National Institute for Health and Care Excellence

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Intrapartum care for women with existing medical conditions or obstetric complications and their babies

Supplement 2: Health economics

NICE guideline NG121

Health economics

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Final

Developed by the National Guideline Alliance, hosted by the Royal College of Obstetricians and Gynaecologists

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Health economics

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- Economic evidence literature reviews.
- Modelling cost effectiveness of antenatal care planning involving a multidisciplinary team for women with existing medical conditions.
- Modelling cost effectiveness of ultrasound needle siting of central neuraxial blockade for women with obesity.
- Modelling cost effectiveness of ultrasound needle siting of central neuraxial blockade for women with obesity.

Economic evidence literature reviews

Women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions

A global health economic literature search was undertaken for women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions. This covered all 26 review questions considered in this part of the guideline. The search strategies are presented in Appendix A.

The search identified 2,841 articles, but after reviewing titles and abstracts, no articles were requested for full-text review. See the study selection flow chart in Appendix B.

Women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons

Two health economic literature searches were undertaken for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons:

- a global search that covered all 17 review questions considered in this part of the guideline
- a search tailored specifically to the review question about clinical and cost effectiveness of antimicrobial therapy for women in labour with sepsis.

The search strategies are presented in Appendix A.

The global search for this part of the guideline identified 2,670 articles, and after reviewing titles and abstracts, 10 articles were requested for full-text review (these did not include the 5 articles requested for full-text review from the search specific to antimicrobials for sepsis in labour; see below for further details). See the study selection flow chart in Appendix B.

Narrative descriptions of 3 studies that were included after full-text review are presented below. All 3 included studies (Grobman 1999, Mrus 2004, Stringer 1999) addressed rapid HIV testing in the intrapartum period for women with no antenatal care. Studies not included in this review with reasons for their exclusion are listed in Appendix C.

A US study (Grobman 1999) used a decision analytic approach to assess the cost effectiveness of voluntary rapid HIV testing in the intrapartum period compared with no testing in women without adequate antenatal care. The analysis assumed an HIV seroprevalence of 1.5%. Women would receive counselling before testing as part of the intervention and those who accepted testing would be offered intrapartum zidovudine therapy if they tested positive. The base-case analysis suggested that voluntary rapid HIV testing would avert 68 cases of paediatric HIV infection per 100,000 women without adequate antenatal care, a reduction of 16.7%. Using 1997 prices, the analysis found that the cost savings from averted paediatric HIV infection, assumed to be $169,642 per case over a lifetime, would more than offset the costs of the intervention. In a univariate sensitivity analysis the study authors reported a break-even point for seroprevalence of 0.71%, with the

intervention ceasing to be cost saving for a lower seroprevalence than this. The study authors also reported that an 11% reduction in HIV transmission represented the break-even point for the effectiveness of the intervention.

Mrus (2004), adopting a societal perspective in the USA, compared rapid HIV testing followed by antiretroviral treatment with no testing for women presenting in labour with no antenatal care. In the basic model women were offered zidovudine treatment if they tested positive, but in additional analyses the study authors considered nevirapine therapy, combination therapy (zidovudine/nevirapine or zidovudine/lamivudine therapy) as well as a strategy of empirical nevirapine therapy. Costs were based on year 2000 prices with future costs discounted at an annual rate of 3%. In the base-case analysis the study authors assumed a prevalence of 0.51% which was lower than in the other included studies in the guideline review. It was assumed in the base-case analysis that, in the absence of antiretroviral treatment, the vertical transmission rate of HIV would be 26.6% and that there would be a 0.62 risk ratio (relative risk) of vertical transmission with antiretroviral treatment. The study authors assumed a $185,000 discounted lifetime cost for a HIV-infected baby and a $105,000 lifetime cost for an HIV-infected woman because testing in the intrapartum period would provide an earlier diagnosis than would otherwise have been the case. The basic model showed that rapid HIV testing followed by zidovudine treatment would avert 27 cases of HIV infection per 50,000 women tested, saving $3 million when compared with no testing. One-way sensitivity analysis suggested that rapid HIV testing would remain cost saving for an HIV prevalence of greater than 0.2%. In a secondary analysis, in which the study authors compared empirical treatment using nevirapine with no intervention, it was reported that 32 HIV cases would be averted, yielding a saving of $2.1 million compared with no treatment. The study authors therefore concluded that an empirical treatment strategy could be considered cost effective in settings where rapid HIV testing was not available.

Stringer (1999) used decision analysis to compare 3 strategies for preventing vertical transmission of HIV from the woman to the baby for unregistered women presenting in labour with no antenatal care in a US study. The strategies were:

- no treatment – described as the current standard for women of unknown HIV status
- rapid HIV testing followed by zidovudine treatment if seropositive
- prophylactic treatment for all women.

To reflect unregistered women being at a much higher risk of infection, a HIV prevalence of 5% was assumed for the base-case analysis. The analysis took the perspective of the health care system and a third-party payer and used a 1998 price year. It assumed a 5-year life expectancy for a paediatric HIV infection. The analysis assumed that the discounted costs of a paediatric infection would be $86,130. In the base-case analysis 183 cases of HIV infection were averted per 100,000 women by rapid HIV testing when compared to no testing. On this basis it was estimated that rapid HIV testing would save the third party payer $10.6 million per 100,000 women. Treating all women averted a further 46 cases than rapid HIV testing, but at an additional cost of $342,068 per additional HIV infection averted. In a sensitivity analysis, the study authors reported that rapid HIV testing remained cost saving relative to no testing for an HIV prevalence of more than 1%.

The second search for this part of the guideline identified 263 articles. After reviewing titles and abstracts, 5 articles were requested for full-text review but no studies were included. Studies not included in this review with reasons for their exclusion are listed in Appendix C.

Modelling cost effectiveness of antenatal care planning involving a multidisciplinary team for women with existing medical conditions

Introduction

Over the last 25 years multidisciplinary teams (MDTs) have emerged as a means to better manage chronic diseases within the NHS. This development has been supported by the Department of Health (Raine 2014). Underpinning this was a sense that hierarchical structures previously prevented the efficient sharing of information. For example, the NHS Management Executive (1993) stated:

"The best and most cost-effective outcomes for patients and clients are achieved when professionals work together, learn together, engage in clinical audit of outcomes together, and generate innovation to ensure progress in practice and service."

The Department of Health commissioned The Health Care Team Effectiveness Project which reported in 2000 (Borill 2000) and the NHS Plan (2000) noted the value of team working:

"Old-fashioned demarcations between staff mean some patients see a procession of health professionals... Information is not shared and investigations are repeated ... Unnecessary boundaries exist between the professions which hold back staff from achieving their true potential"

"Throughout the NHS the old hierarchical ways of working are giving way to more flexible team working between different clinical professionals"

MDTs now permeate many areas of secondary care in England and it has been estimated that it costs approximately £100 million a year to support the functioning of cancer MDT meetings in the NHS (Taylor 2010). However, a systematic review of the literature on the cost effectiveness of MDTs in secondary care suggested that their widespread adoption had not been based on evidence of cost effectiveness (Le 2013).

Women with existing medical conditions are at increased risk of adverse outcomes in pregnancy and during the intrapartum period. Furthermore, deficiencies in multidisciplinary working have been cited in confidential enquiries as a factor in maternal deaths.

The scope for this guideline identified MDT involvement in antenatal care planning for women with existing medical conditions as an issue which could potentially have an impact on commissioning services. It was a topic identified as a priority for health economic analysis and it has previously been acknowledged that MDT meetings can be resource intensive and should be organised to maximise the benefits to patients and the NHS (Raine 2014).

While evidence on MDT for a given guideline population is often absent the clinical review undertaken for this guideline did include a study. Therefore an economic evaluation was undertaken to support guideline recommendations using data from the included study.

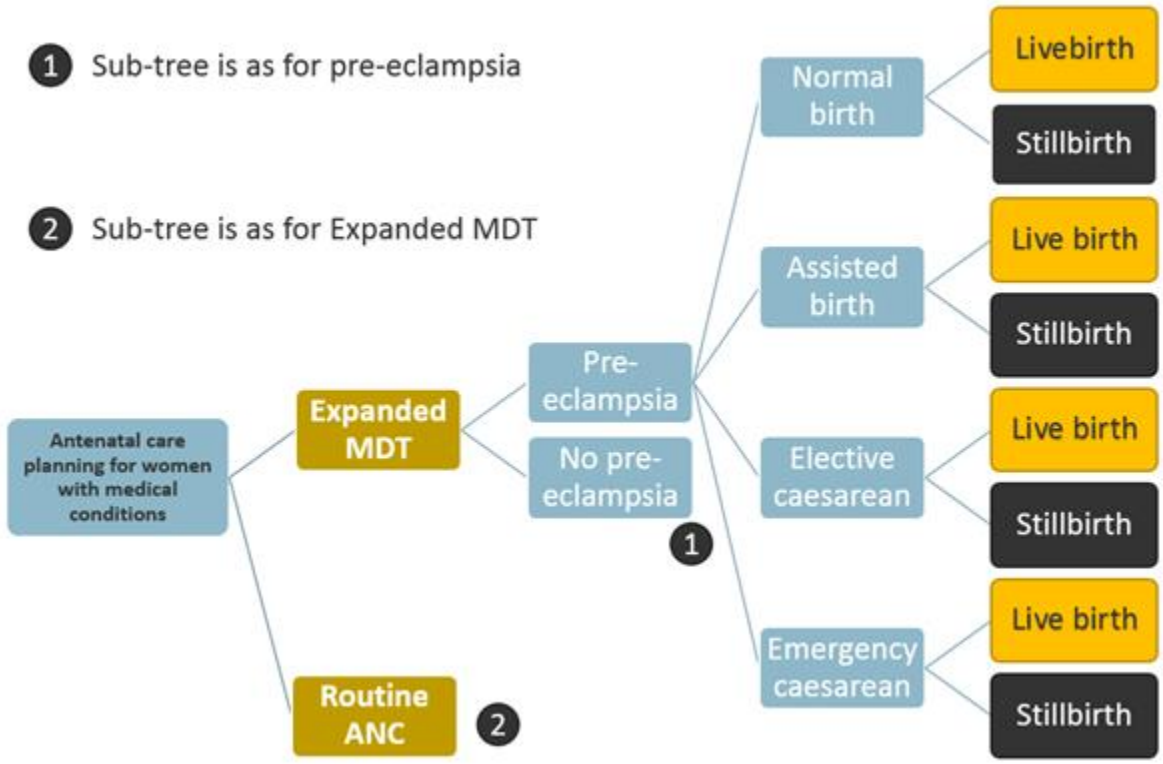
Methods

Model structure

Many alternative MDT configurations are possible and there is a lack of comparative evidence as to the optimum configuration. Therefore, a 'what-if' approach was taken in the model with respect to MDT configuration. It was assumed that the intervention costs of an expanded MDT would always exceed those of routine antenatal care, where the woman does not attend a multiprofessional clinic. Therefore, the analysis considered the cost effectiveness of MDT at different incremental costs relative to routine antenatal care for the clinical effectiveness estimates used in the model.

A simple decision analytic model was developed in Microsoft Excel® to reflect the outcomes reported in the single included study in the systematic clinical review undertaken for this guideline. A schematic of the model is illustrated in Figure 1. The model considers a time horizon from the start of antenatal planning for birth through to the birth, although a life-time perspective was taken to assess the impact on quality adjusted life years (QALYs) of stillbirth.

Figure 1: Model schematic for assessing cost effectiveness of antenatal planning for birth with an expanded multidisciplinary team for intrapartum outcomes for women with existing medical conditions



Setting and population

The model setting was for the NHS and the population was pregnant women identified as being at high risk of adverse outcomes because of the following maternal medical conditions:

- cardiac disease
- asthma
- long-term steroid medication
- haemostatic disorders
- a history of intracranial haemorrhage or a cerebrovascular malformation
- acute kidney injury or have chronic kidney disease
- obesity.

Clinical outcomes

The economic model used the clinical outcomes from the 1 included study (Denison 2017) from the systematic review of the clinical literature undertaken for this guideline. These outcomes and their baseline risk, representing the risk in the absence of a multidisciplinary team, are shown in Table 1. In the model it was possible to use either the trial data from the control arm of the study or population data for England and Wales for the baseline stillbirth data. However, the trial control arm stillbirth data was used as the model base-case default as it was considered to align more closely with the model population of maternities with a high risk of adverse outcomes arising from medical conditions. The effect of using population stillbirth data as the baseline was explored in a sensitivity analysis.

When undertaking probabilistic sensitivity analyses (PSA) these outcome baseline probabilities were sampled using a beta distribution.

Table 1: Baseline probabilities and parameters for probabilistic sensitivity analysis

Outcome	Probability	Alpha	Beta	Source
Stillbirth (trial)	0.0159	8	494	Denison 2017
Stillbirth (ONS)	0.0044	3,112	696,271	NHS Birth Characteristics 2016 (ONS, 2017)
Emergency caesarean section	0.1570	98,501	528,897	NHS Maternity Statistics 2016-17 (NHS Digital, 2017)
Pre-eclampsia	0.0321	132,800	4,004,200	Wallis (2008)

In addition to these outcomes the model utilises the probabilities for non-emergency caesarean section births shown in Table 2. As the various modes of birth have different costs this information is needed to determine the weighted mean cost of births that are not via emergency caesarean sections.

A Dirichlet distribution was used to sample the proportion of non-emergency caesarean section births falling into these 3 categories in the PSA. A count for each mode of birth was sampled using a cumulative gamma function and the sampled value was calculated as its sample count divided by the sum of the sample count for all modes of birth.

Table 2: Non-emergency caesarean section births

Mode of birth	Events	Probability	Source
Unassisted vaginal birth	373,353	0.705	NHS Reference Costs, 2016-17 (NHS Improvement)
Assisted vaginal birth	81,590	0.154	NHS Reference Costs, 2016-17 (NHS Improvement)
Planned caesarean section	74,653	0.141	NHS Reference Costs, 2016-17 (NHS Improvement)

Treatment effectiveness

The relative treatment effects were estimated from the one study (Denison 2017) included in the clinical systematic review undertaken for this guideline and are presented in Table 3 along with their 95% confidence intervals (CIs). These relative treatment effects were applied to the baseline risk in order to estimate the risk of these outcomes for an expanded MDT.

Table 3: Relative treatment effect

Outcome	Relative effect	Lower limit of 95% CI	Upper limit of 95% CI	Source
Stillbirth	0.14[a]	0.02	1.17	Denison 2017
Emergency caesarean section	1.18[b]	0.93	1.48	Denison 2017
Pre-eclampsia	1.38[b]	0.84	2.26	Denison 2017

(a) Odds ratio
(b) Risk ratio

For PSA the relative treatment effects were sampled using a log-normal distribution, with the distribution parameters presented in Table 4, and the standard deviation estimated from the confidence intervals reported in Table 3.

Table 4: Parameters of log-normal distribution for sampling relative treatment effect

Outcome	Mean	Standard deviation
Stillbirth	Ln (0.14)	(Ln (1.17) – Ln (0.14)) ÷ 1.96
Emergency caesarean section	Ln (1.18)	(Ln (1.48) – Ln (1.18)) ÷ 1.96
Pre-eclampsia	Ln (1.38)	(Ln (2.26) – Ln (1.38)) ÷ 1.96

Quality adjusted life years

To estimate the impact of an expanded MDT a QALY decrement was applied to the outcomes of stillbirth and pre-eclampsia. The QALY decrements are shown in Table 5. It was assumed that no QALY decrement was attributable to the mode of birth.

Table 5: Quality adjusted life year decrement associated with adverse outcomes

Outcome	QALY decrement	Source
Stillbirth	23.73	Kind (1999), National Life Tables, England and Wales 2014-16 (ONS, 2017)[a]
Pre-eclampsia	0.0274	Sonnenberg 2004

a Calculated using data from these sources and an annual discount rate of 3.5%

It was assumed that an averted stillbirth would result in a normal life expectancy of 81 years, estimated as a weighted average of male and female life expectancy (ONS, 2017). It was additionally assumed that each year of life would be lived with a health state utility of 0.855. This was based on a publication that estimated that the EQ5D population norms for all ages was 0.86 for males and 0.85 for females (Kind 1999). An annual discount rate of 3.5% was applied to future years of life of life in accordance with NICE methods (https://www.nice.org.uk/Media/Default/About/what-we-do/our-programmes/developing-NICE-guidelines-the-manual.pdf).

Costs and resource use

In accordance with NICE methodology a NHS and Personal Social Services (PSS) perspective was adopted for this analysis (https://www.nice.org.uk/Media/Default/About/what-we-do/our-programmes/developing-NICE-guidelines-the-manual.pdf). Costs were based on a 2016/17 price year reflecting the most recently available NHS Reference Costs at the time of writing. Costs were not discounted as any 'downstream' costs arising from adverse outcomes were assumed to occur around the time of the intervention.

The model allowed an MDT staffing model to be configured with the following categories of staff.

- Consultant
- Band 5 nurses
- Band 6 nurses
- Band 7 nurses
- Scientific & professional band 5
- Scientific & professional band 6
- Scientific & professional band 7
- Scientific & professional band 8a
- Scientific & professional band 8b

It was then possible to able to specify the number of each category of staff in the expanded MDT and their time input per pregnant woman. This information combined with staffing unit costs, described in Table 6, allowed the incremental costs of an expanded MDT relative to routine antenatal care planning to be calculated.

Table 6: Staff unit costs

Staff	Costs per hour	Source
Consultants	£106	Unit Costs of Health and Social Care (PSSRU, 2017)
Band 5 nurses	£37	Unit Costs of Health and Social Care (PSSRU, 2017)
Band 6 nurses	£45	Unit Costs of Health and Social Care (PSSRU, 2017)
Band 7 nurses	£54	Unit Costs of Health and Social Care (PSSRU, 2017)

Staff	Costs per hour	Source
Scientific & professional band 5	£34	Unit Costs of Health and Social Care (PSSRU, 2017)
Scientific & professional band 6	£45	Unit Costs of Health and Social Care (PSSRU, 2017)
Scientific & professional band 7	£55	Unit Costs of Health and Social Care (PSSRU, 2017)
Scientific & professional band 8a	£65	Unit Costs of Health and Social Care (PSSRU, 2017)
Scientific & professional band 8b	£77	Unit Costs of Health and Social Care (PSSRU, 2017)

The PSA was run separately for 10 'what-if' incremental costs of an expanded MDT within a specified range, reflecting the lack of evidence with regard to the optimal configuration of an MDT. However, the deterministic analysis used the hypothetical MDT configuration as outlined in Table 7.

Table 7: Hypothetical multidisciplinary team staffing model

Staff	Quantity	Time (minutes)	Cost
Consultants	3	20	£106
Band 7 nurses	1	15	£13.50
Scientific & professional band 8b	1	15	£19.25
Total cost			£138.75

In addition to the costs associated with an expanded MDT the model took into account the costs associated with the various model outcomes, as outlined in Table 8.

Table 8: Costs associated with model outcomes

Outcome	Cost	Standard error	Distribution	Source
Pre-eclampsia	£4,864 [a]	N/A	Deterministic	NICE 2010
Unassisted vaginal birth	£2,297 [b]	£70 [c]	Normal	NHS Reference Costs, 2016-17 (NHS Improvement)
Assisted vaginal birth	£3,367 [b]	£123 [c]	Normal	NHS Reference Costs, 2016-17 (NHS Improvement)
Planned caesarean section	£3,557 [b]	£79 [c]	Normal	NHS Reference Costs, 2016-17 (NHS Improvement)
Emergency caesarean section	£4,781 [b]	£98 [c]	Normal	NHS Reference Costs, 2016-17 (NHS Improvement)
Stillbirth	£4,361 [d]	N/A	Deterministic	Campbell 2018

a https://www.nice.org.uk/guidance/cg107, Tale K4. Updated to 2016-17 prices using the Hospital and community health services (HCHS) pay and inflation index, with a multiplier of 1.13 derived from the HCHS index for 2008-09 and 2016-17
b weighted average of all relevant currency codes

c The method of estimating a standard error from data included in NHS Reference Costs is described in detail in https://www.nice.org.uk/guidance/ng3. A standard error was estimated for each relevant NHS Reference Cost category and currency code and a pooled standard error was then estimated by weighting according to finished consultant episodes
d Updated to 2016-17 prices using the HCHS pay and inflation index, with a multiplier of 1.04 derived from the HCHS index for 2013-14 and 2016-17

All costs are reported as the cost per woman.

Tornado diagram inputs

The importance of a number of model inputs was assessed using one-way sensitivity analysis and presented in a Tornado diagram. These model inputs and the range of values used are presented in Table 9.

Table 9: Tornado diagram variables and inputs

Variable	Low value	High value
MDT cost	£50	£10,000
Cost of pre-eclampsia	£0	£12,000
QALY loss from stillbirth	15.00	30.00
QALY loss from pre-eclampsia	0.00	2.00
Cost effectiveness threshold	£50 per QALY	£30,000 per QALY

While it is difficult to prescribe an optimal service configuration of the expanded MDT, the ranges chosen for the MDT cost in one-way sensitivity analysis are set to assess the extent to which more resource intensive MDTs would impact on the cost effectiveness conclusions, although this is also tested through PSA.

The default cost of pre-eclampsia is high for a condition that effects approximately 2-8% of pregnancies (WHO 2011) and so the range is set to reflect that mild pre-eclampsia may have a much lower resource impact than indicated in the base-case analyses. The wide range allowed for the importance of this variable as a driver of cost effectiveness to be evaluated.

The ranges for QALY losses for stillbirth and pre-eclampsia allowed for fact that there is some uncertainty with respect to these values and that this was not evaluated as part of the PSA. Again the range was set sufficiently wide to assess the extent to which uncertainty in model inputs would be reflected in the conclusions about the cost effectiveness of an expanded MDT.

Results

Probabilistic sensitivity analysis

The results of the PSA, based on 10,000 Monte Carlo simulations of the model, are presented in Table 10 and Figure 2. For each simulation the results are calculated across different hypothetical or ‘what-if’ costs of the MDT intervention. The incremental mean net monetary benefit (iNMB) is based on a cost effectiveness threshold of £20,000 per QALY.

Table 10: Mean net monetary benefit and probability cost effective for an expanded multidisciplinary team when compared to routine antenatal care planning

MDT cost per woman	Mean iNMB	Probability cost effective
£100	£5,474	95.7%
£1,200	£4,374	93.4%
£2,300	£3,274	88.6%
£3,400	£2,174	80.0%
£4,500	£1,074	66.6%
£5,600	-£26	49.8%
£6,700	-£1,126	34.5%
£7,800	-£2,226	21.9%
£8,900	-£3,326	13.1%
£10,000	-£4,426	7.5%

Figure 2: Probability an expanded multidisciplinary team is cost effective compared to routine antenatal care planning for different costs of the multidisciplinary team

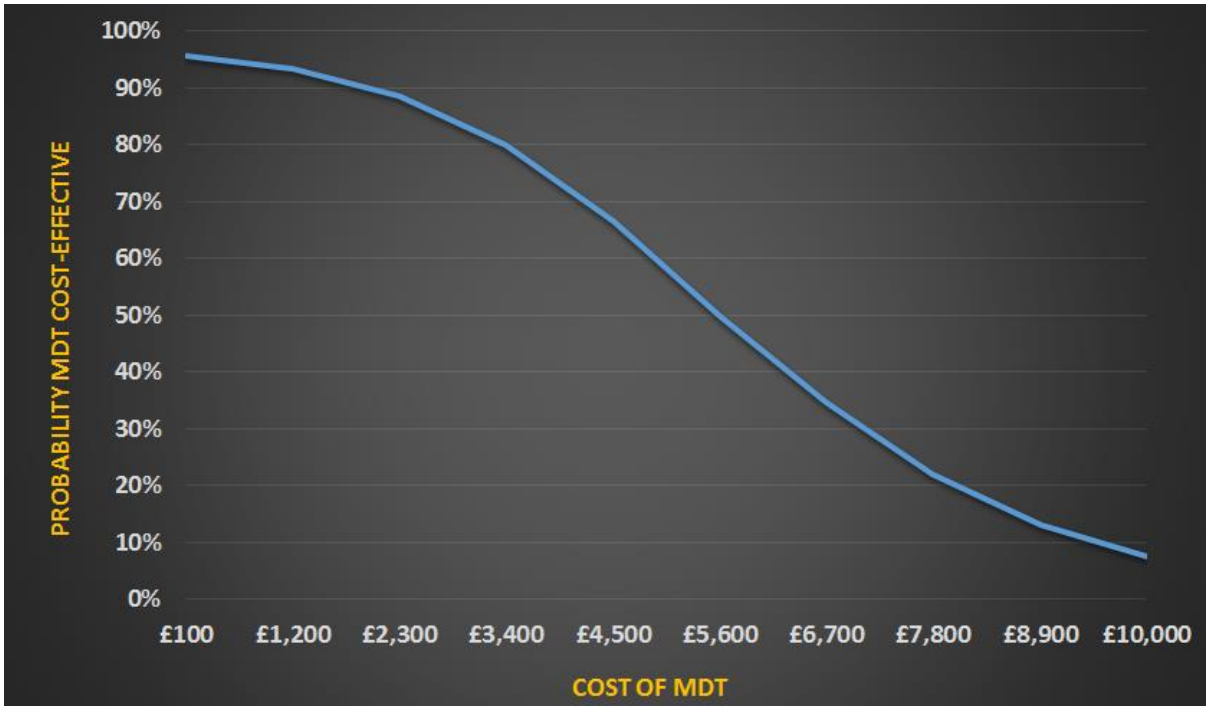


Figure 3 shows the cost effectiveness acceptability curve (CEAC) when the hypothetical incremental cost of an expanded MDT was £4,500. The scatter plot of the individual simulations which generated this probabilistic result is displayed in Figure 4.

Figure 3: Cost effectiveness acceptability curve comparing the probability that an expanded multidisciplinary team or routine antenatal care planning is cost effective when the hypothetical incremental costs of the multidisciplinary team are £4,500

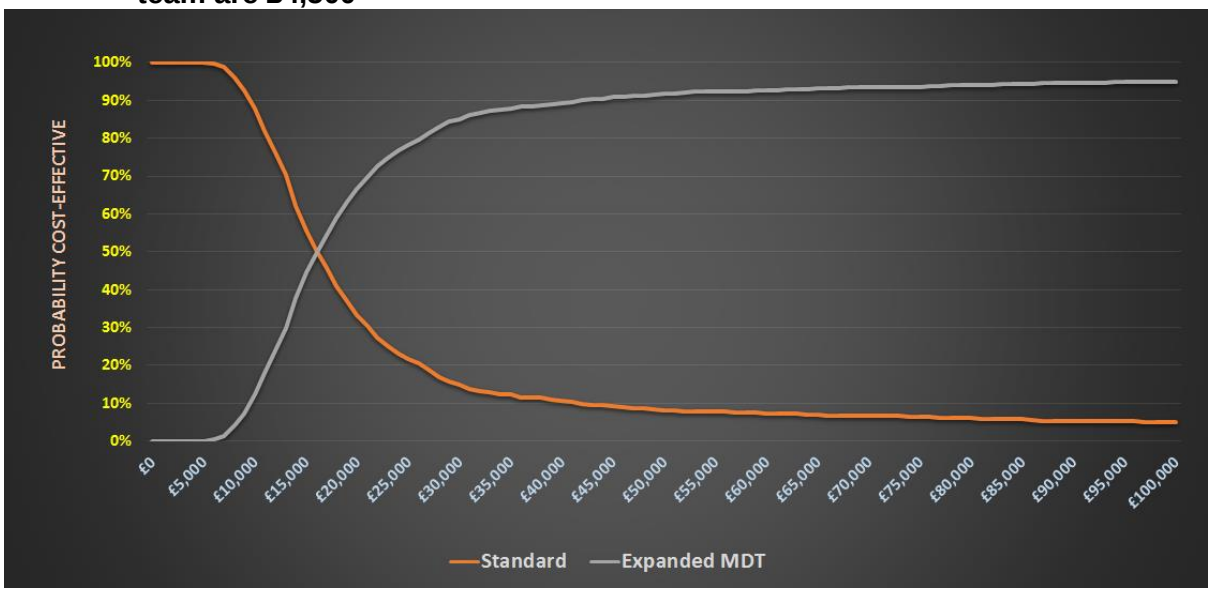
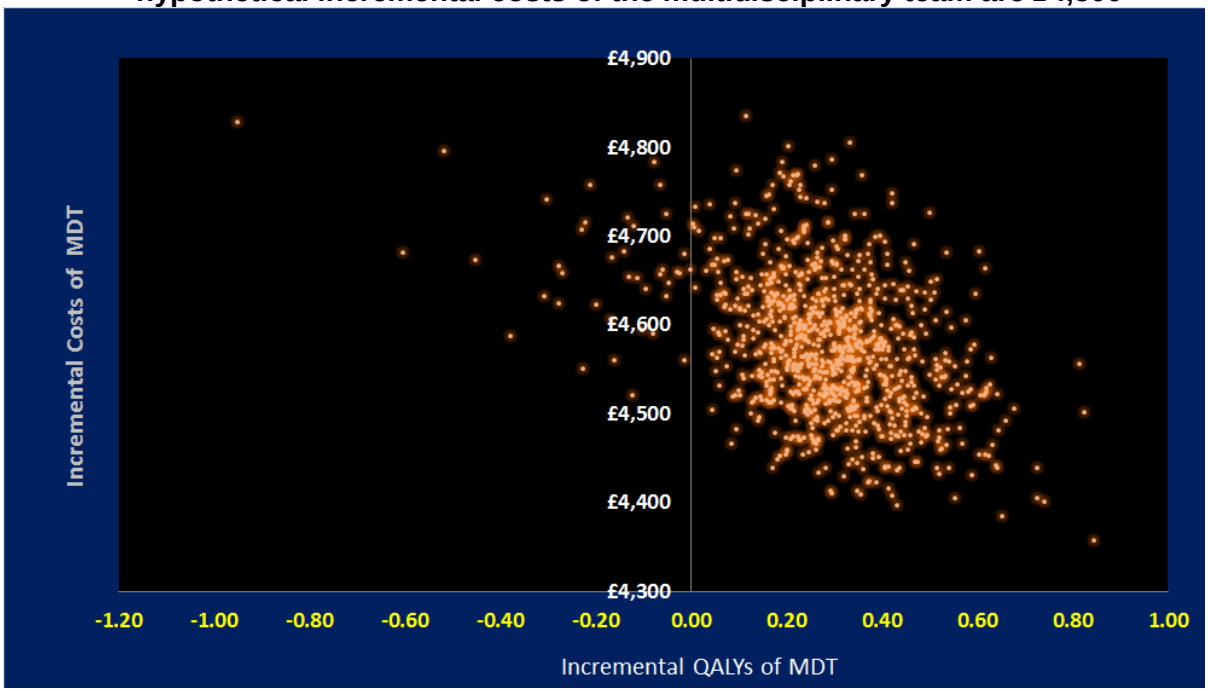


Figure 4: Cost effectiveness plane showing probabilistic simulation results when the hypothetical incremental costs of the multidisciplinary team are £4,500



Deterministic analysis

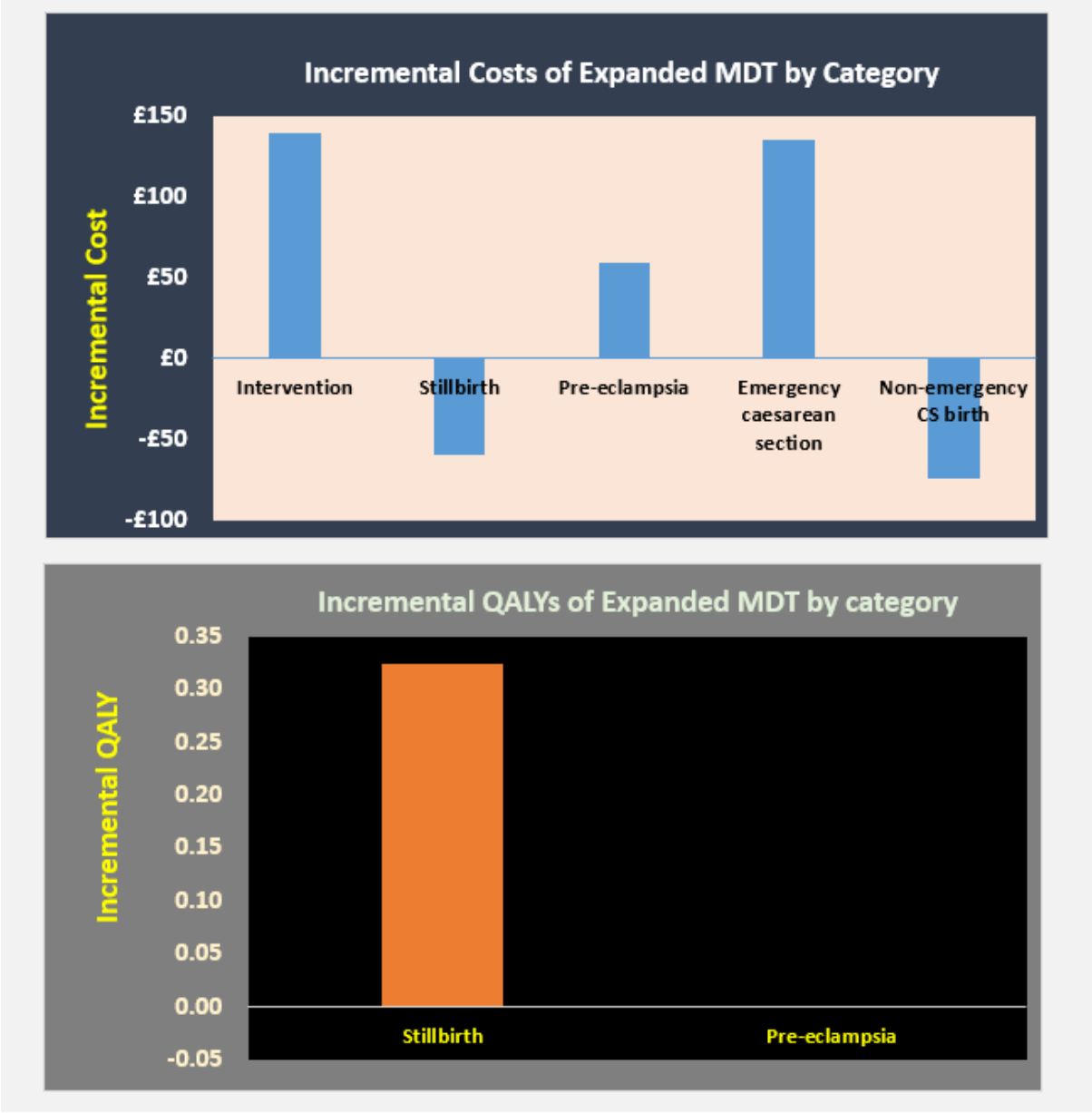
The results of the deterministic analysis are presented in Table 11. In this analysis the hypothetical incremental costs of the expanded MDT when compared to routine antenatal care planning were assumed to be £138.75 as described in Table 7.

Table 11: Comparison of costs and quality adjusted life years from an expanded multidisciplinary team when compared to routine antenatal care planning

Variable/ outcome	Routine antenatal care			Expanded MDT			Incremental	
	Quantity	Cost	QALY loss	Quantity	Cost	QALY	Cost	QALY loss
Intervention	-	-	-	1	£139	-	£139	-
Stillbirths	0.015	£69	0.3782	0.0023	£10	0.0537	-£60	0.3245
Pre-eclampsia	0.0321	£156	0.0009	0.0443	£215	0.0012	£59	-0.0003
Emergency CS	0.1570	£751	-	0.1853	£886	-	£135	-
Unassisted vaginal birth	0.5943	£1,365	-	0.5744	£1,319	-	-£46	-
Assisted vaginal birth	0.1299	£437	-	0.1255	£423	-	-£15	-
Planned CS	0.1188	£423	-	0.1148	£409	-	-£14	-
Total		£3,201	0.3790		£3,400	0.0549	£199	0.3242

The incremental cost effectiveness ratio (ICER) of this hypothetical expanded MDT relative to routine antenatal care was £613 per QALY and MDT had an iNMB of £6,284 at a cost effectiveness threshold of £20,000 per QALY. Figure 5 show the different components of the incremental costs of the expanded MDT intervention relative to routine antenatal care planning.

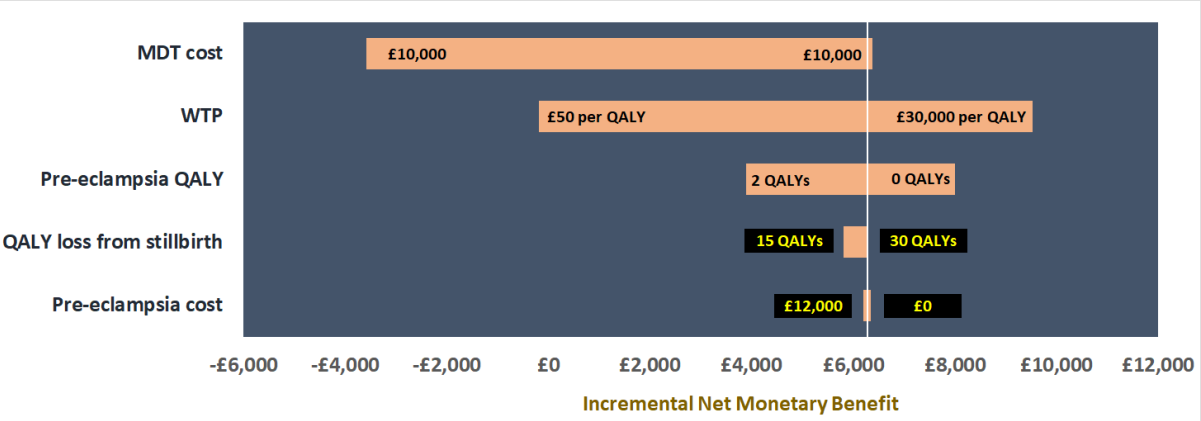
Figure 5: Chart indicating the respective different components of the incremental costs and quality adjusted life years of an expanded multidisciplinary team relative to routine antenatal care planning



Tornado analysis

One-way sensitivity analysis was undertaken to assess the impact of changes to the values of the variables presented in Table 9. In this sensitivity analysis each parameter was varied between a low and high value while holding all other model inputs constant at their base-case value. The results of this analysis are shown in Figure 6.

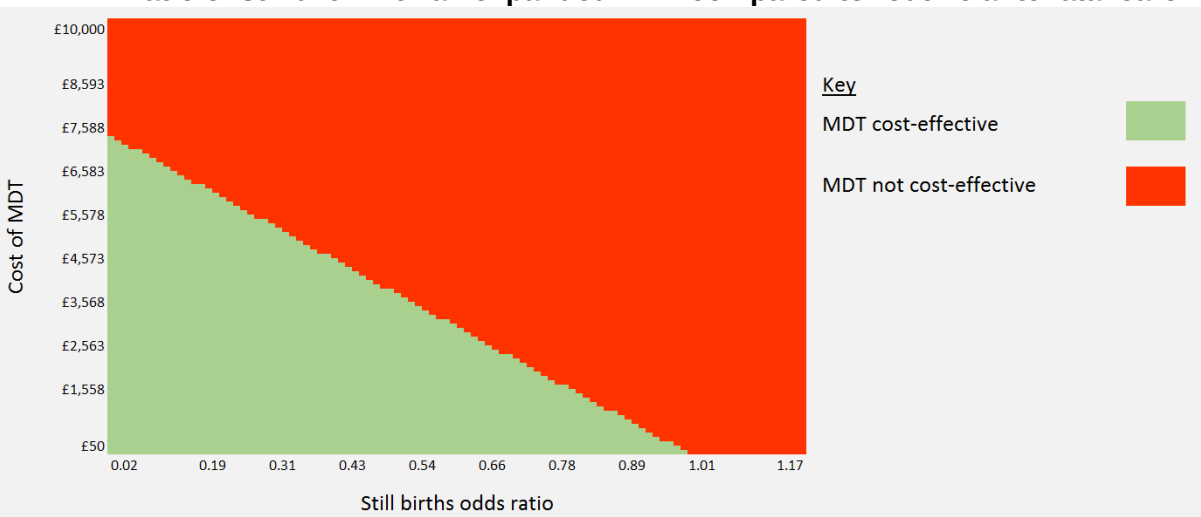
Figure 6: Tornado diagram for an expanded multidisciplinary team when compared to routine antenatal care planning



Two-way sensitivity analysis

A two-way sensitivity analysis was undertaken varying the costs of MDT and the odds ratio (OR) of stillbirth with an expanded MDT compared to routine antenatal care. These were the 2 key drivers of cost effectiveness in the model and yet there is considerable uncertainty with respect to their values. The results of this analysis are shown in Figure 7. The analysis depicts the combinations of MDT cost and stillbirth relative risk where MDT is cost effective holding all other model input parameters constant at their base-case values.

Figure 7: Chart of two-way sensitivity analysis varying the cost of MDT and the odds ratio of stillbirth with an expanded MDT compared to routine antenatal care



Discussion

It is important that the limitations in the study (Denison 2017) that provided the clinical data underpinning this analysis are taken into account when interpreting the results. First, the population in this study was women with a singleton pregnancy and class III obesity. While, this is a relevant population for this guideline it is only a subset of those women with existing medical conditions in pregnancy. In order to support recommendations that cover a broader group of women, it was implicitly assumed that the benefits for women with class III obesity could be generalised to other women with existing medical conditions.

The study used a retrospective cohort design and there may have been systematic differences in the characteristics between women in the intervention and control groups. Furthermore, the intervention and control groups were located in different hospital settings which could influence the respective populations and the reported clinical outcomes. Also the intervention was multi-component and it is not possible to know the extent that any differences in outcomes reflected these additional interventions (for example, dietary advice) rather than the MDT antenatal care per planning per se.

Therefore, the results of the economic analysis may be subject to bias and consequently may over-estimate the benefits of MDT antenatal care planning. Also the costs of the expanded MDT was undertaken on a 'what-if' basis to reflect that there is a lack of evidence with respect to alternative MDT configurations (Bick 2014) .

The model strongly suggests (given the relative treatment effects used in the analysis) that involving an expanded MDT in antenatal care planning is likely to be cost effective compared to routine antenatal care planning providing that the cost per woman is £4,500 or less. So for an MDT antenatal care planning configuration that cost £1,200 per woman the mean iNMB of the MDT would be £4,374 and it would have a 93% probability of being cost effective relative to routine antenatal planning given the sampling uncertainty surrounding the model inputs. Even at a hypothetical MDT cost of £4,500 per woman the iNMB remains positive with a 67% chance of being cost effective. The deterministic analysis, based on an MDT configuration as set out in Table 7 (an MDT cost of £139 per woman), showed an ICER of £613 per QALY for MDT (mean iNMB £6,284) for MDT relative to routine antenatal care planning, again suggesting that MDT was cost effective with the model's assumptions on treatment effects. The reduction in the stillbirth rate with the expanded MDT was an important driver of the cost effectiveness of the intervention especially as the model did not suggest that the MDT would be cost saving even when 'downstream' costs were considered.

Two-way sensitivity analysis showed the joint relationship of the cost of MDT and the OR of stillbirth relative to routine antenatal care in determining the cost effectiveness of MDT. It also indicates the threshold cost of MDT for cost effectiveness for a given OR of stillbirth and conversely the threshold OR for stillbirth for a given cost of MDT. This analysis indicates that when operating at a threshold combination, a reduction in MDT cost of approximately £75 is required for every 0.01 increase in the OR of stillbirth.

The hypothetical configuration of MDT used in the deterministic analysis is less resource intensive than other models and this is important as the Tornado analysis indicates that the cost of the MDT is likely to be an important consideration in determining its cost effectiveness. It is important to note that while this analysis provides some support for an expanded MDT when compared to routine antenatal care for women with existing conditions it does not provide evidence about the optimal configuration of the expanded MDT. As has been previously noted "there is a dearth of evidence to support optimal MDT structure and working practices, or if current MDT model of care have a beneficial impact on maternal and

infant outcomes and healthcare resources" (Bick 2014). An analysis that suggests an expanded MDT costing £4,500 per woman may be cost effective relative to routine antenatal care planning for women with existing medical conditions does not demonstrate that such a resource intensive MDT model would be cost effective if compared to a much less resource intensive configuration.

None of the relative treatment effects for the clinical outcomes included in the model reaches statistical significance at the 5% level. However, such statistical conventions are arbitrary and an irrelevance of inference argument has been made in the context of decision making in the presence of uncertainty (Claxton 1999). The apparent cost effectiveness of MDT in this analysis is driven by a large relative reduction of stillbirths with MDT and whilst the confidence intervals do not indicate statistical significance they do nevertheless suggest a fairly high probability that MDT will lead to reduced stillbirths. This is reflected in the PSA results. It seems unlikely that an MDT would actually lead to an increase in pre-eclampsia even if it is not ultimately protective. However, removing this outcome from the analysis would only further strengthen the cost effectiveness of MDT reported in this evaluation.

Conclusion

Subject to the substantial limitations in the clinical data underpinning the model, this analysis provides support for the recommendations made by the committee with respect to involving an expanded MDT in antenatal care planning for women with existing medical conditions. While the model suggests that an expanded MDT is likely to be cost effective relative to routine antenatal care planning, it does not provide evidence on the optimal way to configure an MDT service.

Modelling cost effectiveness of ultrasound needle siting of central neuraxial blockade for women with obesity

Introduction

Palpation of anatomical landmarks or ultrasound scanning are alternative techniques to identify the needle insertion site for regional anaesthesia or analgesia in obese women who choose a caesarean section under regional block or request epidural analgesia for labour. Anatomical landmarks may be impalpable in obese women and it has been suggested that ultrasound scanning provides an effective alternative to identify the gaps between spinous processes in the lumbar region. Improved needle siting through the use of ultrasound may reduce the time to complete the procedure and the number of failed puncture attempts which has the potential to reduce 'downstream' costs as well as leading to improved health outcomes. However, ultrasound adds to the costs of the procedure and therefore there is an issue as to whether the additional costs constitute good value for money for the NHS. For this reason and because there are differences in practice and opinion, an original health economic analysis was undertaken for this guideline.

Methods

Model structure

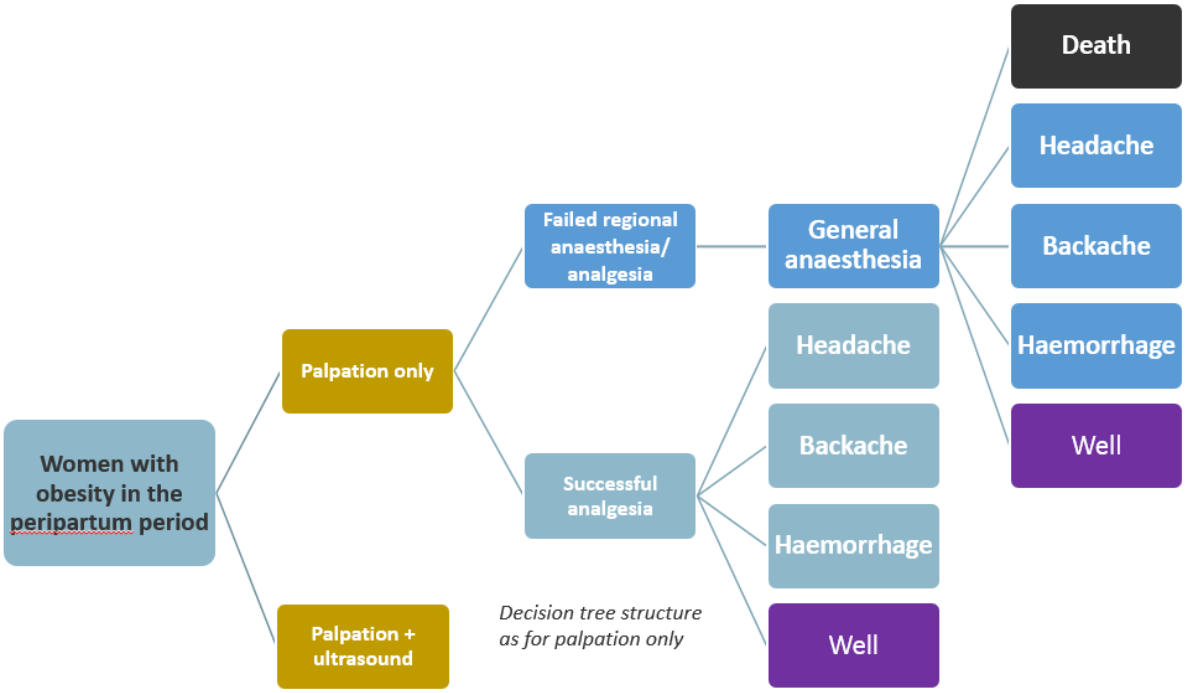
A decision analytic model was developed in Microsoft Excel® to compare the cost effectiveness of ultrasound (plus palpation) with palpation alone, to improve needle siting in obese women. A diagrammatic representation of the decision tree structure is shown in Figure 8. The tree structure is the same for both the model intervention, ultrasound (plus palpation), and the comparator, palpation alone, although the probabilities of the various outcomes vary. The clinical data reports only the overall risk of the outcomes of headache, backache and haemorrhage at the puncture site with no breakdown according to whether or not analgesia failed. Therefore, the model assumed that these adverse outcomes were the same irrespective of whether or not analgesia fails. This assumption does not make any difference in terms of assigning a health state utility loss and cost to these outcomes.

PSA was undertaken using Monte Carlo simulation in order to reflect uncertainty in model input parameters. This involved sampling model inputs from a probability distribution that reflected the uncertainty around the point estimates for model values. Mean costs and QALYs were calculated across all simulations and, as a summary measure of cost effectiveness, a mean iNMB was calculated based on a cost effectiveness threshold of £20,000 per QALY.

One-way deterministic sensitivity analysis was undertaken to explore which model inputs contributed most to the results and where uncertainty with respect to the true model parameter is likely to be the most important. These results are presented in a Tornado diagram which is intended to give some insight into which are the most important variables in driving the results. They indicate how a 'low' value and a 'high' value for a particular model input would change the model result when compared to the base-case value. The Tornado diagrams are presented so that the variables are ordered in descending order of importance

although some caution should be exercised in interpreting this ordering as low or high values may not always have been selected consistently across all variables.

Figure 8: Model schematic for assessing the cost effectiveness of ultrasound (plus palpation) to improve needle siting in obese women



Setting and population

The model setting was for the NHS and the population was obese women (BMI ≥ 30 kg/m^2) and undergoing elective or emergency caesarean section or siting of epidural for analgesia in labour. It was assumed that the women were aged 30 years, reflecting the mean age of women giving birth in England and Wales in 2014 (https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/bulletins/birthsbyparentscharacteristicsinenglandandwales/2014).

Clinical outcomes and baseline risk

The clinical outcomes included in the model reflected the outcomes reported in 3 studies (Wang 2012, Sahin 2014, Urfalioglu 2017) included in the clinical review undertaken for this guideline. All the clinical evidence related to women having an elective caesarean section and therefore the model assumed that the outcomes would be the same in obese woman who were in labour at the time of the procedure. These outcomes and their baseline risk are presented in Table 12. The baseline risk represents the risk for the comparator treatment of palpation alone and was estimated from the control arm of the included studies, pooled when evidence from more than one study was available. The table also includes parameters used for probabilistic sampling in the Monte Carlo simulation.

Table 12: Baseline risk for model outcomes

Outcome	Risk	Alpha	Beta	Distribution	Source
Failed analgesia	0.080	2	23	Beta	Sahin 2014
Backache	0.231	24	80	Beta	Wang 2012, Sahin 2014, Urfalioglu 2017
Headache	0.037	6	98	Beta	Wang 2012, Sahin 2014, Urfalioglu 2017
Haemorrhage	0.236	8	47	Beta	Wang 2012, Sahin 2014

Treatment effectiveness

Treatment effectiveness estimates, shown in Table 13, were derived from 3 studies included in the clinical review. Where data on an outcome was available from more than 1 study the relative treatment effect was estimated from a meta-analysis. The baseline risk was multiplied by the risk ratios from the studies to provide an estimate of the risk of each outcome of interest with the intervention, ultrasound (plus palpation).

Table 13: Relative treatment effect of ultrasound (plus palpation) compared to palpation alone

Outcome	Risk ratio (RR)	Standard Error (ln(RR))	Distribution	Source
Failed analgesia	1.00	0.0834	Log-normal	Sahin 2014
Backache	0.31	0.3778	Log-normal	Wang 2012, Sahin 2014, Urfalioglu 2017
Headache	1.53	0.5083	Log-normal	Wang 2012, Sahin 2014, Urfalioglu 2017
Haemorrhage	0.62	0.4069	Log-normal	Wang 2012, Sahin 2014

Quality adjusted life years

In order to estimate QALYs, a health state utility decrement was estimated for the adverse outcomes of backache, headache and haemorrhage alongside an expected duration. The default values for the health state utility decrement associated with these outcomes and the expected duration are presented in Table 14 and Table 15 respectively. In order to calculate the health state utility decrement a population norm of 0.93 was assumed (Kind 1999) based on the mean weighted health state index for women aged 25 to 34 years. Where a health state utility was established for the adverse outcome from the literature, this was then subtracted from the population norm to give an estimate of the health state utility decrement associated with that outcome.

Table 14: Health state utility decrement

Outcome	HSU Decrement	Standard Error	Distribution	Source
Backache	0.42	0.008	Normal	Whynes 2013 and Abdullayev 2015 [a]
Headache	0.60	None	N/A	Udeh 2014 [b]

Outcome	HSU Decrement	Standard Error	Distribution	Source
Haemorrhage	0.00	None	N/A	N/A

a Whynes 2013 reported a health state utility of 0.62 (95% confidence interval 0.60 to 0.64) for mild backache, 0.48 (95% CI 0.45 to 0.51) for moderate backache and 0.18 (95% CI 0.15 to 0.22) for severe backache. Published data (Abdullayev 2015) was used to estimate to estimate the proportion of women experiencing postdural backache who would be mild (52.6%), moderate (33.8%) or severe (13.5%). These proportions were used to estimate a weighted health state utility loss of 0.51 associated with postdural backache. The standard error was estimated by bootstrapping 10,000 samples of the health state utility values in Whynes 2013.
b Udeh 2014 estimated a health state utility of 0.33 for a post lumbar puncture head for 2 days. A range of 0.25 to 0.41 was reported but no confidence intervals.

Table 15: Duration of adverse outcomes

Outcome	Duration (days)	Standard error	Distribution	Source
Backache	3.2	1.122	Normal	Abdullayev 2015 [a]
Headache	21.2	0.059	Normal	Vandam 1956 [b]
Haemorrhage	N/A	N/A	N/A	N/A

a Based on the control group in that study
b Vandam 1956 reported on the spontaneous recovery from postdural headache. While this occurred within 4 days for a majority of patients, a small percentage of patients took much longer to recover. In this study a total of 10,098 spinal anaesthesia were observed and the overall risk of postdural headache was estimated to be 11%. In order to estimate the uncertainty surrounding the mean duration of postdural headache based on the duration reported by Vandam 1956 (1-2 days = 24%; 3-4 days = 29%; 5-7 days = 19%; 8-14 days = 8%; 3-6 weeks = 5%; 3-6 months = 2%; 7-12 months = 4%) a 1,000 bootstrap case resampling replications were undertaken for 1,110 patients (11% of 10,098) with postdural headache

The estimate of duration of headache represents an upper bound because it is based on spontaneous recovery whereas in current practice women with a postdural puncture headache would be offered an epidural blood patch and this treatment has a high success rate, especially if a second patch is offered to women whose symptoms are only partially relieved after one attempt.

In addition the model estimated a QALY loss for the very small risk of general anaesthetic mortality in the event of general anaesthesia being needed. The model parameters used to derive this loss are presented in Table 16. A discount rate of 3.5% was used to estimate QALY losses occurring into the future in line with NICE methods (https://www.nice.org.uk/media/default/about/what-we-do/our-programmes/developing-nice-guidelines-the-manual.pdf).

Table 16: Quality adjusted life year loss from general anaesthetic mortality

Variable	Value	Source
Remaining Life Expectancy	53 years	ONS, Life Tables 2013-15 [a]
Health state utility decrement from mortality	0.93	Kind 1999
General anaesthetic mortality	0.000077	Lagasse 2002

a Based on a woman aged 30 years

Costs and resource use

In line with NICE methods a NHS and PSS perspective was adopted for this analysis. Costs were based on a 2016/17 price year reflecting the most recently available NHS Reference

Costs at the time of writing. Costs were not discounted as any 'downstream' costs arising from adverse outcomes were assumed to occur within 1 year of treatment.

The incremental nature of the analysis meant that the model sought to capture the additional costs of ultrasound compared to palpation. Palpation would also be used with ultrasound and therefore in the base-case analysis it was assumed that the additional costs of treatment for the intervention relative to the comparator of palpation alone would be captured through the costs of an ultrasound scan. However, given that a key rationale for ultrasound is that it may help facilitate neuraxial blockade, sensitivity analysis explored the possibility that there could be cost differences in treatment arising from differences in the number of puncture attempts or the duration of the procedure.

In addition to treatment, the model also included costs relating to adverse outcomes. The unit costs of the model are shown in Table 17. Model inputs used to assess the impact of puncture attempts and procedure duration are outlined in Table 18 and Table 19 respectively. A Dirichlet distribution was used in the PSA in order to quantify the uncertainty around the number of puncture attempts for both the comparator and intervention.

Table 17: Model unit costs

Cost variable	Value	Standard error [a]	Distribution	Source
Ultrasound	£52	£1.13	Normal	NHS Reference Costs 2016-17 [b]
General anaesthesia	£334	N/A	N/A	University Hospital Southampton [c]
Backache	£50	N/A	N/A	GC estimate [d]
Headache	£112	N/A	N/A	Tung 2012 [e]
Haemorrhage	£50	N/A	N/A	GC estimate [f]
Cost per additional puncture (palpation)	£21	N/A	N/A	PSSRU 2017, Wang 2012 [g]
Cost per additional puncture ultrasound	£52	£1.13	Normal	NHS Reference Costs 2016-17 [a]
Cost per procedure hour	£106 [b]	N/A	N/A	PSSRU 2017

a The method of estimating a standard error from data included in NHS Reference Costs is described in detail in https://www.nice.org.uk/guidance/ng3. Value marked N/A were treated deterministically there was no information on dispersion of values around the point estimate on which to base a sampling distribution
b This was based on an ultrasound scan with duration of less than 20 minutes, without contrast (Currency code RD40Z
c Private Patient Tariff 2017/2018
http://www.uhs.nhs.uk/Media/SUHTInternet/PatientsAndVisitors/Privatepatienttariff2017to2018.pdf (accessed 10/07/2018
d A largely notional value, but reflects that there are a number of low-cost management options that may be employed such as hot or cold massage, mild analgesics and occasionally medical follow-up to rule out more persistent backache
e Based on the costs reported in a US article (Tung 2012) on the costs of an epidural blood patch, a surgical procedure. A US cost of $137.59 in 2011 prices was converted into UK currency using the HM Revenue and Customs monthly exchange rate of £1 = $1.3176 (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/718649/exrates-monthly-0718.csv/preview - July 2018). This was updated to 2016-17 prices using the HCHS pay and inflation index, with a multiplier of 1.07 derived from the HCHS index for 2011-12 and 2016-17
f A largely notional value as this will usually be haematoma formation
g Based on the costs per hour worked of a medical consultant and a procedure duration of 12 minutes (see Table 19)

Table 18: Puncture attempts by needle siting method [a]

Number of attempts	Palpation alone	Ultrasound (plus palpation)
1	13	19
2	7	9
3	1	2
4	9	0

a Wang 2012

Table 19: Duration[a]

	Palpation		Ultrasound (plus palpation)	
Variable	**Mean**	**Standard error**	**Mean**	**Standard error**
Time to determine puncture site	2.60	0.311	0.30	0.061
Procedure duration	9.37	0.776	7.67	0.689

a Wang 2012

Tornado diagram inputs

Values and rationale for one-way sensitivity analysis presented later in a Tornado diagram are shown in Table 20.

Table 20: Values for model inputs in Tornado diagram

Variable	Low value	High value	Rationale for values
Ultrasound cost	£0	£200	Some uncertainty as to most appropriate currency code
Backache cost	£20	£1,000	Wide range to assess sensitivity with respect to this input
Headache cost	£20	£1,000	Wide range to assess sensitivity with respect to this input
Haemorrhage cost	£20	£1,000	Wide range to assess sensitivity with respect to this input
Backache baseline risk	0.01	0.50	Wide range to assess sensitivity with respect to this input
Headache baseline risk	0.01	0.50	Wide range to assess sensitivity with respect to this input
Haemorrhage baseline risk	0.01	0.50	Wide range to assess sensitivity with respect to this input
General anaesthesia risk ratio	0.85	1.18	95% Confidence intervals [a]
Backache risk ratio	0.15	0.65	95% Confidence intervals [a]
Headache risk ratio	0.57	4.05	95% Confidence intervals [a]
Haemorrhage risk ratio	0.28	1.35	95% Confidence intervals [a]
Backache health state utility loss	0.05	0.70	Wide range to assess sensitivity with respect to this input
Headache health state utility loss	0.05	0.70	Wide range to assess sensitivity with respect to this input
Backache mean duration	1 day	50 days	Wide range to assess sensitivity with respect to this input

Variable	Low value	High value	Rationale for values
Headache mean duration	1 day	50 days	Wide range to assess sensitivity with respect to this input

a Values of <1.00 favour ultrasound

Results

Base-case inputs

Probabilistic sensitivity analysis

The output from a PSA using the model's default inputs not taking into account the number of puncture attempts or the duration of the procedure are shown in Table 21, Figure 9 and Figure 10. The results show that in this analysis ultrasound is not cost effective, with a very high probability that the result holds when allowing for parameter uncertainty.

Table 21: Probabilistic sensitivity analysis output for base-case analysis

Measure	Value
Simulations	10,000
Mean incremental cost of ultrasound	£47
Mean incremental QALY of ultrasound	-0.0009
Mean incremental net monetary benefit (iNMB) [a]	-£65
Probability ultrasound cost effective at £20,000 per QALY threshold	1.26%
Probability ultrasound cost effective at £30,000 per QALY threshold	5.00%

a Calculated for a cost effectiveness threshold of £20,000 per QALY

Figure 9: Cost effectiveness plane for base-case analysis

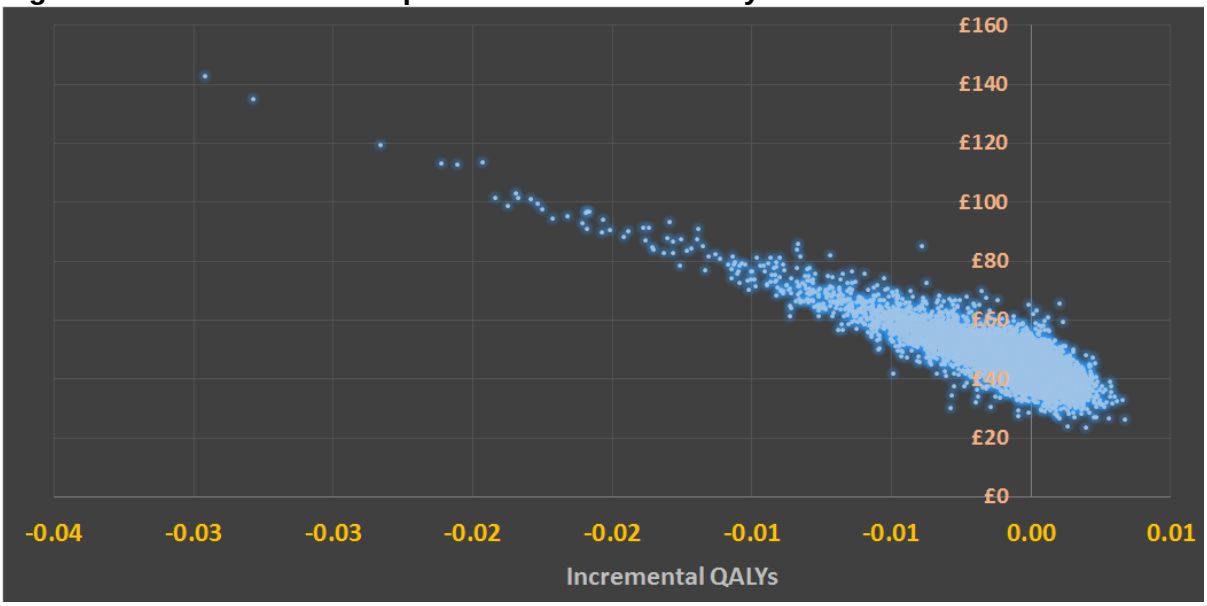
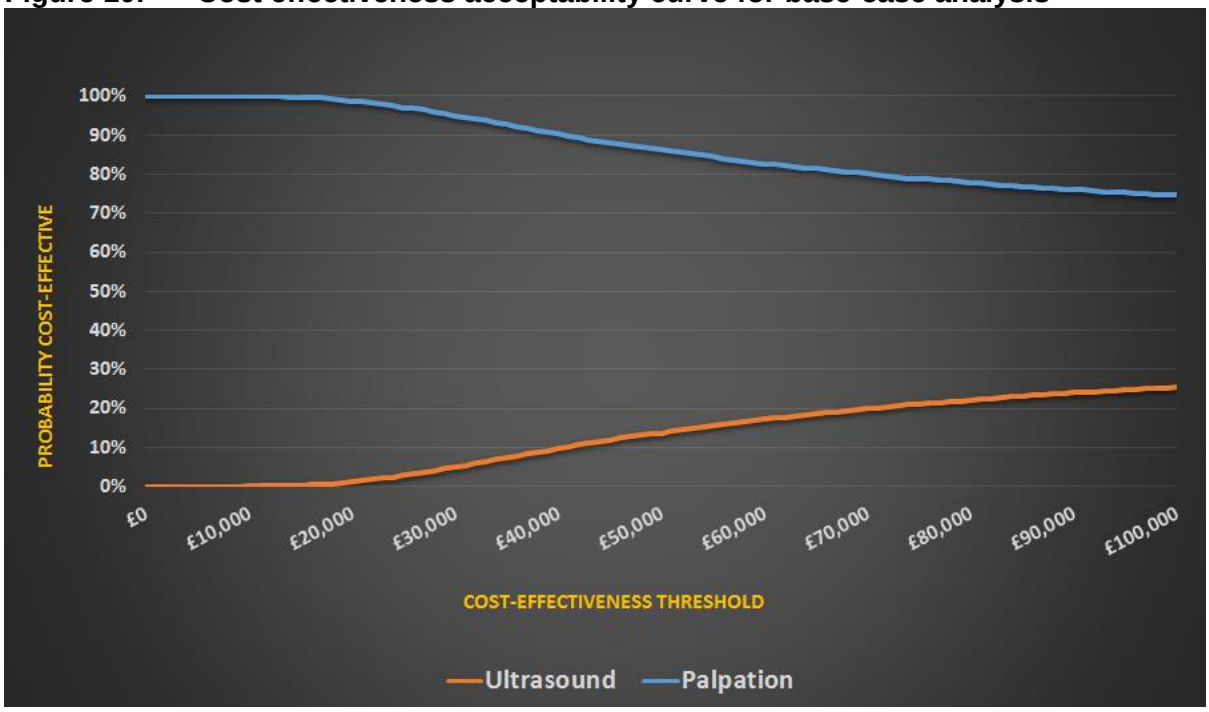


Figure 10: Cost effectiveness acceptability curve for base-case analysis



Deterministic analysis

The results for the deterministic analysis using default model inputs are provided in Table 22. They produce a similar result to the PSA indicating that ultrasound is dominated by palpation alone, with higher costs and lower benefits. The iNMB of ultrasound is -£53.

Table 22: Deterministic analysis for base-case analysis[a]

Measure	Incremental outcomes	Incremental costs	Incremental QALYs
General anaesthesia	0.000	£0.00	N/A
Mortality	0.000	-	0.00000
Backache	-0.159	-£7.97	0.00059
Headache	0.031	£3.44	-0.00107
Haemorrhage at puncture site	-0.090	-£4.48	0.00000
Procedure	-	£52.00	N/A
Total	**N/A**	**£42.99**	**-0.00048**

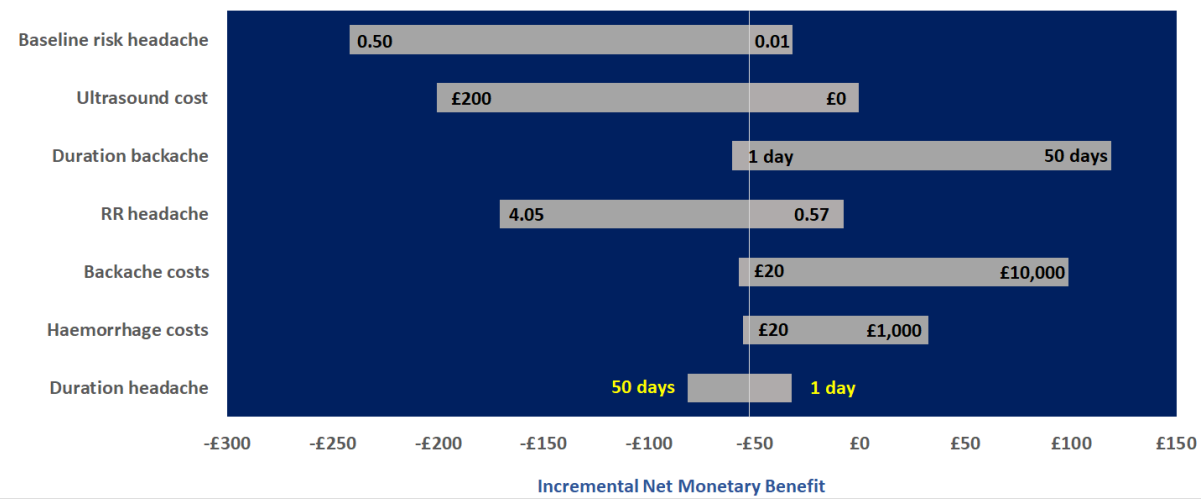
a Results are reported incrementally for ultrasound compared to using palpation alone

Tornado diagram

The results of the Tornado analysis for the base-case analysis are shown in Figure 11 and Figure 12. This involves varying the inputs for the variables presented in Table 20 between

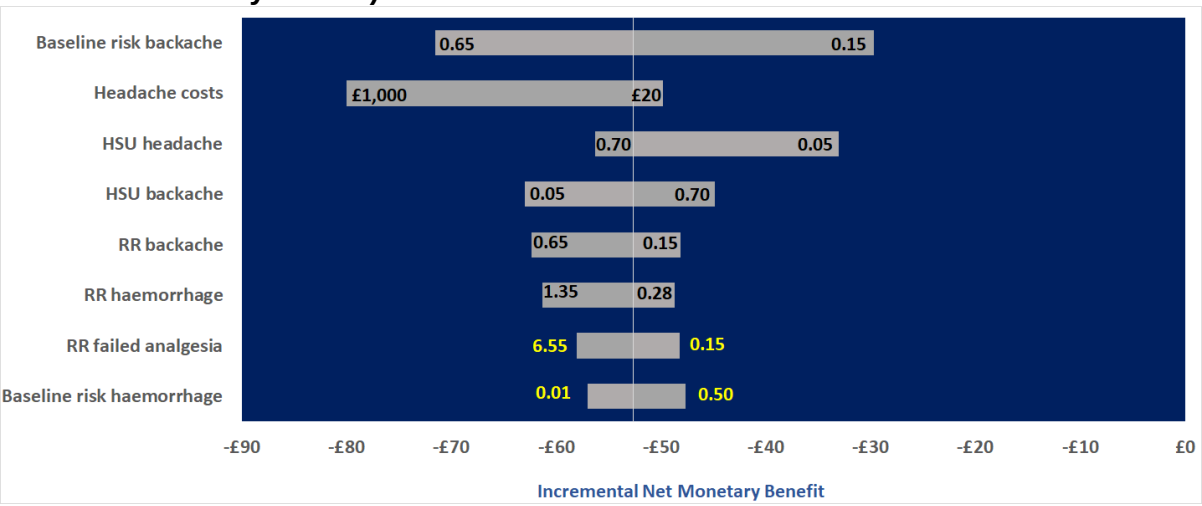
the low and high values as indicated, while holding all other model inputs constant at their default value. Figure 11 shows the variables where varying their value had the greatest impact on iNMB, with Figure 12 displaying the Tornado analysis where varying the variables had a lower impact which is reflected in a much narrow iNMB scale on the horizontal axis..

Figure 11: Tornado diagram for the base-case analysis (larger change in net monetary benefit)



RR = risk ratio

Figure 12: Tornado diagram for the base-case analysis (smaller change in net monetary benefit)



RR = risk ratio; HSU = health state utility

Analysis taking into account puncture attempts

Probabilistic sensitivity analysis

In this analysis the number of puncture attempts is sampled to explore the implications for the costs of the procedure. The results of this analysis are presented in Table 23. The results

show that in this analysis palpation alone is cost effective and with a very high probability when using a cost effectiveness threshold of £20,000 to £30,000 per QALY.

Table 23: Probabilistic sensitivity analysis for analysis taking into account the number of puncture attempts

Measure	Value
Simulations	10,000
Mean incremental cost of ultrasound	£44
Mean incremental QALY of ultrasound	-0.0009
Mean incremental net monetary benefit (iNMB) [a]	-£63
Probability ultrasound cost effective at £20,000 per QALY threshold	2.22%
Probability ultrasound cost effective at £30,000 per QALY threshold	6.59%

a Calculated at a cost effectiveness threshold of £20,000 per QALY

Deterministic analysis

The results for the deterministic analysis are shown in Table 24. Again they produce a similar result to the PSA and indicate that ultrasound remains dominated by palpation alone.

Table 24: Deterministic analysis taking into account the number of puncture attempts [a]

Measure	Incremental outcomes	Incremental costs	Incremental QALYs
General anaesthesia	0.000	£0.00	N/A
Mortality	0.000	-	0.00000
Backache	-0.159	-£7.97	0.00059
Headache	0.031	£3.44	-0.00107
Haemorrhage at puncture site	-0.090	-£4.48	0.00000
Procedure	-	£49.33	N/A
Total	**N/A**	**£40.32**	**-0.0048**

a Results are reported incrementally for ultrasound compared to using palpation alone

Analysis taking into account the duration of the procedure

Probabilistic sensitivity analysis

In this analysis the time to complete the procedure is sampled and factored into the overall costs of the procedure based on the costs per procedure hour (see Table 17). This analysis indicates that the time saving with ultrasound is not sufficient to offset the additional costs of the ultrasound procedure when compared to palpation alone. The mean iNMB of ultrasound is -£59 at a cost effectiveness threshold of £20,000 per QALY. The results are presented in Table 25.

Table 25: Probabilistic sensitivity analysis taking into account the procedure duration

Measure	Value
Simulations	10,000
Mean incremental cost of ultrasound	£40

Measure	Value
Mean incremental QALY of ultrasound	-0.0009
Mean incremental net monetary benefit (iNMB) [a]	-£59
Probability ultrasound cost effective at £20,000 per QALY threshold	2.63%
Probability ultrasound cost effective at £30,000 per QALY threshold	7.52%

a Calculated at a cost effectiveness threshold of £20,000 per QALY

Deterministic analysis

The result of the deterministic analysis is presented in Table 26. It shows that ultrasound is not cost effective as it is dominated by palpation alone, resulting in an iNMB of -£46.

Table 26: Deterministic analysis taking into account the duration of the procedure [a]

Measure	Incremental outcomes	Incremental costs	Incremental QALYs
General anaesthesia	0.000	£0.00	N/A
Mortality	0.000	-	0.00000
Backache	-0.159	-£7.97	0.00059
Headache	0.031	£3.44	-0.00107
Haemorrhage at puncture site	-0.090	-£4.48	0.00000
Procedure	-	£44.93	N/A
Total	**N/A**	**£35.92**	**-0.00048**

a Results are reported incrementally for ultrasound compared to using palpation alone

Scenario analysis increasing the effectiveness of ultrasound

In this analysis the changes outlined in Table 27 were made to model inputs. The effect of these changes was to make the ultrasound intervention less costly relative to palpation alone, while at the same time increasing the benefits of treatment.

Table 27: Scenario analysis with greater ultrasound effectiveness relative to palpation

Variable	Scenario analysis value	Default value
Backache duration	7 days	3.2 days
Backache duration standard error	2 days	1.122 days
Risk ratio for headache [a]	0.57	1.53

a Values of < 1.00 favour ultrasound

Probabilistic sensitivity analysis

The results of the PSA are presented in Table 28, Figure 13 and Figure 14. They show that, in this scenario, there was also considerable uncertainty with respect to cost effectiveness especially for a cost effectiveness threshold of between £20,000 and £30,000 per QALY.

Table 28: Probabilistic sensitivity analysis with greater effectiveness of ultrasound relative to palpation

Measure	Value
Simulations	10,000

Measure	Value
Mean incremental cost of ultrasound	£40
Mean incremental QALY of ultrasound	0.0019
Mean incremental net monetary benefit (iNMB) [a]	-£1.00
Probability ultrasound cost effective at £20,000 per QALY threshold	48.40%
Probability ultrasound cost effective at £30,000 per QALY threshold	75.52%

a Calculated at a cost effectiveness threshold of £20,000 per QALY

Figure 13: Cost effectiveness plane for scenario analysis with greater effectiveness of ultrasound relative to palpation

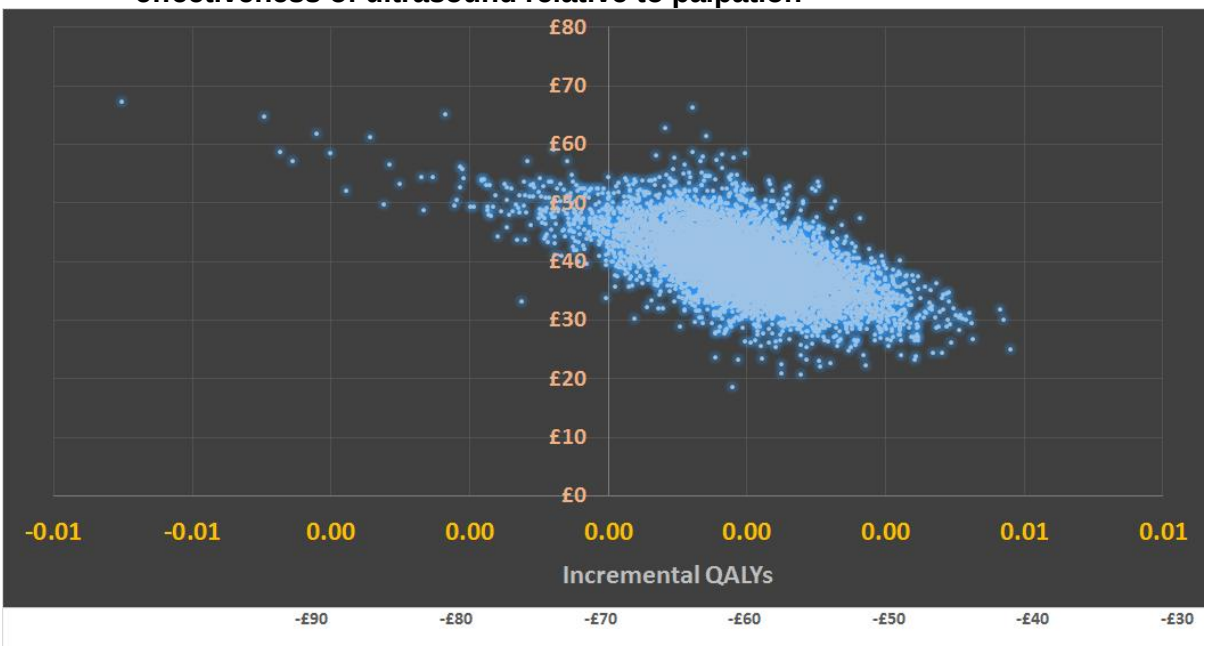
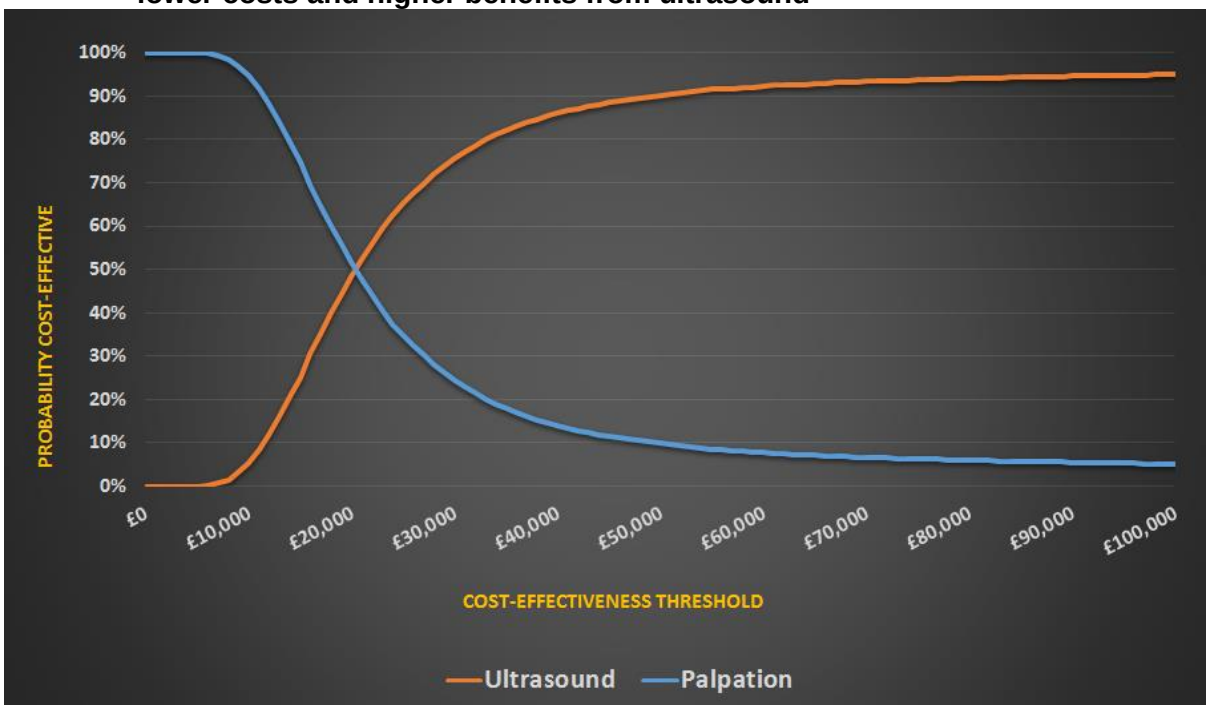


Figure 14: Cost effectiveness acceptability curve for scenario analysis assuming lower costs and higher benefits from ultrasound



Deterministic analysis

Table 29 shows the output of the deterministic analysis for this sensitivity analysis. It suggests that ultrasound (plus palpation) is cost effective at a cost effectiveness threshold of £20,000 per QALY with an ICER of £17,071 per QALY relative to palpation alone. However, an iNMB of £6 is consistent with the PSA suggesting that the finding that the cost effectiveness of ultrasound compared to ultrasound is subject to considerable uncertainty.

Table 29: Deterministic analysis for scenario assuming lower costs and higher benefits from ultrasound [a]

Measure	Incremental outcomes	Incremental costs	Incremental QALYs
General anaesthesia	0.000	£0.00	N/A
Mortality	0.000	-	0.000
Backache	-0.159	-£7.97	0.00128
Headache	-0.025	-£2.79	0.00087
Haemorrhage at puncture site	-0.090	-£4.48	0.00000
Procedure	N/A	£52	N/A
Total	**N/A**	**£36.75**	**0.00215**

a Results are reported incrementally for ultrasound compared to using palpation alone

Discussion

It is important to recognise the limitations of the clinical evidence which underpins this economic evaluation when interpreting the results. Potentially, improved needle siting could reduce the need for general anaesthesia. For obese women, general anaesthesia carries a greater risk than in non-obese women, but there was no evidence reported on related outcomes and the sample size of the included studies in the clinical evidence review meant they would have been underpowered to detect any differences. Therefore, the model was restricted to the outcomes that were reported in the 2 included studies. All the clinical evidence related to women having an elective caesarean section and therefore the model assumed that the outcomes would be the same in obese woman who were in labour at the time of the procedure. Furthermore, the studies were exploratory and generally underpowered to detect differences in outcomes and therefore resulted in very imprecise estimates of treatment effect.

Although the duration of the procedure and the number of failed puncture attempts were not prioritised outcomes for the clinical review, they were reported in the clinical studies and were considered in the evaluation through a sensitivity analysis.

The deterministic sensitivity analysis and the PSA both found that palpation alone was more cost effective than ultrasound (plus palpation) for needle siting. The PSA suggested that there was a 99.8% probability that palpation alone was cost effective and in the deterministic analysis ultrasound (plus palpation) was dominated, being more expensive, principally as a result of the additional procedure cost, and generating fewer QALYs, primarily because the point estimate of the risk ratio for headache suggested an increased risk of this outcome, which combined with the mean duration of headache symptoms is the biggest single driver of QALY differences in the model. While one of the hypotheses underpinning the rationale for using ultrasound (plus palpation) to assist in needle siting is that it might reduce the risk of accidental dural puncture. These punctures can cause headaches that might require an epidural blood patch. However, the limited clinical evidence that informs this model does not provide support for this hypothesis.

The Tornado analysis shows that, at least if all other variables are held constant at their base-case levels, varying one input value by large amounts does not generally alter the cost effectiveness conclusion with only the upper limit of haemorrhage costs leading to a positive iNMB for ultrasound (plus palpation). However, unless the haemorrhage represents a very rare spinal haematoma, it is not considered to be an important clinical issue and will typically be associated with negligible or zero costs. Although the point estimate for the risk ratio indicates a higher risk of headaches with ultrasound, the confidence intervals are wide, and this should be interpreted as a lack of evidence of benefit rather than evidence of harm. However, the Tornado analysis did not suggest that ultrasound was cost effective even when the lower 95% confidence interval for the risk ratio was used.

Sensitivity analysis considered separately the inclusion of procedure duration and the number of puncture attempts. However, in both analyses there was only a negligible improvement in the relative cost effectiveness of ultrasound (plus palpation), with palpation alone remaining the dominant procedure. This is because the savings from a reduced number of puncture attempts or the shorter duration of the procedure only partially offset the higher costs of the procedure, at least with the model assumptions with respect to the additional costs associated with longer duration or more puncture attempts.

A scenario analysis was also undertaken to demonstrate that by moving several model inputs in favour of ultrasound plus palpation, the cost effectiveness of palpation alone

becomes less clear cut. Given the wide imprecision around the inputs in this model then future research may be beneficial in determining whether the cost effectiveness of ultrasound (plus palpation) is better than this current analysis would suggest.

Conclusion

The model results suggest that there is no demonstrable economic benefit in undertaking ultrasound plus palpation to improve needle siting for obese women who choose a caesarean section under regional block or who request epidural analgesia for labour compared to palpation alone. This is unsurprising given that the evidence in the clinical systematic review undertaken for this guideline did not find clinically important differences for any of the outcomes prioritised by the committee. Therefore, the committee chose not to make any recommendations on this topic. However, they did not think that the included evidence provided conclusive evidence that ultrasound (plus palpation) should not be undertaken for needle siting. They therefore refrained from making a recommendation that ultrasound (plus palpation) should not be undertaken for needle siting for central neuraxial blockade anaesthesia for obese women who choose a caesarean section under regional block or for obese women who request epidural analgesia for labour.

Modelling cost effectiveness of mode of birth for women with a large-for-gestational-age baby

Introduction

It is recognised that large for gestational age babies increase the risk of certain adverse outcomes for both the woman and the baby, with the risk rising with increasing birthweight. Of interest in this guideline is the clinical and cost effectiveness of different modes of birth (caesarean section or continuation of labour) for women in labour with a large-for-gestational-age baby. There continues to be variation in practice in the management of pregnancies with a suspected large-for-gestational-age baby. Although, there are published economic evaluations related to the mode of birth for women with a large-for-gestational-age baby, they all focus on a planned birth before labour has started and therefore, it was decided that an original health economic analysis should be undertaken for this guideline which could incorporate this new evidence and more explicitly address a population in labour, where the alternative to continuing with labour would be an emergency caesarean section.

Methods

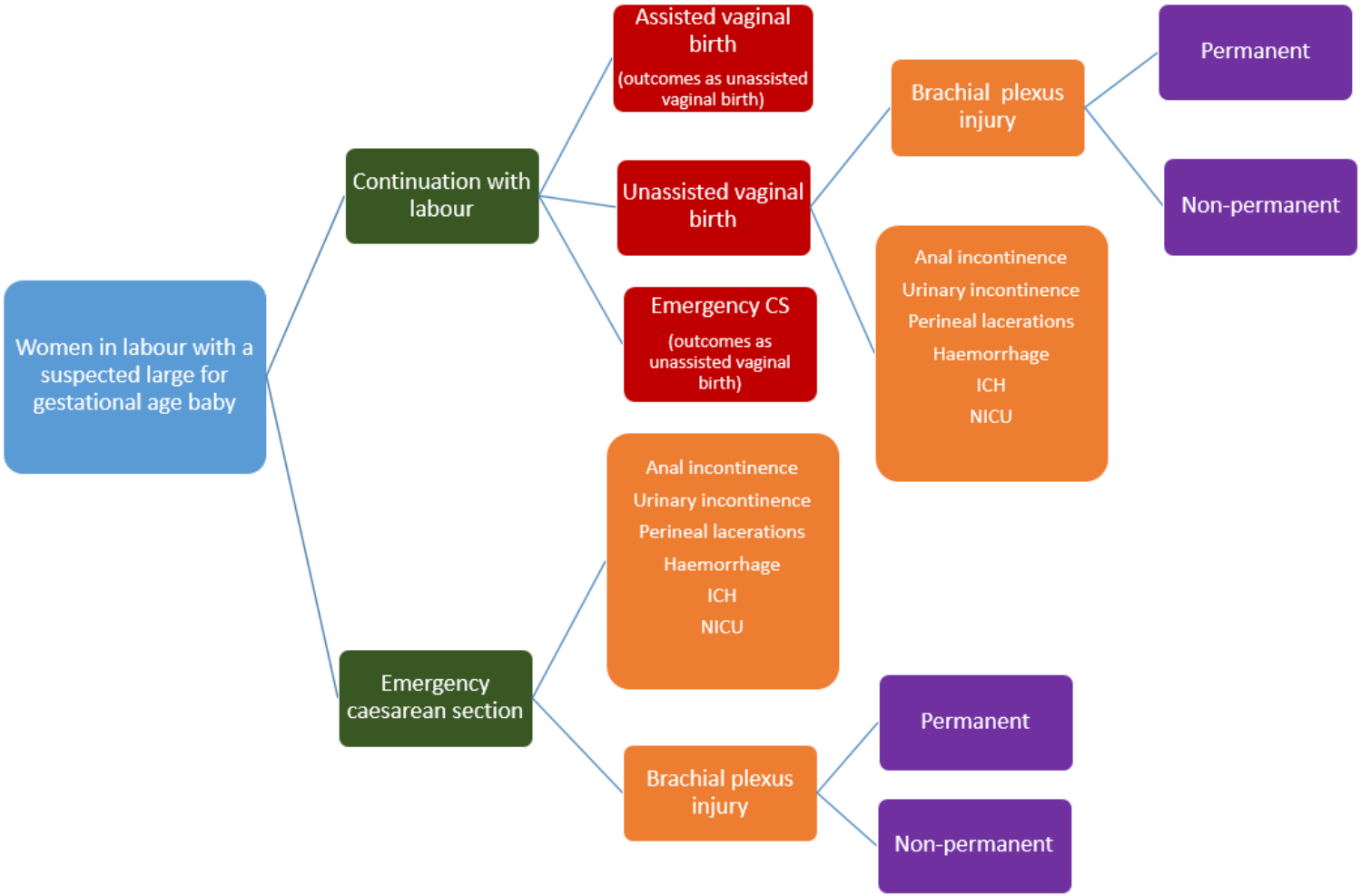
Model structure

A decision analytic model was developed in Microsoft Excel® to compare the cost effectiveness of emergency caesarean section to continuation of labour in women with a suspected large-for-gestational-age baby. A schematic of the model is shown in Figure 15.

The model assumed that a proportion of women who decided to continue with labour would nevertheless require an emergency caesarean section. Outcomes for these women were not differentiated according to the eventual (actual) mode of birth because the data in the included studies did not allow stratification in this way.

The model took a lifetime horizon in order to capture the potential lifelong effects of adverse outcomes for the woman and the baby. Subgroup analysis was undertaken for different birthweights.

Figure 15: Model schematic to compare mode of birth for women in labour with a suspected large for gestational age baby



CS = caesarean section; ICH = intracranial haemorrhage; NICU = neonatal intensive care unit

Setting and population

The model setting was the NHS and the population was women in labour with a suspected large-for-gestational-age baby (>4000 g), although the clinical effectiveness data used in the model was based on a retrospective analysis of births where the birthweight was known. Subgroup analysis was undertaken for women with babies with birthweight:

- 4000 g to 4499 g
- 4500 g to 4999 g
- ≥5000 g

Clinical outcomes

Outcomes were limited to those reported in studies included in the review of clinical evidence undertaken for this guideline. Shoulder dystocia was not included in the model as it was thought that there would be issues with double counting given its relationship to brachial plexus injury, which was included. Clavicle injuries were not included in the model as they are normally self-limiting (that is, there is no need for treatment). Asphyxia and convulsions were also not included in the model as it was considered that these would be closely related to the included outcome of intracranial haemorrhage (ICH). Neonatal mortality or stillbirth was not included as there was no event data for these in any of the included studies.

The 7 outcomes included in the base-case model are listed below:

- brachial plexus injury
- anal incontinence
- urinary incontinence
- third- or fourth-degree perineal lacerations
- haemorrhage
- ICH
- admission to the neonatal intensive care unit (NICU).

The model was constructed in such a way that it could be run with or without any of the outcomes listed above as part of a sensitivity analysis.

All outcomes included in the analysis were assumed to have an associated cost. Additionally, all outcomes other than admission to NICU were assumed to be associated with a loss in health-related quality of life (HRQoL) for the woman or the baby. No HRQoL was assumed for NICU admission as it was considered there would be double counting with other outcomes for the baby that would result in a NICU admission.

Baseline

The baseline risks associated with a continuation of labour were estimated from the studies in the clinical review undertaken for this guideline. These values are presented in Table 30 below. It was assumed that 10% of brachial plexus injuries would lead to permanent disability (Gherman 1998). This was treated as a deterministic variable in PSA but could be varied through a sensitivity analysis.

Table 30: Baseline event probabilities and parameters for probabilistic sensitivity analysis

Outcome (birthweight category)	Probability	Alpha	Beta	Source
Brachial plexus injury (≥4000 g)	0.0059	1,154	194,176	Aberg 2016
Brachial plexus injury (4000-4499 g)	0.0036	563	157,817	Aberg 2016
Brachial plexus injury (4500-4999 g)	0.0127	407	31,615	Aberg 2016
Brachial plexus injury (≥5000 g)	0.0457	184	3,844	Aberg 2016
Anal incontinence	0.1852	25	110	Vercellini 2015
Urinary incontinence	0.4148	56	79	Vercellini 2015
Perineal lacerations	0.1484	19	109	Lipscomb 1995 [a]
Haemorrhage	0.1486	41	235	Vercellini 2015 [a]
ICH (>4000 g)	0.0003	56	195,274	Aberg 2016
ICH (4000-4499 g)	0.0003	41	149,239	Aberg 2016
ICH (4500-4999 g)	0.0004	12	32,019	Aberg 2016
ICH (>5000 g)	0.0007	3	4,025	Aberg 2016
Admission to NICU	0.0136	8	581	Menticoglou 1992

a As meta-analysis was not undertaken the study with the largest number of participants was used where more than 1 study reported on a particular outcome; meta-analysis was not undertaken as these were observational studies, see Supplement 1 (Methods)

It was assumed that a proportion of women where the decision made to continue with labour, would nevertheless ultimately require an emergency caesarean section. Also, a proportion who give birth vaginally would require assisted birth. The values used in the model for the actual mode of birth for women, where the decision is made to continue with labour are provided in Table 31.

Table 31: Actual mode of birth probability for women continuing with labour with a suspected large-for-gestational-age baby

Mode of birth	Probability	Source
Unassisted vaginal birth	0.40	Vercellini 2015, https://www.babycentre.co.uk/a1015615/macrosomia-big-baby (accessed 06/07/2018) [a]
Assisted vaginal birth	0.20	https://www.babycentre.co.uk/a1015615/macrosomia-big-baby (accessed 06/07/2018)
Emergency caesarean section	0.40	Vercellini 2015

a In Vercellini 2015, 40% of women had an emergency caesarean section and 60% had a vaginal birth, but this was not broken down further. The proportion of assisted vaginal births was estimated from an alternative source cited in the table and unassisted vaginal birth was assumed to account for the remainder

Treatment effectiveness

The relative treatment effects were estimated from the studies included in the clinical systematic review undertaken for this guideline. Table 32 presents the relative treatment effects for the model's 7 outcomes along with their 95% CIs. These relative treatment effects were applied to the baseline risk in order to estimate the risk of each outcome for women in labour with a suspected large-for-gestational-age baby who has an emergency caesarean section. It should be noted that these relative treatment effects are based on a retrospective comparison of women who had an emergency caesarean section compared to those had a

vaginal birth when the birthweight was known. This is not the same as a treatment effect among women randomised to continuation of labour (with a mixture of vaginal and emergency caesarean section as the actual mode of birth) or emergency caesarean section, which would be the ideal comparison of interest for decision making purposes.

Table 32: Relative treatment effect for emergency caesarean section in women in labour with a suspected large-for-gestational-age baby

Outcome (birthweight category)	Risk ratio	Lower limit of 95% CI	Upper limit of 95% CI	Source
Brachial plexus injury (≥4000 g)	0.05	0.02	0.12	Aberg 2016
Brachial plexus injury (4000-4499 g)	0.08	0.03	0.22	Aberg 2016
Brachial plexus injury (4500-4999 g)	0.03	0.01	0.14	Aberg 2016
Brachial plexus injury (≥5000 g)	0.01	0.00	0.18	Aberg 2016
Anal incontinence	0.33	0.13	0.82	Vercellini 2015
Urinary incontinence	0.35	0.20	0.61	Vercellini 2015
Perineal lacerations	0.09	0.01	1.49	Lipscom 1995
Haemorrhage	0.70	0.36	1.36	Vercellini 2015
ICH (>4000 g)	1.43	0.68	2.99	Aberg 2016
ICH (4000-4499 g)	1.67	0.71	3.92	Aberg 2016
ICH (4500-4999 g)	1.16	0.26	5.19	Aberg 2016
ICH (>5000 g)	0.59	0.03	11.35	Aberg 2016
NICU	2.79	0.93	8.39	Menticoglou 1992

For PSA the relative treatment effects were sampled using a log-normal distribution, using the distribution parameters presented in Table 33, and the standard deviation estimated from the CIs reported in Table 32.

Table 33: Parameters of log-normal distribution for sampling relative treatment effect for emergency caesarean section in women in labour with a suspected large-for-gestational-age baby

Outcome (birthweight category)	Mean	Standard deviation
Brachial plexus injury (≥4000 g)	Ln (0.05)	(Ln (0.12) – Ln (0.05)) ÷ 1.96
Brachial plexus injury (4000-4499 g)	Ln (0.08)	(Ln (0.22) – Ln (0.08)) ÷ 1.96
Brachial plexus injury (4500-4999 g)	Ln (0.03)	(Ln (0.14) – Ln (0.03)) ÷ 1.96
Brachial plexus injury (≥5000 g)	Ln (0.01)	(Ln (0.18) – Ln (0.01)) ÷ 1.96
Anal incontinence	Ln (0.33)	(Ln (0.82) – Ln (0.33)) ÷ 1.96
Urinary incontinence	Ln (0.35)	(Ln (0.61) – Ln (0.35)) ÷ 1.96
Perineal lacerations	Ln (0.09)	(Ln (1.49) – Ln (0.09)) ÷ 1.96
Haemorrhage	Ln (0.70)	(Ln (1.36) – Ln (0.70)) ÷ 1.96
ICH (>4000 g)	Ln (1.43)	(Ln (2.99) – Ln (1.43)) ÷ 1.96
ICH (4000-4499 g)	Ln (1.67)	(Ln (3.92) – Ln (1.67)) ÷ 1.96
ICH (4500-4999 g)	Ln (1.16)	(Ln (5.19) – Ln (1.16)) ÷ 1.96
ICH (>5000 g)	Ln (0.59)	(Ln (11.35) – Ln (0.59)) ÷ 1.96
NICU	Ln (2.79)	(Ln (8.39) – Ln (2.79)) ÷ 1.96

Costs

In accordance with NICE methodology a NHS and PSS perspective was adopted for this analysis (https://www.nice.org.uk/Media/Default/About/what-we-do/our-programmes/developing-NICE-guidelines-the-manual.pdf). Costs were based on a 2016/17 price year reflecting the most recently available NHS Reference Costs at the time of writing. Costs occurring around the time of the birth were not discounted. Costs that occurred over-time were derived from the literature, and were discounted but not at the 3.5% discount recommended for NICE guidelines (https://www.nice.org.uk/Media/Default/About/what-we-do/our-programmes/developing-NICE-guidelines-the-manual.pdf). This was because the studies were not undertaken in the UK.

The costs used in the analysis are presented in Table 34 alongside their parameters for PSA where applicable.

Table 34: Costs associated with eventual mode of birth and model outcomes

Variable	Cost	Standard error	Distribution	Source
Unassisted vaginal birth	£2,297 [b]	£70 [c]	Normal	NHS Reference Costs, 2016-17 (NHS Improvement)
Assisted vaginal birth	£3,367 [b]	£123 [c]	Normal	NHS Reference Costs, 2016-17 (NHS Improvement)
Emergency caesarean section	£4,781 [b]	£98 [c]	Normal	NHS Reference Costs, 2016-17 (NHS Improvement)
Brachial plexus injury – transient	£685 [b]	£28 [c]	Normal	NHS Reference Costs, 2016-17 (NHS Improvement)
Brachial plexus injury – permanent [a]	£12,487	-	Deterministic	Ohno 2011, Unit Costs of Health and Social Care (PSSRU, 2017) [d]
Anal incontinence	£3,164	-	Deterministic	Culligan 2004, Unit Costs of Health and Social Care (PSSRU, 2017) [e]
Urinary incontinence	£16,276	-	Deterministic	Culligan 2004, Unit Costs of Health and Social Care (PSSRU, 2017) [f]
Perineal lacerations	£11	-	Deterministic	Culligan 2004, Unit Costs of Health and Social Care (PSSRU, 2017) [g]
Haemorrhage	£15,963	-	Deterministic	Pourat 2013, Unit Costs of Health and Social Care (PSSRU, 2017) [h]
ICH	£24,444	-	Deterministic	NICE 2015, Unit Costs of Health and Social Care (PSSRU, 2017) [i]
NICU	£705 [b]	£20 [c]	Normal	NHS Reference Costs, 2016-17 (NHS Improvement)

a NHS Reference Cost Currency Code PB04, Neonatal Diagnoses, Admitted from Other Location or Born in Hospital
b Weighted average of all relevant currency codes
c The method of estimating a standard error from data included in NHS Reference Costs is described in detail in https://www.nice.org.uk/guidance/ng3. A standard error was estimated for each relevant NHS Reference Cost category and currency code and a pooled standard error was then estimated by weighting according to finished consultant episodes
d A reported cost of 15,299 USD in 2009 prices was converted into 2016/17 prices using the hospital and community health services (HCHS) index. It was then converted into UK currency using an exchange rate of £1 = $1.42, reported by HM Revenue and Customs (HMRC). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/702273/exrates-monthly-0518.csv/preview (accessed 01/05/2018). Costs were discounted at 3% (Culligan 2004)

e A reported cost of 2,927 USD in 2001 prices was converted into 2016/17 prices using the hospital and community health services (HCHS) index. It was then converted into UK currency using an exchange rate of £1 = $1.42, reported by HM Revenue and Customs (HMRC). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/702273/exrates-monthly-0518.csv/preview (accessed 01/05/2018). Costs were discounted at 3% (Culligan 2004)
f A reported cost of 15,059 USD in 2001 prices was converted into 2016/17 prices using the hospital and community health services (HCHS) index. It was then converted into UK currency using an exchange rate of £1 = $1.42, reported by HM Revenue and Customs (HMRC). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/702273/exrates-monthly-0518.csv/preview (accessed 01/05/2018). Costs were discounted at 3% (Culligan 2004)
g A reported cost of 10 USD in 2001 prices was converted into 2016/17 prices using the hospital and community health services (HCHS) index. It was then converted into UK currency using an exchange rate of £1 = $1.42, reported by HM Revenue and Customs (HMRC). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/702273/exrates-monthly-0518.csv/preview (accessed 01/05/2018).
h A derived cost of 20,798 USD in 2011 prices was converted into 2016/17 prices using the hospital and community health services (HCHS) index. It was then converted into UK currency using an exchange rate of £1 = $1.42, reported by HM Revenue and Customs (HMRC). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/702273/exrates-monthly-0518.csv/preview (accessed 01/05/2018). Costs were discounted at 3% (Culligan 2004)
I It was assumed that the cost of ICH was the same as the 23,700 GBP cost of Intraventricular haemorrhage reported in the NICE guideline on Preterm labour and birth (https://www.nice.org.uk/guidance/ng25/evidence/full-guideline-pdf-2176838029). This was converted into 2016/17 prices using the hospital and community health services (HCHS) index. The original paper from which the cost of IVH was estimated discounted costs at 5% (Kruse 2009).

Quality adjusted life years

The QALY loss associated with the model outcomes are presented in Table 35. QALYs derived from a lifelong loss in health state utility were discounted at a rate of 3.5% in line with the NICE guidelines manual (https://www.nice.org.uk/Media/Default/About/what-we-do/our-programmes/developing-NICE-guidelines-the-manual.pdf). Remaining life expectancy for the woman and the baby was estimated from national life tables for England 2014-16 (ONS 2017, https://www.ons.gov.uk/releases/nationallifetablesuk2014to2016). For babies this was 81 years and for women it was estimated at 54 years, based on a mean maternal age at birth of the child of 30 years (ONS 2017, https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/bulletins/birthsbyparentscharacteristicsinenglandandwales/2016).

Table 35: Quality adjusted life year losses associated with model outcomes

Outcome	QALY loss	Source
Brachial plexus injury - transient	0.00167	Culligan 2004 [a]
Brachial plexus injury - permanent	11.10	Culligan 2004 [b]
Anal incontinence	12.50	Culligan 2004 [c]
Urinary incontinence	7.50	Culligan 2004 [d]
Perineal lacerations	0.00	Assumption
Haemorrhage	1.00	Culligan 2004 [e]
ICH	2.80	NICE 2015 [f]

a Estimate based a loss of health state utility of 0.01 over 2 months
b Estimate based on a loss of health state utility of 0.4 for the baby with a lifelong duration
c Estimate based on a loss of health state utility of 0.5 for the woman with a lifelong duration
d Estimate based on a loss of health state utility of 0.3 for the woman with a lifelong duration
e Estimate based on a loss of health state utility of 0.04 for the woman with a lifelong duration
f Based on QALY loss used for ICH in the NICE guideline on Preterm labour and birth

Uncertainty

PSA was undertaken using Monte Carlo simulation in order to reflect uncertainty in model input parameters. This involved sampling model inputs from a probability distribution that reflected the uncertainty around point estimates for model parameters. Mean costs and QALYs were calculated across all simulations and, as a summary measure of cost effectiveness, a mean iNMB was calculated based on a cost effectiveness threshold of £20,000 per QALY.

One-way deterministic sensitivity analysis was undertaken to explore which model inputs contributed most to the model results and where uncertainty with respect to the true model parameter was likely to be the most important. These results are presented in a Tornado diagram which is intended to give some insight as to which are the most important variables in driving the model results. They indicate how a 'low' value and a 'high' value for a particular model input would change the model result when compared to the base-case value. The Tornado diagrams presented here show the variables in ascending order of importance although some caution should be exercised in interpreting this ordering as low or high values may not always have been selected consistently across all variables.

Tornado diagram inputs

In order to assess the importance of particular inputs, uncertainty was assessed using one-way sensitivity analysis and presented in a Tornado diagram. The model inputs included in the Tornado analysis with the range of values used are presented in Table 36.

Table 36: Tornado analysis inputs and values

Variable	Low value	High Value
Probability of emergency caesarean section after continuation of labour	0.05	0.60
Baseline anal incontinence probability	0.02	0.25
Baseline urinary incontinence probability	0.05	0.70
Cost of brachial plexus injury permanent	£2,000	£50,000
Cost of anal incontinence	£500	£20,000
Cost of urinary incontinence	£500	£50,000
Cost of haemorrhage	£500	£50,000
Cost of ICH	£10,000	£100,000
QALY loss from brachial plexus injury permanent	2	15
QALY loss from anal incontinence	2	15
QALY loss from urinary incontinence	1	10
QALY loss from haemorrhage	0.05	5
QALY loss from ICH	1	20
Risk ratio brachial plexus injury	0.00	0.18
Risk ratio anal incontinence	0.13	0.82
Risk ratio urinary incontinence	0.20	0.61
Risk ratio haemorrhage	0.36	1.36
Risk ratio ICH	0.03	11.35
Risk ratio NICU	0.93	8.39

Continuation of labour is likely to save some costs with respect to birth but the extent it achieves this will depend on the eventual mode of birth and therefore the probability of emergency caesarean section rate in women in labour with a suspected large-for-gestational-age-baby was included to assess the impact birth costs had on cost effectiveness.

The baseline probability of anal and urinary incontinence were high and the QALY losses associated with these outcomes were substantial, which might not reflect the severity of these conditions for all women across the remaining life expectancy. Therefore, the baseline probability of anal and urinary incontinence were both included in the Tornado analysis.

All deterministic outcomes that had a high cost were included in the Tornado analysis to reflect the large uncertainty that probably exists around the point estimate. Similarly outcomes that had a high associated QALY loss were included.

The range of values chosen for the Tornado analysis was intentionally wide, in order to increase the likelihood that the true value was captured. Furthermore, it was considered useful to assess how sensitive the model was to very large changes in the values of the included variables. However, the exact range was arbitrary to some extent.

Results

Base case

Probabilistic sensitivity analysis

A total of 10,000 Monte Carlo simulations were run with deterministic variables at their base-case value and additionally for each of the subgroups based on eventual birthweight. The results are presented in Table 37. The cost effectiveness plane for each base-case probabilistic analysis is shown in Figure 16, Figure 17, Figure 18 and Figure 19.

Table 37: Mean incremental costs, quality adjusted life years and net monetary benefit of emergency caesarean section compared to continuation of labour for women in labour with a suspected large-for-gestational-age baby – base case

Analysis birthweight	Mean incremental costs of emergency CS	Mean incremental QALYs of emergency CS	Mean iNMB	Probability cost effective	ICER
Brachial plexus injury ≥4000g	-£3,999	3.47	£73,555	100%	Emergency CS dominates
Brachial plexus injury 4000-4499g	-£3,982	3.49	£73,718	99.99%	Emergency CS dominates
Brachial plexus injury 4500-4999g	-£3,993	3.48	£73,640	99.99%	Emergency CS dominates
Brachial plexus injury ≥5000g	-£4,050	3.53	74,772	100%	Emergency CS dominates

CS = caesarean section, QALY = quality adjusted life years, iNMB = incremental net monetary benefit, ICER = incremental cost effectiveness ratio

Figure 16: Cost effectiveness plane for base-case analysis, birthweight ≥ 4000 g

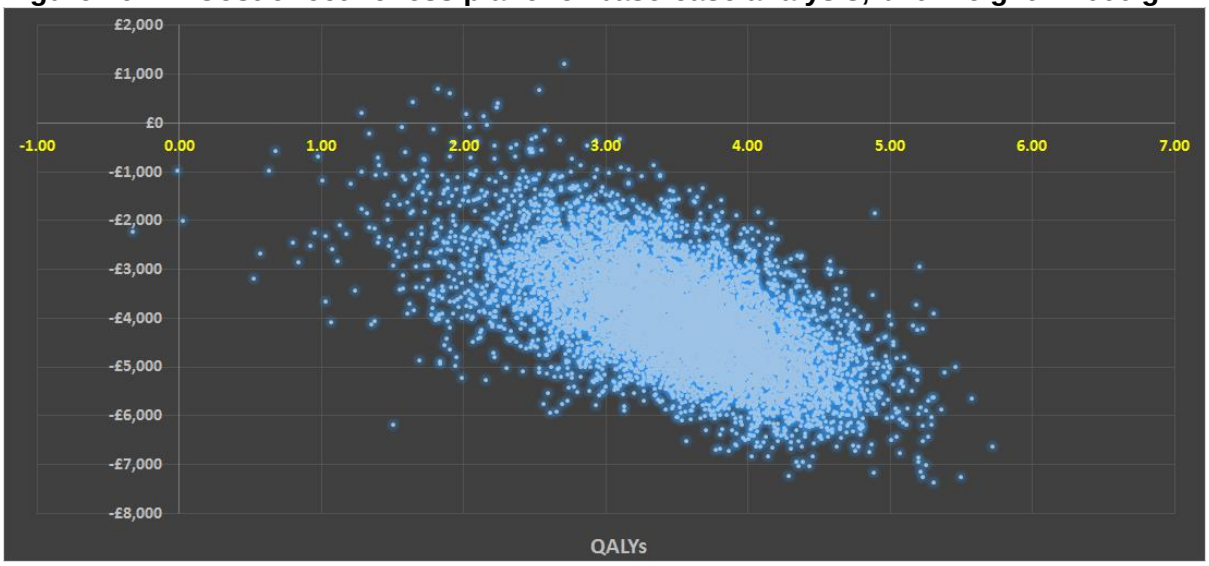


Figure 17: Cost effectiveness plane for base-case analysis, birthweight 4000 g-4499 g

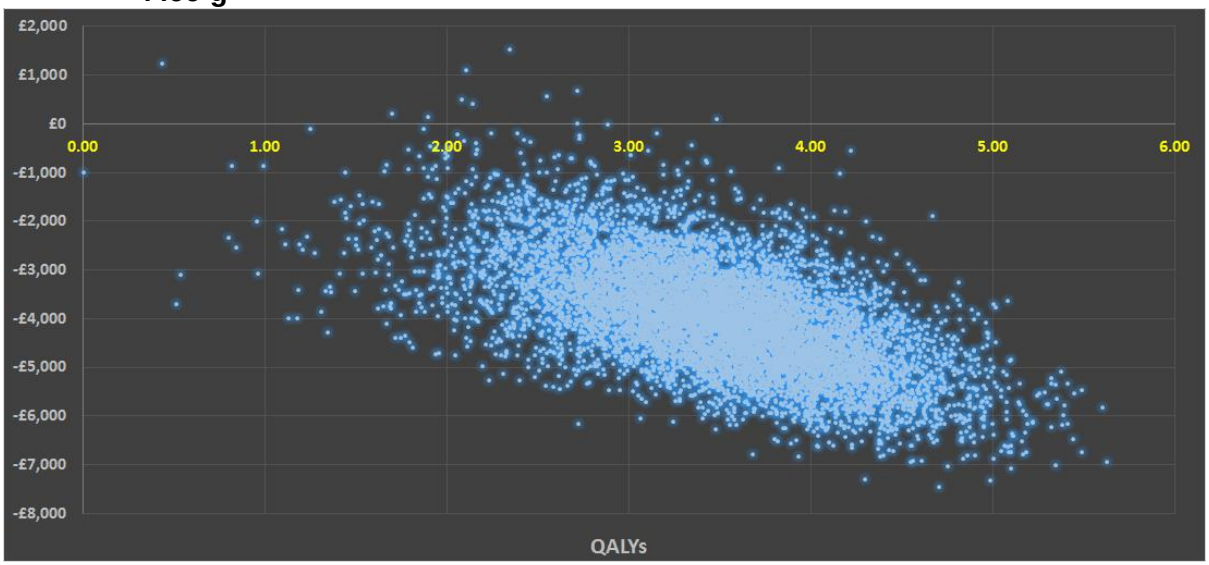


Figure 18: Cost effectiveness plane for base-case analysis, birthweight 4500 g to 4999 g

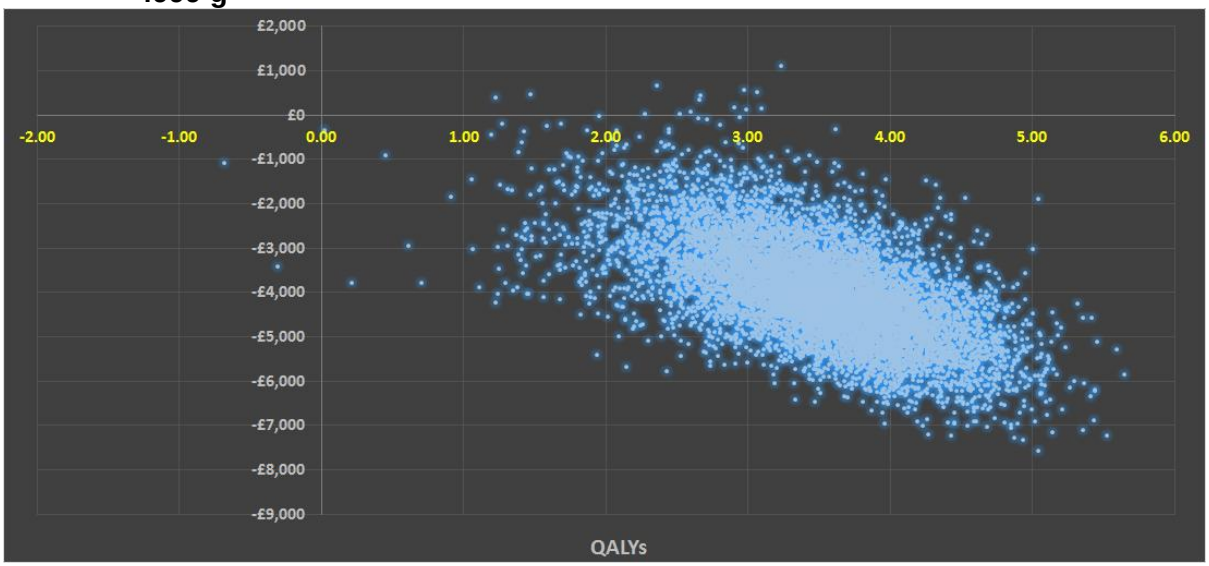
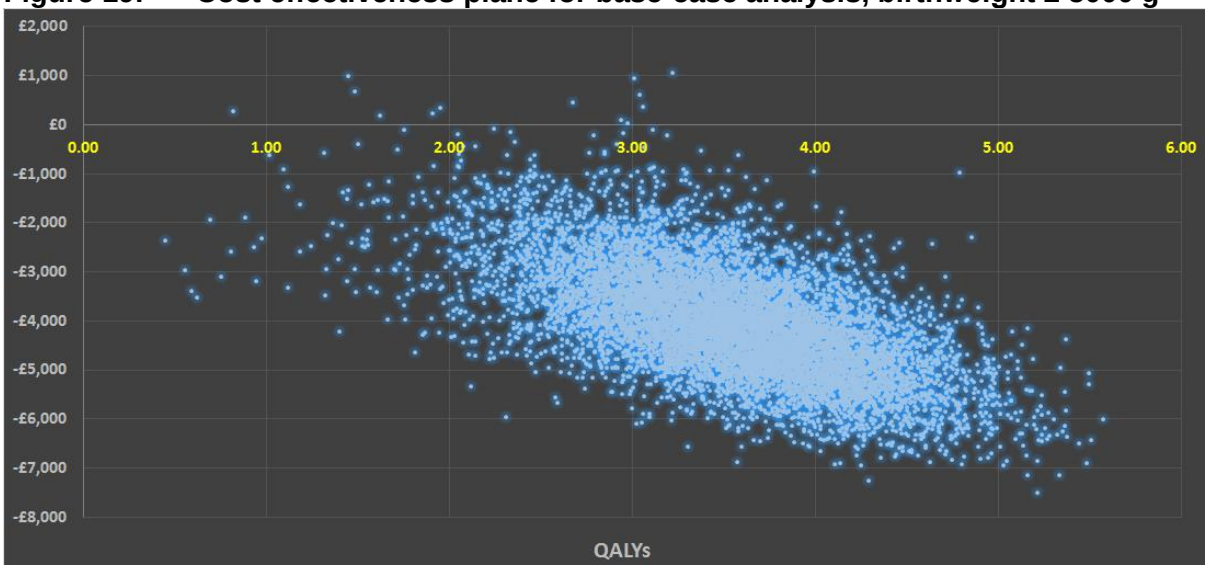


Figure 19: Cost effectiveness plane for base-case analysis, birthweight ≥ 5000 g



Base-case deterministic analysis

The results of the deterministic analysis are presented in Table 38. The breakdown of incremental costs and QALYs for babies with a birthweight greater than 5000 g is illustrated in Figure 20 and Figure 21.

Table 38: Comparison of incremental costs, quality adjusted life years and incremental cost effectiveness ratios of emergency caesarean section compared to continuation of labour for women in labour with a suspected large for gestational age baby – base case

Analysis birthweight	Incremental Costs of emergency CS	Incremental QALYs of emergency CS	ICER	iNMB
Brachial plexus injury ≥4000g	-£4,208	3.62	Emergency CS dominates	£76,680
Brachial plexus injury 4000-4499g	-£4,202	3.61	Emergency CS dominates	£76,620
Brachial plexus injury 4500-4999g	-£4,222	3.63	Emergency CS dominates	£76,847
Brachial plexus injury ≥5000g	-£4,292	3.67	Emergency CS dominates	£77,669

ICER = incremental cost effectiveness ratio; iNMB = incremental net monetary benefit

Figure 20: Graph to show incremental costs of emergency caesarean section by category for women with a baby ≥ 5000 g

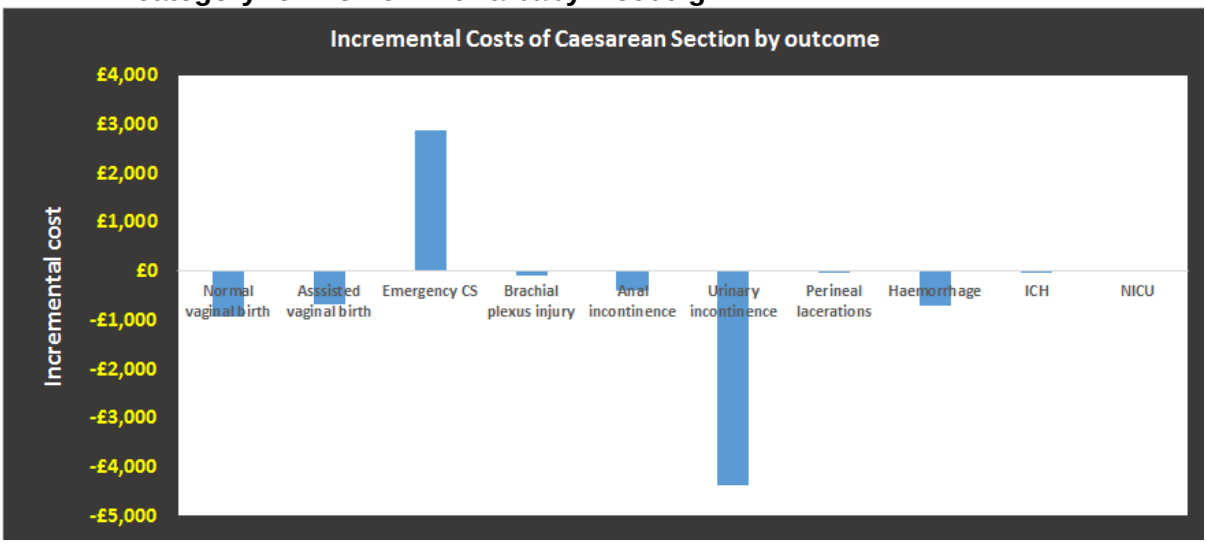
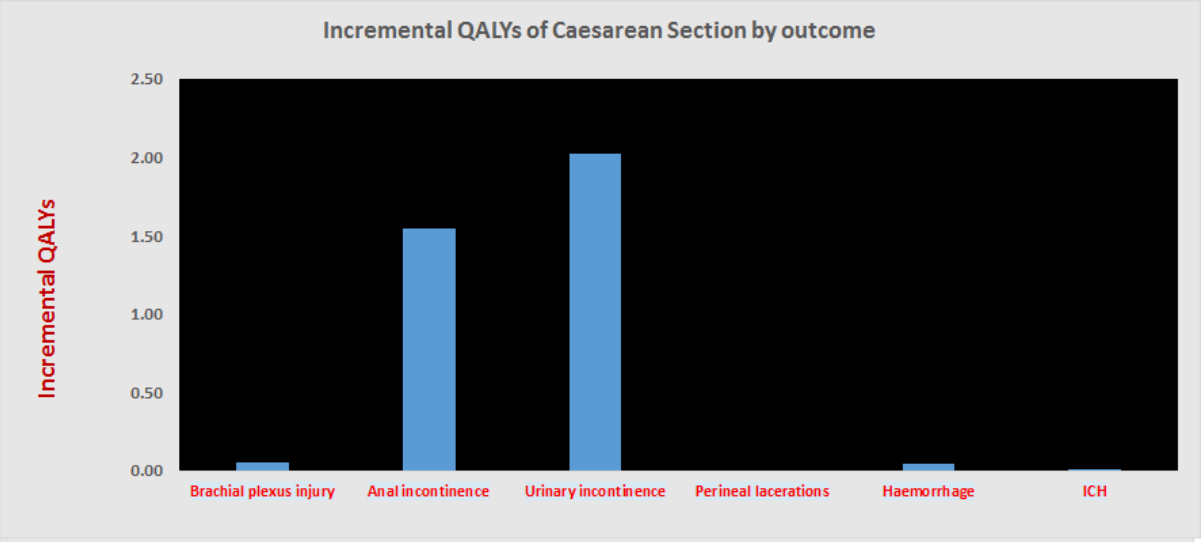


Figure 21: Graph to show incremental costs of emergency caesarean section by outcome for women with a baby ≥ 5000 g



Tornado analysis

A Tornado analysis was undertaking by varying one input value at a time according to the low and high values shown in Table 9 for babies with a birthweight >5000 g. The results of this analysis are shown in Figure 22, Figure 23 and Figure 24.

Figure 22: Tornado diagram indicating how the net monetary benefit of emergency caesarean section compared with continuation of labour changes in response to changes in the input parameters of selected variables (larger change in net monetary benefit) – base case

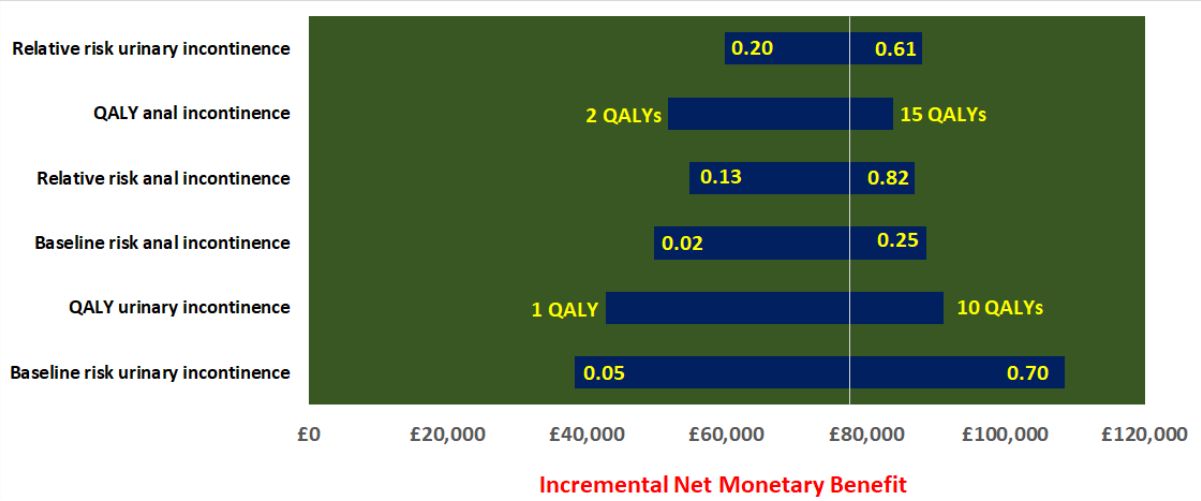


Figure 23: Tornado diagram indicating how the net monetary benefit of emergency caesarean section compared with continuation of labour changes in response to changes in the input parameters of selected variables (smaller change in net monetary benefit) – base case

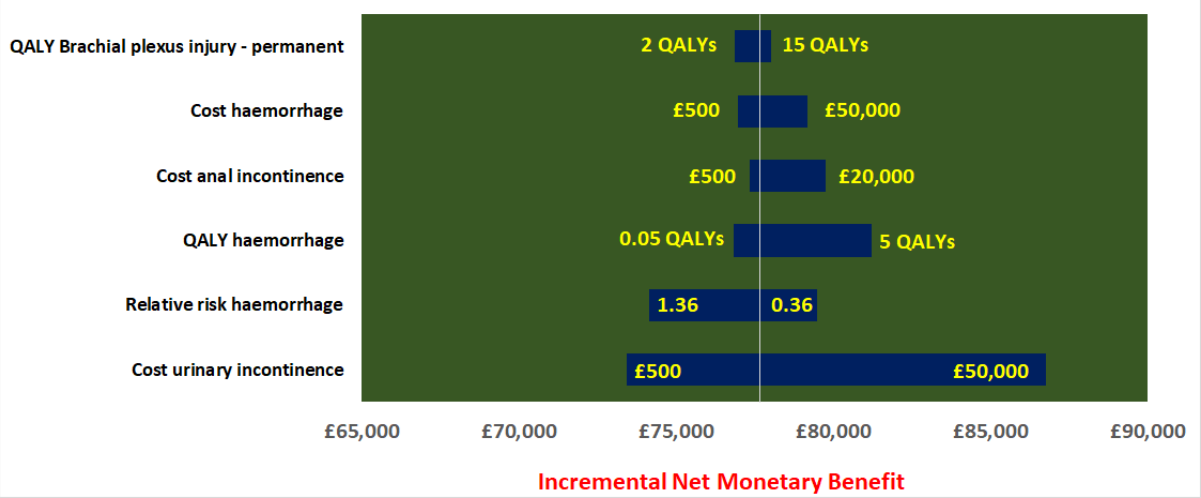


Figure 24: Tornado diagram indicating how the net monetary benefit of emergency caesarean section compared with continuation of labour changes in response to changes in the input parameters of selected variables (least change in net monetary benefit) – base case

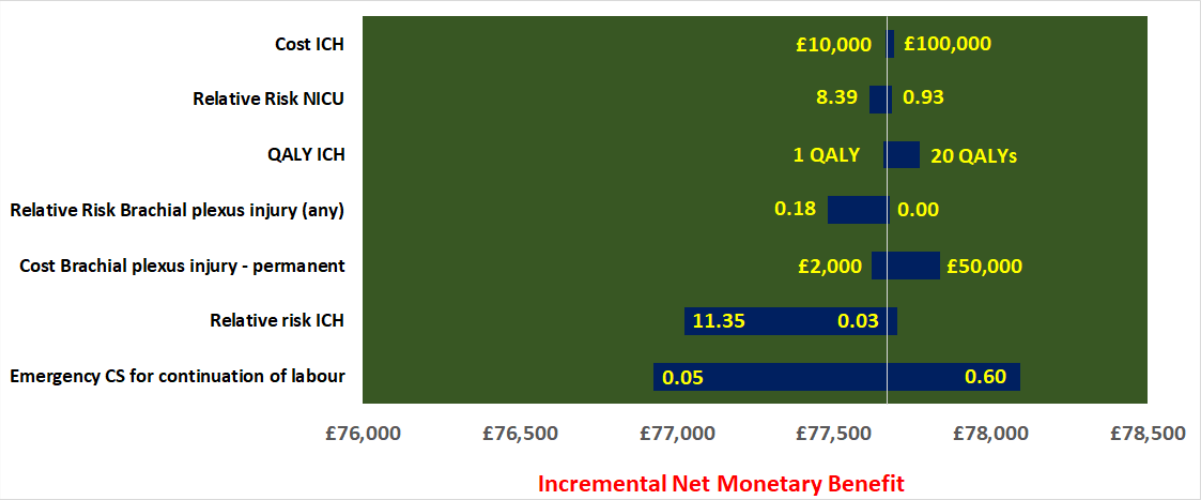


Figure 22 shows the variables where varying the input has the largest impact on iNMB. Note that the iNMB scale for Figure 23 covers a much narrower range of iNMB values compared to those in Figure 22 and Figure 24.

Sensitivity analysis excluding anal and urinary incontinence from the model

The PSA results, based on 10,000 Monte Carlo simulations, are presented in Table 39. The equivalent deterministic results are presented in Table 40.

Table 39: Mean incremental costs, quality adjusted life years and net monetary benefit of emergency caesarean section compared to continuation of labour for women in labour with a suspected large-for-gestational-age baby – anal and urinary incontinence excluded from the model (probabilistic sensitivity analysis)

Analysis birthweight	Mean incremental cost of emergency CS	Mean incremental QALYs of emergency CS	Mean iNMB	Probability cost effective	ICER
Brachial plexus injury ≥4000g	£677	0.044	£215	62.3%	£15,177 per QALY
Brachial plexus injury 4000-4499g	£675	0.042	£172	60.7%	£15,934 per QALY
Brachial plexus injury 4500-4999g	£670	0.052	£361	65.5%	£12,944 per QALY
Brachial plexus injury ≥5000g	£614	0.086	£1,107	81.0%	£7,136 per QALY

CS = caesarean section, ICER = incremental cost effectiveness ratio, iNMB = incremental net monetary benefit, QALY = quality adjusted life year,

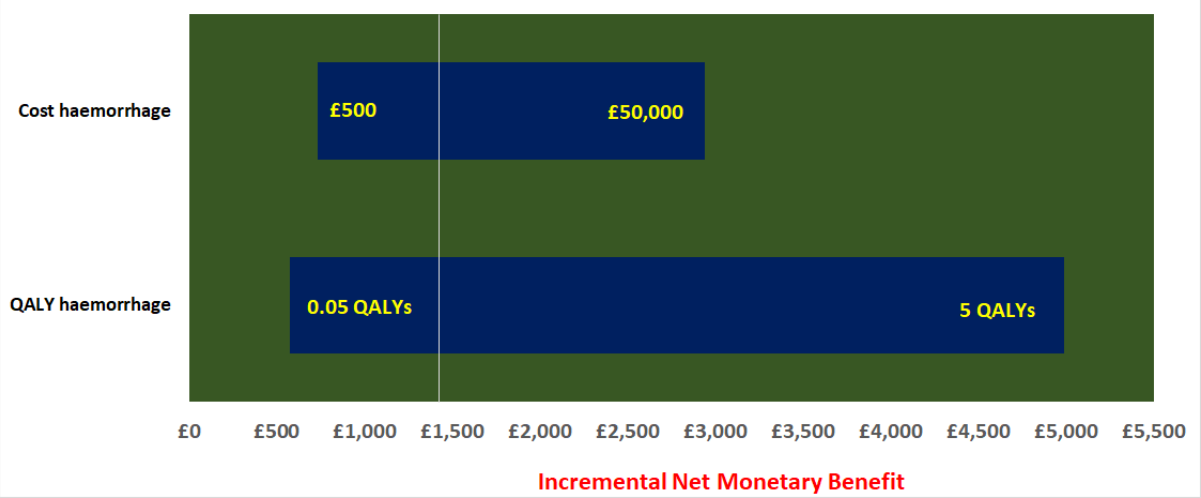
Table 40: Comparison of incremental costs, quality adjusted life years and incremental cost effectiveness ratios of emergency caesarean section compared to continuation of labour for women in labour with a suspected large-for-gestational-age baby – anal and urinary incontinence excluded from the model (deterministic analysis)

Analysis birthweight	Incremental costs of emergency CS	Incremental QALYs of emergency CS	ICER	iNMB
Brachial plexus injury ≥4000g	£567	0.051	£11,029 per QALY	£461
Brachial plexus injury 4000-4499g	£572	0.049	£11,718 per QALY	£404
Brachial plexus injury 4500-4999g	£553	0.059	£9,383 per QALY	£626
Brachial plexus injury ≥5000g	£489	0.096	£5,108 per QALY	£1,425

CS = caesarean section, ICER = incremental cost effectiveness ratio; iNMB = incremental net monetary benefit, QALY = quality adjusted life year

A Tornado analysis displayed in Figure 25 demonstrated the impact of varying the cost and QALY loss from haemorrhage with urinary and anal incontinence excluded from the analysis.

Figure 25: Tornado diagram indicating how the net monetary benefit of emergency caesarean section compared with continuation of labour changes in response to changes in the input parameters of selected variables – anal and urinary incontinence excluded from the model



Sensitivity analysis restricting model outcomes to brachial plexus injuries and intracranial haemorrhage

This sensitivity analysis was restricted to outcomes for which there was different baseline and treatment effectiveness data according to birthweight (that is, brachial plexus injuries and intracranial haemorrhage). The probabilistic analysis is shown in Table 41 and Figure 26 shows the CEAC for the analysis for the subgroup of babies with a birthweight of at least 5000 g. The deterministic results for this sensitivity analysis are presented in Table 42.

Table 41: Mean incremental costs, quality adjusted life years and ne monetary benefit of emergency caesarean section compared to continuation of labour for women in labour with a suspected large for gestational age baby – model outcomes restricted to brachial plexus injuries and intracranial haemorrhage

Analysis birthweight	Mean incremental costs of emergency CS	Mean incremental QALYs of emergency CS	Mean iNMB	Probability cost effective	ICER
Brachial plexus injury ≥4000g	£1,264	0.007	-£1,133	0.00%	£192,624 per QALY
Brachial plexus injury 4000-4499g	£1,272	0.004	-£1,194	0.00%	£329,619 per QALY
Brachial plexus injury 4500-4999g	£1,253	0.014	-£980	0.00%	£91,573 per QALY

Analysis birthweight	Mean incremental costs of emergency CS	Mean incremental QALYs of emergency CS	Mean iNMB	Probability cost effective	ICER
Brachial plexus injury ≥5000g	£1,208	0.048	-£254	5.1%	£25,316 Per QALY

CS = caesarean section, QALY = quality adjusted life year, iNMB = incremental net monetary benefit

Figure 26: Cost effectiveness acceptability curve for women with a large-for-gestational-age baby ≥ 5000 g

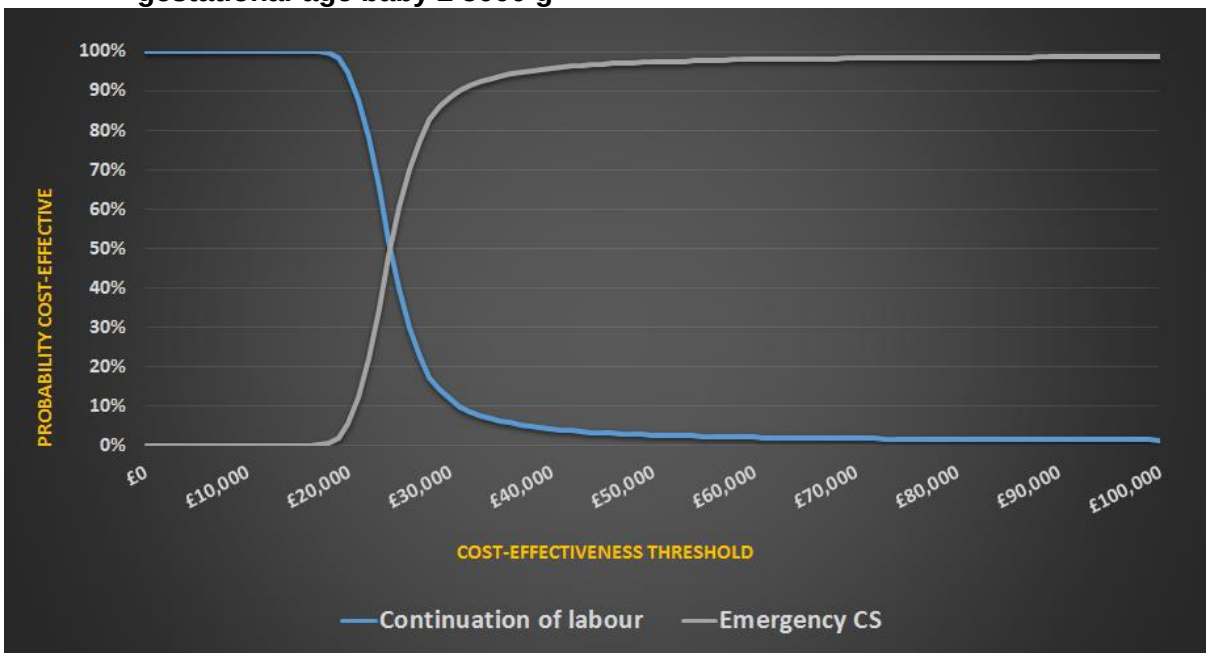


Table 42: Comparison of incremental costs, quality adjusted life years and incremental cost effectiveness ratios of emergency caesarean section compared to continuation of labour for women in labour with a suspected large-for-gestational-age baby – model outcomes restricted to brachial plexus injuries and intracranial haemorrhage

Analysis birthweight	Incremental costs of emergency CS	Incremental QALYs of emergency CS	ICER	iNMB
Brachial plexus injury ≥4000g	£1,269	0.006	£215,323 per QALY	-£1,151
Brachial plexus injury 4000-4499g	£1,275	0.003	£404,336 per QALY	-£1,211
Brachial plexus injury 4500-4999g	£1,255	0.014	£92,709 per QALY	-£984
Brachial plexus injury ≥5000g	£1,185	0.051	£23,172 per QALY	-£162

ICER = incremental cost effectiveness ratio; iNMB = incremental net monetary benefit

Discussion

The clinical evidence which informed this analysis has important limitations. Ideally the clinical data for this analysis would be underpinned by a randomised study design where women in labour with a suspected large-for-gestational-age baby would be randomised to continue with labour or to have an emergency caesarean section. Such a randomised study would represent the decision that is being assessed in this economic evaluation.

However, in the context of the intrapartum period such randomisation is unlikely ever to be feasible. Therefore the included studies were retrospective and compared the outcomes of women who had an emergency caesarean section with those who continued with labour. Such studies are at a high risk of bias as women who have an emergency caesarean section might have an indication for operative birth unrelated to any suspicion of the baby being large for gestational age. Therefore, the women are likely as a population to differ systematically from those who continue with labour. In addition, the included studies reflect outcomes based on eventual birthweight rather than a suspicion of large for gestational age. A clinical diagnosis of large for gestational age is inaccurate and in reality the baby will frequently not be large for gestational age. Conversely, in many cases where the baby is large for gestational age and a birth complication arises, a clinical diagnosis of large for gestational age will not be suspected, although that population was not considered by this analysis.

The base-case analysis suggests that it would be cost effective to offer emergency caesarean section to women in labour with a suspected large-for-gestational-age baby. The deterministic analysis (see Table 38) suggests that emergency caesarean section dominates continuation of labour, being cheaper and more effective, and that this is true for all birthweight subgroups. As expected, the deterministic analysis also shows that cost effectiveness as measured by iNMB increases with increasing birthweight. However, the gradient of this effect is very small. Even in the subgroup where babies had a birthweight of less than 4500 g, the iNMB was £76,620 and almost as high as in the subgroup where babies had a birthweight of at least 5000 g. This is likely to be explained by the importance that the outcomes of anal and urinary incontinence have in driving the overall cost effectiveness results as shown in the Tornado analysis (see Figure 22) and the sensitivity analysis which excluded both outcomes. In the model, neither baseline probability or relative treatment effect for anal and urinary incontinence were varied according to birthweight. Therefore the large absolute impact of anal and urinary incontinence in the analysis was not modified by birthweight and dwarfs any absolute effect of brachial plexus injury and ICH for which the risks are differentiated by birthweight categories.

The PSA for the base-case analysis also suggests that emergency caesarean section is cost effective compared to continuation of labour for women with a suspected large-for-gestational-age baby (see Table 37). Across all subgroups the probability of emergency caesarean section being cost effective is over 99% with a similar iNMB to that found in the deterministic analysis. However, it is less clear in the PSA that the cost effectiveness of emergency caesarean section increases as the birthweight of the baby increases. This is counter-intuitive but is probably explained by the wide CIs for treatment effects, especially for the subgroup analysis, which resulted in the occasional sampling of extreme outliers in terms of relative treatment effect.

A sensitivity analysis was undertaken which excluded urinary and anal incontinence outcomes from the analysis. The committee had reservations about these outcomes. In particular, they questioned the extent to which it can be assumed that these outcomes would relate to a bladder or bowel injury. The base-case analysis indicated that these outcomes were key drivers of the results and dwarfed any effects for other outcomes arising from

birthweight. The probabilistic analysis for this scenario is reported in Table 39 and the deterministic results are shown in Table 40. The analysis continues to show that emergency caesarean section is cost effective. However, it no longer dominates continuation of labour and the iNMB is hugely reduced. Both deterministic and probabilistic analyses indicate increasing cost effectiveness with larger birthweight.

A final sensitivity analysis was restricted to the outcomes of brachial plexus injury and ICH, as both of these had baseline probabilities and treatment effect sizes differentiated by birthweight categories. This sensitivity analysis suggested that continuation of labour could be cost effective (see Table 41). It also showed that the benefits, and cost effectiveness, of emergency caesarean section increased with increasing birthweight. Although the probability of emergency caesarean section being cost effective was only 5.1% even for babies of a birthweight greater than or equal to 5000 g, the CEAC depicted in Figure 26 shows that this result was very sensitive to the cost effectiveness threshold in the region of £20,000 to £30,000 per QALY.

There are many important limitations in the data underpinning this model and therefore considerable caution should be exercised when interpreting the results. The costs of many of the outcomes were derived from US sources and may not necessarily be generalisable to the NHS. For example, Pourat (2013) in their analysis of the costs of maternal haemorrhage note that, while costs are estimated by the agreed per diem rates with private hospitals, actual expenditure will depend on the mix of public-private hospitals as well as variations in practice. In their analysis, the estimate of the cost of a vaginal birth without maternal haemorrhage is $4,504 at 2011 prices. In 2016/17 UK prices this is approximately £3,500, which is higher than the NHS equivalent (see Table 34) although not by a great amount. The costs involved in treating haemorrhage can vary substantially according to severity. When the haemorrhage is not severe, management options may include bed rest, tocolysis, corticosteroids and blood transfusion. For severe haemorrhage arterial ligation, uterine rupture repair or hysterectomy may be required.

Outcomes are based on women who had an emergency caesarean section and in whom an option of continuation of labour was likely to be contraindicated. For this reason, it might be expected that the outcomes of emergency caesarean section would be worse than they would be for women having emergency caesarean section with no medical or obstetric indication other than a suspected large-for-gestational-age baby. On the other hand, the outcomes data for emergency caesarean section are based on eventual birthweight rather than a suspicion of large for gestational age. Large for gestational age can only be determined after the birth and the American College of Obstetricians and Gynaecologists (ACOG 2016) has commented that fetal macrosomia cannot be accurately diagnosed. Therefore, in a decision making context during labour a proportion of women suspected of having a large-for-gestational-age baby would have a baby that was subsequently found not to be large for gestational age. Therefore, the outcomes associated with eventual birthweight are likely to be worse than where a large-for-gestational-age-baby is only suspected. For this reason the model may over-estimate the benefits of emergency caesarean section.

The model analysis was, for pragmatic reasons, limited to the outcomes reported in the evidence reviewed for this guideline. However, many other outcomes which were not included could be affected by mode of birth. The disadvantages of caesarean section on the outcomes of a future pregnancy, for example, were not included. This limitation may give rise to doubts about the apparently overwhelming cost effectiveness of emergency caesarean section in the base-case analysis, even when the birthweight is less than 4500 g. It has already been noted that the committee had certain reservations with respect to the inclusion of urinary and anal incontinence outcomes. While the baseline risks of urinary and anal

incontinence used in the model are not inconsistent with other published literature (such as Thom 2010, Guise 2007) the model does assume that the incontinence is lifelong while the natural history of these conditions suggests that for at least some women this will not be the case. Also, the QALY losses and costs used for these outcomes seem likely to reflect more severe incontinence which has a much lower prevalence than infrequent incontinence. In addition the high costs attributed to these outcomes, particularly urinary incontinence, would suggest that the costs reflect treatment which would be expected to ameliorate symptoms and improve HRQoL and so high rates for costs and QALYs may overstate the potential cost reduction or improvement in HRQoL that could result from the decision to perform an emergency caesarean section.

Conclusion

The results of this model provide sufficient cost effectiveness support for the committee's recommendation to offer women in labour with a suspected large-for-gestational-age baby a choice between continuing in labour (including augmented labour) and caesarean section. The results do suggest that the cost effectiveness of operative birth is likely to increase with larger birthweight. However, limitations in the data mean that it is not possible to estimate a particular (estimated) birthweight threshold for which caesarean section would be the preferred mode of birth.

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Appendices

Appendix A – Literature search strategies

Health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	cost:.mp.
2	cost benefit analys:.mp.
3	health care costs.mp.
4	or/1-3
5	PREGNANCY/
6	PERIPARTUM PERIOD/
7	PARTURITION/
8	exp LABOR, OBSTETRIC/
9	OBSTETRIC LABOR, PREMATURE/
10	pregnan$.ti,ab.
11	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
12	((during or giving or give) adj3 birth?).ti,ab.
13	or/5-12
14	*OBESITY/ or *OBESITY, ABDOMINAL/ or *OBESITY, MORBID/
15	*BODY MASS INDEX/ or *BODY SIZE/ or *OVERWEIGHT/ or *WAIST CIRCUMFERENCE/ or *WAIST-HIP RATIO/
16	body mass index.ti.
17	(obesity or obese or heavy or heavier or overweight or fat$ or BMI).ti.
18	*ADIPOSE TISSUE/ or *ADIPOSE TISSUE, WHITE/
19	or/14-18
20	exp ASTHMA/
21	asthma$.ti,ab.
22	BRONCHIAL SPASM/
23	(Bronchospasm? or bronch$ spasm?).ti,ab.
24	BRONCHOCONSTRICTION/
25	(Bronchoconstrict$ or bronch$ constrict$).ti,ab.
26	or/20-25
27	INTRACRANIAL HEMORRHAGES/
28	SUBARACHNOID HEMORRHAGE/
29	(h?emorrhag$ adj3 (subarachnoid or intracranial$)).ab,ti.
30	SAH?.ab,ti.
31	INTRACRANIAL ARTERIOVENOUS MALFORMATIONS/
32	((Intracranial$ or cerebr$ or brain?) adj5 (arteriovenous or arterio-venous) adj3 malform$).ab,ti.

#	Searches
33	(cerebr$ adj3 malform$).ab,ti.
34	AVM?.ab,ti.
35	(recurr$ adj3 h?emorrhag$).ti,ab.
36	(Cerebr$ adj3 accident?).ti,ab.
37	cva.ti,ab.
38	HEMIPLEGIA/
39	hemiplegia?.ti,ab.
40	cavernoma?.ti,ab.
41	or/27-40
42	exp STEROIDS/
43	exp ADRENAL CORTEX HORMONES/
44	PREDNISONE/
45	exp PREDNISOLONE/
46	exp HYDROCORTISONE/
47	exp DEXAMETHASONE/
48	or/42-47
49	((stress or rescue or maintenance or increment$ or boost$ or supplement$ or additional$ or added$ or increas$) adj3 (dose? or dosag$)).ti,ab.
50	((Temporar$ or short term or physiological$) adj3 increase$).ti,ab.
51	or/49-50
52	48 and 51
53	((steroid$ or corticosteroid? or prednisone or fluprednisolone or methylprednisolone or prednimustine or Hydrocortisone or fludrocortisone or Dexamethasone) adj3 (stress or rescue or maintenance or increment$ or boost$ or supplement$ or additional$ or added$ or increas$ or replace$ or regimen$ or long term)).mp.
54	((steroid$ or corticosteroid? or prednisone or fluprednisolone or methylprednisolone or prednimustine or Hydrocortisone or fludrocortisone or Dexamethasone) adj3 (high$ adj2 (dose? or level?))).mp.
55	or/52-54
56	exp RENAL INSUFFICIENCY, CHRONIC/
57	((Renal$ or kidney?) adj5 (disease? or insuffic$ or fail$) adj5 (chronic$ or end-stage?)).ab,ti.
58	CKD.ab,ti.
59	ESRD.ab,ti.
60	Frasier syndrome.ti,ab.
61	exp ACUTE KIDNEY INJURY/
62	((Renal$ or kidney?) adj5 (injur$ or insuffic$ or fail$) adj5 acute$).ab,ti.
63	(Kidney adj5 tubular necrosis adj5 acute$).ab,ti.
64	(Nephrosis adj5 nephron adj5 lower).ab,ti.
65	AKI.ab,ti.
66	KIDNEY TRANSPLANTATION/
67	((kidney? or renal$) adj3 (transplant$ or graft$)).ti,ab.
68	or/56-67
69	PULMONARY VALVE STENOSIS/

#	Searches
70	(pulmonary adj2 stenos$).ti,ab.
71	DUCTUS ARTERIOSUS, PATENT/
72	(Paten$ adj2 ductus arteriosus).ti,ab.
73	MITRAL VALVE PROLAPSE/
74	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
75	click murmur syndrome?.ti,ab.
76	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
77	HEART SEPTAL DEFECTS, ATRIAL/
78	HEART SEPTAL DEFECTS, VENTRICULAR/
79	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
80	(persist$ adj2 ostium primum).ti,ab.
81	anomal$ pulmonary venous drain$.ti,ab.
82	exp CARDIAC COMPLEXES, PREMATURE/
83	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
84	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
85	"TETRALOGY OF FALLOT"/su [Surgery]
86	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
87	exp *ARRHYTHMIAS, CARDIAC/
88	(arrhythmia? or dysrhythmia?).ti,ab.
89	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
90	(Bradycardia? or bradyarrhythmia?).ti,ab.
91	Brugada Syndrome.ti,ab.
92	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
93	Heart Block.ti,ab.
94	Long QT Syndrome.ti,ab.
95	Parasystole.ti,ab.
96	Pre-Excitation Syndrome?.ti,ab.
97	Tachycardia?.ti,ab.
98	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
99	exp CARDIOMYOPATHY, HYPERTROPHIC/
100	(Hypertrophic adj2 cardiomyopath$).ti,ab.
101	AORTIC VALVE INSUFFICIENCY/
102	MITRAL VALVE INSUFFICIENCY/
103	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
104	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
105	MARFAN SYNDROME/
106	(Marfan$ adj2 syndrome).ti,ab.
107	exp AORTIC DISEASES/
108	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
109	Aortitis.ti,ab.
110	Loeys-Dietz Syndrome.ti,ab.

#	Searches
111	Leriche Syndrome.ti,ab.
112	AORTIC COARCTATION/su [Surgery]
113	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
114	HEART VALVE PROSTHESIS/
115	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
116	"TRANSPOSITION OF GREAT VESSELS"/
117	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
118	FONTAN PROCEDURE/
119	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
120	exp CORONARY DISEASE/
121	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
122	*HEART DEFECTS, CONGENITAL/
123	Cyanotic heart disease?.ti,ab.
124	(complex$ adj10 congenital$ heart disease?).ti,ab.
125	*PULMONARY HYPERTENSION/
126	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
127	exp VENTRICULAR DYSFUNCTION/
128	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
129	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
130	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
131	(previous$ adj5 cardiomyopath$).ti,ab.
132	MITRAL VALVE STENOSIS/
133	(mitral adj2 stenos?s).ti,ab.
134	exp AORTIC VALVE STENOSIS/
135	(aort$ adj2 stenos?s).ti,ab.
136	AORTIC COARCTATION/
137	(Coarctation? adj3 aort$).ti,ab.
138	or/69-137
139	exp CARDIOMYOPATHIES/
140	cardiomyopath$.ti,ab.
141	myocardiopath$.ti,ab.
142	myocardial disease?.ti,ab.
143	PPCM.ti,ab.
144	Arrhythmogenic Right Ventricular Dysplasia.ti,ab.
145	Endocardial Fibroelastos?s.ti,ab.
146	(Isolated Noncompaction adj3 Ventricular Myocardium).ti,ab.
147	Endomyocardial Fibros?s.ti,ab.
148	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).ti,ab.
149	((antopol or danon) adj2 disease?).ti,ab.
150	(Kearn$ adj3 Syndrome).ti,ab.
151	Myocardial Reperfusion Injur$.ti,ab.

#	Searches
152	Myocarditi$.ti,ab.
153	Carditis.ti,ab.
154	Sarcoglycanopath$.ti,ab.
155	or/139-154
156	exp BLOOD PLATELET DISORDERS/
157	(Blood Platelet Disorder? or Bernard-Soulier Syndrome or Gray Platelet Syndrome or Platelet Storage Pool Deficien$ or Hermanski-Pudlak Syndrome or Thrombasthenia or Thrombocytopeni$ or Jacobsen Distal 11q Deletion Syndrome or Kasabach-Merritt Syndrome or Thrombotic Microangiopath$ or Hemolytic-Uremic Syndrome or (Purpura adj3 Thrombocytopeni$) or Glanzmann$ thrombastenia).ti,ab.
158	HELLP SYNDROME/
159	HELLP.ti,ab.
160	HEMOLYTIC-UREMIC SYNDROME/
161	hemolytic uremic syndrome.ti,ab.
162	LUPUS ERYTHEMATOSUS, SYSTEMIC/
163	systemic lupus erythematosus.ti,ab.
164	ANTIPHOSPHOLIPID SYNDROME/
165	((antiphospholipid or anti-phospholipid) adj3 syndrome?).ti,ab.
166	Evans syndrome.ti,ab.
167	(Platelet adj3 (Disorder? or dysfunction$) adj10 (infect$ or human immunodeficiency virus$ or HIV or parvovirus or (Drug adj3 (relat$ or due or induced)) or Liver disease?)).ti,ab.
168	(Bone marrow suppression or myelotoxic$ or myelosuppression).ti,ab.
169	exp HEMORRHAGIC DISORDERS/
170	(Hemorrhagic Disorder? or Afibrinogenemia or Bernard-Soulier Syndrome or Disseminated Intravascular Coagulation or Factor V Deficien$ or Factor VII Deficien$ or Factor X Deficien$ or Factor XI Deficien$ or Factor XII Deficien$ or Factor XIII Deficien$ or H?emophilia? or Hemostatic Disorder? or Cryoglobulinemia or Ehlers-Danlos Syndrome or (Hemangioma? adj3 Cavernous) or Multiple Myeloma or Pseudoxanthoma Elasticum or (Purpura adj3 Hyperglobulinemic) or (Purpura adj3 Schoenlein-Henoch) or Scurvy or Shwartzman Phenomenon or (Telangiectasia adj3 Heredit$) or Waldenstrom Macroglobulinemia or Hypoprothrombinemia? or (Prothrombin adj3 Deficien$) or Platelet Storage Pool Deficien$ or Hermanski-Pudlak Syndrome or (Purpura adj3 Thrombocytopeni$) or Thrombasthenia or Thrombocythemia or Vitamin K Deficien$ or von Willebrand Disease? or Waterhouse-Friderichsen Syndrome or Wiskott-Aldrich Syndrome or (Fibrinogen adj3 Deficien$) or Dysfibrinogenemia or Hypofibrinogenemia).ti,ab.
171	exp BLOOD COAGULATION DISORDERS, INHERITED/
172	((Blood Coagulation Disorder? adj3 Inherit$) or Activated Protein C Resistan$ or Antithrombin III Deficien$ or Protein C Deficien$).ti,ab.
173	PREGNANCY COMPLICATIONS, HEMATOLOGIC/
174	or/156-173
175	19 or 26 or 41 or 55 or 68 or 138 or 155 or 174
176	13 and 175
177	PREGNANCY, HIGH-RISK/
178	(pregnan$ adj3 high$ adj3 risk$).ab,ti.
179	(pregnan$ adj10 (exist$ or preexist$) adj5 condition?).ab,ti.
180	or/177-179

#	Searches
181	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
182	PREGNANCY COMPLICATIONS, HEMATOLOGIC/
183	176 or 180 or 181 or 182
184	limit 183 to english language
185	LETTER/
186	EDITORIAL/
187	NEWS/
188	exp HISTORICAL ARTICLE/
189	ANECDOTES AS TOPIC/
190	COMMENT/
191	CASE REPORT/
192	(letter or comment*).ti.
193	or/185-192
194	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
195	193 not 194
196	ANIMALS/ not HUMANS/
197	exp ANIMALS, LABORATORY/
198	exp ANIMAL EXPERIMENTATION/
199	exp MODELS, ANIMAL/
200	exp RODENTIA/
201	(rat or rats or mouse or mice).ti.
202	or/195-201
203	184 not 202
204	4 and 203

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	cost:.mp.
2	cost benefit analys:.mp.
3	health care costs.mp.
4	or/1-3
5	PREGNANCY/
6	PERIPARTUM PERIOD/
7	PARTURITION/
8	exp LABOR, OBSTETRIC/
9	OBSTETRIC LABOR, PREMATURE/
10	pregnan$.ti,ab,kw.
11	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
12	((during or giving or give) adj3 birth?).ti,ab.
13	or/5-12
14	*OBESITY/ or *OBESITY, ABDOMINAL/ or *OBESITY, MORBID/

#	Searches
15	*BODY MASS INDEX/ or *BODY SIZE/ or *OVERWEIGHT/ or *WAIST CIRCUMFERENCE/ or *WAIST-HIP RATIO/
16	body mass index.ti.
17	(obesity or obese or heavy or heavier or overweight or fat$ or BMI).ti.
18	*ADIPOSE TISSUE/ or *ADIPOSE TISSUE, WHITE/
19	or/14-18
20	exp ASTHMA/
21	asthma$.ti,ab,kw.
22	BRONCHIAL SPASM/
23	(Bronchospasm? or bronch$ spasm?).ti,ab,kw.
24	BRONCHOCONSTRICTION/
25	(Bronchoconstrict$ or bronch$ constrict$).ti,ab,kw.
26	or/20-25
27	INTRACRANIAL HEMORRHAGES/
28	SUBARACHNOID HEMORRHAGE/
29	(h?emorrhag$ adj3 (subarachnoid or intracranial$)).ab,ti.
30	SAH?.ab,ti.
31	INTRACRANIAL ARTERIOVENOUS MALFORMATIONS/
32	((Intracranial$ or cerebr$ or brain?) adj5 (arteriovenous or arterio-venous) adj3 malform$).ab,ti.
33	(cerebr$ adj3 malform$).ab,ti.
34	AVM?.ab,ti.
35	(recurr$ adj3 h?emorrhag$).ti,ab.
36	(Cerebr$ adj3 accident?).ti,ab.
37	cva.ti,ab.
38	HEMIPLEGIA/
39	hemiplegia?.ti,ab,kw.
40	cavernoma?.ti,ab,kw.
41	or/27-40
42	exp STEROIDS/
43	exp ADRENAL CORTEX HORMONES/
44	PREDNISONE/
45	exp PREDNISOLONE/
46	exp HYDROCORTISONE/
47	exp DEXAMETHASONE/
48	or/42-47
49	((stress or rescue or maintenance or increment$ or boost$ or supplement$ or additional$ or added$ or increas$) adj3 (dose? or dosag$)).ti,ab.
50	((Temporar$ or short term or physiological$) adj3 increase$).ti,ab.
51	or/49-50
52	48 and 51
53	((steroid$ or corticosteroid? or prednisone or fluprednisolone or methylprednisolone or prednimustine or Hydrocortisone or fludrocortisone or Dexamethasone) adj3 (stress or rescue

#	Searches
	or maintenance or increment$ or boost$ or supplement$ or additional$ or added$ or increas$ or replace$ or regimen$ or long term)).mp.
54	((steroid$ or corticosteroid? or prednisone or fluprednisolone or methylprednisolone or prednimustine or Hydrocortisone or fludrocortisone or Dexamethasone) adj3 (high$ adj2 (dose? or level?))).mp.
55	or/52-54
56	exp RENAL INSUFFICIENCY, CHRONIC/
57	((Renal$ or kidney?) adj5 (disease? or insuffic$ or fail$) adj5 (chronic$ or end-stage?)).ab,ti.
58	CKD.ab,ti.
59	ESRD.ab,ti.
60	Frasier syndrome.ti,ab,kw.
61	exp ACUTE KIDNEY INJURY/
62	((Renal$ or kidney?) adj5 (injur$ or insuffic$ or fail$) adj5 acute$).ab,ti.
63	(Kidney adj5 tubular necrosis adj5 acute$).ab,ti.
64	(Nephrosis adj5 nephron adj5 lower).ab,ti.
65	AKI.ab,ti.
66	KIDNEY TRANSPLANTATION/
67	((kidney? or renal$) adj3 (transplant$ or graft$)).ti,ab.
68	or/56-67
69	PULMONARY VALVE STENOSIS/
70	(pulmonary adj2 stenos$).ti,ab.
71	DUCTUS ARTERIOSUS, PATENT/
72	(Paten$ adj2 ductus arteriosus).ti,ab.
73	MITRAL VALVE PROLAPSE/
74	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
75	click murmur syndrome?.ti,ab,kw.
76	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
77	HEART SEPTAL DEFECTS, ATRIAL/
78	HEART SEPTAL DEFECTS, VENTRICULAR/
79	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
80	(persist$ adj2 ostium primum).ti,ab.
81	anomal$ pulmonary venous drain$.ti,ab,kw.
82	exp CARDIAC COMPLEXES, PREMATURE/
83	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
84	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
85	"TETRALOGY OF FALLOT"/su [Surgery]
86	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
87	exp *ARRHYTHMIAS, CARDIAC/
88	(arrhythmia? or dysrhythmia?).ti,ab,kw.
89	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
90	(Bradycardia? or bradyarrhythmia?).ti,ab,kw.
91	Brugada Syndrome.ti,ab,kw.

#	Searches
92	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
93	Heart Block.ti,ab,kw.
94	Long QT Syndrome.ti,ab,kw.
95	Parasystole.ti,ab,kw.
96	Pre-Excitation Syndrome?.ti,ab,kw.
97	Tachycardia?.ti,ab,kw.
98	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
99	exp CARDIOMYOPATHY, HYPERTROPHIC/
100	(Hypertrophic adj2 cardiomyopath$).ti,ab.
101	AORTIC VALVE INSUFFICIENCY/
102	MITRAL VALVE INSUFFICIENCY/
103	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
104	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
105	MARFAN SYNDROME/
106	(Marfan$ adj2 syndrome).ti,ab.
107	exp AORTIC DISEASES/
108	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
109	Aortitis.ti,ab,kw.
110	Loeys-Dietz Syndrome.ti,ab,kw.
111	Leriche Syndrome.ti,ab,kw.
112	AORTIC COARCTATION/su [Surgery]
113	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
114	HEART VALVE PROSTHESIS/
115	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
116	"TRANSPOSITION OF GREAT VESSELS"/
117	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
118	FONTAN PROCEDURE/
119	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
120	exp CORONARY DISEASE/
121	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
122	*HEART DEFECTS, CONGENITAL/
123	Cyanotic heart disease?.ti,ab,kw.
124	(complex$ adj10 congenital$ heart disease?).ti,ab.
125	*PULMONARY HYPERTENSION/
126	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
127	exp VENTRICULAR DYSFUNCTION/
128	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
129	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
130	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
131	(previous$ adj5 cardiomyopath$).ti,ab.
132	MITRAL VALVE STENOSIS/

#	Searches
133	(mitral adj2 stenos?s).ti,ab.
134	exp AORTIC VALVE STENOSIS/
135	(aort$ adj2 stenos?s).ti,ab.
136	AORTIC COARCTATION/
137	(Coarctation? adj3 aort$).ti,ab.
138	or/69-137
139	exp CARDIOMYOPATHIES/
140	cardiomyopath$.ti,ab,kw.
141	myocardiopath$.ti,ab,kw.
142	myocardial disease?.ti,ab,kw.
143	PPCM.ti,ab.
144	Arrhythmogenic Right Ventricular Dysplasia.ti,ab,kw.
145	Endocardial Fibroelastos?s.ti,ab,kw.
146	(Isolated Noncompaction adj3 Ventricular Myocardium).ti,ab.
147	Endomyocardial Fibros?s.ti,ab,kw.
148	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).ti,ab.
149	((antopol or danon) adj2 disease?).ti,ab.
150	(Kearn$ adj3 Syndrome).ti,ab.
151	Myocardial Reperfusion Injur$.ti,ab,kw.
152	Myocarditi$.ti,ab,kw.
153	Carditis.ti,ab,kw.
154	Sarcoglycanopath$.ti,ab,kw.
155	or/139-154
156	exp BLOOD PLATELET DISORDERS/
157	(Blood Platelet Disorder? or Bernard-Soulier Syndrome or Gray Platelet Syndrome or Platelet Storage Pool Deficien$ or Hermanski-Pudlak Syndrome or Thrombasthenia or Thrombocytopeni$ or Jacobsen Distal 11q Deletion Syndrome or Kasabach-Merritt Syndrome or Thrombotic Microangiopath$ or Hemolytic-Uremic Syndrome or (Purpura adj3 Thrombocytopeni$) or Glanzmann$ thrombastenia).ti,ab,kw.
158	HELLP SYNDROME/
159	HELLP.ti,ab.
160	HEMOLYTIC-UREMIC SYNDROME/
161	hemolytic uremic syndrome.ti,ab,kw.
162	LUPUS ERYTHEMATOSUS, SYSTEMIC/
163	systemic lupus erythematosus.ti,ab,kw.
164	ANTIPHOSPHOLIPID SYNDROME/
165	((antiphospholipid or anti-phospholipid) adj3 syndrome?).ti,ab.
166	Evans syndrome.ti,ab,kw.
167	(Platelet adj3 (Disorder? or dysfunction$) adj10 (infect$ or human immunodeficiency virus$ or HIV or parvovirus or (Drug adj3 (relat$ or due or induced)) or Liver disease?)).ti,ab.
168	(Bone marrow suppression or myelotoxic$ or myelosuppression).ti,ab,kw.
169	exp HEMORRHAGIC DISORDERS/

#	Searches
170	(Hemorrhagic Disorder? or Afibrinogenemia or Bernard-Soulier Syndrome or Disseminated Intravascular Coagulation or Factor V Deficien$ or Factor VII Deficien$ or Factor X Deficien$ or Factor XI Deficien$ or Factor XII Deficien$ or Factor XIII Deficien$ or H?emophilia? or Hemostatic Disorder? or Cryoglobulinemia or Ehlers-Danlos Syndrome or (Hemangioma? adj3 Cavernous) or Multiple Myeloma or Pseudoxanthoma Elasticum or (Purpura adj3 Hyperglobulinemic) or (Purpura adj3 Schoenlein-Henoch) or Scurvy or Shwartzman Phenomenon or (Telangiectasia adj3 Heredit$) or Waldenstrom Macroglobulinemia or Hypoprothrombinemia? or (Prothrombin adj3 Deficien$) or Platelet Storage Pool Deficien$ or Hermanski-Pudlak Syndrome or (Purpura adj3 Thrombocytopeni$) or Thrombasthenia or Thrombocythemia or Vitamin K Deficien$ or von Willebrand Disease? or Waterhouse-Friderichsen Syndrome or Wiskott-Aldrich Syndrome or (Fibrinogen adj3 Deficien$) or Dysfibrinogenemia or Hypofibrinogenemia).ti,ab,kw.
171	exp BLOOD COAGULATION DISORDERS, INHERITED/
172	((Blood Coagulation Disorder? adj3 Inherit$) or Activated Protein C Resistan$ or Antithrombin III Deficien$ or Protein C Deficien$).ti,ab.
173	PREGNANCY COMPLICATIONS, HEMATOLOGIC/
174	or/156-173
175	19 or 26 or 41 or 55 or 68 or 138 or 155 or 174
176	13 and 175
177	PREGNANCY, HIGH-RISK/
178	(pregnan$ adj3 high$ adj3 risk$).ab,ti.
179	(pregnan$ adj10 (exist$ or preexist$) adj5 condition?).ab,ti.
180	or/177-179
181	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
182	PREGNANCY COMPLICATIONS, HEMATOLOGIC/
183	176 or 180 or 181 or 182
184	4 and 183

Database: NHS Economic Evaluation Database

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.tw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
8	((during or giving or give) adj3 birth?).tw.
9	or/1-8
10	OBESITY/ or OBESITY, ABDOMINAL/ or OBESITY, MORBID/
11	BODY MASS INDEX/ or BODY SIZE/ or OVERWEIGHT/ or WAIST CIRCUMFERENCE/ or WAIST-HIP RATIO/
12	body mass index.tw.
13	(obesity or obese or heavy or heavier or overweight or fat$ or BMI).ti.
14	ADIPOSE TISSUE/ or ADIPOSE TISSUE, WHITE/

#	Searches
15	or/10-14
16	exp ASTHMA/
17	asthma$.tw.
18	BRONCHIAL SPASM/
19	(Bronchospasm? or bronch$ spasm?).tw.
20	BRONCHOCONSTRICTION/
21	(Bronchoconstrict$ or bronch$ constrict$).tw.
22	or/16-21
23	INTRACRANIAL HEMORRHAGES/
24	SUBARACHNOID HEMORRHAGE/
25	(h?emorrhag$ adj3 (subarachnoid or intracranial$)).tw.
26	SAH?.tw.
27	INTRACRANIAL ARTERIOVENOUS MALFORMATIONS/
28	((Intracranial$ or cerebr$ or brain?) adj5 (arteriovenous or arterio-venous) adj3 malform$).tw.
29	(cerebr$ adj3 malform$).tw.
30	AVM?.tw.
31	(recurr$ adj3 h?emorrhag$).tw.
32	(Cerebr$ adj3 accident?).tw.
33	cva.tw.
34	HEMIPLEGIA/
35	hemiplegia?.tw.
36	cavernoma?.tw.
37	or/23-36
38	exp STEROIDS/
39	exp ADRENAL CORTEX HORMONES/
40	PREDNISONE/
41	exp PREDNISOLONE/
42	exp HYDROCORTISONE/
43	exp DEXAMETHASONE/
44	or/38-43
45	((stress or rescue or maintenance or increment$ or boost$ or supplement$ or additional$ or added$ or increas$) adj3 (dose? or dosag$)).tw.
46	((Temporar$ or short term or physiological$) adj3 increase$).tw.
47	or/45-46
48	44 and 47
49	((steroid$ or corticosteroid? or prednisone or fluprednisolone or methylprednisolone or prednimustine or Hydrocortisone or fludrocortisone or Dexamethasone) adj3 (stress or rescue or maintenance or increment$ or boost$ or supplement$ or additional$ or added$ or increas$ or replace$ or regimen$ or long term)).mp.
50	((steroid$ or corticosteroid? or prednisone or fluprednisolone or methylprednisolone or prednimustine or Hydrocortisone or fludrocortisone or Dexamethasone) adj3 (high$ adj2 (dose? or level?))).mp.
51	or/48-50

#	Searches
52	exp RENAL INSUFFICIENCY, CHRONIC/
53	((Renal$ or kidney?) adj5 (disease? or insuffic$ or fail$) adj5 (chronic$ or end-stage?)).tw.
54	CKD.tw.
55	ESRD.tw.
56	Frasier syndrome.tw.
57	KIDNEY FAILURE, ACUTE/
58	((Renal$ or kidney?) adj5 (injur$ or insuffic$ or fail$) adj5 acute$).tw.
59	(Kidney adj5 tubular necrosis adj5 acute$).tw.
60	(Nephrosis adj5 nephron adj5 lower).tw.
61	AKI.tw.
62	KIDNEY TRANSPLANTATION/
63	((kidney? or renal$) adj3 (transplant$ or graft$)).tw.
64	or/52-63
65	PULMONARY VALVE STENOSIS/
66	(pulmonary adj2 stenos$).tw.
67	DUCTUS ARTERIOSUS, PATENT/
68	(Paten$ adj2 ductus arteriosus).tw.
69	MITRAL VALVE PROLAPSE/
70	(mitral valve? adj2 (prolapse? or floppy)).tw.
71	click murmur syndrome?.tw.
72	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw.
73	HEART SEPTAL DEFECTS, ATRIAL/
74	HEART SEPTAL DEFECTS, VENTRICULAR/
75	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw.
76	(persist$ adj2 ostium primum).tw.
77	anomal$ pulmonary venous drain$.tw.
78	exp CARDIAC COMPLEXES, PREMATURE/
79	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw.
80	((Atrial or ventricular) adj2 extrasystole?).tw.
81	"TETRALOGY OF FALLOT"/
82	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw.
83	exp ARRHYTHMIA/
84	(arrhythmia? or dysrhythmia?).tw.
85	(Atrial adj2 (Fibrillation or Flutter)).tw.
86	(Bradycardia? or bradyarrhythmia?).tw.
87	Brugada Syndrome.tw.
88	(premature adj2 (atrial or ventricular) adj2 contraction?).tw.
89	Heart Block.tw.
90	Long QT Syndrome.tw.
91	Parasystole.tw.
92	Pre-Excitation Syndrome?.tw.

#	Searches
93	Tachycardia?.tw.
94	(Ventricular adj2 (Fibrillation or Flutter)).tw.
95	exp CARDIOMYOPATHY, HYPERTROPHIC/
96	(Hypertrophic adj2 cardiomyopath$).tw.
97	AORTIC VALVE INSUFFICIENCY/
98	MITRAL VALVE INSUFFICIENCY/
99	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw.
100	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw.
101	MARFAN SYNDROME/
102	(Marfan$ adj2 syndrome).tw.
103	exp AORTIC DISEASES/
104	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw.
105	Aortitis.tw.
106	Loeys-Dietz Syndrome.tw.
107	Leriche Syndrome.tw.
108	AORTIC COARCTATION/
109	(Coarctation? adj10 (repair$ or surgery)).tw.
110	HEART VALVE PROSTHESIS/
111	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw.
112	"TRANSPOSITION OF GREAT VESSELS"/
113	(Transpos$ adj2 great adj2 (vessels or arteries)).tw.
114	FONTAN PROCEDURE/
115	(Fontan$ adj2 (circulat$ or procedure?)).tw.
116	exp *CORONARY DISEASE/
117	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti.
118	HEART DEFECTS, CONGENITAL/
119	Cyanotic heart disease?.tw.
120	(complex$ adj10 congenital$ heart disease?).tw.
121	PULMONARY HYPERTENSION/
122	(Pulmonary adj2 arter$ adj2 hypertens$).tw.
123	exp VENTRICULAR DYSFUNCTION/
124	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw.
125	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw.
126	exp CARDIOMYOPATHIES/ and TIME FACTORS/
127	(previous$ adj5 cardiomyopath$).tw.
128	MITRAL VALVE STENOSIS/
129	(mitral adj2 stenos?s).tw.
130	exp AORTIC VALVE STENOSIS/
131	(aort$ adj2 stenos?s).tw.
132	AORTIC COARCTATION/
133	(Coarctation? adj3 aort$).tw.

#	Searches
134	or/65-133
135	exp HEMATOLOGIC DISEASES/
136	(h?ematolog$ adj3 (disease? or disorder?)).tw.
137	exp BLOOD COAGULATION DISORDERS/
138	(blood adj3 coagula$ adj3 (disease? or disorder?)).tw.
139	(Coagulation Protein Disorder? or Disseminated Intravascular Coagulation or Ecchymosis or Platelet Storage Pool Deficien$ or Protein S Deficien$ or Purpura or Thrombocythemia or Vitamin K Deficien$).tw.
140	exp BLOOD PLATELET DISORDERS/
141	(blood adj3 platelet$ adj3 (disease? or disorder?)).tw.
142	(Bernard-Soulier Syndrome or Gray Platelet Syndrome or Platelet Storage Pool Deficienc$ or Thrombasthenia or Thrombocytopenia or Thrombocytosis or von Willebrand Disease?).tw.
143	or/135-142
144	15 or 22 or 37 or 51 or 64 or 134 or 143
145	9 and 144
146	PREGNANCY, HIGH-RISK/
147	(pregnan$ adj3 high$ adj3 risk$).tw.
148	(pregnan$ adj10 (exist$ or preexist$) adj5 condition?).tw.
149	or/146-148
150	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
151	PREGNANCY COMPLICATIONS, HEMATOLOGIC/
152	145 or 149 or 150 or 151

Database: Health Technology Assessment

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.tw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
8	((during or giving or give) adj3 birth?).tw.
9	or/1-8
10	OBESITY/ or OBESITY, ABDOMINAL/ or OBESITY, MORBID/
11	BODY MASS INDEX/ or BODY SIZE/ or OVERWEIGHT/ or WAIST CIRCUMFERENCE/ or WAIST-HIP RATIO/
12	body mass index.tw.
13	(obesity or obese or heavy or heavier or overweight or fat$ or BMI).tw.
14	ADIPOSE TISSUE/ or ADIPOSE TISSUE, WHITE/
15	or/10-14
16	exp ASTHMA/
17	asthma$.tw.

#	Searches
18	BRONCHIAL SPASM/
19	(Bronchospasm? or bronch$ spasm?).tw.
20	BRONCHOCONSTRICTION/
21	(Bronchoconstrict$ or bronch$ constrict$).tw.
22	or/16-21
23	INTRACRANIAL HEMORRHAGES/
24	SUBARACHNOID HEMORRHAGE/
25	(h?emorrhag$ adj3 (subarachnoid or intracranial$)).tw.
26	SAH?.tw.
27	INTRACRANIAL ARTERIOVENOUS MALFORMATIONS/
28	((Intracranial$ or cerebr$ or brain?) adj5 (arteriovenous or arterio-venous) adj3 malform$).tw.
29	(cerebr$ adj3 malform$).tw.
30	AVM?.tw.
31	(recurr$ adj3 h?emorrhag$).tw.
32	(Cerebr$ adj3 accident?).tw.
33	cva.tw.
34	HEMIPLEGIA/
35	hemiplegia?.tw.
36	cavernoma?.tw.
37	or/23-36
38	exp STEROIDS/
39	exp ADRENAL CORTEX HORMONES/
40	PREDNISONE/
41	exp PREDNISOLONE/
42	exp HYDROCORTISONE/
43	exp DEXAMETHASONE/
44	or/38-43
45	((stress or rescue or maintenance or increment$ or boost$ or supplement$ or additional$ or added$ or increas$) adj3 (dose? or dosag$)).tw.
46	((Temporar$ or short term or physiological$) adj3 increase$).tw.
47	or/45-46
48	44 and 47
49	((steroid$ or corticosteroid? or prednisone or fluprednisolone or methylprednisolone or prednimustine or Hydrocortisone or fludrocortisone or Dexamethasone) adj3 (stress or rescue or maintenance or increment$ or boost$ or supplement$ or additional$ or added$ or increas$ or replace$ or regimen$ or long term)).mp.
50	((steroid$ or corticosteroid? or prednisone or fluprednisolone or methylprednisolone or prednimustine or Hydrocortisone or fludrocortisone or Dexamethasone) adj3 (high$ adj2 (dose? or level?))).mp.
51	or/48-50
52	exp RENAL INSUFFICIENCY, CHRONIC/
53	((Renal$ or kidney?) adj5 (disease? or insuffic$ or fail$) adj5 (chronic$ or end-stage?)).tw.
54	CKD.tw.

#	Searches
55	ESRD.tw.
56	Frasier syndrome.tw.
57	KIDNEY FAILURE, ACUTE/
58	((Renal$ or kidney?) adj5 (injur$ or insuffic$ or fail$) adj5 acute$).tw.
59	(Kidney adj5 tubular necrosis adj5 acute$).tw.
60	(Nephrosis adj5 nephron adj5 lower).tw.
61	AKI.tw.
62	KIDNEY TRANSPLANTATION/
63	((kidney? or renal$) adj3 (transplant$ or graft$)).tw.
64	or/52-63
65	PULMONARY VALVE STENOSIS/
66	(pulmonary adj2 stenos$).tw.
67	DUCTUS ARTERIOSUS, PATENT/
68	(Paten$ adj2 ductus arteriosus).tw.
69	MITRAL VALVE PROLAPSE/
70	(mitral valve? adj2 (prolapse? or floppy)).tw.
71	click murmur syndrome?.tw.
72	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw.
73	HEART SEPTAL DEFECTS, ATRIAL/
74	HEART SEPTAL DEFECTS, VENTRICULAR/
75	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw.
76	(persist$ adj2 ostium primum).tw.
77	anomal$ pulmonary venous drain$.tw.
78	exp CARDIAC COMPLEXES, PREMATURE/
79	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw.
80	((Atrial or ventricular) adj2 extrasystole?).tw.
81	"TETRALOGY OF FALLOT"/
82	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw.
83	exp ARRHYTHMIA/
84	(arrhythmia? or dysrhythmia?).tw.
85	(Atrial adj2 (Fibrillation or Flutter)).tw.
86	(Bradycardia? or bradyarrhythmia?).tw.
87	Brugada Syndrome.tw.
88	(premature adj2 (atrial or ventricular) adj2 contraction?).tw.
89	Heart Block.tw.
90	Long QT Syndrome.tw.
91	Parasystole.tw.
92	Pre-Excitation Syndrome?.tw.
93	Tachycardia?.tw.
94	(Ventricular adj2 (Fibrillation or Flutter)).tw.
95	exp CARDIOMYOPATHY, HYPERTROPHIC/

#	Searches
96	(Hypertrophic adj2 cardiomyopath$).tw.
97	AORTIC VALVE INSUFFICIENCY/
98	MITRAL VALVE INSUFFICIENCY/
99	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw.
100	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw.
101	MARFAN SYNDROME/
102	(Marfan$ adj2 syndrome).tw.
103	exp AORTIC DISEASES/
104	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw.
105	Aortitis.tw.
106	Loeys-Dietz Syndrome.tw.
107	Leriche Syndrome.tw.
108	AORTIC COARCTATION/
109	(Coarctation? adj10 (repair$ or surgery)).tw.
110	HEART VALVE PROSTHESIS/
111	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw.
112	"TRANSPOSITION OF GREAT VESSELS"/
113	(Transpos$ adj2 great adj2 (vessels or arteries)).tw.
114	FONTAN PROCEDURE/
115	(Fontan$ adj2 (circulat$ or procedure?)).tw.
116	exp CORONARY DISEASE/
117	(Coronary adj2 (disease? or aneurysm? or arteriosclerosis or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).tw.
118	HEART DEFECTS, CONGENITAL/
119	Cyanotic heart disease?.tw.
120	(complex$ adj10 congenital$ heart disease?).tw.
121	PULMONARY HYPERTENSION/
122	(Pulmonary adj2 arter$ adj2 hypertens$).tw.
123	exp VENTRICULAR DYSFUNCTION/
124	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw.
125	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw.
126	exp CARDIOMYOPATHIES/ and TIME FACTORS/
127	(previous$ adj5 cardiomyopath$).tw.
128	MITRAL VALVE STENOSIS/
129	(mitral adj2 stenos?s).tw.
130	exp AORTIC VALVE STENOSIS/
131	(aort$ adj2 stenos?s).tw.
132	AORTIC COARCTATION/
133	(Coarctation? adj3 aort$).tw.
134	or/65-133
135	exp CARDIOMYOPATHIES/
136	cardiomyopath$.tw.

#	Searches
137	myocardiopath$.tw.
138	myocardial disease?.tw.
139	Arrhythmogenic Right Ventricular Dysplasia.tw.
140	Endocardial Fibroelastos?s.tw.
141	(Isolated Noncompaction adj3 Ventricular Myocardium).tw.
142	Endomyocardial Fibros?s.tw.
143	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).tw.
144	((antopol or danon) adj2 disease?).tw.
145	(Kearn$ adj3 Syndrome).tw.
146	Myocardial Reperfusion Injur$.tw.
147	Myocarditi$.tw.
148	Carditis.tw.
149	Sarcoglycanopath$.tw.
150	or/135-149
151	exp BLOOD PLATELET DISORDERS/
152	(Blood Platelet Disorder? or Bernard-Soulier Syndrome or Gray Platelet Syndrome or Platelet Storage Pool Deficien$ or Hermanski-Pudlak Syndrome or Thrombasthenia or Thrombocytopeni$ or Jacobsen Distal 11q Deletion Syndrome or Kasabach-Merritt Syndrome or Thrombotic Microangiopath$ or Hemolytic-Uremic Syndrome or (Purpura adj3 Thrombocytopeni$) or Glanzmann$ thrombastenia).tw.
153	HELLP SYNDROME/
154	HELLP.tw.
155	HEMOLYTIC-UREMIC SYNDROME/
156	hemolytic uremic syndrome.tw.
157	LUPUS ERYTHEMATOSUS, SYSTEMIC/
158	systemic lupus erythematosus.tw.
159	ANTIPHOSPHOLIPID SYNDROME/
160	((antiphospholipid or anti-phospholipid) adj3 syndrome?).tw.
161	Evans syndrome.tw.
162	(Platelet adj3 (Disorder? or dysfunction$) adj10 (infect$ or human immunodeficiency virus$ or HIV or parvovirus or (Drug adj3 (relat$ or due or induced)) or Liver disease?)).tw.
163	(Bone marrow suppression or myelotoxic$ or myelosuppression).tw.
164	exp HEMORRHAGIC DISORDERS/
165	(Hemorrhagic Disorder? or Afibrinogenemia or Bernard-Soulier Syndrome or Disseminated Intravascular Coagulation or Factor V Deficien$ or Factor VII Deficien$ or Factor X Deficien$ or Factor XI Deficien$ or Factor XII Deficien$ or Factor XIII Deficien$ or H?emophilia? or Hemostatic Disorder? or Cryoglobulinemia or Ehlers-Danlos Syndrome or (Hemangioma? adj3 Cavernous) or Multiple Myeloma or Pseudoxanthoma Elasticum or (Purpura adj3 Hyperglobulinemic) or (Purpura adj3 Schoenlein-Henoch) or Scurvy or Shwartzman Phenomenon or (Telangiectasia adj3 Heredit$) or Waldenstrom Macroglobulinemia or Hypoprothrombinemia? or (Prothrombin adj3 Deficien$) or Platelet Storage Pool Deficien$ or Hermanski-Pudlak Syndrome or (Purpura adj3 Thrombocytopeni$) or Thrombasthenia or Thrombocythemia or Vitamin K Deficien$ or von Willebrand Disease? or Waterhouse-Friderichsen Syndrome or Wiskott-Aldrich Syndrome or (Fibrinogen adj3 Deficien$) or Dysfibrinogenemia or Hypofibrinogenemia).tw.
166	exp BLOOD COAGULATION DISORDERS, INHERITED/

#	Searches
167	((Blood Coagulation Disorder? adj3 Inherit$) or Activated Protein C Resistan$ or Antithrombin III Deficien$ or Protein C Deficien$).tw.
168	PREGNANCY COMPLICATIONS, HEMATOLOGIC/
169	or/151-168
170	15 or 22 or 37 or 51 or 64 or 134 or 150 or 169
171	9 and 170
172	PREGNANCY, HIGH-RISK/
173	(pregnan$ adj3 high$ adj3 risk$).tw.
174	(pregnan$ adj10 (exist$ or preexist$) adj5 condition?).tw.
175	or/172-174
176	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
177	PREGNANCY COMPLICATIONS, HEMATOLOGIC/
178	171 or 175 or 176 or 177

Database: Embase

#	Searches
1	cost.tw.
2	costs.tw.
3	or/1-2
4	*PREGNANCY/
5	*PERINATAL PERIOD/
6	exp *BIRTH/
7	exp *LABOR/
8	*PREMATURE LABOR/
9	*INTRAPARTUM CARE/
10	pregnan$.ti,ab.
11	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
12	((during or giving or give) adj3 birth?).ti,ab.
13	or/4-12
14	*OBESITY/ or *ABDOMINAL OBESITY/ or *MORBID OBESITY/
15	*BODY MASS/ or *BODY SIZE/ or *WAIST CIRCUMFERENCE/ or *WAIST-HIP RATIO/
16	(body mass index or obesity or obese).ti.
17	(heavy or heavier or overweight or fat$ or BMI).ti.
18	*ADIPOSE TISSUE/ or *WHITE ADIPOSE TISSUE/
19	or/14-18
20	exp ASTHMA/
21	asthma$.ti,ab.
22	BRONCHOSPASM/
23	(Bronchospasm? or bronch$ spasm?).ti,ab.
24	BRONCHOCONSTRICTION/
25	(Bronchoconstrict$ or bronch$ constrict$).ti,ab.
26	or/20-25

#	Searches
27	*BRAIN HEMORRHAGE/
28	*SUBARACHNOID HEMORRHAGE/
29	(h?emorrhag$ adj3 (subarachnoid or intracranial$)).ab,ti.
30	SAH?.ab,ti.
31	*CEREBROVASCULAR MALFORMATION/
32	*BRAIN ARTERIOVENOUS MALFORMATION/
33	((Intracranial$ or cerebr$ or brain?) adj5 (arteriovenous or arterio-venous) adj3 malform$).ab,ti.
34	(cerebr$ adj3 malform$).ab,ti.
35	AVM?.ab,ti.
36	(recurr$ adj3 h?emorrhag$).ti,ab.
37	*CEREBROVASCULAR ACCIDENT/
38	(Cerebr$ adj3 accident?).ti,ab.
39	cva.ti,ab.
40	*HEMIPLEGIA/
41	hemiplegia?.ti,ab.
42	cavernoma?.ti,ab.
43	or/27-42
44	exp *STEROID/
45	exp *CORTICOSTEROID/
46	*PREDNISONE/
47	*PREDNISOLONE/
48	*HYDROCORTISONE/
49	*DEXAMETHASONE/
50	steroid$.mp.
51	corticosteroid?.mp.
52	prednisone.mp.
53	(prednisolone or fluprednisolone or methylprednisolone or prednimustine).mp.
54	(hydrocortisone or fludrocortisone).mp.
55	dexamethasone.mp.
56	or/44-55
57	((stress or rescue or maintenance or increment$ or boost$ or supplement$ or additional$ or added$ or increas$) adj3 (dose? or dosag$)).ti,ab.
58	((Temporar$ or short term or physiological$) adj3 increase$).ti,ab.
59	or/57-58
60	56 and 59
61	((steroid$ or corticosteroid? or prednisone or fluprednisolone or methylprednisolone or prednimustine or Hydrocortisone or fludrocortisone or Dexamethasone) adj3 (stress or rescue or maintenance or increment$ or boost$ or supplement$ or additional$ or added$ or increas$)).mp.
62	((steroid$ or corticosteroid? or prednisone or fluprednisolone or methylprednisolone or prednimustine or Hydrocortisone or fludrocortisone or Dexamethasone) adj3 (high$ adj2 (dose? or level?))).mp.

#	Searches
63	((steroid$ or corticosteroid? or prednisone or fluprednisolone or methylprednisolone or prednimustine or Hydrocortisone or fludrocortisone or Dexamethasone) adj3 replace$).mp.
64	((steroid$ or corticosteroid? or prednisone or fluprednisolone or methylprednisolone or prednimustine or Hydrocortisone or fludrocortisone or Dexamethasone) adj3 (regimen$ or long term)).mp.
65	or/60-64
66	CHRONIC KIDNEY DISEASE/
67	CHRONIC KIDNEY FAILURE/
68	END STAGE RENAL DISEASE/
69	((Renal$ or kidney?) adj5 (disease? or insuffic$ or fail$) adj5 (chronic$ or end-stage?)).ab,ti.
70	CKD.ab,ti.
71	ESRD.ab,ti.
72	Frasier syndrome.ti,ab.
73	ACUTE KIDNEY FAILURE/
74	((Renal$ or kidney?) adj5 (injur$ or insuffic$ or fail$) adj5 acute$).ab,ti.
75	(Kidney adj5 tubular necrosis adj5 acute$).ab,ti.
76	(Nephrosis adj5 nephron adj5 lower).ab,ti.
77	AKI.ab,ti.
78	exp KIDNEY TRANSPLANTATION/
79	((kidney? or renal$) adj3 (transplant$ or graft$)).ti,ab.
80	or/66-79
81	PULMONARY VALVE STENOSIS/
82	(pulmonary adj2 stenos$).ti,ab.
83	PATENT DUCTUS ARTERIOSUS/
84	(Paten$ adj2 ductus arteriosus).ti,ab.
85	MITRAL VALVE PROLAPSE/
86	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
87	click murmur syndrome?.ti,ab.
88	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
89	HEART SEPTUM DEFECT/
90	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
91	(persist$ adj2 ostium primum).ti,ab.
92	anomal$ pulmonary venous drain$.ti,ab.
93	EXTRASYSTOLE/
94	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
95	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
96	FALLOT TETRALOGY/su [Surgery]
97	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
98	exp *HEART ARRHYTHMIA/
99	(arrhythmia? or dysrhythmia?).ti,ab.
100	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
101	(Bradycardia? or bradyarrhythmia?).ti,ab.

#	Searches
102	Brugada Syndrome.ti,ab.
103	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
104	Heart Block.ti,ab.
105	Long QT Syndrome.ti,ab.
106	Parasystole.ti,ab.
107	Pre-Excitation Syndrome?.ti,ab.
108	Tachycardia?.ti,ab.
109	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
110	exp *HYPERTROPHIC CARDIOMYOPATHY/
111	(Hypertrophic adj2 cardiomyopath$).ti,ab.
112	AORTIC VALVE REGURGITATION/
113	MITRAL VALVE REGURGITATION/
114	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
115	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
116	MARFAN SYNDROME/
117	(Marfan$ adj2 syndrome).ti,ab.
118	exp *AORTA DISEASE/
119	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
120	Aortitis.ti,ab.
121	Loeys-Dietz Syndrome.ti,ab.
122	Leriche Syndrome.ti,ab.
123	AORTA COARCTATION/su [Surgery]
124	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
125	exp *HEART VALVE PROSTHESIS/
126	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
127	GREAT VESSELS TRANSPOSITION/
128	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
129	FONTAN PROCEDURE/
130	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
131	exp *CORONARY ARTERY DISEASE/
132	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
133	CYANOTIC HEART DISEASE/
134	Cyanotic heart disease?.ti,ab.
135	*CONGENITAL HEART DISEASE/
136	(complex$ adj10 congenital$ heart disease?).ti,ab.
137	*PULMONARY HYPERTENSION/
138	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
139	exp *HEART VENTRICLE FAILURE/
140	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
141	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
142	exp CARDIOMYOPATHY/ and TIME FACTOR/

#	Searches
143	(previous$ adj5 cardiomyopath$).ti,ab.
144	MITRAL VALVE STENOSIS/
145	(mitral adj2 stenos?s).ti,ab.
146	AORTA VALVE STENOSIS/
147	(aort$ adj2 stenos?s).ti,ab.
148	AORTA COARCTATION/
149	(Coarctation? adj3 aort$).ti,ab.
150	or/81-149
151	exp CARDIOMYOPATHY/
152	cardiomyopath$.ti,ab.
153	myocardiopath$.ti,ab.
154	myocardial disease?.ti,ab.
155	PPCM.ti,ab.
156	Arrhythmogenic Right Ventricular Dysplasia.ti,ab.
157	Endocardial Fibroelastos?s.ti,ab.
158	(Isolated Noncompaction adj3 Ventricular Myocardium).ti,ab.
159	Endomyocardial Fibros?s.ti,ab.
160	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).ti,ab.
161	((antopol or danon) adj2 disease?).ti,ab.
162	(Kearn$ adj3 Syndrome).ti,ab.
163	Myocardial Reperfusion Injur$.ti,ab.
164	Myocarditi$.ti,ab.
165	Carditis.ti,ab.
166	Sarcoglycanopath$.ti,ab.
167	or/151-166
168	exp *THROMBOCYTE DISORDER/
169	(Blood Platelet Disorder? or Bernard-Soulier Syndrome or Gray Platelet Syndrome or Platelet Storage Pool Deficien$ or Hermanski-Pudlak Syndrome or Thrombasthenia or Thrombocytopeni$ or Jacobsen Distal 11q Deletion Syndrome or Kasabach-Merritt Syndrome or Thrombotic Microangiopath$ or Hemolytic-Uremic Syndrome or (Purpura adj3 Thrombocytopeni$) or Glanzmann$ thrombastenia).ti,ab.
170	*HELLP SYNDROME/
171	HELLP.ti,ab.
172	*HEMOLYTIC UREMIC SYNDROME/
173	hemolytic uremic syndrome.ti,ab.
174	*SYSTEMIC LUPUS ERYTHEMATOSUS/
175	systemic lupus erythematosus.ti,ab.
176	*ANTIPHOSPHOLIPID SYNDROME/
177	((antiphospholipid or anti-phospholipid) adj3 syndrome?).ti,ab.
178	Evans syndrome.ti,ab.
179	(Platelet adj3 (Disorder? or dysfunction$) adj10 (infect$ or human immunodeficiency virus$ or HIV or parvovirus or (Drug adj3 (relat$ or due or induced)) or Liver disease?)).ti,ab.
180	(Bone marrow suppression or myelotoxic$ or myelosuppression).ti,ab.

#	Searches
181	*BLEEDING DISORDER/
182	*BLOOD CLOTTING DISORDER/
183	*ACTIVATED PROTEIN C RESISTANCE/
184	exp *BLOOD CLOTTING FACTOR DEFICIENCY/
185	*DISSEMINATED INTRAVASCULAR CLOTTING/
186	(Hemorrhagic Disorder? or Afibrinogenemia or Bernard-Soulier Syndrome or Disseminated Intravascular Coagulation or Factor V Deficien$ or Factor VII Deficien$ or Factor X Deficien$ or Factor XI Deficien$ or Factor XII Deficien$ or Factor XIII Deficien$ or H?emophilia? or Hemostatic Disorder? or Cryoglobulinemia or Ehlers-Danlos Syndrome or (Hemangioma? adj3 Cavernous) or Multiple Myeloma or Pseudoxanthoma Elasticum or (Purpura adj3 Hyperglobulinemic) or (Purpura adj3 Schoenlein-Henoch) or Scurvy or Shwartzman Phenomenon or (Telangiectasia adj3 Heredit$) or Waldenstrom Macroglobulinemia or Hypoprothrombinemia? or (Prothrombin adj3 Deficien$) or Platelet Storage Pool Deficien$ or Hermanski-Pudlak Syndrome or (Purpura adj3 Thrombocytopeni$) or Thrombasthenia or Thrombocythemia or Vitamin K Deficien$ or von Willebrand Disease? or Waterhouse-Friderichsen Syndrome or Wiskott-Aldrich Syndrome or (Fibrinogen adj3 Deficien$) or Dysfibrinogenemia or Hypofibrinogenemia).ti,ab.
187	((Blood Coagulation Disorder? adj3 Inherit$) or Activated Protein C Resistan$ or Antithrombin III Deficien$ or Protein C Deficien$).ti,ab.
188	or/168-187
189	19 or 26 or 43 or 65 or 80 or 150 or 167 or 188
190	13 and 189
191	HIGH RISK PREGNANCY/
192	(pregnan$ adj3 high$ adj3 risk$).ab,ti.
193	(pregnan$ adj10 (exist$ or preexist$) adj5 condition?).ab,ti.
194	or/191-193
195	190 or 194
196	limit 195 to english language
197	letter.pt. or LETTER/
198	note.pt.
199	editorial.pt.
200	CASE REPORT/ or CASE STUDY/
201	(letter or comment*).ti.
202	or/197-201
203	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
204	202 not 203
205	ANIMAL/ not HUMAN/
206	NONHUMAN/
207	exp ANIMAL EXPERIMENT/
208	exp EXPERIMENTAL ANIMAL/
209	ANIMAL MODEL/
210	exp RODENT/
211	(rat or rats or mouse or mice).ti.
212	or/204-211
213	196 not 212

#	Searches
214	3 and 213

Health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	cost:.mp.
2	cost benefit analys:.mp.
3	health care costs.mp.
4	or/1-3
5	PERIPARTUM PERIOD/
6	PARTURITION/
7	exp LABOR, OBSTETRIC/
8	OBSTETRIC LABOR, PREMATURE/
9	DELIVERY, OBSTETRIC/
10	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
11	((during or giving or give) adj3 birth?).ti,ab.
12	or/5-11
13	exp FEVER/
14	(fever$ or pyrexi$ or hyperthermi$).ti,ab.
15	((elevat$ or high$) adj3 temperature?).ti,ab.
16	or/13-15
17	exp SEPSIS/
18	sepsis.ti,ab.
19	BLOOD-BORNE PATHOGENS/
20	(blood$ adj3 (pathogen$ or poison$)).ti,ab.
21	exp SYSTEMIC INFLAMMATORY RESPONSE SYNDROME/
22	"systemic inflammatory response syndrome".ti,ab.
23	SIRS.ti,ab.
24	septic?emi$.ti,ab.
25	((septic or endotoxic or toxic) adj3 shock).ti,ab.
26	(py?emi$ or pyohemi$).ti,ab.
27	(bacter?emi$ or fung?emi$ or parasit?emi$ or vir?emi$ or endotox?emi$ or candid?emi$).ti,ab.
28	or/17-27
29	FETAL MACROSOMIA/
30	macrosomia?.ti,ab.
31	(large adj3 gestational adj3 age?).ab,ti.
32	(large adj3 date?).ab,ti.
33	or/29-32

#	Searches
34	BREECH PRESENTATION/
35	(breech$ adj3 (present$ or complet$ or incomplet$ or frank$)).ab,ti.
36	or/34-35
37	PREGNANCY, PROLONGED/
38	(pregnan$ adj3 prolong$).ab,ti.
39	(pregnan$ adj1 late).ab,ti.
40	(postterm$ or post-term$).ab,ti.
41	(postdate$ or post-date$).ab,ti.
42	(overdue? adj5 (pregnan$ or birth? or childbirth? or labo?r$)).ab,ti.
43	((42 week? or fourty two week? or fourty second week?) adj5 (pregnan$ or birth? or childbirth? or labo?r$)).ab,ti.
44	or/37-43
45	CESAREAN SECTION, REPEAT/
46	CESAREAN SECTION/ and (repeat$ or previous$).ti.
47	CESAREAN SECTION/ and (repeat$ or previous$).ab. /freq=2
48	((c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)) adj3 (repeat$ or previous$)).ti,ab.
49	VAGINAL BIRTH AFTER CESAREAN/
50	(vagina$ adj1 (birth$ or born or deliver$) adj2 after$ adj2 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
51	VBAC.ti,ab.
52	TRIAL OF LABOR/ and CESAREAN SECTION/
53	(trial adj2 labo?r adj3 after$ adj3 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
54	TOLAC.ti,ab.
55	or/45-54
56	INFANT, SMALL FOR GESTATIONAL AGE/
57	GESTATIONAL AGE/ and small.ti.
58	GESTATIONAL AGE/ and small.ab. /freq=2
59	(small adj3 gestational age?).ab,ti.
60	SGA.ti,ab.
61	FETAL GROWTH RETARDATION/
62	((fetal$ or fetus$ or intrauterine) adj3 grow$ adj3 (restrict$ or retard$)).ti,ab.
63	IUGR.ti,ab.
64	INFANT, LOW BIRTH WEIGHT/
65	exp INFANT, VERY LOW BIRTH WEIGHT/
66	(low birthweight? or low birth weight?).ti,ab.
67	LBW.ti,ab.
68	or/56-67
69	*HEALTH SERVICES ACCESSIBILITY/
70	HEALTHCARE DISPARITIES/
71	HEALTH SERVICES MISUSE/
72	NO-SHOW PATIENTS/

#	Searches
73	((no or late or delay$ or lack$ or without) adj5 (antenatal$ or prenatal$ or pre-natal$) adj3 care).ab,ti.
74	((no or unable or retsrict$ or limit$) adj3 access$ adj3 (care or healthcare or service?)).ti,ab.
75	(unbook$ or un-book$ or (late adj3 book$)).ti,ab.
76	walk$ in?.ti,ab.
77	((no or non) adj3 engag$).ti,ab.
78	no show.ti,ab.
79	or/69-78
80	PREGNANCY, UNPLANNED/
81	PREGNANCY, UNWANTED/
82	((conceal$ or hide? or hidden or hiding or unexpected or un-expected or unintended or un-intended or unsuspect$ or un-suspect$ or unaware or un-aware or unplanned or un-planned or unwanted or un-wanted) adj3 pregnan$).ti,ab.
83	or/80-82
84	PERIPARTUM PERIOD/
85	PARTURITION/
86	LABOR, OBSTETRIC/
87	UTERINE CONTRACTION/
88	LABOR ONSET/
89	LABOR STAGE, FIRST/
90	LABOR STAGE, SECOND/
91	OBSTETRIC LABOR, PREMATURE/
92	DELIVERY, OBSTETRIC/
93	(labo?r or childbirth or partur$ or intra?part$ or peri?part$).ti,ab.
94	((during or giving) adj3 birth?).ti,ab.
95	or/84-94
96	HEMORRHAGE/
97	SHOCK, HEMORRHAGIC/
98	UTERINE HEMORRHAGE/
99	or/96-98
100	95 and 99
101	((labo?r or birth? or childbirth? or partur$ or intra?part$ or peri?part$) adj3 (h?emorrhag$ or bleed$)).ti,ab.
102	or/100-101
103	*OBSTETRIC LABOR COMPLICATIONS/
104	((obstetric$ or labo?r) adj2 complication?).ti,ab.
105	or/103-104
106	*PREGNANCY, HIGH-RISK/
107	(pregnan$ adj2 high$ adj2 risk$).ab,ti.
108	or/106-107
109	33 or 36 or 44 or 55 or 102 or 105 or 108
110	12 and (16 or 28 or 68 or 79 or 83)
111	or/109-110

#	Searches
112	limit 111 to english language
113	LETTER/
114	EDITORIAL/
115	NEWS/
116	exp HISTORICAL ARTICLE/
117	ANECDOTES AS TOPIC/
118	COMMENT/
119	CASE REPORT/
120	(letter or comment*).ti.
121	or/113-120
122	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
123	121 not 122
124	ANIMALS/ not HUMANS/
125	exp ANIMALS, LABORATORY/
126	exp ANIMAL EXPERIMENTATION/
127	exp MODELS, ANIMAL/
128	exp RODENTIA/
129	(rat or rats or mouse or mice).ti.
130	or/123-129
131	112 not 130
132	4 and 131

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	cost:.mp.
2	cost benefit analys:.mp.
3	health care costs.mp.
4	or/1-3
5	PERIPARTUM PERIOD/
6	PARTURITION/
7	exp LABOR, OBSTETRIC/
8	OBSTETRIC LABOR, PREMATURE/
9	DELIVERY, OBSTETRIC/
10	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
11	((during or giving or give) adj3 birth?).ti,ab.
12	or/5-11
13	exp FEVER/
14	(fever$ or pyrexi$ or hyperthermi$).ti,ab,kw.
15	((elevat$ or high$) adj3 temperature?).ti,ab.
16	or/13-15
17	exp SEPSIS/
18	sepsis.ti,ab,kw.

#	Searches
19	BLOOD-BORNE PATHOGENS/
20	(blood$ adj3 (pathogen$ or poison$)).ti,ab.
21	exp SYSTEMIC INFLAMMATORY RESPONSE SYNDROME/
22	"systemic inflammatory response syndrome".ti,ab.
23	SIRS.ti,ab.
24	septic?emi$.ti,ab,kw.
25	((septic or endotoxic or toxic) adj3 shock).ti,ab.
26	(py?emi$ or pyohemi$).ti,ab,kw.
27	(bacter?emi$ or fung?emi$ or parasit?emi$ or vir?emi$ or endotox?emi$ or candid?emi$).ti,ab,kw.
28	or/17-27
29	FETAL MACROSOMIA/
30	macrosomia?.ti,ab,kw.
31	(large adj3 gestational adj3 age?).ab,ti.
32	(large adj3 date?).ab,ti.
33	or/29-32
34	BREECH PRESENTATION/
35	(breech$ adj3 (present$ or complet$ or incomplet$ or frank$)).ab,ti.
36	or/34-35
37	PREGNANCY, PROLONGED/
38	(pregnan$ adj3 prolong$).ab,ti.
39	(pregnan$ adj1 late).ab,ti.
40	(postterm$ or post-term$).ab,ti.
41	(postdate$ or post-date$).ab,ti.
42	(overdue? adj5 (pregnan$ or birth? or childbirth? or labo?r$)).ab,ti.
43	((42 week? or fourty two week? or fourty second week?) adj5 (pregnan$ or birth? or childbirth? or labo?r$)).ab,ti.
44	or/37-43
45	CESAREAN SECTION, REPEAT/
46	CESAREAN SECTION/ and (repeat$ or previous$).ti.
47	CESAREAN SECTION/ and (repeat$ or previous$).ab. /freq=2
48	((c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)) adj3 (repeat$ or previous$)).ti,ab.
49	VAGINAL BIRTH AFTER CESAREAN/
50	(vagina$ adj1 (birth$ or born or deliver$) adj2 after$ adj2 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
51	VBAC.ti,ab.
52	TRIAL OF LABOR/ and CESAREAN SECTION/
53	(trial adj2 labo?r adj3 after$ adj3 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
54	TOLAC.ti,ab.
55	or/45-54
56	INFANT, SMALL FOR GESTATIONAL AGE/

#	Searches
57	GESTATIONAL AGE/ and small.ti.
58	GESTATIONAL AGE/ and small.ab. /freq=2
59	(small adj3 gestational age?).ab,ti.
60	SGA.ti,ab.
61	FETAL GROWTH RETARDATION/
62	((fetal$ or fetus$ or intrauterine) adj3 grow$ adj3 (restrict$ or retard$)).ti,ab.
63	IUGR.ti,ab.
64	INFANT, LOW BIRTH WEIGHT/
65	exp INFANT, VERY LOW BIRTH WEIGHT/
66	(low birthweight? or low birth weight?).ti,ab.
67	LBW.ti,ab.
68	or/56-67
69	*HEALTH SERVICES ACCESSIBILITY/
70	HEALTHCARE DISPARITIES/
71	HEALTH SERVICES MISUSE/
72	NO-SHOW PATIENTS/
73	((no or late or delay$ or lack$ or without) adj5 (antenatal$ or prenatal$ or pre-natal$) adj3 care).ab,ti.
74	((no or unable or retsrict$ or limit$) adj3 access$ adj3 (care or healthcare or service?)).ti,ab.
75	(unbook$ or un-book$ or (late adj3 book$)).ti,ab.
76	walk$ in?.ti,ab.
77	((no or non) adj3 engag$).ti,ab.
78	or/69-77
79	PREGNANCY, UNPLANNED/
80	PREGNANCY, UNWANTED/
81	((conceal$ or hide? or hidden or hiding or unexpected or un-expected or unintended or un-intended or unsuspect$ or un-suspect$ or unaware or un-aware or unplanned or un-planned or unwanted or un-wanted) adj3 pregnan$).ti,ab.
82	or/79-81
83	PERIPARTUM PERIOD/
84	PARTURITION/
85	LABOR, OBSTETRIC/
86	UTERINE CONTRACTION/
87	LABOR ONSET/
88	LABOR STAGE, FIRST/
89	LABOR STAGE, SECOND/
90	OBSTETRIC LABOR, PREMATURE/
91	DELIVERY, OBSTETRIC/
92	(labo?r or childbirth or partur$ or intra?part$ or peri?part$).ti,ab,kw.
93	((during or giving) adj3 birth?).ti,ab.
94	or/83-93
95	HEMORRHAGE/

#	Searches
96	SHOCK, HEMORRHAGIC/
97	UTERINE HEMORRHAGE/
98	or/95-97
99	94 and 98
100	((labo?r or birth? or childbirth? or partur$ or intra?part$ or peri?part$) adj3 (h?emorrhag$ or bleed$)).ti,ab.
101	or/99-100
102	*OBSTETRIC LABOR COMPLICATIONS/
103	((obstetric$ or labo?r) adj2 complication?).ti,ab.
104	or/102-103
105	*PREGNANCY, HIGH-RISK/
106	(pregnan$ adj2 high$ adj2 risk$).ab,ti.
107	or/105-106
108	33 or 36 or 44 or 55 or 101 or 104 or 107
109	12 and (16 or 28 or 68 or 78 or 82)
110	or/108-109
111	4 and 110

Database: NHS Economic Evaluation Database

#	Searches
1	PERIPARTUM PERIOD/
2	PARTURITION/
3	exp LABOR, OBSTETRIC/
4	OBSTETRIC LABOR, PREMATURE/
5	DELIVERY, OBSTETRIC/
6	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
7	((during or giving or give) adj3 birth?).tw.
8	or/1-7
9	exp FEVER/
10	(fever$ or pyrexi$ or hyperthermi$).tw.
11	((elevat$ or high$) adj3 temperature?).tw.
12	or/9-11
13	exp SEPSIS/
14	sepsis.tw.
15	BLOOD-BORNE PATHOGENS/
16	(blood$ adj3 (pathogen$ or poison$)).tw.
17	exp SYSTEMIC INFLAMMATORY RESPONSE SYNDROME/
18	"systemic inflammatory response syndrome".tw.
19	SIRS.tw.
20	septic?emi$.tw.
21	((septic or endotoxic or toxic) adj3 shock).tw.
22	(py?emi$ or pyohemi$).tw.

#	Searches
23	(bacter?emi$ or fung?emi$ or parasit?emi$ or vir?emi$ or endotox?emi$ or candid?emi$).tw.
24	or/13-23
25	FETAL MACROSOMIA/
26	macrosomia?.tw.
27	(large adj3 gestational adj3 age?).tw.
28	(large adj3 date?).tw.
29	or/25-28
30	BREECH PRESENTATION/
31	(breech$ adj3 (present$ or complet$ or incomplet$ or frank$)).tw.
32	or/30-31
33	PREGNANCY, PROLONGED/
34	(pregnan$ adj3 prolong$).tw.
35	(pregnan$ adj1 late).tw.
36	(postterm$ or post-term$).tw.
37	(postdate$ or post-date$).tw.
38	(overdue? adj5 (pregnan$ or birth? or childbirth? or labo?r$)).tw.
39	((42 week? or fourty two week? or fourty second week?) adj5 (pregnan$ or birth? or childbirth? or labo?r$)).tw.
40	or/33-39
41	CESAREAN SECTION, REPEAT/
42	CESAREAN SECTION/ and (repeat$ or previous$).tw.
43	CESAREAN SECTION/ and (repeat$ or previous$).tw.
44	((c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)) adj3 (repeat$ or previous$)).tw.
45	VAGINAL BIRTH AFTER CESAREAN/
46	(vagina$ adj1 (birth$ or born or deliver$) adj2 after$ adj2 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).tw.
47	VBAC.tw.
48	TRIAL OF LABOR/ and CESAREAN SECTION/
49	(trial adj2 labo?r adj3 after$ adj3 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).tw.
50	TOLAC.tw.
51	or/41-50
52	INFANT, SMALL FOR GESTATIONAL AGE/
53	GESTATIONAL AGE/ and small.tw.
54	GESTATIONAL AGE/ and small.tw.
55	(small adj3 gestational age?).tw.
56	SGA.tw.
57	FETAL GROWTH RETARDATION/
58	((fetal$ or fetus$ or intrauterine) adj3 grow$ adj3 (restrict$ or retard$)).tw.
59	IUGR.tw.
60	INFANT, LOW BIRTH WEIGHT/
61	exp INFANT, VERY LOW BIRTH WEIGHT/

#	Searches
62	(low birthweight? or low birth weight?).tw.
63	LBW.tw.
64	or/52-63
65	*HEALTH SERVICES ACCESSIBILITY/
66	HEALTHCARE DISPARITIES/
67	HEALTH SERVICES MISUSE/
68	NO-SHOW PATIENTS/
69	((no or late or delay$ or lack$ or without) adj5 (antenatal$ or prenatal$ or pre-natal$) adj3 care).tw.
70	((no or unable or retsrict$ or limit$) adj3 access$ adj3 (care or healthcare or service?)).tw.
71	(unbook$ or un-book$ or (late adj3 book$)).tw.
72	walk$ in?.tw.
73	((no or non) adj3 engag$).tw.
74	no show.tw.
75	or/65-74
76	PREGNANCY, UNPLANNED/
77	PREGNANCY, UNWANTED/
78	((conceal$ or hide? or hidden or hiding or unexpected or un-expected or unintended or un-intended or unsuspect$ or un-suspect$ or unaware or un-aware or unplanned or un-planned or unwanted or un-wanted) adj3 pregnan$).tw.
79	or/76-78
80	PERIPARTUM PERIOD/
81	PARTURITION/
82	LABOR, OBSTETRIC/
83	UTERINE CONTRACTION/
84	LABOR ONSET/
85	LABOR STAGE, FIRST/
86	LABOR STAGE, SECOND/
87	OBSTETRIC LABOR, PREMATURE/
88	DELIVERY, OBSTETRIC/
89	(labo?r or childbirth or partur$ or intra?part$ or peri?part$).tw.
90	((during or giving) adj3 birth?).tw.
91	or/80-90
92	HEMORRHAGE/
93	SHOCK, HEMORRHAGIC/
94	UTERINE HEMORRHAGE/
95	or/92-94
96	91 and 95
97	((labo?r or birth? or childbirth? or partur$ or intra?part$ or peri?part$) adj3 (h?emorrhag$ or bleed$)).tw.
98	or/96-97
99	*OBSTETRIC LABOR COMPLICATIONS/
100	((obstetric$ or labo?r) adj2 complication?).tw.

#	Searches
101	or/99-100
102	*PREGNANCY, HIGH-RISK/
103	(pregnan$ adj2 high$ adj2 risk$).tw.
104	or/102-103
105	29 or 32 or 40 or 51 or 98 or 101 or 104
106	8 and (12 or 24 or 64 or 75 or 79)
107	or/105-106

Database: Health Technology Assessment

#	Searches
1	PERIPARTUM PERIOD/
2	PARTURITION/
3	exp LABOR, OBSTETRIC/
4	OBSTETRIC LABOR, PREMATURE/
5	DELIVERY, OBSTETRIC/
6	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
7	((during or giving or give) adj3 birth?).tw.
8	or/1-7
9	exp FEVER/
10	(fever$ or pyrexi$ or hyperthermi$).tw.
11	((elevat$ or high$) adj3 temperature?).tw.
12	or/9-11
13	exp SEPSIS/
14	sepsis.tw.
15	BLOOD-BORNE PATHOGENS/
16	(blood$ adj3 (pathogen$ or poison$)).tw.
17	exp SYSTEMIC INFLAMMATORY RESPONSE SYNDROME/
18	"systemic inflammatory response syndrome".tw.
19	SIRS.tw.
20	septic?emi$.tw.
21	((septic or endotoxic or toxic) adj3 shock).tw.
22	(py?emi$ or pyohemi$).tw.
23	(bacter?emi$ or fung?emi$ or parasit?emi$ or vir?emi$ or endotox?emi$ or candid?emi$).tw.
24	or/13-23
25	FETAL MACROSOMIA/
26	macrosomia?.tw.
27	(large adj3 gestational adj3 age?).tw.
28	(large adj3 date?).tw.
29	or/25-28
30	BREECH PRESENTATION/
31	(breech$ adj3 (present$ or complet$ or incomplet$ or frank$)).tw.
32	or/30-31

#	Searches
33	PREGNANCY, PROLONGED/
34	(pregnan$ adj3 prolong$).tw.
35	(pregnan$ adj1 late).tw.
36	(postterm$ or post-term$).tw.
37	(postdate$ or post-date$).tw.
38	(overdue? adj5 (pregnan$ or birth? or childbirth? or labo?r$)).tw.
39	((42 week? or fourty two week? or fourty second week?) adj5 (pregnan$ or birth? or childbirth? or labo?r$)).tw.
40	or/33-39
41	CESAREAN SECTION, REPEAT/
42	CESAREAN SECTION/ and (repeat$ or previous$).tw.
43	CESAREAN SECTION/ and (repeat$ or previous$).tw.
44	((c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)) adj3 (repeat$ or previous$)).tw.
45	VAGINAL BIRTH AFTER CESAREAN/
46	(vagina$ adj1 (birth$ or born or deliver$) adj2 after$ adj2 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).tw.
47	VBAC.tw.
48	TRIAL OF LABOR/ and CESAREAN SECTION/
49	(trial adj2 labo?r adj3 after$ adj3 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).tw.
50	TOLAC.tw.
51	or/41-50
52	INFANT, SMALL FOR GESTATIONAL AGE/
53	GESTATIONAL AGE/ and small.tw.
54	GESTATIONAL AGE/ and small.tw.
55	(small adj3 gestational age?).tw.
56	SGA.tw.
57	FETAL GROWTH RETARDATION/
58	((fetal$ or fetus$ or intrauterine) adj3 grow$ adj3 (restrict$ or retard$)).tw.
59	IUGR.tw.
60	INFANT, LOW BIRTH WEIGHT/
61	exp INFANT, VERY LOW BIRTH WEIGHT/
62	(low birthweight? or low birth weight?).tw.
63	LBW.tw.
64	or/52-63
65	*HEALTH SERVICES ACCESSIBILITY/
66	HEALTHCARE DISPARITIES/
67	HEALTH SERVICES MISUSE/
68	NO-SHOW PATIENTS/
69	((no or late or delay$ or lack$ or without) adj5 (antenatal$ or prenatal$ or pre-natal$) adj3 care).tw.
70	((no or unable or retsrict$ or limit$) adj3 access$ adj3 (care or healthcare or service?)).tw.

#	Searches
71	(unbook$ or un-book$ or (late adj3 book$)).tw.
72	walk$ in?.tw.
73	((no or non) adj3 engag$).tw.
74	no show.tw.
75	or/65-74
76	PREGNANCY, UNPLANNED/
77	PREGNANCY, UNWANTED/
78	((conceal$ or hide? or hidden or hiding or unexpected or un-expected or unintended or un-intended or unsuspect$ or un-suspect$ or unaware or un-aware or unplanned or un-planned or unwanted or un-wanted) adj3 pregnan$).tw.
79	or/76-78
80	PERIPARTUM PERIOD/
81	PARTURITION/
82	LABOR, OBSTETRIC/
83	UTERINE CONTRACTION/
84	LABOR ONSET/
85	LABOR STAGE, FIRST/
86	LABOR STAGE, SECOND/
87	OBSTETRIC LABOR, PREMATURE/
88	DELIVERY, OBSTETRIC/
89	(labo?r or childbirth or partur$ or intra?part$ or peri?part$).tw.
90	((during or giving) adj3 birth?).tw.
91	or/80-90
92	HEMORRHAGE/
93	SHOCK, HEMORRHAGIC/
94	UTERINE HEMORRHAGE/
95	or/92-94
96	91 and 95
97	((labo?r or birth? or childbirth? or partur$ or intra?part$ or peri?part$) adj3 (h?emorrhag$ or bleed$)).tw.
98	or/96-97
99	*OBSTETRIC LABOR COMPLICATIONS/
100	((obstetric$ or labo?r) adj2 complication?).tw.
101	or/99-100
102	*PREGNANCY, HIGH-RISK/
103	(pregnan$ adj2 high$ adj2 risk$).tw.
104	or/102-103
105	29 or 32 or 40 or 51 or 98 or 101 or 104
106	8 and (12 or 24 or 64 or 75 or 79)
107	or/105-106

Database: Embase

#	Searches
1	cost.mp.
2	costs.mp.
3	or/1-2
4	*PERINATAL PERIOD/
5	exp *BIRTH/
6	exp *LABOR/
7	*PREMATURE LABOR/
8	*OBSTETRIC DELIVERY/
9	*INTRAPARTUM CARE/
10	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
11	((during or giving or give) adj3 birth?).ti,ab.
12	or/4-11
13	*FEVER/
14	(fever$ or pyrexi$ or hyperthermi$).ti,ab.
15	((elevat$ or high$) adj3 temperature?).ti,ab.
16	or/13-15
17	exp *SEPSIS/
18	sepsis.ti,ab.
19	BLOODBORNE BACTERIUM/
20	(blood$ adj3 (pathogen$ or poison$)).ti,ab.
21	SYSTEMIC INFLAMMATORY RESPONSE SYNDROME/
22	"systemic inflammatory response syndrome".ti,ab.
23	SIRS.ti,ab.
24	septic?emi$.ti,ab.
25	((septic or endotoxic or toxic) adj3 shock).ti,ab.
26	(py?emi$ or pyohemi$).ti,ab.
27	(bacter?emi$ or fung?emi$ or parasit?emi$ or vir?emi$ or endotox?emi$ or candid?emi$).ti,ab.
28	or/17-27
29	MACROSOMIA/
30	macrosomia?.ti,ab.
31	(large adj3 gestational adj3 age?).ab,ti.
32	(large adj3 date?).ab,ti.
33	or/29-32
34	BREECH PRESENTATION/
35	(breech$ adj3 (present$ or complet$ or incomplet$ or frank$)).ab,ti.
36	or/34-35
37	PROLONGED PREGNANCY/
38	(pregnan$ adj3 prolong$).ab,ti.
39	(pregnan$ adj1 late).ab,ti.
40	(postterm$ or post-term$).ab,ti.
41	(postdate$ or post-date$).ab,ti.

#	Searches
42	(overdue? adj5 (pregnan$ or birth? or childbirth? or labo?r$)).ab,ti.
43	((42 week? or fourty two week? or fourty second week?) adj5 (pregnan$ or birth? or childbirth? or labo?r$)).ab,ti.
44	or/37-43
45	REPEAT CESAREAN SECTION/
46	CESAREAN SECTION/ and (repeat$ or previous$).ti.
47	CESAREAN SECTION/ and (repeat$ or previous$).ab. /freq=2
48	((c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)) adj3 (repeat$ or previous$)).ti,ab.
49	VAGINAL BIRTH AFTER CESAREAN/
50	(vagina$ adj1 (birth$ or born or deliver$) adj2 after$ adj2 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
51	VBAC.ti,ab.
52	"TRIAL OF LABOR"/ and CESAREAN SECTION/
53	(trial adj2 labo?r adj3 after$ adj3 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
54	TOLAC.ti,ab.
55	or/45-54
56	*SMALL FOR DATE INFANT/
57	GESTATIONAL AGE/ and small.ti.
58	GESTATIONAL AGE/ and small.ab. /freq=2
59	(small adj3 gestational age?).ab,ti.
60	SGA.ti,ab.
61	*INTRAUTERINE GROWTH RETARDATION/
62	((fetal$ or fetus$ or intrauterine) adj3 grow$ adj3 (restrict$ or retard$)).ti,ab.
63	IUGR.ti,ab.
64	*LOW BIRTH WEIGHT/
65	exp *VERY LOW BIRTH WEIGHT/
66	(low birthweight? or low birth weight?).ti,ab.
67	LBW.ti,ab.
68	or/56-67
69	*HEALTH CARE DISPARITY/
70	PATIENT ATTENDANCE/
71	((no or late or delay$ or lack$ or without) adj5 (antenatal$ or prenatal$ or pre-natal$) adj3 care).ab,ti.
72	((no or unable or retsrict$ or limit$) adj3 access$ adj3 (care or healthcare or service?)).ti,ab.
73	(unbook$ or un-book$ or (late adj3 book$)).ti,ab.
74	walk$ in?.ti,ab.
75	((no or non) adj3 engag$).ti,ab.
76	no show.ti,ab.
77	or/69-76
78	UNPLANNED PREGNANCY/
79	UNWANTED PREGNANCY/

#	Searches
80	((conceal$ or hide? or hidden or hiding or unexpected or un-expected or unintended or un-intended or unsuspect$ or un-suspect$ or unaware or un-aware or unplanned or un-planned or unwanted or un-wanted) adj3 pregnan$).ti,ab.
81	or/78-80
82	*PERINATAL PERIOD/
83	*BIRTH/
84	*LABOR/
85	UTERUS CONTRACTION/
86	LABOR ONSET/
87	LABOR STAGE 1/
88	LABOR STAGE 2/
89	*PREMATURE LABOR/
90	*OBSTETRIC DELIVERY/
91	*INTRAPARTUM CARE/
92	(labo?r or childbirth or partur$ or intra?part$ or peri?part$).ti,ab.
93	((during or giving) adj3 birth?).ti,ab.
94	or/82-93
95	*BLEEDING/
96	OBSTETRIC HEMORRHAGE/
97	INTRAPARTUM HEMORRHAGE/
98	HEMORRHAGIC SHOCK/
99	UTERUS BLEEDING/
100	or/95-99
101	94 and 100
102	((labo?r or birth? or childbirth? or partur$ or intra?part$ or peri?part$) adj3 (h?emorrhag$ or bleed$)).ti,ab.
103	or/101-102
104	*LABOR COMPLICATION/
105	((obstetric$ or labo?r) adj2 complication?).ti,ab.
106	or/104-105
107	*HIGH RISK PREGNANCY/
108	(pregnan$ adj2 high$ adj2 risk$).ab,ti.
109	or/107-108
110	33 or 36 or 44 or 55 or 103 or 106 or 109
111	12 and (16 or 28 or 68 or 77 or 81)
112	or/110-111
113	limit 112 to english language
114	letter.pt. or LETTER/
115	note.pt.
116	editorial.pt.
117	CASE REPORT/ or CASE STUDY/
118	(letter or comment*).ti.

#	Searches
119	or/114-118
120	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
121	119 not 120
122	ANIMAL/ not HUMAN/
123	NONHUMAN/
124	exp ANIMAL EXPERIMENT/
125	exp EXPERIMENTAL ANIMAL/
126	ANIMAL MODEL/
127	exp RODENT/
128	(rat or rats or mouse or mice).ti.
129	or/121-128
130	113 not 129
131	3 and 130

Health economics search for intrapartum care for women with sepsis – antimicrobial therapy

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	PREGNANCY/

#	Searches
23	PREGNANCY, HIGH-RISK/
24	exp PREGNANCY, MULTIPLE/
25	PERIPARTUM PERIOD/
26	PARTURITION/
27	exp LABOR, OBSTETRIC/
28	OBSTETRIC LABOR, PREMATURE/
29	DELIVERY, OBSTETRIC/
30	pregnan$.ti,ab.
31	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
32	((during or giving or give) adj3 birth?).ti,ab.
33	or/22-32
34	exp SEPSIS/
35	sepsis.ti,ab.
36	BLOOD-BORNE PATHOGENS/
37	(blood$ adj3 (pathogen$ or poison$)).ti,ab.
38	exp SYSTEMIC INFLAMMATORY RESPONSE SYNDROME/
39	"systemic inflammatory response syndrome".ti,ab.
40	SIRS.ti,ab.
41	septic?emi$.ti,ab.
42	((septic or endotoxic or toxic) adj3 shock).ti,ab.
43	(py?emi$ or pyohemi$).ti,ab.
44	(bacter?emi$ or fung?emi$ or parasit?emi$ or vir?emi$ or endotox?emi$ or candid?emi$).ti,ab.
45	or/34-44
46	STREPTOCOCCAL INFECTIONS/
47	group A strep$.ti,ab.
48	group B strep$.ti,ab.
49	exp ESCHERICHIA COLI INFECTIONS/
50	Escherichia coli.ti,ab.
51	e-coli.ti,ab.
52	exp PNEUMOCOCCAL INFECTIONS/
53	(streptococ$ adj3 pneumon$).ti,ab.
54	INFLUENZA, HUMAN/
55	flu.ti,ab.
56	influenza.ti,ab.
57	or/46-56
58	45 or 57
59	ANTI-BACTERIAL AGENTS/
60	(Antibacterial? or anti-bacterial? or antibiotic? or anti-biotic?).ti,ab.
61	(Alamethicin or Amoxicillin or Anisomycin or Aurodox or Azlocillin or Aztreonam or Bacitracin or Bacteriocin? or Bambermycin? or Bongkrekic Acid or Calcimycin or Capreomycin or Carfecillin or Chloramphenicol or Chlortetracycline or Ciprofloxacin or Citrinin or Clavulanic Acid? or Colistin or Dactinomycin or Daptomycin or Demeclocycline or Diketopiperazine? or

#	Searches
	Distamycin? or Doxycycline or Echinomycin or Edeine or Enoxacin or Enviomycin or Fluoroquinolone? or Fosfomycin or Fusidic Acid or Gramicidin or Lactam? or Lasalocid or Leucomycin? or Levofloxacin or Lincomycin or Lincosamide? or Linezolid or Lymecycline or Methacycline or Mezlocillin or Mikamycin or Minocycline or Moxalactam or Mupirocin or Mycobacillin or Nalidixic Acid or Nigericin or Nisin or Norfloxacin or Novobiocin or Ofloxacin or Oxolinic Acid or Oxytetracycline or Pefloxacin or Penicillic Acid or Pipemidic Acid or Piperacillin or Pivampicillin or Polymyxin B or Polymyxin? or Pristinamycin or Prodigiosin or Rifabutin or Rifamycin? or Rolitetracycline or Roxarsone or Streptogramin? or Sulfamerazine or Sulfamethoxypyridazine or Talampicillin or Tetracycline or Thiamphenicol or Thiostrepton or Trimethoprim or Tyrocidine or Tyrothricin or Valinomycin or Vernamycin B or Viomycin or Virginiamycin or beta-Lactam?).mp.
62	or/59-61
63	exp CEPHALOSPORINS/
64	(Cephalosporin? or Cefamandole or Cefoperazone or Cefazolin or Cefonicid or Cefsulodin or Cephacetrile or Cefotaxime or Cefixime or Cefmenoxime or Cefotiam or Ceftizoxime or Ceftriaxone or Cefuroxime or Cephalothin or Cephapirin or Cephalexin or Cefaclor or Cefadroxil or Cefatrizine or Cephaloglycin or Cephradine or Cephaloridine or Ceftazidime or Cephamycin? or Cefmetazole or Cefotetan or Cefoxitin or Ceftaroline or Ceftobiprole).mp.
65	or/63-64
66	exp AMINOGLYCOSIDES/
67	(Aminoglycoside? or Anthracycline? or Aclarubicin or Daunorubicin or Carubicin or Doxorubicin or Epirubicin or Idarubicin or Nogalamycin or Menogaril or Plicamycin or Butirosin Sulfate or Gentamicin? or Sisomicin or Netilmicin or Hygromycin or Kanamycin or Amikacin or Dibekacin or Nebramycin or Tobramycin or Metrizamide or Neomycin or Framycetin or Paromomycin or Ribostamycin or Puromycin or Spectinomycin or Streptomycin or Dihydrostreptomycin Sulfate or Streptothricin? or Streptozocin).mp.
68	or/66-67
69	exp PENICILLINS/
70	(Penicillin? or Amdinocillin or Cyclacillin or Methicillin or Nafcillin or Oxacillin or Cloxacillin or Dicloxacillin or Floxacillin or Penicillanic Acid or Ampicillin or Carbenicillin or Sulbenicillin or Sulbactam or Ticarcillin).mp.
71	or/69-70
72	exp GLYCOPEPTIDES/
73	(Glycopeptide? or Bleomycin or Peplomycin or Phleomycin? or Peptidoglycan or Ristocetin or Teicoplanin or Vancomycin or Oritavancin or Telavancin).mp.
74	or/72-73
75	exp MACROLIDES/
76	(Macrolide? or Lucensomycin or Maytansine or Mepartricin or Miocamycin or Natamycin or Nystatin or Oleandomycin or Troleandomycin or Oligomycin? or Rutamycin or Sirolimus or Everolimus or Tacrolimus or Tylosin or Amphotericin B or Antimycin A or Brefeldin A or Bryostatin? or Candicidin or Epothilone? or Erythromycin or Azithromycin or Clarithromycin or Ketolide? or Roxithromycin or Filipin or Ivermectin or Josamycin or Leucomycins or Kitasamycin or Spiramycin or Fidaxomicin).mp.
77	CLINDAMYCIN/
78	Clindamycin.mp.
79	or/75-78
80	exp CARBAPENEMS/
81	(Carbapenem? or Thienamycin? or Imipenem or Meropenem or Ertapenem).mp.

#	Searches
82	CILASTATIN/
83	Cilastatin.mp.
84	or/80-83
85	exp NITROIMIDAZOLES/
86	(Nitroimidazole? or Dimetridazole or Etanidazole or Ipronidazole or Metronidazole or Misonidazole or Nimorazole or Ornidazole or Ronidazole or Tinidazole).mp.
87	or/85-86
88	exp ANTIVIRAL AGENTS/ not (exp ANTI-RETROVIRAL AGENTS/ or exp VIRAL FUSION PROTEIN INHIBITORS/)
89	(Antiviral? or anti-viral?).ti,ab.
90	(1-Deoxynojirimycin or Acetylcysteine or Ac?clovir or Amantadine or Aphidicolin or Brefeldin or Bromodeoxyuridine or Cytarabine or Deoxyglucose or Dideoxyadenosine or Dideoxynucleoside? or Ditiocarb or Emtricitabine or Filipin or Foscarnet or Ganc?clovir or Idoxuridine or Inosine Pranobex or Interferon? or Methisazone or Netropsin or Oseltamivir or Palivizumab or Phosphonoacetic Acid or Poly A-U or Poly I-C or Pyran Copolymer or Ribavirin or Rimantadine or Simeprevir or Sofosbuvir or Streptovaricin or Tenofovir or Tenuazonic Acid or Tilorone or Trifluridine or Tunicamycin or Vidarabine or Zanamivir).mp.
91	or/88-90
92	DRUG EVALUATION/
93	(drug? and (evaluat$ or effective$ or efficacy)).ti,ab.
94	or/92-93
95	exp ANTI-BACTERIAL AGENTS/pd [Pharmacology]
96	exp DECISION SUPPORT TECHNIQUES/
97	(decision? adj5 (aid? or analys$ or model$ or support$ or model$ or techni$)).ti,ab.
98	(Clinical$ adj3 predict$ adj3 rule?).ti,ab.
99	(data adj5 (interpret$ or analys$)).ti,ab.
100	or/96-99
101	FETAL DEATH/
102	STILLBIRTH/
103	PERINATAL DEATH/
104	((fetal or fetus) adj3 death?).ti,ab.
105	(stillbirths? or stillborn?).ti,ab.
106	(intrauterine adj3 death?).ti,ab.
107	(perinatal adj3 death?).ti,ab.
108	or/101-107
109	((sepsis adj5 manag$) and (maternal or mother?)).ti,ab.
110	(sepsis adj5 (pregnan$ or partu$ or intra?part$ or peri?part$)).ti.
111	or/109-110
112	UK Obstetric Surveillance System.ti,ab.
113	UKOSS.ti,ab.
114	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
115	MBRRACE.ti,ab.
116	Scottish confidential audit of severe maternal morbidity.ti,ab.

#	Searches
117	SCASMM.ti,ab.
118	"Confidential Enquiry into Maternal and Child Health".ti,ab.
119	CEMACH.ti,ab.
120	or/112-119
121	33 and 58 and 65 and (68 or 71 or 74 or 79 or 84 or 87)
122	33 and 58 and 68 and (65 or 71 or 74 or 79 or 84 or 87)
123	33 and 58 and 71 and (65 or 68 or 74 or 79 or 84 or 87)
124	33 and 58 and 74 and (65 or 68 or 71 or 79 or 84 or 87)
125	33 and 58 and 79 and (65 or 68 or 71 or 74 or 84 or 87)
126	33 and 58 and 84 and (65 or 68 or 71 or 74 or 79 or 87)
127	33 and 58 and 87 and (65 or 68 or 71 or 74 or 79 or 84)
128	33 and 58 and (62 or 65 or 68 or 71 or 74 or 79 or 84 or 87) and 91
129	33 and 58 and (62 or 65 or 68 or 71 or 74 or 79 or 84 or 87 or 91) and 94
130	33 and 58 and 95
131	33 and 58 and (62 or 65 or 68 or 71 or 74 or 79 or 84 or 87 or 91) and 100
132	58 and (62 or 65 or 68 or 71 or 74 or 79 or 84 or 87 or 91) and 108
133	(62 or 65 or 68 or 71 or 74 or 79 or 84 or 87 or 91) and 111
134	58 and 120
135	or/121-134
136	limit 135 to english language
137	LETTER/
138	EDITORIAL/
139	NEWS/
140	exp HISTORICAL ARTICLE/
141	ANECDOTES AS TOPIC/
142	COMMENT/
143	CASE REPORT/
144	(letter or comment*).ti.
145	or/137-144
146	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
147	145 not 146
148	ANIMALS/ not HUMANS/
149	exp ANIMALS, LABORATORY/
150	exp ANIMAL EXPERIMENTATION/
151	exp MODELS, ANIMAL/
152	exp RODENTIA/
153	(rat or rats or mouse or mice).ti.
154	or/147-153
155	136 not 154
156	21 and 155

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	PREGNANCY/
23	PREGNANCY, HIGH-RISK/
24	exp PREGNANCY, MULTIPLE/
25	PERIPARTUM PERIOD/
26	PARTURITION/
27	exp LABOR, OBSTETRIC/
28	OBSTETRIC LABOR, PREMATURE/
29	DELIVERY, OBSTETRIC/
30	pregnan$.ti,ab,kw.
31	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
32	((during or giving or give) adj3 birth?).ti,ab.
33	or/22-32
34	exp SEPSIS/
35	sepsis.ti,ab,kw.
36	BLOOD-BORNE PATHOGENS/
37	(blood$ adj3 (pathogen$ or poison$)).ti,ab.
38	exp SYSTEMIC INFLAMMATORY RESPONSE SYNDROME/
39	"systemic inflammatory response syndrome".ti,ab,kw.
40	SIRS.ti,ab.
41	septic?emi$.ti,ab,kw.

#	Searches
42	((septic or endotoxic or toxic) adj3 shock).ti,ab.
43	(py?emi$ or pyohemi$).ti,ab,kw.
44	(bacter?emi$ or fung?emi$ or parasit?emi$ or vir?emi$ or endotox?emi$ or candid?emi$).ti,ab,kw.
45	or/34-44
46	STREPTOCOCCAL INFECTIONS/
47	group A strep$.ti,ab,kw.
48	group B strep$.ti,ab,kw.
49	exp ESCHERICHIA COLI INFECTIONS/
50	Escherichia coli.ti,ab,kw.
51	e-coli.ti,ab,kw.
52	exp PNEUMOCOCCAL INFECTIONS/
53	(streptococ$ adj3 pneumon$).ti,ab.
54	INFLUENZA, HUMAN/
55	flu.ti,ab,kw.
56	influenza.ti,ab,kw.
57	or/46-56
58	45 or 57
59	ANTI-BACTERIAL AGENTS/
60	(Antibacterial? or anti-bacterial? or antibiotic? or anti-biotic?).ti,ab,kw.
61	(Alamethicin or Amoxicillin or Anisomycin or Aurodox or Azlocillin or Aztreonam or Bacitracin or Bacteriocin? or Bambermycin? or Bongkrekic Acid or Calcimycin or Capreomycin or Carfecillin or Chloramphenicol or Chlortetracycline or Ciprofloxacin or Citrinin or Clavulanic Acid? or Colistin or Dactinomycin or Daptomycin or Demeclocycline or Diketopiperazine? or Distamycin? or Doxycycline or Echinomycin or Edeine or Enoxacin or Enviomycin or Fluoroquinolone? or Fosfomycin or Fusidic Acid or Gramicidin or Lactam? or Lasalocid or Leucomycin? or Levofloxacin or Lincomycin or Lincosamide? or Linezolid or Lymecycline or Methacycline or Mezlocillin or Mikamycin or Minocycline or Moxalactam or Mupirocin or Mycobacillin or Nalidixic Acid or Nigericin or Nisin or Norfloxacin or Novobiocin or Ofloxacin or Oxolinic Acid or Oxytetracycline or Pefloxacin or Penicillic Acid or Pipemidic Acid or Piperacillin or Pivampicillin or Polymyxin B or Polymyxin? or Pristinamycin or Prodigiosin or Rifabutin or Rifamycin? or Rolitetracycline or Roxarsone or Streptogramin? or Sulfamerazine or Sulfamethoxypyridazine or Talampicillin or Tetracycline or Thiamphenicol or Thiostrepton or Trimethoprim or Tyrocidine or Tyrothricin or Valinomycin or Vernamycin B or Viomycin or Virginiamycin or beta-Lactam?).mp.
62	or/59-61
63	exp CEPHALOSPORINS/
64	(Cephalosporin? or Cefamandole or Cefoperazone or Cefazolin or Cefonicid or Cefsulodin or Cephacetrile or Cefotaxime or Cefixime or Cefmenoxime or Cefotiam or Ceftizoxime or Ceftriaxone or Cefuroxime or Cephalothin or Cephapirin or Cephalexin or Cefaclor or Cefadroxil or Cefatrizine or Cephaloglycin or Cephradine or Cephaloridine or Ceftazidime or Cephamycin? or Cefmetazole or Cefotetan or Cefoxitin or Ceftaroline or Ceftobiprole).mp.
65	or/63-64
66	exp AMINOGLYCOSIDES/
67	(Aminoglycoside? or Anthracycline? or Aclarubicin or Daunorubicin or Carubicin or Doxorubicin or Epirubicin or Idarubicin or Nogalamycin or Menogaril or Plicamycin or Butirosin Sulfate or Gentamicin? or Sisomicin or Netilmicin or Hygromycin or Kanamycin or Amikacin or Dibekacin

#	Searches
	or Nebramycin or Tobramycin or Metrizamide or Neomycin or Framycetin or Paromomycin or Ribostamycin or Puromycin or Spectinomycin or Streptomycin or Dihydrostreptomycin Sulfate or Streptothricin? or Streptozocin).mp.
68	or/66-67
69	exp PENICILLINS/
70	(Penicillin? or Amdinocillin or Cyclacillin or Methicillin or Nafcillin or Oxacillin or Cloxacillin or Dicloxacillin or Floxacillin or Penicillanic Acid or Ampicillin or Carbenicillin or Sulbenicillin or Sulbactam or Ticarcillin).mp.
71	or/69-70
72	exp GLYCOPEPTIDES/
73	(Glycopeptide? or Bleomycin or Peplomycin or Phleomycin? or Peptidoglycan or Ristocetin or Teicoplanin or Vancomycin or Oritavancin or Telavancin).mp.
74	or/72-73
75	exp MACROLIDES/
76	(Macrolide? or Lucensomycin or Maytansine or Mepartricin or Miocamycin or Natamycin or Nystatin or Oleandomycin or Troleandomycin or Oligomycin? or Rutamycin or Sirolimus or Everolimus or Tacrolimus or Tylosin or Amphotericin B or Antimycin A or Brefeldin A or Bryostatin? or Candicidin or Epothilone? or Erythromycin or Azithromycin or Clarithromycin or Ketolide? or Roxithromycin or Filipin or Ivermectin or Josamycin or Leucomycins or Kitasamycin or Spiramycin or Fidaxomicin).mp.
77	CLINDAMYCIN/
78	Clindamycin.mp.
79	or/75-78
80	exp CARBAPENEMS/
81	(Carbapenem? or Thienamycin? or Imipenem or Meropenem or Ertapenem).mp.
82	CILASTATIN/
83	Cilastatin.mp.
84	or/80-83
85	exp NITROIMIDAZOLES/
86	(Nitroimidazole? or Dimetridazole or Etanidazole or Ipronidazole or Metronidazole or Misonidazole or Nimorazole or Ornidazole or Ronidazole or Tinidazole).mp.
87	or/85-86
88	exp ANTIVIRAL AGENTS/ not exp ANTI-RETROVIRAL AGENTS/
89	(Antiviral? or anti-viral?).ti,ab,kw.
90	(1-Deoxynojirimycin or Acetylcysteine or Ac?clovir or Amantadine or Aphidicolin or Brefeldin or Bromodeoxyuridine or Cytarabine or Deoxyglucose or Dideoxyadenosine or Dideoxynucleoside? or Ditiocarb or Emtricitabine or Filipin or Foscarnet or Ganc?clovir or Idoxuridine or Inosine Pranobex or Interferon? or Methisazone or Netropsin or Oseltamivir or Palivizumab or Phosphonoacetic Acid or Poly A-U or Poly I-C or Pyran Copolymer or Ribavirin or Rimantadine or Simeprevir or Sofosbuvir or Streptovaricin or Tenofovir or Tenuazonic Acid or Tilorone or Trifluridine or Tunicamycin or Vidarabine or Zanamivir).mp.
91	or/88-90
92	DRUG EVALUATION/
93	(drug? and (evaluat$ or effective$ or efficacy)).ti,ab.
94	or/92-93
95	exp ANTI-BACTERIAL AGENTS/pd [Pharmacology]

#	Searches
96	exp DECISION SUPPORT TECHNIQUES/
97	(decision? adj5 (aid? or analys$ or model$ or support$ or model$ or techni$)).ti,ab.
98	(Clinical$ adj3 predict$ adj3 rule?).ti,ab.
99	(data adj5 (interpret$ or analys$)).ti,ab.
100	or/96-99
101	FETAL DEATH/
102	STILLBIRTH/
103	PERINATAL DEATH/
104	((fetal or fetus) adj3 death?).ti,ab.
105	(stillbirths? or stillborn?).ti,ab,kw.
106	(intrauterine adj3 death?).ti,ab.
107	(perinatal adj3 death?).ti,ab.
108	or/101-107
109	((sepsis adj5 manag$) and (maternal or mother?)).ti,ab.
110	(sepsis adj5 (pregnan$ or partu$ or intra?part$ or peri?part$)).ti.
111	or/109-110
112	UK Obstetric Surveillance System.ti,ab.
113	UKOSS.ti,ab.
114	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
115	MBRRACE.ti,ab.
116	Scottish confidential audit of severe maternal morbidity.ti,ab.
117	SCASMM.ti,ab.
118	"Confidential Enquiry into Maternal and Child Health".ti,ab.
119	CEMACH.ti,ab.
120	or/112-119
121	33 and 58 and 65 and (68 or 71 or 74 or 79 or 84 or 87)
122	33 and 58 and 68 and (65 or 71 or 74 or 79 or 84 or 87)
123	33 and 58 and 71 and (65 or 68 or 74 or 79 or 84 or 87)
124	33 and 58 and 74 and (65 or 68 or 71 or 79 or 84 or 87)
125	33 and 58 and 79 and (65 or 68 or 71 or 74 or 84 or 87)
126	33 and 58 and 84 and (65 or 68 or 71 or 74 or 79 or 87)
127	33 and 58 and 87 and (65 or 68 or 71 or 74 or 79 or 84)
128	33 and 58 and (62 or 65 or 68 or 71 or 74 or 79 or 84 or 87) and 91
129	33 and 58 and (62 or 65 or 68 or 71 or 74 or 79 or 84 or 87 or 91) and 94
130	33 and 58 and 95
131	33 and 58 and (62 or 65 or 68 or 71 or 74 or 79 or 84 or 87 or 91) and 100
132	58 and (62 or 65 or 68 or 71 or 74 or 79 or 84 or 87 or 91) and 108
133	(62 or 65 or 68 or 71 or 74 or 79 or 84 or 87 or 91) and 111
134	58 and 120
135	or/121-134
136	21 and 135

Database: NHS Economic Evaluation Database

#	Searches
1	PREGNANCY/
2	PREGNANCY, HIGH-RISK/
3	exp PREGNANCY, MULTIPLE/
4	PERIPARTUM PERIOD/
5	PARTURITION/
6	exp LABOR, OBSTETRIC/
7	OBSTETRIC LABOR, PREMATURE/
8	DELIVERY, OBSTETRIC/
9	pregnan$.tw.
10	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
11	((during or giving or give) adj3 birth?).tw.
12	or/1-11
13	exp SEPSIS/
14	sepsis.tw.
15	BLOOD-BORNE PATHOGENS/
16	(blood$ adj3 (pathogen$ or poison$)).tw.
17	exp SYSTEMIC INFLAMMATORY RESPONSE SYNDROME/
18	"systemic inflammatory response syndrome".tw.
19	SIRS.tw.
20	septic?emi$.tw.
21	((septic or endotoxic or toxic) adj3 shock).tw.
22	(py?emi$ or pyohemi$).tw.
23	(bacter?emi$ or fung?emi$ or parasit?emi$ or vir?emi$ or endotox?emi$ or candid?emi$).tw.
24	or/13-23
25	STREPTOCOCCAL INFECTIONS/
26	group A strep$.tw.
27	group B strep$.tw.
28	exp ESCHERICHIA COLI INFECTIONS/
29	Escherichia coli.tw.
30	e-coli.tw.
31	exp PNEUMOCOCCAL INFECTIONS/
32	(streptococ$ adj3 pneumon$).tw.
33	INFLUENZA, HUMAN/
34	flu.tw.
35	influenza.tw.
36	or/25-35
37	24 or 36
38	ANTI-BACTERIAL AGENTS/
39	(Antibacterial? or anti-bacterial? or antibiotic? or anti-biotic?).tw.
40	(Alamethicin or Amoxicillin or Anisomycin or Aurodox or Azlocillin or Aztreonam or Bacitracin or Bacteriocin? or Bambermycin? or Bongkrekic Acid or Calcimycin or Capreomycin or

#	Searches
	Carfecillin or Chloramphenicol or Chlortetracycline or Ciprofloxacin or Citrinin or Clavulanic Acid? or Colistin or Dactinomycin or Daptomycin or Demeclocycline or Diketopiperazine? or Distamycin? or Doxycycline or Echinomycin or Edeine or Enoxacin or Enviomycin or Fluoroquinolone? or Fosfomycin or Fusidic Acid or Gramicidin or Lactam? or Lasalocid or Leucomycin? or Levofloxacin or Lincomycin or Lincosamide? or Linezolid or Lymecycline or Methacycline or Mezlocillin or Mikamycin or Minocycline or Moxalactam or Mupirocin or Mycobacillin or Nalidixic Acid or Nigericin or Nisin or Norfloxacin or Novobiocin or Ofloxacin or Oxolinic Acid or Oxytetracycline or Pefloxacin or Penicillic Acid or Pipemidic Acid or Piperacillin or Pivampicillin or Polymyxin B or Polymyxin? or Pristinamycin or Prodigiosin or Rifabutin or Rifamycin? or Rolitetracycline or Roxarsone or Streptogramin? or Sulfamerazine or Sulfamethoxypyridazine or Talampicillin or Tetracycline or Thiamphenicol or Thiostrepton or Trimethoprim or Tyrocidine or Tyrothricin or Valinomycin or Vernamycin B or Viomycin or Virginiamycin or beta-Lactam?).mp.
41	or/38-40
42	exp CEPHALOSPORINS/
43	(Cephalosporin? or Cefamandole or Cefoperazone or Cefazolin or Cefonicid or Cefsulodin or Cephacetrile or Cefotaxime or Cefixime or Cefmenoxime or Cefotiam or Ceftizoxime or Ceftriaxone or Cefuroxime or Cephalothin or Cephapirin or Cephalexin or Cefaclor or Cefadroxil or Cefatrizine or Cephaloglycin or Cephradine or Cephaloridine or Ceftazidime or Cephamycin? or Cefmetazole or Cefotetan or Cefoxitin or Ceftaroline or Ceftobiprole).mp.
44	or/42-43
45	exp AMINOGLYCOSIDES/
46	(Aminoglycoside? or Anthracycline? or Aclarubicin or Daunorubicin or Carubicin or Doxorubicin or Epirubicin or Idarubicin or Nogalamycin or Menogaril or Plicamycin or Butirosin Sulfate or Gentamicin? or Sisomicin or Netilmicin or Hygromycin or Kanamycin or Amikacin or Dibekacin or Nebramycin or Tobramycin or Metrizamide or Neomycin or Framycetin or Paromomycin or Ribostamycin or Puromycin or Spectinomycin or Streptomycin or Dihydrostreptomycin Sulfate or Streptothricin? or Streptozocin).mp.
47	or/45-46
48	exp PENICILLINS/
49	(Penicillin? or Amdinocillin or Cyclacillin or Methicillin or Nafcillin or Oxacillin or Cloxacillin or Dicloxacillin or Floxacillin or Penicillanic Acid or Ampicillin or Carbenicillin or Sulbenicillin or Sulbactam or Ticarcillin).mp.
50	or/48-49
51	exp GLYCOPEPTIDES/
52	(Glycopeptide? or Bleomycin or Peplomycin or Phleomycin? or Peptidoglycan or Ristocetin or Teicoplanin or Vancomycin or Oritavancin or Telavancin).mp.
53	or/51-52
54	exp MACROLIDES/
55	(Macrolide? or Lucensomycin or Maytansine or Mepartricin or Miocamycin or Natamycin or Nystatin or Oleandomycin or Troleandomycin or Oligomycin? or Rutamycin or Sirolimus or Everolimus or Tacrolimus or Tylosin or Amphotericin B or Antimycin A or Brefeldin A or Bryostatin? or Candicidin or Epothilone? or Erythromycin or Azithromycin or Clarithromycin or Ketolide? or Roxithromycin or Filipin or Ivermectin or Josamycin or Leucomycins or Kitasamycin or Spiramycin or Fidaxomicin).mp.
56	CLINDAMYCIN/
57	Clindamycin.mp.
58	or/54-57
59	exp CARBAPENEMS/

#	Searches
60	(Carbapenem? or Thienamycin? or Imipenem or Meropenem or Ertapenem).mp.
61	CILASTATIN/
62	Cilastatin.mp.
63	or/59-62
64	exp NITROIMIDAZOLES/
65	(Nitroimidazole? or Dimetridazole or Etanidazole or Ipronidazole or Metronidazole or Misonidazole or Nimorazole or Ornidazole or Ronidazole or Tinidazole).mp.
66	or/64-65
67	exp ANTIVIRAL AGENTS/ not exp ANTI-RETROVIRAL AGENTS/
68	(Antiviral? or anti-viral?).tw.
69	(1-Deoxynojirimycin or Acetylcysteine or Ac?clovir or Amantadine or Aphidicolin or Brefeldin or Bromodeoxyuridine or Cytarabine or Deoxyglucose or Dideoxyadenosine or Dideoxynucleoside? or Ditiocarb or Emtricitabine or Filipin or Foscarnet or Ganc?clovir or Idoxuridine or Inosine Pranobex or Interferon? or Methisazone or Netropsin or Oseltamivir or Palivizumab or Phosphonoacetic Acid or Poly A-U or Poly I-C or Pyran Copolymer or Ribavirin or Rimantadine or Simeprevir or Sofosbuvir or Streptovaricin or Tenofovir or Tenuazonic Acid or Tilorone or Trifluridine or Tunicamycin or Vidarabine or Zanamivir).mp.
70	or/67-69
71	DRUG EVALUATION/
72	(drug? and (evaluat$ or effective$ or efficacy)).tw.
73	or/71-72
74	exp ANTI-BACTERIAL AGENTS/pd [Pharmacology]
75	exp DECISION SUPPORT TECHNIQUES/
76	(decision? adj5 (aid? or analys$ or model$ or support$ or model$ or techni$)).tw.
77	(Clinical$ adj3 predict$ adj3 rule?).tw.
78	(data adj5 (interpret$ or analys$)).tw.
79	or/75-78
80	FETAL DEATH/
81	STILLBIRTH/
82	PERINATAL DEATH/
83	((fetal or fetus) adj3 death?).tw.
84	(stillbirths? or stillborn?).tw.
85	(intrauterine adj3 death?).tw.
86	(perinatal adj3 death?).tw.
87	or/80-86
88	((sepsis adj5 manag$) and (maternal or mother?)).tw.
89	(sepsis adj5 (pregnan$ or partu$ or intra?part$ or peri?part$)).tw.
90	or/88-89
91	UK Obstetric Surveillance System.tw.
92	UKOSS.tw.
93	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".tw.
94	MBRRACE.tw.
95	Scottish confidential audit of severe maternal morbidity.tw.

#	Searches
96	SCASMM.tw.
97	"Confidential Enquiry into Maternal and Child Health".tw.
98	CEMACH.tw.
99	or/91-98
100	12 and 37 and 44 and (47 or 50 or 53 or 58 or 63 or 66)
101	12 and 37 and 47 and (44 or 50 or 53 or 58 or 63 or 66)
102	12 and 37 and 50 and (44 or 47 or 53 or 58 or 63 or 66)
103	12 and 37 and 53 and (44 or 47 or 50 or 58 or 63 or 66)
104	12 and 37 and 58 and (44 or 47 or 50 or 53 or 63 or 66)
105	12 and 37 and 63 and (44 or 47 or 50 or 53 or 58 or 66)
106	12 and 37 and 66 and (44 or 47 or 50 or 53 or 58 or 63)
107	12 and 37 and (41 or 44 or 47 or 50 or 53 or 58 or 63 or 66) and 70
108	12 and 37 and (41 or 44 or 47 or 50 or 53 or 58 or 63 or 66 or 70) and 73
109	12 and 37 and 74
110	12 and 37 and (41 or 44 or 47 or 50 or 53 or 58 or 63 or 66 or 70) and 79
111	37 and (41 or 44 or 47 or 50 or 53 or 58 or 63 or 66 or 70) and 87
112	(41 or 44 or 47 or 50 or 53 or 58 or 63 or 66 or 70) and 90
113	37 and 99
114	or/100-113

Database: Health Technology Assessment

#	Searches
1	PREGNANCY/
2	PREGNANCY, HIGH-RISK/
3	exp PREGNANCY, MULTIPLE/
4	PERIPARTUM PERIOD/
5	PARTURITION/
6	exp LABOR, OBSTETRIC/
7	OBSTETRIC LABOR, PREMATURE/
8	DELIVERY, OBSTETRIC/
9	pregnan$.tw.
10	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
11	((during or giving or give) adj3 birth?).tw.
12	or/1-11
13	exp SEPSIS/
14	sepsis.tw.
15	BLOOD-BORNE PATHOGENS/
16	(blood$ adj3 (pathogen$ or poison$)).tw.
17	exp SYSTEMIC INFLAMMATORY RESPONSE SYNDROME/
18	"systemic inflammatory response syndrome".tw.
19	SIRS.tw.
20	septic?emi$.tw.

#	Searches
21	((septic or endotoxic or toxic) adj3 shock).tw.
22	(py?emi$ or pyohemi$).tw.
23	(bacter?emi$ or fung?emi$ or parasit?emi$ or vir?emi$ or endotox?emi$ or candid?emi$).tw.
24	or/13-23
25	STREPTOCOCCAL INFECTIONS/
26	group A strep$.tw.
27	group B strep$.tw.
28	exp ESCHERICHIA COLI INFECTIONS/
29	Escherichia coli.tw.
30	e-coli.tw.
31	exp PNEUMOCOCCAL INFECTIONS/
32	(streptococ$ adj3 pneumon$).tw.
33	INFLUENZA, HUMAN/
34	flu.tw.
35	influenza.tw.
36	or/25-35
37	24 or 36
38	ANTI-BACTERIAL AGENTS/
39	(Antibacterial? or anti-bacterial? or antibiotic? or anti-biotic?).tw.
40	(Alamethicin or Amoxicillin or Anisomycin or Aurodox or Azlocillin or Aztreonam or Bacitracin or Bacteriocin? or Bambermycin? or Bongkrekic Acid or Calcimycin or Capreomycin or Carfecillin or Chloramphenicol or Chlortetracycline or Ciprofloxacin or Citrinin or Clavulanic Acid? or Colistin or Dactinomycin or Daptomycin or Demeclocycline or Diketopiperazine? or Distamycin? or Doxycycline or Echinomycin or Edeine or Enoxacin or Enviomycin or Fluoroquinolone? or Fosfomycin or Fusidic Acid or Gramicidin or Lactam? or Lasalocid or Leucomycin? or Levofloxacin or Lincomycin or Lincosamide? or Linezolid or Lymecycline or Methacycline or Mezlocillin or Mikamycin or Minocycline or Moxalactam or Mupirocin or Mycobacillin or Nalidixic Acid or Nigericin or Nisin or Norfloxacin or Novobiocin or Ofloxacin or Oxolinic Acid or Oxytetracycline or Pefloxacin or Penicillic Acid or Pipemidic Acid or Piperacillin or Pivampicillin or Polymyxin B or Polymyxin? or Pristinamycin or Prodigiosin or Rifabutin or Rifamycin? or Rolitetracycline or Roxarsone or Streptogramin? or Sulfamerazine or Sulfamethoxypyridazine or Talampicillin or Tetracycline or Thiamphenicol or Thiostrepton or Trimethoprim or Tyrocidine or Tyrothricin or Valinomycin or Vernamycin B or Viomycin or Virginiamycin or beta-Lactam?).mp.
41	or/38-40
42	exp CEPHALOSPORINS/
43	(Cephalosporin? or Cefamandole or Cefoperazone or Cefazolin or Cefonicid or Cefsulodin or Cephacetrile or Cefotaxime or Cefixime or Cefmenoxime or Cefotiam or Ceftizoxime or Ceftriaxone or Cefuroxime or Cephalothin or Cephapirin or Cephalexin or Cefaclor or Cefadroxil or Cefatrizine or Cephaloglycin or Cephradine or Cephaloridine or Ceftazidime or Cephamycin? or Cefmetazole or Cefotetan or Cefoxitin or Ceftaroline or Ceftobiprole).mp.
44	or/42-43
45	exp AMINOGLYCOSIDES/
46	(Aminoglycoside? or Anthracycline? or Aclarubicin or Daunorubicin or Carubicin or Doxorubicin or Epirubicin or Idarubicin or Nogalamycin or Menogaril or Plicamycin or Butirosin Sulfate or Gentamicin? or Sisomicin or Netilmicin or Hygromycin or Kanamycin or Amikacin or Dibekacin or Nebramycin or Tobramycin or Metrizamide or Neomycin or Framycetin or Paromomycin or

#	Searches
	Ribostamycin or Puromycin or Spectinomycin or Streptomycin or Dihydrostreptomycin Sulfate or Streptothricin? or Streptozocin).mp.
47	or/45-46
48	exp PENICILLINS/
49	(Penicillin? or Amdinocillin or Cyclacillin or Methicillin or Nafcillin or Oxacillin or Cloxacillin or Dicloxacillin or Floxacillin or Penicillanic Acid or Ampicillin or Carbenicillin or Sulbenicillin or Sulbactam or Ticarcillin).mp.
50	or/48-49
51	exp GLYCOPEPTIDES/
52	(Glycopeptide? or Bleomycin or Peplomycin or Phleomycin? or Peptidoglycan or Ristocetin or Teicoplanin or Vancomycin or Oritavancin or Telavancin).mp.
53	or/51-52
54	exp MACROLIDES/
55	(Macrolide? or Lucensomycin or Maytansine or Mepartricin or Miocamycin or Natamycin or Nystatin or Oleandomycin or Troleandomycin or Oligomycin? or Rutamycin or Sirolimus or Everolimus or Tacrolimus or Tylosin or Amphotericin B or Antimycin A or Brefeldin A or Bryostatin? or Candicidin or Epothilone? or Erythromycin or Azithromycin or Clarithromycin or Ketolide? or Roxithromycin or Filipin or Ivermectin or Josamycin or Leucomycins or Kitasamycin or Spiramycin or Fidaxomicin).mp.
56	CLINDAMYCIN/
57	Clindamycin.mp.
58	or/54-57
59	exp CARBAPENEMS/
60	(Carbapenem? or Thienamycin? or Imipenem or Meropenem or Ertapenem).mp.
61	CILASTATIN/
62	Cilastatin.mp.
63	or/59-62
64	exp NITROIMIDAZOLES/
65	(Nitroimidazole? or Dimetridazole or Etanidazole or Ipronidazole or Metronidazole or Misonidazole or Nimorazole or Ornidazole or Ronidazole or Tinidazole).mp.
66	or/64-65
67	exp ANTIVIRAL AGENTS/ not exp ANTI-RETROVIRAL AGENTS/
68	(Antiviral? or anti-viral?).tw.
69	(1-Deoxynojirimycin or Acetylcysteine or Ac?clovir or Amantadine or Aphidicolin or Brefeldin or Bromodeoxyuridine or Cytarabine or Deoxyglucose or Dideoxyadenosine or Dideoxynucleoside? or Ditiocarb or Emtricitabine or Filipin or Foscarnet or Ganc?clovir or Idoxuridine or Inosine Pranobex or Interferon? or Methisazone or Netropsin or Oseltamivir or Palivizumab or Phosphonoacetic Acid or Poly A-U or Poly I-C or Pyran Copolymer or Ribavirin or Rimantadine or Simeprevir or Sofosbuvir or Streptovaricin or Tenofovir or Tenuazonic Acid or Tilorone or Trifluridine or Tunicamycin or Vidarabine or Zanamivir).mp.
70	or/67-69
71	DRUG EVALUATION/
72	(drug? and (evaluat$ or effective$ or efficacy)).tw.
73	or/71-72
74	exp ANTI-BACTERIAL AGENTS/pd [Pharmacology]
75	exp DECISION SUPPORT TECHNIQUES/

#	Searches
76	(decision? adj5 (aid? or analys$ or model$ or support$ or model$ or techni$)).tw.
77	(Clinical$ adj3 predict$ adj3 rule?).tw.
78	(data adj5 (interpret$ or analys$)).tw.
79	or/75-78
80	FETAL DEATH/
81	STILLBIRTH/
82	PERINATAL DEATH/
83	((fetal or fetus) adj3 death?).tw.
84	(stillbirths? or stillborn?).tw.
85	(intrauterine adj3 death?).tw.
86	(perinatal adj3 death?).tw.
87	or/80-86
88	((sepsis adj5 manag$) and (maternal or mother?)).tw.
89	(sepsis adj5 (pregnan$ or partu$ or intra?part$ or peri?part$)).tw.
90	or/88-89
91	UK Obstetric Surveillance System.tw.
92	UKOSS.tw.
93	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".tw.
94	MBRRACE.tw.
95	Scottish confidential audit of severe maternal morbidity.tw.
96	SCASMM.tw.
97	"Confidential Enquiry into Maternal and Child Health".tw.
98	CEMACH.tw.
99	or/91-98
100	12 and 37 and 44 and (47 or 50 or 53 or 58 or 63 or 66)
101	12 and 37 and 47 and (44 or 50 or 53 or 58 or 63 or 66)
102	12 and 37 and 50 and (44 or 47 or 53 or 58 or 63 or 66)
103	12 and 37 and 53 and (44 or 47 or 50 or 58 or 63 or 66)
104	12 and 37 and 58 and (44 or 47 or 50 or 53 or 63 or 66)
105	12 and 37 and 63 and (44 or 47 or 50 or 53 or 58 or 66)
106	12 and 37 and 66 and (44 or 47 or 50 or 53 or 58 or 63)
107	12 and 37 and (41 or 44 or 47 or 50 or 53 or 58 or 63 or 66) and 70
108	12 and 37 and (41 or 44 or 47 or 50 or 53 or 58 or 63 or 66 or 70) and 73
109	12 and 37 and 74
110	12 and 37 and (41 or 44 or 47 or 50 or 53 or 58 or 63 or 66 or 70) and 79
111	37 and (41 or 44 or 47 or 50 or 53 or 58 or 63 or 66 or 70) and 87
112	(41 or 44 or 47 or 50 or 53 or 58 or 63 or 66 or 70) and 90
113	37 and 99
114	or/100-113

Database: Embase

#	Searches
1	HEALTH ECONOMICS/
2	exp ECONOMIC EVALUATION/
3	exp HEALTH CARE COST/
4	exp FEE/
5	BUDGET/
6	FUNDING/
7	RESOURCE ALLOCATION/
8	budget*.ti,ab.
9	cost*.ti,ab.
10	(economic* or pharmaco?economic*).ti,ab.
11	(price* or pricing*).ti,ab.
12	(financ* or fee or fees or expenditure* or saving*).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	resourc* allocat*.ti,ab.
15	(fund or funds or funding* or funded).ti,ab.
16	(ration or rations or rationing* or rationed).ti,ab.
17	or/1-16
18	*PREGNANCY/
19	*HIGH RISK PREGNANCY/
20	exp *MULTIPLE PREGNANCY/
21	*PERINATAL PERIOD/
22	*BIRTH/
23	exp *LABOR/
24	*PREMATURE LABOR/
25	*OBSTETRIC DELIVERY/
26	*INTRAPARTUM CARE/
27	pregnan$.ti,ab.
28	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
29	((during or giving or give) adj3 birth?).ti,ab.
30	or/18-29
31	exp *SEPSIS/
32	sepsis.ti,ab.
33	*BLOODBORNE BACTERIUM/
34	(blood$ adj3 (pathogen$ or poison$)).ti,ab.
35	*SYSTEMIC INFLAMMATORY RESPONSE SYNDROME/
36	"systemic inflammatory response syndrome".ti,ab.
37	SIRS.ti,ab.
38	septic?emi$.ti,ab.
39	((septic or endotoxic or toxic) adj3 shock).ti,ab.
40	(py?emi$ or pyohemi$).ti,ab.
41	(bacter?emi$ or fung?emi$ or parasit?emi$ or vir?emi$ or endotox?emi$ or candid?emi$).ti,ab.

#	Searches
42	or/31-41
43	exp *GROUP A STREPTOCOCCAL INFECTION/
44	exp *GROUP B STREPTOCOCCAL INFECTION/
45	group A strep$.ti,ab.
46	group B strep$.ti,ab.
47	*ESCHERICHIA COLI INFECTION/
48	Escherichia coli.ti,ab.
49	e-coli.ti,ab.
50	exp *PNEUMOCOCCAL INFECTION/
51	(streptococ$ adj3 pneumon$).ti,ab.
52	exp *INFLUENZA/ not SWINE INFLUENZA/
53	flu.ti,ab.
54	influenza.ti,ab.
55	or/43-54
56	42 or 55
57	ANTIINFECTIVE AGENT/
58	(Antibacterial? or anti-bacterial? or antibiotic? or anti-biotic?).ti,ab.
59	(Alamethicin or Amoxicillin or Anisomycin or Aurodox or Azlocillin or Aztreonam or Bacitracin or Bacteriocin? or Bambermycin? or Bongkrekic Acid or Calcimycin or Capreomycin or Carfecillin or Chloramphenicol or Chlortetracycline or Ciprofloxacin or Citrinin or Clavulanic Acid? or Colistin or Dactinomycin or Daptomycin or Demeclocycline or Diketopiperazine? or Distamycin? or Doxycycline or Echinomycin or Edeine or Enoxacin or Enviomycin or Fluoroquinolone? or Fosfomycin or Fusidic Acid or Gramicidin or Lactam? or Lasalocid or Leucomycin? or Levofloxacin or Lincomycin or Lincosamide? or Linezolid or Lymecycline or Methacycline or Mezlocillin or Mikamycin or Minocycline or Moxalactam or Mupirocin or Mycobacillin or Nalidixic Acid or Nigericin or Nisin or Norfloxacin or Novobiocin or Ofloxacin or Oxolinic Acid or Oxytetracycline or Pefloxacin or Penicillic Acid or Pipemidic Acid or Piperacillin or Pivampicillin or Polymyxin B or Polymyxin? or Pristinamycin or Prodigiosin or Rifabutin or Rifamycin? or Rolitetracycline or Roxarsone or Streptogramin? or Sulfamerazine or Sulfamethoxypyridazine or Talampicillin or Tetracycline or Thiamphenicol or Thiostrepton or Trimethoprim or Tyrocidine or Tyrothricin or Valinomycin or Vernamycin B or Viomycin or Virginiamycin or beta-Lactam?).mp.
60	or/57-59
61	exp CEPHALOSPORIN DERIVATIVE/
62	(Cephalosporin? or Cefamandole or Cefoperazone or Cefazolin or Cefonicid or Cefsulodin or Cephacetrile or Cefotaxime or Cefixime or Cefmenoxime or Cefotiam or Ceftizoxime or Ceftriaxone or Cefuroxime or Cephalothin or Cephapirin or Cephalexin or Cefaclor or Cefadroxil or Cefatrizine or Cephaloglycin or Cephradine or Cephaloridine or Ceftazidime or Cephamycin? or Cefmetazole or Cefotetan or Cefoxitin or Ceftaroline or Ceftobiprole).mp.
63	or/61-62
64	exp AMINOGLYCOSIDE ANTIBIOTIC AGENT/
65	(Aminoglycoside? or Anthracycline? or Aclarubicin or Daunorubicin or Carubicin or Doxorubicin or Epirubicin or Idarubicin or Nogalamycin or Menogaril or Plicamycin or Butirosin Sulfate or Gentamicin? or Sisomicin or Netilmicin or Hygromycin or Kanamycin or Amikacin or Dibekacin or Nebramycin or Tobramycin or Metrizamide or Neomycin or Framycetin or Paromomycin or Ribostamycin or Puromycin or Spectinomycin or Streptomycin or Dihydrostreptomycin Sulfate or Streptothricin? or Streptozocin).mp.

#	Searches
66	or/64-65
67	exp PENICILLIN DERIVATIVE/
68	(Penicillin? or Amdinocillin or Cyclacillin or Methicillin or Nafcillin or Oxacillin or Cloxacillin or Dicloxacillin or Floxacillin or Penicillanic Acid or Ampicillin or Carbenicillin or Sulbenicillin or Sulbactam or Ticarcillin).mp.
69	or/67-68
70	GLYCOPEPTIDE/
71	VANCOMYCIN/
72	VANCOMYCIN DERIVATIVE/
73	ORITAVANCIN/
74	TELAVANCIN/
75	(Glycopeptide? or Bleomycin or Peplomycin or Phleomycin? or Peptidoglycan or Ristocetin or Teicoplanin or Vancomycin or Oritavancin or Telavancin).mp.
76	or/70-75
77	exp MACROLIDE/
78	(Macrolide? or Lucensomycin or Maytansine or Mepartricin or Miocamycin or Natamycin or Nystatin or Oleandomycin or Troleandomycin or Oligomycin? or Rutamycin or Sirolimus or Everolimus or Tacrolimus or Tylosin or Amphotericin B or Antimycin A or Brefeldin A or Bryostatin? or Candicidin or Epothilone? or Erythromycin or Azithromycin or Clarithromycin or Ketolide? or Roxithromycin or Filipin or Ivermectin or Josamycin or Leucomycins or Kitasamycin or Spiramycin or Fidaxomicin).mp.
79	CLINDAMYCIN/
80	Clindamycin.mp.
81	or/77-80
82	CARBAPENEM DERIVATIVE/
83	MEROPENEM/
84	ERTAPENEM/
85	(Carbapenem? or Thienamycin? or Imipenem or Meropenem or Ertapenem).mp.
86	CILASTATIN/
87	Cilastatin.mp.
88	or/82-87
89	exp NITROIMIDAZOLE DERIVATIVE/
90	(Nitroimidazole? or Dimetridazole or Etanidazole or Ipronidazole or Metronidazole or Misonidazole or Nimorazole or Ornidazole or Ronidazole or Tinidazole).mp.
91	or/89-90
92	exp ANTIVIRUS AGENT/ not (exp ANTIRETROVIRUS AGENT/ or exp VIRUS FUSION INHIBITOR/)
93	(Antiviral? or anti-viral?).ti,ab.
94	(1-Deoxynojirimycin or Acetylcysteine or Ac?clovir or Amantadine or Aphidicolin or Brefeldin or Bromodeoxyuridine or Cytarabine or Deoxyglucose or Dideoxyadenosine or Dideoxynucleoside? or Ditiocarb or Emtricitabine or Filipin or Foscarnet or Ganc?clovir or Idoxuridine or Inosine Pranobex or Interferon? or Methisazone or Netropsin or Oseltamivir or Palivizumab or Phosphonoacetic Acid or Poly A-U or Poly I-C or Pyran Copolymer or Ribavirin or Rimantadine or Simeprevir or Sofosbuvir or Streptovaricin or Tenofovir or Tenuazonic Acid or Tilorone or Trifluridine or Tunicamycin or Vidarabine or Zanamivir).mp.
95	or/92-94

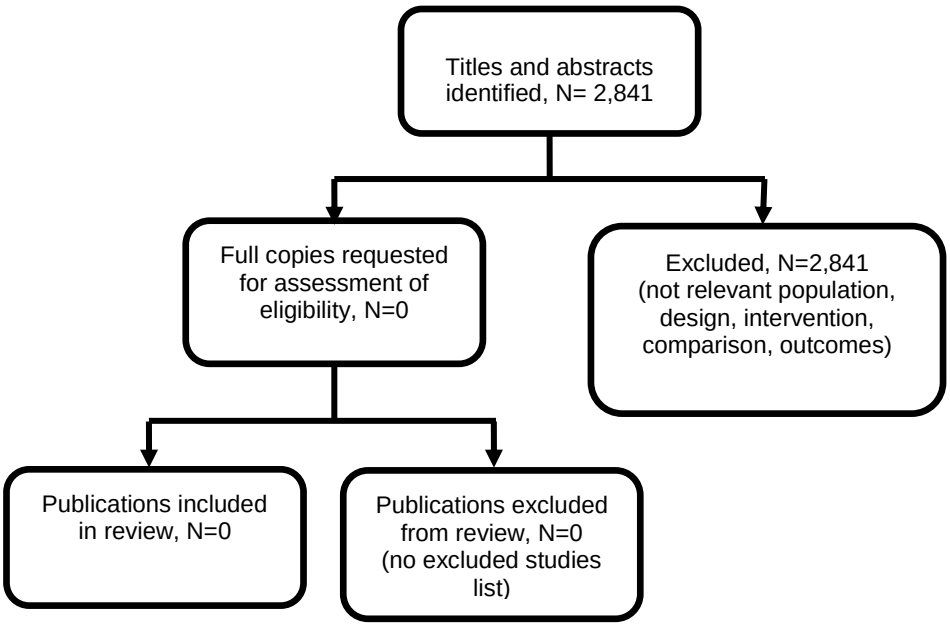
#	Searches
96	DRUG EFFICACY/
97	(drug? and (evaluat$ or effective$ or efficacy)).ti,ab.
98	or/96-97
99	exp ANTIINFECTIVE AGENT/pd [Pharmacology]
100	exp ANTIINFECTIVE AGENT/cm [Drug Comparison]
101	exp DECISION SUPPORT SYSTEM/
102	(decision? adj5 (aid? or analys$ or model$ or support$ or model$ or techni$)).ti,ab.
103	(Clinical$ adj3 predict$ adj3 rule?).ti,ab.
104	(data adj5 (interpret$ or analys$)).ti,ab.
105	or/101-104
106	*FETUS DEATH/
107	*STILLBIRTH/
108	*PERINATAL DEATH/
109	((fetal or fetus) adj3 death?).ti,ab.
110	(stillbirths? or stillborn?).ti,ab.
111	(intrauterine adj3 death?).ti,ab.
112	(perinatal adj3 death?).ti,ab.
113	or/106-112
114	((sepsis adj5 manag$) and (maternal or mother?)).ti,ab.
115	(sepsis adj5 (pregnan$ or partu$ or intra?part$ or peri?part$)).ti.
116	or/114-115
117	UK Obstetric Surveillance System.ti,ab.
118	UKOSS.ti,ab.
119	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
120	MBRRACE.ti,ab.
121	Scottish confidential audit of severe maternal morbidity.ti,ab.
122	SCASMM.ti,ab.
123	"Confidential Enquiry into Maternal and Child Health".ti,ab.
124	CEMACH.ti,ab.
125	or/117-124
126	30 and 56 and 63 and (66 or 69 or 76 or 81 or 88 or 91)
127	30 and 56 and 66 and (63 or 69 or 76 or 81 or 88 or 91)
128	30 and 56 and 69 and (63 or 66 or 76 or 81 or 88 or 91)
129	30 and 56 and 76 and (63 or 66 or 69 or 81 or 88 or 91)
130	30 and 56 and 81 and (63 or 66 or 69 or 76 or 88 or 91)
131	30 and 56 and 88 and (63 or 66 or 69 or 76 or 81 or 91)
132	30 and 56 and 91 and (63 or 66 or 69 or 76 or 81 or 88)
133	30 and 56 and (60 or 63 or 66 or 69 or 76 or 81 or 88 or 91) and 95
134	30 and 56 and (60 or 63 or 66 or 69 or 76 or 81 or 88 or 91 or 95) and 98
135	30 and 56 and 99
136	30 and 56 and 100

#	Searches
137	30 and 56 and (60 or 63 or 66 or 69 or 76 or 81 or 88 or 91 or 95) and 105
138	56 and (60 or 63 or 66 or 69 or 76 or 81 or 88 or 91 or 95) and 113
139	(60 or 63 or 66 or 69 or 76 or 81 or 88 or 91 or 95) and 116
140	56 and 125
141	or/126-140
142	limit 141 to english language
143	letter.pt. or LETTER/
144	note.pt.
145	editorial.pt.
146	CASE REPORT/ or CASE STUDY/
147	(letter or comment*).ti.
148	or/143-147
149	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
150	148 not 149
151	ANIMAL/ not HUMAN/
152	NONHUMAN/
153	exp ANIMAL EXPERIMENT/
154	exp EXPERIMENTAL ANIMAL/
155	ANIMAL MODEL/
156	exp RODENT/
157	(rat or rats or mouse or mice).ti.
158	or/150-157
159	142 not 158
160	17 and 159

Appendix B – Economic evidence study selection

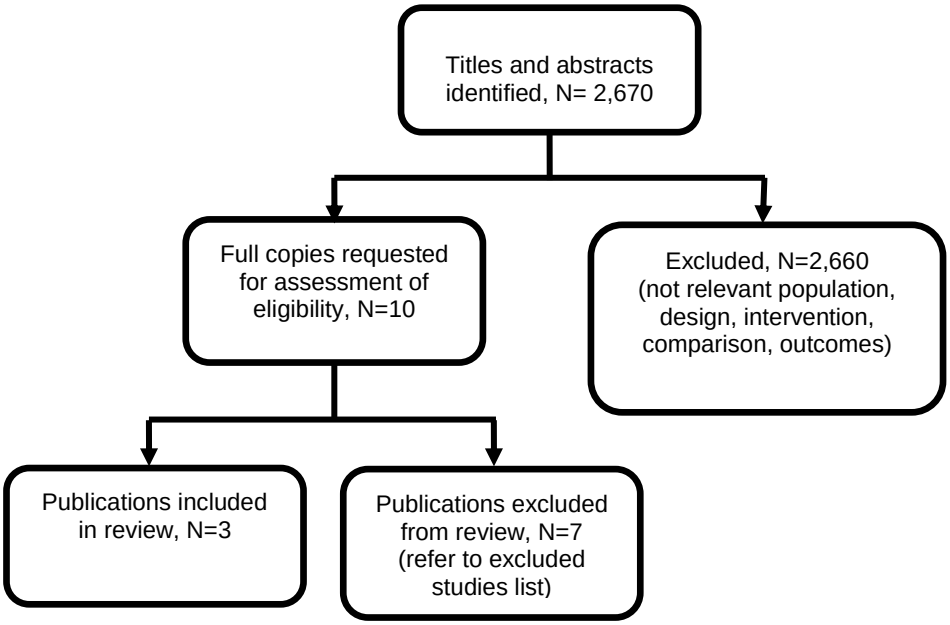
Health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions

Figure 27: Flow diagram of economic article selection for global health economic search for women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions



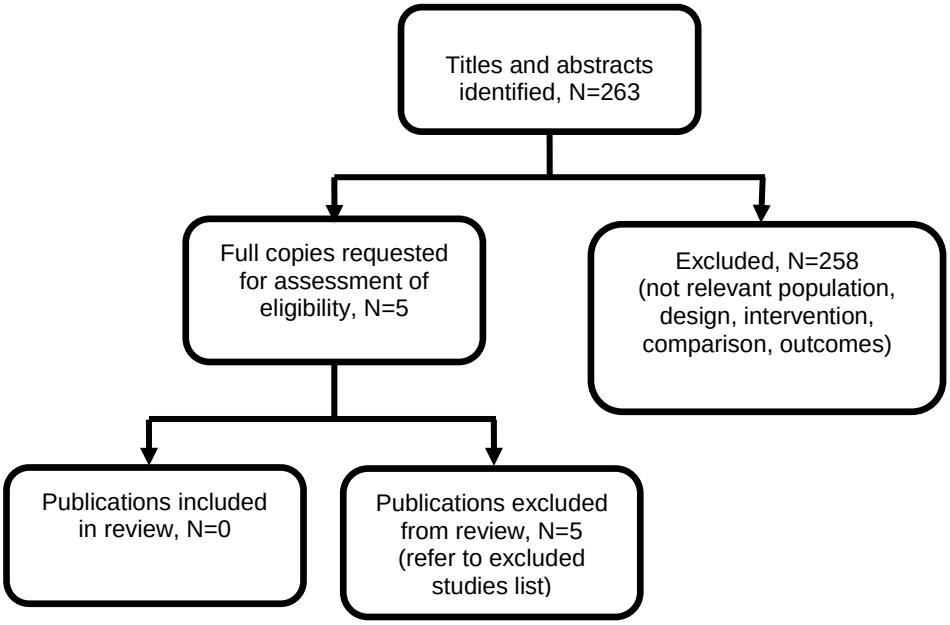
Health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons

Figure 28: Flow diagram of economic article selection for global health economic search for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons



Health economics search for intrapartum care for women with sepsis – antimicrobial therapy

Figure 29: Flow diagram of economic article selection for intrapartum care for women with sepsis – antimicrobial therapy



Appendix C – Excluded studies

Health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions

No full-text copies of articles were requested for this review and so there is no excluded studies list.

Health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons

Study	Reason for exclusion
Centre for, Reviews, Dissemination,, A cost-effectiveness analysis of the intrapartum fetal pulse oximetry multicentre randomised controlled trial (the FOREMOST trial) (Structured abstract), 2006	Population is women with a non-reassuring cardiotocograph trace, which does not match the populations for the fetal monitoring review questions considered in the guideline
Culligan,P.J., Myers,J.A., Goldberg,R.P., Blackwell,L., Gohmann,S.F., Abell,T.D., Elective	Population is pregnant women at 39 weeks of gestation, but not intrapartum

Study	Reason for exclusion
cesarean section to prevent anal incontinence and brachial plexus injuries associated with macrosomia - A decision analysis, International Urogynecology Journal and Pelvic Floor Dysfunction, 16, -28, 2005	
Herbst,M.A., Treatment of suspected fetal macrosomia: a cost-effectiveness analysis, American Journal of Obstetrics and Gynecology, 193, 1035-1039, 2005	Population is pregnant women, but not intrapartum
Ozmen, B., Sukur, Y. E., Yuce, T., Bayramov, V., Olmus, H., Sonmezer, M., Atabekoglu, C. S., Mode of delivery and birth complications in fetal macrosomia: A simple cost-effectiveness analysis, Turkish Journal of Medical Sciences, 42, 119-125, 2012	Cost analysis rather than a full economic evaluation; also based on a retrospective analysis and a setting that may be of limited relevance to the UK
Palencia,R., Gafni,A., Hannah,M.E., Ross,S., Willan,A.R., Hewson,S., McKay,D., Hannah,W., Whyte,H., Amankwah,K., Cheng,M., Guselle,P., Helewa,M., Hodnett,E.D., Hutton,E.K., Kung,R., Saigal,S., The costs of planned cesarean versus planned vaginal birth in the Term Breech Trial, Canadian Medical Association Journal, 174, 1109-1113, 2006	Breech presentation is not in labour
Rouse,D.J., Owen,J., Goldenberg,R.L., Cliver,S.P., The effectiveness and costs of elective cesarean delivery for fetal macrosomia diagnosed by ultrasound, JAMA, 276, 1480-1486, 1996	Population is not women in the intrapartum period
Vijgen, S. M., Westerhuis, M. E., Opmeer, B. C., Visser, G. H., Moons, K. G., Porath, M. M., Oei, G. S., Van Geijn, H. P., Bolte, A. C., Willekes, C., Nijhuis, J. G., Van Beek, E., Graziosi, G. C., Schuitemaker, N. W., Van Lith, J. M., Van Den Akker, E. S., Drogtrop, A. P., Van Dessel, H. J., Rijnders, R. J., Oosterbaan, H. P., Mol, B. W., Kwee, A., Cost-effectiveness of cardiotocography plus ST analysis of the fetal electrocardiogram compared with cardiotocography only, Acta Obstetricia et Gynecologica Scandinavica, 90, 772-8, 2011	Not clear that population includes any small-for-gestational-age babies and clinical data probably outdated

Health economics search for intrapartum care for women with sepsis – antimicrobial therapy

Study	Reason for exclusion
Benitz,W.E., Gould,J.B., Druzin,M.L., Preventing early-onset group B streptococcal sepsis: strategy development using decision analysis, Pediatrics, 103, e76-, 1999	No comparison of alternative antibiotics
Colbourn, T. E., Asseburg, C., Bojke, L., Philips, Z., Welton, N. J., Claxton, K., Ades, A. E., Gilbert, R. E., Preventive strategies for group B streptococcal and other bacterial infections in	Although fever in labour is a risk group considered in the article, it is addressed only in terms of route of administration of antibiotics

Study	Reason for exclusion
early infancy: cost effectiveness and value of information analyses, BMJ, 335, 655, 2007	
Colbourn,T., Asseburg,C., Bojke,L., Philips,Z., Claxton,K., Ades,A.E., Gilbert,R.E., 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 Technology Assessment, 11, 21-108, 2007	Although fever in labour is a risk group considered in the article, it is addressed only in terms of route of administration of antibiotics
Uyemura, A., Nguyen, N., Griffin, E., Werner, E., Pereira, L., Caughey, A., Cost-effectiveness analysis of antibiotic treatment for women with an epidural that have an intrapartum fever, American Journal of Obstetrics and Gynecology, 1), S215, 2014	Abstract only and no comparison of alternative antibiotics
Van Den Akker-Van Marle, M. E., Rijnders, M. E. B., Van Dommelen, P., Fekkes, M., Van Wouwe, J. P., Amelink-Verburg, M. P., Verkerk, P. H., Cost-effectiveness of different treatment strategies with intrapartum antibiotic prophylaxis to prevent early-onset group B streptococcal disease, BJOG: An International Journal of Obstetrics and Gynaecology, 112, 820-826, 2005	Mainly considers alternative screening strategies and does not compare alternative antimicrobials for women in labour with sepsis

Appendix D – Economic evidence tables

Health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions

No economic evidence was identified for this review and so there are no evidence tables.

Health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons

Table 43: Health economic evidence tables (health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons)

Study Country Study type	Intervention details	Study population Study design Data sources	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments
Grobman 1999 USA Cost effectiveness analysis Conflict of interest: not reported Funding: not reported	Interventions: Rapid HIV testing versus no HIV testing Women would receive counselling before testing as part of the rapid HIV testing intervention and antiretroviral treatment for those who tested positive	Women without adequate antenatal care Modelling (decision analytic model) Source of clinical effectiveness data: review of published literature Source of resource use data: unclear Source of unit costs: unclear Cost data from published literature supplemented with expert opinion	Costs: rapid HIV test, western blot, pre- and post-test counselling, intrapartum zidovudine, neonatal zidovudine, additional treatment for women because of early diagnosis of HIV-seropositive status, additional treatment for women falsely diagnosed as being HIV seropositive, additional surveillance of HIV-exposed babies, lifetime cost of paediatric HIV infection Mean cost per 100,000 women: • no test: $69 million • rapid testing: $63 million • difference: -$6 million Primary measure of outcome: HIV cases prevented Mean HIV cases per 100,000 women: • no test: 407 • rapid HIV testing: 339 • difference: -68	Rapid HIV testing dominant Sensitivity analysis: The findings were sensitive to changes in HIV seroprevalence among women without adequate antenatal care, the reduction in transmission after intrapartum and neonatal zidovudine, the reduction in transmission after neonatal zidovudine alone, the lifetime costs of paediatric HIV infection, and the incrementally greater costs incurred by a woman after early diagnosis of HIV infection	Perspective: health care payer Currency: USD Cost year: 1997 Time horizon: lifetime Discounting: 5% for costs Applicability: partially applicable Quality: potentially serious limitations
Mrus 2004 USA Cost effectiveness	Interventions: Rapid HIV testing versus no HIV testing followed	Unregistered women presenting in labour with no antenatal care	Costs: intrapartum zidovudine (additional cost if combined with nevirapine or lamivudine), infant follow-up with zidovudine prophylaxis (additional cost if combined with nevirapine or lamivudine),	Rapid HIV testing dominant using HIV cases prevented as an outcome measure Sensitivity analysis:	Perspective: societal (however seems to be healthcare) Currency: USD

Study Country Study type	Intervention details	Study population Study design Data sources	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments
and cost-utility analysis Conflict of interest: not reported Funding: not reported	by treatment with zidovudine, nevirapine, or combination therapy for those testing positive	Modelling (decision analytic model) Source of clinical effectiveness data: review of published literature Source of resource use data: unclear Source of unit costs: unclear Cost data was obtained from various published studies supplemented with expert option. Where possible national unit costs were used	rapid HIV test with pre-test counselling, western blot, post-test counselling, HIV-infected infant lifetime costs, HIV-infected woman lifetime costs, additional cost associated with earlier HIV treatment Absolute costs were not reported. However, assuming 50,000 women without antenatal care, rapid HIV testing saves $3 million each year. Primary measure of outcome: HIV cases prevented and QALYs Absolute HIV cases prevented not reported. However, assuming 50,000 women without antenatal care, rapid HIV testing prevents 27 cases of HIV. QALYs not reported	The results were robust to changes in the model inputs. Rapid HIV testing would not be cost effective only if the acceptance rate of rapid testing was 0.26 (base case: 0.86); if the proportion of women giving birth before treatment was effective was 0.70 (base case: 0.25); if the prevalence of HIV in women without antenatal care was 2/1000 (base case: 5.1/1000); if the relative risk reduction in vertical HIV transmission was 0.25 (base case: 0.62); if the additional cost associated with earlier HIV treatment (compared with delayed treatment) was $13,000 (base case: no difference). Rapid HIV testing remained potentially cost effective in a more extreme scenario where testing	Cost year: 2000 Time horizon: lifetime Discounting: 3% for costs and outcomes Applicability: partially applicable Quality: potentially serious limitations

Study Country Study type	Intervention details	Study population Study design Data sources	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments
				acceptance rate was 0.04, the proportion giving birth before the treatment was effective was 0.95, the prevalence of HIV was 0.3/1000 in women without antenatal care, or the relative risk reduction in HIV transmission was 0.04. Earlier diagnosis of maternal HIV compared with diagnosis later in the disease would have to more than double the discounted lifetime cost of HIV care to make rapid testing not cost effective. Also, treatment side effects from therapy to reduce the risk of transmission and from earlier treatment of HIV would need to reduce the discounted quality-adjusted life expectancy in HIV-infected women and babies by a total of 2.4 QALYs to negate QALYs gained through prevention of HIV transmission	

Study Country Study type	Intervention details	Study population Study design Data sources	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments
Stringer 1999 USA Cost effectiveness analysis Conflict of interest: not reported Funding: not reported	Interventions: Rapid HIV testing followed by antiretroviral treatment with zidovudine for women who tested positive versus prophylactic treatment for all women versus no treatment (usual care for women with unknown HIV status)	Unregistered women presenting in labour with no antenatal care Modelling (decision analytic model) Source of clinical effectiveness data: review of published literature Source of resource use data: unclear Source of unit costs: various sources. However, where possible national unit costs were used. Cost data was obtained from various published studies supplemented with expert opinion. Some of the resource use was based on local hospital estimates	Costs: rapid testing, ELISA assay test, western blot, intrapartum zidovudine, zidovudine syrup, evaluation of uninfected and HIV-exposed babies, lifetime cost of neonatal HIV infection Mean incremental cost per 100,000 women (versus no testing or treatment): Rapid HIV testing: $10.6 million savings Prophylactic treatment: $5.1 millions Difference prophylactic treatment (versus rapid HIV testing): $15.7 millions Primary measure of outcome: HIV cases prevented Mean HIV cases per 100,000 women: Rapid HIV testing: 183 Prophylactic treatment: 229 Difference prophylactic treatment (versus rapid HIV testing): 46	The incremental cost effectiveness ratio (ICER) of prophylactic treatment (versus rapid HIV testing): $342,068 per additional case of HIV prevented Sensitivity analysis: At the lower HIV prevalence of 0.0017 (base case: 0.05) the rapid-test strategy was not cost saving with an ICER of $360,747 per case of HIV prevented the rapid testing remained the cost-saving strategy at treatment efficacy values between 18–87% (base case: 0.18); the rapid-test strategy was cost saving for the lifetime cost of $70,000-130,000 for paediatric HIV infection (base case: $103,700), whereas the prophylactic treatment strategy remained unfavourable compared with rapid testing. The value for	Perspective: health care payer Currency: USD Cost year: 1998 Time horizon: lifetime Discounting: 5% for costs Applicability: partially applicable Quality: potentially serious limitations

Study Country Study type	Intervention details	Study population Study design Data sources	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments
				the lifetime cost of paediatric HIV below which the rapid-test strategy failed to be cost saving was $33,626; varying the pharmaceutical costs and costs of all test assays did not change the conclusions. In a scenario analysis where both treatment efficacy and lifetime costs were set to a minimum 0.18 and $70,000, respectively; the HIV prevalence would need to be 0.016 or above for the rapid-test strategy to be cost effective. Similarly, with both inputs set at the maximum of 0.87 and $130,000, the HIV prevalence would need to be 0.0014 or above for the rapid-test strategy to be cost effective	

Health economics search for intrapartum care for women with sepsis – antimicrobial therapy

No clinical evidence was identified for this review and so there are no evidence tables.

Appendix E – Health economic evidence methodology checklists

Health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions

No economic evidence was identified for this review and so there are no health economic evidence methodology checklists.

Health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons

Table 44: Health economics quality assessment for Grobman 1999 (health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons)

Study identifier: Grobman 1999		
Guidance topic: intrapartum care for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons		**Question no: rapid HIV testing for women in labour with no antenatal care**
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no/unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	Women without adequate antenatal care
1.2 Are the interventions appropriate for the review question?	Yes	Rapid HIV testing in the intrapartum period compared with no testing
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	US study
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Unclear	Not reported explicitly but appears to be healthcare perspective
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	Has not considered health-related quality of life (HRQoL)
1.6 Are all future costs and outcomes discounted appropriately?	Partly	5% for lifetime costs
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	HIV cases prevented
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued	NA	
1.9 Overall judgement: Partially applicable		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no/unclear/NA	Comments
2.2 Does the model structure adequately reflect the nature of the topic under evaluation	Yes	
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Lifetime

Study identifier: Grobman 1999		
2.3 Are all important and relevant outcomes included?	Partly	HIV cases prevented
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	Review of the published literature relevant to the US setting
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	Review of diagnostic studies
2.6 Are all important and relevant costs included?	Yes	
2.7 Are the estimates of resource use from the best available source?	Partly	Published literature supplemented with exert opinion
2.8 Are the unit costs of resources from the best available source?	Unclear	
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Deterministic sensitivity analysis. However, no probabilistic sensitivity analysis
2.11 Is there any potential conflict of interest?	Unclear	Funding and conflict of interest not reported
2.12 Overall assessment: Potentially serious limitations		
Other comments		

Table 45: Health economics quality assessment for Mrus 2004 (health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons)

Study identifier: Mrus 2004		
Guidance topic: intrapartum care for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons		Question no: rapid HIV testing for women in labour with no antenatal care
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no/unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	Women presenting in labour without antenatal care
1.2 Are the interventions appropriate for the review question?	Yes	Rapid HIV testing in the intrapartum period compared with no testing

Study identifier: Mrus 2004		
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	US study
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Unclear	Reported to be societal, however, seems to be healthcare perspective
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	Partly	3% for costs and quality adjusted life years (QALYs)
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	Utility weights obtained from various published studies. The measures of HRQoL that were used to inform the utility weights were not reported
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued	NA	
1.9 Overall judgement: Partially applicable		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no/unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation	Yes	
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Lifetime
2.3 Are all important and relevant outcomes included?	Yes	HIV cases prevented and QALYs
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	Review of the published literature relevant to the US setting
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	Review of published literature
2.6 Are all important and relevant costs included?	Yes	
2.7 Are the estimates of resource use from the best available source?	Unclear	Cost data was obtained from various published studies supplemented with expert opinion
2.8 Are the unit costs of resources from the best available source?	Unclear	Cost data was obtained from various published studies

Study identifier: Mrus 2004		
		supplemented with expert opinion. Where possible national unit costs were used
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Deterministic sensitivity analysis. However, no probabilistic sensitivity analysis
2.11 Is there any potential conflict of interest?	Unclear	
2.12 Overall assessment: Potentially serious limitations		
Other comments		

Table 46: Health economics quality assessment for Stringer 1999 (health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons)

Study identifier: Stringer 1999		
Guidance topic: intrapartum care for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons		Question no: rapid HIV testing for women in labour with no antenatal care
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no/unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	Women without antenatal care
1.2 Are the interventions appropriate for the review question?	Yes	No testing or treating, rapid HIV testing, prophylactic treatment of all unregistered women
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	US study
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Healthcare
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	Has not considered HRQoL
1.6 Are all future costs and outcomes discounted appropriately?	Partly	5% for costs

Study identifier: Stringer 1999		
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	HIV cases prevented
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued	NA	
1.9 Overall judgement: Partially applicable		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no/unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation	Yes	
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Lifetime
2.3 Are all important and relevant outcomes included?	Partly	HIV cases prevented
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	Review of the published literature relevant to the US setting
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	Review of diagnostic studies
2.6 Are all important and relevant costs included?	Partly	Has not considered costs associated with HIV-infected women
2.7 Are the estimates of resource use from the best available source?	Partly	Cost data was obtained from various published studies supplemented with expert opinion. Some of the resource use was based on local hospital estimates
2.8 Are the unit costs of resources from the best available source?	Unclear	Cost data was obtained from various published studies supplemented with expert opinion. Where possible national unit costs were used
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Deterministic sensitivity analysis. However, no probabilistic sensitivity analysis

Study identifier: Stringer 1999		
2.11 Is there any potential conflict of interest?	Unclear	
2.12 Overall assessment: Potentially serious limitations		
Other comments		

Health economics search for intrapartum care for women with sepsis – antimicrobial therapy

No economic evidence was identified for this review and so there are no health economic evidence methodology checklists.

Appendix F – Health economic evidence profiles

Health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions

No economic evidence was identified for this review and so there are no health economic evidence profiles.

Health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons

Table 47: Health economic evidence profile (health economics global search for women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons)

Study	Limitations	Applicability	Other comments	Costs	Effects	Incremental cost effectiveness	Uncertainty
Grobman 1999 US	Potentially serious limitations[1]	Partially applicable[2]	Cost effectiveness analysis Outcome measure: HIV cases prevented Time horizon: lifetime	-$6 million per 100,000 women	68 per 100,000 women	Rapid HIV testing dominant	The findings were sensitive to changes in HIV seroprevalence among women without adequate antenatal care, the reduction in transmission after intrapartum and neonatal zidovudine, the reduction in transmission after neonatal zidovudine alone, the lifetime costs of paediatric HIV infection, and the incrementally greater costs incurred by a woman after early diagnosis of HIV infection
Mrus 2004 US	Potentially serious limitations[3]	Partially applicable[4]	Cost-utility analysis Outcome measure: HIV	-$3 million per annum	27 cases per annum	Rapid HIV testing dominant	The results were robust to changes in the model inputs.

			cases prevented and quality-adjusted life years (QALYs) Time horizon: lifetime		Incremental QALYs were not reported		Rapid HIV testing would not be cost effective only if the acceptance rate of rapid testing was 0.26 (base case: 0.86); if the proportion of women giving birth before treatment was effective was 0.70 (base case: 0.25); if the prevalence of HIV in women without antenatal care was 2/1000 (base case: 5.1/1000); if the relative risk reduction in vertical HIV transmission was 0.25 (base case: 0.62); if the additional cost associated with earlier HIV treatment (compared with delayed treatment) was $13,000 (base case: no difference). Rapid HIV testing remained potentially cost effective in a more extreme scenario where the testing acceptance

							rate was 0.04, the proportion giving birth before the treatment was effective was 0.95, the prevalence of HIV was 0.3/1000 in women without antenatal care, or the relative risk reduction in HIV transmission was 0.04. Earlier diagnosis of maternal HIV compared with diagnosis later in the disease would have to more than double the discounted lifetime cost of HIV care to make rapid testing not cost effective. Also, treatment side effects from therapy to reduce the risk of transmission and from earlier treatment of HIV would need to reduce the discounted quality-adjusted life expectancy in HIV-infected women and

							babies by a total of 2.4 QALYs to negate QALYs gained through prevention of HIV transmission
Stringer 1999	Potentially serious limitations[1]	Partially applicable[5]	Cost effectiveness analysis Outcome measure: HIV cases prevented Time horizon: lifetime	Rapid HIV testing (versus no testing): -$10.6 million per 100,000 unregistered parturients Prophylactic treatment (versus. rapid HIV testing): $15.7 million per 100,000 unregistered parturients	Rapid HIV testing (versus. no testing): 183 cases per 100,000 unregistered parturients Prophylactic treatment (versus. rapid HIV testing): 46 cases per 100,000 unregistered parturients	$342,068 (prophylactic treatment versus rapid HIV testing)	At the lower HIV prevalence of 0.0017 (base case: 0.05) the rapid-test strategy was not cost saving with an incremental cost effectiveness ratio (ICER) of $360,747 per case of HIV prevented the rapid testing remained the cost-saving strategy at treatment efficacy values between 18–87% (base case: 0.18); the rapid-test strategy was cost saving for the lifetime cost of $70,000-130,000 for paediatric HIV infection (base case: $103,700), whereas the prophylactic treatment strategy remained unfavourable compared with rapid testing. The value for

							the lifetime cost of paediatric HIV below which the rapid-test strategy failed to be cost saving was $33,626; varying the pharmaceutical costs and costs of all test assays did not change the conclusions. In a scenario analysis where both treatment efficacy and lifetime costs were set to a minimum 0.18 and $70,000, respectively; the HIV prevalence would need to be 0.016 or above for the rapid-test strategy to be cost effective. Similarly, with both inputs set at the maximum of 0.87 and $130,000, the HIV prevalence would need to be 0.0014 or above for the rapid-test strategy to be cost effective

1. US study, no QALYs

2. Some model inputs based on study authors' assumptions, the source of unit costs was unclear, and no probabilistic sensitivity analysis was undertaken

3. US study

4. Some model inputs, including those relating to relative treatment effectiveness, based on study authors' assumptions, and no probabilistic sensitivity analysis was undertaken

5. Has not considered costs associated with HIV-infected women, some resource-use estimates based on local hospital estimates, and no probabilistic sensitivity analysis was undertaken

Health economics search for intrapartum care for women with sepsis – antimicrobial therapy

No economic evidence was identified for this review and so there are no health economic evidence profiles.