Cost-consequences evaluation between bivalent and quadrivalent HPV vaccines in Italy: the potential impact of different cross-protection profiles

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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 clinical and cost impact of two alternative human papillomavirus vaccines, in Italy. The authors concluded that the bivalent vaccine could prevent more pre-cancerous and cervical cancer lesions than the quadrivalent vaccine, resulting in cost savings. The methods had a number of limitations and the authors' conclusions should be treated with caution.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study assessed the clinical and cost impact of two alternative human papillomavirus (HPV) vaccines, in Italy.

Interventions
The interventions were a bivalent vaccine against HPV 16 and 18 and a quadrivalent vaccine against HPV 6, 11, 16, and 18.

Location/setting
Italy/out-patient care.

Methods
Analytical approach:
A prevalence-based model was used to estimate the net difference in HPV-related lesions and the associated costs averted, by the bivalent vaccine compared with the quadrivalent vaccine. It evaluated a one-year period at a steady state, assuming that the whole population was vaccinated. The authors reported that the perspective was that of the Italian National Health Service.

Effectiveness data:
The clinical and effectiveness data were from a number of published studies. The main effectiveness estimate was the vaccine efficacy against cervical intraepithelial neoplasia (CIN) stage one and stages two or three, cervical cancer, and genital warts, associated with the HPV types that were vaccinated against. These estimates were from a number of clinical trials. The incidences were from published Italian sources, except for genital warts, where the incidence was the European average from published studies.

Monetary benefit and utility valuations:
None.

Measure of benefit:
The benefit measure was the number of cases of abnormal Papanicolaou (Pap) smear, CIN, cervical cancer, or genital warts prevented.

Cost data:
The direct costs were those of the treatment of HPV lesions of all types. This information was from published studies. It was reported that 25% to 40% of all genital wart cases were treated in the public sector and the rest in private
settings; those costs borne by the private sector were not included. The authors assumed that the two vaccines had the same price, and this cost was not included. The price year was 2010 and all costs were reported in Euros (EUR).

Analysis of uncertainty:
One- and two-way sensitivity analyses were undertaken, varying the key model parameters by ±20%. A probabilistic sensitivity analysis was performed, with uniform distributions assigned to the vaccine effectiveness, incident cases, and treatment costs. The cost difference between the two vaccines was replicated 10,000 times, sampling from the specified distributions. The authors varied the duration of vaccine protection, and the additional benefit from vaccination in the prevention of vulvar and vaginal cancer.

Results
In Italy, the additional cases prevented with the bivalent vaccine, compared with the quadrivalent vaccine, were 7,976 for abnormal Pap smears, 601 for CIN1, 1,826 for CIN2/3, and 295 for cervical cancer. The bivalent vaccine did not target the HPV types known to cause genital warts, so the quadrivalent vaccine prevented an additional 25,848 cases.

The total cost saving with the bivalent vaccine, compared with the quadrivalent vaccine, was EUR 2,385,354 per year.

The probabilistic sensitivity analysis showed that the parameters driving the difference in costs were genital wart parameters (treatment costs, difference in vaccine efficacy, and incidence), then cervical cancer parameters. The duration of protection also influenced the results.

Authors’ conclusions
The authors concluded that, in Italy, the bivalent vaccine could prevent more pre-cancerous and cervical cancer lesions than the quadrivalent vaccine, resulting in cost savings, despite the prevention of genital warts with the quadrivalent vaccine.

CRD commentary
Interventions:
The vaccination strategies were clearly reported. The authors stated that the model considered all women in Italy, but the age of vaccination was not reported, which reduces the transparency of the analysis. The usual practice was not stated.

Effectiveness/benefits:
The authors did not report a systematic review, so it is unclear if the best available evidence was used. The clinical sources included phase III randomised controlled trials, which are considered methodologically sound and have good internal validity. The authors stated that they assumed lifelong protection for the two vaccines, but it is unclear how this assumption was incorporated into the model considering that the time horizon was one year. This short time horizon does not appear to have adequately captured the long-term health benefits of vaccination, such as the reduction in cervical cancer mortality, nor its impact on quality of life outcomes (measured in quality-adjusted life-years), which would have been an appropriate measure of benefit and allowed broader comparisons with other health care interventions and diseases.

Costs:
The perspective was clearly reported. The costs of the two vaccines were assumed to be the same, but no evidence was provided to support this assumption. The costs were appropriately not discounted as the time horizon was one year. The lifetime treatment costs for each case prevented were considered and it was unclear if these were discounted. The sources of the unit costs for the treatment and follow-up of HPV-related lesions were provided and most of them were Italian. A breakdown of resource quantities was not presented.

Analysis and results:
The authors reported that all the evidence on costs and outcomes was synthesised, using a model, but no diagram was given, which leaves the model’s structure unclear. The authors performed an appropriate incremental analysis and the results were generally well reported. The calculation of a cost-effectiveness ratio was not required because the bivalent vaccine was more effective (except for genital warts) and less costly than the quadrivalent vaccine. The overall model...
uncertainty was examined in probabilistic sensitivity analysis and the results were generally clearly reported. One- and two-way sensitivity analyses were conducted. The authors stated that the main limitation was that the efficacy data were from studies with different populations and designs, but they did not describe these studies.

Concluding remarks:
The methods had a number of limitations and the authors’ conclusions should be treated with caution.

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