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Cholesterol lowering intervention for cardiovascular prevention in elderly

A systematic review and meta-analysis of randomized clinical trials

2017 - 7 - 1

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This report should be referenced as follows:
TrialResults-center.org; Results of all major randomized clinical trials about Cholesterol lowering intervention for cardiovascular prevention in elderly.

Contents

0.1 Synthesis of the meta-analysis results

We found 11 trials concerning statins.
Results obtained by the meta-analysis are reported in the following tables, with the endpoints categorized according their results. Three classes are considered: endpoints for wich a benefit effect was detected, endpoints revealing a harmful effect and the other for wich no statistically significant difference was obtained (no evidence).
Reports of 11 trials (including 23,540 patients) were identified .
Among these comparisons, two trials are about fluvastatin,one about lovastatin,5 about pravastatin,one about rosuvastatin and two about simvastatin.
No trial was excluded on grounds of potentially flawed methodology or incomplete presentation of results. No ongoing trial was found.

Fluvastatin

Results obtained with fluvastatin for all the endpoints with data in at least one trial are summarized table 1.

Table 1: *Results summary - Fluvastatin*

Benefit	Harmful	No evidence
	Fluvastatin versus placebo	

* $p < 0.05$; † $p < 0.01$; ¶ $p < 0.001$ RR: relative risk

H: heterogeneity with fixed effect model detected (heterogeneity test $p < 0.05$)

Lovastatin

Results obtained with lovastatin for all the endpoints with data in at least one trial are summarized table 2.

Table 2: *Results summary - Lovastatin*

Benefit	Harmful	No evidence
	Lovastatin versus placebo	

* $p < 0.05$; † $p < 0.01$; ¶ $p < 0.001$ RR: relative risk

H: heterogeneity with fixed effect model detected (heterogeneity test $p < 0.05$)

Pravastatin

Results obtained with pravastatin for all the endpoints with data in at least one trial are summarized table 3.

Table 3: *Results summary - Pravastatin*

Benefit	Harmful	No evidence
	Pravastatin versus placebo	
↓ cardiovascular events RR=0.87* [0.77;0.98] k=1 ↓ coronary death and non fatal MI RR=0.83* [0.71;0.96] k=1 ↓ coronary event RR=0.83* [0.71;0.96] k=1 ↓ MACE RR=0.87* [0.78;0.98] k=1		→ cardiovascular death RR=0.87^{NS} [0.69;1.08] k=1 → stroke (fatal and non fatal) RR=1.04^{NS} [0.82;1.31] k=1 → coronary death RR=0.78^{NS} [0.60;1.01] k=1 → death from cancer RR=1.27^{NS} [0.97;1.67] k=1 → rhabdomyolysis RR=1.01^{NS} [0.02;50.77] k=1 → myopathy RR=1.13^{NS} [0.71;1.82] k=1 → non fatal MI RR=0.88^{NS} [0.74;1.05] k=1 → all cause death RR=0.98^{NS} [0.84;1.14] k=1

* $p < 0.05$; † $p < 0.01$; ¶ $p < 0.001$ RR: relative risk

H: heterogeneity with fixed effect model detected (heterogeneity test $p < 0.05$)

Rosuvastatin

Results obtained with rosuvastatin for all the endpoints with data in at least one trial are summarized table 4.

Table 4: *Results summary - Rosuvastatin*

Benefit	Harmful	No evidence
	Rosuvastatin versus placebo	

* $p < 0.05$; † $p < 0.01$; ¶ $p < 0.001$ RR: relative risk

H: heterogeneity with fixed effect model detected (heterogeneity test $p < 0.05$)

Simvastatin

Results obtained with simvastatin for all the endpoints with data in at least one trial are summarized table 5.

Table 5: *Results summary - Simvastatin*

Benefit	Harmful	No evidence
	Simvastatin versus placebo	

* $p < 0.05$; † $p < 0.01$; ¶ $p < 0.001$ RR: relative risk

H: heterogeneity with fixed effect model detected (heterogeneity test $p < 0.05$)

1 Introduction

1.1 Aim of the report

This report review all the randomized clinical trials of cholesterol lowering intervention for the treatment of cardiovascular prevention in elderly.

1.2 Search strategy

The search aimed to identify all randomized clinical trials relating to the clinical effectiveness of cholesterol lowering intervention for the treatment of cardiovascular prevention in elderly.

1.2.1 Sources searched

The following electronic databases were searched for relevant published literature for the period up to 2017 - 7 - 1:

- MEDLINE,
- EMBASE,
- Cochrane Database of Systematic Reviews (CDSR),
- Cochrane Central Register of Controlled Trials (CCTR),
- Health Technology Assessment (HTA) database,
- ISI Web of Science Proceedings (Index to Scientific and Technical Proceedings),
- ISI Web of Science Science Citation Index Expanded,

Each database was searched as far back as possible, with no language restrictions.
Search strategies of relevant clinical keywords were developed through reference to published strategies, and by iterative searching, whereby keywords identified in references retrieved by initial scoping searches were used to extend the search strategy and so increase the sensitivity of retrieval.
In addition, the reference lists of relevant articles were handsearched.
Attempts to identify further studies were made by consulting health technology assessment and guideline producing agencies, and research and trials registers via the Internet.
Titles and, when available, abstracts of all studies identified in the searches were assessed by a single researcher for relevance to the review. In cases of doubt, the full article was obtained.

1.2.2 Search restrictions

No language, study/publication or date restrictions were applied to the main searches.

1.3 Inclusion criteria

Participants only those studies were included in which the participants had been diagnosed as having established cardiovascular prevention.

Interventions studies in which cholesterol lowering intervention was used.

Studies using other interventions in addition to cholesterol lowering intervention therapy were included only if the treatment received by the intervention and control groups was identical in all respects other than the use of cholesterol lowering intervention.

Methodology randomised controlled trials (RCTs). Trials were accepted as RCTs if the allocation of subjects to treatment groups was described by the authors as either randomised or double-blind.

1.4 Exclusion criteria

Studies considered methodologically unsound. The list of excluded studies with reason of their exclusion are given in a separate section for each treatment categories considered.

1.5 Meta-analysis strategy

Studies that met the reviews entry criteria were eligible for inclusion in the meta-analyses provided that they reported outcomes in terms of the number of subjects suffering clinical outcomes, as only this would allow calculation of the relative risk of subjects in the intervention group developing each outcome, compared with subjects in the control group.

Studies that only presented results in the form of relative risks, relative hazards or odds ratios, without the underlying numbers were also include in the meta-analyses.

Binary outcomes were analysed using the fixed-effect model. For continuous outcomes, weighted mean differences (WMDs) were analysed, using a fixed-effect model.

Heterogeneity was tested by the chi-2 test and the I2 statistic was obtained to describe the proportion of the variability.

Where quantitative heterogeneity was indicated, analysis using a random-effects model was conducted for comparison with results of fixed effect-based analysis. Results of the meta-analysis should be considered as being based on fixed-effect model unless stated otherwise.

Meta-analyses were conducted for data on Cardiovascular death, Coronary death, stroke (fatal and non fatal), MACE, Coronary event, Non fatal MI, Coronary death and non fatal MI, cardiovascular events, Myopathy, Death from cancer, Rhabdomyolysis, All cause death, .

1.6 Structure of the report

Each of the eligible studies is summarised in part **??**. A summary of the studies together with an evaluation of their quality is given in part **??** to **??**, listed by therapeutic class. The therapeutic classes included statins,

In these sections, studies in which an active intervention was compared with placebo or no treatment are discussed first, by intervention, followed by a discussion of those studies in which two or more active interventions were compared.

2 Overview of statins

2.1 Included trials

A total of 11 randomized comparisons which enrolled 23540 patients were identified. In all, 2 randomized comparisons concerned fluvastatin , one lovastatin , 5 pravastatin , one rosuvastatin and two simvastatin.
The detailed descriptions of trials and meta-analysis results is given in section 3 (page 23) for fluvastatin, in section 4 (page 30) for lovastatin, in section 5 (page 35) for pravastatin, in section 6 (page 51) for rosuvastatin and in section 7 (page 56) for simvastatin.

The average study size was 2615 patients (range 94 to 10697). The first study was published in 1994, and the last study was published in 2009.
All trials were double blind in design. All included studies were reported in English language. We did not found any unpublished trial.
The table 2.1 (page 13) summmarizes the main characteristics of all the included trials. More detailed description is given in the following section.

2.2 Summary of meta-analysis results

The meta-analysis of the available trials about statins provide the results listed in tables 2.2 to 2.6 (page 15) and in the following graphs.

2.2.1 Fluvastatin

Data were insufficient to compare **fluvastatin** to **placebo**. There were 2 eligible trials but none provided sufficient information about the endpoints considered by this meta-analysis.

2.2.2 Lovastatin

Data were insufficient to compare **lovastatin** to **placebo**. There was an eligible trial but it did not provided sufficient information about the endpoints considered by this meta-analysis.

2.2.3 Pravastatin

Pravastatin was superior to **placebo** in terms of cardiovascular events (RR=0.87, 95% CI 0.77 to 0.98, p=0.0243, 1 trial), coronary death and non fatal MI (RR=0.83, 95% CI 0.71 to 0.96, p=0.0105, 1 trial), coronary event (RR=0.83, 95% CI 0.71 to 0.96, p=0.0105, 1 trial)and MACE (RR=0.87, 95% CI 0.78 to 0.98, p=0.0221, 1 trial). However, no significant difference was found on cardiovascular death (RR=0.87, 95% CI 0.69 to 1.08, p=0.2101, 1 trial), stroke (fatal and non fatal) (RR=1.04, 95% CI 0.82 to 1.31, p=0.7533, 1 trial), coronary death (RR=0.78, 95% CI 0.60 to 1.01, p=0.0602, 1 trial)and non fatal MI (RR=0.88, 95% CI 0.74 to 1.05, p=0.1489, 1 trial).

2.2.4 Rosuvastatin

Data were insufficient to compare **rosuvastatin** to **placebo**. There was an eligible trial but it did not provided sufficient information about the endpoints considered by this meta-analysis.

2.2.5 Simvastatin

Data were insufficient to compare **simvastatin** to **placebo**. There were 2 eligible trials but none provided sufficient information about the endpoints considered by this meta-analysis.

Table 2.1: *Main study characteristics - statins*

Trial	Patients	Treatments	Trial design and method
Fluvastatin			
Fluvastatin versus placebo			
FLARE (subgroup), 1999 [1, 2] n = 179 vs. 187	CAD requiring PCI, subgroup of age 65-80 y	fluvastatin 80mg **versus**	double blind parallel groups
LIPS (subgroup), 2002 [3] n = 324 vs. 299	CAD requiring PCI, subgroup of age 65-80 y	fluvastatin 80mg **versus**	double blind parallel groups
Lovastatin			
Lovastatin versus placebo			
CRISP 20mg, 1994 [1, 2] n = NA vs. NA	elderly (mean 71y) with low-density lipoprotein cholesterol levels greater than 4.1 and less than 5.7 mmol/L	lovastatin 20mg daily **versus** placebo	double blind parallel groups Primary endpoint: changes in blood lipid levels
Pravastatin			
Pravastatin versus placebo			
CARE (subgroup), 1998 [1] n = 640 vs. 643	MI 320 months, subgroup of age 65-75 y	pravastatin 40mg **versus**	double blind parallel groups
LIPID (sub group), 2001 [2] n = 1741 vs. 1773	MI or unstable angina, subgroup of age 65-75 y	pravastatin 40mg **versus**	double blind parallel groups
PLAC I (sub group), 1995 [3] n = 42 vs. 52	angiographic CAD or recent MI, subgroup of age 65-75 y	pravastatin 40mg **versus**	double blind parallel groups
REGRESS (subgroup), 1995 [4] n = 75 vs. 63	angiographic CAD, subgroup of age 65-70 y	pravastatin 40mg **versus**	double blind parallel groups

continued...

Trial	Patients	Treatments	Trial design and method
PROSPER, 2002 [5] n = 2891 vs. 2913	men and women aged 70-82 years with a history of, or risk factors for, vascular disease	pravastatin 40mg daily **versus** placebo	double blind parallel groups Primary endpoint: death, MI , stroke multicenter, Ecosse, Irelande, Pays bas
Rosuvastatin			
Rosuvastatin versus placebo			
JUPITER (sub group), 2009 [1] n = 5695 vs. NA	healthy individuals aged >=70 years with normal LDL cholesterols but with CRP levels >=2.0 mg/dL	rosuvastatin 20mg daily **versus** placebo	double blind parallel groups Primary endpoint: cv event
Simvastatin			
Simvastatin versus placebo			
4S (subgroup), 1997 [1] n = 518 vs. 503	MI 6 months or stable angina, subgroup of age 65-70 y	simvastatin 20-40mg **versus**	double blind parallel groups
HPS (subgroup), 2002 [2] n = 5366 vs. 5331	vascular disease or diabetes, subgroup of age 65-80 y	simvastatin 40mg **versus**	double blind parallel groups

Table 2.2: *Summary of all results for fluvastatin*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
fluvastatin versus placebo						
No data were presented in the trial identified						

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Table 2.3: *Summary of all results for lovastatin*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
lovastatin versus placebo						
No data were presented in the trial identified						

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Table 2.4: *Summary of all results for pravastatin*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
pravastatin versus placebo						
cardiovascular events	RR=0.87	0.77;0.98	0.0243	1.0000 (0.00)	1	5804
cardiovascular death	RR=0.87	0.69;1.08	0.2101	1.0000 (0.00)	1	5804
stroke (fatal and non fatal)	RR=1.04	0.82;1.31	0.7533	1.0000 (0.00)	1	5804
coronary death and non fatal MI	RR=0.83	0.71;0.96	0.0105	1.0000 (0.00)	1	5804
coronary event	RR=0.83	0.71;0.96	0.0105	1.0000 (0.00)	1	5804
coronary death	RR=0.78	0.60;1.01	0.0602	1.0000 (0.00)	1	5804
MACE	RR=0.87	0.78;0.98	0.0221	1.0000 (0.00)	1	5804
death from cancer	RR=1.27	0.97;1.67	0.0795	1.0000 (0.00)	1	5804
rhabdomyolysis	RR=1.01	0.02;50.77	0.9970	1.0000 (0.00)	1	5804
myopathy	RR=1.13	0.71;1.82	0.6037	1.0000 (0.00)	1	5804
non fatal MI	RR=0.88	0.74;1.05	0.1489	1.0000 (0.00)	1	5804
all cause death	RR=0.98	0.84;1.14	0.8061	1.0000 (0.00)	1	5804

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Table 2.5: *Summary of all results for rosuvastatin*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
rosuvastatin versus placebo						
No data were presented in the trial identified						

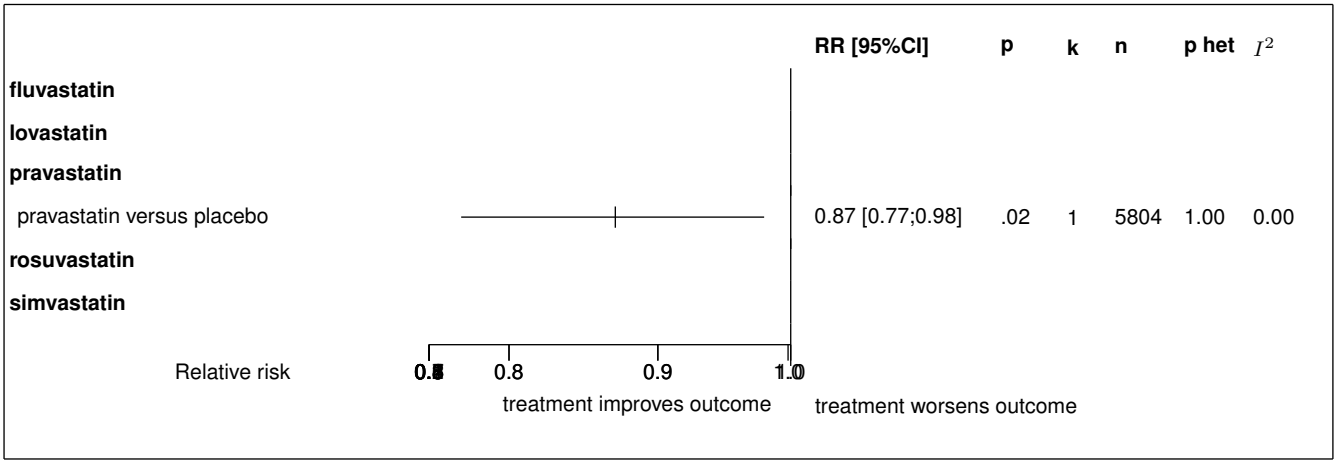
CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Table 2.6: *Summary of all results for simvastatin*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
simvastatin versus placebo						
No data were presented in the trial identified						

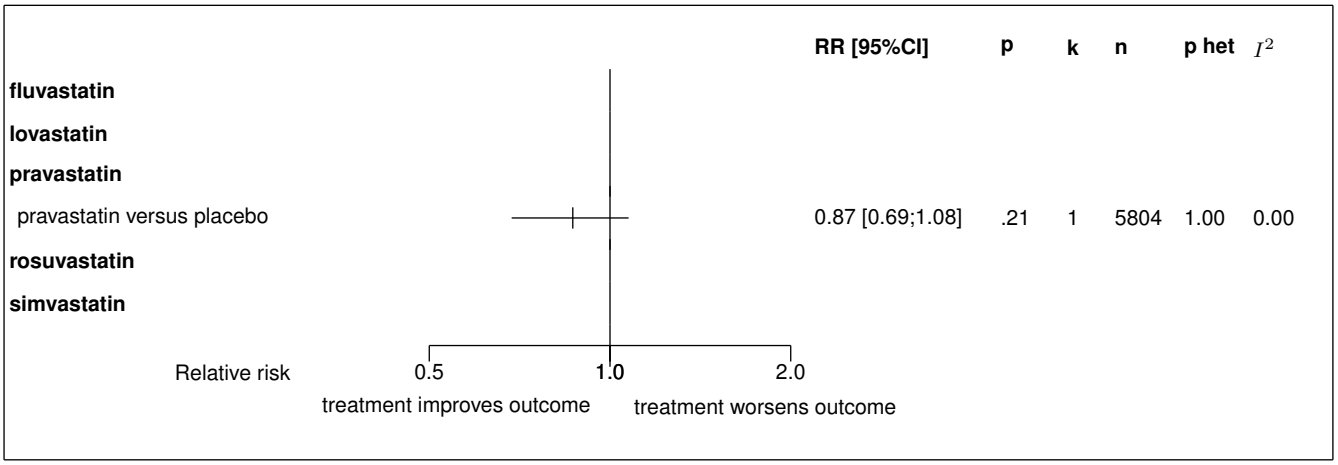
CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Figure 2.1: *Forest's plot for cardiovascular events*



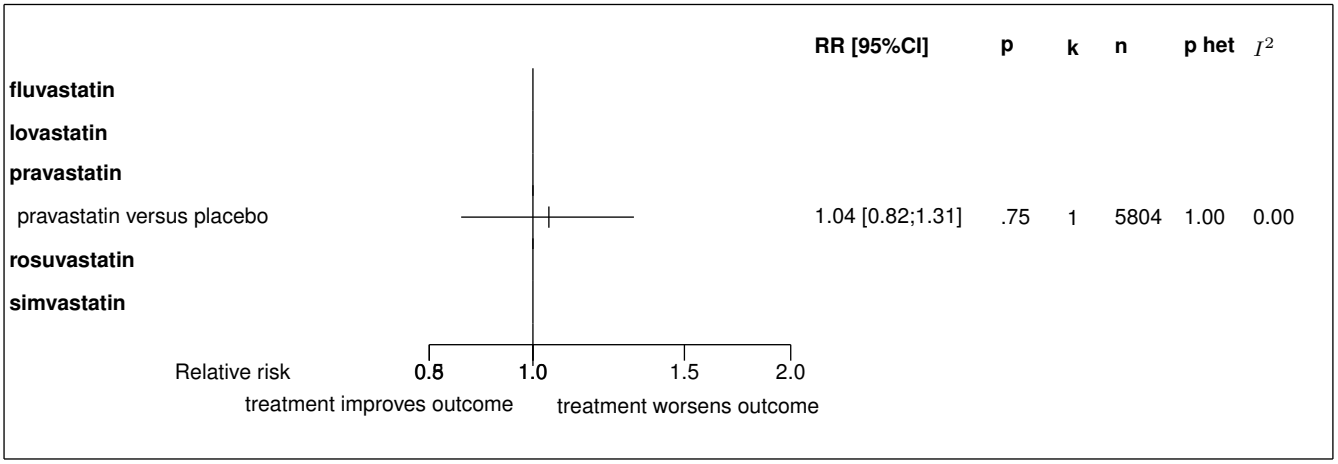
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ^{r}: random effect model used

Figure 2.2: *Forest's plot for cardiovascular death*



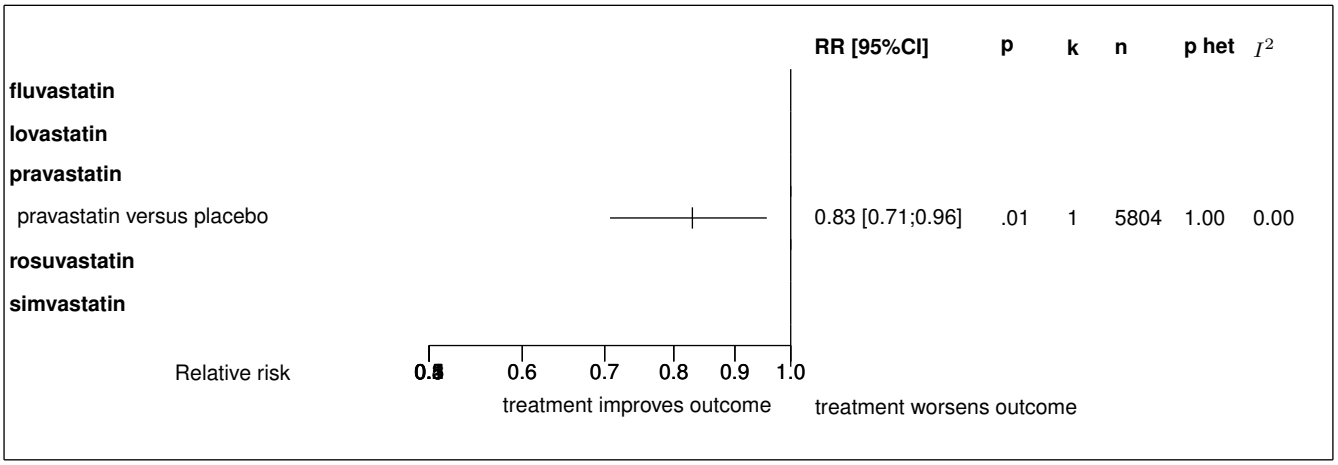
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ʳ: random effect model used

Figure 2.3: *Forest's plot for stroke (fatal and non fatal)*



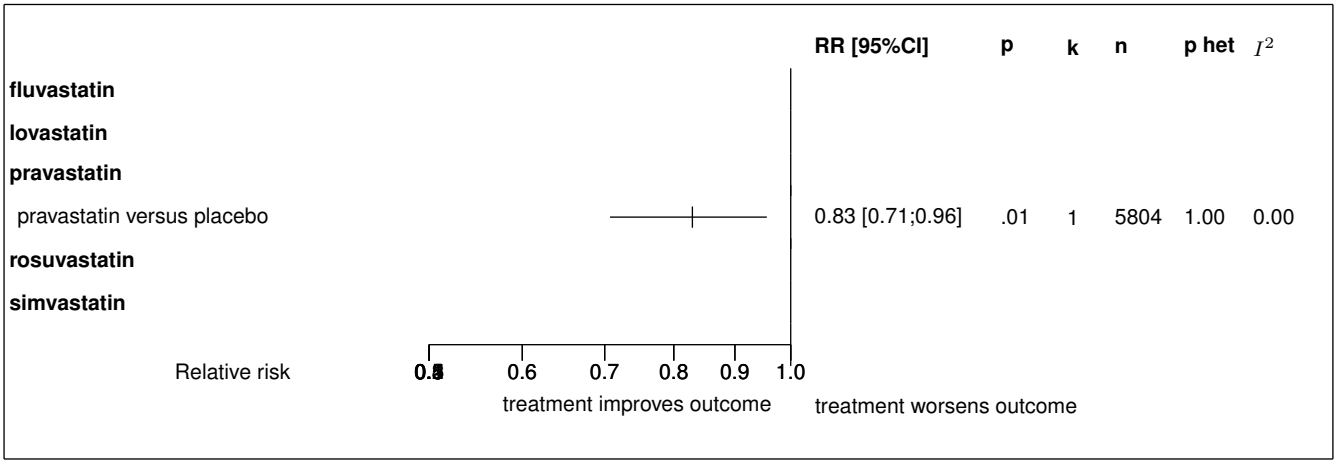
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ʳ: random effect model used

Figure 2.4: *Forest's plot for coronary death and non fatal MI*



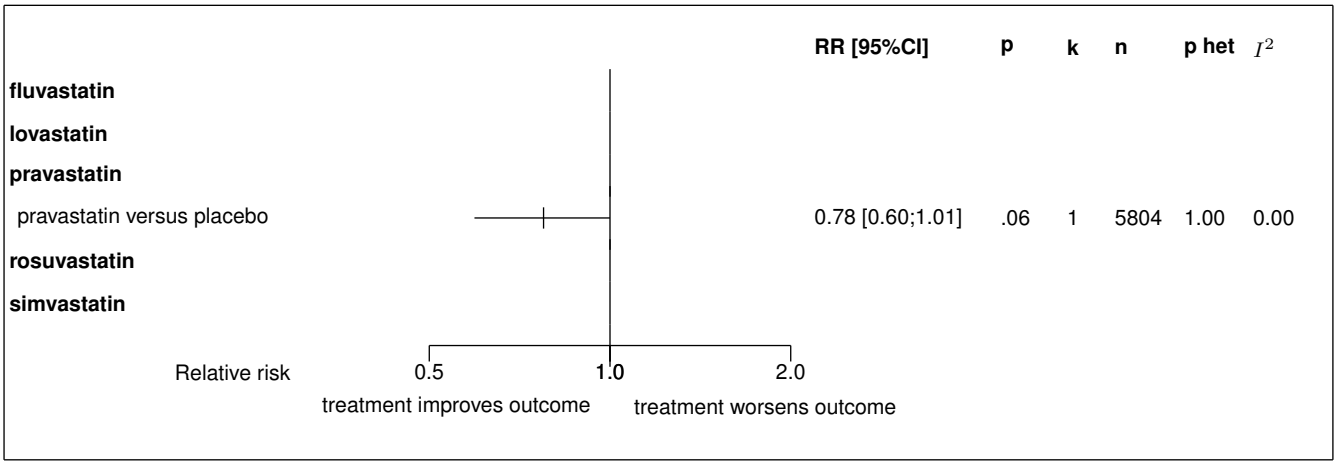
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ʳ: random effect model used

Figure 2.5: *Forest's plot for coronary event*



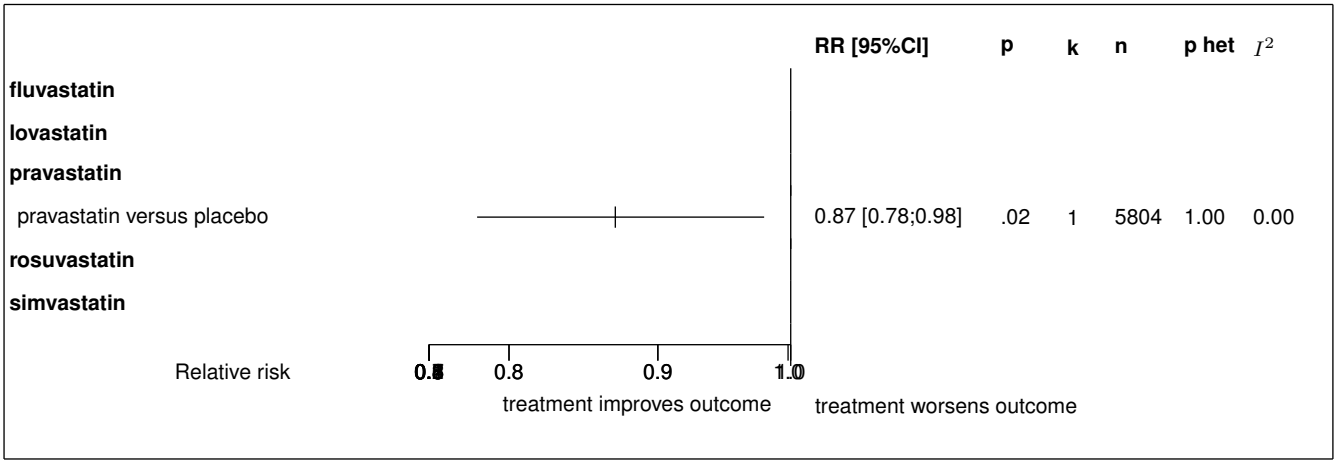
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ʳ: random effect model used

Figure 2.6: *Forest's plot for coronary death*



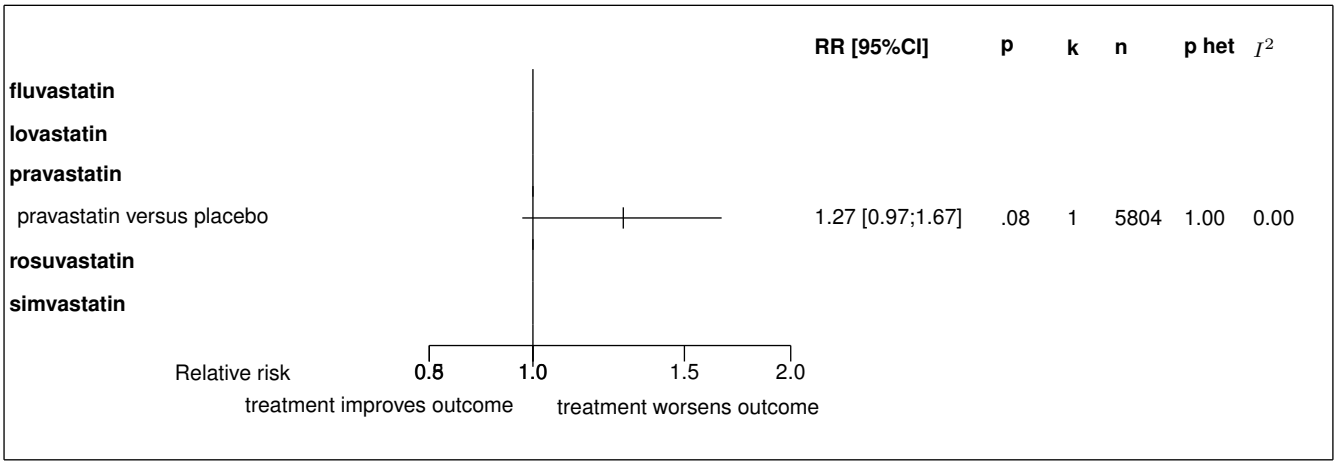
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ᶠ: random effect model used

Figure 2.7: *Forest's plot for MACE*



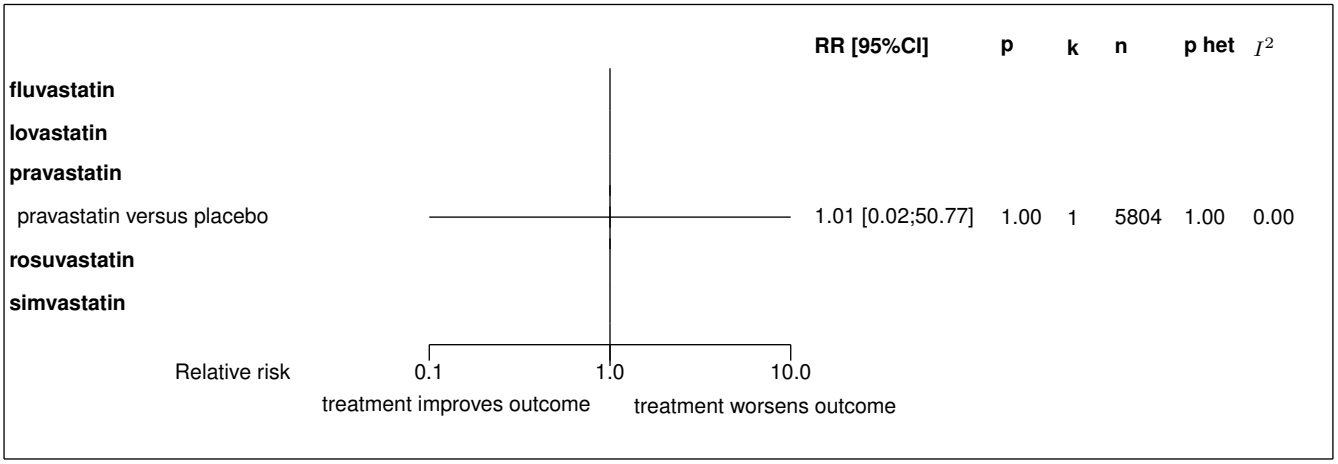
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ᶠ: random effect model used

Figure 2.8: *Forest's plot for death from cancer*



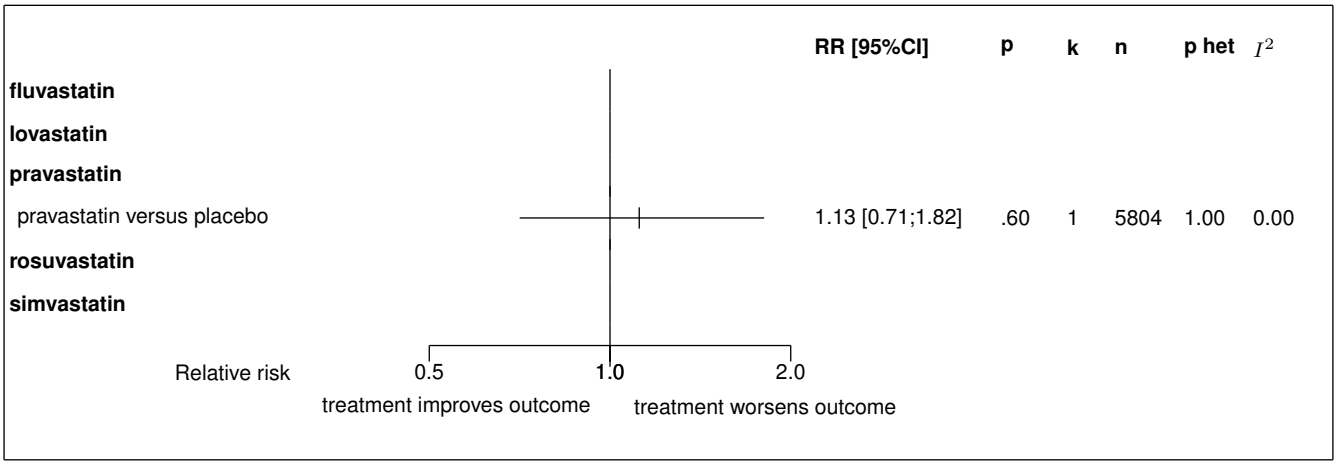
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ʳ: random effect model used

Figure 2.9: *Forest's plot for rhabdomyolysis*



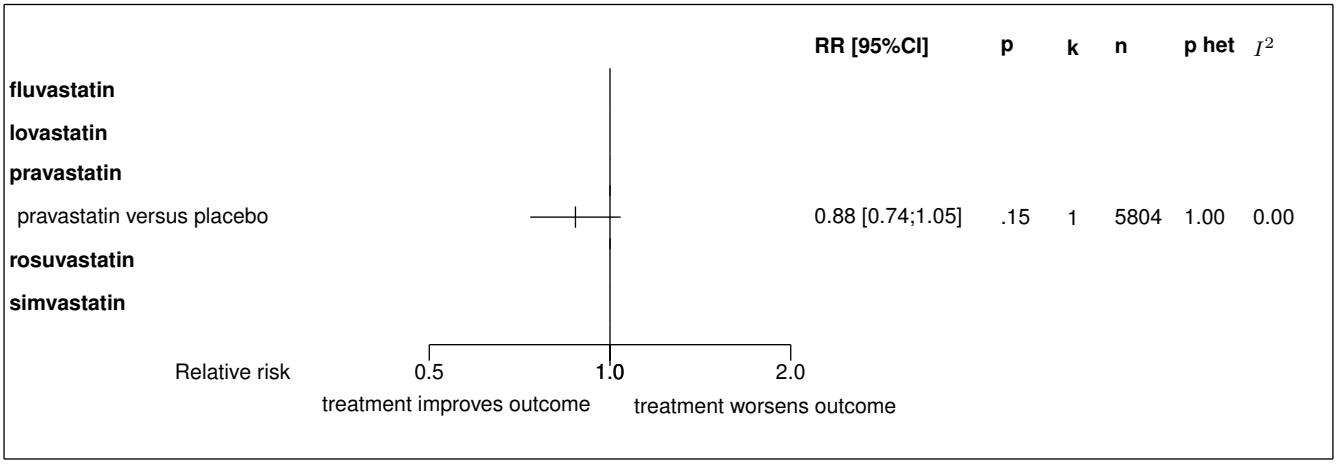
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ʳ: random effect model used

Figure 2.10: *Forest's plot for myopathy*



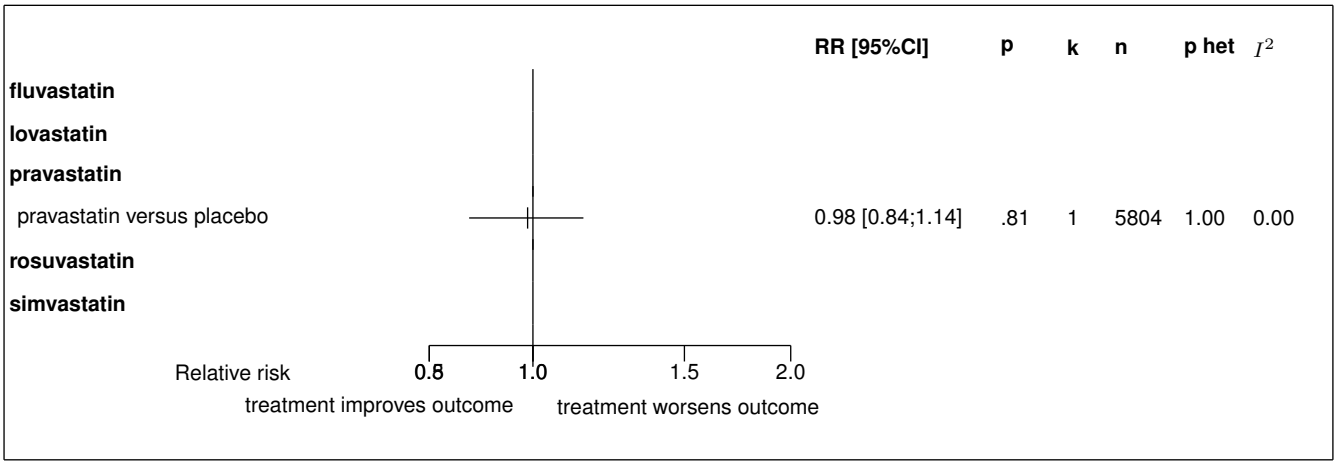
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ʳ: random effect model used

Figure 2.11: *Forest's plot for non fatal MI*



Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ʳ: random effect model used

Figure 2.12: *Forest's plot for all cause death*



Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity test; ˡ: random effect model used

3 Detailed results for fluvastatin

3.1 Available trials

A total of 2 RCTs which randomized 989 patients were identified: all compared fluvastatin with placebo.
The average study size was 494 patients (range 366 to 623). The first study was published in 1999, and the last study was published in 2002.
All trials were double blind in design. All included studies were reported in English language. We did not found any unpublished trial.
data was reported in trials;
Following tables 3.1 (page 23), 3.2 (page 23), 3.4 (page 25), and 3.3 (page 24) summarized the main characteristics of the trials including in this systematic review of randomized trials of fluvastatin.

Table 3.1: *Treatment description - statins - fluvastatin*

Trial	Studied treatment	Control treatment
Fluvastatin versus placebo		
FLARE (subgroup) (1999) [1, 2]	Fluvastatin 80mg	
LIPS (subgroup) (2002) [3]	Fluvastatin 80mg	

Table 3.2: *Descriptions of participants - statins - fluvastatin*

Trial	Patients
Fluvastatin versus placebo	
FLARE (subgroup) (1999) [1, 2]	CAD requiring PCI, subgroup of age 65-80 y
LIPS (subgroup) (2002) [3]	CAD requiring PCI, subgroup of age 65-80 y

Table 3.3: *Design and methodological quality of trials - statins - fluvastatin*

Trial	Design	Duration	Centre	Primary end-point
Fluvastatin versus placebo				
FLARE (subgroup), 1999 [1, 2] n=366	parallel groups double blind exploratory trial	0.8y		
LIPS (subgroup), 2002 [3] n=623	parallel groups double blind exploratory trial	3.9y		

Table 3.4: *Trial characteristics - statins - fluvastatin*

Trial
Fluvastatin versus placebo
FLARE (subgroup), 1999 [1, 2]
LIPS (subgroup), 2002 [3]

3.2 Meta-analysis results

The results are detailed in table 3.5 (page 26). This table is followed by the Forest's plot corresponding to each endpoint.

Fluvastatin versus placebo

No data were presented in the 2 trials identified

Table 3.5: *Results details - statins - fluvastatin*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
fluvastatin versus placebo						
No data were presented in the trial identified						

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2: inconsistance degree

References

[1] Serruys PW, Foley DP, Jackson G, Bonnier H, Macaya C, Vrolix M, Branzi A, Shepherd J, Suryapranata H, de Feyter PJ, Melkert R, van Es GA, Pfister PJ. A randomized placebo-controlled trial of fluvastatin for prevention of restenosis after successful coronary balloon angioplasty; final results of the fluvastatin angiographic restenosis (FLARE) trial. Eur Heart J 1999;20:58-69. [PMID=10075142]

[2] Serruys PW, Foley DP, Jackson G, Bonnier H, Macaya C, Vrolix M, Branzi A, Shepherd J, Suryapranata H, de Feyter PJ, Melkert R, van Es GA, Pfister PJ. A randomized placebo-controlled trial of fluvastatin for prevention of restenosis after successful coronary balloon angioplasty; final results of the fluvastatin angiographic restenosis (FLARE) trial. Eur Heart J 1999;20:58-69. [PMID=10075142]

[3] Serruys PW, de Feyter P, Macaya C, Kokott N, Puel J, Vrolix M, Branzi A, Bertolami MC, Jackson G, Strauss B, Meier B. Fluvastatin for prevention of cardiac events following successful first percutaneous coronary intervention: a randomized controlled trial. JAMA 2002;287:3215-22. [PMID=12076217]

3.3 Individual trial summaries

Table 3.6: *FLARE (subgroup), 1999 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=366 (179 vs. 187) **Follow-up duration:** 0.8y **Study design:** Randomized controlled trial parallel groups Double blind Exploratory trial	CAD requiring PCI, subgroup of age 65-80 y	**Studied treatment:** Fluvastatin 80mg **Control treatment:**	

References

Serruys PW, Foley DP, Jackson G, Bonnier H, Macaya C, Vrolix M, Branzi A, Shepherd J, Suryapranata H, de Feyter PJ, Melkert R, van Es GA, Pfister PJ. A randomized placebo-controlled trial of fluvastatin for prevention of restenosis after successful coronary balloon angioplasty; final results of the fluvastatin angiographic restenosis (FLARE) trial. Eur Heart J 1999;20:58-69 [PMID=10075142]
Serruys PW, Foley DP, Jackson G, Bonnier H, Macaya C, Vrolix M, Branzi A, Shepherd J, Suryapranata H, de Feyter PJ, Melkert R, van Es GA, Pfister PJ. A randomized placebo-controlled trial of fluvastatin for prevention of restenosis after successful coronary balloon angioplasty; final results of the fluvastatin angiographic restenosis (FLARE) trial. Eur Heart J 1999;20:58-69 [PMID=10075142]

Table 3.7: *LIPS (subgroup), 2002 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=623 (324 vs. 299) **Follow-up duration:** 3.9y **Study design:** Randomized controlled trial parallel groups Double blind Exploratory trial	CAD requiring PCI, subgroup of age 65-80 y	**Studied treatment:** Fluvastatin 80mg **Control treatment:**	

Reference

Serruys PW, de Feyter P, Macaya C, Kokott N, Puel J, Vrolix M, Branzi A, Bertolami MC, Jackson G, Strauss B, Meier B. Fluvastatin for prevention of cardiac events following successful first percutaneous coronary intervention: a randomized controlled trial. JAMA 2002;287:3215-22 [PMID=12076217]

4 Detailed results for lovastatin

4.1 Available trials

Only one trial which randomized 0 patients was identified: it compared lovastatin with placebo.
This trial included NaN patients and was published in 1994.
This trial was double blind in design.
It was reported in English language.
data was reported in trials;
Following tables 4.1 (page 30), 4.2 (page 30), 4.4 (page 31), and 4.3 (page 30) summarized the main characteristics of the trial including in this systematic review of randomized trials of lovastatin.

Table 4.1: *Treatment description - statins - lovastatin*

Trial	Studied treatment	Control treatment
Lovastatin versus placebo		
CRISP 20mg (1994) [1, 2] [a]	lovastatin 20mg daily	placebo

a) 3 arms placebo, lovastatin 20mg and 40mg

Table 4.2: *Descriptions of participants - statins - lovastatin*

Trial	Patients
Lovastatin versus placebo	
CRISP 20mg (1994) [1, 2]	Elderly (mean 71y) with low-density lipoprotein cholesterol levels greater than 4.1 and less than 5.7 mmol/L

Table 4.3: *Design and methodological quality of trials - statins - lovastatin*

Trial	Design	Duration	Centre	Primary end-point
Lovastatin versus placebo				
CRISP 20mg, 1994 [1, 2] n=NaN	Parallel groups double blind exploratory trial	1 years		changes in blood lipid levels

Table 4.4: *Trial characteristics - statins - lovastatin*

Trial	LDL change, end of study (mg/DL)	cholesterol change (mmol/L)	CRP change	LDL change, at 1 y (mg/dL)
Lovastatin versus placebo				
CRISP 20mg, 1994 [1, 2]				

4.2 Meta-analysis results

The results are detailed in table 4.5 (page 32). This table is followed by the Forest's plot corresponding to each endpoint.

Lovastatin versus placebo

No data were presented in the 1 trial identified

Table 4.5: *Results details - statins - lovastatin*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
lovastatin versus placebo						
No data were presented in the trial identified						

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2: inconsistance degree

References

[1] LaRosa JC, Applegate W, Crouse JR 3rd, Hunninghake DB, Grimm R, Knopp R, Eckfeldt JH, Davis CE, Gordon DJ. Cholesterol lowering in the elderly. Results of the Cholesterol Reduction in Seniors Program (CRISP) pilot study. Arch Intern Med 1994;154:529-39. [PMID=8122946]

[2] Stoy DB, Curtis RC, Dameworth KS, Dowdy AA, Hegland J, Levin JA, Sousoulas BG. The successful recruitment of elderly black subjects in a clinical trial: the CRISP experience. Cholesterol Reduction in Seniors Program. J Natl Med Assoc 1995;87:280-7. [PMID=7752281]

4.3 Individual trial summaries

Table 4.6: *CRISP 20mg, 1994 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=NA (NA vs. NA) **Follow-up duration:** 1 years **Study design:** Randomized controlled trial Parallel groups Double blind Exploratory trial	Elderly (mean 71y) with low-density lipoprotein cholesterol levels greater than 4.1 and less than 5.7 mmol/L	**Studied treatment:** lovastatin 20mg daily **Control treatment:** placebo **note:** 3 arms placebo, lovastatin 20mg and 40mg	

References

LaRosa JC, Applegate W, Crouse JR 3rd, Hunninghake DB, Grimm R, Knopp R, Eckfeldt JH, Davis CE, Gordon DJ. Cholesterol lowering in the elderly. Results of the Cholesterol Reduction in Seniors Program (CRISP) pilot study. Arch Intern Med 1994;154:529-39 [PMID=8122946]
Stoy DB, Curtis RC, Dameworth KS, Dowdy AA, Hegland J, Levin JA, Sousoulas BG. The successful recruitment of elderly black subjects in a clinical trial: the CRISP experience. Cholesterol Reduction in Seniors Program. J Natl Med Assoc 1995;87:280-7 [PMID=7752281]

5 Detailed results for pravastatin

5.1 Available trials

A total of 5 RCTs which randomized 10833 patients were identified: all compared pravastatin with placebo.
The average study size was 2166 patients (range 94 to 5804). The first study was published in 1995, and the last study was published in 2002.
All trials were double blind in design. All included studies were reported in English language. We did not found any unpublished trial.
Cardiovascular death data was reported in 1 trials; 1 trials reported data on coronary death; 1 trials reported data on stroke (fatal and non fatal); 1 trials reported data on MACE; 1 trials reported data on coronary event; 1 trials reported data on non fatal MI; 1 trials reported data on coronary death and non fatal MI; 1 trials reported data on cardiovascular events; 1 trials reported data on myopathy; 1 trials reported data on death from cancer; 1 trials reported data on rhabdomyolysis; and 1 trials reported data on all cause death.
Following tables 5.1 (page 35), 5.2 (page 36), 5.4 (page 38), and 5.3 (page 36) summarized the main characteristics of the trials including in this systematic review of randomized trials of pravastatin.

Table 5.1: *Treatment description - statins - pravastatin*

Trial	Studied treatment	Control treatment
Pravastatin versus placebo		
CARE (subgroup) (1998) [1]	Pravastatin 40mg	
LIPID (sub group) (2001) [2]	Pravastatin 40mg	
PLAC I (sub group) (1995) [3]	Pravastatin 40mg	
REGRESS (subgroup) (1995) [4]	Pravastatin 40mg	
PROSPER (2002) [5]	pravastatin 40mg daily	placebo

Table 5.2: *Descriptions of participants - statins - pravastatin*

Trial	Patients	
Pravastatin versus placebo		
CARE (subgroup) (1998) [1]	MI 320 months, subgroup of age 65-75 y	
LIPID (sub group) (2001) [2]	MI or unstable angina, subgroup of age 65-75 y	
PLAC I (sub group) (1995) [3]	Angiographic CAD or recent MI, subgroup of age 65-75 y	
REGRESS (subgroup) (1995) [4]	Angiographic CAD, subgroup of age 65-70 y	
PROSPER (2002) [5]	Men and women aged 70-82 years with a history of, or risk factors for, vascular disease	
	Inclusion criteria: men and women aged 7082 years; either pre-existing vascular disease (coronary, cerebral, or peripheral) or raised risk of such disease because of smoking, hypertension, or diabetes; total cholesterol between 4090 mmol/L; triglyceride less than 60 mmol/L	**Exclusion criteria:** poor cognitive function (mini mentalstate examination score $<$24)

Table 5.3: *Design and methodological quality of trials - statins - pravastatin*

Trial	Design	Duration	Centre	Primary endpoint
Pravastatin versus placebo				
CARE (subgroup), 1998 [1] n=1283	parallel groups double blind exploratory trial	5.0y		
LIPID (sub group), 2001 [2] n=3514	parallel groups double blind exploratory trial	6.1y		
PLAC I (sub group), 1995 [3] n=94	parallel groups double blind exploratory trial	2.3y		
REGRESS (subgroup), 1995 [4] n=138	parallel groups double blind exploratory trial	2.0y		

continued...

Trial	Design	Duration	Centre	Primary endpoint
PROSPER, 2002 [5] n=5804	Parallel groups double blind confirmatory trial at low risk of bias	3.2 years inclusion period: dec 1997, May 1999	Ecosse, Irelande, Pays bas multicenter	death, MI , stroke

Table 5.4: *Trial characteristics - statins - pravastatin*

Trial
Pravastatin versus placebo
CARE (subgroup), 1998 [1]
LIPID (sub group), 2001 [2]
PLAC I (sub group), 1995 [3]
REGRESS (subgroup), 1995 [4]
PROSPER, 2002 [5]
-1.1

5.2 Meta-analysis results

The results are detailed in table 5.5 (page 39). This table is followed by the Forest's plot corresponding to each endpoint.

Pravastatin versus placebo

Only one of the 5 studies eligible for this comparison provided data on **cardiovascular events**. The analysis detected a statistically significant difference in favor of pravastatin in cardiovascular events, with a RR of 0.87 (95% CI 0.77 to 0.98, p=0.0243).
Only one of the 5 studies eligible for this comparison provided data on **cardiovascular death**. No statistically significant difference between the groups was found in cardiovascular death, with a RR of 0.87 (95% CI 0.69 to 1.08, p=0.2101).
Only one of the 5 studies eligible for this comparison provided data on **stroke (fatal and non fatal)**. No statistically significant difference between the groups was found in stroke (fatal and non fatal), with a RR of 1.04 (95% CI 0.82 to 1.31, p=0.7533).
Only one of the 5 studies eligible for this comparison provided data on **coronary death and non fatal MI**. The analysis detected a statistically significant difference in favor of pravastatin in coronary death and non fatal MI, with a RR of 0.83 (95% CI 0.71 to 0.96, p=0.0105).
Only one of the 5 studies eligible for this comparison provided data on **coronary event**. The analysis detected a statistically significant difference in favor of pravastatin in coronary event, with a RR of 0.83 (95% CI 0.71 to 0.96, p=0.0105).
Only one of the 5 studies eligible for this comparison provided data on **coronary death**. No statistically significant difference between the groups was found in coronary death, with a RR of 0.78 (95% CI 0.60 to 1.01, p=0.0602).
Only one of the 5 studies eligible for this comparison provided data on **MACE**. The analysis detected a statistically significant difference in favor of pravastatin in MACE, with a RR of 0.87 (95% CI 0.78 to 0.98, p=0.0221).
Only one of the 5 studies eligible for this comparison provided data on **non fatal MI**. No statistically significant difference between the groups was found in non fatal MI, with a RR of 0.88 (95% CI 0.74 to 1.05, p=0.1489).

Table 5.5: *Results details - statins - pravastatin*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
pravastatin versus placebo						
cardiovascular events	RR=0.87	[0.77;0.98]	0.0243	1.0000 (I^2=0.00)	1	5804
cardiovascular death	RR=0.87	[0.69;1.08]	0.2101	1.0000 (I^2=0.00)	1	5804
stroke (fatal and non fatal)	RR=1.04	[0.82;1.31]	0.7533	1.0000 (I^2=0.00)	1	5804
coronary death and non fatal MI	RR=0.83	[0.71;0.96]	0.0105	1.0000 (I^2=0.00)	1	5804
coronary event	RR=0.83	[0.71;0.96]	0.0105	1.0000 (I^2=0.00)	1	5804
coronary death	RR=0.78	[0.60;1.01]	0.0602	1.0000 (I^2=0.00)	1	5804
MACE	RR=0.87	[0.78;0.98]	0.0221	1.0000 (I^2=0.00)	1	5804
death from cancer	RR=1.27	[0.97;1.67]	0.0795	1.0000 (I^2=0.00)	1	5804

continued...

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
rhabdomyolysis	RR=1.01	[0.02;50.77]	0.9970	1.0000 (I^2=0.00)	1	5804
myopathy	RR=1.13	[0.71;1.82]	0.6037	1.0000 (I^2=0.00)	1	5804
non fatal MI	RR=0.88	[0.74;1.05]	0.1489	1.0000 (I^2=0.00)	1	5804
all cause death	RR=0.98	[0.84;1.14]	0.8061	1.0000 (I^2=0.00)	1	5804

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2: inconsistance degree

Figure 5.1: *Forest's plot for cardiovascular events*

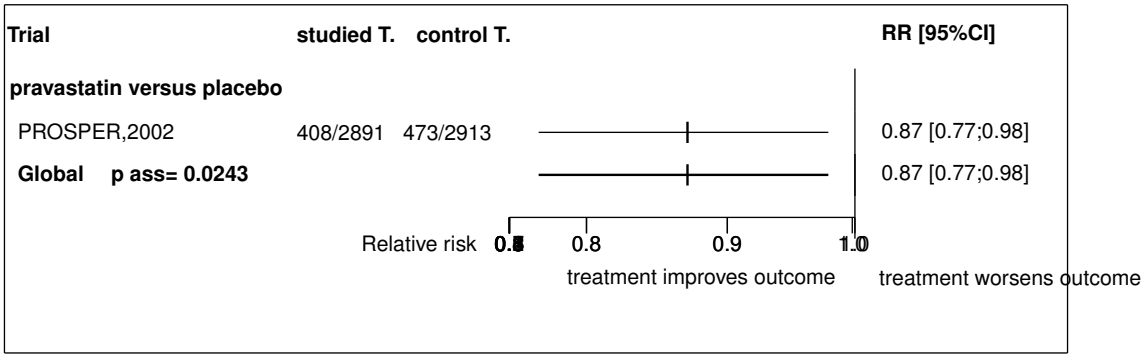


Figure 5.2: *Forest's plot for cardiovascular death*

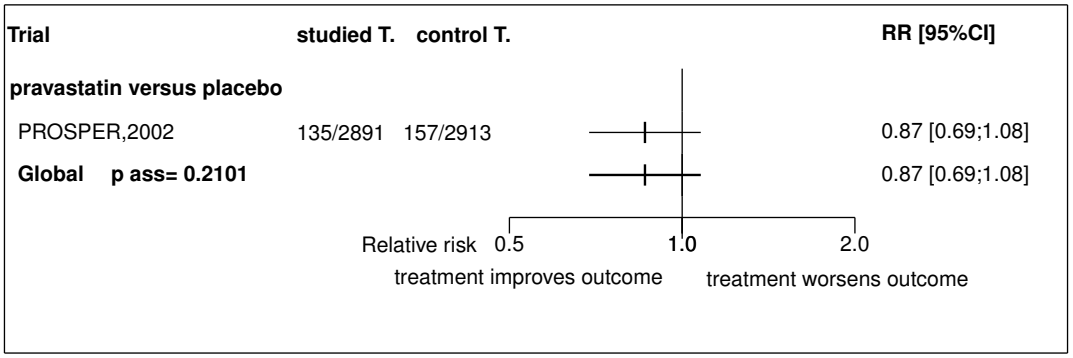


Figure 5.3: *Forest's plot for stroke (fatal and non fatal)*

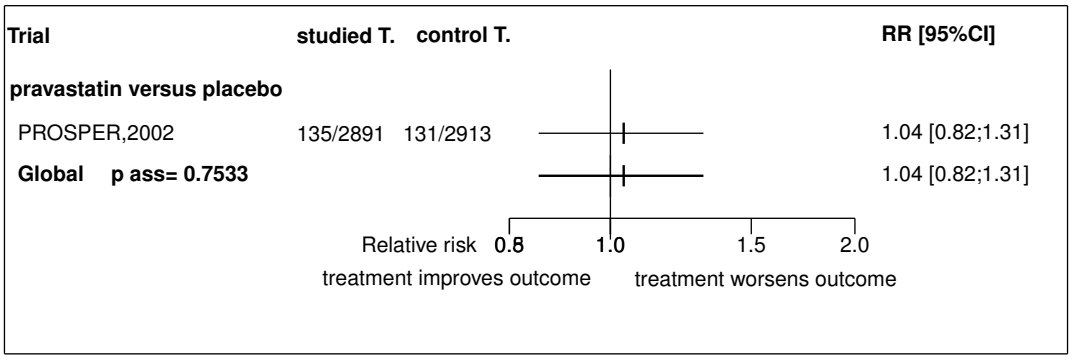


Figure 5.4: *Forest's plot for coronary death and non fatal MI*

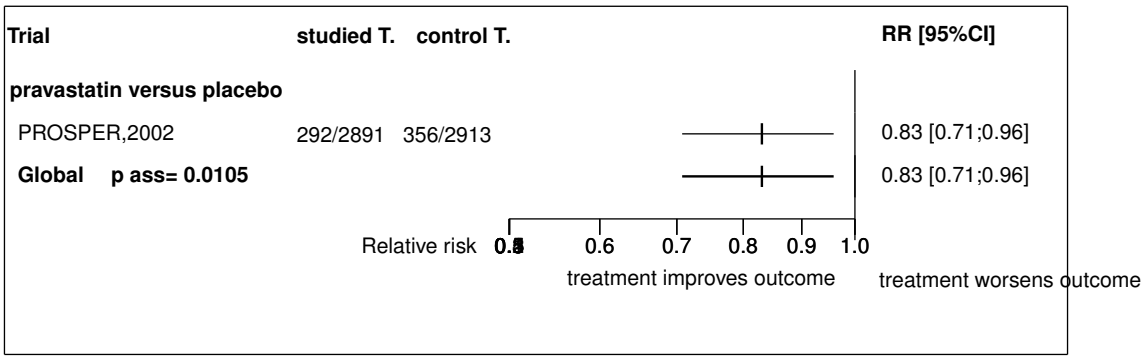


Figure 5.5: *Forest's plot for coronary event*

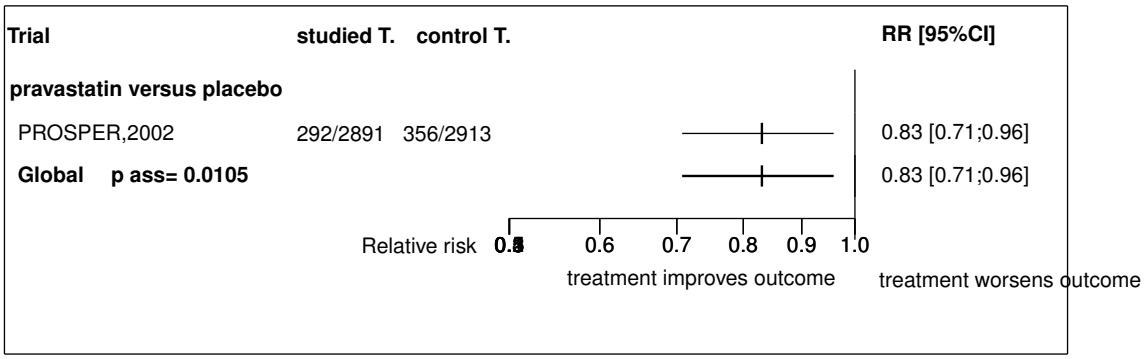


Figure 5.6: *Forest's plot for coronary death*

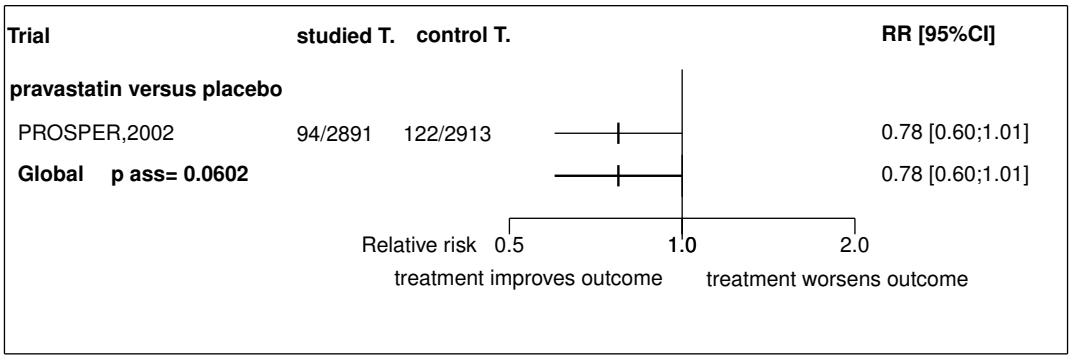


Figure 5.7: *Forest's plot for MACE*

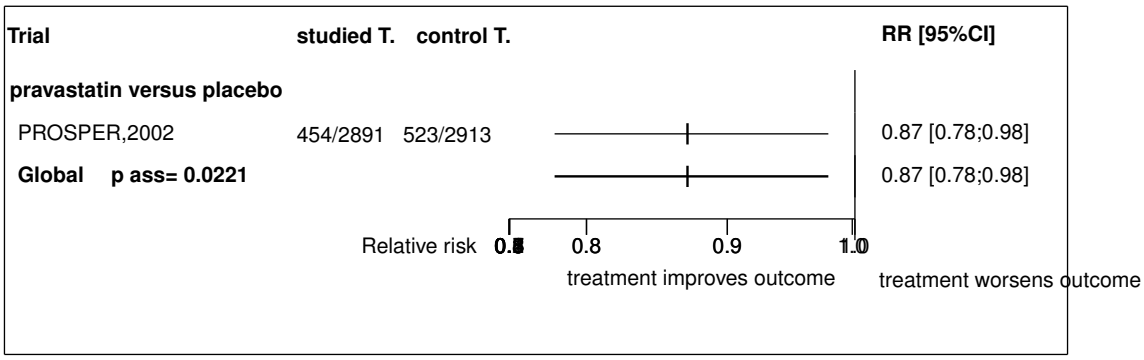


Figure 5.8: *Forest's plot for death from cancer*

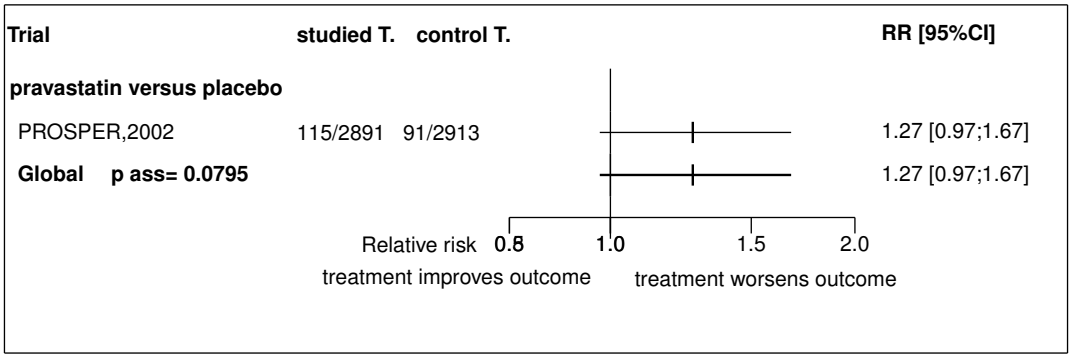


Figure 5.9: *Forest's plot for rhabdomyolysis*

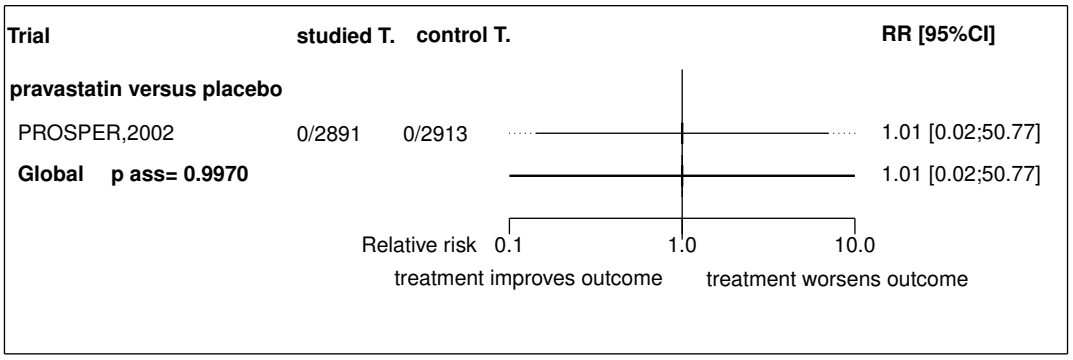


Figure 5.10: *Forest's plot for myopathy*

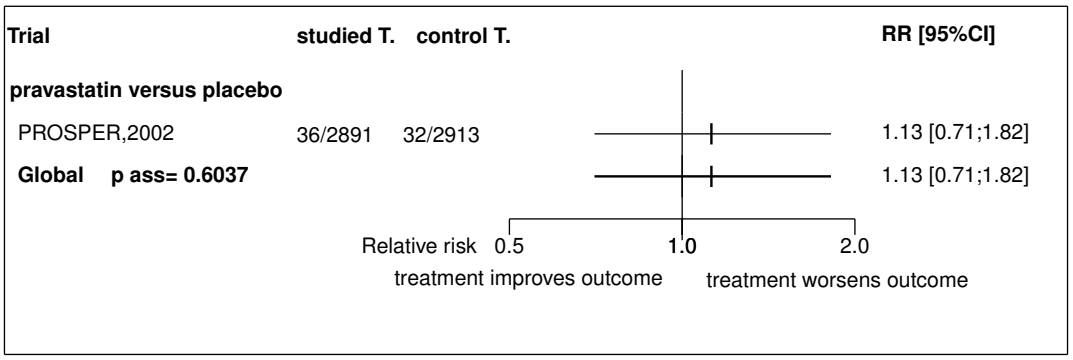


Figure 5.11: *Forest's plot for non fatal MI*

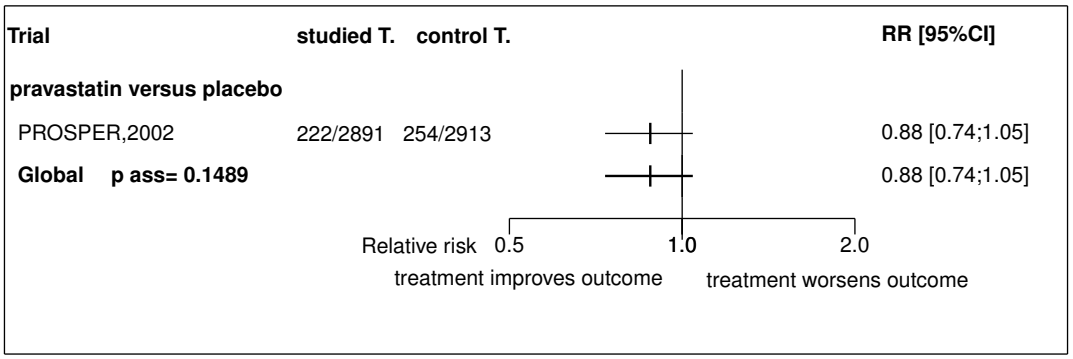
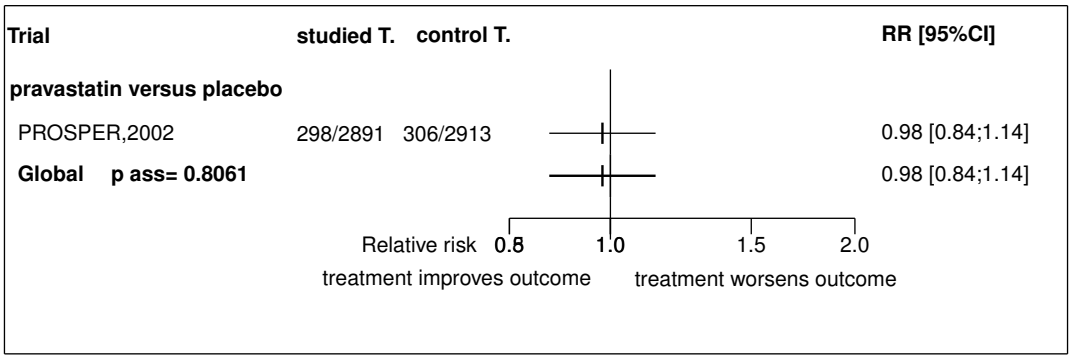


Figure 5.12: *Forest's plot for all cause death*



References

[1] Lewis SJ, Moye LA, Sacks FM, Johnstone DE, Timmis G, Mitchell J, Limacher M, Kell S, Glasser SP, Grant J, Davis BR, Pfeffer MA, Braunwald E. Effect of pravastatin on cardiovascular events in older patients with myocardial infarction and cholesterol levels in the average range. Results of the Cholesterol and Recurrent Events (CARE) trial. Ann Intern Med 1998;129:681-9. [PMID=9841599]

[2] Hunt D, Young P, Simes J, Hague W, Mann S, Owensby D, Lane G, Tonkin A. Benefits of pravastatin on cardiovascular events and mortality in older patients with coronary heart disease are equal to or exceed those seen in younger patients: Results from the LIPID trial. Ann Intern Med 2001;134:931-40. [PMID=11352694]

[3] Pitt B, Mancini GB, Ellis SG, Rosman HS, Park JS, McGovern ME. Pravastatin limitation of atherosclerosis in the coronary arteries (PLAC I): reduction in atherosclerosis progression and clinical events. PLAC I investigation. J Am Coll Cardiol 1995;26:1133-9. [PMID=7594023]

[4] Jukema JW, Bruschke AV, van Boven AJ, Reiber JH, Bal ET, Zwinderman AH, Jansen H, Boerma GJ, van Rappard FM, Lie KI. Effects of lipid lowering by pravastatin on progression and regression of coronary artery disease in symptomatic men with normal to moderately elevated serum cholesterol levels. The Regression Growth Evaluation Statin Study (REGRESS). Circulation 1995;91:2528-40. [PMID=7743614]

[5] Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, Ford I, Gaw A, Hyland M, Jukema JW, Kamper AM, Macfarlane PW, Meinders AE, Norrie J, Packard CJ, Perry IJ, Stott DJ, Sweeney BJ, Twomey C, Westendorp RG,. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Lancet 2002; 360:1623-30. [PMID=12457784]

5.3 Individual trial summaries

Table 5.6: *CARE (subgroup), 1998 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=1283 (640 vs. 643) **Follow-up duration:** 5.0y **Study design:** Randomized controlled trial parallel groups Double blind Exploratory trial	MI 320 months, subgroup of age 65-75 y	**Studied treatment:** Pravastatin 40mg **Control treatment:**	

Reference

Lewis SJ, Moye LA, Sacks FM, Johnstone DE, Timmis G, Mitchell J, Limacher M, Kell S, Glasser SP, Grant J, Davis BR, Pfeffer MA, Braunwald E. Effect of pravastatin on cardiovascular events in older patients with myocardial infarction and cholesterol levels in the average range. Results of the Cholesterol and Recurrent Events (CARE) trial. Ann Intern Med 1998;129:681-9 [PMID=9841599]

Table 5.7: *LIPID (sub group), 2001 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=3514 (1741 vs. 1773) **Follow-up duration:** 6.1y **Study design:** Randomized controlled trial parallel groups Double blind Exploratory trial	MI or unstable angina, subgroup of age 65-75 y	**Studied treatment:** Pravastatin 40mg **Control treatment:**	

Reference

Hunt D, Young P, Simes J, Hague W, Mann S, Owensby D, Lane G, Tonkin A. Benefits of pravastatin on cardiovascular events and mortality in older patients with coronary heart disease are equal to or exceed those seen in younger patients: Results from the LIPID trial. Ann Intern Med 2001;134:931-40 [PMID=11352694]

Table 5.8: *PLAC I (sub group), 1995 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=94 (42 vs. 52) **Follow-up duration:** 2.3y **Study design:** Randomized controlled trial parallel groups Double blind Exploratory trial	Angiographic CAD or recent MI, subgroup of age 65-75 y	**Studied treatment:** Pravastatin 40mg **Control treatment:**	

Reference

Pitt B, Mancini GB, Ellis SG, Rosman HS, Park JS, McGovern ME. Pravastatin limitation of atherosclerosis in the coronary arteries (PLAC I): reduction in atherosclerosis progression and clinical events. PLAC I investigation. J Am Coll Cardiol 1995;26:1133-9 [PMID=7594023]

Table 5.9: *REGRESS (subgroup), 1995 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=138 (75 vs. 63) **Follow-up duration:** 2.0y **Study design:** Randomized controlled trial parallel groups Double blind Exploratory trial	Angiographic CAD, subgroup of age 65-70 y	**Studied treatment:** Pravastatin 40mg **Control treatment:**	

Reference

Jukema JW, Bruschke AV, van Boven AJ, Reiber JH, Bal ET, Zwinderman AH, Jansen H, Boerma GJ, van Rappard FM, Lie KI. Effects of lipid lowering by pravastatin on progression and regression of coronary artery disease in symptomatic men with normal to moderately elevated serum cholesterol levels. The Regression Growth Evaluation Statin Study (REGRESS). Circulation 1995;91:2528-40 [PMID=7743614]

Table 5.10: *PROSPER, 2002 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=5804 (2891 vs. 2913) **Follow-up duration:** 3.2 years **Study design:** Randomized controlled trial Parallel groups Double blind Confirmatory trial at low risk of bias Ecosse, Irelande, Pays bas, multicenter **Inclusion period:** dec 1997, May 1999	Men and women aged 70-82 years with a history of, or risk factors for, vascular disease **Inclusion criteria:** men and women aged 7082 years; either pre-existing vascular disease (coronary, cerebral, or peripheral) or raised risk of such disease because of smoking, hypertension, or diabetes; total cholesterol between 4090 mmol/L; triglyceride less than 60 mmol/L **Exclusion criteria:** poor cognitive function (mini mentalstate examination score <24)	**Studied treatment:** pravastatin 40mg daily **Control treatment:** placebo	Cardiovascular events RR=0.87 [0.77;0.98] Cardiovascular death RR=0.87 [0.69;1.08] Stroke (fatal and non fatal) RR=1.04 [0.82;1.31] Coronary death and non fatal MI RR=0.83 [0.71;0.96] Coronary event RR=0.83 [0.71;0.96] Coronary death RR=0.78 [0.60;1.01] MACE RR=0.87 [0.78;0.98] Death from cancer RR=1.27 [0.97;1.67]

Reference
Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, Ford I, Gaw A, Hyland M, Jukema JW, Kamper AM, Macfarlane PW, Meinders AE, Norrie J, Packard CJ, Perry IJ, Stott DJ, Sweeney BJ, Twomey C, Westendorp RG,. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Lancet 2002; 360:1623-30 [PMID=12457784]

6 Detailed results for rosuvastatin

6.1 Available trials

Only one trial which randomized 0 patients was identified: it compared rosuvastatin with placebo.
This trial included NaN patients and was published in 2009.
This trial was double blind in design.
It was reported in English language.
data was reported in trials;
Following tables 6.1 (page 51), 6.2 (page 51), 6.4 (page 52), and 6.3 (page 51) summarized the main characteristics of the trial including in this systematic review of randomized trials of rosuvastatin.

Table 6.1: *Treatment description - statins - rosuvastatin*

Trial	Studied treatment	Control treatment
Rosuvastatin versus placebo		
JUPITER (sub group) (2009) [1]	rosuvastatin 20mg daily	placebo

Table 6.2: *Descriptions of participants - statins - rosuvastatin*

Trial	Patients
Rosuvastatin versus placebo	
JUPITER (sub group) (2009) [1]	Healthy individuals aged >=70 years with normal LDL cholesterols but with CRP levels >=2.0 mg/dL

Table 6.3: *Design and methodological quality of trials - statins - rosuvastatin*

Trial	Design	Duration	Centre	Primary end-point
Rosuvastatin versus placebo				
JUPITER (sub group), 2009 [1] n=NaN	Parallel groups double blind exploratory trial	double-blind		Cv event

Table 6.4: *Trial characteristics - statins - rosuvastatin*

Trial
Rosuvastatin versus placebo
JUPITER (sub group), 2009 [1]

6.2 Meta-analysis results

The results are detailed in table 6.5 (page 53). This table is followed by the Forest's plot corresponding to each endpoint.

Rosuvastatin versus placebo

No data were presented in the 1 trial identified

Table 6.5: *Results details - statins - rosuvastatin*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
rosuvastatin versus placebo						
No data were presented in the trial identified						

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2: inconsistance degree

References

[1] Glynn RJ, Koenig W, Nordestgaard BG, Shepherd J, Ridker PM. Rosuvastatin for primary prevention in older persons with elevated C-reactive protein and low to average low-density lipoprotein cholesterol levels: exploratory analysis of a randomized trial. Ann Intern Med 2010;152:488-96, W174. [PMID=20404379]

6.3 Individual trial summaries

Table 6.6: *JUPITER (sub group), 2009 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=NA (5695 vs. NA) **Follow-up duration:** double-blind **Study design:** Randomized controlled trial Parallel groups Double blind Exploratory trial	Healthy individuals aged >=70 years with normal LDL cholesterols but with CRP levels >=2.0 mg/dL	**Studied treatment:** rosuvastatin 20mg daily **Control treatment:** placebo	

Reference

Glynn RJ, Koenig W, Nordestgaard BG, Shepherd J, Ridker PM. Rosuvastatin for primary prevention in older persons with elevated C-reactive protein and low to average low-density lipoprotein cholesterol levels: exploratory analysis of a randomized trial. Ann Intern Med 2010;152:488-96, W174 [PMID=20404379]

7 Detailed results for simvastatin

7.1 Available trials

A total of 2 RCTs which randomized 11718 patients were identified: all compared simvastatin with placebo.
The average study size was 5859 patients (range 1021 to 10697). The first study was published in 1997, and the last study was published in 2002.
All trials were double blind in design. All included studies were reported in English language. We did not found any unpublished trial.
data was reported in trials;
Following tables 7.1 (page 56), 7.2 (page 56), 7.4 (page 58), and 7.3 (page 57) summarized the main characteristics of the trials including in this systematic review of randomized trials of simvastatin.

Table 7.1: *Treatment description - statins - simvastatin*

Trial	Studied treatment	Control treatment
Simvastatin versus placebo		
4S (subgroup) (1997) [1]	Simvastatin 20-40mg	
HPS (subgroup) (2002) [2]	Simvastatin 40mg	

Table 7.2: *Descriptions of participants - statins - simvastatin*

Trial	Patients
Simvastatin versus placebo	
4S (subgroup) (1997) [1]	MI 6 months or stable angina, subgroup of age 65-70 y
HPS (subgroup) (2002) [2]	Vascular disease or diabetes, subgroup of age 65-80 y

Table 7.3: *Design and methodological quality of trials - statins - simvastatin*

Trial	Design	Duration	Centre	Primary endpoint
Simvastatin versus placebo				
4S (subgroup), 1997 [1] n=1021	parallel groups double blind exploratory trial	5.4y		
HPS (subgroup), 2002 [2] n=10697	parallel groups double blind exploratory trial	5.0y		

Table 7.4: *Trial characteristics - statins - simvastatin*

Trial
Simvastatin versus placebo
4S (subgroup), 1997 [1]
HPS (subgroup), 2002 [2]

7.2 Meta-analysis results

The results are detailed in table 7.5 (page 59). This table is followed by the Forest's plot corresponding to each endpoint.

Simvastatin versus placebo

No data were presented in the 2 trials identified

Table 7.5: *Results details - statins - simvastatin*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
simvastatin versus placebo						
No data were presented in the trial identified						

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2: inconsistance degree

References

[1] Miettinen TA, Pyörl K, Olsson AG, Musliner TA, Cook TJ, Faergeman O, Berg K, Pedersen T, Kjekshus J. Cholesterol-lowering therapy in women and elderly patients with myocardial infarction or angina pectoris: findings from the Scandinavian Simvastatin Survival Study (4S). Circulation 1997;96:4211-8. [PMID=9416884]

[2] Champagne J, Geelen P, Philippon F, Brugada P. Recurrent cardiac events in patients with idiopathic ventricular fibrillation, excluding patients with the Brugada syndrome. BMC Med 2005;3:1. [PMID=15627402]

7.3 Individual trial summaries

Table 7.6: *4S (subgroup), 1997 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=1021 (518 vs. 503) **Follow-up duration:** 5.4y **Study design:** Randomized controlled trial parallel groups Double blind Exploratory trial	MI 6 months or stable angina, subgroup of age 65-70 y	**Studied treatment:** Simvastatin 20-40mg **Control treatment:**	

Reference

Miettinen TA, Pyörl K, Olsson AG, Musliner TA, Cook TJ, Faergeman O, Berg K, Pedersen T, Kjekshus J. Cholesterol-lowering therapy in women and elderly patients with myocardial infarction or angina pectoris: findings from the Scandinavian Simvastatin Survival Study (4S). Circulation 1997;96:4211-8 [PMID=9416884]

Table 7.7: *HPS (subgroup), 2002 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=10697 (5366 vs. 5331) **Follow-up duration:** 5.0y **Study design:** Randomized controlled trial parallel groups Double blind Exploratory trial	Vascular disease or diabetes, subgroup of age 65-80 y	**Studied treatment:** Simvastatin 40mg **Control treatment:**	

Reference

Champagne J, Geelen P, Philippon F, Brugada P. Recurrent cardiac events in patients with idiopathic ventricular fibrillation, excluding patients with the Brugada syndrome. BMC Med 2005;3:1 [PMID=15627402]

8 Global meta-analysis: all statins

8.1 Global meta-analysis: all statins versus placebo

Table 8.1: *All statinsversus placebo*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
cardiovascular events	RR=0.87	0.77;0.98	0.0243	1.0000 (0.00)	1	5804
cardiovascular death	RR=0.87	0.69;1.08	0.2101	1.0000 (0.00)	1	5804
stroke (fatal and non fatal)	RR=1.04	0.82;1.31	0.7533	1.0000 (0.00)	1	5804
coronary death and non fatal MI	RR=0.83	0.71;0.96	0.0105	1.0000 (0.00)	1	5804
coronary event	RR=0.83	0.71;0.96	0.0105	1.0000 (0.00)	1	5804
coronary death	RR=0.78	0.60;1.01	0.0602	1.0000 (0.00)	1	5804
MACE	RR=0.87	0.78;0.98	0.0221	1.0000 (0.00)	1	5804
non fatal MI	RR=0.88	0.74;1.05	0.1489	1.0000 (0.00)	1	5804

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2: inconsistance degree

9 Ongoing studies

No ongoing trial was identified.

10 Excluded studies

No trial was excluded.

References