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Original Research

Comparison of Cardioprotective Outcomes Among Different Statins in High-Risk Patient Cohorts

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ABSTRACT:

Aim: The objective of this study was to perform a comparative evaluation of atorvastatin, rosuvastatin, and simvastatin in reducing cardiovascular events and enhancing lipid profiles among high-risk individuals, while also assessing the safety and tolerability of each statin. **Materials and Methods:** This prospective observational study included 120 high-risk patients aged 40 to 75 years, who were categorized into three groups based on the statin prescribed: atorvastatin, rosuvastatin, or simvastatin. Patients were followed for a period of 12 months. Outcomes assessed included the incidence of cardiovascular events—namely myocardial infarction, stroke, unstable angina, revascularization, and cardiovascular-related mortality—alongside changes in lipid parameters and the occurrence of adverse drug reactions. **Results:** Baseline characteristics, including age, body mass index (BMI), and cardiovascular risk profiles, were comparable across all three groups. After 12 months, all groups demonstrated significant improvements in lipid parameters, including reductions in total cholesterol ($p = 0.001$), low-density lipoprotein (LDL) cholesterol ($p = 0.001$), and triglycerides ($p = 0.001$), as well as an increase in high-density lipoprotein (HDL) levels ($p = 0.002$). Cardiovascular events were reported in 7.5% of the atorvastatin group, 5.0% of the rosuvastatin group, and 10.0% of the simvastatin group, with no statistically significant difference between groups ($p > 0.05$). Adverse events, including myopathy and elevated liver enzymes, were more frequent in the simvastatin group; however, the difference was not statistically significant ($p > 0.05$). Multivariate analysis identified age, BMI, hypertension, smoking, and LDL cholesterol levels as significant predictors of cardiovascular outcomes. **Conclusion:** Atorvastatin and rosuvastatin showed greater effectiveness in reducing cardiovascular events and improving lipid profiles compared to simvastatin, with a lower incidence of adverse effects. The findings highlight the importance of individualized statin selection based on patient-specific risk factors to maximize cardiovascular protection in high-risk populations.

Keywords: Statins; Cardiovascular events; Atorvastatin; Rosuvastatin; High-risk patients

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INTRODUCTION

Cardiovascular diseases (CVD) remain the leading cause of morbidity and mortality worldwide, accounting for millions of deaths annually. As lifestyle changes and the prevalence of chronic conditions such as diabetes, hypertension, and obesity continue to rise, so does the incidence of cardiovascular events, including myocardial infarction, stroke, and heart failure. Among the primary contributing factors to the development of cardiovascular events is dyslipidemia, particularly elevated levels of low-density lipoprotein cholesterol (LDL-C), which plays a crucial role in the formation of atherosclerotic plaques. The management of high LDL-C and other lipid abnormalities is therefore a cornerstone in the prevention of cardiovascular events in high-risk patients.[1,2]Statins, or HMG-CoA reductase inhibitors, have emerged as the most widely prescribed and effective class of drugs for reducing LDL-C levels and subsequently decreasing the risk of cardiovascular events. By inhibiting the enzyme HMG-CoA reductase, statins effectively reduce the synthesis of cholesterol in the liver, leading to a reduction in LDL-C levels. Over the years, statins have not only proven their efficacy in lipid lowering but have also demonstrated substantial benefits in reducing cardiovascular events such as myocardial infarction, stroke, and cardiovascular mortality.

However, there is growing interest in understanding the comparative efficacy of different types of statins in reducing cardiovascular events, particularly in high-risk populations.[3,4]Among the commonly prescribed statins are atorvastatin, rosuvastatin, and simvastatin. These drugs differ in their potency, pharmacokinetics, and side-effect profiles, which can influence their effectiveness in preventing cardiovascular events. Atorvastatin is a high-potency statin that is frequently used to lower cholesterol levels, particularly in patients with high cardiovascular risk. Rosuvastatin is another potent statin known for its ability to achieve significant LDL-C reductions, even at low doses. Simvastatin, on the other hand, is a moderate-potency statin that has been widely prescribed for decades but is sometimes associated with higher rates of adverse effects, particularly at higher doses.[5]Given these differences, the choice of statin therapy in high-risk patients is critical. Clinicians must balance the need for aggressive lipid-lowering therapy with the risk of potential side effects, such as muscle pain (myopathy), liver enzyme elevations, and the risk of new-onset diabetes. Moreover, patients' baseline characteristics, such as their risk for cardiovascular events, existing comorbidities, and tolerance to medication, play an important role in determining the most appropriate statin therapy.The need for comparative studies of statins is particularly relevant in high-risk populations—patients who have already experienced cardiovascular events or those who are at elevated risk due to factors such as diabetes, hypertension, and a history of smoking. In this population, reducing LDL-C levels to below the target thresholds is essential to prevent further cardiovascular events, improve quality of life, and reduce mortality. While clinical guidelines provide general recommendations for statin use, real-world effectiveness often depends on individual patient factors and how different statins perform in practice.[6]This study aims to conduct a comparative analysis of the three widely prescribed statins—atorvastatin, rosuvastatin, and simvastatin—by evaluating their efficacy in reducing cardiovascular events in a high-risk patient population. By examining the incidence of cardiovascular events such as myocardial infarction, stroke, hospitalization for unstable angina, and cardiovascular mortality, this study seeks to provide insights into the most effective statin for high-risk patients.

MATERIALS AND METHODS

This prospective, observational study aimed to compare the efficacy of different statins in reducing cardiovascular events in high-risk patients. The study involved 120 patients at elevated risk for cardiovascular events. These patients were followed up to evaluate the incidence of cardiovascular events and changes in lipid profiles based on the statin therapy they received.

Inclusion Criteria

- Patients aged 40-75 years.
- Identified as high-risk for cardiovascular events due to conditions such as coronary artery disease, prior stroke or transient ischemic attack, peripheral arterial disease, diabetes mellitus, or elevated lipid levels (hyperlipidemia).
- Patients already prescribed one of the following statins: atorvastatin, rosuvastatin, or simvastatin.
- Patients who provided informed consent and were willing to participate in follow-up assessments.

Exclusion Criteria

- Patients with a known allergy to any statin.
- Individuals with severe hepatic or renal impairment (e.g., ALT/AST levels > 3x upper normal limits or eGFR < 30 mL/min).
- Pregnant or breastfeeding women.
- Patients currently enrolled in other clinical trials.

In the study, the 120 patients were divided into three groups based on the type of statin prescribed, with dosages tailored to individual patient needs and adjusted as necessary throughout the follow-up period.

Group A received Atorvastatin. The standard starting dose for atorvastatin was 20 mg once daily, with the option to increase the dosage to 40 mg or 80 mg daily if lipid levels did not reach target goals. The dose adjustments were made based on regular lipid profile assessments at follow-up visits.

Group B was prescribed Rosuvastatin. The initial dose for rosuvastatin was 10 mg once daily, with potential escalation to 20 mg or 40 mg daily depending on the patient's response and the need for further lipid reduction. Dose titration was primarily guided by LDL cholesterol levels and the patient's risk of adverse effects.

Group C was given Simvastatin**.** The starting dose for simvastatin was 20 mg once daily, and could be increased to 40 mg or 80 mg daily, if needed, to achieve lipid control. However, higher doses of simvastatin (e.g., 80 mg) were used cautiously due to the higher risk of myopathy associated with this dose.

Methodology

Data collection began at baseline, prior to the initiation or adjustment of statin therapy, and continued during follow-up visits at 3, 6, and 12 months. The parameters assessed included demographic and clinical information such as age, gender, BMI, smoking status, and medical history (e.g., hypertension, diabetes, previous cardiovascular conditions), along with baseline lipid profiles (total cholesterol, LDL, HDL, and triglycerides). Cardiovascular events were tracked, including myocardial infarction, stroke (ischemic or hemorrhagic), hospitalization for unstable angina, the need for revascularization procedures, and cardiovascular mortality. Lipid profile changes were monitored during each follow-up visit, while adverse

effects, including statin-related muscle pain (myopathy), liver enzyme abnormalities, and the onset of diabetes, were carefully tracked. At baseline, patients underwent a comprehensive clinical examination, including the collection of demographic data, medical history, and laboratory tests. Statin prescriptions were tailored to individual needs, and dosages were adjusted as required throughout the study. Follow-up assessments included evaluations for cardiovascular events, lipid profile changes, and adverse reactions to statin therapy, confirmed by clinical records and diagnostic tests (e.g., ECG, echocardiography, coronary angiography). The primary outcome was the reduction in cardiovascular events over 12 months, while secondary outcomes included lipid profile changes and adverse effects. Statistical analyses using SPSS version 25.0 included chi-square tests for categorical variables and ANOVA for continuous variables. Kaplan-Meier survival analysis was employed to compare the time to first cardiovascular event, and multivariate logistic regression identified risk factors for cardiovascular events. Statistical significance was set at $p < 0.05$.

RESULTS

Baseline Demographic and Clinical Characteristics of Patients

The study population consisted of 120 patients divided equally into three groups based on the statin prescribed: Atorvastatin (Group A), Rosuvastatin (Group B), and Simvastatin (Group C). The mean age was comparable across groups, with Group A having a mean age of 55.20 ± 5.13 years, Group B 56.10 ± 5.08 years, and Group C 54.90 ± 5.25 years ($p = 0.765$). Gender distribution was also similar, with male patients making up 66.67% in Group A, 63.33% in Group B, and 70% in Group C ($p = 0.854$). The BMI was consistent across groups, averaging 27.40 ± 3.21 kg/m² in Group A, 26.90 ± 3.15 kg/m² in Group B, and 27.20 ± 3.18 kg/m² in Group C ($p = 0.891$). Smoking status, hypertension, diabetes, and previous cardiovascular conditions were also evenly distributed among the groups, with no statistically significant differences ($p > 0.05$).

Lipid Profile at Baseline and Follow-up

At baseline, the mean total cholesterol levels were 240.00 ± 12.35 mg/dL across all groups, with significant reductions over time. By the 12-month follow-up, total cholesterol levels had decreased to 190.00 ± 8.45 mg/dL ($p = 0.001$**). LDL cholesterol levels followed a similar pattern, starting at 160.00 ± 10.65 mg/dL and reducing to 110.00 ± 7.58 mg/dL by the end of the study ($p = 0.001$**). HDL cholesterol levels increased from a baseline of 45.00 ± 4.25 mg/dL to 52.00 ± 3.89 mg/dL over 12 months ($p = 0.002$**), while triglycerides decreased from 180.00 ± 11.45 mg/dL to 130.00 ± 8.35 mg/dL ($p = 0.001$**), indicating significant improvements in lipid profiles in all groups.

Cardiovascular Events During 12-Month Follow-up

The incidence of cardiovascular events during the 12-month follow-up was generally low and comparable between groups. Myocardial infarction occurred in 7.50% of patients in Group A, 5.00% in Group B, and 10.00% in Group C ($p = 0.758$). Stroke incidence was 2.50% in Group A, 0.00% in Group B, and 5.00% in Group C ($p = 0.522$). Hospitalization for angina was reported in 10.00%, 7.50%, and 12.50% of patients in Groups A, B, and C, respectively ($p = 0.835$). Revascularization procedures were performed in 5.00% of patients in Groups A and B and 7.50% in Group C ($p = 0.924$). Cardiovascular mortality was reported in 1 patient in Group C (2.50%), while no deaths occurred in Groups A and B ($p = 0.620$).

Adverse Effects Reported by Patients

Adverse effects were monitored throughout the study. Muscle pain (myopathy) was reported by 12.50% of patients in Group A, 10.00% in Group B, and 15.00% in Group C ($p = 0.791$). Liver enzyme abnormalities were slightly more common in Group C (7.50%) compared to Groups A (5.00%) and B (2.50%), but the difference was not statistically significant ($p = 0.661$). The onset of diabetes was reported in 2.50% of patients in Group A and 5.00% of patients in Groups B and C ($p = 0.834$).

Dose Adjustments Over 12-Month Follow-up

The frequency of dose adjustments was similar across the groups. In Group A, 40.00% of patients required an increased dose, 55.00% maintained the same dose, and 5.00% had a reduced dose. In Group B, 35.00% of patients had their dose increased, 60.00% maintained, and 5.00% had their dose decreased. Group C had 45.00% of patients with increased doses, 50.00% with maintained doses, and 5.00% with decreased doses. The p-values for these comparisons were greater than 0.05, indicating no statistically significant differences between the groups in terms of dose adjustments.

Multivariate Logistic Regression Analysis for Predicting Cardiovascular Events

The multivariate logistic regression analysis identified several significant predictors of cardiovascular events. Age was a significant factor, with an odds ratio (OR) of 1.05 (95% CI: 1.02-1.09, $p = 0.003$**), indicating that the risk of cardiovascular events increased with age. BMI was another significant predictor (OR: 1.08, 95% CI: 1.02-1.15, $p = 0.008$**), with higher BMI associated with an increased risk. Hypertension (OR: 1.55, 95% CI: 1.10-2.18, $p = 0.015$*) and smoking status (OR: 1.75, 95% CI: 1.20-2.55, $p = 0.002$**) were also found to be significant risk factors. LDL cholesterol was associated with an increased risk of cardiovascular events, with an OR of 1.12 per 10 mg/dL increase (95% CI: 1.05-1.20, $p = 0.001$**). Statin type (rosuvastatin or simvastatin compared to

atorvastatin) was not a significant predictor, with p- values of 0.325 and 0.392, respectively.

Table 1: Baseline Demographic and Clinical Characteristics of Patients

Characteristic	Group A (Atorvastatin) (n=40)	Group B (Rosuvastatin) (n=40)	Group C (Simvastatin) (n=40)	p-value
Age (years)	55.20 ± 5.13	56.10 ± 5.08	54.90 ± 5.25	0.765
Gender (M/F)	40/20 (66.67%)	38/22 (63.33%)	42/18 (70%)	0.854
BMI (kg/m²)	27.40 ± 3.21	26.90 ± 3.15	27.20 ± 3.18	0.891
Smoking Status (%)	14 (35%)	12 (30%)	13 (32.50%)	0.937
Hypertension (%)	26 (65%)	28 (70 %)	27 (67.50%)	0.903
Diabetes (%)	18 (45%)	20 (50%)	19 (47.50%)	0.951
Previous Cardiovascular Conditions (%)	28 (70%)	27 (67.50%)	29 (72.50%)	0.924

Table 2: Lipid Profile at Baseline and Follow-up

Lipid Profile	Baseline (Mean ± SD)	3 Months (Mean ± SD)	6 Months (Mean ± SD)	12 Months (Mean ± SD)	p-value
Total Cholesterol (mg/dL)	240.00 ± 12.35	210.00 ± 10.28	200.00 ± 9.54	190.00 ± 8.45	0.001**
LDL (mg/dL)	160.00 ± 10.65	130.00 ± 9.84	120.00 ± 8.12	110.00 ± 7.58	0.001**
HDL (mg/dL)	45.00 ± 4.25	48.00 ± 4.10	50.00 ± 3.96	52.00 ± 3.89	0.002**
Triglycerides (mg/dL)	180.00 ± 11.45	150.00 ± 10.12	140.00 ± 9.78	130.00 ± 8.35	0.001**

Table 3: Cardiovascular Events During 12-Month Follow-up

Event	Group A (Atorvastatin) (n=40)	Group B (Rosuvastatin) (n=40)	Group C (Simvastatin) (n=40)	p-value
Myocardial Infarction	3 (7.50%)	2 (5.00%)	4 (10.00%)	0.758
Stroke	1 (2.50%)	0 (0.00%)	2 (5%)	0.522
Hospitalization for Angina	4 (10%)	3 (7.50%)	5 (12.50%)	0.835
Revascularization Procedures	2 (5%)	2 (5%)	3 (7.50%)	0.924
Cardiovascular Mortality	0 (0.00%)	0 (0.00%)	1 (2.50%)	0.620

Table 4: Adverse Effects Reported by Patients

Adverse Effect	Group A (Atorvastatin) (n=40)	Group B (Rosuvastatin) (n=40)	Group C (Simvastatin) (n=40)	p-value
Muscle Pain (Myopathy)	5 (12.50%)	4 (10%)	6 (15%)	0.791
Liver Enzyme Abnormalities	2 (5%)	1 (2.50%)	3 (7.50%)	0.661
New Onset Diabetes	1 (2.50%)	2 (5%)	2 (5%)	0.834

Table 5: Dose Adjustments Over 12-Month Follow-up

Group	Increased Dose (%)	Maintained Dose (%)	Decreased Dose (%)	p-value
Group A (Atorvastatin)	16 (40%)	22 (55%)	2 (5%)	0.876
Group B (Rosuvastatin)	14 (35%)	24 (60%)	2 (5%)	0.942
Group C (Simvastatin)	18 (45%)	20 (50%)	2 (5%)	0.853

Table 6: Multivariate Logistic Regression Analysis for Predicting Cardiovascular Events

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Age (per 1-year increase)	1.05	1.02 - 1.09	0.003**
Male Gender	1.25	0.90 - 1.75	0.188
BMI (per 1-unit increase)	1.08	1.02 - 1.15	0.008**
Hypertension	1.55	1.10 - 2.18	0.015*
Diabetes	1.30	0.95 - 1.80	0.105

Smoking Status	1.75	1.20 - 2.55	0.002**
LDL (per 10 mg/dL increase)	1.12	1.05 - 1.20	0.001**
Statin (Rosuvastatin vs Atorvastatin)	0.85	0.55 - 1.25	0.325
Statin (Simvastatin vs Atorvastatin)	1.20	0.78 - 1.85	0.392

DISCUSSION

In this study, the mean age of patients across the atorvastatin, rosuvastatin, and simvastatin groups was 55.20 ± 5.13, 56.10 ± 5.08, and 54.90 ± 5.25 years, respectively (p = 0.765). This age distribution aligns with the patient population from the De Vera et al. (2010) study, where the average age of high-risk cardiovascular patients was around 56 years.[7] Similar gender distribution was observed, with males comprising 66.67% of Group A, 63.33% of Group B, and 70% of Group C (p = 0.854), which is comparable to Collins R et al (2002), where the proportion of males was 70%.[8]

BMI was also consistent across groups in this study, with an average of 27.40 ± 3.21 kg/m² in Group A, 26.90 ± 3.15 kg/m² in Group B, and 27.20 ± 3.18 kg/m² in Group C (p = 0.891). These values closely mirror those reported in the TNT trial (LaRosa et al., 2005), which found a mean BMI of approximately 28 kg/m² in patients receiving atorvastatin.[9] Hypertension, diabetes, and previous cardiovascular conditions were evenly distributed across groups in the current study, consistent with findings from Baigent et al. (2010), who reported similar rates of comorbidities in patients on statins.[10]

In this study, total cholesterol levels decreased from a baseline of 240.00 ± 12.35 mg/dL to 190.00 ± 8.45 mg/dL over 12 months (p = 0.001**). Similar reductions were observed in LDL cholesterol, from 160.00 ± 10.65 mg/dL to 110.00 ± 7.58 mg/dL (p = 0.001**), and triglycerides, from 180.00 ± 11.45 mg/dL to 130.00 ± 8.35 mg/dL (p = 0.001**). These improvements are in line with Ridker et al., (2008), which showed significant reductions in total and LDL cholesterol in patients receiving rosuvastatin, with LDL reductions from 155 mg/dL to 110 mg/dL.[11] Similarly, LaRosa et al., (2005) demonstrated a reduction in LDL from 164 mg/dL to 98 mg/dL with atorvastatin, comparable to the LDL reductions seen in this study's atorvastatin group.[9]HDL cholesterol levels in this study increased from 45.00 ± 4.25 mg/dL to 52.00 ± 3.89 mg/dL (p = 0.002**), which aligns with the Barter et al. (2007) study, which found HDL increases of around 7% in patients treated with statins. This increase in HDL is crucial, as even modest improvements in HDL levels have been associated with cardiovascular risk reduction in previous studies.[12]Cardiovascular events, including myocardial infarction, stroke, and angina, occurred at low rates across all groups. In this study, myocardial infarction occurred in 7.50% of patients in Group A, 5.00% in Group B, and 10.00% in Group C (p = 0.758). These rates are consistent with those reported in the Heart Protection Study (HPS, 2002), where major cardiovascular events occurred in around 9% of patients receiving simvastatin. Similarly, the Cannon et al. (2004) reported myocardial infarction rates of around 7% in patients receiving atorvastatin, which is comparable to the results observed here.[13]Stroke incidence in this study was 2.50% in Group A, 0.00% in Group B, and 5.00% in Group C (p = 0.522), which is similar to the stroke rates observed in the Jones PH et al, (2008) (2-3%).[14] Hospitalization for angina was reported in 10.00%, 7.50%, and 12.50% of patients in Groups A, B, and C, respectively (p = 0.835), which is comparable to hospitalization rates seen in the TNT trial (LaRosa et al., 2005), where around 11% of high-risk patients were hospitalized for angina despite statin therapy.[9]

Muscle pain (myopathy) was reported in 12.50% of patients in Group A, 10.00% in Group B, and 15.00% in Group C (p = 0.791), rates that are consistent with those found in the Jones et al. (2003)**,** which reported myopathy rates ranging from 10% to 16%, particularly at higher doses of statins like simvastatin.[14] Liver enzyme abnormalities were slightly more common in Group C (7.50%) compared to Groups A (5.00%) and B (2.50%), though the difference was not statistically significant (p = 0.661). These findings align with the Link et al. (2008), where elevated liver enzymes were more frequently observed with higher doses of simvastatin.[15]New-onset diabetes was reported in 2.50% of patients in Group A and 5.00% of patients in Groups B and C (p = 0.834). This is consistent with findings from the Sattar et al. (2010) meta-analysis, which identified a small but significant risk of diabetes associated with statin use, particularly at higher doses.[16]Dose adjustments were needed for 40.00% of patients in Group A, 35.00% in Group B, and 45.00% in Group C (p = 0.876). This pattern is in line with the Jones et al. (2003), which found that simvastatin often required dose escalation to achieve target lipid levels compared to rosuvastatin and atorvastatin, both of which were more potent in lower doses.[14] Maintenance of doses was common across all groups in this study, with 55.00%, 60.00%, and 50.00% of patients in Groups A, B, and C, respectively, maintaining their doses, which is consistent with findings from the TNT trial (LaRosa et al., 2005), where most patients remained on their initial dose throughout the follow-up period.[9]The regression analysis in this study revealed significant predictors of cardiovascular events. Age had an odds ratio (OR) of 1.05 (95% CI: 1.02-1.09, p = 0.003**), indicating that older age increases cardiovascular risk. This finding is supported by the Framingham Heart Study (2001), which identified age as one of the most significant risk factors for cardiovascular events. BMI was also a significant predictor, with an OR of 1.08 (95% CI: 1.02-1.15, p = 0.008**), consistent with the

ASCOT trial (Sever et al., 2003), which emphasized the role of obesity in cardiovascular risk.[17]Hypertension (OR: 1.55, 95% CI: 1.10-2.18, p = 0.015*) and smoking status (OR: 1.75, 95% CI: 1.20-2.55, p = 0.002**) were also significant predictors, aligning with findings from the Yusuf et al., (2004), which highlighted the substantial impact of these modifiable risk factors.[18] Interestingly, the type of statin (rosuvastatin or simvastatin compared to atorvastatin) did not emerge as a significant predictor of cardiovascular events, a finding that is consistent with the Cannon et al. (2004), which demonstrated comparable cardiovascular event rates across different statin therapies when used at appropriate doses.[16]

CONCLUSION

In conclusion, this study underscores the relative efficacy of atorvastatin, rosuvastatin, and simvastatin in mitigating cardiovascular events among high-risk individuals. While all three statins were effective in improving lipid profiles, atorvastatin and rosuvastatin demonstrated a potentially greater cardioprotective effect with a more favorable safety profile compared to simvastatin. These findings emphasize the necessity of individualized statin therapy, where selection is guided by both clinical efficacy and patient tolerability. Personalizing statin treatment strategies is essential for maximizing cardiovascular risk reduction and improving long-term outcomes in high-risk populations.

REFERENCES

1. Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA, Theroux P, Darius H, Lewis BS, Ophuis TO, Jukema JW, De Ferrari GM, Ruzyllo W, De Lucca P, Contos C, Kiss RG, Giugliano G, Huber K, Weerakkody G, Murphy SA, Tall AR, Braunwald E, Califf RM. Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes. N Engl J Med. 2015 Jun 18;372(25):2387-97.
2. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet*. 1994 Nov 19;344(8934):1383–9.
3. Shepherd J, Cobbe SM, Ford I, Isles CG, Lorimer AR, MacFarlane PW, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. *N Engl J Med*. 1995 Nov 16;333(20):1301–7.
4. Pedersen TR, Faergeman O, Kastelein JJ, Olsson AG, Tikkanen MJ, Holme I, et al. High-dose atorvastatin vs usual-dose simvastatin for secondary prevention after myocardial infarction: the IDEAL study: a randomized controlled trial. *JAMA*. 2005 Nov 16;294(19):2437–45.
5. LaRosa JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart JC, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med*. 2005 Apr 7;352(14):1425–35.
6. Cannon CP, Steinberg BA, Murphy SA, Mega JL, Braunwald E. Meta-analysis of cardiovascular outcomes trials comparing intensive versus moderate statin therapy. *J Am Coll Cardiol*. 2006 Aug 1;48(3):438–45.
7. De Vera MA, Bhole V, Burns LC, Lacaille D. Impact of statin adherence on cardiovascular disease and mortality outcomes: a systematic review. Br J Clin Pharmacol. 2010 Apr;69(6):714-24.
8. Collins R, Armitage J, Parish S, Sleigh P, Peto R; Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet. 2002 Jul 6;360(9326):7-22.
9. LaRosa JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart JC, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. N Engl J Med. 2005 Apr 7;352(14):1425-35.
10. Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet. 2005 Oct 8;366(9493):1267-78.
11. Ridker PM, Danielson E, Fonseca FA, Genest J, Gotto AM Jr, Kastelein JJ, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med. 2008 Nov 20;359(21):2195-207.
12. Barter PJ, Caulfield M, Eriksson M, Grundy SM, Kastelein JJ, Komajda M, et al. Effects of torcetrapib in patients at high risk for coronary events. N Engl J Med. 2007 Nov 22;357(21):2109-22.
13. Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, Joyal SV, Hill KA, Pfeffer MA, Skene AM. Intensive vs moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med. 2004 Apr 8;350(15):1495-504.
14. Jones PH, Davidson MH, Stein EA, Bays HE, McKenney JM, Miller E, Cain VA, Blasetto JW. Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin across doses (STELLAR Trial). Am J Cardiol. 2003 May 15;91(5):581-6.
15. Link E, Parish S, Armitage J, Bowman L, Wallendszus K, Matthews DR, Collins R, SLCO1B1 Variants and Statin-Induced Myopathy Consortium. SLCO1B1 variants and statin-induced myopathy—a genomewide study. N Engl J Med. 2008 Aug 21;359(8):789-99.
16. Sattar N, Preiss D, Murray HM, Welsh P, Buckley BM, de Craen AJ, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. Lancet. 2010 Feb 27;375(9716):735-42.
17. Sever PS, Dahlöf B, Poulter NR, Wedel H, Beevers G, Caulfield M, et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. Lancet. 2003 Apr 5;361(9364):1149-58.
18. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004 Sep 11;364(9438):937-52.