The health and economic impact of cervical cancer screening and human papillomavirus vaccination in kidney transplant recipients

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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 various screening and vaccination options for the prevention of cervical cancer in kidney transplant recipients. The authors concluded that conventional annual cytology screening was cost-effective, but liquid-based cytology or vaccination did not provide sufficient benefits to warrant their costs. Despite some limitations, the methods were appropriate and comprehensive. The results were adequately reported and the conclusions reached by the authors appear to be appropriate.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to evaluate the cost and health benefits of several screening and vaccination options for the prevention of cervical cancer in kidney transplant recipients, who have been found to be at a greater risk of cervical cancer. The hypothetical cohort consisted of 1,000 women, aged 18 to 69 years, who had received a kidney transplant and had not undergone a hysterectomy.

Interventions
Conventional cytologic Papanicolaou smear testing was compared with no screening and with a new liquid-based cytology. As human papillomavirus (HPV) might cause cervical cancer, HPV vaccination was compared with no screening and conventional cytology. Vaccination included initial and booster doses against oncogenic HPV types 6, 11, 16, and 18, for the prevention of cervical dysplasia. All screening ceased when women reached the age of 69 years.

Location/setting
Australia/primary care.

Methods
Analytical approach:
Three Markov models were used to simulate the costs and effects of the screening options, using published data from scientific literature and other sources. The analysis covered a 50-year period and, each year, the patients chose whether or not to be screened. The authors stated that the study was carried out from a health system perspective.

Effectiveness data:
The screening effectiveness was the reduction in the overall age-specific prevalence of cervical dysplasia within the cohort; it was assumed that the benefits of vaccination were limited to those vaccinated and there was no herd immunity. This approach was consistent with the recommendations of the US Food and Drug Association and the Australian Pharmaceutical Benefit Advisory Committee. These data were primarily from published studies, including four systematic reviews. The best available published evidence was used for the additional benefits of liquid-based cytology screening. The age-specific screening participation rates were from the National Cervical Cancer Screening Programme. The stage distribution of cervical dysplasia in the screened and unscreened groups was from the Australian and New Zealand Dialysis and Transplant Registry. The HPV vaccine efficacy and its duration were from three phase II or III randomised controlled trials. The remaining clinical inputs were from a comprehensive literature review that identified published studies of kidney transplant patients and general populations.
Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The measure of benefit was days of life or life-years saved and the benefits were discounted at 5% per annum.

Cost data:
The direct medical costs were those of initial and booster vaccinations, imaging, pathology and procedures for the screening and treatment of cervical cancer, consultations, surgical and adjuvant therapies, and treatment of recurrences. The unit costs were based on data from Australian-Refined Diagnostic Related Groups, the Medicare Benefits Schedule of Australia, the Cancer Institute of New South Wales, and published literature. The costs were discounted at 5% per annum and adjusted to 2005 Australian dollars (AUD), using the Medicare component of the Consumer Price Index and Purchasing Power Parities.

Analysis of uncertainty:
The uncertainty was measured in one-way and multi-way sensitivity analyses on the model parameters, using their 95% confidence intervals or plausible minimum and maximum estimates. Two scenario analyses were undertaken, in which the vaccine efficacy waned after five years and all women were vaccinated regardless of their HPV exposure. The results were presented in various diagrams.

Results
The incremental cost of annual conventional cytology screening, compared with no screening, was AUD 608. Compared with conventional cytology, the incremental cost was AUD 254 with liquid-based cytology and AUD 457 with HPV vaccination. The incremental benefit of conventional screening, compared with no screening, was 0.05 life-years or 18.2 days of life saved. Compared with conventional cytology, the additional days of life saved were 0.70 with liquid-based cytology and 1.1 with HPV vaccination.

The incremental cost per life-year saved was AUD 12,160 with conventional screening compared with no screening, AUD 127,000 with liquid-based cytology screening compared with conventional screening, and AUD 152,333 with HPV vaccination compared with conventional screening.

The incremental cost per life-year saved with conventional screening compared with no screening remained under AUD 50,000 when the parameters were varied, in one- and two-way sensitivity analyses. For the other two models and additional scenarios, the cost-effectiveness ratios remained very high, when parameters were varied, even with the most optimistic values.

Authors' conclusions
The authors concluded that conventional screening was cost-effective in reducing cancer-specific mortality, in the kidney transplant population, while the liquid-based screening test added negligible gains at a large increase in cost. HPV vaccination with annual screening was unlikely to be cost-effective, but more evidence was needed on its effects in the transplant population.

CRD commentary
Interventions:
The interventions were adequately described and appear to have been appropriate comparators. Conventional cytology screening was the usual practice, and was included. The authors stated that their model setting was a developed country with a publicly funded cervical cancer screening programme, which might be applicable for many settings.

Effectiveness/benefits:
The clinical effectiveness parameters were from newly published research trials and systematic reviews, which appear to have been good-quality sources. The evidence appears to have been comprehensive. The conservative approach that did not include reductions in quality of life or morbidity from HPV vaccination nor a dynamic herd immunity effect, meant that the full benefits and costs might not have been captured. The measure of benefit seems to have been appropriate given the lack of quality of life data available for the kidney transplant population. Appropriate discounting...
was undertaken.

Costs:
A health system perspective was used and the relevant costs appear to have been included. An adequate account of the unit costs and their sources was provided; these costs were appropriately discounted and adjusted for inflation.

Analysis and results:
Adequate details of the model structure were reported, and the economic evaluation appears to have appropriately synthesised the information. The results were combined into incremental cost-effectiveness ratios, making them generalisable to other settings. The authors acknowledged a number of limitations to their study, including the lack of evidence on vaccination and HPV infection among transplant recipients. A probabilistic sensitivity analysis, in which the uncertainty in parameters is tested by varying the parameters simultaneously, would have been useful.

Concluding remarks:
Despite some limitations with the availability of data, which limited the scope of the three models, the methods were appropriate and comprehensive. The results were adequately reported and the conclusions reached by the authors appear to be appropriate.

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