Cost-effectiveness of palivizumab in New Zealand

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 use of palivizumab prophylaxis, compared with no prophylaxis, in preterm infants of less than 32 weeks' gestation with respiratory syncytial virus (RSV). Palivizumab, an intramuscular humanised monoclonal antibody preparation, is a prophylaxis for RSV infection in preterm infants.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised preterm infants of less than 32 weeks' gestation that had been cared for at the National Women's Hospital and Middlemore, Waikato, Wellington and Christchurch neonatal units in New Zealand.

Setting
The setting was secondary care. The economic study was carried out in New Zealand.

Dates to which data relate
The effectiveness and epidemiological data were collected between 1997 and 1999. Some effectiveness data were retrieved from studies published between 1998 and 1999. All the costs were reported for the price year 2000.

Source of effectiveness data
The effectiveness data were derived from two studies (a major published trial and a retrospective cohort study conducted by the authors).

Link between effectiveness and cost data
The costing was carried out retrospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The sample size was not planned in the planning phase, nor were there any power calculations performed retrospectively. The participants were selected from a list of all preterm infants of less than 32 weeks' gestation that had been cared for in the five neonatal units, during 1997. The study sample comprised 437 infants born at less than 32 weeks' gestation, of whom 197 (45%) were of no more than 28 weeks' gestation and 50 (11%) were on oxygen at 36 weeks postmenstrual age. Nineteen (4%) infants were discharged home on oxygen. Of these, all but two were born at 28 weeks or less.
Study design
The relative treatment effect of the use of prophylaxis compared with no prophylaxis was taken from the IMPACT trial, the methods of which were reported elsewhere (see Other Publications of Related Interest). However, to obtain absolute outcome data, a retrospective cohort analysis was conducted in New Zealand to obtain the readmission incidence rates for different sub-groups with no prophylaxis treatment. The cohort of infants was obtained from five neonatal units. The duration of follow-up was 2 years.

Analysis of effectiveness
The primary health outcome was the estimated risk of hospitalisation with RSV before 1 year corrected age in infants who did and did not receive palivizumab prophylaxis.

Effectiveness results
The risk of rehospitalisation was highest for those discharged home on oxygen (42.1%). The risk was moderate for infants of 28 weeks' gestation or less with chronic lung disease (CLD; 22.9%) and without CLD (18.5%). In contrast, the risk of rehospitalisation was substantially lower for infants of 29 to 31 weeks' gestation, both with (10.2%) and without (12.4%) CLD.

Data coming from the IMPACT study, (see Other Publications of Related Interest) estimated that the risk of hospitalisation was reduced when using palivizumab prophylaxis in infants by 39% for those with CLD and 78% for those without.

Clinical conclusions
The authors concluded that, since children discharged home on oxygen had significantly the highest readmission rates, prophylaxis will be most beneficial if given to this group.

Methods used to derive estimates of effectiveness
Some estimates of effectiveness were based on authors’ assumptions.

Estimates of effectiveness and key assumptions
Estimated risk of hospitalisation with RSV was calculated using all documented RSV-positive admissions. The authors assumed that untested admissions had the same proportion of RSV infections as the tested admissions.

Measure of benefits used in the economic analysis
The primary measure of benefit used was the number of hospitalisations averted due to palivizumab prophylaxis. This absolute outcome measure was derived from the two studies, as explained already. A secondary outcome assessed was the number-needed-to-treat (NNT) to prevent one hospitalisation.

Direct costs
The costs to the health service and patient's family were included in the study. The costs were derived from actual data and were reported for the year 2000, but no details of the adjustment were given. Although it was not reported whether discounting had been carried out, it would not have been relevant as the time horizon of the study was only 5 months. The costs and the quantities were reported separately. They were derived from various sources such as hospitals, a pharmaceutical company (cost of the drug), and the Department of Statistics, New Zealand. The hospitalisation costs due to RSV were reported aggregated and it is impossible to identify which aspects of the costs were included. However, the authors mentioned that overhead costs were included. The source and year for the cost of a nurse's home visit were not reported. The medical costs were for palivizumab and its administration, and for RSV-related hospitalisation. The direct costs to the family consisted of time lost due to hospitalisation and time lost due to
prophylaxis administration.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not reported.

Currency
New Zealand dollars (NS$).

Sensitivity analysis
Sensitivity analyses were carried out to investigate variability in the data. The variables investigated were:

- prophylaxis dosage (from five to four doses),
- prophylaxis wastage (one dose = one vial),
- infant weight (from 5 to 3kg),
- efficacy of prophylaxis (55% average efficacy as opposed to sub-group specific efficacy), and
- hospital costs (+/- 50%).

Estimated benefits used in the economic analysis
The estimated benefits were reported only as the NNT to prevent one hospitalisation. For infants of 28 weeks' gestation or less, the NNT was 11 for those with CLD and 7 for those without CLD. For the group of infants of 29 to 31 weeks' gestation, the NNTs were 26 (with CLD) and 16 (without CLD), respectively. The NNT was 6 for the sub-group of infants discharged home on oxygen.

Cost results
The total costs were not reported in the paper. However, the unit costs and all cost inputs were clearly reported. The authors gave an estimation that the total net cost for prophylaxis for all infants of 28 weeks' gestation or less nationwide, who survived the neonatal period in 1998, would be NZ$1,090,000 (see Synthesis of Costs and Benefits).

Synthesis of costs and benefits
An incremental cost-effectiveness analysis was conducted. The net cost of prophylaxis per hospitalisation averted was:

- NZ$29,000 for infants discharged home on oxygen,
- NZ$65,000 (with CLD) and NZ$32,000 (without CLD) for infants of 28 weeks' gestation or less, and
- NZ$167,000 (with CLD) and NZ$98,000 (without CLD) for infants of 29 to 31 weeks' gestation.

The sensitivity analysis showed that reducing the number of doses from five to four significantly increased cost-effectiveness. Reducing the average infant weight from 5 to 3 kg more than doubled the cost-effectiveness of prophylaxis for infants of 28 weeks' gestation or less without CLD, and markedly improved the cost-effectiveness in all other sub-groups. Increasing drug wastage to the worst-case scenario of using a new vial for each infant increased the costs in every sub-group. The cost of prophylaxis per hospitalisation averted varied from NZ$42,000 for infants
discharged home on oxygen, to NZ$223,000 for infants of 29 to 31 weeks’ gestation with CLD.

Authors’ conclusions
The authors reported that their analysis did not indicate cost-savings associated with the use of palivizumab for any subgroup. In terms of relative cost-effectiveness, the authors concluded that the priority groups for prophylaxis are preterm infants discharged home on oxygen, then infants at no more than 28 weeks’ gestation or less without chronic lung disease (CLD), and finally with CLD. They reported “infants 20-31 weeks’ gestation with and without CLD would incur higher net costs.”

CRD COMMENTARY - Selection of comparators
The comparators were justified on the grounds that palivizumab is used in New Zealand on ad hoc basis, and there is a lack of evidence about local disease patterns. Due to its high cost, the authors stressed the need to determine the cost-effectiveness of using palivizumab prophylaxis for local paediatric practice, by sub-groups. You should decide if this is a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The authors conducted a retrospective cohort study to determine the incidence rates of readmissions, so that absolute outcomes could be derived from the relative treatment effects of prophylaxis provided by the IMPACT trial. The IMPACT trial methods were not reported in this paper as they had been reported elsewhere. The study sample of the retrospective study included approximately 80% of the infants born at less than 32 weeks’ gestation nationwide, and it was therefore representative of the study population.

Validity of estimate of measure of benefit
The estimation of benefits was obtained directly from the effectiveness analysis. Adverse effects or long-term benefits of prophylaxis were not considered, and mortality was not assessed as an outcome. Therefore, the authors felt that their estimates might be conservative in terms of overall cost-effectiveness.

Validity of estimate of costs
Although the study perspective was societal, the indirect costs were not included in the analysis. This might have been appropriate given that the patients were infants. However, the authors should have discussed this issue. Whilst relevant categories of direct costs were included, the use of summary costs for hospitalisation due to RSV makes it impossible to know what aspects of costs were included in this category. It was stated, though, that overhead costs were included. All the costs were adjusted to the year 2000, although the dates to which the prices related was not reported, nor were any details of the method of adjustment. The sources of the resources used were reported. A sensitivity analysis on the quantities used was not conducted, which may limit the interpretation of the study findings. However, the authors carried out appropriate sensitivity analyses to estimate the impact of changes in the costs.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, suggesting that other studies also indicated that prophylaxis incurred a net cost in all groups. Their results differed as far as the most favourable group is concerned. Explanations for these differences, such as different assumptions in the base-case analysis, were proposed. The authors proposed some reasons as to why their cost-effectiveness estimates might have been conservative. You should compare the stated reasons and assess the implications within your own setting.

The authors did not discuss the generalisability of the results to other settings. However, the sensitivity analyses improve the generalisability of the results. The authors pointed out some limitations of the study. For example, the study was retrospective and, therefore, it is possible that some RSV cases might have been overlooked. They also included aspects that they had not considered, such as compliance with treatment, patient education, underlying hospitalisation rates, long-term outcomes of infants treated with palivizumab, and important intangible costs borne by parents that could not
be quantified in the study. The results were not reported selectively and seem to be within the scope of the analysis.

**Implications of the study**
The authors did not make any explicit recommendations for changes in policy. Further research on the long-term outcomes of infants treated with palivizumab was proposed. In addition, the discussion highlighted some areas where assumptions were made, implying the need for further research.

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**Other publications of related interest**

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