Cost-effectiveness analysis of human papillomavirus DNA testing and Pap smear for cervical cancer screening in a publicly financed health-care system

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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 strategies for human papillomavirus (HPV) deoxyribonucleic acid (DNA) testing combined with Papanicolaou (Pap) smear for healthy women aged 30 years or older. HPV DNA testing was cost-effective compared with no screening or annual Pap smear, in Taiwan. HPV DNA testing then three- or five-yearly Pap was most cost-effective, with five-yearly intervals being best for the publicly financed health care system. The study was generally well conducted and the authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The study examined the cost-effectiveness of various strategies for human papillomavirus (HPV) deoxyribonucleic acid (DNA) testing combined with Papanicolaou (Pap) smear for healthy women aged 30 years or older.

Interventions
Three screening strategies were considered: Pap smear alone; HPV DNA test followed by Pap smear for positive DNA results; and HPV DNA testing combined with Pap smear. Positive Pap smear tests were followed by biopsy, except in the combined strategy, where a repeat smear test was performed, with a biopsy for positive results. Three screening intervals were considered: annual, every three years, and every five years. This created nine possible screening strategies and a background strategy of no screening was considered.

Location/setting
Taiwan/primary care.

Methods
Analytical approach:
The analysis was based on a published decision-analytic model, with a lifetime horizon. The authors stated that the perspective of the health care system was adopted.

Effectiveness data:
The clinical data were from a selection of relevant studies. Most of the epidemiological data, the screening coverage rates, and the survival rates were from Taiwanese studies and registries. The natural history of cervical disease was from a published study. The key input of the model was the accuracy (sensitivity and specificity) of the screening tests. These data were from a clinical trial and a published meta-analysis of clinical uses of the HPV DNA testing.

Monetary benefit and utility valuations:
The utility values were from a published economic evaluation that used US estimates.

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

Cost data:
The economic analysis included the costs of the screening tests, diagnosis including the repeat Pap test and colposcopy with biopsy, and treatment for both pre-cancerous lesions and cervical cancer. The costs of the Pap smear included sampling (selecting eligible women), pelvic examination, and cytological examination. Most of the costs were from official National Health Insurance (NHI) reimbursement rates, while others were from published sources. The unit costs were reported for the screening and diagnostic tests, while category costs were presented for the treatment of pre-cancerous lesions and cancer. The costs were in Taiwan dollars (TWD) and a 3% annual discount rate was applied.

Analysis of uncertainty:
The uncertainty was assessed in a probabilistic sensitivity analysis, which used published ranges of values for the clinical inputs and arbitrary ±50% variations for the cost inputs. Pre-determined probability distributions were applied for each set of parameters. Cost-effectiveness acceptability curves were generated for various willingness-to-pay thresholds. A scenario analysis considered 100% coverage rate for all screening options.

Results
The projected QALYs were 25.5583 with no screening, 25.5612 with five-yearly Pap, 25.5620 with three-yearly Pap, 25.5629 with annual Pap, 25.5636 with HPV then five-yearly Pap, 25.5639 with five-yearly combined, 25.5644 with HPV then three-yearly Pap, 25.5645 with three-yearly combined, 25.5647 with HPV then annual Pap, and 25.5648 with annual combined screening.

The costs were TWD 425 with no screening, TWD 2,352 with five-yearly Pap, TWD 3,045 with three-yearly Pap, TWD 4,242 with annual Pap, TWD 5,202 with HPV then five-yearly Pap, TWD 6,088 with five-yearly combined, TWD 6,261 with HPV then three-yearly Pap, TWD 7,301 with three-yearly combined, TWD 7,507 with HPV then annual Pap, and TWD 8,696 with annual combined screening.

When the decision threshold was three times the gross domestic product per capita (TWD 1,620,000), all strategies were cost-effective compared with no screening. Excluding dominated strategies that were less effective and more expensive or less cost-effective, compared with the next most effective strategy, the incremental cost per QALY gained was TWD 659,966 with five-yearly Pap, TWD 888,718 with three-yearly Pap, TWD 1,323,497 with HPV then five-yearly Pap, and TWD 1,357,692 with HPV then three-yearly Pap. The remaining non-dominated strategies had costs per QALY higher than the threshold.

Compared with annual Pap, which was the usual strategy in Taiwan, the incremental cost per QALY gained was TWD 1,302,645 with HPV then three-yearly Pap, and TWD 1,246,883 with HPV then five-yearly Pap. Increasing the coverage rate to 100% increased the costs and QALYs of the annual screening strategies. The probabilistic analysis showed that the greatest expected net benefits were achieved with HPV then five-yearly Pap, and HPV then three-yearly Pap.

Authors' conclusions
The authors concluded that HPV DNA screening was cost-effective compared with no screening or annual Pap smear, in Taiwan. Extending the screening interval from annual Pap to HPV then three- or five-yearly Pap was most cost-effective, with five-yearly intervals being best for the publicly financed health care system.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear. All possible screening strategies and reasonable intervals were considered. The usual care was annual Pap smear. The comparators appear to be relevant for other settings.

Effectiveness/benefits:
No systematic review was reported to identify the relevant sources of evidence, but the use of Taiwanese registries and databases for the epidemiological data and coverage rates was appropriate, as these are country-specific inputs. The use of a clinical trial and a meta-analysis for the screening accuracy data should guarantee high internal validity, but the methods of these sources were not reported in detail, which reduces the ability to judge the validity of the data. The authors did not consider any heterogeneity between these studies. QALYs were an appropriate benefit measure, given the impact of the cervical cancer on both survival and quality of life, but the derivation of the utility values, including...
who provided them and the instrument used, was not reported.

Costs:
The cost categories were consistent with the perspective of the public reimbursement authority. The unit costs were presented for some categories, but the treatment costs were reported as category totals. They were from published sources, but the methods used to calculate them were not reported. This approach is common in the assessment of cancer treatment costs, but it reduces the transparency of the analysis. Some information on resource consumption was given and it appears that the data were from a study conducted in Taiwan and representative of the authors’ context. The price year was not explicitly stated, which will hinder reflation exercises. Discounting was clearly reported.

Analysis and results:
The projected costs and benefits of the screening strategies were clearly reported and synthesised in a valid incremental analysis, which excluded the inferior or dominated strategies. The uncertainty was satisfactorily investigated in a probabilistic analysis and the findings were clearly illustrated and discussed. The authors acknowledged some limitations to their analysis, which mainly related to the lack of good quality data for some items and the need for some assumptions. They noted that the study focused on women aged 30 years or older, while HPV was common in women under 30 years old. They compared their results with those from other published economic evaluations and pointed out the differences in costs between Taiwan and other developed countries.

Concluding remarks:
The study was generally well conducted and the authors’ conclusions appear to be robust.

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