CRD summary
This review evaluated the effect of pravastatin therapy on cancer risk, according to age. The authors concluded that pravastatin may be associated with an increased risk of cancer among elderly people, but further verification was needed. The conclusions should be regarded with some caution because of limitations in the review process.

Authors' objectives
To evaluate the effect of pravastatin therapy on cancer risk modified by age.

Searching
MEDLINE (1966 to February 2006) and Science Citation Index Expanded (1970 to February 2006) were searched for papers in any language; the search terms were reported. The references of retrieved articles were also checked for additional papers.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) with a minimum duration of 1 year were eligible.

Specific interventions included in the review
Studies comparing pravastatin therapy with placebo or usual care were eligible for inclusion. The majority of the included studies compared pravastatin therapy with placebo.

Participants included in the review
No inclusion criteria for the participants were specified. The participants in the included studies had an overall mean age of 63 years, with mean ages across the studies of between 55 and 75 years.

Outcomes assessed in the review
The included studies needed to report cancer rates.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two reviewers extracted the data independently, and any discrepancies were resolved by consensus.

Methods of synthesis
How were the studies combined?
The pooled relative risk (RR) and 95% confidence intervals (CIs) were calculated using the Mantel-Haenszel fixed-effect model and the DerSimonian and Laird random-effects model. Publication bias was assessed using Begg's adjusted rank correlation test and Egger's regression asymmetry test.

How were differences between studies investigated?
Heterogeneity was assessed using Cochran's Q test and the I-squared statistic. Sensitivity and subgroup analyses were conducted, based on method of control, sample size and duration of treatment. A weighted meta-regression analysis was conducted to investigate cancer risk by patient age, based on the mean age of patients in each study.
Results of the review
Twelve studies (n=42,902) were included in the review.

There was no significant difference in cancer risk between the pravastatin group and all control groups when using either a fixed-effect model (RR 1.06, 95% CI: 0.99, 1.13; 12 studies) or a random-effects model (RR 1.06, 95% CI: 0.97, 1.14; 12 studies). There was no statistically significant heterogeneity between trials or statistical evidence of publication bias. There was also no significant difference in cancer risk between treatment groups for studies involving at least 3,000 patients and with a minimum duration of 3 years.

There was a statistically significant positive association between cancer risk and mean age, with an increasing relative risk of cancer in the pravastatin group with increasing mean age (p=0.006). This statistical significance remained when restricting trials to those evaluating pravastatin versus placebo, trials with at least 3,000 participants and a minimum duration of three years, and when adjusting for duration of follow-up.

Authors’ conclusions
Pravastatin may be associated with an increased risk of cancer among elderly people, but further verification was warranted.

CRD commentary
The research question was clear and the review stated some defined inclusion criteria. No language restrictions were applied to the search, which reduced the risk of language bias. There was no attempt to identify unpublished studies, which introduced the possibility of publication bias; however, the authors tested for this and found no evidence of its existence. The authors did not state how the papers were selected for the review, which made it difficult to assess the potential for errors and bias. It was also difficult to appraise the validity of the included studies as no quality assessment was performed. Measures were taken to minimise errors and bias in the data extraction process.

Statistical heterogeneity was assessed and was present for some analyses. It should be noted that the age effect was based on the mean value (study level), rather than the age of individual patients, which appeared necessary to establish a reliable correlation. Some limitations of the study were discussed, such as the effects of confounding by other study characteristics on the results.

The authors’ conclusions should be regarded with some caution given the outlined limitations.

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

Research: The authors stated that an analysis of cancer risk by patient age should be carried out on individual patient databases. They also recommended greater follow-up periods to identify long-term effects.

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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.