

Statins and Their Impact on Atherosclerotic Cardiovascular Disease

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DESCRIPTION

Statins have emerged as the most widely prescribed class of medications for both the prevention and treatment of Atherosclerotic Cardiovascular Disease (ASCVD). These drugs exert their primary effect by inhibiting the enzyme HMG-CoA reductase, a key regulator in the liver's cholesterol synthesis pathway. By reducing endogenous cholesterol production, statins significantly lower circulating levels of Low-Density Lipoprotein Cholesterol (LDL-C), which is a major contributor to plaque formation and cardiovascular events. Numerous studies have shown a strong correlation between LDL-C reduction and decreased risk of myocardial infarction, ischemic stroke and cardiovascular-related death. One of the earliest and most influential trials, the Scandinavian Simvastatin Survival Study (4S), demonstrated that statin therapy could significantly reduce cardiac events in individuals with existing coronary heart disease. This groundbreaking research set the stage for further investigations, including WOSCOPS, HPS and JUPITER, which consistently confirmed statins' effectiveness in both primary and secondary prevention across different demographics, age groups and risk profiles. The strength and consistency of this evidence led to statins being incorporated into nearly all international cardiovascular treatment guidelines.

Beyond their lipid-lowering capabilities, statins also exhibit several pleiotropic effects benefits that go beyond cholesterol management. These include improving endothelial function, stabilizing atherosclerotic plaques, reducing oxidative stress and attenuating vascular inflammation. These additional mechanisms are believed to enhance cardiovascular protection and may help explain why clinical outcomes sometimes surpass expectations based on LDL-C reduction alone. In particular, the anti-inflammatory properties of statins have gained attention, as chronic inflammation is now recognized as a key factor in plaque instability and thrombotic events. Despite their widespread use and favorable benefit-risk profile, statins are not without side effects. The most commonly reported adverse effects are muscle-related symptoms, which range from mild myalgia to the rare but

serious condition known as rhabdomyolysis. Liver enzyme elevations can also occur but are generally mild and reversible upon discontinuation of therapy. Another point of concern is a modest increase in the risk of developing type 2 diabetes, especially among individuals with predisposing factors. However, the absolute cardiovascular benefits of statins typically outweigh these risks and professional guidelines continue to endorse their use in appropriately selected patients. Clinicians must remain vigilant, monitor laboratory values regularly and tailor treatment to individual tolerability.

Statins vary in both potency and pharmacokinetics. High-intensity statins such as atorvastatin and rosuvastatin are recommended for patients at high or very high cardiovascular risk, as they can lower LDL-C by more than 50%. Moderate- and low-intensity statins such as simvastatin, pravastatin and fluvastatin may be appropriate for patients with lower risk profiles or for those who are unable to tolerate higher doses due to side effects. The introduction of generic statins has greatly enhanced global accessibility, particularly in low- and middle-income countries, contributing to their widespread adoption. Medication adherence, however, remains a significant challenge in long-term statin therapy. Many patients discontinue use due to concerns about side effects, misinformation about the safety of cholesterol-lowering drugs, or underestimation of their personal cardiovascular risk. Studies have shown that poor adherence significantly reduces the protective effects of statins. Addressing this issue requires comprehensive patient education, clear communication about benefits and risks and the use of shared decision-making to empower patients in their care. Additionally, fixed-dose combinations—such as statin-ezetimibe or statin-antihypertensive pairings can simplify treatment regimens and improve compliance.

Ongoing research is expanding the potential uses of statins beyond traditional cardiovascular indications. Statins are currently being investigated for their possible roles in chronic kidney disease, non-alcoholic fatty liver disease, rheumatoid arthritis and even certain cancers, owing to their anti-

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inflammatory and immunomodulatory properties. While newer lipid-lowering agents such as PCSK9 inhibitors, inclisiran and bempedoic acid offer powerful alternatives for patients with statin intolerance or those requiring additional LDL-C reduction, statins remain the foundation of lipid-lowering therapy due to their long-established efficacy, safety profile and cost-effectiveness. In summary, the introduction of statins has revolutionized the management of atherosclerotic cardiovascular disease. These agents have consistently demonstrated the ability

to lower cholesterol, reduce cardiovascular events and improve survival. Their effects extend beyond lipid lowering to include beneficial vascular and anti-inflammatory properties. Despite some limitations and concerns regarding side effects, statins remain an indispensable component of cardiovascular pharmacotherapy. With continued patient education and careful clinical monitoring, they will continue to play a central role in reducing the global burden of cardiovascular disease.