Model for assessing human papillomavirus vaccination strategies
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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.

Health technology
The study examined five strategies for human papillomavirus (HPV) vaccination. The strategies were:

- routine vaccination of girls by age 12 years (F-12);
- routine vaccination of girls and boys by age 12 years (FM-12);
- routine vaccination of girls by age 12 years and catch-up vaccination for females aged 12 - 24 (F-12/CU-F);
- routine vaccination of boys and girls by age 12 years and catch-up vaccination for females aged 12 - 24 (FM-12/CU-F);
- and routine vaccination of boys and girls by age 12 years and catch-up vaccination for females and males aged 12 - 24 (FM-12/CU-FM).

All strategies used a prophylactic quadrivalent HPV (16/18/6/11) vaccine. All vaccination strategies were compared with current screening and HPV disease treatment practice (no vaccination).

Type of intervention
Primary prevention (vaccination).

Economic study type
Cost-utility analysis.

Study population
The study population depended on the vaccination strategy.

Setting
The setting was primary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1981 and 2005. Some costs and resource use data were derived from sources published between 2001 and 2003. The price year was 2005.

Source of effectiveness data
The model inputs were:

- behavioural parameters for the sexually active population,
biological parameters for HPV disease, such as progression or regression of disease and duration of acute HPV
infection,

all-cause death rates,

the death rate due to cervical cancer,

hysterectomy rates,

screening rates, and

other treatment parameters.

Modelling
The dynamic model used in the analysis had two main components: demographic and epidemiological. The
demographic model defined the demographic characteristics of the population being simulated and described how
persons enter, age, and exit various categories. The population was divided into 17 age groups with low, high or medium
sexual activity. The epidemiological model simulated HPV transmission and the occurrence of cervical intraepithelial
neoplasia (CIN), cervical cancer and external genital warts in an age-structured population. The structure of the model
was reported. The time horizon of the model was 100 years. Further details of the model structure, transition
probabilities and formulae were presented in the study appendix.

Sources searched to identify primary studies
Death rates among adolescent girls and women with cervical cancer were obtained from Surveillance Epidemiology and
End Results (SEER) Program data for 1997 to 2002. Death rates for males and for females without cervical cancer
were obtained from Vital Statistics data on gender- and age-specific mortality rates. Information on the other sources of
data was limited.

Methods used to judge relevance and validity, and for extracting data
The clinical and epidemiological data were identified through a systematic search of the literature. Some data were
provided by the vaccine manufacturer. Some assumptions were also made (lifelong duration of protection, linear
increase of vaccine coverage during the first 5 years, degree of protection from the vaccine etc.).

Measure of benefits used in the economic analysis
The summary benefit measure used was the expected number of quality-adjusted life-years (QALYs). These were
estimated using a modelling approach, where survival data were combined with utility weights derived from different
published studies. No details of these studies (such as the instruments used to obtain utility weights or the population
from which the data were derived) were provided. The benefits were discounted at an annual rate of 3%.

Direct costs
The analysis of the costs appears to have been restricted to the perspective of the third-party payer. It included the costs
associated with cytology screening, treatment and vaccination. The costs were mainly presented as macro-categories.
The unit costs were not presented separately from the quantities of resources used. Limited information on the sources
of the costs and resource use was provided. Most of the costs appear to have been derived from some published
sources, which were not described. Discounting was relevant, as the long-term costs were evaluated, and an annual rate
of 3% was used. The price year was 2005.

Statistical analysis of costs
The costs were treated deterministically in the base-case.
Indirect Costs
The productivity costs were not included.

Currency
US dollars ($).

Sensitivity analysis
A univariate sensitivity analysis was carried out to assess the robustness of the model results to variations in vaccine parameters (duration and degree of protection, coverage, cost, target age), quality of life weights, discounting and duration of natural immunity. A pessimistic scenario was considered in a multivariate sensitivity analysis. The key aspect of herd immunity was also investigated.

Estimated benefits used in the economic analysis
In a population of 100,000 persons, the lifetime discounted expected QALYs were:

- 2,698,711 with no vaccination,
- 2,699,178 with F-12,
- 2,699,327 with FM-12,
- 2,699,343 with F-12/CU-F,
- 2,699,461 with FM-12/CU-F, and
- 2,699,506 with FM-12/CU-FM (most effective strategy).

Cost results
In a population of 100,000 persons, the expected lifetime discounted costs were:

- $72,659,302 with no vaccination,
- $74,042,990 with F-12,
- $78,707,825 with FM-12,
- $74,815,667 with F-12/CU-F,
- $79,746,357 with FM-12/CU-F, and
- $81,761,210 with FM-12/CU-FM.

Synthesis of costs and benefits
Incremental cost-utility ratios were calculated in order to combine the costs and benefits of the alternative vaccination strategies.

The FM-12 strategy was dominated by the F-12/CU-F strategy, which was both less expensive and more effective.

The incremental cost per QALY gained over the preceding non-dominated strategy was $2,964 with F-12 (versus no vaccination), $4,666 with F-12/CU-F (versus F-12), $41,803 with FM-12/CU-F (versus F-12/CU-F) and $45,056 with FM-12/CU-FM (versus FM-12/CU-F).
The sensitivity analysis produced the following results. The cost per QALY of all strategies increased when the duration of vaccine protection was reduced from lifelong to 10 years. Lower coverage made vaccinating adolescent boys and men more cost-effective. Increasing vaccination cost and quality of life weights increased the cost-effectiveness ratios. Lower discount rates for costs and benefits led to higher costs and QALYs for each vaccination strategy. A higher HPV prevalence rate resulted in more favourable cost-utility ratios. Earlier vaccinations resulted in greater benefits, but vaccination by age 12 became less efficient the higher the vaccination coverage became among older age groups.

In the pessimistic scenario, the cost per QALY increased from $4,666 to $29,053 for the F-12/CU-F strategy and from $45,056 to $124,063 for the FM-12/CU-FM strategy.

When it was assumed that persons had no protection against HPV 6/11 infection, the cost per QALY increased to $11,254 for the F-12/CU-F strategy and to $74,151 for the FM-12/CU-FM strategy. When the effect of herd immunisation was also removed, the incremental cost per QALY for F-12/CU-F increased to $21,404.

Authors' conclusions
Vaccinating girls and women against human papillomavirus (HPV) in the USA was a cost-effective preventive strategy. Including men and boys in the programme was the most effective strategy, with an incremental cost per quality-adjusted life-year (QALY) of $45,056.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear in that both the existing pattern of care (no vaccination) and all possible vaccination strategies were considered in the analysis. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The parameters were derived from published research. The authors did not report any search methods or inclusion criteria, and did not provide any justification for the estimates they selected. It was stated that a review of the literature was carried out, but the methods and conduct of the review were not reported. Moreover, no information on the primary studies was provided. It was therefore not possible to assess the validity of the primary data.

Validity of estimate of measure of benefit
The estimation of QALYs was modelled using a decision tree model. The methods used to estimate the utility weights were not described as they were taken from published sources. Discounting was appropriately carried out. The choice of QALYs was appropriate, not only because they capture the most important aspects of health (survival and quality of life) but also because they can be compared with the benefits of other health care interventions.

Validity of estimate of costs
The analysis of the costs appears to have been performed from the perspective of a third-party payer. All the relevant categories of costs have been included in the analysis. The cost categories were reported but a breakdown of the cost items was not. The authors stated that the inclusion of indirect costs would have lowered the cost-utility ratios, thus making the vaccination strategies more appealing. Little information on the sources of the data was provided. The price year was reported, which will simplify reflation exercises in other time periods. Statistical analyses of the costs were not performed, but the impact of changing key cost estimates was investigated in the sensitivity analysis.

Other issues
The authors stated that, in general, their findings were consistent with the results of previous research. However, the results differed substantially from a recently published economic evaluation, although the authors attempted to explain the possible reasons for these differences. The issue of the generalisability of the study results to other settings was implicitly addressed in the sensitivity analysis, in which alternative scenarios were considered. The authors noted some further strengths of their analysis, such as the use of validated data and model flexibility/transparency. Some limitations
of the analysis were also pointed out, such as the fact that the current version of the model focused on heterosexual transmission of HPV and did not incorporate transmission between homosexual and heterosexual persons. However, most of the assumptions made were biased against vaccination strategies.

**Implications of the study**
The study results appear to support the implementation of HPV vaccination. The authors stated that more studies on health utilities data on HPV disease states are needed.

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None stated.

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**Other publications of related interest**
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**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
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