Preventive strategies for group B streptococcal and other bacterial infections in early infancy: cost effectiveness and value of information analyses


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
This study investigated five strategies for preventing neonatal infection with group B streptococci (GBS) and other bacteria in the UK. These strategies were:

Strategy one: do nothing;
Strategy two: test vaginal and rectal swabs by culture at 35 to 37 weeks of pregnancy and treat women with at least one positive result, using either oral erythromycin or intravenous penicillin;
Strategy three: test swabs by polymerase chain reaction at presentation in labour and treat those with a positive result using oral erythromycin or intravenous penicillin;
Strategy four: oral or intravenous treatment without testing; and
Strategy five: vaccinate at 28 weeks, in addition to each of the previous four strategies.

Type of intervention
Screening, primary prevention and treatment.

Economic study type
Cost-utility analysis, cost-benefit analysis

Study population
The population comprised a hypothetical cohort of 680,000 pregnant women and their future offspring. This was divided into 12 maternal risk groups which, in order of risk, were:

Preterm Deliveries (before 37 weeks):
1) planned caesarean section;
2) previous baby with GBS infection;
3) positive urine or vaginal swab for GBS in current pregnancy;
4) fever of at least 38°C in labour;
5) rupture of membranes before the onset of labour;
6) spontaneous labour (membrane rupture less than two hours before or after the onset of labour);

Term Deliveries (at 37 weeks or later):
7) planned caesarean section;
8) previous baby with GBS infection;
9) positive urine or vaginal swab for GBS in current pregnancy;
10) fever of at least 38°C in labour;
11) membrane rupture for 18 hours or more; and
12) no risk factors.

Setting
The setting was in-patient secondary care, in the UK.
Dates to which data relate
The authors did not report the time period from which the effectiveness and resource use data were derived, but they referred readers to a full report (Colbourn, et al. 2007, see 'Other Publications of Related Interest' below for bibliographic details), with details of all the sources. The price year was not reported.

Modelling
The authors constructed a decision analytic model to quantify the effects of different testing, treatment, and vaccination strategies on serious bacterial infection in early infancy. The authors did not report the nature of the model used.

Study designs and other criteria for inclusion in the review
The clinical and epidemiological data included: evidence of the risk of GBS transmission (including information on maternal colonisation, baby colonisation, and early onset of GBS); evidence on the risk of infection in babies (including information on early onset GBS and other infections, and late onset GBS); evidence on the proportion of all deliveries occurring at preterm or at term; and evidence on the effectiveness of intravenous penicillin, oral penicillin and erythromycin, and vaccination.

Sources searched to identify primary studies
The authors reported that published studies, primary datasets and expert opinion were used to derive the clinical and epidemiological data. They also reported that the only parameter that was derived exclusively from expert opinion was the vaccine efficacy.

Methods used to derive estimates of effectiveness
Systematic reviews were conducted to answer 32 questions to inform the model parameters. The methods of the reviews were not reported in this paper, but the main study report contained details of each review and data sources in full (Colbourn, et al. 2007). As for the systematic reviews, no details of how expert opinion was elicited were reported in this paper.

Measure of benefits used in the economic analysis
The measure of benefit was quality-adjusted life-years (QALYs) gained. The sources used to derive the quality of life were not reported. Discounting of QALYs was relevant as the benefits could be incurred over the lifetime of the child and it does appear to have been performed, but the discount rate was not reported. For the cost-benefit analysis, QALYs gained were valued using a willingness-to-pay threshold of £25,000.

Direct costs
The direct costs to the UK National Health Service (NHS) were included in the analysis. The authors did not report the cost categories nor the costs included, and so it is unclear if all the relevant costs were included. It is likely that a full summary of the costs was given in the full report (Colbourn, et al. 2007). The methods used to the estimate the costs, and the sources, from which the resource use and unit costs were derived, were not reported. The incremental costs were reported.

Statistical analysis of costs
Costs were reported as point estimates, which means that the data were deterministic.

Indirect Costs
Productivity costs were not included.

Currency
UK pounds sterling (£).

Sensitivity analysis
The authors conducted the analyses for each of the 12 risk groups and then for all possible combinations of interventions that had more than a 1% probability of being cost-effective for each risk group. The potential value of further research was quantified by calculating the expected value of perfect information (EVPI) for the UK population based on the difference between the expected net benefit with perfect and current information, assuming a 10-year time horizon.
Estimated benefits used in the economic analysis
As a large number of intervention strategies were assessed (different combinations of interventions for different patient subgroups) only the intervention strategies with the lowest and highest number of QALYs gained, in comparison with no intervention, are reported here.

A strategy, based on the recommendations of the Royal College of Obstetricians and Gynaecologists (RCOG), which included treating risk groups 2 to 4 and 8 to 10 with intravenous penicillin without testing and not treating risk groups 1, 5 to 7, 11 and 12, generated 340 QALYs.

The same strategy, but offering patients in risk group 5 treatment with oral erythromycin without testing (i.e. current best practice), generated 741 QALYs.

Strategies based on test by culture at 35 to 37 weeks, with treatment of positive cases using intravenous penicillin, for groups 11 and 12, and treatment of groups 1 to 10 without testing, generated between 1,870 and 1,897 QALYs, compared with no intervention.

Strategies based on test by polymerase chain reaction, with treatment of positive cases using intravenous penicillin, for groups 11 and 12, and treatment of groups 1 to 10 without testing, generated between 1,958 and 1,965 QALYs, compared with no intervention.

Cost results
As with benefits, only those intervention strategies with the lowest and highest incremental costs, compared with no intervention, are reported.

Strategies based on treating risk groups 1 to 10, and no intervention for groups 11 and 12, generated the highest savings of between £4.7 million and £4.8 million compared with no intervention.

Strategies based on tests by polymerase chain reaction, with treatment of positive cases using intravenous penicillin, for groups 11 and 12, and treatment of groups 1 to 10 without testing, generated the most incremental costs, ranging between £2.1 million and 2.9 million, in comparison with no intervention.

Synthesis of costs and benefits
The costs and benefits were combined using the net benefit approach (i.e. the additional costs minus the additional benefits valued in monetary terms). The strategies with the lowest net benefit included the one based on RCOG guidelines (£9.7 million) and the current best practice (£21.4 million). The strategies with the highest net benefit included those involving culture tests for risk groups 11 and 12, and treatment without tests for risk groups 1 to 10 (ranging between £48.1 million and £48.5 million).

If vaccination was assumed not to be available, the EVPI for the UK for choosing between all the strategies was £28.9 million. Most of this value of information was driven by the uncertainty about the choice between intravenous and oral antibiotic treatment for certain preterm groups. If vaccination was available, the EVPI was £67.3 million, which reflected the potential, but uncertain increase in net benefit and increased options.

Authors’ conclusions
The authors concluded that, as all the cost-effective interventions involved treating all preterm and high-risk term groups without testing, the treatment of these groups would be beneficial and should be prioritised.

CRD COMMENTARY - Selection of comparators
The authors compared numerous interventions, including current practice and no intervention, for multiple patient groups. You should decide if these interventions are widely used technologies in your setting.

Validity of estimate of measure of effectiveness
The parameters were derived from published research, primary datasets and expert opinion. To identify the relevant
published research the authors undertook systematic reviews of the literature to answer 32 questions. The data were combined using multi parameter evidence synthesis. The authors did not report the methods used to elicit opinions from the experts, but referred readers to the full report (Colbourn, et al. 2007). The evidence used to populate the parameters appears to have had a high level of internal validity. For example, in their synthesis of evidence, the authors simultaneously estimated each parameter using all the relevant data inputs that directly or indirectly informed that parameter.

**Validity of estimate of measure of benefit**

The estimation of health benefit (QALYs) was derived appropriately using a decision analytic model. It was unclear from the article if discounting was performed. As the authors undertook a cost-benefit analysis, QALYs gained were appropriately converted into monetary benefits using a £25,000 threshold, similar to the implicit threshold used by the National Institute for Health and Clinical Excellence (NICE) to determine whether an intervention is cost-effective in the UK.

**Validity of estimate of costs**

Very little information was provided in this article about how the resource use and cost data were derived or the sources used. The authors only reported that the analysis was conducted from the perspective of the UK NHS. In order to determine the validity of the costs, the full report of this study should be assessed (Colbourn, et al. 2007). In light of the detailed literature reviews and synthesis of benefits performed, it should be safe to assume that the analysis of costs was carried out just as rigorously.

**Other issues**

The authors did not compare their results with findings from other studies, probably due to the lack of both effectiveness and cost-effectiveness evidence. Due to the large number of interventions being assessed in various subgroups, the issue of generalisability to other settings was evaluated. The authors also reported the value of future research. They do not appear to have presented their results selectively, and their conclusions reflected the scope of their analysis. They reported a number of limitations to their study, such as the restriction of outcomes to the current pregnancy, which underestimated the net benefits of vaccination for subsequent births; the focus on culture positive bacteraemia or meningitis; and that the adverse effects of intra-partum antibiotic treatment on pathogen selection and antibiotic resistance were not included.

**Implications of the study**

The authors recommended that policy makers immediately consider the extension of antibiotic treatment to all women with preterm and high-risk term deliveries.

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**Other publications of related interest**

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publication is significantly linked to or informed by other publications, these will be referenced in the text of the
abstract and their bibliographic details recorded here for information.

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