The epidemiological and economic impact of a quadrivalent human papillomavirus vaccine (6/11/16/18) in the UK
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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 study assessed the cost-effectiveness of a prophylactic quadrivalent human papillomavirus (6/11/16/18) vaccination programme (including possible catch-up strategies) for the prevention of cervical cancer, cervical intraepithelial neoplasia, and genital warts in the female and male population aged 12 years or older. The authors concluded that the vaccination programme was a cost-effective strategy from the perspective of the UK NHS. The study methodology appears to be based on a sound approach, although some sources of data were not satisfactorily described. On the whole, the authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The general objective was to assess the cost-effectiveness of a prophylactic quadrivalent human papillomavirus (HPV) (6/11/16/18) vaccination programme (including possible catch-up strategies) for the prevention of cervical cancer, cervical intraepithelial neoplasia (CIN) grades 2 and 3, CIN grade 1, and genital warts in the female and male population 12 years or older.

Interventions
The main vaccination strategy was routine HPV vaccination of girls at age 12 years. Other strategies under examination were: routine female vaccination at age 12 years and catch-up female vaccination for ages 12 to 14 years; routine female vaccination at age 12 years and catch-up female vaccination for ages 12 to 17 years; routine female vaccination at ages 12 years and catch-up female vaccination for ages 12 to 24 years. All vaccination strategies were combined with current cervical cancer screening and HPV disease treatment practices.

Location/setting
UK/community (school) and primary care.

Methods
Analytical approach:
A previous disease transmission model was used to determine the clinical and economic impact of the different strategies. A lifetime horizon (100 years) was adopted and the authors stated that the perspective was that of the UK National Health Service (NHS).

Effectiveness data:
A comprehensive literature review was undertaken to identify clinical inputs for the decision model. Little information on search methods, inclusion and exclusion criteria was reported. A few details about some sources of the data were reported. For example, some data on screening were obtained from the 2005 to 2006 Cervical Cancer Screening Programme in England, and the behavioural data were obtained from a national survey of sexual attitudes and lifestyle.

Monetary benefit and utility valuations:
Utility valuations were derived from published studies, details of which were not given. However, it was stated that, due to the lack of UK data, utility weights were taken from the US population.
Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure. A 3.5% annual discount rate was applied. The number of disease events (e.g. genital warts, cervical cancer, CIN etc) prevented was also reported.

Cost data:
The health service costs included in the analysis were: cytology screening; vaccination; diagnosing and treating detected invasive cervical cancer, CIN or genital warts; and following false-positive results of the screening test. The costs were derived from published sources and were likely to reflect NHS prices. A volume-based discount for the price of vaccine was assumed. The source of data on resource consumption was not explicitly stated. Costs were in UK pounds sterling (£) and the price year was 2006. Long-term costs were discounted at an annual rate of 3.5%.

Analysis of uncertainty:
The sensitivity analysis focused on key model inputs that were considered to be the most influential, as shown in other modelling studies on HPV disease. These model inputs were; duration and degree of vaccine protection, coverage rates, utility valuations, vaccine costs, and discount rate. A pessimistic scenario and a scenario, in which the vaccine was assumed to protect only against infection with HPV 6 and 11, were also considered.

Results
In a hypothetical cohort of 100,000 individuals, the expected costs and QALYs were £9,045,921 and 2,352,770 with screening only; £11,826,382 and 2,353,242 with routine vaccination of 12-year-olds; £11,976,113 and 2,353,268 with routine vaccination and catch-up at 12 to 14 years; £12,129,737 and 2,353,294 with routine vaccination and catch-up at 12 to 17 years; £12,504,693 and 2,353,327 with routine vaccination and catch-up at 12 to 24 years.

The incremental analysis suggested that the reference strategy (routine vaccination of 12-year-olds) was weakly dominated (had higher cost-effectiveness ratios compared with the next most effective strategy). The incremental cost, per QALY gained, over the next non-dominated alternative was: £5,882 with routine vaccination and 12 to 14 year-old catch-up (versus no screening); £5,971 with routine vaccination and 12 to 17 year-old catch-up (versus 12 to 14 year-old catch-up); and £11,412 with routine vaccination and 12 to 24 year-old catch-up (versus 12 to 17 year-old catch-up).

The sensitivity analysis indicated that the two most influential model inputs were health utility values and duration of vaccine protection. In general, a shorter duration of vaccine protection and smaller quality-of-life benefits decreased the cost-effectiveness of all vaccination strategies. However, the strategy of routine vaccination and 12 to 24 year-old catch-up was always associated with an incremental cost per QALY of less than £30,000 compared with the next most effective strategy.

Authors’ conclusions
The authors concluded that the prophylactic quadrivalent HPV (6/11/16/18) vaccination programme was a cost-effective strategy from the perspective of the UK NHS.

CRD commentary
Interventions:
The selection of the comparators appears appropriate because several vaccination strategies were considered. These strategies were compared with the current screening programme.

Effectiveness/benefits:
The approach used to identify clinical inputs was appropriate as a literature search was undertaken, although the authors did not report the methods and conduct of this review. The key characteristics of the primary sources of data were not reported, except for some national databases which were used for specific epidemiological and behavioural inputs. The authors referred to a previous publication of the model for more details. This limits the possibility of judging the validity and robustness of these data. Furthermore, the issue of homogeneity and comparability of these sources was not specifically addressed. Little information on the derivation of QALYs was given. The authors did not describe the approach used to elicit utility valuations, but stated that they reflected the US setting due to the lack of available data from the UK setting. QALYs are an appropriate and validated benefit measure.
Costs:
The categories of costs were consistent with the perspective stated by the authors. However, costs were presented as macro-categories, and a detailed breakdown of cost items was not provided. The sources of costs were not extensively described, especially with respect to the data on resource consumption. The authors took into consideration volume-based discount for vaccination acquisition, which is a typical approach in the UK. The price year was reported and the discount rate for long-term costs was appropriately applied. The variability in cost estimates was limited to the cost of treatment, which was tested in the sensitivity analysis.

Analysis and results:
The synthesis of costs and benefits was performed and presented clearly. The issue of sensitivity analysis was only partially addressed since the authors focused on some key model inputs, although these do appear to have been the most relevant. The model results were validated using real-world data for a short time horizon. The authors acknowledged some limitations of the study such as the exclusion of potential adverse events of the vaccination or the exclusion of recent efficacy data, on the vaccine, which were not available at the time of the model analysis.

Concluding remarks:
The study methodology appears to be robust and based on a sound approach, although some sources used were not satisfactorily described. On the whole, the authors’ conclusions appear to be valid.

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