Cost-effectiveness analysis of adding a quadrivalent HPV vaccine to the cervical cancer screening programme in Switzerland
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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
The objective was to estimate the cost-effectiveness of a quadrivalent human papillomavirus (HPV) vaccine for girls aged 11 years, followed by a cervical cancer screening programme, versus the screening programme alone. The authors concluded that HPV vaccination was likely to be cost-effective. The methodology appears to have been appropriate and, on the whole, was clearly and transparently reported. The authors’ conclusions are appropriate and reflect the available evidence.

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

Study objective
The objective was to estimate the cost-effectiveness of a quadrivalent human papillomavirus (HPV) vaccine for girls aged 11 years, followed by a cervical cancer screening programme, compared with a cervical cancer screening programme alone.

Interventions
The quadrivalent prophylactic recombinant HPV vaccine (Gardasil), targeting HPV types 6, 11, 16 and 18, was delivered in three doses. The cervical cancer screening programme was a conventional Papanicolaou (Pap) smear or liquid-based cytology every two years.

Location/setting
Switzerland/primary care.

Methods
Analytical approach:
A Markov model was developed and populated with efficacy and cost data from a range of different sources. The model contained a hypothetical cohort of 41,200 girls aged 11 years. It had an annual cycle length and a lifetime horizon. The health states were: well, infected with HPV, cervical intraepithelial neoplasia (CIN) 1, CIN 2, CIN 3, cervical cancer, and death. The natural history of HPV was based on data from the United Kingdom (Canfell, et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic details). The incidence of HPV infection and the probability of progression, from CIN 3 to cancer at Federation Internationale de Gynecologie et d'Obstetrique (FIGO) stage one, were modified to fit the observed age-specific cervical cancer incidence in Switzerland.

The cervical cancer five-year survival rates and age-specific incidence rates of genital warts were based on data from France and Germany. The age-specific mortalities from all causes in the general female population, and age-specific incidence rates of hysterectomy in Switzerland, were based on standard sources. The cervical cancer screening coverage was based on a survey conducted in Switzerland (Balthasar, et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic details). It was assumed that genital warts were cured within a year and that women who underwent benign hysterectomy did not develop cervical cancer. The authors reported that the analysis was carried out from a direct health care cost perspective.

Effectiveness data:
The efficacy of the quadrivalent HPV vaccine was derived from two Phase III clinical trials. This was then combined
with data on the proportion of precancerous lesions, invasive cancers, and genital warts attributable to HPV 6, 11, 16 and 18 (from Garland, et al. 2007, and The FUTURE II Study Group. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details) to estimate the reduction in incidence of CIN 1, CIN 2, CIN 3, cervical cancer, and genital warts. It was assumed that protection was lifelong without the need for a booster, and that vaccine coverage was 80%. Both these assumptions were tested in the sensitivity analysis.

Monetary benefit and utility valuations:
The utility values for each health state were derived from a US study (Elbasha, et al. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details). The utility for those surviving cervical cancer was assumed to be one. Disutilities were associated with patients having a routine Pap smear, diagnosis as a result of a smear, and genital warts.

Measure of benefit:
The primary measures of benefit were the quality-adjusted life-year (QALY) and the life-year gained (LYG). The discount rate was 1.5% per annum.

Cost data:
The cost categories included the costs of diagnosis (gynaecologist visit, Pap smear, HPV deoxyribonucleic acid (DNA) test, colposcopy, and colposcopy biopsy), treatment for CIN 1, 2, 3, cervical cancer, and genital warts, and vaccine acquisition and administration (half by a general practitioner and half by a gynaecologist). These costs were based on a review of patients treated at a single centre over a five-year period, expert opinion, and two standard data sources. They were reported in Swiss francs (CHF) and the discount rate was 3% per annum.

Analysis of uncertainty:
One-way sensitivity analyses were performed on the duration of efficacy, vaccine efficacy, utilities, duration of genital warts, management costs, discount rates, school programme administration, and co-administration with the hepatitis B vaccine.

Results
The quadrivalent HPV vaccine was found to be 100% effective against HPV types 6, 11, 16 and 18, but a conservative approach was taken and a 95% efficacy rate was assumed. The vaccine was estimated to reduce the incidence of CIN 1 by 33%, CIN 2 and 3 by 52%, cervical cancer by 71%, and genital warts by 86%.

Based on the cohort of 41,200 girls, the cervical cancer deaths were 76 with cervical cancer screening alone and 29 with HPV vaccination followed by cervical cancer screening. Patients experienced 43.030 life-years and 42.987 QALYs with screening alone compared with 43.043 life-years and 43.007 QALYs with HPV vaccination followed by screening. The average treatment cost was CHF 1,809.00 per patient with screening alone compared with CHF 2,329.10 per patient with HPV vaccination followed by screening.

The incremental cost-effectiveness ratio (ICER) was CHF 40,008 per LYG and CHF 26,005 per QALY.

The sensitivity analysis indicated that the ICER was sensitive to the need for a booster 10 years after the first doses to provide lifetime protection (ICER CHF 45,400 per QALY) and discount rates (ICER CHF 105,145 per QALY), but the it did not change substantially with vaccine efficacy, utilities, management costs, school programme administration, or co-administration with the hepatitis B vaccine.

Authors’ conclusions
The authors concluded that HPV vaccination was likely to be cost-effective given the standard threshold in Europe and the implementation of other health interventions in Switzerland.

CRD commentary
Interventions:
The interventions were well described and relevant to the primary health care setting.

Effectiveness/benefits:
The effectiveness of the vaccine was reported, but it was not clear whether a systematic review was conducted to identify all the relevant estimates. The methodologies of the Phase III clinical trials were not reported. The authors acknowledged the limitation that the natural history data needed to be calibrated to fit the age-specific cancer incidence curve observed in Switzerland. The estimation of the utility values was well reported and the authors acknowledged that these values were not based on a European study. Both the vaccine efficacy and the utility valuations were explored in the analysis of uncertainty.

**Costs:**
The costs were relevant to the perspective taken. The unit costs and resource quantities were well reported in tables. The price year was not reported, which makes it impossible to revalue the results in future years.

**Analysis and results:**
The use of a Markov model was appropriate for the disease and the methodology was well reported. The reporting of the results in terms of both cost-utility and cost per LYG was appropriate and generalisable to other settings. The results and uncertainty analysis were well reported. The results of the sensitivity analysis were fully reported, but one-way sensitivity analysis was a limited approach to account for the uncertainty in the model. A multi-way or a probabilistic sensitivity analysis would have been more appropriate.

**Concluding remarks:**
The methodology appears to have been appropriate and, on the whole, was clearly and transparently reported. The authors’ conclusions are appropriate and reflect the available evidence.

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