

Interpretation of the evidence for the efficacy and safety of statin therapy.

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Abstract

This Review is intended to help clinicians, patients, and the public make informed decisions about statin therapy for the prevention of heart attacks and strokes. It explains how the evidence that is available from randomised controlled trials yields reliable information about both the efficacy and safety of statin therapy. In addition, it discusses how claims that statins commonly cause adverse effects reflect a failure to recognise the limitations of other sources of evidence about the effects of treatment. Large-scale evidence from randomised trials shows that statin therapy reduces the risk of major vascular events (ie, coronary deaths or myocardial infarctions, strokes, and coronary revascularisation procedures) by about one-quarter for each mmol/L reduction in LDL cholesterol during each year (after the first) that it continues to be taken. The absolute benefits of statin therapy depend on an individual's absolute risk of occlusive vascular events and the absolute reduction in LDL cholesterol that is achieved. For example, lowering LDL cholesterol by 2 mmol/L (77 mg/dL) with an effective low-cost statin regimen (eg, atorvastatin 40 mg daily, costing about £2 per month) for 5 years in 10 000 patients would typically prevent major vascular events from occurring in about 1000 patients (ie, 10% absolute benefit) with pre-existing occlusive vascular disease (secondary prevention) and in 500 patients (ie, 5% absolute benefit) who are at increased risk but have not yet had a vascular event (primary prevention). Statin therapy has been shown to reduce vascular disease risk during each year it continues to be taken, so larger absolute benefits would accrue with more prolonged therapy, and these benefits persist long term. The only serious adverse events that have been shown to be caused by long-term statin therapy-*ie*, adverse effects of the statin-are myopathy (defined as muscle pain or weakness combined with large increases in blood concentrations of creatine kinase), new-onset diabetes mellitus, and, probably, haemorrhagic stroke. Typically, treatment of 10 000 patients for 5 years with an effective regimen (eg, atorvastatin 40 mg daily) would cause about 5 cases of myopathy (one of which might progress, if the statin therapy is not stopped, to the more severe condition of rhabdomyolysis), 50-100 new cases of diabetes, and 5-10 haemorrhagic strokes. However, any adverse impact of these side-effects on major vascular events has already been taken into account in the estimates of the absolute benefits. Statin therapy may cause symptomatic adverse events (eg, muscle pain or weakness) in up to about 50-100 patients (ie, 0.5-1.0% absolute harm) per 10 000 treated for 5 years. However, placebo-controlled randomised trials have shown definitively that almost all of the symptomatic adverse events that are attributed to statin therapy in routine practice are not actually caused by it (ie, they represent misattribution). The large-scale evidence available from randomised trials also indicates that it is

unlikely that large absolute excesses in other serious adverse events still await discovery. Consequently, any further findings that emerge about the effects of statin therapy would not be expected to alter materially the balance of benefits and harms. It is, therefore, of concern that exaggerated claims about side-effect rates with statin therapy may be responsible for its under-use among individuals at increased risk of cardiovascular events. For, whereas the rare cases of myopathy and any muscle-related symptoms that are attributed to statin therapy generally resolve rapidly when treatment is stopped, the heart attacks or strokes that may occur if statin therapy is stopped unnecessarily can be devastating.

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