Cost-effectiveness of influenza vaccination in high-risk children in Argentina
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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 influenza vaccine was examined.

Type of intervention
Vaccination.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised children aged 6 months to 15 years at high-risk for severe influenza. High-risk children included those with haemodynamically significant cardiac disease, chronic pulmonary disorders, chronic metabolic diseases, renal dysfunction, haemoglobinopathies or immunosuppression. Children receiving aspirin therapy were considered at risk for developing Reye's syndrome after influenza infection.

Setting
The setting was the community. The economic study was carried out in Argentina.

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1960 to 2000. The price year was 1998.

Source of effectiveness data
The effectiveness evidence was derived from published studies, augmented by the authors' assumptions.

Modelling
A decision analytic model was constructed to model the costs and effectiveness of the influenza programme and the no-vaccination strategy in the population of 10,047,651 children under 15 years old in Argentina. In the no-vaccination branch, theoretically, all children were susceptible to infection and each case of influenza could develop into no complications, minor or major complications requiring ambulatory treatment of hospitalisation. In the vaccination branch, the proportion of children vaccinated was determined by the coverage rate, while the proportion of children developing complications was determined by the efficacy rate of the vaccine.

Outcomes assessed in the review
The exact number of high-risk children in Argentina was identified using a number of variables. These included the overall population of children under 15 years old, the prevalence of congenital heart disease and the proportion of those
with haemodynamically significant heart disease, and the prevalence of other conditions (severe form of asthma, cystic fibrosis, cancer, and insulin-dependent diabetes). Once the cohort was identified, the variables derived from the published studies and used as model inputs were:

- vaccine efficacy,
- vaccine side-effects,
- the incidence of disease,
- the number of vaccine doses per child,
- the proportion of children requiring physician consultation,
- the number of outpatient visits per case,
- the proportion of patients having X-ray,
- the proportion of cases requiring antiviral therapy,
- the proportion of those developing otitis and requiring antibiotic therapy,
- the proportion of hospitalised patients,
- the average duration of hospitalisation, and
- the number of parental days out of work.

**Study designs and other criteria for inclusion in the review**
Not stated.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
The effectiveness data were obtained from 40 primary studies.

**Methods of combining primary studies**
The primary studies were combined using narrative methods.

**Investigation of differences between primary studies**
Not carried out.
Results of the review
The overall population of children under 15 years old in Argentina numbered 10,047,651.

The prevalence of congenital heart disease was 4% and the proportion of those with haemodynamically significant heart disease was one third. This resulted in an affected population of 133,968 children.

The prevalence of severe form of asthma was 10% (conservative estimated) and the number of diagnosed cases of cystic fibrosis was 100. This resulted in 1,005,065 children at high risk.

The prevalence of cancer was 55 in 100,000, resulting in a further 5,526 children.

The HIV prevalence was 0.3%, equating to 30,142 children.

The prevalence of insulin-dependent diabetes was 1 in 1,000, representing a further 10,047 children.

The high-risk children cohort was composed of 1,184,748 children.

The vaccine efficacy was 70% and the side-effects were 1%. The incidence of disease was 25% and the number of vaccine doses per child was 2. The proportion of children requiring physician consultation was 100%. There was one outpatient visit per case, and 16% of the patients had an X-ray. One hundred per cent of cases required antiviral therapy, while 30% of those developing otitis required antibiotic therapy. Four per cent of patients were hospitalised, and the average duration of hospitalisation was 7 days. The number of parental days out of work was 3.

Methods used to derive estimates of effectiveness
The authors made some assumptions to augment the data derived from the published studies.

Estimates of effectiveness and key assumptions
The proportion of patients requiring antipyretic therapy was assumed to be 100% and the vaccination coverage 100%.

Measure of benefits used in the economic analysis
The benefit measure used in the economic analysis was the number of cases of influenza avoided. The illness rate was also reported. Both were derived from the decision model. No discount rate was used since the time horizon of the study was one year.

Direct costs
No discounting was performed since the costs were incurred over one year. The unit costs were reported separately from the quantities of resources. The economic analysis included hospitalisation costs and outpatient costs. The hospitalisation costs were for medication, hospital stay and professional services. The outpatient costs were for vaccine cost, outpatient visit, antipyretic therapy (acetaminophen), X-ray, amantadine, and antibiotic for the treatment of otitis (amoxycillin). The cost/resource boundary adopted reflected that of the society, while the direct costs were assessed from the point of view of the hospital. The costs were estimated using actual charges at the Garrahan children's hospital, a public paediatric hospital in Buenos Aires, and drug acquisition prices. The quantities of resources were estimated from the authors' assumptions, which in turn, were based on experts' recommendations and personal communications from staff of the Garrahan children's hospital. The price year was 1998.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs (lost workdays) were included in the analysis since a societal perspective was adopted in the study.
The indirect costs were estimated using the average daily wage for a full-time worker in Argentina. The unit cost was reported, including payroll taxes. No discounting was performed as the time horizon of the model was one year. The price year was 1998.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way sensitivity analyses were performed to test the robustness of the estimated incremental cost-effectiveness ratio to variations in the model inputs. These included vaccine efficacy (10 - 90%), vaccine price ($5 - $30), incidence of influenza infection (5 - 40%), coverage rate (5 - 80%), days lost by the parents (0 - 7 days), and hospitalisation costs ($100 to $500). A second-order Monte Carlo simulation was also performed to assess the probable range of outcomes. This simultaneously varied vaccine efficacy, vaccine price, incidence of influenza, and the number of days lost by the parent.

**Estimated benefits used in the economic analysis**
The illness rate was 7.5% in the vaccinated group and 25% in the non-vaccinated group. The number of patients was 88,856 in the vaccinated group and 296,187 in the non-vaccinated group, with 207,331 cases of influenza avoided.

**Cost results**
The total (direct and indirect) costs were $39,286,244 in the vaccinated group and $51,181,114 in the non-vaccinated group. The vaccination programme resulted in cost-savings of $11,894,870 (net benefit to the society), which equates to $10.04 per vaccinated child.

**Synthesis of costs and benefits**
An incremental cost-effectiveness analysis was conducted to combine the costs and benefits of the programme. The vaccination programme was the dominant strategy over no vaccination, as it was associated with lower costs and higher number of influenza episodes averted. The sensitivity analyses showed that the dominance of the vaccination strategy was sensitive to variations in vaccine efficacy, disease incidence and vaccine costs. The Monte Carlo simulation indicated that the cost-effectiveness ratio fell below 0 (cost-saving) in 64% of the cases, and below $50 per case averted in 80% of the cases.

**Authors' conclusions**
Routine vaccination of high-risk children against influenza proved to be a cost-saving strategy from the perspective of society in Argentina. This conclusion was robust under reliable conditions.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparator was clear. No intervention was selected, as the aim of the study was to assess the active value of the intervention. You should decide whether it represents a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness estimates were derived from published studies, although a formal review of the literature was not performed. The authors did not report any details of the primary studies, such as the validity. The effectiveness estimates were combined using narrative methods. In addition, the impact of differences between the primary studies was not considered when estimating the effectiveness. Some of the estimates were somewhat specific to the Argentinean setting. The authors also made some conservative assumptions, which were used in the decision model.
Sensitivity analyses were performed due to the uncertainty in some estimates.

**Validity of estimate of measure of benefit**
The number of influenza cases avoided represented the benefit measure used in the economic analysis. It was appropriately modelled.

**Validity of estimate of costs**
The cost analysis was carried out from a societal perspective, and it appears that all the relevant categories of costs have been included in the study. The unit costs and the quantities of resources were reported separately and the price year was given. These factors facilitated reflation exercises to other settings. A complete breakdown of the costs was provided. The source of cost data was reported. The costs were treated deterministically in the base-case, but several sensitivity analyses were performed. The cost estimates were specific to the setting of the study.

**Other issues**
The authors made some comparisons of their findings with those from other studies. In terms of the issue of the generalisability of the study results to other settings, the authors stated that their study was carried out under specific conditions, thus further studies should be performed to generalise the results. However, the external validity of the analysis is likely to be high given the performance of several sensitivity analyses. In addition, the costs and the quantities were reported separately. The study referred to high-risk children younger than 15 years of age, and this was reflected in the conclusions of the study. The authors stated that the estimated cost-savings may have been underestimated due to the conservative assumptions used in the decision model.

**Implications of the study**
The authors stated that their findings may provide useful information "to persuade decision-makers that vaccination could be the best means of intervention in the management of influenza in high-risk children".

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None stated.

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