Adding a quadrivalent human papillomavirus vaccine to the UK cervical cancer screening programme: a cost-effectiveness analysis

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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 evaluated the cost-effectiveness of adding a quadrivalent human papillomavirus (HPV) vaccine to the current cervical cancer screening programme in the UK. The authors concluded that, subject to some caveats, an HPV vaccination programme could potentially be cost-effective. The methods used in the study were appropriate and comprehensively reported. Despite some limitations, overall, the authors’ conclusions appear reasonable.

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

Study objective
The purpose of the study was to assess the potential effectiveness and cost-effectiveness of adding a human papillomavirus (HPV) vaccine for the prevention of cervical cancer, pre-cancerous lesions and genital warts, to an existing screening programme. The costs and effects of the vaccine additional to the current UK cervical cancer screening programme were compared with the screening programme alone.

Interventions
The costs and effects of quadrivalent (6/11/16/18) HPV vaccine in combination with the current UK National Health Service (NHS) Cervical Screening Programme were compared with the screening programme on its own. The vaccine was designed to be administered to schoolgirls aged 12 years, with a booster dose for 22-year-olds. The current cervical screening programme schedule is every 3 years in women aged 25 to 49 years and every 5 years for women between 50 and 64 years.

Location/setting
UK/primary prevention.

Methods
Analytical approach:
A Markov model was used to synthesise published data. The costs and effects were analysed for a cohort of 100,000 UK women from age 12 to 85 years, encompassing a lifetime horizon. The authors stated that the study perspective was that of the NHS.

Effectiveness data:
The effectiveness data were derived from a combination of published literature (Canfell et al. 2004 and Myers et al. 2000, see ‘Other Publications of Related Interest’ below for bibliographic details) and national cancer resources. The methods used to identify the literature were not stated. The main clinical end point used in the analysis was the lifetime risk of cancer. Other clinical outcomes were deaths and counts of cervical cancers, genital warts and various grades of cervical intraepithelial neoplasia. Several assumptions were made to model parameters; these were reported clearly and were supported with appropriate references.

Monetary benefit and utility valuations:
Utilities were based on one published and one unpublished study reporting patient preferences for the health states of Pap smears, warts, cervical intraepithelial neoplasia, and stage or severity of cancer (Myers et al. 2004 and Insinga et al. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details). Time in the health states was based
on one expert’s opinion. Utilities were obtained from a US population. The techniques used to determine these utility scores were not stated. The authors made an assumption about the utility of surviving cervical cancer.

**Measure of benefit:**
The two measures of benefit used were the quality-adjusted life years (QALYs) and life-years saved. These were discounted at a rate of 3.5%.

**Cost data:**
The types of resources addressed in the analysis included the direct costs for vaccination and its administration, screening, diagnosis and treatment for cervical cancer and genital warts. The prices were sourced from published studies (Wolstenholme et al. 1998 and Curtis et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details) and the unit costs and sources were reported. Vaccine prices were adjusted to reflect bulk purchases. The costs were discounted at a rate of 3.5% and the Hospital and Community Services Pay and Prices Index was used to inflate the costs to 2005 UK pounds sterling (£).

**Analysis of uncertainty:**
One-way and multi-way sensitivity analyses were performed to test the base-case results against changes in key parameters. A range of incremental cost-effectiveness ratios was presented.

**Results**
In combination with cervical screening, the proposed HPV vaccination programme would reduce the lifetime risk of cancer from 0.71% to 0.29%. With a cohort of 100,000 women, it was estimated that roughly 418 cervical cancers, 127 deaths, 2,554 cervical intraepithelial neoplasia (CIN) (grade 1), 1,683 CIN (grade 2), 2,479 CIN (grade 3) and 4,798 genital warts could be avoided. The total or incremental costs for the HPV vaccination and screening programme versus screening alone were not reported.

The HPV vaccination programme was predicted to yield an incremental cost-effectiveness ratio of £21,059 per QALY gained compared with no vaccination. If the assumption of lifetime efficacy of the vaccine was limited to 10 years, the ratio increased over 3-fold to £68,417 per QALY gained. The results were moderately sensitive to time with an abnormality, and also vaccine cost, and were very sensitive to variations in the discount rates for costs and benefits.

**Authors’ conclusions**
The authors concluded that adding HPV vaccination to the current cervical screening programme was potentially cost-effective in the UK and depended on the duration of vaccine efficacy and subsequent need for a booster to achieve adequate protection against HPV infection.

**CRD commentary**

**Interventions:**
The two options for cervical cancer prevention were described clearly. The profile of the intended patient population, vaccine scheduling and screening tests were reported.

**Effectiveness/benefits:**
The effectiveness data were derived from various published studies. However, the methods used to select these particular studies were not provided. The clinical end points used to assess the merits of the two options were consistently in favour of the vaccine and screening option. Some health benefits were excluded. The derivation of utilities involved one published and one unpublished source, as well as authors’ and expert opinion, which could have introduced biases. It is not possible to assess the quality of the utility methods given the information provided. An illustration of the model structure was not presented, although a thorough description of the health states and possible transitions between them was described.

**Costs:**
The costs included in the analysis appear to have reflected those applicable to the NHS perspective taken. The costing methods, adjustments, their sources and unit costs were documented clearly and in detail. The costs were adjusted for inflation but the cost results for the two options were not reported. In addition, intervention resource quantities were not
reported separately from their costs.

Analysis and results:
The health outcomes and net costs were synthesised into cost-effectiveness ratios. The validity of the cancer risk parameters of cervical cancer was supported by epidemiological observational data in the UK. The one-way sensitivity analyses were comprehensive and tested key parameters over sufficiently large ranges. The authors identified and justified a number of limitations of their study, including the lack of strong utility data for the relevant health states, the lack of a probabilistic sensitivity analysis and potential underestimation of the health benefits. The authors discussed their results in comparison with other economic studies and their potential generalisability.

Concluding remarks:
Overall, the study methods were appropriate and explicitly reported, although there were some limitations relating to the utility estimation, cost reporting and lack of a probabilistic sensitivity analysis. The authors’ conclusions appears to be a reasonable assessment of the analysis undertaken.

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Bibliographic details
Kulasingam S L, Benard S, Barnabas R V, Largeron N, Myers E R. Adding a quadrivalent human papillomavirus vaccine to the UK cervical cancer screening programme: a cost-effectiveness analysis. Cost Effectiveness and Resource Allocation 2008; 6:4

Other publications of related interest
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Wolstenholm JL, Whynes DK. Stage-specific treatment costs for cervical cancer in the United Kingdom. Eur J Cancer 1998;34:1889-93.

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Indexing Status
Subject indexing assigned by CRD

MeSH
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