Towards evidence-based guidelines for the prevention of venous thromboembolism: systematic reviews of mechanical methods, oral anticoagulation, dextran and regional anaesthesia as thromboprophylaxis

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Executive summary

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Objectives
The objectives of this study were to assess the benefits in terms of reductions in the risks of deep vein thrombosis (DVT) and of pulmonary embolism (PE), and hazards in terms of major bleeding, of: (i) mechanical compression (graduated compression stockings, intermittent pneumatic compression, footpumps); (ii) oral anticoagulants; (iii) dextran; and (iv) regional anaesthesia (as an alternative to general anaesthesia) in surgical and medical patients.

Search strategy
The strategy involved a systematic search of electronic databases (MEDLINE, EMBASE, BIOSIS, Derwent), search of the Antithrombotic Trialists’ Collaboration database, contact with trialists and manufacturers, and scrutiny of bibliographies of identified papers and reviews of thromboprophylaxis.

Selection criteria
Properly randomised trials were selected, including those reported in a non-English language, with at least one unconfounded comparison of the effect of one of the methods under review versus control, or a direct comparison between different versions of a method, or a direct comparison between a pharmacological agent (dextran or an oral anticoagulant) and low molecular weight or unfractionated heparin. Trials were included only if systematic assessment of DVT by radiological methods was planned.

Data collection and analysis
All trials identified as fitting the selection criteria were independently assessed by at least two review authors for methodological quality and the numbers of patients with primary and secondary outcomes were recorded. The primary outcomes were DVT, PE and major bleeding events, and proximal venous thrombosis (PVT) and fatal PE were secondary outcomes. Trials were subdivided into those that had assessed a method as the only means of thromboprophylaxis (‘monotherapy’) and those that had assessed the effects of adding a method to another form of thromboprophylaxis (‘adjunctive therapy’).

Main results
Mechanical compression methods reduced the risk of DVT by about two-thirds when used as monotherapy and by about half when added to a pharmacological method. These benefits were similar irrespective of the particular method used (graduated compression stockings, intermittent pneumatic compression or footpumps) and similar in each of the surgical groups studied. Mechanical methods reduced the risk of PVT by about half and the risk of PE by two-fifths.

Oral anticoagulants, when used as monotherapy, reduced the risk of DVT and of PVT by about half, and this protective effect appeared similar in each of the surgical groups studied. There was an apparently large four-fifths reduction in the role of PE, but not only was the magnitude of this reduction statistically uncertain, but also pulmonary embolism was reported by a minority of trials, so it may be subject to selection bias. Oral anticoagulant regimens approximately doubled the risk of major bleeding. Oral anticoagulant regimens appeared less effective at preventing DVT than heparin regimens [64% (standard error (SE) 8) greater risk of DVT], although were associated with less major bleeding [35% (10) risk reduction for major bleeds].

Dextran reduced the risk of DVT and of PVT by about half, again irrespective of the type of surgery, but too few studies had reported PE to provide reliable estimates of effect on this outcome. Dextran appeared to be less effective at preventing DVT than the heparin regimens studied. Dextran was associated with an increased risk of bleeding, but too few bleeds had occurred for the size of this excess risk to be estimated reliably.

Compared with general anaesthesia, regional anaesthesia reduced the risk of DVT by about half,
and this benefit appeared similar in each of the surgical settings studied. Regional anaesthesia was associated with less major bleeding than general anaesthesia.

**Conclusion**

In the absence of a clear contraindication (such as severe peripheral arterial disease), patients undergoing a surgical procedure would be expected to derive net benefit from a mechanical compression method of thromboprophylaxis (such as graduated compression stockings), irrespective of their absolute risk of venous thromboembolism. Patients who are considered to be at particularly high risk of venous thromboembolism may also benefit from a pharmacological thromboprophylactic agent, but since oral anticoagulant and dextran regimens appear less effective at preventing DVT than standard low-dose unfractionated heparin or low molecular weight heparin regimens, they may be less suitable for patients at high risk of venous thromboembolism, even though they are associated with less bleeding. Whenever feasible, the use of regional anaesthesia as an alternative to general anaesthesia may also provide additional protection against venous thromboembolism. There is little information on the prevention of venous thromboembolism among high-risk medical patients (such as those with stroke), so further randomised trials in this area would be helpful.

**Publication**

NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the ‘National Knowledge Service’ that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. ‘Health technologies’ are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA Programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, service-users groups and professional bodies such as Royal Colleges and NHS Trusts. Research suggestions are carefully considered by panels of independent experts (including service users) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or conducting a trial to produce new evidence where none currently exists.

Additionally, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme is able to commission bespoke reports, principally for NICE, but also for other policy customers, such as a National Clinical Director. TARs bring together evidence on key aspects of the use of specific technologies and usually have to be completed within a short time period.

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Reports are published in the HTA monograph series if (1) they have resulted from work commissioned for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in Health Technology Assessment are termed ‘systematic’ when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this monograph was commissioned by the HTA Programme as project number 93/10/01. The contractual start date was in May 1997. The draft report began editorial review in February 2004 and was accepted for publication in May 2005. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors’ report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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