Human papillomavirus transmission and cost-effectiveness of introducing quadrivalent HPV vaccination in Denmark

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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 assessed the cost-effectiveness of quadrivalent human papillomavirus (HPV) vaccination for the prevention of HPV, genital warts, cervical intraepithelial neoplasia, and cervical cancer, in a Danish heterosexual population. The authors concluded that vaccination added to the usual cervical cancer screening created vaccination costs, but saved treatment costs and improved quality of life and survival. The methods were valid and, despite some limitations in the reporting of the data sources and the results, the authors’ conclusions appear to be appropriate.

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

Study objective
This study assessed the cost-effectiveness of quadrivalent human papillomavirus (HPV) vaccination for the prevention of HPV, genital warts, cervical intraepithelial neoplasia (CIN), and cervical cancer, in a heterosexual population.

Interventions
The introduction of routine HPV vaccination of girls aged 12 years, in addition to the existing Danish cervical cancer three-yearly screening programme for women aged 23 to 59 years, was compared with no vaccination (screening alone). Other strategies assessed were: vaccination of girls aged 12 years with catch-up vaccination up to 15-year-olds or 26-year-olds, and vaccination of girls and boys aged 12 years.

Location/setting
Denmark/primary care.

Methods
Analytical approach:
The analysis was based on an adapted version of a published Danish dynamic transmission model accounting for herd immunity (National Board of Health. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details). A time horizon of 62 years was used. The model was initially calibrated to fit the observed Danish incidence and prevalence data for HPV 6/11/16/18, genital warts, CIN grades one to three, and cervical cancer, before the introduction of vaccination. The authors stated that the perspective was that of the health care or third-party payer.

Effectiveness data:
The authors selected the most appropriate estimates from the available evidence and the details of some of the data sources were reported. A few clinical estimates, such as the vaccine efficacy and the duration of protection, were based on the authors’ assumptions. The data on HPV progression, CIN regression and progression rates, and the risk of HPV infection were mostly from a US study (Elbasha, et al. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details). The data on screening, such as the participation rate, were from Danish sources, as were other epidemiological data, such as the incidence and prevalence of HPV 6/11/16/18, genital warts, and cervical cancer.

Monetary benefit and utility valuations:
The utility values were from unpublished Danish general population survey data, and from a published US cohort study of CIN grades one to three, genital warts, and cervical cancer (Elbasha, et al. 2007).
Measure of benefit:
The measures of benefit were life-years and quality-adjusted life-years (QALYs) and a 3% annual discount rate was applied. The number of disease events (cases of genital warts, CIN, or cervical cancer) avoided was reported.

Cost data:
The health care costs were those of vaccination acquisition and administration; and treatment of genital warts, CIN, and cervical cancer. The cost estimates were mostly based on a recent Danish health technology assessment (National Board of Health, 2007). They were in Euros (EUR) and the price year was 2007. Future costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
Univariate sensitivity analyses were performed on the model inputs such as: vaccine efficacy, duration of vaccine protection (lifelong in the base case), treatment costs, vaccine price, discount rate, genital wart prevalence, bivalent HPV 16/18 vaccination (quadrivalent in the base case), and the time horizon. Alternative scenarios, assuming different vaccination rates, additional catch-up programmes, or additional vaccination of boys, were analysed.

Results
HPV types 6, 11, 16, and 18 were estimated to be eliminated after 50 years of vaccination; the prevalence after 49 years was zero for all four types. This led to decreases in the cases of genital warts, CIN grades one to three, and cervical cancer.

At the Danish population level, the incremental cost per year was EUR 1.0 million, with the routine vaccination of girls aged 12 years in addition to screening, compared with screening alone. The mean life-years saved were 494.6 and the mean QALYs gained were 531.8, generating an incremental cost-effectiveness ratio (ICER) of EUR 2,061 per life-year saved or EUR 1,917 per QALY gained.

The sensitivity analysis indicated that these base-case results were most influenced by variations in the discount rate, time horizon, treatment costs, and vaccine price, and the inclusion of a booster dose. The scenario analyses suggested that the inclusion of a catch-up programme up to 26-year-olds increased the ICERs to EUR 9,374 per life-year or EUR 8,727 per QALY gained, as did a higher vaccination rate of 85% (EUR 5,720 per life-year or EUR 5,327 per QALY gained). The additional vaccination of boys aged 12 years yielded the highest ICERs of EUR 20,555 per life-year or EUR 18,677 per QALY gained.

Authors' conclusions
The authors concluded that vaccination added to the usual cervical cancer screening created vaccination costs, but saved treatment costs and improved quality of life and survival.

CRD commentary
Interventions:
The selection of the comparators was appropriate and adequately described. The proposed vaccination strategies, combined with the usual screening programme, were compared with no vaccination (screening alone), which was the usual care in the authors' setting in Denmark before vaccination was introduced in 2009.

Effectiveness/benefits:
No systematic review was conducted and no justification was given for the choice of primary studies, which were not assessed for their quality. The authors referred to a publication of the original model for more details. This means it is not possible to determine the internal validity of the effectiveness estimates, nor if all the relevant information was included. The data appear to have been appropriate and from a mix of published and unpublished Danish, US, or Canadian sources; authors' assumptions were made for inputs, such as the vaccine efficacy. The authors did not describe the approach used to elicit the utility values, which limits the transferability of the results. QALYs were an appropriate benefit measure.

Costs:
The categories of costs were consistent with the perspective stated, but total categories were presented without a
breakdown of individual items, making it difficult to replicate the analysis for other settings. The sources of costs were presented, with most estimates based on a recent health technology assessment (National Board for Health, 2007), but few details of resource use were reported. The price year and time horizon were stated and the discount rate for long-term costs was appropriately applied. All the cost categories, such as treatment and vaccine price, appear to have been tested in the sensitivity analyses.

Analysis and results:
The analytic approach was appropriate and the model structure was presented in a supplementary file. A synthesis of costs and benefits was performed, but only the incremental results were reported. The uncertainty was partly investigated in a univariate sensitivity analysis, but no probabilistic sensitivity analysis was performed, because of the excessive computer processing time needed. Several alternative vaccination scenarios were considered and comparisons with other studies were made. The authors acknowledged several limitations of their study, such as the exclusion of transmission between homosexual and heterosexual people, a reduction in sexual contacts as individuals aged, and no reintroduction of HPV once treated.

Concluding remarks:
The methods were valid and, despite some limitations in the reporting of the data sources and the results, the authors’ conclusions appear to be appropriate.

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