Cost-effectiveness evaluation of a quadrivalent human papillomavirus vaccine in Belgium
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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 compared the cost-effectiveness of a programme of vaccination against human papillomavirus for girls aged 12 years, in addition to cervical cancer screening for women. The authors concluded that a quadrivalent vaccine for girls, in addition to the cervical cancer screening, was cost-effective. The methods were satisfactory, but more detail on the effectiveness data and the costs would have strengthened the findings. Despite this, the authors’ conclusions appear to reflect the scope of their analysis.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study assessed the cost-effectiveness of providing a quadrivalent human papillomavirus (HPV) vaccine for girls aged 12 years, in addition to a cervical cancer screening programme for women.

Interventions
The intervention was a quadrivalent vaccine, targeting HPV types 6, 11, 16, and 18 and administered to girls at 12 years old, in addition to cytology-based cervical screening, and this was compared with the cervical screening alone.

Location/setting
Belgium/primary care.

Methods
Analytical approach:
A published and validated Markov transition model was slightly modified for this economic analysis and a life-time horizon (up to the age of 85 years) was used. The authors reported that the perspective of the Belgian health care payer was adopted.

Effectiveness data:
The effectiveness data were mainly from published studies and, where necessary, several official datasets, such as the UK Cancer Registry. Several assumptions were also required to facilitate the modelling and these were reported. The primary clinical outcomes were the efficacy of the vaccine against cervical cancer, cervical intraepithelial neoplasia (CIN) one to three, and genital warts, all due to HPV6, 11, 16 or 18; the natural progression of HPV infection to invasive disease; survival; and mortality.

Monetary benefit and utility valuations:
The utility weights were primarily from a published study conducted in the USA, which elicited the utilities, using the time trade-off technique, from 150 female volunteers. In this US study the expected time in each disease health state was based on expert opinion. The utility value for the survival of cervical cancer was from another study.

Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years gained (LYG) were the measures of benefit and they were discounted at an annual rate of 1.5%.

Cost data:
The economic analysis included the costs of screening for cervical cancer, vaccine plus general practitioner (GP)
administration, treatment of pre-cancerous lesions, and hospital treatment for cervical cancer or genital warts. The screening costs included Papanicolaou (Pap) smear tests, HPV tests, biopsies, and gynaecologist or GP visits. These costs were reported as total categories. The unit costs were from either official national sources or published literature. They were reported for the price year 2006 in Euros (EUR) and they were discounted at an annual rate of 3%.

Analysis of uncertainty:
The parameter uncertainty was investigated using one-way sensitivity analysis on the: vaccine efficacy, duration of protection, cost of a dose of vaccine, treatment costs, Pap smear sensitivity, discount rates, time spent in CIN and genital wart states, and utility values for cervical cancer at Federation Internationale de Gynecologie et d'Obstetrique (FIGO) stages I, II or III, and IV. A scenario, in which a booster vaccination was administered at 10 years to achieve vaccine protection for either 20 years or a lifetime, was also tested. Two-way sensitivity analysis was conducted by varying both the duration of the vaccine protection and the vaccine efficacy.

Results
Assuming a coverage of 80% in Belgium (60,000 girls vaccinated), the vaccine combined with the screening programme resulted in 2,529,060 LYG or 2,527,800 QALYs. Screening alone resulted in 2,527,680 LYG or 2,526,000 QALYs. The discounted lifetime costs, for the cohort of 60,000 vaccinated females, were EUR 28.38 million for the vaccine with screening versus EUR 9.396 million for screening alone.

Compared with screening alone, screening plus vaccination resulted in an incremental cost-effectiveness ratio (ICER) of EUR 13,756 per LYG or EUR 10,546 per QALY gained.

Sensitivity analyses demonstrated that the results were sensitive to the addition of a booster vaccination, but the ICER remained below or within EUR 30,000 to EUR 45,000 per QALY gained, for vaccination compared with screening alone. The results were also more sensitive to variation in the discount rates.

Authors’ conclusions
The authors concluded that the addition of a quadrivalent HPV vaccine, for girls aged 12 years, to the existing screening programme in Belgium, appeared to be cost-effective.

CRD commentary
Interventions:
The rationale for the interventions was reported and the usual care in the authors’ setting was included. It was not clear if other strategies could have been compared.

Effectiveness/benefits:
No systematic search of the literature was reported. No details of the primary sources, such as their design, study population, and power calculations, were reported. The methods used to combine the data from various sources were not reported. This lack of information makes it difficult to assess the validity of the clinical estimates and it is impossible to be sure that the best available evidence was used. Similarly, little information was provided for the utilities, making a full assessment of their validity difficult. Time trade-off is a valid method for eliciting utilities, but it was not clear how generalisable the utilities from the USA were to Belgium. Some discussion of these issues might have been helpful.

Costs:
The cost categories appear to have reflected the perspective adopted, but the costs were reported as total categories, without the unit costs and resource quantities, which limits the transparency of the analysis. Different discount rates were used for the costs and the benefits, which might reflect Belgium guidelines, but should be considered when generalising the results to other settings. Adjustments for inflation, were necessary, but were not reported, while the price year was reported.

Analysis and results:
The model structure was reported, with the modelling assumptions, but a diagram was only presented for the diagnosis of high-grade squamous intraepithelial lesions, as an example. The sensitivity analysis was restricted to a deterministic...
approach for specific model parameters. A probabilistic approach would have strengthened the analysis. The results of the base-case and sensitivity analyses were presented satisfactorily, with a tornado diagram. Due to the complexity of the disease, a large amount of data was produced and the authors presented a good conceptual overview of their modelling, but the details for some areas might be insufficient.

Concluding remarks:
: The methods were satisfactory, but more detail on the effectiveness data and the costs would have strengthened the findings. Despite this limitation, the authors' conclusions appear to reflect the scope of the analysis.

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