Pretransplant varicella vaccination is cost-effective in pediatric renal transplantation

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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.

Health technology
The vaccination against varicella zoster virus (VZV) of all children with chronic renal failure (CRF) before renal transplantation (Tx) was examined.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of children undergoing Tx because of CRF. Children with a prior history of varicella infection or vaccination were not included.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1978 and 1994. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies and experts' opinions.

Modelling
A decision tree model was constructed to examine the clinical and economic outcomes associated with the two strategies under evaluation (immunisation versus non-immunisation) in a cohort of children undergoing Tx. Limited information on the decision tree was provided.

Outcomes assessed in the review
The outcomes assessed from the literature were the probabilities of:

- exposure to varicella per year,
- varicella infection per year,
- protection by varicella,
recognised protection by VZIG, and sub-clinical infection.

**Study designs and other criteria for inclusion in the review**

It was not stated whether a systematic review of the literature had been undertaken to identify relevant studies. No information on the designs and characteristics of the primary studies was provided.

**Sources searched to identify primary studies**

Not stated.

**Criteria used to ensure the validity of primary studies**

Not stated.

**Methods used to judge relevance and validity, and for extracting data**

Not stated.

**Number of primary studies included**

Five primary studies provided the clinical evidence.

**Methods of combining primary studies**

A narrative method appears to have been used to combine the primary estimates.

**Investigation of differences between primary studies**

Not stated.

**Results of the review**

The probabilities were:

- 0.223 (range: 0.16 - 0.248) for exposure to varicella per year,
- 0.111 (range: 0.08 - 0.124) for varicella infection per year,
- 0.950 (range: 0.83 - 0.95) for protection by varicella,
- 0.9 (range: 0.5 - 0.95) for recognised protection by VZIG, and
- 0.06 (range: 0.04 - 0.15) for sub-clinical infection.

**Methods used to derive estimates of effectiveness**

Some assumptions based on experts' opinions were made.

**Estimates of effectiveness and key assumptions**

The probability of recognising exposure to varicella was 0.8 (range: 0.7 - 0.95). The probability of receiving VZIG once exposed was 0.9 (range: 0.50 - 0.95).
Measure of benefits used in the economic analysis
The model outputs were the probability of receiving VZIG, the probability of infection, and the probability of hospitalisation for acyclovir treatment with the immunisation and non-immunisation strategies.

Direct costs
The time horizon of the study was unclear, but the authors applied an annual discount rate of 5% to costs incurred after the second year. The unit costs were not reported separately from the quantities of resources used as the costs were presented as macro-categories (cost per episode of treatment). The health services included in the economic evaluation were immunisation, VZIG treatment and hospital admission for acyclovir treatment. The authors stated that all the direct costs were included in the analysis. For example, the cost of immunisation included the costs of two doses of vaccine, a visit and vaccine administration. The cost/resource boundary of the study was not stated, but it could have been that of the hospital. The resource use data were estimated on the basis of published evidence and experts’ opinions. The costs came from hospital databases. The price year was not reported.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
Univariate and multivariate sensitivity analyses were performed to examine the robustness of the estimated costs to variations in the model inputs. A worst-case scenario was also considered, where model assumptions were chosen to limit the cost-effectiveness of vaccination. The ranges of values used in the analysis were derived from the literature and from experts’ opinions.

Estimated benefits used in the economic analysis
The probability of receiving VZIG was 0% with immunisation and 64.8% with non-immunisation.

The probability of infection was 2.8% with immunisation and 45% with non-immunisation.

The probability of hospitalisation for acyclovir treatment was 2.2% with immunisation and 42.3% with non-immunisation.

Cost results
The estimated costs per patient were $250 with immunisation and $2,700 with non-immunisation.

The cost of vaccination in the immunisation strategy was totally offset by the avoided hospital admissions.

The sensitivity analysis showed that immunisation remained the dominant strategy under all scenarios examined. Only the magnitude of the cost-savings changed. In particular, when the cost of hospitalisation rose, the rate of exposure to varicella increased, as did the rate of protection from vaccination and the cost-savings rose. When the cost of vaccination increased, the number of patients receiving VZIG increased and the efficacy of VZIG improved, then the cost-savings fell. Even in the worst-case scenario (multivariate analysis with all the worst values for vaccination), immunisation remained cost-saving compared with non-immunisation ($300 versus $588, respectively).
Synthesis of costs and benefits
A synthesis of the costs and benefits was not relevant since immunisation dominated non-immunisation, which was both more costly and less effective.

Authors' conclusions
Vaccination for varicella pre-transplant was a cost-effective strategy for patients with chronic renal failure (CRF) in comparison with usual care, which comprised treatment with varicella zoster immunoglobulin (VZIG) as prophylaxis and subsequent hospitalisation and treatment with parenteral acyclovir if VZIG prophylaxis failed.

CRD COMMENTARY - Selection of comparators
The selection of the comparator was appropriate since it reflected usual care. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came mainly from published evidence. However, it was not stated whether a systematic review of the literature had been undertaken to identify primary studies. Further, no information on the characteristics and patient populations of the primary studies was provided. The methods used to extract and then combine the primary estimates were not described. Similarly, no comments on the quality and comparability of the primary sources were made. Experts' opinions were used to derive some clinical estimates. Almost all of the clinical inputs were varied in the sensitivity analysis.

Validity of estimate of measure of benefit
The summary benefit measures were specific to the interventions considered in the study and are not comparable with the benefits of other health care interventions. Such measures were obtained using the decision model. They are intermediate outputs since they do not reflect the direct impact of the interventions on the patients' health. The use of a more direct and generalisable measure would have been helpful.

Validity of estimate of costs
The perspective adopted in the study was unclear. Only the costs strictly related to the immunisation and non-immunisation strategies were considered in the analysis. The authors noted that even further cost-savings could have been generated if the avoided costs of graft rejection had been included in the cost analysis. A detailed breakdown of the cost items was not provided since the costs were presented as macro-categories. This reduces the possibility of replicating the results of the study. The source of the economic data was provided. The costs were treated deterministically but some cost estimates were varied in the sensitivity analysis. The price year was not reported, which makes reflation exercises in other settings difficult.

Other issues
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Sensitivity analyses were performed, which partially enhance the external validity of the analysis. A decision model was used to examine the costs and benefits of the interventions examined in the study. However, little information on the model was provided.

Implications of the study
The authors recommended that varicella vaccine be given to all children with CRF prior to Tx.

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Other publications of related interest


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MeSH
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