

EDITORIALS



Statins for primary prevention of cardiovascular disease

Patients need better tools to navigate divergent recommendations

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Statins are beneficial in patients with known cardiovascular disease (CVD) but less well established for primary prevention in asymptomatic patients.¹ At least five authoritative guidelines, including the recent publication from the US Preventive Services Task Force, cover this issue.²⁻⁷ Their differing recommendations, however, suggest considerable uncertainty in the underlying data, causing confusion for both clinicians and patients.

The guidelines share several common themes. The essential elements for primary prevention include a healthy lifestyle, treatment of modifiable risk factors, and measurement of serum lipid concentrations in patients aged over 40 years. They agree that statins are appropriate in patients with a high risk of cardiovascular disease—for example, people over 40 with diabetes. All guidelines also recommend statins in other patients with increased cardiovascular risk but with considerable divergence in the details.

The US task force guideline recommends initiating low-to-moderate dose statins in adults aged 40 to 75 years without a history of cardiovascular disease who have at least one risk factor (dyslipidaemia, diabetes, hypertension, or smoking) and a calculated 10 year cardiovascular event risk $\geq 10\%$.² It also recommends statins for selected patients with a calculated 10 year event risk of 7.5-10%. This guideline was based on a commissioned systematic review of the pooled evidence published in medical journals, which included over 70 000 patients.⁸

Similarly, the UK National Institute for Health and Care Excellence (NICE) guidelines recommend offering atorvastatin 20 mg to people whose 10 year risk of developing cardiovascular disease is $\geq 10\%$.³⁻⁴ The American College of Cardiology/American Heart Association (ACC/AHA) guidelines,⁵ the European Society of Cardiology/ European Atherosclerosis Society (ESC/EAS),⁶ and the Canadian Cardiovascular Society (CCS)⁷ also base recommendations for statin therapy on a calculated risk score.

But there, the similarities end. Each of these guidelines uses a different method for estimating risk. The US task force and ACC/AHA guidelines use the pooled cohort risk calculator to estimate 10 year risk of cardiovascular disease, even though

there is considerable evidence that this score overestimates risk and is strongly dependent on patient age.²⁻⁵ The CCS uses Framingham risk score in combination with serum lipid levels.⁷ The ESC/EAS combines the European SCORE tool with serum low density lipoprotein (LDL) cholesterol concentrations⁶ and the Joint British Societies (JBS3) and NICE guidelines use the QRISK2 assessment tool.³⁻⁹

Different risk scores may make sense because each has been validated in the population covered in the particular guideline. None of the clinical trials on which these recommendations are based used risk scores as entry criteria, but a subsequent meta-analysis using individual patient data showed similar relative effects between low and high risk groups and suggested that statins benefit even lower risk patients. Nevertheless, this remains controversial.¹⁰⁻¹²

The second major difference between guidelines is whether a fixed dose statin is recommended, as in the two US guidelines, or whether treatment is titrated to achieve a target serum LDL level, as in the other three guidelines. There is strong evidence that benefit is determined by the degree of LDL lowering. On the other hand, more intensive treatment is costlier, requires more monitoring, and may be associated with increased incident diabetes.¹³ Thus, the choice for a healthcare system depends as much on available resources as on benefit-risk considerations.

The third major difference is in the age range recommended for statin therapy. The US task force guideline focuses on people aged 40 to 75 years and considers the evidence inadequate to make recommendations for people over 75. Similarly, the ACC/AHA recommendations apply only to ages 40 to 75 years. In contrast, the NICE guidelines use the QRISK2 risk score in people up to age 84 years and considers everyone older than 84 at increased cardiovascular risk. The European and Canadian guidelines have no upper age limit.

All guidelines emphasise shared decision making but none provides the tools needed for fully informed decisions. If we are truly committed to informing clinicians and patients, we need interactive tools integrated into the electronic medical record that are accessible, easy to use, and provide individualised

graphic displays of absolute benefits and harms in multilayered formats.¹⁴

There is much we still do not know. Many patients in clinical practice do not match those in clinical trials; data are sparse for women, people aged over 75, and non-white populations. Clinical trials are relatively short term, so the effects of 20-40 years of statin treatment are unknown. Statin side effects seem to be low but this remains controversial¹⁵; smart devices would allow data to be gathered on adverse effects as experienced by patients, rather than as recorded by clinical trial researchers. If side effects are confirmed to be low, we need to reassure patients and encourage compliance with statins.

Despite the imperfections in the evidence base, the available research supports the benefit of statins for primary prevention of cardiovascular disease in selected asymptomatic patients. What we need now is clarity on optimal patient selection and treatment goals. We must also remember that statins are not the only way to reduce cardiovascular risk. Statins are not a substitute for smoking cessation, treating hypertension, maintaining a healthy weight, eating a healthy diet, and exercising regularly.

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