Statin use and the prevention of venous thromboembolism: a meta-analysis

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CRD summary
This review concluded that available evidence suggested that statins can reduce patients' odds of developing venous thromboembolism. This conclusion reflected the data presented, but weaknesses in the review process and analysis mean that it should be interpreted cautiously.

Authors' objectives
To evaluate the effectiveness of statins in preventing development of venous thromboembolism.

Searching
MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Database of Systematic Reviews were searched to 2009. Search terms were reported and no language restrictions were applied. Bibliographies of included studies were screened for additional articles.

Study selection
Randomised controlled trials (RCTs) or observational studies that evaluated the effects of statin therapy on the incidence of venous thromboembolisms were eligible for inclusion. Observational studies were included only if they reported an adjusted estimate of effect (such as multivariate regression or covariate matching).

Study populations, exclusion criteria and variables adjusted for in results varied (details reported). Study participants were aged between 18 and 79 years, where reported. Baseline lipid levels were reported rarely (two out of 10 studies). The rate of venous thromboembolism in control groups in included studies ranged from 0.21 to 1.09 events per 100 person years.

The authors did not state how many reviewers performed study selection.

Assessment of study quality
The methodological quality of included studies was assessed by two reviewers, using methods recommended by the US Preventative Services Task Force. Criteria considered were study design, sample size, magnitude of effect size; and appropriateness of methods to control for confounding. Studies were given an overall ranking of good, fair or poor.

Data extraction
Adjusted odds ratios (OR) with 95% confidence interval (CI) for overall venous thromboembolism, deep vein thrombosis (DVT) and pulmonary embolism were extracted as reported in individual studies.

Data were independently extracted by two reviewers using a standardised data extraction form. Any disagreements were resolved by consensus or discussion with a third reviewer.

Methods of synthesis
Adjusted odds ratios were pooled using a DerSimonian-Laird random-effects model weighted by inverse variance. Summary effect sizes, with 95% CIs, were calculated for the three outcomes (venous thromboembolism, DVT and pulmonary embolism). Subgroup analyses were conducted to include only observational studies and to exclude studies with a poor quality rating.

Between-study heterogeneity was assessed using $I^2$. Publication bias was assessed by visual inspection of funnel plots and Egger's weighted regression.

Results of the review
Ten studies (n=971,307 participants, range 504 to 729,529) were included in the analysis: one RCT (n=17,802) and nine observational studies (six case control, two retrospective cohort and one prospective cohort). The RCT was rated as good quality. Seven observational studies were rated as fair quality and two were rated as poor quality.

Statin use was associated with a significantly decreased risk of venous thromboembolism (adjusted OR 0.68, 95% CI 0.54 to 0.86); nine studies, n=845,445), a significantly decreased risk of DVT (adjusted OR 0.59, 95% CI 0.43 to 0.82) five studies, n=234,730) and a significantly decreased risk of pulmonary embolism, (adjusted OR 0.70, 95% CI 0.53 to 0.94; four studies, n=108,868). Results were similar for all subgroup analyses. Heterogeneity was high in all analyses ($I^2=67%$ to 89%).

The funnel plot and Egger's weighted regression statistic suggested a low likelihood of publication bias.

**Authors' conclusions**
Currently available evidence suggests that statins can reduce patients' odds of developing venous thromboembolism.

**CRD commentary**
The review stated a clear research objective and defined appropriate inclusion criteria. A number of sources were searched for relevant studies and no language restrictions were applied, which minimised the likelihood of language bias. Tests for publication bias were performed and it was deemed to be unlikely. Measures to reduce error and bias were applied to the data extraction and quality assessment components of the review; it was unclear whether similar methods were applied to study selection. An assessment of the methodological quality of included studies was undertaken, but reporting of this was uninformative as only an overall rating was provided. Studies included in the meta-analyses appeared clinically and statistically heterogeneous, which limited the values of pooled estimates.

The authors' conclusions reflected the data presented, but should be interpreted cautiously given the limitations in the review process and analysis.

**Implications of the review for practice and research**

**Practice:** The authors did not state any recommendations for practice.

**Research:** The authors did not state any recommendations for future research.

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