Screening for thrombophilia in high-risk situations: a meta-analysis and cost-effectiveness analysis


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Several thrombophilia screening strategies were compared. These included universal screening versus no screening for four different patient populations, and selective screening versus no screening for the same four different patient populations.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
Four hypothetical study populations were studied. The population groups were women prior to prescribing oral contraceptives, women at the onset of pregnancy, women prior to prescribing hormone replacement therapy, and patients prior to major orthopaedic surgery.

Setting
The setting was not explicitly stated as the study was based on hypothetical patients. It would appear that the study was based in the community for three of the groups (women prescribed oral contraceptives, women at the onset of pregnancy and women being prescribed hormone replacement), while the fourth group (patients prior to major orthopaedic surgery) would presumably have been based in a tertiary care centre. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness data were derived from studies published between 1992 and 2004. The resource use parameters and unit costs were derived from expert opinion and literature published between 2000 and 2003. The price year was 2002.

Source of effectiveness data
The effectiveness data were derived from a review of the literature. Some efficiency data were supplemented by expert panel opinion and authors' assumptions.

Modelling
A decision analytical model was developed to analyse the range of possible clinical events associated with screening and no screening in hypothetical populations. The same model was re-populated for each different patient population. Adverse events were considered in the model. The time horizon of the model was not explicitly reported.
Outcomes assessed in the review
The outcomes assessed in the review related to the risk of vascular complications in the different patient groups, in addition to the risk of adverse pregnancy outcomes due to thrombophilia in the pregnant group.

Study designs and other criteria for inclusion in the review
The inclusion and exclusion criteria employed were not reported.

Sources searched to identify primary studies
The authors stated that all major electronic databases were searched, but did not specify the actual sources searched.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Approximately 14 primary studies were included in the review.

Methods of combining primary studies
The authors stated that meta-analysis was conducted on the basis of a random-effects model and that heterogeneity was tested by the standard chi-squared test where appropriate. The authors also used data from three published meta-analyses (Robertson et al. 2004, Wu et al. 2005 and Wu et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details).

Investigation of differences between primary studies
Not reported.

Results of the review
The proportion of women with a prior personal and/or family history of venous thromboembolism (VTE) was 12%.

The effectiveness of prophylaxis was 50%.

Prophylactic low molecular weight heparin in pregnancy in those who test positive for thrombophilia would result in a 50% reduction in the occurrence of vascular complications and early pregnancy loss.

The extension of thromboprophylaxis for 4 weeks after surgery would result in a 50% reduction in VTE.

The probabilities in different clotting disorders, based on the odds ratios of VTE in the general population, ranged from 2.2 to 12.62.

Methods used to derive estimates of effectiveness
The authors made some estimates based on their assumptions.

Estimates of effectiveness and key assumptions
The overall specificity and sensitivity of the thrombophilia screening tests was assumed to be 80%.

The proportion of patients with prior VTE history was assumed to be 20% in the orthopaedic surgery group and 15% in the hormone replacement therapy group.

**Measure of benefits used in the economic analysis**
The effectiveness of screening was measured in terms of the number of major clinical adverse outcomes averted.

**Direct costs**
The direct costs included those associated with thrombophilia screening and the treatment of associated adverse clinical complications. The authors estimated the costs from the perspective of the UK NHS. It was not reported whether discounting had been carried out. Given that the time horizon for the estimation of the costs was not reported, it is not possible to assess whether discounting was necessary in this study. The costs and the quantities were reported separately. The authors reported that the quantity of resource use was determined by a Delphi study carried out among obstetric and orthopaedic consultants, while the unit costs for health care resource use were obtained from routinely collected data and the literature. The authors did not specify the source of the routinely collected data. The price year was 2002.

**Statistical analysis of costs**
No statistical analysis of the costs was reported.

**Indirect Costs**
The indirect costs were not included.

**Currency**
UK pounds sterling (€).

**Sensitivity analysis**
A univariate sensitivity analysis was conducted on those variables considered to be the least robust and those that were expected to impact on the estimated cost-effectiveness of thrombophilia screening. These included thrombophilia test sensitivity and specificity (sensitivity range 50% to 100% was explored), the effectiveness of prophylaxis in preventing major clinical outcomes (sensitivity range 20 to 80% explored), the impact of varying unit cost data (inflated and reduced by 20%) and model probabilities (the extreme values of the 95% confidence intervals associated with the calculated odds ratios were used). A scenario analysis was conducted to test other assumptions. Instead of testing the most commonly used drugs for contraception and hormone replacement, the second most commonly prescribed drugs were tested in the sensitivity analysis. The cost-effectiveness of prescribing transdermal preparations for hormone replacement in women who tested positive for thrombophilia was also tested. In addition, the authors tested the cost-effectiveness of no thrombophilia testing and prescribing prophylaxis and extended prophylaxis, based on the patients' VTE history, in pregnancy and orthopaedic surgery groups, respectively.

**Estimated benefits used in the economic analysis**
Universal screening prior to oral oestrogen could avoid adverse clinical complications in 3 women in the hypothetical model of 10,000 patients. It could avoid 60 adverse events in the pregnancy group, 42 in the hormone replacement cohort and 88 in the orthopaedic surgery group.

Selective screening compared with no screening would avoid 1 complication in the oral oestrogen group, 8 in the pregnancy group, 14 in the hormone replacement group and 26 in the orthopaedic surgery cohort.
Cost results
The cost of adverse clinical complications with no screening was 119,147 for patients on oral contraceptives, 535,814 for pregnant women, 1,185,427 for patients on hormone replacement therapy and 1,217,935 for patients undergoing orthopaedic surgery.

The costs of universal screening and clinical complications in these groups were 708,640 for patients on oral contraceptives, 5,384,319 for pregnant women, 1,469,464 for patients on hormone replacement therapy and 2,466,343 for patients undergoing orthopaedic surgery.

Selective screening, plus the cost of clinical complications, cost 189,371 for patients on oral contraceptives, 1,081,232 for pregnant women, 1,220,316 for patients on hormone replacement therapy and 1,459,103 for patients undergoing orthopaedic surgery.

Synthesis of costs and benefits
Incremental cost-effectiveness ratios (ICERs) were reported. Universal screening of patients prior to prescribing hormone replacement therapy and restricting prescribing to those testing negative for thrombophilia would prevent 42 VTE events in the hypothetical population. This was the most cost-effective strategy (ICER 6,824) among those examined. In contrast, screening prior to oral contraceptives would only prevent 3 VTE events and was the least cost-effective strategy (ICER 200,402). Overall, selective screening based on the presence of personal and/or family history of VTE prevented fewer cases of adverse clinical complications, but was more cost-effective than universal screening in all four screening scenarios.

The one-way univariate sensitivity analysis showed that the results of the model were relatively robust. The model was most sensitive to test sensitivity and specificity, but changes in the key parameters did not significantly alter the overall results.

The scenario analysis showed that prescribing transdermal hormone replacement therapy in place of withholding therapy for those testing positive would incur an additional cost of 491,434. The ICER was approximately 12,404.

In the scenario analysis with the second most commonly prescribed oral contraceptive and second most commonly prescribed hormone replacement therapy, the relative cost-effectiveness between groups remained unchanged.

Authors’ conclusions
The universal screening of women prior to prescribing hormone replacement therapy was the most cost-effective strategy tested. The universal screening of women prior to prescribing combined oral contraceptives was the least cost-effective strategy. Selective thrombophilia screening based on personal and/or family history of venous thromboembolism (VTE) was more cost-effective than universal screening in all patient groups.

CRD COMMENTARY - Selection of comparators
Universal and selective screening for thrombophilia was compared with no screening in different high-risk patient groups. No explicit justification was given for the comparators used, but they would appear to reflect current practice in the authors’ setting. You should decide if it is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness parameters used to populate the model were based on both the literature and authors’ assumptions. Although it was stated that all major databases were searched and a quality assessment was undertaken, the authors have not reported sufficient detail. The authors also indicated that, where relevant, a meta-analysis based on a random-effects model and tests of heterogeneity were conducted. More detailed reporting of the review methods would have allowed the quality of the effectiveness parameters to be judged; as it is, the quality is difficult to ascertain.
Validity of estimate of measure of benefit
The measure of effectiveness was the number of major adverse clinical outcomes prevented. This referred to an aggregation of VTE and adverse pregnancy events in the pregnant cohort and to VTE events in the three other cohorts. The authors acknowledged that such an aggregated measure of outcomes is not ideal, but it allows standardised comparison across the patient groups and offers some prioritisation order. They suggested that a generic outcome measure such as quality-adjusted life-years (QALYs) would have been more useful, but QALYs related to the foetus are difficult to quantify.

Validity of estimate of costs
The perspective adopted in the study was explicitly stated with the unit costs and resource use presented separately. Resources were obtained from a Delphi panel rather than directly from a relevant patient population in a clinical trial. The unit costs were derived from relevant literature and a sensitivity analysis was performed by varying the costs within a reasonable range. The time horizon was not reported. Hence the relevance of discounting could not be established. The price year was reported, which will aid future relflation exercises.

Other issues
The issue of generalisability to other settings was not explicitly addressed. The authors made limited comparisons of their findings with those from other studies and highlighted a number of limitations to their analysis. The sensitivity analyses suggested that the results are fairly robust. It appears that the conclusions reached were within the scope of the analysis.

Implications of the study
There were no recommendations for further research.

Source of funding
None stated.

Bibliographic details

PubMedID
16173967

DOI
10.1111/j.1365-2141.2005.05715.x

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Contraceptives, Oral, Combined; Cost-Benefit Analysis; Decision Support Techniques; Delphi Technique; Estrogen Replacement Therapy; Female; Humans; Mass Screening /economics /methods; Middle Aged; Patient Selection; Pregnancy; Pregnancy Trimester, First; Risk Assessment; Thrombophilia /diagnosis /genetics; Venous Thrombosis /genetics

AccessionNumber
22005006564

Date bibliographic record published
31/01/2007

Date abstract record published
31/01/2007