Should female relatives of factor V Leiden carriers be screened prior to oral contraceptive use? A cost-effectiveness analysis
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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.

CRD summary
The objective was to evaluate factor V Leiden (FVL) screening, counselling, and prophylactic anticoagulation strategies, in asymptomatic female relatives of FVL carriers, prior to starting oral contraceptive pills. The authors concluded that FVL screening, followed by counselling, and anticoagulation during high risk periods, was very cost-effective. It is unclear whether the best available evidence was used and so the authors’ conclusions should be considered with caution.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to evaluate factor V Leiden (FVL) screening, counselling, and prophylactic anticoagulation (AC) strategies with the aim of reducing the risk of venous thromboembolism (VTE) in asymptomatic female relatives of FVL carriers prior to starting oral contraceptive pills (OCPs).

Interventions
The usual care, with no screening for FVL, was compared with:

- screening alone, without counselling on the risks of using OCPs and without prophylactic AC;
- screening, followed by counselling, without prophylactic AC;
- screening, followed by counselling, with prophylactic AC during high risk periods (such as pregnancy, surgery, immobilisation, bed rest, or air flight), using low molecular weight heparin (LMWH);
- and screening, followed by counselling, with long-term prophylactic AC, using LMWH.

Location/setting
USA/primary care.

Methods
Analytical approach:
A decision tree was used to model the clinical pathway, using data from various sources and a time horizon of 30 years. The authors did not report the perspective.

Effectiveness data:
Data from published studies were used to estimate the risk of VTE in patients who were FVL positive, using OCPs, or pregnant, and the effectiveness of LMWH prophylaxis in reducing the risk of VTEs (Couturaud, et al. 2006, Couturaud, et al 2008, and Middeldorp. 2001, see 'Other Publications of Related Interest' below for bibliographic details).

Monetary benefit and utility valuations:
The utility estimates were derived from a published study (Aujesky, et al. 2005, see 'Other Publications of Related Interest' below for bibliographic details).
Measure of benefit:
The measure of benefit was the quality-adjusted life-year (QALY) gained and these were discounted at an annual rate of 3%.

Cost data:
The direct costs included those of screening and counselling, short and long-term LMWH, VTEs including deep vein thrombosis and pulmonary embolism, adverse events including bleeds and postphlebitic syndrome following LMWH use, and death. The drug costs were obtained from The Red Book in 2006. Other unit costs were derived from a published study (Aujesky, et al. 2005). All costs were reported in US dollars ($) and the annual discount rate was 3%.

Analysis of uncertainty:
One-way sensitivity analysis was used to explore the parameter uncertainty and the results for the most sensitive variables were presented in a table. Further sensitivity analysis was conducted on whether non-hormonal birth control was as effective as OCPs and on the cost of pregnancies, which were not included in the base case. Probabilistic sensitivity analysis was also conducted, with the distributions reported for each parameter and the results presented using cost-effectiveness acceptability curves.

Results
The expected QALYs per patient were 20.040 for no screening, 20.037 for screening alone, 20.054 for screening and counselling, 20.137 for screening, counselling and high risk AC, and 20.141 for screening, counselling and long term AC. The total costs were $806.60 for no screening, $871.00 for screening, $779.70 for screening and counselling, $791.90 for screening, counselling and high risk AC, and $3,536.30 for screening, counselling and long term AC. Screening and counselling without AC was the least expensive strategy.

The incremental cost-effectiveness ratio (ICER) of screening, counselling and high risk AC compared with screening and counselling was $147 per QALY. The no screening strategy and screening alone strategy were more expensive and less effective compared with the two more effective strategies, and so were dominated. The ICER of screening, counselling and long term AC compared with screening, counselling and high risk AC was $639,500 per QALY.

The authors stated that these results were robust to variation in most of the parameter values.

Based on a threshold of $20,000 per QALY, the probabilistic sensitivity analysis revealed that the probability of being the most cost-effective strategy was 74% for screening, counselling and high risk AC, 13% for screening and counselling, and 10% for no screening.

Authors’ conclusions
The authors concluded that FVL screening, prior to the use of OCPs, followed by counselling on the risks of using OCPs, and prophylactic AC at high-risk periods, was cost-effective and the small benefit gained by long-term prophylactic AC did not justify its increased cost.

CRD commentary
Interventions:
Each strategy was well described and appropriately compared with usual practice.

Effectiveness/benefits:
No systematic review of the literature was reported, so it is unclear whether the best available evidence was used. The baseline estimates and sources were reported, but no further details on the methods used in the source studies were given. The reporting of the assumptions was appropriate.

Costs:
As the authors did not report the perspective, it is unclear whether the costs reflected the perspective. A breakdown of the unit costs and the sources was provided. The drug costs were derived from a standard source, but the sources for the other cost data were not described, so it is not clear how valid they were for the population and setting. Details on the price year and any pricing adjustments were not given.
Analysis and results:
The analytical approach was satisfactorily reported and the model structure was reported in full, with a diagram. The time horizon was appropriate for the strategies considered and the use of an incremental analysis was appropriate. The impact of uncertainty was acceptably explored through one-way and probabilistic sensitivity analysis. The results of the base case and sensitivity analyses were satisfactorily reported and extensively discussed. The authors also pointed out the possible limitations of their model.

Concluding remarks:
The methods and results were well reported, but there were limitations to the methodology, mainly due to a lack of information upon which to assess whether the best available evidence was used, and consequently the authors' conclusions should be considered with caution.

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