Effect of type-specific human papillomavirus incidence on screening performance and cost
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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 assessed the effectiveness and costs of type-specific human papillomavirus screening to prevent persistent infection and cervical intraepithelial neoplasia (CIN) in women aged 25 to 34 years. The authors concluded that a combination of cytology and colposcopy was the most sensitive strategy and missed the fewest cases of CIN3 or higher. The study had methodological weaknesses and was not reported transparently, so the authors’ conclusions should be considered with caution.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim was to assess the effectiveness and costs of type-specific human papillomavirus (HPV) screening to prevent persistent infection and cervical intraepithelial neoplasia (CIN). The population was a cohort of women aged 25 to 34 years.

Interventions
Three screening strategies were evaluated. All three started with a type-specific HPV test (HPV16, 18, and other high-risk types). If the result was negative, all women in each strategy were invited back for another screening in three years. If the result was positive, patients in the first strategy were referred for cytology, patients in the second strategy were referred for cytology and colposcopy together, and patients in the third strategy were referred for colposcopy.

Location/setting
Europe/primary care.

Methods
Analytical approach:
The study used an age-dependent Markov model to synthesise the evidence from published studies, to estimate the costs and effectiveness for a hypothetical cohort of 100,000 women. The time horizon was 10 years. The authors did not state the study perspective.

Effectiveness data:
The effectiveness data for screening were from published studies, which were referenced in an online appendix. The main clinical effectiveness estimates were the sensitivity and specificity of the tests; the transition rates between model health states; and the incidence of disease. These and all other background data appear to have been from the published studies. The data for cytology alone were adapted from Cuzick, et al. 200 (see 'Other Publications of Related Interest' below for bibliographic details) and the data for cytology and colposcopy together were adapted from Ronco, et al. 200 (see 'Other Publications of Related Interest' below for bibliographic details).

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The measure of benefit was the total number of missed cases of stage CIN3 or higher, per 100,000 patients after 10 years of screening.
Cost data:
The cost categories were the cost per diagnosed case of stage CIN3 or higher; the cost of triage; and the total cost of screening, which included the costs of HPV deoxyribonucleic acid (DNA) testing, cytology, colposcopy, and combined colposcopy plus biopsy. These cost estimates were from a published study, which provided the weighted mean of four European countries. They were given in US dollars ($) and discounted at a rate of 3% per annum.

Analysis of uncertainty:
One-way sensitivity analysis was performed by varying the sensitivity of the HPV test, and the cytology, colposcopy, and combined tests. The sensitivity of the HPV test was varied from 90% to 99%; that of the cytology test was varied from 70% to 90%; that of the colposcopy test was varied from 75% to 95%; and that of the combined tests was varied from 80% to 99%.

Results
The cumulative percentages of CIN3+ cases missed, after 10 years of screening, were 34.7% for cytology; 8.8% for cytology and colposcopy; and 18.4% for colposcopy. The type-specific incidence of high-risk HPV infections affected the absolute number of CIN3+ cases missed after 10 years of screening.

The cost per detected case of CIN3+ was found to decrease with increasing HPV incidence in all three strategies. For low rates of HPV infection, the combination of tests was found to be cheaper per detected CIN3+ than both individual tests, while colposcopy was cheaper than cytology. The incidence of HPV16 or 18 was a more significant contributor to the cost per detected CIN3+ than the incidence of other high-risk types.

The sensitivity analysis found that the proportion of CIN3+ cases missed could vary between 15% and 53% for cytology; between 2% and 28% for combined tests; and between 6% and 33% for colposcopy. The combination of tests was always the most effective option, followed by colposcopy, and then cytology, while the combination was always the most expensive option, followed by colposcopy, and then cytology.

Authors’ conclusions
The authors concluded that a combination of cytology and colposcopy was the most sensitive strategy and missed the fewest CIN3+ cases. The type-specific HPV incidence was found to affect the absolute number of missed CIN3+ cases and the associated costs.

CRD commentary
Interventions:
The interventions were described and appear to have been appropriate comparators, but it was unclear if the usual care was included. The study population was described.

Effectiveness/benefits:
The reporting of the effectiveness data was very limited. The authors provided a few details, with further data available online. The methods used to identify the clinical data were not reported and it was unclear if a systematic review was undertaken, making it impossible to know if all the best available evidence was included. It was unclear if the benefit measure was the most relevant clinical endpoint. It does not appear to have been discounted and this could affect the results.

Costs:
The perspective was not stated, making it unclear if all the relevant cost categories were included. The costs and resource use data were from one study, which should be consulted to assess its quality. The time horizon was reported, the currency was mentioned in a diagram, and the costs were appropriately discounted, but the price year was not stated and the costs might not have been adjusted for inflation.

Analysis and results:
The costs and outcomes were appropriately synthesised in a decision model. The results were not presented well. Very few absolute results were provided and no incremental analysis was given. The uncertainty was assessed for the sensitivities of the HPV, cytology, colposcopy, and combination tests, but these might not have been the only...
uncertain inputs. The authors reported a number of limitations to their study.

Concluding remarks:
The study had methodological weaknesses and was not reported transparently, so the authors’ conclusions should be considered with caution.

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