Health Technology Assessment 2007; Vol. 11: No. 29

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August 2007

Health Technology Assessment
NHS R&D HTA Programme
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Prenatal screening and treatment strategies to prevent group B streptococcal and other bacterial infections in early infancy: cost-effectiveness and expected value of information analyses

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Declared competing interests of authors: none

Published August 2007

This report should be referenced as follows:

Colbourn T, Asseburg C, Bojke L, Philips Z, Claxton K, Ades AE, *et al*. Prenatal screening and treatment strategies to prevent group B streptococcal and other bacterial infections in early infancy: cost-effectiveness and expected value of information analyses. *Health Technol Assess* 2007;**11**(29).

Health Technology Assessment is indexed and abstracted in *Index Medicus*/MEDLINE, *Excerpta Medica*/EMBASE and *Science Citation Index Expanded (SciSearch®)* and *Current Contents®*/Clinical Medicine.

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The research reported in this monograph was commissioned by the HTA Programme as project number 04/51/01. The contractual start date was in June 2005. The draft report began editorial review in July 2006 and was accepted for publication in November 2006. 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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ISSN 1366-5278

Published by Gray Publishing, Tunbridge Wells, Kent, on behalf of NCCHTA.
Printed on acid-free paper in the UK by St Edmundsbury Press Ltd, Bury St Edmunds, Suffolk.

Abstract

Prenatal screening and treatment strategies to prevent group B streptococcal and other bacterial infections in early infancy: cost-effectiveness and expected value of information analyses

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Objectives: To determine the cost-effectiveness of prenatal strategies for preventing group B streptococci (GBS) and other serious bacterial infections in early infancy and to establish the expected value of further information.

Data sources: Electronic databases were searched up to March 2006. Expert opinion was also sought.

Review methods: Twelve mutually exclusive maternal risk groups were defined at presentation in labour and the consequences considered of early-onset GBS and non-GBS bacterial infections and late onset GBS infection, measured in terms of lifetime NHS costs and quality-adjusted life-years (QALYs). These were for preterm delivery (<37 weeks): (1) planned Caesarean section, (2) previous baby with GBS disease, (3) positive urine or vaginal swab for GBS in current pregnancy, (4) fever ≥38°C during labour, (5) membrane rupture ≥2 hours before labour onset, (6) membrane rupture <2 hours before labour onset. For term delivery (≥37 weeks): (7) planned Caesarean section, (8) previous baby with GBS disease, (9) positive urine or vaginal swab for GBS in current pregnancy, (10) fever ≥38°C during labour, (11) membrane rupture ≥18 hours, and (12) none of the above risk factors. Fourteen intervention strategies were applied to each maternal risk group. Data inputs were obtained from systematic reviews, primary data and expert opinion. The model parameters were simultaneously estimated from the data inputs using Bayesian evidence synthesis. The expected net benefit was calculated relative to no intervention for each intervention within each risk group for two scenarios, with and without vaccination. Interventions with more than a 1% probability of being cost-effective (i.e. maximising net benefit at a threshold of £25,000 per QALY gained) in a specific risk group were combined to form strategies. To limit antibiotic exposure, women who were low risk at presentation could not be treated without a positive culture or polymerase chain reaction result.

Results: Current best practice, comprising intravenous treatment for pyrexia, previous GBS baby and previous GBS swab or urine culture, and oral treatment for preterm pre-labour membrane rupture (groups 2–5 and 8–10) was not cost-effective. All cost-effective options involved treatment of all preterm groups and high-risk term groups (groups 8–10). Testing high-risk women for maternal GBS colonisation would not be cost-effective, as even those with negative results would be better off treated to reduce the risk of early-onset non-GBS infection. In the absence of vaccination, culture-based testing of women in groups 11 and 12, combined with treatment for the rest, would be the most cost-effective strategy. If vaccination was available, vaccination for all and treatment for groups 1–10 would be marginally more cost-effective than treatment for groups 1–10 and culture for groups 11 and 12, but this is uncertain and is based on expert opinion on vaccine efficacy. The expected value of perfect information results suggest that moderate investment in research would be worthwhile.

Conclusions: Based on our findings, immediate extension of current practice to treat all preterm and high-risk term groups would be beneficial. Further research aimed at the realisation of a GBS vaccine should be prioritised.

Contents

Glossary and list of abbreviations

Technical terms and abbreviations are used throughout this report. The meaning is usually clear from the context, but a glossary is provided for the non-specialist reader. In some cases, usage differs in the literature, but the term has a constant meaning throughout this review.

Glossary

Beta Beta distribution, a statistical distribution suitable for probability parameters

Binomial distribution A discrete probability distribution of the number of successes in a sequence of n independent yes/no experiments, each of which yields success with probability p

Dirichlet Dirichlet distribution, a generalisation of the Beta distribution for probability parameters, where there are more than two categories

Dominated When an intervention has higher costs and lower outcomes than its comparator

EQ-5D A health-related quality of life (HRQoL) descriptive system consisting of five dimensions, mobility, self-care, usual activity, pain/discomfort, and anxiety/depression

Extended dominated Situation in which the intervention has lower outcomes for a higher incremental cost-effectiveness ratio (ICER)

Gamma distribution A continuous probability distribution expressed in terms of shape $((\mu/s)^2)$ and scale (s^2/μ) parameters

Incremental cost-effectiveness ratio The cost at which an additional unit of outcome (usually a QALY) will be gained relative to the next most cost-effective strategy

Multinomial distribution A generalisation of the binomial distribution in which instead of each trial resulting in 'success' or 'failure', each trial results in one of some fixed finite number k of possible outcomes, with probabilities p_1, …, p_k, and there are n independent trials

Net benefit Increase in health outcome (QALYs) minus health expenditure costs

Polymerase chain reaction A type of rapid diagnostic test based on the amplification of small amounts of DNA

Posterior distribution The posterior distribution is a combination of information from the prior distribution and the data likelihood

Predictive distribution A Bayesian analysis allows us to obtain a prediction, in the form of a probability distribution, for a parameter, or for what might be observed in a study of a given size, based on our model, priors and data inputs. In random effects models, a predictive distribution for the value of a parameter in a future study

Prior An assumed distribution that reflects our beliefs about the data in question

Quality-adjusted life year One healthy, disability-free year of life, a measurement of health outcome

Stillbirth *In utero* death at ≥24 weeks of gestation

Willingness to pay The amount of money that the health provider is willing to pay for one QALY gained in health outcome

List of abbreviations

BNF	British National Formulary
BPSU	British Paediatric Surveillance Unit
CDC	Centers for Disease Control and Prevention
CI	confidence interval
CSF	cerebrospinal fluid
DOR	diagnostic odds ratio
EOGBS	early onset (less than 7 days of age) group B streptococcal disease
EO non-GBS	early onset (less than 7 days of age) disease caused by a bacterial pathogen other than group B *Streptococcus*
EVPI	expected value of perfect information
EVPPI	expected value of partial parameter information
EVSI	expected value of sample information
GBS	group B streptococcus
HCHS	Hospital and Community Health Services
HES	Hospital Episode Statistics
HPA	Health Protection Agency
HUI	Health Utilities Index
IAP	intrapartum antibiotic prophylaxis
ICER	incremental cost-effectiveness ratio
IEER	incremental exposure per QALY (effect) ratio
LOGBS	late onset (between 7 and 90 days of age) group B streptococcal disease
Logit	log odds
LOR	log odds ratio
LOS	length of stay
LSCS	lower section Caesarean section
MPES	multi-parameter evidence synthesis
NB	net benefit
NICE	National Institute for Health and Clinical Excellence
NICU	neonatal intensive care unit
NNT	number needed-to-treat (to prevent one case of disease/death)
NPEU	National Paediatric Epidemiology Unit
OR	odds ratio
PCR	polymerase chain reaction
p(CE)£25k	probability (%) that the strategy is cost-effective at a WTP of £25,000 per QALY
PSSRU	Personal Social Services Research Unit
QALY	quality-adjusted life-year
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	randomised controlled trial
RG	risk group
ROC	receiver operating characteristic
ROM	rupture of membranes
SCBU	special care baby unit
SD	standard deviation
SMMIS	St Mary's Maternity Information System
VOI	value of information
WTP	willingness to pay

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 at the end of the table.

Executive summary

Background

Prenatal screening for maternal colonisation with group B streptococcus (GBS) is well established in many western industrialised countries but is not currently recommended in the UK because evidence is lacking about its effectiveness.

Aims

The aims were to determine the cost-effectiveness of prenatal strategies for preventing GBS and other serious bacterial infections in early infancy and to establish the expected value of further information.

Methods

Twelve mutually exclusive maternal risk groups were defined at presentation in labour (see below) and the consequences considered of early-onset GBS and non-GBS bacterial infections and late onset GBS infection, measured in terms of lifetime NHS costs and quality-adjusted life-years (QALYs).

The maternal risk groups were (in hierarchical order from 1 to 6 and from 7 to 12):

Preterm delivery (<37 weeks):
1. planned Caesarean section
2. previous baby with GBS disease
3. positive urine or vaginal swab for GBS in current pregnancy
4. fever ≥38°C during labour
5. membrane rupture ≥2 hours before labour onset
6. membrane rupture <2 hours before labour onset.

Term delivery (≥37 weeks):
7. planned Caesarean section
8. previous baby with GBS disease
9. positive urine or vaginal swab for GBS in current pregnancy
10. fever ≥38°C during labour
11. membrane rupture ≥18 hours
12. none of the above risk factors.

Fourteen intervention strategies were applied to each maternal risk group: doing nothing; culture of a vaginal and rectal swab at 35–37 weeks and treating women with at least one positive result at onset of labour with oral erythromycin or intravenous penicillin; polymerase chain reaction (PCR) testing of vaginal and rectal swabs at presentation in labour and treating one or more positive results; oral or intravenous treatment without testing; and vaccination alone or in addition to each of the six interventions. Data inputs were obtained from systematic reviews, primary data and expert opinion. The model parameters were simultaneously estimated from the data inputs using Bayesian evidence synthesis.

The expected net benefit relative to no intervention was calculated for each intervention within each risk group for two scenarios, with and without vaccination. Interventions with more than a 1% probability of being cost-effective (i.e. maximising net benefit at a threshold of £25,000 per QALY gained) in a specific risk group were combined to form strategies. To limit antibiotic exposure, women who were low risk at presentation (groups 11 and 12) could not be treated without a positive culture or PCR result.

Results

Current best practice, comprising intravenous treatment for pyrexia, previous GBS baby and previous GBS swab or urine culture, and oral treatment for preterm pre-labour membrane rupture (groups 2–5 and 8–10) was not cost-effective. All cost-effective options involved treatment of all preterm groups and high-risk term groups (groups 8–10). Testing high-risk women for maternal GBS colonisation would not be cost-effective, as even those with negative results would be better off treated to reduce the risk of early-onset non-GBS infection. In the absence of vaccination, culture-based testing of women in groups 11 and 12, combined with treatment for the rest, would be the most cost-effective strategy. If vaccination was available, vaccination for all and treatment for groups 1–10 would be marginally more cost-effective than treatment for groups 1–10 and culture for groups 11 and 12, but this is

uncertain and is based on expert opinion on vaccine efficacy. The expected value of perfect information (EVPI) results suggest that moderate investment in research would be worthwhile.

Implications for policy

Two limitations of the analysis are the exclusion of adverse effects of antibiotics and organisational costs to implement (or reverse) a new intervention. In outlining policy, we assume that limiting antibiotic exposure is worthwhile and that adding to current practice would be easier to implement than changing it.

Current best practice involves treating 7.4% of women. Extension of clinical recommendations to treat all preterm women, while continuing to give the same treatments to high-risk term women would gain an additional £14 million net benefit for the UK per year and increase the proportion of women exposed to antibiotics to 11%.

In the absence of vaccination, the cost-effective option is culture-based testing of women in groups 11 and 12, combined with treatment for the rest. An alternative strategy, in which women with elective Caesarean section at term (group 7) also undergo culture testing, would generate marginally less benefit, but reduce treatment to 21% (from 27%) of women.

If vaccination becomes available, the cost-effective strategy (net benefit £50.5 million) would be vaccination for all and treatment of risk groups 1–10 (19% of all women treated). Therefore, an advantage of vaccine is that strategies which provide more net benefit can be adopted without an increase in antibiotic exposure.

Conclusions

Based on our findings, immediate extension of current practice to treat all preterm and high-risk term deliveries would be beneficial.

Thereafter, it is not clear whether the optimal choice would be culture-based testing for low-risk women, or vaccination plus treatment of all preterm and high-risk term women. There are also important issues of timing. Vaccination is unlikely to be available for the next 5 years and could not be implemented without Phase III trials, which will substantially reduce uncertainty over vaccine efficacy. In the meantime, implementation of culture testing for low-risk women appears to be the most cost-effective option but implementation costs could be significant and not recouped if, subsequently, a vaccination strategy was adopted.

Recommendations for further research

The EVPI analyses indicated that spending on further research could be worthwhile and would provide maximum returns of between £29 million and £67 million. These results suggest that adoption of treatment for preterm and high-risk term women and research into vaccine efficacy may be beneficial before deciding whether to adopt culture-based screening for low-risk women, or vaccination for all without screening. Cost-effectiveness of vaccine compared with other interventions should be re-evaluated after Phase III trials, which are needed anyway to gain a licence.

Studies comparing culture with PCR testing or no intervention in the low-risk term groups (7, 11 and 12) might also be informative, but would need to be extremely large.

The proposed very large cluster randomised trial of culture-based testing versus no intervention for low-risk women, plus treatment for high-risk women in both arms, would base the primary results on aggregate rates of neonatal infection. The high-risk pregnancies would account for 41% of early-onset GBS, but would not be separately identifiable. This would complicate interpretation of the trial and the consequent dilution of the treatment effect would require a large increase in sample size compared with a trial in which risk groups were identifiable.

Comparison of oral and intravenous treatment could also be valuable, as this might better inform treatment in preterm groups 1, 5 and 6. Finally, study designs other than clinical trials could contribute important information. For example, more information on the consequences of infection outcomes for disability, quality of life, healthcare costs and life expectancy could be valuable. Further EVPI analysis aimed at specific sets of parameters could throw light on the research priorities.

Chapter 1
Background

Group B streptococcus (GBS) is just one of the species of bacteria that make up the normal vaginal flora. Inevitably, these bacteria are transmitted to the baby during delivery. Most are non-pathogenic and colonise the baby's skin, nasopharynx and gut, making an important contribution to the diversity of the infant gut flora. Rarely, maternally transmitted bacteria result in disseminated infection that presents as stillbirth, rapid deterioration after birth or symptoms of infection in the first few days of life. Because infection takes time to become established, symptomatic bacterial infection in the first few days of life is most likely to be due to organisms acquired from the mother. In contrast, bacterial infections after the first week of life are mostly acquired from the environment and predominantly affect preterm and sick babies admitted to the neonatal intensive care unit (NICU). As a result, antibiotic treatment of women during labour will have most impact on early onset bacterial infection, defined in the present study as the first week of life.

The UK and Finland are among the few western industrialised countries where prenatal screening for GBS is rarely offered.[1,2] In contrast, screening based on risk factors for GBS disease and/or testing for maternal GBS colonisation is established practice in North America, Australasia and many parts of Europe.[3] During the 1990s, there was widespread controversy about whether to offer screening based on culture for maternal vaginal colonisation with GBS or to use risk factors such as preterm onset of labour, prolonged rupture of membranes, GBS bacteriuria during pregnancy, intrapartum pyrexia and a previous baby with GBS disease.[4] These strategies were evaluated in a large US case–control study. The results led to revised recommendations from the Centers for Disease Control and Prevention (CDC) in 2002 in favour of universal rectal and vaginal culture-based screening[5] at 35–37 weeks of gestation using enriched medium and overnight incubation, followed by intravenous penicillin or ampicillin 4 hourly until delivery.[6,7] As culture takes 48 hours, women presenting in labour before screening are treated with intravenous antibiotics.[7] In North America, this approach has led to approximately 30–50% of women receiving intravenous prophylactic antibiotics during labour or delivery.[5,8] More recently, rapid tests have been introduced that can be administered at the bedside and have the advantage of detecting colonised women who present in preterm labour or those who fail to be screened during antenatal care.[9,10]

At the heart of the controversy about whether screening for GBS should be introduced into the UK is uncertainty about whether the incidence of early-onset group B streptococcal disease (EOGBS) is sufficiently high for the benefits of universal screening and intravenous antibiotics to outweigh the harms and costs. In the USA, the incidence of early onset disease fell from 1.7/1000 to 0.5/1000 in the 1990s, and to 0.3/1000 in 2004 after CDC recommended universal culture-based screening in 2002.[4,11] However, the incidence in the UK is already 0.5/1000 and the characteristics of affected babies differ from those in the USA. In the UK, 37% of neonates with early-onset disease were born preterm, compared with 17% in the USA, and 45% had prolonged rupture of the membranes, compared with 14% in the USA.[5,12] The implication is that screening at 35–37 weeks, instead of treating all women in these high-risk groups, would miss a much larger proportion of GBS disease in the UK than in the USA.

A second issue is the uncertainty about the harms of GBS screening, particularly related to the selection pressures for other neonatal pathogens caused by the widespread use of prenatal antibiotics.[3,13–15] Third, there is concern about the medicalisation of pregnancy in terms of the impact of swabbing and intravenous treatment on women and on healthcare resources.[16] Systems to ensure prompt transmission of laboratory results to labour wards would be required. In addition, GBS-colonised women could not be managed in the primary care setting and may need earlier admission to the labour ward in order to start intravenous prophylaxis. Fourth, screening needs to be judged in terms of the additional benefits achievable over and above current good clinical practice, relative to the additional costs. Use of oral antibiotics as prophylaxis is now widely recommended for women with preterm prelabour ruptured membranes to increase the duration of

pregnancy, reduce neonatal infections more generally and reduce intracranial lesions.[17] To date, there has been no analysis of the cost-effectiveness of such practice or of the additional costs and benefits of screening for GBS.

Finally, the option of vaccination against GBS infection is now a realistic possibility.[18–21] Policy makers need to decide whether to invest in primary research to inform decisions about GBS screening and treatment or to invest in randomised controlled trials (RCTs) to determine vaccine efficacy. Both options would be costly but are particularly relevant questions for the UK: such trials can only be conducted in a setting where GBS screening is not widely available as it would be considered unethical to withhold screening and antibiotic prophylaxis.

Chapter 2

Aims and objectives

There were two aims of the study: first, to determine the cost-effectiveness of prenatal strategies for preventing GBS and other serious bacterial infections in early infancy, and second, to determine the cost-effectiveness of further research and identify research priorities using expected value of perfect information (EVPI) analysis.

How to read this report

The study can be split into three key areas: (1) the construction of the statistical model of GBS disease and other neonatal bacterial infections; (2) the analysis of the cost-effectiveness of alternative interventions; and (3) the analysis of the value of information that could be gained from further research.

1. The section 'Model structure' (p. 5) gives an overview of the model of the natural history of EOGBS, other early-onset bacterial infections and late-onset group B streptococcal disease (LOGBS). The section 'Limitations of the model' (p. 11) details issues not addressed. The section 'Search strategy and review methods' (p. 13) describes how the data inputs to the statistical model were obtained from a series of systematic reviews of the literature as well as primary data sources. The section 'Data synthesis methods' (p. 13) reports the statistical methods used to derive model outputs, taking into account all related inputs to the model. Chapter 5 details how the specific inputs to the model were derived and reports the outputs in 'results' tables.
2. The analysis of the cost-effectiveness of interventions to prevent GBS and other neonatal bacterial infections is outlined in the section 'Model structure' (p. 5) and then described in detail in Chapter 6. Chapter 7 provides an interpretation of the results of the cost-effectiveness analysis in relation to concerns about antibiotic exposure which could not be formally considered in the analysis.
3. Chapter 8 explains the concepts behind the EVPI analyses and describes the methods and results in detail.

All three areas of the study project are discussed in Chapter 9. The appendices are referred to when appropriate in the text of Chapters 3–9.

Chapter 3
Decision model

Overview

A decision model was developed to reflect the effect of prenatal screening for GBS, antibiotic treatment and vaccination on serious bacterial infection in early infancy defined by positive culture of bacterial pathogens in blood or cerebrospinal fluid. The decision model was probabilistic[22,23] and based on Bayesian methods of multi-parameter evidence synthesis (see the section 'Data synthesis methods', p. 13).[24,25] A UK population of women attending hospital for delivery was considered and intervention strategies compared that involved vaccination for GBS, testing for GBS and treating those with a positive result, and treating specific risk groups. The analysis sought to determine the most cost-effective strategy in terms of health service costs per quality-adjusted life-year (QALY) from the perspective of NHS healthcare providers. The time horizon started from 24 weeks of gestation and continued for the lifetime of the child. Outcomes were restricted to events or life states that had a clinically important effect on the child. *Figure 1* shows the key events of the model in chronological order to aid understanding of the full model structure which is detailed below. Interventions are in shaded boxes and key disease outcomes are in bold-bordered boxes.

Model structure

The model structure was based on a review of the literature (both natural history of GBS and previous cost-effectiveness studies) and discussions with experts (see decision trees 1, 2 and 3 in *Figures 2*, *3* and *4*, respectively). What follows is an explanation for the inclusion of each node in the model. Data inputs are reported in detail in Chapter 5.

Natural history model

Maternal risk groups

The natural history model was based on a representative population of women in the UK with singleton pregnancies divided into 12 risk groups (RGs) according to clinical characteristics at presentation in suspected labour that trigger different approaches to antibiotic treatment. The women were first divided into preterm and term deliveries, as preterm delivery is an important risk factor for early-onset bacterial infection in the baby and its sequelae [Tree 1 (*Figure 2*) and *Table 1*].

Preterm and term deliveries were then divided into a hierarchy of six groups, and the fact that a small proportion of women delivering at term would have presented in suspected labour before 36 completed weeks (i.e. preterm) was ignored. Women undergoing elective Caesarean section were at the top of the hierarchy for preterm and term deliveries (groups 1 and 7) as they did not present in labour. Next were women presenting in suspected labour with known risk factors for EOGBS (groups 2, 3, 8 and 9). Any other women who developed pyrexia during labour entered groups 4 and 10. Women who delivered preterm but presented with preterm prelabour rupture of membranes (ROM) entered group 5, and the remainder, those with preterm onset of labour before ROM, entered group 6. Among term deliveries, women with ROM for 18 hours or more entered group 11 and the remaining deliveries group 12. *Table 1* gives the group definitions and summarises the existing treatment recommendations in the UK, highlighting additional groups for whom treatment is recommended in the USA or Australia. Groups 7 and 12 are the only groups for whom treatment is not recommended in any of the protocols that were reviewed.

Maternal and baby colonisation with GBS

The proportion of women colonised with GBS varied according to the maternal RG. The review showed that the risk of maternal colonisation was higher in women delivering preterm than at term, and in those with a previous GBS positive swab or bacteriuria (see Chapter 5). In addition, the model was allowed to attribute higher than average rates of colonisation for women with preterm ROM or prolonged ROM, as colonisation could predispose to these conditions.

The baby becomes colonised with GBS from the mother while *in utero*, due to ascending organisms from the vagina, particularly after ROM or blood-borne transmission in women with bacteraemia, and during vaginal delivery.[26] Based on *a priori*

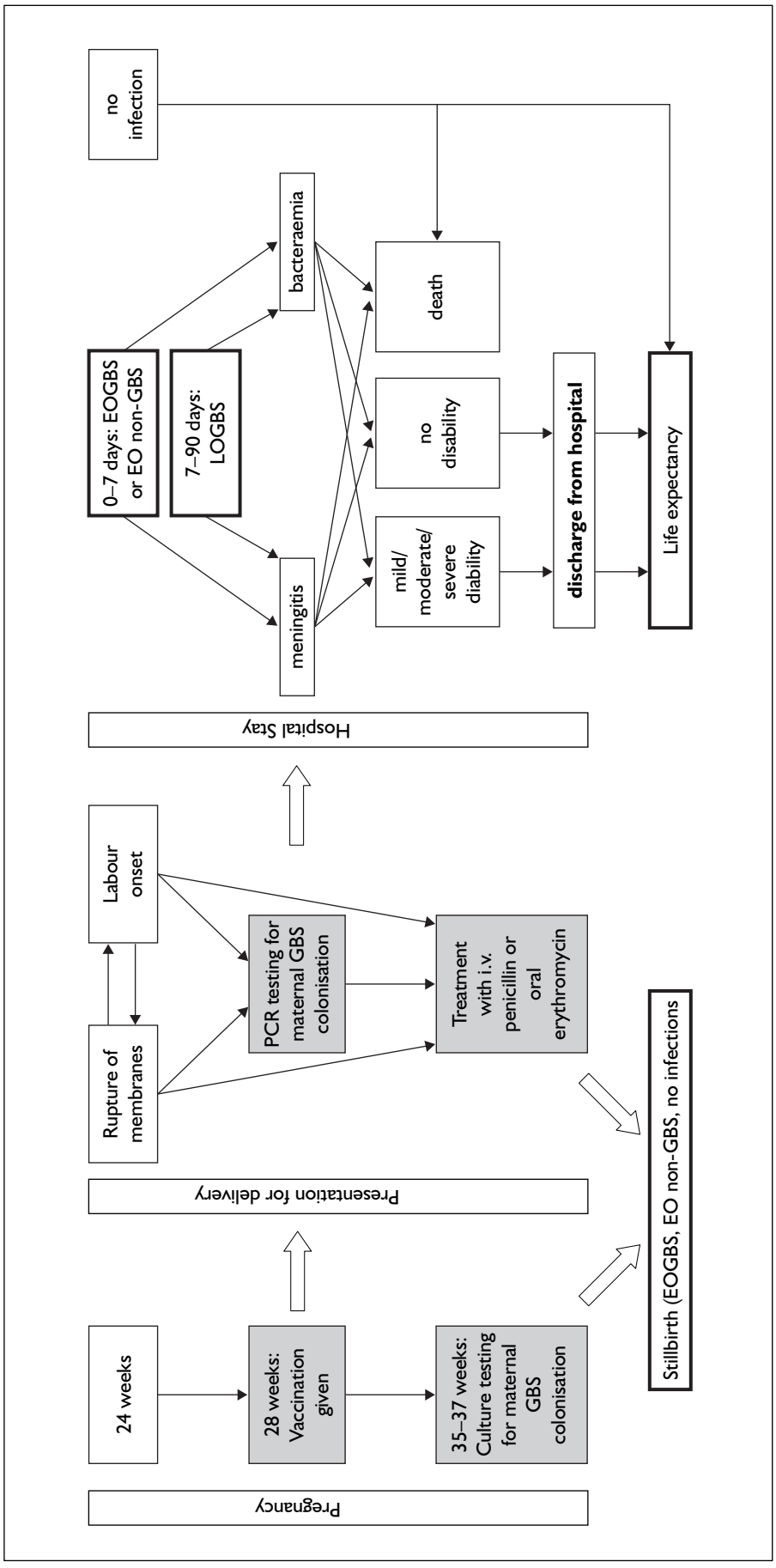

FIGURE 1 *Flow diagram to show testing and treatment procedures for, and the natural history of, neonatal GBS disease and other bacterial infections during pregnancy, presentation for delivery and hospital stay. PCR, polymerase chain reaction.*

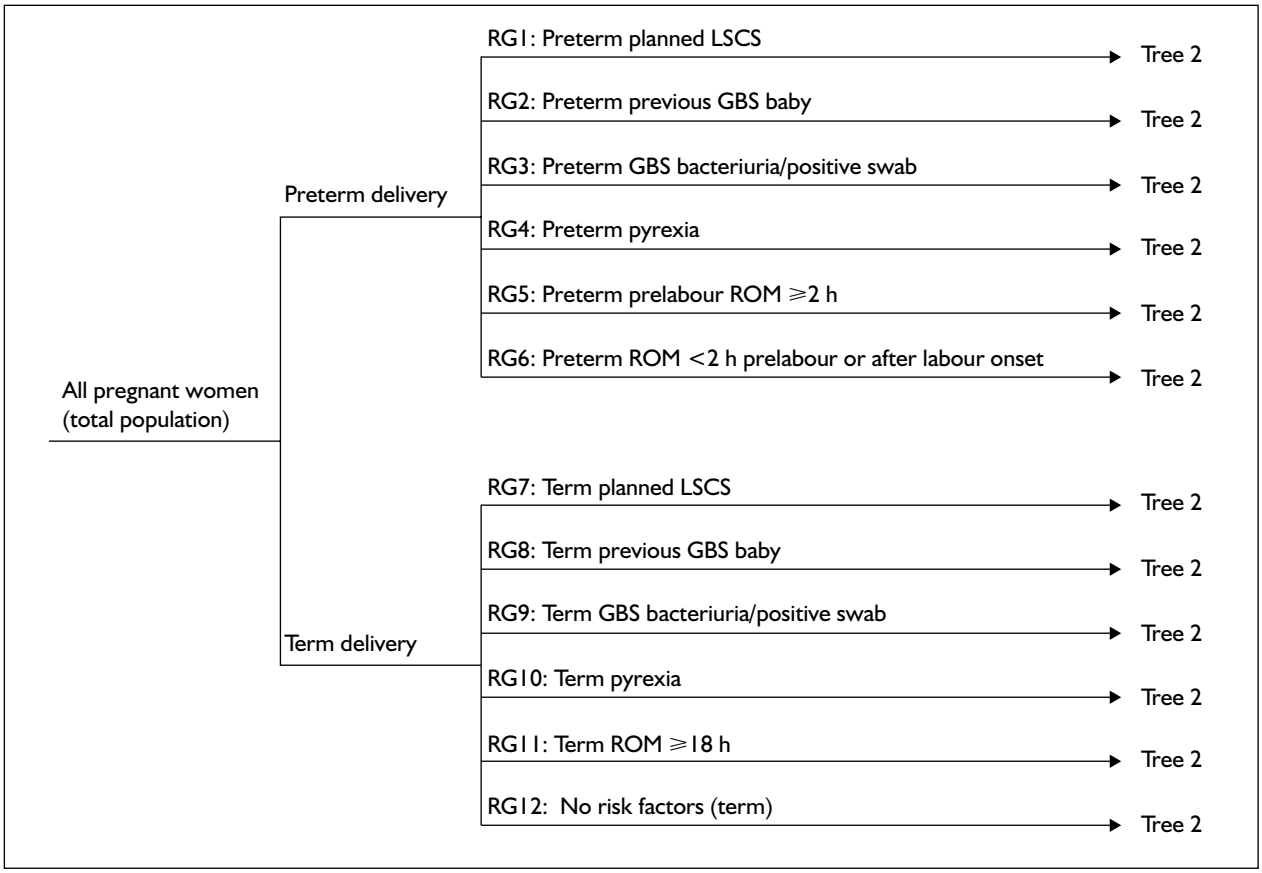

FIGURE 2 *Tree 1: maternal risk groups (RGs) for EOGBS. LSCS, lower section Caesarian section; ROM, rupture of membranes.*

reasoning in view of physiological mechanisms, we allowed the risk of mother to baby transmission of GBS infection to be higher in women with prolonged ROM (RG11) or preterm ROM (RG5) than in women undergoing planned Caesarean section (RG1 and 7). In the model, it was assumed that only babies with colonised mothers could become colonised.

The natural history is shown in Tree 2 (*Figure 3*).

GBS and non-GBS disease in the infant

Bacterial infection was defined by a positive blood or cerebrospinal fluid (CSF) culture, due to GBS or non-GBS pathogens (excluding coagulase-negative staphylococci). Culture-negative disease was not considered as the incidence and characteristics are poorly defined and serious consequences were assumed to be much lower than in culture-positive disease. GBS infection could result in stillbirth, or a livebirth with EOGBS (positive culture before 7 days of age) or LOGBS (positive culture between 7 and 90 days of age). Non-GBS infection could result in stillbirth or early-onset infection (EO non-GBS). Late-onset non-GBS infections were not considered as these are largely nosocomially acquired and are not affected by any of the maternal treatment or vaccination strategies in the model. A 7-day cut-off between early- and late-onset infections was used to maximise the potential benefits of maternal interventions on early-onset infection. EOGBS disease could only occur in GBS-colonised babies, whereas EO non-GBS and LOGBS disease were considered to be equally likely in GBS-colonised and uncolonised babies. As the initial infection determined the long-term costs and outcomes, it was not necessary to model the very rare possibility of multiple infections.

Stillbirth, postnatal death, meningitis and disability

Stillbirth could occur after EOGBS, EO non-GBS and no infection. In live-born babies, infection (EOGBS, EO non-GBS or LOGBS) could result in meningitis or bacteraemia alone, and both could result in death or permanent disability. Disability was defined by three levels of function: 'mild', 'moderate' and 'severe', which corresponded to functional states in studies of long-term outcomes of meningitis and cerebral palsy and to decrements in life expectancy and quality of life (see the section 'Disability', p. 37).

TABLE 1 *Definition of maternal risk groups*[a 7,16]

Risk group	Definition	Description of risk group and current management if no GBS testing done
Preterm		
RG1	Delivery by planned Caesarean section at <37 weeks of gestation	No treatment recommended as low risk of neonatal infection.[7,16] I.v. treatment recommended in USA pending culture results[2]
RG2	Preterm delivery in a woman who had a previous baby with GBS disease	In UK, intrapartum i.v. penicillin treatment recommended without further testing for GBS[7,16]
RG3	Preterm delivery and a positive urine or vaginal swab culture for GBS in the current pregnancy	As for group 2
RG4	Preterm delivery and a fever ⩾38°C during labour	High risk for neonatal bacteraemia and maternal infection. Broad spectrum i.v. antibiotic treatment widely recommended (not specifically for EOGBS)
RG5	Preterm delivery and ROM ⩾2 hours before onset of labour	Oral antibiotic treatment recommended to prolong duration of pregnancy and prevent neonatal infection. Two hours of ROM specified in the model to allow time for assessment and decision to treat
RG6	Preterm delivery and membrane rupture <2 hours before onset of labour	No treatment recommended in the UK. As for group 1 in the USA
Term		
RG7	Delivery by planned Caesarean section at ⩾37 weeks of gestation	No treatment recommended as low risk of neonatal infection[7,16]
RG8	Term delivery in a woman who had a previous baby with GBS disease	As for group 2
RG9	Term delivery and a positive urine or vaginal swab culture for GBS in the current pregnancy	As for group 2
RG10	Term delivery and fever ⩾38°C during labour	As for group 4
RG11	Term delivery and membrane rupture ⩾18 hours	No treatment recommended in the UK. I.v. treatment recommended in Australia (Isaacs D, Westmead Children's Hospital, Australia; personal communication, June 2006) and the USA[7]
RG12	Women with none of the above risk factors	As for group 7

[a] In hierarchical order from 1 to 6 and from 7 to 12.

Interventions

We modelled the cost-effectiveness of 14 interventions in each of the maternal RGs [Tree 3 (*Figure 4*) and *Table 2*].

Apart from those women who delivered before a strategy could be administered, it was assumed that all women offered an intervention would accept. We assumed that women were vaccinated at 28 weeks of gestation but effective transplacental transfer of protective antibodies did not occur until 32 weeks of gestation. Hence women delivering before 28 weeks were not vaccinated and mothers delivering between 28 and 32 weeks were vaccinated but their babies were unprotected. Details of the type of vaccine and efficacy are given in the section 'Vaccination' (p. 45).

Of the two screening options considered, one involved enriched culture of a vaginal and rectal swab between 35 and 37 weeks, which is the recommended method in North America.[7] The second option involved rapid polymerase chain reaction (PCR) testing on the labour ward of a vaginal and rectal swab, which is the most accurate of the currently available rapid tests.[27] The advantage of the PCR test is that women who deliver preterm or who would fail to attend for a swab at 35–37 weeks can be tested on presentation in labour. A positive test was followed by intravenous penicillin or oral erythromycin, which was started on admission in suspected labour. It was assumed that intravenous antibiotic treatment would be with penicillin and oral treatment with erythromycin, as this is currently recommended for RG5.[28,29] Oral antibiotics could be given during labour up to 6 hours before delivery. As the duration of both intravenous and oral treatment was limited by the time between presentation at onset of labour or ROM and delivery, different numbers of treatment doses were applied to each RG. The treatment effect was assumed to be independent of the number of doses and it was assumed that women complied with treatment.

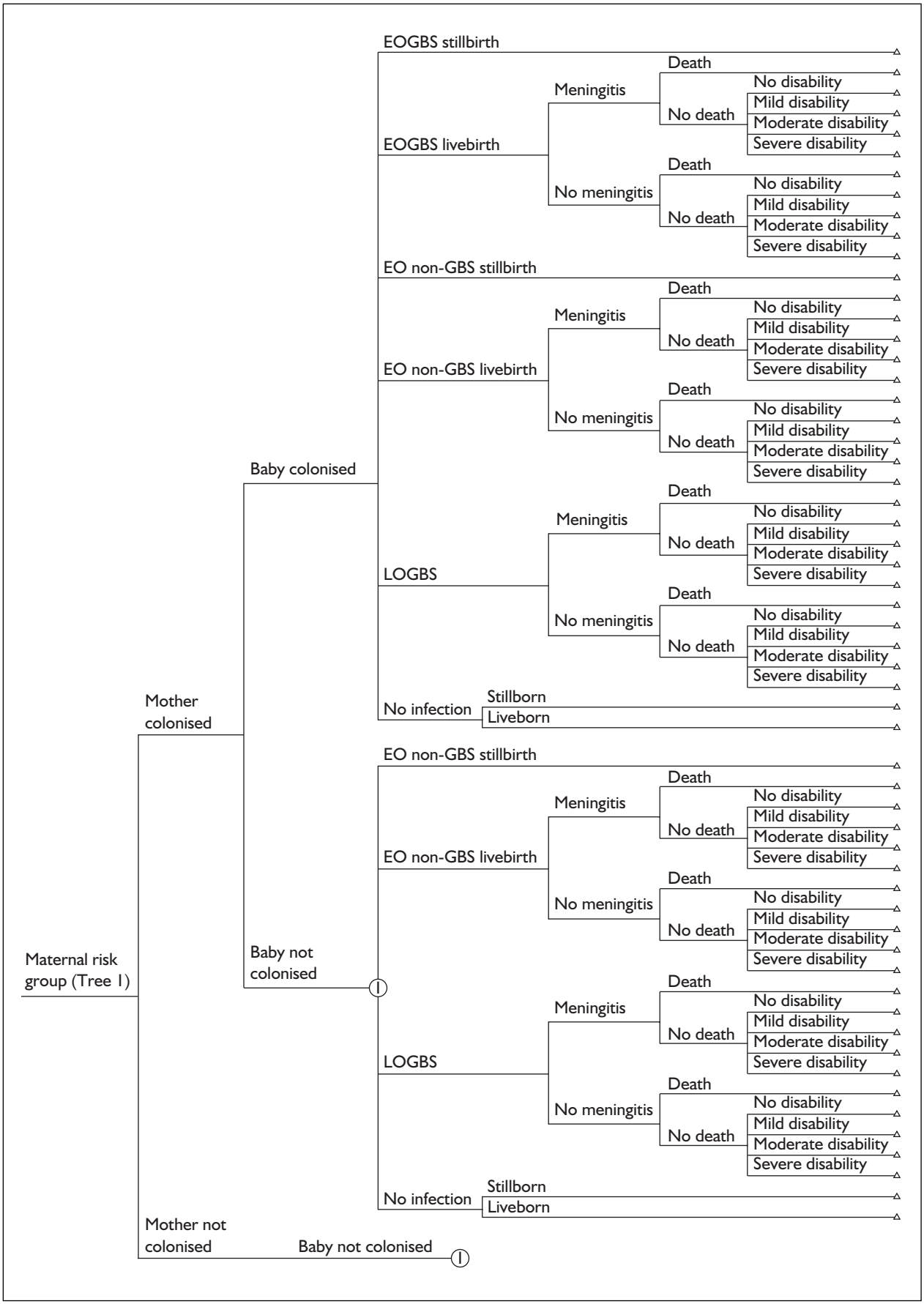

FIGURE 3 *Tree 2: natural history*

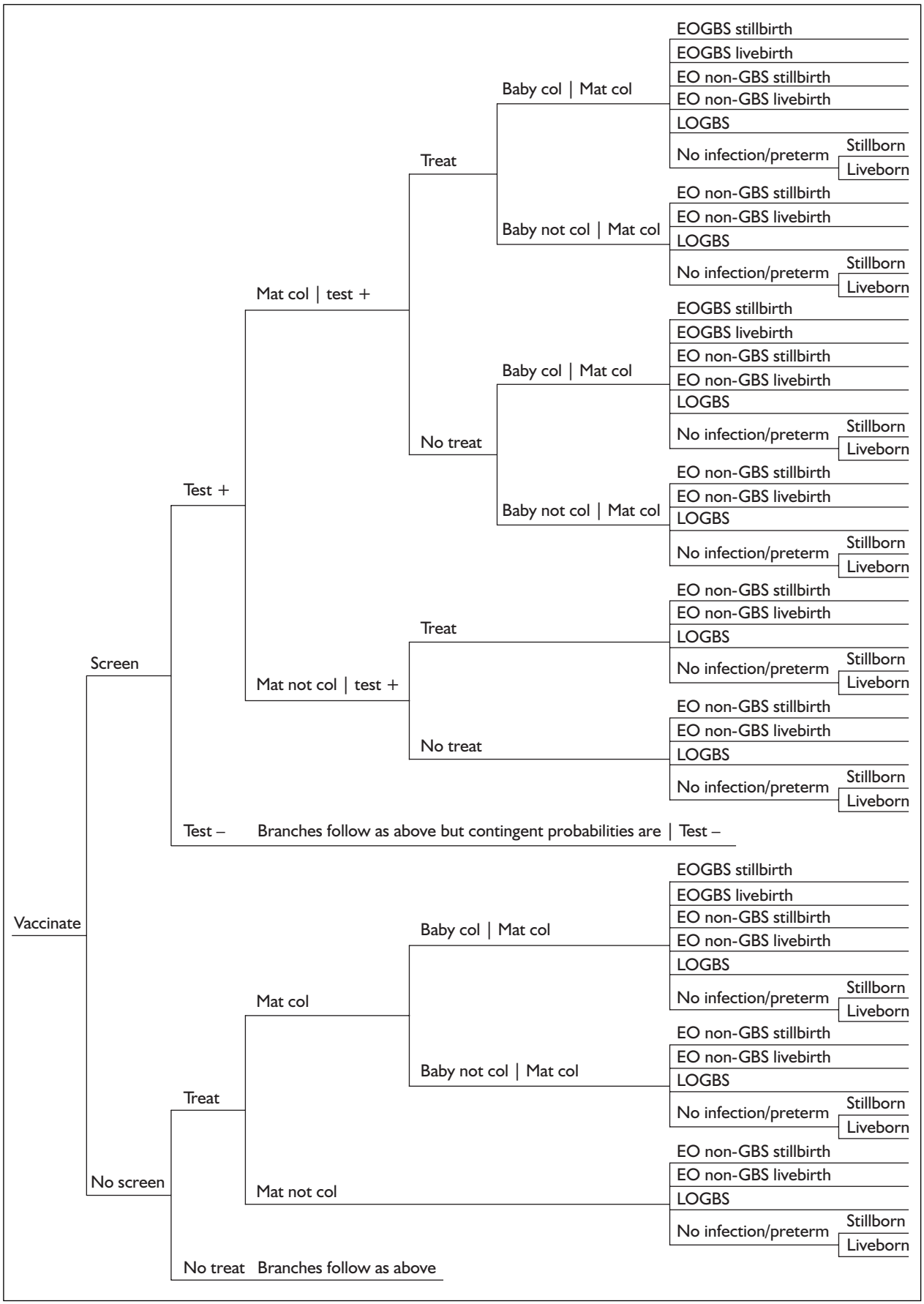

FIGURE 4 *Tree 3: vaccination, screening and treatment*

TABLE 2 *Bacterial infection prevention interventions*

No.	Intervention	Code
1	Vaccinate all	V
2	Screen all at 35–37 weeks and treat positive with oral antibiotics	CO
3	Screen all at 35–37 weeks and treat positive with i.v. antibiotics	CI
4	Screen all at labour with PCR and treat positive with oral antibiotics	PO
5	Screen all at labour with PCR and treat positive with i.v. antibiotics	PI
6	Treat all with i.v. antibiotics	I
7	Treat all with oral antibiotics	O
8	Do nothing	n
9	Vaccinate all then screen all at 35–37 weeks and treat positive with oral antibiotics	VCO
10	Vaccinate all then screen all at 35–37 weeks and treat positive with i.v. antibiotics	VCI
11	Vaccinate all then screen all at labour with PCR and treat positive with oral antibiotics	VPO
12	Vaccinate all then screen all at labour with PCR and treat positive with i.v. antibiotics	VPI
13	Vaccinate all then treat all with i.v. antibiotics	VI
14	Vaccinate all then treat all with oral antibiotics	VO

Antibiotic treatment had an independent effect on GBS colonisation in the baby and on live- and stillbirths with EOGBS and EO non-GBS. Vaccination reduced maternal colonisation and stillbirths due to EOGBS and livebirths with EOGBS or LOGBS. The effects of vaccination and antibiotic treatment were assumed to be additive.

Outcomes

A cost–utility framework was used, in which benefits (health outcomes) were measured in QALYs, to allow interventions to be compared within and across programmes.[30,31] To generate QALYs, a utility on a scale ranging from 0 (death) to 1 (perfect health) was assigned to four levels of disability that could result in the child (no disability and mild, moderate or severe disability). The benefit of an intervention was then calculated as the increase in utility that was generated, multiplied by the life expectancy for each level of disability.

Lifetime costs were defined as those that were attributable to the infant, in addition to costs relating to labour and delivery and the screening and treatment strategies. Costs for the mother after delivery were not included. Babies with infection but no disability incurred only the healthcare costs of the initial infection and no decrement in life expectancy or quality of life in comparison with uninfected babies.

Cost-effectiveness analysis

The cost-effectiveness of each of the 14 interventions for each of the 12 maternal RGs was determined. In a second step, the most cost-effective combinations of interventions across all 12 RGs were selected first with, and then without, vaccination. The selection process stipulated constraints including: women in groups 11 and 12 could only be treated based on a positive GBS test result, and the strategy in group 11 could not differ from that in group 12 (further details are given in the section 'Methods', p. 60). Also included were policy-relevant strategies representing the Royal College of Obstetricians and Gynaecologists' (RCOG) recommendations (intravenous antibiotics for RG2, 3, 4, 8, 9 and 10; do nothing for RG1, 5, 6, 7, 11 and 12) and current standards of good clinical practice (intravenous antibiotics for RG2, 3, 4, 8, 9 and 10; oral antibiotics for RG5; do nothing for RG1, 6, 7, 11 and 12). In total 713 different prevention strategies were modelled (combinations of interventions; see the section 'Cost-effectiveness analysis for strategies', p. 60).

Interventions were compared in terms of QALYs gained and costs, the decision rule being to maximise QALYs for a given budget constraint. This budget constraint [willingness to pay (WTP) for a QALY gained] is uncertain; however, values ranging from £20,000 to £30,000 have been suggested for England and Wales. The net benefit of an intervention was expressed as QALYs multiplied by the appropriate threshold minus the total cost of an intervention. Incremental cost-effectiveness ratios (ICERs) were determined for non-dominated and extendedly dominated (see Chapter 7) strategies.

Limitations of the model

Six important factors were not considered in the model because of time and resource constraints, as outlined below.

Maternal outcomes and adverse effects of interventions

Maternal benefits of treatment were not considered (e.g. reduced risk of endometritis) as prophylactic treatment would not be offered solely for this purpose. In addition, the benefits of oral erythromycin or vaccination on prolongation of pregnancy in women with preterm prelabour rupture of membranes were not considered.[17]

Adverse effects of antibiotic treatment or vaccination in the mother or baby were addressed only as costs and not in terms of QALYs for reasons discussed in the section 'Interventions' (p. 40). Similarly, the cascade of testing and treatment consequences for the baby or the effects on parental anxiety and medicalisation of the experience of childbirth were not considered, because of the difficulties in defining and quantifying these consequences in terms of QALYs and because these outcomes were expected to result in a negligible QALY decrement when viewed over a lifetime. We ignored potential costs of requiring women receiving intravenous treatment to deliver in an obstetric unit rather than at home or in a GP unit, although these are recognised as potential issues of implementation.

Subsequent pregnancies

Any protective effect of a GBS vaccine in subsequent pregnancies was not considered, despite the fact that GBS vaccine is likely to have such an effect.[32] This was because the model only considered the costs and outcomes of one pregnancy per woman.

Antibiotic resistance

The effect of maternal antibiotic treatment on the diversity of gut flora in the mother and baby or on the presence of antibiotic-resistant organisms was not considered. Treatment can change the maternal gut flora, allowing overgrowth of other pathogens or of resistant organisms. In the baby, these organisms may cause disease or become tolerated and persist in the infant gut for months or years.[33] As babies are prime dispersers of gut flora, they may contribute to community-acquired resistance. Finally, concerns have been raised that early exposure to antibiotics reduces the diversity of gut flora, with possible long-term effects on the child's immunity.[33] Although important, none of these outcomes were considered because of lack of evidence on the relative contribution of maternal intrapartum antibiotics compared with other uses of antibiotics in the mother and baby. However, the proportion of women treated as a secondary outcome measure for each of the intervention strategies was included.

Type of antibiotic

The options for antibiotic treatment were restricted to intravenous penicillin and oral erythromycin as these are currently recommended treatments in the UK. There remains an important policy question about the relative cost-effectiveness of strategies using intravenous ampicillin and those using intravenous penicillin as ampicillin is still widely used for intrapartum treatment in the USA[7,34] and Australia (Isaacs D, Westmead Children's Hospital, Australia: personal communication, June 2006). Ampicillin affects a broader spectrum of bacteria and may therefore be more effective against EO non-GBS. However, such benefit needs to be weighed against possible selection of resistant organisms.

Treatment effects on mortality

We assumed that the treatment effect of intrapartum antibiotics on culture-positive cases translates into the same proportionate reduction in mortality. This is due to the lack of data available. Only one systematic review previously carried out looked at the effect of intrapartum antibiotics on mortality from EOGBS.[35] Two studies were found which measured this outcome and, of these, one had zero events in both the control and treatment arms and the other had two deaths (out of 79 babies) in the control group and zero (out of 85 babies) in the treatment group. This meant that any pooled effect could not be accurately determined.

Culture negative sepsis

Culture negative sepsis, which may be between 1.2 and 2.3 times more common than culture positive disease, was not considered.[36,37] Inclusion of culture-negative cases would change the net benefit of strategies involving treatment but, provided that a negative culture was equally likely given in EOGBS or EO non-GBS disease, would not affect the ranking of cost-effective strategies.

Chapter 4

Overview of review methods

Systematic reviews and analyses of primary data were carried out in order to populate each branch of the decision tree with data. For most data inputs, systematic reviews and meta-analyses of the published research literature were conducted, selecting studies based on the inclusion criteria for each data input (see Chapter 5 for details). However, for some of the natural history model parameters, the data required for multiple subgroups were obtained from primary datasets that were representative of the UK. As no research data were available for the treatment effects of vaccination and of antibiotic treatment on stillbirths, estimates from experts were used.

Search strategy and review methods

A broad search strategy was developed to generate a large pool of abstracts from which were selected potentially eligible studies for each review question. A simultaneous search was made of the entire literature of 10 databases using the NHS KA24 service on 29 September 2005 and the following search terms: (GBS OR Group ADJ B ADJ Streptococ$ OR S ADJ DOT ADJ agalactiae) AND (maternal OR mother OR pregnan$ OR neonat$ OR baby OR infan$). These were the only terms used as they encompass all areas of the GBS literature used in the review (except for those concerning life expectancy and utilities, which are detailed below). One reviewer (TC) scanned all the abstracts, retrieved full text for all potentially eligible studies, examined them against the inclusion criteria and extracted the data. Inclusion decisions and data extraction for all treatment effects were scrutinised by a second reviewer (RG).

For information on life expectancy, we carried out a separate search of MEDLINE (on 17 February 2006) for studies reporting life expectancy in children with cerebral palsy or other causes of disability. The terms used were (Life expectancy or Mortality) AND (Children or Pediatric$) AND (Cerebral Palsy or Meningitis or disability), supplemented by a search of articles on http://www.lifeexpectancy.com/articles.shtml (last accessed 28 March 2006).

Data on resource use (see the section 'Utilities', p. 39) and costs (see the section 'Costs', p. 52) were obtained from the following: published cost databases [Personal Social Services Research Unit (PSSRU) and the British National Formulary (BNF)]; primary data analysed by S Petrous [National Paediatric Epidemiology Unit (NPEU)] on the duration of stay and levels of care for serious neonatal bacterial infection; the investigators of an ongoing study on screening tests for GBS (J Gray, Consultant Microbiologist, Birmingham Children's Hospital; and K Khan, Consultant in Obstetrics and Gynaecology, Birmingham Women's Hospital); and published literature.

Results of searches

The main search of ten databases generated 3366 records (excluding duplicates) from MEDLINE (1129), EMBASE (1992), CINAHL, the British Nursing Index (225) Department of Health database (1) and PsycINFO (19). *Table 3* shows the number of potentially eligible and included studies for each review question. The MEDLINE search for studies of life expectancy generated four potentially relevant studies and seven further studies from the website. One study was included (see the section 'Life expectancy', p. 37).

Data synthesis methods

The study used probabilistic decision analysis,[23] which seeks to characterise each input parameter in terms of a probability distribution describing a best estimate and its credible range. The distributions were based where possible on data, either on a single study or on a meta-analysis of several studies or, in the absence of data, expert opinion. In this way, the uncertainty in the data inputs was propagated forward through the model, using Monte Carlo simulation, to generate uncertainty in net benefits (NBs) and uncertainty in the decision. The approach is inherently Bayesian[22,38] because of the focus on uncertainty in parameters given data, rather than the probability of data given values of parameters.

Briefly, strategies, $S = (1, 2, \ldots, s, \ldots)$, were compared in terms of their expected NB, which is a function of many uncertain parameters θ, thus

TABLE 3 *Search results and potentially eligible and included studies*

Question addressed	No. of abstracts scanned	No. potentially eligible	No. of papers meeting inclusion criteria
Natural history			
1. Proportion of total population in maternal RGs for GBS	20	9	6
2. Prevalence of maternal colonisation	314	17	8
3. Maternal RGs for maternal colonisation	129	17	11
4. Baby colonisation (vertical transmission risk)	125	11	7
5. Maternal RGs for baby colonisation	13	3	0
6. Proportion of all EOGBS that are stillborn	19	7	0
7. Risk factors for EOGBS stillbirth	1	0	0
8. Incidence of EOGBS	205	24	1
9. Maternal RGs for EOGBS	147	12	5
10. Proportion of colonised babies with EOGBS	27	13	5
11. Proportion of all EO non-GBS that are stillborn	9	1	0
12. Risk factors for EO non-GBS stillbirth	0	0	0
13. Incidence of EO non-GBS	90	6	0
14. Ratio of EOGBS to EO non-GBS	81	6	0
15. Risk factors for EO non-GBS	26	0	0
16. Incidence of LOGBS	66	7	0
17. Risk factors for LOGBS	56	2	1
18. Proportion of EOGBS with meningitis	58	8	0
19. Proportion of EO non-GBS with meningitis	20	3	0
20. Proportion of LOGBS with meningitis	20	2	0
21. EOGBS mortality rate	101	13	0
22. EO non-GBS mortality rate	43	5	0
23. LOGBS mortality rate	34	3	0
24. Proportion disabled from meningitis	27	3	0
25. Proportion disabled from sepsis/pneumonia (non-meningitis illness from infection)	10	3 [7][a]	1 [3]
Interventions			
26. Effect of antibiotic treatment on baby colonisation given maternal colonisation	29	13	7
27. Effect of antibiotic treatment in reducing EOGBS given maternal colonisation	64	12	6
28. Effect of antibiotic treatment in reducing EOGBS given baby colonisation	21	11	5
29. Effect of antibiotic treatment in reducing EO non-GBS	0 [13]	0 [7]	0 [2]
30. Effect of vaccination for EOGBS	90	0	0
Testing			
31. PCR screening tests – sensitivity/specificity	30	4 (5)	1
32. Sensitivity/specificity of culture screening at 35–37 weeks	18	13	4
Total (unique papers)	**1906 (1411)**	**240 (~150)**	**72 (~50)**

[a] Numbers in brackets are papers found from reference lists.

NB(s, θ). The expected NB can be found by averaging over our distributions for θ. Then, a Bayesian decision-maker should choose the optimal strategy S^* as the one with the highest expected NB:

$$S^* = \text{ArgMax}_s\{E_\theta[\text{NB}(s, \theta)]\}$$

The evidence synthesis approach adopted in this study shares all these features with probabilistic decision analysis, but also includes the possibility of incorporating information on both parameters and **functions of parameters**. This has been called multi-parameter evidence synthesis (MPES)[24] because blocks of parameters are estimated jointly from a common set of data. These methods have been developed independently in several areas,[39] using a range of computational methods to generate a Bayesian posterior analysis. The increasing availability of Bayesian Markov chain

Monte Carlo estimation, via packages such as WinBUGS,[40] has made this type of synthesis a practical possibility, with an increasing stream of applications.[41–48] Among the advantages of this approach are:

- It combines all available information, whether 'direct' or 'indirect', so avoiding arbitrary selection of data.
- It 'calibrates' model predictions to probabilistically agree with observations on model outputs – for example, the observed population rate of EOGBS.
- It allows examination of whether sources of data are consistent (external validation)
- It correctly propagates uncertainty backwards from the data inputs onto the parameters, then forward on to the decision outputs.

An important property of MPES is that it induces correlations between parameters. This has significance for calculation of expected value of information measures (see below).

For example, *Tables 5* and *8* (see later) set out a wide range of data relating to the proportions of women in each risk group, and the maternal colonisation rates in each group, respectively. One of the data items (Input 13 in *Table 8*) gives an average colonisation rate of 13.6% [95% confidence interval (CI) 9.6 to 18.3%], which is in effect a weighted average of the colonisation rates in the 12 groups, with the group sizes as the weights. In fact, this item is redundant, in the sense that the other items of data are sufficient to inform a prediction for the average colonisation rate. Because MPES synthesises all these data together, it is likely that the posterior distributions of parameters will differ from their direct data inputs. In this case the posterior (*Table 9*, item 13) had a mean 12.2% (95% CI: 9.03 to 15.9%), suggesting that the direct and indirect evidence on this parameter were not in conflict. Checking that there is no conflict between evidence inputs is an important part of validating an MPES model.

Expected value of information methods

The probabilistic cost-effectiveness analysis was extended to determine the expected value of information, part of Bayesian decision theory.[49,50] The principle is that the decision that is optimal **under currently available evidence** may yet be the wrong decision, in the sense that another strategy would yield a higher expected net benefit. Consequently, uncertainty leads to an expected opportunity loss. This is known as the expected value of perfect information (EVPI) and is equal to the difference between the expected value of a decision based on perfect information and the value of the decision based on current information (see the section 'Overview of methods', p. 85 for further details):

$$\text{EVPI} = E_\theta\{\text{Max}_s[\text{NB}(s, \theta)]\} - \text{Max}_s\{E_\theta[\text{NB}(s, \theta)]\}$$

EVPI can be readily calculated by Monte Carlo simulation.

Chapter 5

Model inputs and outputs

Overall approach to evidence inclusion

The aim was to include all the available relevant evidence that met the inclusion criteria for each data input to the model. In general, inclusion criteria were restricted to studies in a UK population or, if available, primary data representing a contemporary UK population were used for questions that related to the burden of disease. For information on relative rates, for example the **relative** risk of maternal colonisation in preterm versus term deliveries, studies could be included from any industrialised country. The data inputs are presented as they were used in the model: as log odds (logits) or log odds ratios (LORs), together with the standard deviation (SD). Where data were based on a prior, for example, expert, opinion, this was characterised as a beta distribution, which is commonly used to represent binomial proportions.

The following section describes how the data inputs for the model were derived and the results (outputs) for each parameter presented. All meta-analyses were done using a random effects distribution, unless stated otherwise.

Natural history model

Maternal risk group distribution

Table 4 shows the 12 maternal RGs and the parameter θ_j, used to represent each group: this is the proportion of women in each RG out of all women delivering at 24 weeks or more of gestation. Because no nationally representative data provided information for all 12 RGs, we derived the proportion (θ_j) in each RG from multiple sources using the series of analyses outlined below.

Proportion of all deliveries that were preterm (Input 1)

The proportion of deliveries that were preterm were determined from NHS Hospital Episode Statistics (HES) for England for 2003–4,[51] as this gave the most representative data for the UK. The number of preterm deliveries out of the total, 42,200/575,900 (7.3%), provided an estimate of θ_P, the proportion of preterm deliveries in the total population.

Eight maternal categories based on data from the St Mary's Maternity Information System (SMMIS) (Inputs 2–9, Table 5*)*

The SMMIS dataset was used [unpublished data: St Mary's Maternity Information System (SMMIS)

TABLE 4 *Model parameters representing the maternal risk groups (see* Table 7 *for model output, p. 19)*

Risk group	Description	Parameter
RG1	Preterm: LSCS <37 weeks of gestation	θ_1
RG2	Preterm: previous GBS baby	θ_2
RG3	Preterm: urine/vaginal swab positive for GBS	θ_3
RG4	Preterm: fever ⩾38°C in labour	θ_4
RG5	Preterm: prelabour ROM	θ_5
RG6	Preterm: labour intact membranes	θ_6
RG7	Term: LSCS <37 weeks of gestation	θ_7
RG8	Term: previous GBS baby	θ_8
RG9	Term: urine/vaginal swab positive for GBS	θ_9
RG10	Term: fever ⩾38°C in labour	θ_{10}
RG11	Term: membrane rupture ⩾18 h	θ_{11}
RG12	Term: no risk factors	θ_{12}
RG1–RG6	Preterm delivery <37 weeks of gestation	θ_P
RG7–RG12	Term delivery ⩾37 weeks of gestation	$1-\theta_P$

TABLE 5 *Proportion of women in SMMIS[a] categories, parameters estimated and data inputs*

Input	SMMIS category	Parameters estimated	Data input[b]	% (95% CI)
	Preterm deliveries			
2	Proportion that are planned LSCS	$\theta_{P1} = \theta_1/\theta_P$	475/4,365	10.9 (10.0 to 11.8)
3	Proportion with pyrexia	$\theta_{P2} = \theta_4(1 + \theta_2 + \theta_3)/\theta_P$	151/4,365	3.6 (3.1 to 4.1)
4	Proportion with prelabour ROM >2 h	$\theta_{P3} = \theta_5(1 + \theta_2 + \theta_3)/\theta_P$	1,510/4,365	34.8 (33.4 to 36.2)
5	Proportion with prelabour ROM ≤2 h	$1 - \theta_{P1} - \theta_{P2} - \theta_{P3}$	2,229/4,365	50.8 (49.3 to 52.2)
	Total		4,365	100
	Term deliveries			
6	Proportion that are planned LSCS	$\theta_{T1} = \theta_7/(1 - \theta_P)$	5,587/64,794	8.6 (8.4 to 8.9)
7	Proportion with pyrexia	$\theta_{T2} = \theta_{10}(1 + \theta_8 + \theta_9)/(1 - \theta_P)$	1,159/64,794	1.8 (1.7 to 1.9)
8	Proportion with ROM ≥18 h	$\theta_{T3} = \theta_{11}(1 + \theta_9 + \theta_9)/(1 - \theta_P)$	6,100/64,794	9.4 (9.2 to 9.6)
9	Proportion with no risk factors	$1 - \theta_{T1} - \theta_{T2} - \theta_{T3}$	51,948/64,794	80.2 (79.9 to 80.5)
	Total		64,794	100

LSCS, lower section Caesarean section.
[a] SMMIS database, 2005.
[b] Shows number in each SMMIS category divided by total number of preterm or term deliveries. The data likelihood was based on two four-way multinomial distributions.

maternity database of 17 NHS trusts in north-west London (1988–2000); provided by M Little and P Steer, Imperial College London, in September 2005; hereafter referred to as SMMIS database, 2005] to provide two four-way breakdowns of maternal RGs, one for term and the other for preterm deliveries. *Table 5* shows how the eight RGs reported in SMMIS relate to the 12 maternal RGs. SMMIS data were used as national data (HES or the Scottish Maternity Dataset) lacked information on key variables (pyrexia, duration of ROM or duration of labour). SMMIS is compiled from routinely collected data in 17 NHS trusts in north-west London. Data for 1999–2000 were used, the most recent years with validated data. We restricted analyses to 69,159 deliveries (out of a total of 88,188) that occurred at 24 weeks of gestation or more and had complete data for the eight subgroups. The SMMIS categories provide data on only eight of the 12 maternal RGs. Data for RG2, 3, 8 and 9 were not recorded on the database and these groups are mixed within the other categories. For example, 'preterm pyrexia' (Input 3) contains women in RG2 and 3. It therefore overestimates the proportion of women that would be in the preterm pyrexia group (group 4) as used in the model. Before the proportions in the SMMIS categories could be adjusted to reflect the proportions in the maternal RGs, the proportions in the missing RGs (2, 3, 8 and 9) had to be estimated using other data inputs.

Data on the proportion of deliveries in maternal risk groups not represented in SMMIS (RG2, 3, 8 and 9) (Inputs 10–12, Table 6)

Table 6 shows the data inputs used to estimate functions of the proportions of women in each of the four RGs. It was assumed that the proportion of women with a previous GBS baby (Input 10) ranged from 0.1 to 1 per 1000 and this risk was partitioned between preterm and term deliveries (groups 2 and 8) using the proportion of preterm deliveries (Input 1). Much higher rates reported in three UK studies[52–54] (see Appendix 1, *Table 69*) were inconsistent with the incidence of EOGBS in the UK and suggest recall bias or mislabelling of neonatal infection as a 'GBS baby'. RG3 and 9 include women with GBS bacteriuria or a previous positive swab for GBS during pregnancy; therefore, to estimate the size of these groups, data on the number of women meeting each of these criteria was sought. The proportion of women with GBS bacteriuria was based on three UK studies (see Appendix 1, *Table 69*),[55–57] all of which carried out universal testing during pregnancy [mean proportion based on a random effects model was 2.1% (95% CI: 0.8 to 4.0%; input as log odds mean –3.9028; SD 0.3930]. To determine the proportion of women with a previous GBS swab in the current pregnancy, an unpublished audit from Birmingham Women's Hospital was used (1500/6500 deliveries, 23.1%, had a vaginal swab during pregnancy) (Gray J, Department of Microbiology, Birmingham

TABLE 6 *Derivation of proportions of women in maternal risk groups not represented in the SMMIS dataset (risk groups 2, 3, 8 and 9)*

Input	Description of data input	Parameters estimated	Data input	Mean (%) or odds ratio (95% CI)	Source
10	Prevalence of a previous GBS baby[a]	$\theta_2 + \theta_8$	1.2/4,000	0.03% (0.01 to 0.1%)	Clinical opinion
11	Prevalence of bacteriuria or previous positive swab (groups 3 and 9)	Logit($\theta_3 + \theta_9$)	Logit: median –2.8195, SD 0.3192	5.8% (3.0 to 9.6%)	Estimated in WinBUGS using data described in the text
12	Odds ratio of preterm delivery given GBS bacteriuria or swab	$(\theta_3/\theta_9) \times [(1 - \theta_P - \theta_9)/(\theta_P - \theta_3)]$	LOR: median 0.6678, SD 0.3733	2.08 (0.91 to 4.04)	Meta-analysis of 5 studies[55,57–60] (Appendix 1, *Table 69*)

[a] Partitioned into preterm and term using HES data (Input 1).

Women's Hospital: personal communication, 2005). The 95% probability range was between 8.3 and 42.2% to reflect variation in the frequency of swabbing between hospitals (input as a beta distribution: 4.8779, 16.3304). It was assumed that women who were swabbed had the same risk of a positive result as the average for all women swabbed in labour (Input 13, *Table 8*). The proportion of women with positive bacteriuria and/or a positive swab (groups 3 and 9; Input 11) was estimated in WinBUGS using the following equation, where the overlap (women with positive bacteriuria **and** a positive swab) was allowed to vary between 10 and 90%:

$$p(\text{bacteriuria or positive swab}) = [p(\text{bacteriuria}) + p(\text{positive swab})]/[1 + p(\text{overlap})]$$

The proportion of these women delivering preterm (RG3) was calculated by applying results from a meta-analysis of five studies[55,57–60] on the relative risk of preterm delivery given previous GBS bacteriuria (Input 12) to the combined group of women with GBS bacteriuria or positive swab.

Proportion of women in each of the 12 maternal risk groups (Outputs 1–12, Table 7*)*

To derive the proportion of women in each of the 12 RGs, the inputs from SMMIS for groups 1 and 7 and the inputs from *Table 6* for groups 2, 3, 8 and 9 were used. The proportions were then reduced in groups further down the hierarchy of preterm (4, 5 and 6) and term deliveries (10, 11 and 12) by the proportion of group 2 and 3 out of all preterm deliveries $[(\theta_2 + \theta_3)/\theta_P]$ and the proportion of group 8 and 9 out of all term deliveries $[(\theta_8 + \theta_9)/(1 - \theta_P)]$.

The derived sizes of the 12 RGs are given in *Table 7*.

TABLE 7 *Proportion of the total pregnant population in each of the 12 maternal risk groups (see* Table 4 *for model inputs, p. 17)*

Output	Parameter	Proportion (%)	
		Mean	95% CI
1	RG1. Preterm planned LSCS	0.80	0.73 to 0.87
2	RG2. Preterm previous GBS baby	0.01	0.00 to 0.01
3	RG3. Preterm GBS bacteriuria/positive swab	0.44	0.22 to 0.76
4	RG4. Preterm pyrexia	0.25	0.21 to 0.29
5	RG5. Preterm prelabour ROM	2.41	2.27 to 2.53
6	RG6. Preterm labour with intact membranes	3.43	3.19 to 3.62
7	RG7. Term planned LSCS	7.99	7.79 to 8.19
8	RG8. Term previous GBS baby	0.08	0.02 to 0.18
9	RG9. Term GBS bacteriuria/positive swab	3.51	1.95 to 5.75
10	RG10. Term pyrexia	1.60	1.51 to 1.70
11	RG11. Term prolonged ROM	8.37	8.10 to 8.62
12	RG12. No risk factors (term)	71.10	69.10 to 72.50

It should be noted that in calculating these figures, the model also considers the data inputs involving other 'downstream' parameters such as mother colonisation, baby colonisation, EOGBS given baby colonisation and the percentage of EOGBS cases in each of the 12 RGs. This is because some data items, for example proportion of EOGBS in each group, provide indirect information on the maternal risk group sizes **and** these other parameters. The posteriors are therefore not independent.

As is clear from the table, most women (71.1%) have none of the risk factors [RG12: no risk factors (term)]. The largest groups for women delivering at preterm gestation are RG5, preterm prelabour ROM, and RG6, preterm labour with intact membranes, which between them make up the majority of preterm women. It will be noted later (see *Figure 5*, p. 28) that although some of the groups are small they have a disproportionate risk of EOGBS disease (this is true, for example, for the pyrexia group).

Maternal colonisation with GBS

The prevalence of maternal colonisation with GBS in the 12 RGs was estimated by combining a pooled estimate for the UK average maternal colonisation rate with information on the prevalence of colonisation in specific maternal RGs. Women with a previous positive bacteriuria or vaginal swab (groups 3 and 9) have the highest risk of colonisation, and it was assumed that women with preterm pyrexia or prolonged ROM (groups 4 and 5) have a higher risk than the remaining low-risk groups (groups 1, 2 and 6). A common odds ratio was used for the increased risk of colonisation in women delivering preterm to determine the risk in the corresponding high- and low-risk term groups.

Prevalence of maternal colonisation in the total population (Input 13, Table 8*)*

As colonisation rates vary between countries, we restricted studies to women in the UK who had not received antibiotic treatment prior to being swabbed in suspected labour. Nine studies (2971 women), including one on-going unpublished study from Birmingham Women's Hospital (Gray J, Department of Microbiology, Birmingham Women's Hospital: personal communication, October 2005; 286 women), met the inclusion criteria. All used enriched media for culture. Four studies (879 women) used only vaginal swabs; the remainder (2092 women) used results from a positive vaginal or rectal swab. The mean colonisation rate was 13.59% (95% CI: 9.56 to 18.28%).

Prevalence of colonisation given a previous GBS bacteriuria or positive swab (group 3 or 9) (Input 14, Table 8*)*

The risk of GBS colonisation in labour given a previous positive urine or vaginal swab depends on the time interval between the two tests (see the section 'Culture screening at 35–37 weeks', p. 47) and the clinical indications for testing. Data from four studies of women with GBS bacteriuria in labour[60–63] (see Appendix 1, *Table 70*) produced a pooled prevalence of colonisation in labour (i.e. at the same time) of 77.70% (95% CI: 62.72 to 89.69%). To take account of the delay between a previous positive urine or vaginal swab and labour, we assumed a lower prevalence of 65%, with a 95% probability range of 50–80%.

High- versus low-risk preterm deliveries (Input 15, Table 8*)*

No studies were found that separately reported the risk of colonisation in women delivering preterm with pyrexia or ROM before labour. It was therefore assumed that high-risk groups (4 and 5) were 1.5 times more likely to be colonised than low-risk groups (1, 2 and 6), with a 95% probability range of 1.0–2.25. It was also assumed that the odds ratio (OR) was 1.5 (95% CI: 1.0 to 2.25) and the model was allowed to estimate the risk of colonisation for the low-risk preterm group assuming a uniform prior distribution.

Odds ratio for preterm versus term deliveries (Input 16, Table 8*)*

Studies from any country were included provided that women were swabbed in labour (using any method), had not been treated and the numbers of preterm and term deliveries were reported (see Appendix 1, *Table 70*). Eleven studies (12,527 women, 1585 preterm deliveries) met the inclusion criteria, three of which were case–control studies. The median OR of 1.49 (95% CI: 1.11 to 2.01) was used in the model to estimate the risk of colonisation in the term high- and low-risk groups and group 9, relative to the risk in the corresponding preterm groups.

Output for maternal colonisation (Outputs 13–27, Table 9*)*

Taking all of the data on maternal colonisation into consideration, the model determined the GBS colonisation rate during labour for each of the 12 maternal RGs as shown in *Table 9*.

The colonisation rate varies between RGs. The likelihood of colonisation (see LR column in the table) and is higher in all preterm groups than their term counterparts. Within each set of six

TABLE 8 *Parameters estimating the prevalence of maternal GBS colonisation in labour in maternal risk groups (see* Table 9 *for model output)*

Input	Description of data input	Parameter estimated	Data input	Mean (%) or odds ratio (95% CI)	Source[a]
13	Prevalence of maternal colonisation in all women	$\Sigma_{j=1-12}\theta_j\mu_j/\Sigma_{j=1-12}\theta_j$	Logit: median –1.8592, SD 0.1883	13.6% (9.6 to 18.3%)	Meta-analysis of 9 UK studies[64–71]
14	Maternal colonisation given previous positive swab/bacteriuria	$\theta_3\mu_3 + \theta_9\mu_9/\theta_3 + \theta_9$	Beta (26, 14)	65% (50 to 79%)	Clinical opinion
15	OR of maternal colonisation in high- vs low-risk preterm groups	$\text{logit}(\mu_{high}/\mu_{low})$	LOR: median 0.405, SD 0.043	1.5 (1.0 to 2.5)	Clinical opinion
16	OR for maternal colonisation in preterm vs term groups	$\text{logit}(\mu_j) - \text{logit}(\mu_{j+6})$	LOR: median 0.3873, SD 0.1506	1.49 (1.11 to 2.01)	Meta-analysis of 11 studies worldwide[60,72–81]

μ, Prevalence of maternal colonisation; suffix denotes maternal risk group, or high (RG4, 5) or low preterm risk groups (RG1, 2, 6).
[a] See Appendix 1, *Table 70* for details of the studies used in the meta-analyses.

TABLE 9 *Maternal colonisation with GBS (see* Table 8 *for model inputs)*

Output	Parameter	Proportion (%)		LR[a]
		Mean	95% CI	
13	Overall maternal colonisation (RG1–12)	12.2	9.03 to 15.9	1.00
14	Women delivering preterm (RG1–6)	23.8	17.2 to 31.4	1.96
15	Women delivering at term (RG7–12)	11.1	8.26 to 14.8	0.92
16	RG1. Preterm planned LSCS	18.30	12.4 to 25.2	1.50
17	RG2. Preterm previous GBS baby	18.30	12.4 to 25.2	1.50
18	RG3. Preterm GBS bacteriuria/positive swab	62.00	47.0 to 76.2	5.08
19	RG4. Preterm pyrexia	26.60	17.9 to 36.6	2.18
20	RG5. Preterm prelabour ROM	26.60	17.9 to 36.6	2.18
21	RG6. Preterm labour with intact membranes	18.30	12.4 to 25.2	1.50
22	RG7. Term planned LSCS	9.42	6.5 to 13.0	0.77
23	RG8. Term previous GBS baby	9.42	6.5 to 13.0	0.77
24	RG9. Term GBS bacteriuria/positive swab	43.60	28.1 to 60.9	3.57
25	RG10. Term pyrexia	14.50	9.8 to 20.2	1.19
26	RG11. Term prolonged ROM	14.50	9.8 to 20.2	1.19
27	RG12. No risk factors (term)	9.42	6.5 to 13.0	0.77

[a] Likelihood ratio of colonisation compared with the average colonisation rate.

RGs, the likelihood of colonisation is considerably higher for women with bacteriuria/a previous positive swab for GBS (5.08 times higher than the overall average colonisation rate for women with preterm bacteriuria/previous positive swab and 3.57 times higher than the average for women with the same risk factor but who deliver at term). This makes sense when considering that GBS has already been identified in the urine/vagina of these women previously in pregnancy. Maternal colonisation in women with pyrexia and women with prelabour or prolonged ROM is also higher than average, as was thought when the inputs for the model were being considered. Maternal colonisation is lower than average in women who undergo planned lower section Caesarean section (LSCS).

Baby colonisation with GBS

The risk of baby GBS colonisation given maternal GBS colonisation in the 12 risk groups was estimated by combining data on the average risk

of baby colonisation with estimates of the relative risk of colonisation in high- compared with low-risk groups.

Average risk of baby colonisation given maternal colonisation (Input 17, Table 10*)*

UK studies were reviewed in which untreated women were swabbed during labour and their babies were swabbed within 24 hours of birth. Any method of swabbing or culture was accepted. Six studies were found[64,67–70,82] (308 colonised women, 117 colonised babies), of which five (268 colonised women, 97 colonised babies) used enriched culture. The number of sites sampled in the baby varied from 2 to 8 (see Appendix 1, *Table 71*).

Relative risk of baby colonisation given maternal colonisation in high-risk groups (Inputs 18 and 19, Table 10*)*

Based on clinical reasoning, it was considered that babies whose mothers had premature or prolonged rupture of membranes (RG5 and 11) or pyrexia (RG4 and 10) were more likely to be colonised than babies in the other 'medium-risk' groups (2, 3, 6, 8, 9 and 12). Premature or prolonged ROM leads to an increased likelihood of ascending infection and baby colonisation *in utero* and pyrexia indicates infection which may be associated with more intense maternal and baby colonisation. No relevant published studies were found in any country (two potentially relevant studies were excluded; see Appendix 1, *Table 71*), the model was used to estimate the risk independently in each of these two pairs of RGs (4 and 10, and 5 and 11) assuming the OR shown in the table. It should also be noted that studies were sought that examined an association with preterm delivery and baby colonisation given maternal colonisation, but only three potentially relevant studies were found, all of which were excluded (see Appendix 1, *Table 71*, for studies and reasons for exclusion).

Relative risk of baby colonisation given maternal colonisation in women undergoing elective Caesarean section (Input 20, Table 10*)*

No published studies were found that adequately compared baby colonisation in colonised women undergoing elective Caesarean section with babies delivered by other methods; two potentially relevant studies were excluded (see Appendix 1, *Table 71*, for studies and reasons for exclusion). It was assumed that the risk of transmission of GBS to the baby during elective LSCS would be approximately one-third of that in other RGs because the membranes are usually intact and there is no contact with vaginal organisms [OR: 0.31 (95% CI: 0.20 to 0.50)].

TABLE 10 *Data inputs for parameters informing the prevalence of baby colonisation at birth given maternal colonisation in labour in each of the maternal risk groups (see* Table 11 *for model output)*

Input	Description of data input	Parameters estimated	Data input	Mean (%) or odds ratio (95% CI)	Source
17	Prevalence of baby colonisation given maternal colonisation: all women	$\Sigma_{j=1-12}\theta_j\beta_j/\Sigma_{j=1-12}\theta_j$	Logit: median –0.5474, SD 0.2020	36.5% (26.7 to 45.1%)	Meta-analysis of 6 UK studies[64,67–70,82] (Appendix 1, *Table 71*)
18	OR of baby colonisation given mother colonisation in women with pyrexia vs low-risk women	Logit(β_{pyr}/β_{med})	LOR: median 0.97, SD 0.2694	2.64 (1.56 to 4.47)	Clinical opinion
19	OR of baby colonisation given mother colonisation in women with preterm or prolonged ROM vs low-risk women	Logit(β_{rom}/β_{med})	LOR: median 0.97, SD 0.2694	2.64 (1.56 to 4.47)	Clinical opinion
20	OR of baby colonisation given mother colonisation in women undergoing LSCS vs low-risk women	Logit(β_{lscs}/β_{med})	LOR: median –1.16, SD 0.24	0.31 (0.20 to 0.50)	Clinical opinion

β, Prevalence of baby colonisation given maternal colonisation; suffix denotes maternal RG, or pyrexia (pyr; RG4, 10), ROM (rom; RG5, 11), elective Caesarean section (lscs; RG1, 7) or medium-risk groups (med; RG2, 3, 6, 8, 9, 12).

TABLE 11 *Baby colonisation with GBS at birth given maternal colonisation with GBS during labour (see* Table 10 *for model inputs)*

Output	Parameter	Proportion (%)		LR[a]
		Mean	95% CI	
28	Overall baby colonisation given maternal colonisation (RG1–12)	32.4	24.7 to 40.8	1
29	Women delivering preterm (RG1–6)	36.6	28.4 to 45.9	1.14
30	Women delivering at term (RG7–12)	31.5	24.1 to 40.0	0.98
31	RG1. Preterm planned LSCS	11.1	6.6 to 17.2	0.34
32	RG2. Preterm previous GBS baby	30.0	22.4 to 38.6	0.93
33	RG3. Preterm GBS bacteriuria/positive swab	30.0	22.4 to 38.6	0.93
34	RG4. Preterm pyrexia	59.7	46.1 to 72.3	1.84
35	RG5. Preterm prelabour ROM	50.0	37.6 to 63.2	1.54
36	RG6. Preterm labour with intact membranes	30.0	22.4 to 38.6	0.93
37	RG7. Term planned LSCS	11.1	6.6 to 17.2	0.34
38	RG8. Term previous GBS baby	30.0	22.4 to 38.6	0.93
39	RG9. Term GBS bacteriuria/positive swab	30.0	22.4 to 38.6	0.93
40	RG10. Term pyrexia	59.7	46.1 to 72.3	1.84
41	RG11. Term prolonged ROM	50.0	37.6 to 63.2	1.54
42	RG12. No risk factors (term)	30.0	22.4 to 38.6	0.93

[a] Likelihood ratio of colonisation as compared with the average colonisation rate.

The prevalence of baby colonisation given maternal colonisation in the 'medium-risk' groups (the remaining groups: RG2, 3, 6, 8, 9, 12) was estimated by the model given the average rate and the other inputs. In order for this to be estimated, a uniform prior was assigned to these groups.

Output for baby colonisation given maternal colonisation (Outputs 28–42, Table 11*)*

Taking all of the data on baby colonisation given mother colonisation into consideration, the model determined the rate in each of the 12 maternal risk groups as shown in *Table 11*.

The proportion of all babies who are colonised with GBS at birth was calculated to be 3.9%. This proportion is directly dependent on the maternal colonisation rate as it is determined by the rate of baby colonisation given mother colonisation, which was calculated as 32.4% (95% CI: 24.7 to 40.8%). The rate of baby colonisation given mother colonisation varies according to maternal RG as determined by the model.

Risk of EOGBS in colonised babies or colonised mothers

The average risk of EOGBS in colonised babies for all maternal risk groups and the risk of EOGBS in colonised mothers were estimated. Colonised babies that deliver preterm are at higher risk of EOGBS than term babies because they are relatively immune immature. In addition, babies whose mother had pyrexia or prolonged rupture of membranes (groups 4, 5, 10 and 11), may be exposed to a greater intensity of maternal GBS colonisation[83] or transplacental GBS bacteraemia. A high-risk group was therefore defined for EOGBS comprising preterm deliveries and groups 10 and 11. An odds ratio was derived for high versus low risk based on cohort studies that reported EOGBS in colonised babies, and included information on EOGBS in high- or low-risk colonised mothers.

Average risk of EOGBS in colonised babies or colonised mothers (Input 21, Table 12*)*

Five cohort studies were identified that reported the risk of EOGBS in colonised babies (in total, 16 EOGBS events, 576 colonised babies).[72,84–87] All studies defined baby colonisation using between two and four surface swabs taken within 24 hours of birth and cultured on enriched media. The mothers were not treated and surface swabs and blood cultures were taken before any antibiotics were given to the baby. The pooled estimate is shown in *Table 12*. No attempt was made to modify the estimate to take into account possible overestimation of EOGBS due to routine blood sampling. The predictive distribution from the meta-analysis was used to give more uncertainty around the estimate to reflect the large between-study variation in the observed risks of EOGBS given baby colonisation. No additional studies were found that reported EOGBS in colonised mothers.

TABLE 12 *Estimation of the prevalence of EOGBS in colonised babies and colonised mothers (see* Table 13 *for model output)*

Input	Description of data input	Parameter estimated	Data input	Mean % or odds ratio (95% CI)	Source[a]
21	Prevalence of EOGBS in all colonised babies	$\Sigma_{j=1-12}\gamma_{2,j}$	Logit: median –3.6005, SD 0.4607	2.7% (1.4 to 4.6%)	Meta-analysis of 5 studies[72,84–87]
22	OR for EOGBS given baby colonisation in high- vs low-risk groups (groups 1–6, 10, 11 vs 7–9, 12)	$\text{Logit}[(\gamma_{2,\text{High}})/(\gamma_{2,\text{Low}})]$	LOR: median 0.5425, SD 0.6005	1.74	Ratio derived from meta-analysis of 4 high-risk studies[88–91] and one low-risk study[92]
23	Prevalence of EOGBS given maternal colonisation in high-risk groups (1–6, 10, 11)	$\beta_{\text{High}}\gamma_{2,\text{High}}$	4/111	3.6% (1.4 to 8.9%)	One study[93]

$\gamma_{2,j}$, EOGBS livebirth given baby colonisation in risk group *j*, or in high-risk groups (RG1–6, 10, 11) or low-risk groups (RG7, 8, 9, 12).
[a] See Appendix 1, *Table 72* for details of the studies used in the meta-analyses.

Differential risk of EOGBS in high- versus low-risk colonised babies (Input 22, Table 12*)*

Four studies were identified that reported EOGBS in high-risk colonised babies (13 EOGBS, 123 colonised babies),[88–91] and one study for low-risk babies (two EOGBS, 59 colonised babies).[92] All five studies were based on results from the untreated arm of an RCT. All studies defined baby colonisation based on four or five surface swabs, although only two studies[90,91] reported using enriched media. EOGBS was defined by bacteraemia, and in one study[91] included symptoms of pneumonia or sepsis. As all colonised babies had blood cultures taken, the risk of EOGBS may have been overestimated. In the trial in low-risk babies, two surface swabs were cultured using enriched media but no information was given as to whether blood cultures were taken routinely or in response to symptoms. Using the results of a meta-analysis of the four studies on the risk of EOGBS in high-risk colonised babies (9.5%; 95% CI: 4.8 to 16.5%) and the one study on the risk of EOGBS in low-risk babies (5.7%; 95% CI: 2.1 to 12.9%), an OR of EOGBS given baby colonisation in high- versus low-risk groups was calculated. This was then used in the model to provide more information on the risk of EOGBS given baby colonisation in the different maternal RGs.

Risk of EOGBS in high-risk colonised mothers (Input 23, Table 12*)*

One further trial was found that reported the risk of EOGBS in the untreated control arm of colonised mothers.[93] Maternal colonisation was defined by a positive vaginal swab using enriched media and all babies had a blood culture within 2 hours of birth. As this trial was in high-risk women, we applied the risk of EOGBS given mother colonisation to risk groups 1–6, 10 and 11.

Output for risk of EOGBS given baby colonisation and risk of EOGBS given mother colonisation (Outputs 43–60, Table 13*)*

The top section of *Table 13* shows the average risk of EOGBS in colonised babies and the risk in the high- and low-risk groups, as estimated by the model. The estimates are lower than the data inputs, particularly for the high-risk groups. This disparity illustrates the influence of parameters throughout the model: such high rates of EOGBS given baby colonisation were not consistent with data giving the overall risk of EOGBS, the proportion of women in high-risk groups and the intervening parameters for maternal colonisation and mother to baby transmission of GBS. The bottom section of *Table 13* shows that although there was only one data input for EOGBS given maternal colonisation, the model has used the data available for EOGBS by RG and for proximal parameters to estimate the risk of EOGBS in each of the 12 maternal RGs. This part of the table may be easier to digest using the 'Colonised mothers per EOGBS case' column. Women who are colonised and in RG4 and 10 are most likely to have a baby with EOGBS, with one in every 78 (95% CI: 115 to 54) affected. Other high-risk groups include RG5 and 11, with one in 93 (95% CI: 135 to 66) GBS-colonised women in either of these groups likely to have a baby with EOGBS;

TABLE 13 *Prevalence of EOGBS in GBS colonised babies and mothers (see* Table 12 *for model inputs)*

Output	Parameter	Proportion (%)		LR[a]	Colonised mothers per EOGBS case
		Mean	95% CI		
43	Average EOGBS given baby colonisation (RG1–12)	1.27	0.86 to 1.83	1	
44	EOGBS given baby colonisation in high-risk groups (RG1–6, 10, 11)	2.17	1.45 to 3.19	1.71	
45	EOGBS given baby colonisation in low-risk groups (RG7, 8, 9, 12)	0.79	0.51 to 1.18	0.62	
46	Average EOGBS given mother colonisation	0.66	0.49 to 0.88	1	152
47	In women delivering preterm (RG1–6)	0.76	0.55 to 1.04	1.16	131
48	In women delivering at term (RG7–12)	0.48	0.37 to 0.63	0.74	206
49	RG1. Preterm planned LSCS	0.24	0.14 to 0.38	0.36	421
50	RG2. Preterm previous GBS baby	0.64	0.44 to 0.91	0.97	155
51	RG3. Preterm GBS bacteriuria/positive swab	0.64	0.44 to 0.91	0.97	155
52	RG4. Preterm pyrexia	1.30	0.87 to 1.85	1.95	78
53	RG5. Preterm prelabour ROM	1.10	0.74 to 1.51	1.62	93
54	RG6. Preterm labour with intact membranes	0.64	0.44 to 0.91	0.97	155
55	RG7. Term planned LSCS	0.09	0.05 to 0.14	0.13	1165
56	RG8. Term previous GBS baby	0.23	0.17 to 0.32	0.35	430
57	RG9. Term GBS bacteriuria/positive swab	0.23	0.17 to 0.32	0.35	430
58	RG10. Term pyrexia	1.30	0.87 to 1.85	1.95	78
59	RG11. Term prolonged ROM	1.10	0.74 to 1.51	1.62	93
60	RG12. No risk factors (term)	0.23	0.17 to 0.32	0.35	430

[a] Likelihood ratio of colonisation as compared with the average colonisation rate.

and RG2, 3 and 6, with one in every 155 (95% CI: 227 to 110) GBS-colonised women in any of these groups likely to have a baby with EOGBS. The explanation for groups having identical outputs is again due to the model inputs. The fact that all the preterm RGs are again at higher risk than their term counterparts should also be noted.

Risk of EOGBS livebirth in the total population

Data from the British Paediatric Surveillance Unit (BPSU) surveillance study were used (details are given in Appendix 1, *Table 73*) to determine the risk of EOGBS in the total population.[12] Cases were ascertained during 2000 from active monthly reporting by paediatricians across the UK and Ireland, routine reporting by laboratories, notifications from reference laboratories, and reports from parents. Cases were defined as liveborn children with GBS isolated from blood or CSF taken before 7 days of age. Other UK surveillance studies[52,53,94–96] were not used for the risk estimation, as although the results were consistent with the BPSU study, ascertainment of cases and the denominator populations were considered to be less reliable.

A total of 377 EOGBS cases were confirmed for 794,037 livebirths in the UK and Ireland (Input 24, *Table 14*): a risk of 0.474/1000 live births.

Proportion of EOGBS cases in each maternal risk group

The proportion of EOGBS babies in each maternal risk group was determined using data from a regional surveillance study[53] and estimates were based on functions of parameters (indirect estimates) from the BPSU dataset (unpublished data: database from BPSU study on EOGBS and LOGBS (1 February 2000–28 February 2001);[12] provided by P Heath, St George's Hospital, London, June 2005; hereafter referred to as BPSU database, 2005) and aggregate results in published UK surveillance studies.[52,94–96] A similar approach for integrating information was used on some but not all RGs as was used to define the distribution of maternal RGs (see the section 'Maternal risk group distribution', p. 17). First, primary data from the 3-year surveillance study in the northern region (1990–2000) were used to provide information on each of the 12 maternal RGs. As this study included only 39 cases, of which 35 had data on RGs, the estimates were very uncertain (Inputs 25–36, *Table 14*).[53] Second, the prevalence of preterm delivery was determined as a proportion of all livebirths with EOGBS based on a meta-analysis of UK studies that included four published studies and one unpublished dataset[52,94–96] [unpublished data: database of neonatal bacteraemia from the Royal Free

TABLE 14 *Estimation of the prevalence of EOGBS in the 12 maternal risk groups (see* Table 15 *for model output)*

Input	Description of parameter input	Parameter estimated	Data input	Mean rate (%) or odds ratio (95% CI)	Source[a]
24	Proportion of all livebirths with EOGBS	$E = \theta_A\mu_A\beta_A\gamma_A$	377/794037	0.47/1000	BPSU database, 2005
Proportion of all EOGBS in each maternal RG					
25	Preterm LSCS (RG1)	$E_1 = \theta_1\mu_1\beta_1\gamma_{2,1}/E$	1/35	2.9% (0.1 to 14.5)	Northern Region database, 2005[b]
26	Preterm previous GBS baby (RG2)	$E_2 = \theta_2\mu_2\beta_2\gamma_{2,2}/E$	0/35	0% (0 to 9.9)	As above
27	Preterm GBS bacteriuria/positive swab (RG3)	$E_3 = \theta_3\mu_3\beta_3\gamma_{2,3}/E$	2/35	5.7% (1.6 to 18.6)	As above
28	Preterm pyrexia (RG4)	$E_4 = \theta_4\mu_4\beta_4\gamma_{2,4}/E$	1/35	2.9% (0.1 to 14.5)	As above
29	Preterm prelabour ROM (RG5)	$E_5 = \theta_5\mu_5\beta_5\gamma_{2,5}/E$	5/35	14.3% (6.3 to 29.4)	As above
30	Preterm labour intact membranes (RG6)	$E_6 = \theta_6\mu_6\beta_6\gamma_{2,6}/E$	4/35	11.4% (4.5 to 25.6)	As above
31	Term LSCS (RG7)	$E_7 = \theta_7\mu_7\beta_7\gamma_{2,7}/E$	0/35	0% (0 to 9.9)	As above
32	Term previous GBS baby (RG8)	$E_8 = \theta_8\mu_8\beta_8\gamma_{2,8}/E$	0/35	0% (0 to 9.9)	As above
33	Term GBS bacteriuria/positive swab (RG9)	$E_9 = \theta_9\mu_9\beta_9\gamma_{2,9}/E$	1/35	2.9% (0.1 to 14.5)	As above
34	Term pyrexia (RG9)	$E_{10} = \theta_{10}\mu_{10}\beta_{10}\gamma_{2,10}/E$	4/35	11.4% (4.5 to 25.6)	As above
35	Term ROM >18 h (RG11)	$E_{11} = \theta_{11}\mu_{11}\beta_{11}\gamma_{2,11}/E$	8/35	22.9% (12.1 to 39.0)	As above
36	No risk factors (term) (RG12)	$E_{12} = \theta_{12}\mu_{12}\beta_{12}\gamma_{2,12}/E$	9/35 (Mn)	25.7% (14.1 to 42.1)	As above
Proportion of EOGBS cases that are preterm					
37	Proportion of EOGBS cases that are preterm	E_P	Logit: median –0.381, SD 0.178	40.4% (31.5 to 48.3)	Meta-analysis of 5 UK studies[52,94–96] (also NICU database, 2005)
Proportion of preterm EOGBS in each of 4 BPSU categories					
38	LSCS	$E_{P1} = E_1/E_P$	4/124	1.2% (0.5 to 3.1)	BPSU database, 2005
39	GBS bacteriuria/positive swab	$E_{P2} = E_4(1 + E_2 + E_3)/E_P$	6/124	1.8% (0.8 to 3.9)	As above
40	ROM before labour	$E_{P3} = E_5(1 + E_2 + E_3)/E_P$	74/124	22.4% (18.2 to 27.2)	As above
41	Labour intact membranes	$(1 - E_{P1} - E_{P2} - E_{P3})/E_P$	40/124 (Mn)	12.1% (9.0 to 16.0)	As above
Proportion of term EOGBS in each of 4 BPSU categories					
42	LSCS	$E^{(T)}{}_1 = E_7/(1 - E_P)$	1/207	0.3% (0.1 to 1.7)	As above
43	GBS bacteriuria/positive swab	$E^{(T)}{}_2 = E_4(1 + E_8 + E_9)/(1 - E_P)$	6/207	1.85 (0.8 to 3.9)	As above
44	Prolonged ROM	$E^{(T)}{}_3 = E_5(1 + E_8 + E_9)/(1 - E_P)$	67/207	20.2% (16.3 to 24.9)	As above
45	No risk factors	$[1 - E^{(T)}{}_1 - E^{(T)}{}_2 - E^{(T)}{}_3]/(1 - E_P)$	133/207 (Mn)	40.2% (35.0 to 45.6)	As above
Proportion of EOGBS in maternal RGs not represented in the BPSU dataset					
46	Proportion of EOGBS with previous GBS baby (RG2, 8)	Logit($E_2 + E_8$)	Logit: median –5.307, SD 1.302	0.7% (0.02 to 2.7)	Meta-analysis of 3 UK studies[52,94,95]
47	Proportion of EOGBS with pyrexia (RG4, 10)	Logit($E_3 + E_9$)	LOR: median –1.273, SD 0.244	22.1% (14.5 to 30.8)	Meta-analysis of 3 UK studies[52,94,95]
48	Proportion of EOGBS with any risk factor (i.e. not in RG12)	Logit($\Sigma_{j=1-11}E_j$)	LOR: median 0.589, SD 0.334	63.8% (47.4 to 77.6)	Meta-analysis of 3 UK studies[52,94,95]

$\gamma_{2,j}$, EOGBS livebirth given baby colonisation in risk group j; Mn, multinomial.

[a] See Appendix 1, *Table 74* for details of the studies used in the meta-analyses.

[b] Unpublished data: database for Northern Region EOGBS study (2002);[53] provided by S Oddie, Bradford Royal Infirmary, November 2005; hereafter referred to as Northern Region database, 2005.

TABLE 15 *Proportion of total EOGBS cases that are preterm and that are in each of the 12 maternal risk groups (see* Table 14 *for model inputs)*

Output	Parameter	Proportion (%)	
		Mean	95% CI
61	Average risk of EOGBS in the total population (RG1–12)	0.000483	0.000436 to 0.000531
62	Proportion of EOGBS that are preterm (RG1–6)	27.90	23.90 to 32.20
63	RG1. Preterm planned LSCS	0.70	0.43 to 1.07
64	RG2. Preterm previous GBS baby	0.02	0.00 to 0.04
65	RG3. Preterm GBS bacteriuria/positive swab	3.54	1.82 to 5.81
66	RG4. Preterm pyrexia	1.70	1.28 to 2.19
67	RG5. Preterm prelabour ROM	13.80	11.60 to 16.20
68	RG6. Preterm labour with intact membranes	8.17	6.02 to 10.60
69	RG7. Term planned LSCS	1.30	0.85 to 1.85
70	RG8. Term previous GBS baby	0.04	0.01 to 0.09
71	RG9. Term GBS bacteriuria/positive swab	7.19	3.72 to 11.90
72	RG10. Term pyrexia	6.00	4.82 to 7.38
73	RG11. Term prolonged ROM	26.10	22.80 to 29.40
74	RG12. No risk factors (term)	31.50	26.00 to 36.80

Hospital, Royal London Hospital and University College London Hospital (1996–2004); provided by D Acolet (Royal Free Hospital), M Millar (Royal London Hospital) and S Harding and P Ostro (University College London Hospital); hereafter referred to as NICU database, 2005]. The pooled estimate is shown in *Table 14* (Input 37). The BPSU and northern region studies were excluded to avoid using the same data twice. Third, the BPSU dataset was used to determine the proportion of preterm and term EOGBS babies in each of four maternal RGs (Inputs 38–45, *Table 14*). Fourth, three published studies were found[52,94,95] that reported the proportion of all EOGBS cases that had a previous GBS baby (RG2 and 8): the pooled estimate, based on one case, is shown (Input 46). Finally, these same three studies were used to estimate the proportion of EOGBS in which pyrexia was reported during labour (RG4 and 10; Input 47), and the proportion of EOGBS cases with any maternal risk factors (RG1–11; Input 48). The meta-analyses were calculated in WinBUGS. Characteristics of the source studies are outlined in Appendix 1 (*Table 74*).

Output for proportion of EOGBS cases in each maternal risk group (Outputs 61–74, Table 15*)*

The estimated proportions of EOGBS babies in each maternal risk group are shown in *Table 15*. Note that these estimates were informed by the data inputs in *Table 14* and by the parameters on the proportion of the total population in each RG, the RG-specific rates of maternal and baby colonisation and the risk of EOGBS in a colonised baby. *Figure 5* juxtaposes the percentage of EOGBS from each RG with the percentages of all deliveries from each RG. The most important RGs are RG12 'no risk factors' and RG11 'term prolonged ROM' which together account for 57.6% of all EOGBS but 79.5% of all deliveries. Preterm deliveries account for 27.9% of EOGBS and 7.3% of deliveries, and 'high-risk' groups (RG3, 4, 5, 6, 9, 10 and 11) for 40.5% of EOGBS and 12.5% of all deliveries.

The main discrepancy between the data inputs and model output is in the groups with maternal pyrexia, for which the model estimates are lower than the source studies. It is likely that this is due to a number of factors, namely recall bias in the observational studies, favouring reporting of pyrexia that might not be routinely recorded in maternity records, and underestimation of the risks of maternal colonisation, baby colonisation or EOGBS-given baby colonisation, for women with pyrexia.

EO non-GBS livebirths

Risk of EO non-GBS livebirths in the total population (Input 49, Table 16*)*

No studies were found that reported the prevalence of EO non-GBS bacteraemia and were both representative of the UK and achieved a level of ascertainment that was similar to the BPSU study. Instead, unpublished data were used from the Health Protection Agency (HPA) reporting the numbers of GBS and non-GBS bacterial bacteraemia (excluding coagulase negative staphylococci) in the first week of life based on voluntary reporting from the majority of

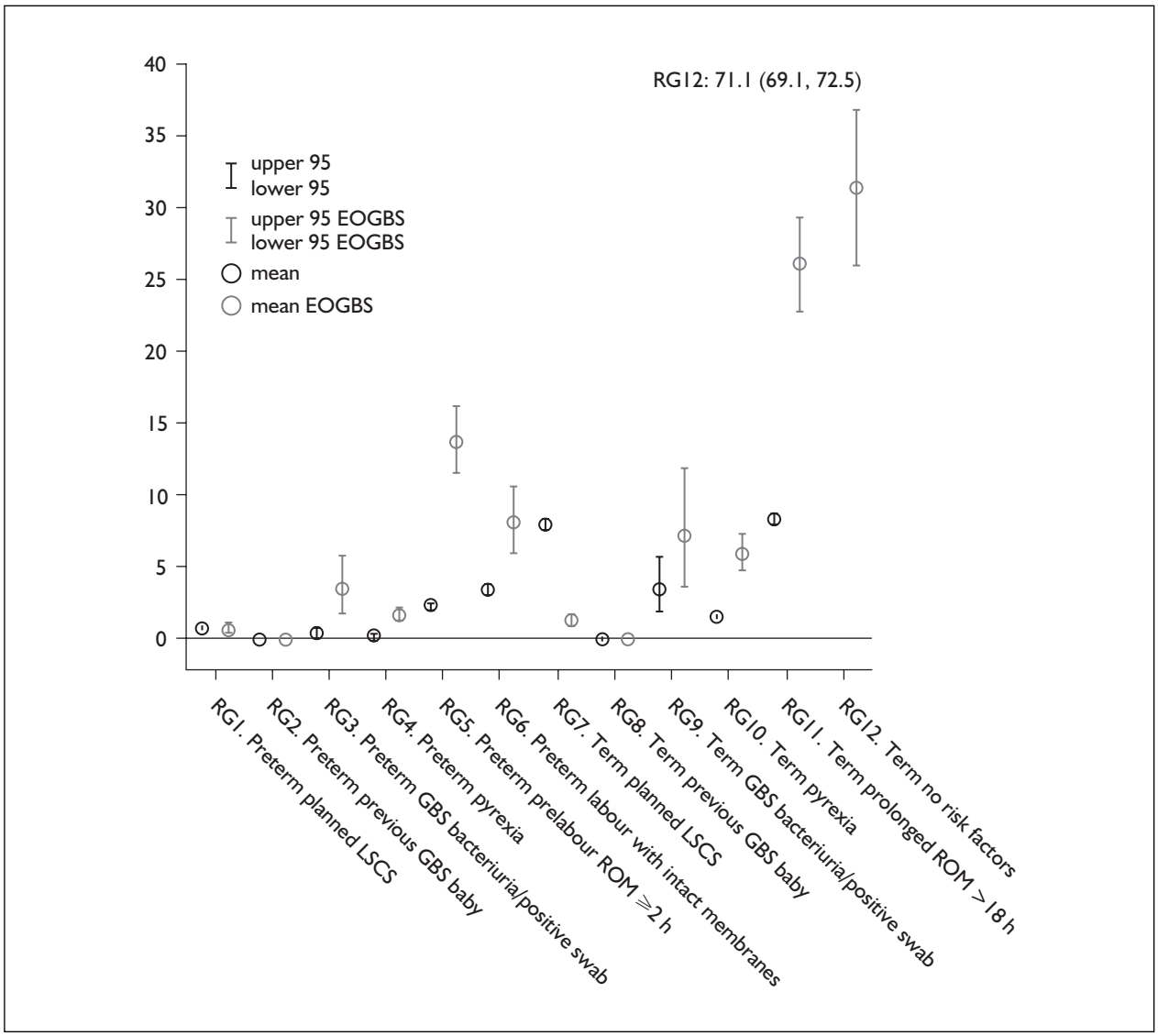

FIGURE 5 *Comparison of the percentage of the total population that is in each risk group and percentage of EOGBS cases coming from each risk group*

TABLE 16 *Prevalence of EO non-GBS in all babies and according to maternal risk groups: data inputs and parameters estimated (see* Table 17 *for model output)*

Input	Description of data input	Parameter estimated	Data input	Mean (%) or odds ratio (95% CI)	Source[a]
49	Proportion of EO disease that is EO non-GBS	$En/Eo = \theta_A\gamma_{4,A}/(\theta_A\gamma_{4,A} + E)$	Logit: median 0.6868, SD 0.0715	66.5% (63.2 to 69.5%)	Meta-analysis of HPA data (Duckworth and colleagues, 2005)
50	Proportion of EO Non-GBS cases that are preterm	En_P	39/74	52.7% (41.5 to 63.7%)	NICU database (2005)

E, EOGBS (Input 21, *Table 14*); En, EO non-GBS; Eo, all EO disease (EOGBS and EO non-GBS); $\gamma_{4,A}$, risk of EO non-GBS (suffix A denotes all maternal RGs).
[a] See Appendix 1, *Table 75* for source studies.

TABLE 17 *Prevalence of EO non-GBS in all babies and in preterm and term babies (see* Table 16 *for model inputs)*

Output	Parameter	Cases per 1000 babies		One case in		LR[a]
		Mean	95% CI	Mean	95% CI	
75	Average risk of EO non-GBS (RG1–12)	0.965	0.807 to 1.14	1036	1239 to 877	1
76	In preterm babies (RG1–6)	6.97	5.19 to 9.01	143	193 to 111	7.22
77	In term babies (RG7–12)	0.498	0.363 to 0.65	2008	2755 to 1538	0.52

[a] Likelihood ratio of EO non-GBS as compared with the average EO non-GBS rate.

laboratories in England and Wales (HPA, unpublished data. Voluntary reporting of bacteraemias in children <1 week old from LabBase2 reports; England and Wales, 1993–2003. Provided by G Duckworth, T Lamagni and C Goodall, Health Protection Agency, UK, September 2005; hereafter referred to as Duckworth and colleagues, 2005). These data underestimated the total number of cases of bacteraemia as only 168 cases of EOGBS were reported for 2000 when the BPSU identified 323 cases in a 13-month period (1 February 2000–28 January 2001) in England and Wales.[12] As under-reporting is unlikely to be related to the type of organism, we used the odds of EO non-GBS to EOGBS reports in the HPA dataset combined with the rate of EOGBS based on the BPSU study, to obtain the rate of EO non-GBS in the total population (Input 49, *Table 16*). The ratio of EO non-GBS to EOGBS reports was based on a random effects pooled estimate of each of the last 5 years for which HPA data were available (1999–2003; see Appendix 1, *Table 75* for actual figures). As *Table 16* shows, nearly twice as many EO non-GBS as EOGBS cases were reported.

Proportion of EO non-GBS babies in each maternal risk group (Input 50, Table 16)

UK studies were sought to provide information on the distribution of EO non-GBS cases in the 12 maternal RGs. The restriction to the UK was based on the need to ensure that mothers were not treated during labour, and because of differences in the prenatal and neonatal management between countries. As no published studies were found, a primary dataset of 5683 admissions to three NICUs in London was used to determine the proportion of all babies with a first episode of EO non-GBS (excluding coagulase-negative staphylococcal infection) that were born preterm (see Appendix 1, *Table 75* for details). No further information could be found on the distribution of EO non-GBS within the preterm and term groups.

Output for risk of EO non-GBS in the total population and in preterm and term babies (Outputs 75–77, Table 17)

As *Table 17* shows, given the inputs, the model estimates that the risk of EO non-GBS is higher than the risk of EOGBS in the total population (0.965/1000 for EO non-GBS compared with 0.483/1000 – Output 61, *Table 15*). Also, the risk of EO non-GBS in preterm babies is about fourteen times that of the risk in term babies.

Late-onset GBS disease (LOGBS)

Prevalence of LOGBS in the total population (Input 51: 191/794,037)

The BPSU surveillance study (see Appendix 1, *Table 73* for details) was used to determine the prevalence of LOGBS, as cases were reported by three sources (paediatricians, routine laboratory reporting and the GBS reference laboratory) ascertainment was high and the results provided a recent estimate that was representative of the UK[12] (also, BPSU database, 2005). The results from one regional study[94] were consistent with the BPSU results but were not used because estimates of the numerator and denominator were less reliable. The BPSU study identified 191 cases of LOGBS (defined as GBS-positive blood or CSF culture following symptoms between 7 and 90 days of age) out of 794,037 livebirths (annual livebirths in UK and Ireland adjusted for the 13-month study period): the incidence of LOGBS was 0.241/1000.

Proportion of LOGBS cases that are preterm (Input 52)

Findings from a regional surveillance study in Bedfordshire showed preterm delivery to be an important risk factor for LOGBS.[94] However, no evidence was found for an association between specific maternal RGs and LOGBS. A constant rate of LOGBS was therefore assumed in each of the six preterm groups and six term groups, although the overall risk of LOGBS was higher given preterm birth. The BPSU data provided data on the proportion of babies with LOGBS born preterm (Input 52): 85/187 (45%).

TABLE 18 *Prevalence of LOGBS in all babies and in preterm and term babies*

Output	Parameter	Cases per 1000 babies		One case in		LR[a]
		Mean	95% CI	Mean	95% CI	
78	Average risk of LOGBS (RG1–12)	0.245	0.211 to 0.277	4082	4739 to 3610	1
79	In preterm babies (RG1–6)	1.51	1.20 to 1.84	662	833 to 543	6.16
80	In term babies (RG7–12)	0.145	0.114 to 0.165	6897	8772 to 6061	0.59

[a] Likelihood ratio of EO non-GBS as compared with the average EO non-GBS rate.

TABLE 19 *Prevalence of meningitis*[a] *(see* Table 22 *for model output, p. 32)*

Input	Description of data input	Parameter estimated	Data input[b]	Mean (%) or odds (95% CI)	Source
53	Proportion of preterm EOGBS with meningitis	$\eta_{1,P}$	13/129	10.1% (6.0 to 16.5%)	BPSU database, 2005
54	Proportion of term EOGBS with meningitis	$\eta_{1,T}$	27/227	11.9% (8.3 to 16.8%)	BPSU database, 2005
55	Proportion of preterm LOGBS with meningitis	$\eta_{2,P}$	31/85	36.5% (26.8 to 47.0%)	BPSU database, 2005
56	Proportion of term LOGBS with meningitis	$\eta_{2,T}$	50/102	49.0% (39.3 to 58.5%)	BPSU database, 2005
57	Odds of preterm EO non-GBS with meningitis	$\eta_{3,P} = [\eta_{En/E}/(En/E \times En_P/E_P)]\eta_{1,P}$	See *Table 21*	0.045 (0.018 to 0.094)	R calculations (see *Table 21*)
58	Odds of term EO non-GBS with meningitis	$\eta_{3,T} = (\eta_{En/E}/\{En/E \times [1/(En_P/E_P)]\})\eta_{1,T}$	See *Table 21*	0.208 (0.093 to 0.398)	R calculations (see *Table 21*)

η, Meningitis given EOGBS (suffix 1), LOGBS (suffix 2) or EO non-GBS (suffix 3) in preterm (suffix P) or term (suffix T) babies; E, EOGBS; En, EO non-GBS.
[a] EOGBS preterm and term cases do not add up to the total of 377 due to missing data for gestation.
[b] Put in as Beta distributions, e.g. 13/129 becomes Beta (13,116).

Output for risk of LOGBS in the total population and in preterm and term babies (Outputs 78–80, Table 18*)*

At 0.245 cases/1000 livebirths (95% CI: 0.211/1000 to 0.277/1000), the incidence of LOGBS is about half that of EOGBS, meaning that of all cases of neonatal GBS disease up to 3 months of age, two-thirds are in the first week of life. As with EOGBS and EO non-GBS, the likelihood of LOGBS is considerably higher in preterm babies (where the rate of LOGBS is 6.16 times higher than the baseline rate in the total population) than in term babies (where the rate of LOGBS is 0.59 times as high as the baseline risk in the total population).

Meningitis

To determine the prevalence of meningitis in babies with EOGBS, EO non-GBS and LOGBS, studies were sought involving UK populations that separately specified outcomes in term and preterm deliveries. No further subdivision was made of meningitis, or any subsequent outcomes (death or disability), into the 12 maternal RGs as it was considered that the main determinant of these outcomes was preterm or term delivery. Studies from outside the UK were excluded as differences in the frequency of sampling CSF, and also overall management, could alter the risk of reported meningitis.

Prevalence of meningitis given EOGBS or LOGBS (Inputs 53–56, Table 19*)*

The BPSU database (see Appendix 1, *Table 73*) provided the most comprehensive data for EOGBS and LOGBS, subdivided into preterm and term deliveries. The data inputs are shown in *Table 19*.

Prevalence of meningitis given EO non-GBS (Inputs 57–58, Table 19*)*

Two national surveillance studies were found (see Appendix 1, *Table 76* for details) that reported all cases of meningitis by infecting organism in the

UK. In the first study, cases were ascertained over 2 years (1985–7), and comprised all meningitis occurring in infancy.[97] The second study used the same methods, but restricted reports to meningitis in the first 28 days of life ascertained over an 18-month period in 1996–7.[98] Both studies followed up the children through their parents, GPs and paediatricians to determine developmental outcomes at 5 years of age. The primary datasets for 1985–7 were combined [unpublished data: Database of neonatal meningitis in England and Wales, 1985–7; follow-up at 5 years of age; provided by H Bedford (Institute of Child Health, London), J de Louvois and S Halket (Karim Centre for Meningitis Research, Imperial College School of Medicine, London), December 2005; hereafter referred to as Bedford and colleagues, 2005] and for 1996–7 [unpublished data: Database of neonatal meningitis in England and Wales, 1996–7; provided by S Halket and J de Louvois (Karim Centre for Meningitis Research, Imperial College School of Medicine, London), December 2005; hereafter referred to as Halket and colleagues, 2005], which included responders at 5 years and deaths before this age. Over 90% of children were followed up.[97,98] As both studies appeared to have substantially under-ascertained cases compared with the BPSU study conducted in 2000, the data were not used to derive incidence rates. Instead, data on separate populations of babies with meningitis and bacteraemia were used (see *Table 20*) to derive ratio measures.

Table 21 shows how the prevalence of meningitis in EO non-GBS cases ($a/a + c$) was calculated. First, the combined dataset of early onset bacterial meningitis was used to derive the odds of EO non-GBS to EOGBS meningitis (a/b). Second, the odds of EO non-GBS to EOGBS bacteraemia were derived using the HPA surveillance data for 1993–7, years for which data were available and closest to the years in the meningitis studies (c/d in *Table 21*; see Appendix 1, *Table 75* for data). The odds were assumed to be the same for bacteraemia alone as for any bacteraemia. Third, the OR for meningitis in EO non-GBS versus EOGBS [$(a/b)/(c/d)$; derived from the two odds] was multiplied by the OR for meningitis in EOGBS (b/d; figures obtained from the BPSU database) to derive the odds of meningitis in EO non-GBS. This was then converted to a rate ($a/a + c$).

TABLE 20 *Meningitis and bacteraemia in babies with early onset infection*

	EO non-GBS	EOGBS
Meningitis	*a*	*b*
Bacteraemia alone	*c*	*d*

These calculations were repeated for preterm and term deliveries modified as follows. It was assumed that the odds of EO non-GBS to EOGBS meningitis were the same in preterm and term deliveries (a/b). The odds of EO non-GBS to EOGBS bacteraemia were adjusted by multiplying them by the OR for preterm delivery in EO non-GBS versus EOGBS. The odds of preterm in EO non-GBS were calculated from primary data for a study of bacteraemia in NICU inpatients in three London Trusts (NICU database, 2005) (39 preterm/35 term; Appendix 1, *Table 75*). The odds of preterm given EOGBS were obtained from the BPSU database (130/227; odds ratio = 1.946). This OR was inverted in the calculations for term babies. Finally, the odds of meningitis in EOGBS cases were derived from data for preterm and term babies in the BPSU dataset.

TABLE 21 *Derivation of the prevalence of meningitis in EO non-GBS cases*

	$Odds^{EO\ non\text{-}GBS}$		$OR_{M,\ EO\ non\text{-}GBS}$ $[(a/b)/(c/d)]$	$Odds_M$		$Prevalence_M$ in EO non-GBS (%) $[a/(a + c)]$
	In meningitis (a/b)	In bacteraemia alone (c/d)		In EOGBS (b/d)	In EO non-GBS $[(a/b)/(c/d) \times b/d]$	
All[a]	82/64	1987/1157	0.746	40/316	0.094	8.56
Preterm	82/64[b]	$1987/1157 \times OR_{PT}$	0.383	13/116	0.0430	4.12
Term	82/64[b]	$1987/1157 \times (1/OR_{PT})$	1.451	27/200	0.1960	16.38

$OR_{M,\ EO\ non\text{-}GBS}$, odds of meningitis in EO non-GBS vs EOGBS (suffix M denotes meningitis throughout table); OR_{PT}, odds of preterm in EO non-GBS vs EOGBS = 1.946.
[a] Not used in the model.
[b] Odds assumed to be constant in preterm and term.

TABLE 22 *Risk of meningitis in EOGBS, LOGBS and EO non-GBS preterm and term babies (see* Table 19 *for model inputs, p. 3.)*

Output	Parameter	Proportion (%)	
		Mean	95% CI
81	Meningitis given EOGBS preterm	10.1	5.6 to 15.6
82	Meningitis given EOGBS term	11.9	8.1 to 16.4
83	Meningitis given LOGBS preterm	36.4	26.4 to 47.2
84	Meningitis given LOGBS term	49.0	39.4 to 58.3
85[a]	Meningitis given EO non-GBS preterm	4.5	1.8 to 9.4
86[a]	Meningitis given EO non-GBS term	20.8	9.3 to 39.8

[a] 85 and 86 marginally overestimate the risk as, in error, the odds were taken to be the risk in the model (Inputs 57 and 58 were odds instead of risks); the true values should approximate to those in *Table 21*.

As none of the parameters included in the model after infection status [see Tree 2 (*Figure 3*, p. 9)] were correlated, data inputs were programmed in R software rather than WinBUGS. Ten thousand simulations were performed to estimate the mean and 95% CI. Uncertainty in the EO non-GBS inputs (see *Table 21*) was also taken into account, and 95% CIs were calculated by simulation.

Table 19 summarises the data inputs for the prevalence of meningitis in EOGBS, LOGBS and EO non-GBS preterm and term deliveries.

Output for risk of meningitis in EOGBS, LOGBS and EO non-GBS preterm and term babies (Outputs 81–86, Table 22*)*

The percentage of EOGBS cases manifesting as meningitis is broadly similar for preterm and term EOGBS cases at 10.1% (95% CI: 5.6 to 15.6%) and 11.9% (95% CI: 8.1 to 16.4%), respectively. The percentage of EO non-GBS cases that manifest themselves as meningitis is lower for preterm EO non-GBS babies [4.5% (95% CI: 1.8 to 9.4%)] than term EO non-GBS babies [20.1% (95% CI: 9.3 to 39.8%)]. The risk of meningitis in LOGBS babies is notably higher than in EOGBS and EO non-GBS babies, both for preterm [36.5% (95% CI: 26.5 to 47.0%) of LOGBS cases are meningitis] and term [49.1% (95% CI: 39.5 to 58.7%) of LOGBS cases are meningitis]. The fact that the CIs do not overlap with those of the values for EOGBS and EO non-GBS meningitis shows that this difference is statistically significant at the 5% level.

Deaths

Death in babies with EOGBS or LOGBS (Inputs 59–66, Table 23*)*

The BPSU database (see Appendix 1, *Table 73*) was used to provide data on the risk of death before hospital discharge in babies reported with EOGBS or LOGBS. The mortality risk was separately extracted for preterm and term deliveries, and for babies with meningitis or bacteraemia only.

EO non-GBS deaths (Inputs 67 and 68, Table 23*)*

The Northern Region study database (see Appendix 1, *Table 77*) of neonatal deaths from infection was used (unpublished data: database of all neonatal deaths from infection in the Northern Health Region 1981–2000; provided by N Embleton, Royal Victoria Infirmary, September 2005; hereafter referred to as Embleton, 2005) to provide information on EO non-GBS deaths as case ascertainment was based on multiple routine data sources and included data on preterm and term status. The Northern Region study was not used to estimate the risk of mortality in the total population because the result might not have been comparable with the mortality rate for EOGBS reported in the BPSU study due to differences in reporting definitions, ascertainment of cases and regional variation. Instead, a ratio of EO non-GBS deaths to EOGBS deaths was derived and the risk of death in babies with EO non-GBS was calculated using a similar method to that described to determine the prevalence of meningitis given EO non-GBS (see the section 'Meningitis', p. 30, *Tables 20* and *21* for meningitis; and below, *Tables 24* and *25* for deaths). In view of the lack of evidence to the contrary, it was assumed that the mortality rate in a preterm or term baby with EO non-GBS was the same for meningitis and for bacteraemia alone.

As for meningitis, the inputs for death were programmed in R software and 10,000 simulations were performed to estimate the mean and 95% CI. The R software also allowed the correct estimation of the EO non-GBS death rates (Inputs 67 and 68) using the data in *Table 25*. *Table 23* summarises the data inputs for the prevalence of death in EOGBS

TABLE 23 *Mortality from EOGBS, LOGBS and EO non-GBS (see* Table 26 *for model output, p. 35)*

Input	Description of data input	Parameter estimated	Data input[a]	Mean (%) (95% CI)	Source
59	Proportion of preterm EOGBS with meningitis that died	$\chi_{1men,P}$	3/13	23.1% (8.2 to 50.3%)	BPSU database, 2005
60	Proportion of term EOGBS with meningitis that died	$\chi_{1men,T}$	3/27	11.1% (3.9 to 28.1%)	BPSU database, 2005
61	Proportion of preterm LOGBS with meningitis that died	$\chi_{2men,P}$	4/31	12.9% (5.1 to 28.9%)	BPSU database, 2005
62	Proportion of term LOGBS with meningitis that died	$\chi_{2men,T}$	5/50	10.0% (4.4 to 21.4%)	BPSU database, 2005
63	Proportion of preterm EOGBS with bacteraemia alone that died	$\chi_{1nmen,P}$	20/116	17.2% (11.5 to 25.1%)	BPSU database, 2005
64	Proportion of term EOGBS with bacteraemia alone that died	$\chi_{1nmen,T}$	10/200	5.0% (2.7 to 9.0%)	BPSU database, 2005
65	Proportion of preterm LOGBS with bacteraemia alone that died	$\chi_{2nmen,P}$	3/54	5.6% (1.9 to 15.1%)	BPSU database, 2005
66	Proportion of term LOGBS with bacteraemia alone that died	$\chi_{2nmen,T}$	3/52	5.8% (2.0 to 15.6%)	BPSU database, 2005
67	Odds of death given preterm EO non-GBS	$\chi_{3,P} = [\chi_{En/E}/(En_{93-00}/E_{93-00} \times En_P/E_P)]\chi_{1,P}$	see *Table 25*	0.151 (0.068 to 0.293)	R calculations (see *Table 25*)
68	Odds of death given term EO non-GBS	$\chi_{3,T} = (\chi_{En/E}/\{En_{93-00}/E_{93-00} \times [1/(En_P/E_p)]\})\chi_{1,T}$	see *Table 25*	0.152 (0.052 to 0.344)	R calculations (see *Table 25*)

χ, Death given EOGBS (suffix 1), LOGBS (suffix 2) or EO non-GBS (suffix 3) meningitis (suffix men) or non-meningitis (bacteraemia alone, suffix nmen) in preterm (suffix P) or term (suffix T) babies; E, EOGBS; En, EO non-GBS.

[a] Put in as Beta distributions, e.g. 3/13 becomes Beta(3,10).

TABLE 24 *Death and survival in babies with early onset infection*

	EO non-GBS	EOGBS
Death	*a*	*b*
No death	*c*	*d*

and LOGBS preterm and term deliveries and for babies with meningitis or bacteraemia only, and EO non-GBS preterm and term deliveries.

Output for mortality from EOGBS, LOGBS and EO non-GBS preterm and term babies with meningitis or bacteraemia alone (Outputs 87–96, Table 26*)*

The mortality rate from EOGBS differs depending on whether the disease manifests as meningitis or bacteraemia alone (no meningitis) and whether it is in preterm or term babies. In preterm babies with EOGBS meningitis, the mortality rate was determined by the model to be 30.0% (95% CI: 7.3 to 60.0%), the large amount of uncertainty in this value being due to the small numbers used as inputs to determine it. In preterm EOGBS babies without meningitis, the mortality rate is 20.8% (95% CI: 13.3 to 29.4%). In term babies, who are less vulnerable to severe infection and death, the mortality rates are lower: 12.4% (95% CI: 2.7 to 27.7%) for term EOGBS babies with meningitis and 5.3% (95% CI: 2.5 to 8.8%) for term EOGBS babies without meningitis. As the data illustrate, EOGBS is more deadly when it manifests as meningitis, irrespective of the gestation of the baby.

LOGBS mortality is similar to that of EOGBS and EO non-GBS, although there are some notable differences. *Table 26* highlights the fact that mortality from LOGBS in preterm babies is lower than mortality from EOGBS, both when the disease is manifest as meningitis and more clearly (the 95% CIs barely overlap) when the disease is not meningitis. One factor in the lower mortality of preterm LOGBS compared with preterm EOGBS or preterm EO non-GBS could be the fact that all LOGBS babies have already survived up to 1 week of age and as such have a greater chance of survival (many of the EOGBS and EO non-GBS babies die in the first week following acute infection). Mortality from term LOGBS is again lower than that for term EOGBS and EO non-GBS; however, it should be noted that this relationship is by no means statistically significant given that the confidence limits for LOGBS broadly overlap those for EOGBS and EO non-GBS.

The mortality rate for EO non-GBS is not split by whether the disease was meningitis or not, due to lack of data, but is given separately for preterm EO non-GBS and term EO non-GBS as 15.1% (95% CI: 6.8 to 29.3%) and 15.2% (95% CI: 5.2 to 34.4%), respectively. These rates are comparable to those for EOGBS especially on consideration of the wide CIs surrounding both sets of values in question.

Stillbirths

Risk of stillbirth due to EOGBS and EO non-GBS (Inputs 69–72, Table 27*)*

Nationally representative studies were sought that had complete ascertainment of all stillbirths, thorough investigation for the type of infection and details on maternal risk groups, in order to determine the prevalence of stillbirths due to GBS and non-GBS infection. One study was found from the Northern Region that met these

TABLE 25 *Derivation of mortality risk given EO non-GBS*

	$Odds^{EO\ non\text{-}GBS}$		$OR_{Death,\ EO\ non\text{-}GBS}$ [(*a*/*b*)/(*c*/*d*)]	$Odds_{Death}$		$Risk_{Death}$ in EO non-GBS (%) [*a*/(*a* + *c*)]
	In death (*a*/*b*)	In bacteraemia alone[b] (*c*/*d*)		In EOGBS (*b*/*d*)	In EO non-GBS [(*a*/*b*)/(*c*/*d*) × *b*/*d*]	
All[a]	190/91	3002/1740	1.210	38/320 (10.61%)	0.1437	12.57
Preterm	152/71	3002/1740 × OR_{PT}	0.638	24/106 (18.46%)	0.1444	12.62
Term	38/19	3002/1740 × (1/OR_{PT})	2.256	13/214 (5.73%)	0.1370	12.05

$OR_{Death,\ EO\ non\text{-}GBS}$, odds of death in EO non-GBS vs EOGBS; OR_{PT}, odds preterm in EO non-GBS vs EOGBS = 1.946 (see the section 'Meningitis', p. 30).

[a] Not used in model.

[b] HPA data differ from *Table 21* as based on years 1993–2000.

TABLE 26 *Mortality from EOGBS, LOGBS and EO non-GBS preterm and term babies with meningitis or bacteraemia alone (see* Table 23 *for model inputs, p. 33)*

Output	Parameter	Proportion (%)	
		Mean	95% CI
87	Death given EOGBS preterm and meningitis	30.0	7.3 to 60.0
88	Death given EOGBS term and meningitis	12.4	2.7 to 27.7
89	Death given EOGBS preterm and no meningitis	20.8	13.3 to 29.4
90	Death given EOGBS term and no meningitis	5.3	2.5 to 8.8
91	Death given LOGBS preterm and meningitis	14.8	4.4 to 30.2
92	Death given LOGBS term and meningitis	11.1	3.7 to 21.6
93	Death given LOGBS preterm and no meningitis	5.9	1.2 to 13.5
94	Death given LOGBS term and no meningitis	6.1	1.2 to 14.1
95[a]	Death given EO non-GBS preterm	15.1	6.8 to 29.3
96[a]	Death given EO non-GBS term	15.2	5.2 to 34.4

[a] 95 and 96 marginally overestimate the risk as, in error, the odds were taken to be the risk in the model (Inputs 67 and 68 were odds instead of risks); the true values should be approximate to those in *Table 25*.

TABLE 27 *EOGBS, EO non-GBS and no infection stillbirths (see* Table 28 *for model output, p. 36)*

Input	Description of data input	Parameter estimated	Data input	Mean (%) (95% CI)	Source
69	Proportion of preterm EOGBS that are stillborn	$E_{S,P} = \chi_{1,P}\sigma_{1,P}$	See text	4.4 (2.5 to 7.0)	R calculations (see text)
70	Proportion of term EOGBS that are stillborn	$E_{S,T} = \chi_{1,T}\sigma_{1,T}$	See text	2.0 (0.8 to 3.9)	R calculations (see text)
71	Proportion of preterm EO non-GBS that are stillborn	$En_{S,P} = \chi_{3,P}\sigma_{2,P}$	See text	4.4 (2.5 to 7.0)	R calculations (see text)
72	Proportion of term EO non-GBS that are stillborn	$En_{S,T} = \chi_{3,T}\sigma_{2,T}$	See text	2.0 (0.8 to 3.9)	R calculations (see text)
73	Proportion of total preterm births that are stillbirths	$\theta^{(P)}_S = \lambda_P + E_{S,P} + En_{S,P}$	215/5211	4.1 (3.6 to 4.7)	SMMIS database, 2005
74	Proportion of total term births that are stillbirths	$\theta^{(T)}_S = \lambda_T + E_{S,T} + En_{S,T}$	136/66357	0.20 (0.17 to 0.24)	SMMIS database, 2005

σ, Stillbirth given EOGBS (suffix 1), or EO non-GBS (suffix 3) in preterm (suffix P) or term (suffix T) babies. E, EOGBS; En, EO non-GBS; suffix denotes proportion of all EOGBS/EO non-GBS that are stillbirths; λ, no infection stillbirths.

criteria (see Appendix 1, *Table 77*), and access was given to the primary dataset[99] (and Embleton, 2005). Cases were ascertained by reviewing all obstetric, paediatric and pathology case notes of all the reported infant deaths or stillbirths in the region from 1981 to 2000. Notes of any stillbirths or deaths before 28 days in which infection was potentially contributory were further reviewed by a neonatologist. Cases were classified according to whether there was microbiological or histopathological evidence of infection (positive culture of blood, CSF or tracheal aspirate or positive superficial swab with histopathological evidence of systemic infection) or clinical evidence of infection but no supportive laboratory evidence.

Only those cases with microbiological or histopathological evidence of infection and classified as GBS and non-GBS stillbirths were included. This numerator could not be used directly with the Northern Region birth rate as the denominator, as the criterion for infection in stillbirths differed from that used to define the prevalence of EOGBS livebirths in the BPSU study (which was based on positive blood or CSF culture). The proportion (for both preterm and term babies) of GBS stillbirths out of all EOGBS deaths and stillbirths in the Northern Region study [18/71 for preterm ($\sigma_{1,P}$) and 7/19 for term ($\sigma_{1,T}$)] was therefore determined and this proportion was multiplied by the rate of death in preterm/term EOGBS cases (none of which are stillbirths) in the

BPSU study [24/130 for preterm ($\chi_{1,P}$) and 13/227 for term ($\chi_{1,T}$)] to give ratios of preterm/term EOGBS stillbirths to preterm/term EOGBS livebirths which were then input into the model to provide estimates on the number of EOGBS stillbirths in relation to EOGBS livebirths in each maternal risk group. These calculations were repeated for EO non-GBS: the proportion of non-GBS stillbirths out of all EO non-GBS deaths and stillbirths in the Northern Region study [47/152 for preterm ($\sigma_{3,P}$) and 7/38 for term ($\sigma_{3,T}$)] was multiplied by the rate of death in preterm/term EO non-GBS cases (none of which are stillbirths) which were derived in the section 'Deaths' (p. 32) (Input 67, $\chi_{3,P}$, for preterm and Input 68, for term $\chi_{3,T}$).

Stillbirths not due to bacterial infection (Inputs 73–74, Table 27*)*

As the rate of stillbirth due to infection was extremely low, we assumed that the total stillbirth rate was equivalent to the rate of stillbirths that were not due to GBS or non-GBS infection. Using the SMMIS database (see Appendix 1, *Table 69*), the risk of stillbirth in preterm deliveries was 215/5211 (4.13%) and in term deliveries 136/66,357 (0.20%).

Output for risk of stillbirth in EOGBS, EO non-GBS and uninfected preterm and term babies (Outputs 97–115, Table 28*)*

Table 28 gives rates of EOGBS stillbirths, both for the total population and for each risk group. As the data inputs used to inform these outputs illustrate, EOGBS stillbirths are much rarer than EOGBS livebirths with typically only around one in 35 total EOGBS cases being stillbirths. The risk groups of colonised women at highest risk of having a baby that is still born as a result of EOGBS infection broadly match those at highest risk of having a liveborn baby with EOGBS; this is due to the link between EOGBS stillbirth and

TABLE 28 *Risk of stillbirth in EOGBS, EO non-GBS and uninfected preterm and term babies (see* Table 27 *for model inputs, p. 35)*

Output	Parameter	Cases per 1000 babies		One case in		LR[a]
		Mean	95% CI	Mean	95% CI	
97	EOGBS stillbirths in the total population (RG1–12)	0.000014	(0.000008 to 0.000022)	77,600	(46,000 to 127,000)	1
98	In women delivering preterm (RG1–6)	0.000086	(0.000046 to 0.000143)	12,600	(6,990 to 21,700)	6.27
99	In women delivering at term (RG7–12)	0.000008	(0.000003 to 0.000015)	149,000	(64,800 to 333,000)	0.58
100	Average EOGBS stillbirths given maternal colonisation	0.000116	(0.000061 to 0.000196)	8,621	(5,102 to 16,313)	1
EOGBS stillbirth given maternal colonisation in:						
101	RG1. Preterm planned LSCS	0.000111	(0.000049 to 0.000213)	10,300	(4,690 to 20,500)	0.96
102	RG2. Preterm previous GBS baby	0.000302	(0.000149 to 0.000533)	3,690	(1,880 to 6,720)	2.61
103	RG3. Preterm GBS bacteriuria/ positive swab	0.000302	(0.000149 to 0.000533)	3,690	(1,880 to 6,720)	2.61
104	RG4. Preterm pyrexia	0.000603	(0.000292 to 0.001080)	1,850	(922 to 3,420)	5.21
105	RG5. Preterm prelabour ROM	0.000503	(0.000246 to 0.000893)	2,220	(1,120 to 4,070)	4.35
106	RG6. Preterm labour with intact membranes	0.000302	(0.000149 to 0.000533)	3,690	(1,880 to 6,720)	2.61
107	RG7. Term planned LSCS	0.000018	(0.000006 to 0.000040)	69,100	(25,100 to 169,000)	0.16
108	RG8. Term previous GBS baby	0.000050	(0.000018 to 0.000101)	24,600	(9,880 to 56,900)	0.43
109	RG9. Term GBS bacteriuria/ positive swab	0.000050	(0.000018 to 0.000101)	24,600	(9,880 to 56,900)	0.43
110	RG10. Term pyrexia	0.000275	(0.000096 to 0.000573)	4,500	(1,740 to 10,400)	2.38
111	RG11. Term prolonged ROM	0.000229	(0.000080 to 0.000475)	5,380	(2,100 to 12,500)	1.98
112	RG12. No risk factors (term)	0.000050	(0.000018 to 0.000101)	24,600	(9,880 to 56,900)	0.43
113	EO non-GBS stillbirths in the total population (RG1–12)	0.000034	(0.000020 to 0.000052)	31,400	(19,100 to 50,400)	1
114	In women delivering preterm (RG1–6)	0.000327	(0.000165 to 0.000552)	3,360	(1,810 to 6,050)	9.66
115	In women delivering at term (RG7–12)	0.000011	(0.000004 to 0.000022)	114,000	(46,600 to 262,000)	0.31

[a] Likelihood ratio of stillbirth as compared with the relevant average stillbirth rate.

EOGBS livebirths provided by the EOGBS stillbirth-to-livebirth ratio used in the model.

As with EOGBS stillbirths, EO non-GBS stillbirths are rare (around one in 30 total EO non-GBS cases are stillbirths).

Disability

Disability due to meningitis (Inputs 75–82, Table 29*)*

Primary data were combined from the two national surveillance studies of meningitis (Bedford and colleagues, 2005 and Halket and colleagues, 2005) to determine the prevalence of severe, moderate, mild or no disability at 5 years old (see Appendix 1, *Table 76* for details of the databases and definitions of the different categories of disability). As no evidence was found for an effect of gestational age at birth or EOGBS/EO non-GBS status on the risk of disability (data not shown), a constant rate was assumed across these groups. Specific rates of disability were calculated for children with early-onset infection and late-onset infection, regardless of preterm or term status. To take into account the 32/1717 children who died before the 5-year follow-up, it was assumed that all had severe disability (in addition to the total of 92 infants in the entire dataset already recorded as having severe disability). The size of the severe groups was therefore enlarged by 35% (32/92).

Disability due to bacteraemia without meningitis (Inputs 83–86, Table 29*)*

Three studies were found that looked at disability from bacteraemia without meningitis caused by GBS/non-GBS;[100–102] four potentially relevant studies were excluded (see Appendix 1, *Table 78* for details of included and excluded studies). None of the studies examined whether gestational age was correlated with disability from non-meningitis bacterial infection. The disabilities were described in the papers and split by the reviewer into the four categories used for meningitis disability based on the same criteria (see Appendix 1, *Table 76* for definitions of categories and Appendix 1, *Table 78* for details of the cases of non-meningitis disability). Given the limitations of the data, cases of non-meningitis were only split into the four categories of disability, which were then assumed to be the same for EOGBS, EO non-GBS and LOGBS and for preterm and term babies. A random effects meta-analysis of the results from the three studies was carried out in WinBUGS using a Dirichelet distribution to calculate the sizes of the four categories of disability relative to each other. *Table 29* (Inputs 83–86) shows results of the WinBUGS meta-analyses which were input into the model. These inputs are the same as the outputs as these parameters were not correlated with other parameters used in the model.

Output for risk of disability from meningitis or non-meningitis caused by EOGBS, EO non-GBS or LOGBS: (Outputs 116–127, Table 30*)*

As *Table 30* shows, for EO disease, the more severe the disability the rarer it is: with 61.4% (95% CI: 53.5 to 69.2%) of cases not suffering disability; 19.6% (95% CI: 13.6 to 26.4%) suffering mild disability; 12.9% (95% CI: 8.1 to 18.7%) suffering moderate disability; and 6.1% (95% CI: 2.9 to 10.4%) suffering from severe disability. The same pattern is evident with disability from LOGBS. Disability from bacteraemia without meningitis disease did not follow this pattern as there were fewer cases of mild disability than moderate or severe disability, possibly owing to the lack of characterisation of mild disability in the studies used to produce this output (see Appendix 1, *Table 78*).

Life expectancy

Life expectancy in children with no, mild, moderate or severe disability (Inputs 87–89, Table 31*)*

ONS data on life expectancy at birth for men and women were used to provide an overall figure for life expectancy at birth for children with no or mild disability.[103]

For children with severe disability, a re-analysis of one study was used that reported life expectancy at 1 year of age for three subgroups of severe disability[104] (see Appendix 1, *Table 79*). A weighted mean life expectancy was calculated for all three groups and the means of the most and least severe groups were used to provide a 95% probability range. It was assumed that life expectancy at 1 year applied to survivors of the acute episode of early-onset or late-onset infection.[104,105] Nine studies were excluded because of incomplete data on life expectancy or inappropriate definitions of disability (see Appendix 1, *Table 79*). No data were available for life expectancy given moderate disability (as defined in the study by Bedford and colleagues; see Appendix 1, *Table 76*). It was therefore assumed that half the group had the same life expectancy as children with no disability (Input 87). The other half had a life expectancy that ranged from the upper limit given severe disability (42.7 years) to the mean life expectancy for children with no disability with a uniform distribution between these points.

TABLE 29 *Disability from meningitis and non-meningitis infections caused by EOGBS, EO non-GBS and LOGBS (see* Table 30 *for model output, p. 39)*

Input	Description of data input	Parameter estimated	Data input	Mean (%) (95% CI)	Source[a]
Disability from EO (GBS/non-GBS) meningitis at 5 years of age					
75	No disability	$1 - \delta_{mild:1,A} - \delta_{mod:1,A} - \delta_{sev:1,A}$	91/148	61.5 (53.5 to 68.9)	Two national databases of neonatal meningitis (Bedford and Colleagues, 2005; Halket and colleagues, 2005)
76	Mild disability	$\delta_{mild:1,A}$	29/148	19.6 (14.0 to 26.7)	As above
77	Moderate disability	$\delta_{mod:1,A}$	19/148	12.8 (8.4 to 19.2)	As above
78	Severe disability	$\delta_{sev:1,A}$	9/148	6.1 (3.2 to 11.2)	As above
Disability from LOGBS meningitis at 5 years of age					
79	No disability	$1 - \delta_{mild:2,A} - \delta_{mod:2,A} - \delta_{sev:2,A}$	69/132	52.3 (43.8 to 60.6)	As above
80	Mild disability	$\delta_{mild:2,A}$	26/132	19.7 (13.8 to 27.3)	As above
81	Moderate disability	$\delta_{mod:2,A}$	19/132	14.4 (9.4 to 21.4)	As above
82	Severe disability	$\delta_{sev:2,A}$	18/132	13.6 (8.8 to 20.5)	As above
Disability from all (EO non-GBS, EOGBS, LOGBS) bacteraemia without meningitis at 5 years of age					
83	No disability	$1 - \delta_{mild:3,A} - \delta_{mod:3,A} - \delta_{sev:3,A}$	0.746 (95% CI 0.641 to 0.838)	74.6 (64.1 to 83.8)	Meta-analysis of three studies[100–102]
84	Mild disability	$\delta_{mild:3,A}$	0.0453 (95% CI 0.0105 to 0.0996)	4.5 (1.1 to 10.0)	As above
85	Moderate disability	$\delta_{mod:3,A}$	0.139 (95% CI 0.0716 to 0.222)	13.9 (7.2 to 22.2)	As above
86	Severe disability	$\delta_{sev:3,A}$	0.0701 (95% CI 0.0232 to 0.138)	7.0 (2.3 to 13.8)	As above

δ, Mild (suffix mild), moderate (suffix mod) or severe (suffix sev) disability given EOGBS/EO non-GBS meningitis (suffix 1), LOGBS meningitis (suffix 2) or any non-meningitis (suffix 3) in all risk groups (suffix A).

[a] See Appendix 1, *Tables 76* and *78* for details of the studies used.

TABLE 30 *Risk of disability from meningitis or non-meningitis caused by EOGBS, EO non-GBS or LOGBS (see* Table 29 *for model inputs)*

Output	Parameter	Cases per 1000 babies	
		Mean (%)	95% CI
Disability due to EO meningitis at 5 years old			
116	No disability given EO-(GBS or non-GBS)	61.4	(53.5 to 69.2)
117	Mild disability given EO-(GBS or non-GBS)	19.6	(13.6 to 26.4)
118	Moderate disability given EO-(GBS or non-GBS)	12.9	(8.1 to 18.7)
119	Severe disability given EO-(GBS or non-GBS)	6.1	(2.9 to 10.4)
Disability due to LO meningitis at 5 years old			
120	No disability given LOGBS	52.3	(43.7 to 60.9)
121	Mild disability given LOGBS	19.7	(13.4 to 26.8)
122	Moderate disability given LOGBS	14.3	(8.9 to 20.9)
123	Severe disability given LOGBS	13.6	(8.4 to 20.1)
Disability due to (EO non-GBS, EOGBS, LOGBS) bacteraemia without meningitis at 5 years old			
124	No disability	74.6	(64.1 to 83.8)
125	Mild disability	4.5	(1.1 to 10.0)
126	Moderate disability	13.9	(7.2 to 22.2)
127	Severe disability	7.0	(2.3 to 13.8)

TABLE 31 *Life expectancy (years) of children with no, mild, moderate or severe disability*

Input	Description of data input	Parameter estimated	Data input	Mean (years)[a] (95% CI) (these are also the outputs)	Source[b]
87	Life expectancy (no disability or mild disability)	$\varepsilon_{no/mild,A}$	Men: mean, 76.25; SD, 0.02 Women: mean, 80.69; SD, 0.02 Overall = (men + women)/2	78.5 (78.4 to 78.5)	ONS[103]
88	Life expectancy with moderate disability	$\varepsilon_{mod,A}$	*Half* = Input 87 *Other half:* lower limit, 42.7; upper limit, Input 87 Mean, uniform distribution	67.8 (38.1 to 78.5)	Estimated
89	Life expectancy with severe disability	$\varepsilon_{sev,A}$	Mean, 24.5; lower limit, 11.2; upper limit, 42.7	26.1 (14.5 to 38.8)	Katz (2003)[104]

ε, Life expectancy given no or mild (suffix no/mild), moderate (suffix mod) or severe (suffix sev) disability in all risk groups (suffix A).
[a] At birth for no/mild disability; at age 1 year for moderate or severe disability.
[b] See Appendix 1, *Table 79* for details of the studies used.

Table 31 details the data inputs. These are the same as the data outputs as life expectancy was calculated using Excel and was not included in the analyses using WinBUGS.

Utilities

The reference values from the EQ-5D[106] were used for children without disability. To obtain utility values for children with disability, MEDLINE was searched for studies that reported utility values during childhood associated with disability due to cerebral palsy or meningitis using the following terms: pediatric/childhood; life expectancy; disability; meningitis; cerebral palsy; utility; quality of life. Eight potentially relevant papers were identified, one of which provided utilities for the consequences of meningitis during childhood.[107] Oostenbrinka and colleagues[107] used the EQ-5D instrument[108] and the Health Utilities Index (HUI)[109] to elicit 28 paediatricians' valuations of the utility of specific impairments during childhood resulting from bacterial meningitis. Given that the EQ-5D has valuations available for a UK population, it was decided to use this instrument for this analysis.

TABLE 32 *Utility values used in the model*

Input	Description of data input	Data input: mean (SD)	Source
No disability at age (years)			
90	<25	0.94 (0.12)	EQ-5D reference values[106]
91	25–34	0.93 (0.15)	As above
92	35–44	0.91 (0.16)	As above
93	45–54	0.85 (0.25)	As above
94	55–64	0.80 (0.26)	As above
95	65–74	0.78 (0.26)	As above
96	75+	0.73 (0.26)	As above
Mild disability			
97	Deafness, mild	0.81 (0.15)	Oostenbrinka (2002)[107]
98	Hearing loss	0.91 (0.08)	As above
99	Epilepsy	0.83 (0.08)	As above
Moderate disability			
100	Mild mental retardation	0.62 (0.11)	As above
101	Leg paresis	0.67 (0.12)	As above
Severe disability			
102	Epilepsy, mild mental retardation and leg paresis	0.47 (0.25)	As above

The mean utility values for deafness, mild hearing loss and epilepsy, which are all long-term consequences of meningitis or sepsis, were used for mild disability and the average of mild mental retardation and leg paresis for moderate disability. Children with severe disability were assigned the utility value for epilepsy, mild mental retardation and leg paresis (see *Table 32*).[107]

For the cost-effectiveness analysis, years of life expectancy were converted into QALYs using utility weights representing the quality of life at each age and for each of the four long-term states (not disabled and mild, moderate or severely disabled). Weights were measured on a scale anchored between 0 (equivalent to death) to 1 (equivalent to good health) and the resulting QALYs were discounted at 3% per year. To provide an estimate of the QALYs for all four disability states at all ages, a QALY decrement was calculated using the age-standardised utilities in *Table 32* and the utility values for disability in childhood. Given no disability, the first age group (<25 years) had a decrement from good health of 1–0.94, which was incorporated into the model as a gamma distribution with a mean of 0.06 and SD of 0.12. Utility values for no disability in the subsequent age groups were represented as a percentage of the first age group (e.g. 0.93/0.94) multiplied by the decrement for age group 1, e.g. (0.93/0.94) × (1 – distribution on decrement group 1). Disability utilities were then calculated relative to the no disability utility expected for that age category: for example, for the first age group, (1 – distribution on decrement group 1) × utility percentage decrement for mild disability (0.81/0.94). The total QALYs for a person with mild disability was the sum of utilities for each age group. Age at death was based on random sampling from the distribution of life expectancy for each health state.[106]

Certain samples from the mild disability utility indicated a better quality of life in the disabled state than in the state with no disability. Given that this is an unrealistic assumption, such samples were replaced by the mean value for mild disability.

Interventions

Antibiotic treatment

Treatment effects were separately determined for early-onset infection in liveborn babies and for stillbirth caused by GBS or non-GBS infection. It was assumed that maternal treatment had no effect on LOGBS and that oral treatment had no effect on stillbirth caused by infection. Six treatment effects were estimated:

1. the effect of intravenous penicillin on EOGBS
2. the effect of oral erythromycin on EOGBS
3. the effect of intravenous penicillin on EO non-GBS
4. the effect of oral erythromycin on EO non-GBS

TABLE 33 *Outcomes of studies of antibiotic treatment on baby colonisation and EOGBS: empirical odds ratios based on normal approximation compared with model predictions*

Study	Antibiotic	Treat		Control		Normal approx. OR	Model OR (95% CI)
		n	*N*	*n*	*N*		
Stage I: Effect on baby colonisation (*n*) given maternal colonisation (*N*)							
Boyer (1982)[88]	Ampicillin	2	69	46	82	0.023	0.032 (0.008 to 0.08)
Boyer (1983)[89]	Ampicillin	1	43	13	37	0.044	0.034 (0.006 to 0.09)
Boyer (1986)[90]	Ampicillin	8	85	40	79	0.098	0.081 (0.028 to 0.18)
Matorras (1991)[91]	Ampicillin	2	54	24	56	0.051	0.040 (0.010 to 0.10)
Easmon (1983)[110]	Penicillin	0	38	17	49	0.025	0.025 (0.003 to 0.07)
Morales (1986)[92]	Penicillin	0	135	59	128	0.004	0.016 (0.002 to 0.04)
Yow (1979)[111]	Ampicillin	0	34	14	24	0.0105	0.025 (0.003 to 0.07)
Pooled effect (random)							*0.028 (0.002 to 0.12)*
Stage II: Effect on EOGBS (*n*) given baby colonisation (*N*)							
Boyer (1982)[88]	Ampicillin	0	2	4	46	2.65	NA
Boyer (1983)[89]	Ampicillin	0	1	1	13	6.0	NA
Boyer (1986)[90]	Ampicillin	0	8	5	40	0.5	NA
Morales (1986)[92]	Penicillin	0	0	2	59	NA	NA
Matorras (1991)[91]	Ampicillin	0	2	3	24	1.75	NA
Pooled effect (fixed)							*0.93 (0.054 to 3.73)*
Stage III: Effect on EOGBS (*n*) given maternal colonisation (*N*)							
Tuppurainen (1989)[93]	Penicillin	1	88	4	111	0.31	0.050 (0.020 to 0.24)

NA, not applicable.

5. the effect of intravenous penicillin on stillbirth due to EOGBS
6. the effect of intravenous penicillin on stillbirth due to EO non-GBS.

Intravenous penicillin for EOGBS

It was assumed that the effects of antibiotics on EOGBS reduced **both** the risk of baby colonisation given mother colonisation **and** the risk of EOGBS given baby colonisation, and the data available were used to generate estimates of both these effects. However, for the purposes of the cost-effectiveness analysis, the treatment effects on each stage were combined to produce estimates of the 'net' treatment effect on EOGBS given maternal colonisation.

RCTs conducted in any setting that compared intravenous intrapartum ampicillin or penicillin with placebo or no treatment were included. Trials of colonised women were included if any measures of GBS colonisation in the baby or EOGBS were reported. Trials were also included that reported EOGBS in colonised babies or these data were extracted from the trials of colonised women (see Appendix 1, *Table 80* for details of included and excluded studies). *Table 33* shows the results for the eight included trials: seven reported baby colonisation in colonised women and five of these provided data on EOGBS in colonised babies. Data from these seven studies for the effect of treatment on EOGBS given maternal colonisation were not used to avoid using the same data twice. One further trial, by Tuppurainen and colleagues,[93] reported EOGBS only in colonised mothers. Five of the trials compared ampicillin and three compared penicillin with no treatment. It was assumed that all of the relative treatment effects on EOGBS and EO non-GBS were constant across maternal risk groups.

Analytic method, Stage I model

For treatment effects on baby colonisation given maternal colonisation, a random effects meta-analysis was assumed, in which for each trial j the trial-specific LORs were drawn from a common distribution: $\delta_j \sim N(d_1, \sigma_d^2)$. The logit of the probability of baby colonisation, $p_j^{(1)}$, takes a trial-specific baseline value in the control arm, μ_j, and $\mu_j + \delta_j$ in the treatment arm:

$$\text{logit}[p_j^{(1)}] = \mu_j + \delta_j \quad \text{in the treated arm}$$
$$\text{logit}[p_j^{(1)}] = \mu_j \quad \text{in the placebo arm}$$

Stage II model

The effect of treatment on EOGBS given baby colonisation was modelled as a fixed effect, d_2.

The probability of EOGBS given baby colonisation in trial j, $p_j^{(2)}$, was then

$$\text{logit}[p_j^{(2)}] = \nu_j + d_2 \quad \text{in the treated arm}$$
$$\text{logit}[p_j^{(2)}] = \nu_j \quad \text{in the placebo arm}$$

These models correspond to the conventional meta-analysis model proposed by Smith and colleagues[112] and used routinely in Bayesian meta-analysis. However, the number of trials with zero cell counts can cause numerical instability even in a Bayesian analysis and a number of technical refinements were introduced to avoid this. First, the trial-specific baselines were assumed to come from random effect distributions: $\mu_j \sim N(m, \sigma_m^2)$, $\nu_j \sim N(n, \sigma_m^2)$, with mean logit of m, and n, and the same between-trials variation σ_m^2. Second, the between-trial variation in the baselines, σ_m^2, was given a prior that reflected a belief that 95% of trials had baselines within a factor of two of the median. Third, the between-trials variation in the treatment effects, σ_d^2, was given a prior that reflected a belief that 95% of trial-specific LORs were within a factor of three from their median. Fourth, it was stipulated that the combined 'net' treatment OR could not be less than 1/1000, and the median Stage I LOR, $\exp(d_1)$, could not be less than 1/100.

The output of the analysis is the 'net' LOR, which is the sum of the treatment LORs for the baby colonisation given maternal colonisation and the treatment LOR for EOGBS given baby colonisation, i.e. $d_{IV} = d_1 + d_2$. The model set out above provides estimates of d_1 and d_2 from the trial evidence on the first and second stages, from which the combined 'net' estimate can be formed. Because of the relative rarity of events, the treatment effect ORs are treated as risk ratios (see *Table 35*).

The Tuppurainen trial (Stage III in *Table 33*) contributes to the estimates as it provides data on the **products** of the probability of baby colonisation given maternal colonisation and the probability of EOGBS given baby colonisation in each arm, that is, on $p^{(1)}_{C,Tup}\, p^{(2)}_{C,Tup}$ in the control arm and $p^{(1)}_{T,Tup}\, p^{(2)}_{T,Tup}$ in the treatment arm, where these quantities can be defined from the basic parameters of the Stage I and Stage II models, as follows:

$$\begin{aligned}
\text{logit}[p^{(1)}_{C,Tup}] &= \mu_{Tup} & \mu_{Tup} &\sim N(m, \sigma_m^2)\\
\text{logit}[p^{(1)}_{T,Tup}] &= \mu_{Tup} + \delta_{Tup} & \delta_{Tup} &\sim N(d_1, \sigma_d^2)\\
\text{logit}[p^{(2)}_{C,Tup}] &= \nu_{Tup} & \nu_{Tup} &\sim N(n, \sigma_m^2)\\
\text{logit}[p^{(2)}_{T,Tup}] &= \nu_{Tup} + d_2
\end{aligned}$$

Output for treatment effect of intravenous penicillin on EOGBS (*Tables 33* and *35*)

Table 35 shows the estimated net effect of intravenous treatment on EOGBS. The Bayesian method[112] relies on the full binomial likelihood attaching to each trial arm, rather than the Normal approximation based on the empirical LOR and its variance. In the present case the Bayesian approach offers a significant advantage as the addition of 0.5 to zero cells, required for the Normal approximation, leads to serious distortions of the evidence. *Table 33* compares the trial-specific LORs based on the normal approximation, which would be the input into a standard non-Bayesian meta-analysis, with the trial-specific LORs predicted by the Bayesian analysis.

Oral erythromycin for EOGBS

No RCTs were found that reported EOGBS or baby colonisation in colonised women treated prior to or during labour with oral penicillin, ampicillin or erythromycin. The criteria were therefore expanded to include studies of any women with any measure of GBS bacteraemia. Only one large trial was found, the MRC ORACLE multicentre trial,[28,29,113] that compared oral erythromycin or co-amoxiclav (ampicillin plus clavulinic acid) or both with placebo in women presenting with preterm prelabour ruptured membranes or spontaneous onset of labour with intact membranes (see Appendix 1, *Table 81* for details). The data for all the women randomised were combined for all the treatment arms, as it was assumed that the treatment effect of co-amoxiclav would be similar to that of erythromycin. No data were collected on the proportion of women colonised or the age at GBS bacteraemia. Blood cultures were taken only if clinically indicated. The trial found that 22/6581 babies in the treatment groups and 19/2216 in the placebo group had GBS bacteraemia.

Analytic method

The ORACLE study, like the Tuppurainen trial, provided information on EOGBS given mother colonisation. It was considered that a prior distribution for the baseline (control arm) logit of EOGBS given maternal colonisation could be generated as $\mu_{Ora} + \nu_{Ora}$, with $\mu_{Ora} \sim N(m, \sigma_m^2)$ and $\nu_{Ora} \sim N(n, \sigma_m^2)$.

The logit of EOGBS given maternal colonisation in the treatment arm would therefore be

$$\text{logit}(p_C) = \mu_{Ora} + \nu_{Ora} \quad \text{in the control arm}$$
$$\text{logit}(p_{T,Oral}) = \mu_{Ora} + \nu_{Ora} + d_{Oral} \quad \text{in the treatment arm}$$

where d_{Oral} is the LOR associated with oral treatment. However, adjustments had to be made to take into account the fact that the ORACLE study (shown below as $p_{C,Kenyon}$ and $p_{T,Kenyon}$): (a) reported **all** GBS, not only early onset; and (b) was not restricted to colonised women but was carried out in a population of women presenting preterm. Hence the control and treatment arms provided estimates of the products, respectively:

$p_{C,Kenyon} = p_C$ × average maternal colonisation rate in preterm × proportion of all preterm GBS that is EOGBS

$p_{T,Kenyon} = p_{T,Oral}$ × average maternal colonisation rate in preterm × proportion of all preterm GBS that is EOGBS

Output for treatment effect of oral erythromycin on EOGBS (*Table 35*)

Based on an analysis of data from three London-based NICUs (NICU database, 2005; see Appendix 1, *Table 75*) the proportion of all preterm GBS that occurred in the first week (i.e. is EOGBS) was 0.59 (95% CI: 0.36 to 0.82). The estimate from the model output was used for the average maternal colonisation rate in preterm women: 0.22 (95% CI: 0.15 to 0.30). The uncertainty in these distributions was propagated through the calculations to give an estimated 'net' effect of oral erythromycin on EOGBS of 0.28 (95% CI: 0.015 to 0.61; see *Table 35*). The model's predictions for what should have been observed in the ORACLE trial was 0.0086 (95% CI: 0.0056 to 0.123) in the control arm (observed 19/2216 = 0.0086) and 0.0031 (95% CI: 0.0021 to 0.0048) in the treatment arm (observed 22/6581 = 0.0033).

Intravenous penicillin for EO non-GBS

For the effect of intravenous penicillin on EO non-GBS, we considered that treatment acted in a single step and was independent of colonisation with GBS. No published studies were found that reported the effect of intravenous penicillin on EO non-GBS (see Appendix 1, *Table 80*). Expert opinion was therefore used to estimate the proportion of early-onset non-GBS bacteraemia pathogens reported in 961 admissions to three NICUs in London between 1996 and 2004 (NICU database, 2005) that were sensitive to penicillin (Gray J, Department of Microbiology, Birmingham Women's Hospital: personal communication, May 2006). It was assumed that sensitivity of non-GBS pathogens to penicillin in the laboratory corresponded to the proportion of EO non-GBS cases that would be prevented by intrapartum intravenous penicillin.

Output for treatment effect of intravenous penicillin on EO non-GBS (*Table 35*)

The average proportion, weighted by the frequency of each group of bacteria, was 73% (95% CI: 64 to 81%). This figure was used for the OR for the effect of intravenous penicillin.

Oral erythromycin for EO non-GBS

The effect of oral erythromycin on EO non-GBS was estimated indirectly using the results from the ORACLE trial[113] (see Appendix 1, *Table 81* on p. 141). The data for erythromycin and co-amoxiclav were combined, based on the assumption that the effectiveness of these drugs on EO non-GBS was equivalent.

Analytic method

To estimate the treatment effect, the following assumptions and adjustments were made:

1. There was a lower limit to efficacy. A prior distribution for the LOR was used to express the belief that the upper limit was an OR of 1, but that there would be a 2.5% chance of a slight negative effect with an OR of up to 1.6. This gave an upper limit to the OR with a mean distribution of 1.17 (95% CI: 1.01 to 1.6).
2. At the other extreme, it was assumed that oral treatment with erythromycin must be less effective than the effect of intravenous treatment with ampicillin on EO non-GBS. For this purpose the effect of intravenous ampicillin was estimated using expert opinion as described for penicillin in the section 'Intravenous penicillin for EO non-GBS' (previous column): the OR was 0.46 (95% CI: 0.38 to 0.56).
3. The ORACLE trial did not distinguish between early- and late-onset non-GBS but treatment was assumed to be effective only for EO non-GBS.
4. The ORACLE trial was restricted to preterm women, and EO non-GBS disproportionately affects preterm rather than term babies.

The control and treatment arms estimated, respectively,

$p_{Control\ ORACLE} = p_C$ × proportion of all non GBS that is EO non-GBS × proportion of all non-GBS in preterm

$p_{Treatment\ ORACLE} = p_T$ Oral × proportion of all non-GBS that is EO non-GBS × proportion of all non-GBS in preterm

TABLE 34 *Expert opinion of the effects of intravenous antibiotics on GBS stillbirth (see* Table 35 *for model outputs)*

Question	Mean (95% CI)				Range of estimates
	Expert 1	Expert 2	Expert 3	Expert 4	
Reduction of EOGBS stillbirth (%)	24 (15 to 34)	70 (50 to 90)	30 (20 to 60)	5 (0 to 10)	0–95

TABLE 35 *Risk ratios for the effect of maternal antibiotics on early-onset disease (see* Tables 33 *and* 34 *for model inputs)*

Treatment	Mean	Median	95% CI
Effect on EOGBS in GBS-colonised women			
I.v. penicillin	0.028	0.017	0.0015 to 0.12
Oral erythromycin	0.28	0.28	0.015 to 0.61
Effect on EO non-GBS in all women			
I.v. penicillin	0.73	0.73	0.64 to 0.81
Oral erythromycin	0.74	0.71	0.44 to 1.21
Effect on EOGBS stillbirth in GBS-colonised women			
I.v. penicillin	0.692	0.72	0.23 to 0.97
Effect on EO non-GBS stillbirth in all women			
I.v. penicillin	0.87	0.85	0.72 to 1.10

Finally, to estimate the treatment effect $d_{\text{Oral EO non-GBS}}$ the usual logistic model was assumed:

$$\text{logit}(p_{\text{T Oral}}) = \text{logit}(p_{\text{C}}) + d_{\text{Oral EO non-GBS}}$$

The additional parameters were based on the natural history model and data from three London NICUs. This data showed that, on average, 28.8% (95% CI: 20.5% to 45.6%) of all preterm non-GBS was early-onset non-GBS. The risk of EO non-GBS in preterm births was estimated at 0.021 (95% CI: 0.016 to 0.038) based on data inputs to the natural history model. The uncertainties in these estimates and on the prior upper and lower limits for the treatment effects were all propagated through the model.

Output for treatment effect of oral erythromycin on EO non-GBS (*Table 35*)

The final estimate of the effect of oral erythromycin on EO non-GBS was an OR of 0.74 (95% CI: 0.44 to 1.21).

Intravenous penicillin for GBS and non-GBS stillbirth

No studies were found that reported the effect of antibiotic treatment on the risk of stillbirth due to GBS or non-GBS infection. Instead, four experts were asked to provide mean estimates and 95% ranges for the relative risks of intravenous penicillin on GBS stillbirth (see *Table 34*; questionnaire available from authors). The estimates were pooled in a random effects meta-analysis using WinBUGS. To estimate the effect of intravenous penicillin on non-GBS stillbirth this rate was then adjusted by a ratio consistent with the ratio of the effect of intravenous penicillin on EO non-GBS and EOGBS livebirths. Because oral treatment is likely to take longer to penetrate fetal tissues than intravenous treatment, it was assumed that oral antibiotics had no effect on stillbirth.

Summary of outputs for treatment effects (*Table 35*)

The outputs of the models of antibiotic treatment are summarised in *Table 35*. In the case of EOGBS, these should be interpreted as the ORs for EOGBS that would be observed in studies of GBS-colonised women (as observed, for example, in the Tuppurainen study). These distributions do not feature directly in the cost-effectiveness analysis, which is based instead on the estimated effects in each of Stages I and II (mother colonisation → baby colonisation, and baby colonisation → EOGBS), but they are shown here for illustration.

Results for treatment effects in the context of previous reports

The OR for the effect of intravenous antibiotic therapy on EOGBS given maternal colonisation as estimated here (mean 0.028, median 0.017, 95%

TABLE 36 *Expert opinion of the effects, type and cost of a likely GBS vaccine (see* Table 37 *for model output)*

Question	Mean (95% CI)				Range of estimates
	Expert 1	Expert 2	Expert 3	Expert 4	
Reduction in maternal colonisation (%)	Upper genital tract: 65 (35 to 80) Lower vagina/rectum: 25 (10 to 40)	Unknown if any reduction	80 (30 to 95)	10–20 (0 to 30)	0 to 95
Reduction of EOGBS (%)	50 (not given)	70 (50 to 90)	30 (10 to 45)	85 (75 to 95)	10 to 95
Reduction of LOGBS	75 (50 to 85)	60 (40 to 80)	70 (60 to 95)	95 (90 to 100)	40 to 100
Vaccine type	Carbohydrate	Conjugate	Conjugate	Glycoconjugate	
Vaccine cost	£27.50	$100–120	£60+ (if research costs included)	$100	$50–120

CI: 0.0015 to 0.12), and used in the cost-effectiveness analysis, is somewhat less than that reported by Smaill in the Cochrane Library (0.17, 95% CI: 0.07 to 0.39).[35] The Cochrane review was based on four trials.[90–93] This, however, is not the main reason for the difference. The Cochrane estimate is based on the Peto 'one-step' method.[114] This is a fixed-effect estimator which is known to produce seriously biased estimates when the true treatment effects are large (as in the present analysis).[115,116] An equivalent Bayesian fixed-effect analysis of the same dataset was carried out. An estimate was obtained of 0.051 (median 0.034, 95% CI: 0.0012 to 0.19), and a random-effects analysis of these four studies gave an OR of 0.038 (median 0.037, 95% CI: 0.017 to 0.69). Work on fixed-effect models has shown that Bayesian methods produce the better CI coverage than methods that use zero-cell corrections, and confirmed that the Peto method gives inaccurate intervals when effects are extreme.[117,118] In summary, therefore, when analysed by appropriate statistical methods, the reduced database examined in the Cochrane study produced substantially the same results as the more inclusive evidence synthesis performed here.

Adverse effects of antibiotic treatment

Two possible hazards of antibiotic treatment were reviewed.

Fatal anaphylaxis in the mother

The incidence of fatal anaphylaxis due to penicillin or ampicillin was reviewed in a working party report by Law and colleagues.[54] No subsequent studies were found that were relevant. Law and colleagues reported US data showing zero deaths in an estimated 1.8 million women given intravenous ampicillin or penicillin between 1997 and 2001. Between 1992 and 1996 there were six deaths, giving a total incidence of one death per 600,000 women treated between 1992 and 2001. A UK-based study of 1225 hospital admissions for adverse drug effects reported none that were due to penicillin.[119] Given the very low risk of fatal anaphylaxis in the mother, this outcome was not included in the model.

Fetal effects of maternal anaphylaxis

One case report was found of fetal damage due to maternal anaphylaxis.[120] Given so few published reports, it was considered that serious fetal consequences of maternal anaphylaxis are so rare as to have a negligible effect on the outcomes in the model.

Short-term adverse drug effects such as vomiting or rash, were not reviewed as transient symptoms would have a negligible effect on the QALYs gained over a lifetime. However, the costs of treatment were adjusted upwards to take account of such short-term adverse drug effects (see *Table 42*, pp. 51–2).

Vaccination

Vaccination for GBS is in the early phases of development. No effectiveness trials have yet been conducted, although various vaccines have been tested in women in Phase I and II trials.[19,20,121–123] In 2006, the most promising candidate for a vaccine is a carbohydrate or glycoconjugate against all the five major serotypes of GBS (*Table 36*).[54,123,124] It is estimated that an adequate GBS vaccination may be available in the UK within the next 4–5 years (Baker C, Baylor College of Medicine, Houston, TX, USA: personal communication, July 2006; Heath P, St George's Hospital, London: personal communication, July

TABLE 37 *Odds ratios for the effect of maternal GBS vaccination on GBS outcomes: predictive distributions based on a meta-analysis of four expert opinions (see* Table 36 *for model inputs)*

Outcome	Mean	Median	95% CI
Maternal GBS colonisation	0.66	0.66	0.44 to 0.848
EOGBS (livebirth and stillbirth)	0.375	0.361	0.111 to 0.73
LOGBS	0.199	0.186	0.0559 to 0.418

2006). However, due to ethical concerns this is likely to be dependent on the acceptance of serological correlates of immunity in maternal sera as the means for licensing (Baker C, Baylor College of Medicine, Houston, TX, USA: personal communication, July 2006). It was assumed that vaccination would be given between 24 and 28 weeks of pregnancy.[124]

Vaccination is expected to act by inducing mucosal immunity in the mother. The potential consequences for GBS disease in the baby would be as follows. First, vaccination is likely to reduce the prevalence of maternal GBS colonisation and consequently the risk of baby colonisation. Second, significant levels of protective vaccine-induced antibodies will have crossed the placenta after 32 weeks of gestation[125] and protect against disseminated disease manifesting as stillbirth, early-onset or late-onset GBS disease. Protective maternal antibodies are expected to persist in the baby for about 3 months after birth.[125]

No comparative studies were found that evaluated the effect of vaccine on maternal colonisation, EOGBS, GBS stillbirth or LOGBS. Instead, four experts were asked to provide a mean estimate and 95% probability range for each of these parameters (*Table 36*; questionnaire available from authors). We used the predictive distribution (see Glossary) calculated from a random effects meta-analysis of the inputs provided by each expert using WinBUGS.

Output for effects of vaccine (*Table 37*)
The results for the vaccine treatment effects used in the model are shown in *Table 37*.

Any potential adverse effects of GBS vaccination were ignored given the limited use of GBS vaccine to date on which to base any estimates.

Accuracy of tests for maternal GBS colonisation

Two types of test for maternal GBS colonisation were compared: a rapid test, which can be performed on admission in labour, and culture at 35–37 weeks of gestation. Both tests are performed on a vaginal and a rectal swab taken at the same time. A positive result was defined as a positive vaginal or rectal swab or both. Although several different types of rapid test are available, the real-time PCR test was selected, which was reported to be the most accurate test in a previous systematic review.[27] Culture based testing at 35–37 weeks was chosen as the alternative test as this is standard practice in the USA.

PCR test

Real-time PCR tests typically give results within 1 hour of sampling. Newer versions of this test (e.g. the Roche light-cycler) can be carried out on the labour ward without specialised laboratory personnel. Inclusion criteria were restricted to studies of untreated women who used the test in routine practice. We included one study based on routine practice in five centres in North America (802 women in total, 167 colonised).[10] All centres used the IDI-Strep B test (Infectio Diagnostics, now BD Diagnostics – GeneOhm, San Diego, CA, USA) compared with a reference standard of enriched culture of swabs taken at the same time. Three further studies were excluded: two because of the tightly controlled methods that would not be feasible in routine practice and one because testing was not performed immediately (see Appendix 1, *Table 82*).

A random effects meta-analysis was carried out using the results from each of the five study centres to calculate a mean diagnostic odds ratio (DOR) and 95% confidence interval. The DOR is represented by the mean receiver operating characteristic (ROC) curve (plot of sensitivity against 1 – specificity) for all the studies. Using the method of Littenberg and colleagues,[126,127] no evidence was found that the DOR varied between study centres, a proxy marker for different thresholds for a positive test result. To estimate the range of test accuracy that could occur in practice, the mean and 95% CI of the DOR were used to estimate the mean and 95% CI for sensitivity for each value of specificity between the highest and lowest mean values observed in the five centres (92.67–99.21%). This range was considered to

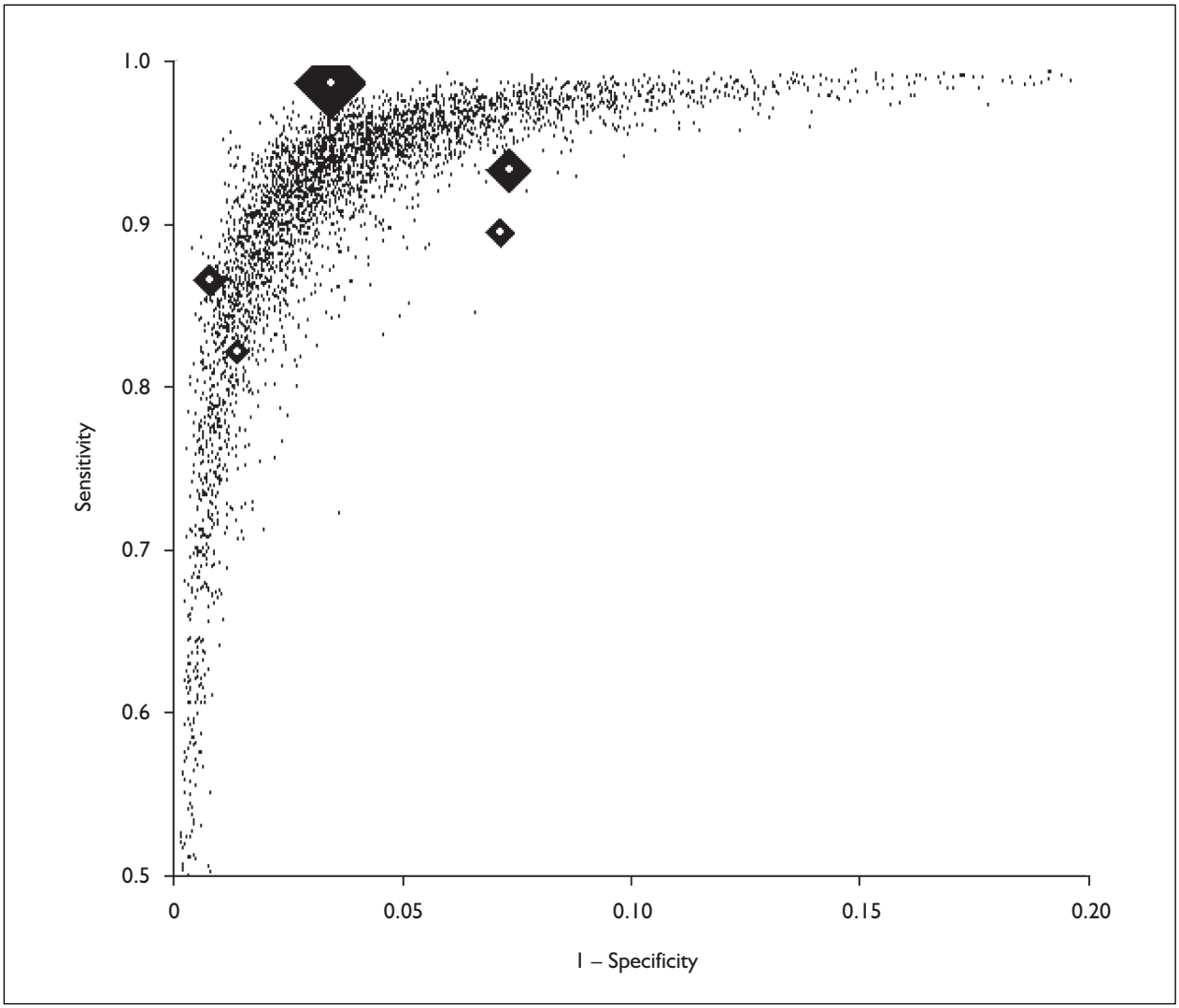

FIGURE 6 *Pooled ROC curve for PCR testing for maternal GBS colonisation in labour*

represent realistic variation in good practice. The analyses were done in WinBUGS based on the equations below, using data inputs for the number of true positives (TP), false positives (FP), false negatives (FN) and true negatives (TN), in each of the five centres (see Appendix 1, *Table 82*; 0.5 was added to all four values of each of the two studies with a zero as one of the values):

$$\text{sensitivity} = TP/(TP + FN)$$
$$\text{specificity} = TN/(FP + TN)$$
$$DOR = [\text{sensitivity}/(1 - \text{sensitivity})]/(1 - \text{specificity})/\text{specificity})$$

$$\text{Hence: sensitivity} = 1/(1 + (1/\{DOR \times [(1 - \text{specificity})/\text{specificity})]\})$$

Output for accuracy of PCR (Figure 6)

The ROC curve in *Figure 6* shows the correlation between sensitivity and the false positive rate (1 – specificity) based on the mean and 95% CI of the DOR (mean 406; 95% CI: 192 to 876). The diamonds represent the five centres; their size is proportional to total numbers tested.

The mean sensitivity (89.2%; 95% CI: 49.1 to 98.7%) and specificity (95.8%; 95% CI: 86.7 to 99.7%) underestimate the mean ROC curve because the overall mean values ignore the correlation between sensitivity and specificity.[128]

Culture screening at 35–37 weeks

The inclusion criteria were restricted to studies of untreated women in which the large majority (>95%) were tested between 35 and 37 weeks, as test accuracy diminishes with increasing time between testing and labour. Included studies used enriched culture for the reference standard swabs taken during labour and also for the swabs taken at 35–37 weeks. Four studies were found (3994

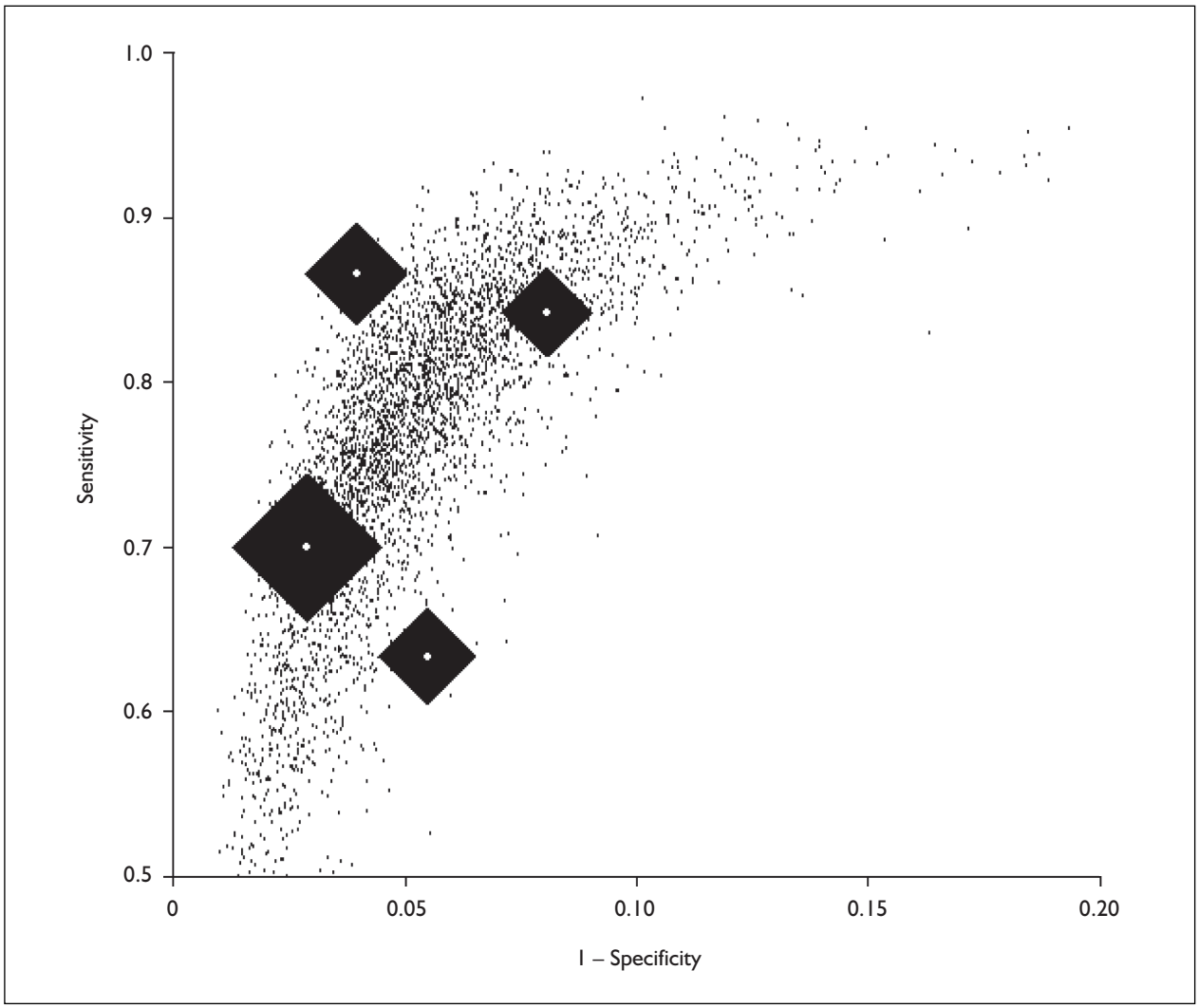

FIGURE 7 *Sensitivity and false positive rate of screening at 35–37 weeks in detecting GBS colonisation during labour*

women in total, 486 colonised; see Appendix 1, *Table 83* for details). All used vaginal and rectal swabs and enriched media. The sensitivity and specificity of culture screening at 35–37 weeks were determined in the same manor as for PCR testing: using WinBUGS analyses based on the equations given above, using data inputs for the number of true positives (TP), false positives (FP), false negatives (FN) and true negatives (TN), in each of the four studies used (see Appendix 1, *Table 83*).

Output for accuracy of culture at 35–37 weeks (Figure 7)

The ROC curve in *Figure 7* shows the correlation between sensitivity and the false positive rate (1 – specificity) based on the mean and 95% CI limits of the DOR (mean 72; 95% CI: 37.7 to 126.0). The range of specificity entered into the model, as for PCR testing, was that observed in the studies used, 91.93–97.11%. The mean sensitivity was 75.8% (95% CI: 47.2 to 91.5%) and specificity 94.7% (95% CI: 88.5 to 98.5%). The diamonds represent the four studies; their size is proportional to total women tested.

Proportion of women receiving testing and treatment and number of doses received

The analyses took into account the fact that some women would deliver before they could undergo testing or treatment as the proportion of women undergoing these interventions affects the relative cost and effectiveness of strategies. It was assumed that all women able to do so underwent each intervention and ignored the possibility that some might decline. As a result, the model addresses the decision options for policy makers given complete uptake of strategies, and for women when deciding which strategy to undergo.

TABLE 38 *Criteria for undergoing testing and treatment*

Vaccination	Women delivering before 28 weeks were not vaccinated (99% of all women were). Vaccine had an effect only on women who delivered after 32 weeks (75% of preterm deliveries, 100% of term deliveries) to allow for antibody transfer across the placenta
Culture test at 35–37 weeks	Women delivering before 35 weeks were not tested. It was assumed that all those delivering after 35 weeks were tested (this means 47.5% of preterm deliveries and 100% of term deliveries) and had a result (taking 48 hours) in time to be treated
PCR screen	All women could be tested. Test results were available 1 hour later
Treatment	Treatment started at the onset of labour or membrane rupture, whichever came first
Oral treatment	Oral treatment was not given in established labour which we defined as less than 6 hours before delivery. No set-up time was required. The treatment effect in *Table 35* was assumed to apply to all women receiving treatment
I.v. treatment	I.v. treatment took 1 hour set-up time to allow for insertion of the i.v. line. Hence women who delivered within 1 hour of onset of labour or a positive PCR result were not treated

TABLE 39 *Proportion of women undergoing testing and/or treatment according to risk group (see* Table 40 *for model output)*

Risk group	Vaccination (%)	Culture test at 35–37 weeks (%)	PCR test (%)	Oral treatment (% of all women or those testing positive at 35–37 weeks)	Oral treatment; PCR test (% of positive women)	I.v. treatment (% of all women or those testing positive at 35–37 weeks)	I.v. treatment; PCR test (% of positive women)
1[a]	99	47.5	100	100.00	100.00	100.00	100.00
2	99	47.5	100	38.02	31.13	81.65	73.98
3	99	47.5	100	38.02	31.13	81.65	73.98
4	99	47.5	100	71.20	68.00	74.83	72.19
5	99	47.5	100	90.47	86.55	76.16	67.62
6	99	47.5	100	38.02	31.13	81.65	73.98
7[a]	99	100	100	100.00	100.00	100.00	100.00
8	99	100	100	56.58	48.31	89.91	84.52
9	99	100	100	56.58	48.31	89.91	84.52
10	99	100	100	93.78	92.41	87.83	86.97
11	99	100	100	100.00	100.00	88.31	85.90
12	99	100	100	56.58	48.31	89.91	84.52
Total	99	100	100	64.75	58.18	89.93	85.17

[a] Given that the Caesarean section is elective, it is assumed that women will always be able to undergo screening/treatment.

Proportion of women tested and treated

Table 38 shows the criteria used to determine the proportion of women in each maternal risk group who were available to undergo each intervention, i.e. had enough time before delivery to undergo treatment (and PCR testing immediately beforehand if applicable). The proportions were calculated using the SMMIS database and are shown in *Table 39*.

In determining the proportion of women treated with intravenous penicillin no account was taken of the proportion of women who report allergy to penicillin (around 10–15% of all women; Steer P, Charing Cross and Westminster Medical School, London: personal communication, June 2006) and are given an alternative antibiotic such as erythromycin. This was because the proportion of women with true penicillin allergy, estimated to be much lower (around 2%; Steer P, personal communication), can be identified by careful history taking. A further reason is that alternative treatment, although possibly being less effective against EOGBS, due to resistance, may be more effective against EO non-GBS disease given its broader spectrum of antimicrobial activity, and so may not alter the results of our model greatly.

*Output for the proportion of women treated (***Table 40***)*

A calculation was made of the proportion of women treated with antibiotics in each risk group

TABLE 40 *Proportion (%) of women receiving antibiotics in each maternal risk group given each of the 14 interventions (see* Table 39 *for model input)*

	Risk group												
Intervention[a]	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**Average**
1. V	0	0	0	0	0	0	0	0	0	0	0	0	0
2. CO	8.6	3.3	8.9	8.1	10.3	3.3	11.9	6.8	20.4	14.5	15.5	6.8	8.5
3. CI	8.6	7.1	19.0	8.6	8.7	7.1	11.9	10.7	32.4	13.6	13.7	10.7	11.7
4. PO	19.7	6.1	17.7	18.2	23.1	6.1	12.2	5.9	19.9	15.2	16.5	5.9	8.5
5. PI	19.7	14.6	42.0	19.3	18.1	14.6	12.2	10.3	34.8	14.3	14.1	10.3	12.3
6. I	100	81.7	81.7	74.8	76.2	81.7	100	89.9	89.9	87.8	88.3	89.9	89.9
7. O	100	38.0	38.0	71.2	90.5	38.0	100	56.6	56.6	93.8	100	56.6	64.8
8. n	0	0	0	0	0	0	0	0	0	0	0	0	0
9. VCO	7.1	2.7	6.9	6.5	8.3	2.7	9.7	5.5	14.5	11.3	12.1	5.5	6.8
10. VCI	7.1	5.8	14.7	6.9	7.0	5.8	9.7	8.7	23.1	10.6	10.6	8.7	9.4
11. VPO	15.8	4.9	13.5	14.3	18.2	4.9	9.5	4.6	13.9	11.4	12.3	4.6	6.6
12. VPI	15.8	11.7	32.2	15.2	14.2	11.7	9.5	8.0	24.3	10.7	10.6	8.0	9.4
13. VI	100	81.7	81.7	74.8	76.2	81.7	100	89.9	89.9	87.8	88.3	89.9	89.9
14. VO	100	38.0	38.0	71.2	90.5	38.0	100	56.6	56.6	93.8	100	56.6	64.8

[a] C, culture test at 35–37 weeks; I; i.v. antibiotics; n, no treatment; O, oral antibiotics; P, PCR test at labour; V, vaccination.

TABLE 41 *Average number of doses of each treatment per treated woman according to risk group (model input)*

Risk group	**Vaccination**	**Culture test at 35–37 weeks**	**PCR test**	**Oral treatment (% of all women or those testing positive at 35–37 weeks)**	**Oral treatment; PCR test (% of positive women)[b]**	**I.v. treatment (% of all women or those testing positive at 35–37 weeks)**	**I.v. treatment; PCR test (% of positive women)[b]**
1[a]	1	1	1	1	1	1	1
2	1	1	1	1.468	1.458	2.032	1.944
3	1	1	1	1.468	1.458	2.032	1.944
4	1	1	1	7.270	7.400	2.584	2.477
5	1	1	1	7.611	7.806	1.770	1.695
6	1	1	1	1.468	1.458	2.032	1.944
7[a]	1	1	1	1	1	1	1
8	1	1	1	1.434	1.409	2.123	1.982
9	1	1	1	1.434	1.409	2.123	1.982
10	1	1	1	3.676	3.561	3.488	3.264
11	1	1	1	6.576	6.370	2.826	2.653
12	1	1	1	1.434	1.409	2.123	1.982
Total	1	1	1	2.026	1.994	2.094	1.965

[a] Given that the Caesarean section is elective it is assumed that women will only be given one dose of treatment before.
[b] For the strategies involving PCR testing, an extra 1 hour is required for the test. Therefore, there will be slightly fewer doses per women as fewer women will be treatable.

given each of the 14 interventions using information on: the risk of maternal colonisation; test accuracy; the effect of vaccination on maternal colonisation; and information from *Table 39*. The results are shown in *Table 40*. This information was used to determine the proportion of all pregnant women who would be treated with antibiotics under each of the 713 strategies included in the cost-effectiveness analyses.

Number of treatment doses according to risk group

The estimated number of doses of oral or intravenous antibiotics for women in each of the 12 maternal risk groups is shown in *Table 41*. These data inputs were used to determine the costs of treatment for each strategy (see *Table 42* for information on the cost of the initial dose and subsequent doses of intravenous and oral

TABLE 42 *Baseline costs*[a]

Input	Description of data input	Data input: mean (95% CI) unless stated otherwise		Source
Cost of delivery at gestation of				
103	<28 weeks	Gamma (mean £6569.35, SD £9187.95)		Petrou, 2003[129]
104	28–31 weeks	Gamma (mean £6700.27, SD £5678.13)		As above
105	32–36 weeks	Gamma (mean £1921.51, SD £1639.03)		As above
106	37+ weeks	Gamma (mean £751.83, SD £763.11)		As above
107	Preterm delivery (<37 weeks)[a]	£2880 (£611, £7190)		Calculated using inputs 103–105
108	Term delivery (≥37 weeks)[a]	£831 (£18.8, £3110)		Calculated using input 106
Costs of disease[b] (fatal/non-fatal EOGBS, EO non-GBS, LOGBS: meningitis or bacteraemia alone)				
109	Alive EOGBS/EO non-GBS meningitis	Proportion split: ICU = 0.24, SCBU = 0.55, general = 0.21 Total LOS: mean = 21.12, SE = 1.93		BPSU database, 2005 and Curtis and Netten, 2005[130]
110	Alive EOGBS/EO non-GBS **bacteraemia alone**	Proportion split: ICU = 0.17, SCBU = 0.60, general = 0.23 Total LOS: mean = 15.94, SE = 0.95		As above
111	Dead EOGBS/EO non-GBS meningitis	Proportion split: ICU = 1, SCBU = 0, general = 0 Total LOS: mean = 2.33, SE = 0.68		As above
112	Dead EOGBS/EO non-GBS **bacteraemia alone**	Proportion split: ICU = 0.97, SCBU = 0.03, general = 0 Total LOS: mean = 3.46, SE = 0.25		As above
113	Alive LOGBS meningitis	Proportion split: ICU = 0.16, SCBU = 0.25, general = 0.59 Total LOS: mean = 27.86, SE = 2.48		As above
114	Alive LOGBS **Bacteraemia alone**	Proportion split: ICU = 0.15, SCBU = 0.30, general = 0.55 Total LOS: mean = 32.95, SE = 3.75		As above
115	Dead LOGBS meningitis	Proportion split: ICU = 0.64, SCBU = 0.18, general = 0.18 Total LOS: mean = 25.64, SE = 3.68		As above
116	Dead LOGBS **Bacteraemia alone**	Proportion split: ICU = 1, SCBU = 0, general = 0 Total LOS: mean = 16.83, SE = 2.40		As above
Other costs				
117	Vaccine	£51.99 at 2005 mean (gamma: alpha = 9.908, beta = 5.247)		Expert opinion
118	Cost stillborn	£871.00 (fixed[c])		Reference costs[134]
119	**Culture screen**			Various sources[29,130,134–137]
	Explanation	Midwife (10 minutes)		£3.50
	Materials	Gloves	£0.02	
		Swab	£0.01	
		Transport medium	£0.16	
		Selective agar plates	£0.87	
		Enrichment broth	£0.16	
	Carrying out test	Biomedical scientist (10 minutes)	£2.03	
	Delivery of results	Midwife (15 minutes)	£5.25	
	Total cost		£11.99 (fixed[c])	
120	**PCR screen**			As above
	Explanation	Midwife (10 minutes)	£3.50	
	Materials	Gloves	£0.02	
		Swab	£0.01	
		PCR reagents	£0.54	
		Pipette tips	£0.01	
		PCR machine[d]	£2.35	

continued

TABLE 42 *Baseline costs[a] (cont'd)*

Input	Description of data input	Data input: mean (95% CI) unless stated otherwise		Source
	Carrying out test	Healthcare assistant (40 minutes)	£7.27	
	Delivery of results	Midwife (15 minutes)	£5.25	
	Total cost		£19.03 (fixed[c])	
	Oral antibiotics			BNF[133] and PSSRU[130]
121	**Initial dose**			
	Erythromycin	1 dose	£0.21	
	Explanation/delivery	Midwife (10 minutes)	£3.50	
	Total cost		£3.71 (fixed[c])	
122	**Subsequent doses**			
	Erythromycin	1 dose	£0.21	
	I.v. antibiotics			Various sources[130,133,138–140]
123	**Initial dose**			
	Setting up i.v.	Midwife (15 minutes)	£5.25	
	Materials	Cannula	£2.59	
		Saline flush (5 ml)	£0.33	
		5-ml syringe	£0.05	
		Saline for injection (20 ml)	£1.04	
	Delivery	SHO (5 minutes)	£3.08	
	Penicillin	3 g	£3.75	
	Adverse effects per patient	Mild (5%)	£2.37	
	(anaphylaxis)	Severe (0.01%)	£0.06	
	Total cost		£18.52 (fixed[c])	
124	**Subsequent doses**			
	Delivery	Midwife (5 minutes)	£1.75	
	Penicillin	1.5 g	£1.88	
	Materials	Saline flush (5 ml)	£0.33	
		5 ml syringe	£0.05	
		Saline for injection (20 ml)	£1.04	
	Total cost		£5.05 (fixed[c])	

ICU, intensive care unit; SCBU, special care baby unit; SE, standard error; SHO, Senior House Officer.
[a] At 2005 prices.
[b] Event costed according to time in hospital. ICU = £1570, SCBU = £356, general ward = £188; Dirichelet distribution specified for each proportional split, summing to total LOS which is specified as a gamma distribution.
[c] Fixed means no measure of uncertainty around cost estimate.
[d] Cost of PCR machine is £35,250 for 5-year life-span (Gray J, Birmingham Women's Hospital: personal communication, May 2006); There will be one PCR machine per maternity unit in the UK; given that there are 220 maternity units in the UK, with a population of 680,000 deliveries per year, each unit will deliver (test) ca 15,000 women over the 5-year life-span of the machine; This is an upper limit of the costs given that up to 16 tests can be done at once, every 40 minutes, by the healthcare assistant and we are assuming only one is done at a time.

antibiotics). The estimates in *Table 41* were based on data from SMMIS, which were used to calculate the interval between the onset of labour or membrane rupture to delivery, or, in the case of oral treatment, 6 hours before birth. The dosing frequency was as follows:

- Oral treatment is given every 6 hours for 10 days maximum (40 doses) or until 6 hours before delivery, commencing at start of ROM or start of labour (whichever occurs first).
- Intravenous treatment is every 4 hours until delivery, commencing 1 hour (set-up time) after the start of labour.

Costs

The healthcare costs associated with states and events in the decision model were grouped into baseline costs (associated with delivery, intervention strategies and immediate infection

TABLE 43 *Long-term costs*

Input	Description of data input	Data input	Source
125	Cost of long-term mild disability	Fixed £541.07 per year undiscounted	Trotter and Edmunds, 2002[141]
126	Cost of long-term moderate disability	Fixed £541.07 per year undiscounted	As above
127	Cost of long-term severe disability	Fixed £21,500 per year undiscounted	As above

outcomes; see *Table 42*) and long-term costs associated with disability (*Table 43*). The costs of delivery according to gestational age at birth were taken from a study by Petrou and colleagues.[129] These costs were inflated to current prices using the Hospital and Community Health Services (HSHS) index.[130] The mean cost for preterm and term deliveries was based on a weighted average using the proportions delivering in each category of gestational age from the Petrou study.[129] Data were used from the BPSU database on the duration of stay in each type of ward before death or hospital discharge for babies with EOGBS or LOGBS disease. A Dirichelet distribution[131] was used to ensure that the division of time spent in each type of ward summed to the total length of stay (LOS) for that particular episode. For EO non-GBS sepsis or meningitis, the same LOS was assumed as the mean for EOGBS outcomes in the same maternal risk group. The costs per night of stay in each type of hospital ward were derived from the PSSRU at 2005 costs.[130]

The costs of testing using PCR or culture at 35–37 weeks were based on the costs of coordination of the programme (staff, materials and laboratory costs) and the delivery of results (see Inputs 119 and 120 in *Table 42*). Antibiotic treatment costs included the costs for the initial dose and for subsequent doses, multiplied by the number of doses given which varied according to maternal risk and intervention strategy (detailed in *Table 41*). As *Table 42* shows, the initial dose of antibiotics took into account the cost of setting up the intravenous line and the cost of treating the adverse effect anaphylaxis, which were estimated to affect 5% of patients mildly and 0.01% of patients severely.[132] Drug costs for oral and intravenous antibiotics were taken from the BNF.[133]

The cost of vaccine was based on the mean of four expert opinions using a random effects model (see *Table 36*; £27.50, £63.10, £60 and £57.37; UK costs for 2005). Using these estimates, the alpha and beta parameters of a gamma distribution were defined.

Long-term healthcare costs of mild, moderate and severe disability were taken from a study that examined the use of meningococcal C vaccine.[141] The yearly costs were multiplied by the life expectancy, which was sampled from the distribution of life expectancy.

Chapter 6

Cost-effectiveness: principles, methods and results

Overview

The purpose of the cost-effectiveness analysis was to inform decision-making about how best to prevent GBS and other bacterial infections in early infancy. To this end, the evaluation addressed two closely related questions:[142,143] (1) given existing evidence, which interventions appear cost-effective for particular risk groups and which strategies or policies appear cost-effective for the whole patient population?; and (2) what is the uncertainty surrounding these choices within risk groups and between strategies and is further evidence required to reduce this decision uncertainty? This chapter addresses the first of these questions. Question 2 is addressed in Chapter 8.

To address the first question, we need to estimate the costs and QALYs associated with each of the interventions within risk groups and the strategies across risk groups. It is then possible to assess if a particular intervention/strategy is cost-effective relative to other interventions/strategies. To determine if an intervention/strategy is cost-effective, standard decision rules are applied.[144] Dominated and extendedly dominated interventions/strategies are excluded and ICERs are then calculated for remaining interventions/strategies. To identify the optimal intervention/strategy, ICERs are compared with accepted thresholds for cost-effectiveness.[144]

Principles of cost-effectiveness analysis

It was first determined which interventions were most cost-effective for each of the 12 maternal risk groups. Standard decision rules were applied,[144] as illustrated in the following example (*Figure 8*). The example will also assist in explaining the results described in the next section.

Imagine that six interventions are compared, S1–S6, producing the cost and QALY results shown in *Table 44*. The first step in determining which strategy is the most cost-effective is to exclude dominated interventions. An intervention is said to be dominated if there is another intervention with higher QALYs and lower costs.

TABLE 44 *Cost-effectiveness decision rule example: costs and QALYS*

Intervention	Costs (£)	QALYs
S1	0	0
S2	600	0.06
S3	750	0.065
S4	920	0.073
S5	900	0.075
S6	1200	0.085

TABLE 45 *Cost-effectiveness decision rule example: ICERs*

Intervention	Costs (£)	QALYs	ICER (£)
S1	0	0	–
S2	600	0.06	10,000
S3	750	0.065	30,000
S5	900	0.075	20,000
S6	1200	0.085	30,000

In this example, S4 is dominated, as S5 offers higher QALYs at a lower cost (see *Figure 8*).

The remaining non-dominated interventions are then ranked according to ascending QALYs, and ICERs (in terms of cost per QALY gained) are then presented for each successively more effective intervention. The ICER is calculated as incremental costs ($Costs_{S1} – Costs_{S2}$) divided by incremental QALYs ($QALY_{S1} – QALY_{S2}$), where $Costs_{S1}$ and $QALY_{S1}$ relate to the intervention of interest (S1) and $Costs_{S2}$ and $QALY_{S2}$ relate to the next best (next most effective) intervention (S2). The ICERs for each of the remaining five interventions in the example can be seen in *Table 45*.

The second step is to exclude interventions that are subject to extended dominance.[144] An intervention is said to be extendedly dominated if it has a higher ICER than the next more effective alternative. In this example, S3 is extendedly dominated, as it is associated with lower QALYs than S5 but has a higher ICER (£30,000 compared with £20,000) (see *Figure 8*). When dominated and extendedly dominated interventions have been excluded, ICERs for the remaining interventions are then recalculated (as shown in *Table 46*). However, the ICER does not by itself indicate if a

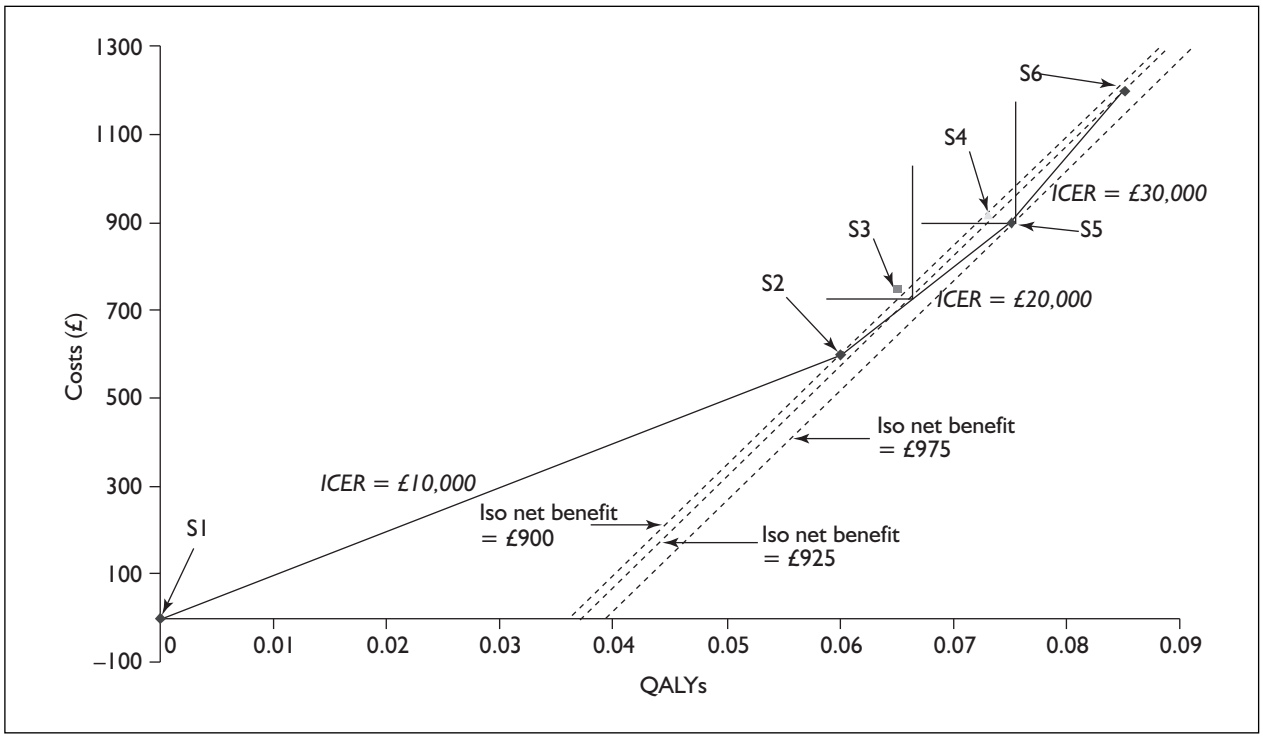

FIGURE 8 *Example of decision rule with multiple strategies*

TABLE 46 *Cost-effectiveness decision rule example: net benefit*

Intervention	Costs (£)	QALYs	ICER (£)	NB (at λ = £25,000) (£)
S1	0	0	–	0
S2	600	0.06	10,000	900
S5	900	0.075	20,000	975
S6	1200	0.085	30,000	925

strategy is cost-effective – we also need to know where health (measured in QALYs) will be displaced elsewhere in the healthcare system, i.e. we need a threshold for cost-effectiveness.

Depending on the cost-effectiveness threshold [willingness to pay (WTP)] operated for policy decisions, the optimal intervention can then be identified. Threshold values of between £20,000 and £30,000 per QALY have been suggested for the UK and this range is currently used by the National Institute for Health and Clinical Excellence (NICE) when issuing guidance to England and Wales. Once a threshold has been established, QALYs can be transformed into monetary values. The net benefit (NB) of each intervention can then be calculated as the difference between the QALYs gained multiplied by the threshold value (λ) and the costs for an intervention:

$$NB_S = (QALY_{SS} \times \lambda) - Costs_S$$

The results for NB for the non-dominated interventions in the example, based on a cost-effectiveness threshold of £25,000 per QALY, are shown in *Table 46*.

The decision based on the cost-effectiveness results is to choose the intervention with the highest number of QALYs subject to the threshold (λ). Therefore, we are maximising health subject to the budget constraint. This is equivalent to choosing the strategy with the highest NB. Less effective interventions become displaced along with more effective interventions that exceed the threshold (budget). If the threshold is below £10,000, S1 would be regarded as the optimum intervention. If the threshold was between £10,000 and £20,000, S2 would be regarded as optimum. At thresholds between £20,000 and £30,000, S5 would be regarded as optimum, and finally at thresholds above £30,000, S6 would be regarded as optimum. NB is calculated here at a threshold

value of £25,000. The intervention with the highest NB at this threshold is S5.

Each of the cost and QALYs pairs from the six interventions (*Table 44*) can be plotted on a cost-effectiveness plane (*Figure 8*) to illustrate further the principles of cost-effectiveness decision rules.

Non-dominated and non-extendedly dominated strategies (S1, S2, S5, and S6) lie on the frontier (solid line). The frontier shows that to gain the additional QALYs offered by S2 compared with S1, one must be willing to pay £10,000 per QALY. Similarly, to gain the additional QALYs offered by S5, one must be willing to pay £20,000. It can be seen that S5 offers a higher NB than S6; therefore, if one were to choose S6 as opposed to S5 one would lose £50 of NB per patient. If it is assumed that the relevant population is 100,000, this loss in NB translates to a total loss of £5,000,000 or 200 QALYs (at a threshold of £25,000 per QALY).

Dominated and extendedly dominated strategies (S3 and S4) do not appear on the frontier and are located to its north-west. S3 and S4 are located fairly close to the frontier; however, as before, it is not the closeness to the frontier that matters but how much NB one would lose if one does not choose the cost-effective intervention (S5 at a threshold of £25,000). The Iso NB lines (lines at which the same NB exists) at a threshold of £25,000 are also shown in *Figure 8*. The difference between strategies (measured in terms of QALYs) is the horizontal distance from the best Iso NB line that can be obtained (measured in monetary terms, it is the vertical difference from the best Iso NB line). Strategies to the south-east of an Iso NB line will have a higher NB, but will not be affordable in terms of the budget constraint. Strategies to the north-west of an Iso NB line will have a lower NB and should not therefore be adopted in favour of strategies with a higher NB that satisfy the budget constraint.

Cost-effectiveness analysis for risk groups

Methods

Using the methodology described in the previous section, the cost-effectiveness of the 14 interventions included in this analysis (see the section 'Interventions', p. 8) was determined for the 12 maternal RGs (see the section 'Maternal risk groups', p. 5). In order to illustrate the differences between the interventions (which are very small in some cases), costs and QALYs (per woman) were calculated relative to the 'no treatment' option (intervention 8). NB was determined from these figures and optimal interventions were determined on the basis of the highest NB.

Due to concerns regarding antibiotic resistance (see the section 'Accounting for antibiotic exposure', p. 69), the option of treating all women with antibiotics (without screening first) in RG11 and RG12 was not permitted, therefore excluding Interventions 6, 7, 13 and 14 (treatment of all women with intravenous or oral antibiotics with and without vaccination) from the analysis for these groups. RG11 was included in addition to RG12 (the majority of the population) because it is not possible to determine if a woman will have prolonged ROM (be in RG11) when she presents in labour with no other risk factors (is in RG12).

Two scenarios were modelled, one where vaccination is plausible (Scenario A) and the other where vaccination is not plausible (Scenario B). In Scenario A, all 14 interventions were compared for each risk group, apart from RG11 and 12, where the 'treat all' strategies were excluded. In Scenario B, given that seven of the 14 interventions involve vaccination, only the seven non-vaccination interventions were compared for each RG, apart from RG11 and 12, where the 'treat all' strategies were again excluded.

Results

The full cost-effectiveness results by RG can be seen in Appendix 2, *Tables 84–95*, for Scenario A and Appendix 3, *Tables 96–107*, for Scenario B. A summary of the cost-effectiveness results for RGs, only showing those interventions with greater than 1% probability of being cost-effective at a threshold of £25,000 per QALY, is presented in *Table 47* for Scenario A and in *Table 48* for Scenario B. The probability of being cost-effective is based on the average uncertainty in the determination of NB over all the iterations of the model that were run (see the section 'Overview of methods', p. 79); it is shown in Appendices 2 and 3, *Tables 84–107*, and was used in the determination of the list of relevant strategies (combinations of interventions for all 12 RGs) to be modelled (see the section 'Methods', p. 60). As explained in the section 'Principles of cost-effectiveness analysis' (p. 55), for each RG, the intervention with the highest NB is the most cost-effective.

Scenario A

In scenario A, using a threshold value of £25,000, the results for preterm risk groups (see *Table 47*)

TABLE 47 *Summary of cost-effectiveness by risk group, Scenario A*

Risk group	Intervention	Cost (£)	QALYs	Result (£)	NB at 25,000 (£)[a]
Preterm					
1. Elective LSCS	13: Vaccination + i.v.	–0.362	0.000164	ICER to 14: 13,900	4.46
	14: Vaccination + oral	–0.483	0.000155	ICER to 7: 979	4.36
2. Previous GBS baby	13: Vaccination + i.v.	–0.00345	0.00000154	ICER to 6: 547	0.04
	14: Vaccination + oral	–0.00246	0.00000104	Dominated	0.03
3. Previous positive swab/bacteriuria	12: Vaccination, PCR + i.v.	–0.367	0.000161	Dominated	4.39
	13: Vaccination + i.v.	–0.564	0.000197	Base for ICER	5.49
	14: Vaccination + oral	–0.413	0.000141	Dominated	3.94
4. Pyrexia	13: Vaccination + i.v.	–0.26	0.0000959	ICER to 14: 1,460	2.66
	14: Vaccination + oral	–0.273	0.0000867	Base for ICER	2.44
5. Prelabour ROM >2 hours	13: Vaccination + i.v.	–2.28	0.000844	ICER to 14: 471,000	23.38
	14: Vaccination + oral	–2.73	0.000843	Base for ICER	23.81
6. Intact membranes	13: Vaccination + i.v.	–1.82	0.000813	ICER to 6: 546	22.15
	14: Vaccination + oral	–1.3	0.000547	Dominated	14.98
Term					
7. Elective LSCS	6: I.v.	0.925	0.0000932	Extended dominated	1.41
	7: Oral	–0.213	0.0000852	Base for ICER	2.34
	14: Vaccination + oral	3.39	0.000143	ICER to 7: 61,800	0.19
8. Previous GBS baby	6: I.v.	0.00881	0.00000128	ICER to 7: 19,400	0.02
	7: Oral	–0.00279	0.000000684	Base for ICER	0.02
	13: Vaccination + i.v.	0.0458	0.00000192	ICER to 6: 58,100	0.00
	14: Vaccination + oral	0.032	0.0000016	Extended dominated	0.01
9. Previous positive swab/bacteriuria	6: I.v.	–0.466	0.000158	ICER to 7: 534	4.42
	13: Vaccination + i.v.	1.02	0.000203	ICER to 6: 32,600	4.06
	14: Vaccination + oral	0.549	0.000175	Extended dominated	3.83
10. Pyrexia	6: I.v.	–0.512	0.000119	ICER to 7: 7,140	3.49
	7: Oral	–0.691	0.0000936	Base for ICER	3.03
	13: Vaccination + i.v.	0.109	0.00015	ICER to 14: 54,000	3.64
	14: Vaccination + oral	–0.208	0.000144	ICER to 6: 11,800	3.81
11. ROM >18 hours	1: Vaccination	0.505	0.000493	Extended dominated	11.82
	3: Culture + i.v.	–1.63	0.000364	Base for ICER	10.73
	4: PCR + oral	–1.24	0.000346	Dominated	9.89
	5: PCR + i.v.	–1.44	0.000415	ICER to 3,700	11.82
	9: Vaccination, culture + oral	0.897	0.000574	Extended dominated	13.45
	10: Vaccination, culture + i.v.	0.976	0.00059	ICER to 5: 13,700	13.77
	11: Vaccination, PCR + oral	1.38	0.000586	Dominated	13.27
	12: Vaccination, PCR + i.v.	1.46	0.000603	ICER to 10: 38,100	13.62
12. No risk factors	1: Vaccination	28.5	0.000979	Extended dominated	4.03
	3: Culture + i.v.	6.49	0.0005	Base for ICER	6.01
	5: PCR + i.v.	11.1	0.000543	ICER to 3: 3,700	2.48
	8: Nothing	0	0	Dominated	0.00

[a] Per woman.

show that apart from in RG5 (preterm, prelabour ROM >2 hours), vaccination followed by intravenous antibiotics (Intervention 13) is the most cost-effective intervention (that with the most NB). In RG5, vaccination followed by oral treatment (Intervention 14) is the optimal decision as it has marginally more NB than vaccination followed by intravenous treatment. For term RGs, the most cost-effective interventions are as follows. In RG7 (term, elective LSCS), treating all women with oral antibiotics (Intervention 7) has the highest NB and is therefore the most cost-effective intervention. For RG8 (term, previous GBS baby) and RG9 (term, previous positive swab/bacteriuria), treating all women with intravenous antibiotics (Intervention 6) is the most cost-effective, having more NB than

TABLE 48 *Summary of cost-effectiveness by risk group, Scenario B*

Risk group	Intervention	Cost (£)	QALYs	Result (£)	NB at 25,000 (£)[a]
Preterm					
1. Elective LSCS	6: I.v.	–0.42	0.000124	ICER to 7: 8,170	3.52
	7: Oral	–0.527	0.000111	Base for ICER	3.30
2. Previous GBS baby	6: I.v.	–0.00368	0.00000112	Base for ICER	0.03
	7: Oral	–0.00202	0.000000441	Dominated	0.01
3. Previous positive swab/bacteriuria	6: I.v.	–0.537	0.000153	Base for ICER	4.36
	7: Oral	–0.236	0.0000551	Dominated	1.61
4. Pyrexia	6: I.v.	–0.241	0.0000704	Base for ICER	2.00
	7: Oral	–0.224	0.0000524	Dominated	1.53
5. Prelabour ROM >2 hours	6: I.v.	–2.17	0.000621	ICER to 7: 9,470	17.70
	7: Oral	–2.52	0.000583	Base for ICER	17.10
6. Intact membranes	6: I.v.	–1.94	0.000594	Base for ICER	16.79
	7: Oral	–1.07	0.000233	Dominated	6.90
Term					
7. Elective LSCS	6: I.v.	0.925	0.0000932	ICER to 7: 142,000	1.41
	7: Oral	–0.213	0.0000852	Base for ICER	2.34
8. Previous GBS baby	6: I.v.	0.00881	0.00000128	ICER to 7: 19,400	0.02
	7: Oral	–0.00279	0.000000684	Base for ICER	0.02
9. Previous positive swab/bacteriuria	6: I.v.	–0.466	0.000158	ICER to 7: 534	4.42
	7: Oral	–0.51	0.0000751	Base for ICER	2.39
10. Pyrexia	5. PCR + i.v.	–0.403	0.0000962	Dominated	2.81
	6: I.v.	–0.512	0.000119	ICER to 7: 7,140	3.49
	7: Oral	–0.691	0.0000936	Base for ICER	3.03
11. ROM >18 hours	2: Culture + oral	–1.41	0.000296	Dominated	8.81
	3: Culture + i.v.	–1.63	0.000364	Base for ICER	10.73
	4: PCR + oral	–1.24	0.000346	Dominated	9.89
	5: PCR + i.v.	–1.44	0.000415	ICER to 3: 3,700	11.82
12. No risk factors	3: Culture + i.v.	6.49	0.0005	ICER to 8: 13,000	6.01
	5: PCR + i.v.	11.1	0.000543	ICER to 3: 107,000	2.48
	8: Nothing	0	0	Base for ICER	0.00

[a] Per woman.

intervention 7, which is the next most cost-effective in both (ICERs are £19,400 and £534 in RG8 and 9, respectively). Vaccination followed by oral antibiotics at labour (Intervention 14) gains the most NB for RG10. In RG11, the most cost-effective intervention involves vaccination followed by culture testing and treating those who test positive for GBS colonisation with i.v. antibiotics (Intervention 10). Finally, the most cost-effective intervention for RG12 is culture + intravenous antibiotics (Intervention 3), which is more cost-effective than vaccination (£6.01 compared with £4.03).

As an illustration of the results in *Table 47*, the cost-effectiveness frontier for RG11 in Scenario A can be seen in *Figure 9*. Interventions (I) 3, 5, 10 and 12 all lie on the frontier, with the optimum intervention at a threshold of £25,000, I10 having an ICER of £13,700. All other interventions are either dominated or extendedly dominated and lie to the north-west of the frontier. For example, no treatment (I8) is dominated and has much less NB than I10 (£0 compared with £13.77). This suggests that current practice of not treating RG11 is not cost-effective and results in a loss of NB.

Scenario B

In Scenario B, using a threshold value of £25,000, the results for preterm RGs (*Table 48*) show that the adoption decision is the same for all six RGs: treatment with intravenous antibiotics (I6) can be regarded as the most cost-effective intervention (it has the highest NB). For term RGs, the adoption

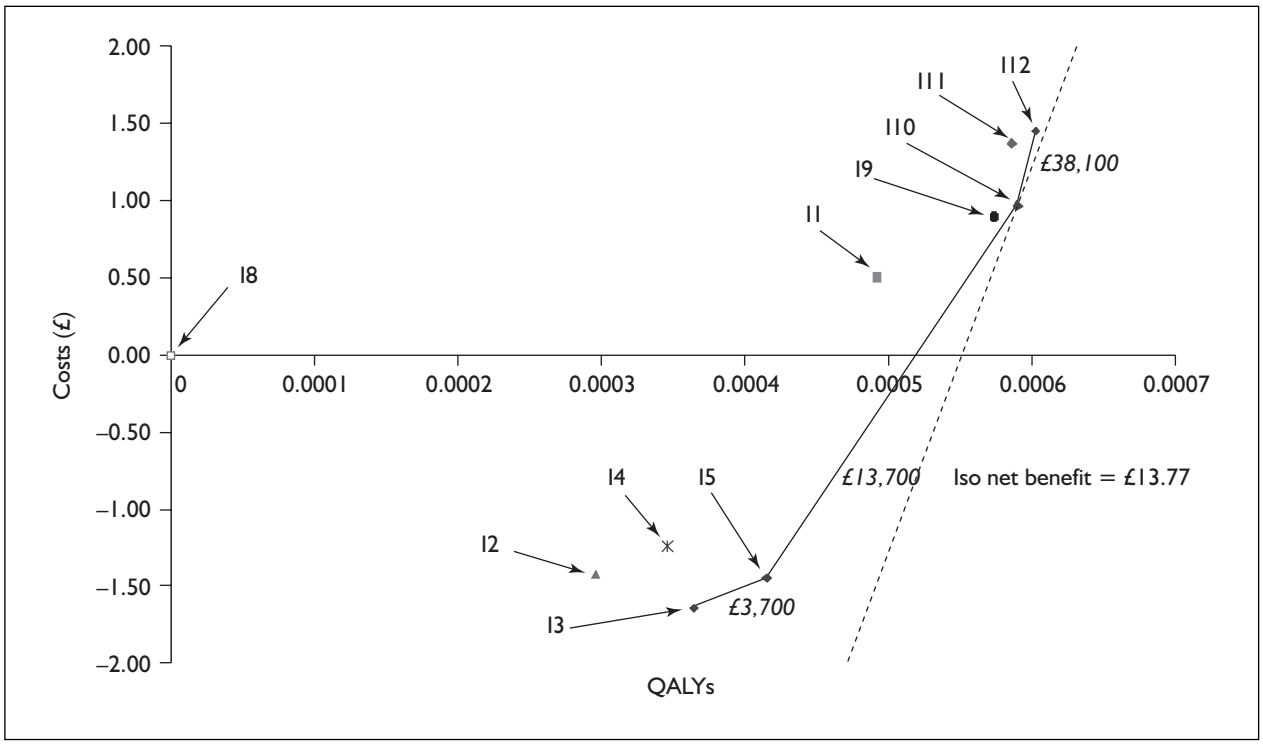

FIGURE 9 *Cost-effectiveness frontier for risk group 11: Scenario A. ICERs are in italic (NB is per woman).*

decision differs. For RG8–10, treatment of all women with intravenous antibiotics (I6) is the most cost-effective intervention (has the highest NB). For RG7, treatment with oral antibiotics (I7) is the most cost-effective. PCR testing followed by intravenous antibiotics at labour is the most cost-effective intervention for RG11, with an ICER of £3700 compared with I3, the next most cost-effective intervention. Finally, culture testing followed by intravenous antibiotics (I3) is optimum for RG12. It should be noted that with regard to the RGs where the most cost-effective interventions in Scenario A do not involve vaccination, the results are the same for Scenario B.

Similarly, the cost-effectiveness frontier for RG11 is illustrated in *Figure 10* for Scenario B. By excluding interventions with vaccine, only I3 and I5 are now on the frontier, with an ICER of £3700 for I5 compared with I3. All other interventions (I2, I4 and I8) lie to the north-west of the frontier, are dominated and offer less expected NB.

Cost-effectiveness analysis for strategies

Methods

A range of strategies (combinations of different interventions for different RGs) which had a realistic chance of being cost-effective were determined using the following methodology. First, those interventions in each RG which had a greater than 1% probability of being cost-effective (for Scenarios A and B those listed in *Tables 47* and *48*, respectively) were selected. This limited the potential number of possible combinations of interventions between the 12 RGs from 12^{14} or 1,283,918,464,548,860 to $2^5 \times 3^3 \times 4^3 \times 8 = 442{,}368$ for Scenario A (see *Table 47*; five RGs with two possible interventions, three RGs with three possible interventions, three RGs with four possible interventions and one RG with eight possible interventions); and to $2^9 \times 3^2 \times 4 = 18{,}432$ for Scenario B (see *Table 48*; nine RGs with two possible interventions, three RGs with two possible interventions and one RG with four possible interventions). Second, logistical and practical constraints were applied to reflect the fact that many of these, still rather computationally challengingly large number of possible strategies, cannot be carried out in reality. These constraints were as follows:

1. Only all RGs or none could be vaccinated, because only RG2 and 8 (previous GBS baby) can be identified at the time of vaccination (28 weeks).
2. Only one testing method (culture or PCR) could be adopted within a strategy.
3. RG11 and 12 had to be given the same intervention because they are not distinguishable at labour onset.

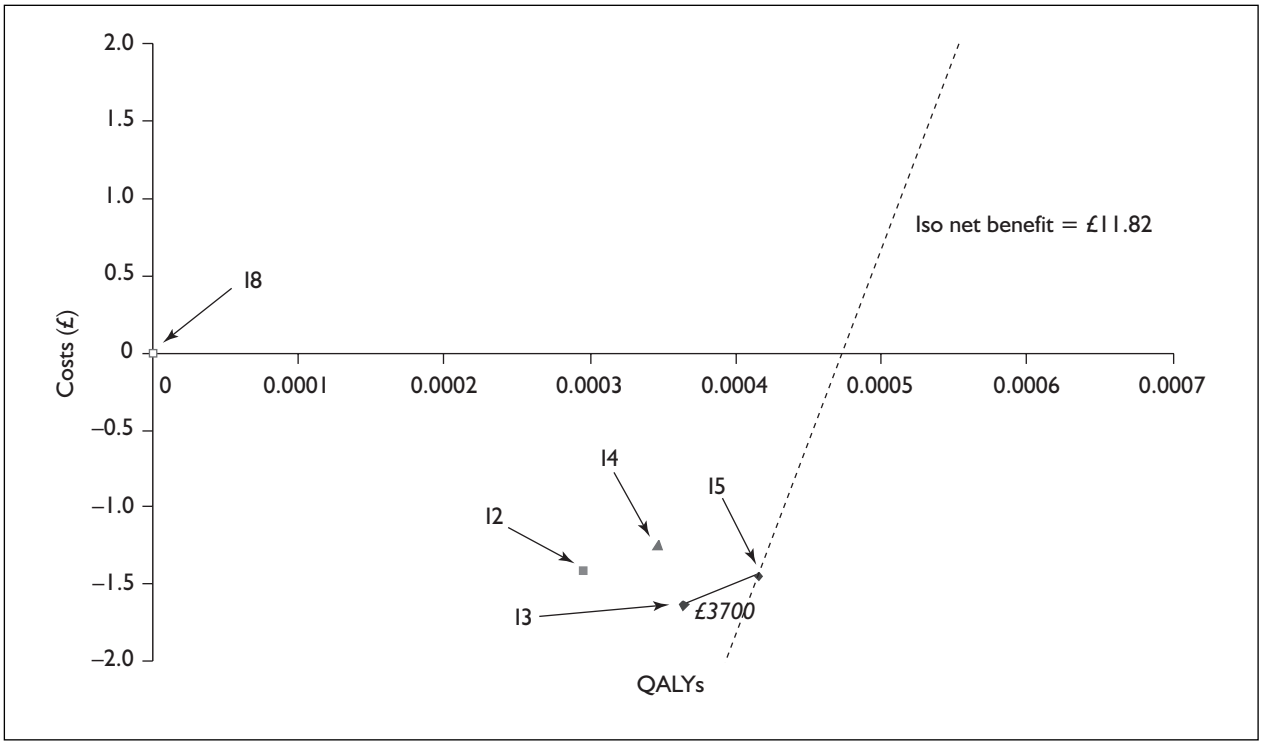

FIGURE 10 *Cost-effectiveness frontier for risk 11: Scenario B. ICERs are in italic (NB is per woman).*

4. Antibiotic treatment (intravenous or oral) could only be given to both groups of women with previously identifiable RGs when either presenting preterm or at term: RG2 and 3 had to be treated together; RG8 and 9 had to be treated together.
5. Oral treatment could not be given to women with pyrexia in labour (RG4 and 10) as it is standard practice to treat these women with intravenous antibiotics.
6. Oral antibiotics could not be given to preterm women when intravenous antibiotics were given to term women.

Applying these constraints reduced the number of possible strategies to 340 under Scenario A and 170 under Scenario B. To these, strategies which were unlikely to be cost-effective but were of policy interest were added. These included those with no treatment for RG7 (which has the lowest risk of disease of all the RGs) due to concerns over unnecessarily increasing antibiotic exposure (see the section 'Accounting for antibiotic exposure', p. 69); those representing no treatment (S30), the current RCOG guidelines for GBS prevention (S1) and current best practice (S3); and those incrementally increasing the number of RGs treated from the RCOG guidelines. This provided a total of 713 strategies for Scenario A (detailed in the first column of Appendix 4, *Table 108*) and 341 strategies for Scenario B (detailed in the first column of Appendix 4, *Table 109*).

As with the cost-effectiveness analysis for RGs (see the section 'Cost-effectiveness analysis for risk groups', p. 57), costs and QALYs (per woman) relative to do nothing, and then NB, were calculated for each strategy and the optimal strategies were determined on the basis of NB. In addition to considering the strategies purely in terms of NB a shortlist of policy-relevant strategies was also drawn up to highlight the trade-offs between intravenous and oral treatment, culture and PCR screening, and increasing antibiotic exposure and net health benefit gained (NB or net QALYs). These policy-relevant strategies were also selected to represent steps in treatment which are logical from a clinical perspective and that of current practice. Separate lists of policy-relevant strategies were determined for Scenarios A and B.

Results

The full cost-effectiveness results for strategies are shown in Appendix 4, *Tables 108* and *109* for Scenarios A and B, respectively. A summary of the cost-effectiveness results for RGs, showing non-dominated strategies, and those strategies deemed to be of policy relevance (see the section 'Cost-effectiveness of policy-relevant strategies', p. 67) is presented in *Table 49* for Scenario A and in

TABLE 49 *Cost-effectiveness results for Scenario A*[a]

Strategy[b]	Risk group												Cost (£)	QALYs	ICER (£)	NB at £25,000 (£)
	1	2	3	4	5	6	7	8	9	10	11	12				
T27	O	I	I	I	O	I	O	O	O	I	–	–	–7.00	0.00179	–	51.75
S86	I	I	I	I	O	I	O	I	I	I	–	–	–6.84	0.00189	ICER to T27: 1,690	54.09
S84	I	I	I	I	O	I	O	I	I	I	CI	CI	–1.98	0.00275	ICER to S86: 5,620	70.73
S99	I	I	I	I	I	I	O	I	I	I	CI	CI	–1.63	0.00279	ICER to S84: 9,470	71.38
S156	**VI**	**VI**	**VI**	**VI**	**VO**	**VI**	**VO**	**VI**	**VI**	**VI**	**V**	**V**	**27.80**	**0.00409**	**ICER to S99: 22,700**	**74.45**
S177	VI	VI	VI	VI	VO	VI	VO	VI	VI	VO	VCI	VCI	36.80	0.00434	ICER to S156: 35,300	71.70
S176	VI	VI	VI	VI	VO	VI	VO	VI	VI	VI	VCI	VCI	37.10	0.00435	ICER to S177: 54,100	71.65
S47	VI	VI	VI	VI	VO	VI	VO	VI	VI	VI	VPI	VPI	42.40	0.00437	ICER to S176: 265,500	66.85
S175	VI	VI	VI	VI	VI	VI	VI	VI	VI	VI	VPI	VPI	44.00	0.00437	ICER to T446: 523,000	65.25
S25	V	V	V	V	V	V	V	V	V	V	V	V	31.40	0.00282	Dominated	39.10
S9	VI	VI	VI	VI	VO	VI	VO	VI	VI	VI	V	V	31.40	0.00305	Dominated	44.85
S11	V	VI	VI	VI	VO	V	V	VI	VI	VI	V	V	29.60	0.00345	Dominated	56.65
T629	VI	VI	VI	VI	VO	VI	V	VO	VO	VI	V	V	27.40	0.00399	Dominated	72.35
S15	VI	VI	VI	VI	VO	VI	V	VI	VI	VI	V	V	27.90	0.00401	Dominated	72.35
S16	VI	VI	VI	VI	VO	VI	VPI	VI	VI	VI	VPI	VPI	44.10	0.00431	Dominated	63.65
T526	VI	VI	VI	VI	VI	VI	VO	VI	VI	VI	VCI	VCI	37.60	0.00435	Extended dominated	71.15
S170	VI	VI	VI	VI	VI	VI	VO	VI	VI	VI	V	V	37.60	0.00409	Extended dominated	74.05
T427	VO	VI	VI	VI	VO	VI	VO	VO	VO	VI	V	V	37.60	0.00405	Extended dominated	74.05
T429	VI	VI	VI	VI	VO	VI	VO	VO	VO	VI	V	V	37.60	0.00400	Extended dominated	74.20

[a] Costs, QALYs and NB are all per woman.
[b] See *Table 2* for codes.

TABLE 50 *Cost-effectiveness results for Scenario B*[a]

Strategy[b]	Risk group												Cost (£)	QALYs	ICER (£)	NB at £25,000 (£)
	1	2	3	4	5	6	7	8	9	10	11	12				
T27	O	I	I	I	O	I	O	O	O	I	–	–	–7.00	0.00179	–	51.75
S86	I	I	I	I	O	I	O	I	I	I	–	–	–6.84	0.00189	ICER to T27: 1,690	54.09
S84	I	I	I	I	O	I	O	I	I	I	CI	CI	–1.98	0.00275	ICER to S86: 5,620	70.73
S99	**I**	**I**	**I**	**I**	**I**	**I**	**O**	**I**	**I**	**I**	**CI**	**CI**	**–1.63**	**0.00279**	**ICER to S84: 9,470**	**71.38**
S80	I	I	I	I	I	I	O	I	I	I	PI	PI	3.13	0.00288	ICER to S99: 51,000	68.87
S102	I	I	I	I	I	I	I	I	I	I	PI	PI	4.27	0.00289	ICER to S80: 142,300	67.98
S30	–	–	–	–	–	–	–	–	–	–	–	–	0.00	0.00000	Dominated	0.00
S1	–	I	I	I	–	–	–	I	I	I	–	–	–1.75	0.00050	Dominated	14.30
S3	–	I	I	I	O	–	–	I	I	I	–	–	–4.27	0.00109	Dominated	31.52
S7	I	I	I	I	O	I	–	I	I	I	–	–	–6.63	0.00180	Dominated	51.63
S8	I	I	I	I	O	I	PI	I	I	I	PI	PI	4.46	0.00279	Dominated	65.29
S83	I	I	I	I	O	I	CI	I	I	I	CI	CI	–0.84	0.00270	Dominated	68.34
S39	I	I	I	I	O	I	O	I	I	I	PI	PI	2.78	0.00285	Extended dominated	68.47
S96	I	I	I	I	I	I	CI	I	I	I	CI	CI	–4.09	0.00273	Dominated	68.74
S101	I	I	I	I	I	I	I	I	I	I	CI	CI	–4.09	0.00280	Extended dominated	70.49
T128	O	I	I	I	I	I	O	I	I	I	CI	CI	–1.74	0.00278	Extended dominated	71.24

[a] Costs, QALYs and NB are all per woman.
[b] See *Table 2* for codes.

Table 50 for Scenario B (policy-relevant strategies are in the shaded bottom panels of the tables).

Scenario A

Each of the 713 strategies for Scenario A are plotted in *Figure 11*. It can be seen that many of these strategies lie far to the west (less effective) and north (more costly) of the Iso NB line, indicating that each of these strategies offers a much lower NB and would not be regarded as cost-effective. Others are to the north-west and are dominated but offer very similar NB to the

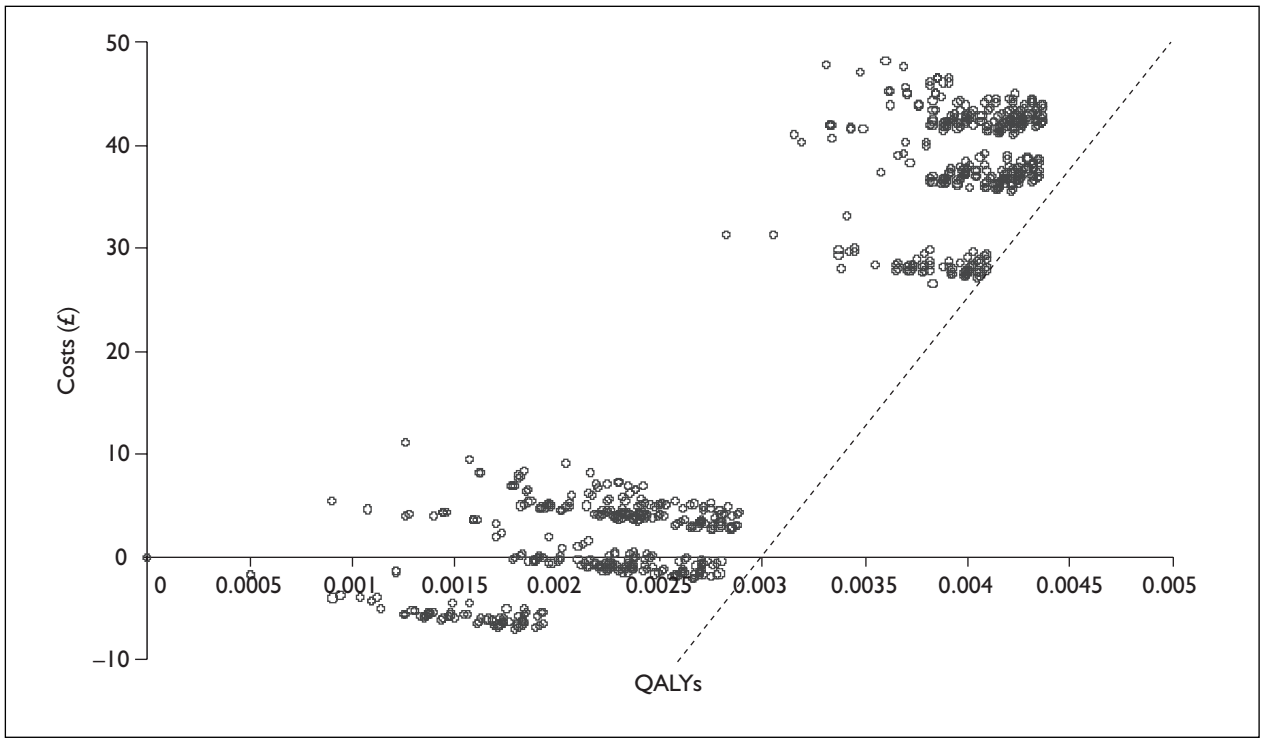

FIGURE 11 *All strategies for Scenario A*

strategy which would be regarded as cost-effective. The cloud to the north-east includes all the vaccination strategies (higher cost but more effective) and the cloud to the south-west includes all the non vaccination strategies.

The non-dominated (those on the cost-effectiveness frontier) and the policy-relevant strategies for Scenario A are plotted on the cost-effectiveness frontier in *Figure 12*. Strategies T27, S86, S84, S99, S156, S177, S176, S47 and S175 all lie on the frontier. The Iso NB line shows that NB is maximised (given a particular threshold) with strategy S156 (NB = £74.45). All the policy-relevant strategies lie to the north-west of the frontier; however, it can be seen that some strategies (T629, T427, T429, T526, S15, S16 and S170) are particularly close to the frontier. It is worth noting that, however, some NB would be foregone if any of these strategies were chosen instead of the optimum strategy for a particular threshold (e.g. S156 at a threshold of £25,000); for example we would forego an NB of £17.80 per patient if we were to choose S11 instead of S156 (see *Table 49*). This equates to a loss of £12,104,000 for the UK population of 680,000 deliveries per year or 484 QALYs (at £25,000 per QALY). However, this loss has to be looked at in the context of the risks of increasing antibiotic exposure (see the section 'Accounting for antibiotic exposure', p. 69).

The full results for these strategies can be seen in *Table 49*. This shows that if vaccine is available, strategy 175 is the most expensive non-dominated strategy but it is also associated with the highest number of QALYs. However, the ICER for S175 (£523,000) is unlikely to be within acceptable cost-effectiveness thresholds. The most cost-effective strategy is likely to be S156 (vaccine + intravenous for RG1–4, 6 and 8–10, vaccine + oral for RG5 and 7 and vaccine alone for RG11 and 12), provided that decision-makers are willing to pay more than £22,700 for a QALY gained. NB is maximised (given a threshold of £25,000) with S156.

Scenario B

Each of the 340 strategies for Scenario B is plotted in *Figure 13* (the cloud of vaccination strategies has been removed). Again it can be seen that many of strategies lie far to the west (less effective) of the Iso NB line, indicating that each of these strategies offers a much lower NB and are therefore not cost-effective. However, many are very close to the Iso NB line and, although they may be dominated, they have very similar NB to the cost-effective strategy (with maximum net benefit).

Selecting non-dominated strategies and policy relevant strategies in *Figure 14*, it can be seen that T27, S86, S84, S99, S80 and S102 all lie on the frontier. The Iso NB line shows that NB is maximised (given a particular threshold) with

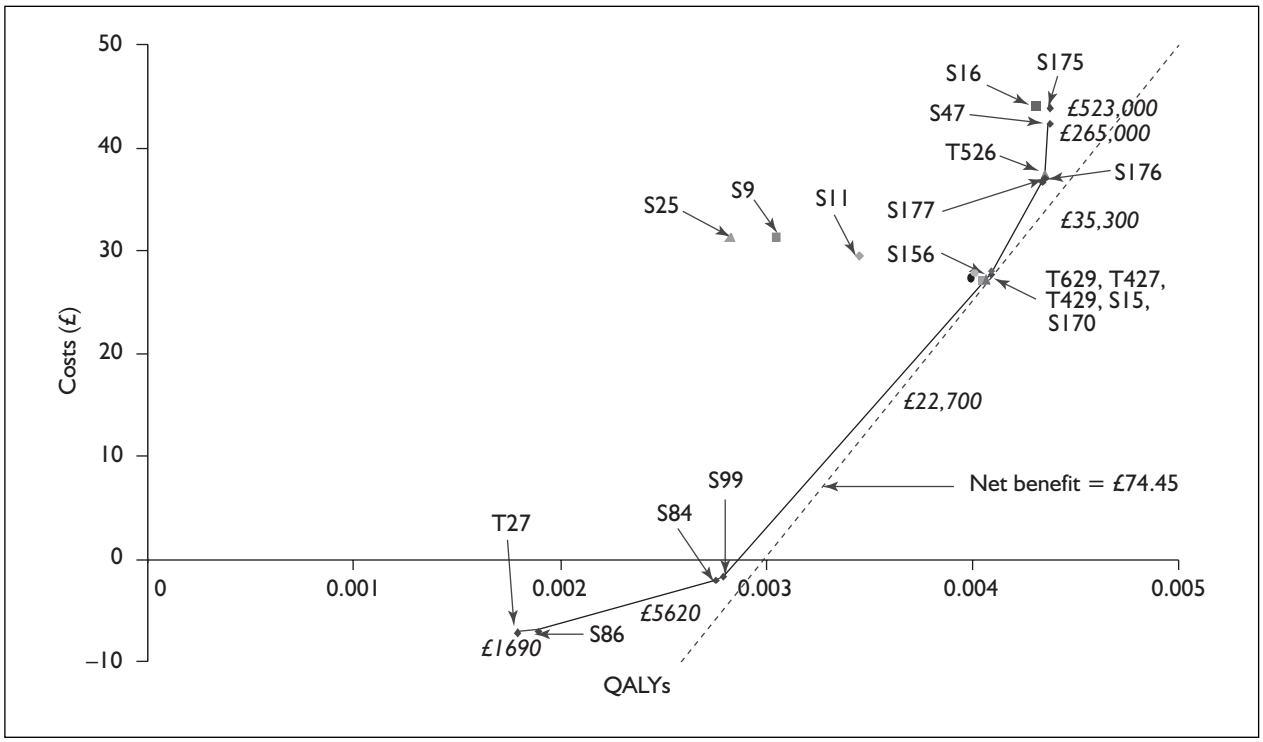

FIGURE 12 *Cost-effectiveness frontier for Scenario A. ICERs are in italic.*

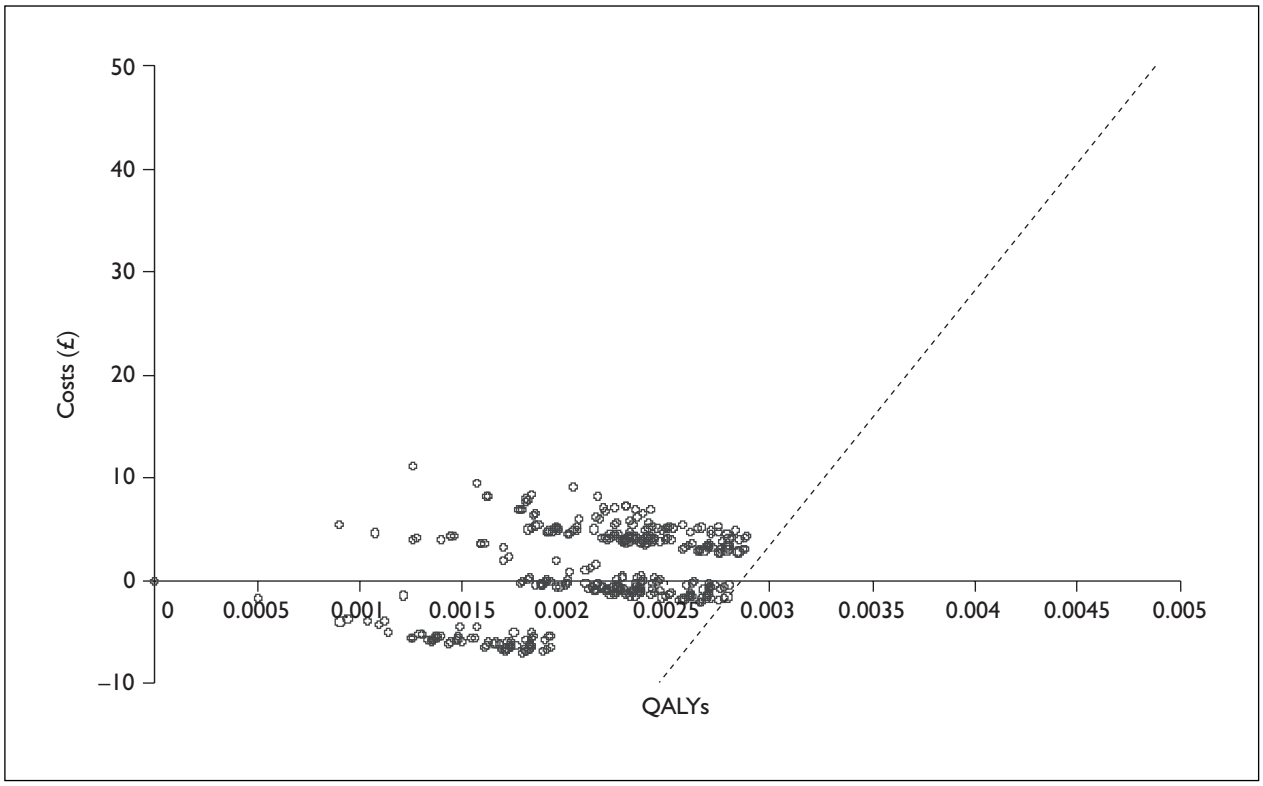

FIGURE 13 *All strategies for Scenario B*

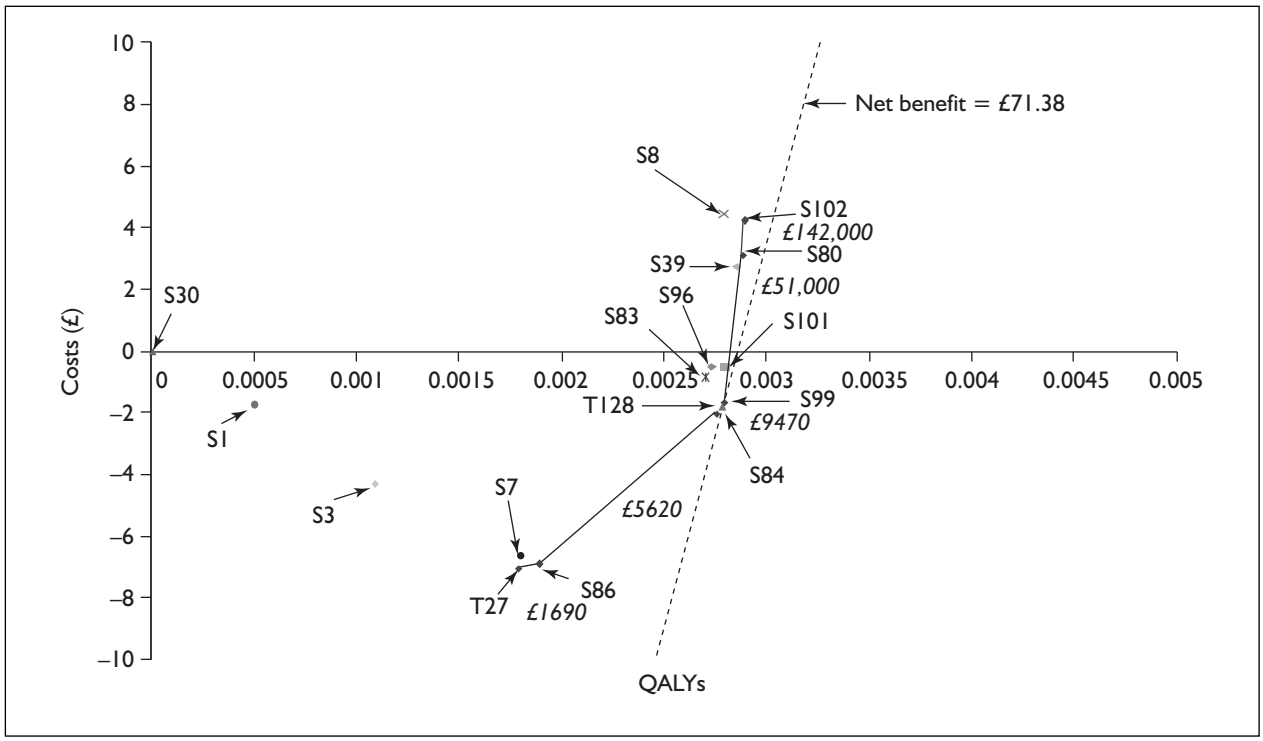

FIGURE 14 *Cost-effectiveness frontier for Scenario B. ICERs are in italic.*

strategy S99 (NB = £71.38). All policy-relevant strategies again lie to the north-west of the frontier, indicating that some NB would be lost if these strategies were chosen instead of the optimum strategy for a particular threshold (S99 at a threshold of £25,000). It is therefore irrelevant to consider how close some policy-relevant strategies are to the frontier (in particular S7, T128, S101 and S39) but relevant to consider the loss of NB resulting from choosing these strategies. For example, NB of £6.09 per patient would be foregone if S8 were chosen instead of S99. This equates to a loss of £4,141,200 over the UK population of 680,000 deliveries per year or 165 QALYs (at £25,000 per QALY). However, as before, this loss has to be looked at in the context of the risks of increasing antibiotic exposure (see the section 'Accounting for antibiotic exposure', p. 69).

The full results for these strategies can be seen in *Table 50*. This shows that strategy S102 is the most expensive strategy non-dominated but it also has the highest number of QALYs. However, the ICER for S102 (£142,000) is unlikely to be within acceptable cost-effectiveness thresholds. The results suggest that if vaccine is not available, strategy 99 (intravenous antibiotics for RG1–6 and 8–10, oral antibiotics for RG7 and culture testing followed by intravenous antibiotics for RG11 and 12) is the most cost-effective strategy, provided that decision-makers are willing to pay more than £9470 for a QALY gained. NB is maximised (given a threshold of £25,000) with S99 at £71.38. The policy-relevant strategies S1, S3, S7, S8, S30, S39, S83, S96, S101 and T128 are again all dominated or extendedly dominated by multiple strategies.

Chapter 7

Interpretation of results in relation to policy

The section 'Methods' (p. 61) described how a series of policy-relevant strategies were selected based on strategies that were close to the cost-effectiveness frontier, minimised the proportion of women exposed to antibiotics and represented feasible programmatic increments from current best practice to the most cost-effective strategies in Scenarios A and B. This chapter considers the decision to adopt each of these policy-relevant strategies, to illustrate the potential gains from treating more of the high-risk groups, of culture-based testing compared with PCR and intravenous compared with oral treatment. These differences are discussed in terms of changes to current policy and the trade-off between gains in NB and antibiotic exposure, all of which impact on decision-making. The next section outlines the main issues of policy relevance. The issue of antibiotic exposure is then explored in more detail in the subsequent section (p. 69) and the final section (p. 75) describes the clinical consequences of each strategy to make explicit the outcomes underlying the costs and QALYs.

Cost-effectiveness of policy-relevant strategies

Scenario B (without vaccination)

Scenario B, where vaccination is not a reality, is discussed first in order to highlight important changes to the results that occur if vaccination is deemed possible (Scenario A). *Table 51* shows the policy-relevant strategies for Scenario B ranked according to increasing net benefit. As shown in *Table 50* and *Figure 13*, most of them are dominated or extendedly dominated by multiple strategies, although for the strategies towards the bottom of *Table 51* the difference in NB compared with the cost-effective strategies in *Table 50* is small.

The shaded strategies are the ones for policy makers to consider and to weigh up while thinking about antibiotic resistance (% of women treated), which is discussed further in the section 'Accounting for antibiotic exposure' (p. 69); they are much better in terms of NB per woman than those strategies in white: doing nothing (S30), the RCOG guidelines (S1) or current best practice (S3). S7 (treating all preterm and high-risk term groups) gives £20.11 more NB per woman than current best practice (S3) but involves treating only 3.6% more women. Using PCR screening for the low-risk groups (RG7, 11 and 12) instead of doing nothing, S8 (PCR testing for low risk) gives £13.76 NB more per woman than S7 (do nothing for low risk) but involves treating 9.4% more women with antibiotics. Using culture instead of PCR for the low-risk groups (S83 instead of S8) generates £2.95 more NB and involves treating only slightly more (0.3%) women. More NB is gained despite the fact that PCR screening is more effective (see the section 'Accuracy of tests for maternal GBS colonisation', p. 46) as the extra cost of PCR in comparison with culture screening (see the section 'Costs', p. 52) outweighs the extra health gains resulting from the superior accuracy of the PCR test. Moving from S83 to S84 (treating RG7; the term Caesarean sections) may not be justified given the additional £2.39 more NB per woman, but involves treatment of 7.0% more women (see the section 'Accounting for antibiotic exposure', p. 69, for more detailed analysis of whether this may or may not be justified). The results also show that there is a slight advantage (gain of £0.65 NB) to treating RG5 with intravenous instead of oral antibiotics (S99 instead of S84); however, this may be offset by the disruption caused by changing from current best practice of treating this group orally to treating intravenously. S83 may be the best strategy bearing in mind the need to limit the percentage of women treated with antibiotics.

The strategy with the highest NB (S99, the most cost-effective strategy as identified in the section 'Results', p. 61) involves intravenous treatment for all preterm women and high-risk term women (RG8–10), oral treatment for RG7, and testing the low-risk term groups (RG11 and 12) using culture. The analysis allowed the option of treating RG7 even though they are at lower risk than RG11 and 12 because they are definable and do not involve treating the whole population (which was not allowed – RG11 and 12 had to be tested first and treated only if they had a positive test result). Treating RG7 gives marginal extra NB and involves treating 7% more of the population.

TABLE 51 *Policy-relevant results for Scenario B*[a]

Strategy[b]	Risk group												Cost (£)	QALYs gained	NB at £25,000 per QALY (£)	Increase in NB (£)	% treated with antibiotics	% of total cases prevented
	1	2	3	4	5	6	7	8	9	10	11	12						
S30	n	n	n	n	n	n	n	n	n	n	n	n	0	0	0		0	0.0
S1	n	I	I	I	n	n	n	I	I	I	n	n	–1.75	0.00050	14.30	14.30	5.2	5.3
S3	n	I	I	I	O	n	n	I	I	I	n	n	–4.27	0.00109	31.52	17.22	7.4	10.1
S7	I	I	I	I	O	I	n	I	I	I	n	n	–6.63	0.00180	51.63	20.11	11.0	15.9
S8	I	I	I	I	O	I	PI	I	I	I	PI	PI	4.46	0.00279	65.39	13.76	20.4	28.7
S83	I	I	I	I	O	I	CI	I	I	I	CI	CI	–0.84	0.00270	68.34	2.95	20.7	27.4
S39	**I**	**I**	**I**	**I**	**O**	**I**	**O**	**I**	**I**	**I**	**PI**	**PI**	**2.78**	**0.00285**	**68.47**		**27.5**	**29.1**
S96	**I**	**I**	**I**	**I**	**I**	**I**	**CI**	**I**	**I**	**I**	**CI**	**CI**	**–0.49**	**0.00273**	**68.74**		**20.3**	**27.4**
S101	**I**	**I**	**I**	**I**	**I**	**I**	**I**	**I**	**I**	**I**	**CI**	**CI**	**–0.49**	**0.00280**	**70.49**		**27.4**	**28.0**
S84	I	I	I	I	O	I	O	I	I	I	CI	CI	–1.98	0.00275	70.73	2.39	27.7	27.9
T128	**O**	**I**	**I**	**I**	**I**	**I**	**O**	**I**	**I**	**I**	**CI**	**CI**	**–1.74**	**0.00278**	**71.24**		**27.4**	**27.9**
S99	I	I	I	I	I	I	O	I	I	I	CI	CI	–1.63	0.00279	71.38	0.65	27.4	27.9

[a] Costs, QALYs and NB are all per woman; multiply by total population of 680,000 per year to determine per year values.
[b] See *Table 2* for codes.

However, if these women are going to be treated anyway, after Caesarean section, practice could be amended so that they are treated before delivery.

In *Table 51*, the strategies in bold are similar in terms of NB to those shaded, but differ slightly in terms of oral versus intravenous treatment and PCR versus culture screening. They are included to illustrate that there is not much difference in terms of NB between oral and intravenous treatment for RG1, 5 and 7 (because oral treatment is cheaper but also less effective), and between PCR and culture screening for low-risk groups RG7, 11 and 12 (again, culture is cheaper but less effective).

Scenario A (with vaccination)

Looking at the same strategies but with vaccination (*Table 52*), the same pattern with regard to increasing NB as the proportion of women treated increases is **not** seen. This is due to the benefits of vaccination. For example, going from S15 (the same as S7 with vaccination) to S16 (S8 with vaccination, shown in italics as NB is less) involves treating 7.3% more women but actually loses £8.70 NB. This is because the benefit of vaccination in RG7, 11 and 12 outweighs the costs of testing and treating colonised women (S16). All other strategies that involve vaccination and testing of RG11 and 12 (e.g. S176 same as S84 with vaccination) and T526 (same as S99 with vaccination) are worse in terms of NB than those that involve vaccination alone for these groups.

More NB can be gained by moving from strategy S15 (S7 with vaccination) to strategies that involve treating RG7 (women at term undergoing elective Caesarean section). An extra NB of £1.70 is gained but 7.7% more women need to be treated. This may not be considered worthwhile, but if women in this group are to be treated anyway during the operation, the timing could be changed to treatment before delivery. It is interesting to note that with vaccination, treating RG5 orally instead of intravenously (S156 instead of S170) has £0.40 more NB; whereas without vaccination it is the other way round (intravenous treatment for RG5 is better), with S99 having £0.60 more NB than S84. The strategies in bold illustrate the point that there is not much difference between oral and intravenous treatment in terms of cost-effectiveness.

In summary, with vaccination available, the best choice may be to adopt S15: this generates almost the entire NB available while treating only 11% of women. The following section explores the rationale underlying this choice in terms of antibiotic exposure for NB gained.

Accounting for antibiotic exposure

This section outlines an approach for valuing the consequences of exposure and for accounting for its possible impact on NB.

The section 'Antibiotic resistance' (p. 12) explained that adverse consequences of antibiotic exposure were not included in the determination of net QALYs due to the complexity of quantifying adverse effects of intrapartum treatment over and above antibiotic use earlier in the pregnancy and in the wider community. Use of antibiotics can affect pathogen selection, for example GBS can be replaced by Gram-negative pathogens, and can lead to selection of bacteria that are resistant to antibiotics. The association between antibiotic exposure and resistance can be characterised by an S-shaped curve. This means that a 5% increase in exposure at a low prevalence of overall exposure will have less impact on resistance than a 5% increase given higher levels of exposure. Exploration of the relationship between antibiotic resistance and exposure in the women delivering in the UK was beyond the scope of the present study. Consequently, it is not possible to specify the number of women who need to be exposed to lose a QALY in health outcome (from adverse effects either to the mother, to the baby or to the population). For this reason, the trade-off has been represented in terms of net QALYs of health outcome gained per total women exposed to antibiotics to quantify how bad antibiotic use would need to be in order to justify rejection of a more cost-effective strategy that involves treating more women.

Figure 15 shows the number of women exposed to antibiotics plotted against net QALYs gained for all strategies in Scenarios A and B. Net QALYs were calculated as QALYs gained minus costs in terms of QALYs (i.e. £/25,000, if the WTP threshold is £25,000 per QALY).

Strategies further south (less women exposed to antibiotics) and east (more net QALYs gained) are better in terms of maximising health benefits whilst treating the least number of women with antibiotics. The graph is set out in the same manner as a cost-effectiveness graph (see, for

TABLE 52 *Policy relevant results for Scenario A*[a]

Strategy[b]	Risk group												Cost (£)	QALYs gained	NB at £25,000 per QALY (£)	Increase in NB (£)	% treated with antibiotics	% of total cases prevented
	1	2	3	4	5	6	7	8	9	10	11	12						
S25	V	V	V	V	V	V	V	V	V	V	V	V	31.40	0.00282	39.10		0	29.6
S9	V	VI	VI	VI	V	V	VI	VI	VI	V	V	V	31.40	0.00305	44.85	5.75	5.2	31.8
S11	V	VI	VI	VI	VO	V	VI	VI	VI	V	V	V	29.60	0.00345	56.65	11.80	7.4	35.2
T629	**VI**	**VI**	**VI**	**VI**	**VO**	**VI**	**V**	**VO**	**VO**	**VI**	**V**	**V**	**27.40**	**0.00399**	**72.35**		**9.8**	**39.5**
S15	VI	VI	VI	VI	VO	VI	V	VI	VI	VI	V	V	27.90	0.00401	72.35	15.70	11.0	39.9
Strategies equivalent to policy-relevant ones in Scenario B, but which may not be policy relevant under Scenario A as vaccine alone is better than screening for RG11 and 12 (NB compared with S15)																		
S16	*VI*	*VI*	*VI*	*VI*	*VO*	*VI*	*VPI*	*VI*	*VI*	*VI*	*VPI*	*VPI*	*44.10*	*0.00431*	*63.65*	*–8.70*	*18.3*	*43.5*
S176	*VI*	*VI*	*VI*	*VI*	*VO*	*VI*	*VO*	*VI*	*VI*	*VI*	*VCI*	*VCI*	*37.10*	*0.00435*	*71.65*	*–0.70*	*26.0*	*43.8*
T526	*VI*	*VI*	*VI*	*VI*	*VI*	*VI*	*VO*	*VI*	*VI*	*VI*	*VCI*	*VCI*	*37.60*	*0.00435*	*71.15*	*–1.20*	*25.7*	*43.5*
S170	VI	VI	VI	VI	VI	VI	VO	VI	VI	VI	V	V	28.20	0.00409	74.05	1.70	18.6	40.3
T427	**VO**	**VI**	**VI**	**VI**	**VO**	**VI**	**VO**	**VO**	**VO**	**VI**	**V**	**V**	**27.20**	**0.00405**	**74.05**		**17.8**	**40.2**
T429	**VI**	**VI**	**VI**	**VI**	**VO**	**VI**	**VO**	**VO**	**VO**	**VI**	**V**	**V**	**27.30**	**0.00406**	**74.20**		**17.8**	**40.2**
S156	VI	VI	VI	VI	VO	VI	VO	VI	VI	VI	V	V	27.80	0.00409	74.45	0.40	19.0	40.5

[a] Costs, QALYs and NB are all per woman; multiply by total population of 680,000 per year to determine per year value.
[b] See *Table 2* for codes.

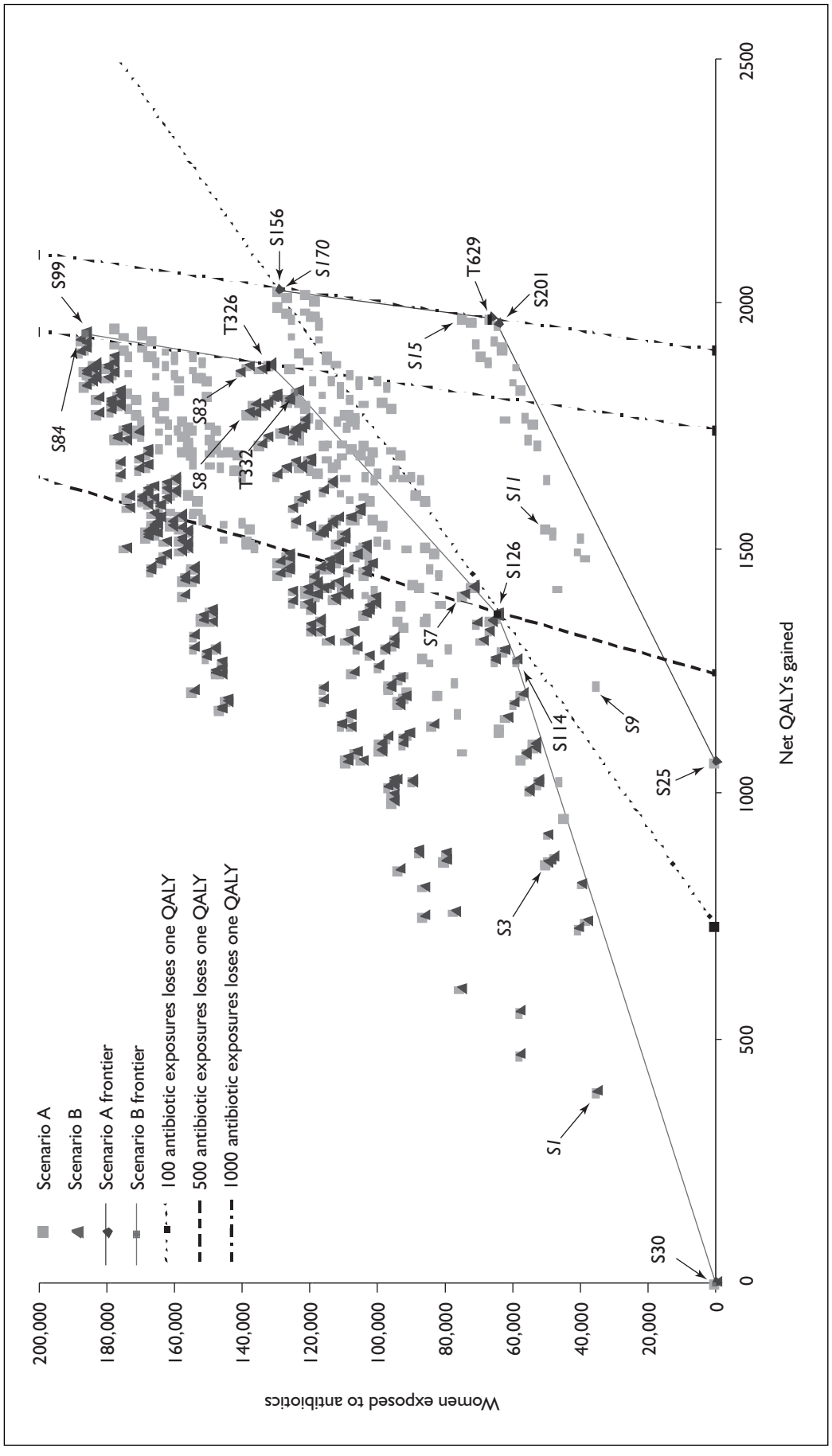

FIGURE 15 *Comparison of net QALY gained and exposure to antibiotic treatment per year (680,000 deliveries)*

TABLE 53 *Strategies on the incremental antibiotic exposure/additional QALYs gained frontier and the IEERs between them*

Strategies[a]	Risk group												Antibiotic exposures		Net QALYs gained[b]	IEER[c]
	1	2	3	4	5	6	7	8	9	10	11	12	No.[b]	%		
Scenario A																
S30	n	n	n	n	n	n	n	n	n	n	n	n	0	0.0	0	
S25	**V**	**V**	**V**	**V**	**V**	**V**	**V**	**V**	**V**	**V**	**V**	**V**	0	0.0	1063.5	0
S201	**VI**	**VI**	**VI**	**VI**	**VI**	**VI**	V	**VO**	**VO**	**VI**	V	V	64,056	9.4	1957.0	72
T629	VI	VI	VI	VI	**VO**	VI	V	VO	VO	VI	V	V	66,436	9.8	1967.9	218
S156	VI	VI	VI	VI	VO	VI	VO	**VI**	**VI**	VI	V	V	129,200	19.0	2025.0	1099
Scenario B																
S30	n	n	n	n	n	n	n	n	n	n	n	n	0	0.0	0	
S114	n	**I**	**I**	**I**	**I**	**I**	n	**O**	**O**	**I**	n	n	58,684	8.6	1269.2	46
S126	**I**	I	I	I	I	I	n	O	O	I	n	n	64,056	9.4	1369.0	54
T332	I	I	I	I	I	I	n	O	O	I	**CI**	**CI**	123,760	18.2	1821.6	132
T326	I	I	I	I	I	I	n	**I**	**I**	I	CI	CI	131,920	19.4	1874.6	154
S99	I	I	I	I	I	I	**O**	I	I	I	CI	CI	186,320	27.4	1941.5	813

[a] See *Table 2* for codes.
[b] Per year for a total population of 680,000 deliveries.
[c] Incremental exposure per additional net QALY gained ratio.

example, *Figure 13*, p. 64). The 'frontier' shows which strategies are optimal for net QALYs gained per antibiotic exposure. Strategies to the north and west of this frontier are 'dominated'. The main difference to the cost-effectiveness analysis in this case, though, is that a threshold value for antibiotic exposure has not been specified, i.e. the number of women who need to be exposed to antibiotics in order to lose one QALY (in the cost-effectiveness analysis it was assumed that one QALY was worth £20,000, £25,000 or £30,000), and therefore cannot determine the NB (net QALYs) gained net of antibiotic exposure.

Table 53 lists the strategies on the frontier for both Scenarios A and B and shows, for a UK population, the additional number of women who would be exposed to antibiotics to gain an additional net QALY: the 'incremental exposure per QALY (effect) ratio' (IEER). This number reflects the value placed on antibiotic exposure: in other words, how many women would need to be exposed to antibiotics to lose one QALY. For example, in Scenario B, if it is considered that more than 154 women need to be exposed to antibiotics to lose a QALY, less than one QALY would be lost due to the harm of antibiotic exposure for every one QALY that would be gained from the NBs. Hence moving from T332 to T326 would be acceptable. However, if it is believed that antibiotics pose a greater risk than this (i.e. less than 154 women would need to be treated to lose a QALY), the decision-maker would adopt strategy T332.

The concept of the IEER is similar to the ICER, (see the section 'Principles of cost-effectiveness analysis', p. 55) in that the IEER has to be below the threshold for the 'value' of antibiotic exposure. The difference is that for the ICERs, the WTP threshold values are known and widely accepted. For the IEERs, these values are not clearly established (and may vary according to total levels of antibiotic exposure). Such threshold values need to be specified by decision-makers using these results.

To take another example from *Table 53*, decision-makers would not move from T326 to S99 unless they were willing to expose more than 813 additional women to antibiotics to gain one additional QALY. In other words, more than 813 women would need to be treated to generate the equivalent of one QALY of adverse health outcome (the risks of exposure would have to be low). The dashed lines in *Figure 15* represent possible threshold values. The two lines representing a value of an additional 1000 women exposed to antibiotics per additional QALY lost highlight the fact that at this threshold, moving from T326 to S99 (the most cost-effective strategy in Scenario B) would be acceptable. In contrast, moving from T629 to S156 (the most cost-effective strategy in Scenario A) would not be acceptable. At the threshold of 1000 or more women treated to lose one QALY, the gains in additional net QALYs by moving from T629 to S156 (1099 additional women are treated to gain one net QALY) would be more than cancelled out by the loss of more

than one QALY due to antibiotic exposure. Whatever threshold value is chosen for the harms of antibiotic exposure, the strategy adopted should remain to the south-east of the dotted line representing this threshold.

In order to contextualise the harms of antibiotic exposure in terms of QALYs, the following are examples of exposures per QALY lost from the model which could be used as comparators:

1. Exposure to GBS bacteriuria/positive swab in pregnancy and then delivering at term (RG9) relative to a term delivery with no risk factors (RG12) is associated with a loss of 0.00374 QALYs per woman when no treatment is involved. For the UK population, this equates to 268 exposures per QALY lost.
2. Exposure to pyrexia during labour at term (RG10) relative to a term delivery with no risk factors (RG12) is associated with a loss of 0.00747 QALYs per woman when no treatment is involved. This equates to 134 exposures per QALY lost for the total population.

One way of using these examples is to ask whether treating an additional 134 women with antibiotics is 'as bad' as some factor that might lead to an additional 134 women becoming pyrexial who previously had no risk factors at term. This analogy is limited as antibiotic exposure has adverse effects for the wider population whereas adding risk factors mainly affects the individual.

Table 53 shows the strategies on the antibiotic exposure/net QALYs gained frontier and highlights in bold the interventions that change with each incremental gain in net QALYs. For example, in Scenario B, moving from S114 to S126 involves treating women in RG1 (preterm elective LSCS) with intravenous antibiotics rather than nothing. As RG1 (preterm elective Caesarean section) is a fairly high-risk group, the IEER is low, indicating that the harms of antibiotic exposure would have to be very high (equivalent to less than 54 women would have to be exposed to antibiotics in order to lose a QALY). Moving from S126 to T332 involves culture testing for RG11 and 12 and treating those who are positive. This may be acceptable unless the harms of antibiotic exposure are valued fairly highly (less than 132 women would have to be exposed to antibiotics in order to lose a QALY). Changing treatment for RG8 and 9 from intravenous to oral (switching from T326 to T332) has a similarly moderate IEER. However, moving from T326 to S99 involves treating RG7 (elective Caesarean section at term). To make this step, decision-makers should value the harms of antibiotic treatment as relatively low: treatment of an additional 813 women should be equivalent to the loss of less than one QALY.

Figure 15 also shows the policy relevant strategies discussed in the cost-effectiveness analysis in the section 'Cost-effectiveness of policy-relevant strategies' (p. 67). It is clear that the RCOG guidelines (S1) and 'current best practice' (S3) are well away from the frontier, as are the equivalent strategies with vaccination added (S9 and S11, respectively). Given that these strategies already perform badly in terms of cost-effectiveness, we need not trouble ourselves further with them. Many of the other 'policy-relevant' strategies are close to the frontier; however, it should be noted that in Scenario B, S8 is not particularly close to the frontier and does not perform well when antibiotic exposure is taken into consideration. Better strategies include T332, or S83, which is listed as one of the policy-relevant strategies in *Table 51*.

Table 54 shows the trade-offs between net QALYs gained and antibiotic exposure (expressed as IEERs) associated with the adoption of a more cost-effective policy-relevant strategy (as discussed in the section 'Cost-effectiveness of policy-relevant strategies', p. 67). The table shows IEERs for moves from particular strategies to more than one other strategy to reflect possible programmatic changes. Certain choices are more beneficial in terms of antibiotic exposures per net QALY gained than others. For example, moving from S7 (treat all preterm and high-risk term groups) to S83 (adding culture-based testing for low-risk groups) involves an IEER of 145 as opposed to the IEER of 172 associated with moving from S7 to S8 (adding PCR testing for low-risk groups). If antibiotic exposure is valued as less harmful than 172 women exposed per QALY lost, this distinction becomes less important. In this case, the decision should be based on the net QALYs gained [i.e. disregarding the additional antibiotic exposure; see Chapter 6)]. The decision to move from S83 to S99 (treating all term women with elective Caesarean section – RG7) would be logical provided that antibiotic exposure of an additional 551 additional women treated (on top of the 20.7% already treated under S83) was valued as less harmful than the loss of one additional QALY.

The benefits of vaccination are clearly illustrated by *Figure 15* and *Table 54*. Vaccination alone for all risk groups (S25) produces a gain of 1063.5

TABLE 54 *Number of additional women exposed to antibiotics per additional QALY gained for each of the policy-relevant strategies*

Strategies[a]	Risk group												Antibiotic exposures		Net QALYs gained[b]	Exposures/QALY gained	IEER[c] from			
	1	2	3	4	5	6	7	8	9	10	11	12	No.[b]	%			S25	S11	S15	
Scenario A																				
S30	n	n	n	n	n	n	n	n	n	n	n	n	0	0.0	0.0	NA				
S25	V	V	V	V	V	V	V	V	V	V	V	V	0	0.0	1063.5	0				
S9	V	VI	VI	VI	V	V	VI	VI	VI	V	V	V	35,292	5.2	1219.9	29				
S11	V	VI	VI	VI	VO	V	VI	VI	VI	V	V	V	50,116	7.4	1540.9	33	105			
S15	VI	VI	VI	VI	VO	VI	V	VI	VI	VI	V	V	74,800	11.0	1967.9	38	83	58		
S170	VI	VI	VI	VI	VI	VI	VO	VI	VI	VI	V	V	126,480	18.6	2014.2	63			1118	
S156	VI	VI	VI	VI	VO	VI	VO	VI	VI	VI	V	V	129,200	19.0	2025.0	64			953	
																	S3	**S7**	**S8**	**S83**
Scenario B																				
S30	n	n	n	n	n	n	n	n	n	n	n	n	0	0.0	0.0	NA				
S1	n	I	I	I	n	n	n	I	I	I	n	n	35,292	5.2	389.0	91				
S3	n	I	I	I	O	n	n	I	I	I	n	n	50,116	7.4	857.3	58				
S7	I	I	I	I	O	I	n	I	I	I	n	n	74,800	11.0	1404.3	53	45			
S8	I	I	I	I	O	I	PI	I	I	I	PI	PI	138,720	20.4	1775.9	78		172		
S83	I	I	I	I	O	I	CI	I	I	I	CI	CI	140,760	20.7	1858.8	76		145		
S84	I	I	I	I	O	I	O	I	I	I	CI	CI	188,360	27.7	1923.9	98			335	732
S99	I	I	I	I	I	I	O	I	I	I	CI	CI	186,320	27.4	1941.5	96			287	551

NA, not applicable.
[a] See *Table 2* for codes.
[b] Per year for a total population of 680,000 deliveries.
[c] Incremental exposure of women per QALY gained ratio.

QALYs per year (assuming 680,000 deliveries) relative to do nothing (S30) with zero women exposed to antibiotics. Strategies which include vaccination result in the gain of far more health benefit (QALYs gained) relative to antibiotic exposure than strategies that do not. The benefit of vaccination is therefore far greater than the modest gains in NB seen when comparing the most cost-effective strategies in Scenario A with the most cost-effective strategies in Scenario B (see *Tables 49* and *50*). When the harms of antibiotic exposure are included, the additional benefit gained by adopting vaccination strategies is greater the more harmful antibiotic exposure is valued. Moving from S7 (treat all preterm and high-risk term groups) in Scenario B (1404.3 net QALYs per year) to S15 in Scenario A (1967.0 net QALYs per year) involves only the addition of vaccination and no additional antibiotic exposure but gains 563.6 QALYs per year. The difference between the strategies with the highest NB in each of the Scenarios further illustrates the benefits of vaccination. S156 gains 83.5 more QALYs per year than S99 and involves exposing 57,120 fewer women per year to antibiotics. Indeed, the exposures per QALY gained ratios shown in *Table 54* clearly illustrate that all the policy-relevant vaccination strategies involve exposing fewer women to antibiotics in order to gain a net QALY in health outcome than the non-vaccination strategies, the distinction being especially clear for the strategies involving the greatest number of net QALYs gained.

Clinical effectiveness of policy-relevant strategies

This section reports the number of infected babies, number of deaths and numbers of women that need to be treated (NNT) in order to prevent these outcomes, for the policy-relevant strategies described in the section 'Cost-effectiveness of policy-relevant strategies' (p. 67). These results are intended to show how the strategies differentially affect overall cases of infection and death due to EOGBS, EO non-GBS and LOGBS, and how total cases and deaths vary by RG. These results are not intended to guide policy decisions as they take no account of the costs of the interventions apart from in crude terms measured as the NNT (which is unweighted for the different costs of different disease outcomes). Policy decisions should be informed by the cost-effectiveness analyses (Chapter 6) and the trade-off between QALYs gained and antibiotic exposure (see the sections 'Cost-effectiveness of policy-relevant strategies', p. 67 and 'Accounting for antibiotic exposure', p. 69).

The model was used to calculate the effect of each of the 713 strategies on each of the disease outcomes examined (EOGBS livebirth, EOGBS stillbirth, EO non-GBS livebirth, EO non-GBS stillbirth and LOGBS), within each of the 12 maternal RGs and overall. This information (for all RGs combined) is given in *Table 55* in terms of total cases per year in the UK (assuming 680,000 livebirths per year) and the percentage of cases prevented, for the policy-relevant strategies in both Scenarios A and B (source data are shown in Appendix 5, *Tables 110–115*).

Table 56 shows the same outputs for the number of deaths per year in the UK (again assuming 680,000 livebirths per year; the information by RG is given in Appendix 5, *Tables 111*, *113* and *116–119*). Comparison with *Table 55* shows that strategies such as S3 (current best practice) and S7 (treat all preterm and high-risk term groups) prevent a higher proportion of deaths than livebirths with early-onset GBS infection. This is because a larger proportion of the deaths occur in preterm and high-risk babies (relative to the proportion of the population that preterm and high-risk babies comprise – see the sections 'Maternal risk group distribution', p. 17 and 'Deaths', p. 32). The rest of the strategies in the table prevent broadly similar proportions of cases as they do deaths. It is clear that, overall, S3 and S7 prevent fewer cases and deaths than strategies that are more cost-effective (i.e. S8, S83, S84, S99 and the vaccination-based strategies of Scenario A).

Tables 55 and *56* also provide information on the total proportion of women treated with antibiotics and the NNT to prevent one case of disease or death for each of the selected strategies. However, given that some of the diseases are more costly in terms of health outcome (QALYs) than others, a better indication of which interventions require the least treatment to gain health is given in *Table 54* in the column 'Exposures/QALY gained'. The issue of the trade-off between health gained from treatment with antibiotics and the harms of antibiotic exposure has been dealt with in the section 'Accounting for antibiotic exposure' (p. 69).

Table 57 details the NNT in order to prevent one case of disease in each RG given intravenous antibiotics with or without vaccination and/or a positive PCR test result. Figures for oral treatment and testing by culture are similar to those for intravenous treatment and PCT testing, respectively (see Appendix 5, *Table 120* for data). The influence of vaccination on maternal colonisation and EOGBS and LOGBS results in

TABLE 55 *Total cases per year[a] in the UK and percentage of cases prevented, according to type of infection, for each of the policy-relevant strategies*

Strategy[b]	EOGBS livebirth		EOGBS stillbirth		EO non-GBS livebirth		EO non-GBS stillbirth		LOGBS		Total cases		% treated with antibiotics	NNT[c]
	Cases per year	% of cases prevented	Cases per year	% of cases prevented	Cases per year	% of cases prevented	Cases per year	% of cases prevented	Cases per year	% of cases prevented	Cases per year	% of cases prevented		
Scenario B: vaccination not allowed														
S30. Do nothing	328	0	9	0	661	0	23	0	167	0	1188	0.0	0.0	NA
S1. (RCOG guidelines): n, I, I, I, n, n, n, I, I, I, n, n	278	15	9	5	650	2	23	1	166	0	1126	5.3	5.2	564
S3. ('Current best practice'): n, I, I, I, O, n, n, I, I, I, n, n	248	24	9	5	623	6	23	1	166	0	1069	10.1	7.4	418
S7. I, I, I, I, O, I, n, I, I, I, n, n	225	32	9	9	579	12	22	6	166	0	1000	15.9	11.0	396
S8. I, I, I, I, O, I, PI, I, I, I, PI, PI	81	75	8	19	571	14	22	6	166	0	848	28.7	20.4	408
S83. I, I, I, I, O, I, CI, I, I, I, CI, CI	97	70	8	18	570	14	22	6	166	0	863	27.4	20.7	432
S84. I, I, I, I, O, I, O, I, I, I, CI, CI	97	70	8	18	564	15	22	6	166	0	857	27.9	27.7	568
S99. I. I. I. I. I. I. O. I. I. I. CI. CI.	93	72	7	23	569	14	21	8	166	0	857	27.9	27.4	561
Scenario A: vaccination allowed														
S25. Vaccinate all	101	69	3	66	661	0	23	0	49	70	837	29.6	0.0	0
S9. V, VI, VI, VI, V, V, V, VI, VI, VI, V, V	85	74	3	68	650	2	23	1	49	70	811	31.8	5.2	1341
S11. V, VI, VI, VI, VO, V, V, VI, VI, VI, V, V	72	78	3	68	623	6	23	1	49	70	770	35.2	7.4	746
S15. VI, VI, VI, VI, VO, VI, V, VI, VI, VI, V, V	62	81	3	69	579	12	22	6	49	70	715	39.9	11.0	609
S170. VI, VI, VI, VI, VI, VI, VO, VI, VI, VI, V, V	59	82	3	72	577	13	21	8	49	70	709	40.3	18.6	991
S156. VI, VI, VI, VI, VO, VI, VO, VI, VI, VI, V, V	61	81	3	69	571	14	22	6	49	70	707	40.5	19.0	987

[a] Assuming 680,000 livebirths per year in the UK.
[b] See *Table 2* for codes.
[c] Number of women needed to treat (NNT) with antibiotics to prevent one case of infection (defined as EOGBS livebirth, EOGBS stillbirth, EO non-GBS livebirth, EO non-GBS stillbirth.

TABLE 56 *Total deaths per year[a] in the UK and percentage of deaths prevented according to type of infection, for each of the policy-relevant strategies*

Strategy[b]	EOGBS livebirth		EOGBS stillbirth		EO non-GBS livebirth		EO non-GBS stillbirth		LOGBS		Total deaths		% treated with antibiotics	NNT[c]
	Deaths per year	% of deaths prevented	Deaths per year	% of deaths prevented	Deaths per year	% of deaths prevented	Deaths per year	% of deaths prevented	Deaths per year	% of deaths prevented	Deaths per year	% of deaths prevented		
Scenario B: vaccination not allowed														
S30. Do nothing	34	0	9	0	100	0	23	0	15	0	181	0	0.0	NA
S1. (RCOG guidelines): n, I, I, I, n, n, n, I, I, I, n, n	29	15	9	5	99	1	23	1	15	0	174	4	5.2	4888
S3. ('Current best practice'): n, I, I, I, O, n, n, I, I, I, n, n	22	34	9	5	95	5	23	1	15	0	164	10	7.4	2807
S7. I, I, I, I, O, I, n, I, I, I, n, n	18	48	9	9	88	12	22	6	15	0	150	17	11.0	2405
S8. I, I, I, I, O, I, PI, I, I, I, PI, PI	9	74	8	19	86	14	22	6	15	0	139	23	20.4	3299
S83. I, I, I, I, O, I, CI, I, I, I, CI, CI	10	71	8	18	86	14	22	6	15	0	140	23	20.7	3423
S84. I, I, I, I, O, I, O, I, I, I, CI, CI	10	71	8	17	86	14	22	6	15	0	140	23	27.7	4485
S99. I. I. I. I. I. I. O. I. I. I. CI. CI.	9	74	7	23	86	14	21	8	15	0	138	24	27.4	4316
Scenario A: vaccination allowed														
S25. Vaccinate all	13	64	3	66	100	0	23	0	4	70	143	21	0.0	0
S9. V, VI, VI, VI, V, V, V, VI, VI, VI, V, V	11	69	3	68	99	1	23	1	4	70	139	23	5.2	9747
S11. V, VI, VI, VI, VO, V, V, VI, VI, VI, V, V	8	77	3	68	95	5	23	1	4	70	133	27	7.4	4700
S15. VI, VI, VI, VI, VO, VI, V, VI, VI, VI, V, V	6	84	3	69	88	12	22	6	4	70	122	33	11.0	3590
S170. VI, VI, VI, VI, VI, VI, VO, VI, VI, VI, V, V	5	85	3	72	88	12	21	8	4	70	121	33	18.6	5688
S156. VI, VI, VI, VI, VO, VI, VO, VI, VI, VI, V, V	6	84	3	69	86	14	22	6	4	70	121	33	19.0	5879

[a] Assuming 680,000 livebirths per year in the UK.
[b] See *Table 2* for codes.
[c] Number of women needed to treat (NNT) with antibiotics to prevent one death (defined as EOGBS death, EOGBS stillbirth, EO non-GBS death, or EO non-GBS stillbirth).

TABLE 57 *Number of women needed to treat (NNT) with antibiotics to prevent one case of disease*

Intervention[a]	Risk group											
	1	2	3	4	5	6	7	8	9	10	11	12
I	441	338	176	193	219	338	4820	2948	910	527	624	2950
PI	269	144	127	78	91	144	1432	602	449	103	123	605
VI	492	430	283	299	329	430	6672	5463	2643	1717	1979	5461
VPI	345	219	188	125	145	218	3155	1605	1117	295	351	1598

[a] I, intravenous antibiotics; P, PCR test in labour; V, vaccination.

TABLE 58 *Number of women needed to treat (NNT) to prevent one death*

Intervention[a]	Risk group											
	1	2	3	4	5	6	7	8	9	10	11	12
I	2,429	1,742	838	938	1,065	1,743	38,279	28,457	11,593	7,127	8,302	28,358
PI	1,331	676	591	354	417	679	16,964	8,005	6,172	1,503	1,787	7,977
VI	2,793	2,326	1,418	1,548	1,696	2,332	44,979	40,675	26,479	19,433	21,535	40,452
VPI	1,826	1,029	903	584	678	1,057	29,782	18,218	13,691	4,165	4,902	17,742

[a] I, intravenous antibiotics; P, PCR test in labour; V, vaccination.

significantly more women needing to be treated with antibiotics to prevent one case of disease. As is apparent in low-risk groups such as RG7 (elective Caesarean section at term), significantly more women require treatment in order to prevent one case of disease. These figures are for consideration by clinicians when determining the risk of disease in the babies of women in specific RGs and determining whether it is worthwhile treating an individual woman as a result. However, in order to appreciate fully whether treatment is worthwhile, the decision should be made in terms of cost-effectiveness for the whole population (see Chapter 6). If the costs of treatment are low, and the consequences of not treating rare but costly, treating low-risk women may be cost-effective. Based on similar reasoning, we wear seatbelts every time we drive.

Table 58 details the NNT to prevent one death due to infection in each RG given intravenous antibiotics with or without vaccination and/or a positive PCR test result (figures for treatment with oral antibiotics and screening with culture are again similar to those for intravenous treatment and screening using PCR testing, respectively, and are given in Appendix 5, *Table 121*). As with the NNT to prevent one case (see *Table 57*), vaccination increases the NNT to prevent one death (comparison of treat all, 'I', and vaccinate and treat all, 'VI').

In order to compare the natural disease burden across RGs and for preterm and term deliveries when no interventions are given, tables are provided in Appendix 6 (*Tables 122–124*). For each RG, these tables show the number of infections and deaths per year in the UK (680,000 deliveries), the percentage of the total cases and the risk (per 1000 women) of infection outcomes or death due to infection.

Chapter 8

Decision uncertainty and value of information analyses

Overview

The expected costs and effects of interventions within each RG and the expected costs and effects of the large number of possible strategies which could be followed were presented in Chapter 6. This analysis indicated which interventions within RGs and which types of strategies might be regarded as cost-effective based on existing evidence. However, a decision to adopt a particular intervention or a strategy must also consider whether the existing evidence is a sufficient basis to implement such polices, or whether more evidence is required to inform these decisions. In essence, the decision to adopt a particular intervention or implement particular strategies cannot be separated from the question of whether existing evidence is sufficient. If it is not sufficient then we must consider what type of evidence would contribute most to informing these policy decisions. For example, is an RCT required, which comparators should be included and for which RGs would further evidence be most valuable?[142,145,146]

The value of additional evidence is that it reduces the uncertainty surrounding these choices and avoids, or rather reduces, the chance that a decision based on current evidence will 'turn out to be wrong'. If a decision is 'wrong', the patient population will have received an intervention which does not provide the highest NB, that is, NB will be foregone. Therefore, the benefit of reducing uncertainty through further research comes from the fact that these NBs foregone can be avoided (the methods of analysis are explained more fully below). However, it should be apparent that the value of additional research will depend on the uncertainty surrounding which intervention or strategy is cost-effective (probability or error), the size of the NB foregone if an error is made (the difference in NB between uncertain strategies) and the size of the relevant population. The analysis in Chapter 6 already suggests there will be considerable uncertainty surrounding the choice between some of the strategies (see *Figures 11* and *13*, where the expected cost-effect points are close to the maximum NB). Some choices will not be uncertain (where the cost-effect point is some distance from the maximum net benefit, e.g. S30, S1, S3 in *Figure 14*). However, where the choice of intervention or strategy is uncertain, the NB foregone may be small (the NBs of the uncertain alternative are similar and therefore the uncertainty is 'less important'). Finally, we should expect different values of information for different RGs which have very different population sizes.

This chapter is organised to reflect this reasoning. In the next section, an overview of the methods used to estimate decision uncertainty is presented, followed by results for the 12 RGs and for the strategies. The subsequent section provides an overview of value of information methods followed by the results for risk groups and for strategies. This is followed by a brief discussion of some of the types of analysis that could be conducted but have not been possible within the resource and time constraints of the current study. Finally, some implications for further research are summarised.

Decision uncertainty

The analysis presented in Chapter 6 indicated the interventions within RGs and the types of strategies which can be regarded as cost-effective based on existing evidence. The value of additional evidence is that it reduces the uncertainty surrounding these choices and reduces the chance that a decision based on current evidence will turn out to be 'wrong'. Therefore, to start to answer the question of whether existing evidence is sufficient or whether more information is needed requires an assessment of the uncertainty surrounding the adoption of particular interventions for each RG and the uncertainty surrounding the implementation of particular strategies for the whole population.

Overview of methods

Establishing the uncertainty surrounding each of these decisions is straightforward. For each iteration of the simulation (each realisation of the

TABLE 59 *Principles of decision uncertainty*[a]

	A	B	C	D	Highest NB
Iteration 1	9	12	*14*	8	C
Iteration 2	*12*	10	8	7	A
Iteration 3	14	*20*	15	12	B
Iteration 4	11	10	*12*	9	C
Iteration 5	*14*	13	11	10	A
Expected NB	12	13	12	9	
Probability cost-effective	0.4	0.2	0.4	0	

[a] Values in italics are the highest.

uncertainty surrounding model parameters) the intervention or strategy which has the highest NB can be recorded. Once the simulation has sampled sufficiently across all the distributions estimated for the parameters in the model, the proportion of times each alternative has the highest NB can be calculated. This provides the probability that the intervention or strategy is cost-effective. For those interventions and strategies identified as cost-effective in Chapter 6, one minus this probability is the error probability (the probability that a decision based on existing information will be 'wrong' based on current information).

These principles can be illustrated in *Table 59*.

In this simple example, there are four alternative strategies (A, B, C, D) and five iterations (or realisations of the uncertainty in all the model parameters). Each iteration provides an estimate of the NB for each alternative. Averaging these NBs across the five iterations provides the expected NB for each strategy. Strategy B has the highest expected NB and can be regarded as cost-effective. However, adopting B is uncertain. In this case, B is only the best alternative (has the highest NB) for one of these five realisations of uncertainty (iteration 3). Alternatives A and C are the best for 2/5 iterations. Therefore, the probability that B is cost-effective is only 0.2 and there is an error probability of 0.8. There are a number of issues to note in this example: (1) alternative B has the highest expected NB but a lower probability of being cost-effective than A or C (due to the skewness of the net benefit – see iteration 3); (2) alternatives A and C are not cost-effective but do contribute to decision uncertainty – to exclude them would underestimate the uncertainty surrounding the choice of B; (3) alternative D is not cost-effective and has no chance of being so – excluding D from consideration will not affect estimates of cost-effectiveness or decision uncertainty (of course, many more than five iterations would be required to exclude it confidently). These simple implications help the interpretation of the following results and provide the intuition behind our procedure of strategy selection outlined in section 'Methods' (p. 60), which was designed to exclude only those which would have had no probability of being cost-effective (like alternative D above). It should be noted that in order to determine confidently the cost-effectiveness and decision uncertainty of the strategies modelled, we used 10,000 iterations as standard.

Results by risk group

The uncertainty surrounding the choice of intervention within each RG is summarised in *Tables 60* and *61* for Scenarios A and B, respectively. Decision uncertainty is only reported for those interventions that had a higher than 0.01 probability of being cost-effective. The interventions that appear to be cost-effective at a threshold of £25,000 are shaded and the associated error probability is recorded for each RG. The results for all interventions available for all RGs and for cost-effectiveness thresholds of £20,000, £25,000 and £30,000 can be found in Appendix 2, *Tables 84–95*, for Scenario A and Appendix 3, *Tables 96–107*, for Scenario B.

Scenario A

It is evident from the results in *Table 60* that there is considerable uncertainty associated with the choice of intervention within most, but not all RGs. For example, the combination of vaccination and intravenous treatment for RG3 is not uncertain and has over a 0.9 probability of being cost-effective. It should be noted that non-vaccination interventions are not cost-effective and this result is not uncertain for preterm RGs, such as RG1, 2, 4 and 6, although there is considerable uncertainty associated with the

TABLE 60 *Summary of decision uncertainty by risk group (Scenario A)*

Risk group	Intervention	Result	NB £25,000 (£)	*p*(CE) £25,000	Error probability
Preterm					
1. Elective LSCS	13: Vaccination + i.v.	ICER to 14: £13,900	4.46	0.5690	0.4310
	14: Vaccination + oral	ICER to 7: £979	4.36	0.4280	
2. Previous GBS baby	13: Vaccination + i.v.	ICER to 6: £547	0.04	0.7910	0.2090
	14: Vaccination + oral	Dominated	0.03	0.2070	
3. Previous positive swab/ bacteriuria	12: Vaccination, PCR + i.v.	Dominated	4.39	0.0043	
	13: Vaccination + i.v.	Base for ICER	5.49	0.9050	0.0950
	14: Vaccination + oral	Dominated	3.94	0.0898	
4. Pyrexia	13: Vaccination + i.v.	ICER to 14: £1,460	2.66	0.6750	0.3250
	14: Vaccination + oral	Base for ICER	2.44	0.3240	
5. Prelabour ROM >2 hours	13: Vaccination + i.v.	ICER to 14: £471,000	23.38	0.5240	
	14: Vaccination + oral	Base for ICER	23.81	0.4740	0.5260
6. Intact membranes	13: Vaccination + i.v.	ICER to 6: £546	22.15	0.7910	0.2090
	14: Vaccination + oral	Dominated	14.98	0.2070	
Term					
7. Elective LSCS	6: I.v.	Extended dominated	1.41	0.3180	
	7: Oral	Base for ICER	2.34	0.6470	0.3530
	14: Vaccination + oral	ICER to 7: £61,800	0.19	0.0264	
8. Previous GBS baby	6: I.v.	ICER to 7: £19,400	0.02	0.5600	0.4400
	7: Oral	Base for ICER	0.02	0.3200	
	13: Vaccination + i.v.	ICER to 6: £58,100	0.00	0.0200	
	14: Vaccination + oral	Extended dominated	0.01	0.0986	
9. Previous positive swab/ bacteriuria	6: I.v.	ICER to 7: £534	4.42	0.5700	0.4300
	13: Vaccination + i.v.	ICER to 6: £32,600	4.06	0.2140	
	14: Vaccination + oral	Extended dominated	3.83	0.2090	
10. Pyrexia	6: I.v.	ICER to 7: £7,140	3.49	0.1530	
	7: Oral	Base for ICER	3.03	0.0650	
	13: Vaccination + i.v.	ICER to 14: £54,100	3.64	0.2230	
	14: Vaccination + oral	ICER to 6: £11,800	3.81	0.5570	0.4430
11. ROM >18 hours	1: Vaccination	Extended dominated	11.82	0.0314	
	3: Culture + i.v.	Base for ICER	10.73	0.0306	
	4: PCR + oral	Dominated	9.89	0.0646	
	5: PCR + i.v.	ICER to 3: £3,700	11.82	0.1150	
	9: Vaccination, culture + oral	Extended dominated	13.45	0.1450	
	10: Vaccination, culture + i.v.	ICER to 5: £13,700	13.77	0.3480	0.6520
	11: Vaccination, PCR + oral	Dominated	13.27	0.0839	
	12: Vaccination, PCR + i.v.	ICER to 10: £38,100	13.62	0.1720	
12. No risk factors	1: Vaccination	Extended dominated	–4.03	0.2080	
	3: Culture + i.v.	Base for ICER	6.01	0.6680	0.3320
	5: PCR + i.v.	ICER to 3: £3,700	2.48	0.0665	
	8: Nothing	Dominated	0.00	0.0529	

cost-effective intervention of vaccination and intravenous treatment, it is only vaccination and oral treatment which have a significant chance of being cost-effective, that is, the decision uncertainty is between these two interventions for these RGs. The result for RG5 is a good example of the fact that the strategy with the most NB may not be the one with the highest probability of being cost-effective: vaccination + oral treatment has the higher NB but a lower probability of being cost-effective than vaccination + intravenous treatment as a result of the skewness of the NB achieved in the iterations of the model (see the section 'Overview of the methods', p. 79).

TABLE 61 *Summary of decision uncertainty by risk group (Scenario B)*

Risk group	Intervention	Result	NB at £25,000 (£)	*p*(CE) at £25,000	Error probability
Preterm					
1. Elective LSCS	6: I.v.	ICER to 7: £8,170	3.52	0.5870	0.4130
	7: Oral	Base for ICER	3.30	0.4120	
2. Previous GBS baby	6: I.v.	Base for ICER	0.03	0.8590	0.1410
	7: Oral	Dominated	0.01	0.1370	
3. Previous positive swab/bacteriuria	6: I.v.	Base for ICER	4.36	0.9730	0.0270
	7: Oral	Dominated	1.61	0.0178	
4. Pyrexia	6: I.v.	Base for ICER	2.00	0.7800	0.2200
	7: Oral	Dominated	1.53	0.2160	
5. Prelabour ROM >2 hours	6: I.v.	ICER to 7: £9,470	17.70	0.5800	0.4200
	7: Oral	Base for ICER	17.10	0.4190	
6. Intact membranes	6: I.v.	Base for ICER	16.79	0.8590	0.1410
	7: Oral	Dominated	6.90	0.1370	
Term					
7. Elective LSCS	6: I.v.	ICER to 7: £142,000	1.41	0.3270	
	7: Oral	Base for ICER	2.34	0.6720	0.3280
8. Previous GBS baby	6: I.v.	ICER to 7: £19,400	0.02	0.6060	0.3940
	7: Oral	Base for ICER	0.02	0.3930	
9. Previous positive swab/bacteriuria	6: I.v.	ICER to 7: £534	4.42	0.9730	0.0270
	7: Oral	Base for ICER	2.39	0.0242	
10. Pyrexia	5. PCR + i.v.	Dominated	2.81	0.0102	
	6: I.v.	ICER to 7: £7,140	3.49	0.7170	0.2830
	7: Oral	Base for ICER	3.03	0.2720	
11. ROM >18 hours	2: Culture + oral	Dominated	8.81	0.0418	
	3: Culture + i.v.	Base for ICER	10.73	0.2000	
	4: PCR + oral	Dominated	9.89	0.1820	
	5: PCR + i.v.	ICER to 3: £3,700	11.82	0.5760	0.4240
12. No risk factors	3: Culture + i.v.	ICER to 8: £13,000	6.01	0.8390	0.1610
	5: PCR + i.v.	ICER to 3: £107,000	2.48	0.0952	
	8: Nothing	Base for ICER	0.00	0.0640	

The picture is somewhat different and more complex for the term RGs. Vaccination interventions are only cost-effective for RG10 and 11 and there is considerable uncertainty associated with this result. For example, vaccination interventions have a significant chance of being cost-effective within all the other term RGs. In addition, the uncertainty is now associated with the choice between a range of possible interventions. For example, the error probability for vaccination, culture screen followed by intravenous treatment in RG11 is high (0.65) and there are five alternative interventions which have a chance of being cost-effective, of which two are non-vaccination interventions. In summary, there is more uncertainty associated with the cost-effective intervention, and more of the other possible interventions contribute to this uncertainty, in term RGs.

Scenario B

When vaccination is removed as a possible intervention the pattern of results is similar (*Table 61*). There remains considerable uncertainty associated with the choice between interventions within most RGs, but there are exceptions. For example, intravenous treatment for RG3 and 9 is not uncertain and has over a 0.97 probability of being cost-effective. For all the other preterm RGs there is uncertainty associated with the intravenous treatment but the uncertain choice is between intravenous and oral treatment. All the other interventions have a negligible probability of being cost-effective (the decision uncertainty is

between intravenous and oral treatment for all preterm RGs).

With the exception of RG9, there is more uncertainty associated with the cost-effective intervention for term RGs. For RG7–10 the uncertainty is associated with the choice between intravenous and oral treatment, and other possible interventions have a negligible probability of being cost-effective. It is only for RG11 and 12 that the uncertainty is associated with more than two interventions. For example, the error probability for PCR screen followed by intravenous treatment in RG11 is high (0.42) and there are three other alternative interventions which have a chance of being cost-effective, most notably, culture screen followed by intravenous treatment with a 0.2 probability of being cost-effective.

The uncertainty surrounding the choice between interventions within each RG indicates those interventions that are not cost-effective and are not uncertain, and in some cases indicates those interventions which are cost-effective and are also not uncertain (RG3 in Scenario A and RG3 and 4 in Scenario B). It also indicates those which may be cost-effective but are also uncertain. However, as explained in Chapter 6, the choice of intervention cannot be made independently RG by RG. The policy decision is which of the possible strategies (combinations of different interventions for different RGs) can be regarded as cost-effective and what the uncertainty is surrounding the choice of strategy.

Results for strategies

The uncertainty surrounding the choice of strategy is summarised in *Tables 62* and *63* for Scenarios A and B respectively at a cost-effective threshold of £25,000. Both tables are separated into three sections. In the first section, all the strategies that are on the cost-effectiveness frontier (see *Figures 12* and *14*) are shown and the cost-effective strategy (highest net benefit) is in bold. The second section includes all those strategies which are of policy interest including current and best practice. The third section includes all other strategies which have a greater than 0.01 probability of being cost-effective. The results for all interventions available for all RGs for cost-effectiveness thresholds of £20,000, £25,000 and £30,000 can be found in Appendix 4, *Tables 108* and *109* for Scenarios A and B, respectively.

Scenario A

When vaccination is available, there is huge uncertainty in the choice between very many of the vaccination and non-vaccination strategies. For example, the error probability associated with S156, the strategy which appears cost-effective (it has the highest expected NB overall) is over 0.97. Not only is the error probability very high but also there are a large number of other vaccination and non-vaccination strategies which may be cost-effective and are just as uncertain.

There are a number of issues to note. First, the uncertainty in the choice between vaccination and non-vaccination strategies is large. For example, S99 is the best non-vaccination strategy (has the highest expected NB of all the non-vaccination strategies) and has a higher probability of being cost-effective (0.0767) than the vaccination strategy S156 (0.0225), which has higher NB. This is an example of the issue illustrated in the section 'Overview of methods' (p. 79), where, due to skewness in NB (for example, due to small chances of large QALY gains and cost savings), the strategy with the highest NB has a lower probability of being cost-effective). The probability that any vaccination strategy will be cost-effective is 0.574, which suggests that a policy of vaccination has substantial error probability (0.426). Second, there is substantial uncertainty in the choice between vaccination strategies. For example, S173 has a probability of being cost-effective of 0.103, which is higher than S156. However, some choices are not uncertain. For example, a number of strategies of policy interest have a zero probability of being cost-effective and there is no uncertainty in rejecting these on grounds of cost-effectiveness. These include S25, S9 and S11, which represent the addition of vaccination to no treatment, the RCOG guidelines (S1) and current best practice (S3), respectively. Finally it should be noted that although the choices are uncertain, the difference in NB between the alternatives is not large – all these uncertain strategies are similar in terms of NB. However, to place differences in NB into a population context an additional £1 of net benefit can be valued at £680,000 per year or 27.2 net QALYs gained per year. Therefore, the difference in net benefit between S156 and S99 (£3.07) would represent a net gain of 83.8 QALYs per year for the healthcare system (this net gain accounts for the QALYs foregone elsewhere due to the additional cost of S156, so more QALYs would be gained for this patient population).

Scenario B

When vaccination is not available, the decision uncertainty is lower [some strategies which have a probability of being cost-effective have been removed – see the section 'Overview of methods'

TABLE 62 *Summary of decision uncertainty for strategies (Scenario A)*

Strategy[a]	Risk group												ICER (£)	NB at £25,000 (£)	*p*(CE) at £25,000 (£)
	1	2	3	4	5	6	7	8	9	10	11	12			
Strategies on the cost-effectiveness frontier															
T27	O	I	I	I	O	I	O	O	O	I	–	–	–	51.75	0.0005
S86	I	I	I	I	O	I	O	I	I	I	–	–	ICER to T27: 1,690	54.09	0.0000
S84	I	I	I	I	O	I	O	I	I	I	CI	CI	ICER to S86: 5,620	70.73	0.0439
S99	I	I	I	I	I	I	O	I	I	I	CI	CI	ICER to S84: 9,470	71.38	0.0767
S156	**VI**	**VI**	**VI**	**VI**	**VO**	**VI**	**VO**	**VI**	**VI**	**VI**	**V**	**V**	**ICER to S99: 22,700**	**74.45**	**0.0225**
S177	VI	VI	VI	VI	VO	VI	VO	VI	VI	VO	VCI	VCI	ICER to S156: 35,300	71.70	0.0102
S176	VI	VI	VI	VI	VO	VI	VO	VI	VI	VO	VCI	VCI	ICER to S177: 54,100	71.65	0.0014
S47	VI	VI	VI	VI	VO	VI	VO	VI	VI	VI	VPI	VPI	ICER to S176: 265,000	66.85	0.0002
S175	VI	VI	VI	VI	VI	VI	VI	VI	VI	VI	VPI	VPI	ICER to T446: 523,000	65.25	0.0015
Policy-relevant strategies															
S25	V	V	V	V	V	V	V	V	V	V	V	V	Dominated	39.10	0.0000
S9	VI	VI	VI	VI	VO	VI	VO	VI	VI	VI	V	V	Dominated	44.85	0.0000
S11	V	VI	VI	VI	VO	V	V	VI	VI	VI	V	V	Dominated	56.65	0.0000
T629	VI	VI	VI	VI	VO	VI	V	VO	VO	VI	V	V	Dominated	72.35	0.0000
S15	VI	VI	VI	VI	VO	VI	V	VI	VI	VI	V	V	Dominated	72.35	0.0000
S16	VI	VI	VI	VI	VO	VI	VPI	VI	VI	VI	VPI	VPI	Dominated	63.65	0.0000
T526	VI	VI	VI	VI	VI	VI	VO	VI	VI	VI	VCI	VCI	Extended dominated	71.15	0.0182
S170	VI	VI	VI	VI	VI	VI	VO	VI	VI	VI	V	V	Extended dominated	74.05	0.0991
T427	VO	VI	VI	VI	VO	VI	VO	VO	VO	VI	V	V	Extended dominated	74.05	0.1090
T429	VI	VI	VI	VI	VO	VI	VO	VO	VO	VI	V	V	Extended dominated	74.20	0.0075
Strategies with >1% probability of cost-effectiveness at 25,000/QALY															
S39	I	I	I	I	O	I	O	I	I	I	PI	PI	Extended dominated	68.47	0.0155
S80	I	I	I	I	I	I	O	I	I	I	PI	PI	Extended dominated	68.87	0.0212
S101	I	I	I	I	I	I	I	I	I	I	CI	CI	Extended dominated	70.49	0.1040
S102	I	I	I	I	I	I	I	I	I	I	PI	PI	Extended dominated	67.98	0.0390
S173	VI	VI	VI	VI	VI	VI	VI	VI	VI	VI	V	V	Extended dominated	72.85	0.1030
S174	VI	VI	VI	VI	VI	VI	VI	VI	VI	VI	VCI	VCI	Extended dominated	70.05	0.0526
S221	VO	VO	VO	VI	VO	VO	VO	VO	VO	VI	V	V	Dominated	65.20	0.0649
T128	V	I	I	I	I	I	O	I	I	I	CI	CI	Extended dominated	71.24	0.0182
T147	O	I	I	I	O	I	O	O	O	I	CI	CI	Extended dominated	68.64	0.0293
T156	O	I	I	I	O	O	O	O	O	I	CI	CI	Dominated	58.77	0.0228
T412	VI	VI	VI	VI	VI	VI	VO	VO	VO	VI	V	V	Extended dominated	73.80	0.0105
T436	VO	VI	VI	VI	VO	VO	VO	VO	VO	VI	V	V	Dominated	66.80	0.0748

[a] See *Table 2* for codes.

(p. 79) but there remains substantial uncertainty surrounding the choice between the remaining strategies. For example, the error probability associated with S99, the strategy which appears cost-effective (it has the highest expected NB), is lower than in Scenario A, but remains over 0.84. The error probability remains high but there are fewer strategies which may be cost-effective and only some of them have a substantial probability of being cost-effective.

There are a number of issues to note. First, the strategy with the highest expected NB (S99) also has the highest probability of being cost-effective (reflecting less skewness in net benefit once vaccination is removed). Second, there is substantial uncertainty in the choice between particular strategies. For example, it is the choice between S99 and S84, S102 or S101 which accounts for most of the decision uncertainty (S84, S102 and S101 contribute 0.435 to the error probability of 0.846), with other strategies contributing more modestly (e.g. S80, S39, T128, T147 and T156 contribute 0.329 of the error probability). Again, for these uncertain choices the difference in net benefit is not large (although at a population level they do represent important net QALYs gains).

Despite the uncertainty in the choice of cost-effective strategies, some choices are not uncertain. For example, many of the strategies of

TABLE 63 *Summary of decision uncertainty for strategies (Scenario B)*

Strategy[a]	Risk group												ICER (£)	NB at £25,000 (£)	*p*(CE) at £25,000 (£)
	1	2	3	4	5	6	7	8	9	10	11	12			
Strategies on the cost-effectiveness frontier															
T27	O	I	I	I	O	I	O	O	O	I	–	–	–	51.75	0.0006
S86	I	I	I	I	O	I	O	I	I	I	–	–	ICER to T27: 1,690	54.09	0.0003
S84	I	I	I	I	O	I	O	I	I	I	CI	CI	ICER to S86: 5,620	70.73	0.1090
S99	**I**	**I**	**I**	**I**	**O**	**I**	**O**	**I**	**I**	**I**	**CI**	**CI**	**ICER to S84: 9,470**	**71.38**	**0.1540**
S80	I	I	I	I	I	I	O	I	I	I	PI	PI	ICER to S99: 51,000	68.87	0.0599
S102	I	I	I	I	I	I	I	I	I	I	PI	PI	ICER to S80: 142,000	67.98	0.1020
Policy-relevant strategies															
S30	–	–	–	–	–	–	–	–	–	–	–	–	Dominated	0.00	0.0009
S1	–	I	I	I	–	–	–	I	I	I	–	–	Dominated	14.30	0.0000
S3	–	I	I	I	O	–	–	I	I	I	–	–	Dominated	31.52	0.0000
S7	I	I	I	I	O	I	–	I	I	I	–	–	Dominated	51.63	0.0000
S8	I	I	I	I	O	I	PI	I	I	I	PI	PI	Dominated	65.29	0.0000
S83	I	I	I	I	O	I	CI	I	I	I	CI	CI	Dominated	68.34	0.0000
S39	I	I	I	I	O	I	O	I	I	I	PI	PI	Dominated	68.47	0.0447
S96	I	I	I	I	I	I	CI	I	I	I	CI	CI	Dominated	68.74	0.0000
S101	I	I	I	I	I	I	I	I	I	I	CI	CI	Extended dominated	70.49	0.2240
T128	O	I	I	I	I	I	O	I	I	I	CI	CI	Extended dominated	71.24	0.0465
>1% *p*(CE) at 25,000/QALY															
T48	I	O	O	I	I	I	O	I	I	I	PI	PI	Extended dominated	68.73	0.0142
T67	O	I	I	I	O	I	O	O	O	I	PI	PI	Dominated	66.13	0.0221
S75	O	O	O	O	O	O	O	O	I	I	PI	PI	Dominated	55.15	0.0350
T147	O	I	I	I	O	I	O	O	O	I	CI	CI	Extended dominated	68.64	0.0788
T156	O	I	I	I	O	O	O	O	O	I	CI	CI	Dominated	58.77	0.0770

[a] See *Table 2* for codes.

policy interest have a zero probability of being cost-effective and there is no uncertainty in rejecting these on the grounds of cost-effectiveness. These include S30, S1 and S3, which represent no treatment, the RCOG guidelines and current best practice, respectively. Here the differences in NB are large. For example, the difference in NB between S99 and S1 (RCOG or current practice) is £57.08, which translates to 1558.3 net QALYs gained per annum for the population: a substantial annual improvement in health outcomes for the healthcare system as a whole (most of these gains in health will accrue to this patient population as S99 is less costly than S1 due to longer term cost savings from avoiding cost-bearing events).

Identifying research priorities

The results of decision uncertainty for the choice between interventions within risk groups and the choice between strategies presented in the previous section suggest that there is substantial decision uncertainty, but over a limited number of particular interventions for certain RGs and over a limited number of strategies. Other interventions in certain RGs and strategies, such as no treatment (S30), RCOG guidelines (S1) and current best practice (S3), are not cost-effective and are not uncertain. The difference in NB across those strategies, for which the choice is uncertain, is not large. However, based only on this type of analysis it is unclear how 'important' this decision uncertainty is or whether it justifies devoting resources to further research focused on particular RGs or strategies. To establish the cost of this uncertainty and therefore the value of acquiring additional information, VOI methods are needed. These are outlined in the next section followed by the results for RGs and strategies.

Overview of methods

Information is valuable because it reduces the expected costs of uncertainty surrounding decisions – it reduces the expected NB foregone due to decision error. Therefore, the expected costs of uncertainty represent the maximum benefit that any amount of additional evidence could provide – it provides an upper bound to the

value of conducting further research. The EVPI can be compared with the costs of proposed research. If the costs of proposed research exceed the EVPI then the value or 'importance' of the uncertainty does not justify further investigation (the costs exceed the maximum benefits). When further research does appear to be justified, the EVPI can be compared with the costs of different types of further investigation. It places a limit on the scale and cost of proposed research. The EVPI for a decision problem can also be compared with other decision problems in healthcare to establish whether this represents a priority area compared with others. Finally, the EVPI across the RGs can be used to identify particular patient groups where further research would be most valuable and identify those where it would not be justified.

Establishing the EVPI is fairly straightforward and can be calculated directly from the simulated output in the same way as decision uncertainty (see the section 'Overview of methods', p. 79). The following provides both some formal notation and an explanation of EVPI to assist with the interpretation of the results for RGs and strategies which follows in the next two sections.

The EVPI can also be thought of as the difference in expected NB with perfect and with current information. With current information, decisions must be made before we know how the uncertainties will be resolved, that is, a decision must now be based on the expected NBs of each of the alternatives. However, with perfect information, decisions could be made once we know how the uncertainties in the model will resolve, so different decisions could be made for different resolutions of net benefit. The EVPI is simply the difference between the pay-off (expected NB) with perfect and current information.[38,145,147–150]

For example, if there are j alternative interventions, with unknown parameters θ, then given the existing evidence, the optimal decision is the intervention that generates the maximum expected NB:

$$\max_j E_\theta \, \mathrm{NB}(j, \theta)$$

that is, choose j with the maximum NBs over all the iterations from the simulation because each iteration represents a possible future realisation of the existing uncertainty (a possible value of θ). With perfect information, the decision-maker would know how the uncertainties would resolve (which value θ will take) before making a decision and could select the intervention that maximises the net benefit given a particular value of θ:

$$\max_j \mathrm{NB}(j, \theta)$$

However, the true values of θ are unknown (we do not know which value θ will take). Therefore, the expected value of a decision taken with perfect information is found by averaging the maximum NB over the joint distribution of θ:

$$E_\theta \max_j \mathrm{NB}(j, \theta)$$

In other words, first calculate the maximum NB for each iteration from the simulation (for a particular value of θ), then take the average over these maximum NBs (over the possible values of θ). The EVPI for an individual patient is simply the difference between the expected value of the decision made with perfect information about the uncertain parameters θ and the decision made on the basis of existing evidence:

$$\mathrm{EVPI} = E_\theta \max_j \mathrm{NB}(j, \theta) - \max_j E_\theta \, \mathrm{NB}(j, \theta)$$

This is illustrated in *Table 64* for the same four alternatives which were illustrated in *Table 59*. The table represents simulated output from five iterations generating NBs for each of the treatments. With current information, the best a decision-maker can do is to choose the alternative with the highest expected NB [$\max_j E_\theta \, \mathrm{NB}(j, \theta)$], which, in this case, is to choose treatment B with an expected NB of £13. With perfect information, the decision-maker could choose the alternative with the maximum NB for each resolution of uncertainty [$\max_j \mathrm{NB}(j, \theta)$], that is, choose C for iteration 1, A for iteration 2 and B for iteration 3, and so on. However, we do not know in advance which of these possibilities will turn out to be true, so the expected NB with perfect information is simply the expectation of the maximum NB (£14.40). The EVPI is then simply the difference between the expected NB with perfect information and the expected NB with current information (£1.40). This is entirely equivalent to taking the expectation of the opportunity losses (the NB foregone) in the last column. This confirms the earlier interpretation that EVPI is also the expected opportunity loss or the expected costs of the uncertainty surrounding the decision.

It should be noted that although alternatives A and C are not cost-effective based on current information, there is a chance that they will be. Excluding A or C will not effect the decision to adopt B but it may effect the decision to conduct

TABLE 64 *Principles of EVPI*[a]

	A	B	C	D	Choice with information	Maximum NB	NB foregone
Iteration 1	9	12	*14*	8	C	*14*	2
Iteration 2	*12*	10	8	7	A	*12*	2
Iteration 3	14	*20*	15	12	B	*20*	0
Iteration 4	11	10	*12*	9	C	*12*	2
Iteration 5	*14*	13	11	10	A	*14*	1
Expected NB	12	**13**	12	9		**14.4**	1.4

[a] Values in italics are the highest; values in bold show the highest expected NB (£13) and the maximum NB with perfect information (£14.40).

further research. For example, if C is excluded the EVPI will fall from £1.40 to £0.80. Alternative D, on the other hand, is never cost-effective in these five iterations (there is no chance that it will be cost-effective) and its inclusion or exclusion has no effect on the EVPI.

The EVPI described above provides the EVPI surrounding the decision as a whole each time this decision is made (for an individual patient or individual episode). However, once information is generated to inform the decision for an individual patient or episode of care, then it is also available to inform the management of all other current and future patients (it has public good characteristics and is non-rival, i.e. the use of information by one patient does not reduce its availability to others). Therefore, EVPI is expressed for the total population of patients who stand to benefit from additional information over the expected lifetime of the decision problem. This requires some assessment of the effective lifetime of the interventions considered in the decision problem (the period over which information about the decision will be useful) (T), and estimates of incidence over this period (I_t).

$$\text{EVPI for the population} = \text{EVPI} \times \sum_{t=1,2,\ldots,T} I_t/(1+r)^t$$

The EVPI associated with future patients is discounted at rate r to provide the total EVPI for the population of current and future patients. The value of information literature in health and other fields such as risk analysis and engineering has generally taken fixed time horizons of 1, 10 or 20 years.[151] In this analysis, a time horizon of 10 years is taken, recognising that the choice faced now will at some time become obsolete as clinical practice and health technologies develop. We used the incidence rate of 680,000 per year and a discount rate of 3.5% over this time horizon. Of course, different views on appropriate time horizons or future incidence rates can easily be incorporated (it simply scales the EVPI up or down). It should be noted that due to discounting even unbounded time horizons do not lead to unbounded EVPI (e.g. £1 per period for an unbounded time horizon is £28.57 at a 3.5% discount rate). So doubling the time horizon from 10 to 20 years does not double the EVPI.

Results by risk group

The EVPI for the RGs is reported in *Tables 65* and *66* for Scenarios A and B, respectively. From the principles outlined in the sections 'Overview of methods' (pp. 79 and 85), it should be apparent that the VOI will be determined by the decision uncertainty (probability of error), the importance of this uncertainty (NBs foregone) and the size of the patient population. Clearly, where the patient population is small, and all other things being equal, the VOI will be lower (it implies that where there is a rare disease or rare risk factor then decisions can be made on the basis of less evidence and more uncertainty). For this reason, the error probability associated with the cost-effective intervention within each RG and the population per year for each RG is also reported.

Scenario A

The EVPI differs substantially across the RGs. For some RGs the EVPI is very low and indicates that additional evidence to inform the choice of intervention for these particular RGs is not justified. For example, the EVPI in RG2 and 8 is particularly low, reflecting the small size of the population and less decision uncertainty in RG2. The low EVPI for RG3 reflects the very low error probability associated with vaccination and intravenous intervention for this group. For other groups where the EVPI is low, more interpretation is required. For example, the EVPI is low in RG10 despite the high error probability and moderate

TABLE 65 *EVPI[a] (£) for risk groups (Scenario A)*

Risk group	EVPI (£)	Error probability	Population (per year)
Preterm			
1. Planned LSCS	5,587,333	0.431	5,440
2. Previous GBS baby	12,807	0.209	68
3. GBS-positive swab	374,000	0.095	2,992
4. Pyrexia	880,600	0.325	1,700
5. Prelabour ROM	12,353,333	0.476	16,388
6. Intact membranes	6,800,000	0.209	23,324
Term			
7. Planned LSCS	1,700,000	0.353	54,332
8. Previous GBS baby	34,000	0.440	544
9. GBS-positive swab	1,394,000	0.430	23,868
10. Pyrexia	716,267	0.443	10,880
11. Prolonged ROM	3,400,000	0.652	56,916
12. No risk factors	9,180,000	0.332	483,480
Total EVPI	42,432,340		

[a] For the total population (680,000 deliveries per year) over a 10-year time horizon.

TABLE 66 *EVPI[a] (£) for risk groups (Scenario B)*

Risk group	EVPI (£)	Error probability	Population (per year)
Preterm			
1. Planned LSCS	5,281,333	0.413	5,440
2. Previous GBS baby	7,820	0.141	68
3. GBS-positive swab	81,600	0.027	2,992
4. Pyrexia	539,467	0.22	1,700
5. Prelabour ROM	12,806,667	0.42	16,388
6. Intact membranes	4,193,333	0.141	23,324
Term			
7. Planned LSCS	1,586,667	0.328	54,332
8. Previous GBS baby	30,600	0.394	544
9. GBS-positive swab	68,000	0.027	23,868
10. Pyrexia	581,400	0.283	10,880
11. Prolonged ROM	4,533,333	0.424	56,916
12. No risk factors	2,040,000	0.161	483,480
Total EVPI	31,750,220		

[a] For the total population (680,000 deliveries per year) over a 10-year time horizon.

size population. This is due to there being little difference in the NBs of those interventions which are uncertain for this group, that is, the uncertainty is less 'important' (see Appendix 2, *Table 93*). The EVPI is substantial and will exceed the cost of much proposed research in a number of RGs, such as RG1, 6, 11 and 12, with RG5 associated with the largest EVPI. This reflects the significant population for RG5, the large error probability and the fact the differences in NBs between uncertain interventions is larger than in other groups (the uncertainty is more important – see Appendix 2, *Table 88*). Although these EVPIs may well exceed the costs of proposed research, they are not large when compared with the other estimates of VOI in health (see the section 'Results for strategies', p. 89) and indicate a limit to the scale and cost of research which can be justified.

Scenario B

The EVPI also differs substantially across the RGs when vaccine is excluded. For RG2, 3, 8 and 9 the EVPI is very low and indicates that additional evidence to inform the choice of intervention is

not justified. This reflects the reduced error probability once vaccine is removed. The EVPI remains substantial and may exceed the cost of some proposed research in some RGs, such as RG1, 5, 6, 7, 11 and 12. Again, RG5 is associated with the largest EVPI. This reflects the significant population for RG5, the large error probability and the fact that the differences in NBs between uncertain interventions are larger than in other groups. The uncertainty is more important and for this group is between oral and intravenous treatment (see *Table 53* and Appendix 3, *Table 100*). Again, even though these EVPIs may well exceed the costs of proposed research, they are not large when compared with the other estimates of VOI in health (see the next section) and indicate limits to the scale and cost of research which can be justified.

Results for strategies

The EVPI for RGs indicates those for which additional evidence would be most valuable to inform the choice between the available interventions. However, as explained previously (see the section 'Methods', p. 60), choice of intervention cannot be made independently RG by RG and the wider policy question is whether further evidence is required to inform the choice of alternative polices or strategies across the RGs. If interventions could be chosen independently by RG then the overall EVPI for the whole patient population would be the sum of the RG EVPIs. However, due to the constraints that RG11 and 12 cannot be treated without first testing, and that vaccination must be initiated before RG membership is known, the EVPI must be estimated for the choice between all the strategies under Scenarios A and B. These estimates of EVPI use the same simulated model output as the decision uncertainty results for strategies which were discussed in the section 'Results for strategies' (p. 83). As with the analysis of EVPI for RGs, the VOI will be determined by the decision uncertainty in choosing between strategies (probability of error) and the importance of this uncertainty (the difference in NB between uncertain strategies). These two issues were presented and discussed in the section 'Results for strategies' (p. 83). The size of the patient population is also important and is clearly the same for Scenarios A and B (680,000 per year). It should be noted that the sum of the RG EVPI is not necessarily the upper bound on the strategy EVPI, even though not all the possible strategies are evaluated. The constraints imposed on the formation of strategies mean that some possible strategies have been excluded (e.g. treatment without prior screening for RG11 and 12). As seen in the section 'Overview of methods' (p. 85) exclusion of a strategy which has some probability of being cost-effective always leads to a reduction in decision uncertainty and often to a reduction in EVPI (strategy EVPI can be less than sum of RG EVPIs as in Scenario B). However, if strategies are removed which have a very similar NB to the cost-effective strategy, then the decision uncertainty will be lower but the difference in NB between the uncertain strategies which remain will be higher; the probability of error falls but the costs of error increase, therefore the EVPI may be greater (for example, in Scenario A).

The EVPIs for strategies are reported in *Table 67* for cost-effectiveness thresholds of £20,000, £25,000 and £30,000. Under both Scenarios A and B the EVPI is substantial and clearly exceeds the cost of most proposed research in this area. This suggests that further research may well be justified but it does place limits on its scale and cost. These overall EVPIs are not particularly large compared with estimates of EVPI for other decision problems in healthcare.[152,153] For example, the EVPI associated with glycoprotein IIb/IIIa antagonists for acute coronary syndrome was estimated to be £171 million and for Clopidogrel and dipyridamole in the secondary prevention of occlusive vascular events it was estimated to be £865 million in the stroke subgroup alone. However, the EVPI results in *Table 67* are in a similar range to other estimates, including for β-interferons and glatiramer acetate in the management of multiple sclerosis (£86.2 million), neurominidase inhibitors for the treatment of influenza (£66.7 million) and screening for age-related macular degeneration (£22.2 million). They are certainly greater than others, including liquid-based cytology screening for cervical cancer (£2.8 million), manual

TABLE 67 *EVPI for strategies*

	Cost-effectiveness threshold (£)		
	20,000	**25,000**	**30,000**
Scenario A			
EVPI (strategies)	56,700,000	67,300,000	63,500,000
EVPI (total RG)	35,009,460	42,432,340	52,658,067
Scenario B			
EVPI (strategies)	22,900,000	28,900,000	35,400,000
EVPI (total RG)	27,559,153	31,750,220	37,082,553

physiotherapy techniques in asthma and in chronic obstructive pulmonary disease (£16.7 million) and long-term low-dose antibiotics in children with recurrent urinary tract infections (£4.6 million). This context suggests that although research may be justified it may not be the highest of research priorities since sufficient evidence already exists to justify moving away from RCOG guidelines and current best practice (S3) [these strategies are not cost-effective and contribute nothing to these estimates of EVPI (since S1 and S3 had a zero probability of being cost-effective)]. It does suggest that further research focused on relevant subgroups (with high EVPI) and using comparators which contribute to uncertainty and EVPI could be worthwhile. However, research which focuses on other RGs or includes comparators which are not uncertain (e.g. S30, S1 and S3, which contribute nothing to decision uncertainty or VOI) will not be worthwhile and cannot be justified based on current estimates of cost-effectiveness.

Further analysis

There are a number of additional analyses which could be conducted and which would help to inform the decision on whether more research is required and, if so, which research designs would be most valuable. These include EVPI for groups of parameters in the model (EVPPI) and an analysis of the expected value of sample information (EVSI). These possible avenues for further analysis are briefly reviewed below.

Expected value of perfect parameter Information (EVPPI)

The EVPI surrounding the decision problem can indicate whether further research is potentially worthwhile. However, it would also be useful to have an indication of what type of additional evidence would be most valuable. Other measures of sensitivity or the importance of parameters rely on linearity, and/or are not directly related to decision uncertainty. Therefore, they cannot provide a measure of value that can be compared with the costs of further investigation. The value of reducing the uncertainty surrounding particular parameters in the decision model can be established using a similar approach to the EVPI for the decision problem as a whole. This type of analysis can be used to focus research on the type of evidence which will be most important by identifying those groups of parameters for which more precise estimates would be most valuable. In some circumstances, this will indicate which endpoints should be included in further experimental research. In other circumstances, it may focus research on getting more precise estimates of particular parameters which may not necessarily require experimental design and may be provided relatively quickly (e.g. evidence related to natural history, resource use and quality of life). The analysis of the VOI associated with groups of parameters is, in principle, conducted in a very similar way to the EVPI for the decision as a whole.[147–9]

More formally, suppose we were interested in the value of perfect information about a parameter or a subset (φ) of all the uncertain parameters θ. With perfect information we would know how φ would resolve (which value it will take) and the expected NB of a decision would be found by choosing the alternative with the maximum expected NB when those expected NBs are averaged over the remaining uncertain parameters in the model (ψ), that is, we take a value of φ and then calculate expected NBs over the remaining uncertainties (ψ) and choose the alternative j that has the maximum expected net benefit:

$$\max_j E_{\psi|\varphi}\, \mathrm{NB}(j, \varphi, \psi)$$

However, as before the true values of φ are unknown (we do not know which value φ will take); therefore, the expected value of a decision taken with perfect information is found by averaging these maximum expected net benefits over the distribution of φ:

$$E_{\varphi} \max_j E_{\psi|\varphi}\, \mathrm{NB}(j, \varphi, \psi)$$

The expected value with current information is the same as before because $\varphi \cup \psi = \theta$):

$$\max_j E_{\theta}\, \mathrm{NB}(j, \theta)$$

Hence the EVPPI for the parameter or group of parameters φ is simply the difference between the expected value of a decision made with perfect information and the expected value with current information:

$$\mathrm{EVPPI}_{\varphi} = E_{\varphi} \max_j E_{\psi|\varphi}\, \mathrm{NB}(j, \varphi, \psi) - \max_j E_{\theta}\, \mathrm{NB}(j, \theta)$$

It should be apparent that although this is conceptually very similar to the calculation for decision EVPI in the section 'Identifying research priorities' (p. 85), it is also more computationally intensive. This is because we have an inner and outer loop of expectation: first we must run the

simulation for parameters ψ but with a particular value of φ (an inner loop), then we must sample a new value of φ (an outer loop) and rerun the simulation. This must be repeated until we have sampled sufficiently from the distribution (or joint distribution) of φ.

The complexity of the evidence synthesis within the model makes this approach computationally very challenging. More efficient methods of estimation (such as the use of emulators) are possible but cannot practically be applied to a model with so many inter-related parameters. The computational requirements can be somewhat simplified if the model has a linear or multilinear relationship between the parameters and NB. If the model is linear in ψ, and φ and ψ are independent, then:

$$E_{\psi|\varphi}\,\mathrm{NB}(j, \varphi, \psi) = \mathrm{NB}[j, \varphi, E(\psi)]$$

This will also be true when NB is multilinear in ψ and where there are no correlations between the parameters in ψ and when φ and ψ are also independent. Multilinearity allows the NB function to contain products of (independent) parameters (as in a decision tree). This model is indeed multilinear. However, there are correlations between the parameters in ψ generated through the synthesis of evidence. Therefore, this 'short cut' is not directly available. However, it is possible to find linear functions of the parameters which will estimate NB correctly. If a linear function can be found and implemented, then EVPPI can be estimated for groups of parameters where φ and ψ are independent even if there are correlations between the parameters in ψ.[38,148] Implementing this type of approach has not been possible within the resource and time constraints of the current study.

Other issues related to VOI which could be explored include exploring the implications for value of information of different assessments of the risk associated with antibiotic exposure (see the section 'Recommendations for research', p. 97 for further discussion and analysis), exploring the sensitivity of estimates of EVPPI to other parameter values, for example new information on the performance of PCR, providing the decision-maker with some indication of the uncertainty in estimates of the value of information and exploring ways to establish an appropriate time horizon in this clinical area including the possibility of accounting for future changes (most notably the availability of vaccine).

Expected value of sample information (EVSI)

The EVPI discussed in this section only places an upper bound on the returns to further research. This provides a necessary condition for conducting further research where additional research about the decision problem as a whole or research about particular groups of parameters may be worthwhile if the EVPI or EVPPI exceeds the cost of conducting further research. However, to establish a sufficient condition, to decide if further research will be worthwhile and identify efficient research design, we need to consider the marginal benefits and marginal cost of sample information (i.e. the costs of research).

The same framework of VOI analysis can be extended to establish the EVSI for particular research designs and to compare these marginal benefits of research with the marginal costs.[145,148] This type of analysis provides a societal payoff to alternative designs and can be used to establish optimal sample size, optimal allocation of patients within a clinical trial, appropriate follow-up and which end-points should be included in the design. Indeed, in principle this framework can be used to identify a portfolio of different types of studies which may be required to provide evidence sufficient to support decisions about interventions for particular RGs and which strategies should be implemented. However, the computational challenges are significant and implementing this type of approach is beyond the resource and time constraints of the current study.

Some implications for research priorities

In the absence of a currently available vaccine, we summarise the implications of the results for Scenario B. Although there is much uncertainty in choice between interventions and strategies, there are some clear implications for research.

Risk groups

1. For all the preterm RGs there is uncertainty associated with choice of intravenous treatment but the uncertain choice is between intravenous and oral treatment. All the other interventions have a negligible probability of being cost-effective. There are exceptions to this. For example, intravenous treatment for RG3 (and RG9) is not uncertain and has over a 0.97 probability of being cost-effective.

2. There is generally more uncertainty associated with the cost-effective intervention for term RGs. For RG7–10 the uncertainty is associated with the choice between intravenous and oral treatment and other possible interventions have a negligible probability of being cost-effective.
3. It is only for RG11 and 12 that the uncertainty is associated with more than two interventions and for interventions other than IV and oral treatment.
4. For RG2, 3, 8 and 9 the EVPI is very low and indicates that additional evidence to inform the choice of intervention is not justified. The EVPI remains substantial and may exceed the cost of some proposed research in RGs, such as RG1, 5, 6, 7, 11 and 12. RG5 is associated with the largest EVPI and any subsequent research must be relevant to this group and address the decision between intravenous and oral treatment to be of most value.

Strategies

1. There is substantial uncertainty in the choice between certain strategies. For example, given Scenario B, the choice between S99 and S84, S102 or S101 accounts for most of the decision uncertainty, with other strategies contributing more modestly or not at all (see probabilities of cost-effectiveness in *Table 55*).
2. For these uncertain choices, the differences in NBs are not large (although at a population level they do represent important net QALYs gains).
3. Some choices are not uncertain. For example, many of the strategies of policy interest have a zero probability of being cost-effective and there is no uncertainty in rejecting these based on existing evidence. These include S30, S1 and S3, which represent the no treatment, RCOG guidelines and current best practice, respectively: the differences in NB between S99 and these strategies are large and could result in a substantial annual improvement in health outcomes for the healthcare system as a whole (see the section 'Results for strategies', p. 83).

Overall EVPI

The EVPI suggests that although research may be justified, it may not be the highest of research priorities, since sufficient evidence already exists to justify moving away from the RCOG guidelines and current best practice. Further research focused on relevant subgroups (with high EVPI) and using comparators which contribute to uncertainty and EVPI may be worthwhile. However, research that focuses on other RGs, or includes comparators which are not uncertain, is unlikely to be worthwhile and may not be justified based on current estimates of costs and effects.

Of course, this summary of implications is based on the cost-effectiveness analysis and the synthesis of evidence on which it is built. There may well be other issues to consider in forming research recommendations, in particular the harms of antibiotic exposure. This is discussed in the section 'Accounting for antibiotic exposure' (p. 69).

Chapter 9
Discussion

Analytic approach

One strength of the study was the consideration of women in 12 separate RGs that could lead to different treatment policies. This approach allowed us to reflect closely the decision options considered by clinicians when assessing women presenting in suspected labour. On a population basis, it provides the most comprehensive assessment yet published of the effectiveness of the range of possible interventions for women to prevent early-onset neonatal bacterial infection. A further strength of the study is the extent to which we included all available data, not just data that directly informed nodes on the decision tree. This approach inevitably led to the inclusion of correlated variables and therefore required the use of Bayesian evidence synthesis methods. Nevertheless, some simplifying assumptions were made. First, it was assumed that the relative treatment effects were constant across all risk groups. This assumption was investigated using trials of prenatal treatment for EOGBS in high- and low-risk women and no evidence was found that the baseline risk in the control groups or relative treatment effects differed. Lack of data meant that this assumption could not be examined for EO non-GBS. Second, it was assumed that the treatment effect on mortality did not differ from the effect on infection status except in the case of stillbirths. Third, by restricting the model to the current pregnancy, the NBs of vaccination, which would protect subsequent births, were underestimated. Fourth, oral antibiotic treatment for preterm prelabour ROM and, possibly, vaccination,[32] increase the duration of pregnancy. These outcomes, and any maternal benefits or harms of treatment, were beyond the scope of the study and were not included. Fifth, the infection outcome was restricted to culture positive bacteraemia or meningitis. Provided that the risk of culture-negative EO non-GBS is similar to that for EOGBS (estimated to be between 1.2 and 2.3 times more common than culture-positive disease.[36,37]), the relative ranking of strategies would not change, although the overall NB would increase (assuming that the interventions reduce culture-negative disease).

The most important omission from the study was the potential for antibiotic treatment to cause pathogen selection and/or the emergence of antibiotic-resistant pathogens, which in turn could cause serious bacterial infection in the baby. This effect has been suggested by time trend analyses of bacteraemia in the USA, which have shown a possible rise in the proportion of early-onset bacteraemia due to Gram-negative bacteria.[3,154] A higher than expected proportion of Gram-negative bacteraemia was due to ampicillin-resistant organisms in two studies and associated with intrapartum treatment with ampicillin. However, this evidence is based on very few cases, and the data from time trend analyses are highly susceptible to publication and reporting bias.[3] Our decision to exclude these adverse effects of antibiotics was based on the fact that the evidence for an association is weak and relates to ampicillin, which was not considered in our model. Second, inclusion would have required a much broader systematic review and a different model structure and analytic approach in order to address the relative contributions of intrapartum treatment, other antibiotic use in the hospital, treatment of women during pregnancy and antibiotic use in the wider community. We considered the last item to be beyond the available evidence and our resources. Nevertheless, a crude analysis was performed to quantify how the harms of antibiotic exposure could be valued in terms of net QALYs (see the section 'Accounting for antibiotic exposure', p. 69).

Generalisability of findings

Generalisability of model outputs

The model was based on data inputs that represented the best available evidence at the time of the review (end of 2005). One characteristic that could change is the prevalence of maternal colonisation. In the model, the mean prevalence of maternal colonisation was 12%, based on a random effects mean estimate from nine UK studies conducted between 1975 and 2005 (and following adjustment by the Bayesian model; see the section 'Maternal colonisation with GBS', p. 20). The most

recent study reported a prevalence of 22% and raises the possibility that prevalence has increased over the last two decades. Many European and North American studies have reported similarly high rates.[7] From a policy perspective, if the mean prevalence of maternal colonisation is 22%, rather than the mean of 12.2% (95% CI: 9.03 to 15.9%) used in the model, and the overall incidence of EOGBS remains constant, there would be less NB to be gained from moving to a strategy involving routine testing of low-risk term groups (e.g. moving from strategy 7, treat all preterm and high-risk term groups, to strategy 83, add culture-based testing to low-risk term women).

Another characteristic that may vary over time or between settings is the proportion of EOGBS compared with EO non-GBS pathogens in each maternal risk group. Data were used for the most recent 5 years of bacteraemia reports in England and Wales (unpublished data provided by the HPA; see Appendix 1, *Table 75*). Overall, EOGBS comprised about one-third of all first-week bacteraemia reports (excluding coagulase-negative staphylococci). Elsewhere, EOGBS has been reported to comprise closer to half of all first-week bacteraemia reports.[155–157] An increase in the proportion of bacteraemia due to EOGBS would increase the relative effectiveness of strategies involving GBS testing compared with treating all high-risk women.

The accuracy of PCR testing is also likely to change over time and between settings. At present there are no data on the accuracy of this test in routine practice in the UK and it was assumed that accuracy would be in the same range as reported in a large multicentre North American study.[158] Test performance could differ in the NHS, and in the future, test development may lead to improved accuracy and/or reduced costs of tests, thereby reversing the relative net benefit of culture-based testing over PCR. The possibility of equivocal or unclassifiable test results was ignored as this problem was not mentioned in the studies reviewed.

Generalisability of model to practice

The model is inevitably a simplification of practice. In reality, women present in one RG and may deliver in another. For example, women may present with suspected preterm labour and intact membranes (RG6), fail to progress and deliver a few weeks later as a low-risk woman with no risk factors (RG12). We chose not to construct a Markov model to reflect movement of women from one RG to another before delivery. Instead, only the last RG that the woman occupied before she delivered was considered and costs of tests or treatments were ignored if they did not pertain to that group or that related to tests undergone before the RG was known and then not used. These costs were greatest for women undergoing culture based testing at 35–37 weeks whose test results were later ignored (about 4% of all women). Up to half of all women who delivered preterm (RG1–6), and those delivering at term with pyrexia (RG10), would have had a culture test result which, even if it were negative, would be ignored, as all women in these groups are better off treated. This additional cost would reduce but not eradicate the higher NB of culture based testing at 35–37 weeks compared with PCR testing (reducing the difference in net costs from approximately £3 to £2.50).

A further cost not included is the additional time required to explain the need for treatment to high-risk women with a negative culture result for EOGBS. We also ignored the possibility that a negative test result might reduce compliance with treatment in the high-risk groups, thereby reducing the NB of strategies involving culture testing.

The model was based on decisions made at presentation in suspected labour. At this point, term women with prolonged ROM (RG11) are indistinguishable from women with no risk factors (RG12). This combined group has a 'low risk' of early-onset neonatal bacterial infection (0.866 per 1000 women; Appendix 6, *Table 124*). However, if considered separately, women with prolonged ROM have a much higher risk of early-onset infection (2.046 per 1000 women) and account for 11% of all early-onset infections (Appendix 6, *Table 123*). An alternative model could evaluate deferral of treatment in RG11 until 18 hours after membrane rupture, provided that women in RG12 were not treated. Given the high risk for RG11, it is likely that deferred treatment would be cost-effective, assuming the same treatment effect as at presentation.

The most appropriate oral treatment will depend on the prevalence of antibiotic resistance. Results were used from the large MRC ORACLE trials in the UK, which evaluated erythromycin, co-amoxiclav or both against placebo. Erythromycin has been recommended for women with preterm prelabour membrane rupture in the UK where resistance of GBS to erythromycin is 10–15%.[1] In countries with higher levels of resistance, a penicillin-based treatment may be more effective.

Data inputs for the timing of testing and treatment were based on the assumption that women present to an obstetric unit at the onset of labour (or at preterm ROM, whichever happened first), when a decision is made about treatment or PCR testing. In practice in the UK, women with no risk factors are encouraged to labour at home, and to attend hospital relatively late in labour (Brocklehurst P, National Perinatal Epidemiology Unit: personal communication, July 2006). The implications for our results are that fewer women in RG11 and 12 would undergo PCR testing and treatment than estimated.

Neonatal care may also differ in practice from that considered in the model. We included costs for the care of babies with early- or late-onset infection, but did not include costs for those admitted for observation and testing. The number admitted may vary depending on the strategy used. For instance, anecdotal reports suggest that some neonatologists require babies born to high-risk women or to women with a positive GBS culture who were treated for less than 4 hours intrapartum to remain in hospital for observation for 12–24 hours.[159] Such practice was not included in the model as it is not based on evidence of benefit or on widely accepted guidelines (Embleton N, Newcastle Neonatal Service: personal communication, June 2006) but could potentially increase costs of testing strategies for low-risk women.

Finally, the model was restricted to consideration of a single type of antibiotic treatment and assumed that women given oral treatment would have treatment stopped once in established labour (assumed to be within 6 hours of delivery), as is current practice for preterm prelabour ROM (Hughes R, Royal College of Obstetricians and Gynaecologists: personal communication, July 2006). In practice, it may be more acceptable to clinicians to continue treatment with intravenous penicillin after the onset of labour, which would add a small additional cost to this strategy. Similarly, when oral treatment is used prior to elective Caesarean section (RG1 and 7), it may make sense to continue with intravenous treatment during the 4 hours prior to operation when no oral intake is allowed.

Comparison with previous cost-effectiveness analyses

The findings cannot be directly compared with previous studies for several reasons. First, none measured the effect of prenatal testing and treatment on early-onset infection due to GBS **and** non-GBS bacterial pathogens. Previous studies may therefore have overestimated the benefits of GBS testing strategies relative to treating all women (or all women in a specific RG) because they ignored the benefits of antibiotic treatment for EO non-GBS. Second, none included as extensive a review of the available data, and data inputs based on our systematic reviews and meta analyses would differ. Third, none of the previous studies used a Bayesian approach to integrate all the available evidence. All previous studies used deterministic modelling methods, which assumed that the GBS natural history parameters were independent and ignored the many correlations between them. Finally, this is the first cost-effectiveness study in a UK context. Previous studies were largely based on North American data for the burden of disease, natural history of GBS and healthcare costs. Results are therefore likely to differ. *Table 68* briefly summarises the previous GBS cost-effectiveness analyses and why they are not comparable to the present study.

Implications for policy

Current best practice, comprising intravenous treatment for pyrexia, previous GBS baby and previous GBS swab or urine culture, and oral treatment for preterm prelabour ROM (RG2, 3, 4, 5, 8, 9, 10, strategy 3) was not cost-effective. All cost-effective options involved treatment of all preterm groups (RG1–6) and high-risk term groups (RG8–10).

Universal screening using PCR or culture was not cost-effective and this result was not uncertain. This is because testing high-risk women for maternal GBS colonisation is not worthwhile as even those with negative results would be better off treated to reduce the risk of early-onset non-GBS infection.

In the absence of vaccination, culture-based testing of women in RG11 and 12, combined with treatment for the rest (strategy 99), would be the cost-effective strategy. If vaccination was available, vaccination for all, and treatment for RG1–10 (strategy 156) would be marginally more cost-effective, but this is uncertain (NB for 680,000 deliveries per year in the UK: £50.6 million, compared with £48.5 million for strategy 99).

Two limitations of the analysis are the exclusion of adverse effects of antibiotics and organisational costs to implement (or reverse) a new intervention.

TABLE 68 *Characteristics of previous cost-effectiveness analyses of GBS prevention strategies*

Study	Strategies compared	Outcomes	Modelling methods	Comments
Mohle-Boetani (1993)[160] USA context	Culture screening followed by treating only positives in high-risk groups vs treat all in high-risk groups with labour complications vs vaccination vs do nothing	Cost per GBS case prevented	Deterministic; all parameters independent of each other	Combinations of strategies not modelled; all cases assumed to have equal costs
Fargason (1997)[161] USA context	CDC guidelines (including PCR testing as well as culture)	Costs per EOGBS case prevented	Deterministic	Model only considers term women; questionable values for some parameters
Mohle-Boetani (1999)[159] USA context	Risk factor-based screening strategy vs do nothing	Costs, benefits in life-years; GBS only considered	Deterministic	Some parameters not based on research evidence
Benitz (1999)[162] USA context	Risk factor-based screening, vs culture screening vs rapid test screening; intrapartum treatment vs intrapartum and postpartum treatment	Number of cases; cost per case of EOGBS prevented	Deterministic	Some parameters not based on research evidence
Stan (2001)[132] Switzerland context	Current risk factor screening vs extended risk factor screening vs culture screening	Number of cases; cost per case of EOGBS prevented	Deterministic	Some parameters not based on research evidence
van den Akker-van Marle (2005)[163] The Netherlands context	Risk factor-based strategy, testing (culture and PCR) and treatment, risk factor-based strategy and screening, Dutch guidelines, do nothing	Cost per QALY; EOGBS only considered	Deterministic	Some parameters not based on research evidence
Sinha (2005)[32] USA context	Vaccination [adolescent, maternal (prenatal), postpartum] vs current practice (culture-based chemoprophylaxis)	GBS cases and deaths prevented only	Deterministic	Costs of interventions not considered

In outlining policy, it is assumed that it is worthwhile to minimise antibiotic exposure, and that adding to current practice would be easier to implement than changing it.

Extension of clinical recommendations

Current best practice involves treating 7.4% of women. Our results suggest that extension of clinical recommendations to treat **all** preterm women, while continuing to give the same treatments to high-risk term women (strategy 7), would increase the NB for the UK per year from £21.4 million to £35.1 million and increase the proportion of women treated to 11%. Although strategy 7 had a zero probability of being cost-effective at a threshold of £25,000, it represents a necessary step in the implementation of more cost-effective strategies for which the optimal choice is uncertain.

Adoption of routine testing

In the absence of vaccination, the cost-effective option is culture-based testing of women in RG11 and 12, combined with treatment for the rest (strategy 99, NB £48.5 million). An alternative strategy, in which women with elective Caesarean section at term (RG7) also undergo culture testing (strategy 83), would generate marginally less benefit (£46.5 million), but reduce treatment to 21% of all women (from 27%). Compared with strategy 7 (treatment of high-risk groups without any routine testing), adoption of strategy 83 would gain a further £11.4 million in NB for the UK per year and would be logical if the harm of exposing every additional 145 women to antibiotics (on top of the 11% already treated under strategy 7) is considered to be equivalent to less than one QALY. Routine testing using culture was less effective than PCR testing, but cheaper, thereby resulting in more NB.

Adoption of vaccination

If vaccination becomes available, the cost-effective strategy (strategy 156, NB £50.6 million) would be vaccination for all and treatment of RG1–10 (19% of all women treated). Fewer women would be treated (11%) for a small loss in NB (NB £49.2 million) if RG7 was not treated (strategy 15). Vaccination for all and no intervention for low-risk women (RG7, 11 and 12; strategy 15) generates £2.7 million more NB for the UK per year than culture-based testing for low-risk women (strategy 83). Moreover, the addition of vaccination would **not** increase exposure to antibiotics. Strategy 15 therefore offers the best of these two options.

Our results suggest that immediate extension of current practice to treat all preterm and high-risk term deliveries could be beneficial. Thereafter, it is not clear whether the optimal choice would be culture-based testing for low-risk women or vaccination plus treatment of all preterm and high-risk term women. There are also important issues of timing. Vaccination is unlikely to be available for the next 5 years and could not be implemented without Phase III trials, which will substantially reduce uncertainty over vaccine efficacy. In the meantime, implementation of culture testing for low-risk women appears to be the most cost-effective option but implementation costs could be significant and not recouped if, subsequently, a vaccination strategy was adopted.

Recommendations for research

The EVPI analyses indicated that further research could be worthwhile (providing maximum returns of between £29 million and £67 million for the UK). The following research is recommended, in order of priority.

1. Research on the effectiveness of GBS vaccination, compared with no treatment or routine testing for low-risk groups, would be valuable and is needed anyway to gain a licence. The results should be used to re-evaluate the cost-effectiveness of vaccine.
2. The proposed very large cluster randomised trial of culture-based testing versus no intervention for low-risk women plus treatment for high-risk women in both arms, would base the primary results on aggregate rates of neonatal infection.[1,16] The difference between the trial arms would be in the low-risk groups, who would receive testing or no intervention. These low-risk groups would not be separately identifiable from high-risk deliveries, who would be treated in both trial arms and would account for 41% of EOGBS. This would complicate interpretation of the trial. The consequent dilution of the treatment effect would require a large increase in sample size compared with a trial in which RGs were identifiable. A trial that compared culture with PCR testing or no intervention in the low-risk term groups (RG7, 11 and 12) would be informative, but would need to be extremely large.
3. More information on the effectiveness of antibiotics is likely to be most valuable for EO non-GBS, for which data are limited. Such information may be available from secondary analyses of datasets from previous studies of intrapartum antibiotics that reported neonatal bacteraemia, but contain data specifying the type and timing of bacteraemia.
4. Comparison of oral and intravenous treatment could be valuable, as this might better inform treatment in preterm groups 1, 5 and 6.
5. More information on the consequences of infection outcomes for disability, quality of life, healthcare costs and life expectancy could be valuable.
6. Further EVPI analysis aimed at specific sets of parameters could throw further light on the research priorities.[38,148]

Acknowledgements

Expert advisors

We are very grateful to the following, who acted as expert advisors to the project. They provided valuable input to the design of the model and contributed information for specific model inputs. Professor Carol J. Baker, Pediatrics and Molecular Virology and Microbiology, Head of the Section of Infectious Diseases, Baylor College of Medicine, Houston, TX, USA; Dr Jim Gray, Consultant Microbiologist, Birmingham Children's Hospital, UK; Professor David Isaacs, Clinical Director of Education and Clinical Professor, University of Sydney, Australia; Ms Sara Kenyon, Senior Research Fellow, University of Leicester, UK; Dr Mike Millar, Consultant Microbiologist, Royal London Hospital, UK; Professor Deirdre Murphy, Professor of Obsterics and Gynaecology, University of Dundee and Ninewells Hospital and Medical School, UK.

The following were co-applicants for this project and provided valuable input into the project, especially during the early stages: Mark Sculpher, Centre for Health Economics, University of York, UK; Khalid Khan, Department of Obstetrics and Gynecology, University of Birmingham, Birmingham Women's Hospital, Birmingham, UK.

Nicky Welton, MRC Health Services Research Unit, Bristol, UK, contributed to the development of the WinBUGS model, particularly in relation to the value of information analyses.

Data contributors

Access to primary datasets was critical to the study and made it possible to develop a relatively detailed model. Data contributors provided their data promptly, free of charge, and responded in full to queries about their data. As far as we are aware, they gain no academic recognition for this.

- *SMMIS database*: Thanks to Mark Little and Phil Steer for access to these data, which provided detailed characteristics of 585,000 pregnant women over a 13-year period.
- *BPSU GBS database*: Thanks to Paul Heath for access to these data, which have details of all cases of EOGBS and LOGBS in the UK and Ireland over a 13-month period.
- *Northern Region EOGBS database*: Thanks to Sam Oddie and Nick Embleton for access to these data, which provided detailed characteristics of 37 cases of EOGBS.
- *HPA data*: Thanks to Georgia Duckworth, Theresa Lamagni and Catherine Goodall for providing data on cases of first-week bacteraemia by organism type from the routine laboratory surveillance programme for England and Wales for a period of 11 years.
- *RFH, RLH, UCL database*: Thanks to Dominique Acolet (Royal Free Hospital), Mike Millar (Royal London Hospital) and Sîan Harding and Paul Ostro (UCL Hospital) for providing data on cases of neonatal infection including gestation at delivery.
- *1985–7 neonatal meningitis database*: Thanks to Helen Bedford, John de Louvois and Sue Halket for providing these data from a national surveillance study of meningitis in infancy in England and Wales between 1985 and 1987, including organism type responsible for infection.
- *1996–7 neonatal meningitis database*: Thanks to Sue Halket and John de Louvois for providing these data from a national surveillance study of neonatal meningitis in England and Wales between 1996 and 1997, including organism type responsible for infection.
- *Northern Region neonatal deaths database*: Thanks to Nick Embleton and the Regional Maternity Survey Office for giving us access to these data from an ongoing regional survey of all deaths in infancy that included 695 cases of neonatal death caused by infection in the former Northern Health Region of England between 1981 and 2000.

Data contributed but not used in the project

Thanks are due to Jim Gray for providing data on the gestation at which 100 high vaginal swabs were taken at Birmingham Women's Hospital. These data were intended to be used to calculate the colonisation rate at pregnancy of women with a previous positive swab but were eventually not required.

Contribution from expert groups

Protocol Development Group – funded by the Health Technology Assessment Programme

We are grateful for comments on the study design and preliminary findings presented to this group at meetings in October 2005 and April and July 2006. Membership of the group is as follows: Julia Drown, Former Chair of Parliamentary Select Committee in Maternity Services (Chair); Dr Peter Brocklehurst, NPEU, Oxford (Project Leader); Dr Rhona Hughes, Obstetrician, Edinburgh (representing Royal College of Obstetricians and Gynaecologists) (co-applicant); Ms Sara Kenyon, Senior Research Fellow, Leicester (co-applicant); Dr Christine McCartney, Health Protection Agency, London, (co-applicant); Mary Newburn, National Childbirth Trust, London (co-applicant); Mr Stavros Petrou, Health Economist, Oxford (co-applicant); Dr Ben Stenson, Neonatologist, Edinburgh (co-applicant). Other members include: Professor Zarko Alfirevic, Obstetrician, Liverpool; Dr Alison Bedford-Russell, Neonatologist, Heart of England NHS Trust; Ursula Bowler, Trials Coordinator, NPEU, Oxford; Professor Malcolm Chiswick, Neonatologist, Manchester; Dr Androulla Efstratiou, Microbiologist, Health Protection Agency, London; Dr Paul Heath, Infectious Disease Paediatrician, London; Professor Jenny Hewison, Psychologist, Leeds; Mervi Jokinen, Midwife, London (representing Royal College of Midwives); Dr Theresa Lamagni, Epidemiologist, Health Protection Agency, London; Professor Neil Marlow, Neonatologist and Developmental Paediatrician, Nottingham; Dr P Melin, Consultant Microbiologist, Liège, Belgium; Dr Jane Norman, Obstetrician, Glasgow; Professor Michael Parker, Ethicist, ETHOX, Oxford; Ms Jane Plumb, GBS Support, London; Maria Quigley, Head of Trials, NPEU, Oxford; Professor David Taylor, Obstetrician, Leicester; Mrs Pat Ward, National Antenatal Screening Programme Coordinator, Northampton; Professor Martin Whittle, Chair Antenatal Subgroup of National Screening Committee, Birmingham; Joanne Woodward, Midwife; Liz Schroeder, Health Economist from the NPEU; Jane Daniels, Trials Unit Coordinator, Birmingham Trials Unit.

UK National Screening Committee Group B Streptococcus Coordinating Group

We are grateful for comments on the preliminary findings of the study, which were presented to a meeting of the group in June 2006. Members of the group at this meeting were: Catherine Peckham (Chair); John Marshall (Project Manager, antenatal screening programmes); Phil Steer (Obstetrician); Jane Plumb (GBS support group); Jennie Carpenter (Department of Health); Ben Stenson (Neonatalogist); Androulla Efstratiou (Health Protection Agency); Rhona Hughes (Obstetrician, RCOG).

Contribution of authors

Tim Colbourn (Research Fellow, Epidemiology) made significant input into the model structure and carried out all the systematic reviews of the literature and analyses of primary data. He was responsible for checking the data used in the model and also the results, wrote much of the report and contributed to the interpretation of the results. Christian Asseburg (Research Fellow, Health Economics) further developed the WinBUGS model following its initial creation by TA, and was responsible for all the modelling in WinBUGS and R. He contributed to the interpretation of the results. Laura Bojke (Research Fellow) contributed to the model structure, modelled the 'downstream' non-correlated parameters of the model using Excel and drafted sections of the report on costs and utilities and cost-effectiveness analyses. Zoe Philips (Health Economist) developed the initial model structure in Excel and produced outputs, which were later superseded by the WinBUGS model, gathered data on costs and utility values and reviewed previous cost-effectiveness studies. Karl Claxton (Professor of Economics) contributed to the development of the model structure and led the cost-effectiveness and value of information analyses. He wrote sections of the report and made a major input to the interpretation of results. Tony Ades (MRC Senior Scientist) helped to conceive and develop the model structure and was responsible for the evidence synthesis approach. He wrote sections of report dealing with the principles of evidence synthesis and treatment effects and made a major input to the interpretation of the results. Ruth Gilbert (Reader in Clinical Epidemiology) was the principal investigator for the project and made significant input into the model structure and systematic reviews. She contributed to decisions in all areas of the project and was responsible for overall coordination and running of the project, writing of the report and interpretation of the results.

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Appendix 1

Systematic reviews: included and excluded studies

TABLE 69 *Maternal risk group distribution*

Preterm delivery rate in the total population
Primary data source

Database name	Details of included cases	Variables measured	Results
NHS Maternity Statistics 2003/04 (HES)[51] UK	All pregnant women delivering in all hospitals in England (85% of UK population, therefore representative of the UK) in 2003–4; routine data collection	Gestation at delivery (also delivery complications, methods of delivery, multiple births, etc.)	See the text[a]

Proportion of the total population of pregnant women in risk groups 1, 4–6, 7, 10–12
Primary data source

Database name	Details of included cases	Variables measured	Results
SMMIS, 2005 UK	All pregnant women giving birth between 1 January 1999 and 31 December 2000 (database contains info from January 1988 to December 2000, but only 1999–2000 used) at St Mary's Hospital, UK	Information on maternal characteristics, history, pregnancy, labour, obstetric complications, the baby	See the text[b]

Previous GBS baby in the total population of pregnant women
Excluded studies: Halliday (2000)[52] (2 out of 1000; 0.2%); Oddie (2002)[53] (2 out of 147; 1.4%); Heath, personal communication from Law (2005)[54] (2 out of 773; 0.3%) – all had too high rates as compared with the background rate of EOGBS in the total population

'GBS bacteriuria/previous positive swab' in the total population of pregnant women
Included studies

Study	Participants – inclusion criteria	Outcome measure	Results	
			No. of women	GBS bacteriuria
White (1984)[55] (correspondence only) UK	Urine samples taken antenatally, culture method not specified	*GBS bacteriuria:* no details	8083	137 (1.7%)
Hastings (1986)[56] UK	Urine samples sent to laboratory from antenatal clinics and processed with enriched media	10^5 CFU/ml^{-1} of uncentrifuged urine (pure bacterial growth) was considered significant bacteriuria	250	4 (1)[c] (0.4%)

continued

TABLE 69 *Maternal risk group distribution (cont'd)*

Study	Participants – inclusion criteria	Outcome measure	Results			
				Pure/predom.	Mixed	Total
McKenzie (1994)[57] UK	Urine samples taken at booking (and 27–29 weeks) and processed using non-enriched culture dip slides	Pure/predominant growth and mixed cultures were reported. Detection limit of 1000 ml^{-1}	**Booking** 1971	16	69	85 (4.3%)
Excluded studies: Halliday (2000);[52] Oddie (2002)[53] – only some and not all of the women were tested in both of these studies						
Preterm/term split of pregnant women with 'GBS bacteriuria/previous positive swab' *Included studies*						
Study	**Participants – inclusion criteria**	**Outcome measure**	**Results**			
				Total	**Preterm**	
White (1984)[55] (correspondence only) UK	Urine samples taken antenatally, culture method not specified	*GBS bacteriuria:* no details *Preterm delivery:* <37 weeks	**GBS bacteriuria** **No GBS bacteriura** OR of preterm delivery given GBS bacteriuria: 1.53	137 7946	10 389	
Moller (1984)[58] Denmark	Urine samples taken between 21 and 38 weeks and processed using non-enriched culture	*GBS bacteriuria:* detection limit of 100 ml^{-1} *Preterm delivery:* <37 weeks	**GBS bacteriuria** **No GBS bacteriura** OR of preterm delivery given GBS bacteriuria: 2.72	68 2677	14 233	
Persson (1986)[60] Sweden	Urine samples taken at delivery and processed using enriched culture *Other inclusion criteria:* this was a case–control study and cases and controls were matched for maternal age *Exclusions:* women were cultured from urine 3 times during gestation and treated with antibiotics when found to have ⩾100,000 GBS ml^{-1}	*GBS bacteriuria:* detection limit of 10 ml^{-1}; divided into ⩾10,000 and <10,000 ml^{-1}	**GBS bacteriuria** **No GBS bacteriura** OR of preterm delivery given GBS bacteriuria: 0.97	125 183	6 9	
Thomsen (1987)[59] Denmark	Urine samples taken between 27 and 31 weeks and processed using non-enriched culture. This study was a trial on i.v. antibiotics for GBS bacteriuria in order to prevent resulting preterm delivery and pROM	*GBS bacteriuria:* detection limit of 100 ml^{-1} *Preterm delivery:* <37 weeks	**GBS bacteriuria** **No GBS bacteriura** OR of preterm delivery given GBS bacteriuria: 12.20	32 4053	12 190	

continued

TABLE 69 *Maternal risk group distribution (cont'd)*

Study	Participants – Inclusion criteria	Outcome measure	Results		
				Total	Preterm
McKenzie (1994)[57] UK	Urine samples taken at booking (and 27–29 weeks) and processed using non-enriched culture dip slides	*GBS bacteriuria:* pure/predominant growth and mixed cultures were reported; detection limit of 1000 ml^{-1} *Preterm delivery:* <37 weeks	**At booking** **GBS bacteriuria**[d] **No GBS bacteriura** OR of preterm delivery given GBS bacteriuria: 0.47	 85 1886	 3 135
Excluded studies: Thomas (1989)[164] – the rate of preterm delivery rate in women with GBS bacteriuria is unclear as the dominator is greater than that given for the total number of bacteriuria cases					

[a] See the section 'Maternal risk group distribution' (p. 17).
[b] See the sections 'Maternal risk group distribution' (p. 17) and 'Stillbirths' (p. 34).
[c] 3 out of the 4 samples were only isolated on enriched media and not using the standard non-enriched media and so were not counted in our analysis.
[d] Includes pure/predominant and mixed cultures.

TABLE 70 *Maternal colonisation with GBS during labour*

Maternal colonisation with GBS in the total population
Included studies: Untreated pregnant women in the UK tested for colonisation during labour/delivery

Study	Participants – inclusion criteria	Outcome measure	Results		
			Total women	No. colonised	% colonised
Reid (1975)[64] Aberdeen	Random sample of women over a 12-week period; swabs taken before ROM where possible *Exclusions:* none stated	Maternal GBS colonisation *When:* before delivery *Where:* vagina *Culture method:* enriched	369	18	4.9
Finch (1976)[65] London	Women in labour with intact membranes, admitted non-consecutively (but unselectively) to maternity unit *Exclusions:* assume that women with prelabour ROM were excluded	Maternal GBS colonisation *When:* labour *Where:* vaginal *Culture method:* enriched	110	7	6.4
Mhalu (1977)[66] London	Women in maternity unit of Hammersmith Hospital *Exclusions:* none stated	Maternal GBS colonisation *When:* labour *Where:* vaginal/rectal *Culture method:* enriched	125	23	18.4
Easmon (1981)[67] London	Mothers from labour and postnatal wards *Exclusions:* none stated	Maternal GBS colonisation *When:* labour *Where:* vaginal/rectal *Culture method:* enriched	600	88	14.7
Murphy (1982)[68] Cardiff	Pregnant women	Maternal GBS colonisation *When:* labour *Where:* vaginal/rectal *Culture method:* enriched	194	40	20.6
Needham (1982)[69] London	Unselected women entering the delivery suite *Exclusions:* none stated	Maternal GBS colonisation *When:* labour *Where:* vaginal *Culture method:* enriched	134	14	10.4
Easmon (1985)[70] London	Prospective cohort (not specifically defined) *Exclusions:* none stated	Maternal GBS colonisation *When:* labour *Where:* vaginal/rectal *Culture method:* enriched	887	151	17.0

continued

TABLE 70 *Maternal colonisation with GBS during labour (cont'd)*

Study	Participants – inclusion criteria	Outcome measure	Results		
			Total women	No. colonised	% colonised
Simpson (1994)[71] London	Women presenting to delivery suite, Homerton Hospital, Hackney *Exclusions:* none stated	Maternal GBS colonisation *When:* labour *Where:* vaginal *Culture method:* enriched	266	38	14.3
Gray (2005) so far (personal communication) Birmingham	Women presenting in labour willing to undergo swabbing	Maternal GBS colonisation *When:* labour *Where:* vaginal/rectal *Culture method:* enriched	286	63	22.0

Association of preterm delivery with GBS colonisation during labour
Included studies

Study	Participants – inclusion criteria	Outcome measure	Results		
				GBS colonised	Not GBS colonised
Baker (1973)[72] USA	GBS-colonised women *When:* admission to labour area *Where:* vagina (and throat) *Culture method:* enriched	Preterm delivery: premature onset of labour <37 weeks	**Preterm** **Term** OR of GBS colonisation given preterm delivery: 1.18	2 50	5 148
Dawodu (1983)[73] Nigeria	GBS-colonised women *When:* labour *Where:* vagina *Culture method:* enriched	Preterm delivery: premature onset of labour <37 weeks	**Preterm** **Term** OR of GBS colonisation given preterm delivery: 1.14	6 3	22 159
Persson (1986)[60] Sweden	GBS-colonised women *When:* admission for delivery *Where:* vagina/rectum/urine *Culture method:* enriched Case–control study	Preterm delivery: delivery <37 weeks	**Preterm** **Term** (159/183 were rectally colonised, 108/183 vaginally and 64/183 had bacteriuria. Therefore, it is highly likely that nearly all of the 183 women were vaginally/rectally colonised) OR of GBS colonisation given preterm delivery: 1.24	11 172	9 174
Joshi (1987)[74] Canada	GBS-colonised women *When:* admission for labour/delivery *Where:* vagina *Culture method:* non-enriched	Preterm delivery: delivery <37 weeks	**Preterm** **Term** OR of GBS colonisation given preterm delivery: 2.96	17 54	289 2718

continued

TABLE 70 *Maternal colonisation with GBS during labour (cont'd)*

Study	Participants – inclusion criteria	Outcome measure	Results		
				GBS colonised	**Not GBS colonised**
Martius (1988)[75] USA	GBS-colonised women *When:* labour *Where:* vagina *Culture method:* enriched *Other inclusion criteria:* case–control study (cases = preterm labour, controls = term delivery). *Exclusions:* women under 16 years, antibiotics in the last 2 weeks, diabetes, chronic heart disease, renal disease, chronic hypertension, pregnancy induced hypertension, cervical cerclage, placental abruption or previa, multiple gestation, congenital malformations	Preterm delivery: delivery <37 weeks	**Preterm** **Term** OR of GBS colonisation given preterm delivery: 2.65	21 25	40 126
McDonald (1991)[76] Australia	GBS-colonised women *When:* admission to labour ward *Where:* vagina *Culture method:* enriched *Other inclusion criteria:* case–control study. Women admitted in preterm or threatened preterm labour. Comparison group was consecutively enrolled women in term labour *Exclusions:* women in threatened preterm labour who did not deliver within 7 days/before 37 weeks gestation	Preterm delivery: delivery <37 weeks	**Preterm** **Term** OR of GBS colonisation given preterm delivery: 0.85	34 52	394 514
Citernesi (1996)[77] Italy	GBS-colonised women *When:* delivery *Where:* vagina *Culture method:* unenriched	Preterm delivery: delivery <37 weeks	**Preterm** **Term** OR of GBS colonisation given preterm delivery: 1.36	18 188	293 4173

continued

TABLE 70 *Maternal colonisation with GBS during labour (cont'd)*

Study	Participants – inclusion criteria	Outcome measure	Results		
				GBS colonised	**Not GBS colonised**
Kubota (1998)[78] Japan	GBS-colonised women *When:* admission for labour *Where:* vagina *Culture method:* non-selective *Other inclusion criteria:* women who had both sets of screening *Exclusions:* women seen after 27 weeks' gestation, those with specimens unavailable on admission and those receiving antibiotics before the second screening	Preterm delivery: premature onset of labour <37 weeks	**Preterm** **Term** OR of GBS colonisation given preterm delivery: 1.50	7 78	30 500
Feikin (2001)[79] Denmark	GBS-colonised women *When:* labour *Where:* vagina *Culture method:* non-selective *Other inclusion criteria:* ⩾18 years, understand Danish, singleton pregnancy *Exclusions:* previous child with congenital malformations, multiple gestation, not delivered at Odense University Hospital, failure to complete questionnaire, moved away, elected withdrawal, induced/spontaneous abortions, fetal loss, home delivery, placenta previa	Preterm delivery: preterm delivery <37 weeks	**Preterm** **Term** OR of GBS colonisation given preterm delivery: 2.11	12 22	72 278
Hammoud (2002)[80] Kuwait	GBS-colonised women *When:* admission to delivery room *Where:* vagina/rectum *Culture method:* not stated	Preterm delivery: premature onset of labour <37 weeks	**Preterm** **Term** OR of GBS colonisation given preterm delivery: 1.01	28 167	132 793
Wilk (2003)[81] Poland	GBS-colonised women *When:* at delivery *Where:* vagina *Culture method:* non-enriched	Preterm delivery: delivery <37 weeks	**Preterm** **Term** OR of GBS colonisation given preterm delivery: 2.39	9 14	134 499

continued

TABLE 70 *Maternal colonisation with GBS during labour (cont'd)*

Excluded studies

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion
McDonald (1989)[165] Australia	GBS-colonised women *When:* 24 weeks; labour *Where:* vagina *Culture method:* enriched	Preterm delivery: premature onset of labour <37 weeks	Preterm/term rate of colonisation was only measured for those colonised at 24 weeks' gestation. Only 27% of colonised women were positive in labour and the paper does not give the preterm/term split of these
Itakura (1996)[166] Japan	GBS-colonised women *When:* within 24 hours of birth *Where:* vagina *Culture method:* enriched	Premature ROM	Premature ROM (prelabour) was the outcome measure, not preterm delivery
Tsolia (2003)[167] Greece	GBS-colonised women *When:* labour (589); ⩾35 weeks (425) *Where:* vagina/rectum *Culture method:* enriched	Preterm delivery delivery <37 weeks	Only 589 of the 1014 women were tested for colonisation in labour, and these were not separately broken down into those delivering prematurely and those delivering at term
Regan (1981)[168] USA	GBS-colonised women *When:* admission for delivery *Where:* vagina *Culture method:* rapid identification system	Preterm delivery: delivery ⩽32 weeks	Preterm delivery was defined as delivery at <32 weeks not delivery at <37 weeks
Lamont (1986)[169] UK	GBS-colonised women *When:* labour *Where:* vagina *Culture method:* enriched *Other inclusion criteria:* case–control study Only preterm women included	Preterm delivery: delivery <37 weeks	Only women delivering prematurely were included
Zhang (1995)[170] China	GBS-colonised women *When:* admission to labour ward *Where:* vagina *Culture method:* enriched	Preterm delivery: delivery <37 weeks	The 78 colonised subjects who are split into preterm and term groups are comprised of colonised mothers (38), colonised babies (30) and colonised mothers and babies (10). The paper gives no breakdown for colonised mothers only

continued

TABLE 70 *Maternal colonisation with GBS during labour (cont'd)*

Association of GBS bacteriuria during pregnancy with GBS colonisation during labour
Included studies: Untreated pregnant women with GBS bacteriuria found to be colonised with GBS at labour in any country

Study	Participants – inclusion criteria	Outcome measure	Results			
				Total	GBS colonised	% colonised
Wood (1981)[61] USA	Pregnant women with GBS bacteriuria *When:* first prenatal visit *Culture method:* enriched *Other inclusion criteria:* 80% of women were from a hospital for acute/chronic diseases; 20% with uncomplicated medical histories. All 59 women tested for both bacteriuria and colonisation had 'less significant' bacteriuria	GBS colonisation *When:* labour *Where:* vagina/rectum *Culture method:* enriched	**GBS bacteriuria**	59	47	79.7
Persson (1986)[60] Sweden	Pregnant women with GBS bacteriuria *When:* admission for delivery *Culture method:* enriched	GBS colonisation *When:* admission for delivery *Where:* vagina/rectum *Culture method:* enriched	**GBS bacteriuria**	64	58	90.6
Hammoud (2003)[62] Kuwait	Pregnant women with GBS bacteriuria *When:* labour *Culture method:* enriched	GBS colonisation *When:* labour *Where:* vagina/rectum *Culture method:* enriched	**GBS bacteriuria**	85	49	57.6
Al-Sweih (2005)[63] Kuwait	Pregnant women with GBS bacteriuria *When:* labour *Culture method:* enriched	GBS colonisation *When:* labour *Where:* vagina *Culture method:* enriched	**GBS bacteriuria**	74	60	81.1

TABLE 71 *Baby colonisation with GBS by at birth*

Baby colonisation with GBS at birth in the total population
Inclusion criteria: Untreated GBS-colonised women in labour and their babies tested for colonisation at birth by any measure (any site/number of swabs)
UK studies only
Included studies

Study	Participants – inclusion criteria	Outcome measure	Results	
			No. of colonised women	No. of colonised babies
Reid (1975)[64] UK prospective study	GBS-colonised women *When:* before delivery *Where:* vagina *Culture method:* enriched *Other inclusion criteria:* swabs taken before ROM where possible	*Baby colonisation:* *Where:* 5 surface sites *When:* not stated (assumed at birth)	18	7 (38.9%)
Easmon (1981)[67] UK	GBS-colonised women *When:* labour *Where:* vaginal/rectal *Culture method:* enriched	*Baby colonisation:* *Where:* 4 surface sites *When:* 6–24 hours after birth	88	31 (35.2%)
Murphy (1982)[68] UK	GBS-colonised women *When:* labour *Where:* vaginal/rectal *Culture method:* non-enriched	*Baby colonisation:* *Where:* 8 surface sites *When:* within minutes of birth	40	20 (50.0%)
Needham (1982)[69] UK	GBS-colonised women *When:* labour *Where:* vaginal *Culture method:* enriched	*Baby colonisation:* *Where:* ear, oropharyngeal aspirate *When:* at birth	14	3 (21.4%)
Ross (1982)[82] UK	GBS-colonised women *When:* labour *Where:* vagina *Culture method:* enriched *Other inclusion criteria:* women who did not pull out earlier in the study	*Baby colonisation:* *Where:* 3 surface sites *When:* at birth	24	4 (16.7%)
Easmon (1985)[70] UK	GBS-colonised women *When:* labour *Where:* vaginal/rectal *Culture method:* enriched	*Baby colonisation:* *Where:* 4 surface sites *When:* within 24 hours of birth	124[a]	52 (41.9%)

continued

TABLE 71 *Baby colonisation with GBS by at birth (cont'd)*

Association of baby colonisation with GBS at birth with preterm delivery (i)/pyrexia or ROM (ii) (high-risk women)
Inclusion criteria: Untreated women colonised with GBS during labour and their babies tested for colonisation at birth by any measure (any site/number of swabs)
Colonisation measured for babies born preterm (<37 weeks' gestation) and babies born at term (≥37 weeks' gestation)
Excluded studies

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion
Hickman (1999)[171] (i) (ii) USA	GBS-colonised women *When:* hospital admission, within 60 hours of birth *Where:* vaginal/rectal *Culture method:* enriched, selective *Other inclusion criteria:* 2 hospitals, one public and one private	*Baby colonisation:* *Where:* 3 surface sites, colonisation counts as being positive at least one site *When:* 24–48 hours after birth *Preterm delivery:* delivery <37 weeks	Of the 153 women, 35 (23%) received IAP. 14 women had either preterm delivery <37 weeks or ROM >18 hours; 6 (43%) of these received IAP. There was no way of knowing which had preterm delivery so the figures could not be used
Hammoud (2003)[62] (i) Kuwait	GBS-colonised women *When:* labour *Where:* vaginal/rectal *Culture method:* enriched *Exclusions:* preterm excluded	*Baby colonisation:* *Where:* 3 surface sites *When:* 10–20 minutes after delivery *Preterm delivery:* delivery <37 weeks	Mean (SD) gestational age was similar in colonised babies (38.79 (2.01)) and non-colonised babies (38.89 (2.05)). However as very preterm babies were excluded this study has to be excluded
Sensini (1997)[172] (i) (ii) Italy	GBS-colonised women *When:* delivery *Where:* vaginal *Culture method:* selective	*Baby colonisation:* *Where:* 3 sites *When:* at birth Multiple risk factors	This study looked at women with any of the following risk factors: preterm delivery <37 weeks; intrapartum fever >38°C; prolonged ROM (>12 hours); multiple births; Caesarean section. There was no separate measure of baby colonisation in preterm/term deliveries

Association of baby colonisation with GBS at birth with delivery by elective LSCS
Inclusion criteria: Untreated women colonised with GBS during labour and their babies tested for colonisation at birth by any measure (any site/number of swabs)
Colonisation measured for babies born preterm (<37 weeks' gestation) and babies born at term (≥37 weeks' gestation)
Excluded studies

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion		
Anthony (1979)[173] USA	GBS-colonised women *When:* intrapartum – all cultures taken since mother's hospitalisation for delivery *Where:* vaginal/rectal *Culture method:* selective medium	*Baby colonisation:* *Where:* 3 surface sites *When:* day of birth or the next day, discharge		**No. of colonised women**	**No. of colonised babies**
			Caesarean	10	4
			Vaginal delivery	54	33
			Exclude – all Caesareans, not just elective		

continued

TABLE 71 *Baby colonisation with GBS by at birth (cont'd)*

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion
Sensini (1997)[172] Italy	GBS-colonised women *When:* delivery *Where:* vaginal *Culture method:* selective	*Baby colonisation:* *Where:* 3 sites *When:* at birth Multiple risk factors	This study looked at women with any of the following risk factors: preterm delivery <37 weeks; intrapartum fever >38°C; prolonged ROM (>12 hours); multiple births; Caesarean section. No separate data for baby colonisation in women with preterm delivery and term delivery

IAP, intrapartum antibiotic prophylaxis.
[a] 24 other women were given antibiotics; none of these transmitted to their babies.

TABLE 72 *Risk of EOGBS in colonised babies or colonised mothers*

Proportion of all babies colonised with GBS at birth that develop EOGBS
Inclusion criteria: Untreated babies tested for colonisation at birth (in the first day of life) by any measure (any site/number of swabs)
EOGBS defined as blood/CSF culture positive cases of infection with GBS in the first 7 days of life
Any country and culture method useful given that this is a relative measure

Included studies

Study	Participants – inclusion criteria	Outcome measure	Results	
			No. of colonised babies	No. with EOGBS
Baker (1973)[72] USA	GBS-colonised babies *When:* mean 18.3 hours after birth *Where:* 3 surface sites *Culture method:* enriched	*EOGBS:* positive blood culture	37	1 (3%)
Pass (1979)[84] USA	GBS-colonised babies *When:* 1–2 hours after birth *Where:* 4 surface sites *Culture method:* enriched *Other inclusion criteria:* low SE group, 60% black	*EOGBS:* blood/CSF culture positive with symptoms; blood cultures taken from sick babies only	290	9 (3%)
Weindling (1981)[85] UK	GBS-colonised babies *When:* first day of life *Where:* 2 surface sites *Culture method:* enriched	*EOGBS:* culture positive and symptomatic. Cultures taken from sick babies only	65	1 (2%)
Visconti (1985)[86] Italy	GBS-colonised babies *When:* within 24 hours after birth *Where:* 3 surface sites *Culture method:* enriched	*EOGBS:* blood culture positive with symptoms. Cultures must have been taken from sick babies only	64	4 (6%)
De Cueto (1998)[87] Spain	GBS-colonised babies *When:* after birth – time not stated *Where:* 3 surface sites *Culture method:* enriched	*EOGBS:* blood culture positive with symptoms. All babies had blood cultures	120	1 (1%)

continued

TABLE 72 *Risk of EOGBS in colonised babies or colonised mothers (cont'd)*

Excluded studies

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion
Moscatelli (1995)[174] Italy	GBS-colonised babies *When:* at birth *Where:* 3 surface sites *Culture method:* non-enriched	*EOGBS:* clinical symptoms (respiratory/meningitis)	Some of the babies were treated with antibiotics after birth
Reid (1975)[64] UK	GBS-colonised babies *When:* not stated, assumed at birth *Where:* 5 surface sites *Culture method:* enriched	*EOGBS:* blood/CSF culture positive with symptoms. Cultures taken when clinically warranted	Babies were only swabbed if thought necessary in the retrospective part of the study which looked at the association of baby colonisation with EOGBS. Therefore, all the babies in this are of undefined high risk
Hammoud (2003)[62] Kuwait	GBS-colonised babies When: 10–20 minutes after delivery *Where:* 3 surface sites *Culture method:* enriched	*EOGBS:* not defined	Preterm babies were excluded from this study
Ferrieri (1977)[175] USA	GBS-colonised babies *When:* within 3 hours of birth *Where:* 3 surface sites *Culture method:* enriched	*EOGBS:* bacteraemia Note: not symptomatic	All three EOGBS 'cases' were treated with antibiotics and showed no definite evidence of GBS disease
Mani (1984)[176] India	GBS-colonised babies *When:* during first 2 days *Where:* 4 surface sites *Culture method:* enriched	*EOGBS:* culture positive and symptomatic. All babies from colonised mothers had blood cultures	Babies were treated with penicillin during the first 5 days of life
Al-Sweih (2005)[63] Kuwait	GBS-colonised babies *When:* after birth – time not stated *Where:* 2 surface sites *Culture method:* enriched	*EOGBS:* not defined. Not stated whether all babies had blood cultures	No definition of EOGBS was given
Allardice (1982)[177] Canada	GBS-colonised babies *When:* on admission (exact time after birth not stated) and at discharge from nursery *Where:* 2 surface sites *Culture method:* enriched	*EOGBS:* blood culture positive with symptoms	49 babies were colonised on admission to hospital and 13 were on discharge from nursery. It is not clear whether all 9 cases came from the 49 initially colonised
Embil (1978)[178] Canada	GBS-colonised babies *When:* within 1 hour of birth *Where:* 1 surface site *Culture method:* enriched	*EOGBS:* symptomatic (no blood cultures)	EOGBS defined as babies that were symptomatic rather than blood culture positive. The symptoms may not have been necessarily due to EOGBS, e.g. 8/12 had pyrexia and these were heavier than normal, which is a confounding factor for pyrexia

continued

TABLE 72 *Risk of EOGBS in colonised babies or colonised mothers (cont'd)*

Proportion of 'high-risk' babies colonised with GBS at birth that develop EOGBS
Included studies: Inclusion criteria as above; all studies used are RCTs of i.v. IAP to prevent GBS (control arm data used to obtain natural history of EOGBS given baby colonisation)

Study	Participants – inclusion criteria	Outcome measure	Results	
		colonised babies?	No. of colonised babies	No. with EOGBS
Boyer (1982)[88] Abstract only USA	GBS-colonised babies *When:* at birth *Where:* 4 surface sites and gastric contents *Culture method:* not stated	*EOGBS:* positive blood culture. All babies tested	46	4 (9%)
Boyer (1983)[89] USA	GBS-colonised babies *When:* at birth *Where:* 5 surface sites *Culture method:* not stated	*EOGBS:* positive blood culture. All babies tested	13	1 (8%)
Boyer (1986)[90] USA	GBS-colonised babies *When:* at birth *Where:* 5 surface sites *Culture method:* enriched	*EOGBS:* positive blood culture. All babies tested	40	5 (13%)
Matorras (1991)[91] USA	GBS-colonised babies *When:* at birth *Where:* 5 surface sites and gastric contents *Culture method:* enriched	*EOGBS/other infection:* bacteraemia or symptoms of sepsis/pneumonia	24	3 (13%)

Proportion of 'low-risk' babies colonised with GBS at birth that develop EOGBS
Included studies: Inclusion criteria as above; study used is an RCT of IV IAP to prevent GBS (control arm data used to obtain natural history of EOGBS given baby colonisation)

Study	Participants – inclusion criteria	Outcome measure	Results	
			No. of colonised babies	No. with EOGBS
Morales (1986)[92] USA	GBS-colonised babies *When:* at birth *Where:* 2 surface sites *Culture method:* enriched *Other inclusion criteria:* control arm of RCT of i.v. IAP to prevent GBS	*EOGBS:* positive blood culture	59 (There was one other infant with heavy colonisation and respiratory distress, but a negative blood culture)	2 (3%)

continued

TABLE 72 *Risk of EOGBS in colonised babies or colonised mothers (cont'd)*

Proportion of 'high-risk' women colonised with GBS during labour who have babies that develop EOGBS
Inclusion criteria: Untreated mothers tested for colonisation during labour
EOGBS defined as blood/CSF culture positive cases of infection with GBS in the first 7 days of life
Any country and culture method useful given that this is a relative measure

Included studies

Study	Participants – inclusion criteria	Outcome measure	Results	
			Colonised women	EOGBS babies
Tuppurainen[93] (1989) Finland	GBS-colonised mothers *When:* admission to delivery unit *Where:* vagina *Culture method:* enriched *Other inclusion criteria:* control arm of RCT of i.v. IAP to prevent GBS. Women entering study were in labour long enough to get test result. This usually meant prolonged ROM. In general the women included in the study were 'high risk' with 7 delivering before 35 weeks' gestation *Exclusions:* 157 women with test results positive for colonisation but who delivered before the test results were available	*EOGBS:* severe symptoms within 48 hours, positive blood or surface cultures, and leucopenia or elevated C-reactive protein. Then classified into sepsis; early-onset infection (surface colonisation + symptoms), pneumonia Blood cultures were taken within 2 hours of birth for all babies born to colonised mothers	111 There were 10 'EOGBS cases' matching the definition: 4 septicaemia; 5 early-onset infection (heavy colonisation); 1 pneumonia. Only the 4 cases of septicaemia were counted as they meet our definition of EOGBS as being blood culture positive	4 (4%)

TABLE 73 *Risk of EOGBS livebirth in the total population*

Inclusion criteria: Risk of EOGBS livebirth in the total population
Population representative of the current situation in the UK
EOGBS defined as blood/CSF culture positive cases of infection with GBS in the first 7 days of life
Cross-sectional/surveillance studies with high ascertainment of total EOGBS cases

Primary data sources

Database name	Details of included cases	Variables measured	Results
BPSU Database UK and Ireland See Heath (2004)[12]	All babies with blood/CSF culture confirmed GBS disease in the first 90 days of life *When:* between 1 February 2000 and 28 February 2001 *Where:* the whole of the UK and Republic of Ireland *Ascertainment of cases:* routine hospital surveillance, microbiology laboratory reports, questionnaires to paediatricians and microbiologists and notifications from parents of babies with GBS disease	For each case of GBS, information was gathered on characteristics of the mother and the infant, many of which pertained to the maternal risk groups of our model, and the outcomes of EOGBS infection	See text[a]

[a] See the sections 'Risk of EOGBS livebirth in the total population' (p. 25), 'Proportion of EOGBS cases in each maternal risk group' (p. 25), 'Late-onset GBS disease (LOGBS)' (p. 29), 'Meningitis' (p. 30), 'Deaths' (p. 32) and 'Stillbirths' (p. 34).

TABLE 74 *Proportion of EOGBS cases in each maternal risk group*

Proportion of EOGBS cases in each of the twelve exclusive maternal risk groups

Inclusion criteria: Proportion of EOGBS cases in each of the 12 exclusive maternal risk groups
Breakdown of all EOGBS cases into the 12 exclusive maternal risk groups for EOGBS
Population representative of the current situation in the UK
Cross-sectional/surveillance studies with high ascertainment of total EOGBS cases

Primary data sources

Database name	Details of included cases	Variables measured	Results
BPSU Database; for details see *Table 73*			
Northern Region EOGBS Database see Oddie (2002)[53]	All babies over 24 weeks' gestation with blood/CSF culture confirmed GBS disease in the first 7 days of life *When:* between 1 April 1998 and 31 March 2000 *Where:* the former Northern Health Region of England (all 15 neonatal units) *Ascertainment of cases:* questioning of all consultant paediatricians, senior neonatal nurses, consultant microbiologists and scientific officers. Cross-checking against cases notified to the Public Health Laboratory Service	For each case of GBS, information was gathered on characteristics of the mother and the infant, many of which pertained to the maternal risk groups of our model	See text[a]

Proportion of EOGBS cases who have mothers who had a previous GBS baby

Inclusion criteria: Population representative of the current situation in the UK
Cross-sectional/surveillance studies with high ascertainment of total EOGBS cases
Data collected on whether the woman with an EOGBS baby has had a previous pregnancy which resulted in a baby which developed EOGBS disease

Included studies

Study	Participants – inclusion criteria	Outcome measure	Results	
			EOGBS cases	Previous GBS baby
Beardsall (2000)[94] UK	*EOGBS babies:* positive blood/CSF culture at <7 days old following clinical signs of infection *When:* January 1993 and December 1998 *Where:* Luton and Dunstable Hospital, South Bedfordshire	*Previous GBS baby:* mother known to have a previous baby that had GBS infection	28	0 (0%)
Halliday (2000)[52] UK	*EOGBS babies:* positive blood/CSF culture at <7 days old *When:* 1992–7 *Where:* 8 of 9 hospitals in Wessex	*Previous GBS baby:* mother known to have a previous baby that had GBS infection	53	0 (0%)

continued

TABLE 74 *Proportion of EOGBS cases in each maternal risk group (cont'd)*

Study	Participants – inclusion criteria	Outcome measure	Results	
			EOGBS cases	**Previous GBS baby**
Mifsud (2004)[95] UK	*EOGBS babies:* positive culture of blood or other normally sterile site at <7 days old *When:* 1990–9 *Where:* 7 maternity units in London	*Previous GBS baby:* mother known to have a previous baby that had GBS infection	55	1 (1.8%)
Proportion of EOGBS cases who have mothers who had pyrexia during labour **Inclusion criteria:** Population representative of the current situation in the UK Cross-sectional/surveillance studies with high ascertainment of total EOGBS cases Data collected on whether the woman with an EOGBS baby had pyrexia >38°C during labour *Included studies*				
Study	**Participants – inclusion criteria**	**Outcome measure**	**Results**	
			EOGBS cases	**Pyrexia**
Beardsall (2000)[94] UK	As above	*Pyrexia:* maternal temperature >38°C	28	5 (18%)
Halliday (2000)[52] UK	As above	*Pyrexia:* maternal temperature ⩾38°C	53	11 (21%)
Mifsud (2004)[95] UK	As above	*Pyrexia:* maternal temperature >38°C	105	26 (25%)
Proportion of EOGBS cases that were preterm **Inclusion criteria:** Population representative of the current situation in the UK Cross-sectional/surveillance studies with high ascertainment of total EOGBS cases Data collected on whether the EOGBS baby was born preterm (<37 weeks) *Included studies*				
Study	**Participants – inclusion criteria**	**Outcome measure**	**Results**	
			EOGBS cases	**Preterm**
Beardsall (2000)[94] UK	As above	*Preterm delivery:* delivery <37 weeks	28	9 (32%)
Halliday (2000)[52] UK	As above	*Preterm delivery:* delivery <37 weeks	53	21 (40%)

continued

TABLE 74 *Proportion of EOGBS cases in each maternal risk group (cont'd)*

Study	Participants – inclusion criteria	Outcome measure	Results	
			EOGBS cases	**Preterm**
Mifsud (2004)[95] UK	As above	*Preterm delivery:* delivery <37 weeks	135	63 (47%)
Moses (1998)[96] UK	*EOGBS babies:* positive blood/CSF culture at <48 hours old with clinical signs of infection. Note that there was only one baby with EOGBS between the ages of 2 and 7 days, therefore this study was included *When:* 1985–96 *Where:* John Radcliffe Hospital, Oxford	*Preterm delivery:* delivery <37 weeks	41	18 (44%)
RFH, RLH, UCL database (NICU database, 2005)	*EOGBS babies:* positive blood/CSF culture at <7 days old *When:* 1995–2005 *Where:* 3 London Hospitals: Royal Free, Royal London, University College London	*Preterm delivery:* delivery <37 weeks	28	8 (29%)

Proportion of EOGBS cases with any risk factor for EOGBS

Inclusion criteria: Population representative of the current situation in the UK
Cross-sectional/surveillance studies with high ascertainment of total EOGBS cases
Data collected on whether there were one or more of the 12 maternal risk factors for EOGBS present in the mothers of babies with EOGBS

Included studies

Study	Participants – inclusion criteria	Outcome measure	Results	
			EOGBS cases	**No. with at least one risk factor present**
Beardsall (2000)[94] UK	As above	*Maternal risk factors for EOGBS:* *Previous GBS baby:* mother known to have a previous baby that had GBS infection *GBS bacteriuria/previous positive swab:* GBS urinary tract infection or localised from maternal swabs (not routine screening) *Preterm delivery:* delivery <37 weeks *Prolonged ROM:* ROM >18 hours *Pyrexia:* maternal temperature >38°C	28	18 (64%)

continued

TABLE 74 *Proportion of EOGBS cases in each maternal risk group (cont'd)*

Study	Participants – inclusion criteria	Outcome measure	Results	
			EOGBS cases	**No. with at least one risk factor present**
Halliday (2000)[52] UK	As above	*Maternal risk factors for EOGBS:* *Previous GBS baby:* mother known to have a previous baby that had GBS infection *GBS bacteriuria:* GBS on previous high vaginal swab (not routine screening) *Preterm delivery:* delivery <37 weeks *Prolonged ROM:* ROM >18 hours *Pyrexia:* maternal temperature ⩾38°C	53	25 (47%)
Mifsud (2004)[95] UK	As above	*Maternal risk factors for EOGBS:* *Previous GBS baby:* mother known to have a previous baby that had GBS infection *Preterm delivery:* delivery <37 weeks *Prolonged ROM:* ROM >18 hours *Pyrexia:* maternal temperature >38°C	140	106 (76%)

[a] See the section 'EO non-GBS livebirths' (p. 27).

TABLE 75 *EO non-GBS livebirths*

EO non-GBS:EOGBS ratio
Primary data source

Database name	Details of included cases	Variables measured	Data			
			Year	EO non-GBS cases	EOGBS cases	EO non-GBS:EOGBS
HPA data[179]	All babies in the first year of life with a bacterial or yeast infection *When:* 1993–2003 *Where:* England and Wales *Ascertainment of cases:* submission of voluntary reports from laboratories across England and Wales for neonates of a known exact age under 1 week. All reports received by 26 October 2005	Bacterial organism, year of infection	1993	360	238	1.51
			1994	371	213	1.74
			1995	403	236	1.71
			1996	424	225	1.88
			1997	429	245	1.75
			1998	347	229	1.52
			1999	354	186	1.90
			2000	314	168	1.87
			2001	363	182	1.99
			2002	351	193	1.82
			2003	495	212	2.33

Preterm EO non-GBS
Primary data source

Database name	Details of included cases	Variables measured	Results
RFH, RLH, UCL database (NICU database, 2005)	All babies in the first year of life with a bacterial or yeast infection *When:* 1995–2005 *Where:* 3 London Hospitals: Royal Free, Royal London, University College London Total of 960 cases of infection from 5683 admissions to the NICU	Date of birth, gestation, death, date of death, age at death, sample data, organism, age at bacteraemia	See text[a]

[a] See the Section 'EO non-GBS livebirths' (p. 27).

TABLE 76 *Meningitis and disability from meningitis*

Primary data sources			
Database name	**Details of included cases**	**Variables measured**	**Results**
1985–1987 neonatal meningitis database (Bedford and colleagues, 2005) See Bedford (2001)[97]	All children at age 5 years who have survived an attack of meningitis in the first year of life *When:* 1985–7 *Where:* England and Wales	Numerous; those used were: gestation, age at meningitis, organism responsible for meningitis, outcome, disability category The conditions specific for each disability category are as follows: **None** = no evidence of developmental problems. However, conditions such as eczema and asthma included in this category **Mild** = having a condition prevalent among children of the same age but not typically associated with meningitis. Middle-ear disease, squint, febrile convulsions, behavioural problems **Moderate** = disability which impairs functioning but is not severe – can attend mainstream school with or without additional support. Mild neuromotor disability, intellectual impairment, moderate sensineural hearing loss, mild/moderate visual impairment, epilepsy controllable by treatment, hydrocephalus without complications **Severe** = unable to attend mainstream school. Severe motor impairment, significant intellectual impairment, severe seizure disorders, severe visual or auditory impairment	See text[a]
1996–1997 neonatal meningitis database (Halket and colleagues, 2005) See Holt (2001)[98]	All children at age 5 years who have survived an attack of meningitis in the first year of life *When:* 1996–7 *Where:* England and Wales	Numerous; those used were gestation, age at meningitis, organism responsible for meningitis, outcome, disability category The conditions specific for each disability category are the same as above	See text[a]

[a] See the sections ‘Meningitis’ (p. 30) and ‘Disability’ (p. 37).

TABLE 77 *Deaths and stillbirths*

Primary data source			
Database name	**Details of included cases**	**Variables measured**	**Results**
Northern Region neonatal deaths database (Embleton, 2005) UK See Embleton (1999)[99]	All babies in the first year of life deemed to have died from an infection *When:* 1981–2000 *Where:* the former Northern Health Region of the UK *Ascertainment of cases:* review of the obstetric, paediatric and pathology case notes of all the reported infant deaths in the region	For each death from infection, information was gathered on the characteristics of the mother and the infant, including the age at infection and which organism was responsible for the death (so they could be split into those caused by EOGBS and those by EO non-GBS) and whether the death was a stillbirth or not	See text[a]

[a] See the sections 'Deaths' (p. 32) and 'Stillbirths' (p. 34).

TABLE 78 *Disability from non-meningitis*

Included studies

Study	Participants – inclusion criteria	Outcome measure	Results				
				Disability			
			n	None	Mild	Moderate	Severe
Horn (1974)[101] USA	Infants surviving an attack of GBS sepsis in the first 2 months of life were followed up between 18 and 32 months of age	*Disability:* general physical examinations were performed and the infants were evaluated developmentally by the Denver Screening Test	12	10 (83%)	0 (0%)	2 (17%)	0 (0%)
			One infant was found to have poor speech and language development, the other to have delayed motor milestones, poor speech and poor fine motor skills. Both were deemed to have 'moderate' disability				
Adriaanse (1996)[102] The Netherlands	Infants surviving an attack of EOGBS sepsis were followed up at at least 1 year of age	*Disability:* a questionnaire was sent to the parents and data from the latest visit to the outpatient clinic was used	44	30 (68%)	2 (5%)	7 (16%)	5 (11%)
			Mild disability (2) = behaviour problems (2) Moderate disability (7) = neuromotor delay (4); logopedia – speech difficulties (3) Severe disability (4) = spastic tetraplegia (3); spastic diplegia (2)				
Alfven (1978)[100] Sweden	Infants surviving an attack of septicaemia/ osteomyelitis (caused by either GBS or non-GBS) between 1969 and 1973 in the first 4 weeks of life were followed up between 2.5 and 6.5 years of age	*Disability:* examination by interview concerning development and previous health and an examination with special attention to neurological, hearing and speech abnormalities	54	44 (81%)	2 (4%)	6 (11%)	2 (4%)
			Mild disability (2) = slight hearing defect; walking with a limp Moderate disability (6) = late psychomotor development (3); shorter leg; severe hearing defect; shorter arm Severe disability (2) = blind + severe mental retardation; cerebral palsy diplegia				

Excluded studies

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion
Bennet (1989)[180]	Survivors of neonatal septicaemia	Disability	Details of disabilities not given, therefore classification into 'mild', 'moderate' and 'severe' categories was not possible
Frederiksen (1993)[181]	Survivors of acute neonatal osteomyelitis and septic arthritis	Disability	Cases of osteomyelitis/arthritis only, not sepsis
Fink (1986)[182]	Children with septic arthritis and osteomyelitis	Disability	Cases of osteomyelitis/arthritis only, not sepsis Infection occurring at <2 years of age (not neonatal)
Ho (1999)[183]	Survivors of EOGBS and LOGBS sepsis	Neurological sequelae	Neurological sequelae during disease episode, not measured at follow-up in childhood

TABLE 79 *Life expectancy*

Inclusion criteria: Population representative of current UK population
Mean life expectancy measured at birth/as young age as possible
Disability categories corresponding to those used by Helen Bedford[97] for classifying disability from meningitis

Primary data source

Database name	Details of included cases	Variables measured	Results
ONS data[103]	Total UK population, 2004	Life expectancy at birth	Men: 76.25 years Women: 80.69 years Combined: 78.46 years SD = 0.02 years

Included studies

Study	Participants – inclusion criteria	Outcome measure	Results
Eyman (1990)[105] USA	Profoundly handicapped people with mental retardation *Inclusions:* those receiving services from the California Department of Developmental Services between March 1984 and October 1987 following prenatal, perinatal or postnatal brain damage	*Life expectancy:* from age 1 year and other older 3 mutually exclusive subgroups were examined: Subgroup 1: immobile, not toilet trained, tube feeding Subgroup 2: immobile, not toilet trained, could eat with assistance Subgroup 3: mobile but not ambulatory, could eat with assistance	The results reported in this, the original paper, were subsequently found to be calculated incorrectly. The correct results are given below in Katz (2003)[104]
Katz (2003)[104] USA	This paper is a review which includes a reanalysis of the Eyman (1990)[105] data with correct statistical methods	As above	**Subgroup (*n*)** 1 1550 2 4513 3 997 1–3 7060 **Life expectancy at 1 year** 11.2 25 42.7 24.5

Excluded studies

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion
Blair (2001)[184]	People with cerebral palsy	Age at death, by type and severity of disability	Life expectancy not given, only incomplete survival curves due to members of the cohort remaining alive
Hemming (2005)[185]	People with cerebral palsy	Age at death, by type and severity of disability	Life expectancy not given, only incomplete survival curves due to members of the cohort remaining alive
Hutton (2006)[186]	People with severe cerebral palsy	Age at death, by type and severity of disability	Life expectancy not given, only incomplete survival curves due to members of the cohort remaining alive

continued

TABLE 79 *Life expectancy (cont'd)*

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion
Hutton (2000)[187]	People with severe cerebral palsy	Age at death, by type and severity of disability	Life expectancy not given, only incomplete survival curves due to members of the cohort remaining alive
Hutton (1994)[188]	People with severe cerebral palsy	Age at death, by type and severity of disability	Life expectancy not given, only incomplete survival curves due to members of the cohort remaining alive
McCurley (1972)[189]	People with mental disability	Average age at death	Poor categorisation of mental disability Institutionalised people only Old study not reflecting recent increases in life expectancy in disabled people Average age at death; not life expectancy as outcome
Patja (2000)[190]	People with mental disability	Life expectancy	Life expectancy measured over a too wide range of years: at ages 2–10 years
Strauss (1998)[191]	People with cerebral palsy	Age at death, by type and severity of disability	Life expectancy not given, only incomplete survival curves due to members of the cohort remaining alive
Wolf (1987)[192]	People with mental disability	Life expectancy	Poor categorisation of mental disability Institutionalised people only Old study not reflecting recent increases in life expectancy in disabled people

TABLE 80 *Intravenous antibiotic prophylaxis*

Effect of i.v. intrapartum antibiotics on EOGBS livebirths

Inclusion criteria: Randomised controlled trial
I.v. ampicillin/penicillin intrapartum; vs no treatment/placebo
Participants are pregnant women in labour who are colonised with GBS
Outcome measure is either baby colonised with GBS at birth or EOGBS livebirth/stillbirth

Included studies

Study	Methods and bias minimisation	Participants – inclusion criteria	Intervention	Outcome measure	Results			
					Group	No.	Babies colonised	EOGBS
High-risk women: premature labour/ROM; prolonged ROM								
Boyer (1982)[88] Abstract only USA	Randomised *Method:* not stated *Blinding:* none	GBS-colonised women *When:* prenatal *Where:* not stated *Culture method:* not stated *Other inclusion criteria:* premature labour or prolonged ROM *Exclusions:* not stated	*Treatment group:* intrapartum i.v. ampicillin. Initial 2-g dose followed by 1 g every 4 hours until delivery *Control group:* no treatment	*Baby colonisation:* 4 surface sites, gastric contents and blood culture *When:* at birth *EOGBS:* positives blood culture	Ampicillin Control RR of babies colonised: 0.05 RR of EOGBS: 0.13	69 82	2 46	0 4
Boyer (1983)[89] USA	Random. Computer-generated sequences, sealed opaque envelopes *Blinding:* none	Vaginal culture on admission in labour 80/196; these women have premature labour/premature ROM	I.v. ampicillin *Control group:* no treatment	Culture of 5 surface sites and blood culture on delivery	Ampicillin Control RR of babies colonised: 0.07 RR of EOGBS: 0.29	43 37	1 13	0 1
Boyer (1986)[90] USA	Randomised *Method:* assignment to groups by random numbers in sealed opaque envelopes *Blinding:* neither patients nor obstetricians were blinded to the assignment to study groups *Blinding:* none	GBS-colonised women *When:* labour *Where:* vaginal/rectal *Culture method:* enriched *Other inclusion criteria:* premature labour (<37 weeks) or prolonged ROM (>12 hours) *Exclusions:* history of allergy to penicillin; those in control group who developed intrapartum fever	*Treatment group:* i.v. ampicillin. Initial 2-g dose followed by 1 g every 4 hours until delivery *Control group:* no treatment	*Baby colonisation:* 5 surface culture and a blood culture *When:* immediately after birth *EOGBS:* bacteraemia	Ampicillin Control RR of babies colonised: 0.19 RR of EOGBS: 0.08	85 79	8 40	0 5

continued

TABLE 80 *Intravenous antibiotic prophylaxis (cont'd)*

Study	Methods and bias minimisation	Participants – inclusion criteria	Intervention	Outcome measure	Results
Matorras (1991)[91] USA	Randomised *Method:* not stated *Blinding:* none	GBS-colonised women *When:* mean (SD) 5.74 (2.09) weeks before delivery *Where:* vaginal/rectal *Culture method:* ? *Other inclusion criteria:* two-thirds high risk with preterm delivery, UTI vaginal bleed or hypertension	*Treatment group:* i.v. ampicillin, 500 mg every 6 hours during labour: 9/54 needed 2 doses instead of one *Control group:* no treatment	*Baby colonisation:* 5 surface sites and gastric contents; severe colonisation defined by 3 or more being positive *EOGBS/other infection:* bacteraemia or symptoms of sepsis/pneumonia. Blood cultures if infection suspected	**Group** **No.** **Babies colonised** **EOGBS** Ampicillin 54 2 0 Control 56 24 3 RR of babies colonised: 0.09 RR of EOGBS: 0.15 Ampicillin group: 60 babies – 6 loss of follow-up. 2 other infections (non-GBS) Control group: 65 babies – 9 loss of follow-up. 6 other infections (non-GBS)
Tuppurainen (1989)[93] Finland	Randomised – sealed envelopes *Blinding:* none	Vaginal swabs on admission to delivery unit Women entering study were in labour long enough to get test result. Rapid test 5–7 hours + agglutination (therefore not high-risk women)	I.v. penicillin for 18 hours, then oral *Control group:* no treatment	Babies cultured at 5 sites within 30 minutes of birth and blood cultures within 2 hours of birth. EOGBS is severe symptoms within 48 hours, positive blood or surface cultures, and leucopenia or elevated C-reactive protein. Then classified into sepsis; early-onset infection (surface colonisation + symptoms), pneumonia	**Group** **No.** **EOGBS** Penicillin 88 1 Control 111 4 RR of EOGBS: 0.32 111 control: 10 EOGBS; 4 septicaemia; 5 early-onset infection (heavy colonisation); 1 pneumonia 88 treated: 1 early-onset infection (heavy colonisation + symptoms). Count as 0, as 0 have sepsis/pneumonia

continued

TABLE 80 *Intravenous antibiotic prophylaxis (cont'd)*

Study	Methods and bias minimisation	Participants – inclusion criteria	Intervention	Outcome measure	Results
Low-risk women					**Group** **No.** **Babies colonised**
Easmon (1983)[110] UK	Randomised – no details *Blinding:* none	GBS-colonised women *When:* admission to labour ward *Where:* vagina/rectum Culture method: enriched *Other inclusion criteria:* all women post-36 weeks	I.m. benzylpenicllin. 7 with a history of allergy to penicillin were given erythromycin *Control group:* no treatment	Babies swabbed at three sites within 24 hours hours of birth	Penicillin 38 0 Control 49 17 RR of babies colonised: 0.04
					Group **No.** **Babies colonised** **EOGBS**
Morales (1986)[92] USA	Quasi-randomised by day of week and chart number *Blinding:* none	GBS-colonised women *When:* preceding week of labour *Where:* vaginal *Culture method:* enriched media *Other inclusion criteria:* all women post-36 weeks and none were febrile and none had elective LSCS. Control group includes penicillin allergy	I.v. penicillin. Neonates treated if signs of symptoms *Control group:* no treatment	*Baby colonisation:* 2 surface sites *When:* at birth *EOGBS:* blood cultures – do not know when	Penicillin 135 0 0 Control 128 59 2 RR of babies colonised: 0.01 RR of EOGBS: 0.24 3 EOGBS: 2 infants with GBS sepsis; 1 heavy colonisation with respiratory distress
					Group **No.**
Yow (1979) USA	Allocation unclear Assumed to be quasi-randomised *Blinding:* not stated	GBS colonised women. *When*: labour *Where*: vaginal/rectal *Culture method*: enriched *Inclusion criteria*: none stated Private hospital population *Exclusions*: none stated	*Treatment group*: IV ampicillin 500 mg every 6 hours during labour: 4/34 women had more than one dose *Control group:* no treatment	*Baby colonisation:* 4 surface sites *When:* mostly within 6 hours of birth	Ampicrum 34 Control 24 RR if baby col.: 0.01

Excluded studies

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion
De Cueto (1998)[87]	Women colonised with GBS during labour	Baby colonisation EOGBS	Not randomised

continued

TABLE 80 *Intravenous antibiotic prophylaxis (cont'd)*

Hickman (1999)[171]	Women colonised with GBS during labour	Baby colonisation EOGBS	Not randomised
Allardice (1982)[177]	Women colonised with GBS during labour	Baby colonisation EOGBS	Not randomised
Pylipow (1994)[193]	Women colonised with GBS during third trimester	Baby colonisation EOGBS	Not randomised
Lim (1986)[194]	Women colonised with GBS in the week preceding week of labour	Baby colonisation EOGBS	Same trial as Morales (1986)[92] but at an earlier stage
Saez-Llorens (1995)[195]	Women colonised with GBS during labour	Baby colonisation EOGBS	Antibiotic on trial was Cephtriaxone, not ampicillin/penicillin

Effect of i.v. intrapartum antibiotics on EO non-GBS livebirths

Inclusion criteria: Randomised controlled trial
I.v. penicillin intrapartum; vs no treatment/placebo
Participants are pregnant women in labour
Outcome measure is early-onset non-GBS livebirth/stillbirth

Excluded studies

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion
Cararach (1998)[196]	Women with singleton gestations ⩾36 weeks, with ROM <12 hours and not in labour	*EO non-GBS:* sepsis within 72 hours of birth (GBS also recorded)	Treatment included intramuscular gentamycin and i.v. ampicillin RR on EO non-GBS: 0.14
Mercer (1997)[197]	Women with singleton gestations 20–34 weeks with prolonged prelabour ROM Grouped according to maternal GBS colonisation or not	*Any neonatal bacteraemia:* positive blood culture. Grouped according to whether bacteraemia occurred at <72 or >72 hours	Bacteraemia not split into GBS and non-GBS Women all giving birth very prematurely RR on all bacteraemia <72 hours in women uncolonised with GBS: 0.79 RR on all bacteraemia >72 hours in women uncolonised with GBS: 0.38 RR on all bacteraemia <72 hours in GBS colonised women: 2.25 RR on all bacteraemia >72 hours in GBS colonised women: 1.63
Johnston (1990)[198]	Women with singleton gestations 20–34 weeks with prelabour ROM	*Any neonatal bacteraemia:* positive blood culture within the first 48 hours of life	Bacteraemia not split into GBS and non-GBS Women all giving birth very prematurely RR (random): 0.22 (95% CI: 0.01 to 4.54)
Svare (1997)[199]	Women with singleton gestations 26–34 weeks ROM	*Any neonatal bacteraemia:* positive blood culture	Bacteraemia not split into GBS and non-GBS Women all giving birth very prematurely RR (random): 0.62 (95% CI: 0.06 to 6.48)
Ovalle (1998)[200]	Women of 37–42 weeks' gestation, singleton pregnancy. ROM less than 12 hours not in labour	*Any neonatal bacteraemia:* positive blood culture	Bacteraemia not split into GBS and non-GBS RR: not estimable
Gordon (1995)[201]	Women 24–35 weeks in labour receiving tocolysis	*Any neonatal bacteraemia:* positive blood culture	Bacteraemia not split into GBS and non-GBS RR (fixed): 1.02 (95% CI: 0.15 to 6.98)

RR, relative risk.

TABLE 81 *Oral antibiotic prophylaxis*

Effect of oral intrapartum antibiotics on EOGBS livebirths and EO non-GBS livebirths

Inclusion criteria: as above for i.v. antibiotics except that treatment is oral antibiotics

Included studies

Study	Methods and bias minimisation	Participants – inclusion criteria	Intervention	Outcome measure	Results			
					Group	No.	GBS	Non-GBS[a]
Gilbert (2005)[113] reanalysis of Kenyon (2001) ORACLE I and II trials[28,29] UK	Randomised *Method*: randomly selected blocks of four by computer *Blinding:* patients and clinicians were blinded	Pregnant women *Inclusions:* <37 weeks' gestation; ROM less than 12 hours and not in labour (prelabour ROM) or intact membranes and spontaneous (preterm) labour *Exclusions:* women who should have been prescribed antibiotics under best practice	*Treatment group:* oral erythromycin (250 mg)/co-amoxiclav (325 mg) *Control group:* placebo	*GBS infection:* positives blood culture *Non-GBS infection:* positives blood culture Timing of infection not recorded	Treatment Control	6581 2216	22 19	100 41
					These numbers were manipulated to estimate the effect on EOGBS and EO non-GBS (see text[b] for details)			

Excluded studies

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion
Mercer (1992)[202]	Women with preterm prelabour ROM at 20–35 weeks' gestation	*Any bacteraemia:* positive blood culture	Although there is a breakdown of the cases of bacteraemia into which organism is responsible, this breakdown is given only for the total number of cases and not separately for the treatment and control groups Very preterm women only RR: 1.00
Almeida (1996)[203]	Women with prelabour ROM at 30–36 weeks	*Any bacteraemia:* positive blood culture at <7 days	Bacteraemia not split into GBS and non-GBS RR (random): 0.17 (95% CI: 0.04 to 0.75)
Oyarzun (1998)[204]	Women thought to be in labour at 22–36 weeks' gestation, singleton pregnancy with intact membranes and cervical dilation <5 cm	*Any bacteraemia:* positive blood culture at <7 days	Bacteraemia not split into GBS and non-GBS RR (fixed): 0.58 (95% CI: 0.05 to 6.24)

[a] Excluding CNS cases.
[b] See the section 'Vaccination' (p. 45).

TABLE 82 *PCR test*

Inclusion criteria: PCR test
Evaluation of test carried out in routine practice representative of likely UK practice
Vaginal/rectal culture at labour/delivery as gold standard for comparison
Figures for true positive (TP), false positive (FP), false negative (FN) and true negative (TN) given to allow calculation of sensitivity and specificity

Included studies

Study	Participants – inclusion criteria	Outcome measure	Results				
					Culture		
					Positive	Negative	
Davies (2004)[10] USA and Canada	Pregnant women *Inclusions:* women attending hospital at labour *Exclusions:* women presenting in labour before 36 weeks' gestation, women with placenta previa, women treated with antibiotics one week prior to admission	Maternal GBS colonisation *When:* labour *Where:* vaginal/rectal *Culture method:* enriched *Rapid test method:* real-time PCR (IDI-Strep b; Infectio Diagnostics)	**Calgary**				
			Rapid tests	**Positive**	TP: 76	FP: 12	**Sensitivity:** 99%
				Negative	FN: 1	TN: 338	**Specificity:** 97%
			Houston				
			Rapid tests	**Positive**	TP: 17	FP: 4	**Sensitivity:** 89%
				Negative	FN: 2	TN: 52	**Specificity:** 93%
			Milwaukee				
			Rapid tests	**Positive**	TP: 11	FP: 0	**Sensitivity:** 85%
				Negative	FN: 2	TN: 35	**Specificity:** 100%
			Montreal				
			Rapid tests	**Positive**	TP: 14	FP: 11	**Sensitivity:** 93%
				Negative	FN: 1	TN: 139	**Specificity:** 93%
			Pittsburgh				
			Rapid tests	**Positive**	TP: 22	FP: 0	**Sensitivity:** 88%
				Negative	FN: 3	TN: 62	**Specificity:** 100%

Excluded studies

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion
Bergernon (2000)[205]	Pregnant women attending hospital for delivery	Vaginal/rectal maternal GBS colonisation during labour *Gold standard:* enriched culture *Rapid test method:* real-time PCR (light cycler)	Not representative of routine practice given that laboratory procedures were carried out extremely strictly
Reglier-Poupet (2005)[206]	Pregnant women attending hospital for delivery	Vaginal/rectal maternal GBS colonisation mid-trimester *Gold standard:* enriched culture *Rapid test method:* real-time PCR (light cycler)	Not representative of routine practice given that laboratory procedures were carried out extremely strictly
Uhl (2005)[207]	Pregnant women attending hospital for delivery *Exclusions:* women who declined to give permission for the use of their specimens	Vaginal/rectal maternal GBS colonisation during pregnancy *Gold standard:* enriched culture *Rapid test method:* real-time PCR (Roche light cycler)	Not representative of routine practice given that laboratory procedures were carried out extremely strictly and not immediately

TABLE 83 *Culture screening at 35–37 weeks*

Inclusion criteria: Culture screening of GBS colonisation between the 35th and 37th week of pregnancy
Evaluation of test carried out in routine practice representative of UK practice
Vaginal/rectal culture at labour/delivery as gold standard for comparison
Figures for true positive (TP), false positive (FP), false negative (FN) and true negative (TN) given to allow calculation of sensitivity and specificity

Included studies

Study	Participants – inclusion criteria	Outcome measure	Results				
					Labour		
					Positive	Negative	
Easmon (1985)[70] UK	Pregnant women *Inclusions:* women attending hospital antenatally, and at labour *Exclusions:* none stated	Maternal GBS colonisation *When:* 36 weeks; labour *Where:* vaginal/rectal *Culture method:* enriched	**36 weeks**	**Positive** **Negative**	TP: 91 FN: 17	FP: 7 TN: 501	**Sensitivity:** 84.3% **Specificity:** 91.9%
Goodman (1997)[208] USA	Pregnant women *Inclusions:* women attending hospital antenatally, and at labour *Exclusions:* none stated	Maternal GBS colonisation *When:* 37 weeks; labour *Where:* vaginal/rectal *Culture method:* enriched	**37 weeks**	**Positive** **Negative**	TP: 57 FN: 33	FP: 36 TN: 621	**Sensitivity:** 63.3% **Specificity:** 94.5%
Natale (1995)[209] Italy	Pregnant women *Inclusions:* women attending hospital antenatally, and at labour *Exclusions:* women with incomplete records; multiple pregnancies	Maternal GBS colonisation *When:* 36 weeks; labour *Where:* vaginal/rectal *Culture method:* enriched	**37 weeks**	**Positive** **Negative**	TP: 170 FN: 73	FP: 44 TN: 1481	**Sensitivity:** 70.0% **Specificity:** 97.1%
Yancey (1996)[210] USA	Pregnant women *Inclusions:* women attending hospital antenatally, and at labour *Exclusions:* women who had received antibiotic therapy in the week before culture	Maternal GBS colonisation *When:* 35–36 weeks; labour *Where:* vaginal/rectal *Culture method:* enriched	**37 weeks**	**Positive** **Negative**	TP: 168 FN: 26	FP: 25 TN: 607	**Sensitivity:** 86.6% **Specificity:** 96.0%

Excluded studies

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion
Pinette (2005)[211]	Pregnant women *Inclusions:* women attending hospital antenatally, and at labour *Exclusions:* none stated	Maternal GBS colonisation *When:* 35–37 weeks; labour *Where:* vaginal/rectal *Culture method:* enriched	This study only allowed the calculation of sensitivity as only the women who tested positive at 35–37 weeks were retested at delivery

continued

TABLE 83 *Culture screening at 35–37 weeks (cont'd)*

Study	Participants – inclusion criteria	Outcome measure	Reason for exclusion
Ferrieri (1977)[175]	Pregnant women *Inclusions:* women attending hospital antenatally, and at labour *Exclusions:* none stated	Maternal GBS colonisation *When:* 36 weeks; labour *Where:* vaginal *Culture method:* enriched	This study only allowed the calculation of sensitivity as only the women who tested positive at labour were checked to see if they had tested positive at 36 weeks
Boyer (1983)[212]	Pregnant women *Inclusions:* women attending hospital antenatally, and at labour *Exclusions:* none stated	Maternal GBS colonisation *When:* 6–10 weeks before delivery, 6 weeks before delivery; delivery *Where:* vaginal/rectal *Culture method:* enriched	Gestation at which women were tested is not given; only the amount of time before delivery is given
Bland (2000)[213]	Pregnant women *Inclusions:* women attending hospital antenatally, and at labour *Exclusions:* women under 18 years	Maternal GBS colonisation *When:* 34–37 weeks; labour *Where:* vaginal/rectal *Culture method:* enriched	This study only allowed the calculation of sensitivity as only the women who tested positive at 34–37 weeks were retested at delivery

Appendix 2

Full cost-effectiveness results of each of the 14 interventions in Scenario A for each risk group

TABLE 84 *RG1: preterm LSCS*

Intervention[a]	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
V	0.00256	0.000055	Dominated	1.10	1.37	1.65	0	0	0
CO	–0.0202	0.0000147	Dominated	0.31	0.39	0.46	0	0	0
CI	–0.0181	0.0000179	Dominated	0.38	0.47	0.56	0	0	0
PO	–0.00294	0.0000348	Dominated	0.70	0.87	1.05	0	0	0
PI	0.0000518	0.0000428	Dominated	0.86	1.07	1.28	0	0	0
I	–0.42	0.000124	Dominated	2.90	3.52	4.14	0.24	0.13	0.06
O	–0.527	0.000111	Base for ICER	2.75	3.30	3.86	0.21	0.13	0.09
n	0	0	Dominated	0.00	0.00	0.00	0.06	0.08	0.09
VCO	0.00418	0.0000645	Dominated	1.29	1.61	1.93	0	0	0
VCI	0.00952	0.0000661	Dominated	1.31	1.64	1.97	0	0	0
VPO	0.0541	0.0000769	Dominated	1.48	1.87	2.25	0	0	0
VPI	0.0648	0.0000808	Dominated	1.55	1.96	2.36	0	0	0
VI	–0.362	0.000164	ICER to 14: £13,900	3.64	4.46	5.28	56.4	56.9	57.3
VO	–0.483	0.000155	ICER to 7: £979	3.58	4.36	5.13	43.1	42.8	42.4

[a] *Tables 84–107*: C, culture test at 35–37 weeks; I, i.v. antibiotics; n, no treatment; O, oral antibiotics; P, PCR test at labour; *p*(CE), probability of being cost-effective; V, vaccination.

TABLE 85 *RG2: preterm previous GBS baby*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
V	–0.000777	0.000000682	Dominated	0.01	0.02	0.02	0	0	0
CO	0.000027	8.09×10^{-8}	Dominated	0.00	0.00	0.00	0	0	0
CI	–0.000436	0.000000227	Dominated	0.00	0.01	0.01	0	0	0
PO	0.000563	0.00000016	Dominated	0.00	0.00	0.00	0	0	0
PI	–0.00054	0.000000499	Dominated	0.01	0.01	0.02	0	0	0
I	–0.00368	0.00000112	Base for ICER	0.03	0.03	0.04	0.11	0.06	0.05
O	–0.00202	0.000000441	Dominated	0.01	0.01	0.02	0.04	0.02	0.02
n	0	0	Dominated	0.00	0.00	0.00	0.07	0.09	0.09
VCO	–0.000605	0.000000727	Dominated	0.02	0.02	0.02	0	0	0
VCI	–0.000823	0.000000803	Dominated	0.02	0.02	0.02	0	0	0
VPO	0.0000818	0.000000769	Dominated	0.02	0.02	0.02	0	0	0
VPI	–0.000442	0.000000944	Dominated	0.02	0.02	0.03	0	0	0
VI	–0.00345	0.00000154	ICER to 6: £547	0.03	0.04	0.05	78.6	79.1	79.4
VO	–0.00246	0.00000104	Dominated	0.02	0.03	0.03	21.1	20.7	20.5

TABLE 86 *RG3: preterm urine/vaginal swab positive for GBS*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
V	–0.256	0.000105	Dominated	2.36	2.88	3.41	0	0	0
CO	–0.0476	0.0000173	Dominated	0.39	0.48	0.57	0	0	0
CI	–0.152	0.0000493	Dominated	1.14	1.38	1.63	0	0	0
PO	–0.0627	0.000035	Dominated	0.76	0.94	1.11	0	0	0
PI	–0.311	0.00011	Dominated	2.51	3.06	3.61	0	0	0
I	–0.537	0.000153	Dominated	3.60	4.36	5.13	0.02	0.02	0.03
O	–0.236	0.0000551	Dominated	1.34	1.61	1.89	0.03	0.01	0
n	0	0	Dominated	0.00	0.00	0.00	0.07	0.09	0.1
VCO	–0.27	0.000115	Dominated	2.57	3.15	3.72	0	0	0
VCI	–0.319	0.000131	Dominated	2.94	3.59	4.25	0	0	0
VPO	–0.251	0.000124	Dominated	2.73	3.35	3.97	0	0	0
VPI	–0.367	0.000161	Dominated	3.59	4.39	5.20	0.35	0.43	0.54
VI	–0.564	0.000197	Base for ICER	4.50	5.49	6.47	90.2	90.5	90.6
VO	–0.413	0.000141	Dominated	3.23	3.94	4.64	9.29	8.98	8.77

TABLE 87 *RG4: preterm pyrexia*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
V	–0.12	0.0000523	Dominated	1.17	1.43	1.69	0	0	0
CO	–0.0427	0.0000139	Dominated	0.32	0.39	0.46	0	0	0
CI	–0.0577	0.0000198	Dominated	0.45	0.55	0.65	0	0	0
PO	–0.0858	0.0000325	Dominated	0.74	0.90	1.06	0	0	0
PI	–0.123	0.0000469	Dominated	1.06	1.30	1.53	0	0	0
I	–0.241	0.0000704	Dominated	1.65	2.00	2.35	0.01	0.01	0.02
O	–0.224	0.0000524	Dominated	1.27	1.53	1.80	0.04	0.02	0.01
n	0	0	Dominated	0.00	0.00	0.00	0.07	0.09	0.1
VCO	–0.135	0.0000592	Dominated	1.32	1.62	1.91	0	0	0
VCI	–0.14	0.0000619	Dominated	1.38	1.69	2.00	0	0	0
VPO	–0.14	0.0000684	Dominated	1.51	1.85	2.19	0	0	0
VPI	–0.154	0.000075	Dominated	1.65	2.03	2.40	0	0	0
VI	–0.26	0.0000959	ICER to 14: £1460	2.18	2.66	3.14	67	67.5	67.9
VO	–0.273	0.0000867	Base for ICER	2.01	2.44	2.87	32.9	32.4	31.9

TABLE 88 *RG5: preterm prelabour ROM*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
V	–0.948	0.000445	Dominated	9.85	12.07	14.30	0	0	0
CO	–0.473	0.000148	Dominated	3.43	4.17	4.91	0	0	0
CI	–0.477	0.000168	Dominated	3.84	4.68	5.52	0	0	0
PO	–0.967	0.000347	Dominated	7.91	9.64	11.38	0	0	0
PI	–0.881	0.000367	Dominated	8.22	10.06	11.89	0	0	0
I	–2.17	0.000621	Dominated	14.59	17.70	20.80	0.01	0.01	0.02
O	–2.52	0.000583	Dominated	14.18	17.10	20.01	0.04	0.02	0.03
n	0	0	Dominated	0.00	0.00	0.00	0.07	0.09	0.1
VCO	–1.13	0.000521	Dominated	11.55	14.16	16.76	0	0	0
VCI	–1.11	0.000528	Dominated	11.67	14.31	16.95	0	0	0
VPO	–1.23	0.00062	Dominated	13.63	16.73	19.83	0	0	0
VPI	–1.13	0.000625	Dominated	13.63	16.76	19.88	0	0	0
VI	–2.28	0.000844	ICER to 14: £471,000	19.16	23.38	27.60	51.9	52.4	52.9
VO	–2.73	0.000843	Base for ICER	19.59	23.81	28.02	48	47.4	47

TABLE 89 *RG6: preterm labour intact membranes*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
V	–0.411	0.00036	Dominated	7.61	9.41	11.21	0	0	0
CO	0.0141	0.0000428	Dominated	0.84	1.06	1.27	0	0	0
CI	–0.231	0.00012	Dominated	2.63	3.23	3.83	0	0	0
PO	0.296	0.0000845	Dominated	1.39	1.82	2.24	0	0	0
PI	–0.287	0.000264	Dominated	5.57	6.89	8.21	0	0	0
I	–1.94	0.000594	Base for ICER	13.82	16.79	19.76	0.11	0.06	0.05
O	–1.07	0.000233	Dominated	5.73	6.90	8.06	0.04	0.02	0.02
n	0	0	Dominated	0.00	0.00	0.00	0.07	0.09	0.09
VCO	–0.32	0.000384	Dominated	8.00	9.92	11.84	0	0	0
VCI	–0.435	0.000424	Dominated	8.92	11.04	13.16	0	0	0
VPO	0.0418	0.000406	Dominated	8.08	10.11	12.14	0	0	0
VPI	–0.235	0.000498	Dominated	10.20	12.69	15.18	0	0	0
VI	–1.82	0.000813	ICER to 6: £546	18.08	22.15	26.21	78.6	79.1	79.4
VO	–1.3	0.000547	Dominated	12.24	14.98	17.71	21.1	20.7	20.5

TABLE 90 *RG7: term LSCS*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
V	3.48	0.0000723	Dominated	–2.03	–1.67	–1.31	0	0	0
CO	0.83	0.0000222	Dominated	–0.39	–0.28	–0.16	0	0	0
CI	0.93	0.0000281	Dominated	–0.37	–0.23	–0.09	0	0	0
PO	1.37	0.0000248	Dominated	–0.87	–0.75	–0.63	0	0	0
PI	1.47	0.0000317	Dominated	–0.84	–0.68	–0.52	0	0	0
I	0.925	0.0000932	Extended dominated	0.94	1.41	1.87	26.7	31.8	35.3
O	–0.213	0.0000852	Base for ICER	1.92	2.34	2.77	71.8	64.7	58.3
n	0	0	Dominated	0.00	0.00	0.00	0.11	0.11	0.11
VCO	4.4	0.0000823	Dominated	–2.75	–2.34	–1.93	0	0	0
VCI	4.51	0.0000839	Dominated	–2.83	–2.41	–1.99	0	0	0
VPO	4.96	0.0000828	Dominated	–3.30	–2.89	–2.48	0	0	0
VPI	5.06	0.0000846	Dominated	–3.37	–2.95	–2.52	0	0	0
VI	4.57	0.000146	ICER to 14: £523,000	–1.65	–0.92	–0.19	0.22	0.71	1.41
VO	3.39	0.000143	ICER to 7: £61,800	–0.53	0.19	0.90	1.25	2.64	4.97

TABLE 91 *RG8: term previous GBS baby*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
V	0.033	0.00000113	Dominated	–0.01	0.00	0.00	0	0	0
CO	0.00792	0.000000271	Dominated	0.00	0.00	0.00	0	0	0
CI	0.0075	0.000000578	Dominated	0.00	0.01	0.01	0	0	0
PO	0.0137	0.000000266	Dominated	–0.01	–0.01	–0.01	0	0	0
PI	0.0128	0.000000627	Dominated	0.00	0.00	0.01	0	0	0
I	0.00881	0.00000128	ICER to 7: £19,400	0.02	0.02	0.03	51.8	56	56.5
O	–0.00279	0.000000684	Base for ICER	0.02	0.02	0.02	41.6	32	24.6
n	0	0	Dominated	0.00	0.00	0.00	0.09	0.09	0.1
VCO	0.0423	0.00000123	Dominated	–0.02	–0.01	–0.01	0	0	0
VCI	0.0432	0.00000132	Dominated	–0.02	–0.01	0.00	0	0	0
VPO	0.0481	0.00000122	Dominated	–0.02	–0.02	–0.01	0	0	0
VPI	0.0488	0.00000133	Dominated	–0.02	–0.02	–0.01	0	0	0
VI	0.0458	0.00000192	ICER to 6: £58,100	–0.01	0.00	0.01	0.76	2	4.51
VO	0.032	0.0000016	Extended dominated	0.00	0.01	0.02	5.78	9.86	14.2

TABLE 92 *RG9: term urine/vaginal swab positive for GBS*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
V	0.688	0.000143	Dominated	2.17	2.89	3.60	0	0	0
CO	0.0391	0.0000503	Dominated	0.97	1.22	1.47	0	0	0
CI	–0.168	0.000109	Dominated	2.35	2.89	3.44	0.01	0.01	0.01
PO	0.285	0.0000503	Dominated	0.72	0.97	1.22	0	0	0
PI	0.0108	0.00012	Dominated	2.39	2.99	3.59	0.01	0	0
I	–0.466	0.000158	ICER to 7: £534	3.63	4.42	5.21	68.8	57	44.6
O	–0.51	0.0000751	Base for ICER	2.01	2.39	2.76	1.18	0.63	0.37
n	0	0	Dominated	0.00	0.00	0.00	0.04	0.06	0.08
VCO	1.01	0.000159	Dominated	2.17	2.97	3.76	0	0	0
VCI	1.06	0.000176	Dominated	2.46	3.34	4.22	0.02	0.02	0.02
VPO	1.26	0.000159	Dominated	1.92	2.72	3.51	0	0	0
VPI	1.29	0.000178	Dominated	2.27	3.16	4.05	0	0	0
VI	1.02	0.000203	ICER to 6: £32,600	3.04	4.06	5.07	11.7	21.4	32.3
VO	0.549	0.000175	Extended dominated	2.95	3.83	4.70	18.3	20.9	22.6

TABLE 93 *RG10: term pyrexia*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
V	–0.0308	0.000111	Dominated	2.25	2.81	3.36	0	0	0
CO	–0.33	0.0000634	Dominated	1.60	1.92	2.23	0	0	0
CI	–0.412	0.0000829	Dominated	2.07	2.48	2.90	0.02	0	0
PO	–0.3	0.0000731	Dominated	1.76	2.13	2.49	0	0	0
PI	–0.403	0.0000962	Dominated	2.33	2.81	3.29	0.06	0.05	0.02
I	–0.512	0.000119	ICER to 7: £7140	2.89	3.49	4.08	22.3	15.3	9.9
O	–0.691	0.0000936	Base for ICER	2.56	3.03	3.50	11	6.5	3.71
n	0	0	Dominated	0.00	0.00	0.00	0.03	0.04	0.08
VCO	0.0281	0.000128	Dominated	2.53	3.17	3.81	0	0	0
VCI	0.0382	0.000133	Dominated	2.62	3.29	3.95	0.01	0	0.02
VPO	0.12	0.000131	Dominated	2.50	3.16	3.81	0	0	0
VPI	0.124	0.000137	Dominated	2.62	3.30	3.99	0.03	0.08	0.1
VI	0.109	0.00015	ICER to 14: £54,100	2.89	3.64	4.39	13.4	22.3	30.4
VO	–0.208	0.000144	ICER to 6: £11,800	3.09	3.81	4.53	53.2	55.7	55.8

TABLE 94 *RG11: term prolonged ROM*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
V	0.505	0.000493	Extended dominated	9.36	11.82	14.29	4.67	3.14	2.17
CO	–1.41	0.000296	Dominated	7.33	8.81	10.29	1.69	0.84	0.44
CI	–1.63	0.000364	Base for ICER	8.91	10.73	12.55	5.77	3.06	1.7
PO	–1.24	0.000346	Dominated	8.16	9.89	11.62	9.32	6.46	4.31
PI	–1.44	0.000415	ICER to 3: £3700	9.74	11.82	13.89	18.4	11.5	7.51
I	NA	NA	NA	NA	NA	NA	NA	NA	NA
O	NA	NA	NA	NA	NA	NA	NA	NA	NA
n	0	0	Dominated	0.00	0.00	0.00	0.09	0.09	0.1
VCO	0.897	0.000574	Extended dominated	10.58	13.45	16.32	13.6	14.5	14.1
VCI	0.976	0.00059	ICER to 5: £13,700	10.82	13.77	16.72	30.4	34.8	35.6
VPO	1.38	0.000586	Dominated	10.34	13.27	16.20	5.42	8.39	10.8
VPI	1.46	0.000603	ICER to 10: £38,100	10.60	13.62	16.63	10.6	17.2	23.3
VI	NA	NA	NA	NA	NA	NA	NA	NA	NA
VO	NA	NA	NA	NA	NA	NA	NA	NA	NA

NA, not applicable.

TABLE 95 *RG12: term, no risk factors*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
V	28.5	0.000979	Extended dominated	–8.92	–4.03	0.87	14.4	20.8	26.9
CO	6.84	0.000235	Dominated	–2.14	–0.97	0.21	0.11	0.15	0.15
CI	6.49	0.0005	Base for ICER	3.51	6.01	8.51	67.4	66.8	60.4
PO	11.8	0.00023	Dominated	–7.20	–6.05	–4.90	0	0	0
PI	11.1	0.000543	ICER to 3: £3700	–0.24	2.48	5.19	3.88	6.65	8.86
I	NA	NA	NA	NA	NA	NA	NA	NA	NA
O	NA	NA	NA	NA	NA	NA	NA	NA	NA
n	0	0	Dominated	0.00	0.00	0.00	14.2	5.29	2.38
VCO	36.5	0.00106	Extended dominated	–15.30	–10.00	–4.70	0	0	0.01
VCI	37.3	0.00114	ICER to 5: £13,700	–14.50	–8.80	–3.10	0.03	0.28	1.27
VPO	41.5	0.00106	Dominated	–20.30	–15.00	–9.70	0	0	0
VPI	42.1	0.00115	ICER to 10: £38,100	–19.10	–13.35	–7.60	0	0.02	0.05
VI	NA	NA	NA	NA	NA	NA	NA	NA	NA
VO	NA	NA	NA	NA	NA	NA	NA	NA	NA

NA, not applicable.

Appendix 3

Full cost-effectiveness results of each of the seven interventions in Scenario B for each risk group

TABLE 96 *RG1: preterm LSCS*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
CO	–0.0202	0.0000147	Dominated	0.31	0.39	0.46	0	0	0
CI	–0.0181	0.0000179	Dominated	0.38	0.47	0.56	0	0	0
PO	–0.00294	0.0000348	Dominated	0.70	0.87	1.05	0	0	0
PI	0.0000518	0.0000428	Dominated	0.86	1.07	1.28	0	0	0
I	–0.42	0.000124	ICER to 7: £8170	2.90	3.52	4.14	0.582	0.587	0.59
O	–0.527	0.000111	Base for ICER	2.75	3.30	3.86	0.417	0.412	0.409
n	0	0	Dominated	0.00	0.00	0.00	0.0006	0.0008	0.0009

TABLE 97 *RG2: preterm previous GBS baby*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
CO	0.000027	8.09E-08	Dominated	0.00	0.00	0.00	0	0	0
CI	–0.000436	0.000000227	Dominated	0.00	0.01	0.01	0	0	0
PO	0.000563	0.00000016	Dominated	0.00	0.00	0.00	0	0	0
PI	–0.00054	0.000000499	Dominated	0.01	0.01	0.02	0.0023	0.0032	0.0039
I	–0.00368	0.00000112	Base for ICER	0.03	0.03	0.04	0.855	0.859	0.861
O	–0.00202	0.000000441	Dominated	0.01	0.01	0.02	0.142	0.137	0.134
n	0	0	Dominated	0.00	0.00	0.00	0.0007	0.0009	0.0009

TABLE 98 *RG3: preterm urine/vaginal swab positive for GBS*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
CO	–0.0476	0.0000173	Dominated	0.39	0.48	0.57	0	0	0
CI	–0.152	0.0000493	Dominated	1.14	1.38	1.63	0	0	0
PO	–0.0627	0.000035	Dominated	0.76	0.94	1.11	0	0	0
PI	–0.311	0.00011	Dominated	2.51	3.06	3.61	0.0073	0.008	0.009
I	–0.537	0.000153	Base for ICER	3.60	4.36	5.13	0.974	0.973	0.973
O	–0.236	0.0000551	Dominated	1.34	1.61	1.89	0.0183	0.0178	0.0166
n	0	0	Dominated	0.00	0.00	0.00	0.0007	0.0009	0.001

TABLE 99 *RG4: preterm pyrexia*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
CO	–0.0427	0.0000139	Dominated	0.32	0.39	0.46	0	0	0
CI	–0.0577	0.0000198	Dominated	0.45	0.55	0.65	0	0	0
PO	–0.0858	0.0000325	Dominated	0.74	0.90	1.06	0	0	0
PI	–0.123	0.0000469	Dominated	1.06	1.30	1.53	0.0025	0.0034	0.0035
I	–0.241	0.0000704	Base for ICER	1.65	2.00	2.35	0.774	0.78	0.784
O	–0.224	0.0000524	Dominated	1.27	1.53	1.80	0.223	0.216	0.212
n	0	0	Dominated	0.00	0.00	0.00	0.0007	0.0009	0.001

TABLE 100 *RG5: preterm prelabour ROM*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
CO	–0.473	0.000148	Dominated	3.43	4.17	4.91	0	0	0
CI	–0.477	0.000168	Dominated	3.84	4.68	5.52	0	0	0
PO	–0.967	0.000347	Dominated	7.91	9.64	11.38	0	0	0
PI	–0.881	0.000367	Dominated	8.22	10.06	11.89	0.0001	0.0001	0.0001
I	–2.17	0.000621	ICER to 7: £9470	14.59	17.70	20.80	0.574	0.58	0.585
O	–2.52	0.000583	Base for ICER	14.18	17.10	20.01	0.425	0.419	0.414
n	0	0	Dominated	0.00	0.00	0.00	0.0007	0.0009	0.001

TABLE 101 *RG6: preterm labour intact membranes*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
CO	0.0141	0.0000428	Dominated	0.84	1.06	1.27	0	0	0
CI	–0.231	0.00012	Dominated	2.63	3.23	3.83	0	0	0
PO	0.296	0.0000845	Dominated	1.39	1.82	2.24	0	0	0
PI	–0.287	0.000264	Dominated	5.57	6.89	8.21	0.0023	0.0032	0.0039
I	–1.94	0.000594	Base for ICER	13.82	16.79	19.76	0.855	0.859	0.861
O	–1.07	0.000233	Dominated	5.73	6.90	8.06	0.142	0.137	0.134
n	0	0	Dominated	0.00	0.00	0.00	0.0007	0.0009	0.0009
VO	0.0141	0.0000428	Dominated	0.84	1.06	1.27	0	0	0

TABLE 102 *RG7: term LSCS*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
CO	0.83	0.0000222	Dominated	–0.39	–0.28	–0.16	0	0	0
CI	0.93	0.0000281	Dominated	–0.37	–0.23	–0.09	0	0	0
PO	1.37	0.0000248	Dominated	–0.87	–0.75	–0.63	0	0	0
PI	1.47	0.0000317	Dominated	–0.84	–0.68	–0.52	0	0	0
I	0.925	0.0000932	ICER to 7: £142,000	0.94	1.41	1.87	0.269	0.327	0.371
O	–0.213	0.0000852	Base for ICER	1.92	2.34	2.77	0.73	0.672	0.628
n	0	0	Dominated	0.00	0.00	0.00	0.0011	0.0011	0.0011

TABLE 103 *RG8: term previous GBS baby*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
CO	0.00792	0.000000271	Dominated	0.00	0.00	0.00	0	0	0
CI	0.0075	0.000000578	Dominated	0.00	0.01	0.01	0	0	0
PO	0.0137	0.000000266	Dominated	–0.01	–0.01	–0.01	0	0	0
PI	0.0128	0.000000627	Dominated	0.00	0.00	0.01	0	0	0
I	0.00881	0.00000128	ICER to 7: £19,400	0.02	0.02	0.03	0.541	0.606	0.649
O	–0.00279	0.000000684	Base for ICER	0.02	0.02	0.02	0.459	0.393	0.35
n	0	0	Dominated	0.00	0.00	0.00	0.0009	0.0009	0.001

TABLE 104 *RG9: term urine/vaginal swab positive for GBS*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
CO	0.0391	0.0000503	Dominated	0.97	1.22	1.47	0	0	0
CI	–0.168	0.000109	Dominated	2.35	2.89	3.44	0.0006	0.0014	0.0017
PO	0.285	0.0000503	Dominated	0.72	0.97	1.22	0	0	0
PI	0.0108	0.00012	Dominated	2.39	2.99	3.59	0.0009	0.0011	0.0019
I	–0.466	0.000158	ICER to 7: £534	3.63	4.42	5.21	0.967	0.973	0.976
O	–0.51	0.0000751	Base for ICER	2.01	2.39	2.76	0.0312	0.0242	0.0201
n	0	0	Dominated	0.00	0.00	0.00	0.0004	0.0006	0.0008

TABLE 105 *RG10: term pyrexia*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
CO	–0.33	0.0000634	Dominated	1.60	1.92	2.23	0	0	0
CI	–0.412	0.0000829	Dominated	2.07	2.48	2.90	0.0009	0.0005	0.0005
PO	–0.3	0.0000731	Dominated	1.76	2.13	2.49	0	0	0
PI	–0.403	0.0000962	Dominated	2.33	2.81	3.29	0.0086	0.0102	0.0111
I	–0.512	0.000119	ICER to 7: £7140	2.89	3.49	4.08	0.684	0.717	0.742
O	–0.691	0.0000936	Base for ICER	2.56	3.03	3.50	0.307	0.272	0.246
n	0	0	Dominated	0.00	0.00	0.00	0.0003	0.0004	0.0008

TABLE 106 *RG11: term prolonged ROM*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
CO	–1.41	0.000296	Dominated	7.33	8.81	10.29	0.0464	0.0418	0.0391
CI	–1.63	0.000364	Base for ICER	8.91	10.73	12.55	0.212	0.2	0.192
PO	–1.24	0.000346	Dominated	8.16	9.89	11.62	0.184	0.182	0.18
PI	–1.44	0.000415	ICER to 3: £3700	9.74	11.82	13.89	0.556	0.576	0.588
I	NA	NA	NA	NA	NA	NA	NA	NA	NA
O	NA	NA	NA	NA	NA	NA	NA	NA	NA
n	0	0	Dominated	0.00	0.00	0.00	0.0009	0.0009	0.001

NA, not applicable.

TABLE 107 *RG12: term, no risk factors*

Intervention	Cost	QALYs	Result	NB at £20,000 (£)	NB at £25,000 (£)	NB at £30,000 (£)	*p*(CE) at £20,000	*p*(CE) at £25,000	*p*(CE) at £30,000
CO	6.84	0.000235	Dominated	–2.14	–0.97	0.21	0.0013	0.0022	0.0026
CI	6.49	0.0005	ICER to 8: £13,000	3.51	6.01	8.51	0.788	0.839	0.828
PO	11.8	0.00023	Dominated	–7.20	–6.05	–4.90	0	0	0
PI	11.1	0.000543	ICER to 3: £107,000	–0.24	2.48	5.19	0.0509	0.0952	0.14
I	NA	NA	NA	NA	NA	NA	NA	NA	NA
O	NA	NA	NA	NA	NA	NA	NA	NA	NA
n	0	0	Base for ICER	0.00	0.00	0.00	0.16	0.064	0.0296

NA, not applicable.

Appendix 4

Full cost-effectiveness results

Costs and QALYs are relative to do nothing (S30).

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A*

Strategy and detail[a]	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
S1: ---.--I.--I.--I.---.---.---.--I.--I.--I.---.---.	–1.75	0.00050	Dominated	11.79	14.30	16.81	0	0	0
S2: -PI.--I.--I.--I.-PI.-PI.-PI.--I.--I.--I.---.---.	–1.45	0.00121	Dominated	25.65	31.70	37.75	0	0	0
S3: ---.--I.--I.--I.--O.---.---.--I.--I.--I.---.---.	–4.27	0.00109	Dominated	26.07	31.52	36.97	0	0	0
S4: -PI.--I.--I.--I.--O.-PI.-PI.--I.--I.--I.-PI.-PI.	6.53	0.00238	Dominated	41.07	52.97	64.87	0	0	0
S5: ---.--I.--I.--I.--O.--I.---.--I.--I.---.---.	–6.21	0.00168	Dominated	39.81	48.21	56.61	0	0	0
S6: -PI.--I.--I.--I.--O.--I.-PI.--I.--I.--I.-PI.-PI.	4.88	0.00271	Dominated	49.32	62.87	76.42	0	0	0
S7: --I.--I.--I.--I.--O.--I.---.--I.--I.--I.---.---.	–6.63	0.00180	Dominated	42.63	51.63	60.63	0	0	0
S8: --I.--I.--I.--I.--O.--I.-PI.--I.--I.--I.-PI.-PI.	4.46	0.00279	Dominated	51.34	65.29	79.24	0	0	0
S9: V--.V-I.V-I.V-I.V--.V--.V--.V-I.V-I.V-I.V--.V--.	31.40	0.00305	Dominated	29.60	44.85	60.10	0	0	0
S10: VPI.V-I.V-I.V-I.VPI.VPI.VPI.V-I.V-I.V-I.V--.V--.	33.10	0.00341	Dominated	35.10	52.15	69.20	0	0	0
S11: V--.V-I.V-I.V-I.V-O.V--.V--.V-I.V-I.V-I.V--.V--.	29.60	0.00345	Dominated	39.40	56.65	73.90	0	0	0
S12: VPI.V-I.V-I.V-I.V-O.VPI.VPI.V-I.V-I.V-I.VPI.VPI.	46.10	0.00391	Dominated	32.10	51.65	71.20	0	0	0
S13: V--.V-I.V-I.V-I.V-O.V-I.V--.V-I.V-I.V-I.V--.V--.	28.20	0.00391	Dominated	50.00	69.55	89.10	0	0	0
S14: VPI.V-I.V-I.V-I.V-O.V-I.VPI.V-I.V-I.V-I.VPI.VPI.	44.50	0.00422	Dominated	39.90	61.00	82.10	0	0	0
S15: V-I.V-I.V-I.V-I.V-O.V-I.V--.V-I.V-I.V-I.V--.V--.	27.90	0.00401	Dominated	52.30	72.35	92.40	0	0	0
S16: V-I.V-I.V-I.V-I.V-O.V-I.VPI.V-I.V-I.V-I.VPI.VPI.	44.10	0.00431	Dominated	42.10	63.65	85.20	0	0	0
S17: ---.V-I.--I.--I.---.---.---.V-I.--I.--I.---.---.	–1.71	0.00050	Dominated	11.77	14.29	16.80	0	0	0
S18: -PI.V-I.--I.--I.-PI.-PI.-PI.V-I.--I.--I.---.---.	–1.41	0.00121	Dominated	25.61	31.66	37.71	0	0	0
S19: ---.V-I.--I.--I.--O.---.---.V-I.--I.--I.---.---.	–4.23	0.00109	Dominated	26.03	31.48	36.93	0	0	0
S20: -PI.V-I.--I.--I.--O.-PI.-PI.V-I.--I.--I.-PI.-PI.	6.57	0.00238	Dominated	41.03	52.93	64.83	0	0	0
S21: ---.V-I.--I.--I.--O.--I.---.V-I.--I.--I.---.---.	–6.17	0.00168	Dominated	39.77	48.17	56.57	0	0	0
S22: -PI.V-I.--I.--I.--O.--I.-PI.V-I.--I.--I.-PI.-PI.	4.92	0.00271	Dominated	49.28	62.83	76.38	0	0	0
S23: --I.V-I.--I.--I.--O.--I.---.V-I.--I.--I.---.---.	–6.59	0.00180	Dominated	42.59	51.59	60.59	0	0	0
S24: --I.V-I.--I.--I.--O.--I.-PI.V-I.--I.--I.-PI.-PI.	4.50	0.00279	Dominated	51.30	65.25	79.20	0	0	0
S25: V--.V--.V--.V--.V--.V--.V--.V--.V--.V--.V--.V--.	31.40	0.00282	Dominated	25.00	39.10	53.20	0	0	0
S26: -CO.-CO.-CO.-CO.-CO.-CO.-CO.-CO.-CO.-CO.-CO.-CO.	5.41	0.00090	Dominated	12.65	17.17	21.68	0	0	0
S27: -CI.-CI.-CI.-CI.-CI.-CI.-CI.-CI.-CI.-CI.-CI.-CI.	4.28	0.00146	Dominated	24.92	32.22	39.52	0	0	0
S28: -PO.-PO.-PO.-PO.-PO.-PO.-PO.-PO.-PO.-PO.-PO.-PO.	11.20	0.00126	Dominated	14.00	20.30	26.60	0	0	0
S29: -PI.-PI.-PI.-PI.-PI.-PI.-PI.-PI.-PI.-PI.-PI.-PI.	9.10	0.00204	Dominated	31.70	41.90	52.10	0	0	0
S30: ---.---.---.---.---.---.---.---.---.---.---.---.	0.00	0.00000	Dominated	0.00	0.00	0.00	0.06	0.09	0.1
S31: VCO.VCO.VCO.VCO.VCO.VCO.VCO.VCO.VCO.VCO.VCO.VCO.	41.10	0.00315	Dominated	21.90	37.65	53.40	0	0	0

[a] Interventions are given for risk groups 1 to 12: C, culture at 35–37 weeks; I, i.v. antibiotics; n, no treatment; O, oral antibiotics; P, PCR test at labour; V, vaccination. Space represents no treatment.

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
S32: VCI.VCI.VCI.VCI.VCI.VCI.VCI.VCI.VCI.VCI.VCI.VCI.	41.90	0.00334	Dominated	24.90	41.60	58.30	0	0	0
S33: VPO.VPO.VPO.VPO.VPO.VPO.VPO.VPO.VPO.VPO. VPO.VPO.	47.80	0.00331	Dominated	18.40	34.95	51.50	0	0	0
S34: VPI.VPI.VPI.VPI.VPI.VPI.VPI.VPI.VPI.VPI.VPI.VPI.	48.30	0.00360	Dominated	23.70	41.70	59.70	0	0	0
S35: -CI.-CI.-CI.-CI.-CO.-CI.-CI.-CI.-CI.-CI.-CI.-CI.	4.29	0.00144	Dominated	24.51	31.71	38.91	0	0	0
S36: -CI.--I.-CI.-CI.-CO.-CI.-CI.--I.-CI.-CI.-CI.-CI.	4.28	0.00144	Dominated	24.52	31.72	38.92	0	0	0
S37: -CI.-CI.--I.-CI.-CO.-CI.-CI.-CI.--I.-CI.-CI.-CI.	3.60	0.00159	Dominated	28.20	36.15	44.10	0	0	0
S38: -CI.--I.--I.-CI.-CO.-CI.-CI.--I.--I.-CI.-CI.-CI.	3.60	0.00159	Dominated	28.20	36.15	44.10	0	0	0
S39: --I.--I.--I.--I.--O.--I.--O.--I.--I.--I.-PI.-PI.	2.78	0.00285	Extended dominated	54.22	68.47	82.72	1.43	1.55	1.38
S40: --I.--I.-CI.--I.--O.--I.--O.--I.-CI.--I.-PI.-PI.	3.46	0.00269	Dominated	50.34	63.79	77.24	0	0	0
S41: --I.-CI.--I.--I.--O.--I.--O.-CI.--I.--I.-PI.-PI.	2.78	0.00284	Dominated	54.02	68.22	82.42	0	0	0
S42: --I.-CI.-CI.--I.--O.--I.--O.-CI.-CI.--I.-PI.-PI.	3.47	0.00269	Dominated	50.33	63.78	77.23	0	0	0
S43: VCI.VCI.VCI.VCI.VCO.VCI.VCI.VCI.VCI.VCI.VCI.VCI.	41.90	0.00333	Dominated	24.70	41.35	58.00	0	0	0
S44: VCI.V-I.VCI.VCI.VCO.VCI.VCI.V-I.VCI.VCI.VCI.VCI.	41.90	0.00333	Dominated	24.70	41.35	58.00	0	0	0
S45: VCI.VCI.V-I.VCI.VCO.VCI.VCI.VCI.V-I.VCI.VCI.VCI.	41.60	0.00343	Dominated	27.00	44.15	61.30	0	0	0
S46: VCI.V-I.V-I.VCI.VCO.VCI.VCI.V-I.V-I.VCI.VCI.VCI.	41.60	0.00343	Dominated	27.00	44.15	61.30	0	0	0
S47: V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-I.V-I.V-I.VPI.VPI.	42.40	0.00437	ICER to S176: £265,000	45.00	66.85	88.70	0	0.02	0.02
S48: V-I.V-I.VCI.V-I.V-O.V-I.V-O.V-I.VCI.V-I.VPI.VPI.	42.70	0.00427	Dominated	42.70	64.05	85.40	0	0	0
S49: V-I.VCI.V-I.V-I.V-O.V-I.V-O.VCI.V-I.V-I.VPI.VPI.	42.40	0.00437	Dominated	45.00	66.85	88.70	0	0	0
S50: V-I.VCI.VCI.V-I.V-O.V-I.V-O.VCI.VCI.V-I.VPI.VPI.	42.70	0.00427	Dominated	42.70	64.05	85.40	0	0	0
S51: -CI.VCI.-CI.-CI.-CO.-CI.-CI.VCI.-CI.-CI.-CI.-CI.	4.32	0.00144	Dominated	24.48	31.68	38.88	0	0	0
S52: -CI.V-I.-CI.-CI.-CO.-CI.-CI.V-I.-CI.-CI.-CI.-CI.	4.32	0.00144	Dominated	24.48	31.68	38.88	0	0	0
S53: -CI.VCI.--I.-CI.-CO.-CI.-CI.VCI.--I.-CI.-CI.-CI.	3.64	0.00159	Dominated	28.16	36.11	44.06	0	0	0
S54: -CI.V-I.--I.-CI.-CO.-CI.-CI.V-I.--I.-CI.-CI.-CI.	3.64	0.00159	Dominated	28.16	36.11	44.06	0	0	0
S55: --I.V-I.--I.--I.--O.--I.--O.V-I.--I.--I.-PI.-PI.	2.82	0.00285	Extended dominated	54.18	68.43	82.68	0	0	0
S56: --I.V-I.-CI.--I.--O.--I.--O.V-I.-CI.--I.-PI.-PI.	3.50	0.00270	Dominated	50.50	64.00	77.50	0	0	0
S57: --I.VCI.--I.--I.--O.--I.--O.VCI.--I.--I.-PI.-PI.	2.82	0.00285	Dominated	54.18	68.43	82.68	0	0	0
S58: --I.VCI.-CI.--I.--O.--I.--O.VCI.-CI.--I.-PI.-PI.	3.50	0.00269	Dominated	50.30	63.75	77.20	0	0	0
S59: V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-I.V-I.V-O.VPI.VPI.	42.10	0.00436	Extended dominated	45.10	66.90	88.70	0	0.03	0.05
S60: V-I.V-I.VCI.V-I.V-O.V-I.V-O.V-I.VCI.V-O.VPI.VPI.	42.40	0.00427	Dominated	43.00	64.35	85.70	0	0	0
S61: V-I.VCI.V-I.V-I.V-O.V-I.V-O.VCI.V-I.V-O.VPI.VPI.	42.10	0.00436	Dominated	45.10	66.90	88.70	0	0	0
S62: V-I.VCI.VCI.V-I.V-O.V-I.V-O.VCI.VCI.V-O.VPI.VPI.	42.40	0.00427	Dominated	43.00	64.35	85.70	0	0	0
S63: -PI.-PI.-PI.--I.--O.-PI.-PI.-PI.-PI.--I.-PI.-PI.	7.24	0.00230	Dominated	38.76	50.26	61.76	0	0	0
S64: -PI.-CI.-PI.--I.--O.-PI.-PI.-CI.-PI.--I.-PI.-PI.	7.24	0.00230	Dominated	38.76	50.26	61.76	0	0	0
S65: VPI.VPI.VPI.V-I.V-O.VPI.VPI.VPI.VPI.V-I.VPI.VPI.	46.60	0.00385	Dominated	30.40	49.65	68.90	0	0	0
S66: VPI.VPI.VPI.V-I.V-O.VPI.V--.VPI.VPI.V-I.VPI.VPI.	45.00	0.00384	Dominated	31.80	51.00	70.20	0	0	0
S67: VPI.VPI.VPI.V-I.V-O.VPI.VPI.V--.VPI.V-I.VPI.VPI.	46.50	0.00385	Dominated	30.50	49.75	69.00	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
S68: VPI.VPI.VPI.V-I.V-O.VPI.V--.V--.VPI.V-I.VPI.VPI.	45.00	0.00384	Dominated	31.80	51.00	70.20	0	0	0
S69: VPI.VCI.VPI.V-I.V-O.VPI.VPI.VCI.VPI.V-I.VPI.VPI.	46.60	0.00385	Dominated	30.40	49.65	68.90	0	0	0
S70: -PI.VPI.-PI.--I.--O.-PI.-PI.VPI.-PI.--I.-PI.-PI.	7.28	0.00230	Dominated	38.72	50.22	61.72	0	0	0
S71: -PI.VCI.-PI.--I.--O.-PI.-PI.VCI.-PI.--I.-PI.-PI.	7.27	0.00230	Dominated	38.73	50.23	61.73	0	0	0
S72: -CO.--O.--O.-CO.-CO.-CO.-CO.--O.--I.-CI.-CO.-CO.	4.62	0.00107	Dominated	16.78	22.13	27.48	0	0	0
S73: --O.--O.--O.--O.--O.--O.--O.--O.--I.--I.-PO.-PO.	4.84	0.00197	Dominated	34.56	44.41	54.26	0.02	0.03	0.01
S74: -CO.--O.--O.-CO.-CO.-CO.-CO.--O.--I.-CI.-CI.-CI.	4.05	0.00140	Dominated	23.95	30.95	37.95	0	0	0
S75: --O.--O.--O.--O.--O.--O.--O.--O.--I.--I.-PI.-PI.	3.85	0.00236	Dominated	43.35	55.15	66.95	0.85	0.74	0.61
S76: -CI.--I.--I.-CI.-CI.-CI.-CI.--I.--I.-CI.-CO.-CO.	4.17	0.00128	Dominated	21.43	27.83	34.23	0	0	0
S77: --I.--I.--I.--I.--I.--I.--I.--I.--I.--I.-PO.-PO.	5.25	0.00251	Dominated	44.95	57.50	70.05	0	0	0
S78: -CI.--I.--I.-CI.-CI.-CI.-CI.--I.--I.-CI.-CI.-CI.	3.60	0.00161	Dominated	28.60	36.65	44.70	0	0	0
S79: --I.--I.--I.--I.--O.--I.--I.--I.--I.---.---.	–5.70	0.00190	Dominated	43.70	53.20	62.70	0	0	0
S80: --I.--I.--I.--I.--I.--I.--O.--I.--I.--I.-PI.-PI.	3.13	0.00288	Extended dominated	54.47	68.87	83.27	2.7	2.12	1.43
S81: -CI.--I.--I.--I.--O.-CI.-CI.--I.--I.--I.-CI.-CI.	1.27	0.00212	Dominated	41.13	51.73	62.33	0	0	0
S82: -CI.--I.--I.--I.--O.--I.-CI.--I.--I.--I.-CI.-CI.	–0.44	0.00259	Dominated	52.24	65.19	78.14	0	0	0
S83: --I.--I.--I.--I.--O.--I.-CI.--I.--I.--I.-CI.-CI.	–0.84	0.00270	Dominated	54.84	68.34	81.84	0	0	0
S84: --I.--I.--I.--I.--O.--I.--O.--I.--I.--I.-CI.-CI.	–1.98	0.00275	ICER to S86: £5620	56.98	70.73	84.48	6.56	4.39	2.94
S85: -CI.-CI.-CI.--I.--O.-CI.-CI.-CI.-CI.--I.-CI.-CI.	1.96	0.00196	Dominated	37.24	47.04	56.84	0	0	0
S86: --I.--I.--I.--I.--O.--I.--O.--I.--I.--I.---.---.	–6.84	0.00189	ICER to T27: £1690	44.64	54.09	63.54	0.03	0	0.01
S87: --I.--I.--I.--I.--O.--I.--I.--I.--I.--I.-CI.-CI.	–0.84	0.00276	Dominated	56.04	69.84	83.64	0.01	0	0.03
S88: --I.--I.--I.--I.--O.--I.--I.--I.--I.--I.-PI.-PI.	3.92	0.00285	Dominated	53.08	67.33	81.58	0.01	0	0
S89: ---.--I.--I.--I.--I.---.---.--I.--I.--I.---.---.	–3.92	0.00112	Dominated	26.32	31.92	37.52	0	0	0
S90: -CI.--I.--I.--I.--I.-CI.-CI.--I.--I.--I.-CI.-CI.	1.62	0.00215	Dominated	41.38	52.13	62.88	0	0	0
S91: -PI.--I.--I.--I.--I.-PI.-PI.--I.--I.--I.-PI.-PI.	6.88	0.00242	Dominated	41.52	53.62	65.72	0	0	0
S92: ---.--I.--I.--I.--I.--I.---.--I.--I.--I.---.---.	–5.86	0.00172	Dominated	40.26	48.86	57.46	0	0	0
S93: -CI.--I.--I.--I.--I.--I.-CI.--I.--I.--I.-CI.-CI.	–0.09	0.00263	Dominated	52.69	65.84	78.99	0	0	0
S94: -PI.--I.--I.--I.--I.--I.-PI.--I.--I.--I.-PI.-PI.	5.23	0.00275	Dominated	49.77	63.52	77.27	0	0	0
S95: --I.--I.--I.--I.--I.--I.---.--I.--I.--I.---.---.	–6.28	0.00184	Dominated	43.08	52.28	61.48	0	0	0
S96: --I.--I.--I.--I.--I.--I.-CI.--I.--I.--I.-CI.-CI.	–0.49	0.00273	Dominated	55.09	68.74	82.39	0	0	0
S97: --I.--I.--I.--I.--I.--I.-PI.--I.--I.--I.-PI.-PI.	4.81	0.00283	Dominated	51.79	65.94	80.09	0	0	0
S98: --I.--I.--I.--I.--I.--I.--O.--I.--I.--I.---.---.	–6.49	0.00193	Extended dominated	45.09	54.74	64.39	0.2	0.08	0.05
S99: --I.--I.--I.--I.--I.--I.--O.--I.--I.--I.-CI.-CI.	–1.63	0.00279	ICER to S84: £9470	57.43	71.38	85.33	12.9	7.67	4.45
S100: --I.--I.--I.--I.--I.--I.--I.--I.--I.--I.---.---.	–5.35	0.00193	Extended dominated	43.95	53.60	63.25	0.03	0	0
S101: --I.--I.--I.--I.--I.--I.--I.--I.--I.--I.-CI.-CI.	–0.49	0.00280	Extended dominated	56.49	70.49	84.49	12.3	10.4	7.94
S102: --I.--I.--I.--I.--I.--I.--I.--I.--I.--I.-PI.-PI.	4.27	0.00289	Extended dominated	53.53	67.98	82.43	3.25	3.9	4.05
S103: ---.--I.--I.--I.--I.---.---.--O.--O.--I.---.---.	–3.97	0.00104	Dominated	24.77	29.97	35.17	0	0	0
S104: -PI.--I.--I.--I.--I.-PI.-PI.--O.--O.--I.-PI.-PI.	6.83	0.00234	Dominated	39.97	51.67	63.37	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
S105: ---.--O.--O.--I.--I.---.---.--O.--O.--I.---.---.	–3.67	0.00094	Dominated	22.49	27.20	31.90	0	0	0
S106: -PI.--O.--O.--I.--I.-PI.-PI.--O.--O.--I.-PI.-PI.	7.13	0.00224	Dominated	37.67	48.87	60.07	0	0	0
S107: ---.--O.--O.--I.--I.-PI.-PI.--O.--O.--I.-PI.-PI.	7.13	0.00219	Dominated	36.67	47.62	58.57	0	0	0
S108: ---.--O.--O.--I.--O.---.---.--O.--O.--I.---.---.	–4.02	0.00090	Dominated	22.10	26.62	31.14	0	0	0
S109: -PI.--O.--O.--I.--O.-PI.-PI.--O.--O.--I.-PI.-PI.	6.78	0.00220	Dominated	37.22	48.22	59.22	0	0	0
S110: -PI.--O.--O.--I.--O.-PI.-PI.--O.--O.--I.-PO.-PO.	7.76	0.00182	Dominated	28.64	37.74	46.84	0	0	0
S111: -PI.--O.--O.--I.--O.-PI.-PO.--O.--O.--I.-PO.-PO.	7.67	0.00181	Dominated	28.53	37.58	46.63	0	0	0
S112: -PI.--O.--O.--I.--O.-PO.-PO.--O.--O.--I.-PO.-PO.	8.25	0.00163	Dominated	24.35	32.50	40.65	0	0	0
S113: -PO.--O.--O.--I.--O.-PO.-PO.--O.--O.--I.-PO.-PO.	8.25	0.00162	Dominated	24.15	32.25	40.35	0	0	0
S114: ---.--I.--I.--I.--I.---.--O.--O.--I.---.---.	–5.91	0.00163	Dominated	38.51	46.66	54.81	0	0	0
S115: -PI.--I.--I.--I.--I.-PI.--O.--O.--I.-PI.-PI.	5.17	0.00267	Dominated	48.23	61.58	74.93	0	0	0
S116: ---.--O.--O.--I.--I.---.--O.--O.--I.---.---.	–5.61	0.00154	Dominated	36.41	44.11	51.81	0	0	0
S117: -PI.--O.--O.--I.--I.-PI.--O.--O.--I.-PI.-PI.	5.48	0.00257	Dominated	45.92	58.77	71.62	0	0	0
S118: ---.--O.--O.--I.--O.--I.---.--O.--O.--I.---.---.	–5.96	0.00150	Dominated	35.96	43.46	50.96	0	0	0
S119: -PI.--O.--O.--I.--O.--I.-PI.--O.--O.--I.-PI.-PI.	5.13	0.00253	Dominated	45.47	58.12	70.77	0	0	0
S120: ---.--O.--O.--I.--O.--I.-PI.--O.--O.--I.-PI.-PI.	5.13	0.00249	Dominated	44.67	57.12	69.57	0	0	0
S121: ---.--O.--O.--I.--O.--O.---.--O.--O.--I.---.---.	–5.09	0.00114	Dominated	27.89	33.59	39.29	0	0	0
S122: -PI.--O.--O.--I.--O.--O.-PI.--O.--O.--I.-PI.-PI.	6.00	0.00217	Dominated	37.40	48.25	59.10	0	0	0
S123: -PI.--O.--O.--I.--O.--O.-PI.--O.--O.--I.-PO.-PO.	6.98	0.00179	Dominated	28.82	37.77	46.72	0	0	0
S124: -PI.--O.--O.--I.--O.--O.-PO.--O.--O.--I.-PO.-PO.	6.89	0.00178	Dominated	28.71	37.61	46.51	0	0	0
S125: -PO.--O.--O.--I.--O.--O.-PO.--O.--O.--I.-PO.-PO.	6.89	0.00177	Dominated	28.51	37.36	46.21	0	0	0
S126: --I.--I.--I.--I.--I.--I.---.--O.--O.--I.---.---.	–6.33	0.00176	Dominated	41.53	50.33	59.13	0	0	0
S127: --I.--I.--I.--I.--I.--I.-PI.--O.--O.--I.-PI.-PI.	4.76	0.00275	Dominated	50.24	63.99	77.74	0	0	0
S128: --I.--O.--O.--I.--I.--I.---.--O.--O.--I.---.---.	–6.03	0.00166	Dominated	39.23	47.53	55.83	0	0	0
S129: --I.--O.--O.--I.--I.--I.-PI.--O.--O.--I.-PI.-PI.	5.06	0.00265	Dominated	47.94	61.19	74.44	0	0	0
S130: --I.--O.--O.--I.--O.--I.---.--O.--O.--I.---.---.	–6.38	0.00162	Dominated	38.78	46.88	54.98	0	0	0
S131: --I.--O.--O.--I.--O.--I.-PI.--O.--O.--I.-PI.-PI.	4.71	0.00261	Dominated	47.49	60.54	73.59	0	0	0
S132: --I.--O.--O.--I.--O.--O.---.--O.--O.--I.---.---.	–5.51	0.00126	Dominated	30.71	37.01	43.31	0	0	0
S133: --I.--O.--O.--I.--O.--O.-PI.--O.--O.--I.-PI.-PI.	5.58	0.00225	Dominated	39.42	50.67	61.92	0	0	0
S134: --O.--O.--O.--I.--O.--O.---.--O.--O.--I.---.---.	–5.61	0.00125	Dominated	30.61	36.86	43.11	0.04	0.01	0
S135: --O.--O.--O.--I.--O.--O.-PI.--O.--O.--I.-PI.-PI.	5.47	0.00224	Dominated	39.33	50.53	61.73	0	0	0
S136: --O.--O.--O.--I.--O.--O.-PI.--O.--O.--I.-PO.-PO.	6.46	0.00186	Dominated	30.74	40.04	49.34	0	0	0
S137: --O.--O.--O.--I.--O.--O.-PO.--O.--O.--I.-PO.-PO.	6.36	0.00185	Dominated	30.64	39.89	49.14	0	0	0
S138: --I.--I.--I.--I.--I.--I.--I.--O.--O.--I.---.---.	–5.41	0.00185	Dominated	42.41	51.66	60.91	0	0	0
S139: --I.--I.--I.--I.--I.--I.--I.--O.--O.--I.-PI.-PI.	4.21	0.00281	Dominated	51.99	66.04	80.09	0	0	0
S140: --I.--I.--I.--I.--I.--I.--I.--O.--O.--O.--I.---.---.	–6.54	0.00184	Dominated	43.34	52.54	61.74	0.01	0.01	0.01
S141: --I.--I.--I.--I.--I.--I.--I.--O.--O.--O.--I.-PI.-PI.	3.08	0.00280	Dominated	52.92	66.92	80.92	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
S142: --I.--O.--O.--I.--I.--I.--O.--O.--O.--I.---.---.	–6.24	0.00174	Dominated	41.04	49.74	58.44	0	0	0
S143: --I.--O.--O.--I.--I.--I.--O.--O.--O.--I.-PI.-PI.	3.38	0.00270	Dominated	50.62	64.12	77.62	0	0	0
S144: --I.--O.--O.--I.--O.--I.--O.--O.--O.--I.---.---.	–6.59	0.00171	Dominated	40.79	49.34	57.89	0	0	0
S145: --I.--O.--O.--I.--O.--I.--O.--O.--O.--I.-PI.-PI.	3.03	0.00266	Dominated	50.17	63.47	76.77	0	0	0
S146: --I.--O.--O.--I.--O.--O.--O.--O.--O.--I.---.---.	–5.72	0.00135	Dominated	32.72	39.47	46.22	0	0	0
S147: --I.--O.--O.--I.--O.--O.--O.--O.--O.--I.-PI.-PI.	3.90	0.00230	Dominated	42.10	53.60	65.10	0	0	0
S148: --O.--O.--O.--I.--O.--O.--O.--O.--O.--I.---.---.	–5.83	0.00133	Dominated	32.43	39.08	45.73	0.04	0.02	0.02
S149: --O.--O.--O.--I.--O.--O.--O.--O.--O.--I.-PI.-PI.	3.79	0.00229	Dominated	42.01	53.46	64.91	0	0	0
S150: --O.--O.--O.--I.--O.--O.--O.--O.--O.--I.-PO.-PO.	4.78	0.00191	Dominated	33.42	42.97	52.52	0	0	0
S151: VCI.V-I.V-I.VCI.VCI.VCI.VCI.V-I.V-I.VCI.VCI.VCI.	41.70	0.00343	Dominated	26.90	44.05	61.20	0	0	0
S152: VCO.V-O.V-O.VCO.VCO.VCO.VCO.V-O.V-O.VCO. VCO.VCO.	40.40	0.00319	Dominated	23.40	39.35	55.30	0	0	0
S153: V-O.V-O.V-O.V-O.V-O.V-O.V-O.V-O.V-O.V-O.VPO. VPO.	41.50	0.00388	Dominated	36.10	55.50	74.90	0.02	0.02	0.05
S154: V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.VPO.VPO.	43.40	0.00426	Dominated	41.80	63.10	84.40	0	0	0
S155: V-O.V-O.V-O.V-O.V-O.V-O.V-O.V-O.V-O.V-O.VPI.VPI.	42.10	0.00399	Dominated	37.70	57.65	77.60	0.02	0.06	0.15
S156: V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-I.V-I.V-I.V--.V--.	27.80	0.00409	ICER to S99: £22,700	54.00	74.45	94.90	1.61	2.25	2.58
S157: V--.V-I.V-I.V-I.V-I.V-I.V--.V-I.V-I.V-I.VPI.VPI.	43.30	0.00419	Dominated	40.50	61.45	82.40	0	0	0
S158: V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.V-I.V-I.V--.V--.	29.00	0.00409	Extended dominated	52.80	73.25	93.70	0	0	0
S159: V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.V-I.V-I.VCI.VCI.	38.30	0.00435	Extended dominated	48.70	70.45	92.20	0	0	0
S160: V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.V-I.V-I.VPI.VPI.	43.60	0.00437	Extended dominated	43.80	65.65	87.50	0	0	0
S161: V--.V-I.V-I.V-I.V-I.V--.V--.V-I.V-I.V-I.V--.V--.	30.10	0.00345	Dominated	38.90	56.15	73.40	0	0	0
S162: VCI.V-I.V-I.V-I.V-I.VCI.VCI.V-I.V-I.V-I.VCI.VCI.	40.40	0.00380	Dominated	35.60	54.60	73.60	0	0	0
S163: VPI.V-I.V-I.V-I.V-I.VPI.VPI.V-I.V-I.V-I.VPI.VPI.	46.50	0.00391	Dominated	31.70	51.25	70.80	0	0	0
S164: V--.V-I.V-I.V-I.V-I.V-I.V--.V-I.V-I.V-I.V--.V--.	28.70	0.00391	Dominated	49.50	69.05	88.60	0	0	0
S165: VCI.V-I.V-I.V-I.V-I.V-I.VCI.V-I.V-I.V-I.VCI.VCI.	39.10	0.00419	Dominated	44.70	65.65	86.60	0	0	0
S166: VPI.V-I.V-I.V-I.V-I.V-I.VPI.V-I.V-I.V-I.VPI.VPI.	45.00	0.00423	Dominated	39.60	60.75	81.90	0	0	0
S167: V-I.V-I.V-I.V-I.V-I.V-I.V--.V-I.V-I.V-I.V--.V--.	28.30	0.00402	Dominated	52.10	72.20	92.30	0	0	0
S168: V-I.V-I.V-I.V-I.V-I.V-I.V-I.VCI.V-I.V-I.V-I.VCI.VCI.	38.70	0.00429	Dominated	47.10	68.55	90.00	0	0	0
S169: V-I.V-I.V-I.V-I.V-I.V-I.V-I.VPI.V-I.V-I.V-I.VPI.VPI.	44.50	0.00431	Dominated	41.70	63.25	84.80	0	0	0
S170: V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.V--.V--.	28.20	0.00409	Extended dominated	53.60	74.05	94.50	9.47	9.91	9
S171: V-I.V-I.V-I.V-I.V-I.V-I.V-I.VCO.V-I.V-I.V-I.VCI.VCI.	38.60	0.00429	Dominated	47.20	68.65	90.10	0	0	0
S172: V-I.V-I.V-I.V-I.V-I.V-I.V-I.VPO.V-I.V-I.V-I.VPI.VPI.	44.40	0.00431	Dominated	41.80	63.35	84.90	0	0	0
S173: V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V--.V--.	29.40	0.00409	Extended dominated	52.40	72.85	93.30	7.67	10.3	10.9
S174: V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.VCI.VCI.	38.70	0.00435	Extended dominated	48.30	70.05	91.80	1.64	5.26	10.6
S175: V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.VPI.VPI.	44.00	0.00437	ICER to T446: £523,000	43.40	65.25	87.10	0.06	0.15	0.47
S176: V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-I.V-I.V-I.VCI.VCI.	37.10	0.00435	ICER to S177: £54,100	49.90	71.65	93.40	0.06	0.14	0.31

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
S177: V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-I.V-I.V-O.VCI.VCI.	36.80	0.00434	ICER to S156: £35,300	50.00	71.70	93.40	0.25	1.02	1.9
S178: VCI.VCI.VCI.V-I.V-O.VCI.VCI.VCI.VCI.V-I.VCI.VCI.	40.30	0.00370	Dominated	33.70	52.20	70.70	0	0	0
S179: VCI.VCI.VCI.V-I.V-O.VCI.V--.VCI.VCI.V-I.VCI.VCI.	39.20	0.00369	Dominated	34.60	53.05	71.50	0	0	0
S180: V--.V-I.V-I.V-I.V-I.V--.V--.V-O.V-O.V-I.V--.V--.	29.60	0.00342	Dominated	38.80	55.90	73.00	0	0	0
S181: VPI.V-I.V-I.V-I.V-I.VPI.VPI.V-O.V-O.V-I.VPI.VPI.	46.10	0.00388	Dominated	31.50	50.90	70.30	0	0	0
S182: V--.V-O.V-O.V-I.V-I.V--.V--.V-O.V-O.V-I.V--.V--.	29.80	0.00337	Dominated	37.60	54.45	71.30	0	0	0
S183: VPI.V-O.V-O.V-I.V-I.VPI.VPI.V-O.V-O.V-I.VPI.VPI.	46.20	0.00382	Dominated	30.20	49.30	68.40	0	0	0
S184: V--.V-O.V-O.V-I.V-O.V--.V--.V-O.V-O.V-I.V--.V--.	29.30	0.00337	Dominated	38.10	54.95	71.80	0	0	0
S185: VPI.V-O.V-O.V-I.V-O.VPI.VPI.V-O.V-O.V-I.VPI.VPI.	45.80	0.00382	Dominated	30.60	49.70	68.80	0	0	0
S186: VPI.V-O.V-O.V-I.V-O.VPI.VPI.V-O.V-O.V-I.VPO.VPO.	45.10	0.00371	Dominated	29.10	47.65	66.20	0	0	0
S187: VPI.V-O.V-O.V-I.V-O.VPI.VPO.V-O.V-O.V-I.VPO.VPO.	45.00	0.00371	Dominated	29.20	47.75	66.30	0	0	0
S188: VPI.V-O.V-O.V-I.V-O.VPO.VPO.V-O.V-O.V-I.VPO.VPO.	45.30	0.00362	Dominated	27.10	45.20	63.30	0	0	0
S189: VPO.V-O.V-O.V-I.V-O.VPO.VPO.V-O.V-O.V-I.VPO.VPO.	45.30	0.00361	Dominated	26.90	44.95	63.00	0	0	0
S190: V--.V-I.V-I.V-I.V-I.V-I.V--.V-O.V-O.V-I.V--.V--.	28.20	0.00388	Dominated	49.40	68.80	88.20	0	0	0
S191: VPI.V-I.V-I.V-I.V-I.V-I.VPI.V-O.V-O.V-I.VPI.VPI.	44.50	0.00420	Dominated	39.50	60.50	81.50	0	0	0
S192: V--.V-O.V-O.V-I.V-I.V-I.V--.V-O.V-O.V-I.V--.V--.	28.40	0.00382	Dominated	48.00	67.10	86.20	0	0	0
S193: VPI.V-O.V-O.V-I.V-I.V-I.V-I.VPI.V-O.V-O.V-I.VPI.VPI.	44.60	0.00414	Dominated	38.20	58.90	79.60	0	0	0
S194: V--.V-O.V-O.V-I.V-O.V-I.V--.V-O.V-O.V-I.V--.V--.	27.90	0.00382	Dominated	48.50	67.60	86.70	0	0	0
S195: VPI.V-O.V-O.V-I.V-O.V-I.VPI.V-O.V-O.V-I.VPI.VPI.	44.20	0.00414	Dominated	38.60	59.30	80.00	0	0	0
S196: V--.V-O.V-O.V-I.V-O.V-O.V--.V-O.V-O.V-I.V--.V--.	28.40	0.00355	Dominated	42.60	60.35	78.10	0	0	0
S197: VPI.V-O.V-O.V-I.V-O.V-O.VPI.V-O.V-O.V-I.VPI.VPI.	44.70	0.00387	Dominated	32.70	52.05	71.40	0	0	0
S198: VPI.V-O.V-O.V-I.V-O.V-O.VPI.V-O.V-O.V-I.VPO.VPO.	44.00	0.00376	Dominated	31.20	50.00	68.80	0	0	0
S199: VPI.V-O.V-O.V-I.V-O.V-O.VPO.V-O.V-O.V-I.VPO.VPO.	43.90	0.00376	Dominated	31.30	50.10	68.90	0	0	0
S200: VPO.V-O.V-O.V-I.V-O.V-O.VPO.V-O.V-O.V-I.VPO.VPO.	43.90	0.00376	Dominated	31.30	50.10	68.90	0	0	0
S201: V-I.V-I.V-I.V-I.V-I.V-I.V--.V-O.V-O.V-I.V--.V--.	27.80	0.00399	Dominated	52.00	71.95	91.90	0	0	0
S202: V-I.V-I.V-I.V-I.V-I.V-I.VPI.V-O.V-O.V-I.VPI.VPI.	44.00	0.00428	Dominated	41.60	63.00	84.40	0	0	0
S203: V-I.V-O.V-O.V-I.V-I.V-I.V--.V-O.V-O.V-I.V--.V--.	28.00	0.00393	Dominated	50.60	70.25	89.90	0	0	0
S204: V-I.V-O.V-O.V-I.V-I.V-I.VPI.V-O.V-O.V-I.VPI.VPI.	44.20	0.00422	Dominated	40.20	61.30	82.40	0	0	0
S205: V-I.V-O.V-O.V-I.V-O.V-I.V--.V-O.V-O.V-I.V--.V--.	27.50	0.00393	Dominated	51.10	70.75	90.40	0	0	0
S206: V-I.V-O.V-O.V-I.V-O.V-I.VPI.V-O.V-O.V-I.VPI.VPI.	43.70	0.00422	Dominated	40.70	61.80	82.90	0	0	0
S207: V-I.V-O.V-O.V-I.V-O.V-O.V--.V-O.V-O.V-I.V--.V--.	28.10	0.00366	Dominated	45.10	63.40	81.70	0	0	0
S208: V-I.V-O.V-O.V-I.V-O.V-O.VPI.V-O.V-O.V-I.VPI.VPI.	44.30	0.00396	Dominated	34.90	54.70	74.50	0	0	0
S209: V-O.V-O.V-O.V-I.V-O.V-O.V--.V-O.V-O.V-I.V--.V--.	27.90	0.00365	Dominated	45.10	63.35	81.60	0	0	0
S210: V-O.V-O.V-O.V-I.V-O.V-O.VPI.V-O.V-O.V-I.VPI.VPI.	44.10	0.00395	Dominated	34.90	54.65	74.40	0	0	0
S211: V-O.V-O.V-O.V-I.V-O.V-O.VPI.V-O.V-O.V-I.VPO.VPO.	43.50	0.00384	Dominated	33.30	52.50	71.70	0	0	0
S212: V-O.V-O.V-O.V-I.V-O.V-O.VPO.V-O.V-O.V-I.VPO.VPO.	43.40	0.00383	Dominated	33.20	52.35	71.50	0	0	0
S213: V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.V--.V--.	28.90	0.00406	Dominated	52.30	72.60	92.90	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
S214: V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.VPI.VPI.	43.60	0.00434	Dominated	43.20	64.90	86.60	0	0	0
S215: V-I.V-O.V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-I.V--.V--.	27.90	0.00400	Dominated	52.10	72.10	92.10	0	0	0
S216: V-I.V-O.V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VPI.VPI.	42.50	0.00428	Dominated	43.10	64.50	85.90	0	0	0
S217: V-I.V-O.V-O.V-I.V-O.V-I.V-O.V-O.V-O.V-I.V--.V--.	27.40	0.00400	Dominated	52.60	72.60	92.60	0	0	0
S218: V-I.V-O.V-O.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VPI.VPI.	42.10	0.00428	Dominated	43.50	64.90	86.30	0	0	0
S219: V-I.V-O.V-O.V-I.V-O.V-O.V-O.V-O.V-O.V-I.V--.V--.	28.00	0.00373	Dominated	46.60	65.25	83.90	0	0	0
S220: V-I.V-O.V-O.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VPI.VPI.	42.60	0.00401	Dominated	37.60	57.65	77.70	0	0	0
S221: V-O.V-O.V-O.V-I.V-O.V-O.V-O.V-O.V-O.V-I.V--.V--.	27.80	0.00372	Dominated	46.60	65.20	83.80	5.52	6.49	6.65
S222: V-O.V-O.V-O.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VPI.VPI.	42.50	0.00401	Dominated	37.70	57.75	77.80	0	0	0
S223: V-O.V-O.V-O.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VPO.VPO.	41.80	0.00390	Dominated	36.20	55.70	75.20	0	0	0
T2: --O.--I.--I.--I.--I.--I.--I.--I.--I.---.---.	–5.46	0.00192	Dominated	43.86	53.46	63.06	0	0	0
T3: --I.--O.--O.--I.--I.--I.--I.--I.--I.---.---.	–5.05	0.00184	Dominated	41.85	51.05	60.25	0	0	0
T5: --I.--I.--I.--I.--I.--O.--I.--I.--I.---.---.	–4.48	0.00157	Dominated	35.88	43.73	51.58	0	0	0
T8: --O.--I.--I.--I.--I.--I.--O.--I.--I.--I.---.---.	–6.60	0.00191	Extended dominated	44.80	54.35	63.90	0.06	0.01	0
T9: --I.--O.--O.--I.--I.--I.--O.--I.--I.--I.---.---.	–6.19	0.00183	Dominated	42.79	51.94	61.09	0	0	0
T11: --I.--I.--I.--I.--I.--O.--O.--I.--I.--I.---.---.	–5.61	0.00156	Dominated	36.81	44.61	52.41	0	0	0
T13: --O.--I.--I.--I.--I.--I.--I.--O.--O.--I.---.---.	–5.51	0.00184	Dominated	42.31	51.51	60.71	0	0	0
T14: --I.--O.--O.--I.--I.--I.--I.--O.--O.--I.---.---.	–5.10	0.00175	Dominated	40.10	48.85	57.60	0	0	0
T15: --I.--I.--I.--I.--O.--I.--I.--O.--O.--I.---.---.	–5.76	0.00181	Dominated	41.96	51.01	60.06	0	0	0
T16: --I.--I.--I.--I.--I.--O.--I.--O.--O.--I.---.---.	–4.53	0.00149	Dominated	34.33	41.78	49.23	0	0	0
T17: --O.--I.--I.--I.--I.--I.--I.--O.--O.--O.--I.---.---.	–6.65	0.00183	Dominated	43.25	52.40	61.55	0	0	0
T20: --I.--I.--I.--I.--I.--O.--O.--O.--O.--I.---.---.	–5.67	0.00148	Dominated	35.27	42.67	50.07	0	0	0
T21: --O.--O.--O.--I.--I.--I.--O.--O.--O.--I.---.---.	–6.35	0.00173	Dominated	40.95	49.60	58.25	0	0	0
T25: --I.--O.--O.--I.--I.--O.--O.--O.--O.--I.---.---.	–5.37	0.00138	Dominated	32.97	39.87	46.77	0	0	0
T27: --O.--I.--I.--I.--O.--I.--O.--O.--O.--I.---.---.	–7.00	0.00179	–	42.80	51.75	60.70	0.09	0.05	0.03
T28: --I.--I.--I.--I.--O.--O.--O.--O.--O.--I.---.---.	–6.02	0.00144	Dominated	34.82	42.02	49.22	0	0	0
T29: --I.--I.--I.--I.--O.--I.--O.--O.--O.--I.---.---.	–6.90	0.00181	Extended dominated	43.10	52.15	61.20	0.02	0	0
T30: --O.--I.--I.--I.--I.--O.--O.--O.--O.--I.---.---.	–5.78	0.00147	Dominated	35.18	42.53	49.88	0	0	0
T36: --O.--I.--I.--I.--O.--O.--O.--O.--O.--I.---.---.	–6.13	0.00143	Dominated	34.73	41.88	49.03	0.15	0.05	0.04
T37: --O.--O.--O.--I.--O.--I.--O.--O.--O.--I.---.---.	–6.70	0.00169	Dominated	40.50	48.95	57.40	0	0	0
T39: --O.--O.--O.--I.--I.--O.--O.--O.--O.--I.---.---.	–5.48	0.00137	Dominated	32.88	39.73	46.58	0	0	0
T42: --O.--I.--I.--I.--I.--I.--I.--I.--I.--I.-PI.-PI.	4.16	0.00288	Dominated	53.44	67.84	82.24	0	0	0
T43: --I.--O.--O.--I.--I.--I.--I.--I.--I.--I.-PI.-PI.	4.57	0.00279	Dominated	51.23	65.18	79.13	0	0	0
T45: --I.--I.--I.--I.--I.--O.--I.--I.--I.--I.-PI.-PI.	5.14	0.00253	Dominated	45.46	58.11	70.76	0	0	0
T48: --O.--I.--I.--I.--I.--I.--I.--O.--I.--I.--I.-PI.-PI.	3.02	0.00287	Extended dominated	54.38	68.73	83.08	0.48	0.46	0.44
T49: --I.--O.--O.--I.--I.--I.--I.--O.--I.--I.--I.-PI.-PI.	3.43	0.00279	Dominated	52.37	66.32	80.27	0	0	0
T51: --I.--I.--I.--I.--I.--O.--O.--I.--I.--I.-PI.-PI.	4.01	0.00252	Dominated	46.39	58.99	71.59	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T53: --O.--I.--I.--I.--I.--I.--I.--O.--O.--I.-PI.-PI.	4.11	0.00280	Dominated	51.89	65.89	79.89	0	0	0
T54: --I.--O.--O.--I.--I.--I.--I.--O.--O.--I.-PI.-PI.	4.52	0.00271	Dominated	49.68	63.23	76.78	0	0	0
T55: --I.--I.--I.--I.--O.--I.--I.--O.--O.--I.-PI.-PI.	3.86	0.00277	Dominated	51.54	65.39	79.24	0	0	0
T56: --I.--I.--I.--I.--I.--O.--I.--O.--O.--I.-PI.-PI.	5.09	0.00245	Dominated	43.91	56.16	68.41	0	0	0
T57: --O.--I.--I.--I.--I.--I.--O.--O.--O.--I.-PI.-PI.	2.97	0.00279	Dominated	52.83	66.78	80.73	0	0	0
T60: --I.--I.--I.--I.--I.--O.--O.--O.--O.--I.-PI.-PI.	3.95	0.00244	Dominated	44.85	57.05	69.25	0	0	0
T61: --O.--O.--O.--I.--I.--I.--O.--O.--O.--I.-PI.-PI.	3.27	0.00269	Dominated	50.53	63.98	77.43	0	0	0
T65: --I.--O.--O.--I.--I.--O.--O.--O.--O.--I.-PI.-PI.	4.25	0.00234	Dominated	42.55	54.25	65.95	0	0	0
T67: --O.--I.--I.--I.--O.--I.--O.--O.--O.--I.-PI.-PI.	2.62	0.00275	Dominated	52.38	66.13	79.88	0.86	0.72	0.65
T68: --I.--I.--I.--I.--O.--O.--O.--O.--O.--I.-PI.-PI.	3.60	0.00240	Dominated	44.40	56.40	68.40	0	0	0
T69: --I.--I.--I.--I.--O.--I.--O.--O.--O.--I.-PI.-PI.	2.72	0.00276	Dominated	52.48	66.28	80.08	0	0	0
T70: --O.--I.--I.--I.--I.--O.--O.--O.--O.--I.-PI.-PI.	3.84	0.00243	Dominated	44.76	56.91	69.06	0	0	0
T76: --O.--I.--I.--I.--O.--O.--O.--O.--O.--I.-PI.-PI.	3.49	0.00239	Dominated	44.31	56.26	68.21	0.19	0.16	0.13
T77: --O.--O.--O.--I.--O.--I.--O.--O.--O.--I.-PI.-PI.	2.92	0.00265	Dominated	50.08	63.33	76.58	0	0	0
T79: --O.--O.--O.--I.--I.--O.--O.--O.--O.--I.-PI.-PI.	4.15	0.00233	Dominated	42.45	54.10	65.75	0	0	0
T82: --O.--I.--I.--I.--I.--I.--I.--I.--I.--I.-PO.-PO.	5.15	0.00250	Dominated	44.85	57.35	69.85	0	0	0
T83: --I.--O.--O.--I.--I.--I.--I.--I.--I.--I.-PO.-PO.	5.56	0.00241	Dominated	42.64	54.69	66.74	0	0	0
T84: --I.--I.--I.--I.--O.--I.--I.--I.--I.--I.-PO.-PO.	4.90	0.00247	Dominated	44.50	56.85	69.20	0	0	0
T85: --I.--I.--I.--I.--I.--O.--I.--I.--I.--I.-PO.-PO.	6.13	0.00215	Dominated	36.87	47.62	58.37	0	0	0
T86: --I.--I.--I.--I.--I.--I.--O.--I.--I.--I.-PO.-PO.	4.12	0.00250	Dominated	45.88	58.38	70.88	0	0	0
T87: --I.--I.--I.--I.--I.--I.--I.--O.--O.--I.-PO.-PO.	5.20	0.00243	Dominated	43.40	55.55	67.70	0	0	0
T88: --O.--I.--I.--I.--I.--I.--O.--I.--I.--I.-PO.-PO.	4.01	0.00249	Dominated	45.79	58.24	70.69	0	0	0
T89: --I.--O.--O.--I.--I.--I.--O.--I.--I.--I.-PO.-PO.	4.42	0.00240	Dominated	43.58	55.58	67.58	0	0	0
T90: --I.--I.--I.--I.--O.--I.--O.--I.--I.--I.-PO.-PO.	3.76	0.00246	Dominated	45.44	57.74	70.04	0	0	0
T91: --I.--I.--I.--I.--I.--O.--O.--I.--I.--I.-PO.-PO.	4.99	0.00214	Dominated	37.81	48.51	59.21	0	0	0
T92: --I.--I.--I.--I.--I.--I.--O.--O.--O.--I.-PO.-PO.	4.06	0.00242	Dominated	44.34	56.44	68.54	0	0	0
T93: --O.--I.--I.--I.--I.--I.--I.--O.--O.--I.-PO.-PO.	5.09	0.00241	Dominated	43.11	55.16	67.21	0	0	0
T94: --I.--O.--O.--I.--I.--I.--I.--O.--O.--I.-PO.-PO.	5.50	0.00233	Dominated	41.10	52.75	64.40	0	0	0
T95: --I.--I.--I.--I.--O.--I.--I.--O.--O.--I.-PO.-PO.	4.85	0.00239	Dominated	42.95	54.90	66.85	0	0	0
T96: --I.--I.--I.--I.--I.--O.--I.--O.--O.--I.-PO.-PO.	6.07	0.00207	Dominated	35.33	45.68	56.03	0	0	0
T97: --O.--I.--I.--I.--I.--I.--O.--O.--O.--I.-PO.-PO.	3.95	0.00241	Dominated	44.25	56.30	68.35	0	0	0
T100: --I.--I.--I.--I.--I.--O.--O.--O.--O.--I.-PO.-PO.	4.93	0.00206	Dominated	36.27	46.57	56.87	0	0	0
T101: --O.--O.--O.--I.--I.--I.--O.--O.--O.--I.-PO.-PO.	4.26	0.00231	Dominated	41.94	53.49	65.04	0	0	0
T104: --I.--O.--O.--I.--O.--I.--O.--O.--O.--I.-PO.-PO.	4.01	0.00228	Dominated	41.59	52.99	64.39	0	0	0
T105: --I.--O.--O.--I.--I.--O.--O.--O.--O.--I.-PO.-PO.	5.24	0.00196	Dominated	33.96	43.76	53.56	0	0	0
T106: --I.--O.--O.--I.--I.--I.--O.--O.--O.--I.-PO.-PO.	4.36	0.00232	Dominated	42.04	53.64	65.24	0	0	0
T107: --O.--I.--I.--I.--O.--I.--O.--O.--O.--I.-PO.-PO.	3.60	0.00237	Dominated	43.80	55.65	67.50	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T108: --I.--I.--I.--I.--O.--O.--O.--O.--I.-PO.-PO.	4.58	0.00202	Dominated	35.82	45.92	56.02	0	0	0
T109: --I.--I.--I.--I.--O.--I.--O.--O.--O.--I.-PO.-PO.	3.71	0.00238	Dominated	43.89	55.79	67.69	0	0	0
T110: --O.--I.--I.--I.--I.--O.--O.--O.--O.--I.-PO.-PO.	4.83	0.00204	Dominated	35.97	46.17	56.37	0	0	0
T116: --O.--I.--I.--I.--O.--O.--O.--O.--O.--I.-PO.-PO.	4.47	0.00201	Dominated	35.73	45.78	55.83	0.01	0.01	0.02
T117: --O.--O.--O.--I.--O.--I.--O.--O.--O.--I.-PO.-PO.	3.90	0.00227	Dominated	41.50	52.85	64.20	0	0	0
T118: --I.--O.--O.--I.--O.--O.--O.--O.--O.--I.-PO.-PO.	4.88	0.00192	Dominated	33.52	43.12	52.72	0	0	0
T119: --O.--O.--O.--I.--I.--O.--O.--O.--O.--I.-PO.-PO.	5.13	0.00195	Dominated	33.87	43.62	53.37	0	0	0
T122: --O.--I.--I.--I.--I.--I.--I.--I.--I.--I.-CI.-CI.	–0.60	0.00278	Dominated	56.20	70.10	84.00	0	0	0
T123: --I.--O.--O.--I.--I.--I.--I.--I.--I.--I.-CI.-CI.	–0.19	0.00270	Dominated	54.19	67.69	81.19	0	0	0
T125: --I.--I.--I.--I.--I.--O.--I.--I.--I.--I.-CI.-CI.	0.38	0.00244	Dominated	48.42	60.62	72.82	0	0	0
T127: --I.--I.--I.--I.--I.--I.--I.--O.--O.--I.-CI.-CI.	–0.55	0.00271	Dominated	54.75	68.30	81.85	0	0	0
T128: --O.--I.--I.--I.--I.--I.--I.--O.--I.--I.--I.-CI.-CI.	–1.74	0.00278	Extended dominated	57.34	71.24	85.14	2.44	1.82	1.31
T129: --I.--O.--O.--I.--I.--I.--I.--O.--I.--I.--I.-CI.-CI.	–1.33	0.00269	Dominated	55.13	68.58	82.03	0	0	0
T131: --I.--I.--I.--I.--I.--I.--O.--O.--I.--I.--I.-CI.-CI.	–0.76	0.00243	Dominated	49.36	61.51	73.66	0	0	0
T132: --I.--I.--I.--I.--I.--I.--I.--O.--O.--O.--I.-CI.-CI.	–1.69	0.00271	Dominated	55.89	69.44	82.99	0	0	0
T133: --O.--I.--I.--I.--I.--I.--I.--I.--O.--O.--I.-CI.-CI.	–0.66	0.00270	Dominated	54.66	68.16	81.66	0	0	0
T134: --I.--O.--O.--I.--I.--I.--I.--I.--O.--O.--I.-CI.-CI.	–0.25	0.00262	Dominated	52.65	65.75	78.85	0	0	0
T135: --I.--I.--I.--I.--I.--O.--I.--I.--O.--O.--I.-CI.-CI.	–0.90	0.00268	Dominated	54.50	67.90	81.30	0	0	0
T136: --I.--I.--I.--I.--I.--I.--O.--I.--O.--O.--I.-CI.-CI.	0.33	0.00235	Dominated	46.67	58.42	70.17	0	0	0
T137: --O.--I.--I.--I.--I.--I.--I.--O.--O.--O.--I.-CI.-CI.	–1.79	0.00269	Dominated	55.59	69.04	82.49	0	0	0
T140: --I.--I.--I.--I.--I.--I.--O.--O.--O.--O.--I.-CI.-CI.	–0.81	0.00235	Dominated	47.81	59.56	71.31	0	0	0
T141: --O.--O.--O.--I.--I.--I.--I.--O.--O.--O.--I.-CI.-CI.	–1.49	0.00260	Dominated	53.49	66.49	79.49	0	0	0
T144: --I.--O.--O.--I.--O.--I.--O.--O.--O.--I.-CI.-CI.	–1.73	0.00257	Dominated	53.13	65.98	78.83	0	0	0
T145: --I.--O.--O.--I.--I.--O.--O.--O.--O.--I.-CI.-CI.	–0.51	0.00225	Dominated	45.51	56.76	68.01	0	0	0
T146: --I.--O.--O.--I.--I.--I.--O.--O.--O.--I.-CI.-CI.	–1.38	0.00261	Dominated	53.58	66.63	79.68	0	0	0
T147: --O.--I.--I.--I.--O.--I.--O.--O.--O.--I.-CI.-CI.	–2.14	0.00266	Extended dominated	55.34	68.64	81.94	4.58	2.93	1.75
T148: --I.--I.--I.--I.--O.--O.--O.--O.--O.--I.-CI.-CI.	–1.16	0.00231	Dominated	47.36	58.91	70.46	0	0	0
T149: --I.--I.--I.--I.--O.--I.--O.--O.--O.--I.-CI.-CI.	–2.04	0.00267	Extended dominated	55.44	68.79	82.14	0	0	0
T150: --O.--I.--I.--I.--I.--O.--O.--O.--O.--I.-CI.-CI.	–0.92	0.00233	Dominated	47.52	59.17	70.82	0	0	0
T156: --O.--I.--I.--I.--O.--O.--O.--O.--O.--I.-CI.-CI.	–1.27	0.00230	Dominated	47.27	58.77	70.27	3.71	2.28	1.38
T157: --O.--O.--O.--I.--O.--I.--O.--O.--O.--I.-CI.-CI.	–1.84	0.00256	Dominated	53.04	65.84	78.64	0	0	0
T158: --I.--O.--O.--I.--O.--O.--O.--O.--O.--I.-CI.-CI.	–0.86	0.00221	Dominated	45.06	56.11	67.16	0	0	0
T159: --O.--O.--O.--I.--I.--O.--O.--O.--O.--I.-CI.-CI.	–0.62	0.00223	Dominated	45.22	56.37	67.52	0	0	0
T160: --O.--O.--O.--I.--O.--O.--O.--O.--O.--I.-CI.-CI.	–0.97	0.00220	Dominated	44.97	55.97	66.97	0.49	0.23	0.13
T161: --I.--I.--I.--I.--I.--I.--I.--I.--I.--I.-CO.-CO.	0.08	0.00246	Dominated	49.12	61.42	73.72	0	0	0
T162: --O.--I.--I.--I.--I.--I.--I.--I.--I.--I.-CO.-CO.	–0.03	0.00245	Dominated	49.03	61.28	73.53	0	0	0
T163: --I.--O.--O.--I.--I.--I.--I.--I.--I.--I.-CO.-CO.	0.38	0.00237	Dominated	47.02	58.87	70.72	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T164: --I.--I.--I.--I.--O.--I.--I.--I.--I.--I.-CO.-CO.	–0.27	0.00243	Dominated	48.87	61.02	73.17	0	0	0
T165: --I.--I.--I.--I.--I.--O.--I.--I.--I.-CO.-CO.	0.96	0.00210	Dominated	41.05	51.55	62.05	0	0	0
T166: --I.--I.--I.--I.--I.--I.--O.--I.--I.--I.-CO.-CO.	–1.06	0.00246	Dominated	50.26	62.56	74.86	0	0	0
T167: --I.--I.--I.--I.--I.--I.--I.--O.--O.--I.-CO.-CO.	0.03	0.00238	Dominated	47.57	59.47	71.37	0	0	0
T168: --O.--I.--I.--I.--I.--I.--O.--I.--I.--I.-CO.-CO.	–1.16	0.00244	Dominated	49.96	62.16	74.36	0	0	0
T169: --I.--O.--O.--I.--I.--I.--O.--I.--I.--I.-CO.-CO.	–0.75	0.00236	Dominated	47.95	59.75	71.55	0	0	0
T170: --I.--I.--I.--I.--O.--I.--O.--I.--I.--I.-CO.-CO.	–1.41	0.00242	Dominated	49.81	61.91	74.01	0.01	0.01	0
T171: --I.--I.--I.--I.--I.--O.--O.--I.--I.--I.-CO.-CO.	–0.18	0.00210	Dominated	42.18	52.68	63.18	0	0	0
T172: --I.--I.--I.--I.--I.--I.--O.--O.--O.--I.-CO.-CO.	–1.11	0.00237	Dominated	48.51	60.36	72.21	0	0	0
T173: --O.--I.--I.--I.--I.--I.--I.--O.--O.--I.-CO.-CO.	–0.08	0.00237	Dominated	47.48	59.33	71.18	0	0	0
T174: --I.--O.--O.--I.--I.--I.--I.--O.--O.--I.-CO.-CO.	0.33	0.00228	Dominated	45.27	56.67	68.07	0	0	0
T175: --I.--I.--I.--I.--O.--I.--I.--O.--O.--I.-CO.-CO.	–0.33	0.00234	Dominated	47.13	58.83	70.53	0	0	0
T176: --I.--I.--I.--I.--I.--O.--I.--O.--O.--I.-CO.-CO.	0.90	0.00202	Dominated	39.50	49.60	59.70	0	0	0
T177: --O.--I.--I.--I.--I.--I.--I.--O.--O.--O.--I.-CO.-CO.	–1.22	0.00236	Dominated	48.42	60.22	72.02	0	0	0
T180: --I.--I.--I.--I.--I.--O.--O.--O.--O.--I.-CO.-CO.	–0.24	0.00201	Dominated	40.44	50.49	60.54	0	0	0
T181: --O.--O.--O.--I.--I.--I.--O.--O.--O.--I.-CO.-CO.	–0.92	0.00226	Dominated	46.12	57.42	68.72	0	0	0
T184: --I.--O.--O.--I.--O.--I.--O.--O.--O.--I.-CO.-CO.	–1.16	0.00224	Dominated	45.96	57.16	68.36	0	0	0
T185: --I.--O.--O.--I.--I.--O.--O.--O.--O.--I.-CO.-CO.	0.06	0.00191	Dominated	38.14	47.69	57.24	0	0	0
T186: --I.--O.--O.--I.--I.--I.--O.--O.--O.--I.-CO.-CO.	–0.81	0.00227	Dominated	46.21	57.56	68.91	0	0	0
T187: --O.--I.--I.--I.--O.--I.--O.--O.--O.--I.-CO.-CO.	–1.57	0.00232	Dominated	47.97	59.57	71.17	0.04	0.02	0.02
T188: --I.--I.--I.--I.--O.--O.--O.--O.--O.--I.-CO.-CO.	–0.59	0.00198	Dominated	40.19	50.09	59.99	0	0	0
T189: --I.--I.--I.--I.--O.--I.--O.--O.--O.--I.-CO.-CO.	–1.46	0.00234	Dominated	48.26	59.96	71.66	0	0	0
T190: --O.--I.--I.--I.--I.--O.--O.--O.--O.--I.-CO.-CO.	–0.35	0.00200	Dominated	40.35	50.35	60.35	0	0	0
T196: --O.--I.--I.--I.--O.--O.--O.--O.--O.--I.-CO.-CO.	–0.70	0.00196	Dominated	39.90	49.70	59.50	0.26	0.16	0.04
T197: --O.--O.--O.--I.--O.--I.--O.--O.--O.--I.-CO.-CO.	–1.27	0.00222	Dominated	45.67	56.77	67.87	0	0	0
T198: --I.--O.--O.--I.--O.--O.--O.--O.--O.--I.-CO.-CO.	–0.29	0.00188	Dominated	37.89	47.29	56.69	0	0	0
T199: --O.--O.--O.--I.--I.--O.--O.--O.--O.--I.-CO.-CO.	–0.04	0.00190	Dominated	38.04	47.54	57.04	0	0	0
T200: --O.--O.--O.--I.--O.--O.--O.--O.--O.--I.-CO.-CO.	–0.40	0.00186	Dominated	37.60	46.90	56.20	0.25	0.12	0.06
T208: --O.--I.--I.--I.--I.---.--I.--I.--I.---.---.	–6.38	0.00183	Dominated	42.98	52.13	61.28	0	0	0
T209: --I.--O.--O.--I.--I.--I.---.--I.--I.--I.---.---.	–5.97	0.00174	Dominated	40.77	49.47	58.17	0	0	0
T211: --I.--I.--I.--I.--I.--O.---.--I.--I.--I.---.---.	–5.40	0.00148	Dominated	35.00	42.40	49.80	0	0	0
T217: --O.--I.--I.--I.--I.--I.---.--O.--O.--I.---.---.	–6.44	0.00174	Dominated	41.24	49.94	58.64	0	0	0
T220: --I.--I.--I.--I.--I.--O.---.--O.--O.--I.---.---.	–5.46	0.00140	Dominated	33.46	40.46	47.46	0	0	0
T221: --O.--O.--O.--I.--I.--I.---.--O.--O.--I.---.---.	–6.14	0.00165	Dominated	39.14	47.39	55.64	0	0	0
T225: --I.--O.--O.--I.--I.--O.---.--O.--O.--I.---.---.	–5.16	0.00130	Dominated	31.16	37.66	44.16	0	0	0
T227: --O.--I.--I.--I.--O.--I.---.--O.--O.--I.---.---.	–6.79	0.00171	Dominated	40.99	49.54	58.09	0.01	0.01	0
T228: --I.--I.--I.--I.--O.--O.---.--O.--O.--I.---.---.	–5.81	0.00136	Dominated	33.01	39.81	46.61	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T229: --I.--I.--I.--I.--O.--I.---.--O.--O.--I.---.---.	–6.68	0.00172	Dominated	41.08	49.68	58.28	0	0	0
T230: --O.--I.--I.--I.--I.--O.---.--O.--O.--I.---.---.	–5.57	0.00138	Dominated	33.17	40.07	46.97	0	0	0
T236: --O.--I.--I.--I.--O.--O.---.--O.--O.--I.---.---.	–5.92	0.00135	Dominated	32.92	39.67	46.42	0	0	0.01
T237: --O.--O.--O.--I.--O.--I.---.--O.--O.--I.---.---.	–6.49	0.00161	Dominated	38.69	46.74	54.79	0	0	0
T239: --O.--O.--O.--I.--I.--O.---.--O.--O.--I.---.---.	–5.26	0.00129	Dominated	31.06	37.51	43.96	0	0	0
T246: --I.--I.--I.--I.--I.--I.---.--I.--I.--I.-PI.-PI.	3.34	0.00280	Dominated	52.66	66.66	80.66	0	0	0
T248: --O.--I.--I.--I.--I.--I.---.--I.--I.--I.-PI.-PI.	3.24	0.00279	Dominated	52.56	66.51	80.46	0	0	0
T249: --I.--O.--O.--I.--I.--I.---.--I.--I.--I.-PI.-PI.	3.65	0.00270	Dominated	50.35	63.85	77.35	0	0	0
T250: --I.--I.--I.--I.--O.--I.---.--I.--I.--I.-PI.-PI.	2.99	0.00276	Dominated	52.21	66.01	79.81	0	0	0
T251: --I.--I.--I.--I.--I.--O.---.--I.--I.--I.-PI.-PI.	4.22	0.00244	Dominated	44.58	56.78	68.98	0	0	0
T252: --I.--I.--I.--I.--I.--I.---.--O.--O.--I.-PI.-PI.	3.29	0.00272	Dominated	51.11	64.71	78.31	0	0	0
T257: --O.--I.--I.--I.--I.--I.---.--O.--O.--I.-PI.-PI.	3.18	0.00270	Dominated	50.82	64.32	77.82	0	0	0
T260: --I.--I.--I.--I.--I.--O.---.--O.--O.--I.-PI.-PI.	4.16	0.00235	Dominated	42.84	54.59	66.34	0	0	0
T261: --O.--O.--O.--I.--I.--I.---.--O.--O.--I.-PI.-PI.	3.48	0.00260	Dominated	48.52	61.52	74.52	0	0	0
T264: --I.--O.--O.--I.--O.--I.---.--O.--O.--I.-PI.-PI.	3.24	0.00258	Dominated	48.36	61.26	74.16	0	0	0
T265: --I.--O.--O.--I.--I.--O.---.--O.--O.--I.-PI.-PI.	4.47	0.00226	Dominated	40.73	52.03	63.33	0	0	0
T266: --I.--O.--O.--I.--I.--I.---.--O.--O.--I.-PI.-PI.	3.59	0.00262	Dominated	48.81	61.91	75.01	0	0	0
T267: --O.--I.--I.--I.--O.--I.---.--O.--O.--I.-PI.-PI.	2.83	0.00266	Dominated	50.37	63.67	76.97	0	0	0
T268: --I.--I.--I.--I.--O.--O.---.--O.--O.--I.-PI.-PI.	3.81	0.00232	Dominated	42.59	54.19	65.79	0	0	0
T269: --I.--I.--I.--I.--O.--I.---.--O.--O.--I.-PI.-PI.	2.94	0.00268	Dominated	50.66	64.06	77.46	0	0	0
T270: --O.--I.--I.--I.--I.--O.---.--O.--O.--I.-PI.-PI.	4.05	0.00234	Dominated	42.75	54.45	66.15	0	0	0
T276: --O.--I.--I.--I.--O.--O.---.--O.--O.--I.-PI.-PI.	3.70	0.00230	Dominated	42.30	53.80	65.30	0	0	0
T277: --O.--O.--O.--I.--O.--I.---.--O.--O.--I.-PI.-PI.	3.13	0.00257	Dominated	48.27	61.12	73.97	0	0	0
T278: --I.--O.--O.--I.--O.--O.---.--O.--O.--I.-PI.-PI.	4.11	0.00222	Dominated	40.29	51.39	62.49	0	0	0
T279: --O.--O.--O.--I.--I.--O.---.--O.--O.--I.-PI.-PI.	4.36	0.00224	Dominated	40.44	51.64	62.84	0	0	0
T280: --O.--O.--O.--I.--O.--O.---.--O.--O.--I.-PI.-PI.	4.01	0.00221	Dominated	40.19	51.24	62.29	0	0	0
T286: --I.--I.--I.--I.--I.--I.---.--I.--I.--I.-PO.-PO.	4.33	0.00242	Dominated	44.07	56.17	68.27	0	0	0
T288: --O.--I.--I.--I.--I.--I.---.--I.--I.--I.-PO.-PO.	4.22	0.00240	Dominated	43.78	55.78	67.78	0	0	0
T289: --I.--O.--O.--I.--I.--I.---.--I.--I.--I.-PO.-PO.	4.63	0.00232	Dominated	41.77	53.37	64.97	0	0	0
T290: --I.--I.--I.--I.--O.--I.---.--I.--I.--I.-PO.-PO.	3.98	0.00238	Dominated	43.62	55.52	67.42	0	0	0
T291: --I.--I.--I.--I.--I.--O.---.--I.--I.--I.-PO.-PO.	5.20	0.00206	Dominated	36.00	46.30	56.60	0	0	0
T292: --I.--I.--I.--I.--I.--I.---.--O.--O.--I.-PO.-PO.	4.27	0.00233	Dominated	42.33	53.98	65.63	0	0	0
T297: --O.--I.--I.--I.--I.--I.---.--O.--O.--I.-PO.-PO.	4.17	0.00232	Dominated	42.23	53.83	65.43	0	0	0
T300: --I.--I.--I.--I.--I.--O.---.--O.--O.--I.-PO.-PO.	5.15	0.00197	Dominated	34.25	44.10	53.95	0	0	0
T301: --O.--O.--O.--I.--I.--I.---.--O.--O.--I.-PO.-PO.	4.47	0.00222	Dominated	39.93	51.03	62.13	0	0	0
T304: --I.--O.--O.--I.--O.--I.---.--O.--O.--I.-PO.-PO.	4.22	0.00220	Dominated	39.78	50.78	61.78	0	0	0
T305: --I.--O.--O.--I.--I.--O.---.--O.--O.--I.-PO.-PO.	5.45	0.00187	Dominated	31.95	41.30	50.65	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T306: --I.--O.--O.--I.--I.--I.---.--O.--O.--I.-PO.-PO.	4.58	0.00224	Dominated	40.22	51.42	62.62	0	0	0
T307: --O.--I.--I.--I.--O.--I.---.--O.--O.--I.-PO.-PO.	3.81	0.00228	Dominated	41.79	53.19	64.59	0	0	0
T308: --I.--I.--I.--I.--O.--O.---.--O.--O.--I.-PO.-PO.	4.79	0.00194	Dominated	34.01	43.71	53.41	0	0	0
T309: --I.--I.--I.--I.--O.--I.---.--O.--O.--I.-PO.-PO.	3.92	0.00230	Dominated	42.08	53.58	65.08	0	0	0
T310: --O.--I.--I.--I.--I.--O.---.--O.--O.--I.-PO.-PO.	5.04	0.00196	Dominated	34.16	43.96	53.76	0	0	0
T316: --O.--I.--I.--I.--O.--O.---.--O.--O.--I.-PO.-PO.	4.69	0.00192	Dominated	33.71	43.31	52.91	0	0	0
T317: --O.--O.--O.--I.--O.--I.---.--O.--O.--I.-PO.-PO.	4.12	0.00218	Dominated	39.48	50.38	61.28	0	0	0
T318: --I.--O.--O.--I.--O.--O.---.--O.--O.--I.-PO.-PO.	5.10	0.00184	Dominated	31.70	40.90	50.10	0	0	0
T319: --O.--O.--O.--I.--I.--O.---.--O.--O.--I.-PO.-PO.	5.34	0.00186	Dominated	31.86	41.16	50.46	0	0	0
T320: --O.--O.--O.--I.--O.--O.---.--O.--O.--I.-PO.-PO.	4.99	0.00182	Dominated	31.41	40.51	49.61	0	0	0
T326: --I.--I.--I.--I.--I.--I.---.--I.--I.--I.-CI.-CI.	–1.42	0.00270	Dominated	55.42	68.92	82.42	0	0	0
T328: --O.--I.--I.--I.--I.--I.---.--I.--I.--I.-CI.-CI.	–1.52	0.00269	Dominated	55.32	68.77	82.22	0	0	0
T329: --I.--O.--O.--I.--I.--I.---.--I.--I.--I.-CI.-CI.	–1.11	0.00261	Dominated	53.31	66.36	79.41	0	0	0
T330: --I.--I.--I.--I.--O.--I.---.--I.--I.--I.-CI.-CI.	–1.77	0.00267	Dominated	55.17	68.52	81.87	0	0	0
T331: --I.--I.--I.--I.--I.--O.---.--I.--I.--I.-CI.-CI.	–0.54	0.00234	Dominated	47.34	59.04	70.74	0	0	0
T332: --I.--I.--I.--I.--I.--I.---.--O.--O.--I.-CI.-CI.	–1.47	0.00262	Dominated	53.87	66.97	80.07	0	0	0
T337: --O.--I.--I.--I.--I.--I.---.--O.--O.--I.-CI.-CI.	–1.58	0.00261	Dominated	53.78	66.83	79.88	0	0	0
T340: --I.--I.--I.--I.--I.--O.---.--O.--O.--I.-CI.-CI.	–0.60	0.00226	Dominated	45.80	57.10	68.40	0	0	0
T341: --O.--O.--O.--I.--I.--I.---.--O.--O.--I.-CI.-CI.	–1.28	0.00251	Dominated	51.48	64.03	76.58	0	0	0
T344: --I.--O.--O.--I.--O.--I.---.--O.--O.--I.-CI.-CI.	–1.52	0.00249	Dominated	51.32	63.77	76.22	0	0	0
T345: --I.--O.--O.--I.--I.--O.---.--O.--O.--I.-CI.-CI.	–0.30	0.00216	Dominated	43.50	54.30	65.10	0	0	0
T346: --I.--O.--O.--I.--I.--I.---.--O.--O.--I.-CI.-CI.	–1.17	0.00252	Dominated	51.57	64.17	76.77	0	0	0
T347: --O.--I.--I.--I.--O.--I.---.--O.--O.--I.-CI.-CI.	–1.93	0.00257	Dominated	53.33	66.18	79.03	0	0	0
T348: --I.--I.--I.--I.--O.--O.---.--O.--O.--I.-CI.-CI.	–0.95	0.00222	Dominated	45.35	56.45	67.55	0	0	0
T349: --I.--I.--I.--I.--O.--I.---.--O.--O.--I.-CI.-CI.	–1.82	0.00258	Dominated	53.42	66.32	79.22	0	0	0
T350: --O.--I.--I.--I.--I.--O.---.--O.--O.--I.-CI.-CI.	–0.71	0.00225	Dominated	45.71	56.96	68.21	0	0	0
T356: --O.--I.--I.--I.--O.--O.---.--O.--O.--I.-CI.-CI.	–1.06	0.00221	Dominated	45.26	56.31	67.36	0	0	0
T357: --O.--O.--O.--I.--O.--I.---.--O.--O.--I.-CI.-CI.	–1.63	0.00247	Dominated	51.03	63.38	75.73	0	0	0
T358: --I.--O.--O.--I.--O.--O.---.--O.--O.--I.-CI.-CI.	–0.65	0.00213	Dominated	43.25	53.90	64.55	0	0	0
T359: --O.--O.--O.--I.--I.--O.---.--O.--O.--I.-CI.-CI.	–0.40	0.00215	Dominated	43.40	54.15	64.90	0	0	0
T360: --O.--O.--O.--I.--O.--O.---.--O.--O.--I.-CI.-CI.	–0.76	0.00211	Dominated	42.96	53.51	64.06	0	0	0
T366: --I.--I.--I.--I.--I.--I.---.--I.--I.--I.-CO.-CO.	–0.84	0.00237	Dominated	48.24	60.09	71.94	0	0	0
T368: --O.--I.--I.--I.--I.--I.---.--I.--I.--I.-CO.-CO.	–0.95	0.00236	Dominated	48.15	59.95	71.75	0	0	0
T369: --I.--O.--O.--I.--I.--I.---.--I.--I.--I.-CO.-CO.	–0.54	0.00227	Dominated	45.94	57.29	68.64	0	0	0
T370: --I.--I.--I.--I.--O.--I.---.--I.--I.--I.-CO.-CO.	–1.20	0.00233	Dominated	47.80	59.45	71.10	0	0	0
T371: --I.--I.--I.--I.--I.--O.---.--I.--I.--I.-CO.-CO.	0.03	0.00201	Dominated	40.17	50.22	60.27	0	0	0
T372: --I.--I.--I.--I.--I.--I.---.--O.--O.--I.-CO.-CO.	–0.90	0.00229	Dominated	46.70	58.15	69.60	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T377: --O.--I.--I.--I.--I.--I.---.--O.--O.--I.-CO.-CO.	–1.01	0.00227	Dominated	46.41	57.76	69.11	0	0	0
T380: --I.--I.--I.--I.--I.--O.---.--O.--O.--I.-CO.-CO.	–0.03	0.00193	Dominated	38.63	48.28	57.93	0	0	0
T381: --O.--O.--O.--I.--I.--I.---.--O.--O.--I.-CO.-CO.	–0.70	0.00218	Dominated	44.30	55.20	66.10	0	0	0
T384: --I.--O.--O.--I.--O.--I.---.--O.--O.--I.-CO.-CO.	–0.95	0.00215	Dominated	43.95	54.70	65.45	0	0	0
T385: --I.--O.--O.--I.--I.--O.---.--O.--O.--I.-CO.-CO.	0.28	0.00183	Dominated	36.32	45.47	54.62	0	0	0
T386: --I.--O.--O.--I.--I.--I.---.--O.--O.--I.-CO.-CO.	–0.60	0.00219	Dominated	44.40	55.35	66.30	0	0	0
T387: --O.--I.--I.--I.--O.--I.---.--O.--O.--I.-CO.-CO.	–1.36	0.00224	Dominated	46.16	57.36	68.56	0	0	0
T388: --I.--I.--I.--I.--O.--O.---.--O.--O.--I.-CO.-CO.	–0.38	0.00189	Dominated	38.18	47.63	57.08	0	0	0
T389: --I.--I.--I.--I.--O.--I.---.--O.--O.--I.-CO.-CO.	–1.25	0.00225	Dominated	46.25	57.50	68.75	0	0	0
T390: --O.--I.--I.--I.--I.--O.---.--O.--O.--I.-CO.-CO.	–0.13	0.00191	Dominated	38.33	47.88	57.43	0	0	0
T396: --O.--I.--I.--I.--O.--O.---.--O.--O.--I.-CO.-CO.	–0.49	0.00188	Dominated	38.09	47.49	56.89	0	0	0
T397: --O.--O.--O.--I.--O.--I.---.--O.--O.--I.-CO.-CO.	–1.06	0.00214	Dominated	43.86	54.56	65.26	0	0	0
T398: --I.--O.--O.--I.--O.--O.---.--O.--O.--I.-CO.-CO.	–0.07	0.00179	Dominated	35.87	44.82	53.77	0	0	0
T399: --O.--O.--O.--I.--I.--O.---.--O.--O.--I.-CO.-CO.	0.17	0.00182	Dominated	36.23	45.33	54.43	0	0	0
T400: --O.--O.--O.--I.--O.--O.---.--O.--O.--I.-CO.-CO.	–0.18	0.00178	Dominated	35.78	44.68	53.58	0	0	0
T402: V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V--.V--.	29.30	0.00408	Dominated	52.30	72.70	93.10	0	0	0
T403: V-I.V-O.V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V--.V--.	29.60	0.00403	Dominated	51.00	71.15	91.30	0	0	0
T405: V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.V-I.V--.V--.	29.90	0.00382	Dominated	46.50	65.60	84.70	0	0	0
T408: V-O.V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.V--.V--.	28.10	0.00408	Dominated	53.50	73.90	94.30	0.17	0.23	0.26
T409: V-I.V-O.V-O.V-I.V-I.V-I.V-O.V-I.V-I.V-I.V--.V--.	28.40	0.00403	Dominated	52.20	72.35	92.50	0	0	0
T411: V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.V-I.V-I.V--.V--.	28.80	0.00382	Dominated	47.60	66.70	85.80	0	0	0
T412: V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-I.V--.V--.	27.70	0.00406	Extended dominated	53.50	73.80	94.10	1.7	1.05	0.56
T413: V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.V--.V--.	28.80	0.00405	Dominated	52.20	72.45	92.70	0	0	0
T414: V-I.V-O.V-O.V-I.V-I.V-I.V-I.V-O.V-O.V-I.V--.V--.	29.10	0.00400	Dominated	50.90	70.90	90.90	0	0	0
T415: V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-O.V-O.V-I.V--.V--.	28.50	0.00406	Dominated	52.70	73.00	93.30	0	0	0
T416: V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-I.V--.V--.	29.50	0.00379	Dominated	46.30	65.25	84.20	0	0	0
T417: V-O.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-I.V--.V--.	27.60	0.00405	Dominated	53.40	73.65	93.90	0.06	0.03	0.02
T420: V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-I.V--.V--.	28.30	0.00379	Dominated	47.50	66.45	85.40	0	0	0
T421: V-O.V-O.V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-I.V--.V--.	27.80	0.00399	Dominated	52.00	71.95	91.90	0	0	0
T425: V-I.V-O.V-O.V-I.V-I.V-O.V-O.V-O.V-O.V-I.V--.V--.	28.40	0.00373	Dominated	46.20	64.85	83.50	0	0	0
T427: V-O.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-O.V-I.V--.V--.	27.20	0.00405	Extended dominated	53.80	74.05	94.30	9.1	10.9	11.2
T428: V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-O.V-I.V--.V--.	27.80	0.00379	Dominated	48.00	66.95	85.90	0	0	0
T429: V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-O.V-I.V--.V--.	27.30	0.00406	Extended dominated	53.90	74.20	94.50	0.99	0.75	0.56
T430: V-O.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-I.V--.V--.	28.20	0.00378	Dominated	47.40	66.30	85.20	0	0	0
T436: V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-O.V-I.V--.V--.	27.70	0.00378	Dominated	47.90	66.80	85.70	6.27	7.48	7.91
T437: V-O.V-O.V-O.V-I.V-O.V-I.V-O.V-O.V-O.V-I.V--.V--.	27.30	0.00399	Dominated	52.50	72.45	92.40	0	0	0
T439: V-O.V-O.V-O.V-I.V-I.V-O.V-O.V-O.V-O.V-I.V--.V--.	28.30	0.00373	Dominated	46.30	64.95	83.60	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T442: V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.VPI.VPI.	43.90	0.00436	Dominated	43.30	65.10	86.90	0	0	0
T443: V-I.V-O.V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-I.VPI.VPI.	44.20	0.00431	Dominated	42.00	63.55	85.10	0	0	0
T445: V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.V-I.VPI.VPI.	44.60	0.00410	Dominated	37.40	57.90	78.40	0	0	0
T446: V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.VPI.VPI.	42.90	0.00437	ICER to S47: £471,000	44.50	66.35	88.20	0	0.05	0.14
T448: V-O.V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.VPI.VPI.	42.70	0.00436	Dominated	44.50	66.30	88.10	0	0	0
T449: V-I.V-O.V-O.V-I.V-I.V-I.V-O.V-I.V-I.V-I.VPI.VPI.	43.00	0.00431	Dominated	43.20	64.75	86.30	0	0	0
T451: V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.V-I.V-I.VPI.VPI.	43.40	0.00410	Dominated	38.60	59.10	79.60	0	0	0
T452: V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VPI.VPI.	42.40	0.00434	Dominated	44.40	66.10	87.80	0	0	0
T453: V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.VPI.VPI.	43.40	0.00433	Dominated	43.20	64.85	86.50	0	0	0
T454: V-I.V-O.V-O.V-I.V-I.V-I.V-I.V-O.V-O.V-I.VPI.VPI.	43.70	0.00428	Dominated	41.90	63.30	84.70	0	0	0
T455: V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-O.V-O.V-I.VPI.VPI.	43.10	0.00434	Dominated	43.70	65.40	87.10	0	0	0
T456: V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-I.VPI.VPI.	44.10	0.00408	Dominated	37.50	57.90	78.30	0	0	0
T457: V-O.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VPI.VPI.	42.30	0.00433	Dominated	44.30	65.95	87.60	0	0	0
T460: V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VPI.VPI.	42.90	0.00407	Dominated	38.50	58.85	79.20	0	0	0
T461: V-O.V-O.V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VPI.VPI.	42.40	0.00427	Dominated	43.00	64.35	85.70	0	0	0
T465: V-I.V-O.V-O.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VPI.VPI.	43.10	0.00402	Dominated	37.30	57.40	77.50	0	0	0
T467: V-O.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VPI.VPI.	41.80	0.00433	Dominated	44.80	66.45	88.10	0	0	0.02
T468: V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VPI.VPI.	42.40	0.00407	Dominated	39.00	59.35	79.70	0	0	0
T469: V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VPI.VPI.	41.90	0.00434	Dominated	44.90	66.60	88.30	0	0	0
T470: V-O.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VPI.VPI.	42.80	0.00406	Dominated	38.40	58.70	79.00	0	0	0
T476: V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VPI.VPI.	42.30	0.00406	Dominated	38.90	59.20	79.50	0	0.02	0.03
T477: V-O.V-O.V-O.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VPI.VPI.	41.90	0.00427	Dominated	43.50	64.85	86.20	0	0	0
T479: V-O.V-O.V-O.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VPI.VPI.	42.90	0.00401	Dominated	37.30	57.35	77.40	0	0	0
T482: V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.VPO.VPO.	43.30	0.00425	Dominated	41.70	62.95	84.20	0	0	0
T483: V-I.V-O.V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-I.VPO.VPO.	43.50	0.00420	Dominated	40.50	61.50	82.50	0	0	0
T484: V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.V-I.V-I.VPO.VPO.	42.90	0.00426	Dominated	42.30	63.60	84.90	0	0	0
T485: V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.V-I.VPO.VPO.	43.90	0.00399	Dominated	35.90	55.85	75.80	0	0	0
T486: V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.VPO.VPO.	42.20	0.00426	Dominated	43.00	64.30	85.60	0	0	0
T487: V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.VPO.VPO.	42.90	0.00423	Dominated	41.70	62.85	84.00	0	0	0
T488: V-O.V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.VPO.VPO.	42.10	0.00425	Dominated	42.90	64.15	85.40	0	0	0
T489: V-I.V-O.V-O.V-I.V-I.V-I.V-O.V-I.V-I.V-I.VPO.VPO.	42.40	0.00420	Dominated	41.60	62.60	83.60	0	0	0
T490: V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-I.V-I.V-I.VPO.VPO.	41.70	0.00426	Dominated	43.50	64.80	86.10	0	0	0
T491: V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.V-I.V-I.VPO.VPO.	42.70	0.00399	Dominated	37.10	57.05	77.00	0	0	0
T492: V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VPO.VPO.	41.70	0.00423	Dominated	42.90	64.05	85.20	0	0	0
T493: V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.VPO.VPO.	42.80	0.00422	Dominated	41.60	62.70	83.80	0	0	0
T494: V-I.V-O.V-O.V-I.V-I.V-I.V-I.V-O.V-O.V-I.VPO.VPO.	43.00	0.00417	Dominated	40.40	61.25	82.10	0	0	0
T495: V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-O.V-O.V-I.VPO.VPO.	42.40	0.00423	Dominated	42.20	63.35	84.50	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T496: V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-I.VPO.VPO.	43.40	0.00396	Dominated	35.80	55.60	75.40	0	0	0
T497: V-O.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VPO.VPO.	41.60	0.00422	Dominated	42.80	63.90	85.00	0	0	0
T500: V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VPO.VPO.	42.20	0.00396	Dominated	37.00	56.80	76.60	0	0	0
T501: V-O.V-O.V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VPO.VPO.	41.70	0.00416	Dominated	41.50	62.30	83.10	0	0	0
T504: V-I.V-O.V-O.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VPO.VPO.	41.40	0.00417	Dominated	42.00	62.85	83.70	0	0	0
T505: V-I.V-O.V-O.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VPO.VPO.	42.40	0.00391	Dominated	35.80	55.35	74.90	0	0	0
T506: V-I.V-O.V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VPO.VPO.	41.90	0.00417	Dominated	41.50	62.35	83.20	0	0	0
T507: V-O.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VPO.VPO.	41.10	0.00422	Dominated	43.30	64.40	85.50	0	0	0.01
T508: V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VPO.VPO.	41.80	0.00396	Dominated	37.40	57.20	77.00	0	0	0
T509: V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VPO.VPO.	41.30	0.00423	Dominated	43.30	64.45	85.60	0	0	0
T510: V-O.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VPO.VPO.	42.10	0.00395	Dominated	36.90	56.65	76.40	0	0	0
T516: V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VPO.VPO.	41.70	0.00395	Dominated	37.30	57.05	76.80	0	0	0
T517: V-O.V-O.V-O.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VPO.VPO.	41.30	0.00416	Dominated	41.90	62.70	83.50	0	0	0
T518: V-I.V-O.V-O.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VPO.VPO.	41.90	0.00390	Dominated	36.10	55.60	75.10	0	0	0
T519: V-O.V-O.V-O.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VPO.VPO.	42.30	0.00390	Dominated	35.70	55.20	74.70	0	0	0
T522: V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.VCI.VCI.	38.60	0.00434	Dominated	48.20	69.90	91.60	0	0	0
T523: V-I.V-O.V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-I.VCI.VCI.	38.90	0.00429	Dominated	46.90	68.35	89.80	0	0	0
T525: V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.V-I.VCI.VCI.	39.30	0.00408	Dominated	42.30	62.70	83.10	0	0	0
T526: V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.VCI.VCI.	37.60	0.00435	Extended dominated	49.40	71.15	92.90	0.63	1.82	3.27
T527: V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.VCI.VCI.	38.30	0.00432	Dominated	48.10	69.70	91.30	0	0	0
T528: V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.VCI.VCI.	37.40	0.00434	Dominated	49.40	71.10	92.80	0.04	0.18	0.31
T529: V-I.V-O.V-O.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.VCI.VCI.	37.70	0.00429	Dominated	48.10	69.55	91.00	0	0	0
T531: V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.V-I.V-I.VCI.VCI.	38.10	0.00408	Dominated	43.50	63.90	84.30	0	0	0
T532: V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VCI.VCI.	37.10	0.00432	Dominated	49.30	70.90	92.50	0	0	0
T533: V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.VCI.VCI.	38.10	0.00431	Dominated	48.10	69.65	91.20	0	0	0
T534: V-I.V-O.V-O.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.VCI.VCI.	38.40	0.00426	Dominated	46.80	68.10	89.40	0	0	0
T535: V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-O.V-O.V-I.VCI.VCI.	37.80	0.00432	Dominated	48.60	70.20	91.80	0	0	0
T536: V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-I.VCI.VCI.	38.80	0.00406	Dominated	42.40	62.70	83.00	0	0	0
T537: V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VCI.VCI.	37.00	0.00431	Dominated	49.20	70.75	92.30	0	0	0.01
T540: V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VCI.VCI.	37.60	0.00405	Dominated	43.40	63.65	83.90	0	0	0
T541: V-O.V-O.V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VCI.VCI.	37.10	0.00425	Dominated	47.90	69.15	90.40	0	0	0
T544: V-I.V-O.V-O.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VCI.VCI.	36.80	0.00426	Dominated	48.40	69.70	91.00	0	0	0
T545: V-I.V-O.V-O.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VCI.VCI.	37.80	0.00400	Dominated	42.20	62.20	82.20	0	0	0
T546: V-I.V-O.V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VCI.VCI.	37.20	0.00426	Dominated	48.00	69.30	90.60	0	0	0
T547: V-O.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VCI.VCI.	36.50	0.00431	Extended dominated	49.70	71.25	92.80	0.31	0.9	1.93
T548: V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VCI.VCI.	37.10	0.00405	Dominated	43.90	64.15	84.40	0	0	0
T549: V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VCI.VCI.	36.60	0.00432	Extended dominated	49.80	71.40	93.00	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T550: V-O.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VCI.VCI.	37.50	0.00404	Dominated	43.30	63.50	83.70	0	0	0
T556: V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VCI.VCI.	37.00	0.00404	Dominated	43.80	64.00	84.20	0.16	0.42	0.87
T557: V-O.V-O.V-O.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VCI.VCI.	36.70	0.00425	Dominated	48.30	69.55	90.80	0	0	0
T558: V-I.V-O.V-O.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VCI.VCI.	37.30	0.00399	Dominated	42.50	62.45	82.40	0	0	0
T559: V-O.V-O.V-O.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VCI.VCI.	37.60	0.00399	Dominated	42.20	62.15	82.10	0	0	0
T560: V-O.V-O.V-O.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VCI.VCI.	37.20	0.00399	Dominated	42.60	62.55	82.50	0.04	0.06	0.16
T561: V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.VCO.VCO.	37.90	0.00425	Dominated	47.10	68.35	89.60	0	0	0
T562: V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-I.VCO.VCO.	37.80	0.00424	Dominated	47.00	68.20	89.40	0	0	0
T563: V-I.V-O.V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-I.VCO.VCO.	38.00	0.00420	Dominated	46.00	67.00	88.00	0	0	0
T564: V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.V-I.V-I.VCO.VCO.	37.40	0.00425	Dominated	47.60	68.85	90.10	0	0	0
T565: V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.V-I.VCO.VCO.	38.40	0.00399	Dominated	41.40	61.35	81.30	0	0	0
T566: V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.VCO.VCO.	36.70	0.00425	Dominated	48.30	69.55	90.80	0	0	0
T567: V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.VCO.VCO.	37.40	0.00422	Dominated	47.00	68.10	89.20	0	0	0
T568: V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-I.VCO.VCO.	36.60	0.00424	Dominated	48.20	69.40	90.60	0	0	0
T569: V-I.V-O.V-O.V-I.V-I.V-I.V-O.V-I.V-I.V-I.VCO.VCO.	36.90	0.00419	Dominated	46.90	67.85	88.80	0	0	0
T570: V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-I.V-I.V-I.VCO.VCO.	36.30	0.00425	Extended dominated	48.70	69.95	91.20	0	0	0
T571: V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.V-I.V-I.VCO.VCO.	37.20	0.00398	Dominated	42.40	62.30	82.20	0	0	0
T572: V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VCO.VCO.	36.20	0.00422	Extended dominated	48.20	69.30	90.40	0	0	0
T573: V-O.V-I.V-I.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-I.VCO.VCO.	37.30	0.00421	Dominated	46.90	67.95	89.00	0	0	0
T574: V-I.V-O.V-O.V-I.V-I.V-I.V-I.V-O.V-O.V-I.VCO.VCO.	37.60	0.00417	Dominated	45.80	66.65	87.50	0	0	0
T575: V-I.V-I.V-I.V-I.V-O.V-I.V-I.V-O.V-O.V-I.VCO.VCO.	36.90	0.00422	Dominated	47.50	68.60	89.70	0	0	0
T576: V-I.V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-I.VCO.VCO.	37.90	0.00396	Dominated	41.30	61.10	80.90	0	0	0
T577: V-O.V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VCO.VCO.	36.10	0.00421	Dominated	48.10	69.15	90.20	0	0	0
T580: V-I.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VCO.VCO.	36.70	0.00396	Dominated	42.50	62.30	82.10	0	0	0
T581: V-O.V-O.V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VCO.VCO.	36.30	0.00416	Dominated	46.90	67.70	88.50	0	0	0
T584: V-I.V-O.V-O.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VCO.VCO.	35.90	0.00416	Dominated	47.30	68.10	88.90	0	0	0
T585: V-I.V-O.V-O.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VCO.VCO.	36.90	0.00390	Dominated	41.10	60.60	80.10	0	0	0
T586: V-I.V-O.V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-I.VCO.VCO.	36.40	0.00416	Dominated	46.80	67.60	88.40	0	0	0
T587: V-O.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VCO.VCO.	35.60	0.00421	Extended dominated	48.60	69.65	90.70	0.03	0.07	0.1
T588: V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VCO.VCO.	36.30	0.00395	Dominated	42.70	62.45	82.20	0	0	0
T589: V-I.V-I.V-I.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VCO.VCO.	35.80	0.00422	Extended dominated	48.60	69.70	90.80	0	0	0
T590: V-O.V-I.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VCO.VCO.	36.60	0.00395	Dominated	42.40	62.15	81.90	0	0	0
T596: V-O.V-I.V-I.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VCO.VCO.	36.20	0.00395	Dominated	42.80	62.55	82.30	0.04	0.11	0.32
T597: V-O.V-O.V-O.V-I.V-O.V-I.V-O.V-O.V-O.V-I.VCO.VCO.	35.80	0.00415	Dominated	47.20	67.95	88.70	0	0	0
T598: V-I.V-O.V-O.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VCO.VCO.	36.40	0.00390	Dominated	41.60	61.10	80.60	0	0	0
T599: V-O.V-O.V-O.V-I.V-I.V-O.V-O.V-O.V-O.V-I.VCO.VCO.	36.80	0.00389	Dominated	41.00	60.45	79.90	0	0	0
T600: V-O.V-O.V-O.V-I.V-O.V-O.V-O.V-O.V-O.V-I.VCO.VCO.	36.30	0.00389	Dominated	41.50	60.95	80.40	0.07	0.22	0.58

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T608: V-O.V-I.V-I.V-I.V-I.V-I.V--.V-I.V-I.V-I.V--.V--.	28.20	0.00401	Dominated	52.00	72.05	92.10	0	0	0
T609: V-I.V-O.V-O.V-I.V-I.V-I.V--.V-I.V-I.V-I.V--.V--.	28.50	0.00396	Dominated	50.70	70.50	90.30	0	0	0
T611: V-I.V-I.V-I.V-I.V-I.V-O.V--.V-I.V-I.V-I.V--.V--.	28.90	0.00375	Dominated	46.10	64.85	83.60	0	0	0
T617: V-O.V-I.V-I.V-I.V-I.V-I.V--.V-O.V-O.V-I.V--.V--.	27.70	0.00398	Dominated	51.90	71.80	91.70	0	0	0
T620: V-I.V-I.V-I.V-I.V-I.V-O.V--.V-O.V-O.V-I.V--.V--.	28.40	0.00372	Dominated	46.00	64.60	83.20	0	0	0
T621: V-O.V-O.V-O.V-I.V-I.V-I.V--.V-O.V-O.V-I.V--.V--.	27.90	0.00392	Dominated	50.50	70.10	89.70	0	0	0
T625: V-I.V-O.V-O.V-I.V-I.V-O.V--.V-O.V-O.V-I.V--.V--.	28.50	0.00366	Dominated	44.70	63.00	81.30	0	0	0
T627: V-O.V-I.V-I.V-I.V-O.V-I.V--.V-O.V-O.V-I.V--.V--.	27.30	0.00398	Dominated	52.30	72.20	92.10	0	0	0
T628: V-I.V-I.V-I.V-I.V-O.V-O.V--.V-O.V-O.V-I.V--.V--.	27.90	0.00372	Dominated	46.50	65.10	83.70	0	0	0
T629: V-I.V-I.V-I.V-I.V-O.V-I.V--.V-O.V-O.V-I.V--.V--.	27.40	0.00399	Dominated	52.40	72.35	92.30	0	0	0
T630: V-O.V-I.V-I.V-I.V-I.V-O.V--.V-O.V-O.V-I.V--.V--.	28.20	0.00371	Dominated	46.00	64.55	83.10	0	0	0
T636: V-O.V-I.V-I.V-I.V-O.V-O.V--.V-O.V-O.V-I.V--.V--.	27.80	0.00371	Dominated	46.40	64.95	83.50	0	0	0
T637: V-O.V-O.V-O.V-I.V-O.V-I.V--.V-O.V-O.V-I.V--.V--.	27.40	0.00392	Dominated	51.00	70.60	90.20	0	0	0
T639: V-O.V-O.V-O.V-I.V-I.V-O.V--.V-O.V-O.V-I.V--.V--.	28.40	0.00365	Dominated	44.60	62.85	81.10	0	0	0
T646: V-I.V-I.V-I.V-I.V-I.V-I.V--.V-I.V-I.V-I.VPI.VPI.	43.00	0.00430	Dominated	43.00	64.50	86.00	0	0	0
T648: V-O.V-I.V-I.V-I.V-I.V-I.V--.V-I.V-I.V-I.VPI.VPI.	42.80	0.00429	Dominated	43.00	64.45	85.90	0	0	0
T649: V-I.V-O.V-O.V-I.V-I.V-I.V--.V-I.V-I.V-I.VPI.VPI.	43.10	0.00424	Dominated	41.70	62.90	84.10	0	0	0
T650: V-I.V-I.V-I.V-I.V-O.V-I.V--.V-I.V-I.V-I.VPI.VPI.	42.50	0.00430	Dominated	43.50	65.00	86.50	0	0	0
T651: V-I.V-I.V-I.V-I.V-I.V-O.V--.V-I.V-I.V-I.VPI.VPI.	43.50	0.00403	Dominated	37.10	57.25	77.40	0	0	0
T652: V-I.V-I.V-I.V-I.V-I.V-I.V--.V-O.V-O.V-I.VPI.VPI.	42.50	0.00427	Dominated	42.90	64.25	85.60	0	0	0
T657: V-O.V-I.V-I.V-I.V-I.V-I.V--.V-O.V-O.V-I.VPI.VPI.	42.30	0.00426	Dominated	42.90	64.20	85.50	0	0	0
T660: V-I.V-I.V-I.V-I.V-I.V-O.V--.V-O.V-O.V-I.VPI.VPI.	43.00	0.00400	Dominated	37.00	57.00	77.00	0	0	0
T661: V-O.V-O.V-O.V-I.V-I.V-I.V--.V-O.V-O.V-I.VPI.VPI.	42.50	0.00420	Dominated	41.50	62.50	83.50	0	0	0
T664: V-I.V-O.V-O.V-I.V-O.V-I.V--.V-O.V-O.V-I.VPI.VPI.	42.20	0.00421	Dominated	42.00	63.05	84.10	0	0	0
T665: V-I.V-O.V-O.V-I.V-I.V-O.V--.V-O.V-O.V-I.VPI.VPI.	43.10	0.00394	Dominated	35.70	55.40	75.10	0	0	0
T666: V-I.V-O.V-O.V-I.V-I.V-I.V--.V-O.V-O.V-I.VPI.VPI.	42.60	0.00421	Dominated	41.60	62.65	83.70	0	0	0
T667: V-O.V-I.V-I.V-I.V-O.V-I.V--.V-O.V-O.V-I.VPI.VPI.	41.90	0.00426	Dominated	43.30	64.60	85.90	0	0	0
T668: V-I.V-I.V-I.V-I.V-O.V-O.V--.V-O.V-O.V-I.VPI.VPI.	42.50	0.00400	Dominated	37.50	57.50	77.50	0	0	0
T669: V-I.V-I.V-I.V-I.V-O.V-I.V--.V-O.V-O.V-I.VPI.VPI.	42.00	0.00427	Dominated	43.40	64.75	86.10	0	0	0
T670: V-O.V-I.V-I.V-I.V-I.V-O.V--.V-O.V-O.V-I.VPI.VPI.	42.90	0.00399	Dominated	36.90	56.85	76.80	0	0	0
T676: V-O.V-I.V-I.V-I.V-O.V-O.V--.V-O.V-O.V-I.VPI.VPI.	42.40	0.00399	Dominated	37.40	57.35	77.30	0	0	0
T677: V-O.V-O.V-O.V-I.V-O.V-I.V--.V-O.V-O.V-I.VPI.VPI.	42.00	0.00420	Dominated	42.00	63.00	84.00	0	0	0
T678: V-I.V-O.V-O.V-I.V-O.V-O.V--.V-O.V-O.V-I.VPI.VPI.	42.70	0.00394	Dominated	36.10	55.80	75.50	0	0	0
T679: V-O.V-O.V-O.V-I.V-I.V-O.V--.V-O.V-O.V-I.VPI.VPI.	43.00	0.00394	Dominated	35.80	55.50	75.20	0	0	0
T680: V-O.V-O.V-O.V-I.V-O.V-O.V--.V-O.V-O.V-I.VPI.VPI.	42.60	0.00393	Dominated	36.00	55.65	75.30	0	0	0
T686: V-I.V-I.V-I.V-I.V-I.V-I.V--.V-I.V-I.V-I.VPO.VPO.	42.30	0.00419	Dominated	41.50	62.45	83.40	0	0	0
T688: V-O.V-I.V-I.V-I.V-I.V-I.V--.V-I.V-I.V-I.VPO.VPO.	42.20	0.00418	Dominated	41.40	62.30	83.20	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T689: V-I.V-O.V-O.V-I.V-I.V-I.V--.V-I.V-I.V-I.VPO.VPO.	42.40	0.00413	Dominated	40.20	60.85	81.50	0	0	0
T690: V-I.V-I.V-I.V-I.V-O.V-I.V--.V-I.V-I.V-I.VPO.VPO.	41.80	0.00419	Dominated	42.00	62.95	83.90	0	0	0
T691: V-I.V-I.V-I.V-I.V-I.V-O.V--.V-I.V-I.V-I.VPO.VPO.	42.80	0.00392	Dominated	35.60	55.20	74.80	0	0	0
T692: V-I.V-I.V-I.V-I.V-I.V-I.V--.V-O.V-O.V-I.VPO.VPO.	41.80	0.00416	Dominated	41.40	62.20	83.00	0	0	0
T697: V-O.V-I.V-I.V-I.V-I.V-I.V--.V-O.V-O.V-I.VPO.VPO.	41.70	0.00415	Dominated	41.30	62.05	82.80	0	0	0
T700: V-I.V-I.V-I.V-I.V-I.V-O.V--.V-O.V-O.V-I.VPO.VPO.	42.30	0.00389	Dominated	35.50	54.95	74.40	0	0	0
T701: V-O.V-O.V-O.V-I.V-I.V-I.V--.V-O.V-O.V-I.VPO.VPO.	41.80	0.00409	Dominated	40.00	60.45	80.90	0	0	0
T704: V-I.V-O.V-O.V-I.V-O.V-I.V--.V-O.V-O.V-I.VPO.VPO.	41.50	0.00410	Dominated	40.50	61.00	81.50	0	0	0
T705: V-I.V-O.V-O.V-I.V-I.V-O.V--.V-O.V-O.V-I.VPO.VPO.	42.50	0.00383	Dominated	34.10	53.25	72.40	0	0	0
T706: V-I.V-O.V-O.V-I.V-I.V-I.V--.V-O.V-O.V-I.VPO.VPO.	42.00	0.00410	Dominated	40.00	60.50	81.00	0	0	0
T707: V-O.V-I.V-I.V-I.V-O.V-I.V--.V-O.V-O.V-I.VPO.VPO.	41.20	0.00415	Dominated	41.80	62.55	83.30	0	0	0
T708: V-I.V-I.V-I.V-I.V-O.V-O.V--.V-O.V-O.V-I.VPO.VPO.	41.90	0.00389	Dominated	35.90	55.35	74.80	0	0	0
T709: V-I.V-I.V-I.V-I.V-O.V-I.V--.V-O.V-O.V-I.VPO.VPO.	41.40	0.00416	Dominated	41.80	62.60	83.40	0	0	0
T710: V-O.V-I.V-I.V-I.V-I.V-O.V--.V-O.V-O.V-I.VPO.VPO.	42.20	0.00388	Dominated	35.40	54.80	74.20	0	0	0
T716: V-O.V-I.V-I.V-I.V-O.V-O.V--.V-O.V-O.V-I.VPO.VPO.	41.80	0.00388	Dominated	35.80	55.20	74.60	0	0	0
T717: V-O.V-O.V-O.V-I.V-O.V-I.V--.V-O.V-O.V-I.VPO.VPO.	41.40	0.00409	Dominated	40.40	60.85	81.30	0	0	0
T718: V-I.V-O.V-O.V-I.V-O.V-O.V--.V-O.V-O.V-I.VPO.VPO.	42.00	0.00383	Dominated	34.60	53.75	72.90	0	0	0
T719: V-O.V-O.V-O.V-I.V-I.V-O.V--.V-O.V-O.V-I.VPO.VPO.	42.40	0.00383	Dominated	34.20	53.35	72.50	0	0	0
T720: V-O.V-O.V-O.V-I.V-O.V-O.V--.V-O.V-O.V-I.VPO.VPO.	41.90	0.00382	Dominated	34.50	53.60	72.70	0	0	0
T726: V-I.V-I.V-I.V-I.V-I.V-I.V--.V-I.V-I.V-I.VCI.VCI.	37.70	0.00428	Dominated	47.90	69.30	90.70	0	0	0
T728: V-O.V-I.V-I.V-I.V-I.V-I.V--.V-I.V-I.V-I.VCI.VCI.	37.50	0.00427	Dominated	47.90	69.25	90.60	0	0	0
T729: V-I.V-O.V-O.V-I.V-I.V-I.V--.V-I.V-I.V-I.VCI.VCI.	37.80	0.00422	Dominated	46.60	67.70	88.80	0	0	0
T730: V-I.V-I.V-I.V-I.V-O.V-I.V--.V-I.V-I.V-I.VCI.VCI.	37.20	0.00428	Dominated	48.40	69.80	91.20	0	0	0
T731: V-I.V-I.V-I.V-I.V-I.V-O.V--.V-I.V-I.V-I.VCI.VCI.	38.20	0.00401	Dominated	42.00	62.05	82.10	0	0	0
T732: V-I.V-I.V-I.V-I.V-I.V-I.V--.V-O.V-O.V-I.VCI.VCI.	37.20	0.00425	Dominated	47.80	69.05	90.30	0	0	0
T737: V-O.V-I.V-I.V-I.V-I.V-I.V--.V-O.V-O.V-I.VCI.VCI.	37.00	0.00424	Dominated	47.80	69.00	90.20	0	0	0
T740: V-I.V-I.V-I.V-I.V-I.V-O.V--.V-O.V-O.V-I.VCI.VCI.	37.70	0.00398	Dominated	41.90	61.80	81.70	0	0	0
T741: V-O.V-O.V-O.V-I.V-I.V-I.V--.V-O.V-O.V-I.VCI.VCI.	37.20	0.00418	Dominated	46.40	67.30	88.20	0	0	0
T744: V-I.V-O.V-O.V-I.V-O.V-I.V--.V-O.V-O.V-I.VCI.VCI.	36.90	0.00419	Dominated	46.90	67.85	88.80	0	0	0
T745: V-I.V-O.V-O.V-I.V-I.V-O.V--.V-O.V-O.V-I.VCI.VCI.	37.80	0.00392	Dominated	40.60	60.20	79.80	0	0	0
T746: V-I.V-O.V-O.V-I.V-I.V-I.V--.V-O.V-O.V-I.VCI.VCI.	37.30	0.00419	Dominated	46.50	67.45	88.40	0	0	0
T747: V-O.V-I.V-I.V-I.V-O.V-I.V--.V-O.V-O.V-I.VCI.VCI.	36.60	0.00424	Dominated	48.20	69.40	90.60	0	0	0
T748: V-I.V-I.V-I.V-I.V-O.V-O.V--.V-O.V-O.V-I.VCI.VCI.	37.20	0.00398	Dominated	42.40	62.30	82.20	0	0	0
T749: V-I.V-I.V-I.V-I.V-O.V-I.V--.V-O.V-O.V-I.VCI.VCI.	36.70	0.00425	Dominated	48.30	69.55	90.80	0	0	0
T750: V-O.V-I.V-I.V-I.V-I.V-O.V--.V-O.V-O.V-I.VCI.VCI.	37.60	0.00397	Dominated	41.80	61.65	81.50	0	0	0
T756: V-O.V-I.V-I.V-I.V-O.V-O.V--.V-O.V-O.V-I.VCI.VCI.	37.10	0.00397	Dominated	42.30	62.15	82.00	0	0	0
T757: V-O.V-O.V-O.V-I.V-O.V-I.V--.V-O.V-O.V-I.VCI.VCI.	36.70	0.00418	Dominated	46.90	67.80	88.70	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T758: V-I.V-O.V-O.V-I.V-O.V-O.V--.V-O.V-O.V-I.VCI.VCI.	37.40	0.00392	Dominated	41.00	60.60	80.20	0	0	0
T759: V-O.V-O.V-O.V-I.V-I.V-O.V--.V-O.V-O.V-I.VCI.VCI.	37.70	0.00392	Dominated	40.70	60.30	79.90	0	0	0
T760: V-O.V-O.V-O.V-I.V-O.V-O.V--.V-O.V-O.V-I.VCI.VCI.	37.30	0.00391	Dominated	40.90	60.45	80.00	0	0	0
T766: V-I.V-I.V-I.V-I.V-I.V-I.V--.V-I.V-I.V-I.VCO.VCO.	36.80	0.00418	Dominated	46.80	67.70	88.60	0	0	0
T768: V-O.V-I.V-I.V-I.V-I.V-I.V--.V-I.V-I.V-I.VCO.VCO.	36.70	0.00417	Dominated	46.70	67.55	88.40	0	0	0
T769: V-I.V-O.V-O.V-I.V-I.V-I.V--.V-I.V-I.V-I.VCO.VCO.	37.00	0.00412	Dominated	45.40	66.00	86.60	0	0	0
T770: V-I.V-I.V-I.V-I.V-O.V-I.V--.V-I.V-I.V-I.VCO.VCO.	36.30	0.00418	Dominated	47.30	68.20	89.10	0	0	0
T771: V-I.V-I.V-I.V-I.V-I.V-O.V--.V-I.V-I.V-I.VCO.VCO.	37.30	0.00391	Dominated	40.90	60.45	80.00	0	0	0
T772: V-I.V-I.V-I.V-I.V-I.V-I.V--.V-O.V-O.V-I.VCO.VCO.	36.30	0.00415	Dominated	46.70	67.45	88.20	0	0	0
T777: V-O.V-I.V-I.V-I.V-I.V-I.V--.V-O.V-O.V-I.VCO.VCO.	36.20	0.00414	Dominated	46.60	67.30	88.00	0	0	0
T780: V-I.V-I.V-I.V-I.V-I.V-O.V--.V-O.V-O.V-I.VCO.VCO.	36.80	0.00388	Dominated	40.80	60.20	79.60	0	0	0
T781: V-O.V-O.V-O.V-I.V-I.V-I.V--.V-O.V-O.V-I.VCO.VCO.	36.30	0.00408	Dominated	45.30	65.70	86.10	0	0	0
T784: V-I.V-O.V-O.V-I.V-O.V-I.V--.V-O.V-O.V-I.VCO.VCO.	36.00	0.00409	Dominated	45.80	66.25	86.70	0	0	0
T785: V-I.V-O.V-O.V-I.V-I.V-O.V--.V-O.V-O.V-I.VCO.VCO.	37.00	0.00383	Dominated	39.60	58.75	77.90	0	0	0
T786: V-I.V-O.V-O.V-I.V-I.V-I.V--.V-O.V-O.V-I.VCO.VCO.	36.50	0.00409	Dominated	45.30	65.75	86.20	0	0	0
T787: V-O.V-I.V-I.V-I.V-O.V-I.V--.V-O.V-O.V-I.VCO.VCO.	35.70	0.00414	Dominated	47.10	67.80	88.50	0	0	0
T788: V-I.V-I.V-I.V-I.V-O.V-O.V--.V-O.V-O.V-I.VCO.VCO.	36.40	0.00388	Dominated	41.20	60.60	80.00	0	0	0
T789: V-I.V-I.V-I.V-I.V-O.V-I.V--.V-O.V-O.V-I.VCO.VCO.	35.90	0.00415	Dominated	47.10	67.85	88.60	0	0	0
T790: V-O.V-I.V-I.V-I.V-I.V-O.V--.V-O.V-O.V-I.VCO.VCO.	36.70	0.00388	Dominated	40.90	60.30	79.70	0	0	0
T796: V-O.V-I.V-I.V-I.V-O.V-O.V--.V-O.V-O.V-I.VCO.VCO.	36.30	0.00387	Dominated	41.10	60.45	79.80	0	0	0
T797: V-O.V-O.V-O.V-I.V-O.V-I.V--.V-O.V-O.V-I.VCO.VCO.	35.90	0.00408	Dominated	45.70	66.10	86.50	0	0	0
T798: V-I.V-O.V-O.V-I.V-O.V-O.V--.V-O.V-O.V-I.VCO.VCO.	36.50	0.00383	Dominated	40.10	59.25	78.40	0	0	0
T799: V-O.V-O.V-O.V-I.V-I.V-O.V--.V-O.V-O.V-I.VCO.VCO.	36.90	0.00382	Dominated	39.50	58.60	77.70	0	0	0
T800: V-O.V-O.V-O.V-I.V-O.V-O.V--.V-O.V-O.V-I.VCO.VCO.	36.40	0.00382	Dominated	40.00	59.10	78.20	0	0	0
T802: -PI.--I.--I.--I.-PI.-PI.-PI.--I.--I.--I.-PI.-PI.	8.17	0.00216	Dominated	35.03	45.83	56.63	0	0	0
T803: -PO.--I.--I.--I.-PO.-PO.-PO.--I.--I.--I.-PO.-PO.	9.55	0.00157	Dominated	21.85	29.70	37.55	0	0	0
T804: -CI.--I.--I.--I.-CI.-CI.-CI.--I.--I.--I.-CI.-CI.	3.31	0.00170	Dominated	30.69	39.19	47.69	0	0	0
T805: -CO.--I.--I.--I.-CO.-CO.-CO.--I.--I.--I.-CO.-CO.	4.03	0.00126	Dominated	21.17	27.47	33.77	0	0	0
T808: -PO.--I.--I.--I.--O.-PO.-PO.--I.--I.--I.-PO.-PO.	8.00	0.00181	Dominated	28.20	37.25	46.30	0	0	0
T810: -CO.--I.--I.--I.--O.-CO.-CO.--I.--I.--I.-CO.-CO.	1.99	0.00170	Dominated	32.01	40.51	49.01	0	0	0
T813: -PO.--I.--I.--I.--O.--I.-PO.--I.--I.--I.-PO.-PO.	5.77	0.00232	Dominated	40.63	52.23	63.83	0	0	0
T815: -CO.--I.--I.--I.--O.--I.-CO.--I.--I.--I.-CO.-CO.	0.03	0.00225	Dominated	44.97	56.22	67.47	0	0	0
T818: -PO.--I.--I.--I.--I.-PO.-PO.--I.--I.--I.-PO.-PO.	8.35	0.00184	Dominated	28.45	37.65	46.85	0	0	0
T820: -CO.--I.--I.--I.--I.-CO.-CO.--I.--I.--I.-CO.-CO.	2.34	0.00173	Dominated	32.26	40.91	49.56	0	0	0
T823: -PO.--I.--I.--I.--I.--I.-PO.--I.--I.--I.-PO.-PO.	6.12	0.00235	Dominated	40.88	52.63	64.38	0	0	0
T825: -CO.--I.--I.--I.--I.--I.-CO.--I.--I.--I.-CO.-CO.	0.39	0.00228	Dominated	45.21	56.61	68.01	0	0	0
T827: VPI.V-I.V-I.V-I.VPI.VPI.VPI.V-I.V-I.V-I.VPI.VPI.	47.70	0.00369	Dominated	26.10	44.55	63.00	0	0	0

continued

TABLE 108 *Full cost-effectiveness results for all 713 strategies modelled for Scenario A (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T828: VPO.V-I.V-I.V-I.VPO.VPO.VPO.V-I.V-I.V-I.VPO.VPO.	47.10	0.00348	Dominated	22.50	39.90	57.30	0	0	0
T829: VCI.V-I.V-I.V-I.VCI.VCI.VCI.V-I.V-I.V-I.VCI.VCI.	41.60	0.00349	Dominated	28.20	45.65	63.10	0	0	0
T830: VCO.V-I.V-I.V-I.VCO.VCO.VCO.V-I.V-I.V-I.VCO.VCO.	40.70	0.00334	Dominated	26.10	42.80	59.50	0	0	0
T833: VPO.V-I.V-I.V-I.V-O.VPO.VPO.V-I.V-I.V-I.VPO.VPO.	45.60	0.00370	Dominated	28.40	46.90	65.40	0	0	0
T834: VCI.V-I.V-I.V-I.V-O.VCI.VCI.V-I.V-I.V-I.VCI.VCI.	40.00	0.00380	Dominated	36.00	55.00	74.00	0	0	0
T835: VCO.V-I.V-I.V-I.V-O.VCO.VCO.V-I.V-I.V-I.VCO.VCO.	39.10	0.00366	Dominated	34.10	52.40	70.70	0	0	0
T838: VPO.V-I.V-I.V-I.V-O.V-I.VPO.V-I.V-I.V-I.VPO.VPO.	43.70	0.00411	Dominated	38.50	59.05	79.60	0	0	0
T839: VCI.V-I.V-I.V-I.V-O.V-I.VCI.V-I.V-I.V-I.VCI.VCI.	38.60	0.00419	Dominated	45.20	66.15	87.10	0	0	0
T840: VCO.V-I.V-I.V-I.V-O.V-I.VCO.V-I.V-I.V-I.VCO.VCO.	37.60	0.00409	Dominated	44.20	64.65	85.10	0	0	0
T841: V--.V-I.V-I.V-I.V-I.V--.V--.--I.--I.--I.V--.V--.	28.00	0.00338	Dominated	39.60	56.50	73.40	0	0	0
T842: VPI.V-I.V-I.V-I.V-I.VPI.VPI.--I.--I.--I.VPI.VPI.	44.40	0.00383	Dominated	32.20	51.35	70.50	0	0	0
T843: VPO.V-I.V-I.V-I.V-I.VPO.VPO.--I.--I.--I.VPO.VPO.	43.90	0.00362	Dominated	28.50	46.60	64.70	0	0	0
T844: VCI.V-I.V-I.V-I.V-I.VCI.VCI.--I.--I.--I.VCI.VCI.	38.30	0.00372	Dominated	36.10	54.70	73.30	0	0	0
T845: VCO.V-I.V-I.V-I.V-I.VCO.VCO.--I.--I.--I.VCO.VCO.	37.40	0.00358	Dominated	34.20	52.10	70.00	0	0	0
T846: V--.V-I.V-I.V-I.V-I.V--.--I.--I.--I.V--.V--.	26.50	0.00383	Extended dominated	50.10	69.25	88.40	0	0	0
T847: VPI.V-I.V-I.V-I.V-I.VPI.--I.--I.--I.VPI.VPI.	42.80	0.00415	Dominated	40.20	60.95	81.70	0	0	0
T848: VPO.V-I.V-I.V-I.V-I.VPO.--I.--I.--I.VPO.VPO.	42.00	0.00403	Dominated	38.60	58.75	78.90	0	0	0
T849: VCI.V-I.V-I.V-I.V-I.VCI.--I.--I.--I.VCI.VCI.	36.90	0.00411	Dominated	45.30	65.85	86.40	0	0	0
T850: VCO.V-I.V-I.V-I.V-I.VCO.--I.--I.--I.VCO.VCO.	35.90	0.00401	Dominated	44.30	64.35	84.40	0	0	0

Costs and QALYs are relative to do nothing (S30).

TABLE 109 *Full cost-effectiveness results for all 341 strategies modelled for Scenario B*

Strategy and detail[a]	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
S1: ---.--I.--I.--I.---.---.---.--I.--I.--I.---.---.	–1.75	0.00050	Dominated	11.79	14.30	16.81	0	0	0
S2: -PI.--I.--I.--I.-PI.-PI.-PI.--I.--I.--I.---.---.	–1.45	0.00121	Dominated	25.65	31.70	37.75	0	0	0
S3: ---.--I.--I.--I.--O.---.---.--I.--I.--I.---.---.	–4.27	0.00109	Dominated	26.07	31.52	36.97	0	0	0
S4: -PI.--I.--I.--I.--O.-PI.-PI.--I.--I.--I.-PI.-PI.	6.53	0.00238	Dominated	41.07	52.97	64.87	0	0	0
S5: ---.--I.--I.--I.--O.--I.---.--I.--I.---.---.	–6.21	0.00168	Dominated	39.81	48.21	56.61	0	0	0
S6: -PI.--I.--I.--I.--O.--I.-PI.--I.--I.--I.-PI.-PI.	4.88	0.00271	Dominated	49.32	62.87	76.42	0	0	0
S7: --I.--I.--I.--I.--O.--I.---.--I.--I.--I.---.---.	–6.63	0.00180	Dominated	42.63	51.63	60.63	0	0	0
S8: --I.--I.--I.--I.--O.--I.-PI.--I.--I.--I.-PI.-PI.	4.46	0.00279	Dominated	51.34	65.29	79.24	0	0	0
S26: -CO.-CO.-CO.-CO.-CO.-CO.-CO.-CO.-CO.-CO.-CO.-CO.	5.41	0.00090	Dominated	12.65	17.17	21.68	0	0	0
S27: -CI.-CI.-CI.-CI.-CI.-CI.-CI.-CI.-CI.-CI.-CI.-CI.	4.28	0.00146	Dominated	24.92	32.22	39.52	0	0	0
S28: -PO.-PO.-PO.-PO.-PO.-PO.-PO.-PO.-PO.-PO.-PO.-PO.	11.20	0.00126	Dominated	14.00	20.30	26.60	0	0	0
S29: -PI.-PI.-PI.-PI.-PI.-PI.-PI.-PI.-PI.-PI.-PI.-PI.	9.10	0.00204	Dominated	31.70	41.90	52.10	0	0	0
S30: ---.---.---.---.---.---.---.---.---.---.---.---.	0.00	0.00000	Dominated	0.00	0.00	0.00	0.06	0.09	0.1
S35: -CI.-CI.-CI.-CI.-CO.-CI.-CI.-CI.-CI.-CI.-CI.-CI.	4.29	0.00144	Dominated	24.51	31.71	38.91	0	0	0
S36: -CI.--I.-CI.-CI.-CO.-CI.-CI.--I.-CI.-CI.-CI.-CI.	4.28	0.00144	Dominated	24.52	31.72	38.92	0	0	0
S37: -CI.-CI.--I.-CI.-CO.-CI.-CI.-CI.--I.-CI.-CI.-CI.	3.60	0.00159	Dominated	28.20	36.15	44.10	0	0	0
S38: -CI.--I.--I.-CI.-CO.-CI.-CI.--I.--I.-CI.-CI.-CI.	3.60	0.00159	Dominated	28.20	36.15	44.10	0	0	0
S39: --I.--I.--I.--I.--O.--I.--O.--I.--I.--I.-PI.-PI.	2.78	0.00285	Extended dominated	54.22	68.47	82.72	3.18	4.47	5.43
S40: --I.--I.-CI.--I.--O.--I.--O.--I.-CI.--I.-PI.-PI.	3.46	0.00269	Dominated	50.34	63.79	77.24	0	0	0
S41: --I.-CI.--I.--I.--O.--I.--O.-CI.--I.--I.-PI.-PI.	2.78	0.00284	Dominated	54.02	68.22	82.42	0	0	0
S42: --I.-CI.-CI.--I.--O.--I.--O.-CI.-CI.--I.-PI.-PI.	3.47	0.00269	Dominated	50.33	63.78	77.23	0	0	0
S63: -PI.-PI.-PI.--I.--O.-PI.-PI.-PI.-PI.--I.-PI.-PI.	7.24	0.00230	Dominated	38.76	50.26	61.76	0	0	0
S64: -PI.-CI.-PI.--I.--O.-PI.-PI.-CI.-PI.--I.-PI.-PI.	7.24	0.00230	Dominated	38.76	50.26	61.76	0	0	0
S72: -CO.--O.--O.-CO.-CO.-CO.-CO.--O.--I.-CI.-CO.-CO.	4.62	0.00107	Dominated	16.78	22.13	27.48	0	0	0
S73: --O.--O.--O.--O.--O.--O.--O.--O.--I.--I.-PO.-PO.	4.84	0.00197	Dominated	34.56	44.41	54.26	0.11	0.11	0.13
S74: -CO.--O.--O.-CO.-CO.-CO.-CO.--O.--I.-CI.-CI.-CI.	4.05	0.00140	Dominated	23.95	30.95	37.95	0	0	0
S75: --O.--O.--O.--O.--O.--O.--O.--O.--I.--I.-PI.-PI.	3.85	0.00236	Dominated	43.35	55.15	66.95	2.55	3.5	4.31
S76: -CI.--I.--I.-CI.-CI.-CI.-CI.--I.--I.-CI.-CO.-CO.	4.17	0.00128	Dominated	21.43	27.83	34.23	0	0	0
S77: --I.--I.--I.--I.--I.--I.--I.--I.--I.--I.-PO.-PO.	5.25	0.00251	Dominated	44.95	57.50	70.05	0	0	0
S78: -CI.--I.--I.-CI.-CI.-CI.-CI.--I.--I.-CI.-CI.-CI.	3.60	0.00161	Dominated	28.60	36.65	44.70	0	0	0
S79: --I.--I.--I.--I.--O.--I.--I.--I.--I.--I.---.---.	–5.70	0.00190	Dominated	43.70	53.20	62.70	0	0	0
S80: --I.--I.--I.--I.--I.--I.--O.--I.--I.--I.-PI.-PI.	3.13	0.00288	ICER to S99: £51,000	54.47	68.87	83.27	5.66	5.99	5.72
S81: -CI.--I.--I.--I.--O.-CI.-CI.--I.--I.--I.-CI.-CI.	1.27	0.00212	Dominated	41.13	51.73	62.33	0	0	0

[a] Interventions are given for risk groups 1 to 12: C, culture at 35–37 weeks; I, i.v. antibiotics; n, no treatment; O, oral antibiotics; P, PCR test at labour; V, vaccination. Space represents no treatment.

continued

TABLE 109 *Full cost-effectiveness results for all 341 strategies modelled for Scenario B (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
S82: -Cl.--I.--I.--I.--O.--I.-Cl.--I.--I.--I.-Cl.-Cl.	–0.44	0.00259	Dominated	52.24	65.19	78.14	0	0	0
S83: --I.--I.--I.--I.--O.--I.-Cl.--I.--I.--I.-Cl.-Cl.	–0.84	0.00270	Dominated	54.84	68.34	81.84	0	0	0
S84: --I.--I.--I.--I.--O.--I.--O.--I.--I.--I.-Cl.-Cl.	–1.98	0.00275	ICER to S86: £5620	56.98	70.73	84.48	11.8	10.9	10.1
S85: -Cl.-Cl.-Cl.--I.--O.-Cl.-Cl.-Cl.-Cl.--I.-Cl.-Cl.	1.96	0.00196	Dominated	37.24	47.04	56.84	0	0	0
S86: --I.--I.--I.--I.--O.--I.--O.--I.--I.--I.---.---.	–6.84	0.00189	ICER to T27: £1690	44.64	54.09	63.54	0.06	0.03	0.01
S87: --I.--I.--I.--I.--O.--I.--I.--I.--I.--I.-Cl.-Cl.	–0.84	0.00276	Dominated	56.04	69.84	83.64	0.02	0.04	0.11
S88: --I.--I.--I.--I.--O.--I.--I.--I.--I.--I.-Pl.-Pl.	3.92	0.00285	Dominated	53.08	67.33	81.58	0.02	0.02	0.06
S89: ---.--I.--I.--I.---.---.--I.--I.--I.---.---.	–3.92	0.00112	Dominated	26.32	31.92	37.52	0	0	0
S90: -Cl.--I.--I.--I.-Cl.-Cl.--I.--I.--I.-Cl.-Cl.	1.62	0.00215	Dominated	41.38	52.13	62.88	0	0	0
S91: -Pl.--I.--I.--I.-Pl.-Pl.--I.--I.-Pl.-Pl.	6.88	0.00242	Dominated	41.52	53.62	65.72	0	0	0
S92: ---.--I.--I.--I.--I.---.--I.--I.---.---.	–5.86	0.00172	Dominated	40.26	48.86	57.46	0	0	0
S93: -Cl.--I.--I.--I.--I.-Cl.--I.--I.-Cl.-Cl.	–0.09	0.00263	Dominated	52.69	65.84	78.99	0	0	0
S94: -Pl.--I.--I.--I.--I.-Pl.--I.--I.-Pl.-Pl.	5.23	0.00275	Dominated	49.77	63.52	77.27	0	0	0
S95: --I.--I.--I.--I.--I.---.--I.--I.---.---.	–6.28	0.00184	Dominated	43.08	52.28	61.48	0	0	0
S96: --I.--I.--I.--I.--I.-Cl.--I.--I.-Cl.-Cl.	–0.49	0.00273	Dominated	55.09	68.74	82.39	0	0	0
S97: --I.--I.--I.--I.--I.-Pl.--I.--I.-Pl.-Pl.	4.81	0.00283	Dominated	51.79	65.94	80.09	0	0	0
S98: --I.--I.--I.--I.--I.--O.--I.--I.---.---.	–6.49	0.00193	Extended dominated	45.09	54.74	64.39	0.24	0.08	0.05
S99: --I.--I.--I.--I.--I.--O.--I.--I.-Cl.-Cl.	–1.63	0.00279	ICER to S84: £9470	57.43	71.38	85.33	20.8	15.4	11.8
S100: --I.--I.--I.--I.--I.--I.--I.---.---.	–5.35	0.00193	Extended dominated	43.95	53.60	63.25	0.03	0.01	0
S101: --I.--I.--I.--I.--I.--I.--I.-Cl.-Cl.	–0.49	0.00280	Extended dominated	56.49	70.49	84.49	20.3	22.4	23.3
S102: --I.--I.--I.--I.--I.--I.--I.-Pl.-Pl.	4.27	0.00289	ICER to S80: £142,000	53.53	67.98	82.43	6.54	10.2	13.6
S103: ---.--I.--I.--I.---.---.--O.--O.--I.---.---.	–3.97	0.00104	Dominated	24.77	29.97	35.17	0	0	0
S104: -Pl.--I.--I.--I.-Pl.-Pl.--O.--O.--I.-Pl.-Pl.	6.83	0.00234	Dominated	39.97	51.67	63.37	0	0	0
S105: ---.--O.--O.--I.---.---.--O.--O.--I.---.---.	–3.67	0.00094	Dominated	22.49	27.20	31.90	0	0	0
S106: -Pl.--O.--O.--I.--I.-Pl.-Pl.--O.--O.--I.-Pl.-Pl.	7.13	0.00224	Dominated	37.67	48.87	60.07	0	0	0
S107: ---.--O.--O.--I.--I.-Pl.-Pl.--O.--O.--I.-Pl.-Pl.	7.13	0.00219	Dominated	36.67	47.62	58.57	0	0	0
S108: ---.--O.--O.--I.--O.---.---.--O.--O.--I.---.---.	–4.02	0.00090	Dominated	22.10	26.62	31.14	0	0	0
S109: -Pl.--O.--O.--I.--O.-Pl.-Pl.--O.--O.--I.-Pl.-Pl.	6.78	0.00220	Dominated	37.22	48.22	59.22	0	0	0
S110: -Pl.--O.--O.--I.--O.-Pl.-Pl.--O.--O.--I.-PO.-PO.	7.76	0.00182	Dominated	28.64	37.74	46.84	0	0	0
S111: -Pl.--O.--O.--I.--O.-Pl.-PO.--O.--O.--I.-PO.-PO.	7.67	0.00181	Dominated	28.53	37.58	46.63	0	0	0
S112: -Pl.--O.--O.--I.--O.-PO.-PO.--O.--O.--I.-PO.-PO.	8.25	0.00163	Dominated	24.35	32.50	40.65	0	0	0
S113: -PO.--O.--O.--I.--O.-PO.-PO.--O.--O.--I.-PO.-PO.	8.25	0.00162	Dominated	24.15	32.25	40.35	0	0	0
S114: ---.--I.--I.--I.--I.---.--O.--O.--I.---.---.	–5.91	0.00163	Dominated	38.51	46.66	54.81	0	0	0
S115: -Pl.--I.--I.--I.--I.--I.-Pl.--O.--O.--I.-Pl.-Pl.	5.17	0.00267	Dominated	48.23	61.58	74.93	0	0	0
S116: ---.--O.--O.--I.--I.--I.---.--O.--O.--I.---.---.	–5.61	0.00154	Dominated	36.41	44.11	51.81	0	0	0
S117: -Pl.--O.--O.--I.--I.--I.-Pl.--O.--O.--I.-Pl.-Pl.	5.48	0.00257	Dominated	45.92	58.77	71.62	0	0	0
S118: ---.--O.--O.--I.--O.--I.---.--O.--O.--I.---.---.	–5.96	0.00150	Dominated	35.96	43.46	50.96	0	0	0

continued

TABLE 109 *Full cost-effectiveness results for all 341 strategies modelled for Scenario B (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
S119: -PI.--O.--O.--I.--O.--I.-PI.--O.--O.--I.-PI.-PI.	5.13	0.00253	Dominated	45.47	58.12	70.77	0	0	0
S120: ---.--O.--O.--I.--O.--I.-PI.--O.--O.--I.-PI.-PI.	5.13	0.00249	Dominated	44.67	57.12	69.57	0	0	0
S121: ---.--O.--O.--I.--O.--O.---.--O.--O.--I.---.---.	–5.09	0.00114	Dominated	27.89	33.59	39.29	0	0	0
S122: -PI.--O.--O.--I.--O.--O.-PI.--O.--O.--I.-PI.-PI.	6.00	0.00217	Dominated	37.40	48.25	59.10	0	0	0
S123: -PI.--O.--O.--I.--O.--O.-PI.--O.--O.--I.-PO.-PO.	6.98	0.00179	Dominated	28.82	37.77	46.72	0	0	0
S124: -PI.--O.--O.--I.--O.--O.-PO.--O.--O.--I.-PO.-PO.	6.89	0.00178	Dominated	28.71	37.61	46.51	0	0	0
S125: -PO.--O.--O.--I.--O.--O.-PO.--O.--O.--I.-PO.-PO.	6.89	0.00177	Dominated	28.51	37.36	46.21	0	0	0
S126: --I.--I.--I.--I.--I.--I.---.--O.--O.--I.---.---.	–6.33	0.00176	Dominated	41.53	50.33	59.13	0	0	0
S127: --I.--I.--I.--I.--I.--I.-PI.--O.--O.--I.-PI.-PI.	4.76	0.00275	Dominated	50.24	63.99	77.74	0	0	0
S128: --I.--O.--O.--I.--I.--I.---.--O.--O.--I.---.---.	–6.03	0.00166	Dominated	39.23	47.53	55.83	0	0	0
S129: --I.--O.--O.--I.--I.--I.-PI.--O.--O.--I.-PI.-PI.	5.06	0.00265	Dominated	47.94	61.19	74.44	0	0	0
S130: --I.--O.--O.--I.--O.--I.---.--O.--O.--I.---.---.	–6.38	0.00162	Dominated	38.78	46.88	54.98	0	0	0
S131: --I.--O.--O.--I.--O.--I.-PI.--O.--O.--I.-PI.-PI.	4.71	0.00261	Dominated	47.49	60.54	73.59	0	0	0
S132: --I.--O.--O.--I.--O.--O.---.--O.--O.--I.---.---.	–5.51	0.00126	Dominated	30.71	37.01	43.31	0	0	0
S133: --I.--O.--O.--I.--O.--O.-PI.--O.--O.--I.-PI.-PI.	5.58	0.00225	Dominated	39.42	50.67	61.92	0	0	0
S134: --O.--O.--O.--I.--O.--O.---.--O.--O.--I.---.---.	–5.61	0.00125	Dominated	30.61	36.86	43.11	0.04	0.01	0
S135: --O.--O.--O.--I.--O.--O.-PI.--O.--O.--I.-PI.-PI.	5.47	0.00224	Dominated	39.33	50.53	61.73	0	0	0
S136: --O.--O.--O.--I.--O.--O.-PI.--O.--O.--I.-PO.-PO.	6.46	0.00186	Dominated	30.74	40.04	49.34	0	0	0
S137: --O.--O.--O.--I.--O.--O.-PO.--O.--O.--I.-PO.-PO.	6.36	0.00185	Dominated	30.64	39.89	49.14	0	0	0
S138: --I.--I.--I.--I.--I.--I.--I.--O.--O.--I.---.---.	–5.41	0.00185	Dominated	42.41	51.66	60.91	0	0	0
S139: --I.--I.--I.--I.--I.--I.--I.--O.--O.--I.-PI.-PI.	4.21	0.00281	Dominated	51.99	66.04	80.09	0	0	0
S140: --I.--I.--I.--I.--I.--I.--I.--O.--O.--O.--I.---.---.	–6.54	0.00184	Dominated	43.34	52.54	61.74	0.01	0.01	0.01
S141: --I.--I.--I.--I.--I.--I.--I.--O.--O.--O.--I.-PI.-PI.	3.08	0.00280	Dominated	52.92	66.92	80.92	0	0	0
S142: --I.--O.--O.--I.--I.--I.--O.--O.--O.--I.---.---.	–6.24	0.00174	Dominated	41.04	49.74	58.44	0	0	0
S143: --I.--O.--O.--I.--I.--I.--O.--O.--O.--I.-PI.-PI.	3.38	0.00270	Dominated	50.62	64.12	77.62	0	0	0
S144: --I.--O.--O.--I.--O.--I.--O.--O.--O.--I.---.---.	–6.59	0.00171	Dominated	40.79	49.34	57.89	0	0	0
S145: --I.--O.--O.--I.--O.--I.--O.--O.--O.--I.-PI.-PI.	3.03	0.00266	Dominated	50.17	63.47	76.77	0	0	0
S146: --I.--O.--O.--I.--O.--O.--O.--O.--O.--I.---.---.	–5.72	0.00135	Dominated	32.72	39.47	46.22	0	0	0
S147: --I.--O.--O.--I.--O.--O.--O.--O.--O.--I.-PI.-PI.	3.90	0.00230	Dominated	42.10	53.60	65.10	0	0	0
S148: --O.--O.--O.--I.--O.--O.--O.--O.--O.--I.---.---.	–5.83	0.00133	Dominated	32.43	39.08	45.73	0.04	0.02	0.02
S149: --O.--O.--O.--I.--O.--O.--O.--O.--O.--I.-PI.-PI.	3.79	0.00229	Dominated	42.01	53.46	64.91	0.01	0.01	0.02
S150: --O.--O.--O.--I.--O.--O.--O.--O.--O.--I.-PO.-PO.	4.78	0.00191	Dominated	33.42	42.97	52.52	0.01	0.01	0
T2: --O.--I.--I.--I.--I.--I.--I.--I.--I.---.---.	–5.46	0.00192	Dominated	43.86	53.46	63.06	0	0	0
T3: --I.--O.--O.--I.--I.--I.--I.--I.--I.--I.---.---.	–5.05	0.00184	Dominated	41.85	51.05	60.25	0	0	0
T5: --I.--I.--I.--I.--I.--O.--I.--I.--I.--I.---.---.	–4.48	0.00157	Dominated	35.88	43.73	51.58	0	0	0
T8: --O.--I.--I.--I.--I.--I.--O.--I.--I.--I.---.---.	–6.60	0.00191	Extended dominated	44.80	54.35	63.90	0.06	0.01	0
T9: --I.--O.--O.--I.--I.--I.--O.--I.--I.--I.---.---.	–6.19	0.00183	Dominated	42.79	51.94	61.09	0	0	0

continued

TABLE 109 *Full cost-effectiveness results for all 341 strategies modelled for Scenario B (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T11: --I.--I.--I.--I.--I.--O.--O.--I.--I.--I.---.---.	–5.61	0.00156	Dominated	36.81	44.61	52.41	0	0	0
T13: --O.--I.--I.--I.--I.--I.--I.--O.--O.--I.---.---.	–5.51	0.00184	Dominated	42.31	51.51	60.71	0	0	0
T14: --I.--O.--O.--I.--I.--I.--I.--O.--O.--I.---.---.	–5.10	0.00175	Dominated	40.10	48.85	57.60	0	0	0
T15: --I.--I.--I.--I.--O.--I.--I.--O.--O.--I.---.---.	–5.76	0.00181	Dominated	41.96	51.01	60.06	0	0	0
T16: --I.--I.--I.--I.--I.--O.--I.--O.--O.--I.---.---.	–4.53	0.00149	Dominated	34.33	41.78	49.23	0	0	0
T17: --O.--I.--I.--I.--I.--I.--O.--O.--O.--I.---.---.	–6.65	0.00183	Dominated	43.25	52.40	61.55	0	0	0
T20: --I.--I.--I.--I.--I.--O.--O.--O.--O.--I.---.---.	–5.67	0.00148	Dominated	35.27	42.67	50.07	0	0	0
T21: --O.--O.--O.--I.--I.--I.--O.--O.--O.--I.---.---.	–6.35	0.00173	Dominated	40.95	49.60	58.25	0	0	0
T25: --I.--O.--O.--I.--I.--O.--O.--O.--O.--I.---.---.	–5.37	0.00138	Dominated	32.97	39.87	46.77	0	0	0
T27: --O.--I.--I.--I.--O.--I.--O.--O.--O.--I.---.---.	–7.00	0.00179	Base for ICER	42.80	51.75	60.70	0.12	0.06	0.03
T28: --I.--I.--I.--I.--O.--O.--O.--O.--O.--I.---.---.	–6.02	0.00144	Dominated	34.82	42.02	49.22	0	0	0
T29: --I.--I.--I.--I.--O.--I.--O.--O.--O.--I.---.---.	–6.90	0.00181	Extended dominated	43.10	52.15	61.20	0.02	0	0
T30: --O.--I.--I.--I.--I.--O.--O.--O.--O.--I.---.---.	–5.78	0.00147	Dominated	35.18	42.53	49.88	0	0	0
T36: --O.--I.--I.--I.--O.--O.--O.--O.--O.--I.---.---.	–6.13	0.00143	Dominated	34.73	41.88	49.03	0.23	0.09	0.07
T37: --O.--O.--O.--I.--O.--I.--O.--O.--O.--I.---.---.	–6.70	0.00169	Dominated	40.50	48.95	57.40	0	0	0
T39: --O.--O.--O.--I.--I.--O.--O.--O.--O.--I.---.---.	–5.48	0.00137	Dominated	32.88	39.73	46.58	0	0	0
T42: --O.--I.--I.--I.--I.--I.--I.--I.--I.--I.-PI.-PI.	4.16	0.00288	Dominated	53.44	67.84	82.24	0	0	0
T43: --I.--O.--O.--I.--I.--I.--I.--I.--I.--I.-PI.-PI.	4.57	0.00279	Dominated	51.23	65.18	79.13	0	0	0
T45: --I.--I.--I.--I.--I.--O.--I.--I.--I.--I.-PI.-PI.	5.14	0.00253	Dominated	45.46	58.11	70.76	0	0	0
T48: --O.--I.--I.--I.--I.--I.--O.--I.--I.--I.-PI.-PI.	3.02	0.00287	Extended dominated	54.38	68.73	83.08	1.04	1.42	1.85
T49: --I.--O.--O.--I.--I.--I.--O.--I.--I.--I.-PI.-PI.	3.43	0.00279	Dominated	52.37	66.32	80.27	0	0	0
T51: --I.--I.--I.--I.--I.--O.--O.--I.--I.--I.-PI.-PI.	4.01	0.00252	Dominated	46.39	58.99	71.59	0	0	0
T53: --O.--I.--I.--I.--I.--I.--I.--O.--O.--I.-PI.-PI.	4.11	0.00280	Dominated	51.89	65.89	79.89	0	0	0
T54: --I.--O.--O.--I.--I.--I.--I.--O.--O.--I.-PI.-PI.	4.52	0.00271	Dominated	49.68	63.23	76.78	0	0	0
T55: --I.--I.--I.--I.--O.--I.--I.--O.--O.--I.-PI.-PI.	3.86	0.00277	Dominated	51.54	65.39	79.24	0	0	0
T56: --I.--I.--I.--I.--I.--O.--I.--O.--O.--I.-PI.-PI.	5.09	0.00245	Dominated	43.91	56.16	68.41	0	0	0
T57: --O.--I.--I.--I.--I.--I.--O.--O.--O.--I.-PI.-PI.	2.97	0.00279	Dominated	52.83	66.78	80.73	0	0	0
T60: --I.--I.--I.--I.--I.--O.--O.--O.--O.--I.-PI.-PI.	3.95	0.00244	Dominated	44.85	57.05	69.25	0	0	0
T61: --O.--O.--O.--I.--I.--I.--O.--O.--O.--I.-PI.-PI.	3.27	0.00269	Dominated	50.53	63.98	77.43	0	0	0
T65: --I.--O.--O.--I.--I.--O.--O.--O.--O.--I.-PI.-PI.	4.25	0.00234	Dominated	42.55	54.25	65.95	0	0	0
T67: --O.--I.--I.--I.--O.--I.--O.--O.--O.--I.-PI.-PI.	2.62	0.00275	Dominated	52.38	66.13	79.88	1.84	2.21	2.79
T68: --I.--I.--I.--I.--O.--O.--O.--O.--O.--I.-PI.-PI.	3.60	0.00240	Dominated	44.40	56.40	68.40	0	0	0
T69: --I.--I.--I.--I.--O.--I.--O.--O.--O.--I.-PI.-PI.	2.72	0.00276	Dominated	52.48	66.28	80.08	0	0	0
T70: --O.--I.--I.--I.--I.--O.--O.--O.--O.--I.-PI.-PI.	3.84	0.00243	Dominated	44.76	56.91	69.06	0	0.01	0
T76: --O.--I.--I.--I.--O.--O.--O.--O.--O.--I.-PI.-PI.	3.49	0.00239	Dominated	44.31	56.26	68.21	0.56	0.67	0.84
T77: --O.--O.--O.--I.--O.--I.--O.--O.--O.--I.-PI.-PI.	2.92	0.00265	Dominated	50.08	63.33	76.58	0	0	0
T79: --O.--O.--O.--I.--I.--O.--O.--O.--O.--I.-PI.-PI.	4.15	0.00233	Dominated	42.45	54.10	65.75	0	0	0

continued

TABLE 109 *Full cost-effectiveness results for all 341 strategies modelled for Scenario B (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T82: --O.--I.--I.--I.--I.--I.--I.--I.--I.--I.-PO.-PO.	5.15	0.00250	Dominated	44.85	57.35	69.85	0	0	0
T83: --I.--O.--O.--I.--I.--I.--I.--I.--I.--I.-PO.-PO.	5.56	0.00241	Dominated	42.64	54.69	66.74	0	0	0
T84: --I.--I.--I.--I.--O.--I.--I.--I.--I.--I.-PO.-PO.	4.90	0.00247	Dominated	44.50	56.85	69.20	0	0	0
T85: --I.--I.--I.--I.--I.--O.--I.--I.--I.--I.-PO.-PO.	6.13	0.00215	Dominated	36.87	47.62	58.37	0	0	0
T86: --I.--I.--I.--I.--I.--I.--O.--I.--I.--I.-PO.-PO.	4.12	0.00250	Dominated	45.88	58.38	70.88	0	0	0
T87: --I.--I.--I.--I.--I.--I.--I.--O.--O.--I.-PO.-PO.	5.20	0.00243	Dominated	43.40	55.55	67.70	0	0	0
T88: --O.--I.--I.--I.--I.--I.--O.--I.--I.--I.-PO.-PO.	4.01	0.00249	Dominated	45.79	58.24	70.69	0	0	0
T89: --I.--O.--O.--I.--I.--I.--O.--I.--I.--I.-PO.-PO.	4.42	0.00240	Dominated	43.58	55.58	67.58	0	0	0
T90: --I.--I.--I.--I.--O.--I.--O.--I.--I.--I.-PO.-PO.	3.76	0.00246	Dominated	45.44	57.74	70.04	0	0	0
T91: --I.--I.--I.--I.--I.--O.--O.--I.--I.--I.-PO.-PO.	4.99	0.00214	Dominated	37.81	48.51	59.21	0	0	0
T92: --I.--I.--I.--I.--I.--I.--O.--O.--O.--I.-PO.-PO.	4.06	0.00242	Dominated	44.34	56.44	68.54	0	0	0
T93: --O.--I.--I.--I.--I.--I.--I.--O.--O.--I.-PO.-PO.	5.09	0.00241	Dominated	43.11	55.16	67.21	0	0	0
T94: --I.--O.--O.--I.--I.--I.--I.--O.--O.--I.-PO.-PO.	5.50	0.00233	Dominated	41.10	52.75	64.40	0	0	0
T95: --I.--I.--I.--I.--O.--I.--I.--O.--O.--I.-PO.-PO.	4.85	0.00239	Dominated	42.95	54.90	66.85	0	0	0
T96: --I.--I.--I.--I.--I.--O.--I.--O.--O.--I.-PO.-PO.	6.07	0.00207	Dominated	35.33	45.68	56.03	0	0	0
T97: --O.--I.--I.--I.--I.--I.--I.--O.--O.--O.--I.-PO.-PO.	3.95	0.00241	Dominated	44.25	56.30	68.35	0	0	0
T100: --I.--I.--I.--I.--I.--I.--O.--O.--O.--O.--I.-PO.-PO.	4.93	0.00206	Dominated	36.27	46.57	56.87	0	0	0
T101: --O.--O.--O.--I.--I.--I.--I.--O.--O.--O.--I.-PO.-PO.	4.26	0.00231	Dominated	41.94	53.49	65.04	0	0	0
T104: --I.--O.--O.--I.--O.--I.--O.--O.--O.--I.-PO.-PO.	4.01	0.00228	Dominated	41.59	52.99	64.39	0	0	0
T105: --I.--O.--O.--I.--I.--O.--O.--O.--O.--I.-PO.-PO.	5.24	0.00196	Dominated	33.96	43.76	53.56	0	0	0
T106: --I.--O.--O.--I.--I.--I.--O.--O.--O.--I.-PO.-PO.	4.36	0.00232	Dominated	42.04	53.64	65.24	0	0	0
T107: --O.--I.--I.--I.--O.--I.--O.--O.--O.--I.-PO.-PO.	3.60	0.00237	Dominated	43.80	55.65	67.50	0	0	0
T108: --I.--I.--I.--I.--O.--O.--O.--O.--O.--I.-PO.-PO.	4.58	0.00202	Dominated	35.82	45.92	56.02	0	0	0
T109: --I.--I.--I.--I.--O.--I.--O.--O.--O.--I.-PO.-PO.	3.71	0.00238	Dominated	43.89	55.79	67.69	0	0	0
T110: --O.--I.--I.--I.--I.--O.--O.--O.--O.--I.-PO.-PO.	4.83	0.00204	Dominated	35.97	46.17	56.37	0	0	0
T116: --O.--I.--I.--I.--O.--O.--O.--O.--O.--I.-PO.-PO.	4.47	0.00201	Dominated	35.73	45.78	55.83	0.01	0.01	0.02
T117: --O.--O.--O.--I.--O.--I.--O.--O.--O.--I.-PO.-PO.	3.90	0.00227	Dominated	41.50	52.85	64.20	0	0	0
T118: --I.--O.--O.--I.--O.--O.--O.--O.--O.--I.-PO.-PO.	4.88	0.00192	Dominated	33.52	43.12	52.72	0	0	0
T119: --O.--O.--O.--I.--I.--O.--O.--O.--O.--I.-PO.-PO.	5.13	0.00195	Dominated	33.87	43.62	53.37	0	0	0
T122: --O.--I.--I.--I.--I.--I.--I.--I.--I.--I.-CI.-CI.	–0.60	0.00278	Dominated	56.20	70.10	84.00	0	0	0
T123: --I.--O.--O.--I.--I.--I.--I.--I.--I.--I.-CI.-CI.	–0.19	0.00270	Dominated	54.19	67.69	81.19	0	0	0
T125: --I.--I.--I.--I.--I.--O.--I.--I.--I.--I.-CI.-CI.	0.38	0.00244	Dominated	48.42	60.62	72.82	0	0	0
T127: --I.--I.--I.--I.--I.--I.--I.--O.--O.--I.-CI.-CI.	–0.55	0.00271	Dominated	54.75	68.30	81.85	0	0	0
T128: --O.--I.--I.--I.--I.--I.--O.--I.--I.--I.-CI.-CI.	–1.74	0.00278	Extended dominated	57.34	71.24	85.14	4.81	4.65	4.39
T129: --I.--O.--O.--I.--I.--I.--O.--I.--I.--I.-CI.-CI.	–1.33	0.00269	Dominated	55.13	68.58	82.03	0	0	0
T131: --I.--I.--I.--I.--I.--O.--O.--I.--I.--I.-CI.-CI.	–0.76	0.00243	Dominated	49.36	61.51	73.66	0.01	0.01	0.01
T132: --I.--I.--I.--I.--I.--I.--O.--O.--O.--I.-CI.-CI.	–1.69	0.00271	Dominated	55.89	69.44	82.99	0	0	0

continued

TABLE 109 *Full cost-effectiveness results for all 341 strategies modelled for Scenario B (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T133: --O.--I.--I.--I.--I.--I.--I.--O.--O.--I.-CI.-CI.	–0.66	0.00270	Dominated	54.66	68.16	81.66	0	0	0
T134: --I.--O.--O.--I.--I.--I.--I.--O.--O.--I.-CI.-CI.	–0.25	0.00262	Dominated	52.65	65.75	78.85	0	0	0
T135: --I.--I.--I.--I.--O.--I.--I.--O.--O.--I.-CI.-CI.	–0.90	0.00268	Dominated	54.50	67.90	81.30	0	0	0
T136: --I.--I.--I.--I.--I.--O.--I.--O.--O.--I.-CI.-CI.	0.33	0.00235	Dominated	46.67	58.42	70.17	0	0	0
T137: --O.--I.--I.--I.--I.--I.--O.--O.--O.--I.-CI.-CI.	–1.79	0.00269	Dominated	55.59	69.04	82.49	0	0	0
T140: --I.--I.--I.--I.--I.--O.--O.--O.--O.--I.-CI.-CI.	–0.81	0.00235	Dominated	47.81	59.56	71.31	0	0	0
T141: --O.--O.--O.--I.--I.--I.--O.--O.--O.--I.-CI.-CI.	–1.49	0.00260	Dominated	53.49	66.49	79.49	0	0	0
T144: --I.--O.--O.--I.--O.--I.--O.--O.--O.--I.-CI.-CI.	–1.73	0.00257	Dominated	53.13	65.98	78.83	0	0	0
T145: --I.--O.--O.--I.--I.--O.--O.--O.--O.--I.-CI.-CI.	–0.51	0.00225	Dominated	45.51	56.76	68.01	0	0	0
T146: --I.--O.--O.--I.--I.--I.--O.--O.--O.--I.-CI.-CI.	–1.38	0.00261	Dominated	53.58	66.63	79.68	0	0	0
T147: --O.--I.--I.--I.--O.--I.--O.--O.--O.--I.-CI.-CI.	–2.14	0.00266	Extended dominated	55.34	68.64	81.94	8.97	7.88	6.82
T148: --I.--I.--I.--I.--O.--O.--O.--O.--O.--I.-CI.-CI.	–1.16	0.00231	Dominated	47.36	58.91	70.46	0	0	0
T149: --I.--I.--I.--I.--O.--I.--O.--O.--O.--I.-CI.-CI.	–2.04	0.00267	Extended dominated	55.44	68.79	82.14	0	0	0
T150: --O.--I.--I.--I.--I.--O.--O.--O.--O.--I.-CI.-CI.	–0.92	0.00233	Dominated	47.52	59.17	70.82	0.01	0	0
T156: --O.--I.--I.--I.--O.--O.--O.--O.--O.--I.-CI.-CI.	–1.27	0.00230	Dominated	47.27	58.77	70.27	8.65	7.7	6.87
T157: --O.--O.--O.--I.--O.--I.--O.--O.--O.--I.-CI.-CI.	–1.84	0.00256	Dominated	53.04	65.84	78.64	0	0	0
T158: --I.--O.--O.--I.--O.--O.--O.--O.--O.--I.-CI.-CI.	–0.86	0.00221	Dominated	45.06	56.11	67.16	0	0	0
T159: --O.--O.--O.--I.--I.--O.--O.--O.--O.--I.-CI.-CI.	–0.62	0.00223	Dominated	45.22	56.37	67.52	0	0	0
T160: --O.--O.--O.--I.--O.--O.--O.--O.--O.--I.-CI.-CI.	–0.97	0.00220	Dominated	44.97	55.97	66.97	1.07	0.98	0.84
T161: --I.--I.--I.--I.--I.--I.--I.--I.--I.--I.-CO.-CO.	0.08	0.00246	Dominated	49.12	61.42	73.72	0	0	0
T162: --O.--I.--I.--I.--I.--I.--I.--I.--I.--I.-CO.-CO.	–0.03	0.00245	Dominated	49.03	61.28	73.53	0	0	0
T163: --I.--O.--O.--I.--I.--I.--I.--I.--I.--I.-CO.-CO.	0.38	0.00237	Dominated	47.02	58.87	70.72	0	0	0
T164: --I.--I.--I.--I.--O.--I.--I.--I.--I.--I.-CO.-CO.	–0.27	0.00243	Dominated	48.87	61.02	73.17	0	0	0
T165: --I.--I.--I.--I.--I.--O.--I.--I.--I.--I.-CO.-CO.	0.96	0.00210	Dominated	41.05	51.55	62.05	0	0	0
T166: --I.--I.--I.--I.--I.--I.--O.--I.--I.--I.-CO.-CO.	–1.06	0.00246	Dominated	50.26	62.56	74.86	0	0	0
T167: --I.--I.--I.--I.--I.--I.--I.--O.--O.--I.-CO.-CO.	0.03	0.00238	Dominated	47.57	59.47	71.37	0	0	0
T168: --O.--I.--I.--I.--I.--I.--O.--I.--I.--I.-CO.-CO.	–1.16	0.00244	Dominated	49.96	62.16	74.36	0	0	0
T169: --I.--O.--O.--I.--I.--I.--O.--I.--I.--I.-CO.-CO.	–0.75	0.00236	Dominated	47.95	59.75	71.55	0	0	0
T170: --I.--I.--I.--I.--O.--I.--O.--I.--I.--I.-CO.-CO.	–1.41	0.00242	Dominated	49.81	61.91	74.01	0.01	0.01	0
T171: --I.--I.--I.--I.--I.--O.--O.--I.--I.--I.-CO.-CO.	–0.18	0.00210	Dominated	42.18	52.68	63.18	0	0	0
T172: --I.--I.--I.--I.--I.--I.--O.--O.--O.--I.-CO.-CO.	–1.11	0.00237	Dominated	48.51	60.36	72.21	0	0	0
T173: --O.--I.--I.--I.--I.--I.--I.--O.--O.--I.-CO.-CO.	–0.08	0.00237	Dominated	47.48	59.33	71.18	0	0	0
T174: --I.--O.--O.--I.--I.--I.--I.--O.--O.--I.-CO.-CO.	0.33	0.00228	Dominated	45.27	56.67	68.07	0	0	0
T175: --I.--I.--I.--I.--O.--I.--I.--O.--O.--I.-CO.-CO.	–0.33	0.00234	Dominated	47.13	58.83	70.53	0	0	0
T176: --I.--I.--I.--I.--I.--O.--I.--O.--O.--I.-CO.-CO.	0.90	0.00202	Dominated	39.50	49.60	59.70	0	0	0
T177: --O.--I.--I.--I.--I.--I.--O.--O.--O.--I.-CO.-CO.	–1.22	0.00236	Dominated	48.42	60.22	72.02	0	0	0
T180: --I.--I.--I.--I.--I.--O.--O.--O.--O.--I.-CO.-CO.	–0.24	0.00201	Dominated	40.44	50.49	60.54	0	0	0

continued

TABLE 109 *Full cost-effectiveness results for all 341 strategies modelled for Scenario B (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T181: --O.--O.--O.--I.--I.--I.--O.--O.--O.--I.-CO.-CO.	–0.92	0.00226	Dominated	46.12	57.42	68.72	0	0	0
T184: --I.--O.--O.--I.--O.--I.--O.--O.--O.--I.-CO.-CO.	–1.16	0.00224	Dominated	45.96	57.16	68.36	0	0	0
T185: --I.--O.--O.--I.--I.--O.--O.--O.--O.--I.-CO.-CO.	0.06	0.00191	Dominated	38.14	47.69	57.24	0	0	0
T186: --I.--O.--O.--I.--I.--I.--O.--O.--O.--I.-CO.-CO.	–0.81	0.00227	Dominated	46.21	57.56	68.91	0	0	0
T187: --O.--I.--I.--I.--O.--I.--O.--O.--O.--I.-CO.-CO.	–1.57	0.00232	Dominated	47.97	59.57	71.17	0.07	0.04	0.04
T188: --I.--I.--I.--I.--O.--O.--O.--O.--O.--I.-CO.-CO.	–0.59	0.00198	Dominated	40.19	50.09	59.99	0	0	0
T189: --I.--I.--I.--I.--O.--I.--O.--O.--O.--I.-CO.-CO.	–1.46	0.00234	Dominated	48.26	59.96	71.66	0	0	0
T190: --O.--I.--I.--I.--I.--O.--O.--O.--O.--I.-CO.-CO.	–0.35	0.00200	Dominated	40.35	50.35	60.35	0	0	0
T196: --O.--I.--I.--I.--O.--O.--O.--O.--O.--I.-CO.-CO.	–0.70	0.00196	Dominated	39.90	49.70	59.50	0.59	0.46	0.32
T197: --O.--O.--O.--I.--O.--I.--O.--O.--O.--I.-CO.-CO.	–1.27	0.00222	Dominated	45.67	56.77	67.87	0	0	0
T198: --I.--O.--O.--I.--O.--O.--O.--O.--O.--I.-CO.-CO.	–0.29	0.00188	Dominated	37.89	47.29	56.69	0	0	0
T199: --O.--O.--O.--I.--I.--O.--O.--O.--O.--I.-CO.-CO.	–0.04	0.00190	Dominated	38.04	47.54	57.04	0	0	0
T200: --O.--O.--O.--I.--O.--O.--O.--O.--O.--I.-CO.-CO.	–0.40	0.00186	Dominated	37.60	46.90	56.20	0.49	0.41	0.3
T208: --O.--I.--I.--I.--I.--I.---.--I.--I.--I.---.---.	–6.38	0.00183	Dominated	42.98	52.13	61.28	0	0	0
T209: --I.--O.--O.--I.--I.--I.---.--I.--I.--I.---.---.	–5.97	0.00174	Dominated	40.77	49.47	58.17	0	0	0
T211: --I.--I.--I.--I.--I.--O.---.--I.--I.--I.---.---.	–5.40	0.00148	Dominated	35.00	42.40	49.80	0	0	0
T217: --O.--I.--I.--I.--I.--I.---.--O.--O.--I.---.---.	–6.44	0.00174	Dominated	41.24	49.94	58.64	0	0	0
T220: --I.--I.--I.--I.--I.--O.---.--O.--O.--I.---.---.	–5.46	0.00140	Dominated	33.46	40.46	47.46	0	0	0
T221: --O.--O.--O.--I.--I.--I.---.--O.--O.--I.---.---.	–6.14	0.00165	Dominated	39.14	47.39	55.64	0	0	0
T225: --I.--O.--O.--I.--I.--O.---.--O.--O.--I.---.---.	–5.16	0.00130	Dominated	31.16	37.66	44.16	0	0	0
T227: --O.--I.--I.--I.--O.--I.---.--O.--O.--I.---.---.	–6.79	0.00171	Dominated	40.99	49.54	58.09	0.01	0.01	0
T228: --I.--I.--I.--I.--O.--O.---.--O.--O.--I.---.---.	–5.81	0.00136	Dominated	33.01	39.81	46.61	0	0	0
T229: --I.--I.--I.--I.--O.--I.---.--O.--O.--I.---.---.	–6.68	0.00172	Dominated	41.08	49.68	58.28	0	0	0
T230: --O.--I.--I.--I.--I.--O.---.--O.--O.--I.---.---.	–5.57	0.00138	Dominated	33.17	40.07	46.97	0	0	0
T236: --O.--I.--I.--I.--O.--O.---.--O.--O.--I.---.---.	–5.92	0.00135	Dominated	32.92	39.67	46.42	0	0	0.01
T237: --O.--O.--O.--I.--O.--I.---.--O.--O.--I.---.---.	–6.49	0.00161	Dominated	38.69	46.74	54.79	0	0	0
T239: --O.--O.--O.--I.--I.--O.---.--O.--O.--I.---.---.	–5.26	0.00129	Dominated	31.06	37.51	43.96	0	0	0
T246: --I.--I.--I.--I.--I.--I.---.--I.--I.--I.-PI.-PI.	3.34	0.00280	Dominated	52.66	66.66	80.66	0	0	0
T248: --O.--I.--I.--I.--I.--I.---.--I.--I.--I.-PI.-PI.	3.24	0.00279	Dominated	52.56	66.51	80.46	0	0	0
T249: --I.--O.--O.--I.--I.--I.---.--I.--I.--I.-PI.-PI.	3.65	0.00270	Dominated	50.35	63.85	77.35	0	0	0
T250: --I.--I.--I.--I.--O.--I.---.--I.--I.--I.-PI.-PI.	2.99	0.00276	Dominated	52.21	66.01	79.81	0	0	0
T251: --I.--I.--I.--I.--I.--O.---.--I.--I.--I.-PI.-PI.	4.22	0.00244	Dominated	44.58	56.78	68.98	0	0	0
T252: --I.--I.--I.--I.--I.--I.---.--O.--O.--I.-PI.-PI.	3.29	0.00272	Dominated	51.11	64.71	78.31	0	0	0
T257: --O.--I.--I.--I.--I.--I.---.--O.--O.--I.-PI.-PI.	3.18	0.00270	Dominated	50.82	64.32	77.82	0	0	0
T260: --I.--I.--I.--I.--I.--O.---.--O.--O.--I.-PI.-PI.	4.16	0.00235	Dominated	42.84	54.59	66.34	0	0	0
T261: --O.--O.--O.--I.--I.--I.---.--O.--O.--I.-PI.-PI.	3.48	0.00260	Dominated	48.52	61.52	74.52	0	0	0
T264: --I.--O.--O.--I.--O.--I.---.--O.--O.--I.-PI.-PI.	3.24	0.00258	Dominated	48.36	61.26	74.16	0	0	0

continued

TABLE 109 *Full cost-effectiveness results for all 341 strategies modelled for Scenario B (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T265: --I.--O.--O.--I.--I.--O.---.--O.--O.--I.-PI.-PI.	4.47	0.00226	Dominated	40.73	52.03	63.33	0	0	0
T266: --I.--O.--O.--I.--I.--I.---.--O.--O.--I.-PI.-PI.	3.59	0.00262	Dominated	48.81	61.91	75.01	0	0	0
T267: --O.--I.--I.--I.--O.--I.---.--O.--O.--I.-PI.-PI.	2.83	0.00266	Dominated	50.37	63.67	76.97	0	0	0
T268: --I.--I.--I.--I.--O.--O.---.--O.--O.--I.-PI.-PI.	3.81	0.00232	Dominated	42.59	54.19	65.79	0	0	0
T269: --I.--I.--I.--I.--O.--I.---.--O.--O.--I.-PI.-PI.	2.94	0.00268	Dominated	50.66	64.06	77.46	0	0	0
T270: --O.--I.--I.--I.--I.--O.---.--O.--O.--I.-PI.-PI.	4.05	0.00234	Dominated	42.75	54.45	66.15	0	0	0
T276: --O.--I.--I.--I.--O.--O.---.--O.--O.--I.-PI.-PI.	3.70	0.00230	Dominated	42.30	53.80	65.30	0	0	0
T277: --O.--O.--O.--I.--O.--I.---.--O.--O.--I.-PI.-PI.	3.13	0.00257	Dominated	48.27	61.12	73.97	0	0	0
T278: --I.--O.--O.--I.--O.--O.---.--O.--O.--I.-PI.-PI.	4.11	0.00222	Dominated	40.29	51.39	62.49	0	0	0
T279: --O.--O.--O.--I.--I.--O.---.--O.--O.--I.-PI.-PI.	4.36	0.00224	Dominated	40.44	51.64	62.84	0	0	0
T280: --O.--O.--O.--I.--O.--O.---.--O.--O.--I.-PI.-PI.	4.01	0.00221	Dominated	40.19	51.24	62.29	0	0	0
T286: --I.--I.--I.--I.--I.--I.---.--I.--I.--I.-PO.-PO.	4.33	0.00242	Dominated	44.07	56.17	68.27	0	0	0
T288: --O.--I.--I.--I.--I.--I.---.--I.--I.--I.-PO.-PO.	4.22	0.00240	Dominated	43.78	55.78	67.78	0	0	0
T289: --I.--O.--O.--I.--I.--I.---.--I.--I.--I.-PO.-PO.	4.63	0.00232	Dominated	41.77	53.37	64.97	0	0	0
T290: --I.--I.--I.--I.--O.--I.---.--I.--I.--I.-PO.-PO.	3.98	0.00238	Dominated	43.62	55.52	67.42	0	0	0
T291: --I.--I.--I.--I.--I.--O.---.--I.--I.--I.-PO.-PO.	5.20	0.00206	Dominated	36.00	46.30	56.60	0	0	0
T292: --I.--I.--I.--I.--I.--I.---.--O.--O.--I.-PO.-PO.	4.27	0.00233	Dominated	42.33	53.98	65.63	0	0	0
T297: --O.--I.--I.--I.--I.--I.---.--O.--O.--I.-PO.-PO.	4.17	0.00232	Dominated	42.23	53.83	65.43	0	0	0
T300: --I.--I.--I.--I.--I.--O.---.--O.--O.--I.-PO.-PO.	5.15	0.00197	Dominated	34.25	44.10	53.95	0	0	0
T301: --O.--O.--O.--I.--I.--I.---.--O.--O.--I.-PO.-PO.	4.47	0.00222	Dominated	39.93	51.03	62.13	0	0	0
T304: --I.--O.--O.--I.--O.--I.---.--O.--O.--I.-PO.-PO.	4.22	0.00220	Dominated	39.78	50.78	61.78	0	0	0
T305: --I.--O.--O.--I.--I.--O.---.--O.--O.--I.-PO.-PO.	5.45	0.00187	Dominated	31.95	41.30	50.65	0	0	0
T306: --I.--O.--O.--I.--I.--I.---.--O.--O.--I.-PO.-PO.	4.58	0.00224	Dominated	40.22	51.42	62.62	0	0	0
T307: --O.--I.--I.--I.--O.--I.---.--O.--O.--I.-PO.-PO.	3.81	0.00228	Dominated	41.79	53.19	64.59	0	0	0
T308: --I.--I.--I.--I.--O.--O.---.--O.--O.--I.-PO.-PO.	4.79	0.00194	Dominated	34.01	43.71	53.41	0	0	0
T309: --I.--I.--I.--I.--O.--I.---.--O.--O.--I.-PO.-PO.	3.92	0.00230	Dominated	42.08	53.58	65.08	0	0	0
T310: --O.--I.--I.--I.--I.--O.---.--O.--O.--I.-PO.-PO.	5.04	0.00196	Dominated	34.16	43.96	53.76	0	0	0
T316: --O.--I.--I.--I.--O.--O.---.--O.--O.--I.-PO.-PO.	4.69	0.00192	Dominated	33.71	43.31	52.91	0	0	0
T317: --O.--O.--O.--I.--O.--I.---.--O.--O.--I.-PO.-PO.	4.12	0.00218	Dominated	39.48	50.38	61.28	0	0	0
T318: --I.--O.--O.--I.--O.--O.---.--O.--O.--I.-PO.-PO.	5.10	0.00184	Dominated	31.70	40.90	50.10	0	0	0
T319: --O.--O.--O.--I.--I.--O.---.--O.--O.--I.-PO.-PO.	5.34	0.00186	Dominated	31.86	41.16	50.46	0	0	0
T320: --O.--O.--O.--I.--O.--O.---.--O.--O.--I.-PO.-PO.	4.99	0.00182	Dominated	31.41	40.51	49.61	0	0	0
T326: --I.--I.--I.--I.--I.--I.---.--I.--I.--I.-CI.-CI.	–1.42	0.00270	Dominated	55.42	68.92	82.42	0	0	0
T328: --O.--I.--I.--I.--I.--I.---.--I.--I.--I.-CI.-CI.	–1.52	0.00269	Dominated	55.32	68.77	82.22	0	0	0
T329: --I.--O.--O.--I.--I.--I.---.--I.--I.--I.-CI.-CI.	–1.11	0.00261	Dominated	53.31	66.36	79.41	0	0	0
T330: --I.--I.--I.--I.--O.--I.---.--I.--I.--I.-CI.-CI.	–1.77	0.00267	Dominated	55.17	68.52	81.87	0	0	0
T331: --I.--I.--I.--I.--I.--O.---.--I.--I.--I.-CI.-CI.	–0.54	0.00234	Dominated	47.34	59.04	70.74	0	0	0

continued

TABLE 109 *Full cost-effectiveness results for all 341 strategies modelled for Scenario B (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T332: --I.--I.--I.--I.--I.--I.---.--O.--O.--I.-CI.-CI.	–1.47	0.00262	Dominated	53.87	66.97	80.07	0	0	0
T337: --O.--I.--I.--I.--I.--I.---.--O.--O.--I.-CI.-CI.	–1.58	0.00261	Dominated	53.78	66.83	79.88	0	0	0
T340: --I.--I.--I.--I.--I.--O.---.--O.--O.--I.-CI.-CI.	–0.60	0.00226	Dominated	45.80	57.10	68.40	0	0	0
T341: --O.--O.--O.--I.--I.--I.---.--O.--O.--I.-CI.-CI.	–1.28	0.00251	Dominated	51.48	64.03	76.58	0	0	0
T344: --I.--O.--O.--I.--O.--I.---.--O.--O.--I.-CI.-CI.	–1.52	0.00249	Dominated	51.32	63.77	76.22	0	0	0
T345: --I.--O.--O.--I.--I.--O.---.--O.--O.--I.-CI.-CI.	–0.30	0.00216	Dominated	43.50	54.30	65.10	0	0	0
T346: --I.--O.--O.--I.--I.--I.---.--O.--O.--I.-CI.-CI.	–1.17	0.00252	Dominated	51.57	64.17	76.77	0	0	0
T347: --O.--I.--I.--I.--O.--I.---.--O.--O.--I.-CI.-CI.	–1.93	0.00257	Dominated	53.33	66.18	79.03	0	0	0
T348: --I.--I.--I.--I.--O.--O.---.--O.--O.--I.-CI.-CI.	–0.95	0.00222	Dominated	45.35	56.45	67.55	0	0	0
T349: --I.--I.--I.--I.--O.--I.---.--O.--O.--I.-CI.-CI.	–1.82	0.00258	Dominated	53.42	66.32	79.22	0	0	0
T350: --O.--I.--I.--I.--I.--O.---.--O.--O.--I.-CI.-CI.	–0.71	0.00225	Dominated	45.71	56.96	68.21	0	0	0
T356: --O.--I.--I.--I.--O.--O.---.--O.--O.--I.-CI.-CI.	–1.06	0.00221	Dominated	45.26	56.31	67.36	0	0	0
T357: --O.--O.--O.--I.--O.--I.---.--O.--O.--I.-CI.-CI.	–1.63	0.00247	Dominated	51.03	63.38	75.73	0	0	0
T358: --I.--O.--O.--I.--O.--O.---.--O.--O.--I.-CI.-CI.	–0.65	0.00213	Dominated	43.25	53.90	64.55	0	0	0
T359: --O.--O.--O.--I.--I.--O.---.--O.--O.--I.-CI.-CI.	–0.40	0.00215	Dominated	43.40	54.15	64.90	0	0	0
T360: --O.--O.--O.--I.--O.--O.---.--O.--O.--I.-CI.-CI.	–0.76	0.00211	Dominated	42.96	53.51	64.06	0	0	0
T366: --I.--I.--I.--I.--I.--I.---.--I.--I.--I.-CO.-CO.	–0.84	0.00237	Dominated	48.24	60.09	71.94	0	0	0
T368: --O.--I.--I.--I.--I.--I.---.--I.--I.--I.-CO.-CO.	–0.95	0.00236	Dominated	48.15	59.95	71.75	0	0	0
T369: --I.--O.--O.--I.--I.--I.---.--I.--I.--I.-CO.-CO.	–0.54	0.00227	Dominated	45.94	57.29	68.64	0	0	0
T370: --I.--I.--I.--I.--O.--I.---.--I.--I.--I.-CO.-CO.	–1.20	0.00233	Dominated	47.80	59.45	71.10	0	0	0
T371: --I.--I.--I.--I.--I.--O.---.--I.--I.--I.-CO.-CO.	0.03	0.00201	Dominated	40.17	50.22	60.27	0	0	0
T372: --I.--I.--I.--I.--I.--I.---.--O.--O.--I.-CO.-CO.	–0.90	0.00229	Dominated	46.70	58.15	69.60	0	0	0
T377: --O.--I.--I.--I.--I.--I.---.--O.--O.--I.-CO.-CO.	–1.01	0.00227	Dominated	46.41	57.76	69.11	0	0	0
T380: --I.--I.--I.--I.--I.--O.---.--O.--O.--I.-CO.-CO.	–0.03	0.00193	Dominated	38.63	48.28	57.93	0	0	0
T381: --O.--O.--O.--I.--I.--I.---.--O.--O.--I.-CO.-CO.	–0.70	0.00218	Dominated	44.30	55.20	66.10	0	0	0
T384: --I.--O.--O.--I.--O.--I.---.--O.--O.--I.-CO.-CO.	–0.95	0.00215	Dominated	43.95	54.70	65.45	0	0	0
T385: --I.--O.--O.--I.--I.--O.---.--O.--O.--I.-CO.-CO.	0.28	0.00183	Dominated	36.32	45.47	54.62	0	0	0
T386: --I.--O.--O.--I.--I.--I.---.--O.--O.--I.-CO.-CO.	–0.60	0.00219	Dominated	44.40	55.35	66.30	0	0	0
T387: --O.--I.--I.--I.--O.--I.---.--O.--O.--I.-CO.-CO.	–1.36	0.00224	Dominated	46.16	57.36	68.56	0	0	0
T388: --I.--I.--I.--I.--O.--O.---.--O.--O.--I.-CO.-CO.	–0.38	0.00189	Dominated	38.18	47.63	57.08	0	0	0
T389: --I.--I.--I.--I.--O.--I.---.--O.--O.--I.-CO.-CO.	–1.25	0.00225	Dominated	46.25	57.50	68.75	0	0	0
T390: --O.--I.--I.--I.--I.--O.---.--O.--O.--I.-CO.-CO.	–0.13	0.00191	Dominated	38.33	47.88	57.43	0	0	0
T396: --O.--I.--I.--I.--O.--O.---.--O.--O.--I.-CO.-CO.	–0.49	0.00188	Dominated	38.09	47.49	56.89	0	0	0
T397: --O.--O.--O.--I.--O.--I.---.--O.--O.--I.-CO.-CO.	–1.06	0.00214	Dominated	43.86	54.56	65.26	0	0	0
T398: --I.--O.--O.--I.--O.--O.---.--O.--O.--I.-CO.-CO.	–0.07	0.00179	Dominated	35.87	44.82	53.77	0	0	0
T399: --O.--O.--O.--I.--I.--O.---.--O.--O.--I.-CO.-CO.	0.17	0.00182	Dominated	36.23	45.33	54.43	0	0	0
T400: --O.--O.--O.--I.--O.--O.---.--O.--O.--I.-CO.-CO.	–0.18	0.00178	Dominated	35.78	44.68	53.58	0	0	0

continued

TABLE 109 *Full cost-effectiveness results for all 341 strategies modelled for Scenario B (cont'd)*

Strategy and detail	Cost (£)	QALYs gained	ICER	Net benefit (£)			% CE at WTP		
				£20,000	£25,000	£30,000	£20,000	£25,000	£30,000
T802: -PI.--I.--I.--I.-PI.-PI.-PI.--I.--I.--I.-PI.-PI.	8.17	0.00216	Dominated	35.03	45.83	56.63	0	0	0
T803: -PO.--I.--I.--I.-PO.-PO.-PO.--I.--I.--I.-PO.-PO.	9.55	0.00157	Dominated	21.85	29.70	37.55	0	0	0
T804: -CI.--I.--I.--I.-CI.-CI.-CI.--I.--I.--I.-CI.-CI.	3.31	0.00170	Dominated	30.69	39.19	47.69	0	0	0
T805: -CO.--I.--I.--I.-CO.-CO.-CO.--I.--I.--I.-CO.-CO.	4.03	0.00126	Dominated	21.17	27.47	33.77	0	0	0
T808: -PO.--I.--I.--I.--O.-PO.-PO.--I.--I.--I.-PO.-PO.	8.00	0.00181	Dominated	28.20	37.25	46.30	0	0	0
T810: -CO.--I.--I.--I.--O.-CO.-CO.--I.--I.--I.-CO.-CO.	1.99	0.00170	Dominated	32.01	40.51	49.01	0	0	0
T813: -PO.--I.--I.--I.--O.--I.-PO.--I.--I.--I.-PO.-PO.	5.77	0.00232	Dominated	40.63	52.23	63.83	0	0	0
T815: -CO.--I.--I.--I.--O.--I.-CO.--I.--I.--I.-CO.-CO.	0.03	0.00225	Dominated	44.97	56.22	67.47	0	0	0
T818: -PO.--I.--I.--I.--I.-PO.-PO.--I.--I.--I.-PO.-PO.	8.35	0.00184	Dominated	28.45	37.65	46.85	0	0	0
T820: -CO.--I.--I.--I.--I.-CO.-CO.--I.--I.--I.-CO.-CO.	2.34	0.00173	Dominated	32.26	40.91	49.56	0	0	0
T823: -PO.--I.--I.--I.--I.--I.-PO.--I.--I.--I.-PO.-PO.	6.12	0.00235	Dominated	40.88	52.63	64.38	0	0	0
T825: -CO.--I.--I.--I.--I.--I.-CO.--I.--I.--I.-CO.-CO.	0.39	0.00228	Dominated	45.21	56.61	68.01	0	0	0

Appendix 5

Full clinical effectiveness results

TABLE 110 *EOGBS livebirth: cases per year (680,000 deliveries)*

Intervention[a]	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Total
V	1.01	0.02	5.12	2.45	19.99	11.83	1.09	0.03	6.02	5.02	21.83	26.38	100.64
CO	1.71	0.05	10.47	4.54	34.75	24.21	1.95	0.08	16.32	9.66	38.96	71.40	214.20
CI	1.50	0.04	8.30	4.11	33.25	19.18	1.12	0.04	7.96	6.94	29.85	34.88	146.88
PO	0.83	0.04	9.32	3.15	20.26	21.49	1.54	0.08	16.32	8.02	30.87	71.40	183.60
PI	0.31	0.02	4.18	2.09	18.77	9.66	0.57	0.03	6.32	4.86	21.90	27.74	96.56
I	0.06	0.01	2.39	1.52	11.76	5.53	0.12	0.02	2.96	2.88	12.10	12.99	52.36
O	0.65	0.04	8.43	2.72	15.91	19.52	1.21	0.07	14.01	6.43	24.14	61.40	154.36
n	2.30	0.05	11.63	5.57	45.29	26.86	4.28	0.12	23.60	19.65	85.68	103.36	328.44
VCO	0.75	0.02	4.62	2.01	15.30	10.68	0.50	0.02	4.16	2.45	9.93	18.22	68.68
VCI	0.66	0.02	3.66	1.82	14.69	8.43	0.29	0.01	2.03	1.77	7.62	8.91	49.84
VPO	0.37	0.02	4.11	1.39	8.91	9.45	0.39	0.02	4.16	2.05	7.89	18.22	56.98
VPI	0.14	0.01	1.84	0.92	8.30	4.26	0.15	0.01	1.61	1.24	5.60	7.07	31.14
VI	0.03	0.00	1.05	0.67	5.19	2.44	0.03	0.00	0.75	0.73	3.09	3.32	17.34
VO	0.29	0.02	3.73	1.20	7.00	8.64	0.31	0.02	3.57	1.64	6.14	15.64	48.14

[a] C, culture test at 35–37 weeks; I, i.v. antibiotics; n, no treatment; O, oral antibiotics; P, PCR test at labour; V, vaccination.

TABLE 111 *EOGBS stillbirths: cases (= deaths) per year (680,000 deliveries)*

Intervention	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Total
V	0.048	0.001	0.241	0.116	0.938	0.556	0.023	0.001	0.129	0.108	0.469	0.566	3.196
CO	0.108	0.002	0.546	0.262	2.128	1.258	0.092	0.003	0.505	0.421	1.829	2.210	9.384
CI	0.096	0.002	0.496	0.240	1.952	1.149	0.070	0.002	0.398	0.335	1.455	1.748	7.956
PO	0.108	0.002	0.546	0.262	2.128	1.258	0.092	0.003	0.505	0.421	1.829	2.210	9.384
PI	0.078	0.002	0.435	0.209	1.734	1.006	0.066	0.002	0.388	0.321	1.401	1.700	7.344
I	0.075	0.002	0.409	0.201	1.632	0.945	0.063	0.002	0.365	0.307	1.333	1.598	6.936
O	0.108	0.002	0.546	0.262	2.128	1.258	0.092	0.003	0.505	0.421	1.829	2.210	9.384
n	0.108	0.002	0.546	0.262	2.128	1.258	0.092	0.003	0.505	0.421	1.829	2.210	9.384
VCO	0.048	0.001	0.241	0.116	0.938	0.556	0.023	0.001	0.129	0.108	0.469	0.566	3.196
VCI	0.042	0.001	0.219	0.105	0.857	0.505	0.018	0.001	0.102	0.086	0.371	0.447	2.754
VPO	0.048	0.001	0.241	0.116	0.938	0.556	0.023	0.001	0.129	0.108	0.469	0.566	3.196
VPI	0.035	0.001	0.192	0.092	0.762	0.443	0.017	0.001	0.099	0.082	0.358	0.435	2.516
VI	0.033	0.001	0.180	0.088	0.721	0.415	0.016	0.000	0.093	0.079	0.341	0.409	2.373
VO	0.048	0.001	0.241	0.116	0.938	0.556	0.023	0.001	0.129	0.108	0.469	0.566	3.196

TABLE 112 *EO non-GBS livebirth: cases per year (680,000 deliveries)*

Intervention	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Total
V	37.81	0.31	20.94	11.70	114.24	162.52	27.06	0.28	11.90	5.43	28.36	240.72	660.96
CO	36.92	0.31	20.40	11.42	110.84	161.16	26.18	0.27	11.22	5.22	27.20	236.64	647.36
CI	36.99	0.30	19.92	11.42	111.52	159.80	26.18	0.27	10.88	5.24	27.34	233.92	643.96
PO	35.84	0.30	19.92	11.08	106.76	159.80	26.18	0.27	11.22	5.21	27.06	236.64	641.24
PI	35.90	0.30	18.63	11.08	108.80	156.40	26.18	0.27	10.81	5.23	27.34	234.60	635.12
I	28.02	0.24	16.52	9.38	91.80	128.52	20.06	0.21	9.11	4.20	21.90	184.96	514.08
O	27.68	0.28	18.77	9.45	86.36	146.20	19.79	0.24	10.06	4.06	20.74	204.00	547.40
n	37.81	0.31	20.94	11.70	114.24	162.52	27.06	0.28	11.90	5.43	28.36	240.72	660.96
VCO	37.06	0.31	20.54	11.49	111.52	161.16	26.32	0.27	11.42	5.26	27.40	237.32	650.08
VCI	37.13	0.30	20.13	11.49	112.20	160.48	26.38	0.27	11.15	5.28	27.54	235.28	647.36
VPO	36.18	0.30	20.13	11.22	108.80	160.48	26.38	0.27	11.42	5.26	27.40	238.00	645.32
VPI	36.24	0.30	19.18	11.22	110.16	157.76	26.38	0.27	11.15	5.28	27.54	235.96	641.24
VI	28.02	0.24	16.52	9.38	91.80	128.52	20.06	0.21	9.11	4.20	21.90	184.96	514.08
VO	27.68	0.28	18.77	9.45	86.36	146.20	19.79	0.24	10.06	4.06	20.74	204.00	547.40

TABLE 113 *EO non-GBS stillbirths: cases (= deaths) per year (680,000 deliveries)*

Intervention	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Total
V	1.775	0.014	0.986	0.548	5.358	7.616	0.579	0.006	0.254	0.116	0.607	5.154	23.052
CO	1.775	0.014	0.986	0.548	5.358	7.616	0.579	0.006	0.254	0.116	0.607	5.154	23.052
CI	1.754	0.014	0.959	0.542	5.297	7.548	0.570	0.006	0.243	0.114	0.596	5.080	22.712
PO	1.775	0.014	0.986	0.548	5.358	7.616	0.579	0.006	0.254	0.116	0.607	5.154	23.052
PI	1.727	0.014	0.932	0.534	5.229	7.480	0.570	0.006	0.243	0.114	0.596	5.080	22.508
I	1.544	0.013	0.877	0.495	4.828	6.800	0.504	0.005	0.224	0.103	0.537	4.549	20.536
O	1.775	0.014	0.986	0.548	5.358	7.616	0.579	0.006	0.254	0.116	0.607	5.154	23.052
n	1.775	0.014	0.986	0.548	5.358	7.616	0.579	0.006	0.254	0.116	0.607	5.154	23.052
VCO	1.775	0.014	0.986	0.548	5.358	7.616	0.579	0.006	0.254	0.116	0.607	5.154	23.052
VCI	1.761	0.014	0.966	0.543	5.304	7.548	0.571	0.006	0.247	0.115	0.598	5.093	22.780
VPO	1.775	0.014	0.986	0.548	5.358	7.616	0.579	0.006	0.254	0.116	0.607	5.154	23.052
VPI	1.741	0.014	0.945	0.537	5.256	7.548	0.572	0.006	0.246	0.115	0.598	5.100	22.644
VI	1.544	0.013	0.877	0.495	4.828	6.800	0.504	0.005	0.224	0.103	0.537	4.549	20.536
VO	1.775	0.014	0.986	0.548	5.358	7.616	0.579	0.006	0.254	0.116	0.607	5.154	23.052

TABLE 114 *LOGBS: cases per year (680,000 deliveries)*

Intervention	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Total
V	3.31	0.03	1.83	1.02	10.00	14.21	1.63	0.02	0.71	0.33	1.71	14.48	49.30
CO	8.16	0.07	4.52	2.52	24.62	35.16	7.89	0.08	3.46	1.58	8.23	70.04	166.60
CI	8.16	0.07	4.52	2.52	24.62	35.16	7.89	0.08	3.46	1.58	8.23	70.04	166.60
PO	8.16	0.07	4.52	2.52	24.62	35.16	7.89	0.08	3.46	1.58	8.23	70.04	166.60
PI	8.16	0.07	4.52	2.52	24.62	35.16	7.89	0.08	3.46	1.58	8.23	70.04	166.60
I	8.16	0.07	4.52	2.52	24.62	35.16	7.89	0.08	3.46	1.58	8.23	70.04	166.60
O	8.16	0.07	4.52	2.52	24.62	35.16	7.89	0.08	3.46	1.58	8.23	70.04	166.60
n	8.16	0.07	4.52	2.52	24.62	35.16	7.89	0.08	3.46	1.58	8.23	70.04	166.60
VCO	3.31	0.03	1.83	1.02	10.00	14.21	1.63	0.02	0.71	0.33	1.71	14.48	49.30
VCI	3.31	0.03	1.83	1.02	10.00	14.21	1.63	0.02	0.71	0.33	1.71	14.48	49.30
VPO	3.31	0.03	1.83	1.02	10.00	14.21	1.63	0.02	0.71	0.33	1.71	14.48	49.30
VPI	3.31	0.03	1.83	1.02	10.00	14.21	1.63	0.02	0.71	0.33	1.71	14.48	49.30
VI	3.31	0.03	1.83	1.02	10.00	14.21	1.63	0.02	0.71	0.33	1.71	14.48	49.30
VO	3.31	0.03	1.83	1.02	10.00	14.21	1.63	0.02	0.71	0.33	1.71	14.48	49.30

TABLE 115 *Total[a] cases per year (680,000 deliveries)*

Intervention	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Total
V	43.96	0.37	29.12	15.83	150.52	196.74	30.38	0.33	19.02	11.00	52.97	287.31	837.15
CO	48.67	0.43	36.93	19.30	177.69	229.40	36.69	0.45	31.76	17.00	76.83	385.44	1060.60
CI	48.50	0.42	34.20	18.84	176.64	222.83	35.83	0.40	22.94	14.21	67.47	345.67	988.11
PO	46.71	0.43	35.29	17.57	159.13	225.32	36.28	0.45	31.76	15.35	68.60	385.44	1023.88
PI	46.18	0.40	28.70	16.44	159.15	209.70	35.28	0.39	21.22	12.11	59.46	339.16	928.13
I	37.86	0.34	24.73	14.12	134.64	176.95	28.63	0.32	16.13	9.07	44.10	274.14	760.51
O	38.37	0.40	33.25	15.50	134.37	209.75	29.56	0.40	28.29	12.61	55.54	342.81	900.80
n	50.15	0.44	38.63	20.60	191.63	233.41	39.91	0.49	39.72	27.21	124.70	421.48	1188.44
VCO	42.95	0.37	28.21	15.18	143.11	194.22	29.04	0.32	16.68	8.27	40.11	275.75	794.31
VCI	42.90	0.36	26.80	14.98	143.04	191.18	28.88	0.31	14.24	7.58	37.83	264.21	772.04
VPO	41.68	0.36	27.29	14.29	134.00	192.32	29.00	0.32	16.68	7.87	38.07	276.43	777.85
VPI	41.47	0.35	23.98	13.79	134.47	184.22	28.74	0.30	13.82	7.05	35.80	263.05	746.84
VI	32.93	0.29	20.46	11.66	112.53	152.39	22.24	0.24	10.90	5.44	27.57	207.72	603.63
VO	33.10	0.34	25.55	12.33	109.66	177.22	22.32	0.28	14.73	6.25	29.66	239.84	671.09

[a] EOGBS livebirth, EOGBS stillbirth, EO non-GBS livebirth, EO non-GBS stillbirth, LOGBS.

TABLE 116 *EOGBS livebirth: deaths per year (680,000 deliveries)*

Intervention	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Total
V	0.221	0.005	1.115	0.534	4.345	2.577	0.067	0.002	0.369	0.308	1.340	1.618	12.512
CO	0.371	0.010	2.278	0.986	7.548	5.263	0.120	0.005	1.000	0.590	2.387	4.386	24.956
CI	0.325	0.008	1.802	0.891	7.208	4.168	0.069	0.002	0.487	0.425	1.829	2.135	19.380
PO	0.180	0.009	2.020	0.687	4.400	4.678	0.095	0.005	1.000	0.493	1.890	4.379	19.856
PI	0.067	0.004	0.904	0.454	4.087	2.101	0.035	0.002	0.388	0.298	1.346	1.700	11.356
I	0.014	0.002	0.520	0.330	2.557	1.204	0.007	0.001	0.182	0.176	0.741	0.796	6.528
O	0.141	0.008	1.836	0.591	3.448	4.243	0.074	0.004	0.857	0.394	1.476	3.760	16.864
n	0.500	0.011	2.523	1.210	9.860	5.841	0.262	0.007	1.442	1.204	5.243	6.338	34.408
VCO	0.164	0.004	1.006	0.436	3.332	2.326	0.031	0.001	0.256	0.151	0.610	1.122	9.452
VCI	0.143	0.003	0.796	0.394	3.189	1.843	0.018	0.001	0.124	0.108	0.466	0.545	7.616
VPO	0.080	0.004	0.891	0.302	1.938	2.060	0.024	0.001	0.255	0.126	0.483	1.122	7.276
VPI	0.030	0.002	0.401	0.201	1.802	0.925	0.009	0.001	0.099	0.076	0.343	0.435	4.325
VI	0.006	0.001	0.230	0.146	1.129	0.531	0.002	0.000	0.046	0.045	0.189	0.204	2.530
VO	0.062	0.004	0.809	0.260	1.523	1.870	0.019	0.001	0.220	0.101	0.377	0.959	6.208

TABLE 117 *EO non-GBS: deaths per year (680,000 deliveries)*

Intervention	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Total
V	5.726	0.047	3.169	1.768	17.272	24.616	4.107	0.042	1.802	0.823	4.304	36.584	99.960
CO	5.596	0.046	3.094	1.727	16.796	24.412	3.971	0.042	1.700	0.796	4.128	35.904	97.920
CI	5.596	0.046	3.012	1.727	16.864	24.208	3.978	0.041	1.652	0.796	4.155	35.564	97.920
PO	5.426	0.046	3.019	1.680	16.184	24.208	3.971	0.042	1.707	0.789	4.114	35.972	97.240
PI	5.433	0.045	2.822	1.680	16.456	23.732	3.978	0.041	1.639	0.796	4.148	35.564	96.560
I	4.243	0.037	2.496	1.428	13.872	19.448	3.046	0.033	1.380	0.637	3.318	28.016	78.200
O	4.189	0.042	2.842	1.428	13.056	22.100	2.999	0.036	1.523	0.617	3.148	31.008	82.960
n	5.726	0.047	3.169	1.768	17.272	24.616	4.107	0.042	1.802	0.823	4.304	36.584	99.960
VCO	5.617	0.046	3.108	1.741	16.864	24.480	3.998	0.042	1.727	0.802	4.162	36.040	98.600
VCI	5.624	0.046	3.046	1.741	17.000	24.276	4.005	0.041	1.693	0.802	4.189	35.700	97.920
VPO	5.481	0.046	3.053	1.700	16.456	24.344	4.005	0.042	1.734	0.802	4.162	36.108	97.920
VPI	5.494	0.045	2.904	1.700	16.660	23.868	4.005	0.041	1.686	0.802	4.189	35.768	97.240
VI	4.243	0.037	2.496	1.428	13.872	19.448	3.046	0.033	1.380	0.637	3.318	28.016	78.200
VO	4.189	0.042	2.842	1.428	13.056	22.100	2.999	0.036	1.523	0.617	3.148	31.008	82.960

TABLE 118 *LOGBS: deaths per year (680,000 deliveries)*

Intervention	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Total
V	0.302	0.002	0.167	0.093	0.911	1.299	0.139	0.001	0.061	0.028	0.146	1.238	4.393
CO	0.748	0.006	0.413	0.230	2.251	3.203	0.675	0.007	0.296	0.135	0.707	6.011	14.688
CI	0.748	0.006	0.413	0.230	2.251	3.203	0.675	0.007	0.296	0.135	0.707	6.011	14.688
PO	0.748	0.006	0.413	0.230	2.251	3.203	0.675	0.007	0.296	0.135	0.707	6.011	14.688
PI	0.748	0.006	0.413	0.230	2.251	3.203	0.675	0.007	0.296	0.135	0.707	6.011	14.688
I	0.748	0.006	0.413	0.230	2.251	3.203	0.675	0.007	0.296	0.135	0.707	6.011	14.688
O	0.748	0.006	0.413	0.230	2.251	3.203	0.675	0.007	0.296	0.135	0.707	6.011	14.688
n	0.748	0.006	0.413	0.230	2.251	3.203	0.675	0.007	0.296	0.135	0.707	6.011	14.688
VCO	0.302	0.002	0.167	0.093	0.911	1.299	0.139	0.001	0.061	0.028	0.146	1.238	4.393
VCI	0.302	0.002	0.167	0.093	0.911	1.299	0.139	0.001	0.061	0.028	0.146	1.238	4.393
VPO	0.302	0.002	0.167	0.093	0.911	1.299	0.139	0.001	0.061	0.028	0.146	1.238	4.393
VPI	0.302	0.002	0.167	0.093	0.911	1.299	0.139	0.001	0.061	0.028	0.146	1.238	4.393
VI	0.302	0.002	0.167	0.093	0.911	1.299	0.139	0.001	0.061	0.028	0.146	1.238	4.393
VO	0.302	0.002	0.167	0.093	0.911	1.299	0.139	0.001	0.061	0.028	0.146	1.238	4.393

TABLE 119 *Total[a] deaths per year (680,000 deliveries)*

Intervention	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Total
V	8.07	0.07	5.68	3.06	28.83	36.66	4.92	0.05	2.62	1.38	6.87	45.16	143.36
CO	8.60	0.08	7.32	3.75	34.08	41.75	5.44	0.06	3.75	2.06	9.66	53.67	170.22
CI	8.52	0.08	6.68	3.63	33.57	40.28	5.36	0.06	3.08	1.80	8.74	50.54	162.34
PO	8.24	0.08	6.98	3.41	30.32	40.96	5.41	0.06	3.76	1.95	9.15	53.73	164.05
PI	8.05	0.07	5.51	3.11	29.76	37.52	5.32	0.06	2.95	1.66	8.20	50.05	152.27
I	6.62	0.06	4.71	2.68	25.14	31.60	4.30	0.05	2.45	1.36	6.64	40.97	126.58
O	6.96	0.07	6.62	3.06	26.24	38.42	4.42	0.06	3.44	1.68	7.77	48.14	146.88
n	8.86	0.08	7.64	4.02	36.87	42.53	5.72	0.07	4.30	2.70	12.69	56.30	181.76
VCO	7.91	0.07	5.51	2.93	27.40	36.28	4.77	0.05	2.43	1.21	5.99	44.12	138.66
VCI	7.87	0.07	5.19	2.88	27.26	35.47	4.75	0.05	2.23	1.14	5.77	43.02	135.70
VPO	7.68	0.07	5.34	2.76	25.60	35.87	4.77	0.05	2.43	1.18	5.87	44.19	135.82
VPI	7.60	0.06	4.61	2.62	25.39	34.08	4.74	0.05	2.19	1.10	5.63	42.97	131.07
VI	6.13	0.05	3.95	2.25	21.46	28.49	3.71	0.04	1.81	0.89	4.53	34.42	107.73
VO	6.38	0.06	5.05	2.45	21.79	33.44	3.76	0.05	2.19	0.97	4.75	38.92	119.79

[a] EOGBS livebirth, EOGBS stillbirth, EO non-GBS livebirth, EO non-GBS stillbirth, LOGBS.

TABLE 120 *Number of women needed to treat with antibiotics to prevent one case of preventable disease*

Intervention	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Average
V	0	0	0	0	0	0	0	0	0	0	0	0	0
CO	318	187	156	105	121	191	2010	912	612	155	184	907	452
CI	284	153	129	81	95	155	1586	684	461	114	136	682	397
PO	311	182	159	100	116	177	1829	808	597	140	167	790	352
PI	269	144	127	78	91	144	1432	602	449	103	123	605	321
I	441	338	176	193	219	338	4820	2948	910	527	624	2950	1429
O	461	373	212	234	259	375	5250	3476	1183	699	823	3478	1532
n	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
VCO	382	284	225	167	183	250	3938	2282	1484	450	536	2296	1076
VCI	365	239	190	134	153	243	3530	1842	1155	337	399	1827	978
VPO	376	256	221	155	181	259	3750	2009	1422	396	470	2040	751
VPI	345	219	188	125	145	218	3155	1605	1117	295	351	1598	709
VI	492	430	283	299	329	430	6672	5463	2643	1717	1979	5461	2618
VO	500	451	319	340	363	454	6744	5808	3153	2147	2442	5765	2654

NA, not applicable.

TABLE 121 *Number of women needed to treat with antibiotics to prevent one preventable death*

Intervention	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Average
V	0	0	0	0	0	0	0	0	0	0	0	0	0
CO	1814	971	830	513	605	978	23190	12530	8951	2463	2909	12420	5006
CI	1390	727	597	368	432	728	18285	9004	6332	1655	1975	8982	4096
PO	1726	928	813	497	578	910	21807	11169	8842	2221	2651	11079	3276
PI	1331	676	591	354	417	679	16964	8005	6172	1503	1787	7977	2836
I	2429	1742	838	938	1065	1743	38279	28457	11593	7127	8302	28358	11078
O	2861	2170	1125	1241	1395	2154	41898	33512	15643	10046	11561	33563	12632
n	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
VCO	2319	1465	1208	873	956	1625	36322	25819	18374	6927	7894	25512	10431
VCI	1939	1115	910	630	731	1132	32099	20377	14200	4724	5514	19742	8320
VPO	2220	1378	1191	798	925	1452	35599	22894	18205	6121	7008	22822	6121
VPI	1826	1029	903	584	678	1057	29782	18218	13691	4165	4902	17742	5340
VI	2793	2326	1418	1548	1696	2332	44979	40675	26479	19433	21535	40452	17426
VO	3200	2764	1802	1942	2107	2750	46981	43862	31534	24684	26870	43885	18909

NA, not applicable.

Appendix 6

Disease burden when no interventions are given

TABLE 122 *Number of cases and deaths per year when no interventions are given*[a]

Number per year in the UK	Preterm	Term	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Total
Delivering women (risk group size)	49,854	630,036	5,426	44	2,999	1,673	16,388	23,324	54,332	560	23,868	10,880	56,916	483,480	680,000
Cases															
EOGBS	92	237	2.30	0.05	11.63	5.57	45.29	26.86	4.28	0.12	23.60	19.65	85.68	103.36	328
EOGBS stillbirth	4	5	0.11	0.00	0.55	0.26	2.13	1.26	0.09	0.00	0.51	0.42	1.83	2.21	9
EO non-GBS	348	314	37.81	0.31	20.94	11.70	114.24	162.52	27.06	0.28	11.90	5.43	28.36	240.72	661
EO non-GBS stillbirth	16	7	1.78	0.01	0.99	0.55	5.36	7.62	0.58	0.01	0.25	0.12	0.61	5.15	23
All early onset	**460**	**562**	**41.99**	**0.38**	**34.10**	**18.08**	**167.02**	**198.25**	**32.01**	**0.41**	**36.26**	**25.62**	**116.48**	**351.44**	**1,022**
LOGBS	75	91	8.16	0.07	4.52	2.52	24.62	35.16	7.89	0.08	3.46	1.58	8.23	70.04	167
All infections	**535**	**654**	**50.15**	**0.44**	**38.63**	**20.60**	**191.63**	**233.41**	**39.91**	**0.49**	**39.72**	**27.21**	**124.70**	**421.48**	**1,188**
Deaths															
EOGBS (including EOGBS stillbirth)	24	20	0.61	0.01	3.07	1.47	11.99	7.10	0.35	0.01	1.95	1.63	7.07	8.55	44
EO non-GBS (including EOGBS stillbirth)	69	54	7.50	0.06	4.16	2.32	22.63	32.23	4.69	0.05	2.06	0.94	4.91	41.74	123
All early onset	**93**	**74**	**8.11**	**0.07**	**7.22**	**3.79**	**34.62**	**39.33**	**5.04**	**0.06**	**4.00**	**2.56**	**11.98**	**50.29**	**167**
LOGBS	7	8	0.75	0.01	0.41	0.23	2.25	3.20	0.68	0.01	0.30	0.14	0.71	6.01	15
All infections	**100**	**82**	**8.86**	**0.08**	**7.64**	**4.02**	**36.87**	**42.53**	**5.72**	**0.07**	**4.30**	**2.70**	**12.69**	**56.30**	**182**

[a] Taken from the 'n' (do nothing) intervention rows from *Tables 110–119*.

TABLE 123 *Percentage of cases and deaths when no intervention is given*

Percentage of total	Preterm	Term	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	Total
Delivering women (risk group size)	7.3%	92.7%	0.8%	0.0%	0.4%	0.2%	2.4%	3.4%	8.0%	0.1%	3.5%	1.6%	8.4%	71.1%	100%
Cases															
EOGBS	27.9%	72.1%	0.7%	0.0%	3.5%	1.7%	13.8%	8.2%	1.3%	0.0%	7.2%	6.0%	26.1%	31.5%	100%
EOGBS stillbirth	45.9%	53.9%	1.2%	0.0%	5.8%	2.8%	22.7%	13.4%	1.0%	0.0%	5.4%	4.5%	19.5%	23.6%	100%
EO non-GBS	52.6%	47.5%	5.7%	0.0%	3.2%	1.8%	17.3%	24.6%	4.1%	0.0%	1.8%	0.8%	4.3%	36.4%	100%
EO non-GBS stillbirth	70.7%	29.1%	7.7%	0.1%	4.3%	2.4%	23.2%	33.0%	2.5%	0.0%	1.1%	0.5%	2.6%	22.4%	100%
All early onset	**45.0%**	**55.0%**	**4.1%**	**0.0%**	**3.3%**	**1.8%**	**16.3%**	**19.4%**	**3.1%**	**0.0%**	**3.5%**	**2.5%**	**11.4%**	**34.4%**	**100%**
LOGBS	45.0%	54.8%	4.9%	0.0%	2.7%	1.5%	14.8%	21.1%	4.7%	0.0%	2.1%	0.9%	4.9%	42.0%	100%
All infections	**45.0%**	**55.0%**	**4.2%**	**0.0%**	**3.3%**	**1.7%**	**16.1%**	**19.6%**	**3.4%**	**0.0%**	**3.3%**	**2.3%**	**10.5%**	**35.5%**	**100%**
Deaths															
EOGBS (including EOGBS stillbirth)	55.4%	44.7%	1.4%	0.0%	7.0%	3.4%	27.4%	16.2%	0.8%	0.0%	4.4%	3.7%	16.1%	19.5%	100%
EO non-GBS (including EOGBS stillbirth)	56.0%	44.2%	6.1%	0.0%	3.4%	1.9%	18.4%	26.2%	3.8%	0.0%	1.7%	0.8%	4.0%	33.9%	100%
All early onset	**55.8%**	**44.3%**	**4.9%**	**0.0%**	**4.3%**	**2.3%**	**20.8%**	**23.6%**	**3.0%**	**0.0%**	**2.4%**	**1.5%**	**7.2%**	**30.1%**	**100%**
LOGBS	46.6%	53.3%	5.1%	0.0%	2.8%	1.6%	15.3%	21.8%	4.6%	0.0%	2.0%	0.9%	4.8%	40.9%	100%
All infections	**55.0%**	**45.0%**	**4.9%**	**0.0%**	**4.2%**	**2.2%**	**20.3%**	**23.4%**	**3.1%**	**0.0%**	**2.4%**	**1.5%**	**7.0%**	**31.0%**	**100%**

TABLE 124 *Risk of infection or death (per 1000 women) when no intervention is given*

Risk (per 1000 woman)	Preterm	Term	RG1	RG2	RG3	RG4	RG5	RG6	RG7	RG8	RG9	RG10	RG11	RG12	RG11 + 12	Total
Cases																
EOGBS	1.839	0.376	0.424	1.129	3.878	3.330	2.764	1.152	0.079	0.214	0.989	1.806	1.505	0.214	0.350	0.483
EOGBS stillbirth	0.086	0.008	0.020	0.045	0.182	0.157	0.130	0.054	0.002	0.005	0.021	0.039	0.032	0.005	0.007	0.014
EO non-GBS	6.971	0.498	6.968	7.003	6.983	6.994	6.971	6.968	0.498	0.500	0.499	0.499	0.498	0.498	0.498	0.972
EO non-GBS stillbirth	0.327	0.011	0.327	0.316	0.329	0.328	0.327	0.327	0.011	0.011	0.011	0.011	0.011	0.011	0.011	0.034
All early onset	**9.223**	**0.892**	**7.739**	**8.494**	**11.372**	**10.808**	**10.191**	**8.500**	**0.589**	**0.731**	**1.519**	**2.355**	**2.046**	**0.727**	**0.866**	**1.503**
LOGBS	1.505	0.145	1.504	1.581	1.507	1.506	1.502	1.507	0.145	0.143	0.145	0.145	0.145	0.145	0.145	0.245
All infections	**10.728**	**1.037**	**9.242**	**9.939**	**12.882**	**12.315**	**11.693**	**10.007**	**0.735**	**0.876**	**1.664**	**2.501**	**2.191**	**0.872**	**1.011**	**1.748**
Deaths															0.000	
EOGBS (including EOGBS stillbirth)	0.486	0.031	0.112	0.294	1.023	0.880	0.732	0.304	0.007	0.018	0.082	0.149	0.124	0.018	0.029	0.064
EO non-GBS (including EOGBS stillbirth)	1.382	0.086	1.382	1.378	1.386	1.385	1.381	1.382	0.086	0.086	0.086	0.086	0.086	0.086	0.086	0.181
All early onset	**1.868**	**0.117**	**1.494**	**1.672**	**2.409**	**2.264**	**2.112**	**1.686**	**0.093**	**0.104**	**0.168**	**0.236**	**0.211**	**0.104**	**0.115**	**0.245**
LOGBS	0.137	0.012	0.138	0.136	0.138	0.137	0.137	0.137	0.012	0.013	0.012	0.012	0.012	0.012	0.012	0.022
All infections	**2.006**	**0.130**	**1.633**	**1.807**	**2.548**	**2.403**	**2.250**	**1.823**	**0.105**	**0.125**	**0.180**	**0.248**	**0.223**	**0.116**	**0.128**	**0.267**

Appendix 7

The model: Winbugs and R code

Details are available from the authors on request.

Appendix 8

Linking this project to the National Screening Committee's criteria for adoption of screening programmes

We interpret these criteria as referring to universal screening of women in labour based on culture or PCR tests for GBS colonisation. The study evaluated universal screening as just two of 713 possible strategies for the management of women, most of which reflect a combination of clinical management, testing for specific clinical risk groups, and primary prevention using vaccination.

UK National Screening Committee: criteria for appraising the viability, effectiveness and appropriateness of a screening programme

Ideally, all of the following criteria should be met before screening for a condition is initiated.

The condition

1. The condition should be an important health problem.
EOGBS disease is an important health problem with an incidence of 0.5/1000 livebirths in the UK and a mortality rate of 10%.

2. The epidemiology and natural history of the condition, including development from latent to declared disease, should be adequately understood and there should be a detectable risk factor, disease marker, latent period or early symptomatic stage.
GBS colonisation of the vagina/rectum of the mother at the time of delivery is necessary in order for the baby to become infected with EOGBS.

3. All the cost-effective primary prevention interventions should have been implemented as far as practicable.
Vaccination in the second trimester is the only option currently considered for primary prevention. Another alternative, treatment of GBS colonisation prior to labour, is thought to be ineffective as maternal colonisation recurs after cessation of treatment. As no studies have evaluated the effect of early prelabour treatment on neonatal colonisation or EOGBS, this option was not evaluated in our study. Vaccination was included in the model of screening strategies.

4. If the carriers of a mutation are identified as a result of screening the natural history of people with this status should be understood, including the psychological implications.
Not applicable (GBS is not a genetic disease).

The test

5. There should be a simple, safe, precise and validated screening test.
Culture screening at 35–37 weeks is the standard screening test; however, new PCR tests that are carried out during labour are now available, and have been validated in previous studies.

6. The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed.
We synthesised results for sensitivity and specificity of both the culture test at 35–37 weeks and the PCR test during labour, based on cut-offs used in routine practice.

7. The test should be acceptable to the population.
Evidence from other similar countries suggests that both the culture screening test and the PCR test are acceptable to the general population.

8. There should be an agreed policy on the further diagnostic investigation of individuals with a positive test result and on the choices available to those individuals.
No further diagnostic tests are required as the decision to treat is based on the screen test result.

9. If the test is for mutations the criteria used to select the subset of mutations to be covered by screening, if all possible mutations are not being tested, should be clearly set out.
Not applicable.

The treatment

10. There should be an effective treatment or intervention for patients identified through early detection, with evidence of early treatment leading to better outcomes than late treatment.
Intravenous or oral antibiotics during labour are effective prophylactic treatments for EOGBS.

11. There should be agreed evidence-based policies covering which individuals should be offered treatment and the appropriate treatment to be offered.
Universal screening and treatment of women with a positive test result was not cost-effective, as some high-risk women with a negative test result were better off treated, and therefore did not benefit from screening.

12. Clinical management of the condition and patient outcomes should be optimised in all healthcare providers prior to participation in a screening programme.
The purpose of the study was to evaluate how clinical management could be optimised and what additional benefits could be gained by routine testing for specific groups of women. Clinicians and policy makers can use these results to decide who should be treated, with and without testing. Universal screening is detrimental provided clinical management is optimised.

The screening programme

13. There should be evidence from high-quality RCTs that the screening programme is effective in reducing mortality or morbidity. Where screening is aimed solely at providing information to allow the person being screened to make an 'informed choice' (e.g. Down's syndrome, cystic fibrosis carrier screening), there must be evidence from high-quality trials that the test accurately measures risk. The information that is provided about the test and its outcome must be of value and readily understood by the individual being screened.
There are no trials of universal screening.

14. There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/intervention) is clinically, socially and ethically acceptable to health professionals and the public.
Evidence from other countries suggests that GBS screening is clinically, socially and ethically acceptable to health professionals and the public. However, it is not known whether the high rates of intravenous antibiotic treatment associated with screening would be acceptable to the UK population.

15. The benefit from the screening programme should outweigh the physical and psychological harm (caused by the test, diagnostic procedures and treatment).
Universal screening is harmful compared with a range of clinical management strategies that combine treatment for high-risk women, and testing for low-risk groups or vaccination for all.

16. The opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (i.e. value for money).
Universal screening was not cost-effective.

17. There should be a plan for managing and monitoring the screening programme and an agreed set of quality assurance standards.
Universal screening was not cost-effective. Consideration of implementation is not relevant.

18. Adequate staffing and facilities for testing, diagnosis, treatment and programme management should be available prior to the commencement of the screening programme.
Universal screening was not cost-effective. Consideration of resources for implementation is not relevant.

19. All other options for managing the condition should have been considered (e.g. improving treatment, providing other services), to ensure that no more cost-effective intervention could be introduced or current interventions increased within the resources available.
The study found that other options that combine treatment for high-risk women, and testing for low-risk groups or vaccination for all, are more cost-effective than universal screening.

20. Evidence-based information, explaining the consequences of testing, investigation and treatment, should be made available to potential participants to assist them in making an informed choice.
The study reports evidence-based estimates of the consequences of testing and treatment for specific clinical risk groups.

21. Public pressure for widening the eligibility criteria for reducing the screening interval, and for increasing the sensitivity of the testing process, should be anticipated. Decisions about these parameters should be scientifically justifiable to the public.
Not applicable. There is no screening interval as screening only occurs once per pregnancy. New, more accurate PCR-based tests are being developed. However, better tests are unlikely to change the finding that universal screening is not cost-effective.

22. If screening is for a mutation the programme should be acceptable to people identified as carriers and to other family members.
Not applicable.

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By Boyle J, McCartney E, Forbes J, O'Hare A.

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By Bryant J, Picot J, Levitt G, Sullivan I, Baxter L, Clegg A.

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Adalimumab, etanercept and infliximab for the treatment of ankylosing spondylitis: a systematic review and economic evaluation. McLeod C, Bagust A, Boland A, Dagenais P, Dickson R, Dundar Y, *et al*.

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Prenatal screening and treatment strategies to prevent group B streptococcal and other bacterial infections in early infancy: cost-effectiveness and expected value of information analyses.
By Colbourn T, Asseburg C, Bojke L, Philips Z, Claxton K, Ades AE, *et al*.

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We look forward to hearing from you.

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ISSN 1366-5278