

# Palivizumab for immunoprophylaxis of respiratory syncytial virus (RSV) bronchiolitis in high-risk infants and young children: systematic review and additional economic modelling of subgroup analyses

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## *Executive summary*

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# Executive summary

## Background

Respiratory syncytial virus (RSV) is a seasonal infectious disease, with epidemics occurring annually from October to March in the UK. It is a very common infection in infants and young children and can lead to hospitalisation particularly in those who are premature or who have chronic lung disease (CLD) or congenital heart disease (CHD). Palivizumab (Synagis®, MedImmune) is a monoclonal antibody designed to provide passive immunity against RSV and thereby prevent or reduce the severity of RSV infection. It is licensed for the prevention of serious lower respiratory tract infection caused by RSV in children at high risk. While it is recognised that a policy of using palivizumab for all children who meet the licensed indication does not meet conventional UK standards of cost-effectiveness, most clinicians feel that its use is justified in some children.

## Objectives

The objective of this report was to use systematic review evidence to estimate the cost-effectiveness of immunoprophylaxis of RSV using palivizumab in different subgroups of children with or without CLD or CHD who are at high risk of serious morbidity from RSV infection.

## Methods

Searches were conducted for prognostic and hospitalisation studies covering 1950–2009 (the original report searches conducted in 2007 covering the period 1950–2007 were rerun in August 2009 to cover the period 2007–9), and the database of all references from the original report was sifted to find any relevant studies that may have been missed. The risk factors identified from the systematic review of included studies were analysed and synthesised using STATA (version 10; StataCorp LP, College Station, TX, USA). The base-case decision tree model developed in the original *Health Technology Assessment* (HTA) journal publication [*Health Technol Assess* 2008;**12**(36)] was used to derive the cost-effectiveness of immunoprophylaxis of RSV using palivizumab in different subgroups of children who are at high risk of serious morbidity from RSV infection. Cost-effective spectra of prophylaxis with palivizumab compared with no prophylaxis for pre-term children without CLD/CHD, with CLD, with acyanotic CHD and with cyanotic CHD were derived.

## Results

Thirteen studies were included in this analysis. Most of the studies were small and they were not powered for the outcomes of interest, and the quality of reporting was also frequently poor.

Analysis of 16,128 subgroups showed that prophylaxis with palivizumab may be cost-effective [at a willingness-to-pay threshold of £30,000/quality-adjusted life-year (QALY)] for some subgroups. For example, for pre-term children without CLD or CHD, the cost-effective subgroups included children under 6 weeks old at the start of the RSV season who had at least two other risk factors that were considered in this report and were born at 24 weeks gestational age (GA) or less, but did not include children who were >9 months old at the start of the RSV season or had a GA of

> 32 weeks. For children with CLD, the cost-effective subgroups included children < 6 months old at the start of the RSV season who were born at 28 weeks GA or less, but did not include children who were > 21 months old at the start of the RSV season. For children with acyanotic CHD, the cost-effective subgroups included children < 6 months old at the start of the RSV season who were born at 24 weeks GA or less, but did not include children who were > 21 months old at the start of the RSV season. For children with cyanotic CHD, the cost-effective subgroups included children < 6 weeks old at the start of the RSV season who were born at 24 weeks GA or less, but did not include children who were > 12 months old at the start of the RSV season.

## Conclusions

Prophylaxis with palivizumab does not represent good value for money based on the current UK incremental cost-effectiveness ratio (ICER) threshold of £30,000/QALY when used unselectively in children without CLD/CHD or children with CLD or CHD. This subgroup analysis showed that prophylaxis with palivizumab may be cost-effective (at a willingness-to-pay threshold of £30,000/QALY) for some subgroups. In summary, the cost-effective subgroups for children who had no CLD or CHD must contain at least two other risk factors apart from GA and birth age. The cost-effective subgroups for children who had CLD or CHD do not necessarily need to have any other risk factors.

The poor quality of the studies feeding numerical results into this analysis means that the true cost-effectiveness may vary considerably from that estimated here. There is a risk that the relatively high mathematical precision of the point estimates of cost-effectiveness may be quite inaccurate because of poor-quality inputs. Because of this we have conducted some credible interval analysis which suggested that, for example, the point estimates of cost-effectiveness of £20,000/QALY could vary between £8000/QALY and £66,000/QALY. It could be useful to derive credible intervals for all of the 16,128 point estimates of cost-effectiveness of prophylaxis with palivizumab compared with no prophylaxis, but they would all suffer from the same problem of poor-quality inputs.

Larger, better quality studies would be needed to generate more accurate input results for the modelling. Unfortunately, much larger, adequately powered studies may be very difficult to do because of a variety of clinical and practical reasons associated with conducting research in at-risk children with multiple risk factors. Also, there were other risk factors, such as lack of or minimal breastfeeding and family history of atopy, which were not considered in the model because of absence of data. Future research should systematically identify the effect size of all of these risk factors and enter them into the model to estimate their effects on the cost-effectiveness results.

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## Publication

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# NIHR Health Technology Assessment programme

The Health Technology Assessment (HTA) programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

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The research reported in this issue of the journal was commissioned by the HTA programme as project number 06/29/02. The contractual start date was in July 2009. The draft report began editorial review in December 2009 and was accepted for publication in September 2010. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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