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Impact of Statin in Patients Depending on Risks and Age Groups: An Explanatory Review

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Abstract: Statins are commonly administered to older individuals; nevertheless, low-risk patients may receive excessive medication, while high-risk patients may receive insufficient treatment. The risk of atherosclerotic cardiovascular disease (ASCVD) and mortality has significantly increased with age in recent times. There are differences over the benefits and drawbacks of statin medication for the elderly; strong data supports secondary prevention but less supports primary prevention. Guidelines and concerns for statin medication are discussed, focusing on the 10-year ASCVD risk of persons without diabetes aged 40-75. For low risk, moderate-to-high-intensity statins are recommended; for intermediate-risk, moderate-to-high-intensity statins; and high-risk, high-intensity statins. Adults with cardiovascular diseases (CVD) are prescribed moderate-intensity statins, whereas those with additional risk factors are prescribed high-intensity statins. This is the updated review focused on the application of statins in patients depending on risk with different age groups to increase the therapeutic efficacy and decrease the toxicity of statins. Primary prevention focuses on lifestyle modifications. Treatment decisions are customized based on life expectancy, comorbidities, and side effects.

Keywords: Statins, Risk factor, Cardiovascular disease, Patients, Prevention, Comorbidities

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Introduction

The appropriateness of statin prescriptions in patients across different age and risk groups, with a particular focus on the elderly population (Dash *et al.*, 2022). This updated review focused on the application of statins to treat patients based on

risk across various age groups to maximize therapeutic efficacy and minimize statin toxicity. This review study aims to determine whether statins are prescribed according to established clinical guidelines and

whether their use is justified based on patient-specific risk factors and potential benefits. It focuses on analyzing the patterns of statin prescriptions among various age brackets, particularly elderly patients aged above 75 years and those aged above 80 years. Globally, high low-density lipoprotein cholesterol (LDL-C) is a key risk factor for atherosclerosis, which causes cardiovascular events including heart attacks and strokes (Khamkat *et al.*, 2022). Due to its capacity to block the enzyme HMG-CoA reductase, which efficiently lowers LDL-C synthesis in the liver, statins, a family of lipid-lowering drugs, have shown to be particularly successful in treating elevated cholesterol levels. Prescription of statins is not a one-size-fits-all approach because there are several factors to consider, such as age, gender, comorbidities, and overall risk profile (Shurraw and Tonelli, 2006). Guidelines from prestigious health organizations provide tailored guidance for different patient groups. Individuals without diabetes between the ages of 40 and 75 who are at risk of atherosclerotic cardiovascular disease (ASCVD) for the next ten years are advised to begin taking statin medication. Statins reduce the incidence of recurrent cardiovascular events, making them crucial for secondary prevention in those with existing ASCVD. To guarantee the safe and efficient use of statins, certain populations, such as women of reproductive age, people with liver disease, and people experiencing muscular complaints associated with statin usage, need special care (Newman, 2022). Despite the widespread use of statins, their appropriateness across different age groups and patient risk categories remains an area of active research.

The study uses a retrospective cross-sectional design over a half-yearly period to analyze statin prescription patterns among patients of different risk and age groups. This comprehensive analysis ensures a comprehensive understanding of prescribing trends, patient demographics, and the effectiveness and appropriateness of statin therapy across diverse patient profiles (Kones and Rumana, 2015a). The plan guarantees a

thorough comprehension of the use of statin medication and its efficacy across a range of patient demographics.

(1) Data Collection:

Setting

Data collection occurs in multiple hospitals and pharmacy outlets across various healthcare providers. This multi-centre approach ensures a representative sample of the population, minimizing regional biases and increasing the generalizability of the study findings.

Participants

The study includes patients who have been prescribed statins for Dyslipidaemia, hypercholesterolemia, or cardiovascular disease prevention. Participants are stratified into different risk categories based on their clinical history, including primary and secondary prevention groups. Furthermore, patients are categorized into four age groups: under 45, 45-64, 65-74, and 75 years and above (Shurraw and Tonelli, 2006).

(2) Survey and Data Extraction:

Survey Administration

A structured survey is administered to patients and healthcare providers at hospitals and pharmacy outlets. The survey includes questions about:

- a. Demographic information (age, gender, etc.)
- b. Medical history (diagnosis, comorbidities, etc.)
- c. Current medications (including dose and duration of statin therapy)
- d. Lifestyle factors (smoking, alcohol consumption, diet, exercise)
- e. Adherence to medication
- f. Side effects and adverse events experienced

Data Extraction from Medical Records

Medical records are reviewed to extract relevant data, including:

- Laboratory results (cholesterol levels, liver function tests)
- Prescription details (type of statin, dosage, frequency)
- Clinical outcomes (incidence of cardiovascular events, hospital admissions)

Risk Stratification

Participants are classified into different risk categories based on established guidelines. Risk factors considered include:

- Age and gender
- Total cholesterol and HDL-C levels
- Blood pressure
- Current Smoking status
- Diabetes mellitus
- Family history on cardiovascular disease

Age Group Classification

Participants are grouped into different age categories to analyse the age-related differences in statin prescription patterns and outcomes. The groups include:

- Below 45 years
- 45-64 years
- 65-74 years
- 75 years and older

(3) Data Analysis:

Statistical Analysis

The baseline characteristics of the study population are obtained using descriptive statistics. The prevalence of statin use, adherence rates, and incidence of adverse effects are calculated for each age and risk group.

Outcome Measures

The percentage of patients who reach their goal cholesterol levels and the frequency of cardiovascular events that occur throughout the research period are the main objectives and measures. Secondary outcomes include

medication adherence rates, the prevalence of adverse effects, and patient-reported quality of life (McGinnis *et al.*, 2007).

Analysis tool

The 10-year ASCVD (Atherosclerotic Cardiovascular Disease) risk calculator is a vital resource for estimating an individual's chance of having a heart attack or stroke, especially if they have dyslipidaemia. Unusual blood lipid levels, or dyslipidaemia, are a substantial risk factor for cardiovascular illnesses (Zoungas *et al.*, 2014). Using this calculator, medical practitioners may assess if statin medication is necessary to control cholesterol levels and lower the risk of cardiovascular disease.

(4) Parameters of ASCVD Risk Calculator:

Lipid Levels

(a) Low-Density Lipoprotein, or LDL Cholesterol: Often called "bad cholesterol," elevated LDL cholesterol levels raise the risk of ASCVD by causing plaque to accumulate in the artery.

(b) High-Density Lipoprotein, or HDL Cholesterol: HDL, also referred to as "good cholesterol," aids in the removal of LDL cholesterol from the blood. Reduced risk of heart disease is linked to higher levels of HDL cholesterol (Kones and Rumana *et al.*, 2015b).

Risk Factors

(a) **Age:** The risk of ASCVD increases with age. The calculator is typically used for adults aged 20-79 years.

(b) **Sex:** Men are generally at higher risk of ASCVD at an earlier age compared to women.

(c) **Blood Pressure:** One of the main risk factors for stroke and heart disease is high blood pressure.

(d) **Smoking Status:** Smoking significantly increases the risk of cardiovascular diseases.

(e) **Diabetes:** Diabetes poses a significant risk for ASCVD.

(f) **Total Cholesterol:** High total cholesterol levels

contribute to a higher ASCVD risk.

(g) **Race:** Certain racial groups, such as African Americans, have higher risks of ASCVD.

(5) *Using the ASCVD Risk Calculator:*

Using the given parameters, the calculator calculates the 10-year risk of a cardiovascular event. The result, which typically indicates the probability of encountering an ASCVD incident during the following ten years, is expressed as a percentage. Healthcare professionals use the Atherosclerotic Cardiovascular Disease (ASCVD) Risk Calculator from the American College of Cardiology (ACC). Another name for it is ASCVD Risk Estimator Plus. This tool evaluates the risk of heart disease over the next ten years for an individual between the ages of 40 and 79. The term "atherosclerotic" describes artery hardening or narrowing. Heart disease gets worse because of this issue. For those aged 20 to 59, the program may also calculate their lifetime risk of heart disease (Wong *et al.*, 2015). This trustworthy heart risk calculator was created in partnership between the American Heart Association (AHA) and the ACC. The online AHA Cardiovascular (CV) Risk Calculator is a more straightforward version of the ASCVD Risk Calculator, requiring fewer answers. Nonetheless, your results ought to be almost the same. Another tool used by clinicians to determine how a certain therapy might increase your risk status is the ASCVD Risk Calculator. For example, lowering high cholesterol with a statin may move you from an intermediate risk to a borderline or low risk. The heart risk calculators from the ACC and AHA both offer suggestions for ways to lower your risk score (Ruscica *et al.*, 2024). Additionally, the ASCVD Risk Calculator can demonstrate how a few of these actions can help avoid heart disease:

(a) Begin taking cholesterol-lowering drugs or up the dosage.

(b) Take a blood pressure medication now or add another.

(c) Begin or carry out aspirin treatment.

(d) Give up smoking.

(6) *Data Visualization:*

Data visualization plays a crucial role in understanding the relationship between ASCVD (Atherosclerotic Cardiovascular Disease) and its risk factors. There are several risk factors associated with ASCVD, and each one affects the total risk uniquely. Complex interactions may be made simpler with the use of visualizations, which can also assist in identifying important patterns and trends that are difficult to see in raw data. It aids in identifying the risk variables that most significantly affect ASCVD. Healthcare professionals may more quickly and reliably identify patients who are at high risk for ASCVD by visualizing patient data. This makes it possible to implement prompt treatments and lifestyle modifications that can stop the disease from starting. Visualization tools may monitor the impact of treatments over time, assisting in the assessment of the efficacy of risk factor reduction initiatives and identifying areas that may require modification (Ruscica *et al.*, 2014). The plotted line graph (Fig. 1) shows the 10-year ASCVD risk percentage across different age groups for hypothetical LDL and HDL levels.

(7) *ASCVD Risk Factors and Their Impact:*

To understand the influence of different risk factors on Atherosclerotic Cardiovascular Disease (ASCVD), we may examine each component separately and its contribution to the total risk (Ruscica *et al.*, 2018). Table 1 shows the contribution of different risk factors to the ASCVD risk score.

High-Risk Individuals

Individuals who have a 20% or greater 10-year risk of ASCVD are deemed high-risk. It is frequently advised to use statin medication to lower LDL cholesterol levels and control risk.

Intermediate-Risk Individuals

Those with a risk of 7.5% to 19.9% may benefit from statins, particularly if other risk factors are present.

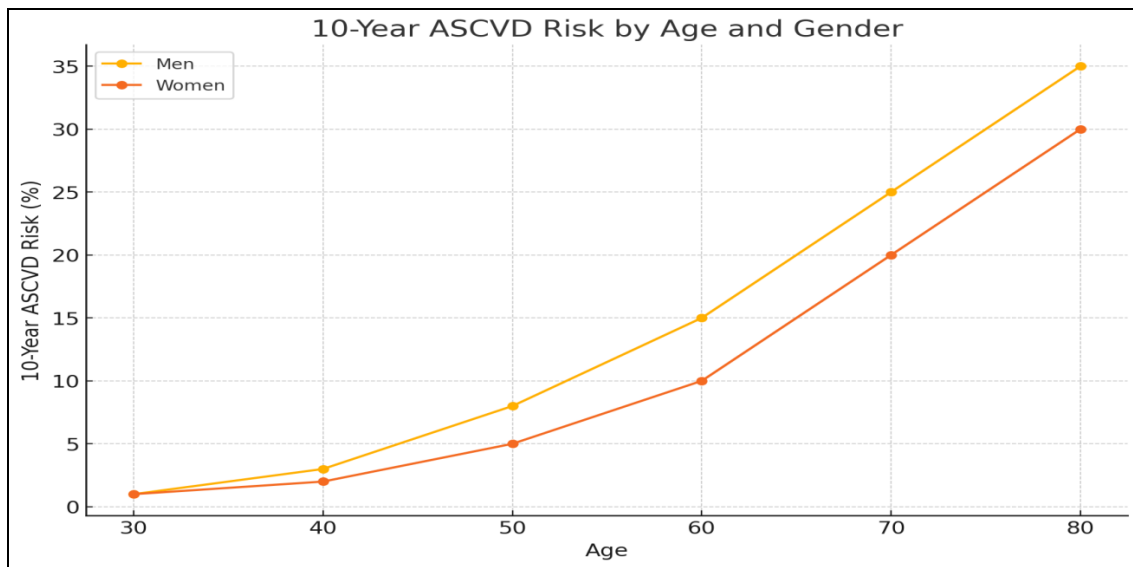


Fig. 1: Graphical representation of Age vs. 10-year ASCVD Risk.

Table 1: List of risk factors with their contribution

Risk Factor	Contribution to Risk
Age	Increases with age
Sex	Men generally higher
LDL Cholesterol	Higher LDL, higher risk
HDL Cholesterol	Higher HDL, lower risk
Blood Pressure	Higher BP, higher risk
Smoking	Significant increase
Diabetes	Significant increase
Total Cholesterol	Higher levels, higher risk
Race	Varies by racial group

Low-Risk Individuals

Individuals with a risk below 7.5% might not need statin therapy but should focus on lifestyle modifications to manage cholesterol levels and overall cardiovascular health.

The ASCVD+ risk calculator is a valuable tool for assessing cardiovascular risk and guiding treatment decisions in individuals with dyslipidaemia. Healthcare practitioners can customize therapies to lower the risk of heart attack and stroke by considering lipid levels, age, sex, blood pressure, smoking status, diabetes, total cholesterol, and race. Visual aids for compre-

hension and communication include tables and line graphs (Kumar *et al.*, 2009).

Applications

Clinical Benefits of Statins:

It has been demonstrated that statins lower LDL-C levels and stop significant cardiovascular events, with large-scale clinical trials showing significant reductions in strokes, myocardial infarctions, and revascularization procedures. According to the Scandinavian Simvastatin Survival Study, statins decreased coronary death by 42% and overall mortality by 30% in individuals with coronary heart disease. In

addition to stabilising atherosclerotic plaques, statins also lower inflammation and enhance endothelial function, which makes them an essential part of both primary and secondary CVD preventive methods (Hendrani *et al.*, 2016).

Safety with Adverse Effects:

Although they are usually well tolerated, statins can have unfavourable side effects such as myopathy and liver damage. Severe muscle toxicity is low but dose-related. Combining statins with other drugs can increase myopathy risk. Careful monitoring and dose adjustments are necessary when statins are prescribed with drugs like cyclosporine, erythromycin, and certain antifungals (Laufs *et al.*, 2019).

Statin Prescription Guidelines:

The American Heart Association, American College of Cardiology, and European Society of Cardiology have developed guidelines for statin therapy, emphasizing its importance in managing patients at risk of cardiovascular events. These guidelines provide detailed recommendations based on patient-specific factors like age, comorbidities, and overall risk profile. Statin therapy is advised by the AHA/ACC guidelines for patients with established atherosclerotic cardiovascular disease, those with LDL-C levels ≥ 190 mg/dl, patients with diabetes who are 40–75 years old and have LDL-C levels 70–189 mg/dl, and non-diabetic individuals whose estimated 10-year risk of ASCVD is 7.5% or higher (Nissen *et al.*, 2023).

Statin Use in Different Age Groups:

Statin therapy is beneficial for younger patients, particularly those under 75 years old, as it reduces LDL-C levels and cardiovascular events. However, older patients (75+ years) are more controversial due to their multiple comorbidities and higher risk of adverse drug reactions. Despite these concerns, evidence suggests that statins can still provide significant cardiovascular benefits in older populations (Kopp *et al.*, 2024). Meta-analyses show that the absolute risk reduction for cardiovascular events with statin therapy is

greater in older patients due to their higher baseline risk. The decision to initiate or continue statin therapy in elderly patients should be individualized (Garg *et al.*, 2018).

Statin Use in Different Risk Groups:

A patient's cardiovascular risk profile is used to determine the course of treatment for statin medication. High-risk individuals, including those with a history of cardiovascular events, hypertension, diabetes, and smoking, benefit the most from statin therapy (Allen Maycock *et al.*, 2002). Moderate-risk patients also benefit from statin therapy, but the absolute risk reduction is smaller. Low-risk patients have fewer clear benefits, and the decision to initiate treatment should be based on a thorough assessment of potential risks and benefits (Chatzizisis *et al.*, 2010).

Compliance with Statin Treatment:

Compliance with statin treatment is crucial for optimal cardiovascular outcomes, but non-adherence is common. Factors influencing adherence include patient understanding of benefits and side effects, medication regimen complexity, and communication quality. Improving adherence requires patient education, simplifying regimens, and addressing side effects concerns. Healthcare providers play a key role in encouraging adherence by discussing the importance of consistent statin use and addressing any barriers patients may face (Bideberi and Mutagaywa, 2022).

Efficacy Across Age Groups

(1) Younger Patients (<75 Years): In those under 75 years old, statins are quite successful in lowering LDL-C levels and avoiding cardiovascular events like strokes and myocardial infarctions. Clinical trials and studies indicate a significant reduction in morbidity and mortality, making statins a cornerstone in managing dyslipidemia and lowering this age group's risk of coronary heart disease (CHD)

(2) Older Patients (75+ Years): Statin treatment

continues to provide significant advantages in reducing LDL-C levels and averting cardiovascular events in patients 75 years of age and above. However, the absolute risk reduction may be less pronounced compared to younger individuals. This is partly due to the higher prevalence of comorbidities and frailty in the elderly, which can influence overall health outcomes and the body's response to medication. Despite this, long-term studies, such as WOSCOPS, have shown enduring benefits of statins in reducing coronary heart disease and major coronary events even in older populations (Carter *et al.*, 2013).

Pharmacokinetics and Age-Related Variations

(1) Statins like pitavastatin, rosuvastatin, and atorvastatin have minimal pharmacokinetic differences between younger and older adults. Pitavastatin shows similar kinetics and higher efficacy in lowering LDL-C compared to pravastatin across all age groups (Krobot *et al.*, 2012). Rosuvastatin shows only slight increases in AUC and C_{max} in younger individuals, suggesting age alone doesn't require significant dose adjustments (Leya and Stone, 2017).

(2) Specific Considerations for Atorvastatin: Atorvastatin displays a higher C_{max} and AUC in elderly patients compared to younger individuals. While these pharmacokinetic differences are notable, they have not translated into clinically significant outcomes in later efficacy trials. This suggests that atorvastatin can still be used effectively in older populations, but with careful consideration and monitoring to avoid potential adverse effects (Onaisi *et al.*, 2023).

Clinical Guidelines and Individualized Care

(1) Statins are advised for primary and secondary cardiovascular events with reduction in older people over 75 by credible organizations such as the AHA/ACC, NLA, and ESC/EAS. They emphasize individualized care, considering health status, comorbidities, and life expectancy when deciding on statin therapy intensity (Khamkat *et al.*, 2022).

(2) Balancing Benefits and Risks: Patients over 80 years, particularly those with significant frailty, should be cautious when deciding to start or continue statin therapy due to the increased risk of adverse effects and the need to strike a balance between lipid-lowering goals and drug-related complications (Heintzman *et al.*, 2023).

Long-term Outcomes and Adverse Effects:

(i) **Long-Term Benefits:** Studies with continuous monitoring show that statins reduce the risk of coronary heart disease and severe cardiovascular events over an extended length of time in a consistent manner. However, the benefits of reducing non-cardiovascular causes of death, such as stroke or cancer mortality, are not as significant in older age groups (Şen *et al.*, 2024).

(ii) **Increased likelihood of Adverse Effects:** As people age, their pharmacokinetic and pharmacodynamic responses to statin medication alter, which raises their likelihood of experiencing negative side effects. Higher rates of adverse effects, including myopathy, aberrant liver enzyme levels, and possible medication-drug interactions, can result from decreased drug clearance and increased free drug concentrations. This highlights the need for regular monitoring and possible dose adjustments to ensure patient safety (Parhofer *et al.*, 2023).

Deprescribing Trends:

Recent studies reveal a rise in statin deprescribing in patients aged 80 and above, especially those with frailty conditions. This is more common in primary prevention settings than secondary prevention, indicating a cautious approach by physicians in managing very old patients. This trend highlights the shift towards personalized medicine, considering patient health and quality of life alongside statin therapy benefits (Sawanny *et al.*, 2023).

Future Aspects

A recent study emphasizes the dynamic nature of statin medication and its consequences for

various age and risk groups, highlighting the need for continued investigation into statin usage.

(1) Risk and Age Group Considerations:

Young Adults: According to recent guidelines, the risk thresholds for ASCVD (Atherosclerotic Cardiovascular Disease) may be underestimated in younger adults, which might result in fewer people taking statins despite their potential advantages. To better identify younger people who may benefit from statins, recommendations that consider other risk variables, such as coronary artery calcium score, are being advised to be adjusted (Thalmann *et al.*, 2023).

Older Adults: The impact of statins on comorbid disorders, such as osteoporosis, in older persons is being investigated. Although the impact is dose-dependent and changes with age, there is evidence to suggest that statin treatment may lower the incidence of osteoporotic fractures.

(2) Efficacy and Safety in Different Populations:

Research contrasting atorvastatin with rosuvastatin shows that while they have distinct safety profiles, they are equally effective at lowering cardiovascular events. For example, rosuvastatin compared to atorvastatin is linked to an increased risk of cataract surgery and diabetes with a new start. This emphasizes how important personalized medicine is when prescribing statins.

Research is also being done on the possibility that statins have advantages outside of decreasing cholesterol, such as anti-inflammatory and neuroprotective properties. Because of these pleiotropic effects, statins may be a useful treatment choice for a greater number of illnesses, such as cancer and cerebrovascular disorders (Sawanny *et al.*, 2023).

(3) Long-Term Effectiveness and Emerging Guidelines:

To maximise the use of statins, new cholesterol guidelines are being established with the goal of minimising needless prescriptions and guaranteeing that individuals who are at risk receive the

right care. Examples of this include a more individualized approach to risk assessment and the potential application of cutting-edge imaging modalities and biomarkers to guide treatment decisions. All things considered, the future of statin therapy entails a more sophisticated strategy that considers unique risk factors, age-specific demands, and the expanding range of therapeutic benefits of statins (Umarje *et al.*, 2023). More studies are necessary to improve recommendations and guarantee that statins are administered safely and efficiently in various groups.

Conclusion

The study suggests that streamlining medication regimens, and administrative processes, and implementing automated telephone interventions by pharmacies may improve patient adherence to statin therapy. However, strategies focusing on education and intensive patient care have inconsistent outcomes. Statins are helpful for those under 75 in decreasing LDL-C levels and avoiding cardiovascular events; most trials extended their intervention to all adult patients. Statin treatment is still beneficial in older patients, but there are still significant gaps in understanding how to increase statin adherence, particularly in older individuals. Variables such as patient beliefs, memory, and anxiety about adverse effects may affect adherence. Successful strategies may involve modifying treatments to target patients' reasons for nonadherence and understanding the mechanisms underlying adherence.

Conflict of Interest

The authors declare no conflicts of interest.

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