Cost-effectiveness analysis of the introduction of a quadrivalent human papillomavirus vaccine in France

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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 determine the cost-effectiveness of human papillomavirus (HPV) vaccination in addition to cervical cancer screening. The authors concluded that adding a quadrivalent HPV vaccine to the current French screening programme was cost-effective. Overall the quality of the methodology was appropriate, and the methods and results, were generally well reported. The authors’ conclusions appear to be appropriate given the scope of the analysis.

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

Study objective
The objective was to determine the cost-effectiveness of a human papillomavirus (HPV) vaccination programme, in adolescent females, in addition to the cervical cancer screening programme, in France.

Interventions
This study investigated the use of a prophylactic quadrivalent HPV (types 6, 11, 16, and 18) recombinant vaccine, designed for the prevention of cervical cancer, pre-cancerous lesions, genital warts, and other HPV-related cancers, in combination with a cervical screening programme. In France, cervical screening was recommended every three years from age 25 to 65 years. This intervention was compared with cervical cancer screening alone.

Location/setting
France/primary care.

Methods
Analytical approach:
A published Markov model (Kulasingam, et al. 2003, see ‘Other Publications of Related Interest’ below for bibliographic details), which simulated the natural history of HPV infection, cervical cancer, and the economic consequences of HPV vaccine in the USA, and subsequently in Europe, was adapted and used to assess the cost-effectiveness of adding HPV vaccine to the current screening programme in France. The time horizon of the analysis was the patient’s lifetime. The authors reported that two perspectives were adopted in the economic analysis, that of the direct health care payer, and that of the third-party payer, which only included the direct costs reimbursed by the Securite Sociale.

Effectiveness data:
The effectiveness and clinical data were derived mainly from published studies. No details were provided on how the relevant studies were identified, or the methods used to derive the clinical estimates. However, the authors did provide a summary of all the clinical model parameters and their sources. The main effectiveness estimate was the efficacy of the quadrivalent HPV vaccine, which was derived from clinical trials and other published literature.

Monetary benefit and utility valuations:
The utilities were derived from a published US study (Elbasha, et al. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details), which used time-trade-off techniques to elicit the utilities from a sample of 150 healthy females.
Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years (LYs) gained were used as the benefit measures. A 1.5% annual discount rate was applied.

Cost data:
The direct costs were those relating to: pap smears; HPV DNA tests; colposcopy and biopsy; treatment of cervical intraepithelial neoplasia and genital warts; and the costs of the vaccine and its administration. The costs of screening, testing, and the vaccine were derived from French Health Insurance sources, or other official sources. The costs of treatment of HPV-related infections were derived from three published French studies. The price year was 2005 and all costs were reported in Euros (EUR). As costs could be incurred over the lifetime of the patient, discounting was relevant and was applied at an annual rate of 3.5%.

Analysis of uncertainty:
A series of one-way sensitivity analyses were performed on the parameters that were considered to have the most influence on the cost-effectiveness results. These parameters were the duration of the vaccine protection, vaccine efficacy, the discount rate, the proportion of cancer cases linked to HPV types 16 and 18, treatment costs, and the utilities.

Results
The average LYs gained was 42.4692 for screening only, compared with 42.4846 for screening and vaccination. The average QALYs gained was 42.4425 with screening only compared with 42.4653 with screening and vaccination.

From a direct health care perspective, the average cost of screening was EUR 274.10 per patient, compared with EUR 548.80 for screening and vaccination.
From a third-party payer perspective, the average cost of screening was EUR 177.80 per patient, compared with EUR 369.50 for screening and vaccination.

The costs and benefits were combined using an incremental cost-effectiveness ratio (i.e. the additional cost per LY gained) and an incremental cost-utility ratio (i.e. the additional cost per QALY gained). From a direct health care perspective, compared with screening only, the incremental cost-effectiveness ratio of screening and vaccination was EUR 20,455, and the incremental cost-utility ratio was EUR 13,809. From a third-party payer perspective, compared with screening only, the incremental cost-effectiveness ratio of screening and vaccination was EUR 12,429, and the incremental cost-utility ratio was EUR 8,408.

Under all the scenarios investigated in the sensitivity analyses, the incremental cost per QALY gained with screening and vaccination over screening alone was never higher than EUR 50,000.

Authors’ conclusions
The authors concluded that the addition of a quadrivalent HPV vaccine to the current screening programme in France was a cost-effective strategy for reducing the burden of cervical cancer.

CRD commentary
Interventions:
Both interventions were reported clearly and in detail. In addition, the explicit justification given, for the comparator used, was that, in France, cervical cancer screening was recommended every three years in women aged 25 to 65 years.

Effectiveness/benefits:
The authors did not report whether a systematic review of the literature was undertaken in order to identify all the relevant clinical and effectiveness data, and no details were given of how the data from the relevant studies were combined. It is not therefore possible to ascertain whether the best available data was used. The authors did however provide a summary of all the model parameters, together with their sources. In addition, the authors clearly reported the sources of the utility estimates.

Costs:
The economic perspectives were clearly stated and all the major costs relevant to the two perspectives appear to have been included. The sources, which were either official French sources or previously published French studies and which were used to derive the costs for each health state, were appropriate and reported. In addition, the authors adequately reported the time horizon of the analysis, the discount rate, the price year, and the currency used.

Analysis and results:
Details of the Markov model, which modelled the costs and outcomes of each intervention, were given, although no diagram was presented. The model was published and validated in US settings and had been updated for the European setting. Although a series of one-way sensitivity analyses were used to measure the impact of uncertainty in the model's results, the use of probabilistic sensitivity analyses would have been a more thorough means of capturing overall model uncertainty. Both the methods and results were adequately reported. The authors acknowledged the limitations of their study in their discussion.

Concluding remarks:
Overall the quality of the methodology was appropriate, and the methods and results, were generally well reported. The authors' conclusions appear to be appropriate given the scope of the analysis.

**Funding**
Funded by Sanofi Pasteur MSD.

**Bibliographic details**

**PubMedID**
18218164

**DOI**
10.1017/S0266462307080026

**Original Paper URL**
http://journals.cambridge.org/download.php?file=%2FTHC%2FTHC24_01%2FS0266462307080026a.pdf&...9718a3d36eebf438633b36

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adolescent; Adult; Aged; Cost-Benefit Analysis; Female; France; Health Care Costs; Humans; Markov Chains; Mass Screening /economics; Middle Aged; Papillomavirus Infections /prevention & control; Papillomavirus Vaccines /classification /economics; Quality-Adjusted Life Years; Uterine Cervical Neoplasms /prevention & control

**AccessionNumber**
22008008076