Cost-effectiveness of human papillomavirus vaccination in the United States
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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 examined the cost-effectiveness of vaccination against human papillomavirus for 12-year-old girls. The authors concluded that vaccination was a cost-effective strategy, especially when the potential benefits of preventing anal, vaginal, vulvar, and oropharyngeal cancers, and herd immunity were included. The study appears to have been based on valid methodology, but the sources of data were not satisfactorily described, which may affect the validity of the authors’ conclusions.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of vaccination against human papillomavirus (HPV) for 12-year-old girls, using a methodology developed by the Institute of Medicine in the United States, both with and without the potential benefits of preventing HPV-related anal, vaginal, vulvar, and oropharyngeal cancers.

Interventions
The HPV vaccination was administered to 12-year-old girls, in three doses before the age of 13 years, and this was compared against a strategy of no vaccination.

Location/setting
USA/primary care.

Methods
Analytical approach:
This economic evaluation was based on a decision analytic model with a lifetime horizon. The base-case analysis considered 12 variations of the model on the basis of four permutations (including or excluding the non-cervical cancers, and including or excluding the benefits of preventing HPV types 6 and 11) of three model versions (a population model with and without herd immunity, and a cohort model without herd immunity). The authors stated that a societal perspective was adopted.

Effectiveness data:
The clinical data were derived from a selection of relevant published sources, including national databases such as the National Program of Cancer Registries (NPCR) and the Surveillance, Epidemiology, and End Results Program (SEER), both of which covered about 96% of the US population in 2003. The vaccine efficacy was taken from randomised controlled trials. The details of the other sources were not reported in the paper itself but are available in an on-line technical appendix. Some estimates such as vaccine coverage and the duration of vaccine efficacy were based on authors’ opinions. The key clinical endpoint was the rate of adverse outcomes averted by vaccination.

Monetary benefit and utility valuations:
The utility valuations were derived from published sources, the main details of which are reported in the on-line technical appendix.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at an annual rate of 3%.
Cost data:
The economic analysis included the costs of vaccination and treatment of various types of cancer. These costs were presented as macro-categories without the details for individual items. The costs and quantities were derived from published studies, details of which are given in the on-line technical appendix. The costs were expressed in US dollars ($) and the price year was 2005. Future costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
One- and multi-way sensitivity analyses were carried out on almost all the model inputs, using alternative values defined by the authors. In an alternative scenario, the effect of herd immunity (i.e. the effect on non-vaccinated people, including a reduction in genital warts in men) was considered using published evidence and authors’ opinions.

Results
The incremental cost per QALY gained with vaccination over no vaccination ranged from $3,906 to $14,723 depending on the model applied. In general, more favourable cost-utility ratios were observed when the herd immunity effect was included, when protection against HPV types 6 and 11 was included, and when the benefits of preventing other cancers in addition to cervical cancer were included.

The base-case findings remained quite stable in the sensitivity analyses. The discount rate and time horizon were the most influential model inputs; assuming a time horizon of 50 years instead of 100 years (the base case), raised the incremental cost per QALY gained to over $80,000.

Authors’ conclusions
The authors concluded that HPV vaccination was a cost-effective strategy, especially when considering the potential benefits of preventing anal, vaginal, vulvar, and oropharyngeal cancers, and when herd immunity was included.

CRD commentary
Interventions:
The selection of the no vaccination scenario as the comparator was appropriate. However, the authors did not provide an explicit description of the no vaccination scenario (namely, which type of cancer screening was applied).

Effectiveness/benefits:
The authors did not report a literature review, therefore the published sources of data were presumably known to the authors, who made their own selection of the most appropriate evidence for the model. These sources of data are documented in the on-line technical appendix. The databases were relevant, given their validity and ability to represent the authors’ setting. The trials, which were used to obtain the treatment effect, were likely to be characterised by high internal validity. The clinical estimates were reported for each parameter and details on their sources can be found in the on-line technical appendix. A similar approach was used for the utility valuations, which were derived from the literature. However, the authors did not describe the instrument used to elicit the preferences for health states, and from whom they were elicited (e.g., patients, the general population, health professionals, etc). The use of QALYs as the summary benefit measure was appropriate because they capture the impact of the disease on patients’ health and allow cross-disease comparisons to be made.

Costs:
The authors’ stated that a societal perspective was adopted, but the analysis appears to have been restricted to those costs incurred by the health care payer. The analysis of costs followed a similar approach to the clinical analysis, in that macro-categories were presented without a detailed breakdown of items. This approach might reduce the transparency of the economic analysis. The price year was reported, which will allow reflation exercises for other time periods. The cost estimates were varied in the sensitivity analysis.

Analysis and results:
The costs and benefits were not reported; only incremental cost-utility ratios were presented, although additional information was reported in the online technical appendix. The sensitivity analysis investigated the issue of uncertainty, using a deterministic approach, which was useful in terms of identifying the most influential model inputs. The authors stated and demonstrated that their findings were consistent with those from other published cost-effectiveness studies.
The authors noted that the main advantage of this model was its simplicity, which required fewer assumptions compared with more complex models. The biggest drawback of their analysis, as the authors stated, was the limited understanding of the impact of changes in screening strategies on the cost-effectiveness of HPV vaccination.

Concluding remarks:
On the whole, the study appears to have been based on valid methodology, and the authors conclusions appear to be valid.

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