Cost-effectiveness of cervical cancer screening: cytology versus human papillomavirus DNA 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.

CRD summary
This economic evaluation examined the cost-effectiveness of strategies to screen for cervical cancer, using cytology, human papillomavirus (HPV) testing, or both, for women who had not been vaccinated against HPV. The authors concluded that increasing the interval between screening, and changing the primary test from cytology to HPV, improved the efficacy and decreased the costs of screening, in the Netherlands. The methods were valid and key areas of uncertainty were investigated. The authors' conclusions appear to be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
This economic evaluation examined the cost-effectiveness of various strategies to screen for cervical cancer, using cytology, human papillomavirus (HPV) testing, or both, for women who had not been vaccinated against HPV.

Interventions
The nine main strategies were cytology with repeat cytology for borderline or mildly abnormal smear tests; HPV testing with cytology or cytology and repeat HPV testing for those who were positive for HPV (four strategies); and cytology with HPV testing or HPV and repeat cytology for those with borderline or mildly abnormal smears (four strategies). Women with abnormal smear tests or positive repeat HPV test underwent colposcopy.

The number of screening rounds, the interval between screening, the age for the first screening, and the type of cytology test (conventional or liquid-based cytology) were varied to include all strategies starting at ages 25, 27, 30, and 32 years that had an interval of at least three years and at most 10 years.

Location/setting
Netherlands/secondary care.

Methods
Analytical approach:
The analysis was based on the Microsimulation Screening Analysis (MISCAN) model, which simulated the clinical and economic outcomes for a hypothetical cohort of 100,000 Dutch women, born between 1939 and 1992. A lifetime horizon was considered. The authors stated that the analysis took the perspective of society.

Effectiveness data:
Most of the epidemiological inputs were from Dutch surveillance databases. Screening coverage was also based on Dutch data. The accuracy (sensitivity and specificity) of each screening strategy was the key input for the model. Some estimates were from the Dutch screening programme, while other data were from published studies. Conventional and liquid-based cytology were assumed to have the same efficacy (sensitivity and specificity).

Monetary benefit and utility valuations:
The utility values were from published sources.

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 screening (including invitations and quality assurance, time and travel for the woman being screened, smear taking, cytological evaluation, repeat tests after an inadequate result, and registration on the Dutch database) and the diagnosis and treatment of various stages of cervical cancer. Most of these costs were from Dutch publications. Some of the cost items were reported. The costs were in Euros (EUR) and a 3% annual discount rate was applied. The price year was 2010.

**Analysis of uncertainty:**
Several sensitivity analyses were carried out to investigate the impact of variations in selected model parameters on the cost-effectiveness results. Alternative assumptions were either based on authors’ opinions or on data from the literature. Life-years were used as the benefit measure in an alternative scenario.

**Results**
In the hypothetical cohort of 100,000 eligible women, the expected QALYs of the efficient strategies ranged from 501 to 618 with the cytology strategies, and from 695 to 1,006 with the HPV strategies. The costs (in thousands) ranged from EUR 1,854 to EUR 2,356 with the cytology strategies, and from EUR 3,090 to EUR 14,648 with the HPV strategies.

The most interesting findings were that the usual screening strategy was cost-effective, at a threshold below EUR 7,000 per QALY gained; all efficient strategies used conventional cytology rather than liquid-based cytology; for strategies that started with an HPV test, then cytology, collecting material for cytology during the HPV test was more cost-effective than asking women return for cytology after two weeks.

At a threshold of EUR 20,000 per QALY gained, the most cost-effective strategy was three screening rounds during a woman’s lifetime, with primary HPV screening. At a threshold of EUR 50,000 per QALY gained, seven screening rounds, with primary HPV testing was most cost-effective.

The sensitivity analysis confirmed that primary HPV screening strategies were the most cost-effective options in most cases. Only increasing the HPV test cost to EUR 45 (EUR 33.87 in the base case) or increasing by three times the utility loss for time spent in triage, changed the findings, making primary cytology screening, with HPV triage, the most cost-effective option.

**Authors’ conclusions**
The authors concluded that increasing the interval between screening rounds and changing the primary test from cytology to HPV testing improved the efficacy and decreased the costs of cervical cancer screening in the Netherlands.

**CRD commentary**
**Interventions:**
The selection of the comparators was appropriate as all possible cervical cancer screening strategies were considered, including the usual screening in the authors’ setting (cytology plus repeat cytology triage for borderline or mildly abnormal smears). The comparators are likely to be relevant for other health care settings.

**Effectiveness/benefits:**
Most of the epidemiological inputs and behavioural data, such as the screening coverage, were from large Dutch databases and local studies, which was appropriate. Test accuracy was from several published sources, which were not fully described. An extensive sensitivity analysis was conducted on all the model parameters. QALYs were a valid benefit measure, since cervical cancer and test results can affect quality of life and survival, but the sources for the utility data were not described.

**Costs:**
The economic analysis took a societal perspective and included a wide range of costs. The unit costs were reported for most items, except the costs of cancer care, which were presented as a total. Limited information on the data sources
and quantities of resources was reported. Most of these data were from a Dutch cost study that was relevant to the authors' setting. The price year was explicitly reported, and reflation exercises are possible. The economic inputs were varied in the sensitivity analyses.

Analysis and results:
All the model outcomes were extensively presented, with full details in an online appendix. An incremental analysis was appropriately used to combine the costs and benefits of the strategies. Conventional cost-effectiveness thresholds of EUR 20,000 and EUR 50,000 per QALY gained were used to identify the most cost-effective strategy. Various deterministic sensitivity analyses were carried out, and the methods and results were clearly reported and illustrated. The authors acknowledged some limitations to their analysis, such as the exclusion of herd immunity from vaccinated women, which could have reduced the need for testing. The authors stated that their findings could not be transferred to most countries since the Netherlands had a low background cervical cancer incidence, but the best strategy was likely to be the same in other countries with similar treatment and testing costs and HPV testing accuracy.

Concluding remarks:
The methods were valid, the comparators were appropriate, and key areas of uncertainty were investigated. The authors' conclusions appear to be robust.

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