Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace (Review)

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Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace

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A B S T R A C T

Background

Fetal scalp blood sampling for lactate estimation may be considered following identification of an abnormal or non-reassuring fetal heart rate pattern. The smaller volume of blood required for this test, compared with the more traditional pH estimation, may improve sampling rates. The appropriate use of this practice mandates systematic review of its safety and clinical effectiveness prior to widespread introduction.

Objectives

To evaluate the effectiveness and risks of fetal scalp lactate sampling in the assessment of fetal well-being during labour, compared with no testing or alternative testing.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 January 2015).

Selection criteria

All published and unpublished randomised and quasi-randomised trials that compared fetal scalp lactate testing with no testing or alternative testing to evaluate fetal status in the presence of a non-reassuring cardiotocograph during labour.

Data collection and analysis

We used the standard methodological procedures of the Cochrane Pregnancy and Childbirth Group. Two review authors independently assessed the studies.

Main results

The search identified two completed randomised controlled trials (RCTs) and two ongoing trials. The two published RCTs considered outcomes for 3348 mother-baby pairs allocated to either lactate or pH estimation of fetal blood samples when clinically indicated in labour. Overall, the published RCTs were of low or unclear risk of bias. There was a high risk of performance bias, because it would not have been feasible to blind clinicians or participants.

No statistically significant between-group differences were found for neonatal encephalopathy (risk ratio (RR) 1.00, 95% confidence interval (CI) 0.32 to 3.09, one study, 2992 infants) or death. No studies reported neonatal seizures. We had planned to report death with other morbidities, for example, neonatal encephalopathy; however, the data were not available in a format suitable for this, therefore death due to congenital abnormality was considered alone. The three reported neonatal deaths occurred in babies with diaphragmatic hernias (n = 2) or congenital cardiac fibrosis (n = 1). All three babies had been randomised to the pH group and were not acidaemic at birth.

There were no statistically significant differences for any of the pre-specified secondary fetal/neonatal/infant outcomes for which data were available. This included low Apgar score at five minutes (RR 1.13, 95% CI 0.76 to 1.68, two studies, 3319 infants) and admission to neonatal intensive care units (RR 1.02, 95% CI 0.83 to 1.25, one study, 2992 infants), or metabolic acidaemia (RR 0.91, 95% CI 0.60 to 1.36, one study, 2675 infants) considered within the studies, either overall or where data were available for those where fetal blood sampling had occurred within 60 minutes of delivery.

Similar proportions of fetuses underwent additional tests to further evaluate well-being during labour, including scalp pH if in the lactate group or scalp lactate if in the pH group (RR 0.22, 95% CI 0.04 to 1.30, two studies, 3333 infants;Tau² 1.00, I² = 58%). Fetal blood sampling attempts for lactate and pH estimation were successful in 98.7% and 79.4% of procedures respectively in the one study that reported this outcome.

There were no significant between-group differences in mode of birth or operative birth for non-reassuring fetal status, either for all women, or within the group where the fetal blood sample had been taken within 60 minutes of delivery (for example, caesarean section for all enrolled, RR 1.09, 95% CI 0.97 to 1.22, two studies, 3319 women; operative delivery for non-reassuring fetal status for all enrolled RR 1.02, 95% CI 0.93 to 1.11, one study, 2992 women).

Neither study reported on adverse effects of fetal scalp lacerations or maternal anxiety.

Authors' conclusions

When further testing to assess fetal well-being in labour is indicated, fetal scalp blood lactate estimation is more likely to be successfully undertaken than pH estimation. Further studies may consider subgroup analysis by gestational age, the stage of labour and sampling within a prolonged second stage of labour. Additionally, we await the findings from the ongoing studies that compare allocation to no fetal blood sample with sampling for lactate and address longer-term neonatal outcomes, maternal satisfaction with intrapartum fetal monitoring and an economic analysis.

PLAIN LANGUAGE SUMMARY

Use of fetal scalp blood lactate for assessing fetal well-being during labour

A fetal heart rate that is abnormal or not reassuring during labour may be caused by the inability of the baby to adapt to decreases in oxygen supply during the birth. Inadequate oxygen supply may lead to the development of acidosis (low pH levels) and increased lactate in the blood. After the amniotic membranes have ruptured and the cervix dilated to around 3 cm, it is possible to measure lactate (or pH) levels in a sample of blood taken from the baby's scalp. A much smaller amount of blood is needed for the lactate test than to measure pH. This review identified two studies of 3348 mother-baby pairs that compared lactate and pH testing in labour. Lactate testing was more likely to be successful than pH testing, but with no differences in newborn outcomes, including the number of babies with low Apgar scores, low pH in their cord blood or admissions to the neonatal intensive care nursery. There were no differences in the number of mothers having caesarean sections, forceps or vacuum births between the two groups. We conclude that lactate testing in labour may be more likely to be successfully achieved than pH testing.

BACKGROUND

Description of the condition

Cardiotocography (CTG), often referred to as electronic fetal monitoring (EFM), records the fetal heart rate and uterine contractions to paper or computer, or both. It was introduced in the 1960s with the aim of improving neonatal outcomes by improving intrapartum fetal surveillance. External monitoring of the fetal heart is achieved using an ultrasound transducer placed on the mother's abdomen, over the region of the baby's heart. Once the amniotic membranes have ruptured, it is also possible to monitor the fetal heart rate by attaching an electrode to the baby's scalp. Fetal heart rate patterns can be classified in a number of ways. These include: (i) normal/reassuring; and (ii) when meeting the criteria for normal or reassuring, a range of terms including non-reassuring, suspicious, atypical, abnormal, pathological or ominous. These classifications are based on the fetal heart rate, its variability and the presence of accelerations or decelerations, compared with the occurrence of uterine contractions.

There is not universal agreement on the definition of these patterns (Di Tommaso 2013). Several groups have published guidelines in an attempt to improve uniformity of interpretation. Examples include the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG 2014), Royal College of Obstetricians and Gynaecologists (NCCWCH 2007), Society of Obstetricians and Gynaecologists of Canada (Liston 2007) and the American College of Obstetricians and Gynecologists (ACOG 2009). Consistent with some of these guidelines and with the clinical practice of the review team, we will generally refer to 'non-reassuring fetal status/CTG/patterns' in this review, rather than the term 'fetal distress' which is sometimes used inappropriately to refer to CTGs that do not meet normal/reassuring/abnormal status (ACOG 2005). Reassuring patterns require no specific action. Non-reassuring patterns occur in approximately 15% to 19% of labours (East 2006a; Umstad 1993) and may prompt clinical actions ranging from simple manoeuvres, such as a change of maternal position, improved maternal hydration, through to expedited birth of the baby (by caesarean section, forceps or vacuum), with the aim of preventing or minimising hypoxia in the fetus.

Non-reassuring CTG patterns may reflect the ability of the individual fetus to adapt to decreases in oxygen supply. Inadequate oxygen supply results in anaerobic metabolism of glucose, which leads to metabolic acidosis. Anaerobic glycolysis results in acidosis through the production of pyruvate, with some conversion to lactate. Low pH is a combined measure of both metabolic acidosis (including base deficit) and the more labile component, respiratory acidosis. The differences in individual fetal responses to a decrease in oxygen (and therefore differences in heart rate changes) mean that the positive predictive value of CTG for adverse outcome is low and the negative predictive value high (Bogdanovic 2014; Holzmann 2015; Nonnenmacher 2010), although this has

the potential for improvement with computerised interpretation of CTGs (Georgieva 2014; Strachan 2001). This means that a normal CTG usually indicates reassuring fetal status, while a non-reassuring CTG does not necessarily equate with 'fetal distress'. These features, combined with marked inter-observer variation in CTG interpretation by midwives (Devane 2005) and doctors (Palomaki 2006), result in variable but inappropriately high operative birth rates for non-reassuring fetal status in many hospitals. Once a non-reassuring fetal heart rate pattern is identified during labour, a number of additional assessments of fetal well-being may be considered. Some clinicians may also consider these in the presence of an ominous pattern, rather than proceeding with immediate delivery. These tests aim to assist the clinician to determine which baby may benefit from expedited birth and for which baby labour may be continued safely. Answers are rarely clear cut and the pros and cons of further tests and potential consequences need to be discussed with the mother. These tests do not replace the CTG, but complement it. Cochrane reviews have examined the safety and efficacy of several additional testing options, including fetal pulse oximetry (East 2014), fetal electrocardiography (ECG) for changes in the ST-segment or PR interval patterns (Neilson 2013), vibroacoustic stimulation (sound and vibration) (East 2013) and near-infrared spectroscopy (a measure of blood oxygen levels) (Mozurkewich 2000). The addition of fetal scalp blood sampling (FBS) for pH estimation to standard EFM may reduce the caesarean section rate, although the odds of having a caesarean birth are still increased compared to intermittent auscultation of the fetal heart (Alfirevic 2013).

Description of the intervention

Following identification of one abnormal or two non-reassuring features on the CTG, the Royal College of Obstetricians and Gynaecologists recommends FBS for pH estimation, with a published action algorithm based on the result (NCCWCH 2007). Collection of a small blood sample from the fetal scalp (a fetal blood sample) for blood gas analysis has been practiced since the 1960s (Saling 1967). It is contra-indicated when the mother is known to have HIV or hepatitis, or where there is suspicion of a bleeding tendency in the fetus (Maiques 1999; Pachydakis 2006). Following rupture of the amniotic membranes and at cervical dilatation greater than or equal to approximately 3 cm, an amnioscope is placed vaginally to allow adequate visualisation of the fetal head. A small sample of blood is then taken from the fetal scalp.

This procedure may be uncomfortable and intrusive for the mother, is invasive to the baby and expensive. Rare complications include infection and haemorrhage (Jaiyesimi 1990; Maiques 1999; Schaap 2011). Traditionally, such testing has required approximately 30 to 50 microlitres of blood, which is often difficult to obtain. Even when the clinician is able to collect this quantity of blood, samples are frequently rejected by the testing equipment due to contamination with air or amniotic fluid. Some equipment

can also analyse for other components, such as lactate. Fetal lactate testing equipment requiring a much smaller blood volume (as little as 5 microlitres) is now available (Wiberg-Itzel 2008).

How the intervention might work

Fetal scalp blood samples of lactate taken within 60 minutes of birth correlate well with umbilical arterial and venous lactate measured following delivery (Bowler 2014; Kruger 1998). Umbilical arterial (UA) lactate values correlate well with UA pH and base deficit values (Kruger 1998; Ramanah 2005). Fetal scalp lactate values correlate significantly with cardiotocography patterns, scalp pH, UA pH, lactate and base deficit, but not with Apgar scores (Holzmann 2015; Ramanah 2010).

Kruger 1999 retrospectively examined the predictive values of simultaneous fetal scalp blood estimation of lactate and pH (n = 326) for Apgar scores, UA pH, UA base deficit and neonatal encephalopathy. Cut-off values were the 75th percentile for lactate (4.8 mmol/L) and the 25th percentile for pH (7.20). The area under the receiver operator curve was significantly larger for lactate than for pH in predicting neonatal encephalopathy and Apgar score less than four at five minutes (Kruger 1999). Ramanah 2010 prospectively examined the predictive value and feasibility of fetal scalp lactate microsampling in the management of non-reassuring fetal status during labour (n = 7617). Using receiver operating characteristic curves, a scalp lactate cut-off value of 5 mmol/L was the most predictive for neonatal acidosis (Ramanah 2010). A retrospective study of 229 scalp lactate measurements reported a positive predictive value of 5% and negative predictive value of 98% of the prediction of an umbilical arterial pH measurement of ≤ 7.10 (Bowler 2014). These findings and evidence from animal studies of the effects of lactate on brain tissue (Engidawork 1997; Myers 1981) suggest that lactate estimation may be a better predictor of severe neonatal morbidity than pH.

Why it is important to do this review

The emerging use of fetal scalp blood sampling for lactate estimation requires systematic evaluation prior to becoming widespread, to ensure the appropriate use of this test in clinical practice (Mulrow 1994). Although many published guidelines of fetal monitoring do not include a recommendation for lactate estimation (including those published by ACOG 2009; Liston 2007; NCCWCH 2007), this trend is changing in some local and national guidelines (for example, Monash Health 2014; RANZCOG 2014; The Women's Hospital 2014).

About this review and its update

The original review (East 2010) and this 2015 update are primarily concerned with the use of fetal scalp lactate sampling in clinical practice. Several of the outcomes of interest would also benefit from a formal review of diagnostic accuracy. However, that is well beyond the scope of this clinical review. Such outcomes include: (i) those that demonstrate the ability of fetal scalp lactate sampling to predict which fetuses are hypoxic or acidaemic, measured after the birth from umbilical arterial cord blood, including pH less than 7.00 (Sehdev 1997) or less than 7.10 (Arikan 2000), lactate (White 2010) and base deficit greater than or equal to 12 mmol/L; (ii) clinical outcomes, including Apgar scores less than seven at five minutes (MacLennan 1999; Sehdev 1997), abnormal neurological status of the baby, possibly caused by inadequate supply of oxygen or blood (neonatal encephalopathy) or long-term infant disability, or both. Other outcomes of interest may include the success rate of fetal blood sampling for lactate measurement, the volume of blood required for lactate evaluation and the number of fetal scalp lacerations, including those which became infected or haemorrhaged.

Interventions resulting from additional tests of fetal well-being during labour are also important. For example, overall modes of birth following different forms of monitoring would usually be included in any analysis of this nature. However, it is important to also record specific interventions, such as operative birth (vacuum, forceps and caesarean section) performed for the indication of non-reassuring fetal status, since assessment of fetal well-being is the purpose of fetal lactate measurement.

Operative birth for non-reassuring fetal status has immediate resource implications and long-term effects. For example, the healthcare facility needs to make provision for an urgent caesarean section. The mother may have an improved likelihood of a vaginal birth in a subsequent pregnancy if the index caesarean was performed for non-reassuring fetal status rather than for another reason such as dystocia (Shipp 2000). Women's satisfaction with differing forms of fetal monitoring is important in determining the provision of appropriate maternity services (East 2006b). A cost-effectiveness analysis of the additional costs of fetal scalp lactate sampling, compared with the potential effect of reducing operative birth rates, is also an important consideration (East 2006c).

OBJECTIVES

To evaluate the effectiveness and risks of fetal scalp lactate sampling in the assessment of fetal well-being during labour, compared with no testing or alternative additional testing (pH, fetal pulse oximetry, etc) for women exhibiting a non-reassuring cardiotocograph trace.

A secondary objective of the review was to determine whether the effectiveness and risks of intrapartum fetal scalp lactate sampling were influenced by the following factors:

- stage of labour;

- gestation less than 37 completed weeks, greater than or equal to 37 completed weeks;

- additional tests performed to confirm the presence or absence of fetal acidaemia during labour.

METHODS

Criteria for considering studies for this review

Types of studies

All published and unpublished randomised and quasi-randomised trials that compared fetal scalp lactate testing with no testing or alternative additional tests (for example, pH, fetal pulse oximetry) to evaluate fetal status in the presence of a non-reassuring cardiotocograph (CTG) during labour.

Types of participants

Women in labour with a non-reassuring fetal heart rate trace who would qualify for fetal scalp blood testing by standard birthing suite protocols.

Types of interventions

Fetal scalp blood sampling for lactate estimation versus no sampling or alternative additional tests of fetal well-being (for example, pH, fetal pulse oximetry).

Types of outcome measures

Primary outcomes

(1) Neonatal seizures
(2) Neonatal encephalopathy
(3) Death or neonatal encephalopathy, or both
(4) Death or neonatal seizures, or both
(5) Death or long-term infant disability, or both

Secondary outcomes

Secondary outcomes: fetal/neonatal/infant

(6) Apgar scores less than seven at five minutes
(7) Apgar scores less than four at five minutes
(8) Umbilical arterial pH less than 7.00
(9) Umbilical arterial pH less than 7.10
(10) Umbilical arterial base deficit greater than 12
(11) Umbilical arterial lactate

(12) Admission to neonatal intensive care unit
(13) Meconium-stained amniotic fluid
(14) Neonatal length of hospital stay
(15) Long-term infant disability
(16) Composite outcome: number of additional tests performed per fetus to evaluate fetal well-being (for example, fetal oxygen saturation monitoring, fetal electrocardiogram waveform analysis, fetal pH estimation)
(17) Fetal oxygen saturation values less than 30%
(18) Fetal electrocardiography (ECG) ST-segment elevation
(19) Fetal ECG PR-interval shortening
(20) Fetal scalp laceration
(21) Fetal scalp laceration infection requiring treatment

Secondary outcomes: maternal

(22) Caesarean section
(23) Assisted vaginal birth (forceps or vacuum)
(24) Caesarean section for non-reassuring fetal status
(25) Assisted vaginal birth (forceps or vacuum) for non-reassuring fetal status
(26) Maternal satisfaction with fetal monitoring in labour
(27) Maternal anxiety
(28) Maternal length of hospital stay

Secondary outcomes: economic

(29) Cost-effectiveness of fetal monitoring

Other outcomes/considerations

We recorded the system used for lactate measurement and whether or not the maternity unit acted on prespecified cut-off values for lactate.

We also considered measures of practical consideration for tests to assess fetal well-being, including the success rate of fetal scalp blood sampling for fetal lactate and the volume of the fetal blood sample(s).

The following methods section of this review is based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

Search methods for identification of studies

The following methods section of this review is based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (31 January 2015).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

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1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);

2. weekly searches of MEDLINE (Ovid);

3. weekly searches of Embase (Ovid);

4. monthly searches of CINAHL (EBSCO);

5. handsearches of 30 journals and the proceedings of major conferences;

6. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE, Embase and CINAHL, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

We did not apply any language or date restrictions.

Data collection and analysis

For methods used in the previous version of this review, *see* East 2010.

For this update, the following methods were used for assessing the reports that were identified as a result of the updated search.

The following methods section of this review is based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

Selection of studies

At least two review authors (C East (CE), L Leader (LL), P Sheehan (PS) independently assessed for inclusion all the potential studies identified as a result of the search strategy. We planned to resolve any disagreement through discussion or, if required, consult another person.

Data extraction and management

We designed a form to extract data. For eligible studies, two review authors (CE, LL) extracted the data using the agreed form. We planned to resolve discrepancies through discussion or, if required, consult another person. We entered data into Review Manager software (RevMan 2014) and checked for accuracy (CE, LL, N Henshall (NH)). If information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

At least two review authors independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We planned to resolve any disagreement by discussion or involving another assessor.

Assessment of risk of bias in included studies

(1) Random sequence generation (checking for possible selection bias)

We considered for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We assessed the method as:

- low risk of bias (any truly random process, e.g. random number table; computer random number generator);
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

We considered for each included study the method used to conceal allocation to interventions prior to assignment and will assess whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment. We assessed these methods as:

- low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
- unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)

We considered for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered studies at low risk of bias if they were blinded, or if we judged that the lack of blinding would be unlikely to have affected the results. We assessed blinding separately for different outcomes or classes of outcomes. We assessed the methods as:

- low, high or unclear risk of bias for participants;
- low, high or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)

We described for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes. We assessed methods used to blind outcome assessment as:

- low, high or unclear risk of bias.

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(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data)

We considered for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or could be supplied by the trial authors, we planned to re-include missing data in the analyses which we undertake.
We assessed methods as:

• low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
• high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomisation);
• unclear risk of bias.

We planned to consider excluding trials where there was more than 20% missing data.

(5) Selective reporting (checking for reporting bias)

We considered for each included study how we investigated the possibility of selective outcome reporting bias and what we found.
We assessed methods as:

• low risk of bias (where it was clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review had been reported);
• high risk of bias (where not all the study's pre-specified outcomes had been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest were reported incompletely and so cannot be used; study failed to include results of a key outcome that would have been expected to have been reported);
• unclear risk of bias.

(6) Other bias (checking for (checking for bias due to problems not covered by (1) to (5) above)

We considered for each included study any important concerns we had about other possible sources of bias.
We assessed whether each study was free of other problems that could have put it at risk of bias:

• low risk of other bias;
• high risk of other bias;
• unclear whether there is risk of other bias.

(7) Overall risk of bias

We made judgments about whether studies are at high risk of bias, according to the criteria given in the *Handbook* (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we considered it was likely to impact on the findings. If necessary, we would have explored the impact of the level of bias through undertaking sensitivity analyses - see Sensitivity analysis.

Measures of treatment effect

Dichotomous data

For dichotomous data, we present results as summary risk ratio with 95% confidence intervals.

Continuous data

For continuous data, we used mean difference to measure continuous data; however, only one trial reported continuous data on outcomes of interest to the review. We planned to use the standardised mean difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomised trials

We planned to include cluster-randomised trials in the analyses along with individually-randomised trials. If we identify cluster-randomised trials in future updates of this review, we will adjust their sample sizes using the methods described in the *Handbook* [Section 16.3.4] using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population. If we use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify both cluster-randomised trials and individually-randomised trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely. We will also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit.

Cross-over trials

Cross-over trials are unlikely to be a valid study design to address this review's outcomes and will be excluded if identified in searches for future updates.

Other unit of analysis issues

We will exclude results of outcomes from multiple pregnancies if they are identified in searches for future updates.

If we identify trials with more than two treatment groups, we will use the methods described in the *Handbook* [Section 16.5.4]. We will combine all relevant experimental intervention groups of the study into a single group and combine all relevant control intervention groups into a single control group.

Dealing with missing data

For included studies, we noted levels of attrition. We would have explored the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis, should it have occurred.

For all outcomes, we planned to carry out analyses on an intention-to-treat basis, i.e. we attempted to include all participants randomised to each group in the analyses, and all participants were analysed in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the Tau², I² and Chi² statistics. We regarded heterogeneity as substantial if an I² was greater than 30% and either the Tau² was greater than zero, or there was a low P value (< 0.10) in the Chi² test for heterogeneity.

Assessment of reporting biases

If we identify 10 or more studies in a future update of the meta-analysis, we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually (Egger 1997). If asymmetry is suggested by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

We carried out statistical analyses using the Review Manager software (RevMan 2014). We used the fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect: i.e. where trials were examining the same intervention, and the trials' populations and methods were judged to be sufficiently similar. If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity was detected, we used random-effects meta-analysis to produce an overall summary, if an average treatment effect across trials was considered clinically meaningful. The random-

effects summary was treated as the average range of possible treatment effects and we discussed the clinical implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful, we would not have combined trials.

Where we used random-effects analyses, the results were presented as the average treatment effect with 95% confidence intervals, and the estimates of Tau² and I².

Subgroup analysis and investigation of heterogeneity

We planned to conduct subgroup analyses of the primary outcomes classifying whole trials by interaction tests as described by Deeks 2001; however, no data were available to allow these analyses.

We planned to carry out the following subgroup analyses:
- stage of labour;
- gestation: less than 37 completed weeks, greater than or equal to 37 completed weeks;
- concurrent use of alternative tests for assessment of fetal well-being (for example, fetal scalp blood sampling pH).

If suitable data are available in future updates. we will assess subgroup differences by interaction tests available within RevMan (RevMan 2014). We will report the results of subgroup analyses quoting the Chi² statistic and P value, and the interaction test I² value.

Sensitivity analysis

We planned to carry out sensitivity analysis of the primary outcomes to explore the effect of trial quality if necessary.

R E S U L T S

Description of studies

See: Characteristics of included studies and Characteristics of ongoing studies.

Results of the search

The original search identified two published randomised controlled trials; we included both. One ongoing study was identified (Flamingo Trial 2011) in the formal search and another (SCALP-trial 2013) whilst searching lactate literature outside this review process. *See* Characteristics of ongoing studies. Two further reports were identified in the search for this review update, which represented a conference abstract and the subsequent manuscript of a secondary analysis of the data in the Wiberg-Itzel 2008 trial, that did not contribute data to this update.

Included studies

The two published randomised controlled trials (RCTs) (Westgren 1998; Wiberg-Itzel 2008) enrolled 3348 mother-baby pairs and reported maternal and fetal/neonatal/infant outcomes following fetal scalp blood sampling for pH or lactate measurement.

The RCT reported by Westgren 1998 compared FBS for pH with FBS for lactate analysis in 341 mother-baby pairs that demonstrated an abnormal fetal heart rate during labour and for whom a FBS was considered clinically appropriate. Outcomes included the frequency and failure rate of the FBS procedures, the interval from incision for the FBS to when result available, mode of birth, birthweight, gestational age, Apgar scores, umbilical arterial blood gas results and admission to neonatal intensive care unit.

Wiberg-Itzel 2008 reported on a multicentre RCT conducted in 10 Swedish hospitals, comparing FBS for pH and lactate analysis in 3007 mother-baby pairs (1504 lactate group; 1503 pH group), with similar inclusion and exclusion criteria to those in the Westgren 1998 study. Outcomes included FBS failure, mode of birth and neonatal outcomes.

See Characteristics of included studies for further details.

Excluded studies

There were no excluded studies.

Risk of bias in included studies

Overall, the published RCTs were of low or unclear risk of bias. There was a high risk of performance bias, because it would not have been feasible to blind clinicians or participants. *See Risk of bias in included studies; Figure 1; Figure 2.*

Figure 1.   'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.
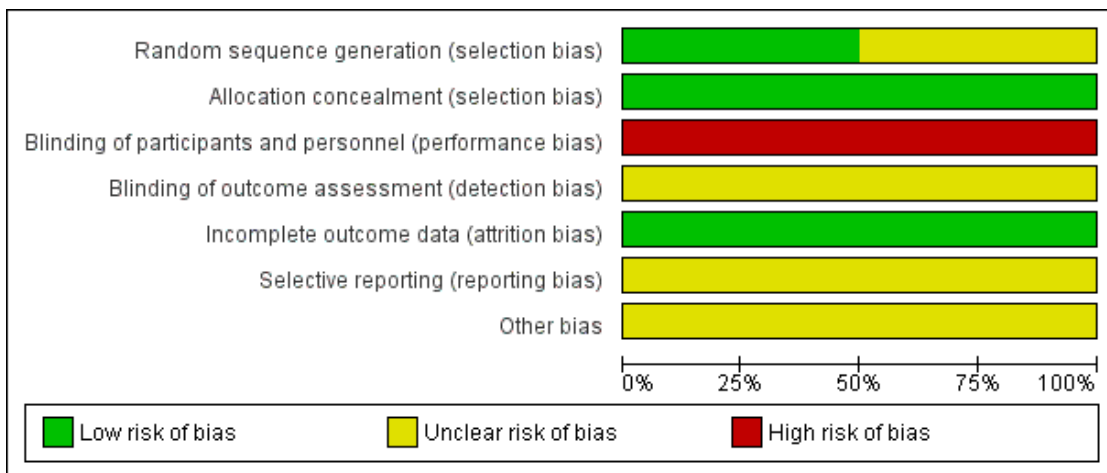
Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

Allocation

Allocation generation was not reported in the study by Westgren 1998. Overall, allocation concealment was considered to be at low risk of bias for both studies.

Blinding

It was not feasible to blind clinicians or participants to study group allocation. We therefore rated the studies as being at high risk of performance bias. Neither study report provided information about whether the outcome assessors were blinded to group allocation or not.

Incomplete outcome data

Outcome data were not reported in cases of protocol violation (n = 1 lactate group; n = 13 in the pH group) in the RCT reported by Westgren 1998. Umbilical cord gas analysis was incomplete for 12% in the lactate group and up to 9% in the pH group of the Wiberg-Itzel 2008 study. All other outcome data were reported, so that we judged these trials to be at low risk of attrition bias.

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Selective reporting

The lack of information in the study reports and lack of published study protocols meant that we were unclear about the risk of reporting bias.

Other potential sources of bias

There was no information in the study reports to indicate the potential for other sources of bias.

Effects of interventions

Comparison - Lactate versus pH analysis of fetal blood sampling

Primary outcomes

No statistically significant between-group differences were found for neonatal encephalopathy (risk ratio (RR) 1.00, 95% confidence interval (CI) 0.32 to 3.09, one study, 2992 infants; Analysis 1.1) or death. No studies reported neonatal seizures. We had planned to report death with other morbidities, for example, neonatal encephalopathy; however, the data were not available in a format suitable for this, therefore death due to congenital abnormality was considered alone. The three reported neonatal deaths occurred in babies with diaphragmatic hernias (n = 2) or congenital cardiac fibrosis (n = 1). All three babies had been randomised to the pH group and were not acidaemic at birth (RR 0.14. 95% CI 0.01 to 2.76, one study, 2992 infants; Analysis 1.2).

Secondary outcomes: fetal/neonatal/infant

There were no statistically significant differences for any of the pre-specified secondary fetal/neonatal/infant outcomes for which data were available. This included low Apgar score at five minutes (RR 1.13, 95% CI 0.76 to 1.68, two studies, 3319 infants; Analysis 1.3) and admission to neonatal intensive care units (RR 1.02, 95% CI 0.83 to 1.25, one study, 2992 infants; Analysis 1.9), or for any categories of low umbilical pH (for example, pH less than 7.00, (RR 0.84, 95% CI 0.47 to 1.50, one study, 2698 infants; Analysis 1.5) or base deficit values (for example, mean difference in base deficit -0.70, 95% CI -1.62 to 0.22, one study, 327 infants; Analysis 1.7) or metabolic acidaemia (RR 0.91, 95% CI 0.60 to 1.36, one study, 2675 infants; Analysis 1.4) considered within the studies, either overall or where data were available for those where fetal blood sampling had occurred within 60 minutes of delivery. Similar proportions of fetuses underwent additional tests to further evaluate well-being during labour, including scalp pH if in the lactate group or scalp lactate if in the pH group (average RR 0.22, 95% CI 0.04 to 1.30, Tau² 1.00, I² = 58%; two studies, 3333 infants; Analysis 1.10). Fetal electrocardiography (specifically ST

segment analysis) was used in some hospitals in the RCT reported by Wiberg-Itzel 2008 as an adjunct to fetal heart rate monitoring, similar numbers were randomised to each of the pH and lactate groups.

Fetal blood sampling attempts for lactate and pH estimation were successful in 98.7% and 79.4% of procedures respectively in the report from Westgren 1998 (Table 1). Failed pH sampling procedures for the 169 original participants of this same study were attributed to birth before the sample could be collected (n = 3), inadequate sample collection (n = 44) and pH meter dysfunction (n = 19). Failed lactate sampling for the study population of 172 was attributed to inadequate sample (n = 1), lactate meter dysfunction (n = 2) or unlikely result (n = 1). Fourteen of these failures were identified as protocol violations and excluded from further analysis, as lactate sampling was then performed in the pH group (n = 13) or pH sampling was performed in the lactate group (n = 1). The report indicated that individuals could have had more than one sampling episode: we have interpreted the reported data to mean that the 14 protocol violations represented 14 mother-baby pairs, rather than 14 of the total 634 samples taken, given the subsequent exclusion of 14 participants. These exclusions translated to the absence of complete data and meant that we were unable to analyse by intention-to-treat. Westgren 1998 suggested that the failure rate was inversely correlated with cervical dilatation in the pH group, but not the lactate group. More scalp incisions were made for each pH sampling attempt (median 2.0, interquartile range (IQR) 1 to 2) than for lactate (median 1.0, IQR 1 to 1) and there was a longer interval from sampling to available result for pH (median 230 seconds (s), IQR 188 to 300s) compared with lactate estimation (120s, IQR 90 to 147s) (Westgren 1998). Although each fetus had a blood sample taken between one and nine times in the study by Wiberg-Itzel 2008, we were only able to identify the total *number* of fetuses for whom fetal blood sampling was undertaken (not the overall number of sampling attempts) in the published report, with slightly greater success in the lactate group than the pH group (RR 1.10, 95% CI 1.08 to 1.12, one study, 2992 infants; Analysis 1.11).

No studies reported data on the remaining outcomes pre-specified for this review, including, for example, fetal scalp laceration infection requiring treatment or long-term infant disability.

Secondary outcomes: maternal

There were no significant between-group differences in mode of birth or operative birth for non-reassuring fetal status, either for all women, or within the group where the fetal blood sample had been taken within 60 minutes of delivery (for example, caesarean section for all enrolled, RR 1.09, 95% CI 0.97 to 1.22, two studies, 3319 women; Analysis 1.14; operative delivery for non-reassuring fetal status for all enrolled RR 1.02, 95% CI 0.93 to 1.11, one study, 2992 women; Analysis 1.15). No studies reported data for the pre-specified outcomes of maternal satisfaction with fetal monitoring,

maternal anxiety, maternal length of stay or cost-effectiveness of fetal monitoring.

Data were not available for conduct of the pre-specified subgroup analyses of stage of labour, gestation or within the subcategories of the additional tests used for assessment of fetal well-being.

DISCUSSION

Summary of main results

This review identified two randomised controlled trials (RCTs) that considered some aspects of the effectiveness and risks of fetal scalp lactate sampling compared with pH estimation for the assessment of fetal well-being, following identification of a non-reassuring cardiotocography trace during 3348 labours. Lactate sampling was more likely to be successful than for pH sampling. This success and speed did not translate to differences in clinical management in terms of mode of birth, or neonatal outcomes evaluated by umbilical cord blood gases, Apgar scores, encephalopathy or admission to the neonatal intensive care unit. The studies were underpowered to assess differences in the low prevalence outcomes.

Overall completeness and applicability of evidence

The studies did not address some of the outcomes of interest for this review, including scalp lacerations/infections, longer-term measures of infant well-being, such as long-term disability, maternal satisfaction with fetal monitoring in labour, maternal anxiety or an economic analysis. Each of these outcomes may impact on the introduction of fetal scalp blood lactate estimation in the clinical setting. One study noted that lower cervical dilatation was associated with greater difficulty in obtaining the fetal blood sampling (FBS) (Westgren 1998). However, it was not clear whether cervical dilatation was similar for each group at the time of sampling. This could be important, particularly for lower dilatations, and may have implications for whether equivalent numbers of women had fetal blood sampling in the latent phase of labour (e.g. less than 3 to 4 cm cervical dilatation) compared with those in the active phase of the first stage of labour.

Further considerations

Cut-off values

The Westgren 1998 study did not mandate clinical action at any given fetal scalp blood lactate value, as they considered it important that the clinician consider the full clinical picture, rather than

act on a single finding. They did acknowledge that a fetal scalp pH of less than 7.20 or lactate greater than 3.08 mmol/L was considered abnormal, while a lactate level between 2.9 and 3.08 was suspicious. The study report did not provide details of lactate values obtained from the FBS attempts or any estimation of the predictive value of the results. The available data would appear to support the action cut-off value greater than 4.8 mmol/L for intervention, measured with the Lactate Pro (Arkray, Kyoto, Japan) in the RCT reported by Wiberg-Itzel 2008. Some hospitals publish internal guidelines on cut-off values: for example, one such guideline uses the same meter as that used by Wiberg-Itzel 2008 and recommends escalating levels of urgent delivery when lactate values exceed 4.7 mmol/L (The Women's Hospital 2014). These cut-off values are considerably higher than the cut-off value of 4.2 mmol/L recommended following an observational study by Allen 2004, using the Accusport (Boeringer, Mannheim, East Sussex, UK) and a report by Smith 1983. Different point-of-care meters such as the Lactate Pro and the Nova Biomedical Statstrip Express may provide differing lactate results, with or without correction for the high haematocrit of fetal blood, when compared with each other and with a laboratory reference standard (Orsonneau 2013; Reif 2014; Stewart 2014; Su 2013). The cut-off lactate value must therefore be considered specifically for the lactate meter in use. Whilst it is beyond the scope of this review to recommend a specific meter or cut-off values, one option for those developing guidelines for their institution may be to base their recommendations on values used in studies performed with the specific lactate meter in use at the hospital's birthing facility.

Normal lactate in umbilical bloods: gestation

Wiberg 2008 studied umbilical blood lactate concentrations in 10,169 "vigorous" newborns, presumably healthy, born vaginally either spontaneously or with instrumental assistance, to establish reference ranges. The study demonstrated a linear relationship between logarithmic lactate values and gestational age commencing from 34 weeks' gestation. The study had relatively few numbers below 34 weeks' gestation (n = 207), so these results may vary if studied in a larger cohort and in addition, may be influenced by the reason for preterm birth. Following exclusion of instrumental deliveries, linear regression analysis revealed duration of second stage as an independent variable. The variation in umbilical arterial lactate values at term ranged from a mean of 3.5 mmol/L at 37 weeks to 4.3 mmol/L at 42 weeks' gestation. According to these data, the use of the cut-off value for lactate as 4.8 mmol/L would not result in any unnecessary interventions, even in babies at 42 weeks' gestation. This study excluded babies with complicated pregnancies and those born by caesarean section. No studies have addressed the significance of a relative rise in lactate levels for a given gestation, rather than a critical cut-off action level applied across all gestations. Future studies could consider receiver operator characteristics for a variety of cut-off values by gestation. The

effect of gestational age on the development of lactic acidosis due to hypoxia, particularly in pregnancies of longer than 42 weeks, also warrants further investigation. We will consider the impact of gestation in this review when data become available from one of the two included studies (Wiberg-Itzel 2008).

Stage of labour

The relationship between maternal and fetal lactate concentrations have been considered in observational studies in labour. The findings demonstrated no significant correlation between duration of first stage of labour and fetal lactate concentration at the beginning of second stage (Nordström 2001). This confirms previous findings suggesting that fetal lactate concentrations are constant during the first stage of labour, in the absence of hypoxia (Nordström 1994; Nordström 1995). Maternal lactate concentrations increase significantly during the active phase of the second stage of labour. The source of the lactate is thought to be maternal skeletal muscles. One estimate for the maternal increase has been given as 2 mmol/L per 30 minutes (Nordström 2001). Fetal lactate concentrations also correlated positively with the duration of active pushing, however at a rate about half that of the maternal lactate (1 mmol/L per 30 minutes). The question of whether this lactate rise is driven by fetal hypoxia or derived from the mother was investigated by studying the arterio-venous lactate difference at delivery, the results of which suggested that the main contributor to the fetal lactate increase is the fetus itself, especially with prolonged second stage (Nordström 2001). This is also supported by animal studies (Milley 1988). These findings suggest that fetal scalp lactates would still be an appropriate indicator of fetal hypoxia in second stage, although the clinical appropriateness of performing a lactate in response to abnormal fetal heart rate monitoring in active second stage would have to be considered. We await data from the authors of the Wiberg-Itzel 2008 study to consider the impact of stage of labour in this review.

Diagnostic accuracy

We constructed this review with the objective of determining the safety and effectiveness of fetal scalp lactate sampling/analysis. The two identified RCTs essentially compared the effectiveness of fetal scalp lactate sampling with what was a more common clinical practice of pH sampling. As such, the available data provide some evidence that the use of lactate monitoring does not result in neonatal or maternal outcomes that differ from those following fetal scalp pH sampling, which had been more commonly used than lactate in many maternity units. Whilst the review was not designed to consider the diagnostic accuracy of fetal lactate estimation during labour, the lack of statistically significant clinical outcomes may provide limited *de facto* support for the equivalence of lactate and pH estimation in identification of the at-risk fetus. Whilst such a concept may warrant further consideration in a formally con-

structed review of diagnostic accuracy, a brief overview of some observational studies may be informative here. Several observational studies have investigated the correlation between fetal scalp lactates and clinical outcomes of interest to this review, although we note that it is potentially problematic to draw conclusions about the relationship between lactate and these low prevalence outcomes in the relatively small published studies. Borruto 2008 reported no correlation between scalp lactates and five-minute Apgar scores, with only 12 of the total 188 neonates assigned an Apgar score less than seven at five minutes. Ramanah 2005 compared fetal scalp lactates to scalp pH, cord blood pH and lactate and Apgar scores. Although good correlations for the former were found in their series of 129 patients, no correlation was found with Apgar scores at one or five minutes. This series included only two babies with Apgars less than seven at one minute of age and in both cases the fetal scalp sample was taken at least 60 minutes prior to delivery. The study of 136 cases by Allen 2004 did not undertake direct correlation of fetal scalp lactate with outcome data. The lack of large, well-conducted studies with sufficient examples of clearly defined intrapartum asphyxia limits the confidence with which fetal scalp lactate estimation can predict intrapartum fetal well-being. Such a deficiency needs to be considered in studies (and a review) of diagnostic accuracy.

Subgroup analyses

The inability to conduct the planned subgroup analyses may be important, particularly given the potential for increases in lactate levels with both advancing gestational age and prolongation of the second stage of labour (Katz 1987; Nordström 2001; Wiberg 2008).

Quality of the evidence

The two RCTs included in this review were judged to be at low or unclear risk of bias overall. The risk of concern was blinding: participants were not blinded, although it could be feasible to achieve this in future studies by analysing all samples outside the birthing room. It was not feasible to blind the clinicians and there was no indication of blinding of outcome assessors. Future studies may incorporate blinding of participants and outcome assessors.

Potential biases in the review process

Potential eligible trials were searched for systematically by the Trials Search Co-ordinator of the Cochrane Pregnancy and Childbirth Group. We also serendipitously identified another trial in a trial register. We are therefore confident that all potentially eligible trials have been identified. The differences in lactate measurements from point-of-care meters represents a potential risk of bias when meta-analysing the findings of trials. The two included trials used

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the same meter and in future updates, we will consider sensitivity analysis if different meters were used in trials added to the meta analysis.

Agreements and disagreements with other studies or reviews

The findings of this review are consistent with observational studies and literature reviews available in the peer-reviewed literature. We are not aware of other published systematic reviews.

AUTHORS' CONCLUSIONS

Implications for practice

When it is clinically determined that further testing is warranted to assess fetal well-being in labour, fetal scalp blood lactate estimation is more likely to be successfully undertaken, with fewer scalp incisions and results more readily available than for pH estimation. The action cut-off values for lactate levels need to be made with consideration of the lactate meter being used. There is no available evidence to determine the effectiveness of fetal scalp blood lactate estimation compared with no sampling, on clinical outcomes.

Implications for research

Future studies may consider the outcomes within the subgroups of gestational age, stage of labour, serial fetal scalp lactate measurements and in the presence of other tests of fetal well-being. Large,

well-conducted studies with sufficient examples of clearly defined intrapartum asphyxia may provide confidence with which fetal scalp lactate estimation can predict intrapartum fetal well-being and inform a systematic review of diagnostic accuracy. Such trials would also compare the effectiveness of fetal scalp blood lactate estimation versus no blood sampling, to reduce clinically important outcomes such as those presented in this review.

Additionally, future studies may address longer-term neonatal outcomes and maternal satisfaction or anxiety with fetal monitoring during labour, as well as conduct of an economic analysis. Outcome assessor blinding would be appropriate in future trials.

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* Indicates the major publication for the study

Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace (Review)   **17**

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Westgren 1998

Methods	RCT comparing FBS for pH or lactate analysis, n = 341 (172 lactate group, 313 sampling procedures; 169 pH group, 321 sampling procedures) Repeat sampling (if required) according to original group allocation
Participants	Women attending Huddinge University Hospital, Karolinska Institute, Stockholm Inclusion criteria: abnormal fetal heart rate during labour and FBS considered necessary by attending clinician Ethics committee determined that informed consent not required from participants
Interventions	FBS for pH (35 microlitres) or lactate (5 microlitres). Performed pH analysis in the delivery ward (ABL 510, Radiometer, Copenhagen) and lactate analysis at bedside (Lactate card, KDK Corporation, Kyoto, Japan) Cut-off action values: pH < 7.20; lactate 2.9-3.08 mmol/L suspicious and > 3.08 mmol/L abnormal. No standard advice regarding action so that clinician could consider full clinical picture rather than isolated value
Outcomes	Frequency and failure rate of FBS procedures; interval from incision to when result available; mode of birth; birthweight; gestational age; Apgar scores, umbilical arterial blood gas results, admission to neonatal intensive care unit
Notes	Acknowledgement statement in publication notes the technical support received from the manufacturers of the lactate meter, but does not indicate or imply any commercial interest in either pH or lactate meters

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Low risk	Randomisation order unknown by investigators and study co-ordinators
Blinding of participants and personnel (performance bias) All outcomes	High risk	*Blinding of participants and personnel* • No blinding of participants. • Blinding of clinicians not feasible.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	*Blinding of outcome assessment* • No mention of blinding of outcome assessors.

Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcomes reported for participants when protocol followed. Those with protocol violations (n = 1 lactate group; n = 13 pH group) excluded from final analysis
Selective reporting (reporting bias)	Unclear risk	Unable to be determined from the report.
Other bias	Unclear risk	Unable to be determined from the report.

Wiberg-Itzel 2008

Methods	RCT comparing FBS for pH and lactate analysis, total n = 3007 (1504 lactate group; 1503 pH group), with later post-randomisation exclusions for final total n = 2992 - see risk of bias) Repeat sampling (if required) according to original group allocation
Participants	Inclusion criteria: singleton pregnancy, cephalic presentation at 34 or more weeks' gestation, with clinical indication for fetal scalp blood analysis during labour (Post-randomisation exclusion: multiple pregnancy, gestational age < 34 weeks.) 10 labour ward departments of Swedish hospitals.
Interventions	FBS for pH or lactate estimation. pH analysis on different blood gas analysers, with regular quality checks from a commercial company (Equalis AB, Uppsala, Sweden). Lactate measured with the Lactate Pro (Arkray, Kyoto, Japan) Guidelines for pH values: normal > 7.25; pre-acidaemia 7.21-7.25; acidaemia < 7.21 Guidelines for lactate values: normal < 4.2 mmol/L; pre-acidaemia 4.2-4.8 mmol/L; acidaemia > 4.8 mmol/L Pre-acidaemia - recommendation for further sampling 20-30 minutes later if no other indications for intervention. Acidaemia - decisions made by attending clinicians
Outcomes	Sampling failure, mode of birth, neonatal outcomes.
Notes	Data for subgroup analyses (stage of labour, gestational age) sought from authors but not yet provided Funding, competing interests and provenance statements confirm no commercial interest in pH or lactate meters used

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Implied by use of Internet based system (www.medscinet.se/laktat, MedSciNet AB, Stockholm, Sweden)

Wiberg-Itzel 2008 (*Continued*)

Allocation concealment (selection bias)	Low risk	Implied by use of Internet based system (www.medscinet.se/laktat, MedSciNet AB, Stockholm, Sweden)
Blinding of participants and personnel (performance bias) All outcomes	High risk	*Blinding of participants and personnel* • No blinding of participants. • Blinding of clinicians not feasible.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	*Blinding of outcome assessment* • No mention of blinding of outcome assessors.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Total enrolled and randomised: n = 3007. Post-randomisation exclusions occurred for 8 of the lactate group (twin pregnancy n = 3; gestational age < 34 weeks n = 5); and for 7 of the pH group (twin pregnancy n = 3; gestational age < 34 weeks n = 4) Appropriate outcomes reported by intention-to-treat for all remaining randomised participants (n = 2992) although FBS not undertaken due to: (1) sampling failure (pH group n = 146; lactate group n = 18) or failed FBS analysis (pH group n = 9; lactate group n = 0); or (2) rapid delivery, need for expedited delivery, reassuring CTG, withdrew consent or no reason given: pH group n = 106; lactate group n = 81) Umbilical cord blood gas analysis incomplete for: (1) metabolic acidaemia: pH group 181/ 1496 (12%); lactate group 136/1496 (9%) ; (2) pH: pH group 174/1496 (12%); lactate group 120/1496 (8%)
Selective reporting (reporting bias)	Unclear risk	Unable to be determined from the report.
Other bias	Unclear risk	Unable to be determined from the report.

CTG: cardiotocography
FBS: fetal scalp blood sampling
RCT: randomised controlled trial

Characteristics of ongoing studies *[ordered by study ID]*

Flamingo Trial 2011

Trial name or title	Fetal lactate measurement to reduce caesarean sections during labour: a randomised trial
Methods	Single-centre randomised controlled trial.
Participants	Women in labour at greater than or equal to 37 weeks' gestation with a non-reassuring fetal heart rate pattern
Interventions	FBS for lactate measurement, compared with no FBS.
Outcomes	Main outcomes: caesarean section following onset of labour, mode of birth, maternal satisfaction with fetal monitoring, neonatal encephalopathy
Starting date	March 2012.
Contact information	flamingo@thewomens.org.au
Notes	Prospectively registered trial: ACTRN12611000172909. The study tests the hypothesis that the addition of lactate measurement will reduce the caesarean section rate from 38% to 25%, which is a 35% relative reduction Country, Australia.

SCALP-trial 2013

Trial name or title	Effectiveness of fetal scalp blood sampling for the prevention of cesarean section in case of suspected fetal distress during labor (SCALP trial): a randomized controlled multicenter study
Methods	Multicentre randomised controlled trial.
Participants	Women in first stage of labour from 36 weeks with an abnormal fetal heart rate pattern
Interventions	FBS for lactate measurement, compared with no FBS. STAN (fetal ECG) may be in use in either group.
Outcomes	Primary outcome: caesarean section. Secondary outcomes: composite poor neonatal outcome (defined), maternal complications, women's birth experience
Starting date	1 March 2013.
Contact information	MPA AMF Heinis, Radboud University Medical Cernter Nijmegen.
Notes	Prospectively registered trial: NTR3837. For those where fECG is used, it is hypothesised that there will be a reduction in caesarean section from 95% in the FBS group to 80% in the no FBS group. When fECG is not used, this will mean a reduction in caesarean birth from 80%in the FBS group to 65% in the no FBS group Country, Netherlands.

ECG: electrocardiograph
FBS: fetal scalp blood sampling
fECG: fetal electrocardiograph

DATA AND ANALYSES

Comparison 1. Lactate versus pH analysis of fetal blood sampling

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Neonatal encephalopathy	1	2992	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.32, 3.09]
2 Neonatal death	1	2992	Risk Ratio (M-H, Fixed, 95% CI)	0.14 [0.01, 2.76]
2.1 Death from congenital abnormalities	1	2992	Risk Ratio (M-H, Fixed, 95% CI)	0.14 [0.01, 2.76]
3 Apgar score < 7 at 5 minutes	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 All study participants	2	3319	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.76, 1.68]
3.2 Fetal blood sample within 60 minutes of delivery	1	1192	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.57, 1.72]
4 Metabolic acidemia (umbilical arterial pH < 7.05 + base defecit > 12 mmol/L)	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 All study participants	1	2675	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.60, 1.36]
4.2 Fetal blood sample within 60 minutes of delivery	1	1192	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.52, 1.65]
5 Low umbilical arterial pH	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 pH < 6.98	1	327	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.14, 1.49]
5.2 pH < 7.00: all study participants	1	2698	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.47, 1.50]
5.3 pH < 7.00: Fetal blood sample within 60 minutes of delivery	1	1192	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.29, 1.58]
5.4 pH < 7.10	1	2698	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.70, 1.12]
6 Umbilical arterial lactate > 4.68 mmol/L	1	327	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.37, 1.07]
7 Umbilical arterial base deficit	1	327	Mean Difference (IV, Fixed, 95% CI)	-0.70 [-1.62, 0.22]
8 Umbilical arterial base deficit > 19.2	1	327	Risk Ratio (M-H, Fixed, 95% CI)	0.30 [0.03, 2.89]
9 Admission to neonatal intensive care unit	1	2992	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.83, 1.25]
10 Number of additional tests to evaluate fetal well-being	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
10.1 Fetal scalp pH (lactate group) or lactate estimation (pH group)	2	3333	Risk Ratio (M-H, Random, 95% CI)	0.22 [0.04, 1.30]
10.2 Fetal ECG (STAN monitor)	1	2992	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.88, 1.12]
11 Success rate of fetal blood sampling	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
11.1 Successful samples (events) in all fetuses sampled (Total)	1	2992	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [1.08, 1.12]
12 Normal vaginal birth	2	3319	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.67, 1.24]

13 Assisted vaginal birth	2	3319	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.81, 1.01]
14 Caesarean section	2	3319	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.97, 1.22]
15 Operative birth for non-reassuring fetal status	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
15.1 Fetal scalp blood sampled within 60 minutes of delivery	1	1192	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.98, 1.22]
15.2 All participants	1	2992	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.93, 1.11]

Analysis 1.1. Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 1 Neonatal encephalopathy.

Review: Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace

Comparison: 1 Lactate versus pH analysis of fetal blood sampling

Outcome: 1 Neonatal encephalopathy

Study or subgroup	Lactate n/N	pH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Wiberg-Itzel 2008	6/1496	6/1496		100.0 %	1.00 [0.32, 3.09]
Total (95% CI)	**1496**	**1496**		**100.0 %**	**1.00 [0.32, 3.09]**
Total events: 6 (Lactate), 6 (pH)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					
Test for subgroup differences: Not applicable					

0.01 0.1 1 10 100

Favours lactate   Favours pH
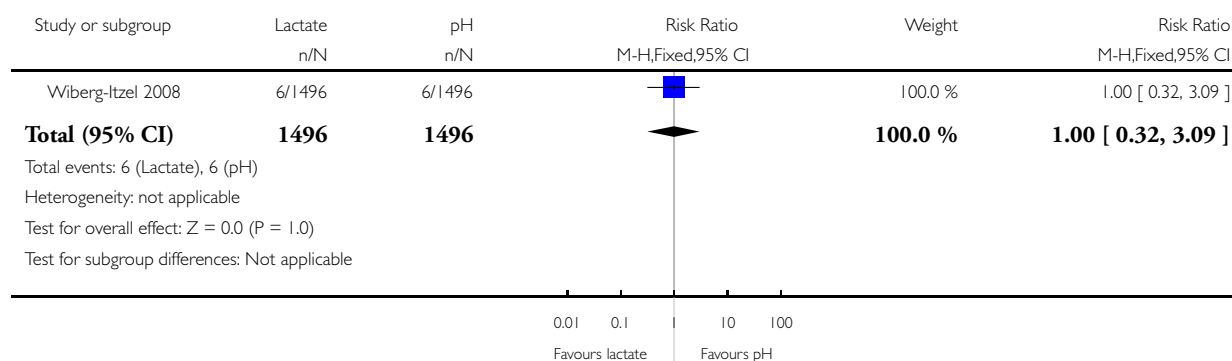
Analysis 1.2.   Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 2 Neonatal death.

Review: Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace

Comparison: 1 Lactate versus pH analysis of fetal blood sampling

Outcome: 2 Neonatal death

Study or subgroup	Lactate n/N	pH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Death from congenital abnormalities					
Wiberg-Itzel 2008	0/1496	3/1496	■	100.0 %	0.14 [0.01, 2.76]
Total (95% CI)	**1496**	**1496**	◆	**100.0 %**	**0.14 [0.01, 2.76]**
Total events: 0 (Lactate), 3 (pH)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.29 (P = 0.20)					
Test for subgroup differences: Not applicable					

```
          0.001 0.01  0.1    1    10  100 1000
          Favours lactate    Favours pH
```

Analysis 1.3. Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 3 Apgar score < 7 at 5 minutes.

Review: Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace

Comparison: 1 Lactate versus pH analysis of fetal blood sampling

Outcome: 3 Apgar score < 7 at 5 minutes

Study or subgroup	Lactate n/N	pH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 All study participants					
Westgren 1998	4/171	4/156		9.5 %	0.91 [0.23, 3.59]
Wiberg-Itzel 2008	46/1496	40/1496		90.5 %	1.15 [0.76, 1.75]
Subtotal (95% CI)	**1667**	**1652**		**100.0 %**	**1.13 [0.76, 1.68]**
Total events: 50 (Lactate), 44 (pH)					
Heterogeneity: Chi² = 0.10, df = 1 (P = 0.75); I² =0.0%					
Test for overall effect: Z = 0.59 (P = 0.56)					
2 Fetal blood sample within 60 minutes of delivery					
Wiberg-Itzel 2008	28/684	21/508		100.0 %	0.99 [0.57, 1.72]
Subtotal (95% CI)	**684**	**508**		**100.0 %**	**0.99 [0.57, 1.72]**
Total events: 28 (Lactate), 21 (pH)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.03 (P = 0.97)					

```
         0.02   0.1       1      10   50
      Favours lactate        Favours pH
```

Analysis 1.4. Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 4 Metabolic acidemia (umbilical arterial pH < 7.05 + base defecit > 12 mmol/L).

Review: Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace

Comparison: 1 Lactate versus pH analysis of fetal blood sampling

Outcome: 4 Metabolic acidemia (umbilical arterial pH < 7.05 + base defecit > 12 mmol/L)

Study or subgroup	Lactate	pH	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Fixed,95% CI		M-H,Fixed,95% CI
1 All study participants					
Wiberg-Itzel 2008	44/1360	47/1315	■	100.0 %	0.91 [0.60, 1.36]
Subtotal (95% CI)	**1360**	**1315**	◆	**100.0 %**	**0.91 [0.60, 1.36]**
Total events: 44 (Lactate), 47 (pH)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.48 (P = 0.63)					
2 Fetal blood sample within 60 minutes of delivery					
Wiberg-Itzel 2008	25/684	20/508	■	100.0 %	0.93 [0.52, 1.65]
Subtotal (95% CI)	**684**	**508**	◆	**100.0 %**	**0.93 [0.52, 1.65]**
Total events: 25 (Lactate), 20 (pH)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.25 (P = 0.80)					

```
        0.01   0.1     1    10   100

        Favours lactate     Favours pH
```

Review: Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace
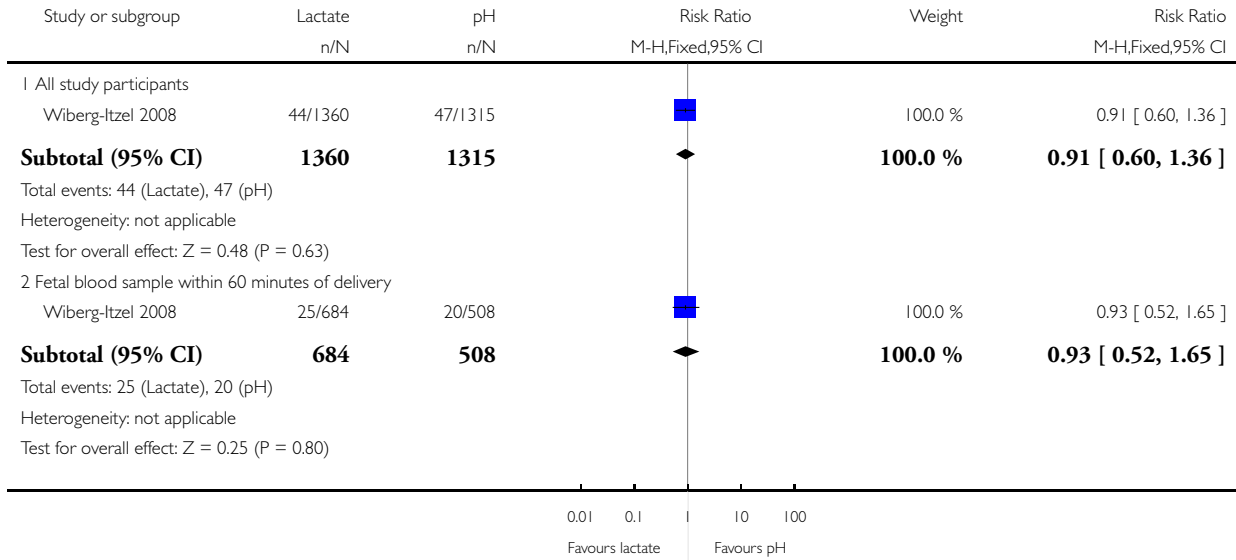
Comparison: 1 Lactate versus pH analysis of fetal blood sampling

Outcome: 5 Low umbilical arterial pH

Study or subgroup	Lactate n/N	pH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 pH < 6.98					
Westgren 1998	4/171	8/156		100.0 %	0.46 [0.14, 1.49]
Subtotal (95% CI)	**171**	**156**		**100.0 %**	**0.46 [0.14, 1.49]**
Total events: 4 (Lactate), 8 (pH)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.30 (P = 0.19)					
2 pH < 7.00: all study participants					
Wiberg-Itzel 2008	21/1376	24/1322		100.0 %	0.84 [0.47, 1.50]
Subtotal (95% CI)	**1376**	**1322**		**100.0 %**	**0.84 [0.47, 1.50]**
Total events: 21 (Lactate), 24 (pH)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.59 (P = 0.56)					
3 pH < 7.00: Fetal blood sample within 60 minutes of delivery					
Wiberg-Itzel 2008	10/684	11/508		100.0 %	0.68 [0.29, 1.58]
Subtotal (95% CI)	**684**	**508**		**100.0 %**	**0.68 [0.29, 1.58]**
Total events: 10 (Lactate), 11 (pH)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.91 (P = 0.36)					
4 pH < 7.10					
Wiberg-Itzel 2008	121/1376	131/1322		100.0 %	0.89 [0.70, 1.12]
Subtotal (95% CI)	**1376**	**1322**		**100.0 %**	**0.89 [0.70, 1.12]**
Total events: 121 (Lactate), 131 (pH)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.99 (P = 0.32)					

0.01   0.1   1   10   100

Favours lactate   Favours pH

Analysis 1.6. Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 6 Umbilical arterial lactate > 4.68 mmol/L.

Review: Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace

Comparison: 1 Lactate versus pH analysis of fetal blood sampling

Outcome: 6 Umbilical arterial lactate > 4.68 mmol/L

Study or subgroup	Lactate n/N	pH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Westgren 1998	20/171	29/156		100.0 %	0.63 [0.37, 1.07]
Total (95% CI)	**171**	**156**		**100.0 %**	**0.63 [0.37, 1.07]**

Total events: 20 (Lactate), 29 (pH)

Heterogeneity: not applicable

Test for overall effect: Z = 1.72 (P = 0.085)

Test for subgroup differences: Not applicable

```
         0.02  0.1      1      10   50
        Favours lactate    Favours pH
```

Analysis 1.7. Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 7 Umbilical arterial base deficit.

Review: Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace

Comparison: 1 Lactate versus pH analysis of fetal blood sampling

Outcome: 7 Umbilical arterial base deficit

Study or subgroup	Lactate N	Mean(SD)	pH N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Westgren 1998	171	8 (3.8)	156	8.7 (4.6)		100.0 %	-0.70 [-1.62, 0.22]
Total (95% CI)	**171**		**156**			**100.0 %**	**-0.70 [-1.62, 0.22]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.49 (P = 0.14)

Test for subgroup differences: Not applicable

```
        -4    -2    0    2    4
       Favours lactate    Favours pH
```

Analysis 1.8. Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 8 Umbilical arterial base deficit > 19.2.

Review: Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace

Comparison: 1 Lactate versus pH analysis of fetal blood sampling
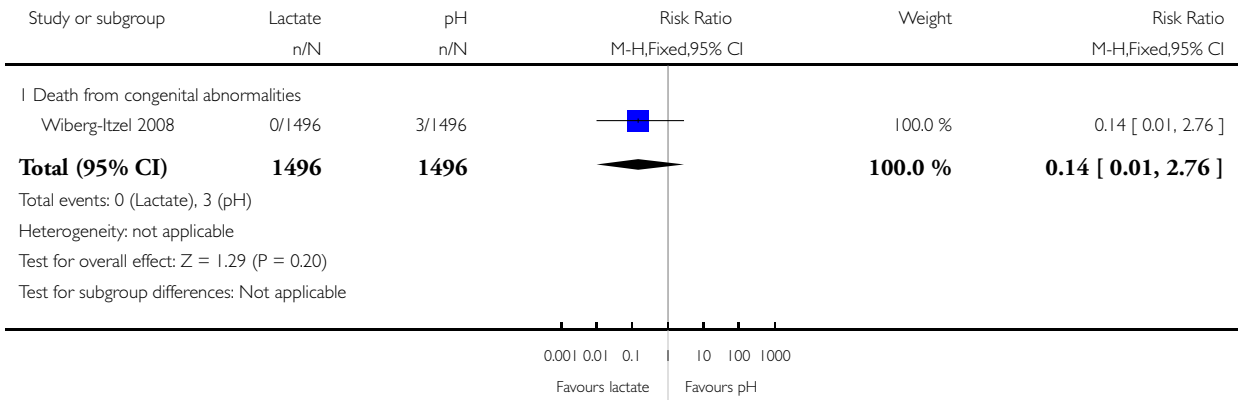
Outcome: 8 Umbilical arterial base deficit > 19.2

Study or subgroup	Lactate n/N	pH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Westgren 1998	1/171	3/156		100.0 %	0.30 [0.03, 2.89]
Total (95% CI)	**171**	**156**		**100.0 %**	**0.30 [0.03, 2.89]**

Total events: 1 (Lactate), 3 (pH)

Heterogeneity: not applicable

Test for overall effect: Z = 1.04 (P = 0.30)

Test for subgroup differences: Not applicable

```
      0.01    0.1     1     10    100
      Favours lactate    Favours pH
```

Analysis 1.9. Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 9 Admission to neonatal intensive care unit.

Review: Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace

Comparison: 1 Lactate versus pH analysis of fetal blood sampling

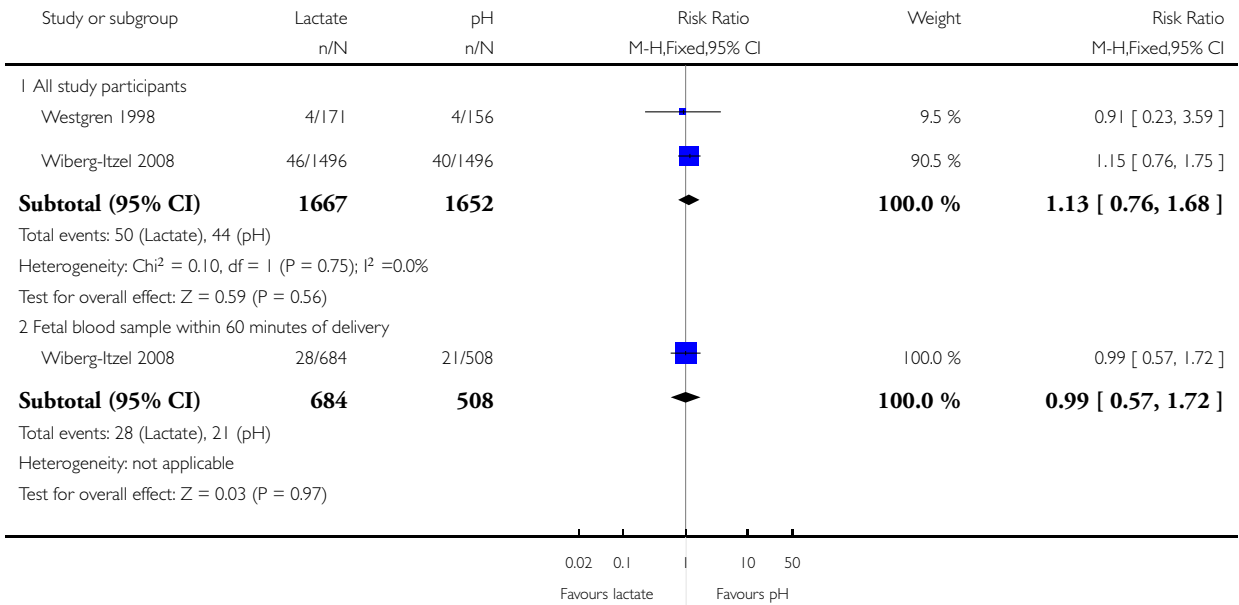Outcome: 9 Admission to neonatal intensive care unit

Study or subgroup	Lactate n/N	pH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Wiberg-Itzel 2008	167/1496	164/1496		100.0 %	1.02 [0.83, 1.25]
Total (95% CI)	**1496**	**1496**		**100.0 %**	**1.02 [0.83, 1.25]**

Total events: 167 (Lactate), 164 (pH)

Heterogeneity: not applicable

Test for overall effect: Z = 0.17 (P = 0.86)

Test for subgroup differences: Not applicable

```
      0.01    0.1     1     10    100
      Favours lactate    Favours pH
```

Analysis 1.10.   Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 10 Number of additional tests to evaluate fetal well-being.

Review: Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace

Comparison: 1 Lactate versus pH analysis of fetal blood sampling

Outcome: 10 Number of additional tests to evaluate fetal well-being

Study or subgroup	Lactate	pH	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
	n/N	n/N			
1 Fetal scalp pH (lactate group) or lactate estimation (pH group)					
Westgren 1998	1/172	13/169		39.7 %	0.08 [0.01, 0.57]
Wiberg-Itzel 2008	4/1496	9/1496		60.3 %	0.44 [0.14, 1.44]
Subtotal (95% CI)	**1668**	**1665**		**100.0 %**	**0.22 [0.04, 1.30]**
Total events: 5 (Lactate), 22 (pH)					
Heterogeneity: Tau² = 1.00; Chi² = 2.40, df = 1 (P = 0.12); I² =58%					
Test for overall effect: Z = 1.67 (P = 0.094)					
2 Fetal ECG (STAN monitor)					
Wiberg-Itzel 2008	392/1496	393/1496		100.0 %	1.00 [0.88, 1.12]
Subtotal (95% CI)	**1496**	**1496**		**100.0 %**	**1.00 [0.88, 1.12]**
Total events: 392 (Lactate), 393 (pH)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.04 (P = 0.97)					

$$0.01 \quad 0.1 \quad 1 \quad 10 \quad 100$$

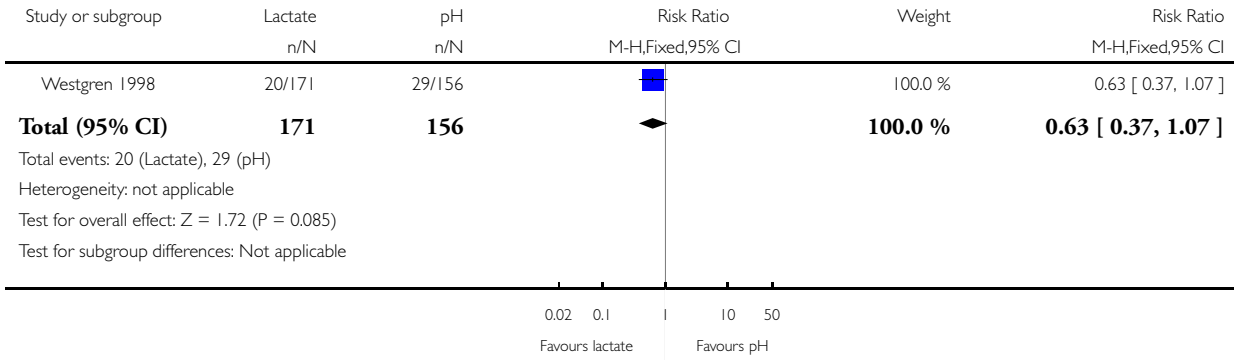Favours lactate   Favours pH

Analysis 1.11. Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 11 Success rate of fetal blood sampling.

Review: Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace

Comparison: 1 Lactate versus pH analysis of fetal blood sampling
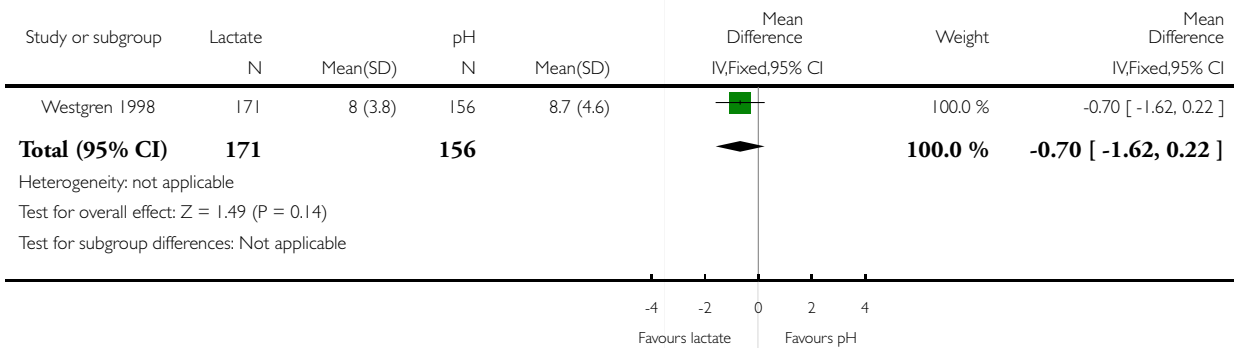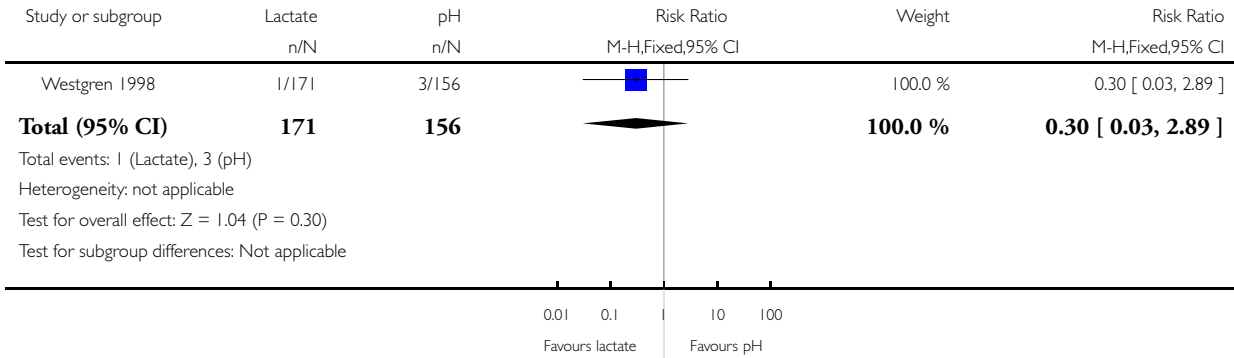
Outcome: 11 Success rate of fetal blood sampling

Study or subgroup	Lactate n/N	pH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Successful samples (events) in all fetuses sampled (Total)					
Wiberg-Itzel 2008	1478/1496	1341/1496		100.0 %	1.10 [1.08, 1.12]
Subtotal (95% CI)	**1496**	**1496**		**100.0 %**	**1.10 [1.08, 1.12]**
Total events: 1478 (Lactate), 1341 (pH)					
Heterogeneity: not applicable					
Test for overall effect: Z = 10.53 (P < 0.00001)					

```
        0.5    0.7    1    1.5    2
          Favours pH    Favours lactate
```

Analysis 1.12. Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 12 Normal vaginal birth.

Review: Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace

Comparison: 1 Lactate versus pH analysis of fetal blood sampling

Outcome: 12 Normal vaginal birth

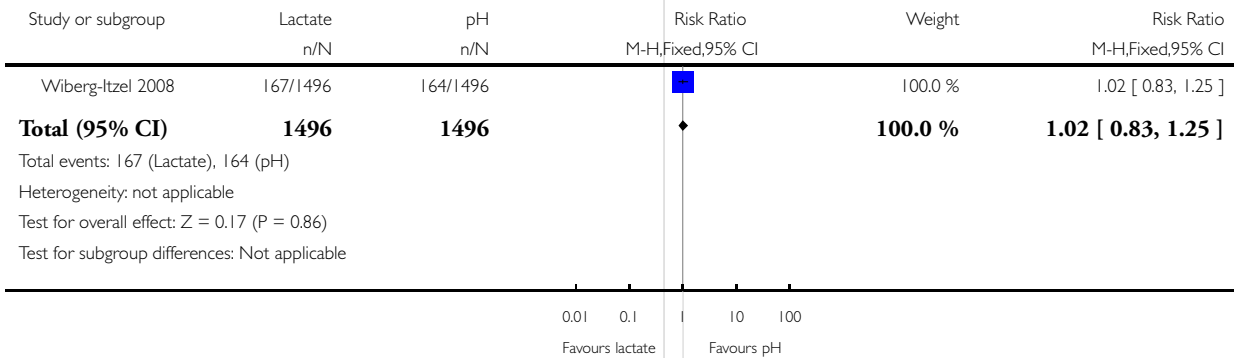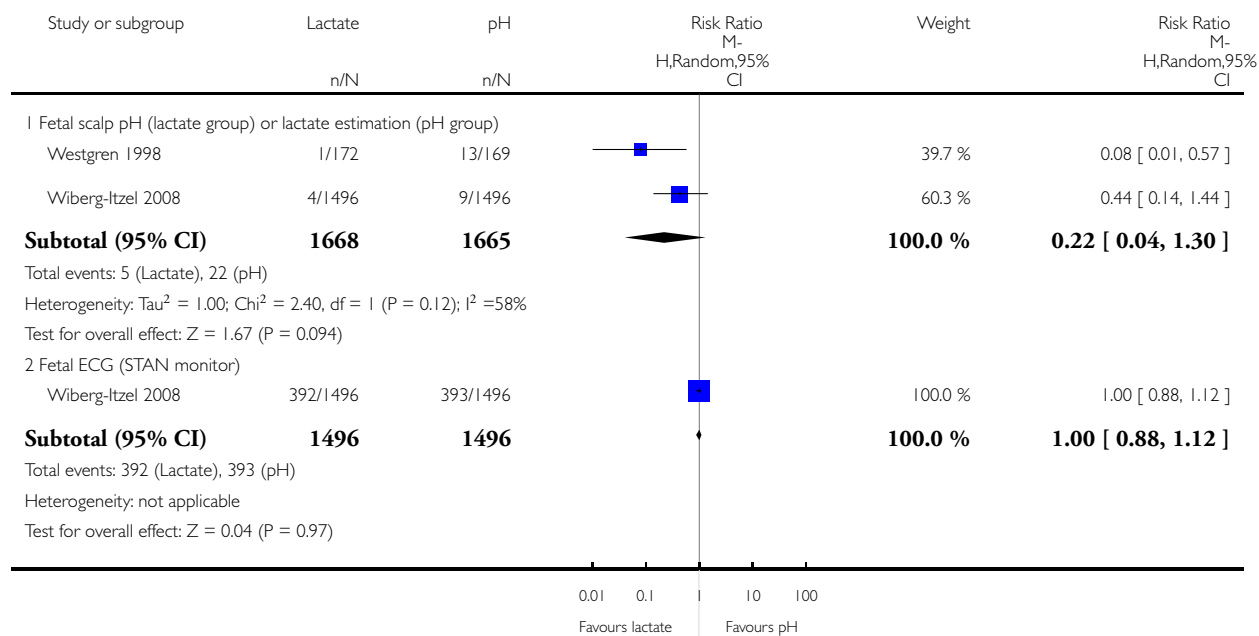| Study or subgroup	Lactate n/N	pH n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Westgren 1998	35/171	44/156		33.3 %	0.73 [0.49, 1.07]
Wiberg-Itzel 2008	674/1496	665/1496		66.7 %	1.01 [0.94, 1.10]
Total (95% CI)	**1667**	**1652**		**100.0 %**	**0.91 [0.67, 1.24]**
Total events: 709 (Lactate), 709 (pH)					
Heterogeneity: Tau^2 = 0.04; Chi^2 = 2.76, df = 1 (P = 0.10); I^2 =64%					
Test for overall effect: Z = 0.62 (P = 0.54)					
Test for subgroup differences: Not applicable					

```
        0.01    0.1    1    10    100
          Favours lactate    Favours pH
```

Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace (Review)

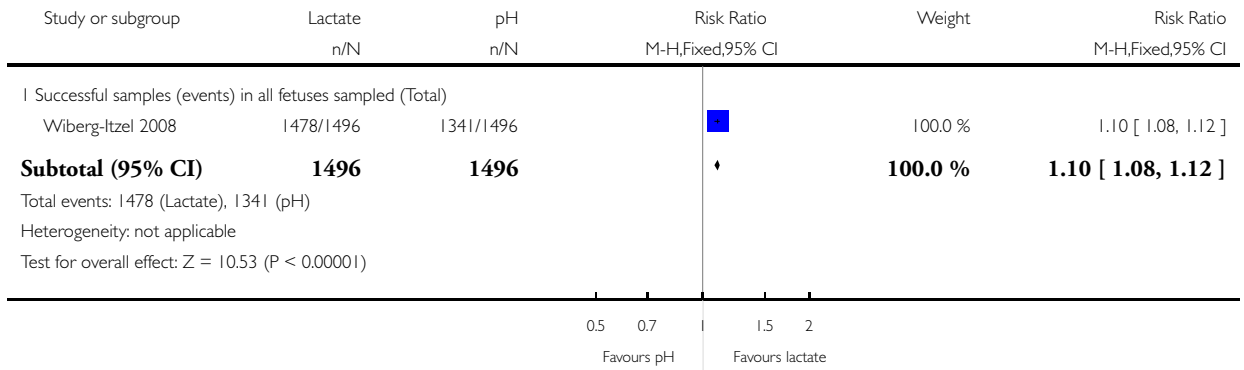Copyright © 2015 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
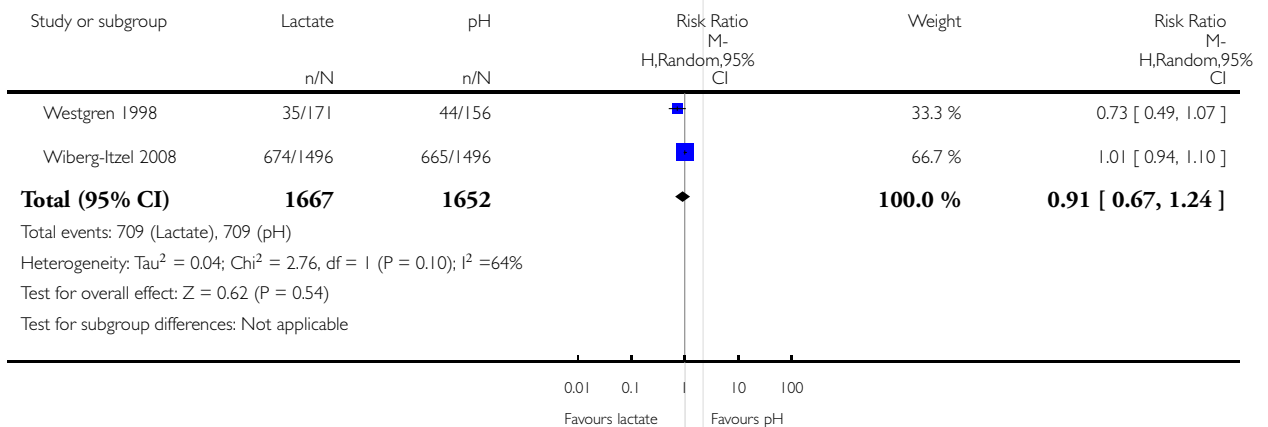
32

Analysis 1.13. Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 13 Assisted vaginal birth.

Review: Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace

Comparison: 1 Lactate versus pH analysis of fetal blood sampling

Outcome: 13 Assisted vaginal birth

Study or subgroup	Lactate n/N	pH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Westgren 1998	45/171	39/156		8.9 %	1.05 [0.73, 1.52]
Wiberg-Itzel 2008	370/1496	416/1496		91.1 %	0.89 [0.79, 1.00]
Total (95% CI)	**1667**	**1652**		**100.0 %**	**0.90 [0.81, 1.01]**

Total events: 415 (Lactate), 455 (pH)

Heterogeneity: Chi² = 0.72, df = 1 (P = 0.40); I² =0.0%

Test for overall effect: Z = 1.73 (P = 0.084)

Test for subgroup differences: Not applicable

```
         0.5    0.7    I    1.5    2
         Favours lactate    Favours pH
```
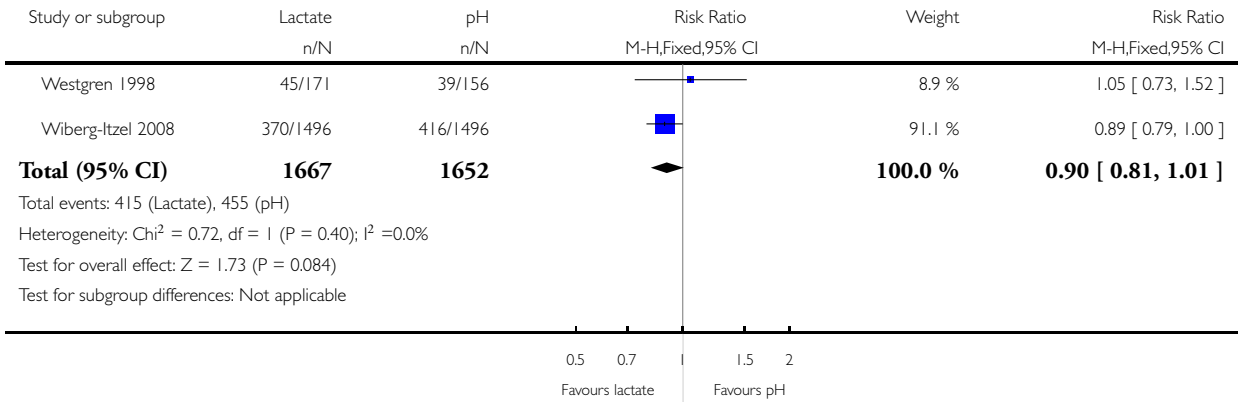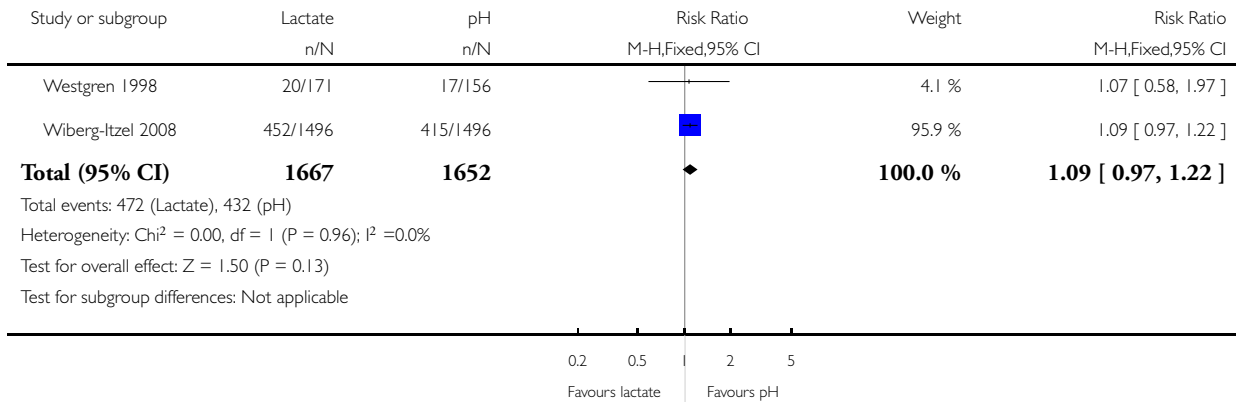
Analysis 1.14. Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 14 Caesarean section.

Comparison: 1 Lactate versus pH analysis of fetal blood sampling

Outcome: 14 Caesarean section

Study or subgroup	Lactate n/N	pH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Westgren 1998	20/171	17/156		4.1 %	1.07 [0.58, 1.97]
Wiberg-Itzel 2008	452/1496	415/1496		95.9 %	1.09 [0.97, 1.22]
Total (95% CI)	**1667**	**1652**		**100.0 %**	**1.09 [0.97, 1.22]**

Total events: 472 (Lactate), 432 (pH)

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.96); I² =0.0%

Test for overall effect: Z = 1.50 (P = 0.13)

Test for subgroup differences: Not applicable
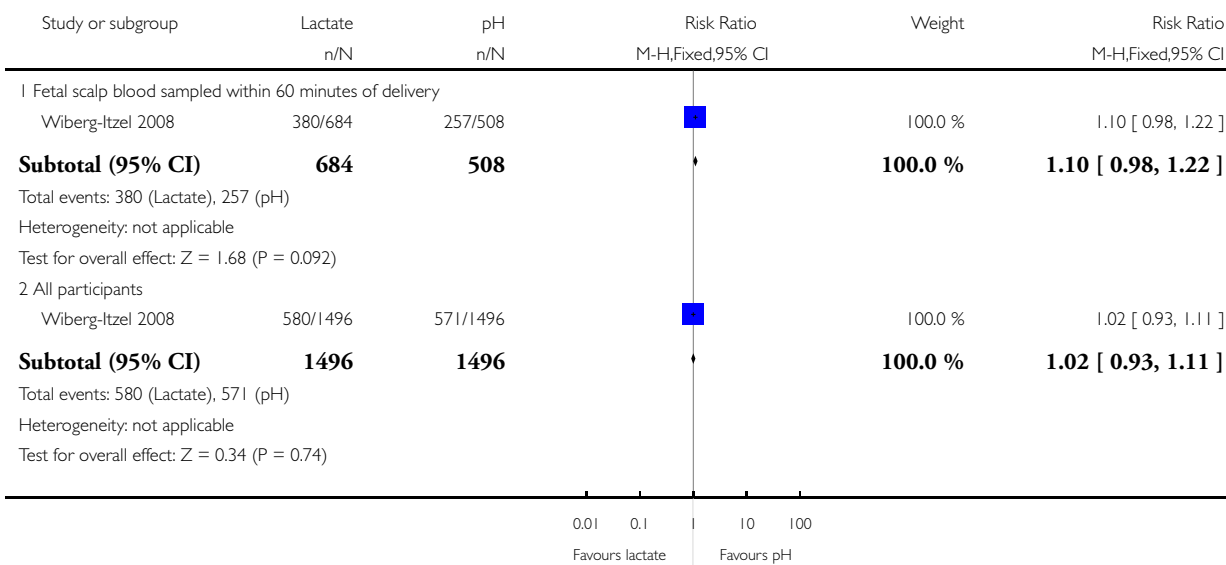
0.2   0.5   1   2   5

Favours lactate   Favours pH

Analysis 1.15. Comparison 1 Lactate versus pH analysis of fetal blood sampling, Outcome 15 Operative birth for non-reassuring fetal status.

Study or subgroup	Lactate n/N	pH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Fetal scalp blood sampled within 60 minutes of delivery					
Wiberg-Itzel 2008	380/684	257/508		100.0 %	1.10 [0.98, 1.22]
Subtotal (95% CI)	**684**	**508**		**100.0 %**	**1.10 [0.98, 1.22]**
Total events: 380 (Lactate), 257 (pH)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.68 (P = 0.092)					
2 All participants					
Wiberg-Itzel 2008	580/1496	571/1496		100.0 %	1.02 [0.93, 1.11]
Subtotal (95% CI)	**1496**	**1496**		**100.0 %**	**1.02 [0.93, 1.11]**
Total events: 580 (Lactate), 571 (pH)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.34 (P = 0.74)					

```
        0.01   0.1    1    10   100
        Favours lactate   Favours pH
```

ADDITIONAL TABLES

Table 1. Success rate of fetal blood sampling

	Lactate success	Lactate attempts	pH success	pH attempts
Westgren 1998	309	313	255	321
	(98.7%)		(79.4%)	

Total enrolled: n = 172 Lactate group; n = 169 pH group

WHAT'S NEW

Last assessed as up-to-date: 31 January 2015.

Date	Event	Description
11 June 2015	Amended	Added Acknowledgements statement.

HISTORY

Protocol first published: Issue 4, 2006

Review first published: Issue 3, 2010

Date	Event	Description
13 February 2015	New search has been performed	Search updated and one ongoing trial was added.
13 February 2015	New citation required but conclusions have not changed	The conclusions remain unchanged.
11 September 2012	Amended	Contact details updated.
11 November 2008	Amended	Converted to new review format. Contact details updated.

CONTRIBUTIONS OF AUTHORS

Christine East compiled the original review with considerable input from each of the co-authors. Christine East and Rosalind Lau updated the literature and methods sections and evaluated the search findings in the 2015 update of this review. All review authors read, advised on, and approved this review.

DECLARATIONS OF INTEREST

C East is the principal investigator for an ongoing randomised controlled trial that will be included in this review upon completion. Two review authors not involved in that trial will evaluate it for inclusion in the review and abstract the results.

SOURCES OF SUPPORT

Internal sources

- Department of Obstetrics and Gynaecology and Pregnancy Research Centre, Department of Perinatal Medicine, University of Melbourne, Royal Women's Hospital, Australia.
  - School of Women's and Children's Health, University of New South Wales, Royal Hospital for Women, Randwick, Australia.
  - Perinatal Research Centre, University of Queensland, Royal Brisbane & Women's Hospital, Australia.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The review methods have been updated to reflect current Cochrane Pregnancy and Childbirth Group methodologies. Rosalind Lau joined the authorship for the 2015 update of the review.

INDEX TERMS

Medical Subject Headings (MeSH)

Acidosis [diagnosis]; Biological Markers [blood]; Blood Specimen Collection [adverse effects; *methods]; Cardiotocography [methods]; Fetal Distress [blood; physiopathology]; Fetal Hypoxia [diagnosis]; Heart Rate, Fetal [*physiology]; Hydrogen-Ion Concentration; Labor, Obstetric; Lactic Acid [*blood]; Randomized Controlled Trials as Topic; Scalp [*blood supply]

MeSH check words

Female; Humans; Pregnancy