Respiratory syncytial virus immune globulin: decisions and costs
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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 use of prophylactic treatment with respiratory syncytial virus immune globulin (RSVIG) in paediatric patients at risk of developing RSV bronchiolitis and in paediatric patients at risk of developing a respiratory illness that would require hospitalisation. The use of RSVIG was compared with no prophylaxis. RSVIG was administered intravenously (IV) by home-based infusions (dose 750 mg/kg monthly) during the RSV season (November to April).

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Two different populations were studied. Population one comprised children at high risk for admission to the intensive care unit (ICU) due to RSV infection. Population two comprised a hypothetical population of children at risk for RSV bronchiolitis who achieved the criteria used by the FDA to allow administration of RSVIG. This included children aged less than 2 years old with bronchopulmonary dysplasia (BPD) and children under 12 months with a history of premature birth (<= 35 weeks’ gestation).

Setting
The setting was secondary care. The economic study was carried out in Arizona, USA.

Dates to which data relate
The effectiveness resource use data were taken from studies published between 1991 and 1997. In addition, some unpublished data from local sources were used. The price year was 1997.

Source of effectiveness data
The effectiveness data were derived from a synthesis of completed studies. A systematic review of the literature was not undertaken.

Modelling
A decision analysis model was constructed for each population studied to determine both the benefits and costs.

Outcomes assessed in the review
The outcomes used in the models were:
children at risk of RSV disease, for population one, aged less than 24 months with BPD or less than 12 months and premature (less than 35 weeks' gestation), and

for population two, infants at risk of ICU admission (less than 8 months and chronic lung disease, current oxygen use, or prior hospitalisations);

RSV admissions in children at risk;

respiratory illness admissions in children at risk;

the percentage of ward admissions;

the percentage of ICU admissions;

the percentage of RSV upper respiratory tract infections/lower respiratory tract infections;

the percentage of children seen in the clinic;

the percentage of phone consultations;

adherence to RSVIG treatment; and

adverse events (fever, decreased oxygen saturation, fluid overload, emesis, diarrhoea, hypertension and tachypnoea or tachycardia).

**Study designs and other criteria for inclusion in the review**
The studies included were clinical trials. Of these, two were randomised controlled clinical trials and one was a 3-year follow-up study of re-hospitalisation in children acquiring RSV after being discharged from a neonatal ICU. Information on the design of the other sources used to derive parameters was not reported. The inclusion or exclusion criteria used to select the studies were also not reported.

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

**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**
Ten primary studies were included in the review.

**Methods of combining primary studies**
Not reported.

**Investigation of differences between primary studies**
Not reported.
Results of the review
The number of RSV admissions/100 children at risk was 13 (range: 6 - 20) with no prophylactic treatment and 4 (range: 0 - 8) with RSVIG treatment.

The number of respiratory illness-related admissions/100 children at risk was 67 (range: 27 - 85) with no prophylactic treatment and 16 with RSVIG treatment.

Ward admissions were 74% (range: 66 - 82) with no treatment and 72% (range: 60 - 83) with RSVIG treatment.

ICU admissions were 26% (range: 18 - 34) with no treatment and 28% (range: 17 - 40) with RSVIG treatment.

The percentage seen in the clinic was 50% for both with and without treatment.

The percent of phone consultations was 25% both with and without treatment.

The number of RSVIG doses was 4 (range: 1 - 5)

Adherence to treatment was 76% (range: 46 - 97).

Adverse events due to RSVIG treatment were 9% (range: 3 - 15).

Methods used to derive estimates of effectiveness
The authors made an assumption about non-adherent patients.

Estimates of effectiveness and key assumptions
It was assumed that the risk of hospitalisation for non-adherent children would be the same as if they had not received prophylaxis. For children who did not complete the therapy course, it was assumed that they received three doses and that risk of RSV bronchiolitis was the same as that for children with no prophylactic RSVIG.

Measure of benefits used in the economic analysis
The measure of benefit used in the economic analysis was the number of hospitalisations avoided.

Direct costs
Discounting was not performed, which was appropriate since the follow-up was carried out within one year. The unit costs were reported, but no resource use was given. The estimation of the quantities and costs was modelled, based on data from published and unpublished sources (confidential financial data from hospitals). Actual costs, instead of charges, were used throughout the study. The direct costs included inpatient and outpatients treatment costs. The inpatient treatment costs encompassed admission and ward only costs, (average) cost of the ICU and the cost of the ICU for high-risk patients. The outpatient treatment costs encompassed phone consultations, office visits, RSVIG IV acquisition cost, RSVIG IV non-drug fixed and variable costs, and adverse events. The costs were calculated in 1997 values. The total cost-differences were presented.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
No indirect costs were included, which was consistent with the perspective adopted.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were performed on the assumptions used when modelling. However, the variables investigated and the types of analysis conducted were not reported. An analysis of extremes (low and high ranges) was performed for each model. In addition, the results of threshold analyses were presented.

Estimated benefits used in the economic analysis
The estimated incremental benefit in population one was a decrease of 18 hospitalisations (range: 23 - 10).

The estimated incremental benefit in population two was presented for two sub-populations. Children aged less than 24 months with BPD, or less than 12 months and premature birth, showed a decrease of 121 hospitalisations due to RSV bronchiolitis (range: -16 - 345). Children aged less than 24 months with BPD, or less than 6 months and premature birth, showed a decrease of 688 hospitalisations due to respiratory illness-related hospitalisation (range: 90 - 1,189).

Cost results
The incremental costs due to RSVIG prophylaxis were -$469,556 (range: -1,028,819 - -39,662) for group one. Group two was again divided into two sub-groups. The incremental costs to prevent RSV bronchiolitis in the group of children aged less than 24 months with BPD, or less than 12 months and premature gestation, were $6,553,165 (range: -1,117,076 - 8,335,265). The incremental costs to prevent all respiratory illness-related hospitalisation in the group of children aged less than 24 months with BPD, or less than 6 months with premature gestation, were $2,670,622 (range: -22,944,732 - 8,125,610).

The costs of adverse events of RSVIG were included.

Synthesis of costs and benefits
The costs and benefits were combined by calculating a cost-effectiveness ratio that showed the cost of one hospitalisation avoided.

The cost-effectiveness ratio for preventing one hospitalisation for severe RSV infection in group one was $26,816, demonstrating a cost-saving per hospitalisation avoided.

The cost-effectiveness ratio for preventing one hospitalisation due to RSV bronchiolitis in group two, sub-group one was $53,945. This indicated an extra cost due to the prophylactic programme.

The cost-effectiveness ratio for preventing one respiratory illness-related hospitalisation in group-two, sub-group two was $3,880, again indicating an extra cost due to the prophylactic programme.

In the model for group one (high risk), the calculated ratio was sensitive to the unit cost of the ICU and the cost for a course of RSVIG. The calculated range of extremes was cost-saving, varying from $3,950 to $44,194 per hospitalisation avoided.

For group two, sub-group one, the cost-effectiveness ratio per avoided hospitalisation due to RSV was primarily sensitive to the cost of RSVIG and the number of doses administered. The calculated range of extremes ranged from a cost-saving of $3,242 to an extra cost of $510,139 per hospitalisation avoided.

For group two, sub-group two, the cost-effectiveness ratio per avoided respiratory illness-related hospitalisation was most sensitive to the costs. Cost neutrality was achieved with a reduction of the cost of RSVIG of almost 40%, or a higher cost of ward admission ($8,000 instead of $2,800) or ICU admission ($26,350 instead of $15,000). The range of extremes was $19,303 to -$90,420.
Authors' conclusions

The authors' conclusions were defined in terms of the short-term cost-consequences of the prophylactic programme. The use of respiratory syncytial virus immune globulin (RSVIG) limited to children at high risk will result in cost-savings of almost $27,000 per hospitalisation avoided. When RSVIG is used for a broad range of children and children at risk for RSV illness regardless of severity, the additional cost per prevented hospitalisation will be approximately $53,000. When RSVIG is intended to prevent hospitalisation due to all respiratory illness, the additional cost is $3,000 per hospitalisation prevented.

CRD COMMENTARY - Selection of comparators

The rationale for the choice of the comparator was clear. The study was aimed at assessing the cost-effectiveness of RSVIG if administered prophylactically to different populations at risk.

Validity of estimate of measure of effectiveness

The authors did not state that a systematic review had been undertaken to select data to populate the decision analysis models. In addition, the authors appear to have used the data from the available studies selectively. No search strategy or inclusion or exclusion criteria were reported, and the impact of any differences between the primary studies was not discussed. Given these limitations, the internal validity of the effectiveness estimates is likely to be low.

Validity of estimate of measure of benefit

The measure of benefit was hospitalisation avoided, which was derived directly from the model. An alternative measure of benefit, to allow the authors to compare the benefits of the treatment alternatives with other cost-effectiveness studies, would have been a quality of life measure.

Validity of estimate of costs

All the categories of cost relevant to the perspective adopted were included in the analysis. The unit costs were reported but the quantities were not, which will affect the generalisability of the cost results obtained. Resource use was taken from published and unpublished sources. A sensitivity analysis of the quantities was not conducted, which may limit the interpretation of the study findings. The unit costs were taken from published and unpublished sources. A sensitivity analysis of the prices was not conducted. Since all the costs were incurred within one year, discounting was unnecessary and was not conducted. The price year was reported, which will aid any future reflation exercises.

Other issues

The results presented were compared with findings from other studies, including studies comparing treatment with RSVIG to an alternative prophylactic drug. These studies reported similar results. The authors do not appear to have presented their results selectively and the results reported were within the scope of the study.

The authors reported a number of limitations to their study. For example, the costs of subsequent long-term medical care of children hospitalised because of RSV infection and the monetary values of intangibles (e.g. pain) were not included. This may lower the relative cost of RSVIG and increase the benefits. The costs of physician and nurses’ time due to infusion-related complications were also not included. Again, the authors suggested that this could have diminished the result.

Implications of the study

The authors concluded that administration to restricted populations would result in optimal costs for greatest patient benefits. If the prophylactic programme is aimed at reducing morbidity and related medical expenditures of both RSV- and non-RSV-related respiratory infection, the drug acquisition cost must be decreased or the programme must be restricted to those children at highest risk for severe disease.
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Other publications of related interest


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