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 strategies to prevent femoral venous catheter-associated pulmonary embolism (PE) were compared. The strategies were physical examination alone without ultrasound and lower extremity unilateral Doppler ultrasound-based screening, performed after 7 days of catheterisation. The ultrasound strategy included unilateral duplex Doppler examination of the proximal veins of the lower extremity catheterised by a femoral central venous line. All patients found to have a deep venous thrombosis (DVT) were given initial anticoagulation with heparin (30,000 U/day) for 5 days followed by coumadin for 3 months.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The population modelled was a hypothetical cohort of 60-year-old patients with acute respiratory failure and requiring mechanical ventilation, with demographics of the most recent US census and a mean age reflecting the epidemiology of ventilated patients.

Setting
The setting was secondary care. The economic evaluation was performed in the USA.

Dates to which data relate
The effectiveness evidence was gathered from studies published between 1960 and 2002. The resource use data were collected from studies published in 1997 and 1998. The prices used related to 2001.

Source of effectiveness data
The effectiveness data were derived from a review of completed studies, and authors' assumptions.

Modelling
A decision analytic model, using a state transition Markov model for long-term survival extrapolation, was used to evaluate the costs and effects of each strategy in a hypothetical cohort of 1,000 patients. The cycle of the model was 1 year. A lifetime horizon was used. The model was based on several assumptions. First, the patients were assumed to receive mechanical ventilation for 7 days, as well as to require ICU care for 8 days and hospital ward stay for an additional 7 days. Second, the patients were assumed to have no contraindications to anticoagulation and received 5,000 units of subcutaneous heparin twice a day. Finally, deaths from recurrent DVT and venous thromboembolic disease
Outcomes assessed in the review
The outcomes assessed were:

- the sensitivity and specificity of ultrasound and physical examination;
- the probability of DVT associated with central venous catheterisation;
- the probability of DVT-associated PE;
- the probability of PE mortality with and without heparin;
- the probability of major heparin-related bleeding or heparin-induced thrombocytopenia;
- the probability of in-hospital death; and
- utilities.

Study designs and other criteria for inclusion in the review
The utility values were obtained from a large cohort of critically ill patients. No further study designs were reported. Although no explicit criteria for inclusion in the review were stated, the authors reported that they included studies that, in their judgement, were of the closest relevance to the target population. They referred the reader to the online supplement for further details.

Sources searched to identify primary studies
MEDLINE was searched from 1966 to April 2002. In addition, a bibliographic search of the reference lists of retrieved articles was conducted.

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
Seventeen studies provided the effectiveness evidence.

Methods of combining primary studies
A narrative method was used to combine the primary studies.

Investigation of differences between primary studies
Not stated.

Results of the review
The sensitivity of ultrasound was 62% (range: 33 - 87) and specificity was 94% (range: 74 - 100).
The sensitivity of physical examination for DVT was 29% (range: 15 - 57) and the specificity was 70% (range: 50 - 88).

The probability of DVT associated with central venous catheterisation was 21.5% (range: 11 - 33).

The probability of DVT-associated PE without heparin was 30% (range: 15 - 45).

PE mortality was 1% (range: 0 - 5) with heparin and 15% (range: 5 - 30) without heparin.

The probability of major heparin-related bleeding was 1.9% (range: 1 - 5).

The probability of heparin-related thrombocytopenia was 1.8% (range: 1 - 2.7).

The baseline probability of in-hospital death was 35.9% (range: 17 - 54).

The utilities were 0.73 for in-hospital survival, 0.79 from discharge until 2 months, and 0.88 thereafter.

Methods used to derive estimates of effectiveness
The authors made some assumptions that were referenced to the literature.

Estimates of effectiveness and key assumptions
The authors incorporated the decreased age-adjusted survival in persons surviving respiratory failure, DVT or PE adjusting. The authors assumed that all recurrent thromboembolic events occurred within one year of discharge, and they assumed an extra decrement in survival of 8% for undiagnosed DVT or PE, and 4% for correctly diagnosed and treated patients. After the initial 2 years, mortality was assumed to parallel population age-, ethnicity-, and sex-appropriate rates from reported 1998 census data.

Measure of benefits used in the economic analysis
The measure of benefit used was the number of quality-adjusted life-years (QALYs) gained. The utility values were taken from a study of critically ill patients that used the time trade-off technique (Tsevat et al., see Other Publications of Related Interest). The secondary outcomes included the number of catheter-related PEs averted and PE-associated deaths averted. Discounting was applied to the benefits and costs at a rate of 3% per year.

Direct costs
Discounting was appropriately performed given the long-term horizon of the study. The costs prior to 2001 were reflated to 2001 using the medical care component of the Consumer Price Index. The quantities and the unit costs were analysed separately for some cost elements considered in the analysis. The direct costs considered included ICU days, hospital ward days, PE episodes, major bleeding episodes and heparin-related thrombocytopenia episodes, which were grouped later into initial treatment costs and future costs categories. Clinically undetected DVTs and PEs, as well as DVTs and PEs not associated with adverse outcomes, were assumed to contribute no increased costs. The quantity/cost boundary adopted was that of the health care payer (health service). The estimates were derived by modelling based on institutional data and published sources. The price year was 2001.

Statistical analysis of costs
The costs were treated as deterministic point estimates, and ranges were evaluated in the sensitivity analysis.

Indirect Costs
No indirect costs were included.

Currency
US dollars ($).

**Sensitivity analysis**
Several types of sensitivity analysis were performed with the probabilities, outcomes and costs. More specifically, one-, two-, three- and four-way analyses, best- and worst-case scenarios, and a probabilistic sensitivity analysis using Monte Carlo analysis. The ranges were chosen by incorporating either the 95% confidence interval of meta-analyses, using the greatest variability observed in the literature, or by halving or doubling values. The probability distributions used in the probabilistic sensitivity analysis were not reported. Sub-group analyses were performed for different age and gender groups.

**Estimated benefits used in the economic analysis**
The QALYs obtained in the base-case scenario were 5.598 with the ultrasound strategy and 5.581 with the no ultrasound strategy (0.016 incremental QALYs or 5.9 quality-adjusted life-days).

The life-years obtained were 6.373 with the ultrasound strategy and 6.355 with the no ultrasound strategy (0.018 incremental life years).

The number of PEs per 1,000 patients was 27.2 with the ultrasound strategy and 53.4 with the no ultrasound strategy (-26.2 incremental PEs per 1,000). The numbers of PE deaths per 1,000 patients were 1.4 (ultrasound) and 2.8 (no ultrasound), respectively (-1.4 incremental PE deaths per 1,000 patients).

By implementing an ultrasound-based strategy, for every 10,000 tests done, 263 nonfatal and 14 fatal PEs would be averted at the expense of 14 major episodes of gastrointestinal bleeding and 13 episodes of heparin-induced thrombocytopenia.

**Cost results**
The initial treatment costs were $16,538 with the ultrasound strategy and $16,409 with the no ultrasound strategy.

Future complication costs were $345 (ultrasound) and $335 (no ultrasound), respectively.

The total costs were $16,883 with the ultrasound strategy and $16,744 with the no ultrasound strategy (incremental costs of $139).

**Synthesis of costs and benefits**
For the ultrasound versus no ultrasound strategies in the base-case analysis of a 60-year-old cohort member, the incremental cost per QALY was $8,688, the incremental cost per life-year was $7,722, the cost per PE averted was $5,305, and the cost per life-year saved from PE death was $99,286. In the probabilistic analysis, the ultrasound strategy was associated with median costs of $12,793/QALY gained (interquartile range: 8,176 - 20,648/QALY gained) and resulted in costs of less than $44,000/QALY in 95% of simulations.

Best- and worst-case scenarios resulted in incremental cost-effectiveness ratios (ICERs) of $1,170/QALY gained (best-case) and $35,342/QALY gained (worst-case), respectively. In the sub-group analysis, the ICER was $8,862/QALY gained for 60-year-old males and $8,124/QALY gained for 60-year-old females. Also, for an average cohort member, the ICER ranged from $6,834/QALY gained for 40-year-olds to $15,211/QALY gained for 80-year-olds.

The ICER was most sensitive to changes in the probability of PE in the setting of DVT without anticoagulation, ultrasound sensitivity, the probability of catheter-associated DVT, the probability of in-hospital death, and the assumptions used for predicting long-term effect of DVT on survival. Complication rates, diagnostic test costs, hospital care costs, treatment hospital days required and illness-associated complications had a minor influence on the ICER.

**Authors' conclusions**
Compared with the strategy of no ultrasound, an ultrasound-based screening strategy could have long-term beneficial effects among critically ill patients with femoral venous catheters at a reasonable cost.

**CRD COMMENTARY - Selection of comparators**
The comparator of not conducting ultrasound was selected, as the authors stated that it is usual practice not to perform routine ultrasound in critically ill patients, a population with a high risk of DVT or PE. Venography was explicitly excluded on the grounds that it is seldom used in the ICU setting. No other potential comparator was mentioned. You should judge if the comparator represents current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The authors stated that the parameters to populate the model came from a review of the literature. While the sources were stated, there were insufficient data in the article to judge their quality, the study selection criteria, and their combination. The general method used to select the ranges for the analysis was stated, but not specifically for each parameter. The probability distributions of parameters for the Monte Carlo analysis were not specified.

**Validity of estimate of measure of benefit**
The authors appropriately modelled the estimation of benefits using a Markov model, but some health states (e.g. adverse events) were not specifically valued and this could slightly alter the results. The assumptions used to derive some model parameters were referenced to the appropriate literature. An extensive sensitivity analysis was performed, which strengthened the conclusions of the study.

**Validity of estimate of costs**
All the cost categories relevant to the stated perspective were included. The costs and the quantities were reported separately for some of the cost elements included in the analysis, which would be helpful in any extrapolation exercises. Resource use was derived from the literature or authors’ assumptions, but no sensitivity analysis was specifically conducted. However, a sensitivity analysis of the prices was conducted, and the ranges used appear to have been appropriate. The date to which the prices referred was reported. These facts improve the generalisability and reproducibility of the results. Discounting was appropriately undertaken since the costs were incurred during the patients’ lifetime. It was stated that the cost methods were described in more detail in the online supplement of the article.

**Other issues**
The authors appropriately compared their study results with the cost-effectiveness of other practices, both in the critical care setting and in other settings. They also addressed the general limitations of a cost-effectiveness analysis in the critically ill, owing to the lack of population-specific data, and some specific limitations of their models. For example, not addressing the relationship of catheterisation duration and DVT risk, and not incorporating catheter-related bloodstream infections. The issue of generalisability to other settings was partially addressed using sensitivity analyses. The results of the analysis were adequately reported.

**Implications of the study**
In the absence of a definitive randomised clinical trial, the results of this study may be useful for decision-making in this patient population where recent guidelines have not directly addressed this issue. In summary, ultrasound screening may improve outcomes among critically ill patients with respiratory failure, and who require femoral venous catheters, at acceptable costs. It could also complement venous thrombosis primary prevention programmes. Further study of the prevention, early detection, and treatment of venous thromboembolic disease among this population may improve outcomes while also reducing the costs of intensive care.

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**Other publications of related interest**

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