The potential health and economic benefits of preventing recurrent respiratory papillomatosis through quadrivalent human papillomavirus vaccination

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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 examine the cost-effectiveness of quadrivalent human papillomavirus (HPV) vaccine, focusing on the benefits of preventing recurrent respiratory papillomatosis (RRP) in children whose mothers had been vaccinated at age 12 years. The prevention of RRP would avert medical costs and save QALYs. Inclusion of these benefits in previous studies of HPV vaccination improved their cost-effectiveness estimates. The study was based on appropriate methodology. Despite some limited reporting of the sources, the authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to examine the cost-effectiveness of quadrivalent human papillomavirus (HPV) vaccine, focusing on the benefits of preventing recurrent respiratory papillomatosis (RRP) in children whose mothers had been vaccinated at age 12 years.

Interventions
The strategy of quadrivalent HPV vaccination of 12-year-old girls was compared with a strategy of no vaccination.

Location/setting
USA/primary care.

Methods
Analytical approach:
This economic evaluation was based on a simple mathematical model which calculated the expected costs and benefits of the alternative strategies. The time horizon of the analysis was from the time of vaccination of the mother, through to the end of RRP in their children. The authors stated that the health care payer’s perspective was adopted.

Effectiveness data:
The clinical data were derived from a selection of known, relevant studies, which appear to have been selected by the authors. Some characteristics of the primary studies were reported, although, in general, little information on these sources was given. The authors selected the most appropriate estimates from among those available in the literature. For example, the data on the incidence of RRP were taken from two large population-based studies conducted in the USA.

Monetary benefit and utility valuations:
The utility values were derived from a study of health-related quality of life in children who had RRP for more than one year. No other details about this study were given.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and a 3% annual discount rate was applied.

Cost data:
The economic analysis included the cost of vaccination and the lifetime costs per case of RRP (RRP-related surgeries and RRP-related tracheostomy) averted as a result of vaccination. The data on costs and resource use were derived from
published studies. The details of cost calculations were reported. All costs were in US dollars ($) and the price year was 2006. Future costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
One- and multi-way deterministic sensitivity analyses were undertaken to investigate the impact of variations in the model inputs on the cost-utility ratios. The ranges of values were derived from the literature or were defined by the authors. A Monte Carlo simulation was carried out to provide a range of possible values for the costs and QALYs.

Results
The inclusion of the benefits associated with the prevention of RRP in the children of vaccinated mothers, gained 0.00016 QALYs and saved $31 per HPV vaccination.

Three scenarios were considered. In the low scenario, the incremental cost per QALY of HPV vaccination versus no vaccination (not considering the benefits to children) was $5,000, in the intermediate, it was $25,000 and in the high, it was $45,000. The inclusion of the benefits to children of prevented RRP reduced the estimated cost per QALY gained for the HPV vaccination, from $5,000 to $3,961 (21% reduction) in the low scenario, from $25,000 to $21,599 (14% reduction) in the intermediate scenario, and from $45,000 to $38,868 (14% reduction) in the high scenario.

These study findings were strongly affected by changes in the incidence of RRP. The percentage reduction in the cost per QALY ranged from 2% to over 100% in the low cost per QALY scenario, and from 1% to over 65% in the intermediate and high cost per QALY scenarios. The magnitude of these changes also depended on the assumptions for costs and lost QALYs.

Authors' conclusions
The authors concluded that the prevention of RRP in the children of vaccinated mothers would avert medical costs and save QALYs. Including these benefits in published economic evaluations of HPV vaccination, improved the cost-effectiveness estimates, although the magnitude of these changes depended on the assumptions for costs, rate of RRP, and lost QALYs. The authors highlighted the need for more reliable data on the incidence of RRP.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear and both strategies were appropriately selected.

Effectiveness/benefits:
The authors provided only limited information on both the approach used to identify the primary sources and the characteristics of these sources. Some details were provided for a few studies. Nevertheless, the authors did report the methods of data extraction and calculation. The extreme values found in the literature were used to generate ranges of estimates for the sensitivity analysis. The use of QALYs as the benefit measure was appropriate and allows comparisons with other diseases, but little information was given on the sources used to obtain the utility weights.

Costs:
The analysis of costs was not extensively reported. Most of the cost estimates were derived from published studies, the methods and results of which were not described. A breakdown of cost items was not given. This makes an objective assessment of the validity of the clinical estimates impossible, and reduces the transparency of the economic analysis. Other details such as the price year and discount rate were reported. Alternative ranges of values were tested in the sensitivity analysis.

Analysis and results:
The use of an incremental analysis was appropriate to synthesise the costs and benefits. Three different incremental cost-utility ratios for HPV vaccination were considered and the impact of including the benefits of preventing RRP was assessed on these scenarios. The issue of uncertainty was extensively addressed in the sensitivity analysis, the key findings of which were reported and discussed. The authors noted some potential limitations of their analysis. First, the benefits of vaccinations were assumed to be of lifelong duration. Second, not all the potential benefits of preventing RRP were considered. Third, non-medical costs were not included although they could be relevant. Finally, most of the
inputs to the model were subject to considerable uncertainty.

**Concluding remarks:**
The study was based on an appropriate and transparent methodology. Despite some limited reporting of the sources, the authors' conclusions appear to be robust.

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