National Institute for Health and Care Excellence

Final

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

[L] Evidence reviews for pyrexia

NICE guideline NG121

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

March 2019

Final

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

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Contents

Intrapartum care for women with pyrexia

This evidence report contains information on 2 reviews relating to intrapartum care for women with pyrexia.

- Does the use of fetal blood sampling (FBS) (in conjunction with electronic fetal monitoring) for women with pyrexia in labour improve outcomes for the baby?
- Does the use of anti-pyretics in women with pyrexia in labour improve outcomes for the woman or the baby?

The recommendations arising from the review about anti-pyretics are presented first in the 'short' version of the guideline because this better reflects the chronology of clinical care for the woman and baby.

Intrapartum care for women with pyrexia – fetal blood sampling

Review question

Does the use of FBS (in conjunction with electronic fetal monitoring) for women with pyrexia in labour improve outcomes for the baby?

Introduction

The aim of this review is to determine whether the use of FBS (in conjunction with electronic fetal monitoring, referred to hereafter as continuous cardiotocography) for women with pyrexia in labour improves outcomes for the baby. The review includes a sub-question that focuses on the value of fetal blood pH analysis and fetal blood lactate analysis for predicting outcomes for the woman and the baby. For reviews related to pyrexia in labour, the committee adopted the definition of fever in labour used in the NICE guideline on intrapartum care for healthy women and babies (CG190), that is a temperature of 38°C or above on a single reading or 37.5°C or above on 2 consecutive readings (1 hour apart).

Summary of the protocol

See Table 1 for a summary of the population, intervention, comparison and outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Women with pyrexia in labour
Intervention	Main review question CTG plus FBS Sub-question CTG plus pH (index test) CTG plus lactate (index test)
Comparison	Main question CTG alone Sub-question CTG alone (reference standard)
Outcomes	Main question For the woman: • mode of birth (and indication whether operative birth) • woman's experience of labour and birth, including experience of the birth companion, and the woman's mobility including trauma (psychological or physical, trauma or distress) For the baby: • mortality

	• major neonatal morbidity (hypoxic ischaemic encephalopathy (HIE), cerebral palsy/neurodevelopmental disability/developmental delay, or trauma/injury to the baby) • Apgar score < 7 at 5 minutes • admission to NICU and duration of hospital stay • cord blood gas values at birth Sub-question • Sensitivity, specificity, positive and negative likelihood ratios for predicting the following outcomes in the baby: ○ neonatal mortality and morbidity (cerebral palsy, hypoxic ischaemic encephalopathy and infection)

CTG: cardiotocography; FBS: fetal blood sample; NICU: neonatal intensive care unit

For further details see the full review protocol in Appendix A. The search strategies are presented in Appendix B.

Clinical evidence

Included studies

No clinical evidence was identified for this review.

See the study selection flow chart in Appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusion are listed in Appendix D.

Summary of clinical studies included in the evidence review

No clinical evidence was identified for this review (and so there are no evidence tables in Appendix E). No meta-analysis was undertaken for this review (and so there are no forest plots in Appendix F).

Quality assessment of clinical studies included in the evidence review

No clinical evidence was identified for this review (and so no quality assessment was undertaken and there are no GRADE tables in Appendix G).

Economic evidence

Included studies

No economic evidence was identified for this review.

See the study selection flow chart in Supplement 2 (Health economics).

Excluded studies

Studies not included in this review with reasons for their exclusion are listed in Supplement 2 (Health economics).

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables in Supplement 2 (Health economics)).

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation (see Supplement 2 (Health economics)).

Evidence statements

No clinical evidence was identified for this review.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The committee prioritised outcomes for the baby as critical outcomes for this review because the review question focuses on the baby rather than the woman. Mortality and major morbidities in the baby such as hypoxic ischaemic encephalopathy, cerebral palsy, neurodevelopmental disability, developmental delay or trauma or injury to the baby were prioritised as critical outcomes because reducing stillbirth and neonatal brain injury are priorities for the NHS and one of the mandate objectives from central government (see Saving babies' lives. A care bundle for reducing stillbirth). Moreover, most of these outcomes are avoidable. An Apgar score of <7 at 5 minutes was chosen as a critical outcome because this is a standard assessment of a baby's wellbeing at birth, therefore it is likely to be reported in the evidence and likely to be recorded more frequently if there is good care.

Important maternal outcomes were mode of birth (and an indication of whether operative birth) and the woman's experience of labour and birth, including experience of her birth companion(s) and the woman's mobility, including trauma (psychological or physical trauma or distress). Mode of birth was chosen as an important outcome because the committee believed that if fetal monitoring including fetal blood sampling was a reliable predictor of fetal wellbeing then unnecessary expedited births could be avoided. The committee discussed that the woman's experience of labour and birth, including related outcomes listed above, were important because they measure the effectiveness of interventions from the woman's perspective. The committee felt that the intervention of interest here (cardiotocography plus fetal blood sampling) was particularly likely to cause distress to the woman and her birth companion(s).

An important outcome for the baby was admission to the neonatal intensive care unit (NICU) and duration of hospital stay because the committee was aware of a national drive to reduce admission of full-term babies to neonatal units (Reducing admission of full term babies to neonatal units), including admissions due to asphyxia (perinatal hypoxic ischaemia)).

Sensitivity and specificity, and positive and negative likelihood ratios were chosen as diagnostic accuracy outcomes for predicting mortality and morbidity in the baby (cerebral palsy, hypoxic ischaemic encephalopathy and infection).

The quality of the evidence

No clinical evidence was identified for this review.

Benefits and harms

The committee wanted to emphasise that if the woman has fever during labour, she should be treated as if she has suspected sepsis for the purpose of fetal blood sampling. The committee expressed their concern about using fetal blood sampling for women with suspected sepsis, and they acknowledged that fetal blood sampling should be used cautiously in conjunction with considering the whole clinical picture, including stage and progress of labour, parity and risk of chorioamnionitis, and with consideration for the individual situation. In addition, the woman's preferences should be considered. The committee was clear that fetal blood sampling is a screening tool, not a treatment, and they emphasised that there are doubts regarding the accuracy of fetal blood sampling in situations when there is suspected sepsis.

The committee was aware that sepsis increases the risk of complications for the baby and clinical judgement is key in determining whether vaginal birth should continue. If sepsis is suspected then reasonable action should be taken. The committee was concerned that, in the presence of sepsis, fetal blood sampling may falsely reassure clinicians as there is no evidence to show at what pH the clinician should be concerned for the baby, therefore fetal blood sampling cannot be used alone, rather the whole clinical picture needs to be considered. The committee suggested that only 1 fetal blood sample should be taken, and saw little advantage in repeated measurements. Extreme caution should be used if sepsis is suspected as fetal blood sampling may increase the risk of infection in the baby. The committee discussed that there is a synergistic effect in babies caused by infection, hypoxia, inflammation and fever, and that all of these can occur even in the absence of sepsis and also when the pH appears normal. Hence the importance of considering the whole clinical picture. The committee acknowledged that it is difficult to provide clear guidance as individual cases differ and no evidence was found to support their clinical experience. The overall belief of the committee was that it was important not to rely solely on fetal blood sampling.

The committee was aware that there are several causes of fever in labour other than sepsis, including epidural analgesia. However, these cannot be reliably confirmed or excluded during labour. Therefore the committee's view was that women with fever in labour should be treated as if they have suspected sepsis for the purpose of fetal blood sampling.

Cost effectiveness and resource use

The committee recognised that cost effectiveness involved striking an appropriate balance between being overly cautious and avoiding multiple fetal blood samples being taken. They additionally noted that the cost effectiveness of fetal blood sampling would depend on the particular characteristics of each woman's situation and that the whole clinical picture needed to be considered alongside any fetal blood sampling.

In the absence of any clinical evidence, the committee hoped that their recommendation would promote cost effective practice in the NHS by increasing the use of fetal blood sampling where appropriate while reducing use where unnecessary sampling is undertaken.

Current practice varies but the committee did not think that the recommendation would have a significant resource impact as increased use of fetal blood sampling in some settings would be offset to some extent by reduced sampling in other settings.

Other factors the committee took into account

The committee adopted the definition of fever in labour used in the NICE guideline on intrapartum care for healthy women and babies (CG190), that is a temperature of 38°C or above on a single reading or 37.5°C or above on 2 consecutive readings (1 hour apart).

The committee was keen to identify evidence that might give guidance about whether fetal blood lactate would be of greater value than fetal blood pH as part of fetal blood sampling. They hoped that finding evidence would help to harmonise practice in using either lactate or pH when interpreting fetal blood sampling results for women in labour with fever. However, no relevant evidence was identified.

Intrapartum care for women with pyrexia – use of anti-pyretics

Review question

Does the use of anti-pyretics in women with pyrexia in labour improve outcomes for the woman or the baby?

Introduction

The aim of this review is to determine whether the use of anti-pyretics in women with pyrexia in labour improves outcomes for the woman or the baby. As noted above, for reviews related to pyrexia in labour, the committee adopted the definition of fever in labour used in the NICE guideline on intrapartum care for healthy women and babies (CG190), that is a temperature of 38°C or above on a single reading or 37.5°C or above on 2 consecutive readings (1 hour apart). The 2014 version of the guideline included a recommendation to 'offer paracetamol if the woman has a raised temperature' but the recommendation was not based on an evidence review and it was stood down in 2017 to allow this guideline to address the topic. For this reason, the review focused on paracetamol as the only pharmacological anti-pyretic to be considered.

Summary of the protocol

See Table 2 for a summary of the population, intervention, comparison and outcome (PICO) characteristics of this review.

Table 2: Summary of the protocol (PICO table)

Population	Women with pyrexia in labour
Intervention	Intervention 1 • Antipyretics (paracetamol) via any route of administration (that is, oral, intravenous or rectal) Intervention 2 • Combination of paracetamol and physical cooling methods (see below for examples)
Comparison	• No antipyretics (no paracetamol) and no other action ('do nothing') • Physical cooling (neck warmer, cool sponging, reducing room temperature, iced drinks, birth pool, or showering) • Combination of physical cooling methods • Different routes of paracetamol administration (oral, intravenous or rectal)
Outcomes	For the woman: • mode of birth • admission to HDU or ITU and duration of hospital stay • woman's experience of labour and birth, including experience of the birth companion • administration of antibiotics

	For the baby: • major morbidities (neonatal infection, hypoxic ischaemic encephalopathy (HIE), or cerebral palsy/neurodevelopmental disability/developmental delay) • mortality • admission to NICU and duration of hospital stay

HDU: high dependency unit; HIE: hypoxic ischaemic encephalopathy; ITU: intensive therapy unit; NICU: neonatal intensive care unit

For further details see the full review protocol in Appendix A. The search strategies are presented in Appendix B.

Clinical evidence

Included studies

One retrospective cohort study was included in this review (see 'Summary of clinical studies included in the evidence review').

This study (Burgess 2017) compared the use of paracetamol (acetaminophen) versus no use of paracetamol (acetaminophen).

Evidence from the studies included in the review is summarised below (see 'Quality assessment of clinical studies included in the evidence review'). Data was reported on the critical outcome, mode of birth, and the important outcome, admission to NICU. There was no evidence identified for the following outcomes for the woman: admission to the high dependency unit (HDU) or intensive therapy unit (ITU) and duration of hospital stay (critical outcome); the woman's experience of labour and birth, including experience of her birth companion(s) (important outcome); administration of antibiotics (outcome of limited importance). There was no evidence for the following outcomes for the baby: major morbidities (neonatal infection, hypoxic ischaemic encephalopathy (HIE), cerebral palsy, neurodevelopmental disability or developmental delay; critical outcomes); mortality (important outcome).

See also the study selection flow chart in Appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusion are listed in Appendix D.

Summary of clinical studies included in the evidence review

Table 3 provides a brief summary of the included study.

Table 3: Summary of included studies

Study	Population	Intervention/Comparison	Outcomes	Comments
Burgess 2017 Retrospective cohort study USA	Women with pyrexia in labour (intrapartum	Paracetamol (acetaminophen; n=41) versus no paracetamol (no	For the woman: • caesarean section	26/54 women received intrapartum antibiotic therapy. The study

Study	Population	Intervention/Comparison	Outcomes	Comments
	temperature ≥38°C) N=54	acetaminophen; n=13)	For the baby: • NICU admission	authors did not report how many of these women were in each of the intervention and control groups. Administration of paracetamol was at the discretion of the treating obstetrician. The study authors reported that 650 mg of paracetamol was administered. However, indications, dose, and route of administration were not standardised

NICU: neonatal intensive care unit

See also the study evidence Appendix E – Clinical evidence tables. No meta-analysis was undertaken for this review (and so there are no forest plots in Appendix F – Forest plots).

Quality assessment of clinical studies included in the evidence review

The clinical evidence profile for this review question is presented in Appendix G – GRADE tables

Economic evidence

Included studies

No economic evidence was identified for this review.

See the study selection flow chart in Supplement 2 (Health economics).

Excluded studies

No full-text copies of articles were requested for this review and so there is no excluded studies list (see Supplement 2 (Health economics)).

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables in Supplement 2 (Health economics)).

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation (see Supplement 2 (Health economics)).

Evidence statements

Paracetamol versus no paracetamol

Outcomes for the woman

Caesarean section

Very low quality evidence from 1 retrospective cohort study in women with pyrexia in labour (N=53) showed no clinically important difference in the number of women who had a caesarean section between women who were administered paracetamol and women who were not administered paracetamol.

Outcomes for the baby

NICU admission

Very low quality evidence from 1 retrospective cohort study in women with pyrexia in labour (N=54) showed no clinically important difference in the number of babies admitted to NICU between women who were administered paracetamol and women who were not administered paracetamol.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The committee prioritised mode of birth as a critical outcome because fever raises the suspicion of infection and therefore increases the risk of interventions such as caesarean section. The committee noted that a caesarean section is more likely to result in separation of the woman and the baby, which can have a negative impact on breastfeeding and perinatal mental health. Maternal admission to HDU or ITU and duration of hospital stay were also prioritised as critical outcomes because they are proxy measures of maternal morbidity, have high economic impact and because they are proxy measures for a woman's experience, including separation of the woman and baby. The committee agreed that major morbidities in the baby (neonatal infection, hypoxic ischaemic encephalopathy (HIE), cerebral palsy, neurodevelopmental disability or developmental delay) should be critical outcomes. The committee noted that the most important outcome for the baby in this review would be major morbidity associated with fever, which may or may not be due to sepsis.

The woman's experience of labour and birth, including experience of her birth companion(s), was chosen as an important outcome because it could, for example, reflect the preferred route of antipyretic administration and the potential cascade of other interventions such as intravenous fluids or antibiotics. Moreover, it is a proxy measure for separation of the woman and the baby.

For the baby, mortality and admission to NICU and duration of hospital stay were prioritised as important outcomes. The committee felt that mortality in the baby was important but not critical for this review because morbidity is more likely to occur than mortality. Admission to NICU and duration of hospital stay were chosen as important outcomes because the committee was aware of a national drive to reduce admission of full term babies to neonatal units (Reducing admission of full term babies to neonatal units), including admissions due to asphyxia (perinatal hypoxia-ischaemia). Pyrexia in conjunction with other criteria can raise the suspicion of sepsis and suspected sepsis is a common reason for babies to be admitted to NICU.

The quality of the evidence

No randomised controlled trials were identified. The included study was a retrospective cohort study. The quality of the evidence from the included study was assessed with GRADE and was rated as very low. There was high risk of selection bias because administration of paracetamol was at the discretion of the treating obstetrician. Therefore it is possible that women who received paracetamol had different baseline characteristics compared to women who did not receive paracetamol. Data on baseline characteristics were reported for all febrile women but were not disaggregated by administration or non-administration of paracetamol. There was also high risk of comparability bias because the study did not control for any factor. There was unclear risk of outcome bias because the study reported only percentages, and so numerators and denominators had to be estimated by the NGA technical team based on the number of women who received paracetamol. Moreover, the decision for admission to NICU was not standardised and was at the discretion of neonatologists and paediatricians. The quality of the evidence was also downgraded for imprecision as the confidence intervals for the risk ratios for both outcomes crossed 1 default minimally important difference threshold. The comparison of interest for the guideline review was not the main comparison in the study and it was carried out only with a subset of the study population (febrile women). The study authors did not report whether they calculated the minimum sample size for this comparison, therefore the analysis may have lacked power to detect a statistically significant difference.

Benefits and harms

The 2014 version of the NICE guideline on intrapartum care for healthy women and babies (CG190) included a recommendation to ‘offer paracetamol if the woman has a raised temperature’ but the recommendation was not based on an evidence review and was stood down in 2017 to allow this guideline to address the topic. For this reason, the review focused on paracetamol as the only pharmacological anti-pyretic to be considered.

The evidence included in the review showed no clinically important difference in the rate of caesarean section or NICU admission between women who had paracetamol for fever and those who did not. However the evidence was of very low quality and came from only 1 study. There was no evidence found that included physical cooling methods as a treatment for fever during labour, or comparing different routes of paracetamol administration. Therefore the committee members used their clinical experience and expertise to make consensus recommendations. The committee agreed that paracetamol is safe and can reduce discomfort when a woman has a raised temperature. Therefore they made a weak recommendation to consider paracetamol for women in labour with a fever. They noted that fever can be a sign of sepsis and agreed that recognising and treating sepsis is a clinical priority. Because paracetamol may mask a worsening fever, they recommended that healthcare professionals should remember that paracetamol is not a treatment for sepsis and should not delay investigation and treatment when sepsis is suspected. The committee noted

that in the context of maternal sepsis there is no evidence that a reduction in maternal temperature secondary to paracetamol administration is associated with benefit or harm to the baby.

Cost effectiveness and resource use

The committee acknowledged that the clinical evidence reviewed did not demonstrate a benefit of anti-pyretics for the outcomes prioritised in the guideline review. However, they noted that paracetamol is inexpensive and safe and that it can reduce discomfort in women who have a raised temperature. Therefore, they considered that their weak recommendation would be cost effective and would have a negligible impact on NHS resources.

With respect to current practice, the committee thought their recommendations would discourage inappropriate use of paracetamol.

Other factors the committee took into account

The committee adopted the definition of fever in labour used in the NICE guideline on intrapartum care for healthy women and babies (CG190), that is a temperature of 38°C or above on a single reading or 37.5°C or above on 2 consecutive readings (1 hour apart).

The committee noted that the recommendation to 'consider' paracetamol for women with a fever in labour was a weaker recommendation than the recommendation in the 2014 version of the NICE guideline on intrapartum care for healthy women and babies (CG190), which recommended an 'offer' of paracetamol if the woman's temperature is raised. The committee noted that this weaker recommendation, in combination with their recommendation to be aware that paracetamol is not a suitable treatment for sepsis and that it should not delay investigation if sepsis is suspected, should reduce the inappropriate use of paracetamol and promote the prompt management of sepsis.

References

Burgess 2017

Burgess, A. P. H., Katz, J. E., Moretti, M., Lakhi, N., Risk Factors for Intrapartum Fever in Term Gestations and Associated Maternal and Neonatal Sequelae, Gynecologic and Obstetric Investigation, no pagination, 2017

Appendices

Appendix A – Review protocols

Intrapartum care for women with pyrexia – fetal blood sampling

Item	Details	Working notes
Area in the scope	Women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons – intrapartum care for women with pyrexia – FBS	
Review question in the scope	Does the use of FBS (in conjunction with electronic fetal monitoring) for women with pyrexia in labour improve outcomes for the baby?	
Review question for the guideline	Does the use of FBS (in conjunction with electronic fetal monitoring) for women with pyrexia in labour improve outcomes for the baby? <u>Sub-question</u> What is the value of the following measures for predicting outcomes for the woman and the baby: • fetal blood pH analysis • fetal blood lactate analysis?	
Objective	The aim of this review is to determine whether the use of FBS (in conjunction with electronic fetal monitoring) for women with pyrexia in labour improve outcomes for the baby. This is an important topic because the incidence of maternal fever in labour is up to 10%, depending on the temperature cut-off used to define pyrexia (Herbst 1997, Impey 2001, Philip 1999), and maternal pyrexia is associated with potentially very serious maternal and neonatal consequences	
Population and directness	Women with pyrexia in labour Pyrexia as defined in studies. Studies in which up to 34% of the women have multiple pregnancy will be included. Evidence in which any of the women have multiple pregnancy should be downgraded for indirectness.	
Intervention	<u>Main review question</u> CTG plus FBS <u>Sub-question</u> CTG plus pH (index test) CTG plus lactate (index test)	
Comparison	<u>Main question</u>	

Item	Details	Working notes
	CTG alone <u>Sub-question</u> CTG alone (reference standard)	

Outcomes	<u>Main question</u>
	Critical outcomes:
	• for the baby:
	  ○ mortality
	  ○ major neonatal morbidity (hypoxic ischaemic encephalopathy (HIE), cerebral palsy/neurodevelopmental disability/developmental delay, or trauma/injury to the baby)
	  ○ Apgar score < 7 at 5 minutes
	
	Important outcomes:
	• for the woman:
	  ○ mode of birth (and indication whether operative birth)
	  ○ woman's experience of labour and birth, including experience of the birth companion, and the woman's mobility including trauma (psychological or physical trauma or distress)
	• for the baby:
	  ○ admission to NICU and duration of hospital stay
	
	Outcomes of limited importance:
	• for the baby:
	  ○ cord blood gas values at birth
	
	<u>Sub-question</u>
	• Sensitivity, specificity, positive and negative likelihood ratios for predicting the following outcomes in the baby:
	  ○ neonatal mortality and morbidity (cerebral palsy, hypoxic ischaemic encephalopathy and infection)	

Importance of outcomes	Preliminary classification of the outcomes for decision making: • critical (up to 3 outcomes) • important but not critical (up to 3 outcomes) • of limited importance (1 outcome)	
Setting	Obstetric units	
Stratified, subgroup and adjusted analyses	Groups that will be reviewed and analysed separately: • women with pyrexia with (any) epidural versus women with pyrexia but no epidural In the presence of heterogeneity, the following subgroups will be considered for sensitivity analysis:	

Item	Details	Working notes
	• women with pyrexia with (any) epidural versus women with pyrexia but no epidural • gestational age Potential confounders: • maternal age • socioeconomic status • parity • prolonged labour • preterm labour • prolonged ruptured membranes • epidural analgesia • internal fetal monitoring • pre-existing infections of the lower genital tract • carriage of group B streptococcus • induced or augmented labour • stage of labour	
Language	English	

Study design	• Published full-text papers only
	• Systematic reviews
	• RCTs
	• Only if RCTs unavailable or there is limited data to inform decision making:
	  ○ prospective or retrospective comparative observational studies (including cohort and case-control studies)
	• Prospective study designs will be prioritised over retrospective study designs
	• Conference abstracts will not be considered
	
	• For the sub-question (diagnostic study designs):
	  ○ studies will be included only if the data reported allows for a 2x2 table to be produced, or if specificity and sensitivity data are reported with confidence intervals
	  ○ conference abstracts will not be considered	

Search strategy	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques were used. See Appendix B – Literature search strategies for full strategies	

Item	Details	Working notes
Review strategy	Appraisal of methodological quality: • for the main question, the methodological quality of each study will be assessed using checklists recommended in the NICE guidelines manual 2014 (for example, AMSTAR or ROBIS for systematic reviews, and Cochrane RoB tool for RCTs) and the quality of the evidence for each outcome (that is, across studies) will be assessed using GRADE • for the sub-question, the methodical quality of each study will be assessed using checklists recommended in the NICE guidelines manual 2014 (QUADAS-2) and the quality of the evidence for an outcome will be assessed using an adapted version of GRADE • if studies report only p-values, this information will be recorded in GRADE tables without an assessment of imprecision Synthesis of data: • meta-analysis will be conducted where appropriate • default MIDs will be used; 0.8 and 1.25 for dichotomous outcomes; 0.5 times the SD of the measurement in the control arm (or median score across control arms if multiple studies are included) for continuous outcomes • for continuous data, change scores will be used in preference to final scores for data from non-RCT studies; final and change scores will not be pooled; if any study reports both, the method used in the majority of studies will be adopted	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies will be resolved through discussion between the first and second reviewers or by reference to a third person. This review question was not prioritised for health economic analysis and so no formal dual weeding, study selection (inclusion/exclusion) or data extraction into evidence tables will be undertaken. However, internal (NGA) quality assurance processes will include consideration of the outcomes of weeding, study selection and data extraction and the committee will review the results of study selection and data extraction
Equalities	Equalities considerations will be considered systematically in relation to the available evidence and draft recommendations. The guideline scope includes women with cognitive or physical disability as populations for whom there may be equalities issues. Women who have received no antenatal care will be considered as a subgroup for all systematic reviews performed within the medical conditions work stream and a specific question has been included in the obstetric complications work stream for this population.	

Item	Details	Working notes
Notes/additional information	• Herbst A, Wolner-Hanssen P, Ingemarsson I. Maternal fever in term labor in relation to fetal tachycardia, cord artery acidaemia and neonatal infection. Br J Obstet Gynaecol 1997;104:363-6 • Impey L, Greenwood C, MacQuillan K, Reynolds M, Sheil O. Fever in labour and neonatal encephalopathy: a prospective cohort study. BJOG. 2001 Jun;108(6):594-7 • Philip J, Alexander JM, Sharma SV, Leveno KJ, McIntire DD, Wiley J. Epidural analgesia during labour and maternal fever. Anaesthesiology 1999;90:1271-5	
Key papers	None identified by the committee	

AMSTAR: Assessing the Methodological Quality of Systematic Reviews; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; CTG: cardiotocography; DARE: Database of Abstracts of Reviews of Effects; FBS: fetal blood sampling; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; NICU: neonatal intensive care unit; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation; ROBIS: Risk of Bias in Systematic Reviews

Intrapartum care for women with pyrexia – use of anti-pyretics

Item	Details	Working notes
Area in the scope	Women at high risk of adverse outcomes for themselves and/or their baby because of obstetric complications or other reasons – intrapartum care for women with pyrexia – use of anti-pyretics	
Review question in the scope	Does the use of anti-pyretics in women with pyrexia in labour improve outcomes for the woman or the baby?	
Review question for the guideline	Does the use of anti-pyretics in women with pyrexia in labour improve outcomes for the woman or the baby?	
Objective	The aim of this review is to determine whether the use of anti-pyretics in women with pyrexia in labour improves outcomes for the woman or the baby. This is an important topic because the incidence of maternal fever in labour is up to 10%, depending on the temperature cut-off used to define pyrexia (Herbst 1997, Impey 2001, Philip 1999), and maternal pyrexia is associated with potentially very serious maternal and neonatal consequences	
Population and directness	Women with pyrexia in labour Pyrexia as defined in studies. Studies in which up to 34% of the women have multiple pregnancy will be included. Evidence in which any of the women have multiple pregnancy should be downgraded for indirectness.	
Intervention	Intervention 1	

Item	Details	Working notes
	• Antipyretics (paracetamol) via any route of administration (that is, oral, intravenous or rectal) <u>Intervention 2</u> • Combination of paracetamol and physical cooling methods (see below for examples) Antipyretics other than paracetamol (for example, NSAIDs) will not be considered because they would not be relevant in labour	
Comparison	• No antipyretics or other action ('do nothing') • Physical cooling (neck warmer, cool sponging, reducing room temperature, iced drinks, birth pool, or showering) • Combination of physical cooling methods • Different routes of paracetamol administration (oral, intravenous or rectal)	
Outcomes	Critical outcomes: • for the woman: ○ mode of birth ○ admission to HDU/ITU and duration of hospital stay • for the baby: ○ major morbidities (neonatal infection, hypoxic ischaemic encephalopathy (HIE), or cerebral palsy/neurodevelopmental disability/developmental delay) Important outcomes: • for the woman: ○ woman's experience of labour and birth, including experience of the birth companion • for the baby: ○ mortality ○ admission to NICU and duration of hospital stay Outcomes of limited importance: • for the woman: ○ administration of antibiotics	
Importance of outcomes	Preliminary classification of the outcomes for decision making: • critical (up to 3 outcomes) • important but not critical (up to 3 outcomes) • of limited importance (1 outcome)	
Setting	Obstetric units	
Stratified, subgroup	Groups that will be reviewed and analysed separately:	

Item	Details	Working notes
and adjusted analyses	• women with pyrexia with (any) epidural versus women with pyrexia but no epidural In the presence of heterogeneity, the following subgroups will be considered for sensitivity analysis: • women with pyrexia with (any) epidural versus women with pyrexia but no epidural • gestational age Potential confounders: • maternal age • socioeconomic status • parity • prolonged labour • prolonged rupture of membranes • epidural analgesia • pre-existing infections of the lower genital tract • carriage of group B streptococcus • induced or augmented labour	
Language	English	
Study design	• Published full text papers only • Systematic reviews • RCTs • Only if RCTs unavailable or there is limited data to inform decision making: ○ prospective or retrospective comparative observational studies (including cohort and case-control studies) • Prospective study designs will be prioritised over retrospective study designs • Conference abstracts will not be considered	
Search strategy	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques were used. See Appendix B – Literature search strategies for full strategies	
Review strategy	Appraisal of methodological quality: • the methodological quality of each study will be assessed using checklists recommended in the NICE guidelines manual 2014 (for example, AMSTAR or ROBIS for systematic reviews, and Cochrane RoB tool for RCTs) and the quality of the evidence for each outcome (that is, across studies) will be assessed using GRADE	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence

Item	Details	Working notes
	• if studies report only p-values, this information will be recorded in GRADE tables without an assessment of imprecision Synthesis of data: • meta-analysis will be conducted where appropriate • default MIDs will be used; 0.8 and 1.25 for dichotomous outcomes; 0.5 times the SD of the measurement in the control arm (or median score across control arms if multiple studies are included) for continuous outcomes • for continuous data, change scores will be used in preference to final scores for data from non-RCT studies; final and change scores will not be pooled; if any study reports both, the method used in the majority of studies will be adopted	recommendations) will be subject to dual weeding and study selection; any discrepancies will be resolved through discussion between the first and second reviewers or by reference to a third person. This review question was not prioritised for health economic analysis and so no formal dual weeding, study selection (inclusion/exclusion) or data extraction into evidence tables will be undertaken. However, internal (NGA) quality assurance processes will include consideration of the outcomes of weeding, study selection and data extraction and the committee will review the results of study selection and data extraction
Equalities	Equalities considerations will be considered systematically in relation to the available evidence and draft recommendations. The guideline scope includes women with cognitive or physical disability as populations for whom there may be equalities issues. Women who have received no antenatal care will be considered as a subgroup for all systematic reviews performed within the medical conditions work stream and a specific question has been included in the obstetric complications work stream for this population.	
Notes/additional information	• Herbst A, Wolner-Hanssen P, Ingemarsson I. Maternal fever in term labor in relation to fetal tachycardia, cord artery acidaemia and neonatal infection. Br J Obstet Gynaecol 1997;104:363-6 • Impey L, Greenwood C, MacQuillan K, Reynolds M, Sheil O. Fever in labour and neonatal encephalopathy: a prospective cohort study. BJOG. 2001 Jun;108(6):594-7	

Item	Details	Working notes
	• Philip J, Alexander JM, Sharma SV, Leveno KJ, McIntire DD, Wiley J. Epidural analgesia during labour and maternal fever. Anaesthesiology 1999;90:1271-5	
Key papers	• Preventing fever in women with labour epidurals using a neck warmer • (http://apps.who.int/trialsearch/Trial2.aspx?TrialID=ISRCTN38665751)	

AMSTAR: Assessing the Methodological Quality of Systematic Reviews; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HDU: high dependency unit; HTA: Health Technology Assessment; ITU: intensive therapy unit; MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; NICU: neonatal intensive care unit; NSAID: non-steroidal anti-inflammatory drugs; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation; ROBIS: Risk of Bias in Systematic Reviews

Appendix B – Literature search strategies

Intrapartum care for women with pyrexia – fetal blood sampling

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

#	Searches
1	PREGNANCY/
2	exp PREGNANCY, MULTIPLE/
3	PERIPARTUM PERIOD/
4	PARTURITION/
5	exp LABOR, OBSTETRIC/
6	OBSTETRIC LABOR, PREMATURE/
7	DELIVERY, OBSTETRIC/
8	pregnan$.ti,ab.
9	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
10	((during or giving or give) adj3 birth?).ti,ab.
11	or/1-10
12	exp FEVER/
13	(fever$ or pyrexi$ or hyperthermi$).ti,ab.
14	((elevat$ or high$) adj3 temperature?).ti,ab.
15	or/12-14
16	FETAL MONITORING/
17	UTERINE MONITORING/
18	HEART RATE, FETAL/ and (monitor$ or assess$).ti,ab.
19	exp FETAL HEART/ and (monitor$ or assess$).ti,ab.
20	FETAL DISTRESS/ and (monitor$ or assess$).ti,ab.
21	((f?etal or f?etus$ or uter$) adj5 (heart$ or monitor$ or assess$)).ti,ab.

#	Searches
22	EFM.ti,ab.
23	FHR.ti,ab.
24	CARDIOTOCOGRAPHY/
25	ELECTROCARDIOGRAPHY/
26	cardiotocogra$.ti,ab.
27	CTG.ti,ab.
28	electrocardiogra$.ti,ab.
29	ECG.ti,ab.
30	EKG.ti,ab.
31	or/16-30
32	SCALP/ and ELECTRODES/
33	((f?etal or f?etus$) adj5 scalp? adj5 electrode?).ti,ab.
34	FSE.ti,ab.
35	or/32-34
36	BLOOD SPECIMEN COLLECTION/
37	FETAL BLOOD/ and (samp$ or analys$ or gas$).ti,ab.
38	((f?etal or f?etus) adj5 (lactate? or pH or scalp? or base$ or acid$ or alk#l$)).ti,ab.
39	((f?etal or f?etus) adj5 blood adj5 (gas$ or sampl$ or analys$)).ti,ab.
40	FBS.ti,ab.
41	exp BLOOD GAS ANALYSIS/
42	exp ACID-BASE IMBALANCE/
43	(blood adj5 (gas$ or oxygen or carbon dioxide or CO2) adj5 analys$).ti,ab.
44	((acidbase or acid base) adj5 (imbalanc$ or equ?l$)).ti,ab.
45	or/36-44
46	(exp PHYSICAL STIMULATION/ or VIBRATION/) and SCALP/
47	((f?etal or f?etus$) adj5 (stimulat$ or stimuli or stimulus)).ti,ab.
48	((scalp? or digit$ or acoustic$ or vibroacoustic$) adj5 (stimulat$ or stimuli or stimulus or punctur$)).ti,ab.
49	((acoustic or artificial) adj laryn$).ti,ab.
50	FSS.ti,ab.
51	or/46-50
52	PREGNANCY OUTCOME/
53	(pregnan$ adj3 outcome?).ti,ab.
54	or/52-53
55	((pregnan$ or labo?r or childbirth or partu$ or intra?part$ or peri?part$ or birth?) adj5 (fever$ or pyrexi$ or hyperthermi$) adj5 manag$).ti,ab.
56	11 and 15 and 31
57	11 and 15 and 35
58	11 and 15 and 45
59	11 and 15 and 51

#	Searches
60	15 and (31 or 35 or 45 or 51) and 54
61	or/55-60
62	limit 61 to english language
63	LETTER/
64	EDITORIAL/
65	NEWS/
66	exp HISTORICAL ARTICLE/
67	ANECDOTES AS TOPIC/
68	COMMENT/
69	CASE REPORT/
70	(letter or comment*).ti.
71	or/63-70
72	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
73	71 not 72
74	ANIMALS/ not HUMANS/
75	exp ANIMALS, LABORATORY/
76	exp ANIMAL EXPERIMENTATION/
77	exp MODELS, ANIMAL/
78	exp RODENTIA/
79	(rat or rats or mouse or mice).ti.
80	or/73-79
81	62 not 80

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	PREGNANCY/
2	exp PREGNANCY, MULTIPLE/
3	PERIPARTUM PERIOD/
4	PARTURITION/
5	exp LABOR, OBSTETRIC/
6	OBSTETRIC LABOR, PREMATURE/
7	DELIVERY, OBSTETRIC/
8	pregnan$.ti,ab,kw.
9	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
10	((during or giving or give) adj3 birth?).ti,ab.
11	or/1-10
12	exp FEVER/
13	(fever$ or pyrexi$ or hyperthermi$).ti,ab,kw.
14	((elevat$ or high$) adj3 temperature?).ti,ab.
15	or/12-14

#	Searches
16	FETAL MONITORING/
17	UTERINE MONITORING/
18	HEART RATE, FETAL/ and (monitor$ or assess$).ti,ab.
19	exp FETAL HEART/ and (monitor$ or assess$).ti,ab.
20	FETAL DISTRESS/ and (monitor$ or assess$).ti,ab.
21	((f?etal or f?etus$ or uter$) adj5 (heart$ or monitor$ or assess$)).ti,ab.
22	EFM.ti,ab.
23	FHR.ti,ab.
24	CARDIOTOCOGRAPHY/
25	ELECTROCARDIOGRAPHY/
26	cardiotocogra$.ti,ab,kw.
27	CTG.ti,ab.
28	electrocardiogra$.ti,ab,kw.
29	ECG.ti,ab.
30	EKG.ti,ab.
31	or/16-30
32	SCALP/ and ELECTRODES/
33	((f?etal or f?etus$) adj5 scalp? adj5 electrode?).ti,ab.
34	FSE.ti,ab.
35	or/32-34
36	BLOOD SPECIMEN COLLECTION/
37	FETAL BLOOD/ and (samp$ or analys$ or gas$).ti,ab.
38	((f?etal or f?etus) adj5 (lactate? or pH or scalp? or base$ or acid$ or alk#l$)).ti,ab.
39	((f?etal or f?etus) adj5 blood adj5 (gas$ or sampl$ or analys$)).ti,ab.
40	FBS.ti,ab.
41	exp BLOOD GAS ANALYSIS/
42	exp ACID-BASE IMBALANCE/
43	(blood adj5 (gas$ or oxygen or carbon dioxide or CO2) adj5 analys$).ti,ab.
44	((acidbase or acid base) adj5 (imbalanc$ or equ?l$)).ti,ab.
45	or/36-44
46	(exp PHYSICAL STIMULATION/ or VIBRATION/) and SCALP/
47	((f?etal or f?etus$) adj5 (stimulat$ or stimuli or stimulus)).ti,ab.
48	((scalp? or digit$ or acoustic$ or vibroacoustic$) adj5 (stimulat$ or stimuli or stimulus or punctur$)).ti,ab.
49	((acoustic or artificial) adj laryn$).ti,ab.
50	FSS.ti,ab.
51	or/46-50
52	PREGNANCY OUTCOME/
53	(pregnan$ adj3 outcome?).ti,ab.
54	or/52-53

#	Searches
55	((pregnan$ or labo?r or childbirth or partu$ or intra?part$ or peri?part$ or birth?) adj5 (fever$ or pyrexi$ or hyperthermi$) adj5 manag$).ti,ab.
56	11 and 15 and 31
57	11 and 15 and 35
58	11 and 15 and 45
59	11 and 15 and 51
60	15 and (31 or 35 or 45 or 51) and 54
61	or/55-60

Database: Cochrane Database of Systematic Reviews

#	Searches
1	PREGNANCY.kw.
2	PREGNANCY, MULTIPLE.kw.
3	PERIPARTUM PERIOD.kw.
4	PARTURITION.kw.
5	LABOR, OBSTETRIC.kw.
6	OBSTETRIC LABOR, PREMATURE.kw.
7	DELIVERY, OBSTETRIC.kw.
8	pregnan$.ti,ab.
9	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
10	((during or giving or give) adj3 birth?).ti,ab.
11	or/1-10
12	FEVER.kw.
13	(fever$ or pyrexi$ or hyperthermi$).ti,ab.
14	((elevat$ or high$) adj3 temperature?).ti,ab.
15	or/12-14
16	FETAL MONITORING.kw.
17	UTERINE MONITORING.kw.
18	HEART RATE, FETAL.kw. and (monitor$ or assess$).ti,ab.
19	FETAL HEART.kw. and (monitor$ or assess$).ti,ab.
20	FETAL DISTRESS.kw. and (monitor$ or assess$).ti,ab.
21	((f?etal or f?etus$ or uter$) adj5 (heart$ or monitor$ or assess$)).ti,ab.
22	EFM.ti,ab.
23	FHR.ti,ab.
24	CARDIOTOCOGRAPHY.kw.
25	ELECTROCARDIOGRAPHY.kw.
26	cardiotocogra$.ti,ab.
27	CTG.ti,ab.
28	electrocardiogra$.ti,ab.
29	ECG.ti,ab.

#	Searches
30	EKG.ti,ab.
31	or/16-30
32	(SCALP and ELECTRODES).kw.
33	((f?etal or f?etus$) adj5 scalp? adj5 electrode?).ti,ab.
34	FSE.ti,ab.
35	or/32-34
36	BLOOD SPECIMEN COLLECTION.kw.
37	FETAL BLOOD.kw. and (samp$ or analys$ or gas$).ti,ab.
38	((f?etal or f?etus) adj5 (lactate? or pH or scalp? or base$ or acid$ or alk#l$)).ti,ab.
39	((f?etal or f?etus) adj5 blood adj5 (gas$ or sampl$ or analys$)).ti,ab.
40	FBS.ti,ab.
41	BLOOD GAS ANALYSIS.kw.
42	ACID-BASE IMBALANCE.kw.
43	(blood adj5 (gas$ or oxygen or carbon dioxide or CO2) adj5 analys$).ti,ab.
44	((acidbase or acid base) adj5 (imbalanc$ or equ?l$)).ti,ab.
45	or/36-44
46	((PHYSICAL STIMULATION or VIBRATION) and SCALP).kw.
47	((f?etal or f?etus$) adj5 (stimulat$ or stimuli or stimulus)).ti,ab.
48	((scalp? or digit$ or acoustic$ or vibroacoustic$) adj5 (stimulat$ or stimuli or stimulus or punctur$)).ti,ab.
49	((acoustic or artificial) adj laryn$).ti,ab.
50	FSS.ti,ab.
51	or/46-50
52	PREGNANCY OUTCOME.kw.
53	(pregnan$ adj3 outcome?).ti,ab.
54	or/52-53
55	((pregnan$ or labo?r or childbirth or partu$ or intra?part$ or peri?part$ or birth?) adj5 (fever$ or pyrexi$ or hyperthermi$) adj5 manag$).ti,ab.
56	11 and 15 and 31
57	11 and 15 and 35
58	11 and 15 and 45
59	11 and 15 and 51
60	15 and (31 or 35 or 45 or 51) and 54
61	or/55-60

Database: Database of Abstracts of Reviews of Effects

#	Searches
1	PREGNANCY.kw.
2	PREGNANCY, MULTIPLE.kw.
3	PERIPARTUM PERIOD.kw.

#	Searches
4	PARTURITION.kw.
5	LABOR, OBSTETRIC.kw.
6	OBSTETRIC LABOR, PREMATURE.kw.
7	DELIVERY, OBSTETRIC.kw.
8	pregnan$.tw,tx.
9	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw,tx.
10	((during or giving or give) adj3 birth?).tw,tx.
11	or/1-10
12	FEVER.kw.
13	(fever$ or pyrexi$ or hyperthermi$).tw,tx.
14	((elevat$ or high$) adj3 temperature?).tw,tx.
15	or/12-14
16	FETAL MONITORING.kw.
17	UTERINE MONITORING.kw.
18	HEART RATE, FETAL.kw. and (monitor$ or assess$).tw,tx.
19	FETAL HEART.kw. and (monitor$ or assess$).tw,tx.
20	FETAL DISTRESS.kw. and (monitor$ or assess$).tw,tx.
21	((f?etal or f?etus$ or uter$) adj5 (heart$ or monitor$ or assess$)).tw,tx.
22	EFM.tw,tx.
23	FHR.tw,tx.
24	CARDIOTOCOGRAPHY.kw.
25	ELECTROCARDIOGRAPHY.kw.
26	cardiotocogra$.tw,tx.
27	CTG.tw,tx.
28	electrocardiogra$.tw,tx.
29	ECG.tw,tx.
30	EKG.tw,tx.
31	or/16-30
32	(SCALP and ELECTRODES).kw.
33	((f?etal or f?etus$) adj5 scalp? adj5 electrode?).tw,tx.
34	FSE.tw,tx.
35	or/32-34
36	BLOOD SPECIMEN COLLECTION.kw.
37	FETAL BLOOD.kw. and (samp$ or analys$ or gas$).tw,tx.
38	((f?etal or f?etus) adj5 (lactate? or pH or scalp? or base$ or acid$ or alk#l$)).tw,tx.
39	((f?etal or f?etus) adj5 blood adj5 (gas$ or sampl$ or analys$)).tw,tx.
40	FBS.tw,tx.
41	BLOOD GAS ANALYSIS.kw.
42	ACID-BASE IMBALANCE.kw.
43	(blood adj5 (gas$ or oxygen or carbon dioxide or CO2) adj5 analys$).tw,tx.

#	Searches
44	((acidbase or acid base) adj5 (imbalanc$ or equ?l$)).tw,tx.
45	or/36-44
46	((PHYSICAL STIMULATION or VIBRATION) and SCALP).kw.
47	((f?etal or f?etus$) adj5 (stimulat$ or stimuli or stimulus)).tw,tx.
48	((scalp? or digit$ or acoustic$ or vibroacoustic$) adj5 (stimulat$ or stimuli or stimulus or punctur$)).tw,tx.
49	((acoustic or artificial) adj laryn$).tw,tx.
50	FSS.tw,tx.
51	or/46-50
52	PREGNANCY OUTCOME.kw.
53	(pregnan$ adj3 outcome?).tw,tx.
54	or/52-53
55	((pregnan$ or labo?r or childbirth or partu$ or intra?part$ or peri?part$ or birth?) adj5 (fever$ or pyrexi$ or hyperthermi$) adj5 manag$).tw,tx.
56	11 and 15 and 31
57	11 and 15 and 35
58	11 and 15 and 45
59	11 and 15 and 51
60	15 and (31 or 35 or 45 or 51) and 54
61	or/55-60

Database: Health Technology Assessment

#	Searches
1	PREGNANCY/
2	exp PREGNANCY, MULTIPLE/
3	PERIPARTUM PERIOD/
4	PARTURITION/
5	exp LABOR, OBSTETRIC/
6	OBSTETRIC LABOR, PREMATURE/
7	DELIVERY, OBSTETRIC/
8	pregnan$.tw.
9	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
10	((during or giving or give) adj3 birth?).tw.
11	or/1-10
12	exp FEVER/
13	(fever$ or pyrexi$ or hyperthermi$).tw.
14	((elevat$ or high$) adj3 temperature?).tw.
15	or/12-14
16	FETAL MONITORING/
17	UTERINE MONITORING/

#	Searches
18	HEART RATE, FETAL/ and (monitor$ or assess$).tw.
19	exp FETAL HEART/ and (monitor$ or assess$).tw.
20	FETAL DISTRESS/ and (monitor$ or assess$).tw.
21	((f?etal or f?etus$ or uter$) adj5 (heart$ or monitor$ or assess$)).tw.
22	EFM.tw.
23	FHR.tw.
24	CARDIOTOCOGRAPHY/
25	ELECTROCARDIOGRAPHY/
26	cardiotocogra$.tw.
27	CTG.tw.
28	electrocardiogra$.tw.
29	ECG.tw.
30	EKG.tw.
31	or/16-30
32	SCALP/ and ELECTRODES/
33	((f?etal or f?etus$) adj5 scalp? adj5 electrode?).tw.
34	FSE.tw.
35	or/32-34
36	BLOOD SPECIMEN COLLECTION/
37	FETAL BLOOD/ and (samp$ or analys$ or gas$).tw.
38	((f?etal or f?etus) adj5 (lactate? or pH or scalp? or base$ or acid$ or alk#l$)).tw.
39	((f?etal or f?etus) adj5 blood adj5 (gas$ or sampl$ or analys$)).tw.
40	FBS.tw.
41	exp BLOOD GAS ANALYSIS/
42	exp ACID-BASE IMBALANCE/
43	(blood adj5 (gas$ or oxygen or carbon dioxide or CO2) adj5 analys$).tw.
44	((acidbase or acid base) adj5 (imbalanc$ or equ?l$)).tw.
45	or/36-44
46	(exp PHYSICAL STIMULATION/ or VIBRATION/) and SCALP/
47	((f?etal or f?etus$) adj5 (stimulat$ or stimuli or stimulus)).tw.
48	((scalp? or digit$ or acoustic$ or vibroacoustic$) adj5 (stimulat$ or stimuli or stimulus or punctur$)).tw.
49	((acoustic or artificial) adj laryn$).tw.
50	FSS.tw.
51	or/46-50
52	PREGNANCY OUTCOME/
53	(pregnan$ adj3 outcome?).tw.
54	or/52-53
55	((pregnan$ or labo?r or childbirth or partu$ or intra?part$ or peri?part$ or birth?) adj5 (fever$ or pyrexi$ or hyperthermi$) adj5 manag$).tw.

#	Searches
56	11 and 15 and 31
57	11 and 15 and 35
58	11 and 15 and 45
59	11 and 15 and 51
60	15 and (31 or 35 or 45 or 51) and 54
61	or/55-60

Database: Embase

#	Searches
1	*PREGNANCY/
2	exp *MULTIPLE PREGNANCY/
3	*PERINATAL PERIOD/
4	*BIRTH/
5	exp *LABOR/
6	*PREMATURE LABOR/
7	*OBSTETRIC DELIVERY/
8	*INTRAPARTUM CARE/
9	pregnan$.ti,ab.
10	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
11	((during or giving or give) adj3 birth?).ti,ab.
12	or/1-11
13	*FEVER/
14	(fever$ or pyrexi$ or hyperthermi$).ti,ab.
15	((elevat$ or high$) adj3 temperature?).ti,ab.
16	or/13-15
17	FETUS MONITORING/
18	UTERINE ACTIVITY MONITORING/
19	FETUS HEART RATE/ and (monitor$ or assess$).ti,ab.
20	FETUS HEART/ and (monitor$ or assess$).ti,ab.
21	FETUS DISTRESS/ and (monitor$ or assess$).ti,ab.
22	((f?etal or f?etus$ or uter$) adj5 (heart$ or monitor$ or assess$)).ti,ab.
23	EFM.ti,ab.
24	FHR.ti,ab.
25	CARDIOTOCOGRAPHY/
26	FETUS ELECTROCARDIOGRAPHY/
27	cardiotocogra$.ti,ab.
28	CTG.ti,ab.
29	electrocardiogra$.ti,ab.
30	ECG.ti,ab.
31	EKG.ti,ab.

#	Searches
32	or/17-31
33	SCALP/ and ELECTRODE/
34	((f?etal or f?etus$) adj5 scalp? adj5 electrode?).ti,ab.
35	FSE.ti,ab.
36	or/33-35
37	FETUS BLOOD SAMPLING/
38	((f?etal or f?etus) adj5 (lactate? or pH or scalp? or base$ or acid$ or alk#l$)).ti,ab.
39	((f?etal or f?etus) adj5 blood adj5 (gas$ or sampl$ or analys$)).ti,ab.
40	FBS.ti,ab.
41	exp BLOOD GAS ANALYSIS/
42	exp "DISORDERS OF ACID BASE BALANCE"/
43	(blood adj5 (gas$ or oxygen or carbon dioxide or CO2) adj5 analys$).ti,ab.
44	((acidbase or acid base) adj5 (imbalanc$ or equ?l$)).ti,ab.
45	or/37-44
46	(STIMULATION/ or VIBRATION/) and SCALP/
47	((f?etal or f?etus$) adj5 (stimulat$ or stimuli or stimulus)).ti,ab.
48	((scalp? or digit$ or acoustic$ or vibroacoustic$) adj5 (stimulat$ or stimuli or stimulus or punctur$)).ti,ab.
49	((acoustic or artificial) adj laryn$).ti,ab.
50	FSS.ti,ab.
51	or/46-50
52	PREGNANCY OUTCOME/
53	(pregnan$ adj3 outcome?).ti,ab.
54	or/52-53
55	((pregnan$ or labo?r or childbirth or partu$ or intra?part$ or peri?part$ or birth?) adj5 (fever$ or pyrexi$ or hyperthermi$) adj5 manag$).ti,ab.
56	12 and 16 and 32
57	12 and 16 and 36
58	12 and 16 and 45
59	12 and 16 and 51
60	16 and (32 or 36 or 45 or 51) and 54
61	or/55-60
62	limit 61 to english language
63	letter.pt. or LETTER/
64	note.pt.
65	editorial.pt.
66	CASE REPORT/ or CASE STUDY/
67	(letter or comment*).ti.
68	or/63-67
69	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.

#	Searches
70	68 not 69
71	ANIMAL/ not HUMAN/
72	NONHUMAN/
73	exp ANIMAL EXPERIMENT/
74	exp EXPERIMENTAL ANIMAL/
75	ANIMAL MODEL/
76	exp RODENT/
77	(rat or rats or mouse or mice).ti.
78	or/70-77
79	62 not 78

Intrapartum care for women with pyrexia – use of anti-pyretics

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

#	Searches
1	PREGNANCY/
2	exp PREGNANCY, MULTIPLE/
3	PERIPARTUM PERIOD/
4	PARTURITION/
5	exp LABOR, OBSTETRIC/
6	OBSTETRIC LABOR, PREMATURE/
7	DELIVERY, OBSTETRIC/
8	pregnan$.ti,ab.
9	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
10	((during or giving or give) adj3 birth?).ti,ab.
11	or/1-10
12	exp FEVER/
13	(fever$ or pyrexi$ or hyperthermi$).ti,ab.
14	((elevat$ or high$) adj3 temperature?).ti,ab.
15	or/12-14
16	exp ANTIPYRETICS/
17	(antipyretic$ or anti-pyretic$).ti,ab.
18	(antifebril$ or anti-febril$).ti,ab.
19	(Apap or acamol or acephen or acetaco or acetamidophenol or acet?minophen or algotropyl or anacin 3 or datril or hydroxyacetanilide or Panadol or paracetamol or Tylenol or p-acetamidophenol or p-hydroxyacetanilide).mp.
20	(acetylsalicylic acid or acetysal or acylpyrin or aloxiprimum or aspirin? or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin).mp.

#	Searches
21	(Algopyrin or analgin or biopyrin or dipyrone or dipyronium or met?amizol? or methampyrone or narone or noramidopyrine methanesulfonate or normelubrine or novalgetol or novalgin or novamidazophen or novaminsulfone or optalgin or pyralgin or sulpyrin?).mp.
22	or/16-21
23	do nothing.ti,ab.
24	((no or avoid$) adj3 interven$).ti,ab.
25	(no adj3 (antipyretic$ or anti-pyretic$ or acetaminophen or paracetamol? or aspirin? or dipyrone)).ti,ab.
26	or/23-25
27	cool$.ti,ab.
28	warm$.ti,ab.
29	spong$.ti,ab.
30	(room? adj3 temperature?).ti,ab.
31	((ice? or cold) adj3 (drink$ or cube?)).ti,ab.
32	BATHS/
33	((birth$ or water) adj3 pool?).ti,ab.
34	shower$.ti,ab.
35	or/27-34
36	exp FEVER/dt [Drug Therapy]
37	exp FEVER/pc [Prevention & Control]
38	exp FEVER/th [Therapy]
39	or/36-38
40	(manag$ adj5 (fever$ or pyrexi$ or hyperthermi$)).ti,ab.
41	11 and 15 and 22
42	11 and 15 and 26
43	11 and 15 and 35
44	11 and 39
45	11 and 40
46	or/41-45
47	limit 46 to english language
48	LETTER/
49	EDITORIAL/
50	NEWS/
51	exp HISTORICAL ARTICLE/
52	ANECDOTES AS TOPIC/
53	COMMENT/
54	CASE REPORT/
55	(letter or comment*).ti.
56	or/48-55
57	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.

#	Searches
58	56 not 57
59	ANIMALS/ not HUMANS/
60	exp ANIMALS, LABORATORY/
61	exp ANIMAL EXPERIMENTATION/
62	exp MODELS, ANIMAL/
63	exp RODENTIA/
64	(rat or rats or mouse or mice).ti.
65	or/58-64
66	47 not 65

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	PREGNANCY/
2	exp PREGNANCY, MULTIPLE/
3	PERIPARTUM PERIOD/
4	PARTURITION/
5	exp LABOR, OBSTETRIC/
6	OBSTETRIC LABOR, PREMATURE/
7	DELIVERY, OBSTETRIC/
8	pregnan$.ti,ab,kw.
9	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
10	((during or giving or give) adj3 birth?).ti,ab.
11	or/1-10
12	exp FEVER/
13	(fever$ or pyrexi$ or hyperthermi$).ti,ab,kw.
14	((elevat$ or high$) adj3 temperature?).ti,ab.
15	or/12-14
16	exp ANTIPYRETICS/
17	(antipyretic$ or anti-pyretic$).ti,ab,kw.
18	(antifebril$ or anti-febril$).ti,ab,kw.
19	(Apap or acamol or acephen or acetaco or acetamidophenol or acet?minophen or algotropyl or anacin 3 or datril or hydroxyacetanilide or Panadol or paracetamol or Tylenol or p-acetamidophenol or p-hydroxyacetanilide).mp.
20	(acetylsalicylic acid or acetysal or acylpyrin or aloxiprimum or aspirin? or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin).mp.
21	(Algopyrin or analgin or biopyrin or dipyrone or dipyronium or met?amizol? or methampyrone or narone or noramidopyrine methanesulfonate or normelubrine or novalgetol or novalgin or novamidazophen or novaminsulfone or optalgin or pyralgin or sulpyrin?).mp.
22	or/16-21
23	do nothing.ti,ab.

#	Searches
24	((no or avoid$) adj3 interven$).ti,ab.
25	(no adj3 (antipyretic$ or anti-pyretic$ or acetaminophen or paracetamol? or aspirin? or dipyrone)).ti,ab.
26	or/23-25
27	cool$.ti,ab.
28	warm$.ti,ab.
29	spong$.ti,ab.
30	(room? adj3 temperature?).ti,ab.
31	((ice? or cold) adj3 (drink$ or cube?)).ti,ab.
32	BATHS/
33	((birth$ or water) adj3 pool?).ti,ab.
34	shower$.ti,ab.
35	or/27-34
36	exp FEVER/dt [Drug Therapy]
37	exp FEVER/pc [Prevention & Control]
38	exp FEVER/th [Therapy]
39	or/36-38
40	(manag$ adj5 (fever$ or pyrexi$ or hyperthermi$)).ti,ab.
41	11 and 15 and 22
42	11 and 15 and 26
43	11 and 15 and 35
44	11 and 39
45	11 and 40
46	or/41-45

Database: Cochrane Database of Systematic Reviews

#	Searches
1	PREGNANCY.kw.
2	PREGNANCY, MULTIPLE.kw.
3	PERIPARTUM PERIOD.kw.
4	PARTURITION.kw.
5	LABOR, OBSTETRIC.kw.
6	OBSTETRIC LABOR, PREMATURE.kw.
7	DELIVERY, OBSTETRIC.kw.
8	pregnan$.ti,ab.
9	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
10	((during or giving or give) adj3 birth?).ti,ab.
11	or/1-10
12	FEVER.kw.
13	(fever$ or pyrexi$ or hyperthermi$).ti,ab.

#	Searches
14	((elevat$ or high$) adj3 temperature?).ti,ab.
15	or/12-14
16	ANTIPYRETICS.kw.
17	(antipyretic$ or anti-pyretic$).ti,ab.
18	(antifebril$ or anti-febril$).ti,ab.
19	(Apap or acamol or acephen or acetaco or acetamidophenol or acet?minophen or algotropyl or anacin 3 or datril or hydroxyacetanilide or Panadol or paracetamol or Tylenol or p-acetamidophenol or p-hydroxyacetanilide).mp.
20	(acetylsalicylic acid or acetysal or acylpyrin or aloxiprimum or aspirin? or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin).mp.
21	(Algopyrin or analgin or biopyrin or dipyrone or dipyronium or met?amizol? or methampyrone or narone or noramidopyrine methanesulfonate or normelubrine or novalgetol or novalgin or novamidazophen or novaminsulfone or optalgin or pyralgin or sulpyrin?).mp.
22	or/16-21
23	do nothing.ti,ab.
24	((no or avoid$) adj3 interven$).ti,ab.
25	(no adj3 (antipyretic$ or anti-pyretic$ or acetaminophen or paracetamol? or aspirin? or dipyrone)).ti,ab.
26	or/23-25
27	cool$.ti,ab.
28	warm$.ti,ab.
29	spong$.ti,ab.
30	(room? adj3 temperature?).ti,ab.
31	((ice? or cold) adj3 (drink$ or cube?)).ti,ab.
32	BATHS.kw.
33	((birth$ or water) adj3 pool?).ti,ab.
34	shower$.ti,ab.
35	or/27-34
36	(manag$ adj5 (fever$ or pyrexi$ or hyperthermi$)).ti,ab.
37	11 and 15 and 22
38	11 and 15 and 26
39	11 and 15 and 35
40	11 and 36
41	or/37-40

Database: Database of Abstracts of Reviews of Effects

#	Searches
1	PREGNANCY.kw.
2	PREGNANCY, MULTIPLE.kw.
3	PERIPARTUM PERIOD.kw.
4	PARTURITION.kw.

#	Searches
5	LABOR, OBSTETRIC.kw.
6	OBSTETRIC LABOR, PREMATURE.kw.
7	DELIVERY, OBSTETRIC.kw.
8	pregnan$.tw,tx.
9	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw,tx.
10	((during or giving or give) adj3 birth?).tw,tx.
11	or/1-10
12	FEVER.kw.
13	(fever$ or pyrexi$ or hyperthermi$).tw,tx.
14	((elevat$ or high$) adj3 temperature?).tw,tx.
15	or/12-14
16	ANTIPYRETICS.kw.
17	(antipyretic$ or anti-pyretic$).tw,tx.
18	(antifebril$ or anti-febril$).tw,tx.
19	(Apap or acamol or acephen or acetaco or acetamidophenol or acet?minophen or algotropyl or anacin 3 or datril or hydroxyacetanilide or Panadol or paracetamol or Tylenol or p-acetamidophenol or p-hydroxyacetanilide).mp.
20	(acetylsalicylic acid or acetysal or acylpyrin or aloxiprimum or aspirin? or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin).mp.
21	(Algopyrin or analgin or biopyrin or dipyrone or dipyronium or met?amizol? or methampyrone or narone or noramidopyrine methanesulfonate or normelubrine or novalgetol or novalgin or novamidazophen or novaminsulfone or optalgin or pyralgin or sulpyrin?).mp.
22	or/16-21
23	do nothing.tw,tx.
24	((no or avoid$) adj3 interven$).tw,tx.
25	(no adj3 (antipyretic$ or anti-pyretic$ or acetaminophen or paracetamol? or aspirin? or dipyrone)).tw,tx.
26	or/23-25
27	cool$.tw,tx.
28	warm$.tw,tx.
29	spong$.tw,tx.
30	(room? adj3 temperature?).tw,tx.
31	((ice? or cold) adj3 (drink$ or cube?)).tw,tx.
32	BATHS.kw.
33	((birth$ or water) adj3 pool?).tw,tx.
34	shower$.tw,tx.
35	or/27-34
36	(manag$ adj5 (fever$ or pyrexi$ or hyperthermi$)).tw,tx.
37	11 and 15 and 22
38	11 and 15 and 26

#	Searches
39	11 and 15 and 35
40	11 and 36
41	or/37-40

Database: Health Technology Assessment

#	Searches
1	PREGNANCY/
2	exp PREGNANCY, MULTIPLE/
3	PERIPARTUM PERIOD/
4	PARTURITION/
5	exp LABOR, OBSTETRIC/
6	OBSTETRIC LABOR, PREMATURE/
7	DELIVERY, OBSTETRIC/
8	pregnan$.tw.
9	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
10	((during or giving or give) adj3 birth?).tw.
11	or/1-10
12	exp FEVER/
13	(fever$ or pyrexi$ or hyperthermi$).tw.
14	((elevat$ or high$) adj3 temperature?).tw.
15	or/12-14
16	exp Analgesics, Non-Narcotic/
17	(antipyretic$ or anti-pyretic$).tw.
18	(antifebril$ or anti-febril$).tw.

#	Searches
19	(Apap or acamol or acephen or acetaco or acetamidophenol or acet?minophen or algotropyl or anacin 3 or datril or hydroxyacetanilide or Panadol or paracetamol or Tylenol or p-acetamidophenol or p-hydroxyacetanilide).mp.
20	(acetylsalicylic acid or acetysal or acylpyrin or aloxiprimum or aspirin? or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin).mp.
21	(Algopyrin or analgin or biopyrin or dipyrone or dipyronium or met?amizol? or methampyrone or narone or noramidopyrine methanesulfonate or normelubrine or novalgetol or novalgin or novamidazophen or novaminsulfone or optalgin or pyralgin or sulpyrin?).mp.
22	or/16-21
23	do nothing.tw.
24	((no or avoid$) adj3 interven$).tw.
25	(no adj3 (antipyretic$ or anti-pyretic$ or acetaminophen or paracetamol? or aspirin? or dipyrone)).tw.
26	or/23-25
27	cool$.tw.
28	warm$.tw.
29	spong$.tw.
30	(room? adj3 temperature?).tw.
31	((ice? or cold) adj3 (drink$ or cube?)).tw.
32	BATHS/
33	((birth$ or water) adj3 pool?).tw.
34	shower$.tw.
35	or/27-34
36	exp FEVER/dt [Drug Therapy]
37	exp FEVER/pc [Prevention & Control]
38	exp FEVER/th [Therapy]
39	or/36-38
40	(manag$ adj5 (fever$ or pyrexi$ or hyperthermi$)).tw.
41	11 and 15 and 22
42	11 and 15 and 26
43	11 and 15 and 35
44	11 and 39
45	11 and 40
46	or/41-45

Database: Embase

#	Searches
1	*PREGNANCY/
2	exp *MULTIPLE PREGNANCY/
3	*PERINATAL PERIOD/
4	*BIRTH/

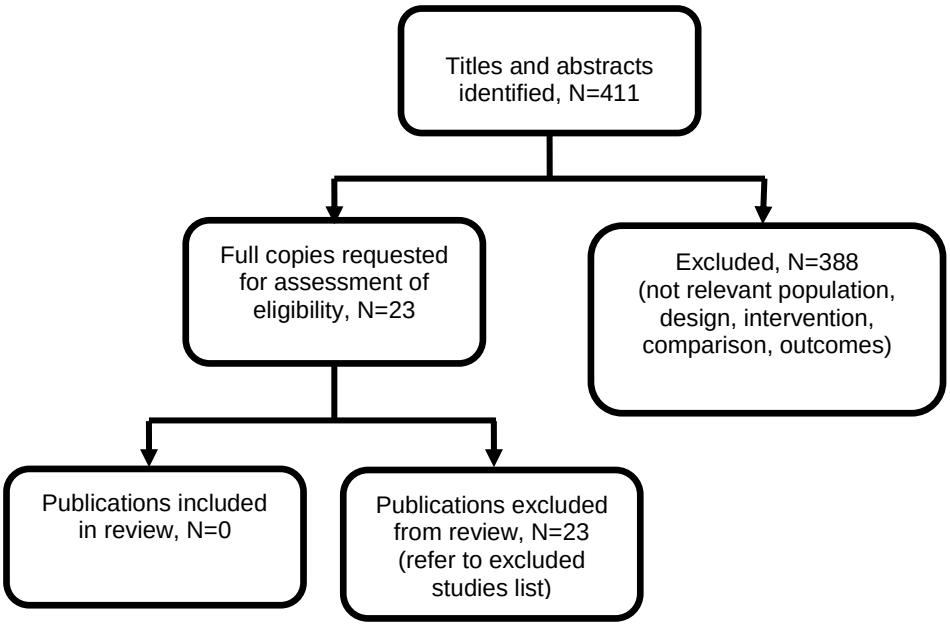
#	Searches
5	exp *LABOR/
6	*PREMATURE LABOR/
7	*OBSTETRIC DELIVERY/
8	*INTRAPARTUM CARE/
9	pregnan$.ti,ab.
10	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
11	((during or giving or give) adj3 birth?).ti,ab.
12	or/1-11
13	FEVER/
14	(fever$ or pyrexi$ or hyperthermi$).ti,ab.
15	((elevat$ or high$) adj3 temperature?).ti,ab.
16	or/13-15
17	ANTIPYRETIC AGENT/
18	PARACETAMOL/
19	ACETYLSALICYLIC ACID/
20	DIPYRONE/
21	(antipyretic$ or anti-pyretic$).ti,ab.
22	(antifebril$ or anti-febril$).ti,ab.
23	(Apap or acamol or acephen or acetaco or acetamidophenol or acet?minophen or algotropyl or anacin 3 or datril or hydroxyacetanilide or Panadol or paracetamol or Tylenol or p-acetamidophenol or p-hydroxyacetanilide).mp.
24	(acetylsalicylic acid or acetysal or acylpyrin or aloxiprimum or aspirin? or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin).mp.
25	(Algopyrin or analgin or biopyrin or dipyrone or dipyronium or met?amizol? or methampyrone or narone or noramidopyrine methanesulfonate or normelubrine or novalgetol or novalgin or novamidazophen or novaminsulfone or optalgin or pyralgin or sulpyrin?).mp.
26	or/17-25
27	do nothing.ti,ab.
28	((no or avoid$) adj3 interven$).ti,ab.
29	(no adj3 (antipyretic$ or anti-pyretic$ or acetaminophen or paracetamol? or aspirin? or dipyrone)).ti,ab.
30	or/27-29
31	cool$.ti,ab.
32	warm$.ti,ab.
33	spong$.ti,ab.
34	(room? adj3 temperature?).ti,ab.
35	((ice? or cold) adj3 (drink$ or cube?)).ti,ab.
36	BATH/
37	((birth$ or water) adj3 pool?).ti,ab.
38	shower$.ti,ab.

#	Searches
39	or/31-38
40	FEVER/dt [Drug Therapy]
41	FEVER/pc [Prevention]
42	FEVER/th [Therapy]
43	or/40-42
44	(manag$ adj5 (fever$ or pyrexi$ or hyperthermi$)).ti,ab.
45	12 and 16 and 26
46	12 and 16 and 30
47	12 and 16 and 39
48	12 and 43
49	12 and 44
50	or/45-49
51	limit 50 to english language
52	letter.pt. or LETTER/
53	note.pt.
54	editorial.pt.
55	CASE REPORT/ or CASE STUDY/
56	(letter or comment*).ti.
57	or/52-56
58	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
59	57 not 58
60	ANIMAL/ not HUMAN/
61	NONHUMAN/
62	exp ANIMAL EXPERIMENT/
63	exp EXPERIMENTAL ANIMAL/
64	ANIMAL MODEL/
65	exp RODENT/
66	(rat or rats or mouse or mice).ti.
67	or/59-66
68	51 not 67

Appendix C – Clinical evidence study selection

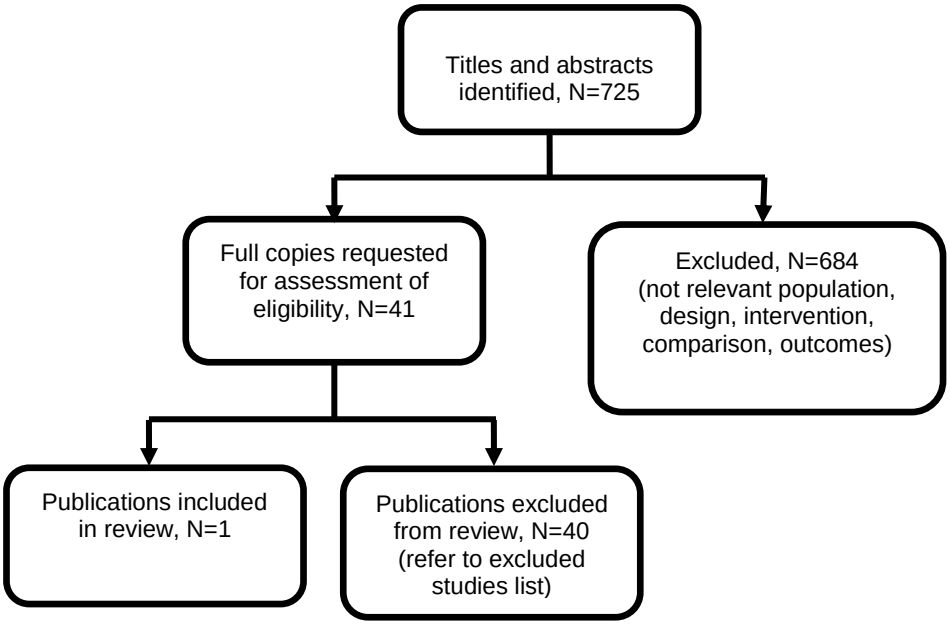
Intrapartum care for women with pyrexia – fetal blood sampling

Figure 1: Flow diagram of clinical article selection for intrapartum care for women with pyrexia – fetal blood sampling



Intrapartum care for women with pyrexia – use of anti-pyretics

Figure 2: Flow diagram of clinical article selection for intrapartum care for women with pyrexia – use of anti-pyretics



Appendix D – Excluded studies

Intrapartum care for women with pyrexia – fetal blood sampling

Clinical studies

Study	Reason for exclusion
Amer-Wahlin, I., Arulkumaran, S., Hagberg, H., Marsal, K., Visser, G. H., Fetal electrocardiogram: ST waveform analysis in intrapartum surveillance, BJOG: An International Journal of Obstetrics & Gynaecology, 114, 1191-3, 2007	A descriptive article about the ST waveform analysis of fetal electrocardiogram (ECG) for intrapartum surveillance (STAN)
Becker, J. H., van Rijswijk, J., Versteijnen, B., Evers, A. C., van den Akker, E. S., van Beek, E., Bolte, A. C., Rijnders, R. J., Mol, B. W., Moons, Kg, Porath, M. M., Drogtrop, A. P., Schuitemaker, N. W., Willekes, C., Westerhuis, M. E., Visser, G. H., Kwee, A., Is intrapartum	Not the comparison of interest. The study examines whether maternal fever is associated with a higher occurrence of ST-events by comparing fetal heart rate (recorded via STAN monitor, using scalp electrode) in women with and without fever

Study	Reason for exclusion
fever associated with ST-waveform changes of the fetal electrocardiogram? A retrospective cohort study, BJOG: An International Journal of Obstetrics & Gynaecology, 119, 1410-6, 2012	
Cahill,A.G., Duffy,C.R., Odibo,A.O., Roehl,K.A., Zhao,Q., Macones,G.A., Number of cervical examinations and risk of intrapartum maternal fever, Obstetrics and Gynecology, 119, 1096-1101, 2012	Not the question of interest. The study examines the association between number of cervical examinations and risk of maternal fever during term labor and birth. FBS is not mentioned
Chan,W.H., Paul,R.H., Toews,J., Intrapartum fetal monitoring. Maternal and fetal morbidity and perinatal mortality, Obstetrics and Gynecology, 41, 7-13, 1973	Not the question of interest. The study examines whether fetal monitoring (via a scalp electrode and an intra-uterine catheter) is associated with maternal and fetal morbidity. No FBS was undertaken
Hagen,D., Maternal febrile morbidity associated with fetal monitoring and cesarean section, Obstetrics and Gynecology, 46, 260-262, 1975	Not the comparison of interest. The study compares morbidity of women who were monitored during labour for continuous fetal heart rate (via an electrode attached to the fetal scalp) and those who were not
Herbst,A., Wolner-Hanssen,P., Ingemarsson,I., Maternal fever in term labour in relation to fetal tachycardia, cord artery acidaemia and neonatal infection, British Journal of Obstetrics and Gynaecology, 104, 363-366, 1997	Not the question of interest. The study examines how often fetal tachycardia precedes maternal fever during term labour, and if such tachycardia predicts neonatal infectious complications. Study population wasinfants whose mothers developed fever during labour and those whose mothers did not develop fever. FBS is not mentioned
Impey,L., Greenwood,C., MacQuillan,K., Reynolds,M., Sheil,O., Fever in labour and neonatal encephalopathy: a prospective cohort study, BJOG: An International Journal of Obstetrics and Gynaecology, 108, 594-597, 2001	Not the question of interest. The study compares neonatal outcomes between women who had no fewer during labour and those who developed fewer before labour
Impey,L., Greenwood,C., Sheil,O., MacQuillan,K., Reynolds,M., Redman,C., The relation between pre-eclampsia at term and neonatal encephalopathy, Archives of Disease in Childhood Fetal and Neonatal Edition, 85, F170-F172, 2001	Not the question of interest. The study examines whether pre-eclampsia at term and neonatal encephalopathy are associated with maternal fever. FBS is not mentioned
Kennedy, D., Management of pain and fever during pregnancy, Medicine Today, 15, 18-23, 2014	A narrative article about treatment options for pregnant women who suffer from pain or fever
Kirshon, B., Moise, K. J., Jr., Wasserstrum, N., Effect of acetaminophen on fetal acid-base balance in chorioamnionitis, Journal of Reproductive Medicine, 34, 955-9, 1989	Not the comparison of interest. The study compares fetal heart rate tracings in women with fever before and after antipyretic therapy
Lavesson, T., Kallen, K., Olofsson, P., Fetal and maternal temperatures during labor and delivery: a prospective descriptive study, Journal of Maternal-Fetal and Neonatal Medicine, 1-9, 2017	Not the question of interest. The study examines the fetal scalp temperature and maternal axillary temperature changes during unassisted vaginal birth relative to progression of labour, and describes normal temperature reference ranges.

Study	Reason for exclusion
	Women with eardrum temperature >=38.0 C were excluded
McCowan,L., Jackson,P., The prophylactic use of metronidazole in caesarean section, New Zealand Medical Journal, 92, 153-155, 1980	Not the question of interest. The article evaluates the effect of metronidazole given prior to caesarean section versus placebo. FBS is not mentioned
Odendaal,H.J., Crawford,J.W., Fetal tachycardia and maternal pyrexia during labour, South African Medical Journal, Suid-Afrikaanse Tydskrif Vir Geneeskunde. 49, 1873-1875, 1975	Not the question of interest. The study examines whether a rise in fetal heart rate during continuous monitoring could be an early warning of intra-uterine infection. Cases were women with pyrexia during labour, controls were women without pyrexia. All women were monitored using CTG. FBS is not mentioned
Perlman,J.M., Maternal fever and neonatal depression: preliminary observations, Clinical Pediatrics, 38, 287-291, 1999	Not the question of interest. The study examines the association between maternal fever and neonatal depression (that is, requiring intensive intervention). Outcomes of infants born to mothers with fever were compared to those born to mothers without fever. FBS is not mentioned
Perloe,M., Curet,L.B., The effect of internal fetal monitoring on cesarean section morbidity, Obstetrics and Gynecology, 53, 354-357, 1979	Not the comparison of interest. The study compares caesarean section morbidity outcomes in women who were monitored with internal fetal monitoring (via a scalp electrode and an internal pressure catheter) and those who were not monitored
Philip,J., Alexander,J.M., Sharma,S.K., Leveno,K.J., McIntire,D.D., Wiley,J., Epidural analgesia during labor and maternal fever, Anesthesiology, 90, 1271-1275, 1999	Not the question of interest. The study examines the association between epidural analgesia and maternal fever. Outcomes of infants born to women with fever were compared to those born to women without fever. FBS is not mentioned
Redrado Gimenez, O., Ruiz, J., Marti, S., Rodrigo, M., Lapresta, M., Rodriguez, L., Campillos, J. M., Adiego, I., Agustin Oliva, A., Cotaina, L., Intrapartum fetal scalp Ph sampling for management of neonatal acidosis, Journal of Perinatal Medicine, 43, 2015	Poster
Reilly,D.R., Oppenheimer,L.W., Fever in term labour, Journal of Obstetrics and Gynaecology Canada: JOGC, 27, 218-223, 2005	Not the question of interest. The study examines the association between maternal, fetal and labour variables, and fever by comparing women whose membranes had been ruptured for less than 24 hours and who were febrile with those who were not. FBS is not mentioned
Rodriguez Fernandez, V., Ramon y Cajal, C. N. L., Ortiz, E. M., Naveira, E. C., Intrapartum and perinatal results associated with different degrees of staining of meconium stained amniotic fluid, European Journal of Obstetrics Gynecology and Reproductive Biology, 224, 192-197, 2018	Not the question of interest. The study examines the association between different degrees of amniotic fluid staining with intrapartum and neonatal outcomes

Study	Reason for exclusion
Steer, P., First do the experiment: Do computerised interpretation of cardiotocography and other widely used interventions improve newborn outcomes?, Early Human Development, 114, 35-37, 2017	A narrative article about intrapartum surveillance
Steer, P. J., The INFANT trial of computer-assisted fetal heart rate pattern interpretation, Obstetrics, Gynaecology and Reproductive Medicine, 27, 322-323, 2017	A short summary of the INFANT trial
Talic, A., Kurjak, A., Honemeyer, U., Effect of maternal fever on fetal behavior assessed by KANET test, Donald School Journal of Ultrasound in Obstetrics and Gynecology, 6, 160-165, 2012	Not the question of interest. The study examines the impact of maternal infection on fetal behaviour. The high risk group was women with fever, the low risk group was women without fever. FBS is not mentioned
Tay, H. S., Audit on the management of pyrexia in labour at Aberdeen Maternity Hospital, Journal of Obstetrics and Gynaecology, 30, 756-757, 2010	Conference abstract

Economic studies

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with pyrexia – use of anti-pyretics

Clinical studies

Study	Reason for exclusion
Acs, N., Banhidy, F., Horvath-Puho, E., Czeizel, A. E., Population-based case-control study of the common cold during pregnancy and congenital abnormalities, European Journal of Epidemiology, 21, 65-75, 2006	No relevant comparison. Not women in labour
Acs,N., Banhidy,F., Puho,E., Czeizel,A.E., Maternal influenza during pregnancy and risk of congenital abnormalities in offspring, Birth Defects Research Part A - Clinical and Molecular Teratology, 73, 989-996, 2005	No relevant comparison. Not women in labour
Andrade, C., Use of acetaminophen (paracetamol) during pregnancy and the risk of attention-deficit/hyperactivity disorder in the offspring, Journal of Clinical Psychiatry, 77, e312-4, 2016	Non-systematic literature review
Bailey, C., Steer, P. J., Maternal temperature in labour, Fetal and Maternal Medicine Review, 18, 67-83, 2007	Non-systematic literature review

Study	Reason for exclusion
Blaser, J. A., Allan, G. M., Acetaminophen in pregnancy and future risk of ADHD in offspring, Canadian Family Physician, 60, 642, 2014	Non-systematic literature review
Brandlistuen, R. E., Ystrom, E., Nulman, I., Koren, G., Nordeng, H., Prenatal paracetamol exposure and child neurodevelopment: a sibling-controlled cohort study, International Journal of Epidemiology, 42, 1702-13, 2013	No subgroup analysis for women with pyrexia in labour
Calhoun, B. C., Brost, B., Emergency management of sudden puerperal fever, Obstetrics & Gynecology Clinics of North America, 22, 357-67, 1995	Non-systematic literature review
de Fays, L., Van Malderen, K., De Smet, K., Sawchik, J., Verlinden, V., Hamdani, J., Dogne, J. M., Dan, B., Use of paracetamol during pregnancy and child neurological development, Developmental Medicine & Child Neurology, 57, 718-24, 2015	Non-systematic literature review
Dreier, J. W., Andersen, A. M., Berg-Beckhoff, G., Systematic review and meta-analyses: fever in pregnancy and health impacts in the offspring, Pediatrics, 133, e674-88, 2014	No relevant studies are included in this systematic review. The review highlights studies that assess the effect of antipyretics. None of these studies focus on women in labour
Herbst,A., Wolner-Hanssen,P., Ingemarsson,I., Maternal fever in term labour in relation to fetal tachycardia, cord artery acidaemia and neonatal infection, British Journal of Obstetrics and Gynaecology, 104, 363-366, 1997	No relevant comparison
Hoover, R. M., Hayes, V. A. G., Erramouspe, J., Association Between Prenatal Acetaminophen Exposure and Future Risk of Attention Deficit/Hyperactivity Disorder in Children, Annals of Pharmacotherapy, 49, 1357-1361, 2015	No relevant studies included
Impey,L., Greenwood,C., MacQuillan,K., Reynolds,M., Sheil,O., Fever in labour and neonatal encephalopathy: a prospective cohort study, BJOG: An International Journal of Obstetrics and Gynaecology, 108, 594-597, 2001	No relevant intervention
Kennedy, D., Management of pain and fever during pregnancy, Medicine Today, 15, 18-23, 2014	Non-systematic literature review
Kirshon, B., Moise, K. J., Jr., Wasserstrum, N., Effect of acetaminophen on fetal acid-base balance in chorioamnionitis, Journal of Reproductive Medicine, 34, 955-9, 1989	No relevant comparison. Uncontrolled before-and-after study involving 8 women with pyrexia in labour who were administered 1 or more acetaminophen (paracetamol) rectal suppositories, but there was no comparison group
Lavesson,T., Akerman,F., Kallen,K., Olofsson,P., Effects on fetal and maternal	Unclear if controls were febrile or afebrile

Study	Reason for exclusion
temperatures of paracetamol administration during labour: a case-control study, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 168, 138-144, 2013	
Li,Z., Ren,A., Liu,J., Pei,L., Zhang,L., Guo,Z., Li,Z., Maternal flu or fever, medication use, and neural tube defects: a population-based case-control study in Northern China, Birth Defects Research, 79, 295-300, 2007	Not women in labour. Analysis focuses on maternal flu or high fever and antipyretic use from 1 month before until 2 months after conception. Results not disaggregated by different antipyretics
Liew, Z., Bach, C. C., Asarnow, R. F., Ritz, B., Olsen, J., Paracetamol use during pregnancy and attention and executive function in offspring at age 5 years, International Journal of Epidemiology, 28, 28, 2016	No subgroup analysis for women in labour
Liew, Z., Ritz, B., Rebordosa, C., Lee, P. C., Olsen, J., Acetaminophen use during pregnancy, behavioral problems, and hyperkinetic disorders, JAMA Pediatrics, 168, 313-20, 2014	No subgroup analysis for women in labour
Liew, Z., Ritz, B., Virk, J., Olsen, J., Maternal use of acetaminophen during pregnancy and risk of autism spectrum disorders in childhood: A Danish national birth cohort study, Autism research : Official Journal of the International Society for Autism Research, 9, 951-8, 2016	No subgroup analysis for women in labour
Linthavong, O. R., Franasiak, J., Ivester, T., Febrile illness in pregnancy: Disseminated herpes simplex virus, Obstetrics and Gynecology, 121, 675-681, 2013	Case report and non-systematic literature review
Lynberg,M.C., Khoury,M.J., Lu,X., Cocian,T., Maternal flu, fever, and the risk of neural tube defects: A population- based case-control study, American Journal of Epidemiology, 140, 244-255, 1994	Not women in labour. Adverse outcomes were reported for women who did or did not take medication during an episode of flu with fever occurring from 1 month before until 3 months after conception
Magnus, M. C., Karlstad, O., Haberg, S. E., Nafstad, P., Davey Smith, G., Nystad, W., Prenatal and infant paracetamol exposure and development of asthma: the Norwegian Mother and Child Cohort Study, International Journal of Epidemiology, 45, 512-22, 2016	No subgroup analysis for women in labour
Nielsen, S. Y., Molbak, K., Henriksen, T. B., Krogfelt, K. A., Larsen, C. S., Villumsen, S., Adverse pregnancy outcomes and Coxiella burnetii antibodies in pregnant women, Denmark, Emerging Infectious Diseases, 20, 925-931, 2014	No relevant population. Two women had pyrexia. It is unclear when they experienced pyrexia. No relevant intervention
Nisha Rani, S. S., Gomathi, S., Sambathkumar, R., Monster phase of acetaminophen use in pregnancy: Current vision of an old drug,	Non-systematic literature review

Study	Reason for exclusion
International Journal of Pharmacy and Pharmaceutical Sciences, 8, 25-27, 2016	
Pastore,L.M., Hertz-Picciotto,I., Beaumont,J.J., Risk of stillbirth from medications, illnesses and medical procedures, Paediatric and Perinatal Epidemiology, 13, 421-430, 1999	No subgroup analysis for women in labour
Philip,J., Alexander,J.M., Sharma,S.K., Leveno,K.J., McIntire,D.D., Wiley,J., Epidural analgesia during labor and maternal fever, Anesthesiology, 90, 1271-1275, 1999	No relevant intervention
Pollock, N. A., Langton, E. E., Management of malignant hyperthermia susceptible parturients, Anaesthesia & Intensive Care, 25, 398-407, 1997	Case series. No relevant intervention
Rebordosa,C., Kogevinas,M., Sorensen,H.T., Olsen,J., Pre-natal exposure to paracetamol and risk of wheezing and asthma in children: a birth cohort study, International Journal of Epidemiology, 37, 583-590, 2008	No subgroup analysis for women in labour
Reilly,D.R., Oppenheimer,L.W., Fever in term labour, Journal of Obstetrics and Gynaecology Canada: JOGC, 27, 218-223, 2005	Data reported are unreliable due to mistakes in relevant table (Table 4); numerators are bigger than denominators; also numbers and percentages do not correspond
Saleeby,E., Chapman,J., Morse,J., Bryant,A., Nygaard,I., H1N1 influenza in pregnancy: Cause for concern, Obstetrics and Gynecology, 114, 885-891, 2009	Case reports and non-systematic literature review
Streissguth, A. P., Treder, R. P., Barr, H. M., Shepard, T. H., Bleyer, W. A., Sampson, P. D., Martin, D. C., Aspirin and acetaminophen use by pregnant women and subsequent child IQ and attention decrements, Teratology, 35, 211-9, 1987	Not women in labour. Acetaminophen (paracetamol) use during the first half of pregnancy
Tanquerav, T. A., Mackenzie, M., Yentis, S. M., Steer, P. J., The effect of neck warming on shivering during labour with epidural analgesia, International Journal of Obstetric Anesthesia, 20, S6, 2011	Conference abstract
Tay, H. S., Audit on the management of pyrexia in labour at Aberdeen Maternity Hospital, Journal of Obstetrics and Gynaecology, 30, 756-757, 2010	Conference abstract
Thompson, J. M., Waldie, K. E., Wall, C. R., Murphy, R., Mitchell, E. A., A. B. C. study group, Associations between acetaminophen use during pregnancy and ADHD symptoms measured at ages 7 and 11 years, PLoS ONE [Electronic Resource], 9, e108210, 2014	No subgroup analysis for women with pyrexia in labour

Study	Reason for exclusion
Tikkanen,J., Heinonen,O.P., Maternal hyperthermia during pregnancy and cardiovascular malformations in the offspring, European Journal of Epidemiology, 7, 628-635, 1991	No relevant intervention
Vaughan, J., MacDonald, D., Daly, L., Puerperal pyrexia--a prospective study, Irish Medical Journal, 72, 317-20, 1979	No relevant comparison. Not women with pyrexia in labour
Vlenterie, R., Wood, M. E., Brandlistuen, R. E., Roeleveld, N., van Gelder, M. M. H. J., Nordeng, H., Neurodevelopmental problems at 18 months among children exposed to paracetamol in utero: A propensity score matched cohort study, International Journal of Epidemiology, 45, 1998-2008, 2016	No subgroup analysis for women in labour
Vogt, G., Puho, E., Czeizel, A. E., Population-based case-control study of isolated congenital cataract, Birth Defects Research Part A - Clinical and Molecular Teratology, 73, 997-1005, 2005	No subgroup analysis for women in labour. Data not disaggregated by different antipyretic medications
Werler, M. M., Sheehan, J. E., Mitchell, A. A., Maternal medication use and risks of gastroschisis and small intestinal atresia, American Journal of Epidemiology, 155, 26-31, 2002	Not women in labour. Analysis focused on use of medication from the first day of the last menstrual period until 84 days after the last menstrual period
Zerbo, O., Iosif, A. M., Walker, C., Ozonoff, S., Hansen, R. L., Hertz-Picciotto, I., Is maternal influenza or fever during pregnancy associated with autism or developmental delays? Results from the CHARGE (CHildhood Autism Risks from Genetics and Environment) study, Journal of Autism & Developmental Disorders, 43, 25-33, 2013	No subgroup analysis for women in labour. Results not disaggregated by different antipyretic medications

Economic studies

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix E – Clinical evidence tables

Intrapartum care for women with pyrexia – fetal blood sampling

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

Intrapartum care for women with pyrexia – use of anti-pyretics

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Burgess, A. P. H., Katz, J. E., Moretti, M., Lakhi, N., Risk Factors for Intrapartum Fever in Term Gestations and Associated Maternal and Neonatal Sequelae, Gynecologic and Obstetric Investigation, no pagination, 2017 **Ref Id** 608942 **Country/ies where the study was carried out** USA **Study type**	**Sample size** N=54 febrile women Acetaminophen (paracetamol): 41/54 No acetaminophen (no paracetamol): 13/54* *Numerator calculated by the NGA technical team **Characteristics** Characteristics of febrile women in labour (n=54): Women who received intrapartum antibiotic therapy, n/N (%): 26/54 (48.1%). The study authors did not report how many women were in the groups that received and did not receive acetaminophen (paracetamol). Babies whose mothers received antibiotics were significantly more likely to be admitted to the NICU (84.66% versus 28.5%, OR 6.46, 95% CI 1.95 to 18.34, p=0.002). There was no difference in the number of caesarean sections	**Interventions** Intervention: acetaminophen (paracetamol) (The study authors mentioned that women were administered 650 mg of acetaminophen; however in the discussion section they commented that dose was not standardised. They also mentioned that indications and route of administration were not standardised.) Comparison: no acetaminophen (no paracetamol)	**Details** **Study setting.** Richmond University Medical Center, New York, USA. The medical centre is a high-risk tertiary centre for obstetrics and neonates. Administration of antibiotics or anti-pyretic therapy was at the discretion of the treating obstetrician. **Data collection.** The medical records of women and their babies were reviewed retrospectively. Neonatal outcomes included incidence of neonatal intensive care admission secondary to respiratory distress, sepsis, hypotonia, and hypoglycaemia (glucose <40 mg/dl). Babies were followed	**Results** Caesarean section (n/N): acetaminophen (paracetamol): 16/41 (39.0%) versus no acetaminophen (no paracetamol): 7/12 (58.3%), p=0.250* NICU admission (n/N): acetaminophen (paracetamol): 35/41 (85.2%) versus no acetaminophen (no paracetamol): 9/13 (69.2%), p=0.145* (The most common reason for NICU admission in the febrile cohort was to rule out neonatal sepsis secondary to the presence of maternal fever at the time of the birth (40/54 of neonates).	**Limitations** Limitations assessed with the Newcastle-Ottawa Quality Assessment Scale: Selection: high risk of bias (The cohort not exposed to acetaminophen (paracetamol) may have been drawn from a different population source compared to the exposed cohort, because administration of anti-pyretic therapy was at the discretion of the treating obstetrician (and was not protocol-specific). The study authors highlighted that it is possible that the sicker appearing women, or those with a higher

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Retrospective study. Study design in relation to the comparison of interest is a cohort study design (although the study focuses mainly on a different comparison with a case-control study design) **Aim of the study** To determine factors associated with intrapartum fever and to assess associated maternal and neonatal outcomes **Study dates** November 2014 to March 2015 **Source of funding**	between women who received antibiotics and those that did not (50% versus 35.7%, p=0.250). Women who met the clinical criteria for diagnosis of chorioamnionitis, n/N (%): 3/54 Time from diagnosis of intrapartum fever to antibiotic administration in minutes, mean (range): 63.70 (1 to 353). Maternal age in years, median (range): 28.57 (18 to 41) Number of previous term births, median (range): 0 (0 to 2) Number of previous vaginal births, median (range): 0 (0 to 2) Number of previous caesarean births, median (range): 0 (0 to 1) Gestational age in weeks, median (range): 40 (35.5 to 41.5) First stage of labour ≥ 720 minutes, n/N (%): 15/52 (28.8%) Second stage of labour ≥ 120 minutes, n/N (%): 15/52 (28.8%) Prostaglandin induction, n/N (%): 15/54 (27.8%)		up for 12 weeks after discharge for ascertainment of neonatal outcomes. **Data analysis.** The study authors provided results relevant for this review as percentages but did not report the numerators and denominators	The most common secondary, non-mutually exclusive, NICU-admitting diagnosis was respiratory distress (14/54 of neonates). Babies admitted for suspected sepsis were given prophylactic IV antibiotics. The mean number of days spent in NICU was 4.9 for babies requiring a sepsis work-up and 5.7 for those requiring respiratory support. Only 1 baby was found to have a positive bacterial culture. None of the babies in the febrile cohort were re-admitted to the hospital secondary to febrile complications during the 12-week follow-up period post-discharge). *Numerators and denominators were calculated by the	temperature, received treatment with acetaminophen (paracetamol). Data on the baseline characteristics were reported for all febrile women but were not disaggregated by receipt or non-receipt of acetaminophen (paracetamol). It is also unclear how many women in the exposed and unexposed groups received antibiotics, and babies whose mothers received antibiotics were significantly more likely to be admitted to the NICU. Notwithstanding the high risk of selection bias, the study had the following strengths in relation to the selection of exposed and non-exposed cohorts: exposure to acetaminophen was ascertained with a

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
The study authors reported that they did not receive funding from any entities listed in the article. They did not report any other sources of funding	Oxytocin augmentation, n/N (%): 34/54 (63.0%) Epidural, n/N (%): 47/54 (87.0%) Rupture of membranes ≥ 240 min, n/N (%): 43/54 (79.6%) BMI ≥ 30 kg/m^2, n/N (%): 25/54 (46.3%) **Inclusion criteria** Women between 36$^{+0/7}$ and 42$^{+0/7}$ gestational weeks who entered active labour (spontaneous or induced) and developed a systemic fever with intrapartum temperature ≥ 38°C **Exclusion criteria** Incomplete medical records, non-singleton gestations, scheduled caesarean section, birth before 36$^{+0/7}$ gestational weeks, stillbirth, or congenital fetal anomalies			NGA technical team based on percentages reported in the article and the overall number of febrile women who received acetaminophen (paracetamol), which was also reported in the article. The NGA team calculated a numerator of 35 for NICU admission in the acetaminophen (paracetamol) group based on data reported in the article (percentage of 85.2%, and 41 women receiving acetaminophen (paracetamol)). However 35/41=85.4%, so the percentage in the paper seems to be incorrect by 0.2%; the NGA team considered whether numerator and denominator may be different from 35 and 41	secure record as the study authors reviewed medical records for this study; there is certainty that the outcomes of interest were not present at start of study given that the outcomes could not occur before labour.) Comparability: high risk of bias (The study did not control for any factor) Outcome: unclear risk of bias (The NGA technical team calculated denominators and numerators based on percentages reported in the article, however in 1 instance the combination of the numerator and denominator estimated by the NGA team gave a somewhat different percentage to that reported in the

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				respectively, however 35 and 41 were selected because in combination they correspond more closely than other combinations to the percentage of 85.2% reported in the article. The NGA team also calculated a denominator of 12 for the non-acetaminophen (non-paracetamol) group in relation to the caesarean section outcome, based on the percentage reported in the article (58.3%) and the number of febrile women who did not receive acetaminophen (paracetamol) (13). There was no numerator that gave the percentage 58.3% with a denominator of 13, while 7/12=58.3%, and so the	article; although the outcomes were assessed through record linkage because the study authors reviewed medical records, the decision to admit to NICU was not standardised and was at the discretion of neonatologists and paediatricians; the follow-up was long enough for outcomes to occur; it is somewhat unclear whether there was an adequate follow-up of cohorts, because the study authors reported percentages and did not state denominators; however the NGA team estimated that there were missing data only for mode of birth for 1 woman in the unexposed group). **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				combination of 7 and 12 was selected	The comparison of interest for the guideline review was not the main comparison in the article and it was carried out with only a subset of the study population (febrile women). The study authors did not report whether they calculated a minimum sample size for this comparison

Appendix F – Forest plots

Intrapartum care for women with pyrexia – fetal blood sampling

No meta-analysis was undertaken for this review and so there are no forest plots.

Intrapartum care for women with pyrexia – use of anti-pyretics

No meta-analysis was undertaken for this review and so there are no forest plots.

Appendix G – GRADE tables

Intrapartum care for women with pyrexia – fetal blood sampling

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

Intrapartum care for women with pyrexia – use of anti-pyretics

Table 4: Clinical evidence profile for paracetamol versus no paracetamol, outcomes for the woman

Quality assessment							Number of women		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Paracetamol	No paracetamol	Relative (95% CI)	Absolute	Quality	Importance
Caesarean section												
1 (Burgess 2017)	Observational studies	Very serious [1]	No serious inconsistency	No serious indirectness	Serious[2]	None	16/41 (39.0%)	7/12 (58.3%)	RR 0.67 (0.36 to 1.23)	192 fewer per 1000 (from 373 fewer to 134 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

CI: confidence interval; MID: minimally important difference; RR: risk ratio
1 The quality of the evidence was downgraded by 2 levels due to high risk of selection and comparability bias, and unclear risk of outcome bias
2 The quality of the evidence was downgraded by 1 level because the 95% CI crosses 1 default MID threshold

Table 5: Clinical evidence profile for paracetamol versus no paracetamol, outcomes for the baby

Quality assessment							Number of babies		Effect			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Paracetamol	No paracetamol	Relative (95% CI)	Absolute	Quality	Importance
NICU admission												

Quality assessment							Number of babies		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Paracetamol	No paracetamol	Relative (95% CI)	Absolute		
1 (Burgess 2017)	Observational studies	Very serious [1]	No serious inconsistency	No serious indirectness	Serious[2]	None	35/41 (85.4%)	9/13 (69.2 %)	RR 1.23 (0.84 to 1.81)	159 more per 1000 (from 111 fewer to 561 more)	⨁⊖⊖⊖ VERY LOW	IMPORTANT

CI: confidence interval; MID: minimally important difference; RR: risk ratio
1 The quality of the evidence was downgraded by 2 levels due to high risk of selection and comparability bias, and unclear risk of outcome bias
2 The quality of the evidence was downgraded by 1 level because the 95% CI crosses 1 default MID threshold

Appendix H – Economic evidence study selection

Intrapartum care for women with pyrexia – fetal blood sampling

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with pyrexia – use of anti-pyretics

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix I – Economic evidence tables

Intrapartum care for women with pyrexia – fetal blood sampling

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with pyrexia – use of anti-pyretics

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix J – Health economic evidence profiles

Intrapartum care for women with pyrexia – fetal blood sampling

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with pyrexia – use of anti-pyretics

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix K – Health economic analysis

Intrapartum care for women with pyrexia – fetal blood sampling

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with pyrexia – use of anti-pyretics

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix L – Research recommendations

Intrapartum care for women with pyrexia – fetal blood sampling

No research recommendations were made for this review.

Intrapartum care for women with pyrexia – use of anti-pyretics

No research recommendations were made for this review.