Statins for the primary prevention of cardiovascular disease

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ABSTRACT

Background
Reducing high blood cholesterol, a risk factor for cardiovascular disease (CVD) events in people with and without a past history of CVD is an important goal of pharmacotherapy. Statins are the first-choice agents. Previous reviews of the effects of statins have highlighted their benefits in people with CVD. The case for primary prevention was uncertain when the last version of this review was published (2011) and in light of new data an update of this review is required.

Objectives
To assess the effects, both harms and benefits, of statins in people with no history of CVD.

Search methods
To avoid duplication of effort, we checked reference lists of previous systematic reviews. The searches conducted in 2007 were updated in January 2012. We searched the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library (2022, Issue 4), MEDLINE OVID (1950 to December Week 4 2011) and EMBASE OVID (1980 to 2012 Week 1). There were no language restrictions.

Selection criteria
We included randomised controlled trials of statins versus placebo or usual care control with minimum treatment duration of one year and follow-up of six months, in adults with no restrictions on total, low density lipoprotein (LDL) or high density lipoprotein (HDL) cholesterol levels, and where 10% or less had a history of CVD.
Two review authors independently selected studies for inclusion and extracted data. Outcomes included all-cause mortality, fatal and non-fatal CHD, CVD and stroke events, combined endpoints (fatal and non-fatal CHD, CVD and stroke events), revascularisation, change in total and LDL cholesterol concentrations, adverse events, quality of life and costs. Odds ratios (OR) and risk ratios (RR) were calculated for dichotomous data, and for continuous data, pooled mean differences (MD) (with 95% confidence intervals (CI)) were calculated. We contacted trial authors to obtain missing data.

Main results
The latest search found four new trials and updated follow-up data on three trials included in the original review. Eighteen randomised control trials (19 trial arms; 56,934 participants) were included. Fourteen trials recruited patients with specific conditions (raised lipids, diabetes, hypertension, microalbuminuria). All-cause mortality was reduced by statins (OR 0.86, 95% CI 0.79 to 0.94); as was combined fatal and non-fatal CVD RR 0.75 (95% CI 0.70 to 0.81), combined fatal and non-fatal CHD events RR 0.73 (95% CI 0.67 to 0.80) and combined fatal and non-fatal stroke (RR 0.78, 95% CI 0.68 to 0.89). Reduction of revascularisation rates (RR 0.62, 95% CI 0.54 to 0.72) was also seen. Total cholesterol and LDL cholesterol were reduced in all trials but there was evidence of heterogeneity of effects. There was no evidence of any serious harm caused by statin prescription. Evidence available to date showed that primary prevention with statins is likely to be cost-effective and may improve patient quality of life. Recent findings from the Cholesterol Treatment Trialists study using individual patient data meta-analysis indicate that these benefits are similar in people at lower (< 1% per year) risk of a major cardiovascular event.

Authors’ conclusions
Reductions in all-cause mortality, major vascular events and revascularisations were found with no excess of adverse events among people without evidence of CVD treated with statins.

**PLAIN LANGUAGE SUMMARY**

**Statins for the primary prevention of cardiovascular disease**

Cardiovascular disease (CVD), which comprises heart attacks (myocardial infarction), angina and strokes, is ranked as the number one cause of mortality and is a major cause of morbidity world wide. High blood cholesterol is linked to CVD events and is an important risk factor. Reducing high blood cholesterol, is thus an important way to reduce the chances of suffering a CVD event. Statins - cholesterol lowering drugs - (e.g. simvastatin, pravastatin, atorvastatin) are the first-choice treatments. Since the early statin randomised controlled trials were reported in the 1990s, several reviews of the effects of statins have been published highlighting their benefits particularly in people with a past history of CVD. Benefits include a reduction in CVD events. Statins have also been shown to reduce the risk of a first event in otherwise healthy individuals at high risk of CVD (primary prevention) but information on possible hazards has not been reported fully. The aim of this updated systematic review is to assess the effects, both in terms of benefits and harms of statins, for the primary prevention of CVD. We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE until 2011. We found 18 randomised controlled trials with 19 trial arms (56,934 patients) dating from 1994 to 2008. All were randomised control trials comparing statins with usual care or placebo. The mean age of the participants was 57 years (range 28 - 97 years), 60.3% were men, and of the eight trials that reported on ethnicity, 85.9 % were Caucasian. Duration of treatment was a minimum one year and with follow-up of a minimum of six months. All-cause mortality and fatal and non-fatal CVD events were reduced with the use of statins as was the need for revascularisation (the restoration of an adequate blood supply to the heart) by means of surgery (coronary artery bypass graft ) or by angioplasty (PTCA). Of 1000 people treated with a statin for five years, 18 would avoid a major CVD event which compares well with other treatments used for preventing cardiovascular disease. Taking statins did not increase the risk of serious adverse effects such as cancer. Statins are likely to be cost-effective in primary prevention.