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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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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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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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Abstract

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

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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: 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.

Data sources: A systematic review of the literature and an economic evalutaion was carried out. The bibliographic databases included the Cochrane Library [Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE) and *Health Technology Assessment* (HTA)] and five other databases, from inception to 2009. Research registries of ongoing trials including Current Controlled Trials metaRegister, Clinical Trials.gov and the National Institute for Health Research Clinical Research Network Portfolio were also searched.

Review 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. The base-case decision tree model developed in the original 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 pre-term infants and young children who are at high risk of serious morbidity from RSV infection. Cost-effective spectra of prophylaxis with palivizumab compared with

no prophylaxis for children without CLD/CHD, children with CLD, children with acyanotic CHD and children with cyanotic CHD were derived.

Results: Thirteen studies were included in this analysis. 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 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.

Limitations: 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.

Conclusions: Prophylaxis with palivizumab does not represent good value for money based on the current UK incremental cost-effectiveness ratio 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. Future research should be directed towards conducting much larger, better powered and better reported studies to derive better estimates of the risk factor effect sizes.

Funding: This report was funded by the HTA programme of the National Institute for Health Research.

Contents

Glossary

Chronic lung disease (CLD) CLD is defined as oxygen dependency for at least 28 days from birth. It is caused by prolonged supplemental oxygen therapy and ventilation and usually develops in the first 4 weeks after birth, most often affecting children born prematurely. It is caused by the pressure and high concentrations of oxygen which, when prolonged, can cause lung tissue to become inflamed and scarred.

Confidence interval (CI) A measure of the precision of a statistical estimate; quantifies the uncertainty in measurement. Usually reported as 95% CI, i.e. the range of values within which one can be 95% sure that the true values for the whole population lie.

Credible interval An indication of the uncertainty in the true location of a parameter value.

Discounting Discounting refers to the process of adjusting the value of costs or benefits that occur at different points of time in the future, so that they may all be compared as if they had occurred at the same time.

Incremental cost-effectiveness ratio (ICER) An expression of the additional cost of health gain associated with an intervention relative to an appropriate comparator. Expressed as the difference in mean costs (relative to the comparator) divided by the difference in mean health gain.

Infant A child up to 1 year old (up to and including 365 days from birth).

Meta-analysis The statistical pooling of the results of a collection of related individual studies, to increase statistical power and synthesise their findings.

Quality of life A concept incorporating all the factors that might impact on an individual's life, including factors such as the absence of disease or infirmity and also other factors which might affect an individual's physical, mental and social well-being.

Quality-adjusted life-year (QALY) An index of health gain where survival duration is weighted or adjusted by the patient's quality of life during the survival period. QALYs have the advantage of incorporating changes in both quantity (mortality) and quality (morbidity) of life.

Odds A ratio of the number of people incurring an event to the number of people who don't have an event.

Odds ratio (OR) Ratio of odds of a specified characteristic in the treated group to the odds in the control group.

Risk ratio (RR) The ratio of risk in the treated group to the risk in the control group.

List of abbreviations

AGE	birth age
CEAC	cost-effectiveness acceptability curve
CI	confidence interval
CLD	chronic lung disease
CHD	congenital heart disease
GA	gestational age
HRQoL	health-related quality of life
HTA	*Health Technology Assessment*
HUI	Health Utilities Index
ICER	incremental cost-effectiveness ratio
MB	multiple birth
NICE	National Institute for Health and Clinical Excellence
OC	overcrowding
OR	odds ratio
PE	parental education
PSA	probabilistic sensitivity analysis
QALY	quality-adjusted life-year
RCT	randomised controlled trial
RR	rate ratio
RSV	respiratory syncytial virus
SAS	siblings at school
SE	smoking exposure

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

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.

Funding

This report was funded by the HTA programme of the National Institute for Health Research.

Chapter 1

Aim of the report

The original *Health Technology Assessment* (HTA) report on this topic was Wang D, Cummins C, Bayliss S, Sandercock J, Burls A. Immunoprophylaxis against respiratory syncytial virus (RSV) with palivizumab in children: a systematic review and economic evaluation. *Health Technol Assess* 2008;**12**(36).[1]

This update report develops the economic model from the first report by exploring cost-effectiveness in different subgroups of children with RSV infection.

Chapter 2

Background

As the original report has full details of the condition, current treatment options and information about palivizumab (Synagis®, MedImmune), only brief details will be given here.

Description of health problem

Respiratory syncytial virus is a seasonal infectious disease, with epidemics occurring annually from October to March in the UK. It is a very common infection in young children, with up to half of all infants becoming infected by the age of 1 year.[1] A proportion of children with RSV are seriously affected by the virus and may need to be hospitalised owing to life-threatening complications such as bronchiolitis (inflammation of the smaller airways of the lung) and pneumonia. Children who are at high risk of hospitalisation for these reasons include premature infants, children with chronic lung disease due to abnormal development of the lungs or cystic fibrosis, children who were born with certain types of heart problems and children who have limited resistance to disease because of a weakened immune system.[2] Many of these high-risk infants may need to be hospitalised and some may require admission to an intensive care unit.[3]

Detection of RSV in children with lower respiratory tract infections is by direct immunofluorescence assay, enzyme immunoassay or a positive viral culture for RSV from nasopharyngeal secretions.

Current service provision

Beyond supportive care (such as mechanical assistance with breathing, intravenous fluids and oxygen), the only treatment available for severe RSV infection causing bronchiolitis is ribavirin (Virazole®, ICN Pharmaceuticals).[4] This is an antiviral treatment available orally and by inhalation. It is licensed for inhaled administration for severe bronchiolitis caused by RSV infection in infants, especially when they have other serious conditions, such as when they are immunocompromised. However, 'there is no evidence that ribavirin produces clinically relevant benefit in RSV bronchiolitis'.[4] Its use requires hospitalisation, which increases the risk of spreading the infection, and it is costly and has a number of unwanted side effects.[4]

Attempts to develop a vaccine to prevent RSV infection have so far been unsuccessful. Strategies to prevent infection are therefore of considerable interest.

Description of technology under assessment

Palivizumab has a proprietary name of Synagis®. It is a monoclonal antibody and is indicated for the prevention of serious lower respiratory tract disease requiring hospitalisation caused by RSV in children at high risk for RSV disease.[4] It is used in the following high-risk groups:

- children < 6 months with haemodynamically significant left to right shunt, congenital heart disease (CHD) or pulmonary hypertension
- children < 2 years with chronic lung disease requiring oxygen at home (or who have been on prolonged oxygen treatment)
- children < 2 years with severe congenital immunodeficiency
- children born at 35 weeks of gestation or less and < 6 months of age at the onset of the RSV season and considered to be at high risk of RSV hospitalisation.[4]

Common side effects of palivizumab include injection site reactions, nervousness and fever. Less common side effects include diarrhoea and vomiting, constipation, haemorrhage, rhinitis, respiratory problems, pain, drowsiness, asthenia, hyperkinesia, leucopenia and rash.[4]

The recommended dose of palivizumab is 15 mg per kg body weight, injected intramuscularly, given once a month during anticipated periods of RSV risk in the community. Where possible, the first dose should be administered prior to commencement of the RSV season. Subsequent doses should be administered monthly throughout the RSV season. To reduce the risk of rehospitalisation, it is recommended that children receiving palivizumab who are hospitalised with RSV continue to receive monthly doses of palivizumab for the duration of the RSV season.[4]

For children undergoing cardiac bypass, it is recommended that a 15 mg/kg injection of palivizumab be administered as soon as the child is stable after surgery to ensure adequate palivizumab serum levels. Subsequent doses should resume monthly through the remainder of the RSV season for children that continue to be at high risk of RSV disease.

The cost of palivizumab (Synagis®) is £360.00 for a 50-mg vial and £663.11 for a 100-mg vial.[4] If a baby at 6 months weighs 7.5 kg the cost of one dose of palivizumab is £1023.11 if vial wastage is assumed, plus cost of administration.

Chapter 3

Definition of the decision problem

This report investigated cost-effectiveness only. We are unaware of any other work investigating the cost-effectiveness of palivizumab by different subgroups, particularly where based on a systematic review.

The original report[1] found the following cost-effectiveness results:

- In pre-term children without chronic lung disease (CLD), the base-case estimate of cost-effectiveness was £475,600/quality-adjusted life-year (QALY). When this was varied by a range of mortality rate estimates the results varied between £24,100/QALY and £3M/QALY.
- In children with CLD the base-case estimate of cost-effectiveness was £66,900/QALY. When this was varied by a range of mortality rate estimates the results varied between £51,000/QALY and £85,000/QALY.
- In children with CHD, the base-case estimate of cost-effectiveness was £83,200/QALY. When this was varied by whether the children had cyanotic or acyanotic CHD, the results varied between £49,100/QALY and £159,400/QALY. When this was varied by age of the child and hospitalisation rates the results varied between £63,300/QALY and £457,900/QALY.

These results are listed in *Table 1*.

There was also further work on the subgroup of CLD children and children with siblings in day care, which provided *Table 2*.

Note that these were point estimates of cost-effectiveness only. There was no information on credible intervals, for example, for the 9000 in the upper left box, i.e. whether it might vary between £8500 and £9500 or between £1000 and £17,000.

The original decision problem for the current report was in two parts.

1. The population is infants and young children at high risk of hospitalisation, morbidity or death due to RSV infection, including children < 2 years of age, and with haemodynamically significant CHD. This group was stratified by age to find out whether administration is cost-effective for any age group.

TABLE 1 Original report[1] cost-effectiveness results

Category	Base estimate (£/QALY)	Sensitivity analyses (£)
Children without CLD	475,600	By mortality rate: 24,100–3,905,500
Children with CLD	66,900	By mortality rate: 51,000–85,000
Children with CHD	83,200	By cyanotic vs not: 49,100–159,400
		By age and hospitalisation rate: 63,300–457,900

TABLE 2 Original report[1] chronic lung disease subgroup analysis with siblings in day care

Birth age (months)	GA (weeks)					
	≤24	24–26	26–28	28–30	30–32	32–34
<3	9000	10,000	12,000	15,000	19,000	25,000
3–6	13,000	15,000	19,000	24,000	33,000	42,000
6–9	19,000	24,000	33,000	42,000	59,000	75,000
9–12	33,000	45,000	58,000	76,000	105,000	141,000
12–15	59,000	83,000	105,000	140,000	212,000	284,000
15–18	105,000	141,000	214,000	286,000	430,000	430,000
18–21	213,000	285,000	42,000	429,000	863,000	866,000
21–24	430,000	431,000	867,00	870,000	859,000	∞000

Incremental cost-effectiveness ratio cost/QALY coding: < £30,000; £30,000–40,000; £40,000–50,000; £50,000–60,000; > £60,000.

2. Using the whole data set, further analyses of other potential risk groups were investigated in healthy children or children with acyanotic or cyanotic CHD or any form of significant CLD:
   i. gestational age (GA)
   ii. male gender
   iii. siblings at school (SAS)
   iv. multiple births (MBs)
   v. exposure to passive smoke (SE)
   vi. overcrowding (OC) in the family home
   vii. parental education (PE)
   viii. age < 6 weeks at the start of the RSV season
   ix. lack of, or minimal, breast feeding
   x. family history of atopy.

The subgroups above were suggested by members of the RSV subcommittee from the UK Joint Committee on Vaccination and Immunisation. The last three listed were not included in the final model owing to lack of good-quality information from included studies.

Chapter 4

Assessment of clinical effectiveness

Methods for reviewing effectiveness

Although this report is on the cost-effectiveness of subgroups of children with potential risk factors for hospitalisation with RSV, the process for finding relevant studies for use in the model is very similar to that used for a systematic review of clinical effectiveness. Therefore, these methods will be described in this section.

Identification of studies

The original searches for this review topic for the previous HTA report were carried out in March 2007, following preliminary scoping in 2006.[1] No date or language limits were applied.

To find appropriate prognostic studies for this report, three main strategies were used:

1. conducting new searches for prognostic and hospitalisation studies covering 1950–2009, making extensive use of searching of reference lists from recently published studies
2. rerunning of the original report searches in August 2009, to cover the interim period 2007–9, for clinical effectiveness and cost-effectiveness research as detailed below
3. sifting through the database of all references from the original report to find any relevant studies that may have been missed.

Prognosis and hospitalisation studies

The following sources were searched for relevant studies:

- Ovid MEDLINE(R) 1950 to July Week 4 2009
- the original HTA review database of all references
- reference lists of relevant studies.

The reason for running the specific prognosis searches on MEDLINE only was because there was a large number of hits, but very few studies of relevance. Therefore, extensive use was made of searching reference lists of relevant studies instead.

Clinical effectiveness review

The following sources were searched for systematic reviews and primary studies:

- Bibliographic databases: Cochrane Library (John Wiley & Sons, Inc. internet version) [Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE) and HTA], 2009 Issue 3, MEDLINE (Ovid) 1950 to July Week 4 2009, MEDLINE In-Process and other Non-Indexed Citations (Ovid) 3 August 2009, EMBASE (Ovid) 1980–2009 Week 31, Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCO Host) 1982 to 4 August 2009 and Science Citation Index (Web of Knowledge) at 4 August 2009.
- Research registries of ongoing trials including Current Controlled Trials metaRegister, Clinical Trials.gov and the National Institute for Health Research Clinical Research Network Portfolio.

- Relevant internet sources.

Searches were limited by date to the period 2007–9 and there were no language restrictions.

Cost-effectiveness review and modelling

Studies on costs, quality of life, cost-effectiveness and modelling were identified from the following sources:

- Bibliographic databases: MEDLINE (Ovid) 1950 to July Week 5 2009, EMBASE (Ovid) 1980 to 2009 Week 32, Cochrane Library (John Wiley & Sons, Inc. internet version) [NHS Economic Evaluation Database (EED) and DARE] 2009 Issue 3.
- Relevant internet sites.

Searches were limited by date to the period 2007–9 and there were no language restrictions. All relevant references were inserted into a new reference manager database.

Inclusion and exclusion criteria

The inclusion criteria for this report are listed in *Table 3*.

Inclusion decisions were made by one reviewer and checked by the modeller. Any disagreements were resolved through discussion.

Data abstraction strategy

Data abstraction was done straight into data tables by one reviewer and checked by the modeller. Any discrepancies were resolved through discussion.

Critical appraisal strategy

Quality assessment was by assessment of four relevant factors derived from the Critical Appraisal Skills Programme checklists for randomised controlled trials (RCTs), cohort and case–control studies (*Appendix 3*).

Data analysis and evidence synthesis

The data analysis and evidence synthesis process consists of the following steps:

(1) The outcomes of the risk factors, including types of population (pre-term infants and children without CLD/CHD or children with CLD or CHD), GA, birth age (AGE), SAS, gender [BOY, SEX(male)], MB, SE, OC, and PE of high school or less (≤ 12 years) were analysed, updated and combined (when it was possible). All values of parameters based on whole weeks, for example

TABLE 3 Inclusion criteria

Population	Infants or children aged up to 5 years, with at least some having confirmed RSV infection, can be term or premature or mixed, healthy or can have CHD or CLD (any definition)
Intervention(s)	–
Comparator(s)	–
Outcomes	Reporting age specific hospitalisation rates
	Reporting ORs and CIs for any of the listed subgroups[a]
Study design	Prospective or retrospective cohort, case–control, cross-sectional

CI, confidence interval; OR, odds ratio.

a If any of the key subgroups (CHD, CLD) had no studies reporting ORs and CIs, reported ORs were used if available or calculated from raw numbers and CI estimated.

34.5 weeks gestational age was rounded to 35 weeks. Meta-analysis was carried out with the STATA program (version 10; StataCorp LP, College Station, TX, USA) using log(odds ratio, OR) and standard error [se(logOR)] for each study and drawing the plot using the meta, rather than metan function because for some studies, only OR and 95% confidence intervals (CIs) were available. Fixed and random effects models were used according to the level of heterogeneity. Heterogeneity was assessed with the *Q* statistic.

(2) It was assumed that the effect of the risk factors follows an addition rule in the log scale. The outcomes of different combinations of risk factors were derived by:

$$\mathrm{OR}_{\mathrm{subgroup}} = e^{\left[x\ln OR_{x} - \ln OR_{GA}(28-GA) - \ln OR_{age}(3-age) + SAS\ln OR_{SAS} + BOY\ln OR_{BOY} + MB\ln OR_{MB} + SE\ln OR_{SE} + OC\ln OR_{OC} + PE\ln OR_{PE}\right]}$$

[Equation 1]

where *x* is an indicator variable for study population, with 0 for children without CLD, CLD for children with CLD, and CHD for children with CHD. SAS, BOY, MB, SE, OC and PE are indicator variables for the presence/absence of the risk factors of siblings at school, gender, MB, smoke exposure, OC and PE of high school or less. Note that the lnORs for GA and AGE are included as negative terms because our model uses increasing risk with lower values compared with the reference (OR > 1), whereas some of the ORs in the papers were reported the other way around (OR < 1).

Establishment of cost-effectiveness

The cost-effectiveness threshold used in this report is a willingness to pay of £30,000 per QALY. This is predefined by the National Institute for Health and Clinical Evidence (NICE) as their normal higher threshold for cost-effectiveness.[5]

Results

Quantity and quality of research available

There were 13 studies included in total (14 papers) and 82 excluded articles for which the full paper was ordered (*Figure 1*). The excluded studies that were closest to being included are listed in *Appendix 2* with their reasons for exclusion. The original report chose studies that were 'of most relevance to the current UK context' so similar studies were used in the update. Therefore, studies from Taiwan and Mexico were excluded. Otherwise, the excluded studies could not have been used as they were too small (total $n = 18$) or carried out in a very specific population with different hospitalisation characteristics (Down's syndrome) or because no subgroup results were given or not with the right metrics, they were replications of included studies or were reviews.

Some of the included studies, provided data for both questions 1 and 2. In the original HTA report, one study[6] provided an estimate of monthly hospitalisation rate in young children with no CLD. It is unclear whether any of the children in this study had CHD. For the update, although five studies were found reporting hospitalisation for RSV by different ages,[6–10] only Rietveld *et al.*[6] reported monthly hospitalisation rates by age so this was used in the model. In the original HTA report, two studies[6,11] were used to estimate subgroup risks of hospitalisation by GA, for CLD and whether there were SAS (see Table 14 in original report[1]). In this update, 13 studies were used, including Carbonell-Estrany *et al.*[11] and Rietveld *et al.*[6] The baseline characteristics of the included studies are shown in *Table 4*. The results for individual subgroups used are shown in *Table 5*. Quality assessment of the included studies is in *Appendix 3*.

Assessment of inputs to model

In the original HTA report, two RCTs[12,13] were used for establishing the relative risk of hospitalisation in children given palivizumab compared with those without. No additional RCTs of palivizumab were found for this update.

There were a number of issues associated with the risk factor inputs to the model. Most of the studies were small and not powered to investigate subgroups, so had wide CIs. The quality of reporting was not always adequate, so it was difficult to determine whether the results were a fair representation or due to biases. Also, there was some difficulty with establishing correct comparators. The required comparator was children hospitalised with RSV who did not have the attribute. For some factors this was straightforward, such as males versus females hospitalised with RSV. Other studies compared, for example, hospitalised males with non-hospitalised males with RSV infection. The results for studies could not be used unless the required comparator was available. Another issue was that some of the studies presented only regression results adjusted for confounding factors whereas other presented raw data. We have used unadjusted results by preference where available. If they were not available, this is shown in *Table 5*. The definitions of CLD, CHD and other risk factors were not reported in most included studies so may have varied between studies.

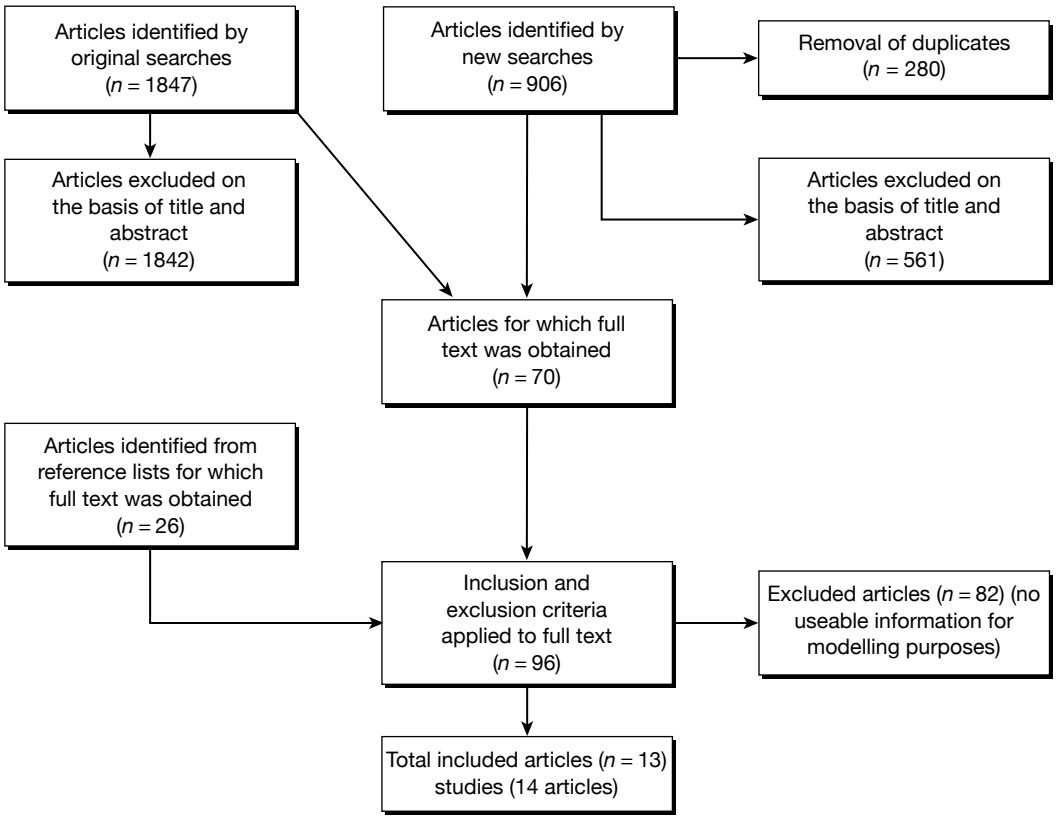


FIGURE 1 Flow diagram showing identification of studies.

TABLE 4 Baseline characteristics of included studies

Study name, date, country	Type	Parameters measured	Number of children in study	Number of children admitted to hospital	Premature/ term/mixed	CHD/CLD/ mixed	Comment
Carbonell-Estrany 2000 Spain[11]	Prospective cohort	GA, CHD, CLD, SAS, SE	584	118	All premature younger than 33 weeks	Mixed	
Carbonell-Estrany 2001 Spain[14]	Prospective cohort	GA, CHD, CLD, SAS, MB, SE	999	207	All premature younger than 33 weeks	Mixed	None given palivizumab
Eriksson 2002 Sweden[15]	Cohort	SAS	48,715 (total population)	1503	Mixed	Mixed	Unclear whether prospective or retrospective
Figueras-Aloy 2004 Spain[16,17]	Prospective case–control	SAS, SE, OC, PE	557	186 cases and 371 controls	All premature (33–35 weeks)	Mixed	Study design odd
Figueras-Aloy 2008 Spain[18]	Prospective cohort	SAS, SE, OC	5441	202	All premature (32–35 weeks)	Mixed	
Frogel 2008 USA[19]	Prospective registry	CHD	19,474	2532	Mixed	Mixed	All given palivizumab
Grimwood 2008 NZ[20]	Prospective cohort	GA, gender, MB	11,270 (total eligible population)	141	Mixed	Mixed	
Kristensen 2009 Denmark[9]	Case–control	Gender	626	313 cases, 313 controls	Mixed	CHD only	
Law 2004 Canada[21]	Prospective cohort	Gender, SAS, SE, OC	1862	1862	All premature (33–35 weeks)	Mixed	
Liese 2003 Germany[25]	Prospective cohort	Gender, CLD	717	76	All premature (35 weeks or less)	Mixed	None given palivizumab
Nielsen 2003 Denmark[23]	Retrospective case–control	GA, SAS	7327	1252 cases, 6075 controls	Mixed	Mixed	
Rietveld 2006 Netherlands[6]	Retrospective cohort	GA, gender	140,661	2469	Mixed	Mixed	
Rossi 2007 Italy[24]	Case–control	GA, gender, SE	440	145	Mixed	Mixed	

TABLE 5 Risk factor outcomes

	Risk factors									
Study	**Age**	**GA**	**Gender (male/female)**	**CHD**	**CLD**	**SAS**	**MB**	**SE**	**OC**	**PE of high school or less (≤12 years)**
Number of studies with this outcome	1	1	6	3	2	6	1	5	3	1
Carbonell-Estrany 2000[11]	–	Combined with Carbonell-Estrany 2001[14]	–	OR = 1.42 (0.57, 3.51) (estimated from raw numbers)	OR = 3.1 (1.22, 7.91) (multivariate logistic regression)	Combined with Carbonell-Estrany 2001[14]	–	Combined with Carbonell-Estrany 2001[14]	–	–
Carbonell-Estrany 2001[14]	–	OR = 0.87 (0.77, 0.97) (multivariate logistic regression)	–	OR = 1.07 (0.41, 2.79) (estimated from raw numbers)	–	OR = 1.64 (1.05, 2.55) (multivariate logistic regression)	–	OR = 1.63 (1.05, 2.56) (multivariate logistic regression)	–	–
Eriksson 2002[15]	–	–	–	–	–	Previously healthy OR 2.42 (2.08, 2.81)	–	–	–	–
Figueras-Aloy 2004[16,17]	–	–	–	–	–	OR = 2.40 (1.61, 3.57) (bivariate analysis)	–	OR = 0.95 (1.01, 2.18) (bivariate analysis)	OR = 1.79 (1.18, 2.72) (bivariate analysis)	OR = 1.48 (0.98, 2.23) (bivariate analysis)
Figueras-Aloy 2008[18]	–	–	–	–	–	OR = 1.96 (1.47, 2.60) (bivariate analysis)	–	OR = 1.59 (1.12, 2.26) (bivariate analysis)	OR 1.37 (0.85, 2.20) (bivariate analysis)	–
Frogel 2008[19]	–	–	–	OR = 1.55 (1.04, 2.31) (CIs estimated)	–	–	–	–	–	–
Grimwood 2008[20]	–	–	Crude RR = 1.30 (0.93, 1.82)	–	–	–	Crude RR = 1.57 (0.83, 2.96)	–	–	–
Kristensen 2009[9]	–	–	Crude OR = 1.10 (0.80, 1.50)	–	–	–	–	–	–	–
Law 2004[21]	–	–	OR = 1.91 (1.10, 3.31) (logistic regression)	–	–	OR = 2.76 (1.51, 5.03) (logistic regression)	–	OR = 1.71 (0.97, 3.00) (logistic regression)	OR = 1.69 (0.93, 3.10) (logistic regression)	–

	Risk factors									
Study	Age	GA	Gender (male/female)	CHD	CLD	SAS	MB	SE	OC	PE of high school or less (≤12 years)
Liese 2003[25]	–	–	OR = 8.7 (2.6, 29.1) (multivariate logistic regression)	–	OR = 3.9 (1.4, 11.2) (multivariate logistic regression)	–	–	–	–	–
Nielsen 2003[23]	–	–	–	–	–	OR = 1.10 (0.92, 1.35) (multivariate logistic regression)	–	–	–	–
Rietveld 2006[6]	OR = 0.8 (0.8, 0.8) (univariable regression analysis)	–	OR = 1.4 (1.3, 1.5) (univariate regression analysis)	–	–	–	–	–	–	–
Rossi 2007[24]	–	–	OR = 0.98 (0.66, 1.47) [calculated from female OR 1.02 (0.68, 1.52)]	–	–	–	–	OR = 0.81 (0.54, 1.21) (bivariate analysis)	–	–

RR, rate ratio.
Ninety-five per cent CIs.

Chapter 5

Assessment of cost-effectiveness

Systematic review of existing cost-effectiveness evidence

No systematic review of cost-effectiveness studies was appropriate for this report as there are no models available investigating the listed subgroups.

Independent economic assessment

Methods

To estimate the cost-effectiveness of immunoprophylaxis of RSV using palivizumab for different subgroups of children who are at high risk of serious morbidity from RSV infection, the base-case decision tree model developed in the original HTA journal publication[1] is used. The model structure is shown in *Figure 2*. All costs are presented in 2006 UK pounds sterling (£). Both costs and benefits are discounted at 3.5%. A time horizon of lifetime is used to take into account the impact of palivizumab on long-term morbidity and mortality from RSV infection. As a large number of subgroup analyses were involved, only the NHS perspective is adopted in this report. The detailed description of the model can be found in the HTA journal publication.[1]

As the best summary estimate for policy-makers is currently considered to be the average ICER from the probabilistic sensitivity analysis (PSA), the results of cost-effectiveness subgroup analysis in this report are expressed as the mean ICER from PSA, where models are run for 5000 simulations for each of the combined risk factors.

Cost-effectiveness for different risk groups

Because the parameters required by the economic model have been updated since the search was made for the original HTA journal publication,[1] and more risk factors have been added, the cost-effectiveness for different risk groups has been re-analysed/extended for children without CLD/CHD, or children with CLD or CHD. All results for such subgroup analyses presented

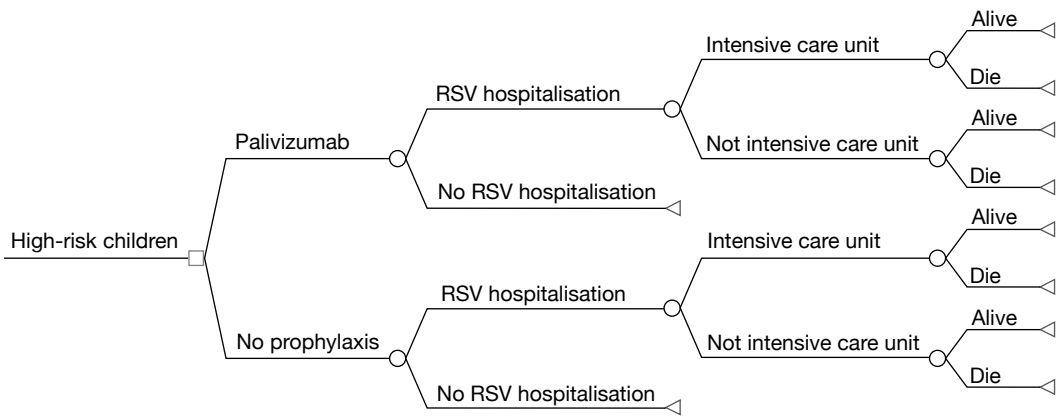


FIGURE 2 Model structure for palivizumab versus no prophylaxis.

in this report overwrite the subgroup analysis results carried out in the original HTA journal publication.[1] In this report, comprehensive subgroup analyses were carried out in four categories:

- children without CLD/CHD
- children with CLD
- children with acyanotic CHD
- children with cyanotic CHD.

In each category, the cost-effectiveness for 64 different combinations of risk factors was derived and is presented. Each combination of risk factors contained 63 subgroups, cross-tabulated by GA and AGE. In total, 256 combinations of risk factors (corresponding to 16,128 subgroups) were analysed.

Results

Risk factors

The studies listed in *Table 5* were identified and used to derive the risk factors.

Hospitalisation at different ages

Only the study by Rietveld *et al.*[6] reported OR per month, which is required by the model. Therefore, an OR of 0.8 (95% CI 0.8 to 0.8) was used to estimate the risk of hospitalisation by age in the model.

Gestational age

Only the study by Carbonell-Estrany *et al.*[14] reported OR per week, which is required by the model. Therefore, an OR of 0.85 (95% CI 0.77 to 0.97) was used to estimate the risk of hospitalisation by GA in the model.

Gender

Six studies[6,9,20,21,24,25] estimated the risk of gender in RSV hospitalisation; a meta-analysis was carried out, heterogeneity was observed ($Q = 15.35$, $p = 0.009$), and thus the OR of 1.37 (95% CI 1.08 to 1.75) from the random effects model was used in the model. The forest plot is shown in *Figure 3*.

Congenital heart disease

No studies were found that gave ORs and CIs for CHD. Three studies[11,14,19] estimated the risk of CHD in RSV hospitalisation and provided sufficient results with which to estimate ORs and CIs. There was no heterogeneity ($Q = 0.489$, $p = 0.783$) so a fixed effects model was used. The meta-analysis gave an OR of 1.46 (95% CI 1.04 to 2.05). The forest plot is shown in *Figure 4*.

Chronic lung disease

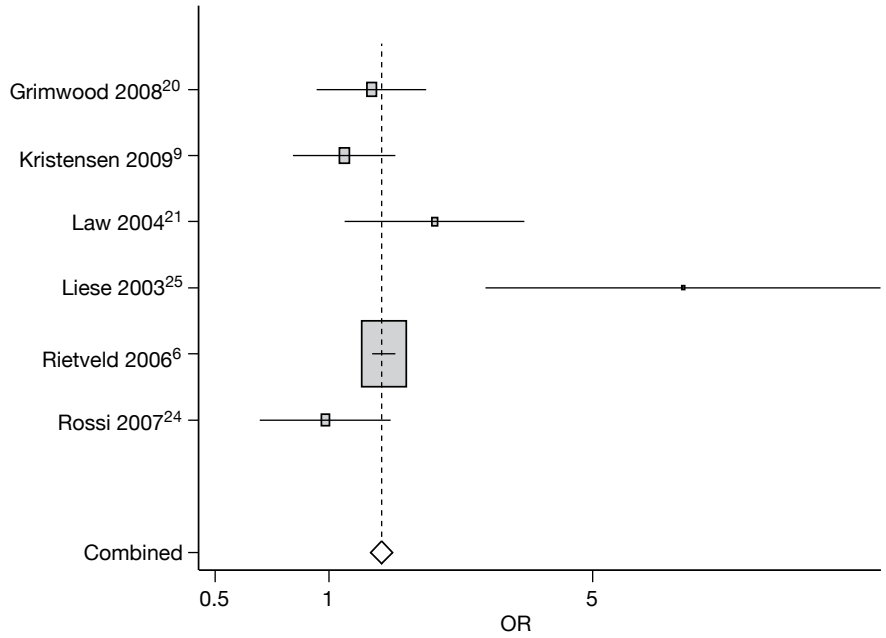
Two studies[14,25] estimated the risk of CLD in RSV hospitalisation; a meta-analysis gave an OR of 3.44 (95% CI 1.71 to 6.88). There was no heterogeneity ($Q = 0.104$, $p = 0.748$) so a fixed effects model was used. The forest plot is shown in *Figure 5*.

Siblings at school (SAS)

Six studies[14–18,21,23] estimated the risk of SAS. Meta-analysis gave an OR of 1.92 (95% CI 1.36 to 2.70). The forest plot is shown in *Figure 6*. Heterogeneity was observed ($Q = 44.26$, $p < 0.001$).

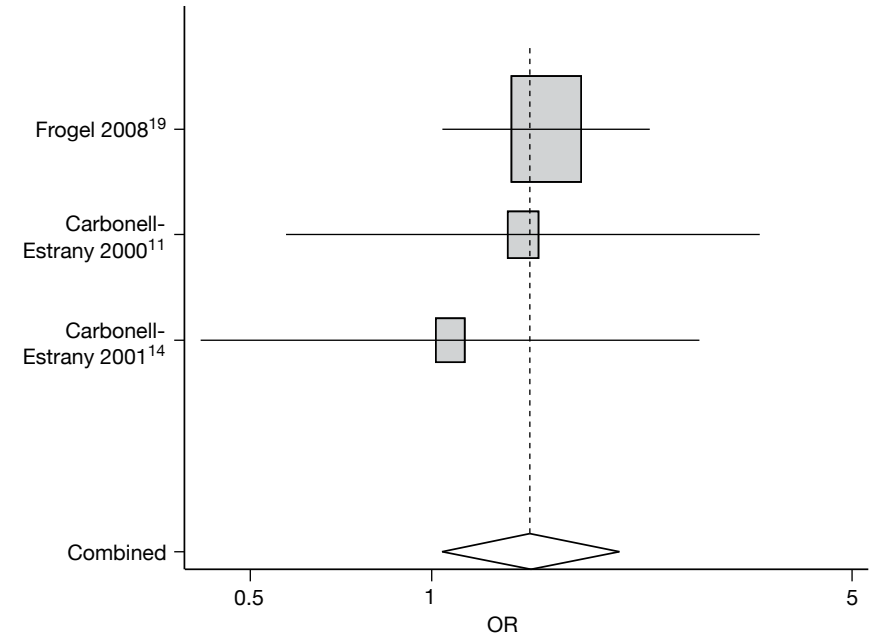
Multiple births

One study, by Grimwood *et al.*,[20] reported OR of MBs for RSV hospitalisation. Therefore, an OR of 1.57 (95% CI 0.83 to 2.96) was used to estimate the risk of MBs in the model.



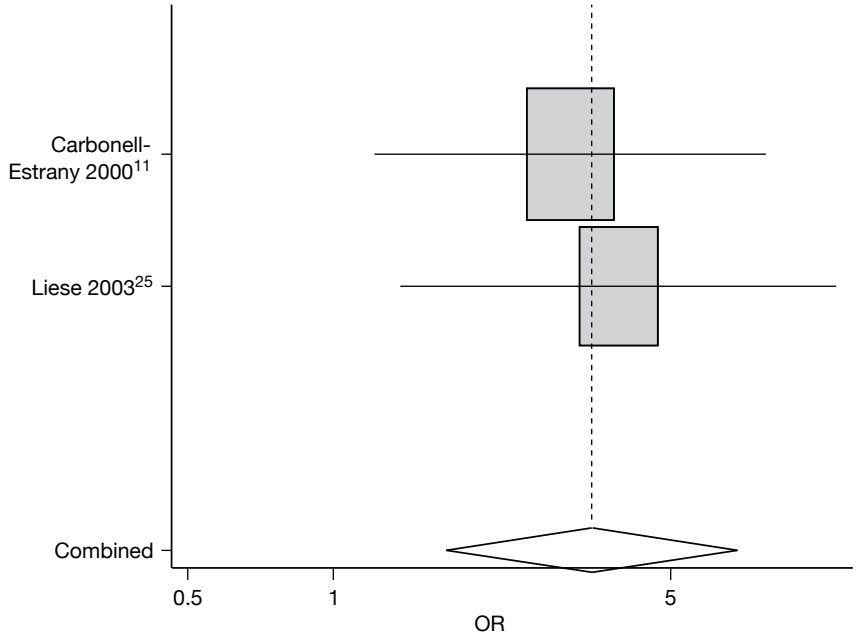
Weights (%)	OR	95% CI	
Random		Lower	Upper
19.02	1.30	0.93	1.82
19.93	1.10	0.80	1.51
11.72	1.91	1.10	3.31
3.53	8.70	2.60	29.11
29.35	1.40	1.30	1.50
16.46	0.98	0.66	1.46
100.00	1.37	1.08	1.75

FIGURE 3 Combined OR for gender (male), random effects model.



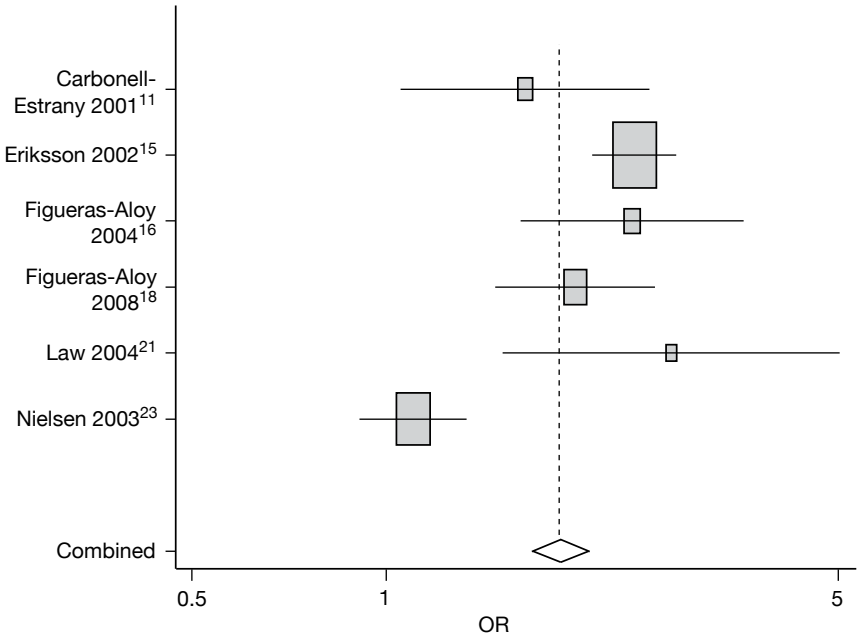
Weights (%)	OR	95% CI	
Fixed		Lower	Upper
73.31	1.55	1.04	2.31
14.04	1.42	0.57	3.51
12.65	1.07	0.41	2.79
100.00	1.46	1.04	2.05

FIGURE 4 Combined OR for CHD, fixed effects model.



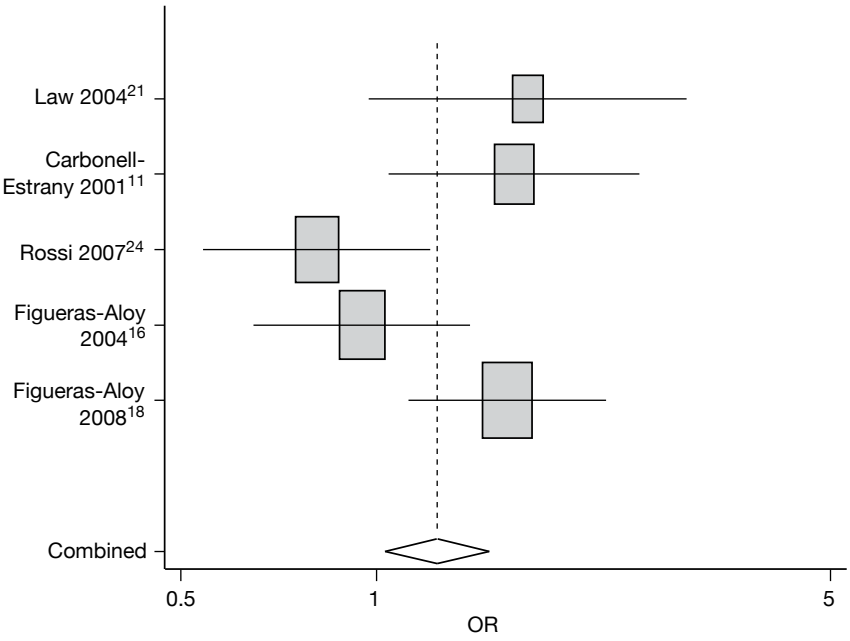
Weights (%)	OR	95% CI	
Fixed		Lower	Upper
55.35	3.10	1.22	7.98
44.65	3.90	1.38	11.03
100.00	3.44	1.71	6.88

FIGURE 5 Combined OR for CLD, fixed effects model.



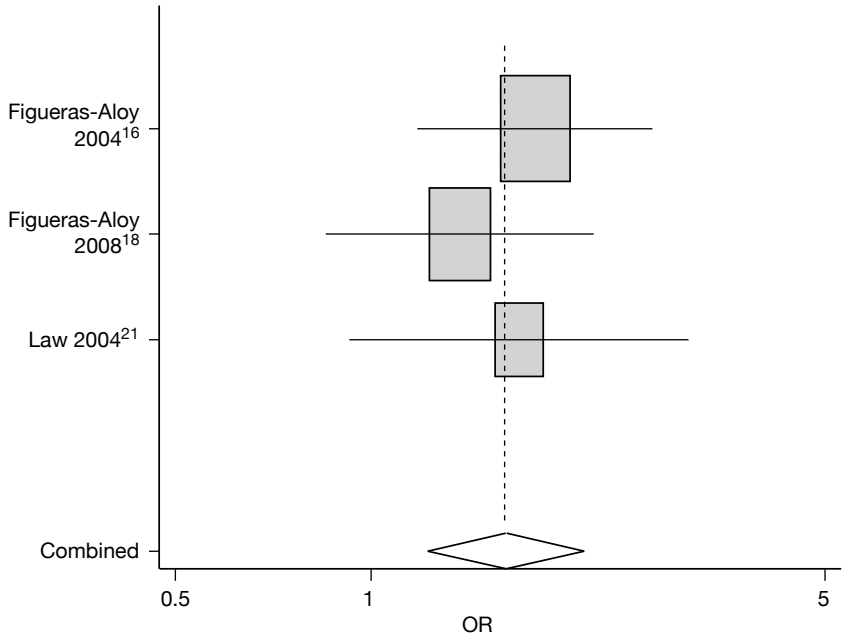
Weights (%)	OR	95% CI	
Random		Lower	Upper
15.13	1.64	1.05	2.56
19.55	2.42	2.08	2.81
15.92	2.40	1.61	3.57
17.82	1.96	1.47	2.61
12.48	2.76	1.51	5.04
19.10	1.10	0.91	1.33
100.00	1.92	1.36	2.70

FIGURE 6 Combined OR for siblings at school, random effects model.



Weights (%)	OR	95% CI	
Random		Lower	Upper
15.53	1.71	0.97	3.01
19.32	1.63	1.04	2.55
20.83	0.81	0.54	1.21
21.53	0.95	0.65	1.40
22.79	1.59	1.12	2.26
100.00	1.26	0.92	1.71

FIGURE 7 Combined OR for SE, random effects model.



Weights (%)	OR	95% CI	
Fixed		Lower	Upper
44.41	1.79	1.18	2.72
34.23	1.37	0.85	2.20
21.36	1.69	0.93	3.09
100.00	1.61	1.22	2.13

FIGURE 8 Combined OR for OC, fixed effects model.

Smoking exposure

Five studies[14,16–18,21,24] estimated the risk of SE in RSV hospitalisation. Meta-analysis gave an OR of 1.26 (95% CI 0.92 to 1.71). The forest plot is shown in *Figure 7*. Heterogeneity was observed ($Q = 10.74$, $p = 0.03$).

Overcrowding

Three studies[16–18,21] estimated the risk of OC in RSV hospitalisation. There was no heterogeneity ($Q = 0.715$, $p = 0.699$) so a fixed effects model was used. Meta-analysis gave an OR of 1.61 (95% CI 1.22 to 2.13). The forest plot is shown in *Figure 8*.

Low parental education

The study by Figueras-Aloy *et al.*[16,17] reported OR of low PE in RSV hospitalisation. Therefore, an OR of 1.48 (95% CI 0.98 to 2.23) was used to estimate the risk of low PE in the model.

Other risk factors

Several studies were identified for the risk factors of age < 6 weeks at the start of the RSV season, lack of or minimal breastfeeding and family history of atopy. Some studies showed association between the risk factors and RSV hospitalisation; others did not. To avoid introducing unreliable parameters into the models, which might reduce the accuracy and precision of the model estimates to an unacceptable degree, we did not include the risk factors of age < 6 weeks at the start of the RSV season, lack of or minimal breastfeeding and family history of atopy in the model. *Table 6* lists all parameters of the considered risk factors that were used in the subgroup analysis.

Costs and outcomes

The costs considered in the model included medical costs, administration costs and hospitalisation costs. The detailed calculation of these costs can be found in the original HTA journal publication.[1] The costs and outcomes for children without CLD, children with CLD, children with acyanotic CHD and children with cyanotic CHD in the base-case model are listed in *Tables 7–10*, respectively. Note that we used a viral sharing scheme in the model, as described in the previous journal publication.[1] For all children, five doses were given. The assumption on vial use was that, among children with or without CLD, 38.7% used a 50-mg vial and 91.3% used a 100-mg vial. For children with CHD, 39.6% used a 50-mg vial, 100.0% used a 100-mg vial, and 3.8% used 200 mg (2 × 100-mg vials). These assumptions were made based on (1) 15 mg/kg weight and (2) the average weight reported in the trials.

Utilities

The study by Greenough *et al.*[26] assessed the health-related quality of life (HRQoL) for pre-term children at the age of 5 years using the Health Utilities Index (HUI). The HUI described a family of genetic health status and HRQoL measures. Parents were sent the HUI2/3 and asked to complete the 15 questions to reflect their child's health over the previous 4 weeks.

TABLE 6 Results of meta-analyses of risk factors used in the model for subgroup analysis

Risk factors, OR (95% CI)									
AGE	GA	SEX (male)	CHD	CLD	SAS	MB	SE	OC	PE (≤ 12 years)
0.80 (0.80 to 0.80)	0.85 (0.77 to 0.97)	1.37 (1.08 to 1.75)	1.46 (1.04 to 2.05)	3.44 (1.71 to 6.88)	1.91 (1.36 to 2.70)	1.57 (0.83 to 2.96)	1.26 (0.92 to 1.71)	1.61 (1.22 to 2.13)	1.48 (0.98 to 2.23)

TABLE 7 Average costs and outcomes for prophylaxis in children without CLD

Parameters	Palivizumab	No prophylaxis	Cost difference	Outcome difference
Costs (£)				
Drug	3437			
Drug administration (GP)	21			
Drug administration (nurse)	39			
Hospital	67	301		
Total cost (NHS)	**3564**	**301**	**3263**	
Outcomes				
Discounting QALYs	26.5163	26.5092		0.0072

GP, general practitioner.

TABLE 8 Average costs and outcomes for prophylaxis in children with CLD

Parameters	Palivizumab	No prophylaxis	Cost difference	Outcome difference
Costs (£)				
Drug	3437			
Drug administration (GP)	21			
Drug administration (nurse)	39			
Hospital	293	475		
Total cost (NHS)	**3790**	**475**	**3315**	
Outcomes				
Discounting QALYs	26.4346	26.3826		0.0520

GP, general practitioner.

TABLE 9 Average costs and outcomes for prophylaxis in children with acyanotic CHD

Parameters	Palivizumab	No prophylaxis	Cost difference	Outcome difference
Costs (£)				
Drug	3714			
Drug administration (GP)	21			
Drug administration (nurse)	39			
Hospital	359	647		
Total cost (NHS)	**4132**	**847**	**3285**	
Outcomes				
Discounting QALYs	26.4187	26.3518		**0.0670**

GP, general practitioner.

TABLE 10 Average costs and outcomes for prophylaxis in children with cyanotic CHD

Parameters	Palivizumab	No prophylaxis	Cost difference	Outcome difference
Costs (£)				
Drug	3714			
Drug administration (GP)	21			
Drug administration (nurse)	39			
Hospital	402	567		
Total cost (NHS)	**4176**	**567**	**3609**	
Outcomes				
Discounting QALYs	26.4128	26.3902		**0.0226**

GP, general practitioner.

The HUI2 measured seven attributes of health status describing 24,000 unique health states, while HUI3 described 972,000 unique health states. The HUI2 was originally developed for paediatric application and clinical evaluation studies, whereas HUI3 was developed for use in adults and population surveys. The median HUI2 multiattribute utility function was 0.88 (range 0.16–1.00) in the RSV-proven children, while the median HUI2 multiattribute utility function was 0.95 (range 0.03–1.00) in the non-RSV children. The median HUI3 multiattribute scores were 0.93 (range –0.05–1.00) for RSV-proven children and 0.97 (range –0.32–1.00) for non-RSV children. These utility values are used in the model for children with or without CLD and are listed in *Table 11*. As mentioned above, the utility estimate was made by asking parents (rather than children themselves) to complete the questions to reflect their child's health. This might introduce a bias in the utility estimate. However, because the utility estimates for children with RSV hospitalisation and without RSV hospitalisation were evaluated in the same way (i.e. parents completed the questionnaire), the effect of utility estimate made by parents for a child on the overall results was likely to be small and conclusions unaltered. Utility data for children and adults with CHD are lacking. The economic evaluation study by Yount *et al.*[27] extrapolated data from congestive heart failure to the CHD population and used a utility of 0.71 for children with CHD. The same utility values for children with CHD as those for children with or without CLD were used here.

Parameter values and their distributions

The parameter values and their distributions used in the subgroup analysis are shown in *Tables 12–15* for children without CLD/CHD, children with CLD, children with acyanotic CHD and children with cyanotic CHD, respectively.

Results of cost-effectiveness subgroup analysis

Detailed numerical results of the outcomes of cost-effectiveness for children without CLD/CHD, children with CLD, children with acyanotic CHD and children with cyanotic CHD alone, plus other risk factors are given below. Detailed numerical results are listed in *Tables 16–19*.

TABLE 11 Estimated utilities

	Utility values		
Category	**RSV hospitalisation**	**Not RSV hospitalisation**	**Source**
Children with or without CLD	0.880	0.950	Greenough 2004,[26] Nuijten 2007[28]
Children with CHD	0.880	0.950	Greenough 2004,[26] Nuijten 2007[28]

TABLE 12a Parameter distributions for children without CLD – beta distributions

Parameter	Expected value	α	β
Probability of RSV hospitalisation (no prophylaxis)	0.081	344.384	3934.08
Mortality rate of RSV hospitalisation	0.0043	17.221	3982.226
Utility of RSV hospitalisation	0.880	702.101	95.770
Utility of non-RSV hospitalisation	0.950	976.417	51.397
Probability of ICU	0.107	26.270	219.218

ICU, intensive care unit.

TABLE 12b Parameter distributions for children without CLD – uniform distributions

Parameter	Expected value	a	b
Dose of palivizumab	5	4	6
Period of morbidity due to RSV	5	2	8

TABLE 12c Parameter distributions for children without CLD – normal distributions

Parameter	Mean	SD^2
Log relative risk of RSV hospitalisation	–1.5404	0.0771
Length of ICU stay	1.370	0.259
Length of general ward stay	6.470	0.644
Life expectancy	77.800	11.830

ICU, intensive care unit; SD, standard deviation.

TABLE 13a Parameter distributions for children with CLD – beta distributions

Parameter	Expected value	α	β
Probability of RSV hospitalisation (no prophylaxis)	0.128	573.974	3900.294
Utility of RSV hospitalisation	0.880	702.101	95.770
Utility of non-RSV hospitalisation	0.950	976.417	51.397
Probability of ICU	0.107	26.270	219.218

ICU, intensive care unit.

TABLE 13b Parameter distributions for children with CLD – uniform distributions

Parameter	Expected value	a	b
Dose of palivizumab	5	4	6
Period of morbidity due to RSV	5	2	8
Mortality rate of RSV hospitalisation	0.040	0.030	0.050

TABLE 13c Parameter distributions for children with CLD – normal distributions

Parameter	Mean	SD^2
Log relative risk of RSV hospitalisation	–0.4826	0.0253
Length of ICU stay	1.370	0.259
Length of general ward stay	6.470	0.644
Life expectancy	77.800	11.830

ICU, intensive care unit; SD, standard deviation.

TABLE 14a Parameter distributions for CHD (acyanotic) – beta distributions

Parameter	Expected value	α	β
Probability of RSV hospitalisation (no prophylaxis)	0.097	21.895	203.830
Mortality rate of RSV hospitalisation	0.0372	8.012	207.920
Utility of RSV hospitalisation	0.880	702.101	95.770
Utility of non-RSV hospitalisation	0.950	976.417	51.397
Probability of ICU	0.387	123.685	195.916

ICU, intensive care unit.

TABLE 14b Parameter distributions for CHD (acyanotic) – uniform distributions

Parameter	Expected value	a	b
Dose of palivizumab	5	4	6
Period of morbidity due to RSV	5	2	8

TABLE 14c Parameter distributions for CHD (acyanotic) – normal distributions

Parameter	Mean	SD^2
Log relative risk of RSV hospitalisation	–0.859	0.088
Length of ICU stay	6.140	1.009
Length of general ward stay	6.250	0.635
Life expectancy	77.110	11.830

ICU, intensive care unit; SD, standard deviation.

TABLE 15a Parameter distributions for CHD (cyanotic) – beta distributions

Parameter	Expected value	α	β
Probability of RSV hospitalisation (no prophylaxis)	0.097	21.895	203.830
Mortality rate of RSV hospitalisation	0.0372	8.012	207.920
Utility of RSV hospitalisation	0.880	702.101	95.770
Utility of non-RSV hospitalisation	0.950	976.417	51.397
Probability of ICU	0.387	123.685	195.916

ICU, intensive care unit.

TABLE 15b Parameter distributions for CHD (cyanotic) – uniform distributions

Parameter	Expected value	a	b
Dose of palivizumab	5	4	6
Period of morbidity due to RSV	5	2	8

TABLE 15c Parameter distributions for CHD (cyanotic) – normal distributions

Parameter	Mean	SD^2
Log relative risk of RSV hospitalisation	–0.340	0.084
Length of ICU stay	6.140	1.009
Length of general ward stay	6.250	0.635
Life expectancy	77.110	11.830

ICU, intensive care unit; SD, standard deviation.

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY)

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE							
< 1.5	78	104	140	192	264	365	831
1.5–3	104	142	196	267	370	497	1147
3–6	200	276	370	515	708	965	2234
6–9	383	520	728	984	1372	1872	4379
9–12	752	1001	1371	1959	2640	3684	8420
12–15	1443	1956	2725	3852	5234	7164	16,437
15–18	2777	3900	5298	7326	10,248	14,121	32,663
18–21	5395	7497	10,309	14,173	19,697	27,134	62,539
21–24	10,578	14,665	20,117	28,330	38,777	54,436	124,424

continued

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus PE ≤ 12 years							
< 1.5	56	73	98	132	180	244	559
1.5–3	74	95	133	182	250	345	776
3–6	137	184	251	348	478	661	1505
6–9	258	355	488	662	920	1280	2980
9–12	501	694	951	1296	1813	2517	5777
12–15	964	1316	1848	2571	3503	4866	11,093
15–18	1867	2592	3572	4957	6815	9442	21,764
18–21	3678	5095	7096	9735	13,485	18,498	42,614
21–24	7127	9827	13,615	18,944	26,094	36,267	83,156
Risk factors GA, AGE, plus OC							
< 1.5	51	66	91	122	166	230	517
1.5–3	67	91	122	167	229	314	721
3–6	126	171	236	325	448	599	1425
6–9	235	329	453	619	836	1181	2737
9–12	463	640	859	1199	1660	2268	5354
12–15	893	1228	1665	2350	3267	4443	10,262
15–18	1739	2386	3280	4578	6289	8627	20,090
18–21	3342	4641	6406	8924	12,401	17,062	39,345
21–24	6518	9135	12,736	17,382	23,827	33,731	77,069
Risk factors GA, AGE, plus SE							
< 1.5	63	84	112	156	208	289	653
1.5–3	86	115	159	214	295	402	918
3–6	157	216	299	408	555	778	1760
6–9	304	423	571	793	1101	1504	3489
9–12	589	792	1103	1539	2119	3039	6752
12–15	1122	1559	2159	2922	4098	5809	13,137
15–18	2182	3052	4336	5844	8164	11,009	26,309
18–21	4358	5978	8224	11,469	15,958	22,160	50,304
21–24	8498	11,730	16,319	22,063	30,773	42,314	96,398
Risk factors GA, AGE, plus MB							
< 1.5	52	70	92	124	171	232	524
1.5–3	70	93	128	170	235	318	735
3–6	130	174	238	327	453	632	1431
6–9	244	340	465	630	888	1215	2752
9–12	480	669	901	1225	1664	2361	5532
12–15	903	1244	1744	2390	3288	4594	10,542
15–18	1771	2466	3364	4637	6456	8811	20,352
18–21	3444	4758	6588	9101	12,582	17,622	40,237
21–24	6632	9313	12,932	18,053	24,955	34,215	77,992

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SEX (male)							
< 1.5	58	78	108	142	196	265	603
1.5–3	79	105	141	196	266	369	845
3–6	147	200	276	373	515	730	1643
6–9	275	381	531	722	1013	1385	3191
9–12	540	733	1008	1408	1956	2657	6296
12–15	1055	1460	1986	2765	3820	5312	12,220
15–18	2020	2779	3865	5379	7550	10,085	23,610
18–21	3866	5411	7545	10,589	14,230	20,087	46,417
21–24	7678	10,694	14,926	20,588	28,282	39,169	90,652
Risk factors GA, AGE, plus SAS							
< 1.5	43	59	78	103	140	192	441
1.5–3	59	77	105	140	190	266	604
3–6	106	146	199	272	374	522	1161
6–9	203	279	385	517	718	1003	2260
9–12	384	543	721	1003	1400	1943	4406
12–15	741	1043	1402	1955	2744	3771	8780
15–18	1450	2010	2780	3851	5340	7369	17,162
18–21	2860	3854	5524	7566	10,420	14,534	33,362
21–24	5589	7604	10,581	15,009	20,458	28,088	64,781
Risk factors GA, AGE, plus OC, PE ≤ 12 years							
< 1.5	36	47	64	85	114	156	359
1.5–3	48	63	84	115	155	216	490
3–6	87	119	160	219	294	412	940
6–9	162	223	308	425	578	796	1832
9–12	314	430	580	818	1126	1593	3587
12–15	594	837	1131	1586	2184	3008	7037
15–18	1156	1637	2226	3073	4273	5828	13,540
18–21	2272	3168	4360	6039	8353	11,509	25,969
21–24	4491	6125	8542	11,747	16,214	22,474	51,712
Risk factors GA, AGE, plus SE, PE ≤ 12 years							
< 1.5	45	59	79	105	143	199	441
1.5–3	60	81	107	145	201	269	618
3–6	109	148	202	280	379	520	1185
6–9	206	282	386	544	739	1020	2365
9–12	403	556	750	1039	1450	1970	4574
12–15	771	1070	1440	2030	2782	3887	9029
15–18	1515	2079	2854	3915	5505	7612	17,155
18–21	2916	3996	5466	7663	10,623	14,445	34,348
21–24	5780	7825	10,819	15,063	20,897	28,700	65,220

continued

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SE, OC							
< 1.5	42	55	72	98	136	183	405
1.5–3	55	73	99	137	184	251	570
3–6	102	135	187	254	347	479	1104
6–9	190	262	360	500	681	937	2157
9–12	364	501	689	976	1304	1831	4227
12–15	704	980	1350	1893	2588	3585	8148
15–18	1354	1855	2642	3608	4976	6915	15,597
18–21	2678	3724	5148	7085	9738	13,903	31,177
21–24	5171	7265	9987	13,794	19,171	26,365	60,631
Risk factors GA, AGE, plus MB, PE ≤ 12 years							
< 1.5	37	49	67	86	118	160	359
1.5–3	50	66	87	119	161	225	498
3–6	89	120	166	226	307	421	969
6–9	170	230	315	427	593	820	1874
9–12	318	445	596	830	1152	1581	3684
12–15	621	856	1188	1626	2223	3087	7116
15–18	1195	1679	2277	3146	4310	5956	14,119
18–21	2351	3210	4448	6147	8450	11,975	27,003
21–24	4580	6348	8819	12,047	16,565	23,112	53,447
Risk factors GA, AGE, plus SEX (male)							
< 1.5	34	45	60	81	107	146	335
1.5–3	46	61	80	110	148	204	457
3–6	82	114	152	210	283	386	903
6–9	154	211	294	400	554	759	
9–12	302	411	572	768	1065	1495	3394
12–15	562	787	1084	1501	2058	2873	6467
15–18	1098	1521	2122	2899	4094	5520	13,045
18–21	2154	2994	4092	5813	7916	10,848	24,742
21–24	4220	5823	7972	10,967	15,332	21,137	48,664
Risk factors GA, AGE, plus MB, SE							
< 1.5	42	56	75	99	137	187	430
1.5–3	57	76	101	139	191	254	582
3–6	104	142	192	264	363	499	1129
6–9	195	270	368	504	691	957	2185
9–12	374	506	717	968	1365	1880	4268
12–15	715	1007	1359	1891	2695	3672	8349
15–18	1394	1953	2658	3695	5188	6983	16,374
18–21	2763	3789	5290	7250	10,058	13,796	31,814
21–24	5390	7452	10,122	13,944	19,885	26,950	62,317

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SEX (male), PE ≤ 12 years							
< 1.5	41	54	75	100	135	182	414
1.5–3	55	74	99	139	180	253	565
3–6	101	136	187	258	353	485	1100
6–9	193	257	364	493	690	931	2128
9–12	368	508	687	952	1309	1833	4152
12–15	695	980	1318	1878	2578	3555	8313
15–18	1414	1880	2636	3656	5059	6907	16,050
18–21	2689	3697	5172	7067	9830	13,465	30,882
21–24	5180	7231	10,027	13,745	19,082	26,551	61,279
Risk factors GA, AGE, plus SEX (male), OC							
< 1.5	38	51	69	89	124	169	387
1.5–3	52	69	91	128	168	234	526
3–6	94	127	174	238	328	442	1022
6–9	177	238	331	452	630	865	2008
9–12	337	459	638	880	1214	1683	3891
12–15	658	884	1227	1721	2338	3275	7535
15–18	1273	1725	2373	3333	4615	6382	14,877
18–21	2453	3421	4724	6485	9111	12,432	28,831
21–24	4830	6626	9260	12,808	17,678	24,225	55,848
Risk factors GA, AGE, plus SEX (male), SE							
< 1.5	48	63	85	113	156	213	493
1.5–3	64	87	115	157	214	296	664
3–6	118	162	218	301	418	572	1310
6–9	219	306	418	576	802	1103	2475
9–12	430	592	806	1142	1554	2121	4943
12–15	824	1144	1588	2181	3011	4135	9836
15–18	1609	2248	3063	4281	5811	8140	18,858
18–21	3134	4346	5971	8206	11,640	16,117	37,082
21–24	6109	8547	11,685	15,968	22,380	31,581	72,274
Risk factors GA, AGE, plus SEX (male), MB							
< 1.5	40	53	70	94	128	169	394
1.5–3	53	70	94	130	173	239	540
3–6	96	132	177	244	330	459	1058
6–9	178	244	336	462	635	889	2034
9–12	346	480	654	917	1243	1745	3965
1288	668	923	1288	1756	2452	3342	7740
24253377	1312	1780	2425	3377	4700	6507	15,079
18–21	2535	3478	4896	6624	9375	12,838	28,966
21–24	4918	6710	9439	12,819	17,920	24,539	58,181

continued

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SAS, PE ≤ 12 years							
< 1.5	31	42	54	71	98	132	299
1.5–3	42	55	72	99	134	186	417
3–6	75	99	134	187	257	348	807
6–9	140	187	259	353	493	675	1567
9–12	266	364	507	681	930	1318	2952
12–15	515	707	980	1328	1863	2534	5880
15–18	1005	1383	1876	2596	3575	4911	11,278
18–21	1940	2672	3694	5099	6985	9669	22,195
21–24	3780	5103	7159	9934	13,633	19,106	43,645
Risk factors GA, AGE, plus SAS, OC							
< 1.5	30	38	51	67	90	122	278
1.5–3	39	51	68	93	124	169	383
3–6	69	94	127	172	235	318	732
6–9	130	177	241	328	456	615	1416
9–12	243	334	465	644	888	1219	2786
12–15	468	647	888	1242	1697	2360	5470
15–18	916	1255	1718	2408	3341	4672	10,756
18–21	1755	2452	3403	4744	6472	8970	20,696
21–24	3431	4838	6650	9248	12,663	17,337	40,181
Risk factors GA, AGE, plus SAS, SE							
< 1.5	37	47	64	84	112	156	346
1.5–3	47	63	86	116	157	213	487
3–6	86	118	156	219	299	413	932
6–9	160	219	303	416	562	775	1817
9–12	314	425	581	813	1110	1513	3501
12–15	597	824	1143	1586	2155	3025	6803
15–18	1157	1597	2217	3064	4276	5912	13,425
18–21	2258	3106	4312	5888	8244	11,361	25,945
21–24	4446	6111	8373	11,525	15,943	22,374	51,355
Risk factors GA, AGE, plus SAS, MB							
< 1.5	31	39	52	70	91	126	285
1.5–3	40	52	70	94	127	172	392
3–6	70	94	129	177	239	329	752
6–9	133	181	245	328	461	641	1432
9–12	247	344	466	649	884	1256	2872
12–15	484	674	905	1255	1760	2465	5557
15–18	929	1295	1807	2455	3441	4738	10,835
18–21	1829	2491	3423	4774	6653	9145	21,118
21–24	3476	4874	6780	9360	12,957	18,070	41,265

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SAS, SEX (male)							
< 1.5	34	44	58	77	106	139	320
1.5–3	44	59	79	107	143	198	449
3–6	81	108	145	202	269	382	863
6–9	150	206	281	394	525	742	1701
9–12	286	387	541	747	1036	1408	3235
12–15	545	751	1025	1437	2009	2767	6340
15–18	1084	1475	2062	2806	3869	5379	12,487
18–21	2100	2894	3972	5453	7795	10,586	24,415
21–24	4002	5534	7770	10,797	14,993	20,601	47,849
Risk factors GA, AGE, plus SE, OC, PE ≤ 12 years							
< 1.5	31	39	52	69	93	125	284
1.5–3	39	52	70	94	128	174	393
3–6	70	93	128	177	237	330	758
6–9	133	180	239	335	462	640	1434
9–12	246	345	467	656	880	1229	2880
12–15	481	658	915	1265	1738	2408	5583
15–18	929	1299	1798	2458	3409	4717	10,838
18–21	1802	2512	3469	4737	6633	9317	21,432
21–24	3589	4827	6770	9373	13,139	17,483	40,239
Risk factors GA, AGE, plus MB, OC, PE ≤ 12 years							
< 1.5	26	33	42	56	76	103	231
1.5–3	33	44	58	76	102	138	313
3–6	59	78	103	143	196	273	611
6–9	106	142	194	269	376	511	1167
9–12	204	273	383	533	731	992	277
12–15	385	531	736	1023	1377	1926	4510
15–18	746	1017	1439	1964	2713	3761	8654
18–21	1426	1981	2740	3841	5333	7224	16,866
21–24	2807	3887	5449	7661	10,376	14,381	33,105
Risk factors GA, AGE, plus MB, SE, PE ≤ 12 years							
< 1.5	31	40	53	71	93	128	288
1.5–3	40	54	72	96	132	180	405
3–6	74	98	131	177	247	339	769
6–9	135	180	255	347	469	638	1513
9–12	256	356	483	658	925	1281	2948
12–15	500	676	946	1280	1809	2465	5728
15–18	977	1298	1844	2574	3510	4900	11,091
18–21	1872	2581	3488	4937	6906	9318	21,707
21–24	3643	5075	6763	9540	13,498	18,451	42,669

continued

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus MB, SE, OC							
< 1.5	29	37	49	65	88	118	269
1.5–3	38	50	67	88	118	162	371
3–6	67	90	121	165	224	314	710
6–9	123	170	231	317	435	601	1369
9–12	238	319	442	611	860	1154	2704
12–15	455	620	859	1186	1687	2250	5171
15–18	892	1198	1680	2318	3231	4446	9963
18–21	1688	2328	3283	4525	6293	8580	19,504
21–24	3305	4619	6294	8818	12,275	16,936	39,178
Risk factors GA, AGE, plus MB, PE ≤ 12 years							
< 1.5	29	37	48	64	86	116	263
1.5–3	37	49	65	87	118	157	363
3–6	67	86	119	163	222	299	686
6–9	123	161	224	313	423	578	1349
9–12	230	314	434	599	814	1117	2609
12–15	445	604	849	1151	1591	2223	5075
15–18	853	1180	1650	2223	3131	4307	9963
18–21	1652	2271	3199	4474	6077	8427	19,593
21–24	3286	4485	6197	8450	11,968	16,420	37,390
Risk factors GA, AGE, plus SEX (male), SE, PE ≤ 12 years							
< 1.5	35	45	60	79	106	149	334
1.5–3	46	60	80	108	146	200	459
3–6	82	110	148	205	283	383	880
6–9	154	211	287	391	548	739	1689
9–12	292	406	561	765	1048	1442	3322
12–15	559	762	1070	1485	2037	2814	6484
15–18	1087	1498	2098	2834	4021	5589	12,750
18–21	2107	2952	4095	5638	7897	10,884	25,124
21–24	4104	5757	7922	11,014	15,059	21,098	47,913
Risk factors GA, AGE, plus SEX (male), SE, OC							
< 1.5	32	42	55	74	99	133	306
1.5–3	42	55	75	100	137	185	418
3–6	75	101	139	189	260	354	814
6–9	140	193	256	359	494	687	1587
9–12	272	371	508	697	954	1343	3114
12–15	512	712	975	1371	1873	2585	5870
15–18	1009	1397	1909	2644	3660	5019	11,692
18–21	1967	2735	3798	5170	6976	9963	22,879
21–24	3829	5302	7238	10,015	13,969	19,709	44,533

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SEX (male), MB, PE ≤ 12 years							
< 1.5	29	37	50	67	87	121	268
1.5–3	37	50	66	88	121	163	370
3–6	66	90	123	167	225	314	715
6–9	126	169	234	311	434	602	1387
9–12	238	321	444	609	852	1166	2682
12–15	452	630	846	1170	1650	2274	5174
15–18	866	1220	1669	2325	3170	4366	10,032
18–21	1708	2346	3230	4423	6214	8668	19,694
21–24	3238	4716	6497	9007	12,334	16,731	39,106
Risk factors GA, AGE, plus SEX (male), MB, OC							
< 1.5	27	35	46	61	82	110	245
1.5–3	36	47	62	82	111	151	339
3–6	62	82	111	152	208	289	653
6–9	115	155	215	292	403	549	1278
9–12	215	297	406	562	785	1072	2503
12–15	425	574	781	1084	1500	2051	4884
15–18	821	1121	1539	2116	2975	4082	9362
18–21	1568	2169	3025	4136	5700	7909	18,155
21–24	3047	4197	5814	8233	11,202	15,502	35,680
Risk factors GA, AGE, plus SEX (male), MB, SE							
< 1.5	33	44	56	76	102	135	314
1.5–3	43	57	75	103	139	194	420
3–6	78	104	142	195	266	366	848
6–9	146	197	268	372	507	703	1625
9–12	276	379	522	724	991	1375	3143
12–15	529	728	997	1396	1921	2625	6295
15–18	1036	1429	2001	2710	3731	5139	11,884
18–21	2003	2798	3767	5257	7387	10,204	23,456
21–24	3914	5529	7424	10,402	14,207	19,872	45,432
Risk factors GA, AGE, plus SAS, OC, PE ≤ 12 years							
< 1.5	23	28	37	48	63	85	193
1.5–3	29	36	48	64	85	117	261
3–6	48	64	86	118	161	219	498
6–9	90	121	165	226	310	419	982
9–12	167	231	314	429	599	823	1905
12–15	317	440	602	840	1146	1607	3685
15–18	618	848	1168	1634	2266	3110	7278
18–21	1207	1642	2267	3141	4401	6038	14,051
21–24	2311	3244	4457	6136	8545	11,783	27,242

continued

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SAS, SE, PE ≤ 12 years							
< 1.5	27	34	44	59	81	107	237
1.5–3	34	45	60	79	106	148	333
3–6	60	82	108	151	200	275	646
6–9	111	152	208	287	392	534	1231
9–12	210	286	397	547	754	1040	2382
12–15	404	554	771	1081	1486	2042	4668
15–18	738	1079	1516	2084	2815	3931	9118
18–21	1515	2128	2916	4081	5543	7711	17,652
21–24	2971	4119	5627	7857	10,901	15,265	34,420
Risk factors GA, AGE, plus SAS, SE, OC							
< 1.5	24	32	42	54	73	97	222
1.5–3	33	42	55	74	100	137	302
3–6	56	75	101	136	187	259	584
6–9	103	140	192	259	363	499	1119
9–12	195	264	370	512	698	976	2198
12–15	373	516	697	974	1349	1884	4309
15–18	727	989	1372	1909	2614	3592	8402
18–21	1390	1935	2674	3684	5206	7186	16,160
21–24	2754	3752	5158	7461	10,121	13,943	32,491
Risk factors GA, AGE, plus SAS, MB, PE ≤ 12 years							
< 1.5	22	29	37	49	66	88	193
1.5–3	29	38	50	66	88	118	265
3–6	50	68	90	121	164	229	512
6–9	93	122	170	232	315	430	982
9–12	171	232	319	452	604	839	1939
12–15	330	453	615	860	1180	1625	3686
15–18	634	871	1215	1689	2300	3167	7254
18–21	1205	1691	2342	3273	4534	6311	14,293
21–24	2393	3295	4554	6263	8688	12,136	27,931
Risk factors GA, AGE, plus SAS, MB, OC							
< 1.5	21	27	36	45	61	81	180
1.5–3	27	35	46	60	83	111	246
3–6	46	62	83	114	151	204	483
6–9	84	113	155	215	289	404	930
9–12	157	214	298	406	568	763	1751
12–15	303	416	565	788	1069	1495	3418
15–18	582	811	1096	1530	2071	2917	6762
18–21	1132	1529	2193	3037	4137	5598	13,239
21–24	2169	3030	4142	5823	8082	10,955	26.042

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SAS, MB, SE							
< 1.5	25	33	43	57	75	103	230
1.5–3	33	43	56	76	100	137	314
3–6	58	79	105	142	192	268	606
6–9	105	145	195	269	365	511	1169
9–12	199	271	376	518	710	977	2258
12–15	386	541	730	992	1383	1927	4389
15–18	740	1009	1426	1911	2696	3743	8593
18–21	1451	1994	2750	3847	5216	7156	16,888
21–24	2798	3892	5488	7261	10,192	14,140	32,426
Risk factors GA, AGE, plus SAS, SEX (male), PE ≤ 12 years							
< 1.5	25	32	42	54	74	100	224
1.5–3	32	42	55	74	99	132	301
3–6	57	75	101	136	185	257	596
6–9	103	141	191	262	355	498	1126
9–12	195	271	370	503	702	956	2210
12–15	374	514	708	970	1350	1844	4324
15–18	732	987	1370	1902	2603	3682	8301
18–21	1407	1906	2648	3688	5138	7050	16,452
21–24	2751	3810	5272	7270	9915	13,822	31,581
Risk factors GA, AGE, plus SAS, SEX (males), OC							
< 1.5	24	30	40	51	69	93	203
1.5–3	30	39	51	69	92	125	281
3–6	52	70	95	127	172	237	536
6–9	94	130	173	242	337	459	1054
9–12	178	245	335	474	642	874	2045
12–15	346	467	646	901	1255	1703	3893
15–18	665	910	1258	1730	2421	3389	7747
18–21	1286	1790	2462	3373	4679	6525	15,110
21–24	2520	3509	4793	6757	9241	12,680	30,006
Risk factors GA, AGE, plus SAS, SEX (male), SE							
< 1.5	28	37	47	63	87	114	256
1.5–3	37	49	65	86	116	160	361
3–6	64	88	119	164	220	297	695
6–9	120	165	223	301	432	573	1359
9–12	225	311	434	601	829	1120	2574
12–15	446	607	830	1146	1580	2225	5085
15–18	858	1170	1611	2240	3070	4269	9910
18–21	1672	2278	3180	4422	6096	8457	19,408
21–24	3229	4456	6110	8522	11,754	16,276	37,137

continued

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SAS, SEX (male), MB							
< 1.5	24	31	40	52	70	93	209
1.5–3	31	39	53	69	95	127	286
3–6	53	73	97	131	177	245	555
6–9	99	134	181	250	341	468	1070
9–12	185	257	347	479	660	902	2082
12–15	347	484	671	922	1277	1751	4027
15–18	664	955	1303	1774	2462	3435	8003
18–21	1318	1832	2551	3541	4861	6684	15,371
21–24	2592	3581	4870	6750	9317	13,004	30,146
Risk factors GA, AGE, plus MB, SE, OC, PE ≤ 12 years							
< 1.5	22	27	36	47	62	81	185
1.5–3	28	35	47	62	83	112	255
3–6	48	62	85	115	156	214	483
6–9	86	116	159	215	296	411	931
9–12	162	222	304	413	578	797	1827
12–15	308	424	578	799	1116	1538	3554
15–18	605	814	1125	1559	2157	2958	6899
18–21	1154	1579	2214	3056	4212	5750	12,407
21–24	2265	3120	4271	5971	8331	11,439	26,311
Risk factors GA, AGE, plus SEX (male), SE, OC, PE ≤ 12 years							
< 1.5	24	30	40	52	71	92	210
1.5–3	31	40	53	70	95	129	286
3–6	53	71	95	128	180	240	561
6–9	98	131	184	249	342	463	1072
9–12	182	250	347	467	652	915	2046
12–15	353	484	661	930	1291	1735	4064
15–18	675	929	1283	1776	2476	3479	7796
18–21	1330	1843	2489	3478	4850	6733	15,208
21–24	2585	3594	4975	6714	9429	12,999	30,536
Risk factors GA, AGE, plus SEX (male), MB, OC, PE ≤ 12 years							
< 1.5	21	26	33	43	57	76	168
1.5–3	26	34	43	57	77	104	236
3–6	44	59	79	107	143	196	449
6–9	80	111	144	196	275	370	870
9–12	151	205	275	387	531	733	1684
12–15	285	389	534	755	1030	1401	3228
15–18	550	760	1032	1421	1982	2736	6398
18–21	1075	1460	2035	2815	3928	5386	12,215
21–24	2085	2853	3940	5482	7623	10,677	24,025

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SEX (male), MB, SE, PE ≤ 12 years							
< 1.5	25	31	40	53	70	96	214
1.5–3	32	41	54	72	96	129	291
3–6	56	74	99	133	184	251	577
6–9	100	133	187	251	344	478	1099
9–12	188	255	353	490	668	926	2123
12–15	357	506	679	939	1302	1783	4146
15–18	696	964	1343	1837	2546	3501	8038
18–21	1370	1862	2589	3588	5050	6957	15,604
21–24	2652	3593	5023	7069	9748	13,752	31,161
Risk factors GA, AGE, plus SEX (male), MB, SE, OC							
< 1.5	23	29	38	49	66	87	197
1.5–3	29	38	50	65	90	119	273
3–6	51	67	89	124	166	233	522
6–9	93	126	170	232	321	434	996
9–12	171	235	329	452	618	854	1962
12–15	330	466	629	871	1203	1662	3723
15–18	645	891	1208	1716	2324	3226	7410
18–21	1264	1687	2399	3360	4604	6348	14,575
21–24	2463	3379	4651	6349	8925	12,290	28,297
Risk factors GA, AGE, plus SAS, SE, OC, PE ≤ 12 years							
< 1.5	19	24	31	40	51	69	153
1.5–3	24	30	40	52	69	92	209
3–6	40	52	69	94	127	178	407
6–9	72	97	132	178	247	336	768
9–12	132	182	246	342	470	653	1496
12–15	258	344	481	660	945	1261	2903
15–18	491	670	940	1298	1771	2461	5644
18–21	941	1327	1842	2494	3458	4767	10,946
21–24	1872	2541	3556	4937	6707	9275	21,672
Risk factors GA, AGE, plus SAS, MB, OC, PE ≤ 12 years							
< 1.5	17	20	26	33	43	56	122
1.5–3	20	26	34	44	57	77	171
3–6	34	45	58	78	103	145	321
6–9	59	80	107	145	202	272	622
9–12	111	146	202	276	376	529	1197
12–15	203	285	383	528	735	1010	2365
15–18	401	543	736	1033	1425	1947	4600
18–21	776	1037	1446	2022	2829	3848	8930
21–24	1492	2056	2861	3865	5526	7581	17,138

continued

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SAS, MB, SE, PE ≤ 12 years							
< 1.5	20	24	30	40	52	70	155
1.5–3	24	31	40	54	71	97	214
3–6	41	55	73	97	134	176	407
6–9	74	98	135	182	254	347	806
9–12	139	192	250	355	480	655	1531
12–15	265	356	494	672	928	1311	2912
15–18	501	703	960	1307	1831	2534	5765
18–21	973	1351	1869	2566	3546	4961	11,259
21–24	1899	2651	3662	5084	6958	9548	21,768
Risk factors GA, AGE, plus SAS, MB, SE, OC							
< 1.5	18	23	29	38	49	67	142
1.5–3	23	29	38	49	65	89	200
3–6	39	50	67	91	121	165	381
6–9	69	92	126	168	233	315	728
9–12	127	173	236	320	451	604	1401
12–15	242	333	448	635	867	1181	2730
15–18	455	620	877	1231	1668	2336	5277
18–21	890	1245	1718	2388	3261	4494	10,331
21–24	1754	2393	3381	4593	6396	8785	20,319
Risk factors GA, AGE, plus SAS, SEX (male), OC, PE ≤ 12 years							
< 1.5	18	22	29	37	49	64	141
1.5–3	22	29	38	48	65	86	193
3–6	37	50	66	88	118	164	365
6–9	67	89	121	165	226	310	697
9–12	125	170	229	315	432	604	1372
12–15	235	325	440	601	831	1145	2667
15–18	461	634	861	1180	1640	2281	5195
18–21	870	1200	1681	2292	3215	4423	10,219
21–24	1725	2354	3255	4451	6332	8597	19,660
Risk factors GA, AGE, plus SAS, SEX (male), SE, PE ≤ 12 years							
< 1.5	21	27	35	45	61	78	179
1.5–3	27	34	45	60	83	109	250
3–6	46	61	82	111	150	205	465
6–9	83	114	151	207	287	395	904
9–12	158	212	290	396	554	758	1726
12–15	299	405	560	777	1054	1509	3447
15–18	581	790	1095	1508	2087	2871	6634
18–21	1117	1547	2122	2938	4093	5575	13,017
21–24	2167	2992	4178	5736	7778	10,929	25,255

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SAS, SEX (male), SE, OC							
< 1.5	20	25	32	42	55	74	169
1.5–3	25	32	42	56	74	101	225
3–6	44	57	76	105	139	189	428
6–9	78	104	142	193	264	366	824
9–12	144	197	270	372	521	711	1630
12–15	272	378	517	720	993	1355	3197
15–18	529	728	1011	1386	1924	2661	6110
18–21	1027	1416	1966	2729	3771	5178	12,123
21–24	2005	2777	3828	5238	7312	10,027	23,334
Risk factors GA, AGE, plus SAS, SEX (male), MB, PE ≤ 12 years							
< 1.5	19	23	29	37	49	67	145
1.5–3	23	30	38	51	66	87	198
3–6	38	51	69	91	124	168	384
6–9	69	92	125	170	231	316	723
9–12	127	172	232	324	449	617	1434
12–15	241	333	452	618	848	1203	2773
15–18	464	641	860	1214	1692	2314	5384
18–21	906	1255	1709	2326	3247	4416	10,527
21–24	1769	2355	3311	4628	6303	8847	20,325
Risk factors GA, AGE, plus SAS, SEX (male), MB, OC							
< 1.5	18	21	26	35	46	61	134
1.5–3	21	28	36	46	60	82	184
3–6	36	47	65	85	113	154	352
6–9	63	86	115	159	215	289	678
9–12	119	159	213	301	408	567	1292
12–15	220	305	412	578	787	1088	2539
15–18	425	584	814	1135	1545	2101	4924
18–21	828	1146	1582	2174	3031	4162	9501
21–24	1650	2224	3082	4261	5892	8054	18,615
Risk factors GA, AGE, plus SAS, SEX (male), MB, SE							
< 1.5	21	26	32	42	57	75	169
1.5–3	25	33	43	57	76	103	228
3–6	44	58	78	105	142	193	440
6–9	80	105	145	199	271	379	851
9–12	146	201	277	381	514	717	1642
12–15	278	386	528	735	1007	1381	3254
15–18	550	759	1019	1419	1950	2720	6312
18–21	1053	1460	1998	2747	3839	5276	12,332
21–24	2078	2805	3936	5443	7349	10,448	23,544

continued

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SAS, SEX (male), MB, SE, OC, PE ≤ 12 years							
< 1.5	17	22	28	36	46	61	137
1.5–3	22	28	37	47	63	84	189
3–6	36	48	65	85	114	156	358
6–9	66	86	121	159	215	298	681
9–12	121	163	223	303	416	581	1342
12–15	224	316	432	600	811	1140	2566
15–18	437	596	830	1152	1591	2184	5038
18–21	841	1178	1628	2216	3071	4265	9908
21–24	1604	2240	3119	4277	6013	8471	19,239
Risk factors GA, AGE, plus SAS, MB, SE, OC, PE ≤ 12 years							
< 1.5	14	18	22	27	35	47	102
1.5–3	18	23	27	36	47	63	137
3–6	28	36	47	64	84	114	257
6–9	48	63	86	115	157	218	502
9–12	88	118	163	221	304	419	965
12–15	167	226	310	422	591	810	1850
15–18	318	434	600	824	1138	1556	3655
18–21	611	854	1147	1595	2188	3103	7051
21–24	1149	1645	2219	3077	4303	5989	13,786
Risk factors GA, AGE, plus SAS, SEX (male), SE, OC, PE ≤ 12 years							
< 1.5	16	20	23	31	39	52	115
1.5–3	20	24	32	41	53	71	156
3–6	31	40	53	72	97	130	295
6–9	54	73	99	133	184	250	559
9–12	101	133	182	251	347	475	1101
12–15	186	258	349	488	684	908	2143
15–18	360	494	684	942	1316	1830	4176
18–21	687	974	1347	1821	2587	3512	8175
21–24	1346	1865	2572	3583	5014	6840	16,027
Risk factors GA, AGE, plus SAS, SEX (male), MB, OC, PE ≤ 12 years							
< 1.5	14	17	20	26	34	44	93
1.5–3	17	21	26	33	44	56	128
3–6	26	34	45	60	79	106	243
6–9	45	60	82	110	148	198	456
9–12	82	111	151	205	277	389	887
12–15	156	210	286	388	560	745	1686
15–18	295	402	546	746	1043	1435	3278
18–21	555	777	1056	1488	2059	2851	6481
21–24	1084	1517	2028	2868	3976	5459	12,490

TABLE 16 Cost-effectiveness subgroup analysis for children without CLD/CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SAS, SEX (male), MB, SE, PE ≤ 12 years							
< 1.5	16	19	25	31	41	53	121
1.5–3	20	24	32	40	54	72	158
3–6	32	41	55	74	101	136	303
6–9	55	75	100	135	187	254	585
9–12	103	140	189	258	355	489	1126
12–15	193	265	369	493	682	948	2208
15–18	369	510	704	973	1347	1852	4226
18–21	716	915	1360	1870	2605	3580	8346
21–24	1405	1902	2607	3675	5085	6967	16,232
Risk factors GA, AGE, plus SAS, SEX (male), MB, SE, OC							
< 1.5	15	18	23	29	38	50	110
1.5–3	19	23	30	38	50	66	147
3–6	30	38	51	69	92	124	279
6–9	52	69	92	126	174	234	525
9–12	94	129	178	235	330	448	1034
12–15	177	243	331	459	632	873	2007
15–18	351	468	645	888	1217	1681	3914
18–21	653	902	1247	1729	2391	3338	7697
21–24	1274	1769	2422	3360	4703	6482	14,873
Risk factors GA, AGE, plus SAS, SEX (male), MB, SE, OC, PE ≤ 12 years							
< 1.5	12	15	18	22	28	35	75
1.5–3	15	18	23	27	36	47	103
3–6	22	28	36	48	64	85	192
6–9	38	49	64	87	116	162	365
9–12	66	90	120	164	223	302	704
12–15	123	167	227	315	429	595	1362
15–18	231	316	437	605	816	1146	2662
18–21	445	616	855	1178	1596	2275	5118
21–24	874	1200	1672	2295	3168	4320	10,097

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY)

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD							
< 1.5	10	11	14	18	22	29	59
1.5–3	12	14	17	22	29	38	78
3–6	18	23	29	38	49	66	147
6–9	29	40	51	71	94	128	289
9–12	53	71	96	129	178	246	560
12–15	97	135	182	253	346	467	1079
15–18	187	257	353	485	668	919	2095
18–21	359	492	672	916	1295	1793	4107
21–24	693	951	1292	1791	2504	3456	7893
Risk factors GA, AGE, CLD plus PE ≤ 12 years							
< 1.5	8	10	11	14	17	21	42
1.5–3	9	11	13	17	22	27	56
3–6	14	17	21	27	36	47	103
6–9	22	27	37	48	65	90	193
9–12	38	49	66	92	125	167	382
12–15	66	92	122	172	233	325	723
15–18	128	174	242	326	450	616	1423
18–21	238	336	468	628	873	1209	2849
21–24	469	638	879	1225	1722	2335	5373
Risk factors GA, AGE, CLD, plus OC							
< 1.5	8	9	11	13	16	20	39
1.5–3	9	11	13	16	20	26	53
3–6	13	16	20	25	33	44	97
6–9	20	26	35	45	61	83	185
9–12	35	46	62	83	114	155	340
12–15	63	85	113	158	215	294	687
15–18	115	159	222	300	419	571	1305
18–21	224	306	418	583	814	1119	2543
21–24	434	590	816	1113	1572	2146	4994
Risk factors GA, AGE, CLD, plus SE							
< 1.5	9	10	12	14	18	22	44
1.5–3	10	12	14	18	22	29	60
3–6	14	18	23	29	39	52	114
6–9	23	30	40	52	70	95	212
9–12	39	53	71	96	129	182	408
12–15	71	97	133	186	250	345	785
15–18	135	187	258	350	488	674	1546
18–21	264	360	485	678	919	1295	2933
21–24	515	687	964	1314	1852	2543	5875

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, plus SAS							
< 1.5	8	9	10	12	14	17	34
1.5–3	9	10	12	14	18	22	45
3–6	12	14	18	22	29	38	83
6–9	18	23	30	39	51	70	156
9–12	30	39	53	71	96	129	293
12–15	53	73	98	133	183	248	571
15–18	100	134	186	255	357	487	1092
18–21	189	266	363	480	688	922	2158
21–24	359	497	708	966	1296	1819	4211
Risk factors GA, AGE, CLD plus OC, PE≤ 12 years							
< 1.5	7	8	9	10	12	15	28
1.5–3	8	9	10	12	15	19	38
3–6	10	13	15	20	25	32	66
6–9	16	19	25	32	42	57	125
9–12	25	32	44	59	78	104	243
12–15	45	59	81	107	145	199	469
15–18	81	109	151	207	286	390	892
18–21	154	209	293	397	547	747	1735
21–24	295	405	559	757	1046	1476	3308
Risk factors GA, AGE, CLD plus SE, PE≤ 12 years							
< 1.5	8	9	10	12	14	18	34
1.5–3	9	10	12	14	18	23	46
3–6	12	15	18	23	29	39	83
6–9	18	23	30	40	53	71	158
9–12	30	40	54	72	98	134	304
12–15	55	72	100	134	188	260	582
15–18	102	138	186	257	360	500	1138
18–21	197	264	367	508	690	951	2204
21–24	370	513	698	994	1368	1863	4259
Risk factors GA, AGE, CLD plus SE, OC							
< 1.5	7	8	10	11	14	17	32
1.5–3	8	10	11	14	17	21	43
3–6	12	14	17	21	28	36	80
6–9	17	22	28	37	49	66	145
9–12	29	38	49	68	91	126	275
12–15	50	70	92	125	170	233	531
15–18	94	128	175	241	330	464	1039
18–21	175	246	334	460	647	867	2047
21–24	341	471	645	907	1244	1720	3939

continued

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus MW, PE≤ 12 years							
< 1.5	7	8	9	10	12	15	29
1.5–3	8	9	10	12	15	19	38
3–6	11	13	15	19	25	32	68
6–9	16	20	26	33	43	58	126
9–12	26	33	44	59	78	109	244
12–15	45	60	81	110	151	208	472
15–18	85	112	155	213	286	396	907
18–21	158	213	295	406	556	759	1767
21–24	302	412	567	791	1093	1529	3483
Risk factors GA, AGE, CLD plus MB, OC							
< 1.5	7	8	9	10	12	15	27
1.5–3	8	9	10	12	15	18	36
3–6	10	12	15	18	24	31	63
6–9	15	19	24	30	40	53	117
9–12	24	31	41	55	75	102	223
12–15	42	55	75	102	140	188	428
15–18	76	102	141	192	266	364	824
18–21	143	198	273	372	516	710	1595
21–24	280	375	524	734	1006	1379	3218
Risk factors GA, AGE, CLD plus MB, SE							
< 1.5	8	8	10	12	14	17	34
1.5–3	9	10	11	14	17	21	43
3–6	12	14	17	22	28	37	80
6–9	17	22	29	38	50	66	149
9–12	29	39	51	69	92	126	285
12–15	53	70	95	130	176	239	553
15–18	96	131	177	252	340	461	1089
18–21	184	249	342	478	660	906	2066
21–24	355	486	667	911	1305	1779	4020
Risk factors GA, AGE, CLD plus SEX (male), PE≤ 12 years							
< 1.5	8	8	10	11	14	17	31
1.5–3	8	10	11	14	17	21	43
3–6	11	14	17	22	28	36	77
6–9	17	22	28	36	50	65	147
9–12	28	37	49	67	92	123	282
12–15	51	68	92	127	171	238	526
15–18	95	129	176	238	331	459	1042
18–21	179	249	331	470	643	896	2025
21–24	348	468	651	917	1213	1707	3951

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus MB, PE≤ 12 years							
< 1.5	7	8	9	11	13	16	30
1.5–3	8	9	11	13	16	20	40
3–6	11	13	16	21	26	34	72
6–9	16	21	27	34	45	60	133
9–12	26	35	47	62	84	112	257
12–15	47	63	85	115	158	217	494
15–18	86	119	158	225	309	422	947
18–21	164	223	306	419	592	815	1889
21–24	317	428	604	827	1143	1601	3597
Risk factors GA, AGE, CLD plus SEX (male)							
< 1.5	8	9	10	12	15	19	37
1.5–3	9	10	12	15	19	24	49
3–6	13	15	20	24	31	43	89
6–9	19	25	32	42	56	76	168
9–12	33	42	58	77	104	140	323
12–15	59	79	107	146	201	276	624
15–18	110	150	207	281	383	537	1234
18–21	210	289	392	544	756	1047	2336
21–24	407	550	761	1047	1461	2053	4746
Risk factors GA, AGE, CLD plus SEX (male), MB							
< 1.5	7	8	9	11	13	16	31
1.5–3	8	9	11	13	16	21	41
3–6	11	13	16	21	26	35	73
6–9	16	21	27	35	46	62	138
9–12	27	36	46	63	86	117	260
12–15	48	66	87	116	162	222	502
15–18	90	124	168	229	312	432	977
18–21	167	232	325	446	603	837	1911
21–24	320	451	628	836	1183	1648	3721
Risk factors GA, AGE, CLD plus SAS, PE≤ 12 years							
< 1.5	7	8	9	9	11	14	25
1.5–3	8	8	10	11	13	17	32
3–6	10	12	14	17	22	28	56
6–9	14	17	22	28	37	49	104
9–12	22	28	37	50	66	90	203
12–15	39	51	67	91	124	174	383
15–18	69	95	128	175	233	325	753
18–21	126	178	241	336	459	639	153
21–24	247	334	468	652	885	1230	2808

continued

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus SAS, OC							
< 1.5	7	7	8	9	11	14	25
1.5–3	8	8	10	11	13	17	32
3–6	10	12	14	17	22	28	56
6–9	14	17	22	28	37	49	104
9–12	22	28	37	50	66	90	203
12–15	39	51	67	91	124	174	383
15–18	69	95	128	175	233	325	753
18–21	126	178	241	336	459	639	1453
21–24	247	334	468	652	885	1230	2808
Risk factors GA, AGE, CLD plus SAS, OC							
< 1.5	7	7	8	9	11	13	23
1.5–3	7	8	9	11	13	16	30
3–6	9	11	13	16	20	26	54
6–9	13	17	20	26	34	45	98
9–12	21	27	34	46	62	84	185
12–15	36	47	63	85	115	158	355
15–18	64	89	118	163	220	298	690
18–21	119	160	225	305	431	582	1355
21–24	227	318	434	588	837	1132	2608
Risk factors GA, AGE, CLD plus SAS, SE							
< 1.5	7	8	9	10	12	15	27
1.5–3	8	9	11	12	15	18	37
3–6	10	13	15	19	24	32	66
6–9	15	19	25	33	42	56	124
9–12	25	32	43	58	76	106	237
12–15	44	57	78	108	147	199	454
15–18	80	111	151	205	282	385	875
18–21	148	211	287	387	549	748	1730
21–24	291	403	555	758	1053	1431	3308
Risk factors GA, AGE, CLD plus SAS, MB							
< 1.5	7	8	9	9	11	13	24
1.5–3	8	8	9	11	13	16	31
3–6	9	11	13	16	21	26	55
6–9	14	16	21	26	35	46	100
9–12	22	27	36	46	63	86	193
12–15	36	48	64	87	120	159	367
15–18	65	88	121	164	225	306	711
18–21	123	167	227	318	429	598	1355
21–24	237	326	444	618	845	1164	2657

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus SAS, SEX (male)							
< 1.5	7	8	9	10	12	14	26
1.5–3	8	9	10	12	14	18	34
3–6	10	12	14	18	23	30	61
6–9	15	18	24	30	40	52	114
9–12	23	30	40	53	72	97	218
12–15	41	55	75	99	138	184	411
15–18	74	100	137	188	256	356	813
18–21	141	191	257	366	499	674	1603
21–24	266	368	507	704	941	1317	3038
Risk factors GA, AGE, CLD plus SE, OC , PE≤ 12 years							
< 1.5	7	7	8	9	11	13	24
1.5–3	8	8	9	11	13	16	31
3–6	9	11	13	17	20	26	55
6–9	13	17	21	27	36	47	99
9–12	21	27	35	46	64	85	189
12–15	36	48	64	86	121	161	363
15–18	66	88	119	164	223	315	705
18–21	122	167	232	318	441	613	1387
21–24	238	319	446	617	844	1166	2656
Risk factors GA, AGE, CLD plus MB, OC, PE≤ 12 years							
< 1.5	7	7	7	8	10	12	20
1.5–3	7	8	9	9	12	14	25
3–6	9	10	12	14	18	22	45
6–9	12	14	18	23	30	38	84
9–12	18	23	29	38	52	69	154
12–15	29	40	52	72	96	131	297
15–18	55	73	97	131	184	242	578
18–21	101	135	187	252	349	479	1105
21–24	188	258	352	492	678	932	2139
Risk factors GA, AGE, CLD plus MB, SE, PE≤ 12 years							
< 1.5	7	8	8	9	11	13	24
1.5–3	8	8	9	11	13	16	31
3–6	10	11	14	17	21	27	55
6–9	14	17	20	27	35	46	103
9–12	22	27	36	50	63	89	193
12–15	36	48	65	89	122	164	372
15–18	67	90	124	167	228	319	723
18–21	126	168	237	318	444	625	1416
21–24	238	325	445	624	872	1188	2804

continued

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus MW, PE≤ 12 years							
< 1.5	7	7	8	9	11	13	23
1.5–3	7	8	9	11	12	15	30
3–6	9	11	13	16	20	25	51
6–9	13	16	20	25	33	45	96
9–12	21	27	33	45	60	80	178
12–15	34	46	60	84	111	152	343
15–18	62	83	113	155	215	289	650
18–21	114	159	215	299	405	564	1291
21–24	221	304	416	569	805	1099	2534
Risk factors GA, AGE, CLD plus SEX (male), OC, PE≤ 12 years							
< 1.5	7	7	8	9	11	13	22
1.5–3	7	8	9	11	12	15	29
3–6	9	11	13	15	19	25	51
6–9	13	16	20	25	33	43	93
9–12	20	26	33	43	58	79	172
12–15	34	44	59	80	108	149	341
15–18	60	82	109	152	206	285	646
18–21	111	154	213	289	396	548	1272
21–24	220	296	408	560	773	1085	2451
Risk factors GA, AGE, CLD plus SEX (male), SE, PE≤ 12 years							
< 1.5	7	8	9	10	12	14	27
1.5–3	8	9	10	12	14	18	35
3–6	10	12	15	18	22	30	62
6–9	15	19	23	31	40	54	117
9–12	24	31	41	55	75	99	218
12–15	42	55	74	101	137	190	428
15–18	74	103	142	195	268	362	841
18–21	144	195	264	364	510	700	1630
21–24	272	380	515	720	1011	1371	3172
Risk factors GA, AGE, CLD plus SEX (male), SE, OC							
< 1.5	7	7	8	10	11	14	25
1.5–3	7	8	10	11	14	16	32
3–6	10	12	14	17	22	28	58
6–9	14	17	22	28	37	49	109
9–12	22	29	38	51	67	91	206
12–15	37	52	68	92	126	175	396
15–18	71	94	130	173	246	334	761
18–21	131	180	249	340	470	642	1490
21–24	253	345	477	658	916	1256	2903

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus SEX (male) MB, PE≤ 12 years							
< 1.5	7	7	8	9	11	13	23
1.5–3	7	8	9	11	13	15	29
3–6	9	11	13	16	19	25	52
6–9	13	16	20	26	33	44	95
9–12	20	26	34	45	61	82	180
12–15	34	45	59	83	112	154	344
15–18	62	86	114	152	214	292	679
18–21	117	157	214	304	414	560	1288
21–24	220	307	412	570	774	1074	2500
Risk factors GA, AGE, CLD plus SEX (male), MB, OC							
< 1.5	7	7	8	9	10	12	21
1.5–3	7	8	9	10	12	15	27
3–6	9	11	13	15	19	24	48
6–9	12	15	19	24	31	41	89
9–12	19	25	31	42	55	74	168
12–15	32	42	57	76	100	140	320
15–18	57	78	104	146	193	269	616
18–21	106	145	199	275	376	520	1165
21–24	202	274	384	532	747	1019	2307
Risk factors GA, AGE, CLD plus SEX (male), MB, SE							
< 1.5	7	8	8	10	11	14	26
1.5–3	8	9	10	12	14	17	33
3–6	10	11	14	17	22	28	59
6–9	15	18	22	29	38	50	111
9–12	23	30	38	52	69	94	209
12–15	39	52	71	94	131	176	408
15–18	71	97	133	177	247	337	767
18–21	135	187	255	349	475	651	1480
21–24	260	356	493	682	952	1323	2998
Risk factors GA, AGE, CLD plus SAS, OC, PE≤ 12 years							
< 1.5	6	7	7	8	9	10	18
1.5–3	7	7	8	9	10	12	22
3–6	8	9	11	13	15	19	38
6–9	11	12	15	19	25	32	68
9–12	16	20	25	33	43	59	127
12–15	25	33	45	58	79	107	238
15–18	45	61	80	110	150	207	485
18–21	82	111	153	210	288	405	915
21–24	156	217	290	404	551	775	1795

continued

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus SAS, SE, PE≤ 12 years							
< 1.5	7	7	8	9	10	12	21
1.5–3	7	8	9	10	12	14	27
3–6	9	10	12	14	18	23	47
6–9	12	15	18	23	30	41	85
9–12	19	24	31	40	55	73	159
12–15	31	41	56	73	101	137	311
15–18	55	75	102	138	191	260	595
18–21	104	141	191	267	368	510	1153
21–24	197	270	370	522	710	987	2294
Risk factors GA, AGE, CLD plus SAS, Se, OC							
< 1.5	6	7	7	8	10	11	20
1.5–3	7	8	8	10	11	14	25
3–6	8	10	11	14	17	21	44
6–9	12	14	17	22	28	37	80
9–12	17	22	28	37	50	67	150
12–15	29	39	52	69	94	126	287
15–18	52	70	94	128	175	238	547
18–21	96	129	181	241	342	462	1079
21–24	181	256	341	469	648	900	2098
Risk factors GA, AGE, CLD plus SAS, MB, PE≤ 12 years							
< 1.5	6	7	7	8	9	11	18
1.5–3	7	7	8	9	11	13	23
3–6	8	9	11	13	15	20	39
6–9	11	13	16	20	25	33	70
9–12	16	20	26	34	45	59	130
12–15	26	34	46	61	82	108	250
15–18	46	61	83	113	154	213	483
18–21	85	114	155	216	303	401	933
21–24	159	215	295	415	580	798	1806
Risk factors GA, AGE, CLD plus SAS, MB, OC							
< 1.5	6	7	7	8	9	10	17
1.5–3	7	7	8	9	10	12	21
3–6	8	9	10	12	15	19	37
6–9	10	12	15	19	23	31	66
9–12	15	19	24	32	41	55	120
12–15	24	32	42	56	74	102	229
15–18	43	57	77	105	144	193	440
18–21	78	107	145	197	273	371	839
21–24	147	207	273	377	520	721	1689

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus SAS, MB, SE							
< 1.5	6	7	8	8	10	11	20
1.5–3	7	8	9	10	11	14	26
3–6	9	10	12	14	17	22	46
6–9	12	14	18	22	29	38	81
9–12	17	22	29	39	51	69	153
12–15	30	39	52	70	95	130	292
15–18	53	71	97	131	183	252	570
18–21	98	132	183	254	351	486	1089
21–24	188	252	352	487	671	927	2126
Risk factors GA, AGE, CLD plus SAS, SEX (male), PE≤ 12 years							
< 1.5	7	7	8	8	10	11	19
1.5–3	7	8	9	10	11	14	25
3–6	8	10	11	14	17	22	44
6–9	12	14	17	22	28	37	80
9–12	18	22	29	38	50	67	149
12–15	30	38	51	68	93	128	287
15–18	52	70	94	128	178	240	541
18–21	93	131	180	246	341	462	1076
21–24	182	255	344	478	665	917	2053
Risk factors GA, AGE, CLD plus SAS, SEX (male), OC							
< 1.5	6	7	7	8	9	11	18
1.5–3	7	7	8	9	11	13	24
3–6	8	9	11	13	16	20	41
6–9	11	13	16	20	26	34	74
9–12	17	20	27	35	46	62	137
12–15	27	36	46	64	87	117	265
15–18	49	64	86	118	163	220	500
18–21	88	122	165	227	313	434	956
21–24	169	231	317	443	604	838	1880
Risk factors GA, AGE, CLD plus SAS, SEX (male), SE							
< 1.5	7	7	8	9	11	12	22
1.5–3	7	8	9	10	12	15	28
3–6	9	11	13	15	19	24	50
6–9	13	16	19	25	33	43	92
9–12	19	25	33	44	59	77	173
12–15	33	44	58	79	106	143	333
15–18	61	80	110	149	208	282	639
18–21	113	150	208	287	395	547	1256
21–24	214	294	408	555	756	1066	2437

continued

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus SAS, SEX (male), MB							
< 1.5	7	7	7	8	10	11	19
1.5–3	7	8	8	9	11	13	25
3–6	8	9	11	13	16	20	41
6–9	11	13	17	21	27	35	75
9–12	17	21	28	36	47	63	142
12–15	28	36	48	65	88	119	271
15–18	49	65	89	123	170	229	525
18–21	91	127	170	234	320	435	1000
21–24	172	238	327	439	627	850	1982
Risk factors GA, AGE, CLD plus MB, SE, OC6, PE≤ 12 years							
< 1.5	6	7	7	8	9	10	17
1.5–3	7	7	8	9	10	12	22
3–6	8	9	10	12	15	19	37
6–9	11	12	15	19	24	31	66
9–12	15	20	25	32	41	57	122
12–15	24	33	44	58	78	103	236
15–18	44	58	78	106	147	200	453
18–21	81	106	148	201	278	384	864
21–24	149	213	282	386	530	747	1687
Risk factors GA, AGE, CLD plus SEX (male), SE, OC, PE≤ 12 years							
< 1.5	6	7	7	8	9	11	19
1.5–3	7	7	8	10	11	13	24
3–6	8	10	11	13	16	20	42
6–9	11	14	17	21	27	35	76
9–12	17	22	27	36	47	64	141
12–15	28	36	49	65	87	120	271
15–18	49	65	89	119	166	228	511
18–21	91	124	170	228	319	444	1006
21–24	171	230	330	451	617	847	1945
Risk factors GA, AGE, CLD plus SEX (male),MB, OC, PE≤ 12 years							
< 1.5	6	6	7	8	8	10	16
1.5–3	6	7	8	9	10	12	21
3–6	8	9	10	12	14	18	34
6–9	10	12	14	18	22	29	63
9–12	15	18	23	30	38	52	112
12–15	23	30	40	52	72	96	214
15–18	41	54	73	97	134	182	412
18–21	73	100	136	184	258	352	811
21–24	137	191	266	358	499	697	1583

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus SEX (male), MB, SE, PE≤ 12 years							
< 1.5	7	7	8	8	10	11	19
1.5–3	7	7	8	9	11	13	24
3–6	9	9	11	13	16	21	43
6–9	11	14	17	21	27	35	77
9–12	17	22	28	36	49	65	141
12–15	28	37	50	66	90	122	277
15–18	50	67	91	123	167	232	532
18–21	93	126	170	237	335	450	1025
21–24	174	243	328	450	628	871	2011
Risk factors GA, AGE, CLD plus SEX (male), MB, SE, OC							
< 1.5	6	7	7	8	9	11	18
1.5–3	7	7	8	9	11	12	23
3–6	8	9	11	13	16	20	40
6–9	11	13	16	20	26	34	71
9–12	16	21	26	34	46	60	133
12–15	26	34	45	61	83	114	256
15–18	47	62	84	115	155	217	483
18–21	84	118	157	221	297	410	954
21–24	163	225	302	434	589	810	1841
Risk factors GA, AGE, CLD plus SAS, SE, OC, PE≤ 12 years							
< 1.5	6	7	7	7	8	9	15
1.5–3	6	7	7	8	10	11	19
3–6	8	8	9	11	13	16	31
6–9	9	11	13	17	21	27	56
9–12	14	17	21	27	36	47	103
12–15	22	28	36	47	65	87	191
15–18	37	49	65	89	121	164	373
18–21	67	89	123	169	226	314	720
21–24	125	168	236	321	438	615	1409
Risk factors GA, AGE, CLD plus SAS, MB, OC, PE≤ 12 years							
< 1.5	6	6	7	7	8	8	13
1.5–3	6	7	7	8	9	10	17
3–6	7	8	9	10	12	14	26
6–9	9	10	12	14	18	23	45
9–12	12	14	18	23	30	39	83
12–15	19	23	30	40	53	70	160
15–18	31	41	54	72	98	132	303
18–21	54	74	100	135	187	255	572
21–24	102	139	187	262	361	487	1120

continued

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus SAS, MB, SE, PE≤ 12 years							
< 1.5	6	7	7	7	8	9	16
1.5–3	6	7	7	8	9	11	19
3–6	8	8	9	11	13	17	32
6–9	10	11	14	17	21	28	57
9–12	14	17	22	28	36	48	104
12–15	22	28	37	49	64	88	198
15–18	37	50	66	91	123	167	385
18–21	68	93	125	169	238	324	738
21–24	129	172	237	328	452	624	1457
Risk factors GA, AGE, CLD plus SAS, MB, SE, OC							
< 1.5	6	6	7	7	8	9	15
1.5–3	6	7	7	8	9	11	18
3–6	7	8	9	11	13	15	30
6–9	9	10	13	16	20	25	54
9–12	13	16	20	26	33	45	96
12–15	21	26	34	46	61	80	184
15–18	34	47	62	85	112	154	352
18–21	62	85	117	159	218	299	676
21–24	118	160	220	307	407	583	1317
Risk factors GA, AGE, CLD plus SAS, SEX (male), OC, PE≤ 12 years							
< 1.5	6	7	7	7	8	9	14
1.5–3	6	7	7	8	9	11	18
3–6	7	8	9	11	13	15	29
6–9	9	10	13	15	20	25	52
9–12	13	16	20	25	33	43	95
12–15	20	26	34	46	60	81	177
15–18	33	45	61	80	113	152	339
18–21	64	85	113	154	212	290	665
21–24	116	157	218	295	400	568	1271
Risk factors GA, AGE, CLD plus SAS, SEX (male), SE, PE≤ 12 years							
< 1.5	6	7	7	7	9	10	17
1.5–3	7	7	8	9	10	12	22
3–6	8	9	10	12	15	18	36
6–9	11	12	15	19	23	31	66
9–12	15	19	24	31	42	54	118
12–15	24	31	42	55	74	102	226
15–18	43	57	75	104	140	195	436
18–21	77	103	144	198	270	371	839
21–24	146	202	278	382	520	715	1663

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus SAS, SEX (male), SE, PE≤ 12 years							
< 1.5	6	6	7	7	8	10	16
1.5–3	7	7	8	8	9	11	20
3–6	8	9	10	11	14	17	33
6–9	10	12	14	17	22	29	60
9–12	14	17	23	28	38	51	110
12–15	23	29	39	52	68	93	211
15–18	39	51	70	94	130	179	410
18–21	72	97	132	178	254	342	774
21–24	137	186	252	346	489	661	1522
Risk factors GA, AGE, CLD plus SAS, SEX (male), MB, PE≤ 12 years							
< 1.5	6	6	7	8	8	9	14
1.5–3	6	7	7	8	9	10	18
3–6	7	8	9	11	13	16	30
6–9	9	11	13	16	20	25	52
9–12	13	16	20	25	35	45	97
12–15	20	26	34	46	61	83	183
15–18	35	46	63	86	114	156	354
18–21	64	85	116	157	216	291	695
21–24	116	159	223	304	421	578	1327
Risk factors GA, AGE, CLD plus SAS, SEX (male), MB, OC							
< 1.5	6	6	7	7	8	9	14
1.5–3	6	7	7	8	9	10	17
3–6	7	8	9	10	12	15	28
6–9	9	11	12	15	19	24	49
9–12	12	16	19	24	31	42	90
12–15	19	24	32	42	56	76	167
15–18	33	43	57	77	104	143	328
18–21	59	79	106	148	202	271	628
21–24	110	148	206	274	387	530	1240
Risk factors GA, AGE, CLD plus SAS, SEX (male), MB, SE							
< 1.5	6	7	7	7	8	10	16
1.5–3	6	7	8	9	10	12	21
3–6	8	9	10	12	14	18	34
6–9	10	12	14	18	23	29	61
9–12	14	18	23	29	39	51	111
12–15	23	30	39	52	70	96	213
15–18	41	54	72	98	134	183	409
18–21	74	99	134	182	249	345	796
21–24	138	190	260	355	486	679	1542

continued

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus SEX (male), MB, SE, OC, PE≤ 12 years							
< 1.5	6	6	7	7	8	9	14
1.5–3	6	7	7	8	9	10	18
3–6	7	8	9	10	12	15	28
6–9	9	10	12	15	19	24	50
9–12	13	15	19	25	32	43	90
12–15	19	25	33	43	57	77	172
15–18	33	44	59	78	107	146	333
18–21	60	80	110	150	205	287	635
21–24	112	154	209	282	391	549	1234
Risk factors GA, AGE, CLD plus SAS, MB, SE, OC							
< 1.5	6	6	6	7	7	8	12
1.5–3	6	6	7	7	8	9	14
3–6	7	7	8	9	10	12	22
6–9	8	9	10	13	15	19	38
9–12	11	12	15	19	24	31	69
12–15	15	20	25	32	43	57	126
15–18	25	34	43	58	80	107	242
18–21	45	59	80	109	147	204	465
21–24	81	110	152	208	285	389	893
Risk factors GA, AGE, CLD plus SAS, SEX (male), SE, OC, PE≤ 12 years							
< 1.5	6	6	6	7	8	8	13
1.5–3	6	6	7	7	8	9	15
3–6	7	8	8	10	11	14	24
6–9	9	9	11	14	17	21	43
9–12	12	14	16	21	27	36	76
12–15	17	22	28	36	49	65	141
15–18	28	36	49	67	89	121	273
18–21	50	66	92	123	172	234	523
21–24	92	125	175	237	327	446	1016
Risk factors GA, AGE, CLD plus SAS, SEX (male), MB, OC, PE≤ 12 years							
< 1.5	6	6	6	7	7	8	11
1.5–3	6	6	7	7	8	9	13
3–6	7	7	8	9	10	12	21
6–9	8	9	10	12	15	18	35
9–12	10	12	15	18	24	30	64
12–15	15	18	24	30	40	52	115
15–18	24	30	41	55	73	99	222
18–21	41	55	74	101	139	189	420
21–24	75	102	139	190	265	360	823

TABLE 17 Cost-effectiveness subgroup analysis for children with CLD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CLD plus SAS, SEX (male), MB, SE, PE≤ 12 years							
< 1.5	6	6	7	7	7	8	13
1.5–3	6	6	7	7	8	10	15
3–6	7	8	8	10	11	13	25
6–9	8	10	11	13	17	21	43
9–12	12	14	17	22	28	37	77
12–15	17	22	29	37	50	67	146
15–18	30	38	50	68	94	124	282
18–21	50	69	95	130	172	239	538
21–24	94	129	174	241	336	453	1015
Risk factors GA, AGE, CLD plus SAS, SEX (male), MB, SE, OC							
< 1.5	6	6	6	7	7	8	12
1.5–3	6	6	7	7	8	9	15
3–6	7	7	8	9	11	13	23
6–9	8	9	11	13	16	20	40
9–12	11	13	16	21	26	35	73
12–15	16	21	27	35	46	62	135
15–18	27	35	46	62	84	115	256
18–21	48	65	86	116	159	220	490
21–24	87	120	162	220	308	423	951
Risk factors GA, AGE, CLD plus SAS, SEX (male), MB, SE, OC							
< 1.5	6	6	6	6	7	7	10
1.5–3	6	6	6	7	7	8	12
3–6	6	7	7	8	9	11	18
6–9	7	8	9	11	12	15	29
9–12	9	11	13	15	19	25	50
12–15	13	16	20	26	33	43	93
15–18	20	26	34	45	59	79	176
18–21	33	45	61	81	109	149	340
21–24	61	82	110	156	212	289	653

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY)

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic)							
< 1.5	8	11	16	22	31	43	100
1.5–3	11	17	22	31	42	59	138
3–6	23	32	44	62	83	114	266
6–9	45	61	86	119	162	224	523
9–12	90	120	166	235	323	443	996
12–15	167	234	324	443	611	854	2021
15–18	333	465	642	874	1221	1613	3960
18–21	641	900	1258	1717	2397	3266	7739
21–24	1253	1761	2439	3434	4593	6473	14,545
Risk factors GA, AGE, CHD (acyanotic) plus PE≤ 12 years							
< 1.5	5	8	10	15	20	28	67
1.5–3	7	11	15	21	29	40	93
3–6	15	22	30	41	56	78	180
6–9	30	42	56	79	110	154	347
9–12	58	80	113	157	217	302	706
12–15	116	158	221	299	417	584	1330
15–18	225	309	421	596	829	1114	2585
18–21	436	606	860	1144	1650	2216	5185
21–24	835	1179	1651	2282	3149	4443	9755
Risk factors GA, AGE, CHD (acyanotic) plus OC							
< 1.5	5	7	10	13	18	27	60
1.5–3	7	10	14	19	26	37	87
3–6	14	19	26	37	52	72	168
6–9	27	39	52	72	102	140	323
9–12	55	75	105	141	199	277	627
12–15	103	140	202	282	399	544	1261
15–18	201	287	395	556	756	1040	2388
18–21	399	556	765	1053	1467	2064	4782
21–24	757	1100	1499	2065	2800	4031	9320
Risk factors GA, AGE, CHD (acyanotic) plus SE							
< 1.5	6	9	12	17	24	32	77
1.5–3	9	13	17	24	34	47	110
3–6	18	25	35	48	65	92	210
6–9	35	49	68	95	131	179	420
9–12	68	95	133	183	255	347	801
12–15	136	183	254	356	495	698	1571
15–18	260	360	504	681	960	1306	3078
18–21	520	713	974	1369	1883	2606	6022
21–24	1012	1393	1908	2640	3679	5232	11,957

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus MB							
< 1.5	5	7	10	14	19	27	61
1.5–3	7	10	14	199	28	37	87
3–6	14	20	27	38	54	75	171
6–9	28	39	54	75	108	143	331
9–12	55	77	107	149	201	277	652
12–15	109	149	209	291	397	545	1230
15–18	212	291	400	558	780	1083	2455
18–21	405	566	780	1103	1502	2119	4816
21–24	792	1102	1525	2163	2955	4009	9519
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male)							
< 1.5	6	8	11	16	22	31	72
1.5–3	8	12	16	23	31	43	99
3–6	16	23	32	43	61	83	195
6–9	32	46	63	85	121	164	375
9–12	63	87	119	170	234	325	748
12–15	125	174	238	330	452	617	1464
15–18	240	342	461	665	894	1209	2892
18–21	468	639	911	1267	1744	2414	5556
21–24	913	1282	1802	2421	3376	4844	11,101
Risk factors GA, AGE, CHD (acyanotic) plus SAS							
< 1.5	4	6	8	11	15	22	52
1.5–3	6	8	11	16	22	31	72
3–6	12	16	22	32	43	61	140
6–9	23	31	46	62	85	117	273
9–12	45	62	87	121	167	232	522
12–15	87	124	170	241	327	458	1019
15–18	177	238	338	462	640	877	2007
18–21	340	467	646	900	1254	1718	4020
21–24	661	926	1266	1740	2432	3350	7724
Risk factors GA, AGE, CHD (acyanotic) plus OC, PE≤ 12 years							
< 1.5	3	4	6	9	13	18	41
1.5–3	5	6	9	13	17	24	60
3–6	9	13	18	25	34	48	113
6–9	18	26	36	48	68	97	220
9–12	35	51	69	95	137	189	429
12–15	70	97	137	191	259	357	837
15–18	141	193	267	371	504	715	1614
18–21	271	386	521	722	1040	1395	3145
21–24	540	749	1010	1384	1951	2688	6046

continued

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus SE, PE≤ 12 years							
< 1.5	4	6	8	12	16	22	52
1.5–3	6	8	12	17	22	31	74
3–6	12	17	23	32	45	62	140
6–9	23	32	46	64	87	120	281
9–12	46	65	88	124	166	236	537
12–15	90	125	174	243	340	461	1053
15–18	181	244	337	481	655	890	2135
18–21	344	489	673	929	1284	1717	4056
21–24	675	943	1306	1754	2515	3487	7991
Risk factors GA, AGE, CHD (acyanotic) plus SE, OC							
< 1.5	4	5	7	11	15	29	48
1.5–3	5	8	11	15	21	29	68
3–6	11	15	21	30	42	56	128
6–9	22	30	42	59	77	109	258
9–12	43	58	81	113	155	222	501
12–15	82	114	160	220	309	424	975
15–18	166	221	313	428	587	836	1884
18–21	315	441	623	864	1184	1632	3679
21–24	631	873	1202	1667	2248	3121	7383
Risk factors GA, AGE, CHD (acyanotic) plus MB, PE≤ 12 years							
< 1.5	3	6	7	10	13	18	43
1.5–3	5	7	9	13	18	25	57
3–6	10	13	19	26	36	50	115
6–9	19	26	36	50	72	95	231
9–12	37	52	71	98	138	193	434
12–15	77	101	138	195	263	365	838
15–18	143	198	271	376	527	714	1709
18–21	280	383	538	747	1012	1380	3240
21–24	547	750	1042	1449	1992	2752	6356
Risk factors GA, AGE, CHD (acyanotic) plus MB, OC							
< 1.5	3	4	6	8	12	16	39
1.5–3	4	6	8	12	17	23	54
3–6	9	12	17	24	32	46	106
6–9	17	23	34	47	67	90	208
9–12	33	47	66	90	124	174	404
12–15	66	92	130	176	254	342	778
15–18	133	180	253	355	483	674	1548
18–21	256	349	491	684	961	1302	3069
21–24	510	690	971	1336	1850	2459	5880

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus MB, SE							
< 1.5	4	5	8	11	14	22	50
1.5–3	6	8	11	16	21	29	68
3–6	11	15	22	31	42	58	135
6–9	22	32	42	59	84	114	263
9–12	45	60	85	118	163	224	524
12–15	84	118	165	226	313	430	1012
15–18	161	238	325	443	612	855	2017
18–21	319	442	623	857	1209	1682	3870
21–24	644	876	1212	1697	2375	3208	7465
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), PE≤ 12 years							
< 1.5	4	6	8	11	15	21	49
1.5–3	5	8	11	15	21	29	67
3–6	11	15	21	29	41	56	133
6–9	22	30	42	57	83	111	257
9–12	42	58	81	112	156	223	511
12–15	85	113	157	224	307	427	979
15–18	161	229	320	440	611	825	1890
18–21	320	440	624	855	1170	1626	3774
21–24	612	864	1212	1646	2282	3154	7333
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), OC							
< 1.5	3	5	7	10	13	18	45
1.5–3	5	7	10	14	20	27	63
3–6	10	14	20	28	36	53	122
6–9	20	28	38	53	72	100	242
9–12	39	54	75	103	143	196	468
12–15	76	105	143	204	285	387	908
15–18	153	211	281	390	540	773	1770
18–21	298	400	561	774	1053	1463	3419
21–24	576	793	1102	1515	2157	2886	6873
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), SE							
< 1.5	5	6	9	12	18	24	59
1.5–3	6	9	13	18	24	34	78
3–6	13	18	25	34	48	67	155
6–9	26	35	50	69	96	130	306
9–12	52	69	97	135	184	261	589
12–15	98	136	190	262	367	493	1139
15–18	193	268	363	519	693	959	2292
18–21	374	523	715	1016	1390	1933	4372
21–24	738	1032	1424	1943	2710	3654	8508

continued

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), MB							
< 1.5	3	5	7	10	14	19	45
1.5–3	5	7	10	14	19	27	65
3–6	11	14	19	28	38	54	127
6–9	21	28	40	55	75	107	245
9–12	40	56	77	106	146	205	473
12–15	77	110	149	211	291	395	925
15–18	155	214	292	410	572	806	1802
18–21	303	412	572	818	1131	1536	3521
21–24	578	821	1122	1545	2144	2953	6868
Risk factors GA, AGE, CHD (acyanotic) plus SAS, PE≤ 12 years							
< 1.5	3	4	5	7	11	15	35
1.5–3	4	5	7	10	15	21	48
3–6	8	11	15	22	29	40	96
6–9	15	21	30	43	59	77	184
9–12	30	42	59	80	114	161	364
12–15	60	82	115	158	219	302	700
15–18	118	163	220	309	439	610	1360
18–21	227	320	442	617	847	1143	2734
21–24	461	624	866	1183	1632	2318	5268
Risk factors GA, AGE, CHD (acyanotic) plus SAS, OC							
< 1.5	2	3	5	7	9	13	32
1.5–3	3	5	7	10	14	19	44
3–6	7	10	14	20	27	38	87
6–9	14	19	28	39	53	72	170
9–12	27	39	53	75	105	144	333
12–15	55	76	104	144	203	286	656
15–18	105	148	205	282	395	548	1284
18–21	209	293	401	557	772	1056	2458
21–24	411	563	801	1107	1516	2122	4798
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SE							
< 1.5	3	4	6	9	13	18	42
1.5–3	5	7	9	12	18	25	58
3–6	9	13	18	24	36	48	115
6–9	18	24	35	48	67	95	218
9–12	35	50	70	97	130	185	424
12–15	69	97	132	182	258	373	810
15–18	139	193	266	368	504	689	1650
18–21	269	371	527	708	994	1390	3105
21–24	539	733	1006	1415	1945	2675	6071

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus SAS, MB							
< 1.5	3	3	5	7	10	14	33
1.5–3	3	5	7	10	14	20	46
3–6	8	10	14	20	27	38	89
6–9	15	20	29	40	53	76	172
9–12	28	40	55	77	106	147	330
12–15	56	77	110	152	212	287	667
15–18	112	153	211	292	409	551	1273
18–21	215	306	416	588	795	1098	2511
21–24	421	582	814	1117	1555	2142	4890
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male)							
< 1.5	3	4	6	8	12	16	38
1.5–3	4	6	8	12	16	22	52
3–6	9	11	16	23	32	45	102
6–9	17	23	32	45	62	86	204
9–12	32	45	65	89	120	166	385
12–15	64	89	124	172	239	328	769
15–18	126	174	238	335	464	640	1483
18–21	248	340	475	662	915	1244	2869
21–24	478	671	934	1278	1794	2444	5595
Risk factors GA, AGE, CHD (acyanotic) plus SE, OC, PE≤ 12 years							
< 1.5	2	4	5	7	10	14	33
1.5–3	3	5	7	10	14	20	46
3–6	7	10	14	19	28	38	88
6–9	14	20	28	39	55	77	172
9–12	29	40	56	75	103	146	338
12–15	57	78	108	148	205	289	660
15–18	110	152	211	296	405	572	1284
18–21	211	298	419	564	784	1110	2488
21–24	417	584	806	1124	1558	2118	4737
Risk factors GA, AGE, CHD (acyanotic) plus MB, OC, PE≤ 12 years							
< 1.5	2	3	4	6	8	11	27
1.5–3	3	4	6	8	11	15	37
3–6	6	8	11	16	22	31	71
6–9	12	17	23	31	43	61	139
9–12	23	32	44	61	85	118	269
12–15	46	63	84	121	171	227	535
15–18	88	124	166	239	326	455	1006
18–21	173	245	325	463	434	875	1983
21–24	337	467	649	908	1232	1729	3970

continued

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus MB, SE, PE≤ 12 years							
< 1.5	3	4	5	7	10	14	34
1.5–3	4	5	7	10	14	20	47
3–6	7	10	15	20	29	40	90
6–9	15	20	29	39	56	76	182
9–12	30	41	57	79	109	149	351
12–15	59	80	112	157	217	298	675
15–18	113	159	218	297	413	574	1301
18–21	216	307	417	587	836	1146	2604
21–24	428	610	838	1126	1579	2224	4982
Risk factors GA, AGE, CHD (acyanotic) plus MB, SE, OC							
< 1.5	2	3	5	7	9	13	31
1.5–3	3	5	7	9	13	18	43
3–6	7	10	13	19	25	36	84
6–9	13	19	26	37	51	70	160
9–12	27	38	53	72	99	137	321
12–15	54	73	102	143	199	274	626
15–18	103	144	195	280	379	542	1223
18–21	197	282	395	539	736	1066	2349
21–24	395	575	742	1029	1466	2008	4664
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), OC, PE≤ 12 years							
< 1.5	2	3	5	7	9	13	30
1.5–3	3	5	6	9	13	18	44
3–6	7	9	13	18	25	35	83
6–9	14	18	25	36	49	68	162
9–12	27	35	51	72	97	134	322
12–15	50	73	101	141	191	271	606
15–18	103	137	194	267	372	519	1175
18–21	198	283	388	523	728	998	2351
21–24	385	534	745	1054	1443	2031	4479
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), SE, PE≤ 12 years							
< 1.5	3	4	6	8	12	16	39
1.5–3	4	66	9	12	16	23	55
3–6	8	12	16	24	33	45	103
6–9	17	24	32	46	65	91	199
9–12	33	48	64	91	124	172	400
12–15	66	92	128	177	242	346	777
15–18	132	180	253	352	474	665	1554
18–21	257	355	493	669	918	1308	3000
21–24	504	691	970	1303	1817	2502	5618

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), SE, OC							
< 1.5	3	4	5	8	11	15	35
1.5–3	4	5	8	11	15	21	51
3–6	8	11	16	21	31	41	98
6–9	16	22	29	42	60	80	183
9–12	32	43	60	83	113	157	369
12–15	62	83	116	157	231	312	717
15–18	118	168	226	322	449	610	1372
18–21	233	316	440	611	847	1164	2745
21–24	460	619	874	1198	1656	2321	5407
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), MB							
< 1.5	2	3	5	7	9	13	31
1.5–3	3	5	7	9	14	18	43
3–6	7	10	13	18	27	36	83
6–9	13	19	27	36	51	73	165
9–12	27	38	52	74	99	136	321
12–15	53	74	102	142	199	270	635
15–18	100	145	199	269	384	547	1244
18–21	208	282	386	536	736	1056	2384
21–24	390	549	764	1038	1443	2054	4710
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), MB, OC							
< 1.5	2	3	4	6	9	12	28
1.5–3	3	4	6	8	12	17	38
3–6	6	9	12	17	23	34	77
6–9	12	17	24	34	46	65	151
9–12	25	34	48	68	91	129	296
12–15	49	67	92	130	177	248	570
15–18	94	136	179	255	353	494	1121
18–21	188	265	355	502	696	957	2124
21–24	368	508	692	973	1327	1843	4328
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), MB, SE							
< 1.5	3	4	6	8	11	15	37
1.5–3	4	6	8	11	16	22	51
3–6	8	11	16	21	31	42	100
6–9	16	22	30	44	59	83	193
9–12	31	44	61	85	120	161	382
12–15	63	85	118	165	234	328	724
15–18	121	167	237	326	467	622	1467
18–21	242	328	460	637	873	1203	2844
21–24	471	644	909	1262	1701	2410	5600

continued

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus SAS, OC, PE≤ 12 years							
< 1.5	1	2	3	5	7	9	22
1.5–3	2	3	5	7	9	13	31
3–6	5	7	9	13	18	25	59
6–9	9	13	18	26	36	49	114
9–12	19	27	36	51	70	96	230
12–15	38	50	69	100	135	190	439
15–18	73	100	137	195	264	365	843
18–21	145	197	271	382	519	720	1629
21–24	268	380	537	737	1027	1396	3291
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SE, PE≤ 12 years							
< 1.5	2	3	4	6	8	12	27
1.5–3	3	4	6	8	11	17	39
3–6	6	8	12	17	23	33	77
6–9	12	17	24	33	47	64	146
9–12	24	34	46	63	90	120	286
12–15	48	67	92	128	173	246	551
15–18	95	128	180	242	346	474	1088
18–21	182	256	345	489	678	919	2089
21–24	360	480	680	930	1320	1846	4187
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SE, OC							
< 1.5	2	3	4	5	7	11	25
1.5–3	3	4	5	8	11	15	36
3–6	5	8	11	15	21	30	69
6–9	11	16	22	30	43	59	138
9–12	23	30	42	61	81	116	261
12–15	44	60	84	118	161	229	504
15–18	85	122	164	227	312	450	1002
18–21	168	231	326	441	607	835	1950
21–24	337	456	623	878	1232	1633	3805
Risk factors GA, AGE, CHD (acyanotic) plus SAS, MB, PE≤ 12 years							
< 1.5	2	2	3	5	6	9	22
1.5–3	2	3	5	6	10	13	31
3–6	5	7	10	13	19	25	61
6–9	10	13	19	27	36	50	117
9–12	19	26	37	51	69	99	229
12–15	39	52	73	103	140	199	446
15–18	73	102	149	194	272	385	889
18–21	149	204	276	400	535	734	1692
21–24	278	399	548	752	1039	1420	3357

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus SAS, MB, OC							
< 1.5	1	2	3	4	6	9	21
1.5–3	2	3	4	6	8	12	28
3–6	4	6	9	12	17	23	56
6–9	9	13	17	24	33	47	101
9–12	18	24	35	48	67	94	210
12–15	35	49	68	96	130	186	401
15–18	70	93	130	182	255	350	807
18–21	136	184	256	358	486	674	1554
21–24	263	362	496	695	974	1358	3128
Risk factors GA, AGE, CHD (acyanotic) plus SAS, MB, SE							
< 1.5	2	3	4	5	8	11	25
1.5–3	3	4	6	8	11	15	36
3–6	6	8	11	15	22	31	72
6–9	12	16	22	30	43	60	142
9–12	22	32	44	61	84	118	275
12–15	44	63	85	17	165	227	531
15–18	90	124	169	236	317	441	1026
18–21	173	242	337	454	631	866	2042
21–24	338	452	637	891	1221	1725	3934
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), PE≤ 12 years							
< 1.5	2	2	4	5	7	11	25
1.5–3	3	4	5	7	11	15	37
3–6	6	8	11	16	21	29	79
6–9	11	16	22	30	42	57	139
9–12	22	31	43	60	83	110	272
12–15	45	61	81	118	161	222	510
15–18	87	118	164	226	311	441	1002
18–21	168	229	317	438	615	853	1989
21–24	323	450	632	866	1209	1648	3892
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), OC							
< 1.5	2	3	4	5	7	10	23
1.5–3	2	3	5	7	10	14	33
3–6	5	7	10	14	20	28	64
6–9	10	15	20	27	39	54	127
9–12	21	29	39	57	75	105	247
12–15	40	55	76	109	149	205	472
15–18	79	109	154	206	293	395	929
18–21	155	210	289	406	559	782	1862
21–24	304	420	578	769	1105	1481	3536

continued

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), SE							
< 1.5	2	3	4	7	9	12	29
1.5–3	3	4	6	9	13	18	42
3–6	6	9	13	18	24	35	81
6–9	13	18	25	36	50	68	158
9–12	26	37	49	70	96	133	311
12–15	53	70	100	139	192	253	589
15–18	101	139	190	269	377	509	1199
18–21	194	270	366	510	712	988	2298
21–24	380	533	723	991	1442	1977	4472
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), MB							
< 1.5	2	2	4	5	7	10	25
1.5–3	3	3	5	7	10	14	34
3–6	5	7	10	14	20	28	67
6–9	10	15	20	29	39	55	127
9–12	21	29	40	56	74	108	251
12–15	40	56	80	108	156	205	483
15–18	80	110	115	215	295	415	961
18–21	158	218	305	425	577	794	1902
21–24	305	424	598	809	1135	1549	3633
Risk factors GA, AGE, CHD (acyanotic) plus MB, SE, OC, PE≤ 12 years							
< 1.5	1	2	3	4	6	8	21
1.5–3	2	3	4	6	9	12	30
3–6	5	6	9	12	18	24	58
6–9	9	13	18	25	35	48	112
9–12	18	26	35	49	67	92	219
12–15	36	50	70	94	132	187	421
15–18	71	96	136	184	268	350	828
18–21	137	188	262	363	505	707	1620
21–24	277	375	507	705	975	1359	3118
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), SE, OC, PE≤ 12 years							
< 1.5	2	2	4	5	7	10	24
1.5–3	2	4	5	7	10	14	34
3–6	5	7	10	14	20	27	64
6–9	11	15	21	28	40	56	128
9–12	20	29	41	55	77	107	243
12–15	42	57	80	109	152	210	477
15–18	80	111	155	216	298	407	925
18–21	159	217	303	413	572	801	1834
21–24	311	435	600	836	1114	1528	3471

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), MB, OC							
< 1.5	1	2	3	4	5	8	19
1.5–3	2	3	4	6	8	11	27
3–6	4	6	8	12	16	23	52
6–9	8	12	16	23	31	44	104
9–12	17	24	32	45	62	87	199
12–15	33	46	63	87	120	172	377
15–18	64	87	122	173	237	331	759
18–21	125	175	247	344	450	657	1470
21–24	249	339	482	654	918	1259	2929
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), MB, SE, PE≤ 12 years							
< 1.5	2	2	4	5	7	10	25
1.5–3	3	4	5	7	10	15	35
3–6	5	7	11	15	21	28	67
6–9	11	16	21	29	40	56	128
9–12	21	30	42	59	77	110	252
12–15	41	59	82	114	158	219	492
15–18	82	116	160	221	308	413	982
18–21	164	220	306	422	586	825	1878
21–24	321	438	596	836	1166	1612	3700
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), MB, SE, OC							
< 1.5	2	2	3	5	7	9	23
1.5–3	2	3	5	6	9	13	32
3–6	5	7	10	14	19	27	61
6–9	10	14	19	27	39	51	120
9–12	20	28	38	53	73	100	236
12–15	39	54	75	102	141	197	450
15–18	75	104	148	205	276	384	868
18–21	150	202	287	394	542	762	1769
21–24	285	404	561	746	1075	1468	3389
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SE, OC, PE≤ 12 years							
< 1.5	1	2	2	3	5	7	17
1.5–3	2	2	4	5	7	10	24
3–6	3	5	7	10	14	20	47
6–9	8	10	15	20	28	40	93
9–12	15	22	29	40	55	76	180
12–15	30	40	58	79	110	151	348
15–18	58	79	110	150	213	301	671
18–21	113	157	220	303	414	564	307
21–24	223	308	426	585	819	1127	2510

continued

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus SAS, MB, OC, PE≤ 12 years							
< 1.5	1	1	2	3	4	6	14
1.5–3	1	2	3	4	5	8	20
3–6	3	4	6	8	11	16	37
6–9	6	9	12	16	23	32	75
9–12	12	17	23	32	45	62	143
12–15	23	32	45	62	88	121	282
15–18	46	64	87	123	172	232	543
18–21	91	126	172	241	334	472	1095
21–24	177	246	328	482	659	902	2070
Risk factors GA, AGE, CHD (acyanotic) plus SAS, MB, SE, PE≤ 12 years							
< 1.5	1	2	2	4	5	7	18
1.5–3	2	3	4	5	7	10	24
3–6	4	5	8	10	15	20	47
6–9	8	11	15	21	29	40	93
9–12	15	21	29	41	55	79	183
12–15	30	41	59	83	113	155	364
15–18	58	82	116	156	214	299	689
18–21	114	157	219	311	438	589	1320
21–24	227	317	437	596	830	1141	2636
Risk factors GA, AGE, CHD (acyanotic) plus SAS, MB, SE, OC							
< 1.5	1	1	2	3	5	7	17
1.5–3	1	2	3	5	7	10	23
3–6	3	5	7	9	14	19	45
6–9	7	10	14	20	26	37	90
9–12	14	19	27	37	50	73	168
12–15	28	39	53	74	101	141	334
15–18	54	75	102	143	196	276	646
18–21	104	146	211	279	388	524	1233
21–24	208	280	396	548	747	1057	2484
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), OC, PE≤ 12 years							
< 1.5	1	1	2	3	5	7	16
1.5–3	1	2	3	5	7	9	22
3–6	3	5	7	9	13	18	44
6–9	7	9	14	19	25	35	85
9–12	13	19	27	37	51	71	160
12–15	27	38	51	72	101	139	315
15–18	54	76	105	142	200	269	632
18–21	105	144	200	278	389	529	1213
21–24	203	276	386	542	743	1041	2364

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), SE, PE≤ 12 years							
< 1.5	1	2	3	4	6	8	20
1.5–3	2	3	4	6	8	12	28
3–6	4	6	9	12	16	23	54
6–9	9	13	17	24	33	46	107
9–12	17	24	35	47	65	88	205
12–15	34	46	67	90	126	176	408
15–18	68	95	128	182	251	338	805
18–21	136	184	253	354	479	666	1539
21–24	261	359	497	699	951	1321	3064
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), SE, OC							
< 1.5	1	2	3	4	5	8	19
1.5–3	2	3	4	6	8	11	27
3–6	4	6	8	11	16	21	51
6–9	8	12	16	22	31	44	99
9–12	16	23	31	44	59	83	190
12–15	33	44	62	85	120	162	392
15–18	63	88	120	165	226	327	732
18–21	121	169	231	329	450	612	1404
21–24	238	326	467	642	869	1209	2851
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), MB, PE≤ 12 years							
< 1.5	1	2	2	3	5	7	16
1.5–3	1	2	3	5	7	9	23
3–6	4	5	7	10	13	19	45
6–9	7	10	14	19	27	36	85
9–12	14	20	27	38	53	72	164
12–15	27	38	53	74	104	141	322
15–18	55	76	107	143	198	281	636
18–21	107	146	206	277	392	545	1255
21–24	212	284	400	548	760	1040	2351
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), MB, OC							
< 1.5	1	1	2	3	4	6	14
1.5–3	1	2	3	4	6	8	21
3–6	3	4	6	9	12	17	41
6–9	6	9	13	18	25	34	80
9–12	13	18	25	34	49	67	160
12–15	26	36	50	68	95	130	299
15–18	49	70	95	134	183	245	585
18–21	99	136	188	257	351	504	1131
21–24	192	266	367	493	711	971	2216

continued

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), MB, SE							
< 1.5	1	2	3	4	6	8	19
1.5–3	2	3	4	5	8	11	26
3–6	4	6	8	12	16	22	52
6–9	8	11	16	23	31	44	100
9–12	17	23	32	45	62	85	195
12–15	33	45	62	85	122	167	394
15–18	64	87	120	172	242	335	735
18–21	129	172	241	330	467	639	1468
21–24	244	344	459	649	915	1241	2926
Risk factors GA, AGE, CHD (acyanotic) plus SEX (male), MB, SE, OC, PE≤ 12 years							
< 1.5	1	1	2	3	4	6	16
1.5–3	2	2	3	4	6	9	22
3–6	3	4	7	9	13	17	41
6–9	7	10	13	18	24	34	80
9–12	13	18	26	35	50	67	155
12–15	25	35	51	69	95	139	307
15–18	52	72	98	138	189	265	615
18–21	99	136	194	269	369	504	1159
21–24	197	266	378	535	705	1001	2293
Risk factors GA, AGE, CHD (acyanotic) plus SAS, MB, SE, OC, PE≤ 12 years							
< 1.5	1	1	1	2	3	4	11
1.5–3	1	1	2	3	4	6	16
3–6	2	3	4	6	9	12	29
6–9	5	7	9	13	18	25	58
9–12	9	13	19	26	35	49	116
12–15	19	26	37	49	70	98	221
15–18	37	51	69	97	136	190	433
18–21	72	100	140	189	269	368	847
21–24	143	192	271	378	505	711	1633
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), SE, OC, PE≤ 12 years							
< 1.5	1	1	2	2	3	5	12
1.5–3	1	2	2	4	5	7	18
3–6	2	4	5	7	10	14	35
6–9	5	7	10	15	21	29	67
9–12	11	15	20	29	40	57	133
12–15	21	30	40	58	77	110	253
15–18	43	58	80	109	153	216	499
18–21	84	115	163	219	304	424	966
21–24	161	220	302	427	592	836	1851

TABLE 18 Cost-effectiveness subgroup analysis for children with acyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), MB, OC, PE≤ 12 years							
< 1.5	1	1	1	2	3	4	11
1.5–3	1	1	2	3	5	6	14
3–6	2	3	4	6	8	11	28
6–9	4	6	8	11	17	23	53
9–12	8	12	17	23	32	45	106
12–15	17	23	32	47	63	88	203
15–18	34	47	66	90	125	171	393
18–21	66	91	125	173	242	343	785
21–24	130	179	244	344	478	646	1504
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), MB, SE, PE≤ 12 years							
< 1.5	1	1	2	3	4	5	13
1.5–3	1	2	2	4	6	8	18
3–6	3	4	5	7	11	15	35
6–9	6	8	11	15	22	30	67
9–12	11	16	22	29	42	57	137
12–15	22	30	43	58	81	114	259
15–18	43	60	82	117	154	218	501
18–21	85	117	162	227	313	429	975
21–24	162	233	314	436	613	843	1961
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), MB, SE, OC							
< 1.5	1	1	2	2	3	5	12
1.5–3	1	2	2	3	5	7	17
3–6	2	3	5	7	10	14	32
6–9	5	7	10	14	19	27	64
9–12	10	14	20	28	37	52	122
12–15	20	28	38	53	75	100	233
15–18	39	55	77	106	147	200	469
18–21	78	106	149	205	286	395	897
21–24	153	212	285	406	556	780	1741
Risk factors GA, AGE, CHD (acyanotic) plus SAS, SEX (male), MB, SE, OC, PE≤ 12 years							
< 1.5	0	1	1	1	2	3	8
1.5–3	1	1	1	2	3	4	11
3–6	1	2	3	5	7	9	23
6–9	3	5	7	9	13	18	42
9–12	7	9	3	18	25	36	83
12–15	14	18	26	35	51	70	159
15–18	26	36	50	70	101	136	310
18–21	52	71	98	138	193	269	608
21–24	100	141	197	272	390	525	1204

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY)

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (cyanotic)							
< 1.5	26	33	41	56	81	100	230
1.5–3	31	47	56	76	101	134	307
3–6	59	78	109	147	184	254	596
6–9	106	140	195	271	357	490	1127
9–12	200	259	368	526	710	946	2068
12–15	367	502	710	964	1319	1850	4364
15–18	761	1043	1421	1898	2627	3417	8903
18–21	1398	1959	2808	3711	5088	7090	17,071
21–24	2723	3848	5431	7525	9736	13,547	30,203
Risk factors GA, AGE, CHD (cyanotic) plus PE≤ 12 years							
< 1.5	21	26	30	40	51	66	155
1.5–3	24	31	44	54	71	95	217
3–6	41	59	76	97	131	177	398
6–9	73	100	127	173	245	354	771
9–12	133	173	255	352	481	658	1596
12–15	263	354	489	643	932	1275	2855
15–18	498	683	901	1309	1830	2408	5658
18–21	935	1275	1854	2450	3674	4641	11,031
21–24	1757	2544	3685	4894	7176	9817	20,326
Risk factors GA, AGE, CHD (cyanotic) plus OC							
< 1.5	20	22	30	37	46	68	133
1.5–3	23	28	38	52	65	90	196
3–6	39	49	61	91	120	163	387
6–9	68	94	125	159	230	311	674
9–12	124	173	235	303	436	607	1325
12–15	232	293	447	618	915	1199	2811
15–18	434	632	853	1247	1677	2277	5062
18–21	876	1202	1677	2192	3098	4609	10,263
21–24	1598	2338	3245	4437	5856	8621	20,345
Risk factors GA, AGE, CHD (cyanotic) plus SE							
< 1.5	21	30	33	43	59	77	177
1.5–3	28	35	45	63	82	115	252
3–6	47	63	86	112	152	209	470
6–9	86	114	150	215	299	393	942
9–12	153	210	294	416	557	752	1763
12–15	299	384	568	781	1061	1574	3458
15–18	570	772	1105	1436	2107	2761	6438
18–21	1154	1520	2129	2980	3954	5694	13,149
21–24	2206	2992	4117	5756	8126	11,306	26,446

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (cyanotic) plus MB							
< 1.5	19	24	30	39	51	67	139
1.5–3	25	29	39	47	68	89	190
3–6	39	53	67	89	130	174	371
6–9	69	90	127	170	248	312	746
9–12	128	178	238	330	443	595	1403
12–15	248	328	479	643	863	1208	2646
15–18	475	643	847	1227	1721	2363	5415
18–21	877	1244	1660	2514	3198	4587	10,222
21–24	1715	2427	3390	4690	6249	8577	21,675
Risk factors GA, AGE, CHD (cyanotic) plus SAS							
< 1.5	18	20	27	33	41	59	126
1.5–3	20	25	31	45	55	74	167
3–6	36	42	56	77	100	137	319
6–9	58	74	110	144	194	256	601
9–12	104	139	191	268	368	508	1097
12–15	198	278	384	539	716	1026	2227
15–18	396	517	749	982	1404	1910	4497
18–21	777	1003	1399	1976	2728	3728	8763
21–24	1390	2021	2724	3657	5346	7206	16,436
Risk factors GA, AGE, CHD (cyanotic) plus OC, PE≤ 12 years							
< 1.5	15	18	21	27	36	47	97
1.5–3	19	23	27	36	45	62	142
3–6	27	36	47	63	81	110	256
6–9	46	64	86	112	152	224	480
9–12	81	119	165	215	312	424	942
12–15	158	212	304	430	563	810	1820
15–18	305	430	589	815	1065	1614	3392
18–21	594	881	1121	1558	2221	3024	6798
21–24	1200	1667	2128	2985	4368	5784	12,620
Risk factors GA, AGE, CHD (cyanotic) plus SE, PE≤ 12 years							
< 1.5	18	20	24	35	42	55	119
1.5–3	21	26	33	47	55	75	164
3–6	35	45	57	77	106	142	305
6–9	59	76	111	152	194	278	606
9–12	110	149	198	276	366	533	1144
12–15	201	281	373	520	746	1003	2256
15–18	399	532	732	1093	1437	1882	4671
18–21	750	1074	1505	2048	2845	3581	8777
21–24	1444	1998	2865	3810	5434	7674	17,116

continued

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (cyanotic) plus SE, OC							
< 1.5	17	20	24	30	40	53	107
1.5–3	19	25	32	40	56	72	156
3–6	35	42	53	74	101	125	272
6–9	55	74	100	143	168	237	564
9–12	98	136	182	245	341	483	1121
12–15	181	249	354	497	687	923	2120
15–18	382	471	685	947	1270	1849	4004
18–21	673	966	1396	1894	2604	3592	7812
21–24	1418	1893	2678	3617	4828	6614	16,790
Risk factors GA, AGE, CHD (cyanotic) plus MB, PE≤ 12 years							
< 1.5	15	18	23	31	36	47	105
1.5–3	18	25	28	37	48	63	126
3–6	31	37	49	66	86	113	256
6–9	49	62	88	114	167	209	510
9–12	90	122	157	221	311	427	919
12–15	186	222	304	427	589	801	1758
15–18	321	435	581	818	1129	1515	3845
18–21	617	826	1137	1650	2203	2884	7095
21–24	1193	1615	2296	3131	4372	6066	13,923
Risk factors GA, AGE, CHD (cyanotic) plus MB, OC							
< 1.5	14	18	21	28	34	42	93
1.5–3	18	22	26	37	46	59	124
3–6	29	35	45	59	77	110	245
6–9	46	59	80	109	155	211	468
9–12	78	109	153	199	272	389	897
12–15	148	209	284	383	554	737	1707
15–18	291	395	542	768	1081	1427	3404
18–21	559	745	1111	1478	2098	2836	6706
21–24	1134	1448	2085	2935	3996	5194	13,168
Risk factors GA, AGE, CHD (cyanotic) plus MB, SE							
< 1.5	16	20	25	33	40	54	120
1.5–3	21	24	32	44	54	72	152
3–6	34	41	55	77	99	134	296
6–9	55	79	98	140	196	267	570
9–12	110	135	199	267	367	502	1203
12–15	189	268	379	498	679	919	2210
15–18	346	534	713	966	1362	1868	4544
18–21	686	937	1357	1906	2724	3750	8474
21–24	1426	1915	2604	3713	5213	6872	16,151

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤24	>24–26	>26–28	>28–30	>30–32	>32–34	≥35
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), PE≤ 12 years							
<1.5	17	22	26	33	40	53	113
1.5–3	19	26	33	41	54	74	151
3–6	33	43	56	70	97	129	293
6–9	54	71	100	126	192	246	581
9–12	96	131	178	245	348	502	1153
12–15	196	249	335	502	667	972	2144
15–18	353	507	735	983	1339	1760	4015
18–21	687	939	1394	1897	2551	3563	8578
21–24	1337	1918	2732	3549	4851	6713	16,047
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), OC							
<1.5	15	19	24	29	38	47	107
1.5–3	17	23	29	38	54	69	144
3–6	29	36	52	70	84	126	280
6–9	50	70	91	125	165	218	539
9–12	91	124	173	219	315	425	1014
12–15	173	228	317	441	636	857	1991
15–18	348	459	603	846	1145	1697	3723
18–21	656	839	1213	1643	2293	3251	7245
21–24	1249	1690	2405	3212	4752	6284	15,765
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), SE							
<1.5	19	22	30	33	48	59	136
1.5–3	23	28	35	47	63	80	171
3–6	36	47	64	81	112	154	332
6–9	66	85	116	161	221	291	679
9–12	126	166	222	311	410	597	1265
12–15	224	292	418	559	810	1073	2494
15–18	425	595	776	1112	1473	2050	4951
18–21	812	1209	1585	2239	3072	4218	9531
21–24	1629	2317	3100	4214	5744	7792	18,295
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), MB							
<1.5	16	20	23	30	39	52	104
1.5–3	20	23	30	41	51	70	155
3–6	33	41	50	70	88	127	285
6–9	55	68	94	127	172	240	535
9–12	92	130	177	233	325	453	1020
12–15	172	246	325	470	652	842	2069
15–18	348	476	624	876	1245	1831	4104
18–21	659	897	1252	1749	2496	3383	7590
21–24	1204	1786	2396	3416	4648	6262	14,784

continued

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (cyanotic) plus SAS, PE≤ 12 years							
< 1.5	14	17	19	24	32	41	82
1.5–3	17	19	25	31	41	55	110
3–6	25	33	44	57	70	95	215
6–9	40	53	77	104	136	169	408
9–12	71	100	132	181	252	356	800
12–15	137	190	261	339	494	654	1491
15–18	266	369	479	680	957	1377	2894
18–21	508	695	966	1322	1818	2486	6169
21–24	1032	1384	1867	2555	3564	5031	11,480
Risk factors GA, AGE, CHD (cyanotic) plus SAS, OC							
< 1.5	14	16	19	25	29	38	76
1.5–3	16	19	24	32	38	51	106
3–6	25	32	41	52	68	93	200
6–9	42	49	70	95	119	166	377
9–12	66	96	121	174	236	321	715
12–15	128	168	234	311	444	674	1485
15–18	240	327	467	615	848	1188	2767
18–21	451	662	873	1193	1699	2287	5270
21–24	876	1207	1760	2370	3261	4576	10,201
Risk factors GA, AGE, CHD (cyanotic) SAS, SE							
< 1.5	15	18	22	28	37	47	99
1.5–3	19	23	26	35	48	64	135
3–6	27	38	51	62	93	113	258
6–9	44	60	83	112	150	218	484
9–12	84	120	161	225	300	414	945
12–15	153	221	289	395	569	842	1765
15–18	313	421	602	799	1063	1469	3640
18–21	593	814	1168	1536	2155	3133	6701
21–24	1161	1601	2275	3156	4220	5783	12,350
Risk factors GA, AGE, CHD (cyanotic) plus SAS, MB							
< 1.5	14	16	19	23	29	38	81
1.5–3	16	20	24	30	38	54	111
3–6	26	29	40	54	67	88	201
6–9	42	52	69	100	122	174	383
9–12	68	95	128	177	239	331	692
12–15	130	172	247	340	468	618	1436
15–18	252	341	470	636	906	1190	2739
18–21	464	683	922	1266	1715	2383	5275
21–24	926	1299	1754	2399	3395	4589	10,165

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤24	>24–26	>26–28	>28–30	>30–32	>32–34	≥35
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male)							
<1.5	16	18	20	27	36	43	88
1.5–3	18	21	28	35	43	56	118
3–6	27	32	42	57	80	106	227
6–9	46	62	77	108	138	194	458
9–12	75	108	155	204	263	361	875
12–15	148	199	273	381	517	719	1686
15–18	274	383	520	747	1001	1391	3240
18–21	531	728	1026	1433	1981	2685	5983
21–24	1052	1445	1997	2791	3942	5135	11,757
Risk factors GA, AGE, CHD (cyanotic) plus SE, OC, PE≤ 12 years							
<1.5	13	16	19	24	29	41	82
1.5–3	16	19	24	29	36	53	108
3–6	24	32	39	48	68	91	193
6–9	40	50	70	92	127	178	377
9–12	69	96	132	163	226	322	746
12–15	135	173	244	323	440	624	1442
15–18	240	345	472	654	881	1249	2813
18–21	447	672	950	1240	1693	2376	5344
21–24	890	1303	1702	2418	3458	4533	9882
Risk factors GA, AGE, CHD (cyanotic) plus MB, OC, PE≤ 12 years							
<1.5	13	16	18	21	25	33	66
1.5–3	14	17	21	26	31	42	87
3–6	21	27	33	43	56	75	161
6–9	35	45	56	78	99	147	310
9–12	60	80	99	136	198	269	582
12–15	110	146	183	276	386	483	1154
15–18	204	274	359	533	718	1012	2119
18–21	387	546	695	1007	1405	1832	4092
21–24	732	1025	1434	2043	2681	3693	8584
Risk factors GA, AGE, CHD (cyanotic) plus MB, SE, PE≤ 12 years							
<1.5	14	16	20	25	31	39	80
1.5–3	16	20	25	30	39	51	109
3–6	23	29	41	49	72	95	200
6–9	42	52	74	91	128	167	407
9–12	76	95	127	184	235	329	785
12–15	139	187	250	365	493	662	1434
15–18	246	353	477	645	889	1255	2733
18–21	463	673	909	1302	1898	2459	5703
21–24	948	1347	1868	2307	3357	4926	10,837

continued

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (cyanotic) plus MB, SE, OC							
< 1.5	14	15	19	22	29	36	74
1.5–3	15	19	22	28	38	48	99
3–6	25	29	37	50	62	85	188
6–9	37	52	64	91	121	154	352
9–12	66	93	125	172	233	303	695
12–15	132	169	235	321	448	590	1335
15–18	226	319	421	623	819	1257	2608
18–21	427	603	870	1185	1597	2334	4933
21–24	864	1303	1619	2197	3228	4348	10,038
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), OC, PE≤ 12 years							
< 1.5	12	15	19	24	27	35	71
1.5–3	16	20	21	27	37	47	104
3–6	23	29	36	49	62	83	194
6–9	37	47	60	85	111	153	348
9–12	68	81	117	166	214	301	733
12–15	116	170	242	314	433	595	1361
15–18	236	299	425	613	796	1122	2550
18–21	440	643	878	1096	1580	2114	5151
21–24	844	1163	1612	2356	3199	4683	9667
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), SE, PE≤ 12 years							
< 1.5	14	18	21	26	36	44	93
1.5–3	17	20	28	34	45	62	129
3–6	26	35	43	60	79	106	233
6–9	45	61	76	107	149	210	422
9–12	80	113	147	203	281	376	870
12–15	150	206	286	399	518	772	1750
15–18	310	412	558	778	1017	1468	3502
18–21	563	802	1082	1449	1946	2878	6474
21–24	1104	1487	2214	2787	3918	5379	11,857
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), SE, OC							
< 1.5	15	18	20	25	32	41	84
1.5–3	18	20	24	31	43	56	120
3–6	24	31	44	55	75	100	221
6–9	44	58	69	100	138	176	388
9–12	80	102	142	186	250	354	790
12–15	137	187	257	339	522	682	1529
15–18	257	388	495	726	1007	1299	2951
18–21	510	698	952	1333	1887	2468	6024
21–24	1017	1366	1894	2516	3569	5097	11,692

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), MB, PE≤ 12 years							
< 1.5	14	15	19	22	30	36	74
1.5–3	15	19	24	28	40	50	98
3–6	23	29	37	46	70	88	186
6–9	36	49	68	86	119	170	371
9–12	68	94	122	179	222	300	719
12–15	124	172	234	314	445	574	1421
15–18	217	323	444	592	846	1246	2777
18–21	471	618	828	1164	1547	2329	5150
21–24	846	1224	1667	2189	3207	4407	10,484
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), MB, OC							
< 1.5	14	15	18	20	28	33	69
1.5–3	13	18	22	27	34	47	89
3–6	22	28	35	45	57	81	172
6–9	33	45	62	86	105	150	330
9–12	64	81	113	159	203	301	658
12–15	118	155	203	283	379	565	1246
15–18	205	306	386	563	745	1070	2334
18–21	417	585	783	1139	1489	2069	4455
21–24	816	1100	1514	2145	2829	3946	9494
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), MB, SE							
< 1.5	15	18	22	25	33	41	91
1.5–3	17	21	25	32	42	56	121
3–6	26	32	44	52	75	97	229
6–9	43	54	74	106	131	195	427
9–12	75	102	139	199	265	333	838
12–15	147	190	259	361	526	729	1473
15–18	269	375	517	719	1046	1372	3306
18–21	534	702	1024	1403	1900	2579	6244
21–24	1017	1436	2073	2746	3633	5329	11,816
Risk factors GA, AGE, CHD (cyanotic) plus SAS, OC, PE≤ 12 years							
< 1.5	12	14	15	18	24	30	54
1.5–3	13	14	19	23	29	36	82
3–6	18	22	29	36	48	62	137
6–9	27	36	47	64	87	113	249
9–12	50	67	83	123	163	214	520
12–15	92	117	153	231	291	407	978
15–18	167	227	295	445	578	775	1777
18–21	321	434	587	854	1165	1560	3466
21–24	571	834	1188	1615	2242	3040	7129

continued

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SE, PE≤ 12 years							
< 1.5	13	14	16	20	25	34	66
1.5–3	15	18	21	27	32	46	95
3–6	22	25	34	44	56	79	177
6–9	36	44	61	79	116	149	321
9–12	62	81	110	149	203	267	614
12–15	111	159	203	290	373	547	1210
15–18	225	282	407	526	796	1063	2391
18–21	400	575	751	1076	1511	1976	4476
21–24	794	1006	1482	2001	2843	4040	9330
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SE, OC							
< 1.5	13	15	17	20	24	33	59
1.5–3	15	17	20	25	34	41	88
3–6	20	25	32	42	54	74	162
6–9	34	44	55	74	102	135	307
9–12	60	73	99	141	180	265	564
12–15	104	135	191	267	359	529	1085
15–18	191	285	350	495	680	1029	2114
18–21	382	518	743	960	1324	1828	4125
21–24	773	1036	1363	1927	2787	3494	8013
Risk factors GA, AGE, CHD (cyanotic) plus SAS, MB, PE≤ 12 years							
< 1.5	12	13	16	19	22	28	59
1.5–3	15	16	20	22	31	36	75
3–6	19	23	30	36	50	63	145
6–9	30	35	52	67	85	117	260
9–12	49	65	89	118	151	222	500
12–15	96	120	166	246	312	457	991
15–18	166	226	335	409	610	873	1964
18–21	347	453	607	897	1176	1564	3644
21–24	592	882	1218	1650	2191	3018	7202
Risk factors GA, AGE, CHD (cyanotic) plus SAS, MB, OC							
< 1.5	11	15	15	18	21	28	55
1.5–3	12	15	17	23	27	37	67
3–6	18	22	28	35	46	58	128
6–9	29	36	45	60	79	115	240
9–12	48	62	85	115	159	217	450
12–15	82	118	157	224	285	446	828
15–18	165	204	281	403	564	770	1773
18–21	304	421	556	802	1072	1448	3289
21–24	588	774	1073	1503	2109	3073	6786

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤24	>24–26	>26–28	>28–30	>30–32	>32–34	≥35
Risk factors GA, AGE, CHD (cyanotic) plus SAS, MB, SE							
<1.5	13	13	18	20	26	33	61
1.5–3	14	16	21	26	33	43	86
3–6	21	26	32	40	56	75	170
6–9	36	46	58	71	103	137	319
9–12	57	77	102	140	190	265	597
12–15	107	148	192	259	365	503	1172
15–18	207	268	375	519	681	969	2286
18–21	395	527	779	961	1349	1897	4519
21–24	744	951	1344	1901	2614	3681	8691
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), PE≤ 12 years							
<1.5	12	13	17	21	24	32	61
1.5–3	15	17	20	24	31	41	91
3–6	21	25	32	42	53	70	159
6–9	32	41	54	73	101	130	328
9–12	57	76	106	137	186	240	621
12–15	105	141	180	274	362	482	1085
15–18	204	268	362	487	682	966	2170
18–21	363	515	690	945	1364	1843	4431
21–24	701	978	1394	1883	2710	3631	8513
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), OC							
<1.5	11	15	17	20	25	31	57
1.5–3	14	16	20	22	31	38	81
3–6	20	26	29	40	51	70	142
6–9	30	40	52	67	92	127	293
9–12	60	68	92	134	168	246	540
12–15	95	127	168	264	330	449	1025
15–18	177	239	356	438	657	847	2008
18–21	353	468	611	887	1172	1732	4139
21–24	667	915	1252	1619	2378	3084	7768
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), SE							
<1.5	13	14	17	23	28	35	71
1.5–3	15	18	22	28	35	48	102
3–6	21	27	37	49	61	83	180
6–9	38	49	62	90	115	157	342
9–12	63	91	110	160	215	298	716
12–15	125	154	232	309	431	542	1277
15–18	234	307	423	601	823	1101	2620
18–21	440	593	778	1101	1533	2179	4977
21–24	821	1146	1602	2157	3241	4375	9666

continued

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), SE							
< 1.5	13	13	16	19	23	31	66
1.5–3	15	15	20	25	28	39	81
3–6	18	24	29	39	52	67	152
6–9	31	40	53	71	95	126	278
9–12	55	72	93	128	163	242	545
12–15	93	130	183	234	361	443	1029
15–18	192	250	347	471	623	910	2196
18–21	339	494	666	966	1244	1682	4328
21–24	666	923	1289	1736	2471	3350	7827
Risk factors GA, AGE, CHD (cyanotic) plus MB, SE, OC, PE≤ 12 years							
< 1.5	11	12	16	18	22	25	54
1.5–3	12	16	18	23	28	35	78
3–6	18	21	27	35	48	62	135
6–9	29	36	48	61	84	115	256
9–12	46	65	82	115	154	200	490
12–15	87	121	157	212	303	425	923
15–18	160	217	312	399	593	770	1829
18–21	305	409	566	812	1107	1535	3573
21–24	617	831	1082	1525	2086	2986	6642
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), SE, OC							
< 1.5	12	14	17	19	26	30	60
1.5–3	14	17	19	23	29	39	85
3–6	19	25	31	40	53	65	144
6–9	32	42	52	70	96	129	281
9–12	49	71	97	127	176	240	525
12–15	101	130	183	249	337	453	1034
15–18	184	247	350	477	635	872	1986
18–21	355	469	671	896	1207	1738	3958
21–24	671	961	1308	1872	2399	3290	7119
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), MB, OC, PE≤ 12 years							
< 1.5	11	12	14	18	19	25	48
14	13	14	15	21	25	32	64
3–6	17	22	26	33	43	59	117
6–9	28	34	41	61	76	102	237
9–12	44	62	79	108	144	198	440
12–15	79	103	142	195	263	385	827
15–18	147	192	272	384	532	716	1714
18–21	272	394	554	770	987	1487	3173
21–24	547	711	1089	1432	2004	2644	6330

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤24	>24–26	>26–28	>28–30	>30–32	>32–34	≥35
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), MB, SE, PE≤ 12 years							
<1.5	12	13	16	20	24	31	63
1.5–3	14	16	20	25	32	42	86
3–6	20	24	32	41	54	71	158
6–9	34	44	55	75	93	128	286
9–12	55	73	100	141	172	245	550
12–15	95	136	186	261	349	496	1085
15–18	180	257	360	489	657	882	2104
18–21	379	479	652	925	1309	1804	4022
21–24	717	935	1279	1816	2555	3528	7756
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), MB, SE, OC							
<1.5	13	14	15	18	23	30	63
1.5–3	14	15	19	22	29	37	77
3–6	19	24	29	38	48	66	137
6–9	30	37	50	66	94	121	265
9–12	50	70	91	126	164	232	541
93	93	126	177	229	308	437	1019
15–18	174	238	338	446	604	819	1844
18–21	343	444	608	870	1176	1644	3900
21–24	609	891	1211	1547	2347	3143	7349
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SE, OC, PE≤ 12 years							
<1.5	11	12	15	16	19	23	46
1.5–3	11	14	16	20	24	32	60
3–6	15	20	25	30	38	49	112
6–9	25	31	41	50	72	94	211
9–12	40	59	72	97	127	171	399
12–15	76	92	131	178	247	333	751
15–18	136	178	244	324	475	673	1426
18–21	250	344	489	691	911	1215	2787
21–24	486	670	928	1241	1819	2490	5209
Risk factors GA, AGE, CHD (cyanotic) plus SAS, MB, OC, PE≤ 12 years							
<1.5	10	11	12	14	19	20	37
1.5–3	11	12	14	18	21	26	51
3–6	15	17	21	23	33	43	87
6–9	21	27	33	43	60	78	175
9–12	35	47	59	76	102	140	323
12–15	60	79	105	144	204	275	614
15–18	111	154	193	271	389	504	1185
18–21	206	281	369	535	723	1109	2399
21–24	386	550	699	1067	1411	2004	4500

continued

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (cyanotic) plus SAS, MB, SE, PE≤ 12 years							
< 1.5	11	12	14	17	18	23	47
1.5–3	11	14	18	20	25	31	58
3–6	17	21	25	30	44	51	111
6–9	26	32	41	54	69	95	205
9–12	40	54	71	98	121	178	401
12–15	77	97	143	189	249	346	798
15–18	135	186	256	341	451	639	1490
18–21	248	335	478	685	951	1300	2810
21–24	495	723	965	1299	1766	2496	5636
Risk factors GA, AGE, CHD (cyanotic) plus SAS, MB, SE, OC							
< 1.5	11	11	14	16	18	23	44
1.5–3	11	13	16	18	22	30	59
3–6	16	20	22	27	39	47	106
6–9	23	31	39	53	64	89	210
9–12	40	48	68	86	113	170	377
12–15	71	94	125	169	222	316	764
15–18	124	174	222	314	429	604	1435
18–21	229	330	479	595	825	1151	2775
21–24	459	608	871	1174	1592	2291	5415
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), OC, PE≤ 12 years							
< 1.5	11	11	13	15	19	24	42
1.5–3	12	13	16	18	23	29	58
3–6	15	18	23	29	37	47	107
6–9	24	29	38	52	63	84	200
9–12	38	48	67	91	117	160	345
12–15	69	91	115	164	232	307	675
15–18	127	179	237	316	467	596	1348
18–21	242	313	438	598	869	1171	2569
21–24	453	606	831	1173	1649	2286	5067
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), SE, PE≤ 12 years							
< 1.5	11	12	15	18	21	26	52
1.5–3	13	15	17	22	26	35	66
3–6	17	22	27	35	41	57	122
6–9	27	36	45	59	80	106	237
9–12	45	61	87	110	144	194	440
12–15	82	106	154	206	269	382	869
15–18	156	215	288	426	564	716	1801
18–21	315	406	569	768	1027	1409	3254
21–24	562	784	1064	1502	2085	2929	6774

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤24	>24–26	>26–28	>28–30	>30–32	>32–34	≥35
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), SE, OC							
<1.5	11	13	14	16	20	26	50
1.5–3	12	14	18	21	25	32	73
3–6	18	21	25	32	44	55	120
6–9	27	34	41	55	77	103	213
9–12	42	59	78	106	134	184	422
12–15	79	102	144	191	272	365	904
15–18	151	198	276	374	491	713	1573
18–21	269	369	509	731	971	1327	3051
21–24	521	688	1042	1409	1948	2579	6383
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), MB, PE≤ 12 years							
<1.5	10	12	12	15	19	23	44
1.5–3	11	14	15	19	23	27	59
3–6	17	19	23	31	37	49	106
6–9	23	29	39	48	64	83	190
9–12	38	51	69	94	127	169	356
12–15	65	89	120	173	236	315	722
15–18	128	174	255	309	432	601	1401
18–21	241	332	454	606	879	1187	2737
21–24	468	629	865	1202	1628	2194	4996
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), MB, OC							
<1.5	11	12	13	15	19	23	39
1.5–3	11	14	16	17	22	26	55
3–6	16	18	22	26	34	46	95
6–9	22	27	37	46	64	82	180
9–12	35	45	64	80	117	159	357
12–15	64	88	121	164	210	291	661
15–18	114	165	210	296	398	521	1236
18–21	222	303	412	551	757	1159	2482
21–24	437	579	778	1064	1570	2100	4715
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), MB, SE							
<1.5	11	12	15	17	22	26	51
1.5–3	13	14	16	19	27	32	65
3–6	17	22	26	35	42	55	121
6–9	26	33	44	60	74	106	218
9–12	45	57	80	108	142	189	426
12–15	81	106	142	188	279	373	907
15–18	147	191	275	387	544	726	1605
18–21	293	373	546	729	1038	1366	3240
21–24	538	791	1013	1381	2014	2696	6283

continued

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (cyanotic) plus SEX (male), MB, SE, OC, PE≤ 12 years							
< 1.5	10	12	13	17	18	22	43
1.5–3	12	13	16	17	21	28	56
3–6	15	18	23	30	36	45	98
6–9	24	31	37	48	59	87	182
9–12	37	49	67	81	117	154	341
12–15	62	84	119	153	210	332	676
15–18	121	164	218	318	422	582	1361
18–21	222	290	440	594	833	1077	2506
21–24	425	585	838	1176	1482	2155	4984
Risk factors GA, AGE, CHD (cyanotic) plus SAS, MB, SE, OC, PE≤ 12 years							
< 1.5	10	11	11	13	16	18	33
1.5–3	10	12	13	15	18	22	43
3–6	12	15	17	22	28	36	72
6–9	19	24	28	37	46	65	137
9–12	27	36	50	64	86	114	258
12–15	51	61	88	116	163	227	502
15–18	91	121	154	212	297	428	947
18–21	160	219	316	426	616	830	1891
21–24	315	430	603	843	1087	1505	3452
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), SE, OC, PE≤ 12 years							
< 1.5	10	10	11	14	16	18	35
1.5–3	11	12	14	17	20	24	49
3–6	13	16	20	23	30	40	84
6–9	19	24	31	41	54	72	152
9–12	31	43	53	74	95	136	310
12–15	54	73	93	132	171	243	555
15–18	108	133	181	236	328	485	1059
18–21	199	257	380	469	675	895	2141
21–24	350	496	680	932	1284	1815	3976
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), MB, OC, PE≤ 12 years							
< 1.5	10	10	12	14	15	18	32
1.5–3	10	11	14	15	17	21	39
3–6	13	14	18	21	27	33	69
6–9	17	22	26	33	47	56	120
9–12	26	35	44	58	78	106	249
12–15	46	60	77	111	141	198	439
15–18	86	111	155	210	282	374	853
18–21	152	206	276	369	541	756	1737
21–24	297	394	541	760	1052	1432	3231

TABLE 19 Cost-effectiveness subgroup analysis for children with cyanotic CHD (£000/QALY) *(continued)*

	GA (weeks)						
AGE (months)	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), MB, SE, PE≤ 12 years							
< 1.5	10	11	14	15	17	19	35
1.5–3	11	12	13	16	22	25	48
3–6	15	16	21	25	33	41	82
6–9	21	25	32	41	56	76	151
9–12	33	42	59	70	101	131	307
12–15	55	76	100	137	179	260	560
15–18	97	136	183	268	341	467	1082
18–21	195	260	359	499	684	923	2101
21–24	354	521	701	934	1367	1894	4298
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), MB, SE, OC							
< 1.5	10	10	11	13	15	18	35
1.5–3	10	12	15	15	20	24	46
3–6	14	16	18	24	29	38	73
6–9	19	25	30	39	51	65	145
9–12	29	39	51	68	87	122	277
12–15	54	67	91	124	174	222	499
15–18	93	130	175	240	335	429	1042
18–21	175	235	320	465	634	855	1962
21–24	348	469	610	898	1225	1737	3634
Risk factors GA, AGE, CHD (cyanotic) plus SAS, SEX (male), MB, SE, OC, PE≤ 12 years							
< 1.5	9	9	10	11	14	15	26
1.5–3	11	11	11	13	15	18	33
3–6	12	13	16	18	23	29	58
6–9	16	18	22	27	36	48	98
9–12	24	27	36	48	61	87	189
12–15	38	46	66	82	118	163	353
15–18	63	86	115	157	233	295	649
18–21	119	163	218	296	440	589	1342
21–24	223	308	425	603	876	1191	2654

Chapter 6

Summary of key results

The assessment group used the decision tree model developed in the original HTA journal publication[1] to assess the cost-effectiveness of prophylaxis with palivizumab, compared with no prophylaxis, for subgroups of pre-term infants and young children with different risk factors. This report covers four categories (children without CLD or CHD, with CLD, with acyanotic CHD and with cyanotic CHD), a total of 256 different combinations of risk factors, corresponding to 16,128 subgroups. Cost-effectiveness is defined as the ICER being less than or equal to the UK conventional cost-effectiveness threshold (a willingness-to-pay threshold of £30,000/QALY).

Compared with no prophylaxis, prophylaxis with palivizumab for children without CLD/CHD:

1. is not cost-effective for any GA and AGE if there are no more than one of the other risk factors that were considered in this report
2. is cost-effective for children < 6 weeks old at the start of the RSV season who had at least two of the other risk factors that were considered in this report and were born at 24 weeks GA or less
3. is cost-effective for children < 6 weeks old at the start of the RSV season who had at least three of the other risk factors that were considered in this report and were born at 26 weeks GA or less
4. is cost-effective for children < 3 months old at the start of the RSV season who had at least four of the other risk factors that were considered in this report and were born at 28 weeks GA or less
5. is cost-effective for children < 6 months old at the start of the RSV season who had at least five of the other risk factors that were considered in this report and were born at 26 weeks GA or less.

Compared with no prophylaxis, prophylaxis with palivizumab for pre-term infants with CLD:

1. is cost-effective for children < 9 months old at the start of the RSV season who had no other risk factors and were born at 24 weeks GA or less, for children < 6 months old at the start of the RSV season who had no other risk factors and were born at 28 weeks GA or less, for children < 3 months old at the start of the RSV season who had no other risk factors and were born at 32 weeks GA or less, and for children < 6 weeks old at the start of the RSV season who had no other risk factors and were born at 34 weeks GA or less.
2. is cost-effective for children < 9 months old at the start of the RSV season who had at least one of the other risk factors that were considered in this report and were born at 26 weeks GA or less
3. is cost-effective for children < 9 months old at the start of the RSV season who had at least two of the other risk factors that were considered in this report and were born at 28 weeks GA or less
4. is cost-effective for children < 12 months old at the start of the RSV season who had at least three of the other risk factors that were considered in this report and were born at 26 weeks GA or less

5. is cost-effective for children < 15 months old at the start of the RSV season who had at least four of the other risk factors that were considered in this report and were born at 24 weeks GA or less
6. is cost-effective for children < 18 months old at the start of the RSV season who had at least five of the other risk factors that were considered in this report and were born at 24 weeks GA or less.

Compared with no prophylaxis, prophylaxis with palivizumab for children with acyanotic CHD:

1. is cost-effective for children < 6 months old at the start of the RSV season who had no other risk factors and were born at 24 weeks GA or less, for children < 3 months old at the start of the RSV season who had no other risk factors and were born at 28 weeks GA or less, and for infants under 6 weeks old at the start of the RSV season who had no other risk factors and were born at 30 weeks GA or less.
2. is cost-effective for children < 6 months old at the start of the RSV season who had at least one of the other risk factors that were considered in this report and were born at 26 weeks GA or less
3. is cost-effective for children < 9 months old at the start of the RSV season who had at least two of the other risk factors that were considered in this report and were born at 24 weeks GA or less
4. is cost-effective for children < 12 months old at the start of the RSV season who had at least three of the other risk factors that were considered in this report and were born at 24 weeks GA or less
5. is cost-effective for children < 9 months old at the start of the RSV season who had at least four of the other risk factors that were considered in this report and were born at 30 weeks GA or less
6. is cost-effective for children < 15 months old at the start of the RSV season who had at least five of the other risk factors and were born at 24 weeks GA or less.

Compared with no prophylaxis, prophylaxis with palivizumab for children with cyanotic CHD:

1. is cost-effective for children < 6 weeks old at the start of the RSV season who had no other risk factors and were born at 24 weeks GA or less
2. is cost-effective for children < 3 months old at the start of the RSV season who had at least one of the other risk factors that were considered in this report and were born at 24 weeks GA or less
3. is cost-effective for children < 6 months old at the start of the RSV season who had at least two of the other risk factors that were considered in this report and were born at 24 weeks GA or less
4. is cost-effective for children < 9 months old at the start of the RSV season who had at least four of the other risk factors and were born at 24 weeks GA or less
5. is cost-effective for children < 12 months old at the start of the RSV season who had at least five of the other risk factors and were born at 24 weeks GA or less.

Credible intervals, cost-effectiveness planes and cost-effectiveness acceptability curves

Credible intervals were derived for one subset of the analysis for illustrative purposes only. The table chosen was acyanotic CHD children who have additional risk factors of GA, AGE and PE ≤ 12 years because this had three results around £20,000 per QALY within it. The mean values of the ICERs and their 95% credible intervals are listed in *Table 20*. The results showed

that for a point estimate of ICERs around £20,000/QALY, the upper 95% credible intervals may far exceeds the UK conventional cost-effective threshold (of £30,000/QALY), and that a point estimate of ICERs has to be < £8000/QALY if its upper 95% credible intervals falls within the UK conventional cost-effective threshold. However, we have some comments on interpretation of these further credible interval analysis results.

- The National Institute for Health and Clinical Excellence (NICE) usually considers the mean values of ICERs when making decisions,[5] i.e. the point estimates of the ICERs presented in the results section of this report.
- As shown in *Table 20*, the 95% credible intervals of the point estimate of £20,000/QALY is £8000/QALY to £66,000/QALY. The wide credible intervals can be explained by the fact that ICER does not follow a normal distribution (see *Figure 9* showing that the distribution has a long tail to the right side).
  - In fact, for this example, the probability of an ICER < £30,000/QALY is 0.74. The probability of ICER < £51,000/QALY is 0.95.

The incremental cost-effectiveness plane and the cost-effectiveness acceptability curve (CEAC) for prophylaxis with palivizumab compared with no prophylaxis for the three cases highlighted in *Table 20* are shown in *Figures 10–15*. These results show that, compared with no prophylaxis, palivizumab has a probability of 74%, 73% and 72% of having an ICER below £30,000/QALY for the three cases, respectively.

TABLE 20 Incremental cost-effectiveness ratios (95% credible intervals) for acyanotic CHD children who have other risk factors of GA, AGE, and PE ≤ 12 years

AGE (months)	GA (weeks)						
	≤ 24	> 24–26	> 26–28	> 28–30	> 30–32	> 32–34	≥ 35
< 1.5	5000 (0 to 27,000)	8 (2000 to 33,000)	10,000 (3000 to 40,000)	15,000 (5000 to 56,000)	20,000 (5000 to 56,000)	28,000 (8000 to 66,000)	67, 000 (31,000 to 246,000)
1.5–3	7000 (2000 to 33,000)	11,000 (3000 to 41,000)	15,000 (6000 to 54,000)	21,000 (9000 to 78,000(	29,000 (11,000 to 112,000)	40,000 (18,000 to 132,000)	93,000 (42,000 to 309,000)
3–6	15,000 (5000 to 57,000)	22,000 (9000 to 75,000)	30,000 (13,000 to 108,000)	41,000 (18,000 to 136,000)	56,000 (26,000 to 177,000)	78,000 (35,000 to 252,000)	180,000 (78,000 to 636,000)
6–9	30,000 (12,000 to 95,000)	42,000 (18,000 to 141,000)	56,000 (24,000 to 179,000)	79,000 (33,000 to 249,000)	110,000 (50,000 to 323,000)	154,000 (69,000 to 494,000)	347,000 (161,000 to 1,151,000)
9–12	58,000 (27,000 to 188,000)	80,000 (37,000 to 254,000)	113,000 (51,000 to 379,000)	157,000 (73,000 to 523,000)	217,000 (103,000 to 747,000)	302,000 (138,000 to 1,060,000)	706,000 (318,000 to 2,323,000)
12–15	116,000 (51,000 to 360,000)	158,000 (71,000 to 547,000)	221,000 (106,000 to 724,000)	299,000 (139,000 to 893,000)	417,000 (185,000 to 1,406,000)	584,000 (286,000 to 1,871,000)	1,330,000 (628,000 to 4,069,000)
15–18	225,000 (102,000 to 717,000)	309,000 (145,000 to 962,000)	421,000 (203,000 to1,286,000)	596,000 (273,000 to 1,906,000)	829,000 (389,000 to 2,411,000)	1,115,000 (499,000 to 3,673,000)	2,586,000 (1,223,000 to 9,295,000)
18–21	436,000 (203,000 to 1,571,000)	607,000 (298,000 to 1,955,00)	860,000 (373,000 to 2,960,000)	1,144,000 (529,000 to 3,820,000)	1,650,000 (775,000 to 4,974,000)	2,216,000 (1,091,000 to 6,390,000)	5,185,000 (2,468,000 to 15,218,000)
21–24	835,000 (379,000 to 2,773,000)	1,179,000 (544,000 to 3,433,000)	1,651,000 (802,000 to 5,112,000)	2,282,000 (1,090,000 to 6,820,000)	3,149,000 (1,412,000 to 9,553,000)	4,443,000 (2,112,000 to 12,917,000)	9,755,000 (4,440,000 to 36,592,000)

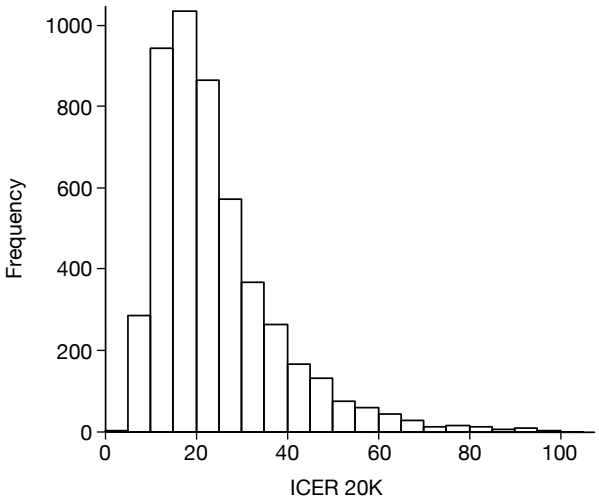


FIGURE 9 Distribution of the ICER with a mean value of £20,000/QALY.

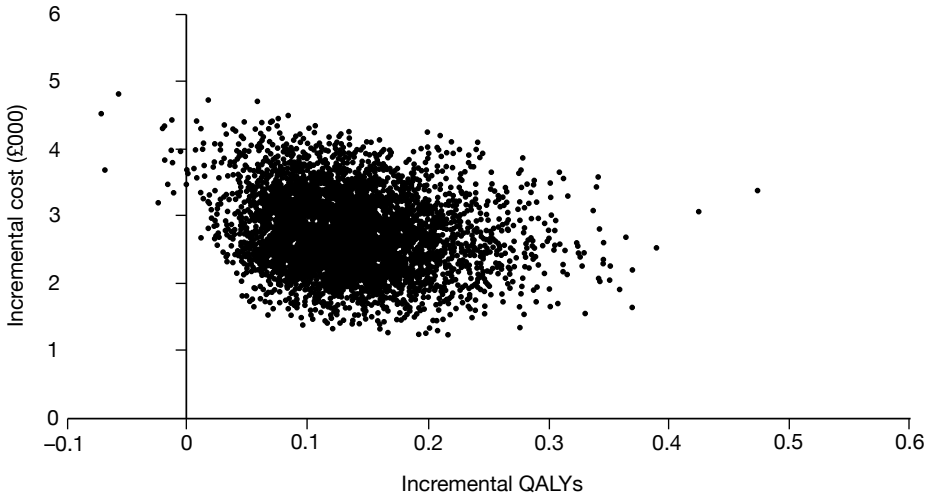


FIGURE 10 Incremental cost-effectiveness plane for prophylaxis with palivizumab compared with no prophylaxis for children < 6 weeks old at the start of the RSV season who had acyanotic CHD and were born at 32 weeks gestational age or less, and whose parental education is < 12 years.

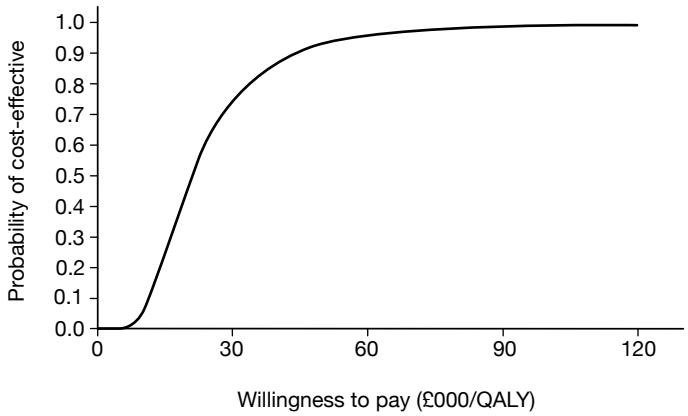


FIGURE 11 Cost-effectiveness acceptability curve for prophylaxis with palivizumab compared with no prophylaxis for children < 6 weeks old at the start of the RSV season who had acyanotic CHD and were born at 32 weeks gestational age or less, and whose parental education is < 12 years.

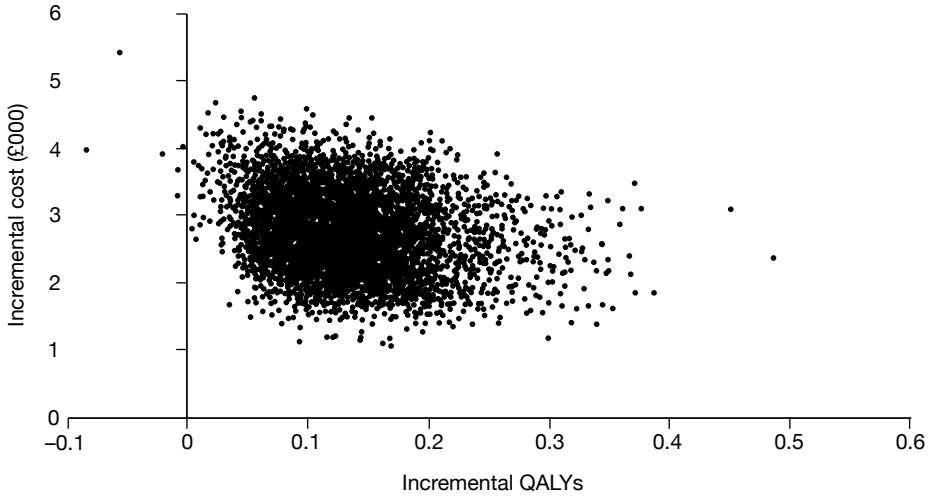


FIGURE 12 Incremental cost-effectiveness plane for prophylaxis with palivizumab compared with no prophylaxis for children < 3 months old at the start of the RSV season who had acyanotic CHD and were born at 30 weeks gestational age or less, and whose parental education is < 12 years.

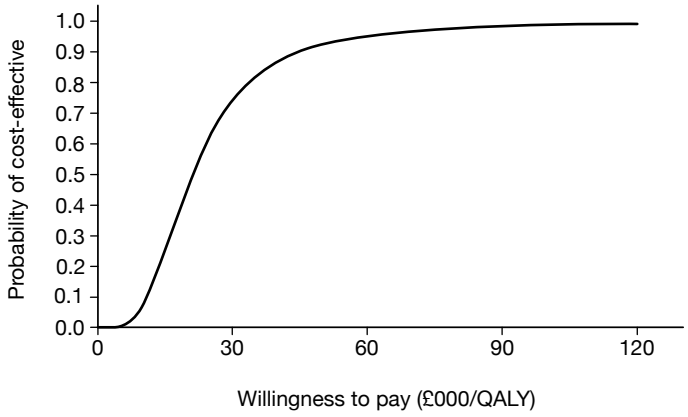


FIGURE 13 Cost-effectiveness acceptability curve for prophylaxis with palivizumab compared with no prophylaxis for children < 3 months old at the start of the RSV season who had acyanotic CHD and were born at 30 weeks gestational age or less, and whose parental education is < 12 years.

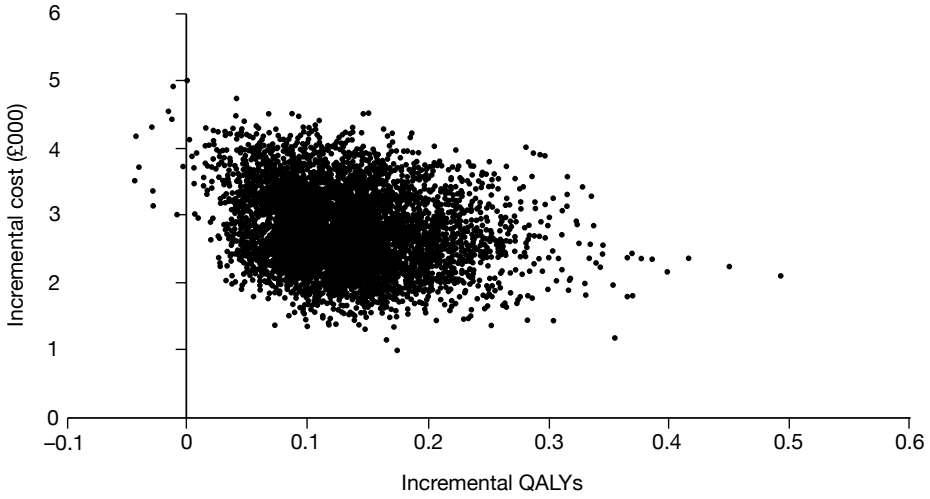


FIGURE 14 Incremental cost-effectiveness plane for prophylaxis with palivizumab compared with no prophylaxis for children < 6 months old at the start of the RSV season who had acyanotic CHD and were born at 26 weeks gestational age or less, and whose parental education is < 12 years.

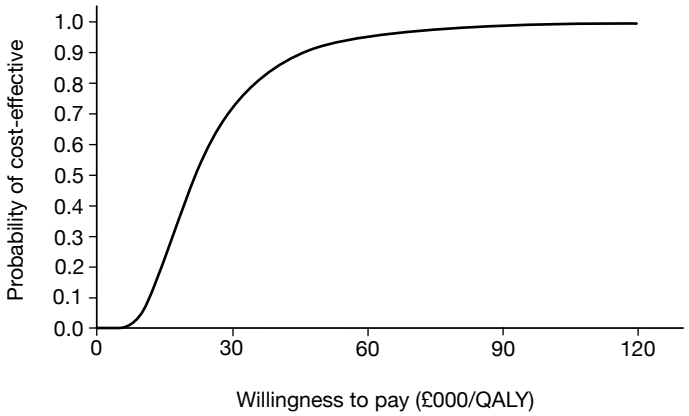


FIGURE 15 Cost-effectiveness acceptability curve for prophylaxis with palivizumab compared with no prophylaxis for children < 6 months old at the start of the RSV season who had acyanotic CHD and were born at 26 weeks gestational age or less, and whose parental education is < 12 years.

Chapter 7

Discussion

Statement of principal findings

For pre-term infants and young children without CLD/CHD, prophylaxis with palivizumab compared with no prophylaxis is not cost-effective for any GA and AGE subgroup if children had no more than one other risk factor. However, from the cost-effective spectra, we did find cost-effective GA and AGE subgroups for children without CLD/CHD who had at least two other risk factors that were considered in this report. For example, prophylaxis with palivizumab compared with no prophylaxis was found to be cost-effective for children < 6 weeks old at the start of the RSV season who had no CLD/CHD, but have at least two of SAS, male, MB, SE, OC or PE of high school or less (≤ 12 years) and were born at 24 weeks GA or less. Furthermore, the cost-effective subgroups would not include children who had no CLD/CHD and were > 9 months old at the start of the RSV season or had a GA of > 32 weeks.

The cost-effective spectra were also derived for children with CLD, children with acyanotic CHD and children with cyanotic CHD. Unlike in the case of children without CLD/CHD, the cost-effective subgroups were found for GA and AGE subgroups for children with CLD, children with acyanotic CHD, and children with cyanotic CHD, who had no SAS, were male, MB, SE, OC or PE of high school or less (≤ 12 years). These include children < 6 months old at the start of the RSV season who had CLD and were born at 28 weeks GA or less, children < 6 months old at the start of the RSV season who had acyanotic CHD and were born at 24 weeks GA or less, and children < 6 weeks old at the start of the RSV season who had cyanotic CHD and were born at 24 weeks GA or less. However, the cost-effective subgroups would not include children who had CLD and were > 21 months old at the start of the RSV season, children who had cyanotic CHD and were > 12 months old at the start of the RSV season, and children who had acyanotic CHD and were > 21 months old at the start of the RSV season.

Strengths and limitations of the assessment

The strengths of the assessment include the following aspects:

- This report presents a comprehensive subgroup analysis for cost-effectiveness of prophylaxis with palivizumab compared with no prophylaxis. It covers four categories of children (pre-term infants and young children without CLD/CHD, with CLD, with acyanotic CHD and with cyanotic CHD), 10 risk factors of RSV hospitalisation, and a total of 16,128 subgroups.
- Meta-analysis was applied to deriving RSV hospitalisation outcomes for gender, CHD, CLD, SAS, SE, and OC.

The assessment includes the following limitations.

- There was only one study contributing to the risk factors of AGE, GA, MB and PE of high school or less (≤ 12 years), which means that these estimates may not be as reliable as when more than one study is available. Therefore, one should be careful when interpreting the

cost-effectiveness for children with different combination of risk factors, especially for the cases that involve risk factors that were derived from only one study.

- Many of the included studies were relatively small and their quality was frequently poor, so it was difficult to know the accuracy of the inputs into the modelling. Therefore several of the meta-analyses had relatively high heterogeneity. The implication of this is that there will be a relatively high degree of uncertainty around the point estimates of cost-effectiveness. To illustrate this, an example estimate of CIs for point estimates was made.
- The definitions of risk factors were not available for most studies and may have varied between studies. This may have been contributing to the heterogeneity seen.
- The diagnosis of RSV was made by different methods in different included studies and unfortunately details were lacking in some of the included studies. This variation in methods will have introduced heterogeneity into the results.
- An additive rule was used to assess the impact of different risk factors. However, it is acknowledged that some of the risk factors will interact with each other to some extent, but this interaction will vary in magnitude and direction by risk factor. Univariate estimates of risk factor OR were used by preference as most studies did not report multivariate estimates. The implications of having interacting risk factors are unknown as they could potentially positively or negatively interact. This interaction is likely to reduce confidence in the point estimates of cost-effectiveness.
- Credible intervals of ICERs were derived for a small subset for illustrative purposes only. It should be noted that, on average, using more risk factors in the estimates will give wider CIs.
- Risk factors of lack of or minimal breastfeeding and family history of atopy were not included in the model due to lack of consistent information from primary studies, giving large amounts of heterogeneity in meta-analyses.
- Assessment of quality of life was derived from parental estimates so may not be accurate. It is not possible to derive accurate preference-based quality of life estimates from infants and young children.

Other relevant factors

There are several factors that may have impact on the evaluation of cost-effectiveness of prophylaxis with palivizumab compared with no prophylaxis. Firstly, other risk factors, such as lack of or minimal breastfeeding and family history of atopy, may further affect the probability that children will be hospitalised for RSV and this will influence the results of ICERs. However, inconsistent results for lack of or minimal breastfeeding and family history of atopy were observed. Without further work to identify relevant studies systematically and consider whether pooling of estimates would be appropriate, there is the risk of reducing the accuracy and precision of the model estimates to an unacceptable degree. Therefore, the risk factors of lack of or minimal breastfeeding and family history of atopy were not included in the model. However, the presence of the two additional risk factors may not play a very important role in making the clinical decision on whether to offer palivizumab prophylaxis to a particular baby as the model considered 10 risk factors.

Secondly, residual confounding is likely to influence the estimate of risk in the included observational studies. Where potential risk factors are associated with each other, the choice of factors entered into the model will influence the factors included in the final model.

Thirdly, vial wastage is an important problem with palivizumab. The drug is packaged in two vial sizes only and cannot be stored once opened. Infants and young children vary in weight so there will be an unknown amount of wastage. A vial sharing scheme was included in the model, using average weights reported in the trials.

Finally, it should be remembered that factors identified as important in one society will not necessarily have the same impact in other settings, for example, the impact of race and rural residence may be different in Northern Europe from Southern USA.

Chapter 8

Conclusions

Implications for service provision

Prophylaxis with palivizumab does not represent good value based on the current UK ICER threshold of £30,000/QALY when used unselectively in pre-term infants and children without CLD/CHD or children with CLD or CHD. This subgroup analysis does show that prophylaxis with palivizumab may be cost-effective for some subgroups, which have been identified in this report. In summary, the cost-effective subgroups for children who had no CLD/CHD have to contain at least two of the other risk factors examined here apart from GA and AGE. The cost-effective subgroups for children who had CLD/CHD do not necessarily have any other of the modelled risk factors apart from GA and AGE.

Suggested research priorities

Future research should be directed towards the following:

- to conduct much larger, better powered and better reported studies to derive better estimates of risk factor effect sizes
- to update the effect sizes of the risk factors used in the current model, especially age, GA, MB and PE as the values of these parameters were derived from only one study
- to systematically identify the effect size of other risk factors, such as lack of or minimal breastfeeding and family history of atopy and enter them into the model to estimate the effect of additional risk factors on the cost-effectiveness
- to derive credible intervals for the 16,128 point estimates of cost-effectiveness of prophylaxis with palivizumab compared with no prophylaxis.

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Contributions of authors

Dechao Wang – Data extraction, data analysis and synthesis, economic modelling, writing report.

Sue Bayliss, – Prepared and ran search strategies, wrote preliminary searching methods section.

Catherine Meads – Inclusion and exclusion of papers, data extraction and data checking, writing report, management and overview of project.

References

1. Wang D, Cummins C, Bayliss S, Sandercock J, Burls A. Immunoprophylaxis against respiratory syncytial virus (RSV) with palivizumab in children: a systematic review and economic evaluation. *Health Technol Assess* 2008;**12**(36).
2. Fjaerli HO, Farstad T, Bratlid D. Hospitalisations for respiratory syncytial virus bronchiolitis in Akershus, Norway, 1993–2000: a population-based retrospective study. *BMC Pediatrics* 2004;**4**(25):1–7.
3. Cabalka AK. Physiologic risk factors for respiratory viral infections and immunoprophylaxis for respiratory syncytial virus in young children with congenital heart disease. *Pediatr Infect Dis J* 2004;**23**:S41–S45.
4. British Medical Association and Royal Pharmaceutical Society of Great Britain. *British national formulary.* No. 59. London: BMA and RPS; 2010.
5. Anon. *Guide to the methods of technology appraisal*. London: National Institute for Health and Clinical Excellence; 2009.
6. Rietveld E, Vergouwe Y, Steyerberg EW, Huysman MW, de Groot R, Moll HA, *et al.* Hospitalization for respiratory syncytial virus infection in young children: development of a clinical prediction rule. *Pediatr Infect Dis J* 2006;**25**(3):201–7.
7. Duppenthaler A, Ammann RA, Gorgievski-Hrisoho M, Pfammatter JP, Aebi C. Low incidence of respiratory syncytial virus hospitalisations in haemodynamically significant congenital heart disease. *Arch Dis Child* 2004;**89**(10):961–5.
8. Feltes TF, Sondheimer HM. Palivizumab and the prevention of respiratory syncytial virus illness in pediatric patients with congenital heart disease. *Expert Opin Biol Ther* 2007;**7**(9):1471–80.
9. Kristensen K, Stensballe LG, Bjerre JV, Roth D, Fisker N, Kongstad T, *et al.* Risk factors for RSV hospitalisation in children with heart disease. *Arch Dis Child* 2009;**94**(10):785–9.
10. Simoes EA, Sondheimer HM, Top FH, Jr, Meissner HC, Welliver RC, Kramer AA, *et al.* Respiratory syncytial virus immune globulin for prophylaxis against respiratory syncytial virus disease in infants and children with congenital heart disease. The Cardiac Study Group. *J Pediatr* 1998;**133**(4):492–9.
11. Carbonell-Estrany X, Quero J, Bustos G, Cotero A, Domenech E, Figueras-Aloy J, *et al.* Rehospitalization because of respiratory syncytial virus infection in premature infants younger than 33 weeks of gestation: a prospective study. IRIS Study Group. *Pediatr Infect Dis J* 2000;**19**(7):592–7.
12. Feltes TF, Cabalka AK, Meissner HC, Piazza FM, Carlin DA, Top FH, Jr, *et al.* Palivizumab prophylaxis reduces hospitalization due to respiratory syncytial virus in young children with hemodynamically significant congenital heart disease. *J Pediatr* 2003;**143**(4):532–40.
13. The IMpact-RSV Study Group. Palivisumab, a humanised respiratory syncytial virus monoclonal antibody, reduces hospitalisation from respiratory syncytial virus infection in high-risk infants. *Pediatrics* 1998;**102**(3):531–7.
14. Carbonell-Estrany X, Quero J, IRIS Study Group. Hospitalization rates for respiratory syncytial virus infection in premature infants born during two consecutive seasons. *Pediatr Infect Dis J* 2001;**20**(9):874–9.

15. Eriksson M, Bennet R, Rotzen-Ostlund M, von Sydow M, Wirgart BZ. Population-based rates of severe respiratory syncytial virus infection in children with and without risk factors, and outcome in a tertiary care setting. *Acta Paediatr* 2002;**91**(5):593–8.

16. Figueras-Aloy J, Carbonell-Estrany X, Quero J, IRIS Study Group. Case-control study of the risk factors linked to respiratory syncytial virus infection requiring hospitalization in premature infants born at a gestational age of 33–35 weeks in Spain. *Pediatr Infect Dis J* 2004;**23**(9):815–20.

17. Simoes EA, Carbonell-Estrany X, Fullarton JR, Liese JG, Figueras-Aloy J, Doering G, *et al.* A predictive model for respiratory syncytial virus (RSV) hospitalisation of premature infants born at 33–35 weeks of gestational age, based on data from the Spanish FLIP Study. *Respir Res* 2008;**9**:78.

18. Figueras-Aloy J, Carbonell-Estrany X, Quero-Jimenez J, Fernandez-Colomer B, Guzman-Cabanas J, Echaniz-Urcelay I, *et al.* FLIP-2 Study: risk factors linked to respiratory syncytial virus infection requiring hospitalization in premature infants born in Spain at a gestational age of 32 to 35 weeks. *Pediatr Infect Dis J* 2008;**27**(9):788–93.

19. Frogel M, Nerwen C, Cohen A, VanVeldhuisen P, Harrington M, Boron M. Prevention of hospitalization due to respiratory syncytial virus: results from the Palivizumab Outcomes Registry. *J Perinatol* 2008;**28**(7):511–17.

20. Grimwood K, Cohet C, Rich FJ, Cheng S, Wood C, Redshaw N, *et al.* Risk factors for respiratory syncytial virus bronchiolitis hospital admission in New Zealand. *Epidemiol Infect* 2008;**136**(10):1333–41.

21. Law BJ, Langley JM, Allen U, Paes B, Lee DS, Mitchell I, *et al.* The Pediatric Investigators Collaborative Network on infections in Canada study of predictors of hospitalization for respiratory syncytial virus infection for infants born at 33 through 35 completed weeks of gestation. *Pediatr Infect Dis J* 2004;**23**(9):806–14.

22. Liese J. Comment on the Austrian consensus paper on prophylaxis of RSV infection with palivizumab and post-RSV respiratory tract disease. *Monatsschrift fur Kinderheilkunde* 2008;**156**(4):384.

23. Nielsen HE, Siersma V, Andersen S, Gahrn-Hansen B, Mordhorst CH, Norgaard-Pedersen B, *et al.* Respiratory syncytial virus infection--risk factors for hospital admission: a case-control study. *Acta Paediatr* 2003;**92**(11):1314–21.

24. Rossi GA, Medici MC, Arcangeletti MC, Lanari M, Merolla R, Paparatti UD, *et al.* Risk factors for severe RSV-induced lower respiratory tract infection over four consecutive epidemics. *Eur J Pediatr* 2007;**166**(12):1267–72.

25. Liese JG, Grill E, Fischer B, Roeckl-Wiedmann I, Carr D, Belohradsky BH. Incidence and risk factors of respiratory syncytial virus-related hospitalizations in premature infants in Germany. *Eur J Pediatr* 2003;**162**(4):230–6.

26. Greenough A, Alexander J, Burgess S, Bytham J, Chetcuti PA, Hagan J, *et al.* Health care utilisation of prematurely born, preschool children related to hospitalisation for RSV infection. *Arch Dis Child* 2004;**89**(7):673–8.

27. Yount LE, Mahle WT, Yount LE, Mahle WT. Economic analysis of palivizumab in infants with congenital heart disease. *Pediatrics* 2004;**114**(6):1606–11.

28. Nuijten MJC, Wittenberg W, Lebmeier M. Cost effectiveness of palivizumab for respiratory syncytial virus prophylaxis in high-risk children: A UK analysis. *Pharmacoeconomics* 2007;**25**(1):55–71.

Appendix 1

Literature search strategies

Clinical effectiveness

Database: Cochrane Library (Wiley) 2009 Issue 3

#1 respiratory next syncytial
#2 rsv
#3 bronchiolitis
#4 MeSH descriptor Bronchiolitis, Viral, this term only
#5 MeSH descriptor Respiratory Syncytial Virus, Human, this term only
#6 (#1 OR #2 OR #3 OR #4 OR #5)
#7 immunoprophylaxis
#8 monoclonal next _ntibody*
#9 MeSH descriptor Antibodies, Monoclonal explode all trees
#10 palivizumab
#11 synagis
#12 (#7 OR #8 OR #9 OR #10 OR #11)
#13 (#6 AND #12)
#14 <nothing>, from 2007 to 2009
#15 (#13 AND #14)

Database: Ovid MEDLINE® In-Process & Other Non-Indexed Citations 3 August 2009

1. respiratory syncytial virus.mp.
2. bronchiolitis.mp. or exp Bronchiolitis, Viral/
3. palivizumab.mp.
4. monoclonal antibod$.mp.
5. synagis.mp.
6. exp Immunotherapy/or immunoprophylaxis.mp.
7. or/1-2
8. or/3-6
9. 7 and 8
10. limit 9 to yr="2007 – 2009"

Database: Ovid MEDLINE® 1950 to week 4 July 2009

1. exp Respiratory Syncytial Virus, Human/or rsv.mp.
2. respiratory syncytial virus.mp.
3. bronchiolitis.mp. or exp Bronchiolitis, Viral/
4. or/1-3
5. palivizumab.mp.
6. monoclonal _ntibody$.mp.
7. exp Antibodies, Monoclonal/
8. synagis.mp.
9. exp Immunotherapy/or immunoprophylaxis.mp.
10. or/5-9
11. 4 and 10

12. (systematic adj review$).tw.
13. (data adj synthesis).tw.
14. (published adj studies).ab.
15. (data adj extraction).ab.
16. meta-analysis/
17. meta-analysis.ti.
18. comment.pt.
19. letter.pt.
20. editorial.pt.
21. animal/
22. human/
23. not (21 and 22)
24. 11 not (18 or 19 or 20 or 23)
25. or/12-17
26. 24 and 25
27. limit 26 to yr="2007 – 2009"

Database: Ovid MEDLINE® 1950 to week 4 July 2009

1. exp Respiratory Syncytial Virus, Human/or rsv.mp.
2. respiratory syncytial virus.mp.
3. bronchiolitis.mp. or exp Bronchiolitis, Viral/
4. or/1-3
5. palivizumab.mp.
6. monoclonal _ntibody$.mp.
7. exp Antibodies, Monoclonal/
8. synagis.mp.
9. exp Immunotherapy/or immunoprophylaxis.mp.
10. or/5-9
11. 4 and 10
12. randomized controlled trial.pt.
13. controlled clinical trial.pt.
14. randomized controlled trials.sh.
15. random allocation.sh.
16. double blind method.sh.
17. single-blind method.sh.
18. or/12-17
19. (animals not human).sh.
20. 18 not 19
21. clinical trial.pt.
22. (clin$adj25 trial$).ti,ab.
23. ((singl$or doubl$or trebl$or tripl$) adj25 (blind$or mask$)).ti,ab.
24. placebos.sh.
25. placebo$.ti,ab.
26. random$.ti,ab.
27. research design.sh.
28. or/21-27
29. 28 not 19
30. 29 not 20
31. comparative study.sh.
32. exp evaluation studies/
33. follow up studies.sh.
34. prospective studies.sh.

35. (control$or _ntibody_ve$or volunteer$).ti,ab.
36. or/31-35
37. not 19
38. 20 or 30 or 38
39. 11 and 39
40. limit 40 to yr="2007 – 2009"

Database: EMBASE 1980 to week 31 2009

1. exp Respiratory Syncytial Pneumovirus/or rsv.mp. or exp Bronchiolitis/
2. bronchiolitis.mp.
3. respiratory syncytial virus.mp.
4. or/1-3
5. palivizumab.mp. or exp PALIVIZUMAB/
6. exp Monoclonal Antibody/or monoclonal _ntibody$.mp.
7. synagis.mp.
8. immunoprophylaxis.mp. or exp IMMUNOPROPHYLAXIS/
9. or/5-8
10. 4 and 9
11. "meta-analysis"/
12. metaanalys$.ti,ab.
13. meta-analys$.ti,ab.
14. meta analys$.ti,ab.
15. cochrane.ti,ab,de.
16. (review$or overview$).ti,ab.
17. (synthes$adj3 (literature$or research$or study or studies or data)).mp.
18. pooled analy$.ti,ab.
19. (systematic$adj2 review$).ti,ab.
20. or/11-19
21. 10 and 20
22. 19 or 11
23. 10 and 22
24. limit 23 to yr="2007 – 2009"

Database: EMBASE 1980 to week 31 2009

1. exp Respiratory Syncytial Pneumovirus/or rsv.mp. or exp Bronchiolitis/
2. bronchiolitis.mp.
3. respiratory syncytial virus.mp.
4. or/1-3
5. palivizumab.mp. or exp PALIVIZUMAB/
6. exp Monoclonal Antibody/or monoclonal _ntibody$.mp.
7. synagis.mp.
8. immunoprophylaxis.mp. or exp IMMUNOPROPHYLAXIS/
9. or/5-8
10. 4 and 9
11. randomized controlled trial/
12. exp clinical trial/
13. exp controlled study/
14. or/11-12
15. 10 and 14
16. limit 15 to yr="2007 – 2009"

Database: CINAHL (EBSCO Host) 1982 to 4 August 2009

Terms used: RSV or respiratory syncytial virus or bronchiolitis or palivizumab or synagis or immunoprophylaxis or monoclonal _ntibody* random* or trial*

Database: Science Citation Index (Web of Science) 1900 to 4 August 2009

Terms used: RSV or respiratory syncytial virus or bronchiolitis or palivizumab or synagis or immunoprophylaxis or monoclonal _ntibody* or random* or trial*

Cost-effectiveness/modelling

Database: Ovid MEDLINE® 1950 to week 5 July 2009

1. exp Respiratory Syncytial Virus, Human/or rsv.mp.
2. respiratory syncytial virus.mp.
3. bronchiolitis.mp. or exp Bronchiolitis, Viral/
4. or/1-3
5. palivizumab.mp.
6. monoclonal _ntibody$.mp.
7. exp Antibodies, Monoclonal/
8. synagis.mp.
9. exp Immunotherapy/or immunoprophylaxis.mp.
10. or/5-9
11. 4 and 10
12. economics/
13. exp "costs and cost analysis"/
14. cost of illness/
15. exp health care costs/
16. economic value of life/
17. exp economics medical/
18. exp economics hospital/
19. economics pharmaceutical/
20. exp "fees and charges"/
21. (econom$or cost or costs or costly or costing or price or pricing or pharmacoeconomic$).tw.
22. (expenditure$not energy).tw.
23. (value adj1 money).tw.
24. budget$.tw.
25. or/12-24
26. 11 and 25
27. limit 26 to yr="2007 –Current"

Database: Ovid MEDLINE® 1950 to week 5 July 2009

1. exp Respiratory Syncytial Virus, Human/or rsv.mp.
2. respiratory syncytial virus.mp.
3. bronchiolitis.mp. or exp Bronchiolitis, Viral/
4. or/1-3
5. palivizumab.mp.
6. monoclonal _ntibody$.mp.)
7. exp Antibodies, Monoclonal/
8. synagis.mp.
9. exp Immunotherapy/or immunoprophylaxis.mp.
10. or/5-9

11. 4 and 10
12. decision support techniques/
13. markov.mp.
14. exp models economic/
15. decision analysis.mp.
16. cost benefit analysis/
17. or/12-16
18. 11 and 17
19. 4 and 17
20. 18 or 19
21. limit 20 to yr="2007 –Current"

Database: Ovid MEDLINE® 1950 to week 5 July 2009

1. exp Respiratory Syncytial Virus, Human/or rsv.mp.
2. respiratory syncytial virus.mp.
3. bronchiolitis.mp. or exp Bronchiolitis, Viral/
4. or/1-3
5. palivizumab.mp.
6. monoclonal _ntibody$.mp.
7. exp Antibodies, Monoclonal/
8. synagis.mp.
9. exp Immunotherapy/or immunoprophylaxis.mp.
10. or/5-9
11. 4 and 10
12. quality of life/
13. life style/
14. health status/
15. health status indicators/
16. or/12-15
17. 4 and 16
18. limit 17 to yr="2007 –Current"

Database: EMBASE 1980 to week 32 2009

1. exp Respiratory Syncytial Pneumovirus/or rsv.mp. or exp Bronchiolitis/
2. bronchiolitis.mp.
3. respiratory syncytial virus.mp.
4. or/1-3
5. palivizumab.mp. or exp PALIVIZUMAB/
6. exp Monoclonal Antibody/or monoclonal _ntibody$.mp.
7. synagis.mp.
8. immunoprophylaxis.mp. or exp IMMUNOPROPHYLAXIS/
9. or/5-8
10. 4 and 9
11. cost benefit analysis/
12. cost effectiveness analysis/
13. cost minimization analysis/
14. cost utility analysis/
15. economic evaluation/
16. (cost or costs or costed or costly or costing).tw.
17. (economic$or pharmacoeconomic$or price$or pricing).tw.
18. (technology adj assessment$).tw.
19. or/11-18

20. 10 and 19
21. limit 20 to yr="2007 –Current"

Database: EMBASE 1980 to week 32 2009

1. exp Respiratory Syncytial Pneumovirus/or rsv.mp. or exp Bronchiolitis/
2. bronchiolitis.mp.
3. respiratory syncytial virus.mp.
4. or/1-3
5. quality of life.mp. or exp "Quality of Life"/
6. health status.mp. or exp Health Status/
7. or/5-6
8. 4 and 7
9. lung transplant$.mp.
10. 8 not 9
11. limit 10 to yr="2007 –Current"

Database: EMBASE 1980 to week 32 2009

1. exp Respiratory Syncytial Pneumovirus/or rsv.mp. or exp Bronchiolitis/
2. bronchiolitis.mp.
3. respiratory syncytial virus.mp.
4. or/1-3
5. palivizumab.mp. or exp PALIVIZUMAB/
6. exp Monoclonal Antibody/or monoclonal _ntibody$.mp.
7. synagis.mp.
8. immunoprophylaxis.mp. or exp IMMUNOPROPHYLAXIS/
9. or/5-8
10. 4 and 9
11. decision support technique$.mp.
12. exp statistical model/or markov model$.mp.
13. exp "cost effectiveness analysis"/or economic model$.mp.
14. decision analysis.mp.
15. or/11-14
16. 10 and 15
17. limit 16 to yr="2007 –Current"

Additional searches:

Prognosis

Database: Ovid MEDLINE® 1950 to week 4 July 2009

1. exp Respiratory Syncytial Virus, Human/or rsv.mp.
2. respiratory syncytial virus.mp.
3. bronchiolitis.mp. or exp Bronchiolitis, Viral/
4. or/1-3
5. prognosis.mp. or exp Prognosis/
6. outcome$.mp.
7. risk$.mp. or exp Risk Factors/
8. hospitali?ation.mp.
9. exp Follow-Up Studies/or follow-up.mp.
10. complication$.mp.
11. exp Cohort Studies/or cohort$.mp.
12. or/5-10

13. 4 and 12
14. 11 and 13
15. limit 14 to yr="2007 – 2009"

Hospitalisation

Database: Ovid MEDLINE® 1950 to week 4 July 2009

1. exp Respiratory Syncytial Virus, Human/or rsv.mp.
2. respiratory syncytial virus.mp.
3. bronchiolitis.mp. or exp Bronchiolitis, Viral/
4. or/1-3
5. hospitali?ation.mp.
6. 4 and 5
7. limit 6 to yr="2007 – 2009"

Appendix 2

Table of excluded studies with rationale

Below are listed studies that were nearly included, with reasons for exclusion. The remaining studies were excluded because they did not report any of the listed subgroups.

Study	Reason for exclusion
Aujard Y, Fauroux B. Risk factors for severe respiratory syncytial virus infection in infants. *Respir Med* 2002;**96**:S9–S14	Review
Bloemers B, van Furth M, Weijerman ME, Gemke RJ, Broers CJ, van den Ende, *et al.* Down syndrome: a novel risk factor for respiratory syncytial virus bronchiolitis – a prospective birth-cohort study. *Pediatrics* 2007;**120**(4):1076–81	All children with Down's syndrome
Boyce TG, Mellen BG, Mitchel EF, Wright PF, Griffin MR. Rates of hospitalisation for respiratory syncytial virus infection among children in Medicaid. *J Pediatr* 2000;**137**:865–70	Reported incidence rate ratios and could not convert to ORs
Breese Hall C, Weinberg GA, Iwane MK, Blumkin AK, Edwards KM, Staat MA, *et al.* The burden of respiratory syncytial virus infection in young children. *N Engl J Med* 2009;**360**(6):588–98	No CIs given for ORs in outcomes where ORs and CIs available from other studies
Cabalka AK. Physiologic risk factors for respiratory viral infections and immunoprophylaxis for respiratory syncytial virus in young children with congenital heart disease. *Pediatr Infect Dis J* 2004;**23**(1):S41–S5	Review
Carbonell-Estrany X, Figueras-Aloy J, IRIpVRS Study Group. Identifying risk factors for severe respiratory syncytial virus among infants born after 33 through 35 completed weeks of gestation. *Pediatr Infect Dis J* 2004;**23**(11):S193–S201	PICNIC and FLIP studies already included
Carbonell-Estrany X, Bont L, Doerling G, Gouyon J-B, Lanari M. Clinical relevance of prevention of respiratory syncytial virus lower respiratory tract infection in pre-term infants born between 33 and 35 weeks gestational age. *Eur J Clin Microbiol Infect Dis* 2008;**27**:891–9	Review
Clark SJ, Beresford MW, Subhedar NV, Shaw NJ. Respiratory syncytial virus infection in high risk infants and the potential impact of prophylaxis in a United Kingdom cohort. *Arch Dis Child* 2000;**83**:313–6	No subgroup results
Doering G, Guselnleitner W, Belohradsky BH, Burdach S, Resch B, Liese JG. The risk of respiratory syncytial virus-related hospitalisation in preterm infants of 29 to 35 weeks gestational age. *Pediatr Infect Dis J* 2006;**25**(12):1188–91	Duplicates Liese *et al.*[25] study
Duppenthaler A, Ammann RA, Gorgievski-Hrisoho M, Pfammatter JP, Aebi C. Low incidence of respiratory syncytial virus hospitalisations in haemodynamically significant congenital heart disease. *Arch Dis Child* 2003;**89**:961–5	No suitable subgroup results
Everard ML. The relationship between respiratory syncytial virus infection and the development of wheezing and asthma in children. *Curr Opin Allergy Clin Immunol* 2006;**6**(1):56–61	Review
Fjaerli HO, Farstad T, Bratlid D. Hospitalisations for respiratory syncytial virus bronchiolitis in Akerhus, Norway, 1993–2000: a population-based retrospective study. *BMC Pediatr* 2004;**4**(25):1–7	No suitable subgroup results
Greenough A, Alexander J, Boit P, Boorman J, Burgess S, Burke A, *et al.* School-age outcome of hospitalisation with respiratory syncytial virus infection of prematurely born infants. *Thorax* 2009;**64**:490–5	No suitable subgroup results
Grimaldi M, Cornet B, Milou C, Gouyon JB. Etude prospective regionale d'une epidemie de bronchiolites a virus respiratoire syncytial (VRS). *Arch Pediatri* 2002;**9**:572–80	Relevant subgroups not given
Groothuis JR, Gutierrez KM, Lauer BA. Respiratory syncytial virus infection in children with bronchopulmonary dysplasia. *Pediatrics* 1988;**82**:199–203	Study too small to use (total $n = 18$ for risk factors)
Henderson J, Hilliard TN, Sherriff A, Stalker D, Al Shammari N, Thomas HM, *et al.* Hospitalisation for RSV bronchiolitis before 12 months of age and subsequent asthma, atopy and wheeze: a longitudinal birth cohort study. *Pediatr Allergy Immunol* 2005;**16**:386–92	No subgroups given
Holberg CJ, Wright AL, Martinez FD, Ray CG, Taussing LM, Lebowitz MD. Risk factors for respiratory syncytial virus-associated lower respiratory illnesses in first year of life. *Am J Epidemiol* 1991;**133**(11):1135–51	RSV hospitalisation related risk factors not given
Kneyber MC, Steyerberg EW, de Groot R, Moll HA. Long term effects of respiratory syncytial virus (RSV) bronchiolitis in infants and young children: a quantitative review. *Acta Paediatr* 2000;**89**:654–60	Early meta-analysis

Study	Reason for exclusion
Lee JT, Chang LY, Wang LC, Kao CL, Shao PL, Lu CY, *et al*. Epidemiology of respiratory syncytial virus infection in northern Taiwan, 2001–2005 – seasonality, clinical characteristics and disease burden. *J Microbiol Immunol Infect* 2007;**40**:293–301	Not generalisable to UK population
Medrano C, Garcia-Guereta L, Grueso J, Insa B, Ballesteros F, Casaldaliga J, *et al*. Respiratory infection in congenital heart disease. Hospitalisations in young children in Spain during 2004 and 2005: the CIVIC Epidemiological Study. *Cardiol Young* 2007;**17**:360–71	No suitable subgroup results given
Navas L, Wang E, de Carvalho V, Robinson J. Improved outcome of respiratory syncytial virus infection in a high risk hospitalised population of Canadian children. *Pediatrics* 1992;**121**(3):347–54	No suitable subgroup results given
Noyola DE, Zuviri-Gonzalez A, Casto-Garcia JA, Ochoa-Zavala JR. Impact of respiratory syncytial virus on hospital admissions in children younger than 3 years of age. *Infection* 2007;**54**:180–4	Study from Mexico and results not UK generalisable
Pedraz C, Carbonell-Estrany X, Figueras-Aloy J, Quero J, Iris Study Group. Effect of palivizumab prophylaxis in decreasing respiratory syncytial virus hospitalisations in premature infants. *Pediatr Infect Dis J* 2003;**22**(9):823–7	Partial duplication of Carbonell-Estrany *et al*. 2000[11] and 2001[14]
Prevent Study Group. Reduction in respiratory syncytial virus hospitalisation among premature infants and infants with bronchopulmonary dysplasia using respiratory syncytial virus immune globulin prophylaxis. *Pediatrics* 1997;**99**:93–9	No suitable subgroups given
Resch B. Palivizumab for the prophylaxis of respiratory syncytial virus infection. *Ped Health* 2008;**2**(3):265–78	Review of other included studies
Simoes EA, Sondheimer HM, Top FH, Meissner C, Welliver RC, Kramer AA, *et al*. Respiratory syncytial virus immune globulin for prophylaxis against respiratory syncytial virus disease in infants and children with congenital heart disease. *J Pediatr* 1998;**133**(4):492–9	No suitable subgroups given
Simoes EA. Environmental and demographic risk factors for respiratory syncytial virus lower respiratory tract disease. *J Pediatr* 2003;**143**:S118–S126	Semi-systematic review
Wang EE, Law BJ, Stephens D, the PICNIC Study Group. Pediatric investigators collaborative network in infections in Canada (PICNIC) prospective study of risk factors and outcomes in patients hospitalised with respiratory syncytial viral lower respiratory tract infection. *J Pediatr* 1995;**126**(2):212–9	PICNIC study already included (Law)
Wang EE, Law BJ, Boucher FD, the PICNIC Study Group. Pediatric investigators collaborative network in infections in Canada (PICNIC) study of admission and management variation in patients hospitalised with respiratory syncytial viral lower respiratory tract infection. *J Pediatr* 1996;**129**(3):310–5	Duplicate of study above

CI, confidence interval.

Appendix 3

Quality assessment of included studies

Study	Patient recruitment	RSV ascertainment method	Measurement methods of subgroups explicit	Clarity of reporting
Carbonell-Estrany 2000[11]	All rehospitalised children	97% antigen test, 3% culture	Interview at O/P or telephone call	Fair
Carbonell-Estrany 2001[14]	All rehospitalised children	Method unclear, 10% not tested for RSV	Interview at O/P or telephone call	Poor. Very difficult to tell where results were from the different population to Carbonell-Estrany 2000[11]
Eriksson 2002[15]	From case records, not consecutive?	Nasopharyngeal lavage, antigen detection and 'virus isolation on the majority of samples'	From case records only	Poor. Included 149 patients not from the catchment area but not clear which tables this in
Figueras-Aloy 2004[16]	Unclear how cases and controls selected, not consecutive?	Not standardised	From questioning, no further details given	Fair. Includes power calculation
Figueras-Aloy 2008[18]	Unclear how cases and controls selected, not consecutive?	Immunofluorescence assay or viral culture	Risk factors defined, collection at first admission	Good
Frogel 2008[19]	Palivizumab treatment registry co-ordinated by drug company	Virology testing (e.g. rapid antigen detection, viral culture)	From registry data take on enrolment	Fair. No CIs given for ORs, *p*-values given instead
Grimwood 2008[20]	Unclear, not consecutive?	Nasopharyngeal aspirate, antigen test	During hospitalisation by nurse administered questionnaire	Good
Kristensen 2009[9]	Unclear, not consecutive?	Not given	Unclear	Poor. Tables and text do not link well
Law 2004[21]	Unclear, not consecutive?	Viral culture/rapid test	Interview by trained researchers	Fair
Liese 2003[25]	All neonates eligible enrolled	Clinical diagnosis or antigen test	Questionnaire sent to parents	Good
Nielsen 2003[23]	All children eligible enrolled	Nasopharyngeal suction, antigen test	Not given	Fair
Rietveld 2006[6]	Unclear, not consecutive?	Nasopharyngeal aspirate, viral culture or immunofluorescence assay	From perinatal registry	Poor. Overly confusing explanations
Rossi 2007[24]	Cases and controls, consecutive acute respiratory infections at emergency departments	Nasal secretion, immunoenzymatic test	From 'osservatorio' database	Fair

CI, confidence interval; O/P, outpatient clinic.

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