Impact of vaccine protection against multiple HPV types on the cost-effectiveness of cervical screening

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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 analysis examined the cost-effectiveness of screening for cervical cancer in women who were vaccinated against human papillomavirus (HPV), considering a broad-spectrum vaccine protecting against multiple HPV types. Four rounds of HPV DNA screening was cost-effective in addition to HPV 16/18 vaccination. One screen in a lifetime was cost-effective in addition to broad-spectrum vaccination. The cost-effectiveness framework was valid and, despite limited reporting of the costs, the authors’ conclusions appear to be robust.

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

Study objective
This analysis examined the cost-effectiveness of various scenarios of screening for cervical cancer in women who were vaccinated against human papillomavirus (HPV), considering the introduction of a broad-spectrum vaccine protecting against multiple HPV types.

Interventions
The analysis considered eight screening strategies that differed in the choice of the screening test and the number of screening rounds. The two screening tests were cytology and HPV DNA. There were seven, six, five, or four screening rounds, corresponding to intervals of five, six, 7.5, or 10 years, between the ages of 30 and 60 years. Vaccination alone was the reference scenario.

The usual care was cytology screening once every five years (seven rounds). Vaccination against HPV 16 and 18 was considered for the main analysis (with or without cross-protection), with vaccination against five (16, 18, 31, 33, and 45) to 13 types of HPV in secondary analyses.

Location/setting
Netherlands/primary care.

Methods
Analytical approach:
The analysis was based on an individual-level simulation of the relationship between 14 HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) and cervical disease, including multiple types of infection. Women were modelled from the age 10 years, over their lifetime. The authors stated that the analysis took a societal perspective.

Effectiveness data:
The data were from published clinical trials, longitudinal studies, and epidemiological databases. Most of the data for HPV prevalence and the screening characteristics were from a randomised controlled population-based screening study, Population Based Screening Study Amsterdam (POBASCAM), that included 44,102 Dutch women aged between 29 and 61 years. Disease progression was from the POBASCAM and observational studies. Some assumptions were made. Vaccine efficacy and cross-protection were key inputs for the model and were from Phase III clinical trials.

Monetary benefit and utility valuations:
The utility values were from published sources.

**Measure of benefit:**
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at an annual rate of 1.5%. Life-years were considered in a sensitivity analysis.

**Cost data:**
The economic analysis included both the direct and indirect costs of vaccination, screening, and the management of disease, as well as productivity losses and travel expenses. These economic data were from published sources. All costs were in Euros (EUR) and a 4% annual discount rate was applied. The price year was 2009.

**Analysis of uncertainty:**
One-way sensitivity analyses were carried out on selected inputs for the model, using alternative assumptions based on published evidence or authors’ opinions.

**Results**
In a scenario with no cross-protection and vaccination against HPV 16/18, after excluding dominated strategies, which were more expensive and less effective than another strategy, the expected costs were EUR 441 with vaccination, EUR 485 with vaccination plus cytology four times, EUR 505 with HPV DNA four times, EUR 521 with HPV DNA five times, and EUR 537 with HPV DNA six times. The QALYs were 42.6914 with vaccination, 42.7075 with cytology four times, 42.7104 with HPV DNA four times, 42.7111 with HPV DNA five times, and 42.7117 with HPV DNA six times.

Excluding the strategies with an incremental cost-utility ratio above the Dutch threshold of EUR 20,000 per QALY gained, the incremental cost per QALY gained was EUR 2,742 (EUR 4,986 with partial cross-protection against types 31, 33, 45 and 58) with cytology four times and EUR 6,707 (EUR 9,994 with partial cross-protection) with HPV DNA four times.

The same results were achieved when using international criteria for the discount rate (3% for both costs and benefits) and a cost-effectiveness threshold of EUR 37,000 per QALY gained based on gross domestic product per capita. In general, the results were confirmed in the sensitivity analysis when only vaccination against HPV 16/18 was considered, except when screening compliance was reduced from 80% to 40% (where seven rounds of DNA screening was the preferred option) or waning of vaccine induced immunity was introduced (and again seven rounds of DNA screening was the preferred option).

The cost-effectiveness results changed when a broad-spectrum of vaccination was assumed. With vaccination against five or more types of HPV, none of the screening options was cost-effective at the EUR 20,000 per QALY threshold. One screening in a lifetime was the only cost-effective option with vaccination against up to 11 types. The use of life-years gained instead of QALYs did not change the cost-effectiveness conclusions.

**Authors’ conclusions**
The authors concluded that four rounds of HPV DNA screening was cost-effective in addition to HPV 16/18 vaccination. One screen during a lifetime was a cost-effective addition to broad-spectrum vaccination against many high-risk HPV types.

**CRD commentary**
**Interventions:**
The selection of the comparators was appropriate to reflect all the possible screening and vaccination strategies. The usual care in the Netherlands was included and no screening was the reference strategy.

**Effectiveness/benefits:**
The clinical data were from several published sources, including a very large population-based screening study that was representative of the authors’ setting and the patients studied. This provided valid estimates for the epidemiological and behavioural inputs. The vaccine efficacy was appropriately from phase III clinical trials that should have had high internal validity. Other data were from published studies that were not fully described. Several
alternative assumptions on cross-protection, waning and the indirect effects of vaccination were considered and tested in scenario analyses. Both life-years saved and QALYs were benefit measures and they were appropriate for cervical cancer and allow comparisons with other economic evaluations. The sources for the utility weights were not described.

Costs:
The economic analysis included a broad range of costs, appropriate for the societal perspective, but the reporting was not satisfactory. The data sources were not described and it was not clear what type of costs were included and how they were calculated. Some of the unit costs were presented, but the patterns of resource consumption were not given. The disease costs were presented as category totals and were not broken down to individual items. The economic inputs were treated deterministically and only some items were varied in the sensitivity analyses. The price year was reported, allowing reflation exercises.

Analysis and results:
The results were extensively presented. An incremental approach was appropriately used to combine the costs and benefits of the strategies and to exclude inferior strategies. Two cost-effectiveness thresholds were used to identify the best strategy. The authors pointed out that a unique characteristic of this analysis was that the decision model not only simulated each individual woman, but also each HPV type. A deterministic approach was used to assess uncertainty. The methods and results of all the sensitivity analyses were clearly reported. The authors stated that the analysis only considered vaccinated women and it results might differ for unvaccinated women for whom screening could be more cost-effective. The findings appear to be specific to the Dutch setting and might be difficult to transfer to other settings without changing key epidemiological and economic parameters.

Concluding remarks:
The cost-effectiveness framework was valid and, despite limited reporting of the economic data, the authors’ conclusions appear to be robust.

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