National Institute for Health and Care Excellence

Final

Fetal monitoring in labour

[A] Evidence review for fetal blood sampling

NICE guideline NG229

Evidence review underpinning recommendation 1.7.1 in the NICE guideline

December 2022

Final

Disclaimer

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Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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Contents

Fetal blood sampling

Review question

What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?

Introduction

Fetal blood sampling is a method of taking a blood sample from the fetal scalp, and is currently used in combination with cardiotocography during labour to assess the wellbeing of the fetus. Fetal blood sampling provides information on the pH and lactate levels of the fetal blood at the time of sampling, which in turn can be used to assess if the baby is receiving enough oxygen. This information can guide clinicians' decision-making regarding the appropriate steps for the ongoing management of labour, including the need to expedite birth. However, the process of fetal blood sampling is unpleasant for the woman and requires a skin prick on the baby's head. There is currently uncertainty around the usefulness of fetal blood sampling in predicting the outcomes for the baby and the mother during labour, and a wide variation in practice regarding its use.

This review aims to address whether fetal blood sampling in labour is a useful tool for improving outcomes for babies and mothers.

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 in labour with a pathological, abnormal or non-reassuring fetal heart rate trace who would qualify for a fetal blood sampling
Intervention	Fetal blood sampling from the scalp during labour
Comparison	• Fetal scalp stimulation • No sampling • Immediate birth (caesarean or instrumental vaginal birth)
Outcome	**Critical** • Neonatal death (death before the age of 28 completed days after live birth) • Apgar score below 7 at 5 minutes • Mode of birth (spontaneous vaginal, instrumental vaginal, caesarean birth) **Important** • HIE • Neonatal admission (includes NICU and SCBU) • Trauma/injury to the baby • Women's experience of labour and birth

HIE: hypoxic ischaemic encephalopathy; NICU: neonatal intensive care unit; SCBU: special care baby unit

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

The population included in the review protocol for this review question included 'women in labour with a pathological, abnormal or non-reassuring fetal heart rate trace'. The committee noted that some of these terms were no longer in use or could have different meanings in terms of fetal wellbeing. However, they agreed to include these in the protocol to ensure that all relevant studies were captured.

The committee agreed that only studies conducted in high-income countries (as defined by the Organisation for Economic Co-operation and Development [OECD]) will be considered for inclusion because many low and middle income countries are likely to lack the facilities or technology to carry out fetal monitoring with the same intensity as monitoring in high-income countries.

To ensure consistency between other intrapartum care reviews, a change to the outcome Apgar score at 5 minutes was made after the protocol was registered on PROSPERO, from 'APGAR score <6 at 5 minutes' to 'Apgar score <7 at 5 minutes'. This had no impact on the studies included in this review as there no additional studies were included, and no studies had to be excluded due to this change.

Effectiveness evidence

Included studies

Two randomised controlled trials (RCTs) were included for this review (East 2021, and Hughes 2020). One study compared fetal blood sampling plus cardiotocography (CTG) to CTG only. One study compared fetal blood sampling to digital fetal scalp stimulation.

The included studies are summarised in Table 2.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review are listed, and reasons for their exclusion are provided in appendix J.

Summary of included studies

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies.

Study	Population	Intervention	Comparison	Outcomes
East 2021 Randomised controlled trial Australia	N=123 women with an abnormal fetal heart rate trace in labour. Nulliparous Intervention: 87%	Fetal scalp blood sampling plus CTG Fetal scalp blood sample taken if a non-reassuring CTG persists despite	CTG only No fetal scalp blood sample taken following a non-reassuring CTG.	• Neonatal death • Apgar score <7 at 5 minutes • Caesarean birth • Instrumental vaginal birth • Spontaneous vaginal birth

Study	Population	Intervention	Comparison	Outcomes
	Comparison: 87% <u>Induction of labour</u> Intervention: 77% Comparison: 76% <u>Birthweight <10th centile</u> Intervention: 8% Comparison: 0% FGR not reported. Most of the women had intrapartum risk factors.	measure to improve. Lactate measured. Birth indicated if lactate >4.8mmol/L	Timing of and progress to birth at the discretion of the clinician.	• Neonatal encephalopathy • Neonatal admission • Neonatal birth trauma
Hughes 2020 Randomised controlled trial Ireland	N=50 pregnant women requiring a CTG in labour and second-line testing. Nulliparous women. <u>Induction of labour</u> Intervention: 60% Comparison: 84% <u>SGA fetus</u> Intervention: 8% Comparison: 8% SGA defined as <10th centile. FGR not reported.	<u>Fetal blood scalp sample</u> Fetal blood scalp sample collected and pH measured. Borderline results repeated after 30 minutes. Abnormal results warrant expedited delivery.	<u>Digital fetal scalp stimulation</u> Digital fetal scalp stimulation performed during the vaginal examination. The examiner rubbed the fetal scalp with the index finder and middle finger for 30 seconds. The CTG was observed for 5 minutes. Digital fetal scalp stimulation repeated after 30 minutes if CTG was borderline. If the obstetrician had concerns following a borderline result, FBS could be taken. If CTG was abnormal, FBS taken or delivery expedited.	• Apgar score <7 at 5 minutes • Caesarean birth • Instrumental vaginal birth • Neonatal encephalopathy • Admission to neonatal unit

CTG: cardiotocography; FGR: fetal growth restriction; mmol/L: millimoles per litre; SGA: small for gestational age

See the full evidence tables in appendix D and the forest plots in appendix E.

Summary of the evidence

Fetal blood sampling was compared to no fetal blood sampling with or without CTG, and to digital fetal scalp stimulation. Across all comparisons, most of the evidence showed no important difference, or no evidence of an important difference on most outcomes.

For the comparison fetal blood sampling plus CTG with CTG alone, there were no neonatal deaths reported. However, fetal blood sampling plus CTG had an important harm in terms of Apgar score less than 7 at 5 minutes. There was no important difference or no evidence of an important difference between the two groups for the other neonatal outcomes, namely neonatal encephalopathy, neonatal admission or neonatal birth trauma. There was also no evidence of an important difference for modes of birth between the two groups. Most of the evidence was very low quality, with only one outcome at moderate quality. There were concerns over risk of bias for all outcomes and imprecision for most outcomes.

Fetal blood sampling plus CTG was compared to digital fetal scalp stimulation plus CTG. The evidence for neonatal outcomes showed no important difference or no evidence of an important difference. There was also no evidence of an important difference for instrumental vaginal births, but more caesarean births in the fetal blood sampling arm compared to the digital scalp stimulation arm. The quality of the evidence was rated low to very low with concerns around imprecision and risk of bias.

Overall the evidence showed no important difference or no evidence of an important difference for most neonatal outcomes, with the exception of Apgar score <7 where fetal blood sampling with CTG showed an important harm, compared to CTG alone. When compared to digital fetal scalp sampling with CTG, fetal blood sampling with CTG showed an increase in caesarean births.

There was no evidence identified for women's experience of labour and birth.

See appendix F for full GRADE tables.

Economic evidence

Included studies

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to this review question.

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

The committee's discussion and interpretation of the evidence

The outcomes that matter most

Neonatal death and Apgar score less than 7 at 5 minutes were prioritised as critical outcomes for this review. An Apgar score is a score based on a baby's heart rate, breathing, muscle tone, reflex response and colour, and is usually recorded at 1 and 5 minutes after birth. The maximum score is 10 and a score less than 7 indicates the baby may require some support to transition to life outside the womb, and is associated with an increased risk of adverse outcomes for the baby. These outcomes were chosen because fetal blood sampling aims to identify compromised or distressed fetuses and provide clarity on the best approach

to prevent neonatal death and optimise outcomes for the neonate. Mode of birth was also prioritised as a critical outcome, because the committee wanted to find out whether the use of fetal blood sampling had an impact on the number of immediate births via caesarean, or instrumental assistance. The committee agreed that together with neonatal outcomes, this would enable them to determine whether fetal blood sampling increased interventions with or without a benefit for the neonate.

The committee also selected important outcomes for the neonate. They agreed that hypoxic ischaemic encephalopathy would be an indicator of future developmental outcomes for the infant. They also chose neonatal admission as an important outcome to assess the fetal wellbeing of the baby. The committee also chose trauma or injury to the baby as an important outcome to look at the direct impact of the fetal blood sampling procedure.

Finally the committee wanted to find out what the experience of taking a fetal blood sample would be like for women. They agreed that the process of taking the sample and the mode of birth could have an impact on a woman's experience of labour. They also discussed that the procedure could either cause or relieve anxieties for women so they hoped to find data that explored this. The committee recognised the great importance of women's experience for this procedure, but they were aware that data on this outcome was likely to be sparse and unlikely to inform decision-making in a meaningful way, so they prioritised other outcomes as critical.

The quality of the evidence

The quality of the evidence for outcomes was assessed with GRADE and ranged from very low to moderate. All of the evidence was downgraded for concerns around risk of bias. Some outcomes were downgraded specifically due to deviations from the intended interventions for some outcomes, where not all of the intervention group received a fetal scalp blood sample measurement. However, this could be expected to happen outside of the trial context. Other outcomes were downgraded for concerns around randomisation as there were differences in baseline characteristics, however these could be attributed to the small sample size. Most of the evidence was also downgraded due to concerns of imprecision around the estimate of effect.

Observational studies were also considered for inclusion in light of the limited RCT evidence, however none met the inclusion criteria of the protocol.

Benefits and harms

The committee discussed that there was a very small quantity of recent evidence and the majority of the evidence around the effectiveness of fetal blood sampling was of very low quality. Therefore, they agreed that it would be useful to consider the evidence, together with their knowledge and experience of current practice when making recommendations.

The committee discussed that the evidence showed harm for fetal blood sampling in combination with CTG, with more babies having an Apgar score below 7 at 5 minutes, when compared to CTG alone. Although the evidence for this outcome was of moderate quality, the committee discussed the risk of bias concerns and the small sample size. The committee discussed that this may be because fetal blood sampling leads to a delay in expediting birth so babies are born in a worse condition.

The committee noted that there was no difference, or no evidence of an important difference for all other outcomes when comparing fetal blood sampling in combination with CTG, compared to CTG alone. However they noted that this evidence was all low quality and that it was important to consider the uncertainty around these outcomes.

The committee next discussed the evidence comparing fetal blood sampling to digital fetal scalp stimulation and noted that it was very low to low quality. They noted that there was

evidence showing an increase in caesarean births in the fetal blood sampling arm. However, they agreed that although this had been selected as a critical outcome it was difficult to define whether it was actually a benefit or a harm: caesarean birth may indicate appropriate care due to the fetal blood sampling results suggesting that expedited birth was necessary. As there was no difference, or no evidence of an important difference for the 3 neonatal outcomes, the committee agreed that this evidence suggested that fetal blood sampling was not more effective at improving outcomes for babies compared to fetal scalp stimulation, nor more harmful.

The committee discussed that, taking into account both comparisons, there was limited evidence for any benefits of fetal blood sampling compared to CTG alone or CTG with fetal scalp stimulation, and there may be a harmful effect on Apgar scores at 5 minutes.

The committee agreed that the evidence could not be used alone to determine the best approach to fetal blood sampling, and that other factors would need to be considered. Using their experiential knowledge, the committee also discussed the other disadvantages of fetal blood sampling. This included the fact that it required a skin prick on the baby's head and the time required to perform the procedure could delay other appropriate interventions such as expediting birth. With limited evidence supporting the use of fetal blood sampling, this could have a big impact on the wellbeing of the mother and baby. The committee also discussed the acceptability of fetal blood sampling for the woman. They agreed that this highly invasive procedure was often uncomfortable and caused anxiety for the mother, particularly in the absence of an effective epidural, and therefore was difficult to justify without the evidence supporting the benefits.

The limited evidence led the committee to discuss the 2017 recommendations that supported the use of fetal scalp stimulation. They discussed that fetal scalp stimulation is less invasive than fetal blood sampling, requires less time, and is more acceptable to women in terms of their overall experience in labour. They agreed that the option to assess fetal wellbeing, using fetal scalp stimulation, had reduced the use of fetal blood sampling. The committee also agreed to amend the existing recommendations on fetal scalp stimulation to clarify that, like CTG and fetal blood sampling, it was only a tool and should be used in conjunction with an assessment of other risk factors, and to add more detail the interpretation of a positive response or no response. In light of the evidence suggesting harm of fetal blood sampling, the committee's discussion around the woman's experience of labour, and the availability of fetal scalp stimulation as another method of assessing fetal wellbeing, which is supported by current guidance, the committee discussed whether it was still appropriate to recommend that the use of fetal blood sampling to assess fetal wellbeing.

The committee were unable to reach a consensus decision on this recommendation and used a vote to reach an agreement, with the majority of the committee (9 votes versus 2 votes) supporting the decision to no longer recommend fetal blood sampling as a tool for assessing fetal wellbeing.

The committee noted that some of the evidence came from pilot data from a current ongoing clinical trial (the FIRSST study) and they agreed that the completion of this trial (https://www.isrctn.com/ISRCTN13295826) would be welcomed. However, it was not expected to complete until the end of 2024, and the committee agreed that on its completion the advice on use of fetal blood sampling may need to be reviewed again. The committee were keen that they did not make a recommendation that hindered completion of this trial, and so although they discussed whether it was appropriate to make a 'do not use fetal blood sampling' recommendation, they agreed that this course of action may impact on recruitment. Instead they chose to remove the existing recommendations that advised the use of fetal monitoring and made a new recommendation stating the lack of evidence to support fetal blood sampling.

Despite the uncertainty of the evidence the committee did not make a research recommendation as they were aware of the ongoing study, described above.

Cost effectiveness and resource use

Although no economic evidence or de novo economic modelling was done for this review, the committee did not consider fetal blood sampling to be cost effective. They reached this conclusion because there was no evidence of benefit, and some evidence of harm, and because there are costs associated with the procedure.

As the committee removed the recommendations to offer fetal blood sampling, there will be no increase in resource use, in terms of the staff and equipment needed to carry out the sampling procedure. Indeed, given there is variation in current practice, some savings are likely to result as a result implementation of this guidance in units which previously offered fetal blood sampling.

Other factors the committee took into account

The committee noted that the previous recommendations had been based on observational studies, with no comparator group, and which had not been controlled for confounders.

Recommendations supported by this evidence review

This evidence review supports recommendation 1.7.1.

References – included studies

Effectiveness

East 2021

East, Christine E., Davey, Mary-Ann, Kamlin, C. Omar F. et al. (2021) The addition of fetal scalp blood lactate measurement as an adjunct to cardiotocography to reduce caesarean sections during labour: The Flamingo randomised controlled trial. The Australian & New Zealand journal of obstetrics & gynaecology

Hughes 2020

Hughes, O. and Murphy, D. J. (2020) Comparing second-line tests to assess fetal wellbeing in Labor: a feasibility study and pilot randomized controlled trial. Journal of Maternal-Fetal and Neonatal Medicine

Appendices

Appendix A Review protocols

Review protocol for review question: What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?

Table 3: Review protocol

Field	Content
PROSPERO registration number	CRD42021269389
Review title	What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?
Review question	What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?
Objective	To update the recommendations in CG190 (2014) for fetal blood sampling. Surveillance has identified ongoing trials that might have an impact on current recommendations.
Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • International Health Technology Assessment database Searches will be restricted by: • No date limitations • English language only • Human studies only Other searches:

Field	Content
	• Inclusion lists of systematic reviews The full search strategies for MEDLINE database will be published in the final review. For each search, the principal database search strategy is quality assured by a second information scientist using an adaptation of the PRESS 2015 Guideline Evidence-Based Checklist. Key papers East 2015 https://doi.org/10.1002/14651858.CD006174.pub3
Condition or domain being studied	Fetal blood sampling following a pathological CTG
Population	Women in labour with a pathological, abnormal or non-reassuring fetal heart rate trace who would qualify for a fetal blood sampling
Intervention	Fetal blood sampling from the scalp during labour
Comparator	• Fetal scalp stimulation • No sampling • Immediate birth (caesarean or instrumental vaginal birth)
Types of study to be included	Include published full-text papers: • Systematic reviews of RCTs • Parallel RCTs (individual or cluster) If not enough evidence from RCTs is found: • Prospective and retrospective cohort studies

Field	Content
	Note: prospective and retrospective studies must make adjustment for confounding factors in their analysis Conference abstracts will not be included because these do not typically have sufficient information to allow full critical appraisal.
Other exclusion criteria	Population: • Women with breech presentation • Women in preterm labour • Women with an intrauterine fetal death • Women pregnant with multiple babies Setting: • Countries other than high income countries (as defined by the OECD) *If any study or systematic review includes <1/3 of women with the above characteristics/ who received care in the above setting, it will be considered for inclusion but, if included, the evidence will be downgraded for indirectness.*
Context	This guideline will partly update the following: Intrapartum care for healthy women and babies (CG190)
Primary outcomes (critical outcomes)	• Neonatal death (death before the age of 28 completed days after live birth) • Apgar score below 7 at 5 minutes • Mode of birth (spontaneous vaginal, instrumental vaginal, caesarean birth)
Secondary outcomes (important outcomes)	• Hypoxic ischaemic encephalopathy (HIE) • Neonatal admission (includes neonatal intensive care unit [NICU] and special care baby unit [SCBU]) • Trauma/injury to infant • Women's experience of labour and birth

Field	Content
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Duplicate screening will not be undertaken for this question. Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and follow-up, relevant outcome data and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.
Risk of bias (quality) assessment	Quality assessment of individual studies will be performed using the following checklists: • ROBIS tool for systematic reviews • Cochrane RoB tool v.2 for RCTs • Cochrane RoB tool v.2 for cluster randomised controlled trials • ROBINS-I tool for non-randomised (clinical) controlled trials and cohort studies The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.
Strategy for data synthesis	Quantitative findings will be formally summarised in the review. Where multiple studies report on the same outcome for the same comparison, meta-analyses will be conducted using Cochrane Review Manager software. A fixed effect meta-analysis will be conducted and data will be presented as risk ratios if possible or odds ratios when required (for example, if only available in this form in included studies) for dichotomous outcomes, and mean differences or standardised mean differences for continuous outcomes. Heterogeneity in the effect estimates of the individual studies will be assessed using the I^2 statistic. Alongside visual inspection of the point estimates and confidence intervals, I^2 values of greater than 50% and 80% will be considered as significant and very significant heterogeneity, respectively. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through subgroup analysis then a random effects model will be used for meta-analysis, or the data will not be pooled.

Field	Content
	The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/ **Minimally important differences:** • Neonatal death (death before the age of 28 completed days after live birth): statistical significance • Validated scales/continuous outcomes: published MIDs where available • All other outcomes & where published MIDs are not available: 0.8 and 1.25 for all relative dichotomous outcomes ; +/- 0.5x control group SD for continuous outcomes

Analysis of subgroups	Evidence will be stratified by:
	• Babies with fetal growth restriction vs babies without fetal growth restriction
	• Women who were induced versus women who were not induced
	
	Stratifications will be dealt with in a hierarchy (this is, first by babies with fetal growth restriction and then by women who were inducted vs those who were not)
	
	Evidence will be subgrouped by the following only in the event that there is significant heterogeneity in outcomes:
	• Age of woman (<35 vs >/= 35)
	• Ethnicity
	  ○ White
	  ○ Asian/Asian British
	  ○ Black/African/Caribbean/Black British
	  ○ Mixed/Multiple ethnic groups
	  ○ Other ethnic group
	• Women with disability vs not
	• Deprived socioeconomic group vs not

Field	Content	
	Where evidence is stratified or subgrouped the committee will consider on a case by case basis if separate recommendations should be made for distinct groups. Separate recommendations may be made where there is evidence of a differential effect of interventions in distinct groups. If there is a lack of evidence in one group, the committee will consider, based on their experience, whether it is reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others.	
Type and method of review	☒	Intervention
	☐	Diagnostic
	☐	Prognostic
	☐	Qualitative
	☐	Epidemiologic
	☐	Service Delivery
	☐	Other (please specify)
Language	English	
Country	England	
Anticipated or actual start date	09/07/2021	
Anticipated completion date	22/03/2023	
Named contact	5a. Named contact National Institute for Health and Care Excellence (NICE) and National Guideline Alliance 5b. Named contact e-mail IPCupdate@nice.org.uk 5c. Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and National Guideline Alliance	

Field	Content
Review team members	From the National Guideline Alliance: • NGA Senior Systematic Reviewer • NGA Systematic Reviewer
Funding sources/sponsor	This systematic review was completed by the National Guideline Alliance which receives funding from NICE.
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/cg190
Other registration details	None
URL for published protocol	https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=269389
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: notifying registered stakeholders of publication publicising the guideline through NICE's newsletter and alerts issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
Keywords	Fetal blood sampling, effectiveness
Details of existing review of same topic by same authors	Not applicable

Field	Content
Additional information	None
Details of final publication	www.nice.org.uk

CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; CTG: cardiotocography; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HIE: hypoxic ischaemic encephalopathy; MID: minimally important difference; NICU: neonatal intensive care unit; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; OECD: Organisation for Economic Co-operation and Development; PRESS: Peer Review of Electronic Search Strategies; RCT: randomised controlled trial; RoB: risk of bias; ROBINS-I: Risk Of Bias In Non-randomised Studies – of Interventions; ROBIS: Risk of Bias in Systematic Reviews; SCBU: special care baby unit; SD: standard deviation

Appendix B Literature search strategies

Literature search strategies for review question: What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?

Review question search strategies

Databases: Medline all

Date of last search: 05/10/2021

#	Searches
1	PREGNANCY/
2	PARTURITION/
3	exp LABOR, OBSTETRIC/
4	exp DELIVERY, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	(pregnan$ or labo?r? or childbirth$ or partu$ or intra?part$ or peri?part$).ab,ti.
7	((during or giving or give) adj5 (birth$ or deliver$)).ti,ab.
8	or/1-7
9	BLOOD SPECIMEN COLLECTION/
10	FETAL BLOOD/ and (samp* or analys* or gas*).ti,ab.
11	((f?etal or f?etus) adj5 (lactate? or pH or base* or acid$ or alk#l*)).ti,ab.
12	((f?etal or f?etus) adj5 blood adj5 (gas* or sampl* or analys*)).ti,ab.
13	FBS.ti,ab.
14	exp BLOOD GAS ANALYSIS/
15	exp ACID-BASE IMBALANCE/
16	(blood adj5 (gas* or oxygen or carbon dioxide or CO2) adj5 analys*).ti,ab.
17	((acidbase or acid base) adj5 (imbalanc$ or equ?l*)).ti,ab.
18	or/9-17
19	SCALP/
20	scalp?.ti,ab.
21	or/19-20
22	8 and 18 and 21
23	limit 22 to english language
24	LETTER/
25	EDITORIAL/
26	NEWS/
27	exp HISTORICAL ARTICLE/
28	ANECDOTES AS TOPIC/
29	COMMENT/
30	CASE REPORT/
31	(letter or comment*).ti.
32	or/24-31
33	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
34	32 not 33
35	ANIMALS/ not HUMANS/
36	exp ANIMALS, LABORATORY/
37	exp ANIMAL EXPERIMENTATION/
38	exp MODELS, ANIMAL/
39	exp RODENTIA/
40	(rat or rats or mouse or mice).ti.
41	or/34-40
42	23 not 41
43	META-ANALYSIS/
44	META-ANALYSIS AS TOPIC/
45	(meta analy* or metanaly* or metaanaly*).ti,ab.
46	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
47	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
48	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
49	(search* adj4 literature).ab.
50	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
51	cochrane.jw.

#	Searches
52	or/43-51
53	randomized controlled trial.pt.
54	controlled clinical trial.pt.
55	pragmatic clinical trial.pt.
56	randomi#ed.ab.
57	placebo.ab.
58	randomly.ab.
59	CLINICAL TRIALS AS TOPIC/
60	trial.ti.
61	or/53-60
62	COHORT STUDIES/
63	FOLLOW-UP STUDIES/
64	LONGITUDINAL STUDIES/
65	PROSPECTIVE STUDIES/
66	RETROSPECTIVE STUDIES/
67	((cohort* or follow-up or follow?up or longitudinal* or prospective* or retrospective*) adj1 (stud* or research or analys*)).tw.
68	(incidence? adj (stud* or research or analys*)).tw.
69	(longitudinal* adj1 (survey* or evaluat*)).tw.
70	(prospective* adj method*).tw.
71	(retrospective* adj design*).tw.
72	or/62-71
73	42 and 52
74	42 and 61
75	42 and 72
76	or/73-75

Databases: Embase; and Embase Classic

Date of last search: 05/10/2021

#	Searches
1	*PREGNANCY/
2	*PERINATAL PERIOD/
3	exp *BIRTH/
4	exp *LABOR/
5	*PREMATURE LABOR/
6	*INTRAPARTUM CARE/
7	(pregnan$ or labo?r? or childbirth$ or partu$ or intra?part$ or peri?part$).ab,ti.
8	((during or giving or give) adj5 (birth$ or deliver$)).ti,ab.
9	or/1-8
10	FETUS BLOOD SAMPLING/
11	((f?etal or f?etus) adj5 (lactate? or pH or base* or acid$ or alk#l*)).ti,ab.
12	((f?etal or f?etus) adj5 blood adj5 (gas* or sampl* or analys*)).ti,ab.
13	FBS.ti,ab.
14	exp BLOOD GAS ANALYSIS/
15	exp "DISORDERS OF ACID BASE BALANCE"/
16	(blood adj5 (gas* or oxygen or carbon dioxide or CO2) adj5 analys*).ti,ab.
17	((acidbase or acid base) adj5 (imbalanc$ or equ?l*)).ti,ab.
18	or/10-17
19	SCALP/
20	scalp?.ti,ab.
21	or/19-20
22	9 and 18 and 21
23	limit 22 to english language
24	letter.pt. or LETTER/
25	note.pt.
26	editorial.pt.
27	CASE REPORT/ or CASE STUDY/
28	(letter or comment*).ti.
29	or/24-28
30	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
31	29 not 30
32	ANIMAL/ not HUMAN/
33	NONHUMAN/
34	exp ANIMAL EXPERIMENT/

#	Searches
35	exp EXPERIMENTAL ANIMAL/
36	ANIMAL MODEL/
37	exp RODENT/
38	(rat or rats or mouse or mice).ti.
39	or/31-38
40	23 not 39
41	SYSTEMATIC REVIEW/
42	META-ANALYSIS/
43	(meta analy* or metanaly* or metaanaly*).ti,ab.
44	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
45	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
46	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
47	(search* adj4 literature).ab.
48	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
49	((pool* or combined) adj2 (data or trials or studies or results)).ab.
50	cochrane.jw.
51	or/41-50
52	random*.ti,ab.
53	factorial*.ti,ab.
54	(crossover* or cross over*).ti,ab.
55	((doubl* or singl*) adj blind*).ti,ab.
56	(assign* or allocat* or volunteer* or placebo*).ti,ab.
57	CROSSOVER PROCEDURE/
58	SINGLE BLIND PROCEDURE/
59	RANDOMIZED CONTROLLED TRIAL/
60	DOUBLE BLIND PROCEDURE/
61	or/52-60
62	COHORT ANALYSIS/
63	FOLLOW UP/
64	LONGITUDINAL STUDY/
65	PROSPECTIVE STUDY/
66	RETROSPECTIVE STUDIES/
67	((cohort* or follow-up or follow?up or longitudinal* or prospective* or retrospective*) adj1 (stud* or research or analys*)).tw.
68	(incidence? adj (stud* or research or analys*)).tw.
69	(longitudinal* adj1 (survey* or evaluat*)).tw.
70	(prospective* adj method*).tw.
71	(retrospective* adj design*).tw.
72	or/62-71
73	40 and 51
74	40 and 61
75	40 and 72
76	or/73-75

Databases: Cochrane Central Register of Controlled Trials; and Cochrane Database of Systematic Reviews

Date of last search: 05/10/2021

#	Searches
#1	MeSH descriptor: [Pregnancy] this term only
#2	MeSH descriptor: [Parturition] this term only
#3	MeSH descriptor: [Labor, Obstetric] explode all trees
#4	MeSH descriptor: [Delivery, Obstetric] explode all trees
#5	MeSH descriptor: [Obstetric Labor, Premature] this term only
#6	(pregnan* or labor* or labour* or childbirth* or partu* or intrapart* or intra-part* or peripart* or peri-part*):ti,ab
#7	((during or giving or give) near/5 (birth* or deliver*)):ti,ab
#8	#1 or #2 or #3 or #4 or #5 or #6 or #7
#9	MeSH descriptor: [Blood Specimen Collection] this term only
#10	MeSH descriptor: [Fetal Blood] this term only
#11	(samp* or analys* or gas*):ti,ab
#12	#10 and #11
#13	((fetal or foetal or fetus or foetus) near/5 (lactate* or pH or base* or acid* or alkal*)):ti,ab
#14	((fetal or foetal or fetus or foetus) near/5 blood near/5 (gas* or sampl* or analys*)):ti,ab
#15	FBS:ti,ab

#	Searches
#16	MeSH descriptor: [Blood Gas Analysis] explode all trees
#17	MeSH descriptor: [Acid-Base Imbalance] explode all trees
#18	(blood near/5 (gas* or oxygen or carbon dioxide or CO2) near/5 analys*):ti,ab
#19	((acidbase or "acid base") near/5 (imbalanc* or equal* or equil*)):ti,ab
#20	#9 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21	MeSH descriptor: [Scalp] this term only
#22	scalp*:ti,ab
#23	#21 or #22
#24	#8 and #20 and #23

Databases: International Health Technology Assessment

Date of last search: 05/10/2021

#	Searches
	All: (fetal or foetal or fetus or foetus)
	AND All: (scalp or scalps)

Health economics search strategies

Databases: Medline all

Date of last search: 13/10/2021

#	Searches
1	PREGNANCY/
2	PARTURITION/
3	exp LABOR, OBSTETRIC/
4	exp DELIVERY, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	(pregnan$ or labo?r? or childbirth$ or partu$ or intra?part$ or peri?part$).ab,ti.
7	((during or giving or give) adj5 (birth$ or deliver$)).ti,ab.
8	or/1-7
9	BLOOD SPECIMEN COLLECTION/
10	FETAL BLOOD/ and (samp* or analys* or gas*).ti,ab.
11	((f?etal or f?etus) adj5 (lactate? or pH or base* or acid$ or alk#l*)).ti,ab.
12	((f?etal or f?etus) adj5 blood adj5 (gas* or sampl* or analys*)).ti,ab.
13	FBS.ti,ab.
14	exp BLOOD GAS ANALYSIS/
15	exp ACID-BASE IMBALANCE/
16	(blood adj5 (gas* or oxygen or carbon dioxide or CO2) adj5 analys*).ti,ab.
17	((acidbase or acid base) adj5 (imbalanc$ or equ?l*)).ti,ab.
18	or/9-17
19	SCALP/
20	scalp?.ti,ab.
21	or/19-20
22	8 and 18 and 21
23	limit 22 to english language
24	LETTER/
25	EDITORIAL/
26	NEWS/
27	exp HISTORICAL ARTICLE/
28	ANECDOTES AS TOPIC/
29	COMMENT/
30	CASE REPORT/
31	(letter or comment*).ti.
32	or/24-31
33	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
34	32 not 33
35	ANIMALS/ not HUMANS/
36	exp ANIMALS, LABORATORY/
37	exp ANIMAL EXPERIMENTATION/
38	exp MODELS, ANIMAL/

#	Searches
39	exp RODENTIA/
40	(rat or rats or mouse or mice).ti.
41	or/34-40
42	23 not 41
43	ECONOMICS/
44	VALUE OF LIFE/
45	exp "COSTS AND COST ANALYSIS"/
46	exp ECONOMICS, HOSPITAL/
47	exp ECONOMICS, MEDICAL/
48	exp RESOURCE ALLOCATION/
49	ECONOMICS, NURSING/
50	ECONOMICS, PHARMACEUTICAL/
51	exp "FEES AND CHARGES"/
52	exp BUDGETS/
53	budget*.ti,ab.
54	cost*.ti,ab.
55	(economic* or pharmaco?economic*).ti,ab.
56	(price* or pricing*).ti,ab.
57	(financ* or fee or fees or expenditure* or saving*).ti,ab.
58	(value adj2 (money or monetary)).ti,ab.
59	resourc* allocat*.ti,ab.
60	(fund or funds or funding* or funded).ti,ab.
61	(ration or rations or rationing* or rationed).ti,ab.
62	ec.fs.
63	or/43-62
64	42 and 63

Databases: Embase; and Embase Classic

Date of last search: 13/10/2021

#	Searches
1	*PREGNANCY/
2	*PERINATAL PERIOD/
3	exp *BIRTH/
4	exp *LABOR/
5	*PREMATURE LABOR/
6	*INTRAPARTUM CARE/
7	(pregnan$ or labo?r? or childbirth$ or partu$ or intra?part$ or peri?part$).ab,ti.
8	((during or giving or give) adj5 (birth$ or deliver$)).ti,ab.
9	or/1-8
10	FETUS BLOOD SAMPLING/
11	((f?etal or f?etus) adj5 (lactate? or pH or base* or acid$ or alk#l*)).ti,ab.
12	((f?etal or f?etus) adj5 blood adj5 (gas* or sampl* or analys*)).ti,ab.
13	FBS.ti,ab.
14	exp BLOOD GAS ANALYSIS/
15	exp "DISORDERS OF ACID BASE BALANCE"/
16	(blood adj5 (gas* or oxygen or carbon dioxide or CO2) adj5 analys*).ti,ab.
17	((acidbase or acid base) adj5 (imbalanc$ or equ?l*)).ti,ab.
18	or/10-17
19	SCALP/
20	scalp?.ti,ab.
21	or/19-20
22	9 and 18 and 21
23	limit 22 to english language
24	letter.pt. or LETTER/
25	note.pt.
26	editorial.pt.
27	CASE REPORT/ or CASE STUDY/
28	(letter or comment*).ti.
29	or/24-28
30	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
31	29 not 30
32	ANIMAL/ not HUMAN/
33	NONHUMAN/
34	exp ANIMAL EXPERIMENT/

#	Searches
35	exp EXPERIMENTAL ANIMAL/
36	ANIMAL MODEL/
37	exp RODENT/
38	(rat or rats or mouse or mice).ti.
39	or/31-38
40	23 not 39
41	HEALTH ECONOMICS/
42	exp ECONOMIC EVALUATION/
43	exp HEALTH CARE COST/
44	exp FEE/
45	BUDGET/
46	FUNDING/
47	RESOURCE ALLOCATION/
48	budget*.ti,ab.
49	cost*.ti,ab.
50	(economic* or pharmaco?economic*).ti,ab.
51	(price* or pricing*).ti,ab.
52	(financ* or fee or fees or expenditure* or saving*).ti,ab.
53	(value adj2 (money or monetary)).ti,ab.
54	resourc* allocat*.ti,ab.
55	(fund or funds or funding* or funded).ti,ab.
56	(ration or rations or rationing* or rationed).ti,ab.
57	or/41-56
58	40 and 57

Database: Cochrane Central Register of Controlled Trials

Date of last search: 13/10/2021

#	Searches
#1	MeSH descriptor: [Pregnancy] this term only
#2	MeSH descriptor: [Parturition] this term only
#3	MeSH descriptor: [Labor, Obstetric] explode all trees
#4	MeSH descriptor: [Delivery, Obstetric] explode all trees
#5	MeSH descriptor: [Obstetric Labor, Premature] this term only
#6	(pregnan* or labor* or labour* or childbirth* or partu* or intrapart* or intra-part* or peripart* or peri-part*):ti,ab
#7	((during or giving or give) near/5 (birth* or deliver*)):ti,ab
#8	#1 or #2 or #3 or #4 or #5 or #6 or #7
#9	MeSH descriptor: [Blood Specimen Collection] this term only
#10	MeSH descriptor: [Fetal Blood] this term only
#11	(samp* or analys* or gas*):ti,ab
#12	#10 and #11
#13	((fetal or foetal or fetus or foetus) near/5 (lactate* or pH or base* or acid* or alkal*)):ti,ab
#14	((fetal or foetal or fetus or foetus) near/5 blood near/5 (gas* or sampl* or analys*)):ti,ab
#15	FBS:ti,ab
#16	MeSH descriptor: [Blood Gas Analysis] explode all trees
#17	MeSH descriptor: [Acid-Base Imbalance] explode all trees
#18	(blood near/5 (gas* or oxygen or carbon dioxide or CO2) near/5 analys*):ti,ab
#19	((acidbase or "acid base") near/5 (imbalanc* or equal* or equil*)):ti,ab
#20	#9 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21	MeSH descriptor: [Scalp] this term only
#22	scalp*:ti,ab
#23	#21 or #22
#24	#8 and #20 and #23
#25	MeSH descriptor: [Economics] this term only
#26	MeSH descriptor: [Value of Life] this term only
#27	MeSH descriptor: [Costs and Cost Analysis] explode all trees
#28	MeSH descriptor: [Economics, Hospital] explode all trees
#29	MeSH descriptor: [Economics, Medical] explode all trees
#30	MeSH descriptor: [Resource Allocation] explode all trees
#31	MeSH descriptor: [Economics, Nursing] this term only
#32	MeSH descriptor: [Economics, Pharmaceutical] this term only
#33	MeSH descriptor: [Fees and Charges] explode all trees
#34	MeSH descriptor: [Budgets] explode all trees
#35	budget*:ti,ab
#36	cost*:ti,ab

#	Searches
#37	(economic* or pharmaco?economic*):ti,ab
#38	(price* or pricing*):ti,ab
#39	(financ* or fee or fees or expenditure* or saving*):ti,ab
#40	(value near/2 (money or monetary)):ti,ab
#41	resourc* allocat*:ti,ab
#42	(fund or funds or funding* or funded):ti,ab
#43	(ration or rations or rationing* or rationed):ti,ab
#44	#25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43
#45	#24 and #44

Databases: International Health Technology Assessment

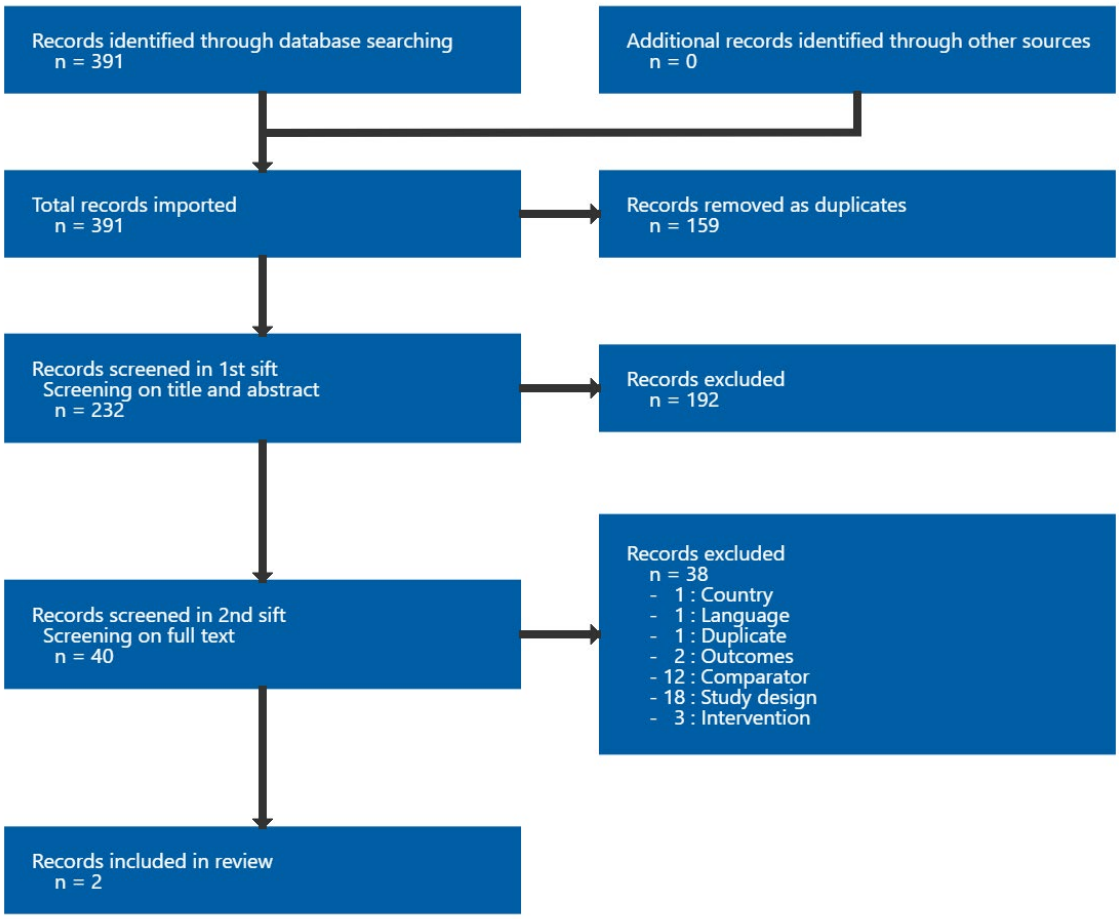
Date of last search: 13/10/2021

#	Searches
	All: (fetal or foetal or fetus or foetus)
	AND All: (scalp or scalps)

Appendix C Effectiveness evidence study selection

Study selection for: What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?

Figure 1: Study selection flow chart



Appendix D Evidence tables

Evidence tables for review question: What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?

Table 4: Evidence tables

East, 2021

Bibliographic Reference	East, Christine E.; Davey, Mary-Ann; Kamlin, C. Omar F.; Davis, Peter G.; Sheehan, Penelope M.; Kane, Stefan C.; Brennecke, Shaun P.; Flamingo Study, Group; The addition of fetal scalp blood lactate measurement as an adjunct to cardiotocography to reduce caesarean sections during labour: The Flamingo randomised controlled trial; The Australian & New Zealand journal of obstetrics & gynaecology; 2021

Study details

Country/ies where study was carried out	Australia
Study type	Randomised controlled trial (RCT)
Study dates	March 2012 to July 2015
Inclusion criteria	• Able to provide informed consent in English • singleton pregnancy • cephalic presentation • ≥37 weeks gestation • cervical dilation ≥3cm • ruptured amniotic membranes • abnormal fetal heart rate trace in labour that does not improve with conservative measures (maternal position change, correction of maternal hypotension, decrease or cessation of oxytocin infusion).
Exclusion criteria	• Planned caesarean section • contraindications for fetal blood sampling (FBS) - known viral infections

	• need for immediate delivery for example due to cord prolapse, or intrapartum haemorrhage • known significant fetal anomaly or bleeding disorder.
Patient characteristics	No significant differences in baseline for maternal age, BMI, gestational age or parity. Ethnicity or socioeconomic status not reported. Intervention: 87% nulliparous Control: 87% nulliparous No information specific to fetal growth restriction. <u>Birthweight <10th centile - n (%):</u> Intervention: 5 (8%) Control: 0 <u>Induction of labour - n (%):</u> Intervention: 47 (77%) Control: 47 (76%) 77% intervention group and 66% of control group had one or more of: maternal pyrexia, ruptured amniotic membranes >18 h, Group B streptococcus positive, meconium-stained amniotic fluid, intrapartum bleed, haematuria, other risk factors.
Intervention(s)/control	<u>Intervention</u> CTG + FBS lactate • If a non-reassuring CTG persists despite measures to improve, fetal blood scalp sampling for lactate will be undertaken. • If lactate <4.0 mmol/L - repeat FBS in 1 hour is fetal heart rate abnormality persists. • If lactate 4.0-4.8 mmol/L - repeat FBS in 30 minutes, or consider expediting the birth if rapid rise since last sample.

	• >4.8 mmol/L - urgent delivery indicated. <u>Control</u> CTG only • Following identification of an eligible CTG - monitoring of fetal well-being will continue. • No FBS taken even if abnormal CTG persists. • Timing of and progress to vaginal, operative vaginal or caesarean birth will be at the discretion of the clinician.
Sources of funding	Not industry funded (funded by an Australian National Health and Medical Research Council)
Sample size	N=123 CTG + FBS, n=61 CTG only, n=62

Outcomes

Outcome	**CTG + FBS, , N = 61**	**CTG only, , N = 62**
Neonatal death No of events	n = 0 ; % = 0	n = 0 ; % = 0
Apgar score <7 at 5 minutes No of events	n = 5 ; % = 8	n = 0 ; % = 0
Caesarean birth For non-reassuring fetal status, or failure to progress, or dystocia No of events	n = 25 ; % = 41	n = 28 ; % = 45

Outcome	CTG + FBS, , N = 61	CTG only, , N = 62
Instrumental vaginal birth vacuum or forceps No of events	n = 23 ; % = 38	n = 23 ; % = 37
Vaginal birth No of events	n = 13 ; % = 21	n = 11 ; % = 18
Neonatal encephalopathy Stage II/III No of events	n = 0 ; % = 0	n = 0 ; % = 0
Neonatal admission NICU and SCN No of events	n = 5 ; % = 8	n = 4 ; % = 6
Neonatal birth trauma Cephalhaematoma for CTG+FBS. Left-sided bruising from forceps for CTG only. No of events	n = 1 ; % = 2	n = 1 ; % = 2

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Allocation sequence was random, concealed and no differences in baseline characteristics between groups.)*

Section	Question	Answer
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Some concerns *(Nearly half of the intervention group (25/61) did not have fetal scalp blood lactate measured and specific reasons why were not provided, although some indication that for some the CTG returned to 'normal', or other clinical decisions. This could have been due to knowledge of intervention, but might be expected to occur outside of a trial context also. The analysis was done by intention to treat.)*
Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)	Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention)	Some concerns *(Not enough information regarding adherence and non-protocol interventions, but no per-protocol analysis)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Data is available for most participants.)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Outcome assessors knew the intervention, but all the outcomes are objective.)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(Data was in accordance with a pre-specified protocol.)*
Overall bias and Directness	Risk of bias judgement	Some concerns *(Some concerns over the number of women who did not receive scalp sampling in the scalp sampling group, but this could be expected to happen outside of a trial context.)*
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	No variation

Hughes, 2020

Bibliographic Reference	Hughes, O.; Murphy, D. J.; Comparing second-line tests to assess fetal wellbeing in Labor: a feasibility study and pilot randomized controlled trial; Journal of Maternal-Fetal and Neonatal Medicine; 2020

Study details

Country/ies where study was carried out	Ireland
Study type	Randomised controlled trial (RCT) Pilot RCT
Study dates	January to May 2018
Inclusion criteria	• Nulliparous women • singleton pregnancy • cephalic presentation • ≥37 weeks gestation • if they required cardiotocography in labour • if a second-line test was required • if the woman was capable of giving informed consent • if the woman had not taken systematic opiates in the last 4 hours.
Exclusion criteria	• Women with a contraindication to fetal blood sampling • limited understanding of English • under 18 years old.
Patient characteristics	Parity: All women were nulliparous.

	Gestational age: 24% of digital fetal scalp stimulation group were gestational age >41 weeks. 16% of fetal blood sampling group were gestational age >41 weeks. No information on fetal growth restricted fetuses or babies. 8% of fetuses in each arm were Small for Gestational Age (<10th percentile on scan). 60% FBS group had labour induced. 84% of dFSS group had labour induced. Study did not report on maternal age, weight/BMI, ethnicity, disability or socioeconomic status.
Intervention(s)/control	Intervention: Fetal blood scalp sampling • Fetal capillary blood samples were collected in heparinized glass tubes and analysed in the delivery suite using the gas analyser. • The results of the first technically reliable sample was interpreted. • Borderline results would need to be repeated in 30 minutes. • Abnormal results warrant expedited delivery in line with clinical circumstances. pH interpretation: • Normal: pH≥7.25 • Borderline: pH 7.21 - 7.24 • Abnormal: pH ≤ 7.20 Comparator: Digital fetal scalp stimulation (dFSS) • Following CTG review, abdominal and vaginal assessment was performed. • Digital fetal scalp stimulation was performed during the vaginal examination.

	• The examiner rubbed the fetal scalp with the index and middle finger over a period of 30 seconds. • The CTG was observed over a 5 minutes interval following the scalp stimulation. • If the CTG was borderline, dFSS would need to be repeated in 30 minutes. • If obstetrician was concerned following a borderline CTG, they could proceed to FBS. • If CTG was abnormal following dFSS, a FBS could be taken or expedited delivery in line with clinical circumstances. <u>CTG interpretation following dFSS</u> Normal: FHR acceleration (15 beats per minute above the baseline for at least 15 seconds) and normal variability (between 5 and 25 beats per minute). Abnormal: No fetal heart rate acceleration and no episode of normal variability, Borderline: Normal variability but not acceleration, or uncertainty.
Sample size	N=50 women randomised FBS, n=25 dFSS, n=25

Outcomes

Outcome	**FBS, , N = 25**	**dFSS, , N = 25**
Apgar score <7 at 5 minutes No of events	n = 0 ; % = 0	n = 1 ; % = 4
Caesarean birth for fetal distress of for poor progress No of events	n = 13 ; % = 52	n = 5 ; % = 20

Outcome	FBS, , N = 25	dFSS, , N = 25
Operative vaginal birth for fetal concerns or for poor progress No of events	n = 9 ; % = 36	n = 13 ; % = 52
Neonatal encephalopathy No of events	n = 0 ; % = 0	n = 0 ; % = 0
Admission to neonatal unit No of events	n = 1 ; % = 4	n = 2 ; % = 8

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(Some differences in baseline characteristics but could be due to small sample size.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(There were no deviations from the intended interventions post randomisation.)*
Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)	Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention)	Some concerns *(Not enough information regarding adherence and non-protocol interventions, but no per-protocol analysis)*

Section	Question	Answer
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Data is available for most participants.)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Outcome assessors knew the intervention, but all the outcomes are objective.)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(Data was in accordance with a pre-specified protocol.)*
Overall bias and Directness	Risk of bias judgement	Some concerns
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	No variation

Renou, 1976

Bibliographic Reference	Renou P; Chang A; Anderson I; Wood C; Controlled trial of fetal intensive care.; American journal of obstetrics and gynecology; 1976; vol. 126 (no. 4)

Study details

Country/ies where study was carried out	Australia
Study type	Randomised controlled trial (RCT)
Study dates	March 1974 - April 1975

Appendix E Forest plots

Forest plots for review question: What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here; the quality assessment for such outcomes is provided in the GRADE profiles in appendix F.

Appendix F GRADE tables

GRADE tables for review question: What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?

Table 5: Evidence profile for comparison 1: Fetal blood sampling + CTG versus CTG only

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fetal blood sampling + CTG	CTG only	Relative (95% CI)	Absolute		
Neonatal death												
1 (East 2021)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/61 (0%)	0/62 (0%)	RD 0.00 (-0.03 to 0.03	0 fewer per 1000 (from 30 fewer to 30 more)	VERY LOW	CRITICAL
Apgar score <7 at 5 minutes												
1 (East 2021)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	5/61 (8.2%)	0/62 (0%)	Peto OR 8.04 (1.35 to 47.81)	8 more per 1000 (from 1 more to 16 more)	MODERATE	CRITICAL
Caesarean birth												
1 (East 2021)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	25/61 (41%)	28/62 (45.2%)	RR 0.91 (0.6 to 1.36)	41 fewer per 1000 (from 181 fewer to 163 more)	VERY LOW	CRITICAL
Instrumental vaginal birth												
1 (East 2021)	randomised trials	serious[1]	no serious inconsistency	serious	very serious[3]	none	23/61 (37.7%)	23/62 (37.1%)	RR 1.02 (0.64 to 1.61)	7 more per 1000 (from 134 fewer to 226 more)	VERY LOW	CRITICAL
Spontaneous vaginal birth												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fetal blood sampling + CTG	CTG only	Relative (95% CI)	Absolute		
1 (East 2021)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	13/61 (21.3%)	11/62 (17.7%)	RR 1.2 (0.58 to 2.47)	35 more per 1000 (from 75 fewer to 261 more)	VERY LOW	CRITICAL
Neonatal encephalopathy												
1 (East 2021)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/61 (0%)	0/62 (0%)	RD 0.00 (-0.03 to 0.03)	0 fewer per 1000 (from 30 fewer to 30 more)	VERY LOW	IMPORTANT
Neonatal admission												
1 (East 2021)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/61 (8.2%)	4/62 (6.5%)	RR 1.27 (0.36 to 4.51)	17 more per 1000 (from 41 fewer to 226 more)	VERY LOW	IMPORTANT
Neonatal birth trauma												
1 (East 2021)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/61 (1.6%)	1/62 (1.6%)	RR 1.02 (0.07 to 15.89)	0 more per 1000 (from 15 fewer to 240 more)	VERY LOW	IMPORTANT

CI: confidence interval; CTG: cardiotocography; OR: odds ratio; RD: risk difference; RR: risk ratio
[1] Serious risk of bias in the evidence contributing to the outcomes as per RoB 2
[2] Sample size <200
[3] 95% CI crosses 2 MIDs

Table 6: Evidence profile for comparison 2: Fetal blood sampling + CTG versus Digital fetal scalp stimulation + CTG

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fetal blood sampling	Digital fetal scalp stimulation	Relative (95% CI)	Absolute	Quality	Importance
Apgar score <7 at 5 minutes												
1 (Hughes 2020)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/25 (0%)	1/25 (4%)	Peto OR 0.14 (0 to 6.82)	34 fewer per 1000 (from 40 fewer to 233 more)	VERY LOW	CRITICAL
Caesarean birth												
1 (Hughes 2020)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	13/25 (52%)	5/25 (20%)	RR 2.6 (1.09 to 6.2)	320 more per 1000 (from 18 more to 1000 more)	LOW	CRITICAL
Instrumental vaginal birth												
1 (Hughes 2020)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	9/25 (36%)	13/25 (52%)	RR 0.69 (0.36 to 1.32)	161 fewer per 1000 (from 333 fewer to 166 more)	VERY LOW	CRITICAL
Neonatal encephalopathy												
1 (Hughes 2020)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/25 (0%)	0/25 (0%)	RD 0.00 (-0.07 to 0.07)	0 fewer per 1000 (from 70 fewer to 70 more)	VERY LOW	IMPORTANT
Admission to neonatal unit												
1 (Hughes 2020)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/25 (4%)	2/25 (8%)	RR 0.5 (0.05 to 5.17)	40 fewer per 1000 (from 76 fewer to 334 more)	VERY LOW	IMPORTANT

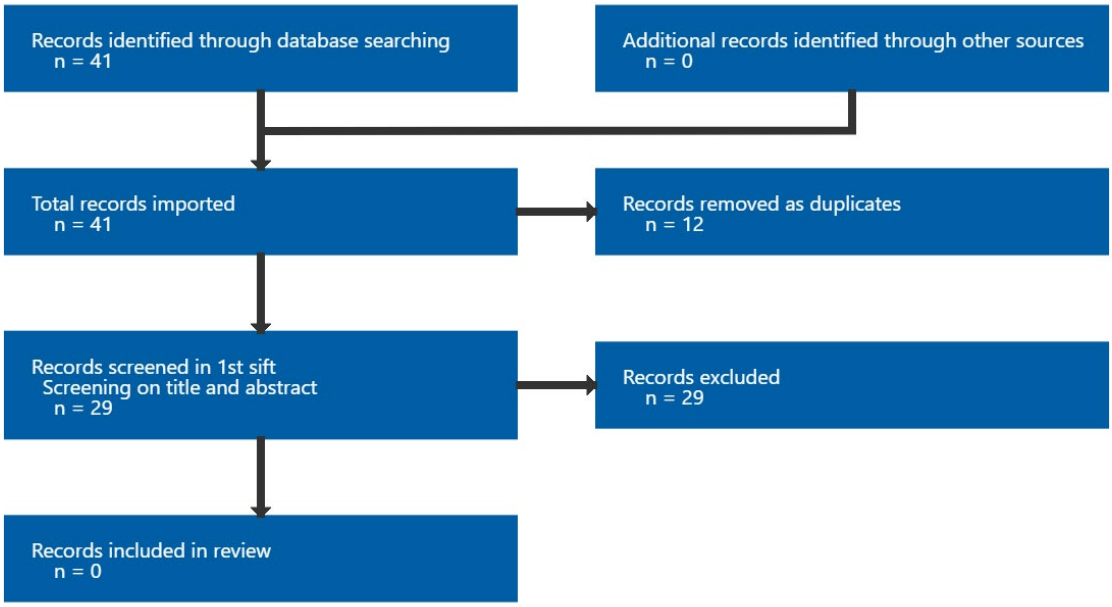
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: risk ratio
[1] Serious risk of bias in the evidence contributing to the outcomes as per RoB 2
[2] 95% CI crosses 2 MIDs
[3] 95% CI crosses 1 MID
[4] Sample size <200

Appendix G Economic evidence study selection

Study selection for: What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?

No economic evidence was identified which was applicable to this review question.

Figure 2: Study selection flow chart



Appendix H Economic evidence tables

Economic evidence tables for review question: What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?

No evidence was identified which was applicable to this review question.

Appendix I Economic model

Economic model for review question: What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?

No economic analysis was conducted for this review question.

Appendix J Excluded studies

Excluded studies for review question: What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?

Excluded effectiveness studies

Table 7: Excluded studies and reasons for their exclusion

Study	Reason for exclusion
Abid, Z. and Heazell, A. (2018) An audit of fetal scalp blood sampling procedures at St Mary's Hospital. BJOG: An International Journal of Obstetrics and Gynaecology 125(supplement3): 10	- Study design *Abstract only. Full text not located as audit only, without a comparison group.*
Al Wattar, Bassel H., Lakhiani, Aarti, Sacco, Adalina et al. (2019) Evaluating the value of intrapartum fetal scalp blood sampling to predict adverse neonatal outcomes: A UK multicentre observational study. European journal of obstetrics, gynecology, and reproductive biology 240: 62-67	- Study design *Observational study without a comparison group*
Al-Abd, Mohammad; Karkour, Tarek; Bakr, Ahmad Fayez (2005) Fetal pulse oximetry and neonatal outcome: A study in a developing country. Journal of Perinatology 25(12): 759-762	- Country *Not a high income country as defined by the OECD - Egypt*
Alfirevic Z, Gyte GML, Cuthbert A, Devane D. Continuous cardiotocography (CTG) as a form of electronic fetal monitoring (EFM) for fetal assessment during labour. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD006066.	- Study design *Included studies checked but none meet the criteria set out in the protocol*
Ayromlooi, J. and Garfinkel, R. (1980) Impact of fetal scalp blood pH on the incidence of cesarean section performed for fetal distress. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics 17(4): 391-2	- Study design *Retrospective before and after study – study did not make adjustments for confounders*
Becker JH, Westerhuis ME, Sterrenburg K, van den Akker ES, van Beek E, Bolte AC, van Dessel TJ, Drogtrop AP, van Geijn HP, Graziosi GC, van Lith JM, Mol BW, Moons KG, Nijhuis JG, Oei SG, Oosterbaan HP, Porath MM, Rijnders RJ, Schuitemaker NW, Wijnberger LD, Willekes C, Visser GH, Kwee A. Fetal blood sampling in addition to intrapartum ST-analysis of the fetal electrocardiogram: evaluation of the recommendations in the Dutch STAN® trial. BJOG. 2011 Sep;118(10):1239-46	- Comparator *Secondary analysis of women who had a fetal blood sample in the intervention arm of a randomised controlled trial. Fetal blood sampling has not been compared to any of the comparators listed in the protocol*

Study	Reason for exclusion
Boujenah, J., Oliveira, J., De La Hosseraye, C. et al. (2016) Should fetal scalp blood sampling be performed in the case of meconium-stained amniotic fluid?. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians 29(23): 3875-8	- Comparator *Not comparing fetal scalp blood sampling to any of the comparators listed in the protocol*
Carbonne, B. (2013) What is the evidence for the use of fetal blood sampling during labour?. Journal of Perinatal Medicine 41(suppl1)	- Study design *Full text is a conference abstract*
Carbonne, Bruno; Pons, Kelly; Maisonneuve, Emeline (2016) Foetal scalp blood sampling during labour for pH and lactate measurements. Best practice & research. Clinical obstetrics & gynaecology 30: 62-7	- Study design *Literature review. Full text checked for relevant studies but none meet the criteria in the PICO.*
Chandraharan, Edwin and Wiberg, Nana (2014) Fetal scalp blood sampling during labor: an appraisal of the physiological basis and scientific evidence. Acta obstetricia et gynecologica Scandinavica 93(6): 544-7	- Study design *Not a systematic review of RCTs or an RCT - appraisal paper.*
Clark, S. L.; Gimovsky, M. L.; Miller, F. C. (1984) The scalp stimulation test: a clinical alternative to fetal scalp blood sampling. American journal of obstetrics and gynecology 148(3): 274-7	- Comparator *Does not compare fetal scalp blood sampling to any of the comparators listed in the protocol*
East, C. E., Kane, S. C., Davey, M. A. et al. (2015) Protocol for a randomised controlled trial of fetal scalp blood lactate measurement to reduce caesarean sections during labour: the Flamingo trial. BMC pregnancy and childbirth 15: 285	- Study design *Protocol only. Full published results included under East 2021*
East, C. E., Sheehan, P., Leader, L. R. et al. (2010) Intrapartum fetal scalp lactate sampling: An updated systematic review. Journal of Paediatrics and Child Health 46(suppl1): 49-50	- Comparator *Fetal blood sampling compared to fetal blood sampling (lactate compared with pH)*
East, C., Davey, M. A., Sheehan, P. et al. (2016) Randomised trial of fetal scalp blood sampling for lactate measurement: The Flamingo trial. BJOG: An International Journal of Obstetrics and Gynaecology 123(supplement2): 158	- Study design *Abstract only. Full published results included under East 2021*

Study	Reason for exclusion
East, Christine E., Leader, Leo R., Sheehan, Penelope et al. (2015) Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace. Cochrane Database of Systematic Reviews 2015(5): cd006174	- Study design *Systematic review of randomised controlled trials. References checked and the relevant references are of trials which were ongoing at the time of publication of this systematic review. One trial, the Flamingo trial - East 2021, has published results and has been included already in this review.*
Haverkamp, A. D., Orleans, M., Langendoerfer, S. et al. (1979) A controlled trial of the differential effects of intrapartum fetal monitoring. American journal of obstetrics and gynecology 134(4): 399-412	- Population *Population indirect as number of women who received a fetal blood sample is less than 33%*
Heinis, Ayesha, van Dillen, Jeroen, Oosting, Janine et al. (2017) Clinical evaluation of Statstrip R Lactate for use in fetal scalp blood sampling. Acta obstetricia et gynecologica Scandinavica 96(3): 334-341	- Comparator *Not comparing fetal blood sampling with any of the comparators listed in the protocol. Looking at lactate compared to pH in fetal blood sampling*
Hoffmann, Scott W., Shaffer, Brian L., Caughey, Aaron B. et al. (2018) Fetal scalp lactate and digital scalp stimulation among those with non-reassuring fetal heart tracings: A decision analytic model. American Journal of Obstetrics and Gynecology 218(1supplement1): S182-S183	- Study design *Full text is a conference abstract only*
Holzmann, Malin, Wretler, Stina, Cnattingius, Sven et al. (2015) Cardiotocography patterns and risk of intrapartum fetal acidemia. Journal of perinatal medicine 43(4): 473-9	- Comparator *Fetal blood sampling not compared to any of the comparators in the protocol*
Irion, O., Stuckelberger, P., Moutquin, J. M. et al. (1996) Is intrapartum vibratory acoustic stimulation a valid alternative to fetal scalp pH determination?. British journal of obstetrics and gynaecology 103(7): 642-7	- Comparator *Study does not compare fetal blood sampling to any of the comparators listed in the protocol*

Study	Reason for exclusion
Isrctn (2018) Comparing second-line tests in labour to assess fetal well-being. http://www.who.int/trialsearch/Trial2.aspx?TrialID=ISRCTN13295826	- Study design *Protocol only. Feasibility results included, but full results not yet published.*
Jorgensen, Jan S. and Weber, Tom (2014) Fetal scalp blood sampling in labor--a review. Acta obstetricia et gynecologica Scandinavica 93(6): 548-55	- Study design *Review of literature. References checked for RCTs but none relevant.*
Langendoerfer, S., Haverkamp, A. D., Murphy, J. et al. (1980) Pediatric follow-up of a randomized controlled trial of intrapartum fetal monitoring techniques. The Journal of pediatrics 97(1): 103-7	- Outcomes *Does not report on any of the outcomes specified in the protocol*
Liston, Robert, Crane, Joan, Hamilton, Emily et al. (2002) Fetal health surveillance in labour. Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC 24(3)	- Study design *Guideline. References checked for studies but none relevant*
Liston, Robert, Crane, Joan, Hughes, Owen et al. (2002) Fetal health surveillance in labour. Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC 24(4): 342-348	- Duplicate *Duplicate of an excluded paper*
Lowe, Belinda and Beckmann, Michael (2016) Involving the consultant before fetal blood sampling. The Australian & New Zealand journal of obstetrics & gynaecology 56(4): 387-90	- Comparator *Not comparing fetal blood sampling to any of the comparators listed in the protocol*
Morin, C., Chartier, M., Goffinet, F. et al. (2017) Fetal scalp pH during labor: Which threshold for intervention?. Journal of Gynecology Obstetrics and Human Reproduction 46(2): 183-187	- Language *Article in French*
Murphy, Deirdre J.; Devane, Declan; Molloy, Eleanor (2020) Fetal scalp stimulation for assessing fetal wellbeing during labour. Cochrane Database of Systematic Reviews 2020(12): cd013808	- Study design *Protocol for a systematic review. Full systematic review not yet available*
Norén, Håkan, Luttkus, Andreas K., Stupin, Jens H., Blad, Sofia, Arulkumaran, Sabaratnam, Erkkola, Risto, Luzietti, Roberto, Visser, Gerard H.A., Yli, Branka and Rosén, Karl G.. "Fetal scalp pH and ST analysis of the fetal ECG as an adjunct to cardiotocography to predict	- Comparator *Secondary analysis of a randomised controlled trial looking at only the cases*

Study	Reason for exclusion
fetal acidosis in labor / A multi-center, case controlled study" Journal of Perinatal Medicine, vol. 35, no. 5, 2007, pp. 408-414.	*with fetal blood sampling. This group was not compared to any other group, and therefore does not meet any of the comparators specified in the protocol*
Ntr (2013) Effectiveness of fetal scalp blood sampling for the prevention of cesarean section in case of suspected fetal distress during labor. http://www.who.int/trialsearch/Trial2.aspx?TrialID=NTR3837	- Study design *Clinical trial entry. Full results not yet published.*
Pascual Mancho, Jara, Marti Gamboa, Sabina, Redrado Gimenez, Olga et al. (2017) Diagnostic accuracy of fetal scalp lactate for intrapartum acidosis compared with scalp pH. Journal of perinatal medicine 45(3): 315-320	- Comparator *Fetal blood sampling not compared to any of the comparators listed in the protocol*
Pexsters, Anne; Hanssens, Myriam; Van De Velde, Marc (2003) Fetal assessment: Do newer technologies offer better assessment and outcomes?. Current Opinion in Anaesthesiology 16(3): 253-256	- Study design *Opinion article. References to fetal blood sampling not relevant to the protocol*
Prouheze, Audrey, Girault, Aude, Barrois, Mathilde et al. (2021) Fetal scalp blood sampling: Do pH and lactates provide the same information?. Journal of gynecology obstetrics and human reproduction 50(4): 101964	- Comparator *No comparator matching the protocol. pH and lactate from fetal blood sampling only.*
Renou P; Chang A; Anderson I; Wood C; Controlled trial of fetal intensive care.; American journal of obstetrics and gynecology; 1976; vol. 126 (no. 4)	- Population *Population is indirect as cannot be certain of the number of women who received a fetal blood sample*
Rimmer, Stephanie; Roberts, Stephen A.; Heazell, Alexander E. P. (2016) Cervical dilatation and grade of doctor affects the interval between decision and result of fetal scalp blood sampling in labour. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians 29(16): 2671-4	- Comparator *Not comparing fetal blood sampling to any of the listed comparators*

Study	Reason for exclusion
Shakouri, Farzaneh, Iorizzo, Linda, Edwards, Hellen Mc Kinnon et al. (2020) Effectiveness of fetal scalp stimulation test in assessing fetal wellbeing during labor, a retrospective cohort study. BMC Pregnancy and Childbirth 20(1): 347	- Intervention *Does not look at the effectiveness of a fetal blood sample - study looking at the effectiveness of fetal scalp stimulation not comparing to fetal blood sample*
Sheehan, P., Kane, S., Brennecke, S. P. et al. (2016) The flamingo trial: A randomised controlled trial of fetal scalp blood lactate measurement to reduce caesarean sections during labour [actrn12611000172909]. Journal of Paediatrics and Child Health 52(supplement2): 24-25	- Study design *Abstract only. Full published results included under East 2021*
Stal, Ingrid, Wennerholm, Ulla-Britt, Ladfors, Lars et al. (2020) Fetal scalp blood sampling during second stage of labor-analyzing lactate or pH? A secondary analysis of a randomized controlled trial. Journal of Maternal-Fetal and Neonatal Medicine	- Comparator *Not comparing fetal blood sampling to any of the comparators listed in the protocol. Comparing fetal blood sampling pH or lactate*
Stein W, Hellmeyer L, Misselwitz B, Schmidt S. Impact of fetal blood sampling on vaginal delivery and neonatal outcome in deliveries complicated by pathologic fetal heart rate: a population based cohort study. J Perinat Med. 2006;34(6):479-83	- Study design *Observational study which did not control for any confounders*
Tahir Mahmood, Uzma, O'Gorman, Catherine, Marchocki, Zibi et al. (2018) Fetal scalp stimulation (FSS) versus fetal blood sampling (FBS) for women with abnormal fetal heart rate monitoring in labor: a prospective cohort study. Journal of Maternal-Fetal and Neonatal Medicine 31(13): 1742-1747	- Outcomes *No outcomes matching those specified in the protocol*
Wiberg-Itzel, E., Lipponer, C., Norman, M. et al. (2008) Determination of pH or Lactate in fetal scalp blood in management of intrapartum fetal distress: randomized controlled multicenter trial. Obstetrical & gynecological survey 63(11): 687-689	- Study design *Editorial commentary*
Wretler, Stina, Nordstrom, Lennart, Holzmann, Malin et al. (2018) Risk factors for intrapartum acidemia-a cohort study. Journal of Maternal-Fetal and Neonatal Medicine 31(24): 3232-3237	- Comparator *No comparison group - all women have fetal blood sampling*

Excluded economic studies

No economic evidence was identified for this review.

Appendix K Research recommendations – full details

Research recommendations for review question: What is the effectiveness of fetal blood sampling in improving outcomes for babies and mothers?

No research recommendations were made for this review question.