Assessment of the cost-effectiveness of a quadrivalent HPV vaccine in Norway using a dynamic transmission model
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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 examined the cost-effectiveness of alternative quadrivalent human papillomavirus (HPV) vaccine strategies in young females. The vaccine protected against infection with, and disease caused by, HPV types 6, 11, 16, and 18. This vaccination programme for girls and women aged 12 to 24 years could be cost-effective from the perspective of the Norwegian health care system. The methodology was appropriate, but few details of the clinical sources were provided. In general, the authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of alternative quadrivalent human papillomavirus (HPV) vaccine strategies in young females. The vaccine protected against infection with, and the diseases caused by, HPV types 6, 11, 16, and 18.

Interventions
The base-case strategy was routine HPV vaccination of girls before the age of 12 years, using three doses of vaccine. The comparison strategy was the routine vaccination of girls before the age of 12 years, together with a temporary five-year catch-up programme of vaccination of females aged 12 to 24 years. These two strategies were compared with no vaccination.

Location/setting
Norway/primary care.

Methods
Analytical approach:
This economic evaluation was based on a published dynamic transmission model, which accounted for both the direct benefits of vaccination upon vaccinees and the indirect benefits upon those not vaccinated (herd immunity). The time horizon of the analysis was 100 years. The authors stated that the perspective of the Norwegian health care system was adopted.

Effectiveness data:
The clinical estimates came from a selection of known, relevant studies. Data on the natural history of disease were based on the inputs of the published model, which represented the US population, but Norwegian data replaced these US inputs. The data on screening and vaccination coverage and other epidemiological data were derived from Norwegian sources, such as the Norwegian cancer registry. Data on vaccine efficacy were taken from clinical trials. Some assumptions were also made and appear to have been based on the authors’ opinions. The key clinical endpoints were vaccine efficacy and coverage.

Monetary benefit and utility valuations:
The utility valuations were derived from a sample of 150 healthy US women using the time trade-off approach.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted yearly at a rate of 3.5%. Other model outputs such as the incidence of cervical intraepithelial neoplasia (CIN), cervical cancer (CC), genital warts (GWs), survival, and deaths from CC were reported.

Cost data:
The economic analysis included the costs of vaccine (acquisition and administration), cytology-screening costs, costs of follow-up of false-positive screening results, and medical costs of cancer screening and treatment of disease resulting from HPV infection, including CIN, CC, and GWs. The resource use and costs were derived mainly from Norwegian sources, including Drug Related Groups, the Fee Schedule of the Norwegian Medical Association, and the Fee Schedule for Public Hospitals. Only the costs of treatment of GWs were derived from US cost data. The cost of the three doses of HPV vaccine was based on authors’ assumptions. Costs were in Norwegian kroner (NOK) for the price year 2005 to 2006. Some were converted to Euros (EUR) at a rate of one NOK equalled EUR 0.12. Future costs were discounted at an annual rate of 3.5%.

Analysis of uncertainty:
A series of one-way sensitivity analyses was carried out on the key model inputs such as the duration of vaccine protection, coverage rate, quality-of-life weights, vaccine costs, duration of vaccine programme, discount rate, cost of GWs, and time horizon. The alternative values appear to have been based on authors’ opinions. A worst-case scenario was considered, in which the cost of HPV-associated diseases was decreased by 25%, while the utilities for the same diseases were increased to 0.97, and the duration of vaccine protection decreased to 10 years (lifelong in the base case).

Results
The model findings were validated using epidemiological data from the Norwegian Cancer Registry.

In a cohort of 100,000 individuals, the expected lifetime costs were NOK 168,418,425 with no vaccination, NOK 198,043,139 with vaccination before 12 years, and NOK 213,523,157 with routine vaccination plus catch-up. The QALYs were 2,349,735 with no vaccination, 2,350,353 with vaccination before 12 years, and 2,350,597 with routine vaccination plus catch-up.

The incremental cost per QALY gained with vaccination before 12 years over no vaccination was NOK 48,001 (EUR 5,996) and with vaccination plus catch-up over routine vaccination it was NOK 63,294 (EUR 8,272).

The results of the sensitivity analysis indicated that in the worst-case scenario, the cost-utility ratio for routine vaccination plus catch-up over no vaccination was NOK 377,467, which was lower than EUR 50,000 per QALY.

Authors’ conclusions
The authors concluded that a routine and catch-up vaccination programme for girls and women aged 12 to 24 years could be a cost-effective strategy from the perspective of the Norwegian health care system. The cost-effectiveness estimate fell within the conventional threshold for the adoption of health care interventions.

CRD commentary
Interventions:
The interventions were appropriate comparators. The authors stated that the vaccination strategies would be combined with the current screening and treatment programme in Norway, which consisted of screening all women aged 25 to 69 years every three years.

Effectiveness/benefits:
The clinical evidence was derived from a selection of published studies and national registries. Other data had already been incorporated in the disease model. The authors did not provide a formal justification for the selection of these sources and their design and other characteristics were not described. This makes an objective assessment of the validity of the clinical estimates difficult. A potential limitation was that the sensitivity analysis considered the uncertainty around only a few estimates. Little detail of the derivation of the utility estimates was provided. QALYs are a validated benefit measure, which capture the impact of the vaccination programmes on the patients’ health and
allow cross-disease comparisons.

Costs:
The categories of costs were consistent with the economic viewpoint, but the economic analysis was not transparently presented. The costs were presented as macro-categories and were not broken down into individual items. The sources of costs were presented, but the calculation of vaccine costs was not clear. In general, the data on resource consumption were not presented. Only a few cost categories were investigated in the sensitivity analysis. These issues might affect the validity of the cost analysis.

Analysis and results:
The costs and benefits were appropriately synthesised using an incremental approach and the findings were clearly presented. The issue of uncertainty was restricted to a limited number of model inputs, and a more comprehensive approach would have been useful. The authors noted that their findings were similar to those from other economic evaluations. The main strength of the analysis was the use of a dynamic model, which simulated the cost-effectiveness of the strategies and included non-vaccinated individuals. The authors pointed out some limitations of their decision model, which might have led to underestimation of the true benefits of the vaccination programmes.

Concluding remarks:
The methodology was appropriate, although more details on some clinical and economic sources would have been useful. In general, the authors’ conclusions appear to be valid.

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