Cost-effectiveness of rescreening conventionally prepared cervical smears by PAPNET testing
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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
PAPNET supplemental, neural network-based rescreening of cervical smears (Neuromedical Systems, Inc. (NSI), Suffern, New York, USA)

Type of intervention
Screening; Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
Women aged 20-64 years.

Setting
Community. The economic study was performed in the USA.

Dates to which data relate
Effectiveness data were extracted from studies dated 1987 to 1994. 1994 price data were used.

Source of effectiveness data
Effectiveness data were derived from a review of previously completed studies.

Modelling
A Markov model, which had been adapted from a model created by Muller et al for the United States Congress Office of Technology Assessment Model, was used to estimate costs and benefits. The model was adjusted to reflect women aged between 18 and 64, while the original model was designed for women aged 65 and over.

Outcomes assessed in the review
Outcomes assessed included incidences, prevalences and mean durations of low grade squamous intraepithelial lesions (LSIL) & high grade squamous intraepithelial lesions (HSIL); the proportion of SIL that regresses spontaneously; the cure probabilities for treated LSIL and HSIL; the proportion of invasive cancers presenting at stage I or II; and the mean survivals associated with invasive cancer at stages I or II and III or IV. Improvements in specificity and sensitivity of screening with PAPNET were also assessed.
Study designs and other criteria for inclusion in the review
Not stated.

Sources searched to identify primary studies
Not stated.

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

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

Number of primary studies included
Four studies were included in the review.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
Incidences of LSIL ranged from 0.5-3.0 cases per 1,000 per year (depending upon age) and the prevalence of LSIL and HSIL prior to screening was 0.5/1,000. The mean duration of LSIL and HSIL was estimated to be 11 years and the proportion of SIL that regresses spontaneously was determined to be 50%. The cure probabilities were relatively high, being 95% for treated LSIL and 98% for treated HSIL. Although the proportion of invasive cancers that presented at stage I or II was 46%, the mean survival associated with invasive cancer at stages I or II (including long-term survivors) was 13 years. For those patients with invasive cancer at stages III or IV, the mean survival was 6.6 years. These results from the review provided the base case estimates for the model. Adding PAPNET improved sensitivity by approximately 30%, so that false negatives were reduced from 25% to 20% in LSIL and 15% to 12% in HSIL. Sensitivity was reduced from 98% to 95% (increasing the false positive rate).

Measure of benefits used in the economic analysis
The measure of benefits used in the economic analysis were life-years gained.

Direct costs
The perspective was that of the health service. Only direct health service costs were considered. Cost packages were calculated by applying 1994 prices to treatment algorithms as detailed in one published study, except that cryotherapy for treatment of SILs was substituted by laser therapy and loop electrosurgical excision (those packages had been derived by reviewing hospital discharge data with relevant ICD-9 codes). The cost for physician services were median 1994 charges submitted by fee-for-service physicians to indemnity plans, and the hospitalization charges used were calculated by the Health Care Financing Administration for 1992 and updated to 1994 dollars using a 10% annual health care inflation rate. NSI provided the charges for PAPNET rescreening.

Statistical analysis of costs
Indirect Costs
Not included.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analysis was performed on the costs and certain attributes of the screening programme (such as the screening interval, smear quality, PAPNET performance, course of follow-up, incidence of cervical neoplasia, prevalence of low grade SIL, and mean duration of preinvasive lesions).

Estimated benefits used in the economic analysis
The life-years gained were not reported for each strategy, but were mentioned to have been discounted at an annual rate of 5%.

Cost results
The costs of the care packages were as follows:

- $23 for screening by cervical smear,
- $30 for PAPNET rescreening,
- $311 for colposcopy.

The evaluation, treatment and follow-up costs (exclusive of colposcopy) were $1944 for LSIL and $9528 for HSIL. The cost of diagnosis, treatment & follow-up for early invasive cancer was $23,015 and for late invasive cancer $34,270. All costs were discounted at 5%.

Synthesis of costs and benefits
The cost-effectiveness ratio for adding PAPNET rescreening to an existing biennial screening program was $48,474 per life-year gained. Sensitivity analysis revealed that costs were not found to have a major influence on the results. If the interval between screening was increased to every three years, the cost-effectiveness ratio improved to $25,185 per life year gained. However if the screening interval was shortened to yearly, the cost-effectiveness ratio worsened to $113,078 per life year gained. If the quality of the smear was decreased, this created a favourable effect on the cost-effectiveness ratio: $17,518 per life year gained when the sensitivity of the smear was 0.65 for LSIL and 0.75 for HSIL. Conversely, the cost-effectiveness ratio became less favourable at $85,891 per life year gained when the quality of the smear was improved to a sensitivity of 0.85 for LSIL and 0.9 for HSIL. When the performance of PAPNET was enhanced, the cost-effectiveness ratio was estimated to be $37,843 per life year gained, while a degraded performance achieved an unfavourable cost-effectiveness ratio of $71,907 per life year gained. Follow-up practices vary according to setting. If abnormal smears were followed up with immediate colposcopy, the cost-effectiveness ratio was $82,851 per life year gained, but if colposcopy were used only for women with repeatedly abnormal smears, the cost-effectiveness ratio was $28,869 per life year gained. Sensitivity analyses were also performed by varying the incidence of cervical neoplasia, prevalence of low grade SIL, and mean duration of preinvasive lesions.

Authors’ conclusions
The PAPNET rescreening programme can reduce morbidity and mortality from cervical cancer, comparing favourably
in terms of cost-effectiveness to other commonly used interventions and diagnostic procedures. This is even though secondary screening techniques such as PAPNET are unlikely to match the cost-effectiveness ratios of original smear screening tests.

**CRD COMMENTARY - Selection of comparators**
Whilst the choice of comparator is not explicitly justified, it appears that the addition of PAPNET is compared to usual practice and is, therefore, sensible.

**Validity of estimate of measure of benefit**
The calculation of life-years gained was not explicit and nor was it immediately obvious in the study.

**Validity of estimate of costs**
Adequate details were given of the sources of the estimates, prices and the price date. However costs were only from the perspective of the purchaser/provider and excluded direct non-medical and indirect costs, which may vary according to the frequency of screening.

**Other issues**
The cost data are unlikely to be generalisable to other countries. The sensitivity and the specificity of the tests are likely to vary from setting to setting. When applied to cost-effectiveness, the term incremental is preferred to marginal.

**Implications of the study**
Given the difficulties associated with adherence rates under intensive screening policies, a screening policy of moderate frequency involving PAPNET would represent a sensible strategy for decreasing morbidity and mortality from cervical cancer.

**Source of funding**
None stated.

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