CRD summary
This review investigated the effect of statin therapy on cancer incidence and death from cancer. The authors concluded that statins have no effect on cancer risk; this finding applied to all statins and all types of cancer investigated. This was a well-conducted review and the authors' conclusions are likely to be reliable.

Authors' objectives
To determine whether statin therapy reduces the risk of developing cancer.

Searching
MEDLINE (1966 to July 2005), EMBASE (1990 to July 2005), CINAHL (1982 to July 2005), Web of Science (1994 to July 2005), Cancerlit (1975 to July 2005) and the Cochrane Database of Systematic Reviews; the search terms were reported. The search was limited to studies published in English. Abstracts presented between 2002 and 2005 at meetings of the American Heart Association, American College of Cardiology, American Society of Clinical Oncologists and American Society of Hematology were searched by hand, as were the reference lists of relevant primary and review articles.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion if they enrolled a minimum of 100 patients and had a mean duration of follow-up of at least 1 year. The follow-up in the included studies ranged from 1.9 to 10.4 years.

Specific interventions included in the review
Studies that compared statins with placebo or standard treatment were eligible for inclusion. The included studies used atorvastatin (10 to 20 mg/day), lovastatin (20 to 80 mg/day), simvastatin (10 to 40 mg/day), cerivastatin (0.4 mg/day), fluvastatin (20 to 80 mg/day) and pravastatin (10 to 40 mg/day).

Participants included in the review
Inclusion criteria for the participants were not specified. In the included studies, the mean age of the patients ranged from 50 to 76 years and 73% of the participants were male.

Outcomes assessed in the review
The studies were required to include cancer diagnosis or cancer death as a primary or secondary outcome.

How were decisions on the relevance of primary studies made?
Three reviewers independently assessed potentially relevant articles.

Assessment of study quality
The studies were assessed for randomisation, random allocation concealment, masking of treatment allocation, blinding and withdrawals. Three independent reviewers judged validity. Any disagreements were resolved by consensus.

Data extraction
Three reviewers independently abstracted the data. Any disagreements were resolved by consensus. Data on the numbers of cancer cases and cancer deaths in the statin and control groups were used to calculate odds ratios (ORs) and their 95% confidence intervals (CIs) for each outcome. Risk differences were calculated for both outcomes.
Methods of synthesis
How were the studies combined?
The studies were combined in a meta-analysis using a DerSimonian and Laird random-effects model. The potential for publication bias was assessed by visual inspection of funnel plots and by the Begg rank correlation method and the Egger weighted regression method.

How were differences between studies investigated?
Statistical heterogeneity was measured using the Q statistic (P<0.1 being considered significant) and assessed by visual examination of L’Abbe plots. Subgroup analyses were used to investigate the effects of statins on the incidence of different cancer diagnoses (breast, prostate, gastrointestinal, colon, respiratory and melanoma), and the effects of individual statins and their properties (hydrophilic or lipophilic and natural or synthetic) on cancer incidence and death. The effects of methodological quality were investigated in a sensitivity analysis in which unblinded or open-label studies were excluded. A second sensitivity analysis compared a fixed-effect meta-analysis (Mantel-Haenszel model) with the main random-effects analysis.

Results of the review
Twenty-six RCTs (n=86,936) were included in the review. Atorvastatin was evaluated in three studies (n=14,398), cerivastatin in one (n=250), fluvastatin in three (n=4,208), lovastatin in three (n=7,206), pravastatin in eleven (n=44,141) and simvastatin in five (n=26,075).

Treatment with statins did not reduce the incidence of cancer (OR 1.02, 95% CI: 0.97, 1.07) or cancer deaths (OR 1.01, 95% CI: 0.93, 1.09). No significant statistical heterogeneity was found (P>0.37 for both meta-analyses).

None of the subgroup analyses produced a statistically significant result, and the conclusions were not altered by varying the assumptions in the sensitivity analyses. Statistical heterogeneity was not significant for any outcome except incidence of breast cancer.

The funnel plots appeared slightly asymmetrical but the Begg and Egger methods did not suggest significant publication bias.

Authors’ conclusions
Statins have a neutral effect on the risk of cancer and cancer death in RCTs.

CRD commentary
The review question and inclusion and exclusion criteria were clear. The authors searched a range of appropriate sources, although confining the search to English language material means that some relevant studies could have been missed. Validity was assessed appropriately and included in a sensitivity analysis. The study selection, validity assessment and data extraction were performed independently by more than one reviewer, thus minimising the risk of bias and errors during the review process. Adequate details of the primary studies were presented, although there was little information on the participants. The studies were combined in a meta-analysis and both statistical and clinical heterogeneity were assessed. Publication bias was assessed using standard methods. The authors’ conclusions follow from the evidence presented and are likely to be reliable.

Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.