Cost-effectiveness of 21 alternative cervical cancer screening strategies

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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
This study examined the cost-effectiveness of 21 cervical cancer screening strategies, using combinations of the Papanicolaou smear (Pap), liquid-based cytology, and human papillomavirus (HPV) deoxyribonucleic acid (DNA) testing. The best strategy was Pap screening, for women aged 18 to 69 years, every three years, with HPV-DNA testing for those aged 30 years or older, who had atypical squamous cells of undetermined significance. Despite limited reporting of the clinical sources, the study was well conducted and the author’s conclusions are robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to examine the cost-effectiveness of 21 cervical cancer screening strategies, which were combinations of the Papanicolaou smear test (Pap), liquid-based cytology, and human papillomavirus (HPV) deoxyribonucleic acid (DNA) testing.

Interventions
There were seven screening and testing comparators and they were evaluated at intervals of one, two, and three years.

In Pap plus Pap, women aged 18 to 69 years were screened, using the Pap, and their management depended on the results of these tests. This was the strategy in use, at the time of the study, in the authors setting, with one-yearly (annual) testing.

In Pap plus HPV plus Pap, the protocol was identical to the previous one, except that women with atypical squamous cells of undetermined significance (ASCUS) were offered a HPV-DNA test for the presence of high-risk oncogenic HPV.

In Pap plus HPV plus Pap at 30 years, the protocol was identical to the first one, except that women aged 30 years or older with ASCUS were offered the HPV-DNA triage test.

In cytology plus HPV plus cytology, women aged 18 to 69 years were screened, using liquid-based cytology and those with a low-grade squamous intra-epithelial lesion (LSIL) were re-tested using cytology six months later, while those with ASCUS were offered a HPV-DNA triage test, management depended on the results of the tests.

In cytology plus HPV plus cytology at 30 years, the protocol was identical to the previous one except that only women aged 30 years or older with ASCUS were offered the HPV-DNA triage test.

In HPV plus cytology plus HPV or cytology, women aged 18 to 69 years were screened, using a HPV-DNA test, and their management depended on the results of this test.

In HPV plus cytology plus HPV or cytology at 30 years, the protocol was identical to the previous one for women aged 30 years or older, while younger women received the cytology plus HPV plus cytology protocol.

Location/setting
Canada/primary and secondary care.
Methods
Analytical approach:
The economic analysis was based on a Markov model of the health of women from entering the model up to the age of 80 years. The author stated that the perspective of the health system was adopted.

Effectiveness data:
The clinical data were from sources selected by the author. Most of the epidemiological evidence was from Alberta-specific sources and the remaining data were from Canadian studies. The details of these sources were not given and neither was their comparability. The key inputs were the transition probabilities across health states and these were from published literature, but the details were not reported.

Monetary benefit and utility valuations:
The utility values were derived from a published report from the Canadian Agency for Drugs and Technologies in Health.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at 3% per annum.

Cost data:
The economic analysis included the costs of general practitioner visits, chest X-ray, tests (Pap, cytology, and HPV-DNA, including labour, equipment, and supplies), colposcopy, cone biopsy, punch biopsy, laser therapy, loop electrosurgical excision procedure, chemotherapy, radiation, pelvic lymphadenectomy, hysterectomy, and end-of-life care for cancer (one year before death). The costs and resource quantities were from Alberta-specific databases of official prices. The price year was 2007 and all costs were in Canadian dollars (CAD) and were discounted at an annual rate of 5%.

Analysis of uncertainty:
The expected mean costs and QALYs were calculated form 6,000 Monte Carlo simulations, using pre-defined distributions and standard errors, which were reported, for each input. A cost attribution analysis was undertaken to consider the impact of the screening strategies on various budgets.

Results
The expected costs and QALYs were only presented graphically.

After excluding dominated strategies, which were less effective and more costly, compared with one-year Pap plus Pap (the current pattern of care), three-year Pap plus HPV plus Pap at 30 years was dominant, while the incremental cost per QALY was CAD 58,512 with one-year Pap plus HPV plus Pap at 30 years, CAD 86,266 with one-year Pap plus HPV plus PAP, and CAD 127,076 with one-year cytology plus HPV plus cytology.

The probabilistic analysis showed that, in more than 98% of simulations, two- and three-year Pap plus Pap and one-, two-, and three-year HPV plus cytology plus HPV or cytology at 30 years were less costly and less effective than one-year Pap plus Pap. In 63% of simulations for three-year Pap plus HPV plus Pap at 30 years and 45% for three-year cytology plus HPV plus cytology at 30 years, they were less costly and more effective than the current pattern of care.

In comparison with one-year Pap plus Pap, three-year Pap plus HPV plus Pap at 30 years was associated with a reduction in testing costs of 22.1% and physician costs of 18.6%, and an increase in in-patient costs of 0.8% and outpatient costs of 27.7%.

Authors' conclusions
The author concluded that three-year Pap plus HPV plus Pap at 30 years was the most cost-effective strategy.

CRD commentary
Interventions:
The strategies were appropriately selected as they covered the full range of possible screening strategies, including the
current pattern of care in the author's setting, which was one-year Pap plus Pap. A clear description of each screening protocol was given. These strategies are generalisable to other settings with similar health care systems.

**Effectiveness/benefits:**
Limited information on the data sources was provided. The author did not describe the types of data used, which prevents an objective assessment of the clinical evidence. This evidence appeared to reflect the Canadian setting and the approach might have been appropriate for representing the epidemiological context of the screening. The utility values were from a published report, the features of which were not reported. QALYs were an appropriate benefit measure given the impact of cervical cancer on both survival and quality of life.

**Costs:**
The analysis of costs was consistent with the perspective stated, for both the cost categories and the sources of data. The details of the derivation of some key costs, such as physician fees were provided. The sources of costs were reported, but the costs were reported as category totals and not broken down into individual items. Other aspects of the economic analysis, such as the price year and the use of discounting, were given. The cost attribution analysis made the findings relevant for various stakeholders. The costs were varied in the probabilistic sensitivity analysis, using appropriate gamma distributions.

**Analysis and results:**
The analytical approach was valid and the decision model was well presented in its pathways and transition patterns. Selected results were reported due to the large number of options compared and only incremental cost-utility ratios were given. The costs and benefits were presented graphically. Sensitivity analyses were appropriately carried out to investigate whether the base-case findings were robust. Most of the data, particularly the epidemiological data, referred to the Canadian health care setting and caution is required if extrapolating these results to other contexts as they might not be similar.

**Concluding remarks:**
Despite limited reporting of the sources of clinical data, the study appears to have been well conducted and the author’s conclusions are robust, as shown in the sensitivity analysis.

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