Statins for Primary Prevention of Cardiovascular Disease

Review of Evidence and Recommendations for Clinical Practice

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KEYWORDS

• Cholesterol • Statin • 10-year risk • Cardiovascular disease • Lipids
• Statin intolerance

KEY POINTS

- Large clinical trials have shown statin therapy to be effective and safe for primary prevention of atherosclerotic cardiovascular disease (CVD) for adults age 40 to 75 years.
- Online 10-year CVD risk calculators can help define eligibility for statin therapy.
- Statin treatment for primary prevention in adults older than 75 years remains uncertain due to sparse research evidence.
- Despite high-quality evidence of effectiveness, safety, and cost-effectiveness, statins are underutilized for primary prevention.
- Decisions around initiation of statin therapy with individual patients should include discussions of benefits and risks of treatment, lifestyle changes, and plans for monitoring for side effects.

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INTRODUCTION

Cardiovascular disease (CVD) remains a leading cause of morbidity and mortality in the United States despite steady improvements over the past several decades.[1] High serum cholesterol, specifically low-density lipoprotein cholesterol (LDL-C), is associated with an increased risk of atherosclerotic CVD. LDL-C reduction with statin therapy has been a cornerstone of CVD prevention since the introduction of statin medications in the late 1980s.[1] Statins are a class of lipid-lowering agents that inhibit the enzyme 3-hydroxy-3-methyl-glutaryl coenzyme A reductase, which catalyzes a rate-limiting step in cholesterol production. Treatment with statins leads to reduced serum levels of total cholesterol, LDL-C, and triglycerides.[2] Seven statin drugs are currently available in the United States and are categorized according to the degree of effect on LDL-C levels: (1) low-intensity statins lower LDL-C by less than 30%; (2) moderate-intensity statins lower LDL-C by 30% to 50%; and (3) high-intensity statins lower LDL-C by 50% or more.

The purpose of this review is both to present the current state of research on statin use in adults for primary prevention of incident atherosclerotic CVD and to provide practical advice for prescribing statins among patients without preexisting atherosclerotic CVD in general medicine practice. In particular, the article focuses on recent reviews of evidence and guidelines from the American College of Cardiology/American Heart Association (ACC/AHA) and the US Preventive Services Task Force (USPSTF).[2,3] Although differing in many specifics, both define the primary prevention target population and statin dosing based on calculations of patients' 10-year risk of having an atherosclerotic CVD event, departing from prior approaches that recommended use of statins to treat populations above certain threshold LDL-C levels. The authors highlight the rationale for this approach as well as address several areas of uncertainty.

EVIDENCE OF EFFICACY, SAFETY, AND COST-EFFECTIVENESS

Statins Are Effective for Primary Prevention of Atherosclerotic Cardiovascular Disease

A large body of evidence from high-quality randomized clinical trials indicates that statins are effective at reducing levels of serum LDL-C and total cholesterol as well as the risk of vascular events and deaths.[4–6] A recent systematic review, commissioned by the USPSTF to inform their guidelines, evaluated evidence from randomized trials comparing statins to placebo in adults older than 40 years of age without a history of atherosclerotic CVD.[4] The review included 19 randomized clinical trials that followed patients for coronary heart disease, stroke, and/or all-cause mortality for up to 6 years. All trials enrolled patients with one or more risk factors for atherosclerotic CVD: one-third used dyslipidemia as the main eligibility criterion; others selected patients based on other atherosclerotic CVD risk factors such as diabetes, hypertension, or early cerebrovascular disease.

In these studies, patients randomized to receiving statins compared with placebo had a 30% decreased risk of adverse cardiovascular outcomes (relative risk [RR] = 0.70, 95% confidence interval [CI]: 0.63–0.78) and a 14% decreased risk of all-cause mortality (RR = 0.86, 95% CI: 0.80–0.93).[4] Patients randomized to statins experienced fewer myocardial infarctions (RR = 0.64, 95% CI: 0.57–0.71), ischemic stroke (RR = 0.71, 95% CI: 0.62–0.82), and cardiovascular mortality (RR = 0.69, 95% CI: 0.54–0.88),[4] findings that are similar in magnitude to results from prior meta-analyses.[6] Absolute benefits in these trials were greater for those with higher baseline risk of atherosclerotic CVD and were not limited to subgroups with hyperlipidemia. The relative reduction in the risk of cardiovascular outcomes was similar