Cost-effectiveness of screening for the factor V Leiden mutation in pregnant women

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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
Two screening strategies for factor V Leiden (FVL) mutation in pregnant women were examined. One was screening all women, while the other was screening only women with a personal or family (first-degree relative) history of venous thromboembolism (VTE).

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised pregnant women attending for antenatal care.

Setting
The setting was secondary care. The economic study was carried out in the UK.

Dates to which data relate
The dates during which the effectiveness and resource use data were gathered were not reported. The price year was 1999.

Source of effectiveness data
The effectiveness evidence was derived from a single study and authors’ assumptions.

Link between effectiveness and cost data
The costing was carried out retrospectively on the same sample of patients as that used in the clinical study.

Study sample
Limited information on the method of selecting the sample was provided. The first 967 women recruited to the GOAL Pregnancy Study (Clark et al., see ‘Other Publications of Related Interest’) were included in the analysis. Universal screening was performed on all 967 women, while selective screening was undertaken on a sample of 113 women with a personal or family history of VTE.

Study design
The authors stated that this was a prospective, unselective study. It would appear that a single cohort of women was
followed and that the impact of the screening strategies was based on assumptions made by the authors. The participants, investigators and doctors were not made aware of FVL status until 6 weeks after delivery, which was the length of follow-up. No details on the loss to follow-up assessment were reported. The number of centres involved was also not reported.

Analysis of effectiveness
The outcome measures used were the number of vascular complications associated with the FVL mutation, including miscarriage, stillbirth or neonatal death, VTE and intrauterine growth restriction, and pre-eclampsia.

Effectiveness results
There were 87 vascular complications. More specifically, 8 miscarriages, 15 cases of stillbirth or neonatal death, one VTE, 45 cases of intrauterine growth restriction, and 18 cases of pre-eclampsia.

Clinical conclusions
The effectiveness results were combined with authors’ assumptions to derive a summary benefit measure.

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

Estimates of effectiveness and key assumptions
It was assumed that enoxaparin prophylaxis, in women identified with the FVL mutation, would have resulted in a 50% reduction in the occurrence of vascular complications. It was also assumed that all individuals (in either strategy) identified as having the FVL mutation would have been given enoxaparin prophylaxis to prevent antenatal and postnatal vascular complications from 12 to 40 weeks’ gestation until 6 weeks postpartum.

Measure of benefits used in the economic analysis
The summary benefit measure used was the number of events prevented by screening. The number of women identified with the FVL mutation and the number of FVL mutations with vascular complications were also reported.

Direct costs
Discounting was not relevant as the costs were incurred during a short timeframe. The unit costs were presented separately from the quantities of resources used for most cost items. The health services included in the economic evaluation were all resources associated with the management of vascular complications (such as inpatient stay, outpatient visits, ultrasound, venograms, heparin, and thromboembolic deterrent stockings) and screening (activated protein C sensitivity ratio and polymerase chain reaction analysis). The cost/resource boundary of the NHS was adopted. Resource use was estimated using data derived from the sample of patients included in the effectiveness study. The costs were derived from NHS hospital trust and from the British National Formulary. The price year was 1999.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not considered.

Currency
UK pounds sterling.

**Sensitivity analysis**
Sensitivity analyses were not performed.

**Estimated benefits used in the economic analysis**
Compared with no screening, the number of women identified with the FVL mutation was 3 with selective screening and 30 with universal screening. The numbers of FVL mutations with vascular complications were 1 (selective screening) and 6 (universal screening), respectively.

Compared with no screening, the number of events prevented was 0.5 with selective screening and 3 with universal screening.

**Cost results**
The total cost of the management strategy was 158,015.49 with no screening (967 women), 161,781.09 with selective screening (113 women) and 197,854.97 with universal screening (967 women).

**Synthesis of costs and benefits**
An incremental cost-effectiveness ratio (ICER) was calculated to combine the costs and benefits of the screening strategy.

The incremental cost per additional event prevented by screening over no screening was 7,535.20 with selective screening and 13,281.16 with universal screening. The ICER for selective screening was 4,418.04 when assuming a 75% reduction with prophylaxis and 2,859.47 when assuming a 100% reduction with prophylaxis. The ICER for universal screening was 8,248.24 when assuming a 75% reduction with prophylaxis and 5,732.44 when assuming a 100% reduction with prophylaxis.

**Authors’ conclusions**
Neither form of screening for the factor V Leiden (FVL) mutation was cost-effective, even if prophylaxis resulted in a 100% reduction in complications and their associated costs.

**CRD COMMENTARY - Selection of comparators**
The selection of the comparator (no screening) was appropriate as it reflected the current standard of care for pregnant women receiving antenatal care. You should decide whether this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness was based on data derived from both a single cohort of women who were prospectively followed and from some authors’ assumptions. Limited information on the design and characteristics of the single studies was provided. Thus, it was difficult to examine the internal validity of the study. Further, sensitivity analyses were not carried out and only one assumption was varied.

**Validity of estimate of measure of benefit**
The summary benefit measure was specific to the interventions considered in the analysis, and is not comparable with the benefits of other health care interventions. As the authors pointed out, the possible benefits to women of knowing they had the FVL mutation were not considered.
Validity of estimate of costs
The authors stated explicitly the perspective adopted in the study and extensive details on the unit costs were provided. The source of the data was reported. Information on resource use was derived from patient-level data. The price year was reported, which aids refiation exercises in other settings. However, the costs were treated deterministically and the cost estimates were specific to the study setting. No sensitivity analyses were carried out.

Other issues
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Sensitivity analyses were not carried out and only one key assumption was varied. This reduced the external validity of the analysis. The authors noted that some of the assumptions made in the analysis had not been assessed in robust studies. Further, the costs to treat adverse events of prophylactic treatment were not considered, although the authors stated that their impact would have been modest. The authors explained the possible reasons for screening being not cost-effective.

Implications of the study
The authors stated that their findings could be extrapolated to other thrombophilic defects, such as prothrombin 2021A. Overall, the study results did not support the implementation of screening for LVF mutation in the population of pregnant women.

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Other publications of related interest

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