated LDL-cholesterol levels were associated with lacunar stroke. The trend in lacunar stroke risk associated with LDL-cholesterol was stronger among carriers of the GG genotype.

Slide 8:

Stroke:

Effects of statins on stroke: Meta-analysis of CHD prevention trials





Effects of statins on stroke: Meta-analysis of CHD prevention trials

This slide summarizes the results of a meta-analysis of cholesterol lowering with statins in stroke prevention. The meta-analysis bases on randomized trials which were designed to investigate the effect of statins on coronary heart disease. Despite the fact that cholesterol is not a strong risk factor for strokes, the long-term use of statins was associated with a significant overall reduction in risk of stroke by 29%. Risk reduction was particularly pronounced in secondary prevention trials.

Slide 9:

**Stroke:
 Risk reduction in major statin trials**

	4S	CARE	LIPID	WOSCOPS	
					
Risk Reduction in the Major Statin Trials					
					
Percentage of women	19	14	17	0	
Age [average] (y)	35-69 [58]	21-75 [59]	31-75 [53]	45-64 [55]	
CHD inclusion criteria	with CHD	with acute MI	with CHD	without MI	
No. of patients	4,444	4,159	9,014	6,595	
Average follow-up period (y)	5.4	5.0	≥ 5	4.9	
<u>Baseline lipid levels (mg/dl)</u>					
Total cholesterol	261	209	213	272	
HDL cholesterol	46	39	37	46	
LDL cholesterol	188	139	157	192	
Triglyceride	133	155	193	163	
<u>Risk reduction (%)</u>					
Nonfatal MI and death from CHD	31 ³	24 ²	23 ³	30 ³	
Nonfatal and fatal stroke	30¹	31¹	20¹	11	
Total mortality	29 ³	9	23 ³	22	

¹ p<0.05
² p<0.01
³ p<0.001

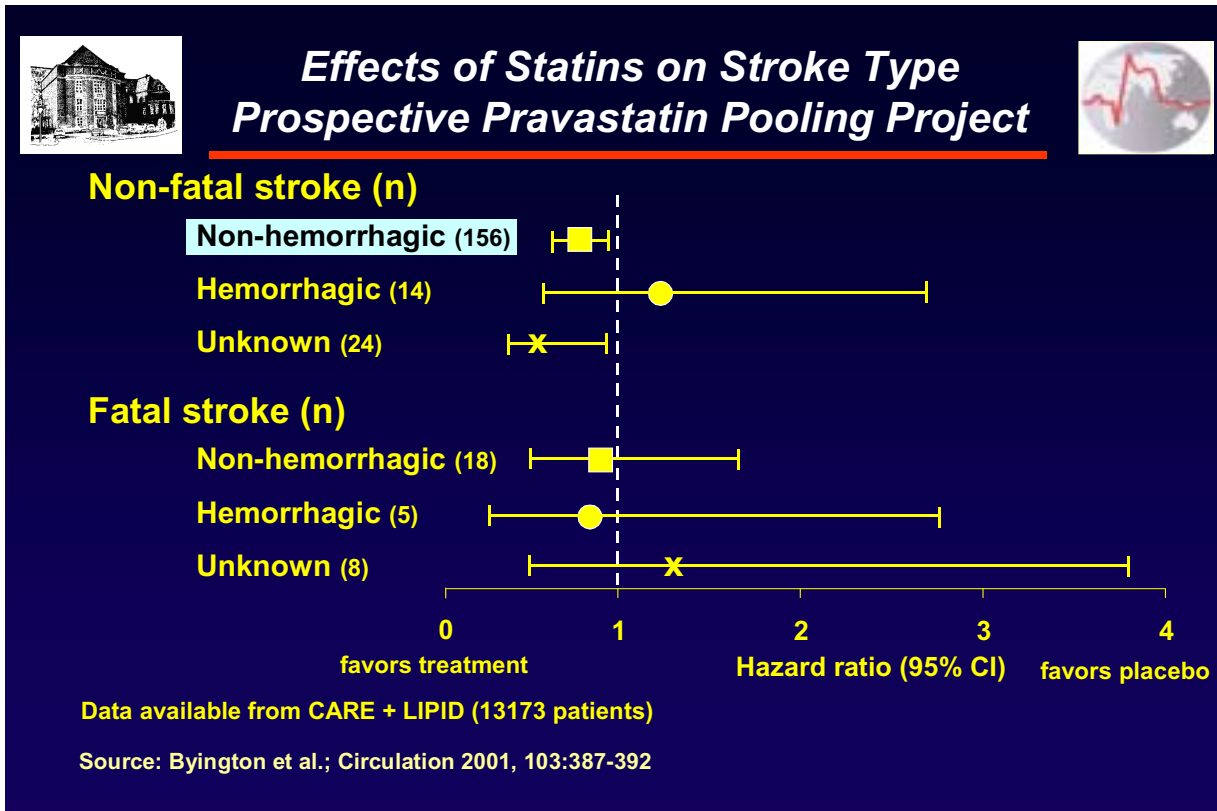
Risk reduction in major statin trials

This slide shows the main characteristics of the major primary (WOSCOPS) and secondary (4S, CARE, LIPID) coronary heart disease prevention trials that used statins. The important point to note is that in the secondary prevention trial statins significantly reduced stroke incidence across a wide range of baseline cholesterol levels.

Slide 10:

Stroke:

Effects of statins on stroke type. Prospective Pravastatin Pooling Project



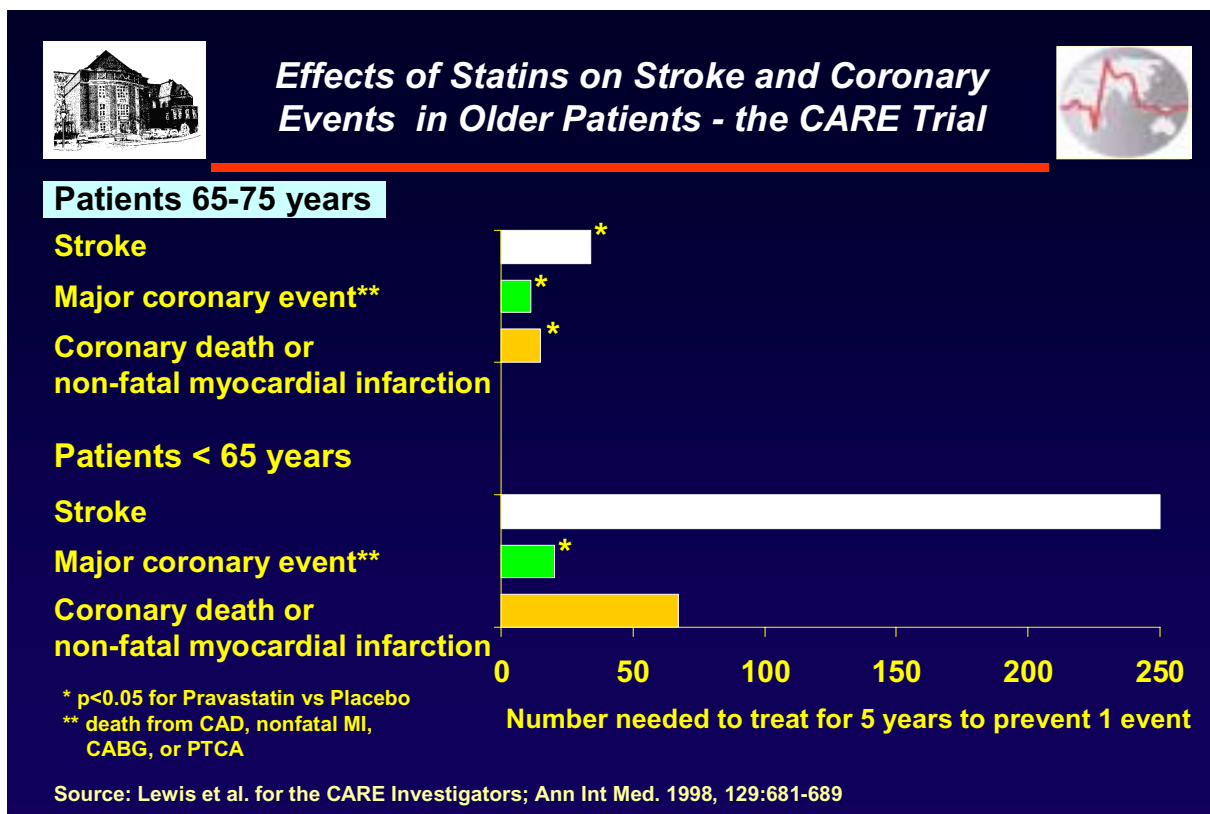
Effects of statins on stroke type. Prospective Pravastatin Pooling Project

This slide shows that the reduced risk for stroke observed in the secondary prevention trials CARE and LIPID was due to a reduction in nonfatal non-hemorrhagic stroke, the predominant type of stroke.

Slide 11:

Stroke:

Effects of statins on stroke and coronary events in older patients - the CARE trial



Effects of statins on stroke and coronary events in older patients - the CARE trial

This slide shows the number of patients needed to treat for 5 years to prevent one stroke or coronary event in the CARE study population. In patients aged 65-75 years who had had a myocardial infarction and cholesterol levels in the average range, pravastatin was associated with a clinically important reduction in risk for major coronary events and stroke. Given the high stroke rate in older patients, the potential for absolute benefit in this age group is substantial.

Slide 12:

Stroke:
Protective effects of statins on ischemic stroke



Protective Effects of Statins on Ischemic Stroke



Downstream effects

- **Stabilization of precerebral atherosclerotic plaques**
- **Favorable hemorheological and antithrombotic effects**

Upstream effects

- **Preserved blood flow and limited neurological loss by simultaneous**
 - **Upregulation of endothelial nitric oxide synthase (eNOS)**
 - **Inhibition of inducible nitric oxide synthase (iNOS)**
- **Attenuated inflammatory neuronal loss**
- **Antioxidant properties**

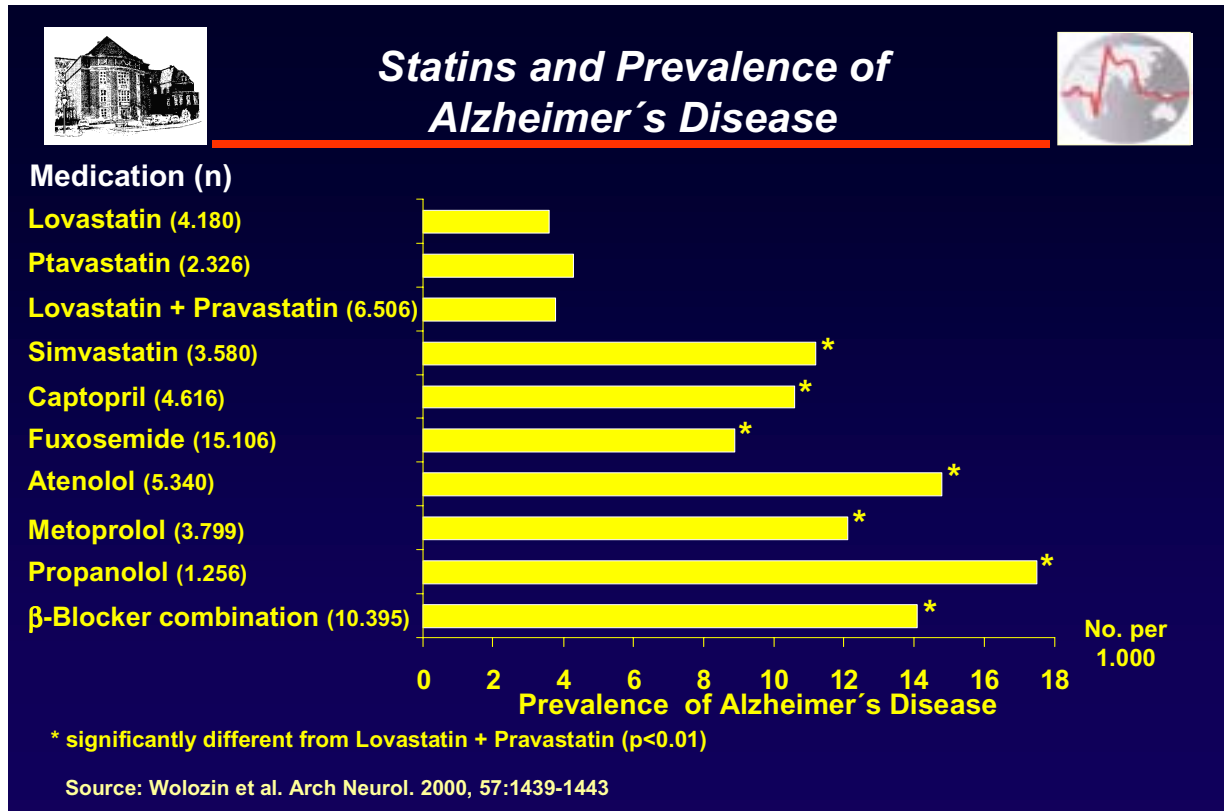
Sources: C.J. Vaughan and N. Delanty; *Stroke* 1999, 30:1969-1973

Protective effects of statins on ischemic stroke

This slide shows which mechanisms are currently thought to play a role in the prevention of stroke by statins. These include downstream effects and neuroprotective properties of statins that likely attenuate the effects of ischemia on the brain vasculature and parenchyma.

Slide 13:

Stroke: Statins and prevalence of Alzheimer's disease

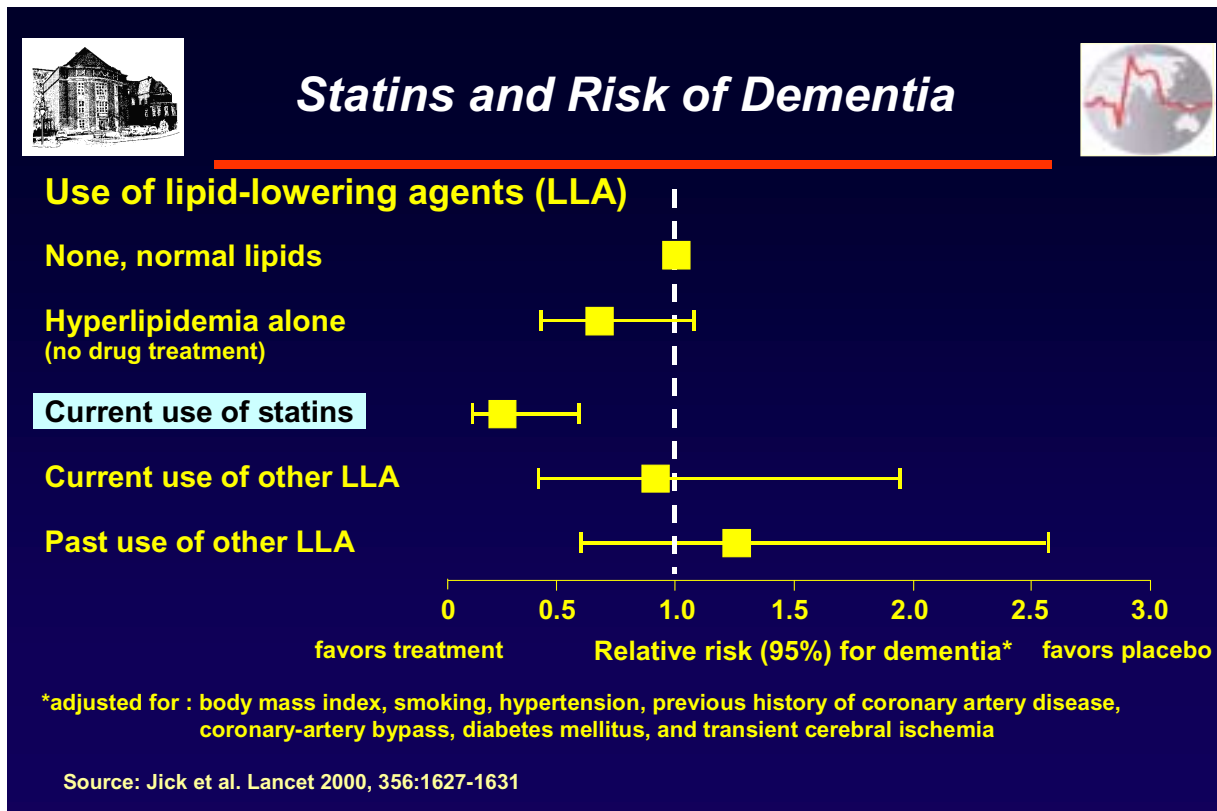


Statins and prevalence of Alzheimer's disease

This slide shows that the neuroprotective properties of statins may also contribute to the prevention of Alzheimer's disease. In a cross-sectional analysis of patients receiving different medications for treating cardiovascular disease, the prevalence of probable Alzheimer's disease in those taking Lovastatin or Pravastatin was 60 to 73% lower than in the total patient population.

Slide 14:

Stroke: Statins and risk of dementia



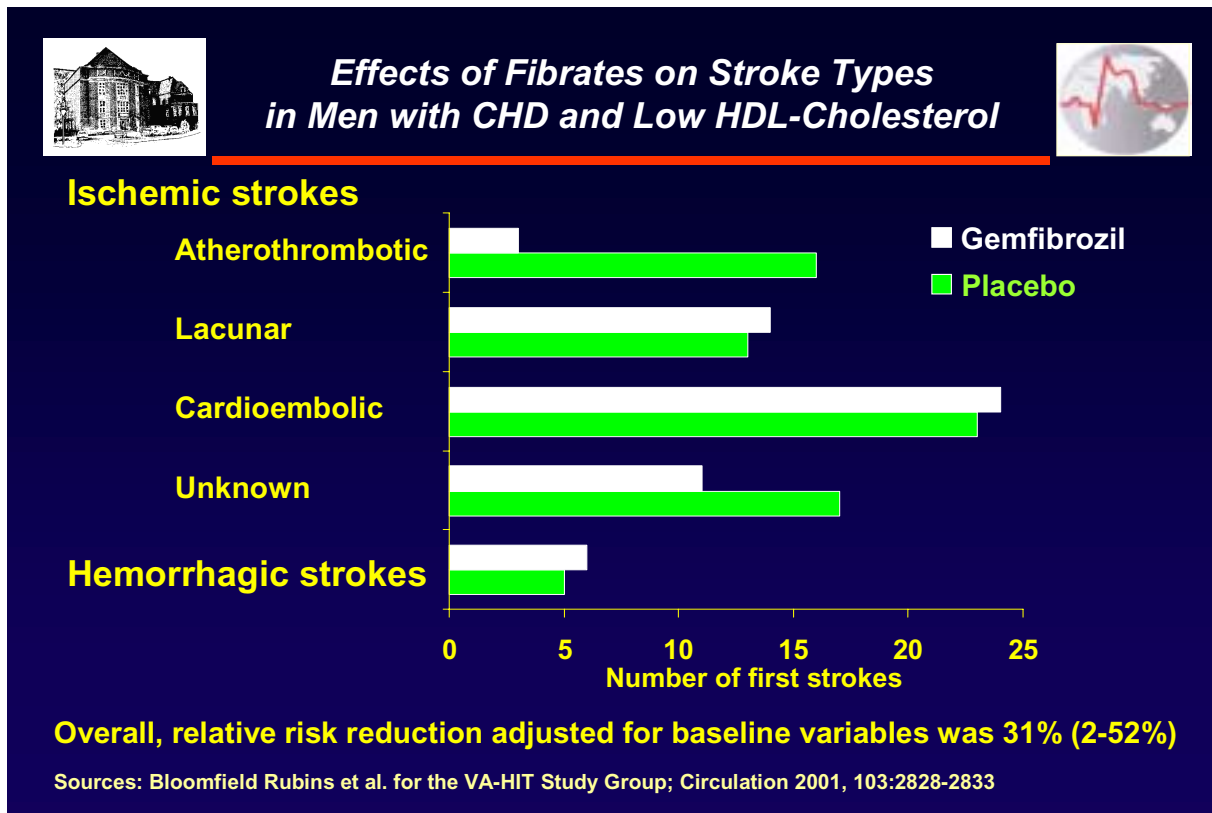
Statins and risk of dementia

This slide shows results from another study indicating that statins may reduce the risk of developing dementia. This nested case-control study included data from patients receiving lipid-lowering agents, individuals with a clinical diagnosis of untreated hyperlipidemia and a randomly selected group of other individuals among whom cases with dementia were identified and matched with up to four controls. Individuals who were prescribed statins had a substantially lowered risk of developing dementia. The available data do not distinguish between Alzheimer's disease and other forms of dementia.

Slide 15:

Stroke:

Effects of fibrates on stroke types in men with CHD and low HDL-cholesterol



Effects of fibrates on stroke types in men with CHD and low HDL-cholesterol

Persons with coronary heart disease who have a low HDL-cholesterol and a low LDL-cholesterol level are commonly treated with fibrates. This slide shows that men treated with fibrates for 5 years also had a reduced incidence of ischemic stroke, namely atherothrombotic strokes.