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

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*Clinical management of risk factors  
of coronary heart disease and stroke*

*Major recent drug trials*

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**Lescol Intervention Prevention Study**

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Slide 1:

## Context and objective



### **The Lescol Intervention Prevention Study (LIPS)**



#### **Context**

- **Percutaneous coronary intervention (PCI) produces excellent short-term improvements in ischemic symptoms. But at 5 years, only 60% of patients - and at 10 years only 33% of patients - remain free of major adverse cardiac events (MACE\*)**

#### **Objective**

- **To determine if lowering cholesterol with 80 mg fluvastatin per day, initiated within days of a successful first PCI - with or without stenting - reduces the incidence of MACE**

\* Cardiac death, nonfatal myocardial infarction, coronary artery bypass grafting (CABG), repeat PCI or PCI for a new lesion

Source: Serruys PWJC et al., JAMA 2002;287:3215-3222

#### **Context and objective**

This slide shows the background and objective of the Lescol Intervention Prevention Study (LIPS). Percutaneous coronary intervention (PCI), a group of procedures that are used to relieve ischemic symptoms due to coronary atherosclerotic narrowing, has a high primary success rate (90-95%). Longer-term prognosis after PCI, however, is relatively poor. Approximately 3 of 5 patients at 5 years and only 1 of 3 patients at 10 years remain free of major adverse cardiac events (MACE). Although several studies have shown that statins can prevent adverse coronary events, few data exist from randomised, prospective studies designed specifically to investigate the effect of these drugs on MACE after PCI. The LIPS findings should thereby help to optimise secondary pharmacotherapy and thereby prolong MACE-free time after first successful PCI.

Slide 2:

## Eligibility



### *Design and Setting*



#### **Conducted at 77 referral centers in Europe, Canada and Brazil**

- **1677 subjects randomized to receive either 80 mg fluvastatin per day or placebo in double-blind fashion following successful first percutaneous coronary intervention**
- **Follow-up for 3 to 4 years**

Source: Serruys PWJC et al., Intern J Cardiovasc Interv 2001;4:165-172

#### **Design and setting**

This slide shows the design and setting of LIPS.

Slide 3:

## Eligibility



### Eligibility



- **Men and women, aged 18 to 80 years**
- **First percutaneous coronary intervention successful: survival, lesions <50% on visual assessment, no evidence of myocardial necrosis, no need for coronary bypass grafting**
- **No lipid-lowering therapy in the 6 weeks before randomization**
- **Total cholesterol levels  $\geq 3.5$  and  $<7.0$  mmol/L ( $\geq 135$  and  $<270$  mg/dl) [ $< 6.0$  mmol/L ( $<232$  mg/dL) in persons with history of diabetes or myocardial infarction]**
- **Triglycerides  $< 400$  mg/dL**



Source: Serruys PWJC et al., Intern J Cardiovasc Interv 2001;4:165-172

#### Eligibility

This slide shows eligibility criteria for recruitment of the LIPS-population. Between April 1996 and October 1998, a total of 1677 patients with stable or unstable angina or silent ischemia were recruited and were randomly assigned to receive either fluvastatin (80mg/d) or placebo.

Slide 4:

## Baseline demographics



### Baseline Demographics

	Fluvastatin	Placebo
<b>Male Sex (n)</b>	<b>711</b>	<b>695</b>
<b>Age (y)</b>	<b>60.0</b>	<b>60.0</b>
<b>Ejection fraction (%)</b>	<b>62.2</b>	<b>61.8</b>
<b>Systolic blood pressure (mmHg)</b>	<b>128.1</b>	<b>128.4</b>
<b>Diastolic blood pressure (mmHg)</b>	<b>75.1</b>	<b>75.6</b>
<b>BMI (kg/m<sup>2</sup>)</b>	<b>26.7</b>	<b>26.4</b>
<b>Indication for PCI (%)</b>		
<b>Unstable angina</b>	<b>417</b>	<b>407</b>
<b>Stable angina</b>	<b>346</b>	<b>325</b>
<b>Silent ischemia</b>	<b>72</b>	<b>91</b>
<b>Multivessel disease</b>	<b>322</b>	<b>292</b>
<b>Stent implanted (n)/total lesions</b>	<b>639/1141</b>	<b>598/1083</b>



Source: Serruys PWJC et al., JAMA 2002;287:3215-3222

### Baseline demographics

This slide shows selected baseline characteristics of the LIPS population. The fluvastatin and placebo groups are well balanced with regard to baseline demographics.

Slide 5:

## Baseline risk factors and lipid levels



	Fluvastatin	Placebo
<b>Risk factors (No.)</b>		
Previous MI	371	373
Diabetes mellitus*	120	82
History of hypertension	330	317
History of stroke	17	27
Peripheral vascular disease	50	57
Current smoking	211	235
Family history of CHD	239	251
<b>Lipids (mg/dl)</b>		
Total cholesterol	200	199
LDL-cholesterol	131	132
HDL-cholesterol	38	37
Triglycerides	160	160

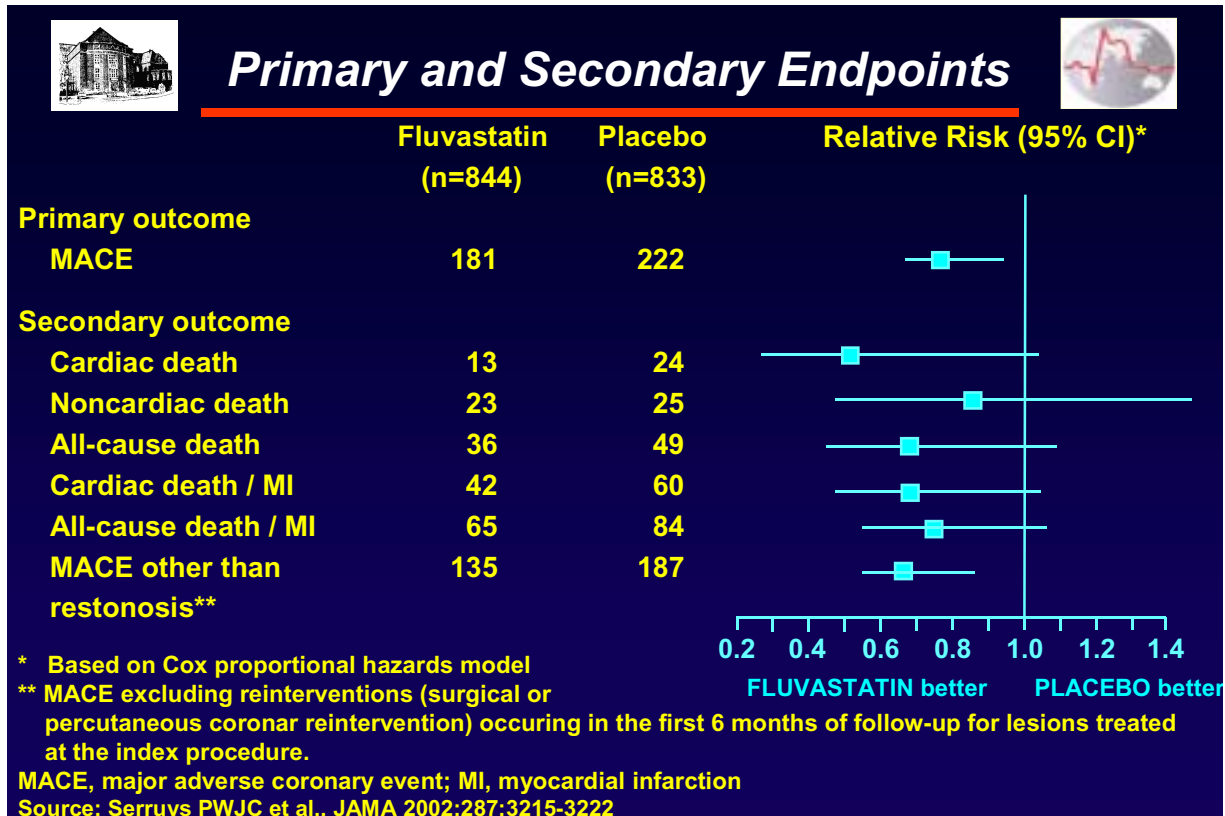
\* significant between-group difference at baseline (odds ratio 4.4%; 95% CI 1.3-7.5)  
Source: Serruys PWJC et al., JAMA 2002;287:3215-3222

### Baseline risk factors and lipid levels

This slide shows baseline risk factors and lipid levels. The treatment groups are also well balanced in baseline risk factors and lipid levels, except for a significant between-group difference in the incidence of diabetes mellitus (1.3-7.5, 95% CI).

Slide 6:

## Primary and secondary endpoints

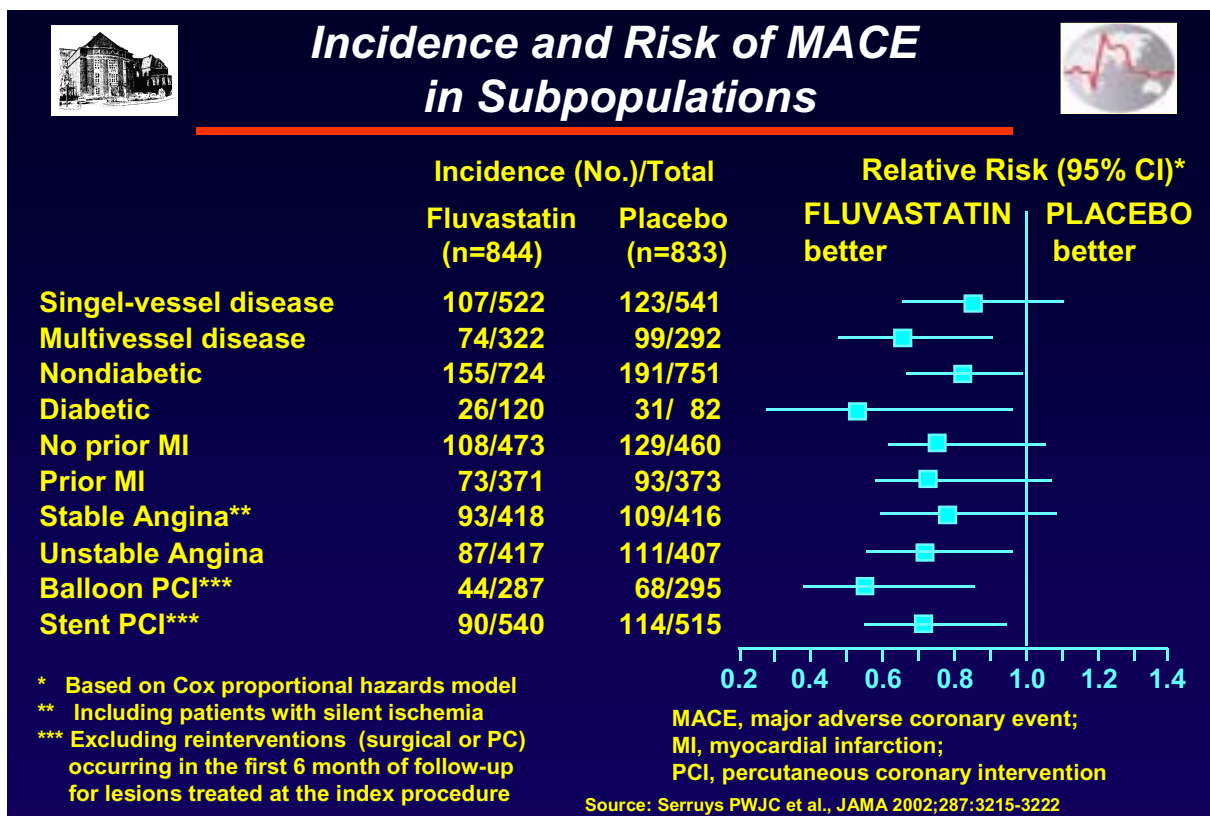


### Primary and secondary endpoints

This slide shows the incidence and risk reduction of primary and secondary endpoints compared to placebo. Fluvastatin compared to placebo significantly reduced the risk of the primary outcome (major adverse cardiac events, MACE) by 22 %. There was also a trend favouring fluvastatin group with regard to prevention for reduction of the secondary endpoints. Median time between PCI-treatment and first dose study medication was 2.0 days.

Slide 7:

**Incidence and risk of MACE in subpopulations**



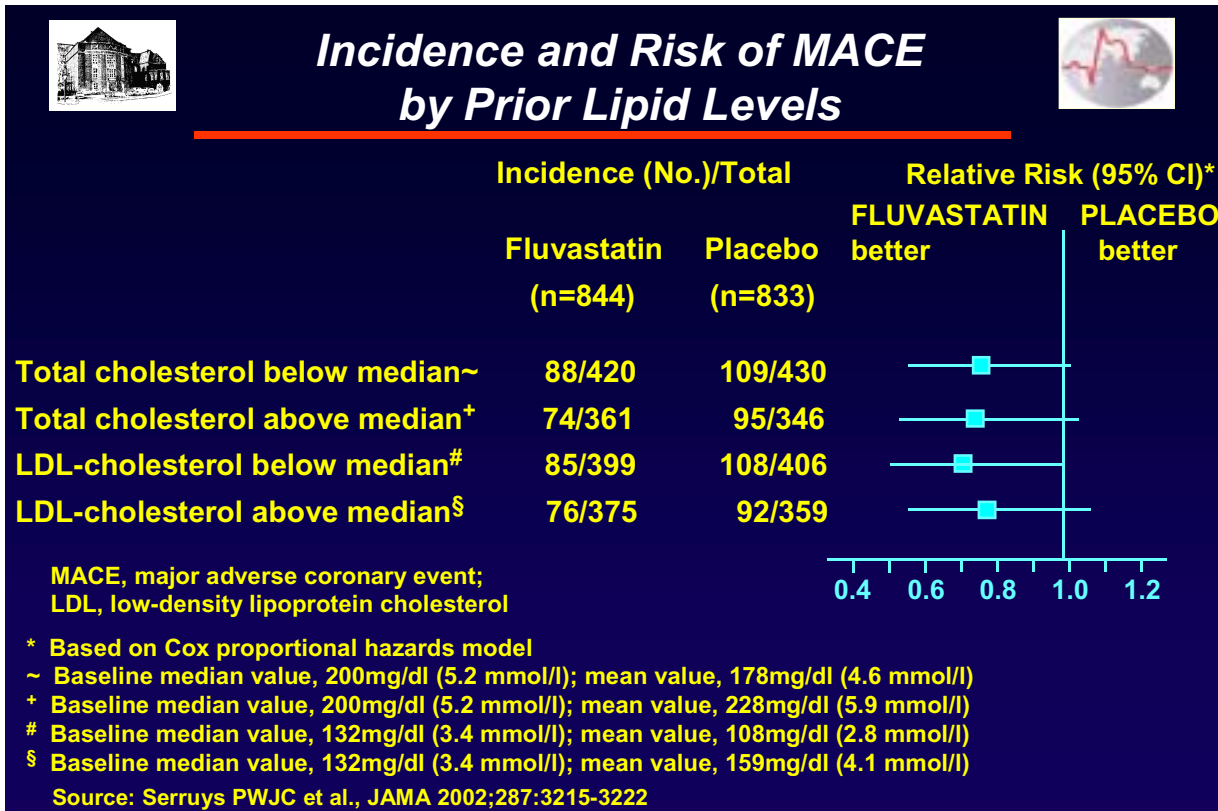
**Incidence and risk of MACE in subpopulations**

This slide shows the incidence and risk reduction of major adverse cardiac events (MACE) in subpopulations of LIPS. Fluvastatin-treatment significantly reduced the risk of MACE in the subgroups of patients with multivessel disease and diabetes as compared to placebo-treatment.

Subgroup analysis by type of PCI-treatment showed risk reductions in MACE achieved with fluvastatin-treatment similar to that observed in the overall study population.

Slide 8:

**Incidence and risk of MACE by prior lipid levels**

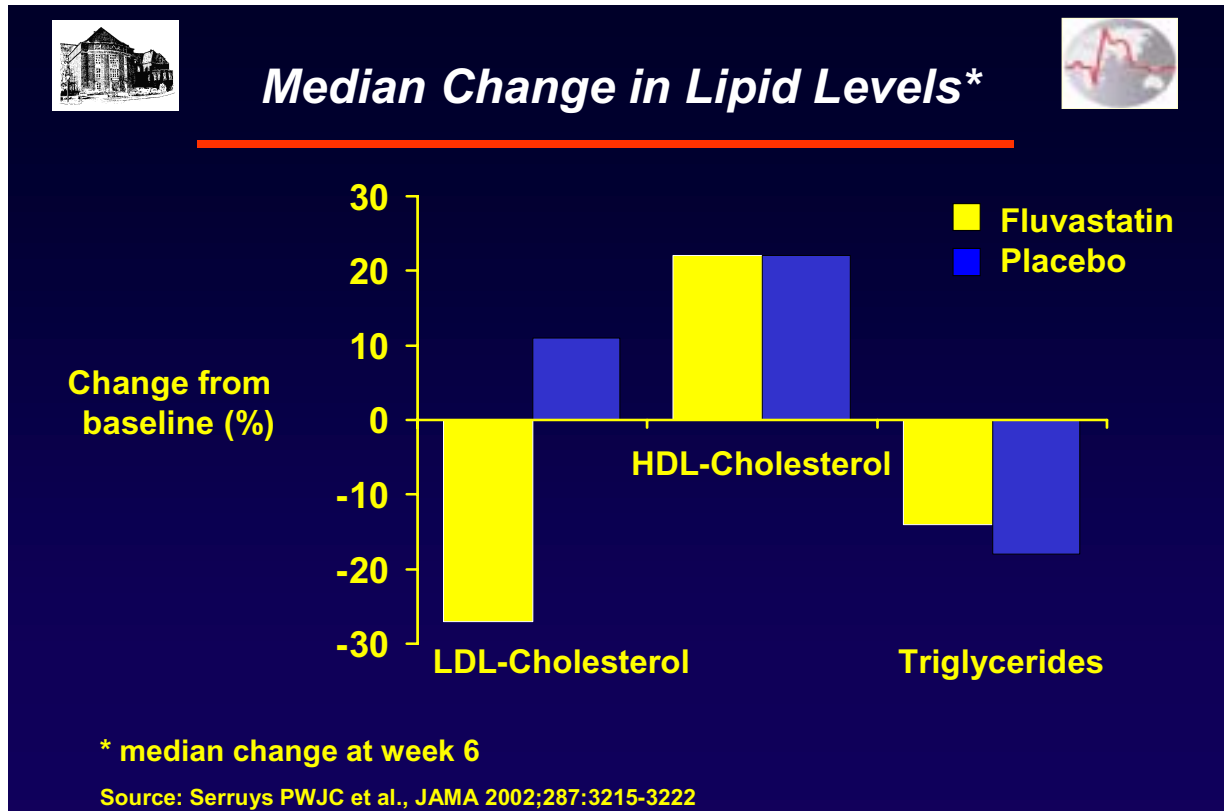


**Incidence and risk of MACE by prior lipid levels**

This slide shows the incidence and risk reduction of major adverse cardiac events (MACE) compared to placebo by baseline lipid levels. Reduction of relative risk of MACE was independent of total baseline total cholesterol levels.

Slide 9:

## Median change in lipid levels




### Median change in lipid levels


This slide shows the median change in lipid levels observed at week 6.

Slide 10:

## Safety



### Safety



	Fluvastatin (%)	Placebo (%)
<b>CPK (<math>\geq 10 \times</math> ULN)</b>	<b>0.0</b>	<b>0.4</b>
<b>AST/ALT (<math>\geq 3 \times</math> ULN repeated)</b>	<b>1.2</b>	<b>0.4</b>
<b>Cancer</b>	<b>1.7</b>	<b>2.2</b>

**No rhabdomyolysis in patients treated with fluvastatin.**

CPK, creatine phosphokinase; ULN, upper limit of normal;  
AST, aspartate aminotransferase; ALT, alanine aminotransferase;

Source: Serruys PWJC et al., JAMA 2002;287:3215-3222

### Safety

This slide illustrates the safety of fluvastatin treatment. No cases of creatine kinase elevations to more than 10-times the upper limit of normal and no severe muscular toxic effects were observed with fluvastatin at a dosage of 80 mg/d, and other adverse effects were reported with similar frequency in the fluvastatin and placebo groups.

Slide 11:

## Conclusions



### Conclusions of LIPS



- **First prospective trial to show significant (22%) reduction in risk of major adverse coronary events by fluvastatin (80mg/d for 4 y), initiated early following successful first percutaneous coronary intervention with or without stent**
- **Supports use of early fluvastatin therapy in patients after percutaneous coronary intervention, regardless of baseline lipids**
- **Risk of major adverse coronary event particularly reduced in patients with diabetes mellitus or multivessel disease**
- **Fluvastatin well tolerated: no CPK >10 times upper limit of normal, no rhabdomyolysis**

Source: Serruys PWJC et al., JAMA 2002;287:3215-3222

#### Conclusions

This slide summarises the major results of LIPS. Considering that 24% of patients in the placebo group were taking other lipid-lowering treatment compared with 10.7% in the fluvastatin group, and that 19.3 % of patients in the fluvastatin group were not compliant with the treatment regimen, the observed risk reduction may have been even greater.