Economic evaluation of strategies for managing women with equivocal cytological results in Brazil


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, from the perspective of the health system in a middle-income setting, of strategies for the management of women whose cervical cytology screening results showed atypical squamous cells of undetermined significance. Strategies included repeat cytology, human papillomavirus (HPV) deoxyribonucleic acid (DNA) testing, and colposcopy. The authors concluded that HPV testing for all women was the most cost-effective strategy. The methods were valid and various alternative scenarios were considered. The authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness, in a middle-income setting, of strategies for the management of women whose cervical cytology screening results showed atypical squamous cells of undetermined significance (ASCUS). The options included repeat cervical cytology, human papillomavirus (HPV) deoxyribonucleic acid (DNA) testing, and colposcopy.

Interventions
The five strategies were: repeat cytology, colposcopy, HPV testing, colposcopy for those aged 30 years or older, and HPV testing for those aged 30 years or older.

Repeat cytology was conducted every six months, with a return to routine three-yearly screening, after two consecutive negative results. Women with a second abnormal result were referred to colposcopy. Women with a positive HPV result were referred to colposcopy and those with a negative result received repeat cytology. In the two referral strategies for women aged 30 years or older, those under 30 years old received repeat cytology.

Location/setting
Brazil/primary care.

Methods
Analytical approach:
The analysis was based on a Markov model, with a lifetime horizon. The authors stated that it was carried out from the perspective of the health system.

Effectiveness data:
The clinical data were from a selection of relevant studies, most of which were national databases. Brazilian or Latin American sources were used where available. For example, the incidence of HPV was from a large cohort study conducted in Brazil. The test characteristics were key inputs for the model. The sensitivity and specificity of colposcopy were from a published meta-analysis. Some assumptions were needed and these were clearly reported.

Monetary benefit and utility valuations:
Not considered.
Measure of benefit:
Life-years were the summary benefit measure and they were discounted at an annual rate of 5%.

Cost data:
The economic analysis included the costs of tests, biopsy, and health care resources associated with cervical disease (medical visits, nurse visits, and hospitalisations). The patterns of resource consumption were from published sources and assumptions. The costs were from official Brazilian sources. The cost of the HPV test was assumed, as it was not available in Brazilian public hospitals. All costs were in US dollars ($) and the price year was 2008. A 5% annual discount rate was applied.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on the key inputs, using ranges of values assumed by the authors or from published sources. Best- and worst-case scenarios were examined by varying both the sensitivity and specificity of the tests. Alternative scenarios considered variations in the incidence of HPV and the price of HPV triage. A probabilistic sensitivity analysis was performed using predetermined probabilistic distributions for the model inputs; cost-effectiveness acceptability curves were generated.

Results
The projected costs per patient were $140.9404 with repeat cytology, $145.9959 with colposcopy, $144.1832 with HPV testing, $142.9630 with colposcopy at 30 plus, and $141.9783 with HPV testing at 30 plus. The life-years per patient were 18.83023 with repeat cytology, 18.83104 with colposcopy, 18.83098 with HPV testing, 18.83081 with colposcopy at 30 plus, and 18.83077 with HPV testing at 30 plus.

The incremental analysis showed that colposcopy at 30 plus was dominated, as it was less effective and less cost-effective than another option. The incremental cost per life-year gained was $1,914.87 with HPV testing at 30 plus (over repeat cytology), $10,303.54 with HPV testing (over HPV testing at 30 plus), and $30,211.19 with colposcopy (over HPV testing).

Using the per capita gross domestic product (GDP) in Brazil, the threshold for a cost-effective intervention was $25,876 and for a highly cost-effective intervention it was $8,625.

The sensitivity analysis confirmed that the base-case findings were robust. The most influential inputs were the cost of colposcopy and the diagnostic accuracy of HPV testing. The size of the cost-effectiveness ratios was affected by the discount rate, but the ranking of alternatives was not altered in most scenarios.

The probability of being highly cost-effective was 0.53 for HPV testing for women aged 30 years or older, and the probability of being cost-effective (at the higher threshold) was 0.49 for HPV testing.

Authors’ conclusions
The authors concluded that HPV testing for all women, with an ASCUS cytology result, was the most cost-effective strategy.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as a wide range of strategies was considered, including the usual care in the authors’ setting (repeat cytology). These tests are likely to be relevant in other settings. The authors stated that HPV vaccination was not available in most low- or middle-income countries, and it was therefore not considered, but its implementation would have a big impact on screening strategies.

Effectiveness/benefits:
No systematic review was reported to identify the relevant sources of evidence, which were mainly national sources. A large cohort study conducted in Brazil provided most of the epidemiological data and so these should have been valid. Other data seem to have been from appropriate sources, but these were not fully described, except that one was a meta-analysis, which is a valid way to synthesise data from various studies. The model was calibrated to account for
uncertainty in some clinical parameters. Life-years were an appropriate benefit measure, given the impact of disease on survival. The authors stated that quality-adjusted life-years were not calculated because of a lack of country-specific quality of life data; they acknowledged that this was a limitation of their analysis.

Costs:
The categories of costs reflected the perspective of the health care system. The unit costs of the test strategies were reported, but the costs for each health state were reported as totals without further details. Typical Brazilian sources were used for the resource use, including hospitals and national databases, which were representative of the authors’ context. Some costs were varied in the sensitivity analysis and stochastic distributions were considered in the probabilistic analysis. Other details, such as the price year and discount rates, were reported.

Analysis and results:
The results were clearly presented and an incremental approach was used to synthesise the costs and benefits of the strategies, excluding inferior (dominated) ones. A common pragmatic approach was used to identify the most cost-effective strategy. The uncertainty was satisfactorily investigated, using various approaches, and the key findings were presented. Details of the model and its calibration procedure were clearly reported. The authors stated that this was the first economic evaluation of strategies for managing women presenting with ASCUS cytology results in low- or middle-income countries. The results can be transferred to similar settings.

Concluding remarks:
The methods were valid and various alternative scenarios were considered. The authors’ conclusions appear to be robust.

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