CRD summary
This review assessed the accuracy of D-dimer assays for the diagnosis of deep venous thrombosis. The authors concluded that there was no support for the use of stand-alone D-dimer assays. The limited search might have resulted in the omission of some relevant studies, and the results varied considerably among the studies identified. However, the authors' conclusions are likely to be robust.

Authors' objectives
To assess the accuracy of D-dimer assays for the diagnosis of lower extremity deep venous thrombosis (DVT).

Searching
MEDLINE was searched from February 1995 to October 2003 for articles published in the English language; the search terms were reported. The reference lists in identified studies were also checked. Abstracts and reports of subgroup analyses of published studies were excluded.

Study selection
Study designs of evaluations included in the review
Diagnostic accuracy studies were eligible for inclusion if they used an accepted reference standard, made the decision to perform the reference standard test independently of the D-dimer result, adequately described the methods of patient selection and enrolled the complete spectrum of patients.

Specific interventions included in the review
Studies of D-dimer assays were eligible for inclusion. The included studies evaluated 21 different D-dimer assays using different methods: first- and second-generation latex agglutination, membrane enzyme-linked immunosorbent assays (ELISAs), erythrocyte agglutination, automated rapid enzyme-linked fluorescence and microplate ELISA; details of the specific tests were reported. For quantitative assays, the included studies reported a range of different cut-off points; in some studies the cut-off points were determined retrospectively to maximise the sensitivity.

Reference standard test against which the new test was compared
Studies that compared D-dimer assays with lower extremity ultrasound or venography were eligible for inclusion.

Participants included in the review
Studies of symptomatic patients with suspected acute DVT were eligible for inclusion. Studies that combined data for patients with suspected DVT and pulmonary embolism were excluded. The included studies used different exclusion criteria (details were reported).

Outcomes assessed in the review
Studies that presented sensitivities and specificities, or provided 2x2 data, were eligible for inclusion. The review reported the prevalence of DVT, sensitivity, specificity, and positive and negative likelihood ratios for each included data set.

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
Studies were assessed on the basis of the following quality criteria: use of an accepted reference standard; independent interpretation of the test results; adequate description of the methods of patient selection; description of at least the...
demographics of the patient population; stratification of the results by disease extent and severity; inclusion of the complete spectrum of patients; decision to perform the reference standard test independently of the D-dimer result; adequate description of the test; sensitivity and specificity reported, or sufficient data for their calculation; evaluation of the reproducibility of the test results in a setting where the test is likely to be used in practice. Two reviewers independently assessed the validity of the studies according to predefined criteria.

Data extraction
Two reviewers independently extracted the data and resolved any disagreements through reaching consensus.

Methods of synthesis
How were the studies combined?
A marginal logistic regression was used to model the diagnostic odds ratio (DOR) as a function of the D-dimer assay. The reference standard, sample size, overall prevalence of disease and patient mix were included as covariates; these covariates were selected a priori. For each study that evaluated more than one D-dimer assay, a cluster of nonindependent assay measures was defined using a repeated measures method.

How were differences between studies investigated?
The independent effect of the a priori covariates on the DOR was examined.

Results of the review
Twenty-three diagnostic accuracy studies (n=3,985) were included. The median sample size was 132 (range: 30 to 474).

Three studies did not report patient demographics. Eight studies stratified their results by proximal and distal DVT. Three studies reported on the reproducibility of the test results in appropriate settings.

The prevalence of DVT in the included studies ranged from 20 to 69%.

Sensitivities, specificities and negative predictive values varied widely across the studies, and there were major differences in study methodology. Sensitivity and negative predictive values were often lower than 90%.

Most DORs of D-dimer assays were not significantly different from each other. The VIDAS assay was significantly better than three assays (Dimertest, Turbiquant, and Nyocard), all different types of assay, but was similar to 17 other assays (five different types of assay).

Increasing prevalence of DVT was associated with poorer test accuracy (P=0.01). The use of venography as the reference standard test was associated with improved test accuracy (P<0.005).

Authors' conclusions
The review did not support the use of stand-alone D-dimer assays for the diagnosis of DVT, as the reported performance characteristics of these assays were frequently inadequate for ruling out DVT (their main clinical application).

CRD commentary
The review question was clear in terms of the study design, test and reference standard, participants and outcomes. Only one database was searched for studies published in English, and this might have resulted in the omission of other relevant studies and the potential for language bias. In addition, there was no attempt to locate unpublished studies, thus raising the possibility of publication bias. The methods used to select the studies were not described, so it is not known whether any efforts were made to reduce errors and bias. Methods were, however, used to minimise bias in the validity assessment and data extraction processes. Validity was assessed using appropriate, specified criteria and only studies meeting minimal quality criteria were included.
Given the heterogeneity among studies, the use of a multivariate analysis to examine factors influencing diagnostic accuracy was appropriate. Despite the wide variability among the studies, the authors' conclusions regarding the lack of support for D-dimer assays are likely to be reliable.

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

**Practice:** The authors stated that they could make no recommendations on specific assays based on the results of their review.

**Research:** The authors stated that more accuracy and management studies are required to determine the place of D-dimer assays in clinical practice. They stated that future studies should be adequately powered, should select the best possible reference standard, and should collect sufficient clinical information on patients to permit stratification by risk of DVT and by conditions that elevate D-dimer values.

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**Other publications of related interest**

These additional published commentaries may also be of interest. Perrier A. Review: several factors are associated with the performance of D-dimer assays for detecting deep venous thrombosis. ACP J Club 2004;141:76. Perrier A. Review: several factors are associated with the performance of D-dimer assays for detecting deep venous thrombosis. Evid Based Med 2004;9:185.

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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.