Cost of influenza hospitalization at a tertiary care children's hospital and its impact on the cost-benefit analysis of the recommendation for universal influenza immunization in children age 6 to 23 months

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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 study compared universal immunisation of children aged 6 to 23 months against influenza with the current strategy of vaccinating only those children with risk factors.

Type of intervention
Primary prevention.

Economic study type
Cost-benefit analysis.

Study population
The study population comprised hospitalised infants and children aged 6 to 23 months with confirmed diagnoses of influenza.

Setting
The setting was a tertiary care children's hospital. The economic study was carried out in Illinois, USA.

Dates to which data relate
The effectiveness evidence and cost data were collected from 2002. The price year was 2002.

Source of effectiveness data
The effectiveness data were derived from a single study and authors' assumptions.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
The medical charts (n=41) for all infants and children hospitalised and diagnosed with influenza as the primary or secondary diagnosis were reviewed. Children with underlying risk factors for influenza were analysed separately. The patients were divided into three groups:

- those requiring admission to the general medical-surgical care units only (Ward);
- those requiring admission to the ward and the paediatric intensive care unit (Ward + PICU); and
those needing mechanical ventilation while in the PICU (Ward + PICU + Vent).

Patients whose influenza was judged to play no role in their hospitalisation were excluded from the analysis (n=4), while the charts for 2 patients were unavailable for review. All 6 of these patients were in the Ward group and were subsequently excluded from the analysis. The remaining 35 charts were analysed. Of these, 27 were in the Ward group, 6 in the Ward + PICU group, and 2 in the Ward + PICU + Vent group. Twenty patients were categorised as high risk and 15 as low risk. The median age of the patients was 26 months in the Ward group and 29 months in the Ward + PICU group. There were only 2 patients in the Ward + PICU + Vent group, one aged 2 months and the other 19 months. Power calculations were not reported.

Study design
This was a single-centred, historical, cross-sectional study.

Analysis of effectiveness
The analysis was conducted on the basis of treatment completers only. The primary health outcomes were the number of hospitalisations and length of stay in each group. No statistical analysis of the outcomes was reported. There was also no information on the comparability of the groups at baseline or adjustments for confounding factors.

Effectiveness results
Twenty-two per cent of patients requiring hospitalisation for influenza were aged between 6 and 23 months, and only 4 of these children were otherwise low risk. Both of the 2 patients who required mechanical ventilation had known risk factors for influenza infection (asthma and pulmonary disease), and one was younger than 6 months.

Sixty-seven per cent of the children who required admission to the PICU, but did not need mechanical ventilation, also had underlying chronic conditions. The other 2 children were older than 2 years.

Fifty-two percent of ward patients had underlying risk factors, one of which was under 6 months. Of the 13 children admitted to the ward who did not have identifiable risk factors, 31% were aged 6 to 23 months.

Forty-six per cent of patients without risk factors for influenza who were hospitalized for the infection were older than 24 months.

The length of stay was 2.7 days for the 4 children aged 6 to 23 months who were without risk factors.

Eighteen of the 20 high-risk children were older than 6 months. The length of stay for these children was 6 days.

The weighted mean length of stay for the entire study population was 5.1 days.

Clinical conclusions
No specific clinical conclusion was reported. The reader is referred to the 'Measure of Benefits Used in the Economic Analysis' section.

Methods used to derive estimates of effectiveness
The study was also based on authors' assumptions.

Estimates of effectiveness and key assumptions
The authors used realistic assumptions in their study. Vaccine efficacy was assumed to be 65%. The hospitalisation rate was assumed to be 1/1,000 for well children aged 6 to 23 months and 1/135 for those with other risk factors (e.g. mortality, morbidity, quality of life, adverse events, sensitivity, specificity of tests, probabilities). Complications from influenza vaccination were not considered as they are rare. Childhood death from influenza was also not considered.
since deaths from influenza in otherwise healthy children are also relatively rare.

**Measure of benefits used in the economic analysis**
The authors used hospitalisations prevented as the measure of benefit. The estimation of benefits was obtained directly from the effectiveness analysis.

**Direct costs**
Total hospital charges, PICU charges, ventilator expenses and the actual cost of administering the vaccine were included. Outpatient and physician charges were excluded, as were costs related to complications from vaccination. All cost categories were estimated using hospital sources. The values were stepped down to costs using a hospital-specific cost-to-charge ratio. Discounting was not carried out, which was appropriate as the costs were incurred during less than two years. The resource quantities and the unit costs were analysed separately but were not reported in great detail. Estimations of the quantities and the costs were based on actual data and were derived using modelling. The price year was 2002.

**Statistical analysis of costs**
No statistical analysis of the costs was conducted.

**Indirect Costs**
The indirect costs were not reported.

**Currency**
US dollars ($).

**Sensitivity analysis**
A sensitivity analysis was carried out in which variability in the data was investigated. The ranges were selected on the basis of published medical literature and authors’ assumptions. Sensitivity analyses on hospitalisation rates, influenza vaccine efficacy and vaccine price were performed.

**Estimated benefits used in the economic analysis**
Immunisation of children aged 6 to 23 months would prevent 18 high-risk hospitalisations and 4 low-risk hospitalisations. To prevent 18 high-risk hospitalisations, approximately 3,738 high-risk children should be vaccinated, while to prevent 4 additional hospitalisations in the otherwise low-risk children aged 6 to 23 months, more than 6,000 children should be vaccinated.

**Cost results**
Protecting all high-risk children over the age of 6 months against influenza would have saved about $350,000 in hospital charges.

Preventing 18 high-risk hospitalisations would have cost almost $187,000, compared with the actual hospital charges of $537,408.

To prevent 4 additional hospitalisations in the otherwise low-risk children aged 6 to 23 months would cost $307,700, compared with savings of $26,908 in total charges.

The sensitivity analysis showed that, when the entire 6- to 23-month cohort was considered, more than $325,000 in hospital charges would have been saved under the best-case scenario.
Synthesis of costs and benefits
In the base-case, for every dollar spent on influenza vaccination of high-risk children, approximately $2.90 in hospital charges was saved, whereas for every $11.40 spent on immunising otherwise healthy 6- to 23-month-old children according to the newest guidelines, approximately $1 in hospital charges was saved. In other words, vaccinating all high-risk children over the age of 6 months would save approximately $90 per child in future hospital charges, whereas vaccinating all healthy 6- to 23-month-olds would cost approximately $46 per child more than the hospital charges saved.

The prevention of hospitalisations in low-risk children aged 6 to 23 months had a cost-benefit ratio of approximately 11.4. On the other hand, considering the entire 6- to 23-month age group, the cost-benefit ratio was 1.0 if the entire group had been inoculated against influenza.

Authors’ conclusions
Preventing hospitalisations in the low-risk children aged 6 to 23 months for whom vaccine is currently recommended would have cost more than the hospital charges saved, approximately $46 per child. When all children aged 6 to 23 months were considered, influenza vaccination was less costly than other prophylactic measures. The addition of indirect costs, deaths, outpatient costs, and the cost of secondary cases would favour the cost-benefit ratio for influenza vaccination of all children aged 6 to 23 months.

CRD COMMENTARY - Selection of comparators
The authors provided an explicit justification for the choice of the comparator, the justification being based on published literature and standard clinical practice. You should judge whether these strategies are relevant in your own setting, or whether other comparators from other vaccination strategies may also be relevant.

Validity of estimate of measure of effectiveness
The authors used data from a single study and authors’ assumptions. The study design, a historical cross-sectional study, was appropriate for the hypothesis although its methodological design was only briefly reported. The main weaknesses of the study were as follows. First, no power calculations were reported. Second, no statistical analyses were undertaken to test for statistically significant differences between the two study groups. Third, it was unclear whether the study sample was representative of the study population. Finally, the patient groups were not shown to be comparable at analysis. These facts may introduce potential bias. The authors justified their choice of assumptions with reference to the medical literature. These estimates were investigated by means of sensitivity analyses, using ranges from the literature.

Validity of estimate of measure of benefit
The authors used hospitalisations prevented as the measure of benefit, and then reported cost-benefit ratios. The estimation of benefits was obtained directly from the effectiveness analysis using the number-needed-to-vaccinate. This choice of analysis was justified. The measure used may have been useful in this study, but it limits comparisons with economic evaluations in other health fields.

Validity of estimate of costs
The authors did not report the perspective of the study, although it appears to have been that of a hospital. Given that perspective, the exclusion of the indirect costs was appropriate. Some influenza vaccination and treatment costs might have been omitted from the analysis, but it is unlikely that this would have affected the authors’ conclusions as it was reported in the sensitivity analyses of the costs. The price values used were stepped down to costs using cost-to-charge ratios. To estimate the total direct costs, the authors considered inpatient care and vaccines only, excluding outpatient care and complications. They were taken from the same source. The resource use quantities and prices were taken from published sources and derived from the model. Sensitivity analyses of the costs were conducted. The price year was reported, which will assist any future reflation exercises. Discounting was appropriately not carried out as the study had
Other issues
The authors compared their findings with those from other studies. However, the issue of generalisability was not explicitly addressed. The authors appear to have presented their results selectively, although their conclusions did reflect the scope of the analysis. The authors stated some limitations. First, their model did not include all the cost categories for influenza vaccination and treatment. Second, the sample was small and was taken from only one relatively mild influenza season, from a single medical centre, and with a relatively smaller percentage of admissions of children aged 6 to 23 months without risk factors for severe influenza. These facts might have influenced the cost-benefit ratio of influenza vaccination.

Implications of the study
The authors stated that, in a season with more severe influenza or with a higher percentage of 6- to 23-month-olds admitted for influenza that did not have risk factors for severe influenza, the cost-benefit ratio of influenza vaccination would be more favourable.

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