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Rosuvastatin for lowering lipids (Review)

Adams SP, Sekhon SS, Wright JM

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[Intervention Review]

Rosuvastatin for lowering lipids

Stephen P Adams[1], Sarpreet S Sekhon[1], James M Wright[1]

[1]Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, Vancouver, Canada

Contact: James M Wright, Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, 2176 Health Sciences Mall, Medical Block C, Vancouver, BC, V6T 1Z3, Canada. jim.wright@ti.ubc.ca.

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ABSTRACT

Background

Rosuvastatin is one of the most potent statins and is currently widely prescribed. It is therefore important to know the dose-related magnitude of effect of rosuvastatin on blood lipids.

Objectives

Primary objective

To quantify the effects of various doses of rosuvastatin on serum total cholesterol, low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein (HDL)-cholesterol, non-HDL-cholesterol and triglycerides in participants with and without evidence of cardiovascular disease.

Secondary objectives

To quantify the variability of the effect of various doses of rosuvastatin.

To quantify withdrawals due to adverse effects (WDAEs) in the randomized placebo-controlled trials.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) Issue 10 of 12, 2014 in *The Cochrane Library*, MEDLINE (1946 to October week 5 2014), EMBASE (1980 to 2014 week 44), Web of Science Core Collection (1970 to 5 November 2014) and BIOSIS Citation Index (1969 to 31 October 2014). No language restrictions were applied.

Selection criteria

Randomized controlled and uncontrolled before-and-after trials evaluating the dose response of different fixed doses of rosuvastatin on blood lipids over a duration of three to 12 weeks.

Data collection and analysis

Two review authors independently assessed eligibility criteria for studies to be included and extracted data. WDAEs information was collected from the placebo-controlled trials.

Main results

One-hundred and eight trials (18 placebo-controlled and 90 before-and-after) evaluated the dose-related efficacy of rosuvastatin in 19,596 participants. Rosuvastatin 10 to 40 mg/day caused LDL-cholesterol decreases of 46% to 55%, when all the trials were combined using the generic inverse variance method. The quality of evidence for these effects is high. Log dose-response data over doses of 1 to 80 mg, revealed strong linear dose-related effects on blood total cholesterol, LDL-cholesterol and non-HDL-cholesterol. When compared to atorvastatin,

rosuvastatin was about three-fold more potent at reducing LDL-cholesterol. There was no dose-related effect of rosuvastatin on blood HDL-cholesterol, but overall, rosuvastatin increased HDL by 7%. There is a high risk of bias for the trials in this review, which would affect WDAEs, but unlikely to affect the lipid measurements. WDAEs were not statistically different between rosuvastatin and placebo in 10 of 18 of these short-term trials (risk ratio 0.84; 95% confidence interval 0.48 to 1.47).

Authors' conclusions

The total blood total cholesterol, LDL-cholesterol and non-HDL-cholesterol-lowering effect of rosuvastatin was linearly dependent on dose. Rosuvastatin log dose-response data were linear over the commonly prescribed dose range. Based on an informal comparison with atorvastatin, this represents a three-fold greater potency. This review did not provide a good estimate of the incidence of harms associated with rosuvastatin because of the short duration of the trials and the lack of reporting of adverse effects in 44% of the placebo-controlled trials.

PLAIN LANGUAGE SUMMARY

The effect of rosuvastatin on cholesterol

Rosuvastatin (Crestor) is one of the most potent statins and is currently widely prescribed. It is therefore important to know how much rosuvastatin lowers cholesterol. We searched for all the trial evidence from trials of three to 12 week duration reporting the effect of rosuvastatin on cholesterol. We found 108 trials involving 19,596 participants. Based on an informal comparison with atorvastatin three-fold lower doses of rosuvastatin are needed to lower cholesterol by the same amount. This review cannot be used to assess harms of rosuvastatin, because of the short duration of these trials and the high risk of bias for this outcome; adverse effects were only reported in 10 of the 18 trials that could be used to assess harms.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. LDL-cholesterol lowering efficacy of rosuvastatin for all trials

LDL-cholesterol lowering efficacy of rosuvastatin

Patient or population: participants**with normal or abnormal lipid profiles**

Settings: clinics of hospitals

Intervention: rosuvastatin

Comparison: LDL-Cholesterol per cent change from baseline for all trials

Comparison: WDAEs rosuvastatin versus placebo

Outcomes	Mean % reduction (95% CI)[1]	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
LDL-Cholesterol **rosuvastatin** 2.5 mg/day	-39.1 (-40.6 to -37.6)	450 (11)	**low[4]** ⊕⊕⊝⊝	Likely an overestimate of the effect; effect predicted from log dose response equation is -36.9%
LDL-Cholesterol **rosuvastatin** 5 mg/day	-41.3 (-42.0 to -40.7)	2602 (25)	⊕⊕⊕⊕ **high[5]**	Effect predicted from log dose response equation is -41.4%.
LDL-Cholesterol **rosuvastatin** 10 mg/day	-45.6 (-46.0 to -45.3)	9855 (74)	⊕⊕⊕⊕ **high[5]**	Effect predicted from log dose response equation is -45.8%.
LDL-Cholesterol **rosuvastatin** 20 mg/day	-49.9 (-50.4 to -49.4)	3675 (28)	⊕⊕⊕⊕ **high[5]**	Effect predicted from log dose response equation is -50.2%.
LDL-Cholesterol **rosuvastatin**	-54.9 (-55.4 to -54.4)	3512 (18)	⊕⊕⊕⊕ **high[5]**	Effect predicted from log dose response equation is -54.6%.

40 mg/day				
WDAE[2] all doses	**RR**[3] (0.84) (0.48 to 1.47)	1330 (10)	⊕⊖⊖⊖ **very low**[6]	Only 10 out of 18 placebo-controlled trials reported withdrawals due to adverse effects.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

1. CI: confidence interval.
2. WDAE: withdrawal due to adverse effects.
3. RR: risk ratio.
4. Small number of studies and participants with relatively wide confidence intervals and high risk of publication bias.
5. Narrow confidence intervals.
6. High risk of selective reporting bias and wide confidence interval.

BACKGROUND

Description of the condition

Cardiovascular disease is the major cause of death and disability in the developed world accounting for more than one-third of total deaths (Kreatsoulas 2010). In the United States, cardiovascular disease causes one in three deaths reported each year (CDC 2011; Roger 2011). Existing evidence shows a weak association between adverse cardiovascular events and blood concentrations of low-density lipoprotein (LDL)-cholesterol in adults (Grundy 2004). The current recommended treatment for secondary prevention of adverse cardiovascular events in addition to diet and lifestyle changes is drug therapy with the drug class widely known as "statins".

Description of the intervention

Rosuvastatin is on of the most potent statins and is currently widely prescribed. Rosuvastatin and the six other marketed statins are prescribed to prevent adverse cardiovascular events and to lower total cholesterol and LDL-cholesterol (Law 2003). Rosuvastatin is rapidly absorbed, reaching peak plasma concentration within three hours. The lipid-lowering effect of rosuvastatin is not influenced by the time-of-day the drug is administered. This is probably due to the relatively long half-life of 20 hours (Goodman 2011). Rosuvastatin and statins as a class have been shown in individual randomized controlled trials (RCTs), systematic reviews, and meta-analyses of RCTs to reduce major vascular events in people with and without occlusive vascular disease (CTT 2005; Mills 2008; Taylor 2013). The effect of statins on morbidity and mortality, however, is not the subject of this systematic review, which is to learn more about the pharmacology of rosuvastatin by characterizing its dose-related effect on the surrogate markers: total cholesterol, LDL-cholesterol, high-density lipoprotein (HDL)-cholesterol and triglycerides. This information will be useful on its own, and will also allow comparison of rosuvastatin with the other statins that are used clinically.

How the intervention might work

Rosuvastatin acts in the liver by inhibiting an enzyme early in the pathway for cholesterol synthesis, 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (HMG-CoA reductase). This enzyme irreversibly converts 3-hydroxy-3-methylglutaryl CoA to mevalonate (Moghadasian 1999). This reaction is the third step in a sequence of reactions resulting in the production of many compounds including cholesterol and its circulating blood derivatives, LDL-cholesterol and very low-density (VLDL)-cholesterol (Gaw 2000). The prevailing hypothesis is that statins reduce mortality and morbidity in patients with occlusive vascular disease by reducing the liver production of cholesterol resulting in a reduction in blood LDL-cholesterol and a decrease in atherogenesis. The HMG Co-A reductase enzyme however is also responsible for the production of ubiquinone (coenzyme Q10), heme A, vitamin D, steroid hormones, and many other compounds. It remains possible that the beneficial effects of statins are due to actions other than the reduction of cholesterol. These effects are commonly referred to as the pleiotropic effects of statins (Liao 2005). Independent of how the drug works, it is important to know the average per cent reduction in the lipid parameters associated with the common doses taken by patients.

The magnitude of effect of the statin is expressed as the per cent reduction from baseline because the per cent reduction is independent of the unit of measurement and of the baseline lipid parameter. Furthermore, the per cent reduction from baseline in blood LDL-cholesterol at the present time represents the best available pharmacological marker of the magnitude of the effect of statins on HMG Co-A reductase.

Most importantly for this review is the fact that a fasting blood lipid profile, consisting of total cholesterol, LDL-cholesterol, non-HDL-cholesterol, HDL-cholesterol, and triglycerides, is used clinically to monitor the magnitude of the effect of a prescribed statin. Therefore, the observed per cent reduction in the five blood lipids constitutes the best available pharmacological markers of the magnitude of the statin effect, and represents the amount by which the HMG Co-A reductase enzyme is inhibited.

Why it is important to do this review

Statins are the most widely prescribed class of drugs in the world. Prescribing of statins is increasing, as are average prescribed doses. At the present time, clinicians have an approximate sense of the different potency of the different statins, but a systematic assessment of the potency, dose-response relationship, and variability of effect has not been completed for any of the statins except for our previous review of atorvastatin (Adams 2012a). It is possible that, in addition to differences in potency, the dose-response relationship or the variability of response differs between different statins. A small number of previous systematic reviews have assessed the effect of statins on serum lipids (Bandolier 2004; Edwards 2003; Law 2003; Ward 2007). They have demonstrated that different statins have different potencies in terms of lipid lowering and that higher doses of statins cause greater lowering of serum lipids than lower doses (Kellick 1997; Schaefer 2004; Schectman 1996). None, however, of these systematic reviews has calculated the slope of the dose response or the variability of effect, and none of them is up-to-date. The most comprehensive systematic review to date is limited in that it presents the data based on the average absolute reduction in LDL concentration rather than on the per cent reduction from baseline (Law 2003). Reporting in this way can be misleading, as the absolute reduction in LDL is dependent on the baseline LDL concentration, in addition to the dose of statin. The purpose of this second systematic review is to build on Law's work.

Since rosuvastatin is the most potent widely-prescribed statin in the world, we have chosen rosuvastatin as the second drug to study in this class. We use the surrogate marker measure of the pharmacological effect of statins, the per cent reduction from baseline, to describe the dose-response relationship of the effect of rosuvastatin on total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides and non-HDL-cholesterol (Boekholdt 2012). We have used the results of this review to compare rosuvastatin with atorvastatin (Adams 2012a). Subsequent reviews of other drugs in the class (i.e. cerivastatin, fluvastatin, lovastatin, pravastatin, simvastatin, and pitavastatin) will also be done, in order to compare the results with rosuvastatin and atorvastatin. The protocol for this review was published in 2012 (Adams 2012b).

OBJECTIVES

Primary objective

To quantify the effects of various doses of rosuvastatin on serum total cholesterol, LDL-cholesterol, HDL-cholesterol, non-HDL-cholesterol and triglycerides in people with, and without, evidence of cardiovascular disease.

Secondary objectives

To quantify the variability of the effect of various doses of rosuvastatin.

To quantify withdrawals due to adverse effects (WDAEs) in the randomized placebo-controlled trials.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized placebo-controlled trials (RCTs) as well as uncontrolled before-and after-trials. Before-and after-trials were included because it has been shown that there is no placebo effect of statins on lipid parameters and that a placebo control for these outcomes is not essential (Tsang 2002). Cross-over trials were included if the outcomes were reported for the parallel arms prior to the cross-over.

Types of participants

Participants could be of any age with, and without, evidence of cardiovascular disease. Participants could can have normal lipid parameters or any type of hyperlipidaemia or dyslipidaemia (conditions involving high levels of lipids in the blood).

We also allowed the inclusion of participants with various co-morbid conditions including type 2 diabetes mellitus, hypertension, metabolic syndrome (combination of medical disorders that increase risk for cardiovascular disease and diabetes), chronic renal failure or cardiovascular disease.

Types of interventions

Rosuvastatin had to be administered at a constant daily dose compared with placebo, or alone for a period of three to 12 weeks. This administration period was chosen to allow at least three weeks for a steady-state effect of rosuvastatin to occur, and to be short enough to minimize participant drop outs. Data from studies where rosuvastatin was administered in the morning, or evening, or where it was not specified were accepted. Trials required a washout baseline dietary stabilization period of at least three weeks where all previous lipid-altering medication was withdrawn. This baseline phase ensures that participants follow a standard lipid-regulating diet, and helps to stabilize baseline lipid values prior to treatment. Baseline dietary stabilization periods were not required in trials where participants were not receiving lipid-altering medications or dietary supplements before receiving the test drug.

Types of outcome measures

Primary outcomes

1. Placebo-controlled RCTs: mean per cent change of LDL-cholesterol from baseline of different doses of rosuvastatin minus per cent change from baseline with placebo.
2. Placebo-controlled RCTs: mean per cent change of non-HDL-cholesterol from baseline of different doses of rosuvastatin minus per cent change from baseline with placebo.
3. Before-and-after trials: mean per cent change of LDL-cholesterol from baseline of different doses of rosuvastatin.
4. Before-and-after trials: mean per cent change of non-HDL-cholesterol from baseline of different doses of rosuvastatin.

Secondary outcomes

1. Placebo-controlled RCTs: mean per cent change of total cholesterol from baseline of different doses of rosuvastatin minus mean per cent change from baseline with placebo.
2. Before-and-after trials: mean per cent change from baseline of total cholesterol of different doses of rosuvastatin. It is recognized that effects on total cholesterol are primarily due to effects on LDL-cholesterol, which is the reason that this is a secondary outcome.
3. Placebo-controlled RCTs: mean per cent change of HDL-cholesterol from baseline of different doses of rosuvastatin minus mean per cent change from baseline with placebo.
4. Before-and-after trials: mean per cent change from baseline of HDL-cholesterol of different doses of rosuvastatin.
5. Placebo-controlled RCTs: mean per cent change of triglycerides from baseline of different doses of rosuvastatin minus mean per cent change from baseline with placebo.
6. Before-and-after trials: mean per cent change from baseline of triglycerides of different doses of rosuvastatin.
7. End of treatment variability (standard deviation) and coefficient of variation of LDL-cholesterol measurements for each dose of rosuvastatin. It was important to know whether rosuvastatin has an effect on the variability of lipid measures and ultimately to compare this with the effect of other statins.
8. Placebo-controlled RCTs: withdrawals due to adverse effects (WDAEs). This is an important measure of harm that can only be assessed in the placebo-controlled trials.

Search methods for identification of studies

Electronic searches

Relevant trials of rosuvastatin were identified through searches of the Cochrane Central Register of Controlled Trials (CENTRAL) Issue 10 of 12, 2014 in T*he Cochrane Library*, MEDLINE (Ovid, 1946 to October week 5 2014), EMBASE (Ovid, 1980 to 2014 week 44), Web of Science Core Collection (Thomson Reuters, 1970 to 5 November 2014) and BIOSIS Citation Index (Thomson Reuters, 1969 to 31 October 2014). Bibliographies of included studies were checked. Please see Appendix 1 for the search strategies.

There were no language restrictions.

Searching other resources

In cases of incomplete reports, further searches were carried out for connected papers. Previously published meta-analysis on the

efficacy of HMG-CoA reductase inhibitors were used to help identify references to trials (CTT 2005; Edwards 2003; Law 2003). A Grey literature search (date up to November week 1 2014) was included by searching other resources.

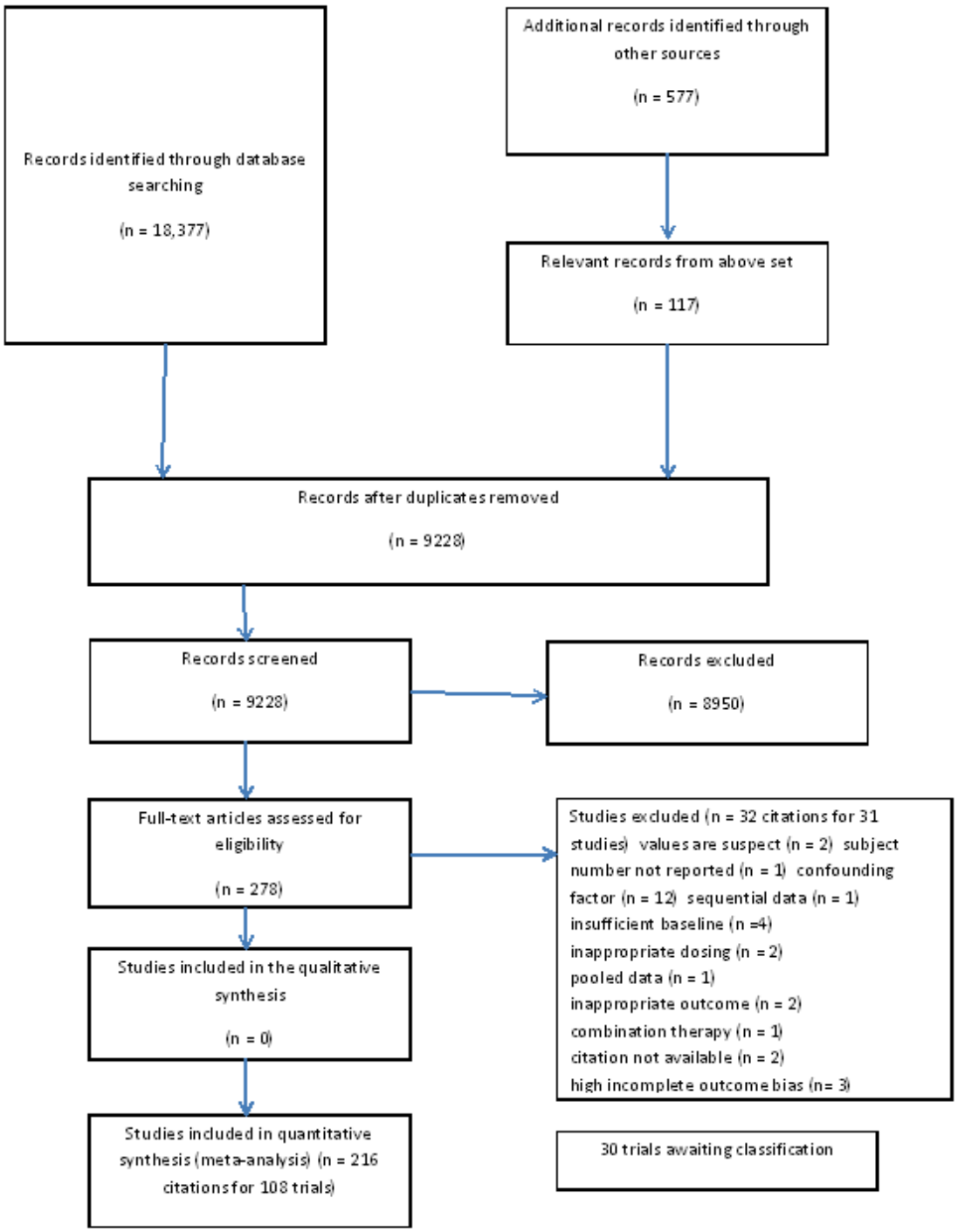
- SciFinder Scholar (scifinder.cas.org/scifinder/view/scifinder/scifinderExplore.jsf)
- ClinicalTrials.gov (www.clinicaltrials.gov/)
- International Pharmaceutical Abstracts database (EBSCO)
- ProQuest Dissertations and Theses (search.proquest.com/pqdtft/advanced?accountid=14656)
- AstraZeneca (www.astrazenecaclinicaltrials.com/)
- US Food and Drug Administration (www.fda.gov/)
- European Patent Office (worldwide.espacenet.com).
- the metaRegister of controlled trials (mRCT) (www.controlled-trials.com/mrct)
- the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (apps.who.int/trialsearch/)

Data collection and analysis

Selection of studies

Initial selection of trials involved reading the titles and abstracts from the electronic searches and excluding those that were obviously irrelevant. We obtained the full text of potentially relevant trials. Two review authors (SA, SS) analyzed the full-text papers independently to decide which trials to include. Disagreements were resolved by a third party (JMW). A PRISMA flow diagram documenting this process is provided (Figure 1).

Figure 1.



Data extraction and management

Two authors (SA, SS) extracted the mean per cent change directly from the data or calculated it from the baseline and endpoint values. If there was a disagreement for a value, consensus was reached by data recalculation to determine the correct value. We also extracted standard deviations and standard errors from the report, or calculated them, when possible. We entered data from placebo-controlled and uncontrolled before-and-after trials

into RevMan 5.3 as continuous and generic inverse variance data, respectively.

Assessment of risk of bias in included studies

We assessed all trials for risk of bias using the Cochrane 'Risk of bias' tool for the following items: adequate sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other biases. We used 'Risk of bias' tables in RevMan 5.3 for assessing the risk of bias in the included studies (Higgins 2011). We used the GRADE method to define the Quality of the evidence in the 'Summary of findings' table as discussed in the *Cochrane Handbook for Systematic Reviews of Interventions*, Section 12.2 (Higgins 2011).

Measures of treatment effect

Initially, we analyzed the treatment effects for each dose of rosuvastatin in the placebo-controlled RCTs, and the before-and-after uncontrolled trials, separately. After determining that the mean effects from the two trial designs were not statistically different, we reanalyzed all efficacy study data using the generic inverse variance fixed-effect model to determine the overall weighted treatment effects and their 95% confidence intervals (CI) for serum total cholesterol, LDL-cholesterol, HDL-cholesterol, non-HDL-cholesterol and triglycerides.

Unit of analysis issues

There were no unit of analysis issues for this review.

Dealing with missing data

We requested missing data from the authors. The most common type of data that was not reported was standard deviation of the change. For studies where standard deviations were not provided, we imputed them. The imputed value used was the average weighted standard deviation of the change from other trials in the review (Furukawa 2006).

Assessment of heterogeneity

Use of the Chi^2 test to identify heterogeneity is not appropriate because it has low power when there are few studies, but has excessive power to detect clinically unimportant heterogeneity when there are many studies. A better statistic used in this review is I^2, which is the between-study variance divided by the between-study variance plus the within-study variance (i.e. between-study variance/(between-study variance + within-study variance)). This measures the proportion of total variation in the estimate of the treatment effect that is due to heterogeneity between studies. This statistic is also independent of the number of studies in the analysis (Higgins 2002). If the I^2 was greater than or equal to 50%, we used the random-effects model to assess whether the pooled effect is statistically significant and to conservatively estimate the measure of the effect.

Assessment of reporting biases

We assessed for publication bias and other reporting biases by creating funnel plots for the primary outcomes. Asymmetry in funnel plots may indicate publication bias. Publication bias occurs as a result of the publication of positive trials and corresponding reduced likelihood that small negative trials were submitted or accepted for publication in peer-reviewed journals (Sterne 2011).

Data synthesis

We entered all placebo-controlled studies into RevMan 5.2 as mean difference (MD) fixed-effect model data to determine the weighted treatment effect and 95% CI for serum total cholesterol, LDL-cholesterol, HDL-cholesterol, non-HDL-cholesterol and triglycerides. We entered all uncontrolled before-and-after studies as generic inverse variance fixed-effect model data to determine the weighted treatment effect. Because the effect in the placebo-controlled trials was not statistically significantly different from the before-and-after trials, we entered the data for all trials and each dose as generic inverse variance to determine the best overall weighted treatment effect for each dose.

We entered the trial data of each study and dose into GraphPad Prism 4 to yield a weighted least squares analyses based on the inverse of the square of the standard error for each lipid parameter to generate weighted log dose-response curves. We also entered the number of participants from placebo-controlled trials who prematurely withdrew due to at least one adverse effect into Revman 5.2 as dichotomous data for each dose and all combined doses of rosuvastatin.

Subgroup analysis and investigation of heterogeneity

The main subgroup analyses were the different doses of rosuvastatin. We assessed heterogeneity within the doses using I^2 (Higgins 2002). If there was significant heterogeneity, we attempted to identify possible causes for this by carrying out a number of planned subgroup analyses, provided there were sufficient numbers of trials (see below).

Subgroups based on the following factors were analyzed when possible.

1. Placebo-controlled trials versus before-and-after trials (described above).
2. Male participants versus female participants.
3. Morning administration time versus evening administration time analysis was not done because there were no trials that reported morning dosing.
4. AstraZeneca-funded versus non-AstraZeneca-funded trials.

Sensitivity analysis

We conducted sensitivity analyses to assess the effect of different co-morbidities, such as familial hyperlipidaemia, on the treatment effect.

RESULTS

Description of studies

This review included 108 trials involving 19,596 participants. There were 90 before-and-after trials, 15 randomized double-blind placebo-controlled trials, two randomized single-blind placebo-controlled trials and one randomized open-label placebo-controlled trial. The number of placebo participants and rosuvastatin participants were 918 and 18,678 respectively. The number of male and female participants reported in 100 of the 108 trials were 9529 and 8656 respectively. Participants could be of any age. There were six familial hypercholesterolaemia trials and 102 non-familial hypercholesterolaemia trials.

Results of the search

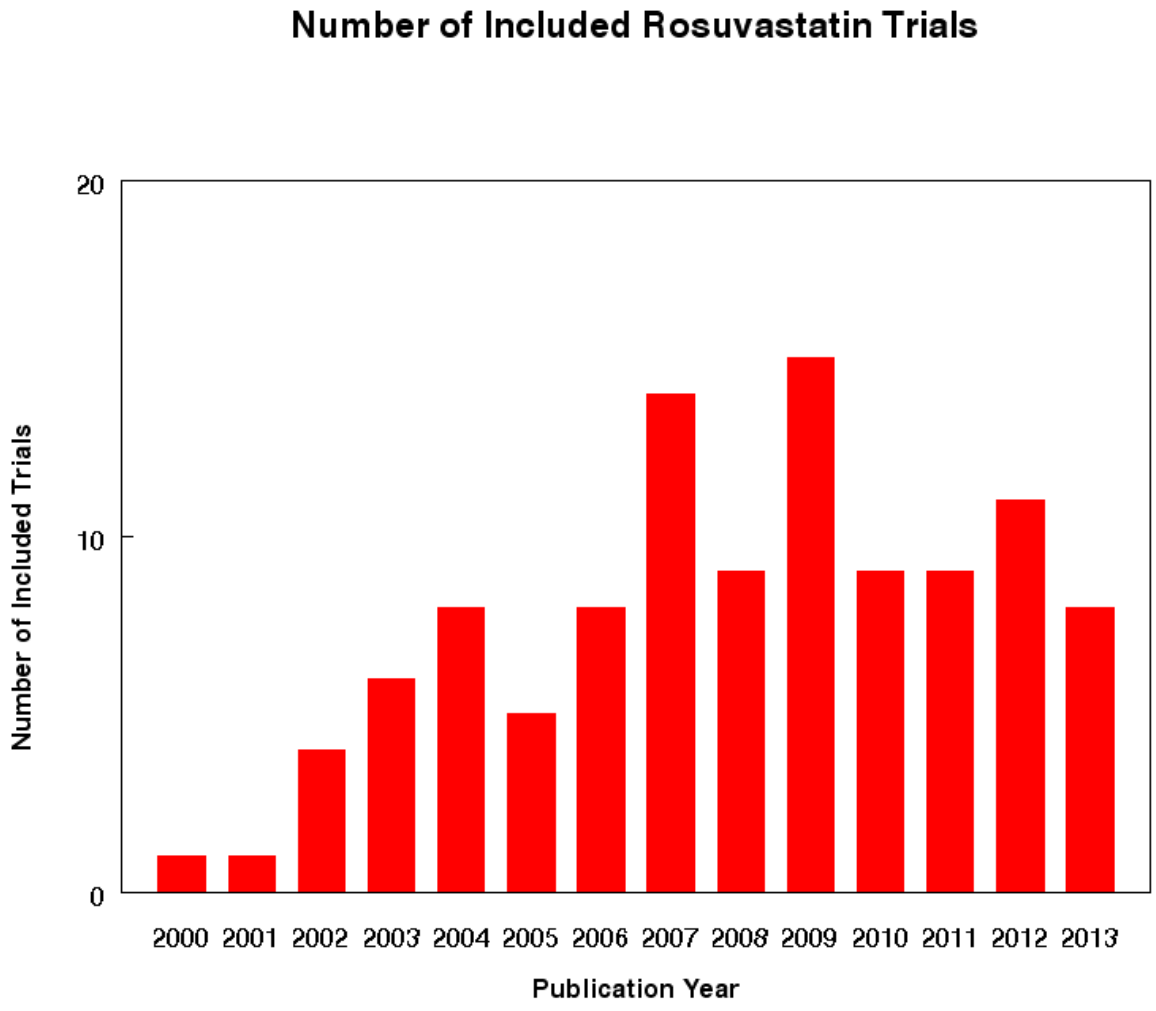
Database searching identified 18,377 citations and 577 other resource citations giving a total of 18,954 records. After irrelevant records and duplicates were removed, 9228 records remained. From these remaining records 278 were obtained as full-text articles assessed for eligibility and 30 articles are awaiting classification (Figure 1).

Included studies

Two-hundred and sixteen citations to 108 trials met the inclusion criteria and had extractable data to evaluate the dose-related blood lipid-lowering effect of rosuvastatin from these 265 full-text articles. Each included study is summarized in the Characteristics of included studies table. The publication languages of the 108 included studies were 98 (91%) English, two (1.8%) Russian, five (4.6%) Chinese, two (1.8%) Japanese and one (0.9%) Hungarian.

Of the 18 placebo-controlled trials, 15 (83.3%) were double-blind, two (11.1%) were single-blind, and one (5.6%) was an open-label trial. Trials evaluating the lipid-altering efficacy of rosuvastatin were first published in 2000. Between 2000 and 2013 the number of available studies increased and then decreased. The year with the most available studies was 2009 (Figure 2).

Figure 2.



The baseline mean (range) lipid parameters were as follows: total cholesterol, 6.9 (4.5 to 15.0) mmol/L, 265 (175 to 580) mg/dL; LDL-cholesterol, 4.6 (2.5 to 13.3) mmol/L, 178 (96 to 514) mg/dL; HDL-cholesterol 1.26 (0.75 to 1.71) mmol/L, 48.6 (29.0 to 66.1) mg/dL; non-HDL-C 5.6 (3.1 to 14.1) mmol/L, 217 (121 to 544) mg/dL and triglycerides, 2.1 (0.8 to 5.8) mmol/L,189 (71 to 511) mg/dL. Trials were available over the dose range of rosuvastatin from 1 to 80 mg daily and were sufficient to generate dose-response regression lines for each of these lipid parameters (Figure 3; Figure 4; Figure 5; Figure 6; Figure 7).

Figure 3. Values represent the results of each trial for each dose comparison. The standard error bars cannot be seen because they all lie within the points.

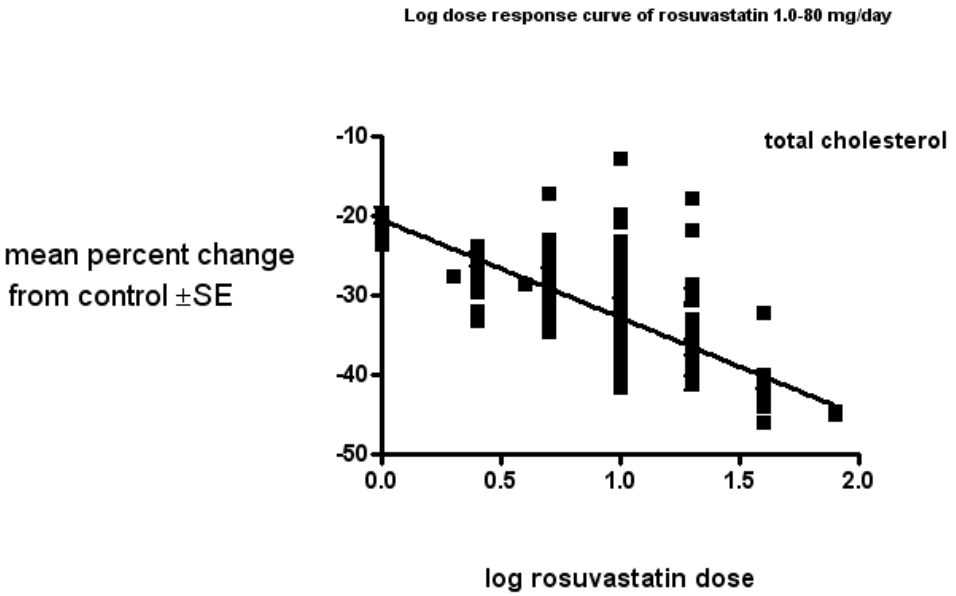


Figure 4. Values represent the results of each trial for each dose comparison. The standard error bars cannot be seen because they all lie within the points.

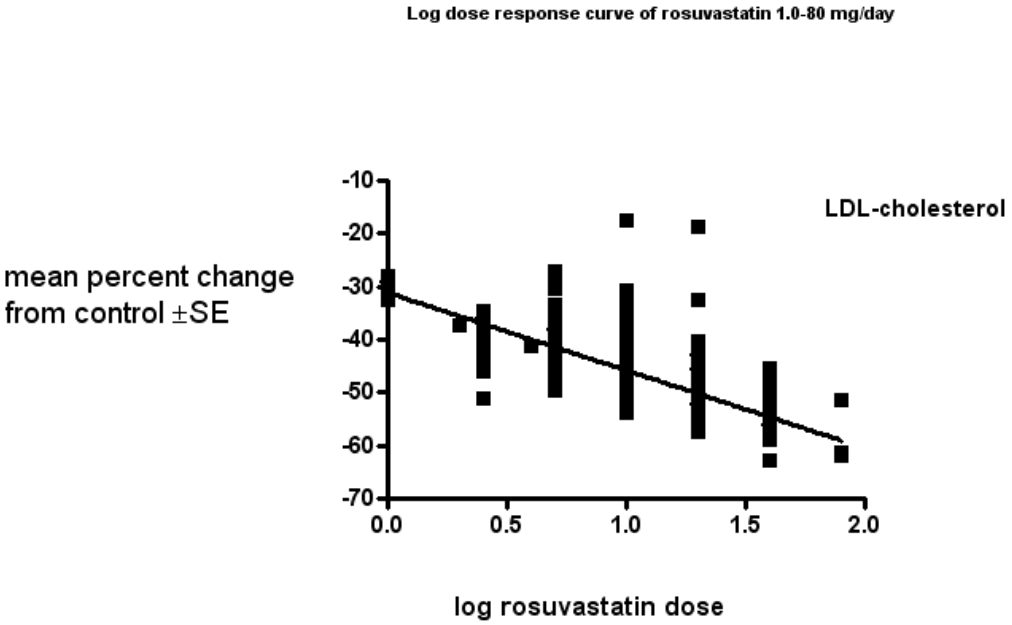


Figure 5. Values represent the results of each trial for each dose comparison. The standard error bars cannot be seen because they all lie within the points.

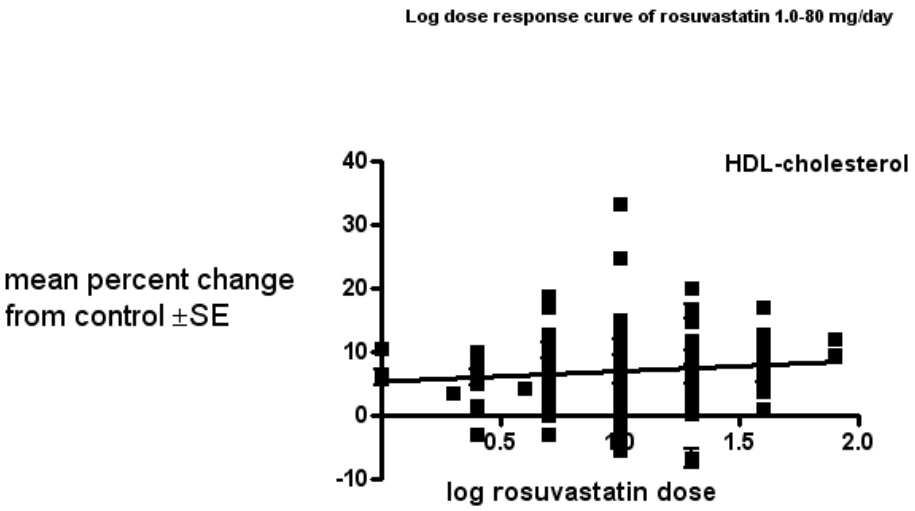


Figure 6. Values represent the results of each trial for each dose comparison. The standard error bars cannot be seen because they all lie within the points.

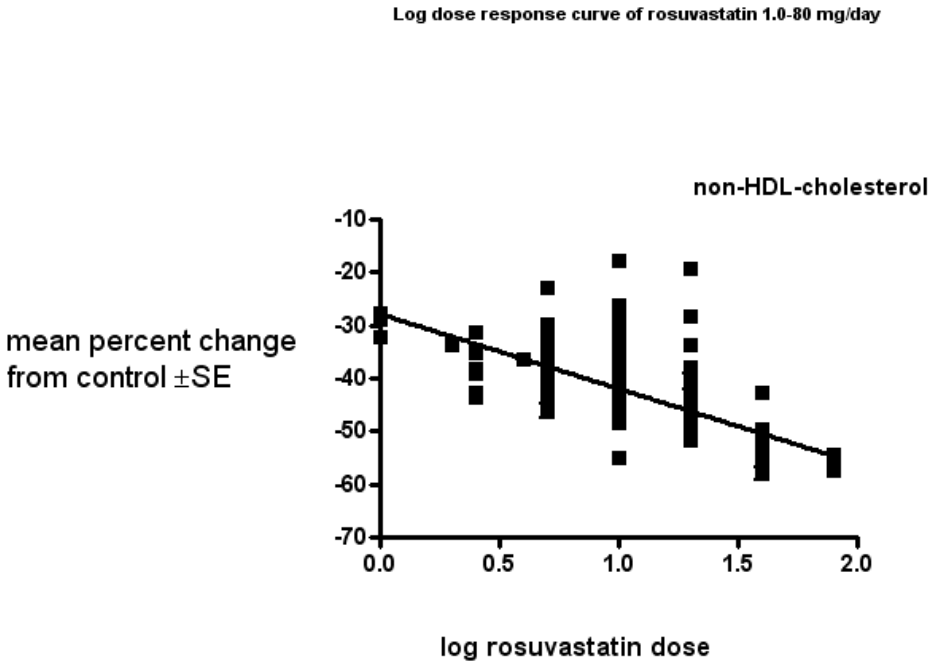
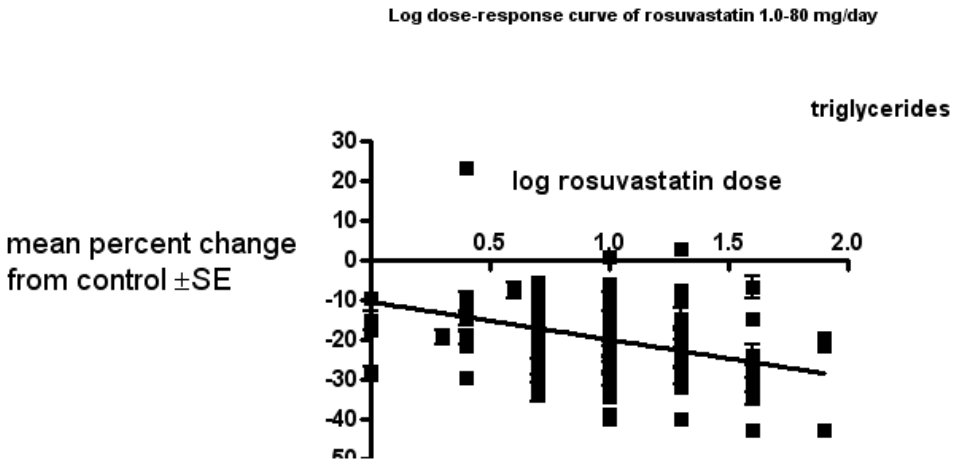


Figure 7. Values represent the results of each trial for each dose comparison. The standard error bars cannot be seen because they all lie within the points.



Excluded studies

Thirty-one studies were excluded because they did not meet the inclusion criteria. Reasons for exclusion included failure to report the number of participants, confounding, sequential data, inappropriate dosing, pooled data, attrition bias, and inadequate dietary baseline stabilization period. The reasons for excluding each trial are listed in the Characteristics of excluded studies table.

Risk of bias in included studies

Sequence generation could not be applied to the 90 before-and-after trials and one open-label placebo-controlled trial. Of the 15 double-blind randomized placebo-controlled trials, two (13.3%) reported adequate sequence generation. This suggests a high risk of bias for sequence generation.

Allocation

Allocation concealment could not be applied to the 90 before-and-after trials and one open-label placebo-controlled trial. Of the 15 double-blind randomized placebo-controlled trials, two (13.3%) reported adequate allocation concealment. This suggests a high risk of bias for allocation concealment.

Blinding

There was a high risk of blinding bias for all the before-and-after trials plus the open-label placebo-controlled trial RCT. However, lack of blinding probably had little effect on the primary outcomes, which were laboratory measurements of lipid parameters. Lack of blinding is likely to have had an effect on the ascertainment of withdrawals due to adverse effects (WDAEs).

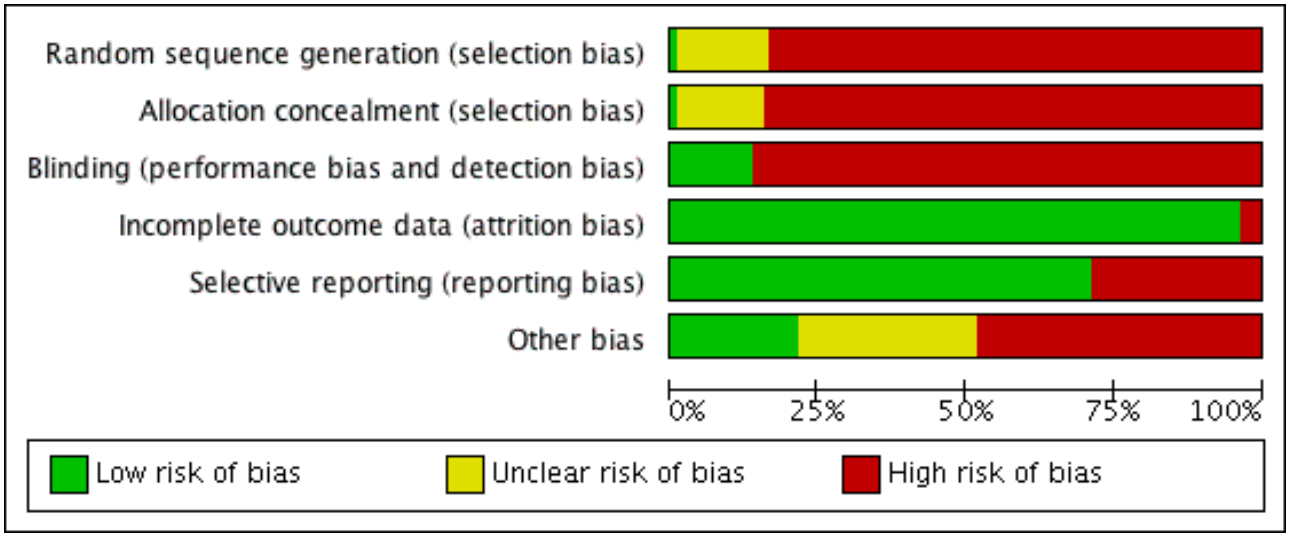
Incomplete outcome data

Incomplete outcome reporting leading to attrition bias was not a problem in this review as few participants were lost to follow-up and 96% of the participants completed the treatment.

Selective reporting

Out of 108 trials, 78 (72.2%) reported all relevant lipid parameters and WDAEs, thus selection bias was a potential source of bias for all outcomes. (Figure 8).

Figure 8. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Other potential sources of bias

The main other potential source of bias is industry funding. Out of the 108 trials, 57 (52.8%) reported funding by industry, 24 (22.2%) reported no industry funding and in 27 (25%) trials, source of funding was not reported. Out of the 57 industry-funded trials 54 (94.7%) were funded by AstraZeneca, the manufacturer of rosuvastatin and three (5.6%) were funded by other pharmaceutical companies. The AstraZeneca-funded trials might be biased in favour of rosuvastatin and would be expected to overestimate the treatment effect while trials funded by rival pharmaceutical companies might be biased against rosuvastatin and be expected to underestimate the treatment effect. In trials where the source of funding was not reported, bias could be for or against the drug.

AstraZeneca-funded versus non-AstraZeneca-funded LDL-cholesterol efficacy data were available for the doses, 5, 10, 20, 40 mg/day. These data were analyzed separately using the generic inverse variance fixed-effect model in RevMan 5. This sensitivity analysis revealed that the lipid-lowering efficacy of rosuvastatin in AstraZeneca-funded versus non-AstraZeneca-funded trials showed statistically significant differences, but they were not consistently in one direction. The LDL-lowering effect (AstraZeneca versus non-AstraZeneca) was 5 mg/day (-39.88 versus -45.29) $P < 0.00001$; 10 mg/day (-46.44 versus -45.14) $P < 0.00001$; 20 mg/day (-49.46 versus -51.02) $P = 0.004$; 40 mg/day (-54.34 versus -56.30) $P = 0.0004$. These results show that AstraZeneca-funded trials are not necessarily biased towards a greater effect of rosuvastatin.

Assessment for publication bias was done by reviewing the funnel plots for all lipid outcomes with 10 or more trials. None of these funnel plots showed significant asymmetry

Effects of interventions

See: **Summary of findings for the main comparison** LDL-cholesterol lowering efficacy of rosuvastatin for all trials

Overall efficacy of rosuvastatin

Doses of 2 and 4 mg had only one trial each so the data are not shown in the Data and analyses section. The trials were included in calculating the log dose-response curve equations. Values from all data describing the efficacy of rosuvastatin to lower the lipid parameters from placebo and before-and-after trials were entered as generic inverse variance data separately into GraphPad Prism 4 to yield log dose-response curves for placebo and before-and-after trials. To compare slope results of placebo versus before-and-after trials t-tests were performed from the slopes and standard errors of the curves for total cholesterol, LDL-cholesterol, non-HDL-cholesterol and triglycerides. The results showed that there were no statistical differences between placebo trials and before-and-after trials for all the lipid parameters studied $P > 0.5$. This demonstrates that the two trial designs provide similar estimates of the lipid-lowering efficacy of rosuvastatin. In addition, two-tailed one sample t-tests were performed from the placebo-controlled trials to test for the difference between placebo mean effects and zero. HDL-cholesterol data were not analyzed because there was no dose response for this parameter. The results of these tests demonstrated the placebo means were not statistically different from zero: total cholesterol: 0.37 (95% CI -1.47 to 2.21) $P > 0.5$, LDL-cholesterol: -1.16 (95% CI -3.12 to 0.81) $0.2 < P < 0.5$, non-HDL-C: -0.74 (95% CI -2.205 to 0.73) $0.2 < P < 0.5$ and triglycerides: 0.72 (95% CI -3.84 to 5.28) $P > 0.5$. The evidence of lack of a placebo effect provided further justification for combining all the trials to determine the overall efficacy. This was done by entering all data into the RevMan 5 using the generic inverse variance model outside of this review (data and analysis are not shown). The mean parameters from this analysis are summarized in Table 1.

Dose-ranging effects of rosuvastatin on blood lipids as calculated from the slopes of the log dose-response curve equations

Data from all trials were also entered into GraphPad Prism 4 to yield a weighted least squares analysis based on the inverse of the square of the standard error for each lipid parameter in order to generate

weighted log dose-response curves for each of the lipid parameters below (Figure 3; Figure 4; Figure 5; Figure 6: Figure 7).

Total cholesterol

The effect of different doses of rosuvastatin on total cholesterol are shown in the Data and analysis section (Analysis 1.1; Analysis 2.1; Analysis 2.6; Analysis 3.1; Analysis 3.6; Analysis 4.1; Analysis 4.6; Analysis 5.1; Analysis 5.6; Analysis 6.1; Analysis 6.6; Analysis 7.1; Analysis 7.6). The analysis for total cholesterol yielded the log dose-response straight-line equation, y = -12.32 log(x) -20.46. This equation provides the best estimate of the mean reductions in blood total cholesterol from baseline for rosuvastatin doses ranging from 1 mg/day to 80 mg/day as it uses all the available data. Using this formula the calculated reductions in total blood cholesterol for the recommended doses of 5 to 40 mg per day was from 29% to 40%. For every two-fold dose increase there was a 3.7% (95% CI 3.3 to 4.1) per cent decrease in blood total cholesterol (Figure 3).

LDL-cholesterol

The effect of different doses of rosuvastatin on LDL-cholesterol are shown in the Data and analysis section (Analysis 1.2; Analysis 2.2; Analysis 2.7; Analysis 3.2; Analysis 3.7; Analysis 4.2; Analysis 4.7; Analysis 5.2; Analysis 5.7; Analysis 6.2; Analysis 6.7; Analysis 7.2; Analysis 7.7). The analysis for LDL-cholesterol yielded the log dose-response straight-line equation, y = -14.67 log(x) -31.11. This equation provides the best estimate of the mean reductions in blood LDL-cholesterol from baseline for rosuvastatin doses ranging from 1 mg/day to 80 mg/day as it uses all the available data. Using this formula the calculated reductions in total blood LDL-cholesterol for the recommended doses of 5 to 40 mg per day was from 41% to 55%. For every two-fold dose increase there was a 4.42% (95% CI 3.85 to 4.99) per cent decrease in blood LDL-cholesterol (Figure 4).

HDL-cholesterol

The GraphPad Prism 4 analysis showed that rosuvastatin doses ranging from 1 mg/day to 80 mg/day had no dose related effect on blood HDL-cholesterol (Figure 5). All doses of rosuvastatin caused a small increase in HDL. When all trials and doses were pooled using generic inverse variance the magnitude of the increase was 7.3% [95% CI 7.1, 7.6].

Non-HDL-cholesterol

The effect of different doses of rosuvastatin on non-HDL-cholesterol are shown in the Data and analysis section (Analysis 1.4; Analysis 2.4; Analysis 2.9; Analysis 3.4; Analysis 3.9; Analysis 4.4; Analysis 4.9; Analysis 5.4; Analysis 5.9; Analysis 6.4; Analysis 6.9; Analysis 7.4; Analysis 7.9). The analysis for non-HDL-cholesterol yielded the log dose-response straight-line equation, y = -14.11 log(x) -27.81. This equation provides the best estimate of the mean reductions in blood non-HDL-cholesterol from baseline for rosuvastatin doses ranging from 1 mg/day to 80 mg/day as it uses all the available data. Using this formula the calculated reductions in non-HDL-cholesterol for the recommended doses of 5 to 40 mg per day ranged from 38% to 50%. For every two-fold dose increase there was a 4.25% (95% CI 3.68 to 4.81) per cent decrease in blood non-HDL-cholesterol (Figure 6).

Triglycerides

The effect of different doses of rosuvastatin on triglycerides are shown in the Data and analysis section (Analysis 1.5; Analysis 2.5; Analysis 2.10; Analysis 3.5; Analysis 3.10; Analysis 4.5; Analysis 4.10; Analysis 5.5; Analysis 5.10; Analysis 6.5; Analysis 6.10; Analysis 7.5; Analysis 7.10). The analysis for triglycerides demonstrated that there was a very weak but statistically significant relationship between dose and reduction in triglycerides (Figure 7). The data summarized in the Additional Table 1 shows that the reduction in triglycerides over the recommended dose range of 5 to 40 mg per day was 18% to 27% (Table 1).

End of treatment variability

In nine of the 18 placebo-controlled trials it was possible to compare the end of treatment variability expressed as coefficient of variation of rosuvastatin for doses of 1, 2.5, 5, 10, 20, 40 and 80 mg/day with placebo. The Kruskal-Wallis test showed no statistically significant difference compared with placebo for end of treatment variability for total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides at all doses of rosuvastatin. There was not enough data to analyze non-HDL-cholesterol.

Withdrawal data

Ten (55.6%) of the 18 placebo-controlled trials reported WDAEs during the three- to 12-week treatment period. In two trials no participant discontinued treatment due to adverse effects or died during the study, therefore risk reduction was not estimable. There was no rosuvastatin dose-response relationship for WDAEs. A pooled estimate for all doses compared to placebo showed an risk ratio (RR) of 0.84 (95% CI 0.48 to 1.47) suggesting no effect of rosuvastatin on WDAEs in these short-term trials (Analysis 8.1).

Overall completeness and applicability of evidence

Male versus female participant data were available for the 10 mg/day dose. These data were analyzed separately for LDL-cholesterol-lowering efficacy using the generic inverse variance fixed-effect model in RevMan 5 outside of this review. The subgroup analysis revealed that the efficacy in male participants was less than in female participants. The efficacy (male versus female participant) was: (-45.07, -49.42) P = 0.02.

Familial versus non-familial participant data were available for the doses 5, 10, 20 and 40 mg/day. These data were analyzed separately for LDL-cholesterol-lowering efficacy using the generic inverse variance fixed-effect model in RevMan 5. The per cent reductions in familial patients versus non-familial were not consistently in one direction: 5 mg/day (-37.00, -41.37) P = 0.17; 10 mg/day (-48.54, -45.64) P = 0.001; 20 mg/day (-44.67, -50.66) P < 0.00001; and 40 mg/day (-55.70, -54.75) P = 0.21.

DISCUSSION

Summary of main results

Long-term, daily rosuvastatin intake is highly effective at lowering blood LDL-cholesterol concentrations and does so in a predictable dose-related manner. The Summary of findings for the main comparison documents the effect of rosuvastatin on LDL-cholesterol over the dose range of 2.5 to 40 mg/day, which is also the range for which this systematic review has the most data. Over this range, LDL-cholesterol is decreased by 39% to 55% (Summary

of findings for the main comparison). These large reductions reflect a reduction in synthesis of cholesterol by the liver and indicate that liver HMG CoA reductase is being inhibited by approximately one half over this dose range. This has significant implications beyond circulating LDL-cholesterol, as LDL-cholesterol is only one of many important biochemical products that are produced by the HMG CoA reductase pathway. Those other products, including co-enzyme Q10, heme A, vitamin D, steroid hormones and many other compounds are also likely to be reduced by about one half over this dose range. It is important to recognize that the long-term consequences of reduction of these products is presently unknown.

In the data and analysis section it can be seen that there are more trials and data with the before-and-after design than from placebo-controlled trials. For the doses where there is a large number of trials and participants, it can be seen that estimates of the effect of rosuvastatin on the lipid parameters are similar with the two different trial designs. This, plus the demonstration that the placebo effect was not different from zero, justified using generic inverse variance and displaying the combined estimates in Table 1. In addition all trial data were entered into GraphPad Prism 4 to calculate the regression lines shown in Figure 3; Figure 4; Figure 5; Figure 6; and Figure 7. The overall efficacy results from GraphPad Prism 4 provide the best estimate of the treatment effect, because it is based on a regression line calculated from all the data for all the doses. The estimates of the average treatment effect from the regression lines are similar to those shown in Table 1.

In this review we have reported on a number of outcomes: total cholesterol (HDL-cholesterol, LDL-cholesterol and triglycerides), non-HDL-cholesterol (LDL-cholesterol and triglycerides), and the individual components: HDL-cholesterol, LDL-cholesterol and triglycerides. In the review of atorvastatin non-HDL-cholesterol was not included. Adding non-HDL-cholesterol as an outcome in the rosuvastatin review was a considerable amount of additional work, but did not add any additional value. It would thus not be worth including in future reviews of other statins.

In this review it was established using regression analysis that there was a correlation between the baseline value and rosuvastatin effect on LDL-cholesterol when the effect was expressed as absolute change from baseline ($P < 0.0001$). There was no correlation between the baseline value and the rosuvastatin effect when the effect was expressed as per cent reduction from baseline ($P = 0.92$). This finding provides strong support for the fact that systematic reviews reporting the effect of statins on absolute changes in lipid parameters are problematic and misleading.

What is the effect of rosuvastatin on the end of treatment variability?

The end of treatment variabilities of rosuvastatin and placebo were compared in order to determine the effect of rosuvastatin on variability of blood lipids when expressed as coefficient of variation. Compared with placebo, rosuvastatin did not increase the coefficient of variation of blood total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides. This suggests that variability in lipid parameters is not increased or decreased by rosuvastatin, however it was based on a relatively small number of comparisons because the end of treatment standard deviation was often not reported.

Does rosuvastatin increase withdrawals due to adverse effects?

Ten of the 18 placebo-controlled trials (55.6%) reported withdrawals due to adverse effects (WDAEs). This analysis only represented 1330 participants, 873 who received rosuvastatin and 457 who received placebo. The results did not show a dose-response relationship of rosuvastatin for WDAE and the pooled estimate for all doses was a RR of 0.84 (95% CI 0.48 to 1.47), demonstrating uncertainty, but the possibility of a reduction or increase in risk remains. Since eight (44.4%) out of 18 placebo-controlled trials did not report WDAEs, there is a high risk of selective reporting bias for this outcome and the null effect may be a result of that bias. Furthermore, this analysis was limited to trials of three to 12 weeks' duration and thus does not reflect the adverse effects of rosuvastatin occurring after longer durations of intake. Furthermore, there is probably a high risk of patient selection bias in these trials as many of the patients studied were likely known to tolerate statins at baseline. Since the trials do not report on this it cannot be specifically assessed.

Overall completeness and applicability of evidence

This review included 108 trials with 19,596 participants. As such it provided us with robust evidence of the dose-related lipid-lowering effects of rosuvastatin. Practitioners can use this evidence to calculate the expected effect of doses of rosuvastatin commonly utilized in society. It is unlikely that further research will change these estimates appreciably. However, there was a fair amount of heterogeneity in many of the estimates and it is possible that this was due to differences in the populations being studied (e.g. gender or genetic differences) (Thompson 2005). To explore this, we compared in the trials where it was possible, the lipid-lowering efficacy of rosuvastatin between male and female participants plus between patients with familial and non-familial hypercholesterolaemia.

The subgroup analysis in male and female participants was limited to the 10 mg dose but showed that the effect in female participants was greater than in male participants. This may be real and would be important to confirm. If it is real, it could be due to the fact that on average women weigh less than men and thus the dose per kilogram is greater in women than men. This demonstrates why it is important for authors to report data separately by sex. If this had been done in most or all of the trials in this review it would have been possible to be more certain whether a sex difference in effect is real.

In a paper by (Choumerianou 2005), statins were less efficacious in lowering LDL-cholesterol in familial hypercholesterolaemia patients than in non-familial hypercholesterolaemia patients. This could have been a possible explanation for some of the heterogeneity found in the review. We we carried out a subgroup analysis comparing the efficacy of rosuvastatin in patients with familial and non-familial hypercholesterolaemia and we found no consistent differences between the two patient groups. More research is needed to determine whether the lipid-lowering efficacy is different in patients with familial hypercholesterolaemia compared to the rest of the population.

The profound and relatively consistent effect of rosuvastatin on lipid parameters shown in this review is well known to clinicians who treat patients with these drugs. This has implications to

statin trials as whether a patient is taking a statin or not is most likely evident to investigators and patients involved in placebo-controlled RCTs. Thus knowledge of the lipid parameters almost certainly leads to loss of blinding in statin RCTs. The present review calls attention to that problem and future statin RCTs must be designed to prevent this loss of blinding bias.

Quality of the evidence

The summary of all 'Risk of bias' tools for the lipid effects suggests a high risk of bias for this review (Figure 8). However the lipid parameter outcomes, because they are performed in a laboratory separate from the conduct of the trial, are probably relatively free of bias. If anything, bias would lead to an overestimate of the lipid-lowering effects rather than an underestimate. However, because of the objectivity of the lipid measurements we think that the effect estimates are reasonably accurate. This view is strengthened by the fact that we could not show evidence of funding bias and review of funnel plots did not suggest evidence of publication bias.

That is not true for the outcome assessing harm and withdrawals due to adverse effects (WDAE). This could only be assessed in the placebo-controlled trials and this outcome was not reported in eight (44.4%) of the 18 placebo-controlled trials. There is therefore a high risk of selective reporting bias and this combined with the high risk of other biases means that we cannot be confident that the finding of no increase in WDAEs is correct (see Summary of findings for the main comparison).

The most likely place to find evidence of funding bias was by comparing AstraZeneca-funded trials where an overestimate of the effect might be expected and non-AstraZeneca-funded trials where a bias towards underestimating the effect of rosuvastatin may be expected. The fact that this comparison did not show a consistent effect one way or the other suggests that lipid measurements are relatively resistant to bias.

Potential biases in the review process

One limitation of this review is that many trials did not report standard deviations for the lipid-lowering effects. In those trials the standard deviation of the per cent change from baseline of the blood lipid parameters were imputed as the average of this parameter from trials that reported it. These values were determined by the method of (Furukawa 2006). Such imputation might weight some studies more or less; however, this has been shown in other reviews not to have much effect on the estimate of the effect size (Heran 2008). Another limitation is that in this review few studies were available to demonstrate the effect of rosuvastatin at very low and very high doses.

Agreements and disagreements with other studies or reviews

The best estimate of the mean per cent reduction in blood LDL-cholesterol for any dose of rosuvastatin can be calculated from our log dose-response equation. Using this equation y = -14.67 log(x) -31.11, a rosuvastatin dose of 40 mg/day reduces LDL-cholesterol by an average of 54.3%. This is within the range of 53.6% to 58.8% reduction in LDL-cholesterol from the five comparative trials from the Drug Effectiveness Review Project (DERP) (Smith 2009), but significantly lower than the manufacturers prescribing information estimate of 63% (Crestor Prescribing Information 2015).

Comparison of the effect with other statins

The greatest value in doing this type of review is the ability to compare rosuvastatin to other statins. At present we can only compare it to atorvastatin, which has been reviewed using the same protocol. When this comparison is done, the slope of the dose-response relationship for total cholesterol is similar for atorvastatin (-12.75) and rosuvastatin (-12.32). This is consistent with the two drugs acting by a similar mechanism. However, rosuvastatin is more potent than atorvastatin meaning that the same reduction in total cholesterol requires less drug for rosuvastatin than atorvastatin. For example, rosuvastatin at a dose of 10 mg day reduces total cholesterol by 33%; the dose of atorvastatin to achieve the same reduction in cholesterol is 29 mg. Making the same comparison for LDL-cholesterol rosuvastatin 10 mg reduces it on average by 46%; the dose of atorvastatin to achieve the same reduction is 30 mg. Therefore, in terms of reduction in LDL-cholesterol, rosuvastatin is three-fold more potent. The dose-response slope for atorvastatin for LDL-cholesterol (-18.13) was statistically greater than rosuvastatin (-14.67), however, in view of the similar slope for total cholesterol, we think that this does not reflect a difference in the mechanism whereby these 2 drugs lower cholesterol in humans.

The three-fold difference in potency between rosuvastatin and atorvastatin shown in this review is greater than the common thinking that rosuvastatin is two-fold more potent than atorvastatin and that 5 to 40 mg of rosuvastatin is approximately equipotent to 10 to 80 mg of atorvastatin.

In contrast to the three-fold greater potency of rosuvastatin on LDL-cholesterol, there is very little difference in potency between the two drugs when it comes to the effect on triglycerides: 10 to 20 mg of rosuvastatin and atorvastatin reduce triglycerides by 21% and 19% respectively, whereas 40 to 80 mg of rosuvastatin and atorvastatin reduce triglycerides by 27% and 30% respectively (Table 1).

When comparing the effect of the two drugs on HDL-cholesterol both rosuvastatin and atorvastatin do not show a dose-related effect and both increase HDL by a small amount. The effect of rosuvastatin on HDL, 7.3% (95%CI 7.1 to 7.6) is significantly greater than the effect of atorvastatin on HDL, 4.1% (95%CI 3.9 to 4.2).

At the present time there is nothing to suggest that one statin is different than another statin in terms of the benefit in reduction of atherosclerotic-related events: myocardial infarction and ischaemic stroke (Taylor 2013). Therefore there is no reason to suggest that the differences demonstrated in this review between atorvastatin and rosuvastatin on surrogate outcomes, would lead to any advantages in terms of the use of statins clinically. It will be useful to complete the reviews of the other statins to know how they compare in terms of the effects on the lipid surrogate outcomes.

AUTHORS' CONCLUSIONS

Implications for practice

Specific findings of the review

1. Rosuvastatin 1 to 80 mg/day causes a linear dose-response reduction in the per cent change from control of blood total cholesterol, LDL-cholesterol, non-HDL-cholesterol and triglycerides, but not for HDL-cholesterol. Manufacturer-recommended rosuvastatin doses of 10 to 40 mg/day resulted

in 45.8% to 54.6% decreases of LDL-cholesterol. From the slope of the lines there was a 3.7%, 4.4%, and 4.2% decrease in blood total cholesterol, LDL-cholesterol, and non-HDL-cholesterol, respectively, for every two-fold dose increase.

2. Based on an informal comparison rosuvastatin was determined to be about three-fold more potent than atorvastatin in reducing total cholesterol and LDL-cholesterol.

3. The percentage LDL-lowering effect of rosuvastatin was similar in individuals with familial hypercholesterolaemia and the general population.

4. All doses of rosuvastatin did not change WDAEs as compared to placebo (RR 0.84; 95% CI 0.48 to 1.47). However, there is a high risk of bias for this outcome and thus it cannot be considered a reliable estimate.

Implication of these findings

Rosuvastatin lowers lipid parameters in a dose-related fashion that is similar to but more potent than atorvastatin; 30 mg of atorvastatin is required to lower total cholesterol and LDL-cholesterol as much as 10 mg of rosuvastatin.

Implications for research

1. More randomized controlled trials (RCTs) for rosuvastatin doses of 1 and 80 mg/day are needed as well as for higher and lower doses to improve the estimate of the dose-response efficacy of rosuvastatin.

2. All placebo-controlled RCTs must accurately report WDAEs.

3. All trials should report the effects separately in men and women so it is possible to determine if there are any clinically significant dose-related sex differences.

4. Further systematic reviews comparing the lipid-lowering effect of rosuvastatin both directly and indirectly with other statins are needed.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Agouridis 2011

Methods	4-week washout period 12-week before-and-after trial
Participants	90 men and women mean age 55 years with mixed dyslipidaemia LDL-C > 160 mg/dl (> 4.14 mmol/l TG > 200 mg/dl (> 2.26 mmol/l) 30 participants randomized to rosuvastatin 40 mg/day

Agouridis 2011 *(Continued)*

	30 participants randomized to rosuvastatin 40 mg/day + fenofibrate 200 mg/day 30 participants randomized to rosuvastatin 40 mg/day + 2 g n-3 fatty acids/day exclusion criteria: known coronary heart disease or atherosclerosis TG > 500 mg/dl (> 5.645 mmol/l), renal disease, diabetes mellitus hypothyroidism, liver disease or dysfunction and medical conditions that would interfere with trial completion uncontrolled hypertension Rosuvastatin 40 mg/day baseline TC : 7.86 mmol/l (304 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 5.28 mmol/l (204 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.29 mmol/l (50 mg/dl) Rosuvastatin 40 mg/day baseline non-HDL-C: 6.54 mmol/l (253 mg/dl)
Interventions	rosuvastatin 40 mg/day rosuvastatin 40 mg/day + fenofibrate 200 mg/day rosuvastatin 40 mg/day + 2 g n-3 fatty acids/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, and non-HDL-C
Notes	rosuvastatin 40 mg/day + fenofibrate 200 mg/day rosuvastatin 40 mg/day + 2 g n-3 fatty acids/day groups were not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of random sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all subjects were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	triglyceride data was not reported
Other bias	Low risk	trial was not funded by industry

Andreou 2010

Methods	4-week washout period 4-week randomized, double-blind, placebo-controlled trial
Participants	65 men and women age 44-80 years with chronic heart failure 18 randomized to placebo 21 randomized to rosuvastatin 10 mg/day 21 randomized to allopurinol 300 mg/day exclusion criteria: acute coronary syndromes during the last 6 months diabetes mellitus, cancer, RA, infections, pulmonary disease, thyroid disease liver dysfunction, severe hyperlipidaemia, renal dysfunction Placebo baseline TC : 5.61 mmol/l (217 mg/dl) Placebo baseline LDL-C : 3.93 mmol/l (152 mg/dl) Placebo baseline HDL-C : 1.06 mmol/l (41 mg/dl) Rosuvastatin 10 mg/day baseline TC : 5.77 mmol/l (223 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.80 mmol/l (147 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.22 mmol/l (47 mg/dl)
Interventions	Placebo Rosuvastatin 10 mg/day Allopurinol 300 mg/day
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C and HDL-C
Notes	Allopurinol 300 mg/day group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	5/65= 7.7% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	High risk	Triglycerides and WDAEs were not included in the analysis
Other bias	Low risk	There is no conflict of interest related with the present manuscript

ANDROMEDA 2007

Methods	4-week washout period 8-week randomized, double-blind study
Participants	509 men and non-pregnant women age ≥ 18 years with type 2 diabetes glucose ≥ 7.0 mmol/l TG ≤ 6.0 mmol/l (531 mg/dl) 254 received rosuvastatin 255 received atorvastatin exclusion criteria: type 1 diabetes mellitus, glycated haemoglobin > 9.0 % history of cardiovascular disease or familial hypercholesterolaemia uncontrolled hypertension CK > 3 X ULN Rosuvastatin 10 mg/day baseline TC : 5.5 mmol/l (213 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.4 mmol/l (131 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.2 mmol/l (46 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.0 mmol/l (177 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 4.3 mmol/l (166 mg/dl)
Interventions	Rosuvastatin 10 mg/day for 8 weeks Rosuvastatin 20 mg/day from 8-16 weeks Atorvastatin 10 mg/day for 8 weeks Atorvastatin 20 mg/day from 8-16 weeks
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Rosuvastatin 20 mg/day from 8-16 weeks Atorvastatin 10 mg/day for 8 weeks Atorvastatin 20 mg/day from 8-16 weeks groups were not included in the analysis SD was imputed for triglycerides

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of random sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable

ANDROMEDA 2007 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	the rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	14/254 were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the study. Data may support bias for rosuvastatin

ARIES 2006

Methods	6-week washout period 6-week before-and-after trial
Participants	774 African-American men and women age ≥ 18 years with type IIa or IIb hypercholesterolaemia LDL-C ≥160 mg/dl and ≤300 mg/dl (≥4.14 mmol/l and 7.76 mmol/l) TG < 400 mg/dl (4.52 mmol/l) 391 randomized to rosuvastatin 383 randomized to atorvastatin exclusion criteria: homozygous familial hypercholesterolaemia or type I, III, or V hyperlipoproteinaemia active arterial disease, uncontrolled hypertension, poorly controlled diabetes mellitus, active liver disease or dysfunction serum CK > 3 X ULN Rosuvastatin 10 mg/day baseline TC : 7.00 mmol/l (271 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.96 mmol/l (192 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.33 mmol/l (51 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.54 mmol/l (136 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.67 mmol/l (219 mg/dl) Rosuvastatin 20 mg/day baseline TC : 7.01 mmol/l (271 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 4.90 mmol/l (189 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.36 mmol/l (53 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.62 mmol/l (143 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C: 5.645 mmol/l (218 mg/dl)
Interventions	Rosuvastatin 10 mg/day Rosuvastatin 20 mg/day Atorvastatin 10 mg/day Atorvastatin 20 mg/day
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C

ARIES 2006 *(Continued)*

Notes	Atorvastatin 10 mg/day Atorvastatin 20 mg/day groups were not included in the analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day and Rosuvastatin 20 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day and Rosuvastatin 20 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day and Rosuvastatin 20 mg/day treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	9/195 were not included in the efficacy analysis for rosuvastatin 10 mg/day 7/196 were not included in the efficacy analysis for rosuvastatin 20 mg/day 4.1 % participants receiving rosuvastatin were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were measured
Other bias	High risk	This research was supported by AstraZeneca. Data may support bias for rosuvastatin

AstraZeneca 2010a

Methods	4-week washout period 0 to 6-week randomized double-blind trial 6 to 12-week open-label trial
Participants	436 men and women ≥ 18 years with hypercholesterolaemia LDL-C ≥ 3.36 mmol/l (130 mg/dl) and < 6.50 mmol/l (250 mg/dl) TG < 4.52 mmol/l (400 mg/dl) history of CHD or a CHD risk equivalent clinical evidence of atherosclerosis 10 year CHD risk of ≥10% 145 patients were randomized to rosuvastatin 5 mg/day for 0-6 weeks 145 patients were randomized to rosuvastatin 10 mg/day for 0-6 weeks

AstraZeneca 2010a *(Continued)*

	146 patients were randomized to atorvastatin 10 mg/day for 0 to 6 weeks 36 patients were titrated from 5 mg to 10 mg rosuvastatin for 6-12 weeks 23 patients were titrated from 10 mg to 20 mg rosuvastatin for 6-12 weeks exclusion criteria: none reported Rosuvastatin 5 mg/day baseline LDL-C : 4.24 mmol/l (164 mg/dl) Rosuvastatin 5 mg/day baseline TG : 1.92 mmol/l (170 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.13 mmol/l (160 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.04 mmol/l (181 mg/dl)
Interventions	rosuvastatin 5 mg/day for 0-6 weeks rosuvastatin 10 mg/day for 0-6 weeks atorvastatin 10 mg/day for 0-6 weeks titrated from 5 mg to 10 mg rosuvastatin for 6-12 weeks titrated from 10 mg to 20 mg rosuvastatin for 6-12 weeks
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	atorvastatin 10 mg/day for 0 to 6 weeks titrated from 5 mg to 10 mg rosuvastatin for 6-12 weeks titrated from 10 mg to 20 mg rosuvastatin for 6-12 weeks groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day for 0-6 weeks and Rosuvastatin 10 mg/day for 0-6 weeks treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day for 0-6 weeks and Rosuvastatin 10 mg/day for 0-6 weeks treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day for 0-6 weeks and Rosuvastatin 10 mg/day for 0-6 weeks treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	rosuvastatin 5 mg/day group 9-11/145 (6.2-7.6)% patients were not included in the efficacy analysis rosuvastatin 10 mg/day group 6/145 (4.1%) patients were not included in the efficacy analysis

AstraZeneca 2010a *(Continued)*

Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the study. Data may support bias for rosuvastatin

AstraZeneca 2010b

Methods	no washout required because participants were not receiving any lipid-altering agents for at least 6 months 8-week randomized, double-blind, placebo-controlled trial
Participants	334 men and women with hypertriglyceridaemia mean age 52 years TG 200-800 mg/dL (2.26-9.03) mmol/l 111 randomized to placebo 111 randomized to rosuvastatin 10 mg/day 112 randomized to rosuvastatin 20 mg/day exclusion criteria: high LDL-C, unstable cardiovascular condition or awaiting a myocardial revascularization congestive heart failure, uncontrolled diabetes mellitus cancer, uncontrolled hypothyroidism, familial hypercholesterolaemia, liver/muscle disease, pregnancy Placebo baseline TC : 5.53 mmol/l (214 mg/dl) Placebo baseline LDL-C : 3.36 mmol/l (130 mg/dl) Placebo baseline HDL-C : 0.84 mmol/l (32 mg/dl) Placebo baseline non-HDL-C : 4.71 mmol/l (182 mg/dl) Placebo baseline TG : 3.49 mmol/l (309 mg/dl) Rosuvastatin 10 mg/day baseline TC : 5.61 mmol/l (216 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.34 mmol/l (129 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 0.87 mmol/l (34 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C : 4.64 mmol/l (179 mg/dl) Rosuvastatin 10 mg/day baseline TG : 3.61 mmol/l (320 mg/dl) Rosuvastatin 20 mg/day baseline TC : 5.57 mmol/l (215 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 3.37 mmol/l (130 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 0.88 mmol/l (34 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C : 4.63 mmol/l (179 mg/dl) Rosuvastatin 20 mg/day baseline TG : 3.35 mmol/l (297 mg/dl)
Interventions	Placebo Rosuvastatin 10 mg/day Rosuvastatin 20 mg/day
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, non-HDL-C and Triglycerides
Notes	SDs were imputed

AstraZeneca 2010b *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	WDAEs were not reported
Other bias	High risk	AstraZeneca funded the trial

ASTRO-2 2009

Methods	no washout required because participants were not receiving any lipid-altering agents for at least 2 months 8-week open-label, randomized study
Participants	877 men and women age > 20 years with hypercholesterolaemia 442 randomized to rosuvastatin 5 mg/day 435 randomized to atorvastatin 10 mg/day exclusion criteria: severe hypertension, type 1 diabetes mellitus, familial hypercholesterolaemia fasting TG > 400 mg/dL, MI or cerebrovascular disorder within 3 months prior to the start of the study serious cardiac insufficiency, revascularization during the study period active hepatic disease, renal dysfunction, pregnancy or possible pregnancy, hypothyroidism muscle disease, drug and alcohol abuse
Interventions	rosuvastatin 5 mg/day atorvastatin 10 mg/day
Outcomes	per cent change from baseline at 8 weeks of plasma LDL-C, HDL-C and triglycerides
Notes	atorvastatin 10 mg/day data were not analyzed
Risk of bias	

ASTRO-2 2009 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	8/450 (1.8%) participants were not included in the efficacy analysis
Selective reporting (reporting bias)	High risk	TC and non-HDL-C data were not provided
Other bias	Low risk	Industry did not fund the trial

ASTRONOMER 2010

Methods	no washout required because participants were not receiving any lipid-altering agents 12-week randomized, double-blind, placebo-controlled trial
Participants	269 men and women age 18-82 years with aortic stenosis 135 randomized to placebo 134 randomized to rosuvastatin 40 mg/day exclusion criteria: Patients with clinical indications for the use of statins as defined by Canadian guidelines such as coronary artery disease cerebrovascular disease, peripheral vascular disease, diabetes and Asian participants Placebo baseline LDL-C : 3.12 mmol/l (121 mg/dl) Placebo baseline HDL-C : 1.55 mmol/l (60 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 3.18 mmol/l (123 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.59 mmol/l (58 mg/dl)
Interventions	Placebo Rosuvastatin 40 mg/day
Outcomes	per cent change from baseline at 12 weeks of blood LDL-C and HDL-C
Notes	SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement

ASTRONOMER 2010 *(Continued)*

Random sequence generation (selection bias)	Low risk	centralized and generated by computer program a third party AstraZeneca Canada Inc
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind "patients, site coordinators, investigators and statisticians were blinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	TC, TGs and WDAEs were not reported
Other bias	High risk	this trial was partially funded by AstraZeneca

ATOROS 2006

Methods	6-week washout period 18-week randomized open-label study
Participants	120 men and women with primary hyperlipidaemia TC > 240 mg/dl (6.2 mmol/l) TG < 350 mg/dl (4.0 mmol/l) 60 patients were randomized to rosuvastatin 60 patients were randomized to atorvastatin exclusion criteria: liver disease or dysfunction, renal dysfunction diabetes mellitus, raised TSH medical condition that could affect outcome of trial Rosuvastatin 10 mg/day baseline TC : 7.37 mmol/l (285 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 5.3 mmol/l (205 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.24 mmol/l (48 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.8 mmol/l (159 mg/dl)
Interventions	Rosuvastatin 10 mg/day 0-6 weeks Rosuvastatin 10 or 20 mg/day 6-24 weeks Atorvastatin 20 mg/day for 0-6 weeks Atorvastatin 20 or 40 mg/day for 6-24 weeks
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	Rosuvastatin 10 or 20 mg/day 6-24 weeks Atorvastatin 20 mg/day for 0-6 weeks

ATOROS 2006 *(Continued)*

	Atorvastatin 20 or 40 mg/day for 6-24 weeks
	groups were not included in the analysis
	SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Low risk	No company nor institution supported the trial financially

Ballantyne 2003

Methods	6-week washout
	12-week randomized open-label trial
Participants	623 men and women mean age 60 years with and without metabolic syndrome
	LDL-C ≥ 160 and < 250 mg/dl (≥ 4.14 and < 6.46 mmol/l)
	TG <400 mg/dl (< 4.52 mmol/l)
	194 metabolic syndrome patients received rosuvastatin 10 mg/day
	382 non-metabolic syndrome patients received rosuvastatin 10 mg/day
	576 patients received rosuvastatin 10 mg/day
	exclusion criteria: none
	Metabolic syndrome group:
	Rosuvastatin 10 mg/day baseline LDL-C : 4.84 mmol/l (187 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.14 mmol/l (44 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.44 mmol/l (216 mg/dl)
	Rosuvastatin 10 mg/day baseline non-HDL-C: 5.94 mmol/l (230 mg/dl)
	Non-metabolic syndrome group:

Ballantyne 2003 *(Continued)*

	Rosuvastatin 10 mg/day baseline LDL-C : 4.81 mmol/l (186 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.40 mmol/l (54 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.75 mmol/l (155 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.61 mmol/l (217 mg/dl) Combined groups: Rosuvastatin 10 mg/day baseline LDL-C : 4.82 mmol/l (186 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.31 mmol/l (51 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.98 mmol/l (175 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.72 mmol/l (221 mg/dl)
Interventions	Rosuvastatin 10 mg/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	TC was calculated from HDL-C and non-HDL-C

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	There was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	There was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	There was only one group of participants analyzed therefore it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	47/623 (7.5%) were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the study. Data may support bias for rosuvastatin

Ballantyne 2004

Methods	6-week washout period 6-week before-and-after trial evening doses
Participants	153 men and women with severe hypercholesterolaemia age ≥ 18 years LDL-cholesterol 190-400 mg/dl (4.9-10.3 mmol/l) TG < 400 mg/dl (4.5 mmol/l) all participants received 40 mg/day rosuvastatin exclusion criteria: liver disease, active arterial disease, cancer history, uncontrolled hypertension or hypothyroidism,

Ballantyne 2004 *(Continued)*

	homozygous familial hypercholesterolaemia or familial dysbetalipoproteinaemia, use of medications known to affect lipid measurements, present a safety concern or interfere with trial participation Rosuvastatin 40 mg/day baseline TC : 8.84 mmol/l (342 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 6.65 mmol/l (257 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.24 mmol/l (48 mg/dl) Rosuvastatin 40 mg/day baseline TG : 2.06 mmol/l (182 mg/dl)
Interventions	Rosuvastatin 40 mg/day
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	There was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	There was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	There was only one group of participants analyzed therefore it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded it. Data may support bias for rosuvastatin

Bellia 2010

Methods	3-week washout period 4-week randomized single-blind trial
Participants	29 men and women age 40-60 years with type 2 diabetes mellitus BMI < 30, good glycaemic control, LDL-C > 2.58 mmol/l (> 100 mg/dl) 14 randomized to rosuvastatin 15 randomized to simvastatin exclusion criteria: history of cardiovascular, neoplastic or other systemic diseases Rosuvastatin 20 mg/day baseline TC : 5.01 mmol/l (194 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 3.46 mmol/l (134 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 0.88 mmol/l (34 mg/dl)

Bellia 2010 *(Continued)*

	Rosuvastatin 20 mg/day baseline non-HDL-C: 4.13 mmol/l (160 mg/dl)
Interventions	Rosuvastatin 20 mg/day Simvastatin 20 mg/day
Outcomes	per cent change from baseline at 4 weeks of serum TC, LDL-C, HDL-C and non-HDL-C
Notes	Simvastatin 20 mg/day group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 20 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 20 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 20 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	triglycerides were not included in the efficacy analysis because they were expressed as medians
Other bias	Low risk	study was not funded by pharmaceutical industry

Briseno 2010

Methods	12-week washout period 8-week open study
Participants	187 men and women with dyslipidaemia Patients were classified according to their vascular risk factors based on the NCEP ATP III 2001 recommendations 98 were randomized to rosuvastatin 10 mg/day 89 were randomized to ezetimibe/simvastatin 10/20 mg/day exclusion criteria: not taking medications appropriately combining test drugs with other lipid-lowering agents baseline or final data were missing Rosuvastatin 10 mg/day baseline TC : 6.42 mmol/l (248 mg/dl)

Briseno 2010 *(Continued)*

	Rosuvastatin 10 mg/day baseline LDL-C : 4.32 mmol/l (167 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.15 mmol/l (44 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.18 mmol/l (193 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.76 mmol/l (223 mg/dl)
Interventions	rosuvastatin 10 mg/day ezetimibe/simvastatin 10/20 mg/day
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	ezetimibe/simvastatin 10/20 mg/day group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	Study was funded by AstaZeneca Mexico. Data may support bias for rosuvastatin

Brown 2002

Methods	6-week washout period 52 week randomized double-blind trial
Participants	477 men and women age ≥ 18 years with hypercholesterolaemia LDL-C ≥160 and < 250 mg/dl (≥ 4.14 and < 6.465 mmol/l) TG ≤ 400 mg/dl (≤ 4.52 mmol/l) 123 patients received 5 mg rosuvastatin 116 patients received 10 mg rosuvastatin 118 patients received 20 mg pravastatin

Brown 2002 *(Continued)*

	120 patients received 20 mg simvastatin exclusion criteria: active liver disease or dysfunction, renal dysfunction, familial hypercholesterolaemia, pregnancy or lactation active arterial disease within 3 months of trial, cancer history, uncontrolled hypertension, hypothyroidism serum CK > 3X ULN Rosuvastatin 5 mg/day baseline TC : 7.15 mmol/l (276 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 4.84 mmol/l (187 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.31 mmol/l (51 mg/dl) Rosuvastatin 5 mg/day baseline TG : 2.18 mmol/l (193 mg/dl) Rosuvastatin 5 mg/day baseline non-HDL-C: 5.84 mmol/l (226 mg/dl) Rosuvastatin 10 mg/day baseline TC : 7.05 mmol/l (273 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.84 mmol/l (187 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.29 mmol/l (50 mg/dl) Rosuvastatin 10 mg/day baseline TG : 4.64 mmol/l (411 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.76 mmol/l (223 mg/dl)
Interventions	Rosuvastatin 5 mg/day for 0-12 weeks Rosuvastatin 5-80 mg/day for 12-52 weeks Rosuvastatin 10 mg/day for 0-12 weeks Rosuvastatin 10-80 mg/day for 12-52 weeks Pravastatin 20 mg/day for 0-12 weeks Pravastatin 20-40 mg/day for 12-52 weeks Simvastatin 20 mg/day for 0-12 weeks Simvastatin 20-80 mg/day for 12-52 weeks
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Rosuvastatin 5-80 mg/day for 12-52 weeks Rosuvastatin 10-80 mg/day for 12-52 weeks Pravastatin 20 mg/day for 0-12 weeks Pravastatin 20-40 mg/day for 12-52 weeks Simvastatin 20 mg/day for 0-12 weeks Simvastatin 20-80 mg/day for 12-52 weeks groups were not included in the analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day for 0-12 weeks, 10 mg/day for 0-12 weeks and 20 mg/day for 0-12 weeks treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable

Brown 2002 *(Continued)*

Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day for 0-12 weeks, 10 mg/day for 0-12 weeks and 20 mg/day for 0-12 weeks treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day for 0-12 weeks, 10 mg/day for 0-12 weeks and 20 mg/day for 0-12 weeks treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	2/123 for rosuvastatin 5 mg/day were not included in the analysis 1/116 for rosuvastatin 10 mg/day were not included in the analysis 1.3% participants were not included in the analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	Trial was supported by AstraZeneca Pharmaceuticals. Data may support bias for rosuvastatin

CAP-Chol 2009

Methods	6-week washout period for participants with ongoing statin treatment no washout required for participants naive to all lipid-lowering treatment 8-week randomized double-blind trial
Participants	317 men and women ≥ 18 years with type IIa and IIb hypercholesterolaemia LDL-C > 160 mg/dl (> 4.14 mmol/l) in the presence of 2 other cardiovascular risk factors LDL-C > 130 mg/dl (> 3.36 mmol/l) in the presence of more than 2 other cardiovascular risk factors 110 patients were randomized to rosuvastatin 5 mg/day 104 patients were randomized to atorvastatin 10 mg/day 103 patients were randomized to pravastatin 40 mg/day exclusion criteria: familial hypercholesterolaemia, TG > 400 mg/dl (> 4.52 mmol/l) 10-year CHD risk > 20 % statin hypersensitivity, concomitant drug use not authorized during the study active liver disease, CPK > 3 X ULN, renal dysfunction poorly controlled hypertension or hypothyroidism
Interventions	rosuvastatin 5 mg/day atorvastatin 10 mg/day pravastatin 40 mg/day
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	atorvastatin 10 mg/day

CAP-Chol 2009 *(Continued)*

	pravastatin 40 mg/day
	groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	non-HDL-C was not included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the trial. Data may support bias for rosuvastatin

Capuzzi 2003

Methods	6-week washout period
	4-week randomized open study
	evening dosing
Participants	270 men and women age ≥ 18 years with combined hyperlipidaemia and low HDL-C
	TC ≥200 mg/dl (≥ 5.17 mmol/l)
	TG 200-800 mg/dl (2.26-9.03 mmol/l)
	HDL-C <45 mg/dl (<1.16 mmol/l)
	46 received rosuvastatin
	72 received niacin
	152 received rosuvastatin and niacin
	exclusion criteria: pregnancy or lactation, liver disease or dysfunction, active arterial disease within 3 months of trial
	uncontrolled hypertension or hypothyroidism
	CK > 3 X ULN use of concomitant medications known to affect serum lipid levels or potential safety concerns

Capuzzi 2003 *(Continued)*

	Rosuvastatin 40 mg/day baseline LDL-C : 3.78 mmol/l (146 mg/dl)
Interventions	Rosuvastatin 40 mg/day for 12 weeks ER niacin 2 g/day for 12 weeks Rosuvastatin/ER niacin 40 mg/1g/day for 12 weeks Rosuvastatin/ER niacin 10 mg/2g/day for 12 weeks
Outcomes	per cent change from baseline at 4,6,12 weeks of serum LDL-C
Notes	ER niacin 2 g/day for 12 weeks Rosuvastatin/ER niacin 40 mg/1g/day for 12 weeks Rosuvastatin/ER niacin 10 mg/2g/day for 12 weeks groups were not included in the analysis SD was imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	TC, HDL-C, TG and non-HDL-C were not included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the study. Data may support bias for rosuvastatin

Catapano 2006

Methods	4-week washout period 6-week double-blind randomized study
Participants	2959 men and women age 18-81 years LDL-C ≥ 145 mg/dl (≥3.7 mmol/l) and ≤ 250 mg/dl (≤ 6.5 mmol/l) TG ≤ 350 mg/dl (≤ 4.0 mmol/l)

Catapano 2006 *(Continued)*

	ALT, AST, CK ≤ 1.5 X ULN haemoglobin Alc < 9.0% in patients with diabetes 1481 received rosuvastatin 1478 received ezetimibe/simvastatin exclusion criteria: none Rosuvastatin 10 mg/day baseline TC : 6.7 mmol/l (259 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.5 mmol/l (174 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.3 mmol/l (50 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C : 5.33 mmol/l (206 mg/dl) Rosuvastatin 20 mg/day baseline TC : 6.7 mmol/l (259 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 4.5 mmol/l (174 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.3 mmol/l (50 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C : 5.35 mmol/l (207 mg/dl) Rosuvastatin 40 mg/day baseline TC : 6.7 mmol/l (259 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 4.5 mmol/l (174 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.3 mmol/l (50 mg/dl) Rosuvastatin 40 mg/day baseline non-HDL-C : 5.35 mmol/l (207 mg/dl)
Interventions	Rosuvastatin 10 mg/day Rosuvastatin 20 mg/day Rosuvastatin 40 mg/day EZ/simvastatin 10/20 mg/day EZ/simvastatin 10/40 mg/day EZ/simvastatin 10/80 mg/day
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and non-HDL-C
Notes	EZ/simvastatin 10/20 mg/day EZ/simvastatin 10/40 mg/day EZ/simvastatin 10/80 mg/day groups were not included in the analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day, Rosuvastatin 20 mg/day, Rosuvastatin 40 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day, Rosuvastatin 20 mg/day, Rosuvastatin 40 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day, Rosuvastatin 20 mg/day, Rosuvastatin 40 mg/day treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial

Catapano 2006 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	17/492 were not included in the efficacy analysis for rosuvastatin 10 mg/day 17/495 were not included in the efficacy analysis for rosuvastatin 20 mg/day 19/494 were not included in the efficacy analysis for rosuvastatin 40 mg/day 3.6 % participants were not included in the efficacy analysis
Selective reporting (reporting bias)	High risk	triglycerides were not included in the efficacy analysis
Other bias	High risk	Merck/Schering-Plough Pharmaceutical funded the study. Data may support bias against rosuvastatin

Celik 2012

Methods	participants were not receiving any lipid-altering agents within 6 months of study no washout period was required 12-week before-and-after trial
Participants	20 women received metformin for 12 weeks 18 women received metformin and 10 mg/day rosuvastatin for 12 weeks LDL-C > 160 mg/dl (> 4.14 mmol/l) exclusion criteria:liver and kidney diseases, patients with Cushing's syndrome hyperprolactinaemia, diabetes mellitus, thyroid disease, congenital adrenal hyperplasia, androgen-secreting tumours insufficient LH syndrome and other endocrinopathies, using drugs that affect insulin sensitivity, participants taking oral contraceptives Rosuvastatin 10 mg/day baseline TC : 6.56 mmol/l (254 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.37 mmol/l (169 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.22 mmol/l (47 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.91 mmol/l (169 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.34 mmol/l (206 mg/dl)
Interventions	metformin metformin and rosuvastatin 10 mg/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	metformin group was not analyzed SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the metformin and rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable

Celik 2012 *(Continued)*

Allocation concealment (selection bias)	High risk	the metformin and rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the metformin and rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Low risk	study was supported by the Research Fund of the University of Istanbul, Turkey not industry-funded

Chiang 2008

Methods	375 LLT-naive participants no washout period required 12-week open-label trial
Participants	375 men and women aged ≥ 18 years with hypercholesterolaemia 375 patients received rosuvastatin 10 mg/day for 12 weeks exclusion criteria: homozygous familial hypercholesterolaemia, secondary hypercholesterolaemia liver disease or dysfunction, CK > 3 X ULN, renal dysfunction and statin hypersensitivity
Interventions	rosuvastatin 10 mg/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	There was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	There was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	There was only one group of participants analyzed therefore it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis

Chiang 2008 *(Continued)*

Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

Coban 2008

Methods	4-week washout period 12-week open trial
Participants	30 men and women mean age 48 years with primary dyslipidaemia TG >200 mg/dl (> 5.17 mmol/l) TC > 200 mg/dl (> 5.17 mmol/l) LDL-C > 130 mg/dl (> 3.36 mmol/l) HDL-C < 35 mg/dl (< 0.905 mmol/l) for men HDL-C < 45 mg/dl (< 1.16 mmol/l) for women 30 patients received rosuvastatin 10 mg/day exclusion criteria: use of lipid-lowering drugs or drug that affect lipid metabolism supplements, hepatic or renal dysfunction, sustained hypertension diabetes mellitus, BMI ≥ 30, smoking , hypothyroidism, infection, cancer and/or major surgery or illness Rosuvastatin 10 mg/day baseline TC : 6.65 mmol/l (257 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.34 mmol/l (168 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.24 mmol/l (48 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.09 mmol/l (185 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.41 mmol/l (209 mg/dl)
Interventions	Rosuvastatin 10 mg/day for 12 weeks
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	SDs were imputed

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	There was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	There was only one group of participants analyzed therefore it is an unblinded trial

Coban 2008 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

Coen 2009

Methods	participants were not receiving any lipid-altering agents no washout period is required 20-week randomized open-label trial
Participants	31 men and women age 40-65 years with hypercholesterolaemia TC > 200 mg/dl (> 5.17 mmol/l) LDL-C > 130 mg/dl (> 3.36 mmol/l) 16 participants were randomized to rosuvastatin 10 mg/day for 0-10 weeks 16 participants were randomized to rosuvastatin 10 mg/day for 10-20 weeks 15 participants were randomized to rosuvastatin 10 mg/day and exercise for 0-10 weeks 15 participants were randomized to rosuvastatin 10 mg/day and exercise for 10-20 weeks exclusion criteria:MI or stroke, liver or kidney disease, physical disability acute illness, hypothyroidism, diabetes mellitus, renal dysfunction other drugs that interfere with the study drug Rosuvastatin 10 mg/day baseline TC : 6.58 mmol/l (254 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.68 mmol/l (181 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.12 mmol/l (43 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.53 mmol/l (136 mg/dl)
Interventions	rosuvastatin 10 mg/day for 0-10 weeks rosuvastatin 10 mg/day for 10-20 weeks rosuvastatin 10 mg/day and exercise for 0-10 weeks rosuvastatin 10 mg/day and exercise for 10-20 weeks
Outcomes	per cent change from baseline at 10 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	rosuvastatin 10 mg/day for 10-20 weeks rosuvastatin 10 mg/day and exercise for 10-20 weeks time periods were not included in the efficacy analysis SDs were imputed
Risk of bias	

Coen 2009 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day 0-10 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day 0-10 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day 0-10 weeks treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca sponsored the trial. Data may support bias for rosuvastatin

COMETS 2005

Methods	4-week washout period
	12-week randomized double-blind placebo-controlled trial
Participants	401 men and women age ≥ 18 years with metabolic syndrome
	LDL-C ≥ 3.36 mmol/l (130 mg/dl)
	TG ≥ 1.70 mmol/l (150 mg/dl)
	HDL-C < 1.04 mmol/l (40 mg/dl) for men
	HDL-C < 1.30 mmol/l (50 mg/dl) for women
	glucose ≥ 6.11 mmol/l (110 mg/dl)
	10 year CHD risk score of > 10%
	79 patients were randomized to placebo
	165 patients were randomized to rosuvastatin
	157 patients were randomized to atorvastatin
	exclusion criteria:patients with diabetes mellitus,, use of lipid-lowering agents within the past 6 months
	TG ≥ 5.65 mmol/l (500 mg/dl), LDL-C ≥ 6.48 mmol/l (250 mg/dl)
	documented history of CHD or other atherosclerotic disease
	familial hypercholesterolaemia, statin hypersensitivity, uncontrolled hypertension or hypothyroidism
	acute liver disease or dysfunction, serum CK > 3 x ULN and the use of concomitant medications

COMETS 2005 *(Continued)*

	Placebo baseline TC : 6.60 mmol/l (255 mg/dl) Placebo baseline LDL-C : 4.42 mmol/l (171 mg/dl) Placebo baseline HDL-C : 1.20 mmol/l (46 mg/dl) Placebo baseline TG : 2.42 mmol/l (214 mg/dl) Placebo baseline non-HDL-C: 5.35 mmol/l (207 mg/dl) Rosuvastatin 10 mg/day baseline TC : 6.48 mmol/l (251 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.4 mmol/l (170 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.13 mmol/l (44 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.34 mmol/l (207 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.4 mmol/l (209 mg/dl)
Interventions	Placebo from 0-6 weeks Rosuvastatin 10 mg/day from 0-6 weeks Atorvastatin 10 mg/day from 0-6 weeks Rosuvastatin 20 mg/day from 6-12 weeks Atorvastatin 20 mg/day from 6-12 weeks
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C WDAEs
Notes	Atorvastatin 10 mg/day from 0-6 weeks Rosuvastatin 20 mg/day from 6-12 weeks Atorvastatin 20 mg/day from 6-12 weeks groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/79 placebo group was not included in the efficacy analysis 1/165 rosuvastatin group was not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	The study was supported by AstraZeneca. Data may support bias for rosuvastatin

CORALL 2005

Methods	6-week washout period 18-week randomized open-label study
Participants	263 men and women ≥ 18 years with type 2 diabetes mellitus LDL-C > 2.99 to ≤ 5.00 mmol/l (>116 to ≤193 mg/dl) TG <4.52 mmol/l (< 400 mg/dl) 131 patients were randomized to rosuvastatin 132 patients were randomized to atorvastatin exclusion criteria:statin hypersensitivity, active cardiovascular disease, uncontrolled hypertension pregnancy lactation, renal dysfunction, uncontrolled hypothyroidism, TSH > 1.5 X ULN homozygous familial hypercholesterolaemia or familial dysbetalipoproteinaemia, active liver disease or dysfunction serum CK > 3 X ULN Rosuvastatin 10 mg/day baseline TC : 6.34 mmol/l (245 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.23 mmol/l (164 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.26 mmol/l (49 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.89 mmol/l (167 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.08 mmol/l (196 mg/dl)
Interventions	Rosuvastatin 10 mg/day for 0-6 weeks Rosuvastatin 20 mg/day for 6-12 weeks Rosuvastatin 40 mg/day for 12-18 weeks Atorvastatin 20 mg/day for 0-6 weeks Atorvastatin 40 mg/day for 6-12 weeks Atorvastatin 80 mg/day for 12-18 weeks
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Rosuvastatin 20 mg/day for 6-12 weeks Rosuvastatin 40 mg/day for 12-18 weeks Atorvastatin 20 mg/day for 0-6 weeks Atorvastatin 40 mg/day for 6-12 weeks Atorvastatin 80 mg/day for 12-18 weeks groups were not included in the analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement

CORALL 2005 *(Continued)*

Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the analysis
Other bias	High risk	AstraZeneca financially supported and monitored the study. Data may support bias for rosuvastatin

Davidson 2002

Methods	6 week washout period 12 week randomized double-blind placebo-controlled trial
Participants	519 men and women age ≥ 18 years with type IIa or IIb hypercholesterolemia LDL-C ≥4.14 mmol/l (160 mg/dl) and <6.47 mmol/l (250 mg/dl) TG ≤4.52 mmol/l (400 mg/dl) 132 randomized to placebo 259 randomized to rosuvastatin 128 randomized to atorvastatin exclusion criteria:active arterial disease within 3 months of study, homozygous familial hypercholesterolemia uncontrolled hypertension, liver disease or dysfunction, glyciated hemoglobin >9% Placebo baseline TC : 7.06 mmol/l (273 mg/dl) Placebo baseline LDL-C : 4.83 mmol/l (187 mg/dl) Placebo baseline HDL-C : 1.26 mmol/l (49 mg/dl) Placebo baseline TG : 2.11 mmol/l (187 mg/dl) Rosuvastatin 5 mg/day baseline TC : 7.18 mmol/l (278 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 4.87 mmol/l (188 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.36 mmol/l (53 mg/dl) Rosuvastatin 5 mg/day baseline TG : 2.10 mmol/l (186 mg/dl) Rosuvastatin 10 mg/day baseline TC : 7.03 mmol/l (272 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.77 mmol/l (184 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.28 mmol/l (49 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.13 mmol/l (189 mg/dl)

Davidson 2002 *(Continued)*

Interventions	Placebo for 12 weeks Rosuvastatin 5 mg/day for 12 weeks Rosuvastatin 10 mg/day for 12 weeks Atorvastatin 10 mg/day for 12 weeks
Outcomes	percent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C and triglycerides WDAEs
Notes	Placebo and rosuvastatin groups were analyzed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/129 was not included in the efficacy analysis for the rosuvastatin 5 mg/day group 1/130 was not included in the efficacy analysis for the rosuvastatin 10 mg/day group 1% of the rosuvastatin group was not in the efficacy analysis all placebo subjects were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the study Data may support bias for rosuvastatin

DISCOVERY-Asia 2007

Methods	6-week washout period for LLT-naive patients 12-week randomized open-label study
Participants	1482 men and women aged ≥ 18 years with primary hypercholesterolaemia LDL-C > 3.5 mmol/l (> 135 mg/dl) TG ≤ 4.52 mmol/l (≤ 400 mg/dl) a history of CHD, atherosclerosis 10-year CHD risk score of > 20% diabetes mellitus

DISCOVERY-Asia 2007 *(Continued)*

	995 patients were randomized to rosuvastatin 10 mg/day 487 patients were randomized to atorvastatin 10 mg/day exclusion criteria: familial hypercholesterolaemia or dysbetalipoproteinaemia secondary hypercholesterolaemia of any cause, uncontrolled hypertension or diabetes mellitus active liver disease or dysfunction, statin hypersensitivity serum CK > 3 X ULN, renal dysfunction and unstable angina within 3 months of the study Rosuvastatin 10 mg/day baseline TC : 6.47 mmol/l (248 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.326 mmol/l (167 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.31 mmol/l (51 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.85 mmol/l (164 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.16 mmol/l (200 mg/dl)
Interventions	Rosuvastatin 10 mg/day 516 naive participants Rosuvastatin 10 mg/day 434 switched participants Atorvastatin 10 mg/day 267 naive participants Atorvastatin 10 mg/day 204 switched participants
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Rosuvastatin 10 mg/day 434 switched participants Atorvastatin 10 mg/day 267 naive participants Atorvastatin 10 mg/day 204 switched participants groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day naive participants treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day naive participants treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day naive participants treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis

DISCOVERY-Asia 2007 *(Continued)*

Other bias	High risk	This study was sponsored by AstraZeneca. Data may support bias for rosuvastatin

Dulay 2009

Methods	4-week washout period 15-week open-label cross-over trial
Participants	45 men and women age 18-80 years with hypercholesterolaemia LDL-C > 3.5 mmol/l (> 135 mg/dl) 41 participants received rosuvastatin 10 mg/day for 0-6 weeks 41 participants received rosuvastatin 20 mg every other day for 0-6 weeks 41 participants received rosuvastatin 20 mg every other day for 9-15 weeks 41 participants received rosuvastatin 10 mg/day for 9-15 weeks
Interventions	rosuvastatin 10 mg/day for 0-6 weeks rosuvastatin 20 mg every other day for 0-6 weeks rosuvastatin 20 mg every other day for 9-15 weeks rosuvastatin 10 mg/day for 9-15 weeks
Outcomes	per cent change from baseline at 6 weeks of serum LDL-C
Notes	rosuvastatin 20 mg every other day for 0-6 weeks rosuvastatin 20 mg every other day for 9-15 weeks rosuvastatin 10 mg/day for 9-15 weeks groups were not included in the efficacy analysis SD was imputed

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias)	Low risk	4/45 (8.9%) participants were not included in the efficacy analysis

Dulay 2009 *(Continued)*
All outcomes

Selective reporting (reporting bias)	High risk	total cholesterol, HDL-C , non-HDL-C and triglycerides were not included in the efficacy analysis
Other bias	Low risk	funded by The Physicians` Services Incorporated Foundatioin, Grant RO4-42

Durrington 2004

Methods	6-week washout period 6-week randomized double-blind placebo-controlled trial
Participants	216 men and women age ≥ 18 years with type 2 diabetes, hypertriglyceridaemia and HbA1c < 10% TG ≥ 200 to < 800 mg/dl (≥2.26 to <9.03 mmol/l) TC ≥ 200 mg/dl (≥ 5.17 mmol/), glycated haemoglobin < 10% 53 randomized to placebo for 5 mg/day rosuvastatin 49 randomized to placebo for 10 mg/day rosuvastatin 60 randomized to rosuvastatin 5 mg/day 54 randomized to rosuvastatin 10 mg/day exclusion criteria:type 1 diabetes, history of diabetic ketoacidosis, use of lipid-lowering drugs or supplements, pregnancy or lactation uncontrolled hypertension, acute ischaemic event within 3 months of trial entry, alcohol abuse, active liver disease or dysfunction serum CK > 3 X ULN Placebo for 5 mg/day Rosuvastatin baseline TC : 6.2 mmol/l (240 mg/dl) Placebo for 5 mg/day Rosuvastatin baseline LDL-C : 3.7 mmol/l (143 mg/dl) Placebo for 5 mg/day Rosuvastatin baseline HDL-C : 1.0 mmol/l (29 mg/dl) Placebo for 5 mg/day Rosuvastatin baseline TG : 3.6 mmol/l (319 mg/dl) Placebo for 10 mg/day Rosuvastatin baseline TC : 6.3 mmol/l (244 mg/dl) Placebo for 10 mg/day Rosuvastatin baseline LDL-C : 3.7 mmol/l (143 mg/dl) Placebo for 10 mg/day Rosuvastatin baseline HDL-C : 1.0 mmol/l (29 mg/dl) Placebo for 10 mg/day Rosuvastatin baseline TG : 4.2 mmol/l (372 mg/dl) 5 mg/day Rosuvastatin baseline TC : 6.5 mmol/l (251 mg/dl) 5 mg/day Rosuvastatin baseline LDL-C: 3.9 mmol/l (151 mg/dl) 5 mg/day Rosuvastatin baseline HDL-C: 1.1 mmol/l (42.5 mg/dl) 5 mg/day Rosuvastatin baseline TG: 3.5 mmol/l (310 mg/dl) 10 mg/day Rosuvastatin baseline TC : 6.4 mmol/l (247 mg/dl) 10 mg/day Rosuvastatin baseline LDL-C: 3.9 mmol/l (151 mg/dl) 10 mg/day Rosuvastatin baseline HDL-C:1.0 mmol/l (38.7 mg/dl) 10 mg/day Rosuvastatin baseline TG: 3.5 mmol/l (310 mg/dl)
Interventions	Placebo for 5 mg/day Rosuvastatin for 6 weeks

Durrington 2004 *(Continued)*

	Placebo for 10 mg/day Rosuvastatin for 6 weeks
	Rosuvastatin 5 mg/day for 6 weeks
	Rosuvastatin 10 mg/day for 6 weeks
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides WDAEs
Notes	all interventions were analyzed for efficacy

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	2/53 placebo for 5 mg/day rosuvastatin were not included in the efficacy analysis 1/54 rosuvastatin 10 mg/day was not included in the efficacy analysis 1.4% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	High risk	non HDL-C was not included in the efficacy analysis
Other bias	High risk	This research was supported by AstraZeneca. Data may support bias for rosuvastatin

Dzhaiani 2008

Methods	participants were not receiving any lipid-altering agents no washout period required 3-week open-label trial
Participants	47 men and women mean age 60 years with acute myocardial infarction 26 participants received rosuvastatin 10 mg/day for 3 weeks 21 participants received standard therapy but no statins exclusion criteria: active liver disease, renal dysfunction myopathy / rhabdomyolysis followed by a persistent increase in CPK more than 3 times upper limit normal prior to taking statins and other lipid-reducing agents, cancer, connective tissue diseases, clinical and lab sign of inflammation and hypothyroidism Rosuvastatin 10 mg/day baseline TC : 5.81 mmol/l (225 mg/dl)

Dzhaiani 2008 *(Continued)*

	Rosuvastatin 10 mg/day baseline LDL-C : 3.29 mmol/l (127 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.40 mmol/l (54 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.39 mmol/l (212 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 4.41 mmol/l (171 mg/dl)
Interventions	rosuvastatin 10 mg/day standard therapy but no statins
Outcomes	per cent change from baseline at 3 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	standard therapy but no statins group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

ECLIPSE 2008

Methods	6-week washout period 24-week open-label randomized trial
Participants	1036 men and women aged ≥18 years with hypercholesterolaemia and a history of CHD, clinical evidence of atherosclerosis or a 10-year CHD risk score > 20% LDL-C ≥ 160 to < 250 mg/dl (4.14 to <6.47 mmol/l) TG <400 mg/dl (< 4.52 mmol/l) 522 participants were randomized to rosuvastatin 10 mg/day 514 participants were randomized to atorvastatin 10 mg/day

ECLIPSE 2008 *(Continued)*

	exclusion criteria: history of statin-induced myopathy, statin hypersensitivity clinical instability after a cardiovascular event, homozygous familial hypercholesterolaemia uncontrolled hypothyroidism, severe hepatic impairment, serum CK > 3 X ULN, renal dysfunction pregnancy, lactation
Interventions	rosuvastatin 10 mg/day for 0-6 weeks rosuvastatin 20 mg/day for 6-12 weeks rosuvastatin 40 mg/day for 12-24 weeks atorvastatin 10 mg/day for 0-6 weeks atorvastatin 20 mg/day for 6-12 weeks atorvastatin 40 mg/day for 12-18 weeks atorvastatin 80 mg/day for 18-24 weeks
Outcomes	per cent change from baseline at 6weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	rosuvastatin 20 mg/day for 6-12 weeks rosuvastatin 40 mg/day for 12-24 weeks atorvastatin 10 mg/day for 0-6 weeks atorvastatin 20 mg/day for 6-12 weeks atorvastatin 40 mg/day for 12-18 weeks atorvastatin 80 mg/day for 18-24 weeks groups were not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	24/522 participants were not included in the efficacy analysis 4.6% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis

ECLIPSE 2008 *(Continued)*

Other bias	High risk	AstraZeneca funded the study. Data may support bias for rosuvastatin

EFFORT 2011

Methods	no lipid-lowering medication had been administered within 3 months of trial enrolment no washout period required 12 week open-label clinical study
Participants	97 men and women age 18-69 years with metabolic syndrome LDL-C > 130 mg/dl (3.36 mmol/l) HDL-C < 40 mg/dl (1.03 mmol/l) in males < 50 mg/dl (1.29 mmol/l) in females TG < 400 mg/dl (4.52 mmol/l) 97 patients received rosuvastatin 10 mg/day for 0-6 weeks 85 patients received rosuvastatin 20 mg/day for 6-12 weeks exclusion criteria:concomitant coronary artery disease uncontrolled hypertension, homozygous familial hypercholesterolaemia uncontrolled hypothyroidism, renal failure, history of MI, renal dysfunction history of severe arrhythmia, heart failure, history of syncope cancer history, statin hypersensitivity or myopathy CK > 3 X ULN, alcohol or drug abuse, pregnancy or lactation concomitant medications with warfarin, cyclosporin, gemfibrozil, antacids participation in another investigational drug study less than 4 weeks before enrolment in the study Rosuvastatin 10 mg/day baseline TC : 6.12 mmol/l (237 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.28 mmol/l (166 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.02 mmol/l (39 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.20 mmol/l (195 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.10 mmol/l (197 mg/dl)
Interventions	rosuvastatin 10 mg/day for 0-6 weeks rosuvastatin 20 mg/day for 6-12 weeks
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	rosuvastatin 20mg/day for 6-12 weeks group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement

EFFORT 2011 *(Continued)*

Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	High risk	12/97 = 12.4% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the study. Data may support bias for rosuvastatin

Erbs 2011

Methods	participants were not receiving any lipid-altering agents no washout period is required 12-week randomized double-blind placebo-controlled trial
Participants	42 men and women with chronic heart failure 22 patients were randomized to rosuvastatin 40 mg/day 20 patients were randomized to placebo exclusion criteria:renal failure, liver dysfunction, type 1 diabetes mellitus valvular heart disease, uncontrolled hypertension, muscle disease previous treatment with statins or other lipid-altering agents fibrates immunosuppressants Placebo baseline LDL-C : 3.91 mmol/l (151 mg/dl) Placebo baseline HDL-C : 1.41 mmol/l (55 mg/dl) Placebo baseline TG : 2.82 mmol/l (250 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 3.66 mmol/l (142 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.13 mmol/l (48 mg/dl) Rosuvastatin 40 mg/day baseline TG : 2.34 mmol/l (207 mg/dl)
Interventions	Placebo Rosuvastatin 40 mg/day
Outcomes	per cent change from baseline at 12 weeks of serum LDL-C, HDL-C and triglycerides
Notes	
Risk of bias	

Erbs 2011 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Low risk	allocation was done by a third party Pharmacy of Heart Center and Parkkrankenhaus, Leipzig
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind "all patients, investigators and lab staff were blinded"
Incomplete outcome data (attrition bias) All outcomes	Low risk	2/42 = 4.8% were not included in the efficacy analysis
Selective reporting (reporting bias)	High risk	total cholesterol and non-HDL-C were not included in the efficacy analysis WDAEs were not reported
Other bias	High risk	AstraZeneca funded the trial. Data may support bias for rosuvastatin

EXPLORER 2007

Methods	6-week washout period 6-week open-label randomized study
Participants	469 men and women at high risk for cardiovascular disease with hypercholesterolaemia age ≥ 18 years LDL-C ≥160 mg/dl and < 250 mg/dl (≥ 4.14 mmol/l and < 6.465 mmol/l) TG < 400 mg/dl (4.516 mmol/l) exclusion criteria: statin-induced myopathy or serious hypersensitivity reaction history unstable heart disease, myocardial revascularization, coronary artery bypass graft, TIA or stroke, severe congestive heart failure, cancer, uncontrolled hypothyroidism homozygous familial hypercholesterolaemia, current active liver disease or dysfunction use of prohibited medications, pregnancy or lactation change in HRT or use of contraceptives within 3 months of enrolment Rosuvastatin 40 mg/day baseline TC : 7.19 mmol/l (278 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 4.94 mmol/l (191 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.29 mmol/l (50 mg/dl) Rosuvastatin 40 mg/day baseline TG : 2.1 mmol/l (186 mg/dl) Rosuvastatin 40 mg/day baseline non-HDL-C: 5.9 mmol/l (228 mg/dl)
Interventions	Rosuvastatin 40 mg/day Rosuvastatin/Ezetimibe 40/10 mg/day combination therapy
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Rosuvastatin group was analyzed

EXPLORER 2007 *(Continued)*

	SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were measured
Other bias	Unclear risk	source of funding not reported

Florentin 2013

Methods	no washout required because participants were not receiving any lipid-altering agents for at least 4 weeks 3 month before-and-after trial
Participants	40 men and women with hypercholesterolaemia and impaired fasting glucose LDL-C > 130 mg/dl (3.36 mmol/l), fasting serum glucose of 100-125 mg/dl (5.6-6.9 mmol/l) exclusion criteria:cardiovascular disease, DM, TG >300 mg/dl (3.39 mmol/l), renal disease hypothyroidism, liver disease, uncontrolled hypertension and patients taking other medications that could affect glucose homeostasis 20 participants received Rosuvastatin 5 mg/day plus colesevelam 3.75 grams/day 20 participants received Rosuvastatin 5 mg/day Rosuvastatin 5 mg/day baseline TC : 6.88 mmol/l (266 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 4.60 mmol/l (178 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.45 mmol/l (56.1 mg/dl) Rosuvastatin 5 mg/day baseline non-HDL-C: 5.35 mmol/l (207 mg/dl)
Interventions	Rosuvastatin 5 mg/day plus colesevelam 3.75 grams/day Rosuvastatin 5 mg/day
Outcomes	per cent change from baseline at 3 months of serum TC, LDL-C, HDL-C, and non-HDL-C

Florentin 2013 *(Continued)*

Notes	Rosuvastatin 5 mg/day plus colesevelam 3.75 g/day group was not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day for 3 months treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day for 3 months treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day for 3 months treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	blood triglycerides were not included in the efficacy analysis because it was a median per cent change
Other bias	Unclear risk	source of funding not reported

Gao 2007

Methods	6-week washout period 12-week randomized double-blind trial
Participants	304 patients age 18-75 years with hypercholesterolaemia LDL-C ≥ 160 mg/dl to < 250 mg/dl (≥ 4.14 mmol/l to < 6.465 mmol/l) TG < 400 mg/dl (< 4.52 mmol/l) 191 patients were randomized to rosuvastatin 99 patients were randomized to atorvastatin Rosuvastatin 10 mg/day baseline TC : 6.81 mmol/l (263 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.99 mmol/l (193 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.46 mmol/l (56 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.03 mmol/l (180 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.35 mmol/l (207 mg/dl)
Interventions	Rosuvastatin 10 mg/day for 0-12 weeks Rosuvastatin 20 mg/day for 12-20 weeks Atorvastatin 10 mg/day for 0-12 weeks
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C

Gao 2007 *(Continued)*

Notes	Rosuvastatin 20 mg/day for 12-20 weeks Atorvastatin 10 mg/day for 0-12 weeks groups were not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the study. Data may support bias for rosuvastatin

Gomez-Garcia 2007

Methods	participants are not on any lipid-altering agents 12-week open-label placebo-controlled trial evening dosing
Participants	48 men and women age ≥ 65 years with hypertension and dyslipidaemia LDL-C ≥100 mg/dl (≥ 2.59 mmol/l) TG ≥150 mg/dl (≥ 1.69 mmol/l) HDL-C <40 mg/dl (<1.03 mmol/l) in men HDL-C <50 mg/dl (<1.29 mmol/l) in women 16 participants received rosuvastatin 10 mg/day 16 participants received metformin 1.7 g/day 16 participants received placebo 10 mg/day Placebo baseline TC : 6.25 mmol/l (242 mg/dl) Placebo baseline LDL-C : 3.37 mmol/l (130 mg/dl)

Gomez-Garcia 2007 *(Continued)*

	Placebo baseline HDL-C : 0.97 mmol/l (38 mg/dl) Placebo baseline TG : 2.72 mmol/l (241 mg/dl) Rosuvastatin 10 mg/day baseline TC : 5.90 mmol/l (228 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.37 mmol/l (130 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.17 mmol/l (45 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.35 mmol/l (208 mg/dl)
Interventions	placebo rosuvastatin metformin
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	metformin 1.7 g/day group was not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	High risk	no allocation concealment
Blinding (performance bias and detection bias) All outcomes	High risk	open-label
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	WDAEs were not included in the analysis
Other bias	Low risk	not funded by the pharmaceutical industry

GRAVITY 2009

Methods	6-week washout period 12-week randomized open-label trial
Participants	833 patients ≥ 18 years with hypercholesterolaemia and CHD or CHD risk score > 20% LDL-C ≥130 to < 220 mg/dl (≥3.36 mmol/l to < 5.69 mmol/l) TG < 400 mg/dl (4.52 mmol/l) 214 participants randomized to rosuvastatin 10 mg/day for 0-6 weeks 214 participants randomized to rosuvastatin 10 mg/day+ezetimibe 10 mg/day for 6-12 weeks 214 participants randomized to rosuvastatin 20 mg/day for 0-6 weeks

GRAVITY 2009 *(Continued)*

	214 participants randomized to rosuvastatin 20 mg/day+ezetimibe 10 mg/day for 6-12 weeks
	202 participants randomized to simvastatin 40 mg/day for 0-6 weeks
	202 participants randomized to simvastatin 40 mg/day+ezetimibe 10 mg/day for 6-12 weeks
	203 participants randomized to simvastatin 80 mg/day for 0-6 weeks
	203 participants randomized to simvastatin 80 mg/day+ezetimibe 10 mg/day for 6-12 weeks
	exclusion criteria: myocardial infarction, recent episode of angina, PTCA, CABG, TIA
	stroke and patients awaiting a planned myocardial revascularization
	statin or ezetimibe hypersensitivity, use of lipid-lowering drugs and other prohibited concomitant medications
Interventions	rosuvastatin 10 mg/day
	rosuvastatin 10 mg/day+ezetimibe 10 mg/day
	rosuvastatin 20 mg/day
	rosuvastatin 20 mg/day+ezetimibe 10 mg/day
	simvastatin 40 mg/day
	simvastatin 40 mg/day+ezetimibe 10 mg/day
	simvastatin 80 mg/day
	simvastatin 80 mg/day+ezetimibe 10 mg/day
Outcomes	LDL-C
Notes	rosuvastatin 10 mg/day+ezetimibe 10 mg/day
	rosuvastatin 20 mg/day+ezetimibe 10 mg/day
	rosuvastatin 20 mg/day+ezetimibe 10 mg/day
	simvastatin 40 mg/day
	simvastatin 40 mg/day+ezetimibe 10 mg/day
	simvastatin 80 mg/day
	simvastatin 80 mg/day+ezetimibe 10 mg/day
	groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable

GRAVITY 2009 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	8/214 participants rosuvastatin 10 mg/day group 15/214 participants rosuvastatin 20 mg/day group 23/428 (5.4%) were not included in the efficacy analysis
Selective reporting (reporting bias)	High risk	only LDL-C was included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the trial. Data may support bias for rosuvastatin

Guo 2012

Methods	participants were not receiving any lipid-altering agents within 3 months of study no washout period was required 12-week before-and-after trial
Participants	30 participants received 10 mg/day rosuvastatin for 12 weeks 30 participants received 40 mg/day simvastatin for 12 weeks 30 participants received control diet for 12 weeks exclusion criteria: hepatic dysfunction, endocrine disorders, recent major surgery or cancer statin intolerance and participation in other clinical trials Rosuvastatin 10 mg/day baseline TC : 6.11 mmol/l (236 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.82 mmol/l (148 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 0.75 mmol/l (29 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.10 mmol/l (186 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.35 mmol/l (207 mg/dl)
Interventions	rosuvastatin 10 mg/day simvastatin 40 mg/day diet
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	simvastatin 40 mg/day and control diet groups were not analyzed SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement

Guo 2012 *(Continued)*

Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	no source of funding was reported

Han 2008

Methods	4-week washout period 4-week randomized single-blind trial
Participants	67 patients 65-70 years with hypercholesterolaemia LDL-C ≥ 4.14 mmol/l and ≤ 6.50 mmol/l (≥ 160 mg/dl and ≤ 251 mg/dl TG ≤ 4.52 mmol/l (≤ 400 mmol/l) 33 patients received rosuvastatin 10 mg/day 34 patients received atorvastatin 20 mg/day Rosuvastatin 10 mg/day baseline TC : 5.5 mmol/l (213 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.4 mmol/l (131 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.24 mmol/l (48 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.1 mmol/l (186 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 4.26 mmol/l (165 mg/dl)
Interventions	rosuvastatin 10 mg/day atorvastatin 20 mg/day
Outcomes	per cent change from baseline at 4 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	atorvastatin 20 mg/day group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement

Han 2008 *(Continued)*

Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding was not reported

HeFH 2003

Methods	6-week washout period 18-week weighted randomized double-blind study
Participants	623 men and women age 45-50 with heterozygous familial hypercholesterolaemia LDL-C 220 to < 500 mg/dl (5.7 to < 12.9 mmol/l) TG ≤ 400 mg/dl (≤4.5 mmol/l) 436 were randomized to rosuvastatin 187 were randomized to atorvastatin exclusion criteria: hepatic dysfunction, active arterial disease within 3 months of trial uncontrolled hypertension, uncontrolled hypothyroidism, renal dysfunction, CK > 3 X ULN cyclic hormone therapy, use of medication that could affect serum lipid profiles or safety issues Rosuvastatin 20 mg/day baseline TC : 9.62 mmol/l (372 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 7.55 mmol/l (292 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.24 mmol/l (48 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.81 mmol/l (160 mg/dl)
Interventions	Rosuvastatin 20 mg/day for 0-6 weeks Rosuvastatin 40 mg/day for 6-12 weeks Rosuvastatin 80 mg/day for 12-18 weeks Atorvastatin 20 mg/day for 0-6 weeks Atorvastatin 40 mg/day for 6-12 weeks Atorvastatin 80 mg/day for 12-18 weeks

HeFH 2003 *(Continued)*

Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	Rosuvastatin 40 mg/day for 6-12 weeks Rosuvastatin 80 mg/day for 12-18 weeks Atorvastatin 20 mg/day for 0-6 weeks Atorvastatin 40 mg/day for 6-12 weeks Atorvastatin 80 mg/day for 12-18 weeks groups were not included in the analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 20 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 20 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 20 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/436 was not included in the efficacy analysis
Selective reporting (reporting bias)	High risk	non-HDL-C was not included in the efficacy analysis
Other bias	High risk	The research was supported by AstraZeneca. Data may support bias for rosuvastatin

Her 2010

Methods	4-week washout period 12-week randomized open-label trial
Participants	90 men and women aged 20-79 years with hypercholesterolaemia LDL-C > 130 mg/dl (> 3.36 mmol/l) TG < 400 mg/dl (< 4.52 mmol/l) 25 were randomized to rosuvastatin 10 mg/day 25 were randomized to atorvastatin 20 mg/day 26 were randomized to atorvastatin/ezetimibe 5 mg/5 mg/day exclusion criteria: familial hypercholesterolaemia, diabetes mellitus

Her 2010 *(Continued)*

	pregnancy, lactation, stroke or MI within 3 months of enrolment renal dysfunction, thyroid dysfunction, serum CK > 2.5 X ULN infection, cancer, history of adverse reaction to test drugs Rosuvastatin 10 mg/day baseline TC : 6.26 mmol/l (242 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.22 mmol/l (163 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.3 mmol/l (50 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.87 mmol/l (166 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 4.96 mmol/l (192 mg/dl)
Interventions	rosuvastatin 10 mg/day for 8 weeks atorvastatin 20 mg/day for 8 weeks atorvastatin/ezetimibe 5 mg/5 mg/day for 8 weeks
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	atorvastatin 20 mg/day for 8 weeks atorvastatin/ezetimibe 5 mg/5 mg/day for 8 weeks groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	2/27 participants in the rosuvastatin group were not included in the efficacy analysis due to protocol violation 7.4% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Low risk	pharmaceutical industry did not fund this study

Hunninghake 2004

Methods	6-week washout period 6-week randomized double-blind placebo-controlled trial

Hunninghake 2004 *(Continued)*

Participants	156 men and women with hypertriglyceridaemia type IIb or IV aged 18 years or older were enrolled in the study TG ≥ 300 and < 800 mg/dl (≥3.39 and < 9.03mmol/l) glucose ≤ 180 mg/dl (≤ 9.99 mmol/l) or glycosylated haemoglobin ≤ 8% 26 were randomized to placebo 26 were randomized to rosuvastatin 5 mg/day 23 were randomized to rosuvastatin 10 mg/day 28 were randomized to rosuvastatin 20 mg/day 26 were randomized to rosuvastatin 40 mg/day 27 were randomized to rosuvastatin 80 mg/day exclusion criteria: pregnancy, lactation, heterozygous or homozygous familial hypercholesterolaemia type III hyperlipoproteinaemia, active arterial disease within 3 months of trial entry, uncontrolled hypertension cancer history, uncontrolled hypothyroidism, alcohol or drug abuse, active liver disease or dysfunction, elevated serum CK concomitant medications known to affect lipid profiles or present a safety concern Placebo baseline TC : 6.62 mmol/l (256 mg/dl) Placebo baseline LDL-C : 2.97 mmol/l (115 mg/dl) Placebo baseline HDL-C : 0.91 mmol/l (35 mg/dl) Placebo baseline TG : 5.77 mmol/l (511 mg/dl) Placebo baseline non-HDL-C : 5.715 mmol/l (221 mg/dl) Rosuvastatin 5 mg/day baseline TC : 6.31 mmol/l (244 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 2.95 mmol/l (114 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 0.93 mmol/l (36 mg/dl) Rosuvastatin 5 mg/day baseline TG : 5.21 mmol/l (461 mg/dl) Rosuvastatin 5 mg/day baseline non-HDL-C : 5.38 mmol/l (208 mg/dl) Rosuvastatin 10 mg/day baseline TC : 6.67 mmol/l (258 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.26 mmol/l (126 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 0.98 mmol/l (38 mg/dl) Rosuvastatin 10 mg/day baseline TG : 5.04 mmol/l (446 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C : 5.69 mmol/l (220 mg/dl) Rosuvastatin 20 mg/day baseline TC : 6.49 mmol/l (251 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 3.08 mmol/l (119 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 0.88 mmol/l (34 mg/dl) Rosuvastatin 20 mg/day baseline TG : 5.04 mmol/l (446 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C : 5.61 mmol/l (217 mg/dl) Rosuvastatin 40 mg/day baseline TC : 6.41 mmol/l (248 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 3.23 mmol/l (125 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 0.91 mmol/l (35 mg/dl) Rosuvastatin 40 mg/day baseline TG : 5.32 mmol/l (471 mg/dl) Rosuvastatin 40 mg/day baseline non-HDL-C : 5.53 mmol/l (214 mg/dl) Rosuvastatin 80 mg/day baseline TC : 7.03 mmol/l (272 mg/dl)

Hunninghake 2004 *(Continued)*

	Rosuvastatin 80 mg/day baseline LDL-C : 3.59 mmol/l (139 mg/dl) Rosuvastatin 80 mg/day baseline HDL-C : 0.93 mmol/l (36 mg/dl) Rosuvastatin 80 mg/day baseline TG : 5.06 mmol/l (448 mg/dl) Rosuvastatin 80 mg/day baseline non-HDL-C : 6.08 mmol/l (235 mg/dl)
Interventions	Placebo Rosuvastatin 5 mg/day Rosuvastatin 10 mg/day Rosuvastatin 20 mg/day Rosuvastatin 40 mg/day Rosuvastatin 80 mg/day
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	3/156 were not included in the efficacy analysis 1.9 % participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were measured WDAEs were also reported
Other bias	High risk	The study was supported by AstraZeneca. Data may support bias for rosuvastatin

Igase 2012a

Methods	no washout period required no participant received lipid-altering agents 4 week before-and-after trial
Participants	137 men and women with dyslipidaemia who suffered acute ischaemic stroke age 60-80 years exclusion criteria: history of previous stroke or lipid-lowering treatment Rosuvastatin 2.5 mg/day baseline TC : 5.87 mmol/l (227 mg/dl) Rosuvastatin 2.5 mg/day baseline LDL-C : 3.85 mmol/l (149 mg/dl) Rosuvastatin 2.5 mg/day baseline HDL-C : 1.27 mmol/l (49 mg/dl)

Igase 2012a *(Continued)*

	Rosuvastatin 2.5 mg/day baseline non-HDL-C : 4.65 mmol/l (180 mg/dl) Rosuvastatin 2.5 mg/day baseline TG : 1.72 mmol/l (152 mg/dl)
Interventions	rosuvastatin 2.5 mg/day for 4 weeks
Outcomes	per cent change from baseline at 4 weeks of serum TC, LDL-C, HDL-C, non-HDL-C and triglycerides
Notes	SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	there was only one group of participants analyzed therefore it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Low risk	pharmaceutical industry did not funded this trial

Igase 2012b

Methods	participants were not receiving any lipid-altering agents no washout period is required 12 week before-and-after trial
Participants	26 postmenopausal women age 55 years or older with dyslipidaemia LDL-C ≥ 140 mg/dl (3.62 mmol/l) exclusion criteria: uncontrolled hypertension, diabetes mellitus, cerebrovascular disease, CAD, peripheral artery disease Rosuvastatin 2.5 mg/day baseline TC : 6.39 mmol/l (247 mg/dl) Rosuvastatin 2.5 mg/day baseline LDL-C : 4.30 mmol/l (166 mg/dl) Rosuvastatin 2.5 mg/day baseline HDL-C : 1.71 mmol/l (66 mg/dl) Rosuvastatin 2.5 mg/day baseline TG : 1.01 mmol/l (89 mg/dl) Rosuvastatin 2.5 mg/day baseline non-HDL-C: 4.68 mmol/l (181 mg/dl)
Interventions	rosuvastatin 2.5 mg/day for 12 weeks
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C

Igase 2012b *(Continued)*

Notes	SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	there was only one group of participants analyzed therefore it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Low risk	not industry funded

IRIS 2007

Methods	6-week washout period 6-week randomized open-label study
Participants	740 men and women at risk of CHD LDL-C ≥100 mg/dl (≥ 2.6 mmol/l); or ≥2 risk factors, 10-year CHD risk 10% to 20% LDL-C≥130 mg/dl (≥ 3.4 mmol/l); or 0 or 1 risk factor LDL-C≥160 mg/dl (≥ 4.1mmol/l) For eligibility, LDL-C ≤ 300 mg/dl (≤ 7.8 mmol/l TG < 500 mg/dl (5.6mmol/l) 371 randomized to rosuvastatin 369 randomized to atorvastatin exclusion criteria: homozygous familial hypercholesterolaemia, type I, III or V hyperlipoproteinaemia active arterial disease within 3 months of entry into trial, uncontrolled hypertension, poorly controlled diabetes mellitus active liver disease or liver dysfunction CK > 3XULN Rosuvastatin 10 mg/day baseline TC : 6.13 mmol/l (237 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.06 mmol/l (157 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.14 mmol/l (44 mg/dl)

IRIS 2007 *(Continued)*

	Rosuvastatin 10 mg/day baseline TG : 2.07 mmol/l (183 mg/dl) Rosuvastatin 20 mg/day baseline TC : 6.03 mmol/l (233 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 3.96 mmol/l (153 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.16 mmol/l (45 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.98 mmol/l (175 mg/dl)
Interventions	Rosuvastatin 10 mg/day for 6 weeks Rosuvastatin 20 mg/day for 6 weeks Atorvastatin 10 mg/day for 6 weeks Atorvastatin 20 mg/day for 6 weeks
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	Atorvastatin 10 mg/day for 6 weeks Atorvastatin 20 mg/day for 6 weeks groups were not included in the analysis SDs were imputed for LDL-C and HDL-C

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	6/189 was not included in the efficacy analysis for the rosuvastatin 10 mg/day group 11/182 was not included in the efficacy analysis for the rosuvastatin 20 mg/day group 3% rosuvastatin participants was not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the study. Data may support bias for rosuvastatin

JART 2012

Methods	1-month washout period

JART 2012 *(Continued)*

	8-week before-and-after trial
Participants	348 patients with hypercholesterolaemia aged 20 years or older LDL-C ≥ 140 mg/dL (≥3.62 mmol/l) with maximum IMT ≥ 1.1 mm measured at the carotid artery 173 patients randomized to rosuvastatin 5 mg/day 175 patients randomized to pravastatin 10 mg/day exclusion criteria: severe carotid artery stenosis (≥ 80%) or severe calcification, familial hypercholesterolaemia or secondary hypercholesterolaemia fasting TG ≥ 400 mg/dL (≥ 4.52 mmol/l), statin hypersensitivity, uncontrolled hypertension, type 1 diabetes mellitus and uncontrolled type 2 diabetes mellitus MI or stroke within 3 months, severe congestive heart failure, hepatic dysfunction or renal dysfunction, cyclosporine treatment, cancer, hypothyroidism, muscle disease drug and alcohol abuse, pregnancy or potential for pregnancy Rosuvastatin 5 mg/day baseline LDL-C : 4.24 mmol/l (164 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.40 mmol/l (54 mg/dl) Rosuvastatin 5 mg/day baseline non-HDL-C : 4.99 mmol/l (193 mg/dl) Rosuvastatin 5 mg/day baseline TG : 1.69 mmol/l (150 mg/dl)
Interventions	Rosuvastatin 5 mg/day for 8 weeks Pravastatin 10 mg/day for 8 weeks
Outcomes	per cent change from baseline at 4 weeks of serum TC, LDL-C, HDL-C, non-HDL-C and triglycerides
Notes	Pravastatin 10 mg/day for 8 weeks group was not analyzed TC was calculated from HDL-C and non-HDL-C

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	High risk	24/173 (13.9%) patients were not included in the LDL-C efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Low risk	pharmaceutical industry did not fund this trial

Jing 2013

Methods	4-week placebo run-in period 4-week before-and-after trial
Participants	345 men and women with hypercholesterolaemia aged 18-70 years TC ≥ 5.72 mmol/l (221 mg/dl) LDL-C ≥ 3.64 mmol/l (141 mg/dl) TG < 4.5 mmol/l (399 mg/dl) exclusion criteria: pregnancy, lactation, liver and kidney dysfunction, myopathy MI major surgery or angioplasty within the last 6 months congestive heart failure or unstable angina, systolic blood pressure ≥180 mmHg and/or diastolic blood pressure ≥ 110 mmHg HMG-CoA reductase inhibitor hypersensitivity Rosuvastatin 5 mg/day baseline TC : 6.74 mmol/l (261 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 4.48 mmol/l (173 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.39 mmol/l (54 mg/dl) Rosuvastatin 5 mg/day baseline TG : 1.93 mmol/l (171 mg/dl) Rosuvastatin 5 mg/day baseline non-HDL-C: 5.35 mmol/l (207 mg/dl) Rosuvastatin 10 mg/day baseline TC : 6.61 mmol/l (256 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.37 mmol/l (169 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.34 mmol/l (52 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.01 mmol/l (178 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.27 mmol/l (204 mg/dl)
Interventions	115 patients randomized to rosuvastatin 5 mg/day 115 patients randomized to rosuvastatin 10 mg/day 115 patients randomized to atorvastatin 10 mg/day
Outcomes	per cent change from baseline at 4 weeks of serum TC, LDL-C, HDL-C, non-HDL-C and triglycerides
Notes	atorvastatin 10 mg/day group was not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day and 10 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day and 10 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day and 10 mg/day treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias)	Low risk	1/115 participants in the rosuvastatin group was not included in the efficacy analysis

Jing 2013 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding was not reported

Jones 2009

Methods	6-week washout period 12-week randomized double-blind trial
Participants	1445 men and women ≥18 years with mixed dyslipidaemia TG ≥ 150 mg/dl (≥ 1.69 mmol/l) HDL-C < 40 mg/dl (< 1.03 mmol/l) for men HDL-C < 50 mg/dl (< 1.29 mmol/l) for women LDL-C ≥ 130 mg/dl (≥ 3.36 mmol/l) 260 participants were randomized to fenofibrate 135 mg/day 265 participants were randomized to rosuvastatin 10 mg/day 261 participants were randomized to fenofibrate/rosuvastatin 135 mg/10 mg/day 266 participants were randomized to rosuvastatin 20 mg/day 262 participants were randomized to fenofibrate/rosuvastatin 135 mg/20 mg/day 131 participants were randomized to rosuvastatin 40 mg/day exclusion criteria: hypersensitivity to test drugs Asian ancestry, type 1 diabetes mellitus, uncontrolled type 2 diabetes mellitus GI disease, hepatic disease, renal disease, unstable cardiovascular disease, myopathy solid organ transplant, HIV positive, drug or alcohol abuse, mental instability changes in HRT, treatment with excluded medications, abnormal TSH study unsuitability Rosuvastatin 10 mg/day baseline TC : 6.68 mmol/l (258 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.93 mmol/l (152 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 0.99 mmol/l (38 mg/dl) Rosuvastatin 10 mg/day baseline TG : 3.31 mmol/l (293 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.66 mmol/l (219 mg/dl) Rosuvastatin 20 mg/day baseline TC : 6.72 mmol/l (260 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 3.98 mmol/l (154 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 0.99 mmol/l (38 mg/dl) Rosuvastatin 20 mg/day baseline TG : 3.32 mmol/l (294 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C: 5.71 mmol/l (221 mg/dl) Rosuvastatin 40 mg/day baseline TC : 6.67 mmol/l (258 mg/dl)

Jones 2009 *(Continued)*

	Rosuvastatin 40 mg/day baseline LDL-C : 3.96 mmol/l (153 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 0.97 mmol/l (38 mg/dl) Rosuvastatin 40 mg/day baseline TG : 3.19 mmol/l (283 mg/dl) Rosuvastatin 40 mg/day baseline non-HDL-C: 5.66 mmol/l (219 mg/dl)
Interventions	fenofibrate 135 mg/day rosuvastatin 10 mg/day fenofibrate/rosuvastatin 135 mg/10 mg/day rosuvastatin 20 mg/day fenofibrate/rosuvastatin 135 mg/20 mg/day rosuvastatin 40 mg/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	fenofibrate 135 mg/day fenofibrate/rosuvastatin 135 mg/10 mg/day fenofibrate/rosuvastatin 135 mg/20 mg/day groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	22/165 participants from the rosuvastatin 10 mg/day group were not included in the efficacy analysis 28/266 participants from the rosuvastatin 20 mg/day group were not included in the efficacy analysis 11/131 participants from the rosuvastatin 40 mg/day group were not included in the efficacy analysis 61/662 = 9.2% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	Financial support was provided by Abbott. Abbott make fenofibrate. Data may be bias against rosuvastatin

Kanazawa 2009

Methods	no one had treatments with any lipid-altering drugs, washout not required 3-month randomized open trial
Participants	36 men and women mean age 60 years with hypercholesterolaemia and type 2 diabetes mellitus LDL-C ≥ 100 mg/dl (≥ 2.59 mmol/l) 18 were randomized to rosuvastatin 2.5 mg/day 18 were randomized to ezetimibe 10 mg/day exclusion criteria: hepatic or renal dysfunction nutritional derangement Rosuvastatin 2.5 mg/day baseline TC : 5.82 mmol/l (225 mg/dl) Rosuvastatin 2.5 mg/day baseline LDL-C : 3.65 mmol/l (141 mg/dl) Rosuvastatin 2.5 mg/day baseline HDL-C : 1.63 mmol/l (63 mg/dl) Rosuvastatin 2.5 mg/day baseline TG : 1.39 mmol/l (123 mg/dl) Rosuvastatin 2.5 mg/day baseline non-HDL-C : 4.19 mmol/l (162 mg/dl)
Interventions	Rosuvastatin 2.5 mg/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	there was only one group of participants analyzed therefore it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Low risk	source of funding not reported

Kim 2013

Methods	no washout required because participants were not receiving any lipid-altering agents within 8 weeks of randomization

Kim 2013 *(Continued)*

	8-week randomized single-blind placebo-controlled trial
Participants	53 men and women with mild to moderate hypertension mean age 60 years SBP < 170 mmHg DBP < 105 mm Hg exclusion criteria: renal disease, hepatic disease, any thyroid disease, uncontrolled diabetes uncontrolled severe hypertension, stroke, acute coronary syndrome and unstable angina Placebo baseline TC : 5.14 mmol/l (199 mg/dl) Placebo baseline LDL-C : 3.28 mmol/l (127 mg/dl) Placebo baseline HDL-C : 1.29 mmol/l (50 mg/dl) Placebo baseline TG : 2.30 mmol/l (204 mg/dl) Placebo baseline non-HDL-C : 3.856 mmol/l (149 mg/dl) Rosuvastatin 20 mg/day baseline TC : 5.64 mmol/l (218 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 3.81 mmol/l (147 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.30 mmol/l (50 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.96 mmol/l (174 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C : 4.345 mmol/l (168 mg/dl)
Interventions	26 participants received placebo for 8 weeks 27 participants received Rosuvastatin 20 mg/day for 8 weeks
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported "medication was provided in envelopes"
Blinding (performance bias and detection bias) All outcomes	High risk	single-blinded, patients were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis WDAE data were provided
Other bias	Low risk	pharmaceutical companies did not fund the trial

Koh 2013

Methods	no washout required because participants were not receiving any lipid-altering agents within 8 weeks of randomization 8-week randomized single-blind placebo-controlled trial
Participants	162 men and women with hypercholesterolaemia age 54-56 years LDL-C ≥ 130 mg/dl (3.36 mmol/l) exclusion criteria: liver disease, renal failure, hypothyroidism, myopathy, uncontrolled diabetes, severe hypertension, stroke acute coronary events, coronary revascularization within 3 months of trial, alcohol abuse Placebo baseline TC : 6.41 mmol/l (248 mg/dl) Placebo baseline LDL-C : 4.29 mmol/l (166 mg/dl) Placebo baseline HDL-C : 1.40 mmol/l (54 mg/dl) Placebo baseline TG : 1.56 mmol/l (138 mg/dl) Placebo baseline non-HDL-C : 5.017 mmol/l (194 mg/dl) Rosuvastatin 20 mg/day baseline TC : 6.36 mmol/l (246 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 4.29 mmol/l (166 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.37 mmol/l (53 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.535 mmol/l (136 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C : 4.991 mmol/l (193 mg/dl)
Interventions	54 participants received placebo 54 participants received rosuvastatin 10 mg/day 54 participants received pravastatin 40 mg/day
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	the pravastatin group was not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	High risk	single-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/54 of the placebo participants were not included in the efficacy analysis 2/54 of the rosuvastatin participants were not included in the efficacy analysis
Selective reporting (reporting bias)	High risk	all lipid parameters were included in the efficacy analysis WDAEs were not reported
Other bias	Low risk	pharmaceutical companies did not fund the trial

Kostapanos 2006

Methods	6-week washout period 12-week open study
Participants	40 men and women with primary dyslipidaemia type IIa age ≥18 years LDL-C > 160 mg/dl (> 4.13 mmol/l) TG ≤ 350 mg/dl (≤ 3.95 mmol/l) 40 patients received rosuvastatin 10 mg/day exclusion criteria:renal impairment, diabetes mellitus, raised thyroid stimulating hormone levels liver disease, child-bearing potential, antihypertensive therapy modified 12 or fewer weeks before enrolment Rosuvastatin 10 mg/day baseline TC : 7.95 mmol/l (307 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 5.56 mmol/l (215 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.6 mmol/l (62 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.55 mmol/l (137 mg/dl)
Interventions	rosuvastatin 10 mg/day
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	there was only one group of participants analyzed therefore it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	non-HDL-C was not included in the efficacy analysis
Other bias	Unclear risk	source of funding not provided

Kostapanos 2007a

Methods	6-week washout period 12-week open-label trial

Kostapanos 2007a *(Continued)*

Participants	75 men and women mean age 52 years with hyperlipidaemia LDL-C >160 mg/dl (> 4.14 mmol/l) TG < 400 mg/dl (< 4.52 mmol/l) 75 received rosuvastatin 10 mg/day exclusion criteria: renal dysfunction, liver disease or dysfunction elevated TSH, diabetes mellitus, childbearing potential lipid-lowering therapy agents within 8 weeks of trial Rosuvastatin 10 mg/day baseline TC : 7.71 mmol/l (298 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 5.35 mmol/l (207 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.47 mmol/l (57 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.63 mmol/l (144 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 6.23 mmol/l (241 mg/dl)
Interventions	Rosuvastatin 10 mg/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	there was only one group of participants analyzed therefore it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Low risk	pharmaceutical companies did not fund this trial

Kostapanos 2007b

Methods	6-week washout period 12-week randomized open-label trial
Participants	130 men and women mean age 52 years with primary hyperlipidaemia

Kostapanos 2007b *(Continued)*

	45 participants randomized to rosuvastatin 10 mg/day 45 participants randomized to rosuvastatin 20 mg/day 40 participants randomized to control dietary treatment only not a placebo exclusion criteria: renal dysfunction, liver disease or dysfunction elevated TSH, diabetes mellitus, child-bearing potential lipid-lowering therapy agents within 8 weeks of trial Rosuvastatin 10 mg/day baseline TC : 7.99 mmol/l (309 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 5.59 mmol/l (216 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.66 mmol/l (64 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.46 mmol/l (129 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 6.34 mmol/l (245 mg/dl) Rosuvastatin 20 mg/day baseline TC : 8.07 mmol/l (312 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 5.82 mmol/l (225 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.63 mmol/l (63 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.43 mmol/l (127 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C: 6.44 mmol/l (249 mg/dl)
Interventions	rosuvastatin 10 mg/day rosuvastatin 20 mg/day control dietary treatment only not a placebo
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	control dietary treatment only not a placebo group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis

Kostapanos 2007b *(Continued)*

Other bias	Unclear risk	source of funding not reported

Kostapanos 2008a

Methods	6-week washout period 12-week randomized open-label trial
Participants	80 men and women mean age 52 years non-diabetic with primary hyperlipidaemia 40 participants randomized to rosuvastatin 10 mg/day 40 participants randomized to control non-statin group dietary treatment only not a placebo exclusion criteria: renal dysfunction, liver disease or dysfunction elevated TSH, diabetes mellitus, childbearing potential lipid-lowering therapy agents within 8 weeks of trial Rosuvastatin 10 mg/day baseline TC : 7.9 mmol/l (305 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 5.4 mmol/l (209 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.6 mmol/l (62 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.7 mmol/l (151 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 6.3 mmol/l (244 mg/dl)
Interventions	Rosuvastatin 10 mg/day control non-statin group dietary treatment only not a placebo
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	control non-statin group dietary treatment only not a placebo group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis

Kostapanos 2008a *(Continued)*

Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

Kostapanos 2008b

Methods	6-week washout period 12-week randomized open-label trial
Participants	120 men and women mean age 50 years with primary dyslipidaemia 60 participants randomized to rosuvastatin 20 mg/day 60 participants randomized to control non-statin group dietary treatment only not a placebo exclusion criteria: renal dysfunction, liver disease or dysfunction elevated TSH, diabetes mellitus, childbearing potential lipid-lowering therapy agents within 8 weeks of trial Rosuvastatin 20 mg/day baseline TC : 8.59 mmol/l (332 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 6.03 mmol/l (233 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.58 mmol/l (61 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C: 7.01 mmol/l (271 mg/dl)
Interventions	Rosuvastatin 20 mg/day control non-statin group dietary treatment only not a placebo
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C and non-HDL-C
Notes	control non-statin group dietary treatment only not a placebo was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	the Rosuvastatin 20 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 20 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 20 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis

Kostapanos 2008b *(Continued)*

Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

Kostapanos 2009

Methods	6-week washout period 12-week randomized open-label trial
Participants	150 men and women mean age 51 years with primary dyslipidaemia 50 participants randomized to rosuvastatin 10 mg/day 50 participants randomized to rosuvastatin 20 mg/day 50 participants randomized to control non-statin group dietary treatment only not a placebo exclusion criteria: renal dysfunction, liver disease or dysfunction elevated TSH, diabetes mellitus, childbearing potential lipid-lowering therapy agents within 8 weeks of trial Rosuvastatin 10 mg/day baseline TC : 7.86 mmol/l (304 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 5.46 mmol/l (211 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.63 mmol/l (63 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.69 mmol/l (150 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 6.23 mmol/l (241 mg/dl) Rosuvastatin 20 mg/day baseline TC : 7.94 mmol/l (307 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 5.59 mmol/l (216 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.55 mmol/l (60 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.74 mmol/l (154 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C: 6.39 mmol/l (247 mg/dl)
Interventions	rosuvastatin 10 mg/day rosuvastatin 20 mg/day control dietary treatment only not a placebo
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	control dietary treatment only not a placebo group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day and Rosuvastatin 20 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable

Kostapanos 2009 *(Continued)*

Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day and Rosuvastatin 20 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day and Rosuvastatin 20 mg/day treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

Lamendola 2005

Methods	6-week washout 12-week randomized open study
Participants	39 men and women with combined dyslipidaemia aged 51-54 years old TC > 200 mg/dl (> 5.17 mmol/l) TG > 200 mg/dl (> 2.26 mmol/l) BMI <33.0 20 participants randomized to rosuvastatin 19 participants randomized to gemfibrozil exclusion criteria: none reported Rosuvastatin 40 mg/day baseline TC : 6.26 mmol/l (242 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 3.57 mmol/l (138 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.03 mmol/l (40 mg/dl) Rosuvastatin 40 mg/day baseline TG : 3.66 mmol/l (324 mg/dl) Rosuvastatin 40 mg/day baseline non-HDL-C: 5.22 mmol/l (202 mg/dl)
Interventions	Rosuvastatin 40 mg/day Gemfibrozil 1.2 g/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Gemfibrozil 1.2 g/day group was not analyzed SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement

Lamendola 2005 *(Continued)*

Random sequence generation (selection bias)	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the trial. Data may support bias for rosuvastatin

Liberopoulos 2013

Methods	participants were not receiving any lipid-altering agents within 3 months of trial no washout required 12-week before-and-after trial
Participants	40 men and women with impaired fasting glucose, hypertension and mixed dyslipidaemia LDL-C >160 mg/dl (4.14 mmol/l) TG >150 mg/dl (1.69 mmol/l) 20 participants were randomized to manidipine and rosuvastatin 10 mg/day 20 participants were randomized to olmesartan and rosuvastatin 10 mg/day exclusion criteria: diabetes mellitus, cardiovascular disease, renal disease hypothyroidism, liver dysfunction and females not taking sufficient contraceptive measures Rosuvastatin 10 mg/day baseline TC : 6.745 mmol/l (261 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.345 mmol/l (168 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.435 mmol/l (55 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.315 mmol/l (206 mg/dl)
Interventions	manidipine and rosuvastatin 10 mg/day for 12 weeks olmesartan and rosuvastatin 10 mg/day for 12 weeks both sets of data were combined
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C and non HDL-C
Notes	SDs were imputed
Risk of bias	

Liberopoulos 2013 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	triglyceride data were not included in the efficacy analysis
Other bias	Low risk	no financial support for the study not industry funded

Lu 2004

Methods	6-week washout period 6-week randomized, double-blind, placebo-controlled trial
Participants	46 men and women with hypercholesterolaemia LDL-C > 160 mg/dl (> 4.14 mmol/l) TG <350 mg/dl (< 3.95 mmol/l) 25 were randomized to placebo 25 were randomized to rosuvastatin exclusion criteria:renal dysfunction, hepatic dysfunction, thyroid disease, chronic or acute inflammation, cancer history, uncompensated heart failure, uncontrolled hypertension uncontrolled diabetes mellitus, acute coronary syndrome within 1 month of trial entry were also excluded Placebo baseline TC : 6.63 mmol/l (256 mg/dl) Placebo baseline LDL-C : 4.61 mmol/l (178 mg/dl) Placebo baseline HDL-C : 1.26 mmol/l (49 mg/dl) Placebo baseline TG : 1.65 mmol/l (146 mg/dl) Rosuvastatin 10 mg/day baseline TC : 6.72 mmol/l (260 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.59 mmol/l (177 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.14 mmol/l (44 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.15 mmol/l (190 mg/dl)
Interventions	Placebo Rosuvastatin 10 mg/day

Lu 2004 *(Continued)*

Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	2/25 placebo group was not included in the efficacy analysis 2/25 rosuvastatin group was not included in the efficacy analysis 8% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca partially funded the study. Data may support bias for rosuvastatin

Lui 2007

Methods	4-week washout period 4-week open-label trial
Participants	146 men and women mean age 56 years with hyperlipidaemia TC ≥ 5.2 mmol/l (≥ 201 mg/dl) TG ≥ 2.3 mmol/l (≥ 204 mg/dl) LDL-C ≥3.4 mmol/l (≥ 131 mg/dl) 146 participants received rosuvastatin 10 mg/day exclusion criteria:renal dysfunction, hepatic dysfunction drugs known to affect lipid profiles or rosuvastatin interaction Rosuvastatin 10 mg/day baseline TC : 7.84 mmol/l (303 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 5.4 mmol/l (209 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.53 mmol/l (59 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.06 mmol/l (182 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 6.3 mmol/l (244 mg/dl)
Interventions	Rosuvastatin 10 mg/day

Lui 2007 *(Continued)*

Outcomes	per cent change from baseline at 4 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	SD was imputed for non-HDL-C

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	there was only one group of participants analyzed therefore it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	9/146 = 6.2% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not provided

LUNAR 2012

Methods	no washout period required no participant received lipid-altering agents for at least 4 weeks 12 week before-and-after trial
Participants	825 patients with acute coronary syndrome age 18 to 75 years LDL-C > 70 mg/dl (1.81 mmol/l) TG< 500 mg/dl (5.645 mmol/l) 277 patients received rosuvastatin 20 mg/day 270 patients received rosuvastatin 40 mg/day 278 patients received atorvastatin 80 mg/day exclusion criteria: HRT within 3 months, Q-wave MI, pulmonary oedema, moderate or severe congestive heart failure severe mitral regurgitation, acute ventricular septal defect, heart disease, stroke, sepsis, coronary artery bypass graft within 3 months HMG CoA reductase inhibitor hypersensitivity, pregnancy, uncontrolled diabetes mellitus, hypertension, hypothyroidism, systolic hypotension hepatic dysfunction, severe anaemia, serum creatinine >2 mg/dL and serum creatine kinase > 3 times ULN Rosuvastatin 20 mg/day baseline TC : 5.19 mmol/l (201 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 3.58 mmol/l (138 mg/dl)

LUNAR 2012 *(Continued)*

	Rosuvastatin 20 mg/day baseline HDL-C : 1.02 mmol/l (39 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C : 4.17 mmol/l (161 mg/dl) Rosuvastatin 20 mg/day baseline TG : 2.04 mmol/l (181 mg/dl) Rosuvastatin 40 mg/day baseline TC : 5.22 mmol/l (202 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 3.59 mmol/l (139 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.00 mmol/l (39 mg/dl) Rosuvastatin 40 mg/day baseline non-HDL-C : 4.21 mmol/l (163 mg/dl) Rosuvastatin 40 mg/day baseline TG : 2.06 mmol/l (182 mg/dl)
Interventions	rosuvastatin 20 mg/day for 12 weeks rosuvastatin 40 mg/day for 12 weeks atorvastatin 80 mg/day for 12 weeks
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, non-HDL-C and triglycerides
Notes	atorvastatin group was not analyzed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 20 mg/day and the Rosuvastatin 40 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 20 mg/day and the Rosuvastatin 40 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 20 mg/day and the Rosuvastatin 40 mg/day treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	31/277 rosuvastatin 20 mg/day were not included in the efficacy analysis 19/270 rosuvastatin 40 mg/day were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the trial. Data may support bias for rosuvastatin

Mabuchi 2004

Methods	8-week washout period 18-week open-label study
Participants	37 men and non-pregnant women age ≥ 18 years with heterozygous familial hypercholesterolaemia LDL-C ≥ 220 and < 500 mg/dl (≥5.69 and < 12.93 mmol/l)

Mabuchi 2004 *(Continued)*

	TG ≤ 400 mg/dl (≤ 4.52 mmol/l) 37 patients received rosuvastatin exclusion criteria: statin sensitivity, serious or unstable medical or psychological conditions that could compromise the patient's safety or successful trial participation history of homozygous FH, use of medications that affect lipid profile or safety concern, drug or alcohol abuse CK > 3 X ULN, renal dysfunction, liver disease or dysfunction Rosuvastatin 10 mg/day baseline TC : 9.91 mmol/l (383 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 7.86 mmol/l (304 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.29 mmol/l (50 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.66 mmol/l (147 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 8.62 mmol/l (333 mg/dl)
Interventions	Rosuvastatin 10 mg/day for 0-6 weeks Rosuvastatin 20 mg/day for 6-12 weeks Rosuvastatin 40 mg/day for 12-18 weeks
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Rosuvastatin 20 mg/day for 6-12 weeks Rosuvastatin 40 mg/day for 12-18 weeks groups were not analyzed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

Makariou 2012

Methods	participants were not receiving any lipid-altering agents within 4 weeks of trial no washout required 12 week before-and-after trial
Participants	60 men and women mean age of 55 years with mixed lipidaemia LDL-C >160 mg/dl (4.14 mmol/l) TG >200 mg/dl (2.26 mmol/l) 22 participants were randomized to rosuvastatin 40 mg/day for 12 weeks 21 participants were randomized to rosuvastatin 10 mg/day plus 200 mg fenofibrate for 12 weeks 17 participants were randomized to rosuvastatin 10 mg/day plus 2 g omega-3 fatty acids for 12 weeks exclusion criteria: coronary heart disease, atherosclerotic disease, TG > 500 mg/dl renal disease, diabetes mellitus, hypothyroidism, liver disease, uncontrolled hypertension Rosuvastatin 40 mg/day baseline TC : 8.22 mmol/l (318 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 5.9 mmol/l (228 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.4 mmol/l (54 mg/dl) Rosuvastatin 40 mg/day baseline non-HDL-C: 6.83 mmol/l (264 mg/dl)
Interventions	rosuvastatin 40 mg/day rosuvastatin 10 mg/day plus 200 mg fenofibrate rosuvastatin 10 mg/day plus 2 g omega-3 fatty acids
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C and non HDL-C
Notes	rosuvastatin 10 mg/day plus 200 mg fenofibrate rosuvastatin 10 mg/day plus 2 g omega-3 fatty acids groups were not analyzed SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis

Makariou 2012 *(Continued)*

Selective reporting (reporting bias)	High risk	triglyceride data were not included in the efficacy analysis
Other bias	Low risk	no financial support for the study not industry funded

Marais 2008

Methods	4-week washout period 0-18 week open-label forced dose titration trial then a 18-24 week randomized double-blind cross-over trial
Participants	44 patients ≥ 10 years with homozygous familial hypercholesterolaemia LDLC ≥ 500 mg/dl (12.9 mmol/l) TG < 600 mg/dl (6.8 mmol/l) 41 patients received rosuvastatin exclusion criteria:active liver disease or dysfunction, serum CK > 3 X ULN, renal dysfunction, uncontrolled hypertension Rosuvastatin 20 mg/day baseline TC : 15.0 mmol/l (580 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 13.3 mmol/l (514 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 0.93 mmol/l (36 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.60 mmol/l (142 mg/dl)
Interventions	Rosuvastatin 20 mg/day for 0-6 weeks Rosuvastatin 40 mg/day for 6-12 weeks Rosuvastatin 80 mg/day for 12-18 weeks Crossover rosuvastatin 80 mg/day and atorvastatin 80 mg/day 18-24 and 24-30 weeks
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	Rosuvastatin 40 mg/day for 6-12 weeks Rosuvastatin 80 mg/day for 12-18 weeks Cros-sover rosuvastatin 80 mg/day and atorvastatin 80 mg/day 18-24 and 24-30 weeks groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 20 mg/day for 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 20 mg/day for 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable

Marais 2008 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 20 mg/day for 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	3/41 participants were not included in the efficacy analysis 7.3% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the study. Data may support bias for rosuvastatin

Marino 2012

Methods	participants were not receiving any lipid-altering agents no washout period required 12-week before-and-after trial
Participants	10 participants had type 2 diabetes and hypercholesterolaemia mean age was 68 years 10 participants had hypercholesterolaemia mean age was 65 years exclusion criteria: infection, smoking habits and competitive sporting activities Rosuvastatin 10 mg/day baseline TC : 6.615 mmol/l (256 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.3 mmol/l (166 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.355 mmol/l (52 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.955 mmol/l (173 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.26 mmol/l (203 mg/dl)
Interventions	rosuvastatin 10 mg/day for 12 weeks
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	there was only one group of participants analyzed therefore it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis

Marino 2012 *(Continued)*

Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding was not reported

MERCURY I 2004

Methods	6-week washout period 16-week randomized open-label trial
Participants	3161 patients ≥ 18 years history of CHD or atherosclerosis type 2 diabetes mellitus CHD risk > 20% over 10 years LDL-C ≥ 2.99 mmol/l (≥ 115 mg/dl) TG <4.52 mmol/l (< 400 mg/dl) 538 participants were randomized to rosuvastatin 10 mg/day for 0-8 weeks 529 participants were randomized to atorvastatin 10 mg/day for 0-8 weeks 925 participants were randomized to atorvastatin 20 mg/day for 0-8 weeks 543 participants were randomized to simvastatin 20 mg/day for 0-8 weeks 521 participants were randomized to pravastatin 40 mg/day for 0-8 weeks 521 participants were randomized to rosuvastatin 10 mg/day for 8-16 weeks 276 participants switched from atorvastatin 10 mg/day to rosuvastatin 10 mg/day for 8-16 weeks 240 participants were randomized to atorvastatin 10 mg/day for 8-16 weeks 293 participants switched from atorvastatin 20 mg/day to rosuvastatin 10 mg/day for 8-16 weeks 305 participants switched from atorvastatin 20 mg/day to rosuvastatin 20 mg/day for 8-16 weeks 299 participants were randomized to atorvastatin 20 mg/day for 8-16 weeks 277 participants switched from simvastatin 20 mg/day to rosuvastatin 10 mg/day for 8-16 weeks 250 participants were randomized to simvastatin 20 mg/day for 8-16 weeks 253 participants switched from pravastatin 40 mg/day to rosuvastatin 10 mg/day for 8-16 weeks 253 participants were randomized to pravastatin 40 mg/day for 8-16 weeks exclusion criteria: pregnancy, lactation homozygous familial hypercholesterolaemia, type III hyperlipoproteinaemia active arterial disease, uncontrolled hypertension, active liver disease or hepatic dysfunction serum CK > 3 X ULN and renal dysfunction Rosuvastatin 10 mg/day baseline LDL-C : 4.26 mmol/l (165 mg/dl)
Interventions	rosuvastatin 10 mg/day for 0-8 weeks atorvastatin 10 mg/day for 0-8 weeks

MERCURY I 2004 *(Continued)*

	atorvastatin 20 mg/day for 0-8 weeks simvastatin 20 mg/day for 0-8 weeks pravastatin 40 mg/day for 0-8 weeks rosuvastatin 10 mg/day for 8-16 weeks switched from atorvastatin 10 mg/day to rosuvastatin 10 mg/day for 8-16 weeks atorvastatin 10 mg/day for 8-16 weeks switched from atorvastatin 20 mg/day to rosuvastatin 20 mg/day for 8-16 weeks atorvastatin 20 mg/day for 8-16 weeks switched from simvastatin 20 mg/day to rosuvastatin 10 mg/day for 8-16 weeks simvastatin 20 mg/day for 8-16 weeks switched from pravastatin 40 mg/day to rosuvastatin 10 mg/day for 8-16 weeks pravastatin 40 mg/day for 8-16 weeks
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	atorvastatin 10 mg/day for 0-8 weeks atorvastatin 20 mg/day for 0-8 weeks simvastatin 20 mg/day for 0-8 weeks pravastatin 40 mg/day for 0-8 weeks rosuvastatin 10 mg/day for 8-16 weeks switched from atorvastatin 10 mg/day to rosuvastatin 10 mg/day for 8-16 weeks atorvastatin 10 mg/day for 8-16 weeks switched from atorvastatin 20 mg/day to rosuvastatin 20 mg/day for 8-16 weeks atorvastatin 20 mg/day for 8-16 weeks switched from simvastatin 20 mg/day to rosuvastatin 10 mg/day for 8-16 weeks simvastatin 20 mg/day for 8-16 weeks switched from pravastatin 40 mg/day to rosuvastatin 10 mg/day for 8-16 weeks pravastatin 40 mg/day for 8-16 weeks groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day for 0-8 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable

MERCURY I 2004 *(Continued)*

Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day for 0-8 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day for 0-8 weeks treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	105/3161 (3.3%) participants were not included in the efficacy analysis
Selective reporting (reporting bias)	High risk	non-HDL-C was not included in the efficacy analysis
Other bias	High risk	Trial was supported by AstraZeneca. Data may support bias for rosuvastatin

MERCURY II 2006

Methods	6-week washout period 8-week open randomized study
Participants	1993 men and women with hypercholesterolaemia age ≥ 18 years LDL-C ≥ 130 to < 250 mg/dl (≥3.36 to < 6.46 mmol/l) TG <400 mg/dl (<4.52 mmol/l) 392 received rosuvastatin 798 received atorvastatin 803 received simvastatin exclusion criteria: pregnancy or lactation, homozygous familial hypercholesterolaemia known hyperlipoproteinaemia types I, III, IV or V, unstable arterial disease within 3 months of trial uncontrolled hypertension, fasting serum glucose of >180 mg/dl (> 10.0 mmol/l) during dietary lead-in active liver disease or dysfunction Rosuvastatin 20 mg/day baseline TC : 6.48 mmol/l (251 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 4.32 mmol/l (167 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.22 mmol/l (47 mg/dl) Rosuvastatin 20 mg/day baseline TG : 2.05 mmol/l (182 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C: 5.26 mmol/l (203 mg/dl)
Interventions	Rosuvastatin 20 mg/day Atorvastatin 10 mg/day Atorvastatin 20 mg/day Simvastatin 20 mg/day Simvastatin 40 mg/day

MERCURY II 2006 *(Continued)*

Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Atorvastatin 10 mg/day Atorvastatin 20 mg/day Simvastatin 20 mg/day Simvastatin 40 mg/day groups were not included in the analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 20 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 20 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 20 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	9/392 were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

Milionis 2005

Methods	6-week washout period 20-week before-and-after trial
Participants	55 men and women age 55-66 years with primary hyperlipidaemia TC > 240 mg/dl (>6.2 mmol/l) TG < 350 mg/dl (4.0 mmol/l) 55 patients received rosuvastatin exclusion criteria: liver disease or dysfunction, renal dysfunction, diabetes mellitus, raised FSH levels, medical conditions that might preclude successful completion of trial participants receiving drugs that could affect lab parameters tested were also excluded Rosuvastatin 10 mg/day baseline TC : 7.63 mmol/l (295 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 5.51 mmol/l (213 mg/dl)

Milionis 2005 *(Continued)*

	Rosuvastatin 10 mg/day baseline HDL-C : 1.37 mmol/l (53 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.67 mmol/l (148 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 6.26 mmol/l (242 mg/dl)
Interventions	Rosuvastatin 10 mg/day for 0-6 weeks Rosuvastatin 10 mg/day for 6-20 weeks
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Rosuvastatin 10 mg/day for 6-20 weeks group was not analyzed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day for 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day for 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day for 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the analysis
Other bias	Unclear risk	source of funding not reported

Mori 2013

Methods	1-month or more washout period 3-month before-and-after trial
Participants	128 men and women with hypercholesterolaemia and type 2 diabetes aged 20-80 years LDL-C ≥ 100 mg /dl (2.59 mmol/l) 44 participants received atorvastatin 42 participants received rosuvastatin 42 participants received pravastatin exclusion criteria: history of stoke or ischaemic heart disease during the previous 6 months hepatic dysfunction, renal dysfunction, females that were pregnant or possibly pregnant Rosuvastatin 5 mg/day baseline TC : 6.25 mmol/l (242 mg/dl)

Mori 2013 *(Continued)*

	Rosuvastatin 5 mg/day baseline LDL-C : 4.17 mmol/l (161 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.58 mmol/l (61 mg/dl) Rosuvastatin 5 mg/day baseline TG : 1.61 mmol/l (143 mg/dl) Rosuvastatin 5 mg/day baseline non-HDL-C: 4.67 mmol/l (181 mg/dl)
Interventions	Atorvastatin 10 mg/day for 3 months Rosuvastatin 5 mg/day for 3 months Pravastatin 10 mg/day for 3 months
Outcomes	per cent change from baseline at 3 months of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Atorvastatin 10 mg/day for 3 months and Pravastatin 10 mg/day for 3 months groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day for 3 months treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day for 3 months treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day for 3 months treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	High risk	5/42 (11.9%) of the rosuvastatin group were not included in the efficacy analysis due to dropout or incomplete evaluation
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the analysis
Other bias	Low risk	no pharmaceutical company funded the study

Moutzouri 2011

Methods	4-week washout period 12-week randomized open-label trial
Participants	153 men and women with primary hypercholesterolaemia TG ≤ 500 mg/dl (≤ 565 mmol/l) 55 participants were randomized to simvastatin 40 mg/day 45 participants were randomized to rosuvastatin 10 mg/day 53 participants were randomized to simvastatin/ezetimibe 10/10 mg/day exclusion criteria:CVD, carotid artery disease, peripheral artery disease

Moutzouri 2011 *(Continued)*

	abdominal aortic aneurysm, diabetes mellitus, renal disease hypothyroidism, liver disease, cancer, inflammatory or infectious diseases, uncontrolled hypertension Rosuvastatin 10 mg/day baseline TC : 7.09 mmol/l (274 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.71 mmol/l (182 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.58 mmol/l (61 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.51 mmol/l (213 mg/dl)
Interventions	rosuvastatin 10 mg/day simvastatin 40 mg/day simvastatin/ezetimibe 10/10 mg/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C and non-HDL-C
Notes	simvastatin 40 mg/day simvastatin/ezetimibe 10/10 mg/day groups were not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	triglycerides were not included in the efficacy analysis
Other bias	Low risk	authors state no conflict of interest

Olsson 2001

Methods	6-week washout period 6-week randomized double-blind placebo-controlled trial
Participants	206 men aged 18-70 and postmenopausal women with hypercholesterolaemia aged 50-70 years

Olsson 2001 *(Continued)*

LDL-C > 4.14 mmol/l (>160 mg/dl) and < 6.21 mmol/l (< 240 mg/dl)

TG < 3.39 mmol/l (< 300 mg/dl)

BMI ≤ 30

29 received placebo

137 received rosuvastatin

23 received atorvastatin

exclusion criteria:active arterial disease, cancer history, uncontrolled hypertension, diabetes mellitus

uncontrolled hypothyroidism, homozygous familial hypercholesterolaemia, active liver disease or dysfunction

CK > 3 X ULN

Placebo baseline TC : 7.00 mmol/l (271 mg/dl)
Placebo baseline LDL-C : 5.10 mmol/l (197 mg/dl)
Placebo baseline HDL-C : 1.40 mmol/l (54 mg/dl)
Placebo baseline TG : 1.40 mmol/l (124 mg/dl)

Rosuvastatin 1 mg/day baseline TC : 6.90 mmol/l (267 mg/dl)
Rosuvastatin 1 mg/day baseline LDL-C : 4.90 mmol/l (189 mg/dl)
Rosuvastatin 1 mg/day baseline HDL-C : 1.40 mmol/l (54 mg/dl)
Rosuvastatin 1 mg/day baseline TG : 1.30 mmol/l (115 mg/dl)

Rosuvastatin 2.5 mg/day baseline TC : 6.80 mmol/l (236 mg/dl)
Rosuvastatin 2.5 mg/day baseline LDL-C : 4.90 mmol/l (189 mg/dl)
Rosuvastatin 2.5 mg/day baseline HDL-C : 1.30 mmol/l (50 mg/dl)
Rosuvastatin 2.5 mg/day baseline TG : 1.40 mmol/l (124 mg/dl)

Rosuvastatin 5 mg/day baseline TC : 7.00 mmol/l (271 mg/dl)
Rosuvastatin 5 mg/day baseline LDL-C : 5.00 mmol/l (193 mg/dl)
Rosuvastatin 5 mg/day baseline HDL-C : 1.30 mmol/l (50 mg/dl)
Rosuvastatin 5 mg/day baseline TG : 1.40 mmol/l (124 mg/dl)

Rosuvastatin 10 mg/day baseline TC : 6.90 mmol/l (267 mg/dl)
Rosuvastatin 10 mg/day baseline LDL-C : 4.90 mmol/l (189 mg/dl)
Rosuvastatin 10 mg/day baseline HDL-C : 1.30 mmol/l (50 mg/dl)
Rosuvastatin 10 mg/day baseline TG : 1.50 mmol/l (133 mg/dl)

Rosuvastatin 20 mg/day baseline TC : 6.80 mmol/l (263 mg/dl)
Rosuvastatin 20 mg/day baseline LDL-C : 4.70 mmol/l (182 mg/dl)
Rosuvastatin 20 mg/day baseline HDL-C : 1.30 mmol/l (50 mg/dl)
Rosuvastatin 20 mg/day baseline TG : 1.60 mmol/l (142 mg/dl)

Rosuvastatin 40 mg/day baseline TC : 6.70 mmol/l (259 mg/dl)
Rosuvastatin 40 mg/day baseline LDL-C : 4.80 mmol/l (186 mg/dl)
Rosuvastatin 40 mg/day baseline HDL-C : 1.40 mmol/l (54 mg/dl)
Rosuvastatin 40 mg/day baseline TG : 1.30 mmol/l (115 mg/dl)

Rosuvastatin 80 mg/day baseline TC : 6.80 mmol/l (236 mg/dl)
Rosuvastatin 80 mg/day baseline LDL-C : 4.90 mmol/l (189 mg/dl)
Rosuvastatin 80 mg/day baseline HDL-C : 1.30 mmol/l (50 mg/dl)
Rosuvastatin 80 mg/day baseline TG : 1.30 mmol/l (115 mg/dl)

Interventions	Placebo Rosuvastatin 1 mg/day Rosuvastatin 2.5 mg/day

Olsson 2001 *(Continued)*

	Rosuvastatin 5 mg/day
	Rosuvastatin 10 mg/day
	Rosuvastatin 20 mg/day
	Rosuvastatin 40 mg/day
	Rosuvastatin 80 mg/day
	Atorvastatin 10 mg/day
	Atorvastatin 80 mg/day
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides WDAEs reported
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	17/206 were not included in the efficacy analysis 8.25 % were not analyzed
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the study. Data may support bias for rosuvastatin

Olsson 2002

Methods	6-week washout period 52-week randomized double-blind trial
Participants	412 men and women aged ≥ 18 years with hypercholesterolaemia LDL-C between 160 and < 250 mg/dl (4.14 and <6.5 mmol/l) TG ≤ 400 mg/dl (≤ 4.5 mmol/l) EPAT score ≤28 138 participants were randomized to rosuvastatin 5 mg/day 134 participants were randomized to rosuvastatin 10 mg/day 140 participants were randomized to atorvastatin 10 mg/day Conventional exclusion criteria for lipid-modifying drugs under development were applied

Olsson 2002 *(Continued)*

	Rosuvastatin 5 mg/day baseline TC : 7.07 mmol/l (273 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 4.86 mmol/l (188 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.41 mmol/l (55 mg/dl) Rosuvastatin 5 mg/day baseline TG : 1.76 mmol/l (156 mg/dl) Rosuvastatin 10 mg/day baseline TC : 7.00 mmol/l (271 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.81 mmol/l (186 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.44 mmol/l (56 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.65 mmol/l (146 mg/dl)
Interventions	Rosuvastatin 5 mg/day for 0-12 weeks Rosuvastatin 5-80 titration mg/day 12-52 weeks Rosuvastatin 10 mg/day for 0-12 weeks Rosuvastatin 10-80 titration mg/day 12-52 weeks Atorvastatin 10 mg/day for 0-12 weeks Atorvastatin 10-80 titration mg/day 12-52 weeks
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	Rosuvastatin 5-80 titration mg/day 12-52 weeks Rosuvastatin 10-80 titration mg/day 12-52 weeks Atorvastatin 10 mg/day for 0-12 weeks Atorvastatin 10-80 titration mg/day 12-52 weeks groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day for 0-12 weeks and Rosuvastatin 10 mg/day for 0-12 weeks treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day for 0-12 weeks and Rosuvastatin 10 mg/day for 0-12 weeks treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day for 0-12 weeks and Rosuvastatin 10 mg/day for 0-12 weeks treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	3/138 participants from the rosuvastatin 5 mg/day group were not included in the efficacy analysis 2/134 participants from the rosuvastatin 10 mg/day group were not included in the efficacy analysis 1.8% participants were not included in the efficacy analysis

Olsson 2002 *(Continued)*

Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded the trial. Data may support bias for rosuvastatin

Paoletti 2009

Methods	6-week washout period 12-week double-blind randomized study evening doses
Participants	502 patients with hypercholesterolaemia age ≥ 18 years LDL-C ≥ 160 mg/dl (4.14 mmol/l) and < 250 mg/dl (6.50 mmol/l) TG ≤ 400 mg/dl (4.52 mmol/l) 235 received rosuvastatin 137 received pravastatin 130 received simvastatin exclusion criteria:active arterial disease within 3 months trial entry, familial hypercholesterolaemia uncontrolled hypertension, liver disease, alcohol or drug abuse, use of cyclic hormonal therapy Rosuvastatin 5 mg/day baseline TC : 7.1 mmol/l (276 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 4.9 mmol/l (189 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.3 mmol/l (50 mg/dl) Rosuvastatin 5 mg/day baseline TG : 1.9 mmol/l (168 mg/dl) Rosuvastatin 10 mg/day baseline TC : 7.0 mmol/l (271 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.8 mmol/l (186 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.4 mmol/l (54 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.8 mmol/l (159 mg/dl)
Interventions	Rosuvastatin 5 mg/day Rosuvastatin 10 mg/day Pravastatin 20 mg/day Simvastatin 20 mg/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	rosuvastatin groups were analyzed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day and Rosuvastatin10 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable

Paoletti 2009 *(Continued)*

Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day and Rosuvastatin10 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day and Rosuvastatin10 mg/day treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	5 mg/day rosuvastatin: 1/120 were not included in the efficacy analysis 10 mg/day rosuvastatin: 4/115 were not included in the efficacy analysis 2.1 % participants were excluded from the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	AstraZeneca funded it. Data may support bias for rosuvastatin

Park 2010

Methods	6-week washout period 6-week randomized open-label trial evening dosing
Participants	351 men and women ≥ 18 years with nondiabetic metabolic syndrome and hypercholesterolaemia LDL-C ≥ 130 mg/dl to < 220 mg/dl (≥ 3.36 mmol/l to < 5.69 mmol/l) TG ≥ 150 mg/dl (1.70 mmol/l) HDL-C < 40 mg/dl (< 1.03 mmol/l) in men HDL-C < 50 mg/dl (< 1.29 mmol/l) in women well-controlled hypertension glucose 110 mg/dl (6.11 mmol/l) to 125 mg/dl (6.94 mmol/l) 172 participants were randomized to rosuvastatin 178 participants were randomized to atorvastatin exclusion criteria: pregnancy, cancer, diabetes mellitus, active arterial disease Rosuvastatin 10 mg/day baseline TC : 6.14 mmol/l (237 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.23 mmol/l (164 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.03 mmol/l (40 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.93 mmol/l (171 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.12 mmol/l (198 mg/dl)
Interventions	Rosuvastatin 10 mg/day for 6 weeks Atorvastatin 10 mg/day for 6 weeks
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C

Park 2010 *(Continued)*

Notes	Atorvastatin 10 mg/day for 6 weeks group was not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	2/170 (1.2%) participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZenca Korea funded the trial. Data might support bias for the drug

Patel 2011

Methods	no washout required because participants were not receiving any lipid-altering agents 4-week before-and-after trial
Participants	11 men and women with chronic hepatitis C mean age 51 years exclusion criteria: patients with CHC with other co-morbid states, renal impairment, hepatic dysfunction, low TC <80 mg/dl familial hypercholesterolaemia, combined hyperlipidaemia, secondary dyslipidaemias participants receiving thiazide diuretics, retinoids, corticosteroids known hypersensitivity and/or myopathy to previous lipid-lowering therapy Rosuvastatin 20 mg/day baseline TC : 4.52 mmol/l (175 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 2.48 mmol/l (96 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.38 mmol/l (53 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.45 mmol/l (128 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C: 3.14 mmol/l (121 mg/dl)
Interventions	Rosuvastatin 20 mg/day for 4 weeks Rosuvastatin 40 mg/day for 4-8 weeks a posttreatment period of 8-16 weeks
Outcomes	per cent change from baseline at 4 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C

Patel 2011 *(Continued)*

Notes	Rosuvastatin 40 mg/day for 4-8 weeks period and the posttreatment period of 8-16 weeks were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	there was only one group of participants analyzed therefore it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	Schering Plough Research Institute supported the study in part. Data might support bias against the drug

Pirro 2007

Methods	no participant was receiving lipid-altering drugs no washout period required 4-week randomized open-label trial
Participants	71 men and women mean age 57 years with primary hypercholesterolaemia LDL-C > 160 mg/dl (> 4.14 mmol/l) 35 patients were randomized to rosuvastatin 10mg/day 36 patients were randomized to diet exclusion criteria: secondary hyperlipidaemia, diabetes mellitus renal, liver dysfunction, thyroid disease, alcohol consumption > 40 g/day active arterial disease Rosuvastatin 10 mg/day baseline TC : 6.67 mmol/l (258 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.65 mmol/l (180 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.34 mmol/l (52 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.55 mmol/l (137 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.33 mmol/l (206 mg/dl)
Interventions	Rosuvastatin 10 mg/day Diet

Pirro 2007 *(Continued)*

Outcomes	per cent change from baseline at 4 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	diet group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

Pirro 2009

Methods	8-week washout period 4-week randomized open-label trial
Participants	48 men and women age 50-60 years with primary hypercholesterolaemia LDL-C > 160 mg/dl (> 4.14 mmol/l) 32 patients were randomized to rosuvastatin 10 mg/day 16 patients were randomized to no pharmacological treatment exclusion criteria: secondary hyperlipidaemia, diabetes mellitus renal, liver dysfunction, thyroid disease, alcohol consumption > 40 g/day active arterial disease Rosuvastatin 10 mg/day baseline LDL-C : 5.35 mmol/l (207 mg/dl)
Interventions	rosuvastatin 10 mg/day no pharmacological treatment
Outcomes	per cent change from baseline at 4 weeks of serum LDL-C

Pirro 2009 *(Continued)*

Notes	no pharmacological treatment group was not included in the efficacy analysis SD was imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	TC, HDL-C, non-HDL-C and triglycerides were not included in the efficacy analysis
Other bias	Low risk	pharmaceutical industry did not fund this study

PLUTO 2010

Methods	6-week washout period 12-week randomized, double-blind placebo-controlled trial
Participants	177 pubertal children ages 10-17 years with familial hypercholesterolaemia LDL-C >160 mg/dl (> 4.14 mmol/l) 46 randomized to placebo 42 randomized to Rosuvastatin 5 mg/day 44 randomized to Rosuvastatin 10 mg/day 44 randomized to Rosuvastatin 20 mg/day Placebo baseline TC : 7.58 mmol/l (293 mg/dl) Placebo baseline LDL-C : 5.92 mmol/l (229 mg/dl) Placebo baseline HDL-C : 1.16 mmol/l (45 mg/dl) Rosuvastatin 5 mg/day baseline TC : 7.76 mmol/l (300 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 6.15 mmol/l (238 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.19 mmol/l (46 mg/dl) Rosuvastatin 10 mg/day baseline TC : 7.68 mmol/l (297 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 5.92 mmol/l (229 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.27 mmol/l (49 mg/dl)

PLUTO 2010 *(Continued)*

	Rosuvastatin 20 mg/day baseline TC : 7.81 mmol/l (302 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 6.13 mmol/l (237 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.22 mmol/l (47 mg/dl)
Interventions	placebo Rosuvastatin 5 mg/day Rosuvastatin 10 mg/day Rosuvastatin 20 mg/day
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C , HDL-C and non-HDL-C
Notes	SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/177 participants were not included in th efficacy analysis
Selective reporting (reporting bias)	High risk	triglycerides were not included because they were expressed as medians WDAEs were not reported
Other bias	High risk	AstraZeneca funded the trial. Data may support bias for rosuvastatin

Polenova 2009

Methods	4-week washout period 12-week randomized open-label trial
Participants	30 men and women age 47-74 years with type 2 diabetes mellitus low HDL-C HDL-C <1.0 mmol/l (< 39 mg/dl) for men HDL-C <1.2 mmol/l (< 46 mg/dl) for women all participants had hypertension, BMI > 25 17 participants were randomized to rosuvastatin 10 mg/day 13 participants were randomized to fenofibrate 200 mg/day

Polenova 2009 *(Continued)*

	exclusion criteria: persistent atrial fibrillation, participants with acute coronary syndrome within the previous 3 months, type 1 diabetes mellitus and decompensated diabetes (glycated haemoglobin level HbA1C > 10.5 %) Rosuvastatin 10 mg/day baseline TC : 5.59 mmol/l (216 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.68 mmol/l (142 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 0.95 mmol/l (37 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.21 mmol/l (1967 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 4.64 mmol/l (179 mg/dl)
Interventions	rosuvastatin 10 mg/day fenofibrate 200 mg/day
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	fenofibrate 200 mg/day group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

Postadzhiyan 2008

Methods	patients received no lipid-altering agents during the past 6 months, no washout was required 12-week randomized trial
Participants	30 men and women age 50-60 years with unstable angina or non STEMI 16 patients received rosuvastatin 10 mg/day 14 patients received rosuvastatin 20 mg/day

Postadzhiyan 2008 *(Continued)*

	exclusion criteria: acute of chronic inflammatory diseases, cancer renal dysfunction, liver disease, on immunosuppressants and antibiotics acute ST elevation MI, diabetes mellitus, active arterial disease within 1 month of trial Rosuvastatin 10 mg/day baseline TC : 5.66 mmol/l (219 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.86 mmol/l (149 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 0.99 mmol/l (38 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.76 mmol/l (156 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 4.67 mmol/l (181 mg/dl) Rosuvastatin 20 mg/day baseline TC : 6.07 mmol/l (235 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 4.27 mmol/l (165 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 0.91 mmol/l (35 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.93 mmol/l (171 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C: 5.16 mmol/l (200 mg/dl)
Interventions	Rosuvastatin 10 mg/day Rosuvastatin 20 mg/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day and Rosuvastatin 20 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day and Rosuvastatin 20 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day and Rosuvastatin 20 mg/day treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

PULSAR 2006

Methods	6-week washout period 6-week open randomized study

PULSAR 2006 *(Continued)*

Participants	996 men and women of high risk with hypercholesterolaemia age ≥ 18 years LDL-C ≥ 3.4 and < 5.7 mmol/l (130 and 220 mg/dl) TG < 4.5 mmol/l (400 mg/dl) 504 received 10 mg rosuvastatin 492 received 20 mg atorvastatin exclusion criteria: history of statin-induced myopathy or hypersensitivity, unstable cardiovascular system cancer history, homozygous familial hypercholesterolaemia, current active liver disease, uncontrolled hypothyroidism history of alcohol and drug abuse, pregnancy or lactation, changes in HRT within 3 months of enrolment Rosuvastatin 10 mg/day baseline TC : 6.49 mmol/l (251 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.27 mmol/l (165 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.3 mmol/l (50 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.01 mmol/l (178 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C : 5.19 mmol/l (201 mg/dl)
Interventions	Rosuvastatin 10 mg/day Atorvastatin 20 mg/day
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	rosuvastatin group was analyzed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	11/504 were not analyzed
Selective reporting (reporting bias)	Low risk	all lipid parameters were measured
Other bias	High risk	AstraZeneca sponsored the trial. Data may support bias for rosuvastatin

RADAR 2005

Methods	6-week washout period 6-week open-label randomized trial
Participants	461 men and women aged 40-80 years with cardiovascular disease and a low HDL-C HDL-C < 1.0 mmol/l (40 mg/dl) TG ≤4.5 mmol/l (400 mg/dl) 230 participants were randomized to rosuvastatin 231 participants were randomized to atorvastatin exclusion criteria: use of lipid-altering drugs or supplements after enrolment, statin hypersensitivity pregnancy lactation, active arterial disease, uncontrolled hypertension, glycated haemoglobin > 8%, cancer history, uncontrolled hypothyroidism homozygous familial hypercholesterolaemia or type III hyperlipoproteinaemia, alcohol or drug abuse, active liver disease serum CK > 3 X ULN, received an investigational drug within 4 weeks of enrolment serious or unstable medical or psychological conditions that could affect the trial or safety concerns Rosuvastatin 10 mg/day baseline TC : 5.8 mmol/l (224 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.6 mmol/l (139 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 0.8 mmol/l (31 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.8 mmol/l (248 mg/dl)
Interventions	Rosuvastatin 10 mg/day for 0-6 weeks Rosuvastatin 20 mg/day for 6-12 weeks Rosuvastatin 40 mg/day for 12-18 weeks Atorvastatin 20 mg/day for 0-6 weeks Atorvastatin 40 mg/day for 6-12 weeks Atorvastatin 80 mg/day for 12-18 weeks
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Rosuvastatin 20 mg/day for 6-12 weeks Rosuvastatin 40 mg/day for 12-18 weeks Atorvastatin 20 mg/day for 0-6 weeks Atorvastatin 40 mg/day for 6-12 weeks Atorvastatin 80 mg/day for 12-18 weeks outcomes were not analyzed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day for 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable

RADAR 2005 *(Continued)*

Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day for 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day for 0-6 weeks treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	The study was supported by AstraZeneca. Data may support bias for rosuvastatin

Raza 2000

Methods	6-week washout period 6-week randomized double-blind placebo-controlled trial evening dosing
Participants	108 men and women ≥ 18 years LDL-C >4.14 mmol/l to < 6.21 mmol/l (> 160 mg/dl to < 240 mg/dl) TG < 3.39 mmol/l (< 300 mg/dl) BMI ≤ 30 12 participants were randomized to placebo 12 participants were randomized to rosuvastatin 1 mg/day 12 participants were randomized to rosuvastatin 2.5 mg/day 12 participants were randomized to rosuvastatin 5 mg/day 12 participants were randomized to rosuvastatin 10 mg/day 12 participants were randomized to rosuvastatin 20 mg/day 12 participants were randomized to rosuvastatin 40 mg/day 12 participants were randomized to atorvastatin 10 mg/day 12 participants were randomized to atorvastatin 80 mg/day exclusion criteria: statin hypersensitivity, active arterial disease cancer, uncontrolled hypertension, diabetes mellitus, uncontrolled hypothyroidism homozygous familial hypercholesterolaemia or type III hyperlipoproteinaemia use of some concomitant medications, alcohol or drug abuse active liver disease or dysfunction, renal dysfunction

Raza 2000 *(Continued)*

	participation in another study less than 3 months before enrolment
	serum CK ? 3 X ULN, serious of unstable medical or psychological conditions that would affect safety or successful participation in the study
	HRT, participants receiving digoxin and/or coumarin anti-coagulants, immunosuppressants
Interventions	placebo
	rosuvastatin 1 mg/day
	rosuvastatin 2.5 mg/day
	rosuvastatin 5 mg/day
	rosuvastatin 10 mg/day
	rosuvastatin 20 mg/day
	rosuvastatin 40 mg/day
	atorvastatin 10 mg/day
	atorvastatin 80 mg/day
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	atorvastatin 10 mg/day
	atorvastatin 80 mg/day
	groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	non-HDL-C and WDAEs were not reported
Other bias	High risk	AstraZeneca funded the trial. Data may support bias for rosuvastatin

ROMEO 2009

Methods	6-week washout period

ROMEO 2009 *(Continued)*

	6 -week randomized open-label trial
Participants	258 men and women ≥ 18 years with metabolic syndrome LDL-C ≥ 130 mg/dl (3.36 mmol/l) < 220 mg/dl (5.69 mmol/l) 132 were randomized to rosuvastatin 126 were randomized to atorvastatin exclusion criteria: none reported
Interventions	rosuvastatin 10 mg/day for 0-6 weeks atorvastatin 10 mg/day for 0-6 weeks
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	atorvastatin 10 mg/day for 0-6 weeks group was not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	5/132 participants from the rosuvastatin group were not included in the efficacy analysis 3.8 % participants were not included in the efficacy analysis
Selective reporting (reporting bias)	High risk	non-HDL-C was not included in the efficacy analysis
Other bias	High risk	AstraZeneca provided the data. Data may support bias for rosuvastatin

Rosenson 2011

Methods	6-week washout period 12-week randomized double-blind trial
Participants	499 patients with mixed dyslipidaemia and type 2 diabetes mellitus LDL-C ≥130 mg/dl (≥3.36 mmol/l) HDL-C < 40/50 mg/dl in men/women (< 1.03/1.29 mmol/l) in men/women TG ≥150 mg/dl (≥ 1.69 mmol/l)

Rosenson 2011 *(Continued)*

	123 participants were randomized to fenofibric acid 135 mg/day 68 participants were randomized to rosuvastatin 5 mg/day 73 participants were randomized to rosuvastatin fenofibric acid 5 mg/135 mg/day 53 participants were randomized to rosuvastatin 10 mg/day 52 participants were randomized to rosuvastatin fenofibric acid 10 mg/135 mg/day 53 participants were randomized to rosuvastatin 20 mg/day 52 participants were randomized to rosuvastatin fenofibric acid 20 mg/135 mg/day 25 participants were randomized to rosuvastatin 40 mg/day exclusion criteria: none reported Rosuvastatin 5 mg/day baseline LDL-C : 3.82 mmol/l (148 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.07 mmol/l (41 mg/dl) Rosuvastatin 5 mg/day baseline TG : 3.49 mmol/l (309 mg/dl) Rosuvastatin 5 mg/day baseline non-HDL-C: 5.63 mmol/l (218 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.79 mmol/l (147 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 0.95 mmol/l (37 mg/dl) Rosuvastatin 10 mg/day baseline TG : 3.58 mmol/l (317 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.62 mmol/l (217 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 3.93 mmol/l (152 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 0.97 mmol/l (38 mg/dl) Rosuvastatin 20 mg/day baseline TG : 3.39 mmol/l (300 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C: 5.75 mmol/l (222 mg/dl)
Interventions	rosuvastatin 5 mg/day rosuvastatin 10 mg/day rosuvastatin 20 mg/day rosuvastatin 40 mg/day fenofibric acid 135 mg/day rosuvastatin fenofibric acid 5 mg/135 mg/day rosuvastatin fenofibric acid 10 mg/135 mg/day rosuvastatin fenofibric acid 20 mg/135 mg/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, non-HDL-C and triglycerides
Notes	fenofibric acid 135 mg/day rosuvastatin fenofibric acid 5 mg/135 mg/day rosuvastatin fenofibric acid 10 mg/135 mg/day rosuvastatin fenofibric acid 20 mg/135 mg/day rosuvastatin 40 mg/day groups were not included in the efficacy analysis

Rosenson 2011 *(Continued)*

	TC was calculated from HDL-C and non-HDL-C

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day, the Rosuvastatin 10 mg/day, the Rosuvastatin 20 mg/day and the Rosuvastatin 40 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day, the Rosuvastatin 10 mg/day, the Rosuvastatin 20 mg/day and the Rosuvastatin 40 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day, the Rosuvastatin 10 mg/day, the Rosuvastatin 20 mg/day and the Rosuvastatin 40 mg/day treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	5 mg rosuvastatin group 2/68 = 2.9% participants were not included in the efficacy analysis 10 mg rosuvastatin group 7/53 = 13.2% participants were not included in the efficacy analysis 4/53 = 7.5% participants were not included in the efficacy analysis all rosuvastatin groups 13/174 = 7.5 % of all the participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	Abbott and AstraZeneca sponsored the studies. Data may support bias for rosuvastatin

Saito 2003

Methods	6-week washout period 6-week randomized, double-blind, placebo-controlled trial evening dosing
Participants	112 men aged 18-70 years and postmenopausal women aged 50-70 years with hypercholesterolaemia LDL-C > 160 and < 240 mg/dl (> 4.14 and < 6.21 mmol/l) TG < 300 mg/dl (< 3.39 mmol/l) 15 participants were randomized to placebo 16 participants were randomized to rosuvastatin 1 mg/day 18 participants were randomized to rosuvastatin 2.5 mg/day

Saito 2003 *(Continued)*

	15 participants were randomized to rosuvastatin 5 mg/day 15 participants were randomized to rosuvastatin 10 mg/day 19 participants were randomized to rosuvastatin 20 mg/day 14 participants were randomized to rosuvastatin 40 mg/day exclusion criteria: use of lipid-lowering agents within 4 weeks of enrolment active arterial disease, BMI > 30, active liver disease or dysfunction, renal dysfunction serum CK > 3 X ULN Placebo baseline TC : 6.96 mmol/l (269 mg/dl) Placebo baseline LDL-C : 4.91 mmol/l (190 mg/dl) Placebo baseline HDL-C : 1.36 mmol/l (53 mg/dl) Placebo baseline TG : 1.52 mmol/l (135mg/dl) Rosuvastatin 1 mg/day baseline TC : 6.80 mmol/l (263 mg/dl) Rosuvastatin 1 mg/day baseline LDL-C : 4.76 mmol/l (184 mg/dl) Rosuvastatin 1 mg/day baseline HDL-C : 1.38 mmol/l (53 mg/dl) Rosuvastatin 1 mg/day baseline TG : 1.45 mmol/l (128 mg/dl) Rosuvastatin 2.5 mg/day baseline TC : 6.94 mmol/l (268 mg/dl) Rosuvastatin 2.5 mg/day baseline LDL-C : 4.78 mmol/l (185 mg/dl) Rosuvastatin 2.5 mg/day baseline HDL-C : 1.43 mmol/l (55 mg/dl) Rosuvastatin 2.5 mg/day baseline TG : 1.59 mmol/l (141 mg/dl) Rosuvastatin 5 mg/day baseline TC : 6.89 mmol/l (266 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 4.69 mmol/l (181 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.56 mmol/l (60 mg/dl) Rosuvastatin 5 mg/day baseline TG : 1.40 mmol/l (124 mg/dl) Rosuvastatin 10 mg/day baseline TC : 6.68 mmol/l (258 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.71 mmol/l (182 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.34 mmol/l (52 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.41 mmol/l (125 mg/dl) Rosuvastatin 20 mg/day baseline TC : 7.02 mmol/l (271 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 4.80 mmol/l (186 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.44 mmol/l (56 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.70 mmol/l (151 mg/dl) Rosuvastatin 40 mg/day baseline TC : 6.94 mmol/l (268 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 4.68 mmol/l (181 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.63 mmol/l (63 mg/dl) Rosuvastatin 40 mg/day baseline TG : 1.38 mmol/l (122 mg/dl)
Interventions	placebo rosuvastatin 1 mg/day rosuvastatin 2.5 mg/day rosuvastatin 5 mg/day rosuvastatin 10 mg/day rosuvastatin 20 mg/day rosuvastatin 40 mg/day

Saito 2003 *(Continued)*

Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides WDAEs were reported
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported (tablets encapsulated in dark-yellowish red, opaque capsule shells)
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	3/15 participants for the placebo group were not included in the efficacy analysis 1/16 participants for the rosuvastatin 1 mg/day group were not included in the efficacy analysis 1/18 participants for the rosuvastatin 2.5 mg/day group were not included in the efficacy analysis 3/15 participants for the rosuvastatin 5 mg/day group were not included in the efficacy analysis 1/15 participants for the rosuvastatin 10 mg/day group were not included in the efficacy analysis 1/19 participants for the rosuvastatin 20 mg/day group were not included in the efficacy analysis 1/14 participants for the rosuvastatin 40 mg/day group were not included in the efficacy analysis 9.8% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	High risk	non-HDL-C was not reported for the efficacy analysis
Other bias	Low risk	AstraZeneca sponsored the trial. Data may support bias for rosuvastatin

Saito 2007

Methods	6-9 week washout period 8-week randomized double-blind placebo-controlled trial
Participants	154 patients age 20-75 years with hypertriglyceridaemia TG ≥ 200 to < 800 mg/dl (≥ 2.26 to < 9.0 mmol/l) 35 patients were randomized to placebo

Saito 2007 *(Continued)*

	32 patients were randomized to rosuvastatin 5 mg/day 34 patients were randomized to rosuvastatin 10 mg/day 26 patients were randomized to rosuvastatin 20 mg/day 27 patients were randomized to bezafibrate 200 mg bid exclusion criteria: pancreatitis, use of glitazones within 3 months of trial entry pregnancy, lactation, active arterial disease, uncontrolled diabetes serum glucose ≥140 mg/dl or glycated haemoglobin ≥8%, serum CK > 3 X ULN active liver disease or hepatic dysfunction, familial hypercholesterolaemia Placebo baseline TC : 7.00 mmol/l (246 mg/dl) Placebo baseline LDL-C : 5.10 mmol/l (138 mg/dl) Placebo baseline HDL-C : 1.40 mmol/l (43 mg/dl) Placebo baseline TG : 1.40 mmol/l (334 mg/dl) Placebo baseline non-HDL-C: 5.24 mmol/l (203 mg/dl) Rosuvastatin 5 mg/day baseline TC : 6.00 mmol/l (232 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 3.22 mmol/l (125 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.08 mmol/l (42 mg/dl) Rosuvastatin 5 mg/day baseline TG : 3.79 mmol/l (336 mg/dl) Rosuvastatin 5 mg/day baseline non-HDL-C: 4.92 mmol/l (190 mg/dl) Rosuvastatin 10 mg/day baseline TC : 6.00 mmol/l (232 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.26 mmol/l (126 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.03 mmol/l (40 mg/dl) Rosuvastatin 10 mg/day baseline TG : 3.82 mmol/l (338 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 4.97 mmol/l (192 mg/dl) Rosuvastatin 20 mg/day baseline TC : 6.06 mmol/l (234 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 3.00 mmol/l (116 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.09 mmol/l (42 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.60 mmol/l (398 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C: 4.49 mmol/l (192 mg/dl)
Interventions	Placebo rosuvastatin 5 mg/day rosuvastatin 10 mg/day rosuvastatin 20 mg/day bezafibrate 200 mg bid
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C WDAEs
Notes	bezafibrate 200 mg bid group was not included the analysis

Risk of bias

Bias	Authors' judgement	Support for judgement

Saito 2007 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis WDAEs were also reported
Other bias	High risk	This study was supported by AstraZeneca. Data may support bias for rosuvastatin

Schneck 2003

Methods	6-week washout period 6-week randomized, double-blind trial
Participants	374 men and women age ≥ 18 years with hypercholesterolaemia without active arterial disease within 3 months of trial entry or uncontrolled hypertension LDL-C ≥ 160 mg/dl (≥ 4.14 mmol/l) and < 250 mg/dl (< 6.47 mmol/l) TG ≤ 400 mg/dl (≤ 4.52 mmol/l) EPAT score of ≤28 38 participants were randomized to rosuvastatin 5 mg/day 45 participants were randomized to rosuvastatin 10 mg/day 39 participants were randomized to rosuvastatin 20 mg/day 45 participants were randomized to rosuvastatin 40 mg/day 42 participants were randomized to rosuvastatin 80 mg/day 165 participants randomized to atorvastatin exclusion criteria:pregnancy, lactation, familial hypercholesterolaemia type III hyperlipoproteinaemia Rosuvastatin 5 mg/day baseline TC : 7.27 mmol/l (281 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 4.99 mmol/l (193 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.37 mmol/l (53 mg/dl) Rosuvastatin 5 mg/day baseline TG : 2.03 mmol/l (180 mg/dl) Rosuvastatin 5 mg/day baseline non-HDL-C : 5.90mmol/l (228 mg/dl) Rosuvastatin 10 mg/day baseline TC : 7.14 mmol/l (276 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.91 mmol/l (190 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.32 mmol/l (51 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.03 mmol/l (180 mg/dl)

Schneck 2003 *(Continued)*

	Rosuvastatin 10 mg/day baseline non-HDL-C : 5.82 mmol/l (225 mg/dl) Rosuvastatin 20 mg/day baseline TC : 6.98 mmol/l (270 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 4.86 mmol/l (188 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.29 mmol/l (50 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.85 mmol/l (164 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C : 5.72 mmol/l (221 mg/dl) Rosuvastatin 40 mg/day baseline TC : 7.14 mmol/l (276 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 4.86 mmol/l (188 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.37 mmol/l (53 mg/dl) Rosuvastatin 40 mg/day baseline TG : 1.99 mmol/l (176 mg/dl) Rosuvastatin 40 mg/day baseline non-HDL-C : 5.77 mmol/l (223 mg/dl) Rosuvastatin 80 mg/day baseline TC : 7.40 mmol/l (286 mg/dl) Rosuvastatin 80 mg/day baseline LDL-C : 5.12 mmol/l (198 mg/dl) Rosuvastatin 80 mg/day baseline HDL-C : 1.34 mmol/l (50 mg/dl) Rosuvastatin 80 mg/day baseline TG : 2.00 mmol/l (177 mg/dl) Rosuvastatin 80 mg/day baseline non-HDL-C : 6.025 mmol/l (233 mg/dl)
Interventions	Rosuvastatin 5 mg/day Rosuvastatin 10 mg/day Rosuvastatin 20 mg/day Rosuvastatin 40 mg/day Rosuvastatin 80 mg/day Atorvastatin 10 mg/day Atorvastatin 20 mg/day Atorvastatin 40 mg/day Atorvastatin 80 mg/day
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Atorvastatin 10 mg/day Atorvastatin 20 mg/day Atorvastatin 40 mg/day Atorvastatin 80 mg/day groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day, the Rosuvastatin 10 mg/day, the Rosuvastatin 20 mg/day, the Rosuvastatin 40 mg/day, and the rosuvastatin 80 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day, the Rosuvastatin 10 mg/day, the Rosuvastatin 20 mg/day, the Rosuvastatin 40 mg/day, and the rosuvastatin 80 mg/day treat-

Schneck 2003 *(Continued)*

		ment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day, the Rosuvastatin 10 mg/day, the Rosuvastatin 20 mg/day, the Rosuvastatin 40 mg/day, and the Rosuvastatin 80 mg/day treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/39 participants in the rosuvastatin 20 mg/day and 1/45 participants in the rosuvastatin 40 mg/day were not included in the efficacy analysis 1.2% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	The research was supported by AstaZeneca. Data may support bias for rosuvastatin

Schwartz 2004

Methods	6-week washout period 24-week randomized, double-blind trial evening dosing
Participants	383 men and women age ≥ 18 years with type 2 diabetes mellitus or atherosclerosis LDL-C ≥ 160 mg/dl (≥ 4.14 mmol/l) and < 250 mg/dl (< 6.47 mmol/l) TG ≤ 400 mg/dl (≤ 4.52 mmol/l) 127 participants received 5/20/80 mg/day rosuvastatin 128 participants received 10/40/80 mg/day rosuvastatin 128 participants received 10/40/80 mg/day atorvastatin exclusion criteria: pregnant, receiving concomitant medications that affect lipid profile or safety concern active arterial disease, familial hypercholesterolaemia, uncontrolled hypertension and hypothyroidism cancer history, acute liver disease or dysfunction, serum CK > 3 X ULN, renal disease uncontrolled diabetes mellitus Rosuvastatin 5 mg/day baseline TC : 7.09 mmol/l (274 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 4.86 mmol/l (188 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.19 mmol/l (46 mg/dl) Rosuvastatin 5 mg/day baseline TG : 2.21 mmol/l (196 mg/dl) Rosuvastatin 5 mg/day baseline non-HDL-C: 5.87 mmol/l (227 mg/dl) Rosuvastatin 10 mg/day baseline TC : 7.03 mmol/l (272 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.81 mmol/l (186 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.22 mmol/l (47 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.20 mmol/l (195 mg/dl)

Schwartz 2004 *(Continued)*

	Rosuvastatin 10 mg/day baseline non-HDL-C: 5.82 mmol/l (225 mg/dl)
Interventions	Rosuvastatin 5 mg/day for 0-12 weeks Rosuvastatin 20 mg/day for 12-18 weeks Rosuvastatin 80 mg/day for 18-24 weeks Rosuvastatin 10 mg/day for 0-12 weeks Rosuvastatin 40 mg/day for 12-18 weeks Rosuvastatin 80 mg/day for 18-24 weeks Atorvastatin 10 mg/day for 0-12 weeks Atorvastatin 40 mg/day for 12-18 weeks Atorvastatin 80 mg/day for 18-24 weeks
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Rosuvastatin 20 mg/day for 12-18 weeks Rosuvastatin 80 mg/day for 18-24 weeks Rosuvastatin 40 mg/day for 12-18 weeks Rosuvastatin 80 mg/day for 18-24 weeks Atorvastatin 10 mg/day for 0-12 weeks Atorvastatin 40 mg/day for 12-18 weeks Atorvastatin 80 mg/day for 18-24 weeks groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca supported the study. Data may support bias for rosuvastatin

Semenova 2009

Methods	1-month washout period 12-week open-label trial
Participants	70 men and women age 57 years with CAD BMI =25-29 40 men and women received aspirin and statins 30 men received rosuvastatin 10 mg/day for 12 weeks exclusion criteria: congestive heart failure, diabetes mellitus, hypothyroidism liver or kidney dysfunction, acute coronary syndrome inflammatory disease and surgical intervention during the last 3 months exclusion criteria in the rosuvastatin group: TG > 4.5 mmol/l (> 399 mg/dl) liver dysfunction, serum CK > 2 X ULN Rosuvastatin 10 mg/day baseline TC : 6.52 mmol/l (252 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.11 mmol/l (159 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.15 mmol/l (44 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.73 mmol/l (242 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.37 mmol/l (208 mg/dl)
Interventions	aspirin and statins rosuvastatin 10 mg/day for 12 weeks
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	aspirin and statins group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis

Semenova 2009 *(Continued)*

Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

Shepherd 2004

Methods	6-week washout 12-week randomized double-blind placebo-controlled trial
Participants	135 postmenopausal women age 55-60 years with hypercholesterolaemia receiving HRT LDL-C ≥ 130 mg/dl (≥ 3.4 mmol/l) and < 250 mg/dl (< 6.5 mmol/l) TG ≤ 400 mg/dl (≤ 4.5 mmol/l) 46 patients were randomized to placebo 45 patients were randomized to rosuvastatin 5 mg/day 44 patients were randomized to rosuvastatin 10 mg/day exclusion criteria: statin hypersensitivity, active arterial disease within 3 months of trial entry cancer history excluded skin cancer, uncontrolled hypertension or hypothyroidism glucose > 180 mg/dl (> 9.99 mmol/l), glucosylated haemoglobin > 9%, familial hypercholesterolaemia use of concomitant medications that affect trial, alcohol or drug abuse active liver disease or dysfunction, serum CK > 3 X ULN serious or unstable medical or psychological condition that could affect safety or trial participation Placebo baseline TC : 6.57 mmol/l (254 mg/dl) Placebo baseline LDL-C : 4.22 mmol/l (163 mg/dl) Placebo baseline HDL-C : 1.50 mmol/l (58 mg/dl) Placebo baseline TG : 1.75 mmol/l (155 mg/dl) Rosuvastatin 5 mg/day baseline TC : 6.72 mmol/l (260 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 4.50 mmol/l (174 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.40 mmol/l (54 mg/dl) Rosuvastatin 5 mg/day baseline TG : 1.78 mmol/l (158 mg/dl) Rosuvastatin 10 mg/day baseline TC : 6.57 mmol/l (254 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.27 mmol/l (165 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.47 mmol/l (57 mg/dl) Rosuvastatin 10 mg/day baseline TG : 1.83 mmol/l (162 mg/dl)
Interventions	Placebo Rosuvastatin 5 mg/day Rosuvastatin 10 mg/day
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	

Shepherd 2004 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported (randomization scheme was predetermined)
Blinding (performance bias and detection bias) All outcomes	Low risk	double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	research was reported by AstraZeneca. Data may support bias for rosuvastatin

SHUKRA 2009

Methods	6-week washout period 6-week randomized double-blind trial
Participants	55 men and women with hypercholesterolaemia LDL-C ≥ 4.00 mmol/l (≥ 155 mg/dl) TG< 4.52 mmol/l (< 400 mg/dl) exclusion criteria: none reported 30 participants were randomized to rosuvastatin 5 mg/day 25 participants were randomized to atorvastatin 10 mg/day
Interventions	rosuvastatin 5 mg/day atorvastatin 10 mg/day
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C and non-HDL-C
Notes	atorvastatin 10 mg/day group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement

SHUKRA 2009 *(Continued)*

Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	serum triglycerides were not included in the efficacy analysis
Other bias	High risk	This study was supported by AstraZeneca. Data may support bias for rosuvastatin

Siddiqi 2013

Methods	no washout required because participants were not receiving any lipid-altering agents within the last 6 months of the trial 12-week before-and-after trial
Participants	135 men and women with metabolic syndrome age 30-70 years LDL-C ≥ 130 mg/dl (≥ 3.36 mmol/l), TG ≥ 150 mg/dl (1.69 mmol/l), HDL-C < 40 mg/dl (1.03 mmol/l) for men, HDL-C < 50 mg/dl (1.29 mmol/l) for women BP ≥ 130/85 mmHg, 10-year CHD risk score of >10% 68 patients received Atorvastatin/Ezetimibe (10/10 mg/day) 67 patients received Rosuvastatin 5 mg/day exclusion criteria: TG ≥ 500 mg/dl (5.65 mmol/l), LDL-C ≥ 250 mg/dl (6.48 mmol/l) documented history of CHD or other atherosclerotic disease, familial hypercholesterolaemia, statin hypersensitivity uncontrolled hypertension, hypothyroidism, acute liver disease of hepatic dysfunction, CK > 3X ULN and the use of prohibited concomitant medications Rosuvastatin 5 mg/day baseline TC : 6.047 mmol/l (234 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 3.787 mmol/l (146 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.255 mmol/l (48.5 mg/dl) Rosuvastatin 5 mg/day baseline TG : 2.185 mmol/l (194 mg/dl) Rosuvastatin 5 mg/day baseline non-HDL-C: 4.792 mmol/l (185 mg/dl)
Interventions	Atorvastatin/Ezetimibe (10/10 mg/day) Rosuvastatin 5 mg/day

Siddiqi 2013 *(Continued)*

Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	The atorvastatin/ezetimibe (10/10 mg/day) group was not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day for 12 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day for 12 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day for 12 weeks treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

SOLAR 2007

Methods	6-week washout period 6-week open-label randomized trial
Participants	1632 men and women 18 years or older at high risk for CHD LDL-C ≥ 130 mg/dl to < 250 mg/dl (≥ 3.36 mmol/l to < 6.465 mmol/l) TG < 400 mg/dl (< 4.52 mmol/l) 542 participants were randomized to rosuvastatin 544 participants were randomized to atorvastatin 546 participants were randomized to simvastatin exclusion criteria: active arterial disease, uncontrolled hypertension glucose ≥180 mg/dl, glucosylated haemoglobin ≥ 9% active liver disease or dysfunction, serum CK > 3 X ULN Rosuvastatin 10 mg/day baseline TC : 6.57 mmol/l (254 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.40 mmol/l (170 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.22 mmol/l (47 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.10 mmol/l (186 mg/dl)

SOLAR 2007 *(Continued)*

	Rosuvastatin 10 mg/day baseline non-HDL-C : 5.35 mmol/l (207 mg/dl)
Interventions	Rosuvastatin 10 mg/day Atorvastatin 10 mg/day Simvastatin 20 mg/day
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Atorvastatin 10 mg/day Simvastatin 20 mg/day were not analyzed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to, it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	6/542 were not included in the efficacy analysis 1.1% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

STARSHIP 2006

Methods	6-week washout period 6-week randomized open study
Participants	696 patients age ≥ 18 years with hypercholesterolaemia with a 10-year risk ≥10% for coronary heart disease or its equivalent LDL-C (130-300 mg/dl) (3.36-7.76 mmol/l) TG < 400 mg/dl (< 4.516 mmol/l) 357 were randomized to rosuvastatin 339 were randomized to atorvastatin exclusion criteria: homozygous familial hypercholesterolaemia, known type I, III, or V hyperlipoproteinaemia

STARSHIP 2006 *(Continued)*

	active arterial disease, uncontrolled hypertension, poorly controlled diabetes active liver disease or dysfunction, serum CK > 3 X ULN Rosuvastatin 10 mg/day baseline TC : 6.465 mmol/l (250 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.27 mmol/l (165 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.19 mmol/l (46 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.21 mmol/l (196 mg/dl) Rosuvastatin 20 mg/day baseline TC : 6.26 mmol/l (242 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 4.11 mmol/l (159 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.22 mmol/l (47 mg/dl) Rosuvastatin 20 mg/day baseline TG : 2.02 mmol/l (179 mg/dl)
Interventions	Rosuvastatin 10 mg/day Rosuvastatin 20 mg/day Atorvastatin 10 mg/day Atorvastatin 20 mg/day
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	Atorvastatin 10 mg/day Atorvastatin 20 mg/day groups were not analyzed SDs were imputed for LDL-C and HDL-C

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day and the Rosuvastatin 20 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day and the Rosuvastatin 20 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day and the Rosuvastatin 20 mg/day treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	10/184 Rosuvastatin 10 mg/day were not included in the efficacy analysis 6/173 Rosuvastatin 20 mg/day were not included in the efficacy analysis 4.5% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstaZeneca supported the study. Data may support bias for rosuvastatin

Stein 2007a

Methods	4-5 week washout period 6-week open-label randomized trial
Participants	626 patients aged 18 years or older with dyslipidaemia LDL-C 175-350 mg/dl (4.52-9.04 mmol/l) TG <400 mg/dl (4.52 mmol/l) 308 participants were randomized to rosuvastatin 318 participants were randomized to simvastatin exclusion criteria:active arterial disease within 3 months of study entry renal dysfunction,uncontrolled hypertension, uncontrolled diabetes mellitus active liver disease or hepatic dysfunction serum CK > 3 X ULN Rosuvastatin 40 mg/day baseline TC : 8.0 mmol/l (309 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 5.8 mmol/l (224 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.3 mmol/l (50 mg/dl) Rosuvastatin 40 mg/day baseline TG : 2.0 mmol/l (177 mg/dl)
Interventions	Rosuvastatin 40 mg/day Simvastatin 80 mg/day
Outcomes	per cent change from baseline at 6 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	Simvastatin 80 mg/day group was not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 40 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	The study was funded by AstraZeneca. Data may support bias for rosuvastatin

Stein 2007b

Methods	6-week washout period 96-week open-label trial
Participants	1382 men and women ≥ 18 years with severe hypercholesterolaemia LDL-C 190-260 mg/dl (4.91-6.72 mmol/l) TG <400 mg/dl (< 4.52 mmol/l) 1382 patients received rosuvastatin 40 mg/day exclusion criteria: homozygous familial hypercholesterolaemia, type III hyperlipoproteinaemia hepatic dysfunction,, active arterial disease serum CK > 3 X ULN, renal dysfunction, poorly controlled diabetes mellitus uncontrolled hypothyroidism Rosuvastatin 40 mg/day baseline TC : 7.81 mmol/l (302 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 5.59 mmol/l (216 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.27 mmol/l (49 mg/dl) Rosuvastatin 40 mg/day baseline TG : 2.12 mmol/l (188 mg/dl) Rosuvastatin 40 mg/day baseline non-HDL-C : 6.54 mmol/l (253 mg/dl)
Interventions	Rosuvastatin 40 mg/day for 0-12 weeks Rosuvastatin 40 mg/day for 12-48 weeks Rosuvastatin 40 mg/day for 48-96 weeks Rosuvastatin 40-20-40 titrated dosing mg/day any time
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	Rosuvastatin 40 mg/day for 12-48 weeks Rosuvastatin 40 mg/day for 48-96 weeks Rosuvastatin 40-20-40 titrated dosing mg/day any time groups were not included in the efficacy analysis

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	the Rosuvastatin 40 mg/day for 0-12 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 40 mg/day for 0-12 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 40 mg/day for 0-12 weeks treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial

Stein 2007b *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	152/1382(11%) were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	The study was sponsored by AstraZeneca. Data may support bias for rosuvastatin

STELLAR 2003

Methods	6-week washout period 6-week multi-centred randomized open-label study evening doses
Participants	2431 men and women from the USA mean age 58 (21-86) LDL-C 160-250 mg/dl (4.14-6.46 mmol/l) TG < 400 mg/dl (4.52 mmol/l) 641 patients received atorvastatin 655 patients received simvastatin 492 patients received pravastatin 643 patients received rosuvastatin exclusion criteria: women who are likely to become pregnant , statin sensitivity, serious or unstable medical conditions, familial hypercholesterolaemia, lipid-altering drug use and drug and alcohol abuse Rosuvastatin 10 mg/day baseline TC : 7.11 mmol/l (275 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 4.86 mmol/l (188 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 1.32 mmol/l (51 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C : 5.79 mmol/l (224 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.02 mmol/l (179 mg/dl) Rosuvastatin 20 mg/day baseline TC : 7.09 mmol/l (274 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 4.84 mmol/l (187 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.32 mmol/l (51 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C : 5.77 mmol/l (223 mg/dl) Rosuvastatin 20 mg/day baseline TG : 2.03 mmol/l (180 mg/dl) Rosuvastatin 40 mg/day baseline TC : 7.24 mmol/l (280 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 5.02 mmol/l (194 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.29 mmol/l (50 mg/dl) Rosuvastatin 40 mg/day baseline non-HDL-C : 5.95 mmol/l (230 mg/dl) Rosuvastatin 40 mg/day baseline TG : 2.06 mmol/l (182 mg/dl)
Interventions	Atorvastatin 10 mg/day Atorvastatin 20 mg/day Atorvastatin 40 mg/day Atorvastatin 80 mg/day

STELLAR 2003 *(Continued)*

	Rosuvastatin 10 mg/day
	Rosuvastatin 20 mg/day
	Rosuvastatin 40 mg/day
	Simvastatin 10 mg/day
	Simvastatin 20 mg/day
	Simvastatin 40 mg/day
	Simvastatin 80 mg/day
	Pravastatin 10 mg/day
	Pravastatin 20 mg/day
	Pravastatin 40 mg/day
Outcomes	per cent change from baseline at 6 weeks of plasma TC, LDL-C, HDL-C, non-HDL-C and triglycerides
Notes	rosuvastatin groups were analyzed
	SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day, the Rosuvastatin 20 mg/day, the Rosuvastatin 40 mg/day, treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day, the Rosuvastatin 20 mg/day, the Rosuvastatin 40 mg/day, treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day, the Rosuvastatin 20 mg/day, the Rosuvastatin 40 mg/day, treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	10 mg/day rosuvastatin: 2/158 were not included in the efficacy analysis 20 mg/day rosuvastatin: 4/164 were not included in the efficacy analysis 40 mg/day rosuvastatin: 1/158 were not included in the efficacy analysis 1.5% participants were excluded from the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	High risk	AstraZeneca funded it. Data may support bias for rosuvastatin

Szapary 2012

Methods	no washout required because participants were not receiving any lipid-altering agents

Szapary 2012 *(Continued)*

	12-week before-and-after trial
Participants	109 men and women age 72 years with cerebrovascular disease exclusion criteria: none Rosuvastatin 20 mg/day baseline TC : 5.47 mmol/l (212 mg/dl) Rosuvastatin 20 mg/day baseline LDL-C : 3.16 mmol/l (122 mg/dl) Rosuvastatin 20 mg/day baseline HDL-C : 1.27 mmol/l (49 mg/dl) Rosuvastatin 20 mg/day baseline non-HDL-C: 4.2 mmol/l (162 mg/dl) Rosuvastatin 20 mg/day baseline TG : 1.47 mmol/l (130 mg/dl)
Interventions	Rosuvastatin 20 mg/day
Outcomes	per cent change from baseline at 12 weeks of blood TC, LDL-C, HDL-C, non-HDL-C and triglycerides
Notes	SD was imputed for non-HDL-C data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	there was only one group of participants analyzed therefore it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding was not reported

Takebayashi 2009

Methods	no patient was receiving lipid-altering medications no washout period was required 12-week randomized open-label trial
Participants	40 men and women age 55-65 with type 2 diabetes mellitus and hyperlipidaemia TC > 220 mg/dl (> 5.69 mmol/l) TG > 150 mg/dl (> 1.69 mmol/l) 20 patients were randomized to rosuvastatin 2.5 mg/day 20 patients were randomized to colestimide 3.0 g/day

Takebayashi 2009 *(Continued)*

	exclusion criteria: liver dysfunction, renal dysfunction, infections autoimmune disease Rosuvastatin 2.5 mg/day baseline TC : 6.60 mmol/l (255 mg/dl) Rosuvastatin 2.5 mg/day baseline LDL-C : 3.97 mmol/l (154 mg/dl) Rosuvastatin 2.5 mg/day baseline HDL-C : 1.39 mmol/l (54 mg/dl) Rosuvastatin 2.5 mg/day baseline TG : 2.35 mmol/l (208 mg/dl) Rosuvastatin 2.5 mg/day baseline non-HDL-C: 5.22 mmol/l (202 mg/dl)
Interventions	rosuvastatin 2.5 mg/day colestimide 3.0 g/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	colestimide 3.0 g/day group was not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 2.5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 2.5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 2.5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/20 (5%) in the rosuvastatin group was not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding was not reported

Tateishi 2011

Methods	participants were not receiving any lipid-altering agents no washout period is required 12 week
Participants	exclusion criteria: none Rosuvastatin 2.5 mg/day baseline LDL-C : 4.22 mmol/l (163 mg/dl) Rosuvastatin 2.5 mg/day baseline HDL-C : 1.33 mmol/l (51 mg/dl) Rosuvastatin 2.5 mg/day baseline TG : 1.885 mmol/l (167 mg/dl)

Tateishi 2011 *(Continued)*

Interventions	rosuvastatin 2.5 mg/day for 0-12 weeks rosuvastatin 5 mg/day for 12-24 weeks atorvastatin 10 mg/day pitavastatin 2 mg/day
Outcomes	per cent change from baseline at 8 weeks of serum LDL-C, HDL-C and triglycerides
Notes	rosuvastatin 5 mg/day for 12-24 weeks atorvastatin 10 mg/day pitavastatin 2 mg/day groups were not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 2.5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 2.5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 2.5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	High risk	total cholesterol and non-HDL-C were not included in the efficacy analysis
Other bias	Unclear risk	source of funding was not reported

Tsunoda 2011

Methods	participants were not receiving any lipid-altering agents no washout period is required 12-week open-label trial
Participants	exclusion criteria: serum triglycerides > 400 mg/dl Rosuvastatin 2.5 mg/day baseline TC : 6.53 mmol/l (253 mg/dl) Rosuvastatin 2.5 mg/day baseline LDL-C : 4.15 mmol/l (160 mg/dl) Rosuvastatin 2.5 mg/day baseline HDL-C : 1.38 mmol/l (53 mg/dl)

Tsunoda 2011 *(Continued)*

	Rosuvastatin 2.5 mg/day baseline TG : 2.19 mmol/l (194 mg/dl)
	Rosuvastatin 2.5 mg/day baseline non-HDL-C: 5.15 mmol/l (199 mg/dl)
Interventions	rosuvastatin 2.5 mg/day
	atorvastatin 10 mg/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	atorvastatin 10 mg/day group was not included in the efficacy analysis
	SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 2.5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 2.5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 2.5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding was not reported

Wang 2012

Methods	participants were not receiving any lipid-altering agents within 1 month of study no washout period was required
	12-week before-and-after trial
Participants	90 patients with mild to moderate chronic kidney disease with dyslipidaemia age 26-81 years
	TC ≥ 5.18 mmol / l, LDL - C ≥ 3.37 mmol / l, TG ≥ 1.7 mmol/l
	30 participants received rosuvastatin 5 mg/day for 12 weeks
	30 participants received rosuvastatin 10 mg/day for 12 weeks
	30 participants received atorvastatin 10 mg/day for 12 weeks
	exclusion criteria: statin allergies, familial hypercholesterolaemia, thyroid dysfunction, acute and chronic liver disease or abnormal liver function severe infection, surgery and trauma history

Wang 2012 *(Continued)*

	Rosuvastatin 5 mg/day baseline TC : 6.18 mmol/l (239 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 3.75 mmol/l (145 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 0.85 mmol/l (33 mg/dl) Rosuvastatin 5 mg/day baseline TG : 2.25 mmol/l (199 mg/dl) Rosuvastatin 5 mg/day baseline non-HDL-C: 5.33 mmol/l (206 mg/dl) Rosuvastatin 10 mg/day baseline TC : 6.21 mmol/l (240 mg/dl) Rosuvastatin 10 mg/day baseline LDL-C : 3.84 mmol/l (148 mg/dl) Rosuvastatin 10 mg/day baseline HDL-C : 0.87 mmol/l (34 mg/dl) Rosuvastatin 10 mg/day baseline TG : 2.23 mmol/l (198 mg/dl) Rosuvastatin 10 mg/day baseline non-HDL-C: 5.34 mmol/l (206 mg/dl)
Interventions	rosuvastatin 5 mg/day rosuvastatin 10 mg/day atorvastatin 10 mg/day
Outcomes	per cent change from baseline at 4 and 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	atorvastatin 10 mg/day group was not analyzed SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day and the Rosuvastatin 10 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day and the Rosuvastatin 10 mg/day treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day and the Rosuvastatin 10 mg/day treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

Weinstein 2013

Methods	6-week washout period 0-8 week before-and-after trial

Weinstein 2013 *(Continued)*

	8-16 week dose escalation study 16-24 week posttreatment washout phase
Participants	280 men and women ≥18 years of age with stage 3 CKD and mixed dyslipidaemia TG ≥ 150 mg/dl (3.88 mmol/l), LDL-C ≥ 130 mg/dl (3.36 mmol/l), HDL-C < 40 mg/dl (1.03 mmol/l) for men and < 50 mg/dl (1.29 mmol/l) for women 140 patients received 45 mg/day fenofibric acid and 5-10 mg/day rosuvastatin 140 patients received 5-10 mg/day rosuvastatin exclusion criteria:hypersensitivity to fenofibrate or fenofibric acid or statins BP >140/90 mm Hg, unstable cardiovascular disease within 3-6 months of trial, type 1 diabetes, uncontrolled type 2 diabetes, history of diabetic ketoacidosis, malignancy except non-melanoma skin cancer within 2 years, neurologic or blood disorders, GI/hepatic dysfunction, myopathy, renal dysfunction and patients of Asian ancestry Rosuvastatin 5 mg/day baseline TC : 6.55 mmol/l (253 mg/dl) Rosuvastatin 5 mg/day baseline LDL-C : 3.605 mmol/l (139 mg/dl) Rosuvastatin 5 mg/day baseline HDL-C : 1.02 mmol/l (39.4 mg/dl) Rosuvastatin 5 mg/day baseline non-HDL-C: 5.53 mmol/l (214 mg/dl)
Interventions	Fenofibric acid 45 mg/day and Rosuvastatin 5 mg/day for 0-8 weeks Fenofibric acid 45 mg/day and Rosuvastatin 10 mg/day for 8-16 weeks Fenofibric acid and Rosuvastatin posttreatment washout phase for 16-24 weeks Rosuvastatin 5 mg/day for 0-8 weeks Rosuvastatin 10 mg/day for 8-16 weeks Rosuvastatin posttreatment washout phase for 16-24 weeks
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, and non-HDL-C
Notes	Fenofibric acid 45 mg/day and Rosuvastatin 5 mg/day for 0-8 weeks Fenofibric acid 45 mg/day and Rosuvastatin 10 mg/day for 8-16 weeks Fenofibric acid and Rosuvastatin posttreatment washout phase for 16-24 weeks Rosuvastatin 10 mg/day for 8-16 weeks Rosuvastatin posttreatment washout phase for 16-24 weeks groups were not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 5 mg/day for 8 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 5 mg/day for 8 weeks treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable

Weinstein 2013 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 5 mg/day for 8 weeks treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	2/140 (1.4%) participants were not included in the efficacy analysis for TC , HDL-C and non-HDL-C 7/140 (5%) participants were not included in the efficacy analysis for LDL-C
Selective reporting (reporting bias)	High risk	blood triglycerides were not included in the efficacy analysis because it was a median per cent change
Other bias	High risk	AbbVie and AstraZeneca sponsored the study. Data may be biased for Rosuvastaitn

Wongwiwatthananukit 2006

Methods	participants were not receiving any lipid-altering agents no washout period is required 8-week randomized open-label trial
Participants	80 men and women > 20 years of age with hypercholesterolaemia coronary heart disease or risk equivalents LDL-C ≥100 mg/dl (≥2.59 mmol/l), ≥2 risk factors and LDL-C ≥130 mg/dl (≥3.36 mmol/l) <2 risk factors and LDL-C ≥160 mg/dl (≥4.14 mmol/l) 38 patients randomized to rosuvastatin 10mg/day 38 patients randomized to rosuvastatin 10 mg EOD exclusion criteria: taking drugs known to affect lipid metabolism or interact with rosuvastatin active liver disease, liver dysfunction, serum CK > 3 X ULN renal dysfunction, pregnancy, lactation Rosuvastatin 40 mg/day baseline TC : 6.63 mmol/l (256 mg/dl) Rosuvastatin 40 mg/day baseline LDL-C : 4.70 mmol/l (182 mg/dl) Rosuvastatin 40 mg/day baseline HDL-C : 1.36 mmol/l (53 mg/dl) Rosuvastatin 40 mg/day baseline TG : 1.75 mmol/l (155 mg/dl) Rosuvastatin 40 mg/day baseline non-HDL-C: 5.27 mmol/l (204 mg/dl)
Interventions	rosuvastatin 10 mg/day rosuvastatin 10 mg EOD
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	rosuvastatin 10 mg EOD group was not included in the efficacy analysis

Risk of bias

Bias	Authors' judgement	Support for judgement

Wongwiwatthananukit 2006 *(Continued)*

Random sequence generation (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 10 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	2/40 = 5% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding was not reported

Yamamoto 2002

Methods	≥ 4 week washout period 8-week randomized double-blind trial
Participants	68 men and women age 28-72 years with primary hypercholesterolaemia TC ≥220 mg/dl (5.68 mmol/l) TG ≤400 mg/dl (4.50 mmol/l) 20 patients were randomized to rosuvastatin 1 mg/day 19 patients were randomized to rosuvastatin 2 mg/day 21 patients were randomized to rosuvastatin 4 mg/day exclusion criteria: none reported Rosuvastatin 1 mg/day baseline TC : 7.61 mmol/l (294 mg/dl) Rosuvastatin 1 mg/day baseline LDL-C : 5.67 mmol/l (219 mg/dl) Rosuvastatin 1 mg/day baseline HDL-C : 1.21 mmol/l (47 mg/dl) Rosuvastatin 1 mg/day baseline TG : 1.60 mmol/l (142 mg/dl) Rosuvastatin 2 mg/day baseline TC : 7.85 mmol/l (304 mg/dl) Rosuvastatin 2 mg/day baseline LDL-C : 5.73 mmol/l (222 mg/dl) Rosuvastatin 2 mg/day baseline HDL-C : 1.30 mmol/l (50 mg/dl) Rosuvastatin 2 mg/day baseline TG : 2.00 mmol/l (177 mg/dl) Rosuvastatin 4 mg/day baseline TC : 7.37 mmol/l (285 mg/dl) Rosuvastatin 4 mg/day baseline LDL-C : 5.27 mmol/l (204 mg/dl) Rosuvastatin 4 mg/day baseline HDL-C : 1.41 mmol/l (55 mg/dl) Rosuvastatin 4 mg/day baseline TG : 1.50 mmol/l (133 mg/dl)
Interventions	rosuvastatin 1 mg/day rosuvastatin 2 mg/day

Yamamoto 2002 *(Continued)*

	rosuvastatin 4 mg/day
Outcomes	per cent change from baseline at 8 weeks of serum TC, LDL-C, HDL-C and triglycerides
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 1 mg/day, the Rosuvastatin 2 mg/day, the Rosuvastatin 4 mg/day, treatment arms were analyzed and since there was no placebo group to compare them to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 1 mg/day, the Rosuvastatin 2 mg/day, the Rosuvastatin 4 mg/day, treatment arms were analyzed and since there was no placebo group to compare them to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 1 mg/day, the Rosuvastatin 2 mg/day, the Rosuvastatin 4 mg/day, treatment arms were analyzed and since there was no placebo group to compare them to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	High risk	8/68 = 11.8% participants were not included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis
Other bias	Unclear risk	source of funding not reported

Yanagi 2011

Methods	no lipid-lowering medication had been administered no washout period required 24-week randomized open-label cross-over trial
Participants	90 men and women with type 2 diabetes mellitus and hyperlipidaemia LDL-C ≥140 mg/dl (≥ 3.62 mmol/l) TG < 300 mg/dl (<3.39 mmol/l) glycated haemoglobin <8.5% serum creatinine < 2.0 mg/d urinary albumin excretion < 300 mg/Cr 21 patients were randomized to rosuvastatin 2.5 mg/day for 0-12 weeks then pitavastatin 2 mg/day for 12-24 weeks 21 patients were randomized to pitavastatin 2 mg/day for 0-12 weeks then rosuvastatin 2.5 mg/day for 12-24 weeks 22 patients were randomized to rosuvastatin 2.5 mg/day for 0-12 weeks then rosuvastatin 2.5 mg/day for 12-24 weeks

Yanagi 2011 *(Continued)*

	22 patients were randomized to pitavastatin 2 mg/day for 0-12 weeks then pitavastatin 2 mg/day for 12-24 weeks exclusion criteria: history of stroke,or other cardiovascular event ROS-PIT group for 0-12 weeks Rosuvastatin 2.5 mg/day baseline LDL-C : 4.98 mmol/l (193 mg/dl) Rosuvastatin 2.5 mg/day baseline HDL-C : 1.36 mmol/l (53 mg/dl) Rosuvastatin 2.5 mg/day baseline TG : 1.82 mmol/l (161 mg/dl) ROS-ROS group for 0-12 weeks Rosuvastatin 2.5 mg/day baseline LDL-C : 4.87 mmol/l (188 mg/dl) Rosuvastatin 2.5 mg/day baseline HDL-C : 1.40 mmol/l (54 mg/dl) Rosuvastatin 2.5 mg/day baseline TG : 1.76 mmol/l (156 mg/dl) Combined groups for 0-12 weeks Rosuvastatin 2.5 mg/day baseline LDL-C : 4.92 mmol/l (190 mg/dl) Rosuvastatin 2.5 mg/day baseline HDL-C : 1.38 mmol/l (53 mg/dl) Rosuvastatin 2.5 mg/day baseline TG : 1.79 mmol/l (159 mg/dl)
Interventions	rosuvastatin 2.5 mg/day for 0-12 weeks pitavastatin 2 mg/day for 12-24 weeks pitavastatin 2 mg/day for 0-12 weeks rosuvastatin 2.5 mg/day for 12-24 weeks
Outcomes	per cent change from baseline at 12 weeks of serum LDL-C, HDL-C and triglycerides
Notes	pitavastatin 2 mg/day for 12-24 weeks pitavastatin 2 mg/day for 0-12 weeks rosuvastatin 2.5 mg/day for 12-24 weeks groups and time periods were not included in the efficacy analysis SDs were imputed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	the Rosuvastatin 2.5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	the Rosuvastatin 2.5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	the Rosuvastatin 2.5 mg/day treatment arm was analyzed and since there was no placebo group to compare it to it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	4/90 = 4.4% participants were not included in the efficacy analysis

Yanagi 2011 *(Continued)*

Selective reporting (reporting bias)	High risk	total cholesterol and non-HDL-C were not included in the efficacy analysis
Other bias	Low risk	authors declare they have no conflict of interest

Yoshino 2012

Methods	6-week dietary washout baseline stabilization period 12-week before-and-after trial
Participants	23 men and women with diabetes and hypercholesterolaemia and 33 non diabetic men and women with hypercholesterolaemia for a total of 56 age 36-78 years all participants received 2.5 mg/day rosuvastatin for 12 weeks exclusion criteria: renal dysfunction, hepatic dysfunction hyperthyroidism, pregnancy, receiving lipid-altering agents within 8 weeks of study diabetic participants receiving pioglitazone Rosuvastatin 2.5 mg/day baseline TC : 6.75 mmol/l (261 mg/dl) Rosuvastatin 2.5 mg/day baseline LDL-C : 4.52 mmol/l (175 mg/dl) Rosuvastatin 2.5 mg/day baseline HDL-C : 1.51 mmol/l (58 mg/dl) Rosuvastatin 2.5 mg/day baseline TG : 1.79 mmol/l (159 mg/dl) Rosuvastatin 2.5 mg/day baseline non-HDL-C: 5.24 mmol/l (203 mg/dl)
Interventions	rosuvastatin 2.5 mg/day
Outcomes	per cent change from baseline at 12 weeks of serum TC, LDL-C, HDL-C, triglycerides and non-HDL-C
Notes	SDs were imputed

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of adequate sequence generation is not applicable
Allocation concealment (selection bias)	High risk	there was only one group of participants analyzed therefore assessment of allocation concealment is not applicable
Blinding (performance bias and detection bias) All outcomes	High risk	there was only one group of participants analyzed therefore it is an unblinded trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	all participants were included in the efficacy analysis
Selective reporting (reporting bias)	Low risk	all lipid parameters were included in the efficacy analysis

Yoshino 2012 *(Continued)*

Other bias	Unclear risk	source of funding not reported

ALT: Alanine transaminase
AST: aspartate aminotransferase
BMI: body mass index
CABG: coronary artery bypass graft
CAD: coronary artery disease
CHD: coronary heart disease
CK: creatine kinase
CKD: chronic kidney disease
CPK: creatine phosphokinase
DBP: diastolic blood pressure
GI: gastrointestinal
HDL-C: high-density lipoprotein cholesterol
HRT: hormone replacement therapy
IMT: intima-media thickness
LDL-C: low-density lipoprotein cholesterol
LLT: lipid-lowering therapy
MI: myocardial infarction
PTCA: percutaneous transluminal coronary angioplasty
SBP: systolic blood pressure
SD: standard deviation
STEMI: ST segment elevation myocardial infarction
TC: total cholesterol
TG: triglycerides
TIA: transient ischaemic attack
TSH: thyroid stimulating hormone
ULN: upper limit of normal
WDAEs: withdrawals due to adverse effects

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
AstraZeneca 2007	Exact number of participants receiving rosuvastatin not reported
Bays 2011	Participants received confounding drug ezetimibe added to the rosuvastatin
Bertolotti 2012	Specific dose not reported, range of doses given
Bottaro 2008	Confounding factor: anti retroviral drugs for the treatment of HIV inappropriate outcomes median per cent change from baseline
Burmeister 2009	Confounding factor: haemodialysis
Calza 2008	Confounding factor: anti retroviral drugs for the treatment of HIV
Calza 2012	Confounding factor: anti retroviral drugs for the treatment of HIV
Calza 2013	Confounding factor: anti retroviral drugs for the treatment of HIV
COMPELL 2007	Titrated dose sequential data
DISCOVERY-Alpha 2006	447/1002 (44.6%) participants were not included in the efficacy analysis high incomplete outcome bias

Study	Reason for exclusion
Domingos 2012	Confounding factor: anti retroviral drugs for the treatment of HIV
Fonseca 2005	Data from statin-naive patients and switched patients were combined. No baseline dietary washout stabilization period for at least 3 weeks was performed for the switched patients
Gadarla 2008	Some participants were receiving confounding drugs
Gliozzi 2013	length of washout period not recorded
Goldberg 2011	No dose of rosuvastatin reported
Johns 2007	Confounding factor: anti retroviral drugs for the treatment of HIV
Jyoti 2008	Not available via interlibrary loan
Katabami 2014	length of washout period not recorded
Khan 2014	length of washout period not recorded
Kiser 2008	Confounding factor: participants are receiving protease inhibitors for the treatment of HIV
Li 2012a	LDL-C values are incorrect from the Friedewald formula all values are suspect
Li 2012b	LDL-C values are incorrect from the Friedewald formula all values are suspect
Polis 2009	Pooled data across all statin doses
Puccetti 2011	Inappropriate outcomes, median per cent change
Riccioni 2012	Article is not available via interlibrary loan
Rossi 2009	4/15 (26.6%) participants were not included in the efficacy analysis high incomplete outcome bias
Roth 2010	Rosuvastatin fenofibrate combination
Talavera 2013	Median per cent change was reported
Van Der Lee, 2007	Confounding factor: participants received protease inhibitors for the treatment of HIV
Van Der Lee, 2008	Confounding factor: participants received protease inhibitors for the treatment of HIV
Yun 2012	167/723 (23%) participants were not included in the efficacy analysis; high incomplete outcome bias

LDL-C: low-density lipoprotein cholesterol

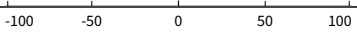
DATA AND ANALYSES

Comparison 1. 1.0 mg vs control

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Total cholesterol	3	93	Mean Difference (IV, Fixed, 95% CI)	-21.83 [-25.59, -18.08]
2 LDL-cholesterol	3	93	Mean Difference (IV, Fixed, 95% CI)	-31.17 [-35.32, -27.02]
3 HDL-cholesterol	3	93	Mean Difference (IV, Fixed, 95% CI)	8.16 [2.93, 13.38]
4 non-HDL-cholesterol	2	69	Mean Difference (IV, Fixed, 95% CI)	-30.13 [-38.06, -22.20]
5 Triglycerides	3	93	Mean Difference (IV, Fixed, 95% CI)	-20.77 [-32.73, -8.80]
6 WDAE	1	31	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 1.1. Comparison 1 1.0 mg vs control, Outcome 1 Total cholesterol.

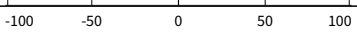
Study or subgroup	Rosuvastatin N	Rosuvastatin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Olsson 2001	13	-23.7 (7.9)	29	-2.2 (7)		56.57%	-21.5[-26.49,-16.51]
Raza 2000	12	-25.3 (12)	12	-5.3 (12)		15.3%	-20[-29.6,-10.4]
Saito 2003	15	-25.5 (9.3)	12	-2 (9.4)		28.13%	-23.5[-30.58,-16.42]
Total ***	**40**		**53**			**100%**	**-21.83[-25.59,-18.08]**
Heterogeneity: Tau²=0; Chi²=0.37, df=2(P=0.83); I²=0%							
Test for overall effect: Z=11.39(P<0.0001)							



Favours rosuvastatin — Favours placebo

Analysis 1.2. Comparison 1 1.0 mg vs control, Outcome 2 LDL-cholesterol.

Study or subgroup	Rosuvastatin N	Rosuvastatin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Olsson 2001	13	-34.3 (9.4)	29	-3.6 (9.2)		46.24%	-30.7[-36.81,-24.59]
Raza 2000	12	-36 (15)	12	-8 (15)		11.98%	-28[-40,-16]
Saito 2003	15	-35.8 (2.7)	12	-3.2 (11.1)		41.78%	-32.6[-39.03,-26.17]
Total ***	**40**		**53**			**100%**	**-31.17[-35.32,-27.02]**
Heterogeneity: Tau²=0; Chi²=0.48, df=2(P=0.79); I²=0%							
Test for overall effect: Z=14.71(P<0.0001)							



Favours rosuvastatin — Favours placebo

Analysis 1.3. Comparison 1 1.0 mg vs control, Outcome 3 HDL-cholesterol.

Study or subgroup	Rosuvastatin N	Rosuvastatin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Olsson 2001	13	10 (13)	29	3.6 (11.8)		39.92%	6.4[-1.87,14.67]
Raza 2000	12	8.8 (16)	12	2.8 (16)		16.65%	6[-6.8,18.8]
Saito 2003	15	11.8 (10.5)	12	1.2 (10.4)		43.43%	10.6[2.67,18.53]
Total ***	**40**		**53**			**100%**	**8.16[2.93,13.38]**
Heterogeneity: Tau²=0; Chi²=0.65, df=2(P=0.72); I²=0%							
Test for overall effect: Z=3.06(P=0)							

Analysis 1.4. Comparison 1 1.0 mg vs control, Outcome 4 non-HDL-cholesterol.

Study or subgroup	Rosuvastatin N	Rosuvastatin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Olsson 2001	13	-32.3 (16)	29	-3.6 (16)		57.38%	-28.7[-39.17,-18.23]
Saito 2003	15	-34.9 (16)	12	-2.8 (16)		42.62%	-32.05[-44.2,-19.9]
Total ***	**28**		**41**			**100%**	**-30.13[-38.06,-22.2]**
Heterogeneity: Tau²=0; Chi²=0.17, df=1(P=0.68); I²=0%							
Test for overall effect: Z=7.45(P<0.0001)							

Analysis 1.5. Comparison 1 1.0 mg vs control, Outcome 5 Triglycerides.

Study or subgroup	Rosuvastatin N	Rosuvastatin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Olsson 2001	13	-18.8 (28.5)	29	-1.3 (26.4)		43.06%	-17.5[-35.73,0.73]
Raza 2000	12	-16.9 (31.5)	12	-1.7 (31.5)		22.53%	-15.2[-40.4,10]
Saito 2003	15	-26.2 (26.7)	12	2.3 (27)		34.41%	-28.5[-48.89,-8.11]
Total ***	**40**		**53**			**100%**	**-20.77[-32.73,-8.8]**
Heterogeneity: Tau²=0; Chi²=0.86, df=2(P=0.65); I²=0%							
Test for overall effect: Z=3.4(P=0)							

Analysis 1.6. Comparison 1 1.0 mg vs control, Outcome 6 WDAE.

Study or subgroup	Rosuvastatin n/N	Placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Saito 2003	0/16	0/15			Not estimable
Total (95% CI)	**16**	**15**			**Not estimable**
Total events: 0 (Rosuvastatin), 0 (Placebo)					
Heterogeneity: Not applicable					

Study or subgroup	Rosuvastatin n/N	Placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Test for overall effect: Not applicable					

0.01 0.1 1 10 100

Comparison 2. 2.5 mg vs control

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Total cholesterol	3	95	Mean Difference (IV, Fixed, 95% CI)	-27.44 [-31.17, -23.70]
2 LDL-cholesterol	3	95	Mean Difference (IV, Fixed, 95% CI)	-38.27 [-42.79, -33.75]
3 HDL-cholesterol	3	95	Mean Difference (IV, Fixed, 95% CI)	6.02 [0.88, 11.16]
4 non-HDL-cholesterol	2	71	Mean Difference (IV, Fixed, 95% CI)	-36.47 [-44.30, -28.63]
5 Triglycerides	3	95	Mean Difference (IV, Fixed, 95% CI)	-13.11 [-24.97, -1.25]
6 Total cholesterol	6	286	% change from baseline (Fixed, 95% CI)	-26.52 [-27.90, -25.13]
7 LDL-cholesterol	8	355	% change from baseline (Fixed, 95% CI)	-39.21 [-40.76, -37.65]
8 HDL-cholesterol	8	355	% change from baseline (Fixed, 95% CI)	4.20 [2.54, 5.85]
9 non-HDL-cholesterol	6	286	Mean Difference (Fixed, 95% CI)	-35.27 [-37.13, -33.41]
10 Triglycerides	8	355	% change from baseline (Fixed, 95% CI)	-13.70 [-16.97, -10.43]
11 WDAE	1	33	Risk Ratio (M-H, Fixed, 95% CI)	2.53 [0.11, 57.83]

Analysis 2.1. Comparison 2 2.5 mg vs control, Outcome 1 Total cholesterol.

Study or subgroup	Rosuvastatin N	Rosuvastatin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Olsson 2001	13	-29.1 (7.9)	29	-2.2 (7)		56%	-26.9[-31.89,-21.91]
Raza 2000	12	-30.8 (12)	12	-5.3 (12)		15.14%	-25.5[-35.1,-15.9]
Saito 2003	17	-31.5 (9.5)	12	-2 (9.4)		28.86%	-29.5[-36.46,-22.54]
Total ***	**42**		**53**			**100%**	**-27.44[-31.17,-23.7]**
Heterogeneity: Tau^2=0; Chi^2=0.54, df=2(P=0.76); I^2=0%							
Test for overall effect: Z=14.39(P<0.0001)							

Favours rosuvastatin -100 -50 0 50 100 Favours placebo

Analysis 2.2. Comparison 2 2.5 mg vs control, Outcome 2 LDL-cholesterol.

Study or subgroup	Rosuvastatin N	Rosuvastatin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Olsson 2001	13	-40.7 (9.4)	29	-3.6 (9.2)		54.63%	-37.1[-43.21,-30.99]
Raza 2000	12	-43 (15)	12	-8 (15)		14.15%	-35[-47,-23]
Saito 2003	17	-45 (10.7)	12	-3.2 (11.1)		31.22%	-41.8[-49.88,-33.72]
Total ***	**42**		**53**			**100%**	**-38.27[-42.79,-33.75]**

Heterogeneity: $Tau^2=0$; $Chi^2=1.16$, df=2(P=0.56); $I^2=0\%$

Test for overall effect: Z=16.61(P<0.0001)

Favours rosuvastatin — Favours placebo

Analysis 2.3. Comparison 2 2.5 mg vs control, Outcome 3 HDL-cholesterol.

Study or subgroup	Rosuvastatin N	Rosuvastatin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Olsson 2001	13	9.3 (13)	29	3.6 (11.8)		38.7%	5.7[-2.57,13.97]
Raza 2000	12	8.8 (16)	12	2.8 (16)		16.14%	6[-6.8,18.8]
Saito 2003	17	7.5 (10.3)	12	1.2 (10.4)		45.16%	6.3[-1.35,13.95]
Total ***	**42**		**53**			**100%**	**6.02[0.88,11.16]**

Heterogeneity: $Tau^2=0$; $Chi^2=0.01$, df=2(P=0.99); $I^2=0\%$

Test for overall effect: Z=2.29(P=0.02)

Favours placebo — Favours rosuvastatin

Analysis 2.4. Comparison 2 2.5 mg vs control, Outcome 4 non-HDL-cholesterol.

Study or subgroup	Rosuvastatin N	Rosuvastatin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Olsson 2001	13	-38.2 (16)	29	-3.6 (16)		56.06%	-34.6[-45.07,-24.13]
Saito 2003	17	-41.7 (16)	12	-2.8 (16)		43.94%	-38.85[-50.67,-27.03]
Total ***	**30**		**41**			**100%**	**-36.47[-44.3,-28.63]**

Heterogeneity: $Tau^2=0$; $Chi^2=0.28$, df=1(P=0.6); $I^2=0\%$

Test for overall effect: Z=9.12(P<0.0001)

Favours Rosuvastatin — Favours Placebo

Analysis 2.5. Comparison 2 2.5 mg vs control, Outcome 5 Triglycerides.

Study or subgroup	Rosuvastatin N	Rosuvastatin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Olsson 2001	13	-10.6 (28.5)	29	-1.3 (26.4)		42.32%	-9.3[-27.53,8.93]
Raza 2000	12	-12.3 (31.5)	12	-1.7 (31.5)		22.14%	-10.6[-35.8,14.6]
Saito 2003	17	-16.9 (26.8)	12	2.3 (27)		35.54%	-19.2[-39.09,0.69]
Total ***	**42**		**53**			**100%**	**-13.11[-24.97,-1.25]**

Favours rosuvastatin — Favours placebo

Study or subgroup	Rosuvastatin N	Rosuvastatin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Heterogeneity: Tau²=0; Chi²=0.57, df=2(P=0.75); I²=0%							
Test for overall effect: Z=2.17(P=0.03)							

Favours rosuvastatin -100 -50 0 50 100 Favours placebo

Analysis 2.6. Comparison 2 2.5 mg vs control, Outcome 6 Total cholesterol.

Study or subgroup	Rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Igase 2012a	137	0	-23.8 (1.025)		47.64%	-23.8[-25.81,-21.79]
Igase 2012b	26	0	-32 (2.353)		9.04%	-32[-36.61,-27.39]
Kanazawa 2009	18	0	-25.8 (2.828)		6.26%	-25.8[-31.34,-20.26]
Takebayashi 2009	19	0	-28.8 (2.753)		6.61%	-28.8[-34.2,-23.4]
Tsunoda 2011	30	0	-33.2 (2.136)		10.97%	-33.2[-37.39,-29.01]
Yoshino 2012	56	0	-26.3 (1.604)		19.47%	-26.3[-29.44,-23.16]
Total (95% CI)					**100%**	**-26.52[-27.9,-25.13]**
Heterogeneity: Tau²=0; Chi²=23.01, df=5(P=0); I²=78.27%						
Test for overall effect: Z=37.47(P<0.0001)						

Favours rosuvastatin -100 -50 0 50 100

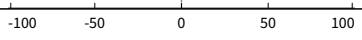
Analysis 2.7. Comparison 2 2.5 mg vs control, Outcome 7 LDL-cholesterol.

Study or subgroup	Rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Igase 2012a	137	0	-34.4 (1.282)		38.43%	-34.4[-36.91,-31.89]
Igase 2012b	26	0	-51 (2.942)		7.29%	-51[-56.77,-45.23]
Kanazawa 2009	18	0	-41.1 (3.536)		5.05%	-41.1[-48.03,-34.17]
Takebayashi 2009	19	0	-38.4 (3.441)		5.33%	-38.4[-45.14,-31.66]
Tateishi 2011	26	0	-39.3 (2.903)		7.49%	-39.35[-45.04,-33.66]
Tsunoda 2011	30	0	-46.1 (2.702)		8.64%	-46.1[-51.4,-40.8]
Yanagi 2011	43	0	-44.4 (2.288)		12.06%	-44.4[-48.88,-39.92]
Yoshino 2012	56	0	-37.3 (2.005)		15.71%	-37.3[-41.23,-33.37]
Total (95% CI)					**100%**	**-39.21[-40.76,-37.65]**
Heterogeneity: Tau²=0; Chi²=43.05, df=7(P<0.0001); I²=83.74%						
Test for overall effect: Z=49.35(P<0.0001)						

Favours rosuvastatin -100 -50 0 50 100

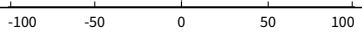
Analysis 2.8. Comparison 2 2.5 mg vs control, Outcome 8 HDL-cholesterol.

Study or subgroup	Rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Igase 2012a	137	0	1.6 (1.367)		38.28%	1.6[-1.08,4.28]
Igase 2012b	26	0	-3 (3.138)		7.26%	-3[-9.15,3.15]
Kanazawa 2009	18	0	7.9 (3.771)		5.03%	7.9[0.51,15.29]
Takebayashi 2009	19	0	6.7 (3.671)		5.31%	6.7[-0.49,13.89]
Tateishi 2011	26	0	6 (3.059)		7.64%	6[0,12]
Tsunoda 2011	30	0	6.7 (2.848)		8.82%	6.7[1.12,12.28]
Yanagi 2011	43	0	10 (2.44)		12.01%	10[5.22,14.78]
Yoshino 2012	56	0	5.1 (2.138)		15.65%	5.1[0.91,9.29]
Total (95% CI)					**100%**	**4.2[2.54,5.85]**
Heterogeneity: Tau²=0; Chi²=17.25, df=7(P=0.02); I²=59.43%						
Test for overall effect: Z=4.96(P<0.0001)						



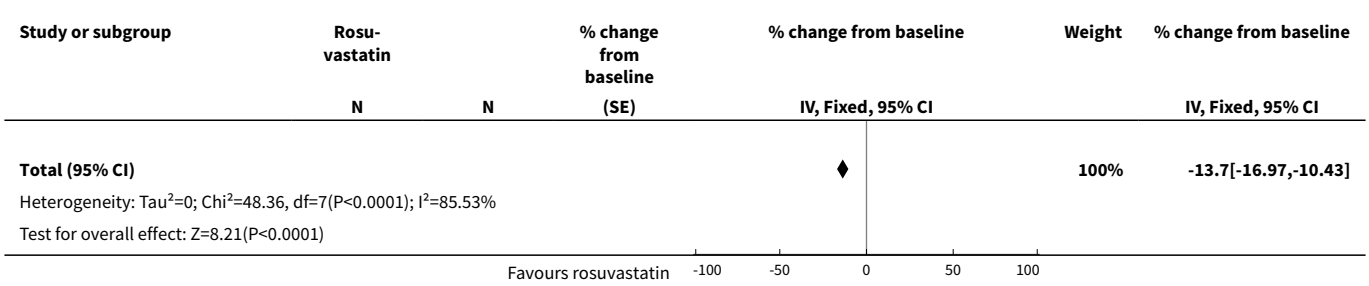
Analysis 2.9. Comparison 2 2.5 mg vs control, Outcome 9 non-HDL-cholesterol.

Study or subgroup	Rosuvastatin N	N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
Igase 2012a	137	0	-31.3 (1.367)		48.15%	-31.3[-33.98,-28.62]
Igase 2012b	26	0	-42.6 (3.138)		9.14%	-42.6[-48.75,-36.45]
Kanazawa 2009	18	0	-38.9 (3.771)		6.33%	-38.9[-46.29,-31.51]
Takebayashi 2009	19	0	-38.3 (3.671)		6.68%	-38.3[-45.49,-31.11]
Tsunoda 2011	30	0	-43.6 (2.994)		10.03%	-43.6[-49.47,-37.73]
Yoshino 2012	56	0	-35.1 (2.138)		19.68%	-35.15[-39.34,-30.96]
Total (95% CI)					**100%**	**-35.27[-37.13,-33.41]**
Heterogeneity: Tau²=0; Chi²=23.24, df=5(P=0); I²=78.49%						
Test for overall effect: Z=37.19(P<0.0001)						

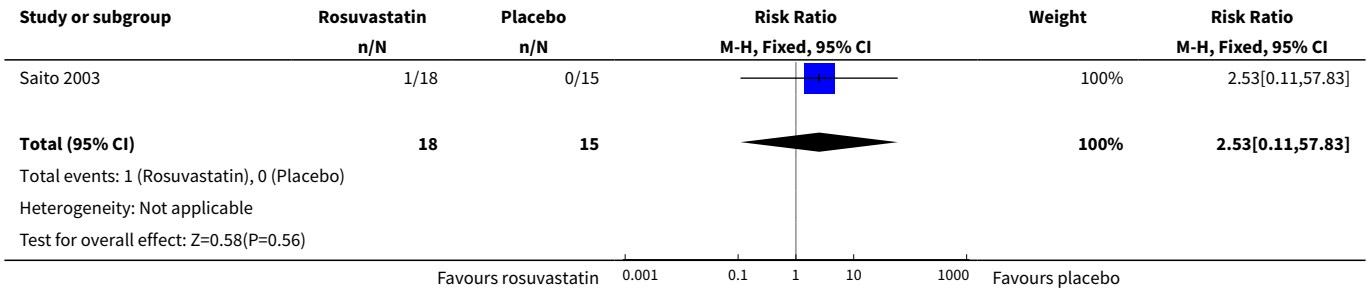


Analysis 2.10. Comparison 2 2.5 mg vs control, Outcome 10 Triglycerides.

Study or subgroup	Rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Igase 2012a	137	0	-13.5 (2.691)		38.4%	-13.5[-18.77,-8.23]
Igase 2012b	26	0	23.3 (6.178)		7.29%	23.3[11.19,35.41]
Kanazawa 2009	18	0	-19.5 (7.425)		5.04%	-19.5[-34.05,-4.95]
Takebayashi 2009	19	0	-14.5 (7.227)		5.32%	-14.5[-28.66,-0.34]
Tateishi 2011	26	0	-9.8 (6.08)		7.52%	-9.8[-21.72,2.12]
Tsunoda 2011	30	0	-29.6 (5.66)		8.68%	-29.6[-40.69,-18.51]
Yanagi 2011	43	0	-14.6 (4.804)		12.05%	-14.6[-24.02,-5.18]
Yoshino 2012	56	0	-21.6 (4.209)		15.69%	-21.6[-29.85,-13.35]



Analysis 2.11. Comparison 2 2.5 mg vs control, Outcome 11 WDAE.



Comparison 3. 5.0 mg vs control

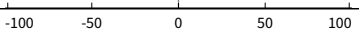
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total cholesterol	9	762	Mean Difference (IV, Fixed, 95% CI)	-29.13 [-30.56, -27.70]
2 LDL-cholesterol	9	762	Mean Difference (IV, Fixed, 95% CI)	-39.12 [-41.11, -37.12]
3 HDL-cholesterol	9	762	Mean Difference (IV, Fixed, 95% CI)	8.64 [6.93, 10.35]
4 non-HDL-cholesterol	8	738	Mean Difference (IV, Fixed, 95% CI)	-36.79 [-38.85, -34.72]
5 Triglycerides	8	674	Mean Difference (IV, Fixed, 95% CI)	-23.08 [-26.97, -19.19]
6 Total cholesterol	15	1411	% change from baseline (Fixed, 95% CI)	-29.11 [-29.69, -28.53]
7 LDL-cholesterol	16	1840	% change from baseline (Fixed, 95% CI)	-41.57 [-42.22, -40.92]
8 HDL-cholesterol	16	1845	% change from baseline (Fixed, 95% CI)	6.69 [6.04, 7.34]
9 non-HDL-cholesterol	14	1307	% change from baseline (Fixed, 95% CI)	-37.77 [-38.53, -37.01]
10 Triglycerides	14	1678	% change from baseline (Fixed, 95% CI)	-16.96 [-18.33, -15.60]
11 WDAE	5	561	Risk Ratio (M-H, Fixed, 95% CI)	1.38 [0.70, 2.72]

Analysis 3.1. Comparison 3 5.0 mg vs control, Outcome 1 Total cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Davidson 2002	128	-28 (11.3)	132	0 (10.3)		29.41%	-28[-30.63,-25.37]
Durrington 2004	60	-31.4 (9.3)	51	1.1 (7.1)		21.8%	-32.5[-35.56,-29.44]
Hunninghake 2004	25	-23 (11)	26	2.5 (11.2)		5.48%	-25.5[-31.59,-19.41]
Olsson 2001	17	-31.1 (7.8)	29	-2.2 (7)		10.06%	-28.9[-33.4,-24.4]
PLUTO 2010	42	-30 (12)	46	0 (12)		8.08%	-30[-35.02,-24.98]
Raza 2000	12	-32.9 (12)	12	-5.3 (12)		2.21%	-27.6[-37.2,-18]
Saito 2003	12	-36.5 (9.4)	12	-2 (9.4)		3.62%	-34.5[-42,-27]
Saito 2007	32	-27.1 (11.3)	35	1.3 (8.2)		8.96%	-28.4[-33.17,-23.63]
Shepherd 2004	45	-25 (10.7)	46	0.8 (10.9)		10.38%	-25.8[-30.23,-21.37]
Total ***	**373**		**389**			**100%**	**-29.13[-30.56,-27.7]**

Heterogeneity: $Tau^2=0$; $Chi^2=11.2$, df=8(P=0.19); $I^2=28.58\%$

Test for overall effect: Z=40.02(P<0.0001)



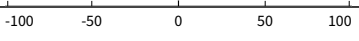
Favours rosuvastatin — Favours placebo

Analysis 3.2. Comparison 3 5.0 mg vs control, Outcome 2 LDL-cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Davidson 2002	128	-40 (14.7)	132	0 (13.8)		33.13%	-40[-43.47,-36.53]
Durrington 2004	60	-40.7 (15.5)	51	-0.6 (11.4)		15.83%	-40.1[-45.12,-35.08]
Hunninghake 2004	25	-28 (20.5)	26	6.2 (21.4)		3.01%	-34.2[-45.7,-22.7]
Olsson 2001	17	-42.5 (9.9)	29	-3.6 (9.2)		11.94%	-38.9[-44.68,-33.12]
PLUTO 2010	42	-38 (15)	46	-1 (15)		10.12%	-37[-43.27,-30.73]
Raza 2000	12	-45 (15)	12	-8 (15)		2.77%	-37[-49,-25]
Saito 2003	12	-52.7 (10.7)	12	-3.2 (11.1)		5.24%	-49.5[-58.22,-40.78]
Saito 2007	32	-31.9 (17.8)	35	3.6 (15.5)		6.19%	-35.5[-43.53,-27.47]
Shepherd 2004	45	-37.6 (14.1)	46	-1.2 (14.2)		11.78%	-36.4[-42.21,-30.59]
Total ***	**373**		**389**			**100%**	**-39.12[-41.11,-37.12]**

Heterogeneity: $Tau^2=0$; $Chi^2=8.72$, df=8(P=0.37); $I^2=8.28\%$

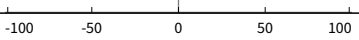
Test for overall effect: Z=38.41(P<0.0001)



Favours rosuvastatin — Favours placebo

Analysis 3.3. Comparison 3 5.0 mg vs control, Outcome 3 HDL-cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Davidson 2002	128	13 (11.3)	132	4 (11.5)		38.03%	9[6.23,11.77]
Durrington 2004	60	9.9 (12.4)	51	1.2 (9.3)		17.86%	8.7[4.66,12.74]
Hunninghake 2004	25	4 (12.5)	26	-2 (12.2)		6.35%	6[-0.78,12.78]
Olsson 2001	17	14 (13.2)	29	3.6 (11.8)		5.05%	10.4[2.8,18]
PLUTO 2010	42	4 (16)	46	7 (16)		6.52%	-3[-9.69,3.69]



Favours rosuvastatin — Favours placebo

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Raza 2000	12	13.2 (16)	12	2.8 (16)		1.78%	10.4[-2.4,23.2]
Saito 2003	12	9.9 (10.4)	12	1.2 (10.4)		4.22%	8.7[0.38,17.02]
Saito 2007	32	14.5 (16.9)	35	1.8 (10.7)		6.23%	12.7[5.86,19.54]
Shepherd 2004	45	11 (11.4)	46	-0.5 (10.9)		13.96%	11.5[6.93,16.07]
Total * **	**373**		**389**			**100%**	**8.64[6.93,10.35]**

Heterogeneity: Tau^2=0; Chi^2=15.4, df=8(P=0.05); I^2=48.05%

Test for overall effect: Z=9.9(P<0.0001)

Favours rosuvastatin -100 -50 0 50 100 Favours placebo

Analysis 3.4. Comparison 3 5.0 mg vs control, Outcome 4 non-HDL-cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Davidson 2002	128	-37.6 (16)	132	-0.9 (16)		28.23%	-36.7[-40.59,-32.81]
Durrington 2004	60	-39.8 (16)	51	1.1 (16)		11.97%	-40.9[-46.87,-34.93]
Hunninghake 2004	25	-27 (12.5)	26	3.3 (12.8)		8.89%	-30.3[-37.23,-23.37]
Olsson 2001	17	-41.4 (16)	29	-3.6 (16)		4.66%	-37.8[-47.38,-28.22]
PLUTO 2010	42	-36.3 (10)	46	-0.8 (11.9)		20.42%	-35.5[-40.07,-30.93]
Saito 2003	12	-49 (16)	12	-2.8 (16)		2.61%	-46.15[-58.95,-33.35]
Saito 2007	32	-36.8 (13.7)	35	1.4 (9.3)		13.34%	-38.2[-43.86,-32.54]
Shepherd 2004	45	-34.5 (16)	46	1.2 (16)		9.88%	-35.7[-42.28,-29.12]
Total * **	**361**		**377**			**100%**	**-36.79[-38.85,-34.72]**

Heterogeneity: Tau^2=0; Chi^2=7.94, df=7(P=0.34); I^2=11.79%

Test for overall effect: Z=34.89(P<0.0001)

Favours rosuvastatin -100 -50 0 50 100 Favours placebo

Analysis 3.5. Comparison 3 5.0 mg vs control, Outcome 5 Triglycerides.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Davidson 2002	128	-17 (27.2)	132	-1 (26.4)		35.61%	-16[-22.52,-9.48]
Durrington 2004	60	-24.5 (27.1)	51	4.7 (20.7)		19.08%	-29.2[-38.1,-20.3]
Hunninghake 2004	25	-18 (22.5)	26	2.9 (22.4)		9.96%	-20.9[-33.23,-8.57]
Olsson 2001	17	-34.6 (29.3)	29	-1.3 (26.4)		5.28%	-33.3[-50.22,-16.38]
Raza 2000	12	-34.8 (31.5)	12	-1.7 (31.5)		2.38%	-33.1[-58.3,-7.9]
Saito 2003	12	-24.5 (27)	12	2.3 (27)		3.24%	-26.8[-48.4,-5.2]
Saito 2007	32	-29 (22)	35	1 (30)		9.64%	-30[-42.53,-17.47]
Shepherd 2004	45	-12.6 (24.8)	46	10.5 (24.4)		14.8%	-23.1[-33.21,-12.99]
Total * **	**331**		**343**			**100%**	**-23.08[-26.97,-19.19]**

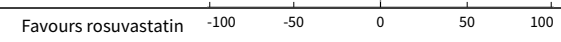
Heterogeneity: Tau^2=0; Chi^2=9.76, df=7(P=0.2); I^2=28.29%

Test for overall effect: Z=11.63(P<0.0001)

Favours rosuvastatin -100 -50 0 50 100 Favours placebo

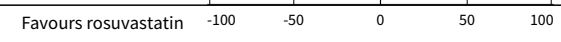
Analysis 3.6. Comparison 3 5.0 mg vs control, Outcome 6 Total cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
AstraZeneca 2010a	135	0	-29.6 (1.92)		2.39%	-29.6[-33.36,-25.84]
Brown 2002	121	0	-28 (1)		8.81%	-28[-29.96,-26.04]
CAP-Chol 2009	103	0	-25.2 (1.38)		4.63%	-25.2[-27.9,-22.5]
JART 2012	151	0	-32.2 (0.977)		9.24%	-32.2[-34.11,-30.29]
Jing 2013	114	0	-30 (1.124)		6.98%	-30[-32.2,-27.8]
Mori 2013	37	0	-32.9 (1.973)		2.26%	-32.9[-36.77,-29.03]
Olsson 2002	135	0	-32 (1)		8.81%	-32[-33.96,-30.04]
Paoletti 2009	119	0	-30 (0.9)		10.88%	-30[-31.76,-28.24]
Rosenson 2011	66	0	-26.3 (1.455)		4.16%	-26.3[-29.15,-23.45]
Schneck 2003	38	0	-29.4 (1.1)		7.28%	-29.4[-31.56,-27.24]
Schwartz 2004	127	0	-29.1 (0.8)		13.77%	-29.1[-30.67,-27.53]
SHUKRA 2009	30	0	-23 (2.191)		1.84%	-23[-27.29,-18.71]
Siddiqi 2013	67	0	-23.8 (1.258)		5.57%	-23.8[-26.27,-21.33]
Wang 2012	30	0	-17.2 (2.191)		1.84%	-17.25[-21.54,-12.96]
Weinstein 2013	138	0	-30.9 (0.874)		11.54%	-30.9[-32.61,-29.19]
Total (95% CI)					**100%**	**-29.11[-29.69,-28.53]**
Heterogeneity: Tau^2=0; Chi^2=95.88, df=14(P<0.0001); I^2=85.4%						
Test for overall effect: Z=98.07(P<0.0001)						



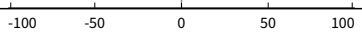
Analysis 3.7. Comparison 3 5.0 mg vs control, Outcome 7 LDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
AstraZeneca 2010a	136	0	-39.7 (1.419)		5.5%	-39.7[-42.48,-36.92]
ASTRO-2 2009	435	0	-44.4 (0.671)		24.58%	-44.4[-45.72,-43.08]
Brown 2002	121	0	-39.1 (1.3)		6.55%	-39.1[-41.65,-36.55]
CAP-Chol 2009	103	0	-37.6 (1.774)		3.52%	-37.6[-41.08,-34.12]
JART 2012	149	0	-47 (1.057)		9.92%	-47[-49.07,-44.93]
Jing 2013	114	0	-42.9 (1.405)		5.61%	-42.9[-45.65,-40.15]
Mori 2013	37	0	-48 (2.466)		1.82%	-48[-52.83,-43.17]
Olsson 2002	135	0	-46 (1.3)		6.55%	-46[-48.55,-43.45]
Paoletti 2009	119	0	-42 (1.3)		6.55%	-42[-44.55,-39.45]
Rosenson 2011	66	0	-28.1 (2.216)		2.26%	-28.1[-32.44,-23.76]
Schneck 2003	38	0	-41.5 (1.4)		5.65%	-41.5[-44.24,-38.76]
Schwartz 2004	127	0	-39.8 (1.1)		9.15%	-39.8[-41.96,-37.64]
SHUKRA 2009	30	0	-33.3 (2.739)		1.48%	-33.3[-38.67,-27.93]
Siddiqi 2013	67	0	-30.3 (1.784)		3.48%	-30.3[-33.8,-26.8]
Wang 2012	30	0	-26.9 (2.739)		1.48%	-26.9[-32.27,-21.53]
Weinstein 2013	133	0	-39.2 (1.371)		5.89%	-39.2[-41.89,-36.51]
Total (95% CI)					**100%**	**-41.57[-42.22,-40.92]**
Heterogeneity: Tau^2=0; Chi^2=194.22, df=15(P<0.0001); I^2=92.28%						
Test for overall effect: Z=124.91(P<0.0001)						



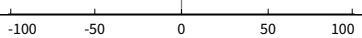
Analysis 3.8. Comparison 3 5.0 mg vs control, Outcome 8 HDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
AstraZeneca 2010a	134	0	5.6 (2.29)		2.11%	5.63[1.14,10.12]
ASTRO-2 2009	435	0	6.8 (0.597)		31.12%	6.8[5.63,7.97]
Brown 2002	121	0	8.2 (1.2)		7.7%	8.2[5.85,10.55]
CAP-Chol 2009	103	0	11.3 (2.03)		2.69%	11.3[7.32,15.28]
JART 2012	151	0	6.3 (1.107)		9.05%	6.3[4.13,8.47]
Jing 2013	114	0	0 (1.499)		4.94%	0[-2.94,2.94]
Mori 2013	37	0	2.3 (2.63)		1.6%	2.3[-2.86,7.46]
Olsson 2002	135	0	6 (1.3)		6.56%	6[3.45,8.55]
Paoletti 2009	119	0	6 (1.2)		7.7%	6[3.65,8.35]
Rosenson 2011	66	0	17 (2.68)		1.54%	17[11.75,22.25]
Schneck 2003	38	0	7.4 (1.8)		3.42%	7.4[3.87,10.93]
Schwartz 2004	127	0	6.6 (1)		11.09%	6.6[4.64,8.56]
SHUKRA 2009	30	0	4.5 (2.921)		1.3%	4.5[-1.23,10.23]
Siddiqi 2013	67	0	3.9 (2.004)		2.76%	3.9[-0.03,7.83]
Wang 2012	30	0	18.9 (2.921)		1.3%	18.85[13.12,24.58]
Weinstein 2013	138	0	7.8 (1.473)		5.11%	7.8[4.91,10.69]
Total (95% CI)					**100%**	**6.69[6.04,7.34]**
Heterogeneity: Tau²=0; Chi²=65.8, df=15(P<0.0001); I²=77.2%						
Test for overall effect: Z=20.09(P<0.0001)						

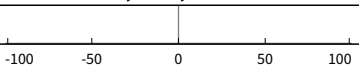


Analysis 3.9. Comparison 3 5.0 mg vs control, Outcome 9 non-HDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
AstraZeneca 2010a	134	0	-38.6 (3.57)		1.19%	-38.6[-45.6,-31.6]
Brown 2002	121	0	-35.9 (1.2)		10.5%	-35.9[-38.25,-33.55]
JART 2012	151	0	-42.6 (0.993)		15.35%	-42.6[-44.55,-40.65]
Jing 2013	114	0	-37.8 (1.499)		6.74%	-37.8[-40.74,-34.86]
Mori 2013	37	0	-44.9 (2.63)		2.19%	-44.9[-50.06,-39.74]
Olsson 2002	135	0	-41.5 (1.377)		7.98%	-41.5[-44.2,-38.8]
Paoletti 2009	119	0	-38.1 (1.467)		7.03%	-38.1[-40.97,-35.23]
Rosenson 2011	66	0	-33.5 (1.86)		4.37%	-33.5[-37.15,-29.85]
Schneck 2003	38	0	-38.1 (1.3)		8.95%	-38.1[-40.65,-35.55]
Schwartz 2004	127	0	-36.3 (1)		15.13%	-36.3[-38.26,-34.34]
SHUKRA 2009	30	0	-29.7 (2.921)		1.77%	-29.72[-35.45,-23.99]
Siddiqi 2013	67	0	-31 (1.955)		3.96%	-31.05[-34.88,-27.22]
Wang 2012	30	0	-23 (2.921)		1.77%	-23[-28.73,-17.27]
Weinstein 2013	138	0	-37.9 (1.075)		13.08%	-37.9[-40.01,-35.79]
Total (95% CI)					**100%**	**-37.77[-38.53,-37.01]**
Heterogeneity: Tau²=0; Chi²=93.37, df=13(P<0.0001); I²=86.08%						

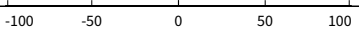


Study or subgroup	rosuvas-tatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Test for overall effect: Z=97.12(P<0.0001)						



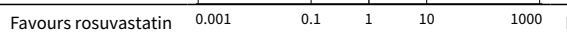
Analysis 3.10. Comparison 3 5.0 mg vs control, Outcome 10 Triglycerides.

Study or subgroup	rosuvas-tatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
AstraZeneca 2010a	135	0	-20.1 (4.72)		2.18%	-20.1[-29.35,-10.85]
ASTRO-2 2009	435	0	-14.4 (1.738)		16.1%	-14.4[-17.81,-10.99]
Brown 2002	121	0	-17.6 (2.5)		7.78%	-17.6[-22.5,-12.7]
CAP-Chol 2009	103	0	-8.7 (3.646)		3.66%	-8.7[-15.85,-1.55]
JART 2012	151	0	-11.2 (3.198)		4.76%	-11.2[-17.47,-4.93]
Jing 2013	114	0	-9.3 (2.95)		5.59%	-9.3[-15.08,-3.52]
Mori 2013	37	0	-31.2 (5.179)		1.81%	-31.2[-41.35,-21.05]
Olsson 2002	135	0	-15 (2.5)		7.78%	-15[-19.9,-10.1]
Paoletti 2009	119	0	-12 (2.9)		5.78%	-12[-17.68,-6.32]
Rosenson 2011	66	0	-23.6 (3.2)		4.75%	-23.6[-29.87,-17.33]
Schneck 2003	38	0	-23.1 (4.6)		2.3%	-23.1[-32.12,-14.08]
Schwartz 2004	127	0	-17.4 (2.2)		10.05%	-17.4[-21.71,-13.09]
Siddiqi 2013	67	0	-21.4 (1.368)		25.98%	-21.4[-24.08,-18.72]
Wang 2012	30	0	-5.3 (5.751)		1.47%	-5.35[-16.62,5.92]
Total (95% CI)					**100%**	**-16.96[-18.33,-15.6]**
Heterogeneity: Tau^2=0; Chi^2=49.63, df=13(P<0.0001); I^2=73.81%						
Test for overall effect: Z=24.32(P<0.0001)						



Analysis 3.11. Comparison 3 5.0 mg vs control, Outcome 11 WDAE.

Study or subgroup	rosuvastatin n/N	placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Davidson 2002	6/128	7/132		50.97%	0.88[0.31,2.56]
Durrington 2004	2/60	3/53		23.56%	0.59[0.1,3.39]
Saito 2003	0/15	0/15			Not estimable
Saito 2007	3/32	0/35		3.54%	7.64[0.41,142.34]
Shepherd 2004	7/45	3/46		21.94%	2.39[0.66,8.65]
Total (95% CI)	**280**	**281**		**100%**	**1.38[0.7,2.72]**
Total events: 18 (rosuvastatin), 13 (placebo)					
Heterogeneity: Tau^2=0; Chi^2=3.59, df=3(P=0.31); I^2=16.49%					
Test for overall effect: Z=0.94(P=0.35)					



Comparison 4. 10 mg vs control

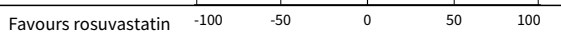
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total cholesterol	15	1442	Mean Difference (IV, Fixed, 95% CI)	-31.34 [-32.45, -30.23]
2 LDL-cholesterol	15	1442	Mean Difference (IV, Fixed, 95% CI)	-42.80 [-44.26, -41.35]
3 HDL-cholesterol	15	1442	Mean Difference (IV, Fixed, 95% CI)	10.46 [9.40, 11.52]
4 non-HDL-cholesterol	14	1418	Mean Difference (IV, Fixed, 95% CI)	-39.28 [-40.82, -37.74]
5 Triglycerides	13	1313	Mean Difference (IV, Fixed, 95% CI)	-19.97 [-22.81, -17.12]
6 Total cholesterol	55	8100	% change from baseline (Fixed, 95% CI)	-32.89 [-33.14, -32.64]
7 LDL-cholesterol	59	8413	% change from baseline (Fixed, 95% CI)	-45.77 [-46.09, -45.46]
8 HDL-cholesterol	55	8085	% change from baseline (Fixed, 95% CI)	6.25 [5.93, 6.58]
9 non-HDL-cholesterol	53	7405	% change from baseline (Fixed, 95% CI)	-42.06 [-42.39, -41.72]
10 Triglycerides	51	7524	% change from baseline (Fixed, 95% CI)	-19.72 [-20.38, -19.07]
11 WDAE	6	724	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.29, 1.39]

Analysis 4.1. Comparison 4 10 mg vs control, Outcome 1 Total cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Andreou 2010	21	-26 (12)	18	2.3 (12)		2.16%	-28.3[-35.85,-20.75]
AstraZeneca 2010b	111	-22.9 (12)	111	0.7 (12)		12.36%	-23.6[-26.76,-20.44]
COMETS 2005	164	-31.9 (10.2)	78	-0.7 (9.7)		17.43%	-31.2[-33.86,-28.54]
Davidson 2002	129	-30 (11.4)	132	0 (10.3)		17.71%	-30[-32.64,-27.36]
Durrington 2004	53	-36.6 (9.5)	49	1.1 (7.1)		11.74%	-37.7[-40.94,-34.46]
Gomez-Garcia 2007	16	-41.5 (12.2)	16	0 (11.7)		1.8%	-41.5[-49.78,-33.22]
Hunninghake 2004	23	-38 (11)	26	2.5 (11.2)		3.18%	-40.5[-46.72,-34.28]
Koh 2013	52	-30.9 (12)	53	-5.6 (12)		5.85%	-25.3[-29.89,-20.71]
Lu 2004	23	-30.2 (12)	23	3.3 (12)		2.56%	-33.5[-40.44,-26.56]
Olsson 2001	16	-35 (8)	29	-2.2 (7)		5.64%	-32.8[-37.48,-28.12]
PLUTO 2010	44	-34 (12)	46	0 (12)		5.01%	-34[-38.96,-29.04]
Raza 2000	12	-36.7 (12)	12	-5.3 (12)		1.34%	-31.4[-41,-21.8]
Saito 2003	14	-35 (9.4)	12	-2 (9.4)		2.36%	-33[-40.23,-25.77]
Saito 2007	34	-31.4 (13.1)	35	1.3 (8.2)		4.6%	-32.7[-37.87,-27.53]
Shepherd 2004	44	-31.3 (10.6)	46	0.8 (10.9)		6.27%	-32.1[-36.53,-27.67]
Total * **	**756**		**686**			**100%**	**-31.34[-32.45,-30.23]**

Heterogeneity: Tau^2=0; Chi^2=62.7, df=14(P<0.0001); I^2=77.67%

Test for overall effect: Z=55.35(P<0.0001)



Analysis 4.2. Comparison 4 10 mg vs control, Outcome 2 LDL-cholesterol.

Study or subgroup	rosuvastatin		placebo		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Andreou 2010	21	-34.7 (15)	18	1.3 (15)		2.38%	-36[-45.44,-26.56]
AstraZeneca 2010b	111	-32.7 (15)	111	2.1 (15)		13.61%	-34.75[-38.7,-30.8]
COMETS 2005	164	-42.7 (14.1)	78	-0.3 (13.2)		16.01%	-42.4[-46.04,-38.76]
Davidson 2002	129	-43 (14.8)	132	0 (13.8)		17.57%	-43[-46.47,-39.53]
Durrington 2004	53	-45.8 (14.6)	49	-0.6 (11.4)		8.27%	-45.2[-50.26,-40.14]
Gomez-Garcia 2007	16	-58.7 (11.7)	16	-5.1 (5.1)		5.42%	-53.65[-59.9,-47.4]
Hunninghake 2004	23	-40 (20.1)	26	6.2 (21.4)		1.57%	-46.2[-57.82,-34.58]
Koh 2013	52	-44.6 (15)	53	-7.8 (15)		6.44%	-36.8[-42.54,-31.06]
Lu 2004	23	-43.4 (15)	23	2.3 (15)		2.82%	-45.7[-54.37,-37.03]
Olsson 2001	16	-50.5 (9.6)	29	-3.6 (9.2)		6.36%	-46.9[-52.67,-41.13]
PLUTO 2010	44	-45 (15)	46	-1 (15)		5.52%	-44[-50.2,-37.8]
Raza 2000	12	-52 (15)	12	-8 (15)		1.47%	-44[-56,-32]
Saito 2003	14	-49.7 (10.5)	12	-3.2 (11.1)		3.04%	-46.5[-54.85,-38.15]
Saito 2007	34	-38.1 (18.6)	35	3.6 (15.5)		3.24%	-41.7[-49.79,-33.61]
Shepherd 2004	44	-49.3 (13.9)	46	-1.2 (14.2)		6.29%	-48.1[-53.91,-42.29]
Total ***	**756**		**686**			**100%**	**-42.8[-44.26,-41.35]**

Heterogeneity: Tau^2=0; Chi^2=41.57, df=14(P=0); I^2=66.32%

Test for overall effect: Z=57.62(P<0.0001)

Analysis 4.3. Comparison 4 10 mg vs control, Outcome 3 HDL-cholesterol.

Study or subgroup	rosuvastatin		placebo		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Andreou 2010	21	-2.1 (16)	18	0 (16)		1.1%	-2.1[-12.17,7.97]
AstraZeneca 2010b	111	10.4 (16)	111	6 (16)		6.3%	4.4[0.19,8.61]
COMETS 2005	164	9.5 (12.8)	78	1.1 (12.4)		9.79%	8.4[5.02,11.78]
Davidson 2002	129	12 (11.4)	132	4 (11.5)		14.47%	8[5.22,10.78]
Durrington 2004	53	10.1 (12.4)	49	1.2 (9.3)		6.23%	8.9[4.67,13.13]
Gomez-Garcia 2007	16	7.3 (1.7)	16	-7.1 (2.9)		40.74%	14.45[12.79,16.11]
Hunninghake 2004	23	6.1 (12.5)	26	-2 (12.2)		2.32%	8.1[1.17,15.03]
Koh 2013	52	0 (16)	53	-5.6 (16)		2.98%	5.6[-0.52,11.72]
Lu 2004	23	14 (16)	23	2.4 (16)		1.31%	11.6[2.35,20.85]
Olsson 2001	16	14.4 (13.2)	29	3.6 (11.8)		1.85%	10.8[3.04,18.56]
PLUTO 2010	44	10 (16)	46	7 (16)		2.55%	3[-3.61,9.61]
Raza 2000	12	13.7 (16)	12	2.8 (16)		0.68%	10.9[-1.9,23.7]
Saito 2003	14	12.8 (10.5)	12	1.2 (10.4)		1.72%	11.6[3.55,19.65]
Saito 2007	34	12.4 (16.3)	35	1.8 (10.7)		2.62%	10.6[4.07,17.13]
Shepherd 2004	44	7.9 (11.3)	46	-0.5 (10.9)		5.32%	8.4[3.82,12.98]
Total ***	**756**		**686**			**100%**	**10.46[9.4,11.52]**

Heterogeneity: Tau^2=0; Chi^2=49.89, df=14(P<0.0001); I^2=71.94%

Test for overall effect: Z=19.4(P<0.0001)

Analysis 4.4. Comparison 4 10 mg vs control, Outcome 4 non-HDL-cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Andreou 2010	21	-32.4 (16)	18	2.8 (16)		2.34%	-35.2[-45.27,-25.13]
AstraZeneca 2010b	111	-29.4 (16)	111	-0.6 (16)		13.39%	-28.8[-33.01,-24.59]
COMETS 2005	164	-40.6 (12.8)	78	-0.9 (12.4)		20.79%	-39.7[-43.08,-36.32]
Davidson 2002	129	-39.3 (16)	132	-0.9 (16)		15.74%	-38.4[-42.28,-34.52]
Durrington 2004	53	-45.3 (16)	49	1.1 (16)		6.14%	-46.4[-52.61,-40.19]
Gomez-Garcia 2007	16	-53.6 (16)	16	1.3 (16)		1.93%	-54.9[-65.99,-43.81]
Hunninghake 2004	23	-45 (12.5)	26	3.3 (12.8)		4.75%	-48.3[-55.37,-41.23]
Koh 2013	52	-39.4 (16)	53	-5.6 (16)		6.33%	-33.8[-39.92,-27.68]
Lu 2004	23	-39.2 (16)	23	-4.6 (16)		2.77%	-34.6[-43.85,-25.35]
Olsson 2001	16	-46.5 (16)	29	-3.6 (16)		2.49%	-42.9[-52.67,-33.13]
PLUTO 2010	44	-42.8 (11.5)	46	-0.8 (11.9)		10.16%	-42[-46.83,-37.17]
Saito 2003	14	-45.8 (16)	12	-2.8 (16)		1.56%	-42.95[-55.29,-30.61]
Saito 2007	34	-41 (16)	35	1.4 (9.3)		6.18%	-42.4[-48.6,-36.2]
Shepherd 2004	44	-42.6 (16)	46	1.2 (16)		5.43%	-43.8[-50.41,-37.19]
Total ***	**744**		**674**			**100%**	**-39.28[-40.82,-37.74]**

Heterogeneity: $Tau^2=0$; $Chi^2=52.53$, df=13(P<0.0001); $I^2=75.25\%$

Test for overall effect: Z=49.98(P<0.0001)

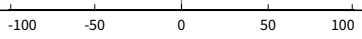
Favours rosuvastatin — Favours placebo

Analysis 4.5. Comparison 4 10 mg vs control, Outcome 5 Triglycerides.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
AstraZeneca 2010b	111	-21.3 (31.5)	111	-7.2 (31.5)		11.77%	-14.1[-22.39,-5.81]
COMETS 2005	164	-19.1 (28.2)	78	-2.8 (27.4)		14.54%	-16.3[-23.76,-8.84]
Davidson 2002	129	-19 (27.3)	132	-1 (26.4)		19.03%	-18[-24.52,-11.48]
Durrington 2004	53	-29.5 (26.9)	49	4.7 (20.7)		9.4%	-34.2[-43.48,-24.92]
Gomez-Garcia 2007	16	-7.5 (18.3)	16	3.9 (4.3)		9.52%	-11.4[-20.61,-2.19]
Hunninghake 2004	23	-37 (22.5)	26	2.9 (22.4)		5.09%	-39.9[-52.5,-27.3]
Koh 2013	52	-10.3 (31.5)	53	5.1 (31.5)		5.57%	-15.4[-27.45,-3.35]
Lu 2004	23	-19.4 (31.5)	23	11.2 (31.5)		2.44%	-30.6[-48.81,-12.39]
Olsson 2001	16	-9.8 (29.2)	29	-1.3 (26.4)		2.72%	-8.5[-25.73,8.73]
Raza 2000	12	-12 (31.5)	12	-1.7 (31.5)		1.27%	-10.3[-35.5,14.9]
Saito 2003	14	-20.1 (26.9)	12	2.3 (27)		1.87%	-22.4[-43.18,-1.62]
Saito 2007	34	-29 (23)	35	1 (30)		5.1%	-30[-42.59,-17.41]
Shepherd 2004	44	-8.9 (24.5)	46	10.5 (14.2)		11.67%	-19.4[-27.72,-11.08]
Total ***	**691**		**622**			**100%**	**-19.97[-22.81,-17.12]**

Heterogeneity: $Tau^2=0$; $Chi^2=31.83$, df=12(P=0); $I^2=62.29\%$

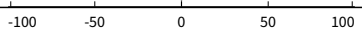
Test for overall effect: Z=13.76(P<0.0001)



Favours rosuvastatin — Favours placebo

Analysis 4.6. Comparison 4 10 mg vs control, Outcome 6 Total cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
ANDROMEDA 2007	240	0	-35.1 (1.064)		1.43%	-35.1[-37.19,-33.01]
ARIES 2006	186	0	-26.6 (1)		1.62%	-26.6[-28.56,-24.64]
AstraZeneca 2010a	139	0	-33.1 (1.91)		0.44%	-33.1[-36.84,-29.36]
ATOROS 2006	60	0	-32.4 (1.549)		0.67%	-32.4[-35.44,-29.36]
Ballantyne 2003	576	0	-34.2 (0.5)		6.48%	-34.2[-35.18,-33.22]
Briseno 2010	98	0	-34.9 (1.212)		1.1%	-34.9[-37.28,-32.52]
Brown 2002	115	0	-33.4 (1)		1.62%	-33.4[-35.36,-31.44]
Catapano 2006	475	0	-32.3 (0.4)		10.12%	-32.3[-33.08,-31.52]
Celik 2012	18	0	-31.4 (2.828)		0.2%	-31.4[-36.94,-25.86]
Chiang 2008	375	0	-31.6 (1.2)		1.12%	-31.6[-33.95,-29.25]
Coban 2008	30	0	-23.1 (2.191)		0.34%	-23.1[-27.39,-18.81]
Coen 2009	31	0	-30.1 (2.155)		0.35%	-30.1[-34.32,-25.88]
CORALL 2005	131	0	-33.2 (1.048)		1.47%	-33.2[-35.25,-31.15]
DISCOVERY-Asia 2007	516	0	-34.2 (0.66)		3.72%	-34.2[-35.49,-32.91]
Dzhaiani 2008	26	0	-26.2 (2.353)		0.29%	-26.2[-30.81,-21.59]
ECLIPSE 2008	498	0	-33.4 (0.538)		5.6%	-33.4[-34.45,-32.35]
EFFORT 2011	85	0	-32.4 (1.269)		1.01%	-32.4[-34.89,-29.91]
Florentin 2013	20	0	-33.9 (2.683)		0.22%	-33.9[-39.16,-28.64]
Gao 2007	191	0	-33.2 (0.868)		2.15%	-33.2[-34.9,-31.5]
Guo 2012	30	0	-19.8 (2.191)		0.34%	-19.8[-24.09,-15.51]
Han 2008	33	0	-12.7 (2.089)		0.37%	-12.7[-16.79,-8.61]
Her 2010	25	0	-35 (2.2)		0.33%	-35[-39.31,-30.69]
IRIS 2007	183	0	-31 (1)		1.62%	-31[-32.96,-29.04]
Jing 2013	115	0	-31.2 (1.119)		1.29%	-31.2[-33.39,-29.01]
Jones 2009	252	0	-32.5 (0.82)		2.41%	-32.5[-34.11,-30.89]
Kostapanos 2006	40	0	-30.7 (1.897)		0.45%	-30.7[-34.42,-26.98]
Kostapanos 2007a	75	0	-32.9 (1.386)		0.84%	-32.9[-35.62,-30.18]
Kostapanos 2007b	45	0	-32.7 (1.789)		0.51%	-32.7[-36.21,-29.19]
Kostapanos 2008a	40	0	-31.6 (1.897)		0.45%	-31.6[-35.32,-27.88]
Kostapanos 2009	50	0	-33.2 (1.697)		0.56%	-33.2[-36.53,-29.87]
Liberopoulos 2013	40	0	-32.5 (1.897)		0.45%	-32.5[-36.22,-28.78]
Lui 2007	137	0	-35.8 (0.752)		2.87%	-35.8[-37.27,-34.33]
Mabuchi 2004	37	0	-39.4 (1.233)		1.07%	-39.4[-41.82,-36.98]
Marino 2012	20	0	-33.6 (2.683)		0.22%	-33.65[-38.91,-28.39]
MERCURY I 2004	552	0	-32.5 (0.511)		6.21%	-32.5[-33.5,-31.5]
Milionis 2005	55	0	-36.9 (1.618)		0.62%	-36.9[-40.07,-33.73]
Moutzouri 2011	45	0	-32.5 (1.789)		0.51%	-32.5[-36.01,-28.99]
Olsson 2002	132	0	-35 (1)		1.62%	-35[-36.96,-33.04]
Paoletti 2009	111	0	-34 (1)		1.62%	-34[-35.96,-32.04]
Park 2010	170	0	-36.1 (0.698)		3.33%	-36.1[-37.47,-34.73]
Pirro 2007	35	0	-24.8 (2.028)		0.39%	-24.8[-28.78,-20.82]
Polenova 2009	17	0	-30.4 (2.91)		0.19%	-30.4[-36.1,-24.7]
Postadzhiyan 2008	16	0	-20.7 (3)		0.18%	-20.7[-26.58,-14.82]
PULSAR 2006	493	0	-30.8 (0.5)		6.48%	-30.8[-31.78,-29.82]
RADAR 2005	230	0	-37.4 (0.7)		3.31%	-37.4[-38.77,-36.03]
ROMEO 2009	127	0	-34.1 (0.99)		1.65%	-34.1[-36.04,-32.16]
Rosenson 2011	46	0	-36.6 (1.697)		0.56%	-36.6[-39.93,-33.27]
Schneck 2003	45	0	-33.3 (0.8)		2.53%	-33.3[-34.87,-31.73]
Schwartz 2004	128	0	-33.9 (0.8)		2.53%	-33.9[-35.47,-32.33]



Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Semenova 2009	30	0	-31.4 (2.191)		0.34%	-31.4[-35.69,-27.11]
SOLAR 2007	536	0	-32 (0.4)		10.12%	-32[-32.78,-31.22]
STARSHIP 2006	174	0	-32 (1)		1.62%	-32[-33.96,-30.04]
STELLAR 2003	156	0	-32.9 (0.961)		1.75%	-32.9[-34.78,-31.02]
Wang 2012	30	0	-19.9 (2.191)		0.34%	-19.9[-24.19,-15.61]
Wongwiwatthananukit 2006	40	0	-36.8 (2.135)		0.36%	-36.8[-40.98,-32.62]
Total (95% CI)					**100%**	**-32.89[-33.14,-32.64]**
Heterogeneity: Tau²=0; Chi²=452.07, df=54(P<0.0001); I²=88.06%						
Test for overall effect: Z=258.47(P<0.0001)						

Favours rosuvastatin -100 -50 0 50 100

Analysis 4.7. Comparison 4 10 mg vs control, Outcome 7 LDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
ANDROMEDA 2007	240	0	-51.3 (0.738)		4.75%	-51.3[-52.75,-49.85]
ARIES 2006	186	0	-37.1 (1.3)		1.53%	-37.1[-39.65,-34.55]
AstraZeneca 2010a	139	0	-43.9 (1.47)		1.2%	-43.9[-46.78,-41.02]
ATOROS 2006	60	0	-43.9 (1.937)		0.69%	-43.9[-47.7,-40.1]
Ballantyne 2003	576	0	-47.7 (0.546)		8.68%	-47.7[-48.77,-46.63]
Briseno 2010	98	0	-47.8 (1.515)		1.13%	-47.8[-50.77,-44.83]
Brown 2002	115	0	-47.4 (1.3)		1.53%	-47.4[-49.95,-44.85]
Capuzzi 2003	46	0	-40.7 (2.212)		0.53%	-40.7[-45.03,-36.37]
Catapano 2006	475	0	-45.8 (0.5)		10.35%	-45.8[-46.78,-44.82]
Celik 2012	18	0	-38.6 (3.536)		0.21%	-38.6[-45.53,-31.67]
Chiang 2008	375	0	-44.2 (1)		2.59%	-44.2[-46.16,-42.24]
Coban 2008	30	0	-35 (2.739)		0.34%	-35[-40.37,-29.63]
Coen 2009	31	0	-43.1 (2.694)		0.36%	-43.1[-48.38,-37.82]
CORALL 2005	131	0	-45.9 (1.311)		1.51%	-45.9[-48.47,-43.33]
DISCOVERY-Asia 2007	515	0	-47.5 (0.9)		3.19%	-47.5[-49.26,-45.74]
Dulay 2009	41	0	-52.3 (2.343)		0.47%	-52.3[-56.89,-47.71]
Dzhaiani 2008	26	0	-33.4 (2.942)		0.3%	-33.4[-39.17,-27.63]
ECLIPSE 2008	498	0	-46.5 (0.672)		5.72%	-46.5[-47.82,-45.18]
EFFORT 2011	85	0	-44.5 (1.605)		1%	-44.5[-47.65,-41.35]
Florentin 2013	20	0	-45 (3.354)		0.23%	-45[-51.57,-38.43]
Gao 2007	191	0	-45.6 (1.085)		2.2%	-45.6[-47.73,-43.47]
GRAVITY 2009	206	0	-46.5 (0.913)		3.11%	-46.5[-48.29,-44.71]
Guo 2012	30	0	-34.3 (2.739)		0.34%	-34.3[-39.67,-28.93]
Han 2008	33	0	-17.6 (2.611)		0.38%	-17.6[-22.72,-12.48]
Her 2010	25	0	-50 (2.6)		0.38%	-50[-55.1,-44.9]
IRIS 2007	183	0	-45 (1.109)		2.1%	-45[-47.17,-42.83]
Jing 2013	115	0	-43.5 (1.399)		1.32%	-43.5[-46.24,-40.76]
Jones 2009	243	0	-38 (1.18)		1.86%	-38[-40.31,-35.69]
Kostapanos 2006	40	0	-40.7 (2.372)		0.46%	-40.7[-45.35,-36.05]
Kostapanos 2007a	75	0	-45.4 (1.732)		0.86%	-45.4[-48.79,-42.01]

Favours rosuvastatin -100 -50 0 50 100

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Kostapanos 2007b	45	0	-44.9 (2.236)		0.52%	-44.9[-49.28,-40.52]
Kostapanos 2008a	40	0	-42.6 (2.372)		0.46%	-42.6[-47.25,-37.95]
Kostapanos 2009	50	0	-46 (2.121)		0.57%	-46[-50.16,-41.84]
Liberopoulos 2013	40	0	-43 (2.372)		0.46%	-43[-47.65,-38.35]
Lui 2007	132	0	-48.8 (1.097)		2.15%	-48.8[-50.95,-46.65]
Mabuchi 2004	37	0	-49.2 (1.644)		0.96%	-49.2[-52.42,-45.98]
Marino 2012	20	0	-46.3 (3.354)		0.23%	-46.35[-52.92,-39.78]
MERCURY I 2004	552	0	-47 (0.638)		6.35%	-47[-48.25,-45.75]
Milionis 2005	55	0	-47.9 (2.023)		0.63%	-47.9[-51.86,-43.94]
Moutzouri 2011	45	0	-45.6 (2.236)		0.52%	-45.6[-49.98,-41.22]
Olsson 2002	132	0	-50 (1.3)		1.53%	-50[-52.55,-47.45]
Paoletti 2009	111	0	-49 (1.3)		1.53%	-49[-51.55,-46.45]
Park 2010	170	0	-48.4 (1.192)		1.82%	-48.4[-50.74,-46.06]
Pirro 2007	35	0	-37.8 (2.536)		0.4%	-37.8[-42.77,-32.83]
Pirro 2009	32	0	-37 (2.652)		0.37%	-37[-42.2,-31.8]
Polenova 2009	17	0	-40.8 (3.638)		0.2%	-40.8[-47.93,-33.67]
Postadzhiyan 2008	16	0	-30.8 (3.75)		0.18%	-30.8[-38.15,-23.45]
PULSAR 2006	493	0	-44.6 (0.6)		7.19%	-44.6[-45.78,-43.42]
RADAR 2005	230	0	-44 (1.5)		1.15%	-44[-46.94,-41.06]
ROMEO 2009	127	0	-45.5 (1.34)		1.44%	-45.5[-48.13,-42.87]
Rosenson 2011	49	0	-43.3 (2.57)		0.39%	-43.3[-48.34,-38.26]
Schneck 2003	45	0	-46.6 (1.1)		2.14%	-46.6[-48.76,-44.44]
Schwartz 2004	128	0	-47.1 (1.1)		2.14%	-47.1[-49.26,-44.94]
Semenova 2009	30	0	-41.6 (2.739)		0.34%	-41.6[-46.97,-36.23]
SOLAR 2007	536	0	-45 (1)		2.59%	-45[-46.96,-43.04]
STARSHIP 2006	174	0	-45 (1.137)		2%	-45[-47.23,-42.77]
STELLAR 2003	156	0	-45.8 (1.201)		1.79%	-45.8[-48.15,-43.45]
Wang 2012	30	0	-34.2 (2.739)		0.34%	-34.25[-39.62,-28.88]
Wongwiwatthananukit 2006	40	0	-48.2 (3.02)		0.28%	-48.2[-54.12,-42.28]
Total (95% CI)					**100%**	**-45.77[-46.09,-45.46]**

Heterogeneity: Tau²=0; Chi²=476.99, df=58(P<0.0001); I²=87.84%

Test for overall effect: Z=284.58(P<0.0001)

-100 -50 0 50 100

Favours rosuvastatin

Analysis 4.8. Comparison 4 10 mg vs control, Outcome 8 HDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
ANDROMEDA 2007	240	0	2 (0.736)		4.96%	2[0.56,3.44]
ARIES 2006	186	0	7 (0.9)		3.32%	7[5.24,8.76]
AstraZeneca 2010a	137	0	6.8 (2.29)		0.51%	6.82[2.33,11.31]
ATOROS 2006	60	0	3.3 (2.066)		0.63%	3.3[-0.75,7.35]
Ballantyne 2003	576	0	9.3 (0.513)		10.23%	9.3[8.3,10.3]
Briseno 2010	98	0	8.3 (1.616)		1.03%	8.3[5.13,11.47]
Brown 2002	115	0	11.9 (1.2)		1.87%	11.9[9.55,14.25]

-100 -50 0 50 100

Favours rosuvastatin

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Catapano 2006	475	0	6.7 (0.5)		10.75%	6.7[5.72,7.68]
Celik 2012	18	0	-1.1 (3.771)		0.19%	-1.1[-8.49,6.29]
Chiang 2008	375	0	1.5 (1.1)		2.22%	1.5[-0.66,3.66]
Coban 2008	30	0	6.9 (2.921)		0.31%	6.9[1.17,12.63]
Coen 2009	31	0	15.1 (2.874)		0.33%	15.1[9.47,20.73]
CORALL 2005	131	0	0.7 (1.398)		1.37%	0.7[-2.04,3.44]
DISCOVERY-Asia 2007	516	0	0.7 (0.88)		3.47%	0.7[-1.02,2.42]
Dzhaiani 2008	26	0	4.3 (3.138)		0.27%	4.3[-1.85,10.45]
ECLIPSE 2008	498	0	7.7 (0.717)		5.23%	7.7[6.29,9.11]
EFFORT 2011	85	0	11.9 (1.692)		0.94%	11.9[8.58,15.22]
Florentin 2013	20	0	-5.5 (3.578)		0.21%	-5.5[-12.51,1.51]
Gao 2007	191	0	6.6 (1.158)		2%	6.6[4.33,8.87]
Guo 2012	30	0	33.3 (2.921)		0.31%	33.3[27.57,39.03]
Han 2008	33	0	4.8 (2.785)		0.35%	4.8[-0.66,10.26]
Her 2010	25	0	3.6 (3.32)		0.24%	3.6[-2.91,10.11]
IRIS 2007	183	0	6.9 (1.183)		1.92%	6.9[4.58,9.22]
Jing 2013	115	0	-2.2 (1.492)		1.21%	-2.2[-5.12,0.72]
Jones 2009	239	0	8.5 (1.32)		1.54%	8.5[5.91,11.09]
Kostapanos 2006	40	0	4 (2.53)		0.42%	4[-0.96,8.96]
Kostapanos 2007a	75	0	1.8 (1.848)		0.79%	1.8[-1.82,5.42]
Kostapanos 2007b	45	0	3.1 (2.385)		0.47%	3.1[-1.57,7.77]
Kostapanos 2008a	40	0	6.2 (2.53)		0.42%	6.2[1.24,11.16]
Kostapanos 2009	50	0	3.2 (2.263)		0.52%	3.2[-1.23,7.63]
Liberopoulos 2013	40	0	1 (2.53)		0.42%	1[-3.96,5.96]
Lui 2007	137	0	3.2 (1.102)		2.21%	3.2[1.04,5.36]
Mabuchi 2004	37	0	9.6 (2.285)		0.51%	9.6[5.12,14.08]
Marino 2012	20	0	-3.8 (3.578)		0.21%	-3.8[-10.81,3.21]
MERCURY I 2004	552	0	9.2 (0.681)		5.79%	9.2[7.87,10.53]
Milionis 2005	55	0	0 (2.157)		0.58%	0[-4.23,4.23]
Moutzouri 2011	45	0	3.3 (2.385)		0.47%	3.3[-1.37,7.97]
Olsson 2002	132	0	8 (1.3)		1.59%	8[5.45,10.55]
Paoletti 2009	111	0	7 (1.3)		1.59%	7[4.45,9.55]
Park 2010	170	0	-1.3 (1.105)		2.2%	-1.3[-3.47,0.87]
Pirro 2007	35	0	1.9 (2.705)		0.37%	1.9[-3.4,7.2]
Polenova 2009	17	0	13.7 (3.881)		0.18%	13.7[6.09,21.31]
Postadzhiyan 2008	16	0	6.1 (4)		0.17%	6.1[-1.74,13.94]
PULSAR 2006	493	0	6.4 (0.5)		10.75%	6.4[5.42,7.38]
RADAR 2005	230	0	3.9 (1)		2.69%	3.9[1.94,5.86]
ROMEO 2009	127	0	9.9 (1.455)		1.27%	9.9[7.05,12.75]
Rosenson 2011	46	0	5.7 (3.2)		0.26%	5.7[-0.57,11.97]
Schneck 2003	45	0	6 (1.7)		0.93%	6[2.67,9.33]
Schwartz 2004	128	0	7.7 (1)		2.69%	7.7[5.74,9.66]
Semenova 2009	30	0	6.1 (2.921)		0.31%	6.1[0.37,11.83]
SOLAR 2007	536	0	7 (1)		2.69%	7[5.04,8.96]
STARSHIP 2006	174	0	5.5 (1.213)		1.83%	5.5[3.12,7.88]
STELLAR 2003	156	0	7.7 (1.281)		1.64%	7.7[5.19,10.21]
Wang 2012	30	0	24.7 (2.921)		0.31%	24.7[18.97,30.43]
Wongwiwatthananukit 2006	40	0	8.6 (2.909)		0.32%	8.6[2.9,14.3]
Total (95% CI)					**100%**	**6.25[5.93,6.58]**

-100 -50 0 50 100 Favours rosuvastatin

Study or subgroup	rosuvas-tatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Heterogeneity: Tau²=0; Chi²=504.93, df=54(P<0.0001); I²=89.31%						
Test for overall effect: Z=38.16(P<0.0001)						

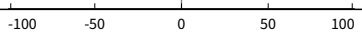
-100 -50 0 50 100 Favours rosuvastatin

Analysis 4.9. Comparison 4 10 mg vs control, Outcome 9 non-HDL-cholesterol.

Study or subgroup	rosuvas-tatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
ANDROMEDA 2007	240	0	-45.4 (0.981)		3.02%	-45.4[-47.32,-43.48]
ARIES 2006	186	0	-34.3 (1.2)		2.02%	-34.3[-36.65,-31.95]
AstraZeneca 2010a	137	0	-46.1 (3.57)		0.23%	-46.08[-53.08,-39.08]
ATOROS 2006	60	0	-39.6 (2.066)		0.68%	-39.6[-43.65,-35.55]
Ballantyne 2003	576	0	-44.3 (0.529)		10.39%	-44.3[-45.34,-43.26]
Briseno 2010	98	0	-44.4 (1.616)		1.11%	-44.4[-47.57,-41.23]
Brown 2002	115	0	-43.5 (1.2)		2.02%	-43.5[-45.85,-41.15]
Catapano 2006	475	0	-41.6 (0.5)		11.64%	-41.6[-42.58,-40.62]
Celik 2012	18	0	-38.4 (3.771)		0.2%	-38.4[-45.79,-31.01]
Chiang 2008	375	0	-43.1 (0.842)		4.11%	-43.1[-44.75,-41.45]
Coban 2008	30	0	-30 (2.921)		0.34%	-30[-35.73,-24.27]
Coen 2009	31	0	-39.4 (2.874)		0.35%	-39.4[-45.03,-33.77]
CORALL 2005	131	0	-42.3 (1.398)		1.49%	-42.3[-45.04,-39.56]
DISCOVERY-Asia 2007	516	0	-42.6 (0.718)		5.65%	-42.6[-44.01,-41.19]
Dzhaiani 2008	26	0	-35.8 (3.138)		0.3%	-35.8[-41.95,-29.65]
ECLIPSE 2008	498	0	-42.7 (0.717)		5.66%	-42.7[-44.11,-41.29]
EFFORT 2011	85	0	-41.1 (1.768)		0.93%	-41.1[-44.57,-37.63]
Florentin 2013	20	0	-42.4 (3.578)		0.23%	-42.4[-49.41,-35.39]
Gao 2007	191	0	-43.9 (1.158)		2.17%	-43.9[-46.17,-41.63]
Guo 2012	30	0	-27.2 (2.921)		0.34%	-27.2[-32.93,-21.47]
Han 2008	33	0	-17.8 (2.785)		0.38%	-17.8[-23.26,-12.34]
Her 2010	25	0	-45.1 (3.26)		0.27%	-45.1[-51.49,-38.71]
IRIS 2007	183	0	-39.7 (1.183)		2.08%	-39.7[-42.02,-37.38]
Jing 2013	115	0	-38.6 (1.492)		1.31%	-38.6[-41.52,-35.68]
Jones 2009	238	0	-39.8 (1.02)		2.8%	-39.8[-41.8,-37.8]
Kostapanos 2006	40	0	-39.5 (2.53)		0.45%	-39.5[-44.46,-34.54]
Kostapanos 2007a	75	0	-41.1 (1.848)		0.85%	-41.1[-44.72,-37.48]
Kostapanos 2007b	45	0	-42 (2.385)		0.51%	-42[-46.67,-37.33]
Kostapanos 2008a	40	0	-41.3 (2.53)		0.45%	-41.3[-46.26,-36.34]
Kostapanos 2009	50	0	-42.7 (2.263)		0.57%	-42.7[-47.13,-38.27]
Liberopoulos 2013	40	0	-41.1 (2.53)		0.45%	-41.1[-46.06,-36.14]
Lui 2007	137	0	-45.3 (1.393)		1.5%	-45.3[-48.03,-42.57]
Mabuchi 2004	37	0	-46.7 (1.447)		1.39%	-46.7[-49.54,-43.86]
Marino 2012	20	0	-41.3 (3.578)		0.23%	-41.35[-48.36,-34.34]
Milionis 2005	55	0	-45 (2.157)		0.63%	-45[-49.23,-40.77]
Moutzouri 2011	45	0	-42.7 (2.385)		0.51%	-42.7[-47.37,-38.03]
Olsson 2002	132	0	-46.1 (1.393)		1.5%	-46.1[-48.83,-43.37]
Paoletti 2009	111	0	-44.3 (1.519)		1.26%	-44.3[-47.28,-41.32]

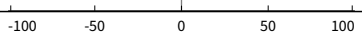
Favours rosuvastatin -100 -50 0 50 100

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Park 2010	170	0	-43 (1.106)		2.38%	-43.05[-45.22,-40.88]
Pirro 2007	35	0	-31.5 (2.755)		0.38%	-31.55[-36.95,-26.15]
Polenova 2009	17	0	-39.4 (3.881)		0.19%	-39.4[-47.01,-31.79]
Postadzhiyan 2008	16	0	-26.3 (4)		0.18%	-26.3[-34.14,-18.46]
PULSAR 2006	493	0	-40.1 (0.6)		8.08%	-40.1[-41.28,-38.92]
RADAR 2005	230	0	-44.3 (0.8)		4.55%	-44.3[-45.87,-42.73]
Rosenson 2011	46	0	-44.6 (2.22)		0.59%	-44.6[-48.95,-40.25]
Schneck 2003	45	0	-42.8 (1)		2.91%	-42.8[-44.76,-40.84]
Schwartz 2004	128	0	-42.6 (1)		2.91%	-42.6[-44.56,-40.64]
Semenova 2009	30	0	-39.5 (2.921)		0.34%	-39.5[-45.23,-33.77]
SOLAR 2007	536	0	-41 (1)		2.91%	-41[-42.96,-39.04]
STARSHIP 2006	174	0	-40.5 (1.213)		1.98%	-40.5[-42.88,-38.12]
STELLAR 2003	156	0	-42.1 (1.281)		1.77%	-42.1[-44.61,-39.59]
Wang 2012	30	0	-27.1 (2.921)		0.34%	-27.15[-32.88,-21.42]
Wongwiwatthananukit 2006	40	0	-48.2 (2.577)		0.44%	-48.16[-53.21,-43.11]
Total (95% CI)					**100%**	**-42.06[-42.39,-41.72]**
Heterogeneity: Tau²=0; Chi²=340.93, df=52(P<0.0001); I²=84.75%						
Test for overall effect: Z=246.55(P<0.0001)						



Analysis 4.10. Comparison 4 10 mg vs control, Outcome 10 Triglycerides.

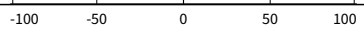
Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
ANDROMEDA 2007	240	0	-21.6 (2.033)		2.7%	-21.6[-25.59,-17.61]
ARIES 2006	186	0	-16 (1.9)		3.09%	-16[-19.72,-12.28]
AstraZeneca 2010a	139	0	-22 (4.69)		0.51%	-22.05[-31.24,-12.86]
ATOROS 2006	60	0	-25.1 (4.067)		0.67%	-25.1[-33.07,-17.13]
Ballantyne 2003	576	0	-20.3 (0.946)		12.47%	-20.3[-22.15,-18.45]
Briseno 2010	98	0	-26.1 (3.182)		1.1%	-26.1[-32.34,-19.86]
Brown 2002	115	0	-21.5 (2.5)		1.78%	-21.5[-26.4,-16.6]
Celik 2012	18	0	-29.8 (7.425)		0.2%	-29.8[-44.35,-15.25]
Chiang 2008	375	0	-16.5 (1.9)		3.09%	-16.5[-20.22,-12.78]
Coban 2008	30	0	-19.7 (5.751)		0.34%	-19.7[-30.97,-8.43]
Coen 2009	31	0	-17.2 (5.658)		0.35%	-17.2[-28.29,-6.11]
CORALL 2005	131	0	-18.8 (2.752)		1.47%	-18.8[-24.19,-13.41]
DISCOVERY-Asia 2007	516	0	-13.5 (1.6)		4.36%	-13.5[-16.64,-10.36]
Dzhaiani 2008	26	0	-28.9 (6.178)		0.29%	-28.9[-41.01,-16.79]
ECLIPSE 2008	498	0	-20.5 (1.412)		5.6%	-20.5[-23.27,-17.73]
EFFORT 2011	85	0	-21.5 (3.362)		0.99%	-21.5[-28.09,-14.91]
Gao 2007	191	0	-22.8 (2.279)		2.15%	-22.8[-27.27,-18.33]
Guo 2012	30	0	-23.8 (5.751)		0.34%	-23.8[-35.07,-12.53]
Han 2008	33	0	-9.5 (5.483)		0.37%	-9.5[-20.25,1.25]
Her 2010	25	0	-6 (7.6)		0.19%	-6[-20.9,8.9]
IRIS 2007	183	0	-19 (2)		2.79%	-19[-22.92,-15.08]



Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Jing 2013	115	0	-11.4 (2.937)		1.29%	-11.4[-17.16,-5.64]
Jones 2009	252	0	-24.4 (1.81)		3.41%	-24.4[-27.95,-20.85]
Kostapanos 2006	40	0	-14.9 (4.981)		0.45%	-14.9[-24.66,-5.14]
Kostapanos 2007a	75	0	-15.3 (3.637)		0.84%	-15.3[-22.43,-8.17]
Kostapanos 2007b	45	0	-10.9 (4.696)		0.51%	-10.9[-20.1,-1.7]
Kostapanos 2008a	40	0	-17.6 (4.981)		0.45%	-17.6[-27.36,-7.84]
Kostapanos 2009	50	0	-20.7 (4.455)		0.56%	-20.7[-29.43,-11.97]
Lui 2007	137	0	-19.6 (2.956)		1.28%	-19.6[-25.39,-13.81]
Mabuchi 2004	37	0	-18.2 (6.116)		0.3%	-18.2[-30.19,-6.21]
Marino 2012	20	0	-27.2 (7.044)		0.22%	-27.25[-41.06,-13.44]
MERCURY I 2004	552	0	-18.9 (1.341)		6.21%	-18.9[-21.53,-16.27]
Milionis 2005	55	0	-23.6 (4.248)		0.62%	-23.6[-31.92,-15.28]
Olsson 2002	132	0	-19 (2.5)		1.78%	-19[-23.9,-14.1]
Paoletti 2009	111	0	-18 (3)		1.24%	-18[-23.88,-12.12]
Park 2010	170	0	-17.6 (2.907)		1.32%	-17.6[-23.3,-11.9]
Pirro 2007	35	0	0.7 (5.325)		0.39%	0.7[-9.74,11.14]
Polenova 2009	17	0	-23.5 (7.64)		0.19%	-23.5[-38.47,-8.53]
Postadzhiyan 2008	16	0	-26.1 (7.875)		0.18%	-26.1[-41.53,-10.67]
PULSAR 2006	493	0	-17.9 (1.2)		7.75%	-17.9[-20.25,-15.55]
RADAR 2005	230	0	-29.2 (1.8)		3.44%	-29.2[-32.73,-25.67]
ROMEO 2009	127	0	-17.2 (3.008)		1.23%	-17.2[-23.1,-11.3]
Rosenson 2011	50	0	-28.6 (3.68)		0.82%	-28.6[-35.81,-21.39]
Schneck 2003	45	0	-22.1 (4.3)		0.6%	-22.1[-30.53,-13.67]
Schwartz 2004	128	0	-19.8 (2.2)		2.3%	-19.8[-24.11,-15.49]
Semenova 2009	30	0	-38.8 (5.751)		0.34%	-38.8[-50.07,-27.53]
SOLAR 2007	536	0	-20 (1)		11.16%	-20[-21.96,-18.04]
STARSHIP 2006	174	0	-20 (2)		2.79%	-20[-23.92,-16.08]
STELLAR 2003	156	0	-19.8 (2.522)		1.75%	-19.8[-24.74,-14.86]
Wang 2012	30	0	-9.2 (5.751)		0.34%	-9.2[-20.47,2.07]
Wongwiwatthananukit 2006	40	0	-20.9 (2.851)		1.37%	-20.95[-26.54,-15.36]
Total (95% CI)					**100%**	**-19.72[-20.38,-19.07]**

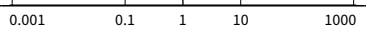
Heterogeneity: Tau²=0; Chi²=135.07, df=50(P<0.0001); I²=62.98%

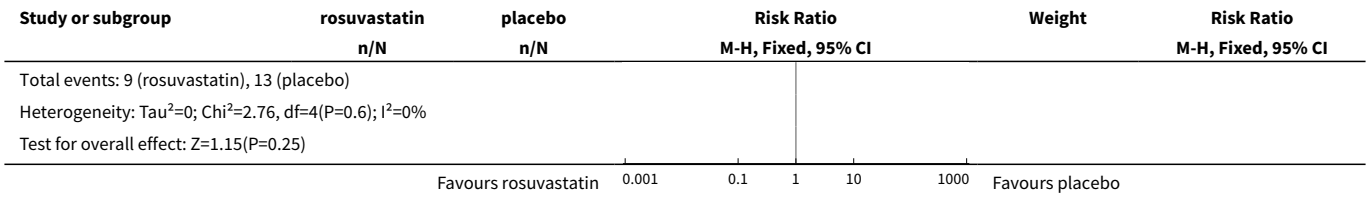
Test for overall effect: Z=59.05(P<0.0001)



Analysis 4.11. Comparison 4 10 mg vs control, Outcome 11 WDAE.

Study or subgroup	rosuvastatin n/N	placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
COMETS 2005	2/163	3/79		27.15%	0.32[0.06,1.89]
Davidson 2002	4/129	7/132		46.48%	0.58[0.18,1.95]
Gomez-Garcia 2007	0/16	0/16			Not estimable
Saito 2003	1/15	0/15		3.36%	3[0.13,68.26]
Saito 2007	1/34	0/35		3.31%	3.09[0.13,73.21]
Shepherd 2004	1/44	3/46		19.7%	0.35[0.04,3.23]
Total (95% CI)	**401**	**323**		**100%**	**0.63[0.29,1.39]**

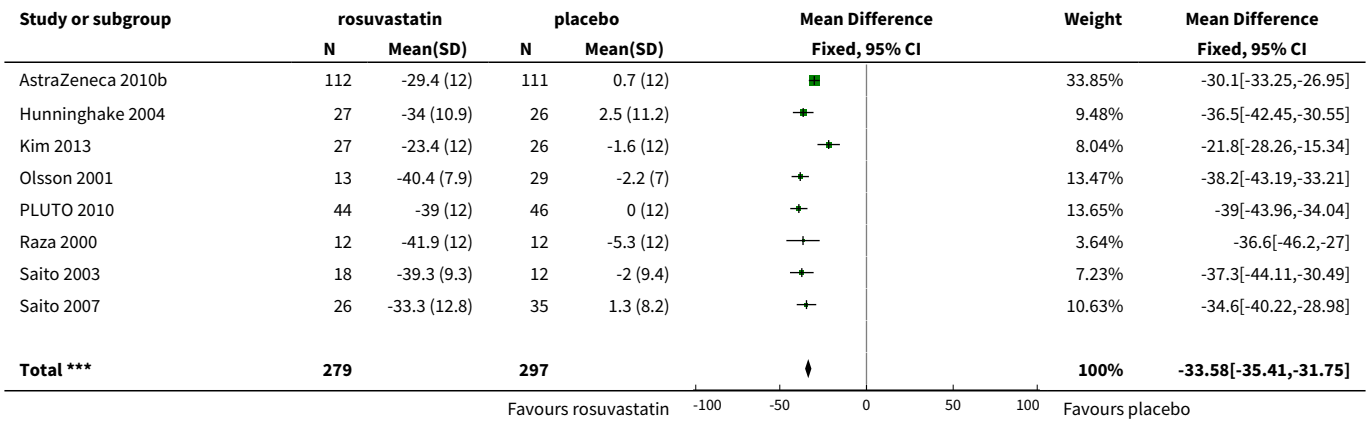




Comparison 5. 20 mg vs control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total cholesterol	8	576	Mean Difference (IV, Fixed, 95% CI)	-33.58 [-35.41, -31.75]
2 LDL-cholesterol	8	576	Mean Difference (IV, Fixed, 95% CI)	-45.83 [-48.22, -43.44]
3 HDL-cholesterol	8	576	Mean Difference (IV, Fixed, 95% CI)	6.82 [4.42, 9.21]
4 non-HDL-cholesterol	7	552	Mean Difference (IV, Fixed, 95% CI)	-40.67 [-43.16, -38.19]
5 Triglycerides	7	486	Mean Difference (IV, Fixed, 95% CI)	-22.61 [-27.94, -17.28]
6 Total cholesterol	19	2915	% change from baseline (Fixed, 95% CI)	-36.30 [-36.70, -35.90]
7 LDL-cholesterol	20	3099	% change from baseline (Fixed, 95% CI)	-50.07 [-50.55, -49.58]
8 HDL-cholesterol	19	2896	% change from baseline (Fixed, 95% CI)	8.03 [7.51, 8.55]
9 non-HDL-cholesterol	18	2461	% change from baseline (Fixed, 95% CI)	-45.77 [-46.31, -45.24]
10 Triglycerides	16	2367	% change from baseline (Fixed, 95% CI)	-21.65 [-22.80, -20.50]
11 WDAE	5	248	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.25, 4.48]

Analysis 5.1. Comparison 5 20 mg vs control, Outcome 1 Total cholesterol.



Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Heterogeneity: Tau²=0; Chi²=27.9, df=7(P=0); I²=74.91%							
Test for overall effect: Z=35.91(P<0.0001)							

Favours rosuvastatin -100 -50 0 50 100 Favours placebo

Analysis 5.2. Comparison 5 20 mg vs control, Outcome 2 LDL-cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
AstraZeneca 2010b	112	-40.8 (15)	111	2.1 (15)		36.8%	-42.85[-46.79,-38.91]
Hunninghake 2004	27	-34 (20.3)	26	6.2 (21.4)		4.52%	-40.2[-51.44,-28.96]
Kim 2013	27	-31 (15)	26	1.5 (15)		8.74%	-32.5[-40.58,-24.42]
Olsson 2001	13	-57 (9.7)	29	-3.6 (9.2)		14.62%	-53.4[-59.65,-47.15]
PLUTO 2010	44	-50 (15)	46	-1 (15)		14.84%	-49[-55.2,-42.8]
Raza 2000	12	-59 (15)	12	-8 (15)		3.96%	-51[-63,-39]
Saito 2003	18	-58.2 (10.6)	12	-3.2 (11.1)		9%	-55[-62.96,-47.04]
Saito 2007	26	-41 (18.3)	35	3.6 (15.5)		7.52%	-44.6[-53.31,-35.89]
Total ***	**279**		**297**			**100%**	**-45.83[-48.22,-43.44]**
Heterogeneity: Tau²=0; Chi²=26.15, df=7(P=0); I²=73.24%							
Test for overall effect: Z=37.61(P<0.0001)							

Favours rosuvastatin -100 -50 0 50 100 Favours placebo

Analysis 5.3. Comparison 5 20 mg vs control, Outcome 3 HDL-cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
AstraZeneca 2010b	112	7.3 (16)	111	6 (16)		32.51%	1.3[-2.9,5.5]
Hunninghake 2004	27	18 (12.5)	26	-2 (12.2)		12.97%	20[13.35,26.65]
Kim 2013	27	0.8 (16)	26	0.6 (16)		7.72%	0.2[-8.42,8.82]
Olsson 2001	13	10 (13)	29	3.6 (11.8)		8.39%	6.4[-1.87,14.67]
PLUTO 2010	44	9 (16)	46	7 (16)		13.11%	2[-4.61,8.61]
Raza 2000	12	9.2 (16)	12	2.8 (16)		3.5%	6.4[-6.4,19.2]
Saito 2003	18	11.3 (10.2)	12	1.2 (10.4)		10.09%	10.1[2.56,17.64]
Saito 2007	26	16.7 (15.7)	35	1.8 (10.7)		11.71%	14.9[7.9,21.9]
Total ***	**279**		**297**			**100%**	**6.82[4.42,9.21]**
Heterogeneity: Tau²=0; Chi²=31.9, df=7(P<0.0001); I²=78.05%							
Test for overall effect: Z=5.58(P<0.0001)							

Favours rosuvastatin -100 -50 0 50 100 Favours placebo

Analysis 5.4. Comparison 5 20 mg vs control, Outcome 4 non-HDL-cholesterol.

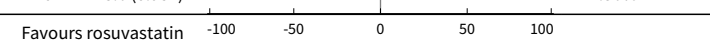
Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
AstraZeneca 2010b	112	-34.3 (16)	111	-0.6 (16)		34.9%	-33.7[-37.9,-29.5]
Hunninghake 2004	27	-42 (12.5)	26	3.3 (12.8)		13.34%	-45.3[-52.09,-38.51]
Kim 2013	27	-30.6 (16)	26	-2.3 (16)		8.29%	-28.35[-36.97,-19.73]
Olsson 2001	13	-52.3 (16)	29	-3.6 (16)		5.62%	-48.7[-59.17,-38.23]
PLUTO 2010	44	-47.7 (13.5)	46	-0.8 (11.9)		22.21%	-46.9[-52.16,-41.64]
Saito 2003	18	-53.4 (16)	12	-2.8 (16)		4.51%	-50.55[-62.24,-38.86]
Saito 2007	26	-44.3 (17.6)	35	1.4 (9.3)		11.14%	-45.7[-53.13,-38.27]
Total ***	**267**		**285**			**100%**	**-40.67[-43.16,-38.19]**
Heterogeneity: Tau^2=0; Chi^2=32.36, df=6(P<0.0001); I^2=81.46%							
Test for overall effect: Z=32.13(P<0.0001)							

Analysis 5.5. Comparison 5 20 mg vs control, Outcome 5 Triglycerides.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
AstraZeneca 2010b	112	-26.5 (31.5)	111	-7.2 (31.5)		41.57%	-19.3[-27.57,-11.03]
Hunninghake 2004	27	-37 (22.3)	26	2.9 (22.4)		19.61%	-39.9[-51.94,-27.86]
Kim 2013	27	-21.4 (31.5)	26	-24.4 (31.5)		9.88%	3[-13.96,19.96]
Olsson 2001	13	-22.9 (28.8)	29	-1.3 (26.4)		8.42%	-21.6[-39.97,-3.23]
Raza 2000	12	-26.2 (31.5)	12	-1.7 (31.5)		4.47%	-24.5[-49.7,0.7]
Saito 2003	18	-16 (27.2)	12	2.3 (27)		7.26%	-18.3[-38.08,1.48]
Saito 2007	26	-31 (39)	35	1 (30)		8.78%	-32[-49.99,-14.01]
Total ***	**235**		**251**			**100%**	**-22.61[-27.94,-17.28]**
Heterogeneity: Tau^2=0; Chi^2=18.56, df=6(P=0); I^2=67.67%							
Test for overall effect: Z=8.31(P<0.0001)							

Analysis 5.6. Comparison 5 20 mg vs control, Outcome 6 Total cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
ARIES 2006	189	0	-33 (1)		4.2%	-33[-34.96,-31.04]
Bellia 2010	14	0	-41.1 (3.207)		0.41%	-41.1[-47.39,-34.81]
Catapano 2006	478	0	-37.3 (0.4)		26.27%	-37.3[-38.08,-36.52]
HeFH 2003	435	0	-37.4 (0.6)		11.68%	-37.4[-38.58,-36.22]
IRIS 2007	171	0	-35 (1)		4.2%	-35[-36.96,-33.04]
Jones 2009	255	0	-37.3 (0.82)		6.25%	-37.3[-38.91,-35.69]
Kostapanos 2007b	45	0	-38.1 (1.789)		1.31%	-38.1[-41.61,-34.59]
Kostapanos 2008b	60	0	-36.4 (1.549)		1.75%	-36.4[-39.44,-33.36]
Kostapanos 2009	50	0	-40.4 (1.697)		1.46%	-40.4[-43.73,-37.07]
LUNAR 2012	246	0	-28.6 (0.982)		4.36%	-28.6[-30.52,-26.68]



Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Marais 2008	41	0	-17.7 (1.952)		1.1%	-17.7[-21.53,-13.87]
MERCURY II 2006	383	0	-37.1 (0.5)		16.81%	-37.1[-38.08,-36.12]
Patel 2011	11	0	-30.2 (3.618)		0.32%	-30.2[-37.29,-23.11]
Postadzhiyan 2008	14	0	-30.1 (3.207)		0.41%	-30.1[-36.39,-23.81]
Rosenson 2011	49	0	-38.7 (1.68)		1.49%	-38.7[-41.99,-35.41]
Schneck 2003	38	0	-37.2 (0.7)		8.58%	-37.2[-38.57,-35.83]
STARSHIP 2006	167	0	-35 (1)		4.2%	-35[-36.96,-33.04]
STELLAR 2003	160	0	-37.6 (0.949)		4.67%	-37.6[-39.46,-35.74]
Szapary 2012	109	0	-30.1 (2.859)		0.51%	-30.1[-35.7,-24.5]
Total (95% CI)					**100%**	**-36.3[-36.7,-35.9]**
Heterogeneity: Tau²=0; Chi²=206.15, df=18(P<0.0001); I²=91.27%						
Test for overall effect: Z=177.06(P<0.0001)						

Favours rosuvastatin -100 -50 0 50 100

Analysis 5.7. Comparison 5 20 mg vs control, Outcome 7 LDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
ARIES 2006	189	0	-45.7 (1.3)		3.65%	-45.7[-48.25,-43.15]
Bellia 2010	14	0	-57.5 (4.009)		0.38%	-57.5[-65.36,-49.64]
Catapano 2006	478	0	-52.3 (0.5)		24.68%	-52.3[-53.28,-51.32]
GRAVITY 2009	199	0	-53.6 (0.744)		11.14%	-53.6[-55.06,-52.14]
HeFH 2003	435	0	-47.1 (0.8)		9.64%	-47.1[-48.67,-45.53]
IRIS 2007	171	0	-50 (1.132)		4.82%	-50[-52.22,-47.78]
Jones 2009	238	0	-45 (1.19)		4.36%	-45[-47.33,-42.67]
Kostapanos 2007b	45	0	-52 (2.236)		1.23%	-52[-56.38,-47.62]
Kostapanos 2008b	60	0	-48.9 (1.937)		1.65%	-48.9[-52.7,-45.1]
Kostapanos 2009	50	0	-51.9 (2.121)		1.37%	-51.9[-56.06,-47.74]
LUNAR 2012	246	0	-42 (1.18)		4.43%	-42[-44.31,-39.69]
Marais 2008	41	0	-18.8 (2.468)		1.01%	-18.8[-23.64,-13.96]
MERCURY II 2006	383	0	-52.1 (0.7)		12.59%	-52.1[-53.47,-50.73]
Patel 2011	11	0	-44.3 (4.523)		0.3%	-44.3[-53.16,-35.44]
Postadzhiyan 2008	14	0	-46.8 (4.009)		0.38%	-46.8[-54.66,-38.94]
Rosenson 2011	51	0	-44.3 (2.52)		0.97%	-44.3[-49.24,-39.36]
Schneck 2003	38	0	-51.7 (0.9)		7.62%	-51.7[-53.46,-49.94]
STARSHIP 2006	167	0	-50 (1.161)		4.58%	-50[-52.27,-47.73]
STELLAR 2003	160	0	-52.4 (1.186)		4.39%	-52.4[-54.72,-50.08]
Szapary 2012	109	0	-43.5 (2.755)		0.81%	-43.55[-48.95,-38.15]
Total (95% CI)					**100%**	**-50.07[-50.55,-49.58]**
Heterogeneity: Tau²=0; Chi²=327.01, df=19(P<0.0001); I²=94.19%						
Test for overall effect: Z=201.57(P<0.0001)						

Favours rosuvastatin -100 -50 0 50 100

Analysis 5.8. Comparison 5 20 mg vs control, Outcome 8 HDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
ARIES 2006	189	0	6.5 (0.9)		8.78%	6.5[4.74,8.26]
Bellia 2010	14	0	9.1 (4.276)		0.39%	9.1[0.72,17.48]
Catapano 2006	478	0	8.1 (0.5)		28.44%	8.1[7.12,9.08]
HeFH 2003	435	0	11.7 (0.9)		8.78%	11.7[9.94,13.46]
IRIS 2007	171	0	6.6 (1.193)		4.99%	6.6[4.26,8.94]
Jones 2009	236	0	10.3 (1.32)		4.08%	10.3[7.71,12.89]
Kostapanos 2007b	45	0	3.2 (2.385)		1.25%	3.2[-1.47,7.87]
Kostapanos 2008b	60	0	8.2 (2.066)		1.67%	8.2[4.15,12.25]
Kostapanos 2009	50	0	5 (2.263)		1.39%	5[0.57,9.43]
LUNAR 2012	246	0	9.7 (1.046)		6.5%	9.7[7.65,11.75]
Marais 2008	41	0	5.1 (3.826)		0.49%	5.1[-2.4,12.6]
MERCURY II 2006	383	0	6.9 (0.6)		19.75%	6.9[5.72,8.08]
Patel 2011	11	0	-6.7 (4.824)		0.31%	-6.7[-16.16,2.76]
Postadzhiyan 2008	14	0	16.5 (4.276)		0.39%	16.5[8.12,24.88]
Rosenson 2011	49	0	11 (3.1)		0.74%	11[4.92,17.08]
Schneck 2003	38	0	9.1 (1.8)		2.19%	9.1[5.57,12.63]
STARSHIP 2006	167	0	5.7 (1.231)		4.69%	5.7[3.29,8.11]
STELLAR 2003	160	0	9.5 (1.265)		4.44%	9.5[7.02,11.98]
Szapary 2012	109	0	9 (3.088)		0.75%	9[2.95,15.05]
Total (95% CI)					**100%**	**8.03[7.51,8.55]**

Heterogeneity: $Tau^2=0$; $Chi^2=56.13$, df=18(P<0.0001); $I^2=67.93\%$

Test for overall effect: Z=30.12(P<0.0001)

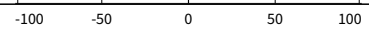
-1000 -500 0 500 1000 Favours rosuvastatin

Analysis 5.9. Comparison 5 20 mg vs control, Outcome 9 non-HDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
ARIES 2006	189	0	-42.3 (1.2)		5.2%	-42.3[-44.65,-39.95]
Bellia 2010	14	0	-51.8 (4.276)		0.41%	-51.8[-60.18,-43.42]
Catapano 2006	478	0	-47.9 (0.5)		29.96%	-47.9[-48.88,-46.92]
IRIS 2007	171	0	-44.9 (1.224)		5%	-44.9[-47.3,-42.5]
Jones 2009	236	0	-45.8 (1.02)		7.2%	-45.8[-47.8,-43.8]
Kostapanos 2007b	45	0	-48.6 (2.385)		1.32%	-48.6[-53.27,-43.93]
Kostapanos 2008b	60	0	-46.5 (2.066)		1.76%	-46.5[-50.55,-42.45]
Kostapanos 2009	50	0	-51.4 (2.263)		1.46%	-51.4[-55.83,-46.97]
LUNAR 2012	246	0	-37.9 (1.046)		6.85%	-37.9[-39.95,-35.85]
Marais 2008	41	0	-19.2 (2.499)		1.2%	-19.2[-24.1,-14.3]
MERCURY II 2006	383	0	-47.2 (0.7)		15.29%	-47.2[-48.57,-45.83]
Patel 2011	11	0	-40.5 (4.824)		0.32%	-40.5[-49.96,-31.04]
Postadzhiyan 2008	14	0	-38.4 (4.276)		0.41%	-38.4[-46.78,-30.02]
Rosenson 2011	49	0	-45.8 (2.16)		1.61%	-45.8[-50.03,-41.57]
Schneck 2003	38	0	-47.5 (0.9)		9.25%	-47.5[-49.26,-45.74]
STARSHIP 2006	167	0	-44.9 (1.238)		4.89%	-44.9[-47.33,-42.47]

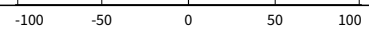
Favours rosuvastatin -100 -50 0 50 100

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
STELLAR 2003	160	0	-48.4 (1.265)		4.68%	-48.4[-50.88,-45.92]
Szapary 2012	109	0	-41.9 (1.533)		3.19%	-41.9[-44.9,-38.9]
Total (95% CI)					**100%**	**-45.77[-46.31,-45.24]**
Heterogeneity: Tau²=0; Chi²=229.67, df=17(P<0.0001); I²=92.6%						
Test for overall effect: Z=167.24(P<0.0001)						



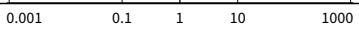
Analysis 5.10. Comparison 5 20 mg vs control, Outcome 10 Triglycerides.

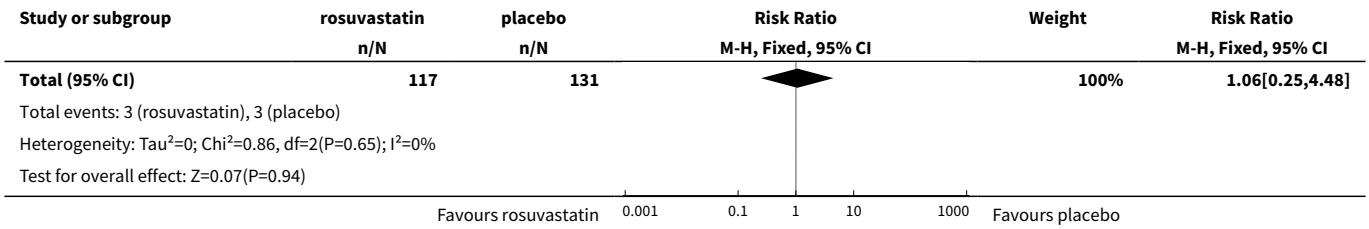
Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
ARIES 2006	189	0	-20.9 (1.9)		9.55%	-20.9[-24.62,-17.18]
HeFH 2003	435	0	-22.9 (1.4)		17.58%	-22.9[-25.64,-20.16]
IRIS 2007	171	0	-22 (2)		8.61%	-22[-25.92,-18.08]
Jones 2009	255	0	-25.6 (1.8)		10.64%	-25.6[-29.13,-22.07]
Kostapanos 2007b	45	0	-16.5 (4.696)		1.56%	-16.5[-25.7,-7.3]
Kostapanos 2009	50	0	-27.3 (4.455)		1.74%	-27.3[-36.03,-18.57]
LUNAR 2012	246	0	-9.5 (2.576)		5.19%	-9.5[-14.55,-4.45]
Marais 2008	41	0	-7.5 (4.638)		1.6%	-7.5[-16.59,1.59]
MERCURY II 2006	383	0	-22.8 (1.3)		20.39%	-22.8[-25.35,-20.25]
Patel 2011	11	0	-14.8 (9.498)		0.38%	-14.8[-33.41,3.81]
Postadzhiyan 2008	14	0	-29 (8.419)		0.49%	-29[-45.5,-12.5]
Rosenson 2011	53	0	-26.9 (3.57)		2.7%	-26.9[-33.9,-19.9]
Schneck 2003	38	0	-18.4 (4.6)		1.63%	-18.4[-27.42,-9.38]
STARSHIP 2006	167	0	-18 (2)		8.61%	-18[-21.92,-14.08]
STELLAR 2003	160	0	-23.7 (2.49)		5.56%	-23.7[-28.58,-18.82]
Szapary 2012	109	0	-24.6 (3.024)		3.77%	-24.65[-30.58,-18.72]
Total (95% CI)					**100%**	**-21.65[-22.8,-20.5]**
Heterogeneity: Tau²=0; Chi²=49.89, df=15(P<0.0001); I²=69.93%						
Test for overall effect: Z=36.89(P<0.0001)						



Analysis 5.11. Comparison 5 20 mg vs control, Outcome 11 WDAE.

Study or subgroup	rosuvastatin n/N	placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Hunninghake 2004	1/28	2/26		61.57%	0.46[0.04,4.82]
Kim 2013	0/27	0/26			Not estimable
Olsson 2001	1/17	1/29		21.94%	1.71[0.11,25.55]
Saito 2003	1/19	0/15		16.49%	2.4[0.1,55.03]
Saito 2007	0/26	0/35			Not estimable

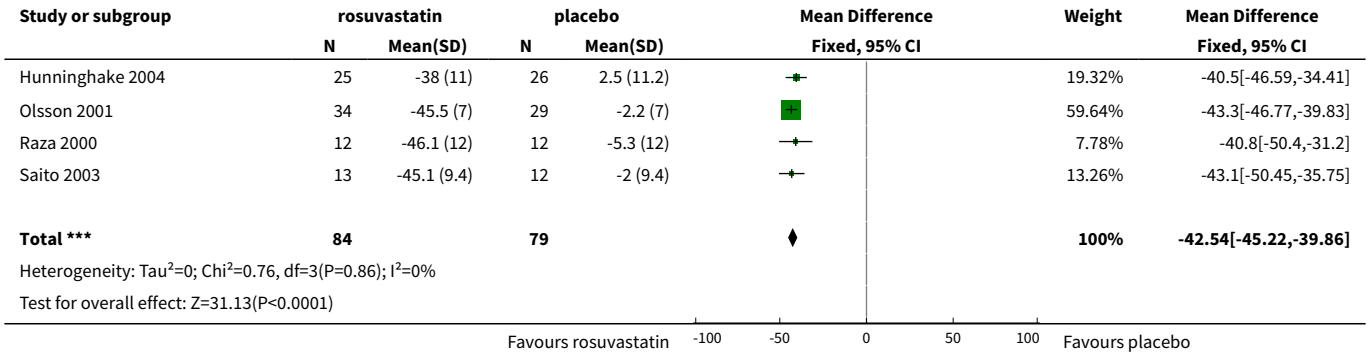




Comparison 6. 40 mg vs control

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Total cholesterol	4	163	Mean Difference (IV, Fixed, 95% CI)	-42.54 [-45.22, -39.86]
2 LDL-cholesterol	6	472	Mean Difference (IV, Fixed, 95% CI)	-55.85 [-58.31, -53.40]
3 HDL-cholesterol	6	472	Mean Difference (IV, Fixed, 95% CI)	6.85 [4.29, 9.40]
4 non-HDL-choles-terol	3	139	Mean Difference (IV, Fixed, 95% CI)	-53.75 [-58.57, -48.94]
5 Triglycerides	5	203	Mean Difference (IV, Fixed, 95% CI)	-31.76 [-39.40, -24.12]
6 Total cholesterol	11	3017	% change from baseline (Fixed, 95% CI)	-40.42 [-40.83, -40.02]
7 LDL-cholesterol	11	3010	% change from baseline (Fixed, 95% CI)	-54.84 [-55.35, -54.33]
8 HDL-cholesterol	11	3005	% change from baseline (Fixed, 95% CI)	9.90 [9.34, 10.46]
9 non-HDL-choles-terol	11	3005	% change from baseline (Fixed, 95% CI)	-50.69 [-51.22, -50.16]
10 Triglycerides	9	2520	% change from baseline (Fixed, 95% CI)	-26.53 [-27.76, -25.29]
11 WDAE	1	29	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 6.1. Comparison 6 40 mg vs control, Outcome 1 Total cholesterol.

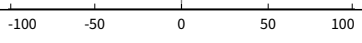


Analysis 6.2. Comparison 6 40 mg vs control, Outcome 2 LDL-cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
ASTRONOMER 2010	134	-54.5 (15)	135	0 (15)		46.9%	-54.5[-58.09,-50.91]
Erbs 2011	20	-55.7 (7.2)	20	-6.9 (22.8)		5.49%	-48.8[-59.28,-38.32]
Hunninghake 2004	25	-39 (20.5)	26	6.2 (21.4)		4.56%	-45.2[-56.7,-33.7]
Olsson 2001	34	-62.6 (8.7)	29	-3.6 (9.2)		30.5%	-59[-63.45,-54.55]
Raza 2000	12	-63 (15)	12	-8 (15)		4.18%	-55[-67,-43]
Saito 2003	13	-66 (10.5)	12	-3.2 (11.1)		8.37%	-62.8[-71.29,-54.31]
Total ***	**238**		**234**			**100%**	**-55.85[-58.31,-53.4]**

Heterogeneity: Tau²=0; Chi²=10.1, df=5(P=0.07); I²=50.51%

Test for overall effect: Z=44.59(P<0.0001)



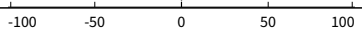
Favours rosuvastatin — Favours placebo

Analysis 6.3. Comparison 6 40 mg vs control, Outcome 3 HDL-cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
ASTRONOMER 2010	134	1.8 (16)	135	-1.9 (16)		44.66%	3.7[-0.12,7.52]
Erbs 2011	20	8.2 (16.1)	20	2.8 (12.5)		8.18%	5.4[-3.53,14.33]
Hunninghake 2004	25	15 (12.5)	26	-2 (12.2)		14.2%	17[10.22,23.78]
Olsson 2001	34	10.1 (11.7)	29	3.6 (11.8)		19.26%	6.5[0.68,12.32]
Raza 2000	12	9.4 (16)	12	2.8 (16)		3.98%	6.6[-6.2,19.4]
Saito 2003	13	9.7 (10.5)	12	1.2 (10.4)		9.72%	8.5[0.3,16.7]
Total ***	**238**		**234**			**100%**	**6.85[4.29,9.4]**

Heterogeneity: Tau²=0; Chi²=11.48, df=5(P=0.04); I²=56.45%

Test for overall effect: Z=5.25(P<0.0001)



Favours rosuvastatin — Favours placebo

Analysis 6.4. Comparison 6 40 mg vs control, Outcome 4 non-HDL-cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Hunninghake 2004	25	-47 (12.5)	26	3.3 (12.8)		48.33%	-50.3[-57.23,-43.37]
Olsson 2001	34	-60.2 (16)	29	-3.6 (16)		36.94%	-56.6[-64.53,-48.67]
Saito 2003	13	-60.8 (16)	12	-2.8 (16)		14.73%	-57.95[-70.5,-45.4]
Total ***	**72**		**67**			**100%**	**-53.75[-58.57,-48.94]**

Heterogeneity: Tau²=0; Chi²=1.88, df=2(P=0.39); I²=0%

Test for overall effect: Z=21.87(P<0.0001)

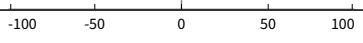
Favours rosuvastatin — Favours placebo

Analysis 6.5. Comparison 6 40 mg vs control, Outcome 5 Triglycerides.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Erbs 2011	20	0.8 (59.9)	20	7.6 (50.1)		4.99%	-6.76[-40.98,27.46]
Hunninghake 2004	25	-40 (22.5)	26	2.9 (22.4)		38.44%	-42.9[-55.23,-30.57]
Olsson 2001	34	-28 (26.2)	29	-1.3 (26.4)		34.37%	-26.7[-39.73,-13.67]
Raza 2000	12	-25.5 (31.5)	12	-1.7 (31.5)		9.19%	-23.8[-49,1.4]
Saito 2003	13	-25.1 (27)	12	2.3 (27)		13.01%	-27.4[-48.58,-6.22]
Total ***	**104**		**99**			**100%**	**-31.76[-39.4,-24.12]**

Heterogeneity: $Tau^2=0$; $Chi^2=6.31$, df=4(P=0.18); $I^2=36.63\%$

Test for overall effect: Z=8.15(P<0.0001)

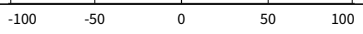


Analysis 6.6. Comparison 6 40 mg vs control, Outcome 6 Total cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Ballantyne 2004	153	0	-40.7 (0.8)		6.62%	-40.7[-42.27,-39.13]
Catapano 2006	475	0	-40.6 (0.4)		26.47%	-40.6[-41.38,-39.82]
EXPLORER 2007	230	0	-42 (0.791)		6.76%	-42[-43.55,-40.45]
Jones 2009	127	0	-42.7 (1.13)		3.32%	-42.7[-44.91,-40.49]
Lamendola 2005	20	0	-43 (2.683)		0.59%	-43[-48.26,-37.74]
LUNAR 2012	251	0	-32.2 (0.991)		4.31%	-32.2[-34.14,-30.26]
Makariou 2012	22	0	-44 (2.558)		0.65%	-44[-49.01,-38.99]
Schneck 2003	44	0	-41.1 (0.8)		6.62%	-41.1[-42.67,-39.53]
Stein 2007a	308	0	-41.5 (0.558)		13.58%	-41.5[-42.59,-40.41]
Stein 2007b	1230	0	-40 (0.4)		26.47%	-40[-40.78,-39.22]
STELLAR 2003	157	0	-40.2 (0.958)		4.62%	-40.2[-42.08,-38.32]
Total (95% CI)					**100%**	**-40.42[-40.83,-40.02]**

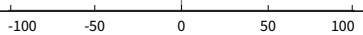
Heterogeneity: $Tau^2=0$; $Chi^2=85.69$, df=10(P<0.0001); $I^2=88.33\%$

Test for overall effect: Z=196.43(P<0.0001)



Analysis 6.7. Comparison 6 40 mg vs control, Outcome 7 LDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Ballantyne 2004	153	0	-52.2 (1.05)		6.15%	-52.2[-54.26,-50.14]
Catapano 2006	475	0	-56.7 (0.5)		27.14%	-56.7[-57.68,-55.72]
EXPLORER 2007	230	0	-57 (0.989)		6.93%	-57[-58.94,-55.06]
Jones 2009	120	0	-50.6 (1.64)		2.52%	-50.6[-53.81,-47.39]
Lamendola 2005	20	0	-55.1 (3.354)		0.6%	-55.1[-61.67,-48.53]
LUNAR 2012	251	0	-46.8 (1.149)		5.14%	-46.8[-49.05,-44.55]



Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Makariou 2012	22	0	-58 (3.198)		0.66%	-58[-64.27,-51.73]
Schneck 2003	44	0	-56.8 (1.1)		5.61%	-56.8[-58.96,-54.64]
Stein 2007a	308	0	-55.7 (0.712)		13.37%	-55.7[-57.1,-54.3]
Stein 2007b	1230	0	-54 (0.5)		27.14%	-54[-54.98,-53.02]
STELLAR 2003	157	0	-55 (1.197)		4.73%	-55[-57.35,-52.65]
Total (95% CI)					**100%**	**-54.84[-55.35,-54.33]**
Heterogeneity: Tau²=0; Chi²=89.05, df=10(P<0.0001); I²=88.77%						
Test for overall effect: Z=210.55(P<0.0001)						

Favours rosuvastatin -100 -50 0 50 100

Analysis 6.8. Comparison 6 40 mg vs control, Outcome 8 HDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Ballantyne 2004	153	0	12.9 (1)		8.19%	12.9[10.94,14.86]
Catapano 2006	475	0	8.1 (0.5)		32.78%	8.1[7.12,9.08]
EXPLORER 2007	230	0	9 (1.055)		7.36%	9[6.93,11.07]
Jones 2009	115	0	9.3 (1.85)		2.39%	9.3[5.67,12.93]
Lamendola 2005	20	0	5 (3.578)		0.64%	5[-2.01,12.01]
LUNAR 2012	251	0	11.9 (1.244)		5.3%	11.9[9.46,14.34]
Makariou 2012	22	0	1 (3.411)		0.7%	1[-5.69,7.69]
Schneck 2003	44	0	12.3 (1.7)		2.84%	12.3[8.97,15.63]
Stein 2007a	308	0	10.8 (0.826)		12%	10.8[9.18,12.42]
Stein 2007b	1230	0	11 (0.6)		22.76%	11[9.82,12.18]
STELLAR 2003	157	0	9.6 (1.277)		5.03%	9.6[7.1,12.1]
Total (95% CI)					**100%**	**9.9[9.34,10.46]**
Heterogeneity: Tau²=0; Chi²=40.66, df=10(P<0.0001); I²=75.41%						
Test for overall effect: Z=34.58(P<0.0001)						

-100 -50 0 50 100 Favours rosuvastatin

Analysis 6.9. Comparison 6 40 mg vs control, Outcome 9 non-HDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Ballantyne 2004	153	0	-49.4 (1.295)		4.33%	-49.4[-51.94,-46.86]
Catapano 2006	475	0	-52 (0.5)		29.04%	-52[-52.98,-51.02]
EXPLORER 2007	230	0	-52.2 (1.055)		6.52%	-52.2[-54.27,-50.13]
Jones 2009	115	0	-51.5 (1.43)		3.55%	-51.5[-54.3,-48.7]
Lamendola 2005	20	0	-52.5 (3.578)		0.57%	-52.5[-59.51,-45.49]
LUNAR 2012	251	0	-42.6 (1.111)		5.88%	-42.6[-44.78,-40.42]

Favours rosuvastatin -100 -50 0 50 100

Study or subgroup	rosuvas-tatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Makariou 2012	22	0	-52 (3.411)		0.62%	-52[-58.69,-45.31]
Schneck 2003	44	0	-52.2 (1)		7.26%	-52.2[-54.16,-50.24]
Stein 2007a	308	0	-51.6 (0.912)		8.73%	-51.6[-53.39,-49.81]
Stein 2007b	1230	0	-50 (0.5)		29.04%	-50[-50.98,-49.02]
STELLAR 2003	157	0	-51 (1.277)		4.45%	-51[-53.5,-48.5]
Total (95% CI)					**100%**	**-50.69[-51.22,-50.16]**
Heterogeneity: Tau²=0; Chi²=68.9, df=10(P<0.0001); I²=85.49%						
Test for overall effect: Z=188.12(P<0.0001)						

Favours rosuvastatin -100 -50 0 50 100

Analysis 6.10. Comparison 6 40 mg vs control, Outcome 10 Triglycerides.

Study or subgroup	rosuvas-tatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Ballantyne 2004	153	0	-30.1 (1.5)		17.6%	-30.1[-33.04,-27.16]
EXPLORER 2007	230	0	-25 (2.077)		9.18%	-25[-29.07,-20.93]
Jones 2009	127	0	-32.1 (2.48)		6.44%	-32.1[-36.96,-27.24]
Lamendola 2005	20	0	-34.9 (7.044)		0.8%	-34.9[-48.71,-21.09]
LUNAR 2012	251	0	-14.6 (3.049)		4.26%	-14.6[-20.58,-8.62]
Schneck 2003	44	0	-25.7 (4.3)		2.14%	-25.7[-34.13,-17.27]
Stein 2007a	308	0	-25.4 (1.698)		13.73%	-25.4[-28.73,-22.07]
Stein 2007b	1230	0	-26 (1)		39.59%	-26[-27.96,-24.04]
STELLAR 2003	157	0	-26.1 (2.514)		6.26%	-26.1[-31.03,-21.17]
Total (95% CI)					**100%**	**-26.53[-27.76,-25.29]**
Heterogeneity: Tau²=0; Chi²=28.77, df=8(P=0); I²=72.19%						
Test for overall effect: Z=42.16(P<0.0001)						

Favours rosuvastatin -100 -50 0 50 100

Analysis 6.11. Comparison 6 40 mg vs control, Outcome 11 WDAE.

Study or subgroup	rosuvastatin n/N	placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Saito 2003	0/15	0/14			Not estimable
Total (95% CI)	**15**	**14**			**Not estimable**
Total events: 0 (rosuvastatin), 0 (placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

Favours rosuvastatin 0.001 0.1 1 10 1000 Favours placebo

Comparison 7. 80 mg vs control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total cholesterol	2	113	Mean Difference (IV, Fixed, 95% CI)	-44.5 [-47.84, -41.16]
2 LDL-cholesterol	2	113	Mean Difference (IV, Fixed, 95% CI)	-59.47 [-64.15, -54.79]
3 HDL-cholesterol	2	113	Mean Difference (IV, Fixed, 95% CI)	10.68 [5.92, 15.44]
4 non-HDL-cholesterol	2	113	Mean Difference (IV, Fixed, 95% CI)	-55.50 [-60.70, -50.29]
5 Triglycerides	2	113	Mean Difference (IV, Fixed, 95% CI)	-34.49 [-43.89, -25.10]
6 Total cholesterol	1	42	% change from baseline (Fixed, 95% CI)	-43.00 [-47.16, -42.84]
7 LDL-cholesterol	1	42	% change from baseline (Fixed, 95% CI)	-61.9 [-64.64, -59.16]
8 HDL-cholesterol	1	42	% change from baseline (Fixed, 95% CI)	9.6 [6.27, 12.93]
9 non-HDL-cholesterol	1	42	% change from baseline (Fixed, 95% CI)	-57.0 [-59.55, -54.45]
10 Triglycerides	1	42	% change from baseline (Fixed, 95% CI)	-19.7 [-28.32, -11.08]
11 WDAE	1	53	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.05, 4.99]

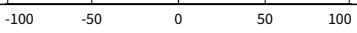
Analysis 7.1. Comparison 7 80 mg vs control, Outcome 1 Total cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Hunninghake 2004	27	-42 (10.9)	26	2.5 (11.2)		31.51%	-44.5[-50.45,-38.55]
Olsson 2001	31	-46.7 (8.9)	29	-2.2 (7)		68.49%	-44.5[-48.54,-40.46]
Total ***	**58**		**55**			**100%**	**-44.5[-47.84,-41.16]**
Heterogeneity: Tau²=0; Chi²=0, df=1(P=1); I²=0%							
Test for overall effect: Z=26.1(P<0.0001)							

Favours rosuvastatin — Favours placebo

Analysis 7.2. Comparison 7 80 mg vs control, Outcome 2 LDL-cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Hunninghake 2004	27	-45 (20.3)	26	6.2 (21.4)		17.33%	-51.2[-62.44,-39.96]
Olsson 2001	31	-64.8 (11.1)	29	-3.6 (9.2)		82.67%	-61.2[-66.35,-56.05]
Total ***	**58**		**55**			**100%**	**-59.47[-64.15,-54.79]**
Heterogeneity: Tau²=0; Chi²=2.51, df=1(P=0.11); I²=60.23%							



Favours rosuvastatin — Favours placebo

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Test for overall effect: Z=24.91(P<0.0001)							

Favours rosuvastatin -100 -50 0 50 100 Favours placebo

Analysis 7.3. Comparison 7 80 mg vs control, Outcome 3 HDL-cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Hunninghake 2004	27	10 (12.5)	26	-2 (12.2)		51.16%	12[5.35,18.65]
Olsson 2001	31	12.9 (15)	29	3.6 (11.8)		48.84%	9.3[2.49,16.11]
Total ***	**58**		**55**			**100%**	**10.68[5.92,15.44]**
Heterogeneity: Tau^2=0; Chi^2=0.31, df=1(P=0.58); I^2=0%							
Test for overall effect: Z=4.4(P<0.0001)							

Favours rosuvastatin -100 -50 0 50 100 Favours placebo

Analysis 7.4. Comparison 7 80 mg vs control, Outcome 4 non-HDL-cholesterol.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Hunninghake 2004	27	-51 (12.5)	26	3.3 (12.8)		58.72%	-54.3[-61.09,-47.51]
Olsson 2001	31	-60.8 (16)	29	-3.6 (16)		41.28%	-57.2[-65.3,-49.1]
Total ***	**58**		**55**			**100%**	**-55.5[-60.7,-50.29]**
Heterogeneity: Tau^2=0; Chi^2=0.29, df=1(P=0.59); I^2=0%							
Test for overall effect: Z=20.9(P<0.0001)							

Favours rosuvastatin -100 -50 0 50 100 Favours placebo

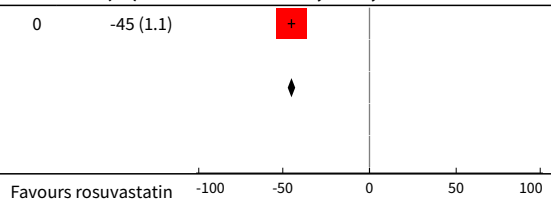
Analysis 7.5. Comparison 7 80 mg vs control, Outcome 5 Triglycerides.

Study or subgroup	rosuvastatin N	rosuvastatin Mean(SD)	placebo N	placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Hunninghake 2004	27	-40 (22.3)	26	2.9 (22.4)		60.9%	-42.9[-54.94,-30.86]
Olsson 2001	31	-22.7 (32.8)	29	-1.3 (26.4)		39.1%	-21.4[-36.42,-6.38]
Total ***	**58**		**55**			**100%**	**-34.49[-43.89,-25.1]**
Heterogeneity: Tau^2=0; Chi^2=4.79, df=1(P=0.03); I^2=79.13%							
Test for overall effect: Z=7.2(P<0.0001)							

Favours rosuvastatin -100 -50 0 50 100 Favours placebo

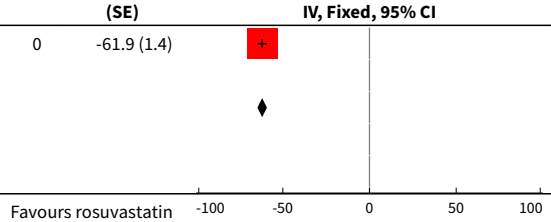
Analysis 7.6. Comparison 7 80 mg vs control, Outcome 6 Total cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Schneck 2003	42	0	-45 (1.1)		100%	-45[-47.16,-42.84]
Total (95% CI)					**100%**	**-45[-47.16,-42.84]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%						
Test for overall effect: Z=40.91(P<0.0001)						



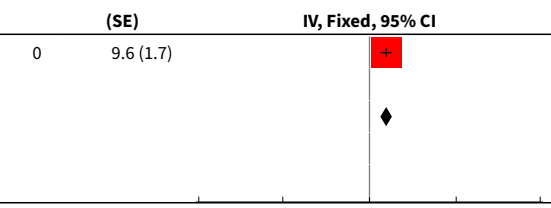
Analysis 7.7. Comparison 7 80 mg vs control, Outcome 7 LDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Schneck 2003	42	0	-61.9 (1.4)		100%	-61.9[-64.64,-59.16]
Total (95% CI)					**100%**	**-61.9[-64.64,-59.16]**
Heterogeneity: Not applicable						
Test for overall effect: Z=44.21(P<0.0001)						



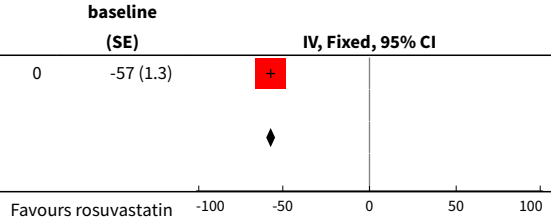
Analysis 7.8. Comparison 7 80 mg vs control, Outcome 8 HDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Schneck 2003	42	0	9.6 (1.7)		100%	9.6[6.27,12.93]
Total (95% CI)					**100%**	**9.6[6.27,12.93]**
Heterogeneity: Not applicable						
Test for overall effect: Z=5.65(P<0.0001)						

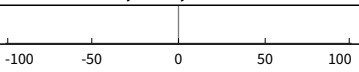


Analysis 7.9. Comparison 7 80 mg vs control, Outcome 9 non-HDL-cholesterol.

Study or subgroup	rosuvastatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Schneck 2003	42	0	-57 (1.3)		100%	-57[-59.55,-54.45]
Total (95% CI)					**100%**	**-57[-59.55,-54.45]**
Heterogeneity: Not applicable						

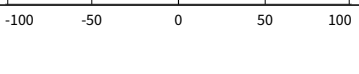


Study or subgroup	rosuvas-tatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Test for overall effect: Z=43.85(P<0.0001)						



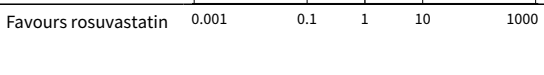
Analysis 7.10. Comparison 7 80 mg vs control, Outcome 10 Triglycerides.

Study or subgroup	rosuvas-tatin N	N	% change from baseline (SE)	% change from baseline IV, Fixed, 95% CI	Weight	% change from baseline IV, Fixed, 95% CI
Schneck 2003	42	0	-19.7 (4.4)		100%	-19.7[-28.32,-11.08]
Total (95% CI)					**100%**	**-19.7[-28.32,-11.08]**
Heterogeneity: Not applicable						
Test for overall effect: Z=4.48(P<0.0001)						



Analysis 7.11. Comparison 7 80 mg vs control, Outcome 11 WDAE.

Study or subgroup	rosuvastatin n/N	placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Hunninghake 2004	1/27	2/26		100%	0.48[0.05,4.99]
Total (95% CI)	**27**	**26**		**100%**	**0.48[0.05,4.99]**
Total events: 1 (rosuvastatin), 2 (placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.61(P=0.54)					

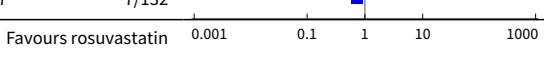


Comparison 8. all doses vs control

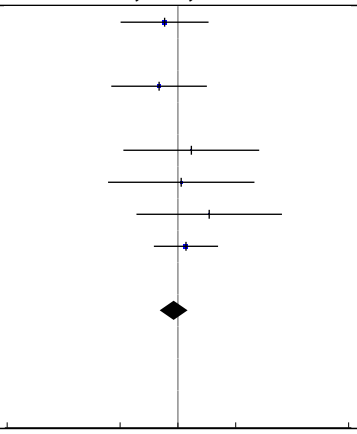
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 WDAEs	10	1330	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.48, 1.47]

Analysis 8.1. Comparison 8 all doses vs control, Outcome 1 WDAEs.

Study or subgroup	rosuvastatin n/N	placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
COMETS 2005	2/163	3/79		15.87%	0.32[0.06,1.89]
Davidson 2002	10/257	7/132		36.32%	0.73[0.29,1.88]



Study or subgroup	rosuvastatin n/N	placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Durrington 2004	2/60	3/53		12.51%	0.59[0.1,3.39]
Gomez-Garcia 2007	0/16	0/16			Not estimable
Hunninghake 2004	2/55	2/26		10.66%	0.47[0.07,3.17]
Kim 2013	0/27	0/26			Not estimable
Olsson 2001	1/17	1/29		2.9%	1.71[0.11,25.55]
Saito 2003	3/97	0/15		3.38%	1.14[0.06,21.1]
Saito 2007	4/92	0/35		2.83%	3.48[0.19,63.08]
Shepherd 2004	8/89	3/46		15.53%	1.38[0.38,4.95]
Total (95% CI)	**873**	**457**		**100%**	**0.84[0.48,1.47]**
Total events: 32 (rosuvastatin), 19 (placebo)					
Heterogeneity: Tau^2=0; Chi^2=3.52, df=7(P=0.83); I^2=0%					
Test for overall effect: Z=0.61(P=0.54)					



ADDITIONAL TABLES

Table 1. Rosuvastatin overall efficacy table

Rosuvastatin dose mg/day	1	2.5	5	10	20	40	80
Mean per cent change from control of total cholesterol	-22.1	-26.6	-29.1	-32.8	-36.2	-40.5	-44.8
95% CI[1]	(-24.9 to -19.3)	(-27.9 to -25.3)	(-29.6 to -28.6)	(-33.1 to -32.6)	(-36.6 to -35.8)	(-40.9 to -40.1)	(-46.6 to -43.1)
Mean per cent change from control of LDL-C[2]	-31.2	-39.1	-41.3	-45.6	-49.9	-54.9	-61.2
95% CI[1]	(-34.5 to -27.9)	(-40.6 to -37.6)	(-42.0 to -40.7)	(-45.95 to -45.3)	(-50.4 to -49.4)	(-55.4 to -54.4)	(-63.6 to -58.9)
Mean per cent change from control of non-HDL-C[3]	-28.9	-35.4	-37.6	-41.9	-45.5	-50.8	-56.7
95% CI[1]	(-34.1 to -23.7)	(-37.2 to -33.5)	(-38.4 to -36.9)	(-42.3 to -41.6)	(-46.1 to -45.0)	(-51.3 to -50.2)	(-59.0 to -54.4)
Mean per cent change from control of triglycerides	-14.4	-13.4	-17.7	-19.7	-21.7	-26.7	-26.6
95% CI[1]	(-22.1 to -6.8)	(-16.5 to -10.2)	(-19.0 to -16.4)	(-20.4 to -19.1)	(-22.8 to -20.6)	(-27.9 to -25.4)	(-32.9 to -20.4)

1. CI: confidence interval
2. LDL-C: low-density lipoprotein cholesterol
3. non-HDL-C: non high-density lipoprotein cholesterol

APPENDICES

Appendix 1. Search strategies

CENTRAL October 2013

1 rosuvastatin
2 crestor
3 s4522
4 zd4522
5 (1 or 2 or 3 or 4)

CENTRAL November 2014

#1rosuvastatin
#2crestor
#3rosuvas
#4"s 4522"
#5s4522
#6"zd 4522"
#7zd4522
#8#1 or #2 or #3 or #4 or #5 or #6 or #7 Publication Year from 2013 to 2014

MEDLINE October 2013

1 rosuvastatin.af
2 crestor.tw
3 s4522.tw
4 zd4522
5 (1 or 2 or 3 or 4)
6 animals/
7 5 not 6

MEDLINE November 2014

1. rosuvastatin.af.
2. crestor.tw.
3. rosuvas.tw.
4. s 4522.tw.
5. s4522.tw.
6. zd 4522.tw.
7. zd4522.tw.
8. or/1-7
9. exp animals/ not humans.sh.
10. 8 not 9
11. (201310* or 201311* or 201312* or 2014*).ed.
12. 10 and 11

EMBASE October 2013

1 rosuvastatin/
2 rosuvastatin.tw
3 crestor.tw
4 s4522.tw
6 zd4522.tw
7 (1 or 2 or 3 or 4 or 5 or 6)
8 exp animals/not humans.sh
9 7 not 8

EMBASE November 2014

1. rosuvastatin/
2. rosuvastatin.tw.
3. crestor.tw.
4. rosuvas.tw.

5. s 4522.tw.
6. s4522.tw.
7. zd 4522.tw.
8. zd4522.tw.
9. or/1-8
10. (animal/ or nonhuman/) not human/
11. 9 not 10
12. limit 11 to embase
13. (201310* or 201311* or 201312* or 2014*).dd.
14. 12 and 13

Web of Science October 2013

1 rosuvastatin or crestor or rosuvas or "s 4522" or s4522 or "zd 4522" or zd4522
2 crestor
3 rosuvas
4 "s 4522"
5 s4522
6 "zd 4522"
7 zd4522
8 (1 or 2 or 3 or 4 or 5 or 6 or 7)

BIOSIS October 2013

1 (rosuvastatin or crestor) AND Taxa Notes=(HUMANS)
2 "s 4522"
3 s4522
4 "zd 4522"
5 zd4522
6 (1 or 2 or 3 or 4 or 5)

Web of Science and BIOSIS November 2014

3 #2 OR #1
2 TS=(rosuvas or "s 4522" or s4522 or "zd 4522" or zd4522)
1 TS=(rosuvastatin or crestor)

WHAT'S NEW

Date	Event	Description
24 January 2017	Amended	corrected minor errors in citations in the Additional references section; moved Adams 2012b to Other published versions of this review section; corrected link to Adams 2012b

HISTORY

Protocol first published: Issue 12, 2012
Review first published: Issue 11, 2014

Date	Event	Description
6 December 2016	Amended	Changed from Pfizer to AstraZeneca in searching other resources section

CONTRIBUTIONS OF AUTHORS

*Both JMW and SA contributed to the design of the protocol.

*Both SA and SS extracted the data.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- University of British Columbia, Canada.

External sources

- None, Canada.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

A subgroup analysis comparing AstraZeneca-funded versus non-AstraZeneca-funded trials was added to the review.

INDEX TERMS

Medical Subject Headings (MeSH)

Cardiovascular Diseases [blood]; Cholesterol [blood]; Cholesterol, HDL [blood]; Cholesterol, LDL [blood]; Dose-Response Relationship, Drug; Drug Administration Schedule; Fluorobenzenes [*administration & dosage]; Hydroxymethylglutaryl-CoA Reductase Inhibitors [*administration & dosage]; Hyperlipidemias [blood] [*drug therapy]; Lipids [*blood]; Pyrimidines [*administration & dosage]; Randomized Controlled Trials as Topic; Rosuvastatin Calcium; Sulfonamides [*administration & dosage]; Triglycerides [blood]

MeSH check words

Humans