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
Three alternative diagnostic strategies for diagnosing pulmonary embolism (PE) were evaluated. All strategies began with a ventilation-perfusion scan, and were then followed by a variety of different strategies in patients with a nondiagnostic result:

- ventilation-perfusion scans and pulmonary angiography;
- ventilation-perfusion scans, single noninvasive leg test, and pulmonary angiography; and
- ventilation-perfusion scans, serial noninvasive leg tests, and pulmonary angiography.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
A sub-set of patients who participated in the PIOPED study served as the basis for this decision analysis. They were patients with suspected PE and a known cardiorespiratory status, who were examined prospectively by ventilation-perfusion lung scanning and pulmonary angiography.

Setting
The setting was secondary and tertiary care. The economic study was conducted in Canada.

Dates to which data relate
The effectiveness evidence related to 1983 to 1995. The resource use data come from the PIOPED trial (1990), while data on side effects and complications came from a 1992 trial. The price year was 1999.

Source of effectiveness data
The effectiveness data were derived from a review of completed trials.

Modelling
A published decision analytic model was updated to estimate both the effectiveness and costs of applying three different diagnostic strategies to the 662 PIOPED patients with a known status of cardiorespiratory reserve (see Other Publications of Related Interest).
Outcomes assessed in the review
The outcomes assessed were:

ventilation-perfusion results in patients with and without adequate cardiorespiratory reserve,

Doppler ultrasound with B mode sensitivity for deep vein thrombosis (DVT) in patients with PE, and

the additional detection rate with serial testing if the initial ultrasound was negative.

Study designs and other criteria for inclusion in the review
The study designs were not specifically reported.

Sources searched to identify primary studies
Not stated.

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

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

Number of primary studies included
Four primary studies were included in the review. This number excluded the authors’ prior decision analysis.

Methods of combining primary studies
The primary studies were combined in a narrative.

Investigation of differences between primary studies
Not stated.

Results of the review
Of the 662 patients, 56% had adequate cardiorespiratory reserve. In this sub-set of 370 patients, ventilation-perfusion scans were near-normal in 72, nondiagnostic in 255, and of high probability in 43.

In patients with inadequate cardiorespiratory reserve (n=292), ventilation-perfusion scans were near-normal in 33, nondiagnostic in 213, and of high probability in 46.

A single Doppler would detect DVT in 50% of patients with PE.

In 3% of patients with adequate cardiorespiratory reserve and negative initial ultrasound, serial ultrasound would detect DVT.

In all strategies, 105 patients had near normal results in the lung scan (treatment subsequently withheld) and 89 of them had high probability scans (and were assumed to be treated).

Measure of benefits used in the economic analysis
Two criteria of effectiveness were used. These were the correct identification of venous thromboembolism; and the
correct identification of the number of patients in whom treatment was correctly withheld.

**Direct costs**
The quantity/cost boundary adopted was that of a third-party payer (health service perspective). The costs included were those for each diagnostic strategy (including physician or specialist charges for interpretation) plus the costs of treating patients who had positive results. The treatment costs included anticoagulant therapy (drugs, laboratory tests, physician fees), hospital "hotel" costs, and the costs of anticoagulant therapy for side effects. Side effects of pulmonary angiography were excluded as they were considered to be non significant. The initial clinical examination was also excluded because it was common to all strategies. The quantities were partly derived from data and partly using modelling. Although some long-term cost components were included in the study (e.g. long-term warfarin treatment of PE), the authors did not report whether discounting was carried out. The quantities and the costs were analysed and reported separately. More detailed cost information can be obtained from the authors if required. The quantities were derived from trials published in 1990 and 1992. The costs came from an urban teaching hospital in western Canada and the price year was 1999 (inflation-adjusted from original data from 1992).

**Statistical analysis of costs**
The costs were treated deterministically and no statistical analysis was carried out.

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

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
Multiple sensitivity analyses were carried out to evaluate variations in the costs of a hospital bed, treatment and diagnostic tests, and the impact of false-positive tests on noninvasive testing. Variations in PE prevalence in symptomatic patients were also analysed to evaluate generalisability. The ranges used were based on authors’ assumptions. The costs of secondary investigation with electrocardiography, chest X-ray, and so on (which common to all strategies) were also evaluated in a sensitivity analysis.

**Estimated benefits used in the economic analysis**
In strategy 1, all patients with nondiagnostic results (468) would undergo angiography. Of these, 105 would receive treatment (positive result) and 363 with negative results would not receive treatment. In strategy 2, all patients with nondiagnostic results (468) would undergo a single Doppler ultrasound, 53 patients with positive Doppler would undergo treatment and the remaining 415 would undergo angiography (53 positive results receiving treatment).

In strategy 3, all patients with nondiagnostic results (468) would undergo a single Doppler ultrasound and 53 patients with positive Doppler would undergo treatment. Of the 415 patients with negative leg tests, 222 would have adequate cardiopulmonary reserve and would undergo serial Doppler ultrasound (7 being detected and treated). Patients with inadequate cardiopulmonary reserve would undergo pulmonary angiography (resulting in 20 patients with positive tests being treated).

Thus, the total number of patients suspected of requiring treatment was 194 with strategy 1, 195 with strategy 2 and 169 with strategy 3.

**Cost results**
The total costs for 662 patients were Can$2,087,568 with strategy 1, Can$2,021,038 with strategy 2, and
Can$1,506,676 with strategy 3.

**Synthesis of costs and benefits**
The costs per patient requiring treatment were Can$10,761 with strategy 1, Can$10,364 with strategy 2, and Can$8,915 with strategy 3.

The costs per patient in whom treatment was correctly withheld were Can$4,461 with strategy 1, Can$4,328 with strategy 2, and Can$3,056 with strategy 3.

The rankings of the strategies were robust during all conditions of the sensitivity analysis. Strategy 3 (ventilation-perfusion lung scanning, combined with serial Doppler ultrasound with B-mode imaging and pulmonary angiography) proved to be the most cost-effective alternative. An incremental analysis was not performed.

**Authors’ conclusions**
Use of serial ultrasonography in patients with nondiagnostic lung scans and adequate cardiorespiratory reserve was the most cost-effective and the less invasive approach. In addition, it allowed anticoagulant therapy to be safely withheld in the greatest number of patients.

**CRD COMMENTARY - Selection of comparators**
The authors justified their selection of the strategies compared, as well as the exclusion of impedance pletismography, which was considered outdated in current practice. Other excluded strategies that were addressed in the discussion were D-dimer testing and spiral computed tomography (CT). D-dimer testing could have avoided serial ultrasound in 57 patients and saved 1.11%. Spiral CT would have a diagnostic cost of Can$283,696 if implemented instead of leg testing for patients with nondiagnostic lung scans. You should judge if the exclusion of these strategies would limit the application of the result to your own setting.

**Validity of estimate of measure of effectiveness**
The authors did not state that a systematic review of the literature had been undertaken. They updated another decision analysis (Stein et al., see Other Publications of Related Interest). The sources searched for the primary studies, the inclusion criteria, and the data extraction and validation methods, were not reported. These facts make it difficult to assess whether the effectiveness data used to populate the model were derived in a systematic way and thus reflect the best available evidence.

**Validity of estimate of measure of benefit**
The estimation of benefit was modelled and appears to have been clinically significant.

**Validity of estimate of costs**
All the categories of cost relevant to the adopted perspective appear to have been included in the analysis. Some excluded costs were common to all strategies (differential costing) but, although this would alter the total costs, it would not change the incremental analysis. The quantities and the costs were analysed and reported separately, which can help translate the results to other decision-making settings. Several other issues strengthen the generalisability of the results to other settings (although mainly to other settings in Canada). For example, the results were robust to the sensitivity analyses conducted on different cost categories, PE prevalence in symptomatic patients, and the impact of false-positive tests. The price date was reported, which will aid reflation exercises. Resource use and the unit costs were taken from published studies and were treated as deterministic estimates. A statistical analysis would have enhanced their validity.

**Other issues**
The authors made no comparisons with other economic evaluations. Generalisability issues to other settings were
appropriately addressed. The conclusions reflected the scope of the analysis. The results appear to have been reported in full.

**Implications of the study**
A combination of ventilation-perfusion lung scanning and serial noninvasive leg tests safely avoids pulmonary angiography in up to 70% of patients. The incorporation of D-dimer testing to exclude PE is a promising diagnostic option. Spiral CT is also promising but needs further study. Some studies showing the similar effectiveness of repeat leg testing with two serial ultrasounds suggested that such a strategy would be expected to provide more savings than the five serial ultrasounds used in this study.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
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**Other publications of related interest**


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