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Fetal and umbilical Doppler ultrasound in normal pregnancy

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Abstract

Background—One of the main aims of routine antenatal care is to identify the 'at risk' fetus in order to apply clinical interventions which could result in reduced perinatal morbidity and mortality. Doppler ultrasound study of umbilical artery waveforms helps to identify the compromised fetus in 'high-risk' pregnancies and, therefore, deserves assessment as a screening test in 'low-risk' pregnancies.

Objectives—To assess the effects on obstetric practice and pregnancy outcome of routine fetal and umbilical Doppler ultrasound in unselected and low-risk pregnancies.

Search methods—We searched the Cochrane Pregnancy and Childbirth Group Trials Register (May 2010).

Selection criteria—Randomised and quasi-randomised controlled trials of Doppler ultrasound for the investigation of umbilical and fetal vessels waveforms in unselected pregnancies compared to no Doppler ultrasound. Studies where uterine vessels have been assessed together with fetal and umbilical vessels have been included.

Data collection and analysis—Two authors independently assessed the studies for inclusion, assessed risk of bias and carried out data extraction.

Main results—We included five trials involving 14,185 women. The methodological quality of the trials was generally unclear because of insufficient data included in the reports.

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CONTRIBUTIONS OF AUTHORS Following discussions with Z Alfirevic (ZA), T Stampallija (TS) re-wrote the protocol section and G Gyte (GG) updated the methods section. TS and GG selected studies and extracted the data. TS entered the data into RevMan 2008 and GG checked the data entry. ZA drew the evidence together in the discussion and recommendations and made further comments.
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Routine fetal and umbilical Doppler ultrasound examination in low-risk or unselected populations did not result in increased antenatal, obstetric and neonatal interventions, and no overall differences were detected for substantive short term clinical outcomes such as perinatal mortality. There is no available evidence to assess the effect on substantive long term outcomes such as childhood neurodevelopment and no data to assess maternal outcomes, particularly psychological effects.

Authors' conclusions—Existing evidence does not provide conclusive evidence that the use of routine umbilical artery Doppler ultrasound, or combination of umbilical and uterine artery Doppler ultrasound in low-risk or unselected populations benefits either mother or baby. Future studies should be designed to address small changes in perinatal outcome, and should focus on potentially preventable deaths.

Medical Subject Headings (MeSH)

*Ultrasonography, Doppler; Perinatal Mortality; Pregnancy Outcome; Randomized Controlled Trials as Topic; Ultrasonography, Prenatal [*methods]; Umbilical Arteries [*ultrasonography]; Uterine Artery [ultrasonography]

MeSH check words

Female; Humans; Pregnancy

BACKGROUND

Description of the condition

One of the main aims of routine antenatal care is to identify the 'at risk' fetus in order to apply clinical interventions which could result in reduced perinatal morbidity and mortality (RCOG 1997). The routine use of a screening test should be based on proven clinical effectiveness, to avoid subjecting a large group of normal women to anxiety and inappropriate intervention with subsequent risk of iatrogenic morbidity and mortality.

In majority of cases the fetal death can be attributed to a 'known' cause such as maternal disorder (hypertension, diabetes and others), fetal pathology (congenital abnormalities, intrauterine growth restrictions (IUGR)), placental pathologies or intrapartum complications. The rate of unexplained fetal deaths decreased from 3.5 per 1000 total births in the 1960s to 1.1 to 1.9 per 1000 in the 1990s (Chibber 2005; Fretts 1992; Huang 2000). Unrecognised IUGR remains the main cause of unexplained stillbirths in otherwise uncomplicated pregnancy. Two recent studies identified the fetal growth restriction in 43% (Gardosi 2005) and 52% (Froen 2004) of unexplained stillbirth respectively, concluding that the IUGR was the strongest risk factor for an unexplained intrauterine death.

It is important to highlight that the fetal growth restriction is often confused with the concept of being small-for-gestational age. Some fetuses are constitutionally small and they do not have increased perinatal mortality or morbidity. Inability to distinguish easily between small but healthy fetuses and those who are failing to reach their growth potential has hampered attempts to find appropriate treatment for growth restriction (Soothill 1993). Growth

restricted fetuses are at increased risk of mortality and morbidity (Bernstein 2000; Fisk 2001). The serious morbidity includes intraventricular haemorrhage, bronchopulmonary dysplasia, necrotising enterocolitis, infection, pulmonary haemorrhage, hypothermia and hypoglycaemia (Fisk 2001). Early antenatal detection, treatment where appropriate, and timely delivery could minimise the risks significantly.

Description of the intervention

Doppler ultrasound technology is based on the Doppler shift, a physical principle of the change of ultrasound frequency when aimed at the moving object (e.g. red cell) (Campbell 1983; Fitzgerald 1977; Nelson 1988; Owen 2001). Different Doppler methods are used in obstetrics: continuous-wave, pulsed-wave, colour and power Doppler flow (Eik-Nes 1980; Mires 2000).

Doppler ultrasound examination can be performed as a part of a more detailed ultrasound assessment that includes fetal biometry and anatomical survey or as a separate ultrasound examination. Flow of the umbilical and fetal arteries is most often quantified either by pulsatility index or resistant index (Burns 1993; Nelson 1988). These indices reflect the down stream vascular resistance by quantifying the differences between the peak systolic and the enddiastolic velocity within blood vessels of interest in each cardiac cycle. A high ratio in umbilical artery indicates a high vascular impedance and possible feto-placental compromise. In extreme circumstance the blood flow at the end of diastole may be absent or even reversed (Figure 2 - we plan to insert a scan picture in a final version).

Initial Doppler studies have been restricted to the umbilical artery, but other fetal vessels have recently become a focus of interest including middle cerebral artery and ductus venosus.

How the intervention might work

Although stillbirths and fetal complications related to placental problems are rare in uncomplicated pregnancy, the impact is devastating. Current methods for the assessment of fetal well-being and detection of compromised fetus in the routine antenatal care include: symphysis fundal height measurement from the 24th week (Neilson 1998a; NICE 2008), fetal movements charts (Mangesi 2007) and antenatal cardiotocography (Pattison 1999). None of them, however, have proven ability to make an impact on perinatal mortality and morbidity.

Observational and longitudinal studies of Doppler ultrasound in unselected or low-risk pregnancies have raised doubts about its efficacy and authors have cautioned against its introduction into obstetric practice without supportive evidence from randomised trials (Beattie 1989; Goffinet 1997; Sijoms 1989). The relatively low incidence of preventable adverse perinatal outcomes in low-risk and unselected populations present a challenge in evaluating the clinical effectiveness of routine Doppler ultrasound, as large numbers are required to provide definitive evidence.

Why it is important to do this review

Any screening test has not only potential for benefit, but also for harm (Barnett 1995). Subjecting a large group of low-risk patients to a screening test with relatively high false positive rate is likely to cause anxiety and lead to inappropriate intervention and subsequent risk of iatrogenic morbidity and mortality.

Although the epidemiological studies and Cochrane review have found no correlation between the use of fetal Doppler ultrasound and adverse neurological outcome in childhood development, childhood malignancies and birth weight (Neilson 1998b; Salvesen 2007), some concern about the association between the left-handedness in males and exposure to Doppler ultrasound has been expressed (Kieler 2001; Kieler 2002; Salvesen 1999).

Considering that no recent studies have been done regarding the fetal exposure to Doppler ultrasound and the fact that the acoustic output of a modern equipment has increased (Barnett 2001; Duck 1991; Henderson 1997) indicates that Doppler ultrasound in obstetrics should be used only if of proven value (in terms of improved outcome, good specificity and sensitivity).

The continuous assessment of the evidence to provide the balanced view of effectiveness, safety and cost effectiveness is, therefore, essential. In this review, we will focus on fetal and umbilical Doppler ultrasound in low-risk and unselected pregnancies. There are other reviews on ‘Fetal and umbilical Doppler ultrasound in high-risk pregnancies’ (Alfirevic 2009) and on ‘Utero-placental Doppler ultrasound for improving pregnancy outcome’ (a Cochrane review in progress).

OBJECTIVES

To assess the effects of routine fetal and umbilical Doppler ultrasound, or a combination of uterine Doppler ultrasound and umbilical Doppler ultrasound, in unselected and low-risk pregnancies on obstetric practice and pregnancy.

A low-risk population is defined as a population where those considered at risk have been excluded. Criteria of ‘at risk’ are defined variably and this is taken into consideration.

In the context of this review ‘unselected’ pregnant population refers to a mixture of pregnant women with no identified risk factors and those who may have some risk factors but the trialists have not reported them separately.

METHODS

Criteria for considering studies for this review

Types of studies—All randomised controlled trials of routine fetal and umbilical Doppler ultrasound, or a combination of uterine Doppler ultrasound and umbilical Doppler ultrasound, in unselected or low-risk pregnancies. We included quasi-randomised trials, but planned to undertake sensitivity analysis by trial quality. Had we identified studies that were published as conference abstracts only, we would have tried to contact the authors for

further details. We would have included them but undertaken sensitivity analyses of trial quality (see Sensitivity analysis).

Types of participants—Pregnant women in both unselected and low-risk populations.

Types of interventions—Routine Doppler ultrasound of the fetal and umbilical artery circulation in pregnancy in unselected or low-risk populations. We included studies that considered the combination of utero-placental Doppler and fetal or umbilical Doppler in normal pregnancies in this review.

If appropriate, we performed stratified analyses of all outcome measures in the following comparisons:

1. all routine Doppler versus no Doppler/concealed Doppler examinations (i.e. caregivers not aware of results);
2. single Doppler measurement versus no Doppler/concealed Doppler examinations;
3. multiple Doppler measurement versus no Doppler/concealed Doppler examinations.

Types of outcome measures—We have selected outcome measures with the help of a proposed core data set of outcome measures (Devane 2007).

Primary outcomes:

1. Any perinatal death after randomisation.
2. Serious neonatal morbidity - composite outcome including hypoxic ischaemic encephalopathy, intraventricular haemorrhage, bronchopulmonary dysplasia, necrotising enterocolitis.

Secondary outcomes:

1. Stillbirth.
2. Neonatal death.
3. Any potentially preventable perinatal death after randomisation (excluding congenital malformations, chromosomal abnormalities, termination of pregnancy).
4. Fetal acidosis.
5. Apgar score less than seven at five minutes.
6. Caesarean section (both elective and emergency).
7. Elective caesarean section.
8. Emergency caesarean section.
9. Spontaneous vaginal birth.
10. Operative vaginal birth.

11. Induction of labour.
12. Neonatal resuscitation required.
13. Infant requiring intubation/ventilation.
14. Neonatal fitting/seizures.
15. Preterm birth (before 37 completed weeks of pregnancy).
16. Infant respiratory distress syndrome.
17. Meconium aspiration.
18. Neonatal admission to special care or intensive care unit, or both.
19. Infant birthweight.
20. Gestational age at birth.
21. Length of infant hospital stay.
22. Long-term infant/child neurodevelopmental outcome.
23. Women's views of care/satisfaction.

We have reported non-prespecified outcomes if we consider them to be important.

Search methods for identification of studies

Electronic searches—We have contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register (May 2010).

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

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL and MEDLINE, 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.

Searching other resources—We have looked for additional studies in the reference lists of the studies identified.

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We have not applied any language restrictions.

Data collection and analysis

The methodology for data collection and analysis was based on the *Cochrane Handbook of Systematic Reviews of Interventions* (Higgins 2009a).

Selection of studies—Two review authors have independently assessed for inclusion all the potential studies we identified as a result of the search strategy. We have resolved any disagreement through discussion; there was no need to consult the third author.

Data extraction and management—We have designed a form to extract data. Two review authors have extracted the data using the agreed form. We have resolved discrepancies through discussion. We have entered data into Review Manager software (RevMan 2008), and checked for accuracy. We did not contact authors of the included studies for additional information.

Assessment of risk of bias in included studies—Two review authors have independently assessed risk of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2009a). We have resolved any disagreement through discussion.

1) Sequence generation (checking for possible selection bias): We have described the methods used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We have assessed the methods as:

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

2) Allocation concealment (checking for possible selection bias): We have described the methods used to conceal the allocation sequence in sufficient detail and determine whether intervention allocation could have been foreseen in advance of, or during, recruitment.

We have assessed the methods as:

- adequate (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- inadequate (open random allocation; alternation; date of birth);
- unclear.

3) Blinding (checking for possible performance bias): We have described all the methods used, if any, to blind study participants and personnel from knowledge of which intervention

a participant received. We have also provided any information relating to whether the intended blinding was effective. Where blinding was not possible, we have assessed whether the lack of blinding was likely to have introduced bias. We have assessed blinding separately for different outcomes or classes of outcomes.

We have assessed the methods as:

- adequate, inadequate or unclear for participants;
- adequate, inadequate or unclear for personnel;
- adequate inadequate or unclear for outcome assessors.

4) Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations): We have described the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. We have stated whether attrition and exclusions were reported, the numbers (compared with the total randomised participants), reasons for attrition/exclusion where reported, and any re-inclusions in analyses which we undertook.

Had there been loss of data greater than 20% we would have considered whether this missing data might impact on outcomes acknowledging that with long-term follow up, complete data are difficult to attain.

5) Selective reporting bias: We have described how the possibility of selective outcome reporting bias was examined by us and what we found.

We have assessed the methods as:

- adequate (where it is clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review have been reported);
- inadequate (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
- unclear.

6) Other sources of bias: We have described any important concerns we have about other possible sources of bias.

We have assessed whether each study was free of other problems that could put it at risk of bias:

- yes;
- no;
- unclear.

7) Overall risk of bias: We have made explicit judgements about whether studies are at high risk of bias, according to the criteria given in the *Cochrane Handbook of Systematic Reviews of Interventions* (Higgins 2009a). With reference to (1) to (6) above, we have assessed the likely magnitude and direction of the bias and whether we considered it was likely to impact on the findings. We would have explored the impact of the level of bias through undertaking sensitivity analyses (*see* Sensitivity analysis) but there were insufficient high-quality studies.

Measures of treatment effect—Where there were multiple pregnancies, we have used the number of women who are randomised as the denominator for maternal outcomes, and the number of babies of women who are randomised as the denominator for neonatal outcomes.

We have also used as the denominator the number of babies of women who were randomised even though some babies could not have attained the outcome; for example, if there was a stillbirth then this baby would not have been able to attain the outcome of 'Admission to special care baby unit'.

None of the studies reported data on twins, with three studies specifically excluding multiple pregnancies (Davies 1992; Mason 1993; Whittle 1994). We would have contacted a statistician concerning how to deal with the non-independence of this data for multiple pregnancies had it been necessary.

Dichotomous data: For dichotomous data, we have presented results as summary risk ratio with 95% confidence intervals.

Continuous data: For continuous data, we have used the mean difference if outcomes were measured in the same way between trials. We have used the standardised mean difference to combine trials that measure the same outcome, but used different methods.

Unit of analysis issues—If there had been several time points for assessment of an outcome, we would have performed separate analyses. In studies including multiple pregnancies because of non-independence, we would have used cluster trial methods in these situations and consulted a statistician to help with the analyses.

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

For all outcomes, we have carried out analyses, as far as possible, on an intention-to-treat basis: i.e. we have attempted to include all participants randomised to each group in the analyses. 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 have assessed statistical heterogeneity in each meta-analysis using the T^2 (tau-squared), I^2 and Chi^2 statistics. We have regarded heterogeneity as substantial if T^2 was greater than zero and either I^2 was greater than 30% or

there was a low P-value (less than 0.10) in the Chi^2 test for heterogeneity. Where we found heterogeneity and used random-effects, we have reported the average risk ratio, or average mean difference or average standard mean difference.

Assessment of reporting biases—If there had been 10 or more studies in a meta-analysis, we would have investigated reporting biases (such as publication bias) using funnel plots. We would have assessed funnel plot asymmetry visually, and would have used formal tests for funnel plot asymmetry. For continuous outcomes, we would have used the test proposed by Egger 1997, and for dichotomous outcomes we would have used the tests proposed by Peters 2006. If we had detected asymmetry by any of these tests or by a visual assessment, we would have performed exploratory analyses to investigate it.

Had there been sufficient studies of high quality we would, where we have suspected reporting bias (*see* 'Selective reporting bias' above), have attempted to contact study authors asking them to provide missing outcome data. Where this was not possible, and the missing data were thought to introduce serious bias, we have explored the impact of including such studies in the overall assessment of results by a sensitivity analysis.

Data synthesis—We have carried out statistical analysis using the Review Manager software (RevMan 2008). We have used 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 sufficiently similar. If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity was detected, we have used random-effects analysis to produce an overall summary, if this was considered clinically meaningful. If an average treatment effect across trials was not clinically meaningful, we have not combined heterogeneous trials. If we used random-effects analyses, the results have been presented as the average treatment effect and its 95% confidence interval, the 95% prediction interval for the underlying treatment effect, and the estimates of T^2 and I^2 (Higgins 2009b).

Subgroup analysis and investigation of heterogeneity—We planned to carry out the following *a priori* subgroup analyses on all outcomes:

- umbilical Doppler ultrasound only or umbilical and uteroplacental Doppler ultrasound.

For fixed-effect meta-analyses, we would have conducted the planned subgroup analyses classifying whole trials by interaction tests as described by Deeks 2001. For random-effects meta-analyses, we would have assessed differences between subgroups by inspection of the subgroups' confidence intervals; non-overlapping confidence intervals indicate a statistically significant difference in treatment effect between the subgroups.

Sensitivity analysis—We were to carry out sensitivity analysis to explore the effect of trial quality for the primary outcomes in the review; however, there was only one study (Whittle 1994) of sufficient quality in terms of low risk of bias for sequence generation and concealment allocation although it did suffer from other potential bias (Figure 1). Where

there was risk of bias associated with a particular aspect of study quality (e.g. inadequate allocation concealment), we were to explore this by sensitivity analysis.

Publication bias: An assessment of publication bias was desired but considered inappropriate here as only five studies were identified, and it is generally recommended that 10 studies are required for publication bias assessments.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search—The search identified 20 publications, of which we have included five studies involving 14,185 women and 26 meta-analyses. We have excluded eight studies. For further details of trial characteristics, please refer to the tables of Characteristics of included studies and Characteristics of excluded studies.

Included studies—The five included studies were all undertaken in the 1990s. Three studies used fetal/umbilical vessels only (French Doppler 1997; Mason 1993; Whittle 1994). Two studies used both uterine vessels and umbilical vessels (Davies 1992; Newnham 1993). One study looked at a single assessment at 28 to 34 weeks (French Doppler 1997), three studies looked more than one assessment (Davies 1992; Mason 1993; Newnham 1993) and one study had a mixture of some women receiving a single assessment and others more than one assessment (Whittle 1994).

Excluded studies—We excluded five studies because they studied uterine Doppler ultrasound only and not fetal and umbilical Doppler or a combination of uterine plus fetal and umbilical Doppler (Ellwood 1997; Goffinet 2001; Snaith 2006; Subtil 2000; Subtil 2003). These studies will be assessed in a separate review on ‘Utero-placental Doppler ultrasound for improving pregnancy outcome’. We excluded two studies because the previous review authors had tried to contact these authors for information needed for studies to be included and had received no response (Gonsoulin 1991; Schneider 1992). We excluded one study because it had high risk of bias; we needed further information before being able to include it and it only reported one outcome relevant to the review (induction of labour) (Scholler 1993).

Risk of bias in included studies

We assessed risk of bias of each included study according to the *Cochrane Handbook of Systematic Reviews of Interventions* (Higgins 2009a) and summarised in Figure 1.

Allocation—Only one study had adequate sequence generation and allocation concealment (Whittle 1994), although the imbalance between the number of women allocated to the two groups (1642 to the intervention group and 1344 to the control group) would suggest a problem with the randomisation process. Two studies had adequate sequence generation but unclear allocation concealment (Mason 1993; Newnham 1993) and two studies had unclear sequence generation and allocation concealment (Davies 1992; French Doppler 1997).

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Blinding—None of the studies could be blinded for clinicians and only ones that had concealed versus revealed groups could be blinded for the women.

Incomplete outcome data—Four studies showed minimal loss of data either by withdrawal after randomisation or by loss to follow up less than 6% (Davies 1992; French Doppler 1997; Mason 1993; Newnham 1993). The fifth study reported no loss of outcome data (Whittle 1994).

Selective reporting—Since we did not assess the trial protocols of the included studies, we cannot comment on whether all the pre-specified outcomes are reported on.

Other potential sources of bias—Three studies appeared to be free from other potential biases (Davies 1992; French Doppler 1997; Newnham 1993) and for one study this seemed unclear (Mason 1993). The fifth study was assessed as having high risk of bias in that there was a considerable difference in the numbers of women allocated to the two groups (1642 and 1344) which probably indicates a problem with the randomisation (Whittle 1994). This was discussed and explained by the authors as "…due to secretarial error in preparation of the envelopes…previously used random numbers had been 'recycled' through the study." This was considered to be a possible high risk of bias in this study.

Effects of interventions

1) All routine Doppler ultrasound versus no Doppler ultrasound (five studies, 14,185 women)—Five studies addressed this comparison (Davies 1992; French Doppler 1997; Mason 1993; Newnham 1993; Whittle 1994).

Primary outcomes

1) Any perinatal death after randomisation: Due to the large heterogeneity for this outcome ($Tau^2 = 0.18$, Chi^2 P = 0.10, $I^2 = 51\%$;), we used a random-effects meta-analysis. The average risk ratio (RR) across studies was 0.85 (95% confidence interval (CI) 0.47 to 1.54; four studies, 11,190 women, Analysis 1.1), indicating that on average there is no statistically significant reduction identified in the risk of perinatal death when Doppler ultrasound is used. A prediction interval for the underlying relative risk in any future study is also very wide (95% prediction interval = 0.09 to 8.01), reflecting the large heterogeneity identified and the small number of studies.

Based on a single study, there was no significant difference identified in serious neonatal morbidity (RR 0.99, 95% CI 0.06 to 15.75; one study, 2016 woman, Analysis 1.2).

Secondary outcomes: We found no significant differences in either the average intervention effect estimate across studies where a random-effects meta-analysis was used, nor in the pooled estimate of the intervention effect from a fixed-effect meta-analysis for the whole range of the secondary outcomes (Analyses 1.3 to 1.21). These included Apgar scores less than seven at five minutes, caesarean section, operative vaginal births, spontaneous vaginal births, induction of labour, neonatal resuscitation and preterm birth.

When looking further into outcomes with substantive heterogeneity, we found the following.

- Stillbirths: there was no evidence of between-study heterogeneity ($Tau^2 = 0$). Overall, no effect was discernable (Analysis 1.3).
- Neonatal death: there was only one study assessing fetal vessels only, showing no statistically significant difference (French Doppler 1997) and two studies using a combination of fetal and utero-placental Doppler (Davies 1992; Newnham 1993) showing large heterogeneity (Analysis 1.4).
- Potentially preventable neonatal deaths: there was extremely large heterogeneity for this outcome and the average intervention effect across studies from a random-effects meta-analysis was not significant (average RR 0.82, 95% CI 0.15 to 4.67; three studies, 9395 babies, random effects ($Tau^2 = 1.87$, Chi^2 $P < 0.01$, $I^2 = 80\%$), Analysis 1.5). This was despite one subgroup appearing to make a difference.

In subgroup analysis with two studies that assessed Doppler ultrasound used only in fetal/umbilical vessels, the heterogeneity disappeared and, in a fixed-effect meta-analysis, there was a statistically significant reduction potentially preventable perinatal deaths (pooled RR 0.35, 95% CI 0.12 to 0.99; two studies, 6884 women, Analysis 1.5.1).

By contrast, in the one study that used a combination of fetal/umbilical vessels and uterine vessels Doppler assessment there was a statistically significant increase potentially preventable perinatal mortality (RR 3.95, 95% CI 1.32 to 11.77; one study, 2475 women, Analysis 1.5.2). Again, caution is strongly advised here as these are subgroup analyses of secondary outcomes containing small number of studies.

- Preterm birth: the subgroup analysis failed to provide an explanation of significant heterogeneity for this outcome. (Analysis 1.17).

2) Single Doppler ultrasound assessment versus no Doppler ultrasound (one study, 3898 women)—One study addressed this comparison (French Doppler 1997).

Primary outcomes: Based on a single study, there was no statistically significant difference identified in any perinatal death after randomisation (RR 0.33, 95% CI 0.09 to 1.23; one study, 3898 women, Analysis 2.1). Serious neonatal morbidity was not assessed.

Secondary outcomes: There were no statistically significant differences identified in any of the secondary outcomes which were assessed (Graphs 2.3 to 2.21).

3) Multiple Doppler ultrasound assessments versus no Doppler ultrasound (three studies, 7301 women)—Three studies addressed this comparison (Davies 1992; Mason 1993; Newnham 1993). One study combined the data from women having one assessment and some having more than one assessment (Whittle 1994); these data are only included in Comparison 1 - ‘All routine Doppler ultrasound versus no Doppler routine ultrasound’.

Primary outcomes: Perinatal deaths showed large heterogeneity ($Tau^2 = 0.13$, Chi^2 $P = 0.14$, $I^2 = 49\%$). A random-effects meta-analysis showed that the average intervention effect across studies was not statistically significant (average RR 1.00, 95% CI: 0.55 to 1.80; three

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studies, 7292 women, Analysis 3.1); the prediction interval for the intervention effect in any future study was an even wider 95% CI. From a single study, for the serious neonatal morbidity outcome the intervention effect was again clearly not significant (RR 0.99, 95% CI 0.06 to 15.75; one study, 2016 women, Analysis 3.2) (Mason 1993).

Secondary outcomes: There were no statistically significant differences identified in any of the secondary outcomes which were assessed (Analyses 3.3 to 3.21).

DISCUSSION

This review includes data from 14,185 women from five studies (Davies 1992; French Doppler 1997; Mason 1993; Newnham 1993; Whittle 1994). No differences in perinatal mortality were demonstrated, although there was considerable heterogeneity and the number of participants remains too small to detect small but potentially significant changes in perinatal outcome (Chalmers 1989).

The pooled data from two studies using umbilical artery Doppler showed a significant reduction in potentially preventable perinatal mortality (French Doppler 1997; Whittle 1994). However, the results from Davies suggested that routine Doppler ultrasound in unselected pregnancies assessing both umbilical and uterine artery Doppler may do more harm than good, but authors acknowledged that increase in perinatal deaths was an unexpected finding which may have occurred by chance (Davies 1992). Furthermore, they state that the study was not designed to test the ability of routine Doppler ultrasound examinations to reduce perinatal mortality, as a much larger number of women would need to be included in a such a trial to test this hypothesis.

In the Perth study (Newnham 1993), there was an unexpected finding of a greater risk of intrauterine growth restriction in the serial ultrasound and Doppler examination group (i.e. the intensive monitoring group). The authors report “A written diagnosis of intrauterine growth restriction was observed more frequently in the medical records of women in the intensive group than in the regular group (relative risk 2.07; 95% CI 1.34 to 3.21)” but they do not provide data in a format in which we can include in our review (we have written to the authors and *Lancet* to try to obtain this data). The authors state that multiple logistic regression analyses indicated that this was probably not a chance effect, and it is possible that frequent exposure to ultrasound may have influenced fetal growth. This finding was not associated with increased perinatal morbidity and mortality, and follow up of these children at one year of age found that the difference in growth was no longer discernible (Newnham 1996). This is, however, a further finding which suggests more harm than good, and the authors stress the need for further investigation of the effects of frequent ultrasound exposure on fetal growth.

AUTHORS’ CONCLUSIONS

Implications for practice

Existing data do not provide conclusive evidence that the use of routine umbilical artery Doppler ultrasound, or combination of umbilical and uterine artery Doppler ultrasound in

low-risk or unselected populations benefits either mother or baby. At present, Doppler ultrasound examination should be reserved for use in high-risk pregnancies (Alfirevic 2009).

Implications for research

If there is to be future research into fetal and umbilical Doppler ultrasound examination in low-risk or unselected populations, a large trial with adequate power to test hypotheses related to perinatal outcome is required. Trials should focus on potentially preventable deaths and inclusion criteria should reflect that. It would be also important to include assessment of neurodevelopment assessment of maternal outcomes and psychological effects on mother.

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Internal sources

- The University of Liverpool, UK.

External sources

- National Institute for Health Research, UK.

NIHR NHS Cochrane Collaboration Programme Grant Scheme award for NHS-prioritised centrally-managed, pregnancy and childbirth systematic reviews: CPGS02

CHARACTERISTICS OF STUDIES

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

Davies 1992

Methods	Randomised controlled trial. Individual women.
Participants	Inclusion criteria • Pregnant women, with singleton pregnancies, at 19-22 weeks pregnant. • Unselected. • Low- and high-risk pregnancies: high risk 189 in Doppler group and 192 in control group. • 2600 women - 79% of eligible population. Exclusion criteria • Multiple pregnancies.
Interventions	Experimental intervention: Doppler ultrasound of umbilical-artery and uterine-artery

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	• Multiple assessments at 20 and 32 weeks. • Women with low-risk pregnancies had Doppler at booking and 32 weeks. Low risk for small-for-gestational age or other compromised infant. • Women at high risk had ultrasound every month. High risk = women identified before entry into trial by: pre-existing medical condition, e.g. hypertension, diabetes, previous small for gestational age baby, previous stillbirth pr neonatal death, hypertension (BP > 140/90 mmHg) in previous pregnancy or at booking, smoking > 10a day. • Any women in low-risk group who had abnormal Doppler was managed subsequently as high risk. If subsequent examination was normal the woman transferred back to low-risk group. • Clinician could have Doppler at other times as requested. • N = 1246. Control/Comparison intervention: no Doppler ultrasound • Intended that women should not have Doppler US at anytime in pregnancy. • Normal AN care with no Doppler. • N = 1229. Multiple estimations were at 20 and 32 weeks' gestation.
Outcomes	Number of days of antenatal admission; number of CTG recordings and US scans; gestational age at birth; mode of birth; birthweight; Apgar scores; need for resuscitation (intermittent positive pressure ventilation either via a mask or endotracheal tube); admission to NICU; fetal and neonatal outcomes The study was not designed to test the ability of Doppler ultrasound to reduce PNM, so the fact that there were more preventable deaths in the Doppler group is likely to be due to chance. However, the authors do theorise that it is possible that a woman's knowledge of a normal result may have resulted in her taking less notice of symptoms that might otherwise have resulted in a review of fetal well-being
Notes	London (UK) 1992 study in previous version of the review (Bricker 2007).

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No information provided.
Allocation concealment?	Unclear	"…cards in sealed opaque envelopes…." no mention of numbers sequence. The handbook says: "…sequentially numbered opaque sealed envelopes…" and that to be really sure "Envelopes were sequentially numbered and opened sequentially only after participants details were written on the envelope"
Incomplete outcome data addressed? All outcomes	Yes	Describe any loss of participants to follow up at each data collection point. Describe any exclusion of participants after randomisation: • 125 women (4.8%) were excluded because: 106 gave birth elsewhere; 8 were randomised then found to have missed abortion; 2 multiple pregnancies; or because randomisation care (7), Doppler data (1) or hospital notes (1) went missing. Demographics similar to rest of study population . Was the analysis ITT? If not has the data been able to be re-included? • Loss was small and unlikely to impact on outcomes.

Free of selective reporting?	Unclear	We did not assess the trial protocol.
Free of other bias?	Yes	If the study was stopped early, explain the reasons: • Not stopped earlier. Describe any baseline in balance: • "Women in the Doppler and the control groups did not differ in their demographic details (Table 1)". So assessed by age, weight at booking, ethnic origins, nulliparous, smoking, shared antenatal care, high risk. • 15 (1.2%) of the 1229 women in the control group had Doppler. Describe any differential diagnosis: • Seems fine.

French Doppler 1997

Methods	Multicentre randomised controlled trial. Individual women. Randomisation in blocks of 4
Participants	Inclusion criteria • Women attending routine AN visit between 28-34 weeks who had a normal US scan (fetal biometry above 10th centile of reference curve). • N = 4187 randomised with 3898 analysed. Exclusion criteria • Women who had indications for Doppler at last 2nd trimester appointment, e.g. medical history of hypertension, diabetes, previous fetal death, IUGR, hypertensive disorder of pregnancy, treatment with beta agonists, insulin-dependent diabetes. • Women who at their last second trimester appointment had indications for umbilical Doppler. • Women who had undergone an umbilical Doppler before 28 weeks for any reason whatever.
Interventions	Experimental intervention: umbilical Doppler ultrasound • Single assessment at 28-34 weeks. • Umbilical Doppler US on day of randomisation, immediately after ultrasound scan monitoring fetal growth. • All further tests performed at clinicians' request according to standard practices in their AN clinics. • N = 2099 with 1950 analysed. Control/comparison intervention: no Doppler ultrasound • No Doppler US on day of randomisation. Access to Doppler studies was allowed on obstetrician's request. • N = 2088 with 1948 analysed. Single estimation between 28-34 weeks.
Outcomes	• AN consultations; days of AN hospitalisation; CTG; ultrasound and Doppler tests.

- Peri and neonatal deaths; fetal distress; Apgars; neonatal resuscitation; neonatal transfer; birthweight; SGA.
- Disorders occurring after randomisation e.g. PIH; pre-eclampsia, uterine bleeding, oligohydramnios, suspected IUGR, abnormal CTG patterns.

Notes	France 1997 study in previous version of the review (Bricker 2007). Authors did report umbilical cord pH < 7.20 but only on a subsample of women and the groups were not randomised groups. Findings were: Doppler 188 / 757 (24.8%) and no Doppler 181/761 (23.8%)

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"…randomly divided…"
Allocation concealment?	Unclear	• "The randomisation procedure using sealed envelopes was standard in each centre and was carried out by the ultrasonographer immediately after verification of the inclusion criteria and performance of the standard ultrasound scan. The envelopes were prepared centrally and were sent to each centre consecutively numbered." No 'opaque' mentioned. • "The randomisation sequence was verified in two ways. After the end of the study every centre was asked to send back the enveloped that had not been used. It was also checked that the envelopes were used in ascending order." • Blocks of 4 means that the sequence may have been predicted for at least ¼ women.
Incomplete outcome data addressed? All outcomes	Yes	Describe any loss of participants to follow up at each data collection point: • 174 women lost to follow up. Doppler; 25 (1.2%) lost just after randomisation and 66 (3.3%) data were not available for analysis. No Doppler: 27 (1.3%) lost just after randomisation and 56 (2.8%) data were not available for analysis. Describe any exclusion of participants after randomisation: • 115 were excluded (58 (2.8%) in Doppler and 57 (2.7%) in No Doppler. All these women were from 3 centres where randomisation was not undertaken properly in that envelopes were not used in ascending order. Was the analysis ITT? If not has the data been able to be re-included? • Appears to be ITT and losses are only small % and evenly distributed between the 2 groups.
Free of selective reporting?	Unclear	We have not assessed the trial protocol.
Free of other bias?	Yes	There appear to be no other biases.

Mason 1993

Methods	Randomised controlled trial, individual women.
Participants	Inclusion criteria

	• Primagravida women with a negative medical and gynaecological history and physical examinations were identified at booking clinic. • N = 2145 were randomised but 2025 analysed. Exclusion criteria • Twin pregnancies.
Interventions	Experimental intervention: umbilical artery Doppler ultrasound • Multiple at 28 weeks and again at 34 weeks. • N = 1073. Control/comparison intervention: routine care, no Doppler ultrasound • Clinician could request Doppler if felt indicated. 3.9% (42 women) were referred for Doppler US. • N = 1072. Multiple estimations were at 28 and 34 weeks' gestation.
Outcomes	Main outcome: obstetric intervention rate, short-term neonatal morbidity
Notes	Leeds (UK) 1993 study in previous version of the review (Bricker 2007).

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"Tables of random numbers were used to generate each random permuted block."
Allocation concealment?	Unclear	"…opaque numbered envelopes which were opened on the fetal assessment unit by a radiographer who had no personal knowledge of the women or her history." No mention if enveloped were sealed.
Incomplete outcome data addressed? All outcomes	Yes	Describe any loss of participants to follow up at each data collection point: • 53/1073 (5%) women in Doppler were lost to follow up. • 67/1072 (6%) women in No Doppler were lost to follow up. Describe any exclusion of participants after randomisation: • 5 sets of twins were excluded from Doppler and 4 from control.
Free of selective reporting?	Unclear	We did not assess the trial protocol.
Free of other bias?	Unclear	If the study was stopped early, explain the reasons: • Not stopped early for benefit or harm. Describe any baseline in balance: • Balanced according to: age, weight before pregnancy, primapara, educational level, gestational age at inclusion, biparietal diameter, transverse abdominal diameter. • 863 (80%) of those offered Doppler attended for assessment. In the control group 42 (3.9%) women were referred for a total of 191 Doppler assessments. • The relatively lower compliance at 34 weeks than at 28 weeks was probably related to the hospital policy of a routine visit at 28 weeks but not at 34 weeks. Describe any differential diagnosis:

- Seems ok.

Newnham 1993

Methods	Randomised controlled trial. Individual women.
Participants	Inclusion criteria • Pregnant women, gestational age 16-20 weeks. Sufficient proficiency in English, expected to give birth in hospital and expected to remain in the Western Australia for childhood follow up. • N = 2834 with data available on 2801.
Interventions	Experimental intervention: umbilical and uterine Doppler US - intense monitoring group • The intense group had ultrasound imaging and Doppler flow studies at approximately 18 weeks and then at 24, 28, 34 and 38 weeks. • Umbilical artery and arcuate artery within the placental vascular bed. • N = 1415. Control/Comparison intervention: no Doppler US - regular group • Ultrasound scan at 18 weeks and any other tests only done at request of clinician. • N = 1419. Multiple estimations were at 18, 24, 28, 34 and 38 weeks' gestation
Outcomes	Induction of labour; caesarean section; ultrasound information
Notes	Perth (Aus) 1993 study in previous version of the review (Bricker 2007). Authors report an increase in IUGR with the Doppler group (RR 2.07, 95% CI 1.34 to 3.21) but do not provide the data for us to enter into RevMan. They report "Multiple logistic regression analyses showed that the increased proportion of growth-restricted fetuses in the intensive arm was not due to a chance effect from differential clustering within the two groups…" though they go on to say that while this may have been a chance finding, it is possible that frequent exposure to ultrasound may have influenced fetal growth. This finding was not associated with increased perinatal morbidity and mortality, and follow up of these children at 1 year of age found that the difference in growth was no longer discernible. We are trying to contact the authors and are writing to the journal to seek further data

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"…computer generated random numbers…"
Allocation concealment?	Unclear	• "..the woman was allocated to a group by a sealed-envelope technique prepared in blocks of 20…" • Suggest this is unclear because no mention of sequentially numbered envelopes not of their needing to be opaque.
Incomplete outcome data addressed? All outcomes	Yes	Describe any loss of participants to follow up at each data collection point: • 13/1415 (1%) in Doppler and 20/1419 (1%) in no Doppler. Describe any exclusion of participants after randomisation:

		• Appeared to be none. • 66 (2.3%) multiple pregnancies excluded but we think before randomisation. Was the analysis ITT? If not has the data been able to be re-included? • Appears to be ITT.
Free of selective reporting?	Unclear	We did not assess the trial protocol.
Free of other bias?	Yes	If the study was stopped early, explain the reasons: • Not stopped early for benefit or harm. Describe any baseline in balance: • Groups similar in terms of: age, height, weight, marital status, race, parity, poor obstetric history and smoking. • 114 (intensive 50 and regular 64) women delivered in other hospitals and their outcomes were still assessed. Describe any differential diagnosis: • Seems ok.

Whittle 1994

Methods	Randomised controlled trial. Individual women.
Participants	Inclusion criteria • Unselected population. • Women attending the AN before 26 weeks' gestation, there was no attempt at selection, so women were eligible for inclusion, regardless of whether they had high-risk features). Exclusion criteria • Multiple pregnancies.
Interventions	Experimental intervention: umbilical Doppler US revealed • Umbilical artery systolic/diastolic ratio revealed. • Doppler US made available from 26 to 30 weeks (1^{st} window) and 34 to 36 weeks (2^{nd} window). • N = 1642. Control/Comparison intervention: no Doppler • Doppler concealed. • N = 1344. Multiple estimations were at 26-30 weeks and 34-36 weeks. Of the 2986 women in the study, 1386 underwent examination at both gestational windows, 1056 at only the first and 544 at only the second

Outcomes	Antenatal complications; antenatal admissions; day care visits; elective delivery; elective CS; CS in labour; CS for FD; birth < 32 weeks; Apgar scores; small for dates; admission to SCBU; ventilations; stillbirth	
Notes	Glasgow (UK) 1994 study in previous version of the review (Bricker 2007).	
Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	"the order was generated by random-number tables."
Allocation concealment?	Yes	"sealed opaque envelopes" "numbered."
Incomplete outcome data addressed? All outcomes	Unclear	Describe any loss of participants to follow up at each data collection point: • No dropouts (in comment). Describe any exclusion of participants after randomisation: • Not specified. Was the analysis ITT? If not has the data been able to be re-included?
Free of selective reporting?	Unclear	We did not assess the trial protocol.
Free of other bias?	No	If the study was stopped early, explain the reasons: • Not stopped earlier. Describe any baseline in balance: • Numbers of women in each group were not similar - see below. Groups were similar for parity and gestational age. The difference in age was small 27.9 vs 27.2 but it was statistically significant. There were more abnormal Doppler at the first window (26 to 30 weeks) namely 33 for revealed and 148 for concealed but similar numbers at the 2nd window (34-36 weeks) namely 69 for revealed and 66 for concealed. Describe any differential diagnosis: • Groups were well matched except for abnormal Doppler at first window. "It is possible that this may have occurred through unintentionally less persistent attempts to obtain a normal waveform in the concealed group than in the revealed group. If this did occur, however, one would have expected to see evidence of the same trend at the second screen, and this was not so." Also: • The numbers in each group were not similar (1642 vs 1344) suggesting a problem with the randomisation. The authors also noticed this and reported "…due to secretarial error in preparation of the envelopes…previously used random numbers had been 'recycled' through the study".

AN: antenatal

BP: blood pressure

CTG: cardiotocography

FD:

ITT: intention to treat

IUGR: intrauterine growth restriction

NICU: neonatal intensive care unit

PIH: pregnancy-induced hypertension

PNM: perinatal mortality

SCBU: special care baby unit

SGA: small-for-gestational age

US: ultrasound

VS: versus

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

Study	Reason for exclusion
Ellwood 1997	Trial studied uterine Doppler ultrasound and not fetal and umbilical
Goffinet 2001	Trial studied uterine Doppler ultrasound and not fetal and umbilical
Gonsoulin 1991	Conference abstract - not clear whether high-risk/low-risk/unselected pregnancies, and no data suitable for inclusion. Further details were sought from the authors by the authors of the previous version of this review (L Bricker and JP Neilson), without success.
Schneider 1992	Conference abstract in English language identified - unexplained difference in numbers (250 vs 329) in Doppler vs control groups suggesting allocation bias. The definitive publication after translation from German did not explain this difference and failed to outline the trial methodology
Scholler 1993	This study was translated from German for us. It was a quasi RCT of 211 women undergoing Doppler ultrasound vs no Doppler ultrasound. It was excluded for a combination of the following reasons: the only outcome relevant to our review was induction of labour; the study had high risk of bias being a quasi RCT; further information was needed from the authors before these data could be included. Data reported for induction of labour: Doppler group 37/108 and no Doppler group 41/103
Snaith 2006	Trial studied uterine Doppler ultrasound and not fetal and umbilical
Subtil 2000	Trial studied uterine Doppler ultrasound and not fetal and umbilical
Subtil 2003	Trial studied uterine Doppler ultrasound and not fetal and umbilical

RCT: randomised controlled trial

vs: versus

DATA AND ANALYSES

Comparison 1

All routine Doppler ultrasound versus no Doppler ultrasound

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Any perinatal death after randomisation	4	11190	Risk Ratio (IV, Random, 95% CI)	0.85 [0.47, 1.54]
1.1 Fetal/umbilical vessels only	2	5914	Risk Ratio (IV, Random, 95% CI)	0.51 [0.20, 1.29]
1.2 Fetal/umbilical vessels + uterine artery	2	5276	Risk Ratio (IV, Random, 95% CI)	1.06 [0.47, 2.38]
2 Serious neonatal morbidity	1	2016	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.06, 15.75]
2.1 Fetal/umbilical vessels only	1	2016	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.06, 15.75]
2.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
3 Stillbirth	4	12160	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.32, 1.97]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Fetal/umbilical vessels only	2	6884	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.12, 0.95]
3.2 Fetal/umbilical vessels + uterine artery	2	5276	Risk Ratio (M-H, Random, 95% CI)	1.41 [0.44, 4.46]
4 Neonatal death	3	9174	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.09, 5.23]
4.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Random, 95% CI)	0.25 [0.03, 2.23]
4.2 Fetal/umbilical vessels + uterine artery	2	5276	Risk Ratio (M-H, Random, 95% CI)	1.44 [0.04, 54.93]
5 Potentially preventable perinatal death	3	9359	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.15, 4.67]
5.1 Fetal/umbilical vessels only	2	6884	Risk Ratio (M-H, Random, 95% CI)	0.35 [0.12, 0.99]
5.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Random, 95% CI)	3.95 [1.32, 11.77]
6 Fetal acidosis	1	1518	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.87, 1.25]
6.1 Fetal/umbilical vessels only	1	1518	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.87, 1.25]
6.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
7 Apgar score < 7 at 5 minutes	4	11375	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.56, 1.39]
7.1 Fetal/umbilical vessels only	3	8900	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.47, 1.29]
7.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	1.48 [0.53, 4.14]
8 Caesarean section (elective and emergency)	2	6373	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.85, 1.13]
8.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.84, 1.16]
8.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.74, 1.29]
9 Elective caesarean section	4	11375	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.87, 1.18]
9.1 Fetal/umbilical vessels only	3	8900	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.87, 1.23]
9.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.70, 1.28]
10 Emergency caesarean section	2	6373	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.74, 1.18]
10.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.71, 1.17]
10.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [0.52, 2.59]
11 Spontaneous vaginal birth	2	6373	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.96, 1.02]
11.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.94, 1.02]
11.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.95, 1.06]
12 Operative vaginal birth	2	6884	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.96, 1.12]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12.1 Fetal/umbilical vessels only	2	6884	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.96, 1.12]
12.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
13 Induction of labour	4	11190	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.97, 1.12]
13.1 Fetal/umbilical vessels only	2	5914	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.97, 1.22]
13.2 Fetal/umbilical vessels + uterine artery	2	5276	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.93, 1.10]
14 Neonatal resuscitation	2	6373	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.84, 1.24]
14.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.80, 1.27]
14.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.74, 1.52]
15 Infant intubation/ventilation	1	2986	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.54, 1.81]
15.1 Fetal/umbilical vessels only	1	2986	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.54, 1.81]
15.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
16 Neonatal seizures/fits	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
16.1 Fetal/umbilical vessels only	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
16.2 Fetal/umbilical vessels + uterine artery	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
17 Preterm birth (before 37 weeks)	4	12162	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.87, 1.18]
17.1 Fetal/umbilical vessels only	2	6884	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.81, 1.29]
17.2 Fetal/umbilical vessels + uterine artery	2	5278	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.83, 1.24]
18 Infant respiratory distress syndrome	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
18.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
18.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
19 Meconium aspiration	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
19.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
19.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
20 Neonatal admission to SCBU/NICU	3	7477	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.84, 1.17]
20.1 Fetal/umbilical vessels only	2	5002	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.82, 1.18]
20.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.67, 1.53]
21 Women’s views/satisfaction	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
21.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
21.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
22 Birthweight	2	5914	Mean Difference (IV, Fixed, 95% CI)	−17.55 [−42.23, 7.13]
22.1 Fetal/umbilical vessels only	2	5914	Mean Difference (IV, Fixed, 95% CI)	−17.55 [−42.23, 7.13]
22.2 Fetal/umbilical vessels + uterine artery	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
23 Gestational age at birth	2	5914	Mean Difference (IV, Fixed, 95% CI)	−0.08 [−0.16, −0.00]
23.1 Fetal/umbilical vessels only	2	5914	Mean Difference (IV, Fixed, 95% CI)	−0.08 [−0.16, −0.00]
23.2 Fetal/umbilical vessels + uterine artery	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable

Comparison 2

Single Doppler ultrasound assessment versus no Doppler ultrasound

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Any perinatal death after randomisation	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.09, 1.23]
1.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.09, 1.23]
1.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
2 Serious neonatal morbidity	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
2.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
2.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
3 Stillbirth	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.40 [0.08, 2.06]
3.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.40 [0.08, 2.06]
3.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
4 Neonatal death	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.25 [0.03, 2.23]
4.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.25 [0.03, 2.23]
4.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
5 Potentially preventable perinatal death	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.06, 1.37]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.06, 1.37]
5.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
6 Fetal acidosis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
6.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
6.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
7 Apgar score < 7 at 5 minutes	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.38, 2.66]
7.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.38, 2.66]
7.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
8 Caesarean section (elective and emergency)	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.84, 1.16]
8.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.84, 1.16]
8.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
9 Elective caesarean section	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.84, 1.34]
9.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.84, 1.34]
9.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
10 Emergency caesarean section	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.71, 1.17]
10.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.71, 1.17]
10.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
11 Spontaneous vaginal birth	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.94, 1.02]
11.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.94, 1.02]
11.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
12 Operative vaginal birth	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.95, 1.26]
12.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.95, 1.26]
12.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
13 Induction of labour	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.99, 1.33]
13.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.99, 1.33]
13.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
14 Neonatal resuscitation	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.80, 1.27]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.80, 1.27]
14.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
15 Infant intubation/ventilation	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
15.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
15.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
16 Neonatal seizures/fits	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
16.1 Fetal/umbilical vessels only	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
16.2 Fetal/umbilical vessels + uterine artery	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
17 Preterm birth (before 37 weeks)	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [0.86, 1.69]
17.1 Fetal/umbilical vessels only	1	3898	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [0.86, 1.69]
17.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
18 Infant respiratory distress syndrome	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
18.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
18.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
19 Meconium aspiration	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
19.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
19.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
20 Neonatal admission to SCBU/NICU	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
20.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
20.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
21 Women’s views/satisfaction	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
21.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
21.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
22 Birthweight	1	3898	Mean Difference (IV, Fixed, 95% CI)	−14.0 [−42.94, 14.94]
22.1 Fetal/umbilical vessels only	1	3898	Mean Difference (IV, Fixed, 95% CI)	−14.0 [−42.94, 14.94]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
22.2 Fetal/umbilical vessels + uterine artery	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
23 Gestational age at birth	1	3898	Mean Difference (IV, Fixed, 95% CI)	−0.10 [−0.19, −0.01]
23.1 Fetal/umbilical vessels only	1	3898	Mean Difference (IV, Fixed, 95% CI)	−0.10 [−0.19, −0.01]
23.2 Fetal/umbilical vessels + uterine artery	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable

Comparison 3

Multiple Doppler ultrasound assessments versus no Doppler ultrasound

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Any perinatal death after randomisation	3	7292	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.55, 1.80]
1.1 Fetal/umbilical vessels only	1	2016	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.21, 2.93]
1.2 Fetal/umbilical vessels + uterine artery	2	5276	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.47, 2.38]
2 Serious neonatal morbidity	1	2016	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.06, 15.75]
2.1 Fetal/umbilical vessels only	1	2016	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.06, 15.75]
2.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
3 Stillbirth	2	5276	Risk Ratio (M-H, Random, 95% CI)	1.41 [0.44, 4.46]
3.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Random, 95% CI)	Not estimable
3.2 Fetal/umbilical vessels + uterine artery	2	5276	Risk Ratio (M-H, Random, 95% CI)	1.41 [0.44, 4.46]
4 Neonatal death	2	5276	Risk Ratio (M-H, Random, 95% CI)	1.44 [0.04, 54.93]
4.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Random, 95% CI)	Not estimable
4.2 Fetal/umbilical vessels + uterine artery	2	5276	Risk Ratio (M-H, Random, 95% CI)	1.44 [0.04, 54.93]
5 Potentially preventable perinatal death	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	3.95 [1.32, 11.77]
5.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
5.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	3.95 [1.32, 11.77]
6 Fetal acidosis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
6.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
6.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7 Apgar score < 7 at 5 minutes	2	4491	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.48, 1.80]
7.1 Fetal/umbilical vessels only	1	2016	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.27, 1.60]
7.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	1.48 [0.53, 4.14]
8 Caesarean section (elective and emergency)	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.74, 1.29]
8.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
8.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.74, 1.29]
9 Elective caesarean section	2	4491	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.70, 1.16]
9.1 Fetal/umbilical vessels only	1	2016	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.49, 1.29]
9.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.70, 1.28]
10 Emergency caesarean section	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [0.52, 2.59]
10.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
10.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [0.52, 2.59]
11 Spontaneous vaginal birth	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.95, 1.06]
11.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
11.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.95, 1.06]
12 Operative vaginal birth	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
12.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
12.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
13 Induction of labour	3	7292	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.93, 1.09]
13.1 Fetal/umbilical vessels only	1	2016	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.83, 1.21]
13.2 Fetal/umbilical vessels + uterine artery	2	5276	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.93, 1.10]
14 Neonatal resuscitation	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.74, 1.52]
14.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
14.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.74, 1.52]
15 Infant intubation/ventilation	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
15.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
15.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
16 Neonatal seizures/fits	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
16.1 Fetal/umbilical vessels only	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
16.2 Fetal/umbilical vessels + uterine artery	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
17 Preterm birth (before 37 weeks)	3	8264	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.82, 1.15]
17.1 Fetal/umbilical vessels only	1	2986	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.64, 1.21]
17.2 Fetal/umbilical vessels + uterine artery	2	5278	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.83, 1.24]
18 Infant respiratory distress syndrome	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
18.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
18.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
19 Meconium aspiration	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
19.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
19.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
20 Neonatal admission to SCBU/NICU	2	4491	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.71, 1.34]
20.1 Fetal/umbilical vessels only	1	2016	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.56, 1.52]
20.2 Fetal/umbilical vessels + uterine artery	1	2475	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.67, 1.53]
21 Women’s views/satisfaction	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
21.1 Fetal/umbilical vessels only	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
21.2 Fetal/umbilical vessels + uterine artery	0	0	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
22 Birthweight	1	2016	Mean Difference (IV, Fixed, 95% CI)	−27.0 [−74.23, 20.23]
22.1 Fetal/umbilical vessels only	1	2016	Mean Difference (IV, Fixed, 95% CI)	−27.0 [−74.23, 20.23]
22.2 Fetal/umbilical vessels + uterine artery	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
23 Gestational age at birth	1	2016	Mean Difference (IV, Fixed, 95% CI)	−0.02 [−0.19, 0.15]
23.1 Fetal/umbilical vessels only	1	2016	Mean Difference (IV, Fixed, 95% CI)	−0.02 [−0.19, 0.15]
23.2 Fetal/umbilical vessels + uterine artery	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable

HISTORY

Protocol first published: Issue 2, 1999

Review first published: Issue 2, 2000

Date	Event	Description
6 November 2008	Amended	Converted to new review format.
5 February 2007	Amended	Review withdrawn from publication.
14 January 2000	New citation required and conclusions have changed	Substantive amendment

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We updated the Background and Methods sections and changed the title from ‘Routine Doppler ultrasound in normal pregnancy’ to ‘Fetal and umbilical Doppler ultrasound in normal pregnancy’.

We changed the outcome of ‘Preterm labour (onset of labour before 37 weeks)’ to ‘Preterm birth (birth less than 37 weeks)’ because this was the outcome reported in the studies.

We have modified the wording in the methods sections for Assessment of heterogeneity, Assessment of reporting biases and Data synthesis to update them with the new methods being used by the group, developed in conjunction with the group’s statisticians, Simon Gates and Richard Riley. We have used these new methods in the review.

WHAT’S NEW

Last assessed as up-to-date: 30 May 2010.

Date	Event	Description
28 January 2010	New citation required but conclusions have not changed	New review team substantially updated the review.
20 May 2009	New search has been performed	Search updated. Six new trials excluded (Ellwood 1997; Goffinet 2001; Scholler 1993; Snaith 2006; Subtil 2000; Subtil 2003).

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* Indicates the major publication for the study

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PLAIN LANGUAGE SUMMARY

Doppler ultrasound of fetal blood vessels in normal pregnancies

One of the main aims of routine antenatal care is to identify babies who are not thriving in the womb. It is possible that medical interventions might improve outcomes for these babies, if they can be identified. Doppler ultrasound uses sound waves to detect the movement of blood in vessels. It is used in pregnancy to study blood circulation in the baby, uterus and placenta. Using it in high-risk pregnancies, where there is concern about baby's condition, shows benefits. However, its value as a screening tool in all pregnancies needs to be assessed as there is a possibility of unnecessary interventions and adverse effects. The review of trials of routine Doppler ultrasound of the baby's vessels in pregnancy identified five studies involving more than 14,000 women and babies. The studies were not of high quality and were all undertaken in the 1990s. There were no improvements identified for either the baby or the mother, though more data would be needed to prove whether it is effective or not for improving outcomes.

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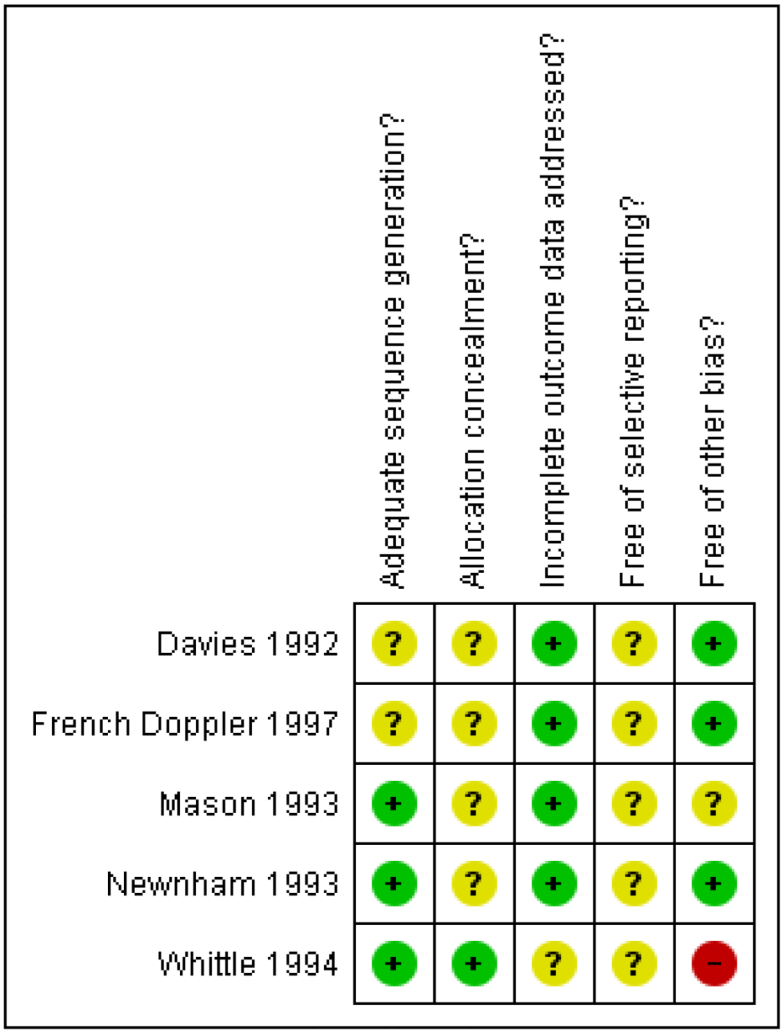

Figure 1 .

Methodological quality summary: review authors' judgements about each methodological quality item for each included study.