RESEARCH PAPER

Comparison of Atorvastatin and Rosuvastatin: A Literature Review

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ABSTRACT

Background:

Cardiovascular diseases (CVDs) are the leading cause of death globally, with a death toll of approximately 17.9 million lives each year. Studies indicate statins (especially Atorvastatin and Rosuvastatin) were effective in reducing cardiovascular events and all-cause mortality in primary prevention populations.

Objective:

To compare Atorvastatin and Rosuvastatin in four key domains: LDL-cholesterol reduction (including diabetic and non-diabetic populations), cardiovascular outcomes, adverse drug reactions, and economic considerations.

Methods:

This literature review was conducted using the PubMed database. Relevant studies were identified using combinations of MeSH terms and relevant keywords related to the study drugs and the outcomes under study.

Results:

The literature comparing Atorvastatin and Rosuvastatin were reviewed in the four major domains of LDL-cholesterol lowering, cardiovascular outcomes, ADRs and cost. It was found that, Rosuvastatin frequently demonstrates greater per-dose efficacy and higher rates of target attainment. Both statins reduce MACEs significantly, with Rosuvastatin showing slightly better outcomes in some populations, though more RCT evidence is needed. Rosuvastatin may have a higher acquisition cost but lower total cost. Overall, both Atorvastatin and Rosuvastatin demonstrate comparable safety profiles, with most adverse effects being dose-related and of low absolute risk, and their cardiovascular benefits substantially outweigh potential harms.

Conclusion:

This review integrates clinical outcomes, adverse effects, and economic considerations to provide a comprehensive comparison between Atorvastatin and Rosuvastatin. Overall, the choice between the two should be individualized based on patient risk profile, tolerability, and economic considerations.

Keywords: Statins, Atorvastatin, Rosuvastatin, Cvd, Ldl-c, Adverse effects, Cost.

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Introduction:

Cardiovascular diseases (CVDs) are the leading cause of death globally, with a death toll of approximately 17.9 million lives each year. Heart attacks and strokes account for more than four out of five CVD deaths, and one third of these deaths occur prematurely in people under 70 years of age (1). Studies indicate statins were effective in reducing cardiovascular events and all-cause mortality in primary prevention populations. Furthermore, data showed that Atorvastatin and Rosuvastatin were most effective in reducing CVD related events (2). Although statins are recommended as lifelong therapy for CVD risk reduction, long-term adherence in routine clinical practice is poor, with many patients discontinuing treatment due to perceived adverse effects, medication burden, and other financial considerations (3). Economic factors also play a crucial role in selecting a particular statin for therapeutic use, with Rosuvastatin frequently incurring higher initial acquisition costs than Atorvastatin despite both possessing similar, relatively higher efficacy in reducing CVD events (4). Existing studies often evaluate these agents individually or focus on the comparison between individual outcomes such as lipid reduction, cardiovascular events, adverse effects, or cost. A comprehensive comparison integrating clinical efficacy at LDL-C reduction, cardiovascular outcomes, safety profile, and economic considerations remains limited. Therefore, the present literature review was conducted to provide an integrated evaluation of Atorvastatin and Rosuvastatin across these key domains, offering a more holistic assessment to enhance clinical decision-making.

Methodology:

● Study Design: This literature review was conducted to compare Atorvastatin and Rosuvastatin in four key domains: LDL-cholesterol reduction (including diabetic and non-diabetic populations), cardiovascular outcomes, adverse drug reactions, and economic considerations.

● Data Source: A literature search was conducted using the PubMed database due to its comprehensive coverage of biomedical and clinical research literature.

● Search Strategy: Relevant studies were identified using combinations of MeSH terms and relevant keywords related to the study drugs and the outcomes under study.

● Eligibility Criteria:

 Inclusion Criteria: Studies comparing atorvastatin and rosuvastatin directly, studies reporting at least one of the following outcomes: LDL-C reduction (including diabetic populations), cardiovascular outcomes, adverse drug reactions, cost-effectiveness, randomized controlled trials, cohort studies, systematic reviews and meta-analyses with one or more of the same domains of study as the present study.

 Exclusion Criteria: None

● Study Selection:

 Titles and abstracts of retrieved articles were screened for relevance.

 Full-text articles of potentially eligible studies were then reviewed to determine suitability for inclusion.

 Studies meeting the eligibility criteria were included in the final analysis.

● Data extraction: Relevant data were extracted from each included study using a structured approach. Extracted information included: Study characteristics (author, year, design), population details (including presence of diabetes), drug type and dosage, key findings related to the four domains of interest.

● Outcomes of Interest:

 LDL-cholesterol reduction (in diabetic and non-diabetic populations)

 Cardiovascular outcomes (e.g., myocardial infarction, stroke, mortality)

 Adverse drug reactions (hepatic, renal, gastrointestinal, and others)

 Cost and cost-effectiveness

Result:

The literature comparing Atorvastatin and Rosuvastatin were reviewed in the four major domains of LDL-cholesterol lowering, cardiovascular outcomes, ADRs and cost. According to randomized controlled trials, observational studies, systematic reviews, meta-analyses and pharmacoeconomic analyses, both statins are clinically highly effective although there are differences in potency, safety profile, economic considerations. The results in the literature are summarized below regarding these domains.

1. **LDL-cholesterol reduction**:

Elevated levels of LDL and triglycerides, along with low levels of HDL, are key contributors to CVD. The two drugs atorvastatin and rosuvastatin are the most commonly used drugs to reduce LDL and triglycerides and increase HDL in patients, which is the central strategy in the primary and secondary prevention of CVD.

Evidence from multiple meta-analyses consistently demonstrates that both Rosuvastatin and Atorvastatin produce substantial reductions in low-density lipoprotein cholesterol (LDL-C), although Rosuvastatin consistently exhibited greater potency. In an East Asian population meta-analysis of 16 randomized controlled trials involving 5,930 participants, rosuvastatin achieved significantly greater LDL-C reduction than atorvastatin (weighted mean difference −7.15 mg/dL). This superiority was significant even when Rosuvastatin was administered at approximately half the dose of Atorvastatin, suggesting intrinsically higher lipid-lowering efficacy rather than a dose-dependent effect. The enhanced efficacy was consistent across both demographic and clinical variables, including age, sex, baseline LDL-C levels, and duration of follow-up, while both agents demonstrated comparable tolerability (5).

Similar findings were reported in a broader systematic review and meta-analysis evaluating changes in LDL, triglycerides (TG), and high-density lipoprotein cholesterol (HDL). In this analysis, Rosuvastatin produced a greater reduction in LDL-C compared with Atorvastatin (approximately 55.7 mg/dL vs. 51.5 mg/dL). Moreover, Rosuvastatin also demonstrated distinguished effects on other lipid parameters, including greater reductions in triglycerides and an optimized increase in HDL levels. These results proved that Rosuvastatin may help achieve a holistic improvement in the overall lipid profile, potentially translating into augmented CVD prevention, even when direct clinical outcomes weren't assessed (6).

Dose-equivalence data further highlight the potency differences between the two drugs. The VOYAGER meta-analysis, which considered 38,052 patient exposures, reported that equivalent reductions in LDL-C require substantially higher doses of atorvastatin compared with rosuvastatin (regarding reductions in LDL-C and non-HDL-C, each rosuvastatin dose is equivalent to doses 3-3.5 times higher for atorvastatin). For instance, rosuvastatin 5 mg produced LDL-C reductions comparable to atorvastatin 15 mg, whereas rosuvastatin 20 mg achieved reductions similar to approximately 70 mg of atorvastatin. At the highest studied dose, rosuvastatin 40 mg reduced LDL-C by about 55%, a magnitude not rivaled even by atorvastatin 80 mg. These findings highlight the substantially higher potency of rosuvastatin in lowering atherogenic lipoproteins (7).

Real-world observational evidence supports the enhanced lipid-lowering efficacy of Rosuvastatin compared with Atorvastatin in routine clinical practice. In a retrospective observational study of 1,100 adults receiving statin therapy for a least three months in a primary care setting, Rosuvastatin yielded the greatest mean reduction in LDL-cholesterol, followed by Atorvastatin. Differences between treatment groups were statistically significant, statin type along with intensity of treatment emerged as autonomous predictors of LDL reduction (8).

Evidence in patients with diabetes mellitus also demonstrates greater LDL-C lowering with Rosuvastatin at equivalent doses. In a cross-sectional analytical study of individuals with type 2 diabetes treated with 10 mg doses of either drug, a greater percentage of patients receiving Rosuvastatin achieved recommended LDL targets compared with those receiving Atorvastatin. This difference was noted as early as one month into therapy. By the end of the follow-up period, target attainment rates were substantially higher in the Rosuvastatin group, reinforcing its superior efficacy in diabetic populations, who typically require more aggressive lipid control due to elevated cardiovascular risk (9).

Network meta-analytic data examining statin therapy in diabetes further emphasize the importance of drug type and intensity of the treatment in lowering atherogenic lipoproteins. Rosuvastatin, at moderate and high intensity doses, and Atorvastatin, at high intensity doses, were most effective at moderately suppressing levels of non-HDL-C in patients with diabetes (10).

Collectively, these findings strengthen the central role of statin potency and intensity in attaining optimal lipid control. Across varied populations, such as primary care patients and individuals with diabetes, both Atorvastatin and Rosuvastatin consistently reduce LDL-cholesterol and related atherogenic lipoproteins. However, rosuvastatin frequently demonstrates greater per-dose efficacy and enhanced achievement of predefined targets.

2. **CVS Outcome Studies**:

Statins play a crucial role in the prevention of cardiovascular diseases. They are primarily used as lipid lowering drugs that reduce the risk of major adverse cardiovascular events (MACEs) by lowering LDL-c levels. Among the statins, Atorvastatin and Rosuvastatin are often preferred for their higher potency and longer duration of action. This literature review aims to summarize existing studies comparing the safety, efficacy of Atorvastatin and Rosuvastatin primarily in MACEs and their cost analysis.

According to a 2021 study, the most common components of MACEs are Acute myocardial infarction (AMI), stroke and all-cause death. This is also referred to as 3-point MACE (11).

Intensive reduction in low density lipoprotein (LDL) cholesterol levels is recommended in people with coronary artery disease or who are regarded as being at high risk or very high risk of future MACEs. Among the various lipid lowering drugs available, 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (statins) are the cornerstone of treatment, and high intensity statins are generally the choice for LDL cholesterol lowering treatment. Multiple studies conducted have not sufficiently evaluated the effect of different types of statins. Few randomized control trials, however have compared the long-term clinical outcomes of the two most potent statins-rosuvastatin and atorvastatin. Atorvastatin 80 mg/day or Rosuvastatin 40 mg/day are defined as high dose of statin because those average daily dosages reduce plasma LDL-C levels by 50% or greater. In addition to statins' efficacy in reducing LDL cholesterol levels and the risk of future adverse cardiovascular events, safety concerns, including statin related adverse effects and intolerance, should also be considered in real world practice (12,13).

Several randomized trials have compared the lipid-lowering efficacy of rosuvastatin and atorvastatin. It has been demonstrated that rosuvastatin reduced LDL cholesterol approximately 8% more than atorvastatin across comparable doses. Similarly, LDL reductions of 40–43% with rosuvastatin compared with approximately 35% with atorvastatin have been reported. Meta-analyses of randomized trials further support the superior LDL-lowering effect of rosuvastatin (14,15).

In a study, rosuvastatin, compared with atorvastatin, was associated with reducing the risk of the 1-year composite of recurrent stroke, MI, and all-cause mortality with an absolute risk reduction of 1% and a relative risk reduction of 11% (16,17).

Multiple studies thereby suggest that both atorvastatin and rosuvastatin significantly reduce the risk of major adverse cardiovascular events. Current evidence suggests rosuvastatin may offer slightly improved outcomes in certain populations, although further randomized trials are required to confirm these findings.

3. **Cost**:

Cost is another major factor that comes into play with statin therapy initiation in developing nations. Availability of Atorvastatin in the generic forms provides a cheaper alternative to the high priced Rosuvastatin. It was reported that in a low to moderate income setting, this difference is critical, as higher cost might ensue low adherence and even unreported discontinuation. In such a case if found to have similar effectiveness, Atorvastatin could be a more cost-effective choice (13).

A prescription bases cost analysis of medicines for cardiovascular risk factors suggests that, there was a huge difference in the price per medicine per year, ranging from INR 426 for generic NLEM(Atorvastatin) to INR 9318 for branded non-NLEM medicines (Rosuvastatin) which is 22 times higher. They also reported that use of Rosuvastatin in 39 million patients with dyslipidemia, costed approximately INR 363.4 billion, which could have been INR 16.6 billion if atorvastatin was prescribed, causing over expenditure of INR 346.8 billion (18).

Whereas in developed countries like USA, Spain, the results favored rosuvastatin A study suggests, Atorvastatin 10 mg had a lower acquisition cost than rosuvastatin 10 mg, yet the total first-year cost of rosuvastatin was lower because of greater effectiveness at the starting dose, which prevented titrations in all but 16% of patients. Moreover, the flat price of rosuvastatin minimized the economic impact when patients were titrated. Conversely, 37% of patients treated with atorvastatin required at least one titration. In addition to more frequent physician monitoring and laboratory tests, drug costs increased substantially at higher doses of atorvastatin (19).

A pharmacoeconomic analysis comparing rosuvastatin with other statins including atorvastatin in patients with high cardiovascular risk in the Spanish population. Although rosuvastatin had a higher acquisition cost, it produced greater health benefits and more quality-adjusted life years, resulting in favourable incremental cost-effectiveness ratios. The study concluded that rosuvastatin is a cost-effective treatment option, particularly in patients with higher baseline cardiovascular risk (20).

4. **Adverse Effects**:

Despite their well-established efficacy and overall favorable safety profile in reduction of cardiovascular mortality and morbidity as well as cardiovascular events in patients with a very high risk of cardiovascular disease (CVD) and also in subjects with high or moderate risk by reducing the levels of low-density lipoprotein cholesterol (LDL-C), statins are frequently associated with concerns regarding adverse effects because of their wide use. There are many concerns that their adverse effects might compromise their proven beneficial effects. Clinically significant adverse effects include myopathy, rare rhabdomyolysis, and reversible elevations in hepatic transaminases, while a modest increase in the risk of type 2 diabetes mellitus has also been reported. Nevertheless, the cardiovascular benefits of statin therapy markedly outweigh these potential risks (21).

In a multi-database cohort study, comparing effectiveness and safety of the two drugs it was noted that among the 285,680 eligible participants in both databases, 6-year all-cause mortality was lower for Rosuvastatin than for Atorvastatin. It was also seen that Rosuvastatin has been associated with a higher risk of development of type 2 diabetes mellitus, while both agents demonstrate similar risks for chronic kidney disease and other statin-related adverse effects, with Rosuvastatin showing a lower risk of major adverse liver outcomes (17).

A prospective observational study in the UAE's multiethnic population undertaken to provide pharmacogenomic insights into Atorvastatin and Rosuvastatin adverse effects focusing on statin-associated muscle symptoms and liver enzyme elevation as main adverse effects, revealed SLCO1B1 and ABCG2 variants as actionable pharmacogenomic markers. In case of Rosuvastatin, a threefold increased risk of liver enzyme elevation was noted in patients carrying ABCG2 rs2231142 variant. Particularly pronounced liver enzyme elevation was also noted among East Asian patients. Drug combination of Rosuvastatin and Ezetimibe was also noted to exacerbate statin-associated muscle symptoms (SAMS) and liver enzyme elevation risks. Atorvastatin was associated with a higher incidence rate of SAMS, with a twofold increased risk in patients with SLCO1B1 rs4149056 variant, higher SAMS rates observed in females and higher SAMS rates observed in Arabs (22).

In a pharmacovigilance comparative study focusing on the occurrence of rhabdomyolysis with statins therapy taking into account 10,657 reports of rhabdomyolysis with statins as identified in VigiBase® (WHO pharmacovigilance database) as of December 31, 2022 included 73.7% of the reports classified as "serious" with 375 fatal cases and 5,363 causing/prolonging hospitalization. A comparative risk ranking was drawn comparing each statin, and Atorvastatin was associated with the second highest risk for rhabdomyolysis reporting followed by Rosuvastatin at the third position (23).

In clinical practice, patients often avoid or cease statin use due to adverse reactions. To elucidate statin adverse reactions, their variability across diseases, and the factors influencing them, a high-quality clinical trial-based meta-analysis was conducted. The study concluded that statins' adverse reactions differ across populations. It was also found that myalgia risk in hypercholesterolemia and coronary disease patients using different statins is comparable, but those with acute coronary syndrome or stroke, especially on high-dose rosuvastatin, have a higher myalgia risk (24).

A study conducted to compare the effects of maximum doses of rosuvastatin and atorvastatin on the plasma levels of the insulin, glycated albumin, adiponectin, and C-reactive protein compared to baseline in hyperlipidemic patients, studied 252 hyperlipidemic men and women who had been randomized to receive atorvastatin 80 mg/day or rosuvastatin 40 mg/day during a 6-week period. The study confirmed concerns about statin effects on glucose homeostasis, with both drugs showing a significant rise median insulin level. However, only Atorvastatin increased glycated albumin levels from the baseline while Rosuvastatin decreased them. Both Atorvastatin and Rosuvastatin caused significant and similar median reductions in the C-reactive protein level of -40% and -26% compared to the baseline values. However, no statistically significant difference was found between the 2 groups in the adiponectin changes from baseline (25).

Statin product labels list certain adverse outcomes as potential treatment-related effects based mainly on non-randomised and non-blinded studies, which might be subject to bias. A study was conducted, aimed to assess the evidence for such undesirable effects more reliably through a meta-analysis of individual participant data from large double-blind trials of statin therapy. 19 trials compared statins versus placebo

(123,940 participants, median follow-up 4·5 years), 66 prespecified adverse outcomes from statin product labels were assessed. Key findings showed on 4 out of 66 outcomes showed significant excess risk (abnormal liver transaminases, other liver function test abnormalities, urinary composition alteration, oedema). The study noted that event rate ratios were significantly greater in the trial of atorvastatin 80 mg versus placebo than the trial of rosuvastatin 20 mg versus placebo for both abnormal liver transaminases and other liver function test abnormalities. Overall, this study demonstrated that the vast majority of adverse effects listed in statin product labels are not supported by evidence from randomized controlled trials, with only liver function abnormalities showing a clear causal relationship, particularly with high-dose atorvastatin (26).

With respect to renal effects, both agents are not associated with clinically significant deterioration in renal function or an increased risk of acute kidney injury, although mild and transient proteinuria may occur, particularly with high-dose therapy, without impacting overall renal function. Rosuvastatin, a hydrophilic statin, requires cautious dose adjustment in patients with severe renal impairment due to its renal handling, whereas atorvastatin, being lipophilic, is less dependent on renal clearance. Hepatic adverse effects are more clearly characterized with Atorvastatin, with dose-dependent elevations in liver enzymes and rare instances of hepatotoxicity, although the absolute risk remains low. High-dose atorvastatin has also been associated with a small increase in hemorrhagic stroke risk in certain high-risk populations, though this has not been consistently supported by larger meta-analyses.

Overall, both Atorvastatin and Rosuvastatin demonstrate comparable safety profiles, with most adverse effects being dose-related and of low absolute risk, and their cardiovascular benefits substantially outweigh potential harms (27).

Results of comparison of Atorvastatin and Rosuvastatin in terms of LDL-C reduction	
Citation	Key Finding
(5)	Rosuvastatin produces a greater LDL-C reduction than Atorvastatin at half the dose, indicating higher intrinsic potency.
(6)	Rosuvastatin shows greater reductions in LDL-C and triglycerides and a larger increase in HDL compared to Atorvastatin. Thus, improving overall lipid profile.
(7)	Rosuvastatin is approximately 3–3.5 times more potent than Atorvastatin.
(8)	Real-world observational evidence confirm Rosuvastatin achieves greater LDL-C reduction than Atorvastatin.
(9)	In type 2 diabetes, Rosuvastatin leads to higher rates of LDL target attainment than Atorvastatin at equivalent doses.
(10)	In diabetic patients, moderate/high dose rosuvastatin and high dose atorvastatin are most effective in reducing non-HDL cholesterol.
Conclusion: Rosuvastatin frequently demonstrates greater per-dose efficacy and higher rates of target attainment**.**	

Results of comparison of Atorvastatin and Rosuvastatin in terms of CVS outcome studies	
Citation	Key Finding
(11)	Major adverse cardiovascular events (MACEs) commonly include AMI, stroke, and all-cause mortality (3-point MACE).

(12,13)	High-intensity statins (atorvastatin 80 mg or rosuvastatin 40 mg) reduce LDL-C by ≥50% and are standard in high-risk patients, though safety and intolerance must be considered.
(14,15)	Rosuvastatin consistently produces greater LDL-C reduction than atorvastatin across comparable doses.
(16,17)	Rosuvastatin is associated with lower 1-year risk of recurrent stroke, MI, and all-cause mortality with an absolute risk reduction of 1% and a relative risk reduction of 11%.
Conclusion: Both statins reduce MACEs significantly, with rosuvastatin showing slightly better outcomes in some populations, though more RCT evidence is needed.	

Results of comparison of Atorvastatin and Rosuvastatin in terms of cost	
Citation	Key Finding
(13)	Atorvastatin is more cost effective in low to middle income settings due to lower price and better adherence compared to expensive Rosuvastatin.
(18)	Large cost differences exist, with Rosuvastatin being approximately 22 times more expensive, leading to massive healthcare over-expenditure compared to Atorvastatin.
(19)	In developed countries, Rosuvastatin may have lower overall treatment cost due to higher efficacy and fewer dose titrations despite having a higher initial cost.
(20)	Rosuvastatin is cost-effective in high-risk patients by providing greater health benefits and improved quality-adjusted life years despite higher acquisition cost.
Conclusion: Rosuvastatin may have higher acquisition cost but lower total cost.	

Results of comparison of Atorvastatin and Rosuvastatin in terms of adverse effects	
Citation	Key Finding
(21)	Statins may cause myopathy, rare rhabdomyolysis, liver enzyme elevation, and slight diabetes risk, but benefits far outweigh risks.
(17)	Rosuvastatin shows lower all-cause mortality but higher diabetes risk, with similar CKD risk and lower major liver adverse outcomes compared to Atorvastatin.
(22)	Pharmacogenomics influences adverse effects: Atorvastatin has higher SAMS risk, while Rosuvastatin shows increased liver enzyme elevation, especially in certain high-risk populations.

(23)	Atorvastatin has the second highest and Rosuvastatin the third highest reported risk of rhabdomyolysis among the statins group.
(24)	Myalgia risk is generally similar across statins, but high-dose Rosuvastatin may increase risk in acute coronary syndrome or stroke patients.
(25)	Both statins increase insulin levels, but Atorvastatin worsens glycemic markers more, while both similarly reduce CRP levels.
(26)	Most statin adverse effects listed in statin product labels aren't backed by RCT evidence, with liver enzyme abnormalities being the main confirmed risk, especially with high-dose Atorvastatin.
(27)	Both statins have comparable safety with low absolute risk. Atorvastatin shows more hepatic effects, while Rosuvastatin requires caution in renal impairment.
Conclusion: Overall, both Atorvastatin and Rosuvastatin demonstrate comparable safety profiles, with most adverse effects being dose-related and of low absolute risk, and their cardiovascular benefits substantially outweigh potential harms.	

Discussion:

1. **LDL-cholesterol reduction**:

Both Atorvastatin and Rosuvastatin produce significant reductions in LDL-C levels across studies. Rosuvastatin consistently showed slightly greater LDL-C reduction compared to Atorvastatin at comparable doses, proving that it's more potent. The consistent superiority of Rosuvastatin is multifactorial including additional enzyme-binding interactions leading to stronger binding to HMG-CoA reductase enzyme which increases its efficiency in inhibiting cholesterol synthesis, its hydrophilic nature also makes it hepatoselective (poor penetration in extrahepatic tissues) leading to poor penetration into extra-hepatic tissues and a more liver-specific action, which's the main site of cholesterol synthesis. On the other hand, Atorvastatin is lipophilic and is widely distributed in extrahepatic tissues and its binding to HMG-CoA reductase is effective but less tight binding. (28,29)

Rosuvastatin achieves the same level of LDL reduction at a dose about three times lower than that of Atorvastatin. Across multiple studies and meta-analyses Rosuvastatin also shows greater increase in HDL and greater reduction in triglycerides, thus making it potent across all lipid parameters, not just LDL. However, high-intensity atorvastatin achieves similar reductions. Though clinically, treatment intensity (moderate vs high) is a stronger determinant of LDL reduction than the specific statin. LDL reduction also varies with patient-factors such as, baseline LDL levels, cardiovascular risk status and presence of other comorbidities. For example, in patients at a greater risk of major cardiovascular events, atorvastatin at high intensity showed the largest reduction in levels of non-HDL-C. Combination therapy is another factor contributing in achieving therapeutic targets along with statins, for example adding ezetimibe significantly increases goal attainment.

Overall, while Rosuvastatin may provide marginally superior LDL-C reduction, both statins demonstrate robust lipid-lowering efficacy, and the choice between them should be directed by patient-specific factors, such as cardiovascular risk profile, tolerability, cost, and therapeutic goals. (5–10)

2. **CVS Outcome Studies**:

Statins play a vital role in the risk of reduction of major CVS events (MACEs), including MI, stroke, and all-cause mortality, primarily through the reduction of LDL-C levels. Among them, Atorvastatin and Rosuvastatin are the most potent agents and are used as high-intensity therapies. On the basis of multiple randomized trials and meta-analyses both drugs significantly reduce LDL-C, while Rosuvastatin provides a modestly greater reduction when compared to Atorvastatin at equivalent doses. Furthermore, evidence suggests rosuvastatin may offer slightly improved outcomes in some populations, although further randomized trials are required to confirm these findings.

The association between increased initiation of rosuvastatin use and lower all-cause mortality versus atorvastatin can be explained by its stronger cardiovascular protective effect. Previous studies have suggested but not confirmed a difference between rosuvastatin and atorvastatin in protecting against MACEs. Rosuvastatin's protective effect may be attributed to its pleiotropic effects. For example, it is more effective than atorvastatin at reducing LDL-C. Previous studies also reported that, compared with atorvastatin, rosuvastatin results in a higher reduction in the inflammatory markers associated with progression of coronary atheroma and decreases levels of C-reactive protein. Additionally, rosuvastatin has a lower likelihood for drug interactions than other statins. (11–17)

3. **Cost**:

Cost is an essential component in statin therapy selection in low- and middle-income settings, Atorvastatin, which is available in generic formulations is much more affordable when compared to Rosuvastatin, and this cost difference plays an important role in influencing drug adherence and long-term persistence. In such settings, atorvastatin may represent a more cost-effective option when clinical effectiveness is comparable.

Whereas in high-income countries, pharmacoeconomic analyses indicate despite its higher acquisition cost, rosuvastatin may be cost-effective due to greater efficacy at lower doses, reduced need for dose titration, and improved quality-adjusted life years. Therefore, cost-effectiveness of these drugs depends on various factors such as the healthcare systems and patient populations.

Cost is a major barrier to access and adherence, in low- and middle-income countries like India, generic Atorvastatin is substantially cheaper. It is also to be noted that price differences can be 5-22 times higher for branded drugs. In case of Atorvastatin, its inclusion in the National List of Essential Medicines (NLEM) along with its generic availability plays a role in reduction of its cost burden. This shows the significance of policy-level decisions (NLEM inclusion) on drug affordability.

Higher upfront cost may also be offset by better therapeutic outcomes. In some analyses, Rosuvastatin proved to be more effective and cheaper overall due to its greater LDL reduction and overall higher therapeutic goal attainment rates. More patients reach targets at initial doses leading to fewer clinical visits, tests and adjustments leading to lower overall costs. On the other hand, Atorvastatin requires more dose escalation. Thus, Rosuvastatin may have higher acquisition cost but lower total cost.

Considering population-level economic impact, small differences per patient yields a massive impact at a population level, leading to billions in potential savings in the healthcare system of the nation. As far as policy and prescribing implications are concerned, generic prescribing and NLEM adherence is encouraged which can significantly reduce healthcare burden. (18–20)

4. **Adverse Effects:**

Statins are widely used in reducing cardiovascular morbidity and mortality. However, their extensive use has raised concerns regarding adverse effects. Clinically significant reactions are uncommon and include myopathy, rare rhabdomyolysis, reversible elevations in hepatic transaminases, and a modest increase in the risk of Type 2 Diabetes Mellitus. Evidence suggests that while both agents share broadly comparable safety profiles, Rosuvastatin may be associated with a slightly higher risk of diabetes, whereas atorvastatin has shown a greater risk for muscle-related symptoms and liver enzyme abnormalities, particularly at higher doses. Pharmacogenomic factors and patient characteristics can further influence adverse effect susceptibility. Importantly, most adverse effects are dose-related, population-specific, and of low absolute risk, and the overall cardiovascular benefits of statin therapy substantially outweigh these potential harms.

The differences in risk for adverse effects between the two drugs were relatively small, and many did not meet traditional standards for statistical significance. Further research is needed to understand whether these findings can be used with confidence in clinical practice. The overall incidence of adverse effects remains comparable between Atorvastatin and Rosuvastatin. Adverse effects appear to be primarily dose-dependent rather than drug-specific, with higher intensity regimens contributing to increased intolerance.

Emerging pharmacogenomic evidence suggests that genetic variability significantly influences statin tolerability, highlighting the potential for individualized therapy. Despite a strong safety profile, perceived adverse effects remain a key contributor to discontinuity of statins in clinical practice. (17,21–27)

Conclusion:

While prior studies have predominantly focused on discrete factors such as efficacy or safety, this review integrates clinical outcomes, adverse effects, and economic considerations to provide a comprehensive comparison between Atorvastatin and Rosuvastatin.

Both Atorvastatin and Rosuvastatin are highly effective statins that significantly reduce LDL-C and thus reduce the risk of cardiovascular morbidity and mortality. Rosuvastatin demonstrates greater per-dose potency and slightly superior lipid-lowering efficacy, although high-intensity Atorvastatin achieves comparable outcomes. The safety profiles of both drugs are broadly similar, with most adverse effects being dose-dependent and clinically mild. Cost remains plays a major role with Atorvastatin being more affordable in low-resource settings, while Rosuvastatin may be more cost-effective in certain high-risk populations. Overall, the choice between the two should be individualized based on patient risk profile, tolerability, and economic considerations.

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