Ultrasound for fetal assessment in early pregnancy (Review)

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[Intervention Review]

Ultrasound for fetal assessment in early pregnancy

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ABSTRACT

Background

Diagnostic ultrasound is a sophisticated electronic technology, which utilises pulses of high frequency sound to produce an image. Diagnostic ultrasound examination may be employed in a variety of specific circumstances during pregnancy such as after clinical complications, or where there are concerns about fetal growth. Because adverse outcomes may also occur in pregnancies without clear risk factors, assumptions have been made that routine ultrasound in all pregnancies will prove beneficial by enabling earlier detection and improved management of pregnancy complications. Routine screening may be planned for early pregnancy, late gestation, or both. The focus of this review is routine early pregnancy ultrasound.

Objectives

To assess whether routine early pregnancy ultrasound for fetal assessment (i.e. its use as a screening technique) influences the diagnosis of fetal malformations, multiple pregnancies, the rate of clinical interventions, and the incidence of adverse fetal outcome when compared with the selective use of early pregnancy ultrasound (for specific indications).

Search strategy

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (September 2009).

Selection criteria

Published, unpublished, and ongoing randomised controlled trials that compared outcomes in women who experienced routine versus selective early pregnancy ultrasound (i.e. less than 24 weeks' gestation). We have included quasi-randomised trials.

Data collection and analysis

Two review authors independently extracted data for each included study. We used the Review Manager software to enter and analyse data.

Main results

Routine/revealed ultrasound versus selective ultrasound/concealed: 11 trials including 37505 women. Ultrasound for fetal assessment in early pregnancy reduces the failure to detect multiple pregnancy by 24 weeks' gestation (risk ratio (RR) 0.07, 95% confidence interval (CI) 0.03 to 0.17). Routine scan is associated with a reduction in inductions of labour for 'post term' pregnancy (RR 0.59, 95% CI 0.42 to 0.83). Routine scans do not seem to be associated with reductions in adverse outcomes for babies or in health service use by mothers and babies. Long-term follow up of children exposed to scan in utero does not indicate that scans have a detrimental effect on children's physical or cognitive development.

Authors' conclusions

Early ultrasound improves the early detection of multiple pregnancies and improved gestational dating may result in fewer inductions for post maturity. Caution needs to be exercised in interpreting the results of aspects of this review in view of the fact that there is considerable variability in both the timing and the number of scans women received.

PLAIN LANGUAGE SUMMARY

Routine compared with selective ultrasound in early pregnancy

Ultrasound is an electronic technology, which uses the reflection of pulses of high frequency sound to produce an image. Ultrasound may be used in a variety of circumstances during pregnancy. It has been assumed that the routine use of ultrasound in early pregnancy will result in the earlier detection of problems and improved management of pregnancy complications when compared with selective use for specific indications such as after clinical complications (e.g. bleeding in early pregnancy), or where there are concerns about fetal growth.

The focus of this review is routine early pregnancy ultrasound (before 24 weeks). We have included 11 randomised controlled trials including 37,505 women. Early ultrasound improved the early detection of multiple pregnancies and improved gestational dating which may result in fewer inductions for post maturity. The detection of fetal malformation was addressed in detail in only two of the trials. There was no evidence of a significant difference between the screened and control groups for perinatal death. Results do not show that routine scans reduce adverse outcomes for babies or lead to less health service use by mothers and babies. Long-term follow up of children exposed to scans before birth did not indicate that scans have a detrimental effect on children's physical or intellectual development. Studies were carried out over three decades and technical advances in equipment, more widespread use of ultrasonography, and increased training and expertise of operators may have resulted in more effective sonography.

BACKGROUND

Diagnostic ultrasound is a sophisticated electronic technology, which utilises pulses of high frequency sound to produce an image. A transducer which is moved across the area to be examined emits pulses of ultrasound which propagate through the tissues. Some pulses are reflected back to the transducer which converts these returning echoes into electronic signals. The strength of the returning echo is determined by tissue interface characteristics. Returning signals are processed by a computer which displays each echo in both strength and position as an image on a screen. The quality of ultrasound imaging is dependent not only on the technical capabilities of the ultrasound equipment but also on the experience and expertise of the operator and standards are variable.

Diagnostic ultrasound examination may be employed in a variety of specific circumstances during pregnancy, such as: after clinical complications (e.g. bleeding in early pregnancy); where the fetus is perceived to be at particularly high risk of malformation; and where there are concerns regarding fetal growth. Because adverse outcomes may also occur in pregnancies without clear risk factors, assumptions have been made that the routine use of ultrasound in all pregnancies will prove beneficial. The rationale for such screening would be the detection of clinical conditions which place the fetus or mother at high risk, which would not necessarily have been detected by other means such as clinical examination, and for which subsequent management would improve perinatal outcome. Routine screening examinations may be planned for

early pregnancy, late gestation, or both. The focus of this review is routine early pregnancy ultrasound, late pregnancy screening will be addressed in another review (Bricker 2008).

The use of ultrasound to identify women at risk of preterm delivery by assessment of the cervix may be a component of screening before 24 weeks; this is outside the remit of this review and is considered elsewhere (Berghella 2009; Crane 2008).

Early pregnancy complications and serum screening

An ultrasound at the time of antenatal booking may enable non-viable pregnancies to be detected earlier than is possible using clinical presentation. This has implications for clinical management of these pregnancies. In addition, earlier detection of ectopic pregnancy may be possible allowing for medical rather than surgical management, or 'minimally invasive' rather than open surgery. Between 11% and 42% of gestational age estimations taken from the menstrual history are reported as inaccurate (Barrett 1991; Geirsson 1991; Peek 1994). A reliable estimate of gestational age is required for maternal serum screening for fetal abnormality to be accurately timed (Owen 1997). Accurate knowledge of gestational age may increase the efficiency of maternal serum screening and some late pregnancy fetal assessment tests.

Multiple pregnancy

Multiple pregnancies are associated with increased perinatal morbidity and mortality compared to singleton pregnancies (Dodd 2005). Determination of chorionicity plays an important role in risk stratification when managing twin pregnancies. Routine early pregnancy scanning in this group may impact on accuracy of assignment of chorionicity in multiple pregnancies, as some studies have shown that this can be done more accurately at earlier gestations (Lee 2006). It is also possible that earlier diagnosis of multiple pregnancy will occur with routine early pregnancy scanning, thus preventing inappropriate maternal serum screening (Persson 1983; Saari-Kemppainen 1990).

Structural fetal abnormalities

In a systematic review, based on 11 studies (one randomised controlled trial, six retrospective cohorts and four prospective cohorts) undertaken to examine the use of routine second trimester ultrasound to detect fetal anomalies, the overall prevalence of fetal anomaly was 2.09%, ranging from 0.76% to 2.45% in individual studies and including major and minor anomalies (Bricker 2000). Using late pregnancy ultrasound scanning overall, detection of fetal anomaly was 44.7%, with a range of 15.0% to 85.3% (Bricker 2000). Optimum timing of such ultrasound scans may be aided by accurate estimation of dates using routine early pregnancy scanning.

Intervention

A recent Cochrane review concluded that a policy of labour induction after 41 completed weeks or later compared to awaiting spontaneous labour either indefinitely or at least one week is associated with fewer perinatal deaths (Gulmezoglu 2006). It is possible that routine early pregnancy scanning will improve the accuracy of pregnancy dating and thereby affect the number of pregnancies undergoing induction for post-maturity. Whilst there is evidence to suggest that ultrasound is very attractive to women and families, studies have also shown that women often lack information about the purposes for which an ultrasound scan is being done and the technical limitations of the procedure (Bricker 2000a). It is therefore essential that patient satisfaction is considered.

Safety

The use of routine pregnancy ultrasound needs to be considered in the context of potential hazards. In theory, some ultrasonic energy propagated through tissue is converted to heat, and in laboratory experiments, biological effects of ultrasound have been observed. However, these effects have been produced using continuous wave ultrasound with long 'dwell' time (time insonating one area) and high-power output. In the clinical setting, diagnostic ultrasound uses pulsed waves (short pulses of sound propagation), and most modern machines are designed so that safe power output limits cannot be exceeded. Operators are always advised to apply the ALARA principle (as low as reasonably attainable) to the ultrasound power output used (EFSUMB 1995), and to ensure time taken for an examination, including the 'dwell' time over a specific target, is kept to a minimum. One of the aims of this review is to assess available data and determine whether clear epidemiological evidence exists from clinical trials that ultrasound examination during pregnancy is harmful.

OBJECTIVES

To assess whether routine early pregnancy ultrasound for fetal assessment (i.e. its use as a screening technique) influences the diagnosis of fetal malformations, multiple pregnancies, the rate of clinical interventions, and the incidence of adverse fetal outcome when compared with the selective use of early pregnancy ultrasound (for specific indications).

METHODS

Criteria for considering studies for this review

Types of studies

All published, unpublished, and ongoing randomised controlled trials with reported data that compared outcomes in women who experienced routine early pregnancy ultrasound with outcomes in women who experienced the selective use of early pregnancy ultrasound. We have included quasi-randomised controlled trials. We planned to include trials reported as abstracts provided that they contained sufficient information for us to assess eligibility and risk of bias, and that results were described in sufficient detail. Where insufficient information was provided in abstracts, we have included studies in "awaiting assessment" until publication of the full study report or until we can obtain further information from authors.

Types of participants

Women with early pregnancies, i.e. less than 24 weeks' gestation.

Types of interventions

Routine ultrasound examination compared with selective ultrasound examination.

Types of outcome measures

Primary outcomes

1. Detection of major fetal abnormality (as defined by the trial authors) prior to 24 weeks' gestation.
2. Detection of multiple pregnancy by 24 weeks' gestation.
3. Induction of labour for 'post-term' pregnancy.
4. Perinatal death (defined as stillbirth after trial entry, or death of a liveborn infant up to 28 days of age).

Secondary outcomes

Detection of
(1) non-viable pregnancy prior to clinical presentation;
(2) ectopic pregnancy prior to clinical presentation;
(3) chorionicity of multiple pregnancy (in first trimester or in second trimester);
(4) multiple pregnancy prior to labour;
(5) soft markers before 24 weeks' gestation (i.e. structural features in the fetus that are of little or no functional significance (e.g. choroid plexus cyst, echogenic bowel) but which can be associated with increased risk of chromosomal disorder, e.g.Trisomy 21);
(6) major anomaly before birth.

Complications for infants and children

(7) Birthweight;
(8) gestation at delivery;
(9) low birthweight (defined as less than 2500 grams at term in singletons);
(10) very low birthweight (defined as less than 1500 grams at term in singletons);
(11) Apgar score less than or equal to seven at five minutes;
(12) admission to neonatal intensive care unit;
(13) respiratory distress syndrome;
(14) death or major neurodevelopmental handicap at childhood follow up;
(15) poor oral reading at school;
(16) poor reading comprehension at school;
(17) poor spelling at school;
(18) poor arithmetic at school;
(19) poor overall school performance;
(20) dyslexia;
(21) reduced hearing in childhood;
(22) reduced vision in childhood;
(23) use of spectacles;
(24) non right-handedness;
(25) ambidexterity;
(26) disability at childhood follow up.

Maternal outcomes

(27) Appropriately timed serum screening tests;
(28) laparoscopic management of ectopic pregnancy;
(29) surgical management of abortion;
(30) appropriately timed anomaly scan (18 to 22 weeks);
(31) termination of pregnancy for fetal abnormality;
(32) antenatal hospital admission;
(33) induction of labour for any reason;
(34) caesarean section.

Measures of satisfaction

(35) Woman not satisfied;
(36) women's preferences for care.

Costs

(37) Costs associated with routine early pregnancy ultrasound versus selective early pregnancy ultrasound;
(38) number of antenatal visits;
(39) length of stay in neonatal intensive care unit;
(40) infant length of hospital stay.

Search methods for identification of studies

Electronic searches

We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register (September 2009).

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 examined cited references, abstracts, letters to the editor, and editorials for additional studies. Where necessary, we contacted the primary investigator directly to obtain further data.

We did not apply any language restrictions.

Data collection and analysis

Selection of studies

We assessed for inclusion all potential studies identified as a result of the search strategy. We resolved any disagreement through discussion.

Data extraction and management

We designed a form to extract data. Two of the review authors independently extracted data for each included study using the agreed form. We resolved discrepancies through discussion. We used the Review Manager software (RevMan 2008) to enter data, and after data entry we checked tables for accuracy.

When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

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 2008). We resolved any disagreement by discussion or by involving a third assessor.

(1) Sequence generation (checking for possible selection bias)

We have described for each included study the method used to generate the allocation sequence.

We 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);
- unclear.

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

We have described for each included study the method used to conceal the allocation sequence and considered whether group allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We assessed the methods as:

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

(3) Blinding (checking for possible performance bias)

With an intervention such as ultrasound it may not be feasible to blind study participants and personnel from knowledge of which intervention a participant received. In studies where both groups received ultrasound but results were not revealed for the control group, blinding participants may be possible, but staff are still likely to be aware of group allocation. We have provided information on whether blinding (or partial blinding) was attempted and assessed whether the intended blinding was effective.

We assessed the methods as:

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

(4) Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)

We have described for each included study, and for each outcome or class of outcomes, the completeness of data including attrition

and exclusions from the analysis. We have noted 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 supplied by the trial authors, we have re-included missing data in the analyses. For outcomes relating to the antenatal period or labour and delivery where data are unavailable for more than 20% of those originally randomised, we had planned that data for that outcome would not be included in the meta-analysis. For long-term outcomes, we have recorded the levels of attrition and where there has been more than 20% loss to follow up we have interpreted results cautiously.

We have assessed methods for dealing with missing data in the included studies as:

- adequate;
- unclear; or
- inadequate

(5) Selective reporting bias

We have described for each included study how the possibility of selective outcome reporting bias was examined by us and what we found.

We assessed the methods as:

- adequate (where it is clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review were reported);
- inadequate (where not all the study's pre-specified outcomes were reported; one or more reported primary outcomes were not pre-specified; outcomes of interest were reported incompletely and so could not be used; or the study failed 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 for each included study any important concerns we had about other possible sources of bias such as baseline imbalance between groups.

We 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 *Handbook* (Higgins 2008). With reference to (1) to (6) above, we have discussed the likely magnitude and direction of the bias and whether we consider it is likely to impact on the findings. We 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 have presented results as summary risk ratio with 95% confidence intervals.

Continuous data

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

Unit of analysis issues

Cross-over designs are unlikely to be appropriate for trials in pregnancy and childbirth and we have not included them.

Cluster-randomised trials

We are aware of potential variations in units of analysis across trials. We planned to include cluster-randomised trials in the analyses along with individually randomised trials. If such trials are identified in the future, we will adjust their standard errors using the methods described in Gates 2005 and Higgins 2008 using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), or from another source. 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 separate meta-analysis. Therefore, we will perform the meta-analysis in two parts as well.

Dealing with missing data

For included studies, we have noted levels of attrition. We planned to explore 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 carried out analyses, as far as possible, on an intention-to-treat basis, i.e. we attempted to include all participants randomised to each group in the analyses 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 examined the forest plots for each analysis to look for signs of heterogeneity between studies, and used the I^2 statistic to quantify heterogeneity among the trials in each analysis. Where we identified moderate or high values of I^2 (I^2 greater than 30%), we repeated the analysis using a random-effects model and also examined the Tau² (T^2) statistic. In the presence of moderate or high levels of heterogeneity we have presented the results of the random-effects analysis, and values for the $I^2$and T^2 statistics along with the 95% prediction interval and the P value for the Chi² test for heterogeneity (a value less than 0.1 indicating significant heterogeneity). In analyses where random-effects analyses have been used, the overall treatment effect represents an average. Where there are moderate or high levels of heterogeneity, we would advise readers to interpret results cautiously.

Data synthesis

We have carried out statistical analysis using the Review Manager software (RevMan 2008). In the absence of heterogeneity we have used fixed-effect meta-analysis for combining data where trials examined the same intervention, and the trials' populations and methods were judged sufficiently similar.

Subgroup analysis and investigation of heterogeneity

Planned subgroup analyses included:

1. parity (nulliparous versus multiparous women);
2. selective performance of ultrasound versus selective reporting of ultrasound findings;
3. first scan occurring in first trimester (up to 14 weeks' gestation) versus second trimester (14 to 24 weeks' gestation).

We carried out subgroup analyses for the review's primary outcomes (induction for post-term pregnancy, perinatal death, and detection of multiple pregnancy and abnormality before 24 weeks' gestation). We assessed differences between subgroups by visual inspection of the forest plots and the subgroups' confidence intervals; non-overlapping confidence intervals indicating a statistically significant difference in treatment effect between the subgroups. If we suspected any differences between subgroups we planned to seek statistical advice.

Sensitivity analysis

We have carried out sensitivity analysis to explore the effect of trial quality on study results. We planned to exclude from the analysis trials assessed as having inadequate or unclear allocation concealment or high levels of attrition in order to assess whether this would make any substantive difference to the overall results. We carried out sensitivity analysis for the review's primary outcomes only (induction for post-term pregnancy, perinatal death, and detection of multiple pregnancy and abnormality before 24 weeks' gestation).

We assessed possible publication bias by visually examining the funnel plots for those outcomes where at least 10 studies contributed data, with funnel plot asymmetry indicating possible publication bias.

RESULTS

Description of studies

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

Results of the search

The search strategy identified 63 papers reporting findings from 24 studies examining ultrasound for fetal assessment in early pregnancy (most studies resulted in several publications or reports). We have included 11 trials in the review and one study is awaiting further assessment (Newcastle). In addition, one of the included studies (Norway) reported long-term, childhood outcome data from two of the included trials (Alesund; Trondheim 1984). We excluded 11 studies.

Included studies

The studies were carried out in a number of countries: Australia (Adelaide 1999); the USA (RADIUS (a multicentre study); Missouri 1990); South Africa (Johannesburg 2007; Tygerberg 1996); Sweden (Sweden); Norway (Alesund; Trondheim 1984); the UK (London 1982; Oxford 2006) and Finland (Helsinki). The earliest trials began recruitment in the late 1970s (Alesund; Trondheim 1984).

All of the trials included an intervention involving an ultrasound examination before the 24th week of pregnancy. The dates of the scans, and the number of scans women received varied in different trials. In the London 1982 trial all women (in both the intervention and control groups) were offered a scan, but while in the intervention group results were revealed in the women's case notes, in the control group results were concealed unless they were

specifically requested by clinical staff. In all other included studies women in the intervention group were offered a "routine" scan whilst those in the control groups received a scan at the discretion of clinical staff ("selective scans"). Ultrasound scans in the intervention group may have been the only "routine" scan offered, or may have been an additional scan, with women in both intervention and control groups having scans scheduled at a later stage of pregnancy.

The gestational age at which index scans were performed, and the purpose of scans, varied in different trials. In the Adelaide 1999, study scans in the intervention group were carried out at between 11 and 14 weeks. The purposes of the scan were to ascertain gestational age (with the aim of improving the timing of other screening tests), identify multiple pregnancies, and to carry out a limited examination of fetal morphology. Women in both treatment and control arms of this study had a routine morphology scan at 18 to 20 weeks' gestation.

In the two Norwegian studies, women in the intervention group were offered two scans, the first at 18 to 20 weeks and then a late ultrasound scan at 32 weeks (Alesund and Trondheim 1984) (with follow-up data for both studies reported in the Norway papers). The purposes of the early scan were to measure biparietal diameter (BPD); to estimate the expected date of delivery (EDD); to identify multiple pregnancies; to note the location of the placenta; and to carry out a general examination of the fetus.

The ultrasound in the intervention group of the Helsinki trial was carried out between 16 and 20 weeks; the aims were similar to those in the Norwegian trials, with the amount of amniotic fluid also being recorded.

The main aim in the London 1982 study was BPD measurement and assessment of the EDD; scans were performed at approximately 16 weeks. In the Missouri 1990 trial, scans generally took place between 10 to 12 weeks (up to 18 weeks) and were carried out to estimate gestational age, identify multiple pregnancies, assess fetal viability and to identify uterine abnormalities. The Sweden study had similar aims; women attending 19 antenatal clinics in Stockholm were invited for a scan at 15 weeks (range 13 to 19 weeks) (intervention) or received selective scans after 19 weeks (control).

In the Oxford 2006 study, women in both the intervention and control groups had routine scans at 18 to 20 weeks, in addition women in the intervention group were offered an early scan (at between eight and 12 weeks) to estimate gestational age.

In a large multi-centre trial in the USA (RADIUS) women in the intervention group were offered scans at 18 to 20 weeks and at 31 to 33 weeks versus selective scans. The purpose of the earlier scan was to identify the location of the placenta, the volume of amniotic fluid, uterine abnormalities, multiple pregnancies, BPD and other measures of fetal size, and a detailed assessment of fetal anatomy.

In the South African study (Tygerberg 1996), a single scan was offered to women in the intervention group; women received a scan which aimed to ascertain gestational age and to identify major fetal anomalies. Finally, in the Johannesburg 2007 trial, scans in the intervention group were carried out between 18 and 23 weeks; the reasons for scans were not described.

Further details of settings, participants and interventions are set out in the Characteristics of included studies tables.

Excluded studies

In four of the excluded studies all participants (in both the intervention and control groups) received early scans; in the studies by Saltvedt 2006 and Schwarzler 1999, the timing of scans was examined (i.e. earlier versus later scans); in the study by Duff 1993, women in the intervention group had an additional scan in the third trimester; and Owen 1994 looked at women with a high risk of fetal anomaly, with women in the intervention group receiving more frequent scans.

In the trial by Bennett 2004, the focus was specifically on the timing of the assessment of gestational age with scans in the first and second trimesters. In the trial by Larsen 1992, the participants were high-risk women, with those in the intervention group receiving an additional scan at 28 weeks. Two trials compared two versus three or four dimensional ultrasound scans (Leung 2006; Rustico 2005). In the Hong Kong study, women in both arms of the trial had two routine scans, in the intervention group the earlier scan was more detailed than in the control group. The study by Belanger 1996 did not include results relevant to the outcomes of the review. We attempted to contact the authors of one report, but results were not available (Wald 1988).

Risk of bias in included studies

Allocation

In the majority of the included studies, no information was provided on the methods used to generate the sequence for randomisation. In the Adelaide 1999 study, a table of random numbers was used to generate the allocation order, and in the RADIUS study the sequence was determined by a computerised random number generator. In two studies there was balanced block randomisation (Missouri 1990 (block size four) and Oxford 2006 (block size six)).

We assessed two studies as having inadequate methods to conceal group allocation; in the London 1982 study there was quasi-random allocation to groups using the women's hospital number to determine allocation, while in the Johannesburg 2007 trial women were allocated to intervention and control groups according to day of the week. In the RADIUS study the methods used for allocating women to randomisation group were not clear. In all the remaining studies, the study allocation was concealed in sealed envelopes; in the Adelaide 1999, Missouri 1990 and Oxford 2006 studies envelopes were described as numbered, opaque, and sealed;

in the Tygerberg 1996 and Sweden studies envelopes were sealed and opaque; while the Alesund, Helsinki, and Trondheim 1984 reports refer to the "sealed envelope method" of randomisation.

Blinding

Blinding women and clinical staff to group allocation was generally not feasible as women in the two treatment arms received different care, and the results of scans were recorded in women's case notes. In the Trondheim 1984 study outcome assessment was described as partially blinded. In the London 1982 study the results of the scan for the control group were not stored in case notes and therefore not available to outcome assessors (although outcome assessors would be aware of group allocation by the presence or absence of the scan report).

The lack of blinding in these studies is unlikely to affect some review outcomes (such as perinatal mortality) but outcomes relying on clinical judgement (e.g. the decision to induce labour for post-term pregnancy) may possibly be influenced by knowledge of group allocation and this is a potential source of bias; such outcomes should be interpreted with caution.

Incomplete outcome data

The loss of women to follow up and levels of missing data for pregnancy outcomes were generally low in these studies (less than 5%). In the Missouri 1990 study 9% of the sample were lost to follow up after randomisation, and in the Oxford 2006 study 15% were lost, but an intention-to-treat analysis, including all women randomised, was carried out for the main study outcomes. There was relatively high attrition in the Johannesburg 2007 trial; 15.7% of women randomised were lost to follow up and there were further missing data for some outcomes; reasons for attrition were not described, and it was not clear how many women from each group were lost.

We have attempted to use consistent denominators in the analyses within this review. For pregnancy and early postnatal outcomes we have tried to include all women randomised less: those women that were not actually pregnant; those who had pre-screening pregnancy termination; and those who experienced an early spontaneous miscarriage. We have included women lost to follow up for other reasons (e.g. did not attend for screening, withdrew from the study, missing data) in the denominators. In some cases it was difficult to determine the denominators, as detailed information on attrition at different stages was not reported (in the Johannesburg 2007 study it was not clear how many women were randomised to each study group, and so we had to use the group denominators for those women available to follow up). For outcomes for "all babies", we have used the total number of babies (including babies from multiple pregnancies); some outcomes (e.g. birthweight) are specified for singletons only. Again, it was not always easy to ascertain the appropriate denominators for babies.

For long-term follow up where there was greater attrition (for example, there was complete data for approximately half of the original sample for some outcomes at childhood follow up in the Sweden study), we have used the denominators reported by the authors in study publications.

For some competing/overlapping outcomes (e.g. perinatal deaths, miscarriages and pregnancy termination for fetal abnormality) we have reported figures provided in the trial reports but we advise caution in interpreting such data. We will return to this issue in the discussion.

Other potential sources of bias

Some of the trials had other potential sources of bias: the Oxford 2006 study was stopped part way through and results are difficult to interpret, and in the Alesund trial there was some baseline imbalance between groups in smoking rates. While not a source of bias as such, large numbers of women were not eligible for inclusion in the RADIUS trial and this may affect the generalisability of results.

Effects of interventions

Routine/revealed ultrasound versus selective ultrasound/concealed results: 11 trials including 37,505 women

Primary outcomes

The detection of fetal abnormalities before 24 weeks in the screened and unscreened groups was reported in two studies; these studies (17,158 pregnancies) recorded a total of 387 fetal abnormalities with most being undetected at 24 weeks (346, 89% not detected by 24 weeks). It was more likely for the screened group to have abnormalities detected by 24 weeks compared with controls (unweighted percentages 16% versus 4%) (risk ratio (RR) 3.46, 95% confidence interval (CI) 1.67 to 7.14).

Failure to detect multiple pregnancies by 24 weeks was reported in seven studies. It was more likely that multiple pregnancies would not be detected by 24 weeks in the unscreened groups; only two of 153 multiple pregnancies were undetected at 24 weeks in the screened groups, compared with 56 of 142 in the control groups (RR 0.07, 95% CI 0.03 to 0.17).

Seven studies reported rates of induction of labour for "post-dates" pregnancy (which accounted for approximately 13% of total inductions). Compared with controls, women offered early routine ultrasound were less likely to be induced for post-maturity. For this outcome there was a high level of heterogeneity between studies. A visual examination of the forest plot reveals that the general direction of findings is the same among studies; however, the size

of the treatment effect and the rates of induction in control groups vary. We used a random-effects model in the meta-analysis and the average treatment effect favoured the screened group (RR 0.59, 95% CI 0.42 to 0.83), (heterogeneity: I^2 = 68%, T^2 = 0.14, Chi^2 test for heterogeneity P = 0.002, prediction interval 0.22 to 1.62). There was no evidence of a significant difference between the screened and control groups for perinatal mortality (unweighted percentages 0.73 versus 0.82%), (RR 0.89, 95% CI 0.70 to 1.12). When lethal malformations were excluded, rates of perinatal death in the screened and unscreened groups were very similar (0.53 versus 0.56%), (RR 0.96, 95% CI 0.72 to 1.27).

Secondary outcomes

Detection of abnormalities and multiple pregnancies prior to delivery

All multiple pregnancies (140) were detected before labour in the intervention groups, whereas 12 of the 133 in the control groups remained undetected at the onset of labour (RR 0.12, 95% CI 0.03 to 0.54). Screened groups were also more likely to have major fetal anomalies detected before birth (RR 3.19, 95% CI 1.99 to 5.11).

Complications for infants and children

There was no evidence of significant differences between groups in terms of the number of low birthweight babies (less than 2500 g) or very low birthweight babies (less than 1500 g); (for these outcomes, some studies reported results for singletons only, and so in the analyses we have set out results for singletons and all babies separately; Analysis 1.8; Analysis 1.9). There was no evidence of statistically significant differences between groups in the number of babies that were small for gestational age, or in mean birthweight (Analysis 1.10; Analysis 1.11). There were high levels of heterogeneity for outcomes relating to low birthweight, and these results should be interpreted with caution.

The number of babies with low Apgar scores (seven or less) at five minutes was similar in the two groups, and there was no difference in rates of admission to neonatal intensive care (Analysis 1.11; Analysis 1.13).

In three studies babies were followed up into childhood (results for children up to nine years in the Alesund and Trondheim 1984 trials are reported together in the Norway study, and the Sweden study includes data for children at eight to nine years and for teenagers aged 15 to 16 years). For children aged eight to nine years, there were no significant differences for any of the outcomes reported including school performance, hearing and vision, disabilities or dyslexia (which was measured in a subset of the main sample) (. Analysis 1.14; Analysis 1.15; Analysis 1.16; Analysis 1.17; Analysis 1.18; Analysis 1.19; Analysis 1.20; Analysis 1.21; Analysis 1.22; Analysis 1.23; Analysis 1.24; Analysis 1.25; Analysis 1.30).There was concern raised regarding an excess of non-right handedness in the intervention group in the Norwegian study; however, the Swedish study did not confirm these findings, and results may have occurred by chance. Examination of the school records of teenagers (aged 15 to 16 years) revealed little difference in the performance of children whose mothers had been randomised to ultrasound or no ultrasound in the Swedish trial. Data were available for 94% of singletons in the original sample. Authors reported that there was no strong evidence of differences between groups for school performance (grades over all subjects) for girls or boys. For physical education there was a small difference in scores for boys; those whose mothers had been randomised to the ultrasound group had slightly lower mean scores compared to those in the control group, but this finding was not statistically significant.

Maternal outcomes

It was more likely that women would undergo pregnancy termination for fetal abnormality in the screened groups, although overall the number of terminations was small (24 of 14,237 pregnancies in screened groups were terminated after detection of abnormality compared with 10 of 14,019 in controls) (RR 2.23, 95% CI 1.10 to 4.54).

There was no significant evidence that ultrasound was associated with reduced numbers of women undergoing delivery by caesarean section (Analysis 1.32). Overall, on average, there were slightly fewer inductions of labour (for any reason, including post-maturity) in women in the screened groups; in view of heterogeneity we used a random-effects model for this outcome (RR 0.78, 95% CI 0.63 to 0.97) (heterogeneity: I^2 = 84%, T^2 = 0.06 Chi^2 test for heterogeneity P = 0.00001, prediction interval 0.39 to 1.56). The rate of induction in the screened group was 18.8% versus 19.8% in the control group (unweighted percentages).

The Adelaide 1999 trial examined whether an early scan would reduce the number of serum screening tests or fetal anomaly scans that needed to be repeated because they had been performed at the wrong gestational age. There was no significant evidence that the numbers of women having repeat testing was reduced in the intervention group (Analysis 1.26; Analysis 1.27). There was also no significant evidence in the Helsinki and Johannesburg 2007 trials that the number of antenatal visits was reduced (Analysis 1.29), and pooled results from five trials showed no significant reduction in antenatal hospital admissions (Analysis 1.30).

In the Adelaide 1999, study investigators examined whether having an early scan was reassuring or worrying to mothers. Fewer mothers in the screened group reported feeling worried about their pregnancies (RR 0.80, 95% CI 0.65 to 0.99).

Costs of care

The impact of screening on costs to women and health services was examined in two trials.

In the Helsinki study, the average time spent in the hospital was 61 minutes and women spent 74 minutes travelling to hospital; 81% of the sample were working, and half of the working women used work time to attend for initial screening (some women may have had to attend for further screening-induced appointments). The cost to health services was not simple to calculate; the cost of the examinations was offset by fewer hospital visits and stays, and in this study there was a lower perinatal mortality rate and increased pregnancy termination in the screened group, leading the authors to conclude that ultrasound resulted in cost savings (Leivo 1996).

The issue of cost was also examined in a trial carried out in a low-resource setting where overall adverse fetal outcome was higher, but where fetal anomalies represented a smaller proportion of adverse outcomes compared with high resource settings. An explicit aim of the Tygerberg 1996 study was to examine whether the costs of routine ultrasound for all women (rather than selective ultrasound) would be offset by a reduction in the use of other healthcare resources. In this study routine ultrasound was perceived as being an expensive luxury: "In our less privileged community, however, the cost of investigation is in direct competition with resources for more urgent needs in healthcare and housing, sanitation, education and unemployment... a routine obstetric ultrasonography policy is expensive and ... the more selective use is not accompanied by an increase in adverse perinatal outcome" (Tygerberg 1996 p.507).

Other outcomes

Included studies did not report data for a number of the secondary outcomes pre-specified in the review protocol including the detection of ectopic pregnancy or chorionicity of multiple pregnancy, laparoscopic management of ectopic pregnancy and surgical management of abortion.

Subgroup and sensitivity analysis

We planned subgroup analysis by parity, by the timing of the early ultrasound (before or after 14 weeks) and by whether the control group had scans (with results concealed) rather than selective scans. We examined subgroups for primary outcomes only.

Parity

Information on parity was not available for us to be able to carry out this analysis.

Timing of early scan

In three studies the early scan was planned for before 14 weeks' gestation. In the Adelaide 1999 study, scans were planned for 11 to 14 weeks, in Oxford 2006 10 to 12 weeks, and in Missouri 1990, while scans could be performed up to 18 weeks, most were carried out between 10 and 12 weeks. There were no clear differences in outcomes in groups where scans were performed earlier rather than later for induction for post-term pregnancy, detection of multiple pregnancy or perinatal death (Analysis 1.34; Analysis 1.35; Analysis 1.36). In the Adelaide 1999 and Oxford 2006 studies, the treatment effect for these outcomes appeared more conservative than in some of the other studies; this may be because women in both arms of these trials had routine ultrasound scheduled at 18 to 20 weeks' gestation.

Concealed results and routine care

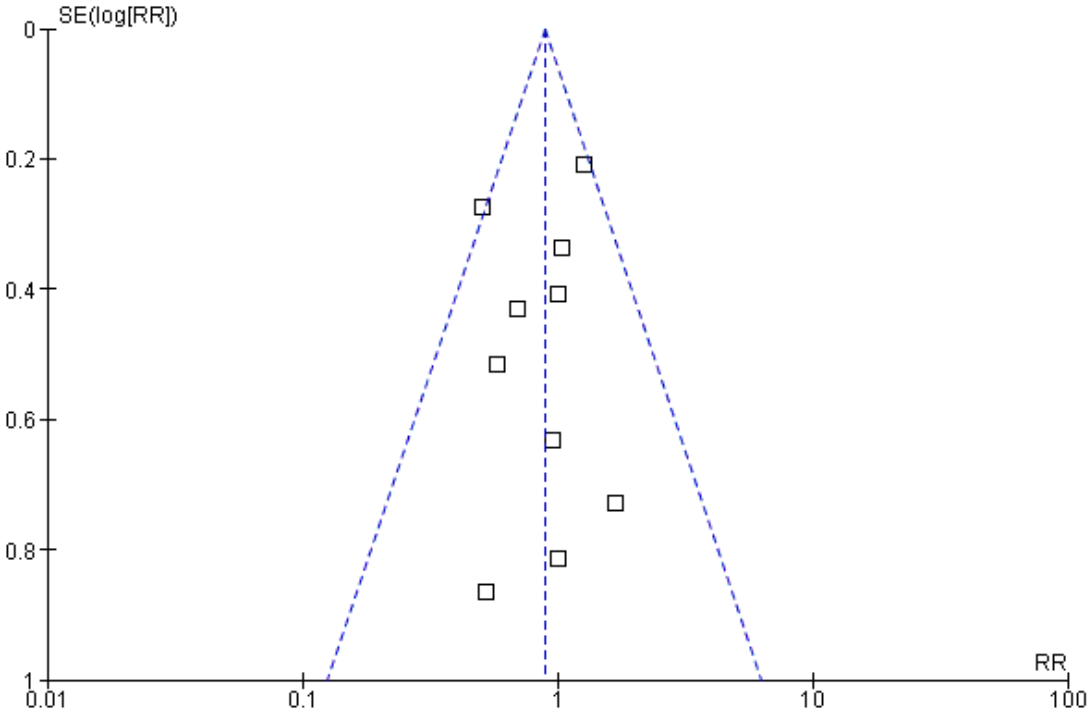
In one study, women in both groups were screened but results were revealed for the intervention group only (London 1982). This study examined two of the review's primary outcomes: detection of multiple pregnancy before 24 weeks and perinatal death. There was considerable overlap in the confidence intervals for these outcomes for the London 1982 study and the other trials, suggesting no clear differences between subgroups.

Sensitivity analysis (allocation concealment assessed as inadequate)

Two studies used a quasi-randomised design (case note number London 1982) (allocation by day of the week Johannesburg 2007); removing these studies from the analysis did not affect overall results for the primary outcomes. None of the studies had very high levels of attrition (more than 20%) for primary outcomes.

Only one outcome (perinatal death) included data from ten studies (Analysis 1.4); we produced a funnel plot to look for plot asymmetry which may suggest publication bias; there was no asymmetry apparent on visual inspection (Figure 1).

Figure 1. Funnel plot of comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, outcome: 1.4 Perinatal death (all babies).



DISCUSSION

Summary of main results

Ultrasound for fetal assessment in early pregnancy increases the chances of the detection of multiple pregnancy before 24 weeks' gestation, and there is some evidence that fetal abnormalities are detected earlier. Routine scan is associated with a reduction in inductions of labour for "post-term" pregnancy, and this contributes to a small reduction in the overall rates of induction (for any indication). Routine scans do not seem to be associated with reductions in adverse outcomes for babies or in health service use by mothers and babies. At the same time, long-term follow up of children exposed to scan in utero does not indicate that scans have a detrimental effect on children's physical or cognitive development. Considerable caution needs to be exercised in interpreting the results of aspects of this review in view of the fact that there is considerable variability in both the timing of the intervention and the number of scans which women received during pregnancy.

The assumed benefits of routine ultrasonography in early pregnancy have been: (1) better gestational age assessment; (2) earlier detection of multiple pregnancies; and (3) detection of clinically unsuspected fetal malformation at a time when termination of pregnancy is possible.

These assumptions appear to have been justified by analysis of data from the studies included in this review. The reduced incidence of induction of labour in the routinely scanned groups presumably results from better gestational 'dating', and earlier detection of multiple pregnancy. However, the high levels of heterogeneity for the former outcome means caution should be applied. Whilst routine ultrasound assessment in early pregnancy has not been shown to improve fetal outcome, much larger numbers of participants would be required to demonstrate that better gestational 'dating' and earlier detection of multiple pregnancy result in improved outcomes for babies.

The detection of fetal malformation has been addressed in detail only in two of the trials. The Helsinki trial showed improved detection with a resultant increase in the termination of pregnancy rate and a drop in perinatal mortality. There were, however, large differences in the detection rates between the two hospitals involved in this study, which shows that variation in skill and expertise can

impact on performance and effectiveness of ultrasonography, and highlights the need for education, training, audit and quality control. This point is further emphasised by the low detection rate of major fetal malformations in the large RADIUS trial - only 17% of such babies were identified in the ultrasound screened group before 24 weeks of pregnancy. Based on the Helsinki trial results and other reports of observational data, this implies unsatisfactory diagnostic expertise. A combination of low detection rates of malformation, together with a gestational age limit of 24 weeks for legal termination of pregnancy in the RADIUS trial, produced minimal impact on perinatal mortality, unlike the Helsinki experience.

The majority of obstetric units in the developed world already practice routine early pregnancy ultrasonography. For those considering its introduction, the benefit of the demonstrated advantages needs to be considered against the theoretical possibility that the use of ultrasound during pregnancy could be harmful, and the need for additional resources. At present, there is no clear evidence that ultrasound examination during pregnancy is harmful. The findings from the follow up of school children and teenagers, exposed as fetuses to ultrasound in the Norwegian and Swedish trials (Norway; Sweden) are generally reassuring; the finding that fewer children in the Norwegian ultrasound groups were right-handed was not confirmed by intention to treat analysis of long-term follow-up data from the Swedish trial. The Norwegian finding is difficult to interpret and may have been a chance observation that emanated from the large number of outcome measures assessed, or from the method of ascertainment. Alternatively, if it was a real consequence of ultrasound exposure, then it could imply that the effect of diagnostic ultrasound on the developing brain may alter developmental pathways. No firm conclusion can be reached from available data, and there is a need to study these children formally rather than to rely on a limited number of questionnaire responses obtained from the parents (Paneth 1998).

Financial costs also need to be considered. Calculations by the authors of the Radius report indicate that screening four million pregnant women in the USA at 200 dollars per scan would increase costs by one billion dollars per year (LeFevre 1993). While costs have been shown to be less in other countries (Henderson 2002; Roberts 2002), economic issues will still be relevant, particularly in low-resource settings. Clinicians, health planners, and pregnant women need to decide if these results justify the expense of providing routine ultrasound examination in early pregnancy. The early Helsinki data may have overestimated the efficiency of scans. Cost savings were assumed on the basis of decreased perinatal mortality which was not borne out in other studies.

Maternal anxiety and satisfaction have not been well explored in the studies included in this review. Parents may not be fully informed about the purpose of routine ultrasonography and may be made anxious, or be inappropriately reassured by scans (Garcia 2002; Lalor 2007). Ultrasound scans are, however, popular - the potential enjoyment that parents can receive from seeing the image of their baby in utero is discussed elsewhere (Neilson 1995).

Overall completeness and applicability of evidence

The review includes several large trials, although the eligibility criteria of some trials (e.g. RADIUS) mean that results may not be generalisable to all women.

The majority of studies were carried out in high-resource settings where overall levels of perinatal mortality are low and the contribution of major fetal abnormality to mortality is higher than in lower-resource settings. Findings in high-resource settings may not apply in less affluent settings.

Studies were carried out over three decades and technical advances in equipment, more widespread use of ultrasonography in the developed world, and training and expertise of operators are likely to have resulted in more effective sonography, particularly for the detection of fetal abnormalities. The two trials which evaluated detection of fetal abnormality are probably not relevant in today's setting.

Quality of the evidence

Overall, the review includes several large, well designed trials but the lack of blinding is a problem common to all of the studies and this may have an effect on some outcomes.

Potential biases in the review process

The possibility of introducing bias was present at every stage of the reviewing process. We attempted to minimise bias in a number of ways; two review authors assessed eligibility for inclusion, carried out data extraction and assessed risk of bias. Each worked independently. Nevertheless, the process of assessing risk of bias, for example, is not an exact science and includes many personal judgements. Further, the process of reviewing research studies is known to be affected by prior beliefs and attitudes. It is difficult to control for this type of bias in the reviewing process.

While we attempted to be as inclusive as possible in the search strategy, the literature identified was predominantly written in English and published in North American and European journals. Although we did attempt to assess reporting bias, constraints of time meant that this assessment largely relied on information available in the published trial reports and thus, reporting bias was not usually apparent.

AUTHORS' CONCLUSIONS

Implications for practice

Routine early pregnancy ultrasonography has been shown to detect multiple pregnancy earlier, and to reduce induction of labour for

post-term pregnancy, both of which could be clinically useful if resources allow.

Implications for research

1) Other benefits which could result from better gestational age assessment, e.g. better management of pregnancies complicated by fetal growth retardation, need to be assessed in much larger studies than have been reported so far.

(2) Earlier detection of twin pregnancies has not been translated into an improvement in fetal outcome. The continuing high perinatal mortality rate from multiple pregnancies is a legitimate cause for concern and requires study on a number of fronts; at least, early detection improves the potential for the proper scientific study of other, potentially useful, interventions in multiple pregnancies.

(3) There is a need to look at the value of the detection of fetal abnormalities in terms of important outcomes (perinatal morbidity, mortality, burden of disease and long-term outcomes) in the context of newer imaging technologies and advancing skill in fetal abnormality detection.

(4) In settings where resources are constrained the question of the added value of ultrasonography should be revisited in the light of technological advances.

(4) In the developed world screening for Down's syndrome and fetal abnormality is moving into the first trimester and there is a need to evaluate the optimal timing of ultrasonography for gestational dating, multiple pregnancy detection including chorionicity determination, and fetal abnormality detection. There is also a need to determine whether one or more scans are needed to provide all this information in a way that is cost effective and acceptable to women.

(5) There is still some debate about the long-term outcomes associated with fetal exposure to ultrasound, especially multiple exposures and the use of colour Doppler in the first trimester.

(6) There is a lack of evidence from trials on women's views; although ultrasound is perceived as a largely benign technology and is popular with women and their families, the finding of structural features in the fetus of uncertain significance can cause great upset. In the context of advancing technology, women's views should be explored as part of future evaluations.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Adelaide 1999

Methods	RCT (women randomised).
Participants	Setting: Adelaide, Australia, 2 hospitals. Study carried out 1991-5. 648 women attending hospital for their first antenatal visit. Inclusion criteria: women attending for antenatal care < 17 weeks' gestation, no previous ultrasound scans this pregnancy, expected to deliver at the study hospital, no clear indication for ultrasound at the first visit.
Interventions	Intervention group (n = 321): ultrasound scan at 11-14 weeks' gestation (at the antenatal booking visit) performed by medical staff with ultrasound training or in the ultrasound department. Control group (n = 327): routine care. All women were offered routine scans at 18-20 weeks and completed assessments of anxiety and feelings about pregnancy.
Outcomes	Number of women whose EDD was adjusted by 10 or more days at the 18-20 weeks' scan. Number of women booked for fetal morphology scan at suboptimal gestation (< 17 or > 20 weeks). Number of women needing repeat serum screening. Number of women who felt worried about pregnancy at the end of the first visit.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Random number tables. Randomisation carried out by external university clinical trials unit.
Allocation concealment?	Yes	Consecutively numbered opaque, sealed envelopes. Envelopes prepared by researcher not involved in clinical care.
Blinding? Women	No	
Blinding? Clinical staff	Unclear	Reports not available to staff carrying out 18-20 week scans.
Incomplete outcome data addressed? All outcomes	Yes	648 randomised (321 in intervention group and 327 controls). All women randomised were included in the analysis for the primary outcome. 37 women miscarried before the mid-trimester morphology scan (18 in the inter-

Adelaide 1999 (*Continued*)

		vention group and 19 in the control group). Few women were lost to follow up (17). Pregnancy outcome data were available for 296/321 of the intervention group and 298/327 of the control group. There were missing data (< 10%) for some outcomes.
Free of other bias?	Yes	Groups balanced at baseline. Primary analysis by ITT.

Alesund

Methods	RCT. Individual randomisation.
Participants	1628 women attending their first antenatal visit at the clinics of 35 general practitioners (nearly all women in that geographical area, including those with 'high-risk' pregnancies) . Recruitment 1979-1981.
Interventions	Intervention group: routine ultrasound examinations at 18 weeks (biparietal diameter measured to predict EDD, multiple pregnancies noted, placenta located and general examination of the fetus) and 32 weeks (biparietal diameter and abdominal circumference, final placental location and presentation noted) with additional examination at 36 weeks if fetus small for gestational age or presenting by the breech. Control group: selective examination for specific clinical indications only (77% of women in the control group did not have an ultrasound examination). Ultrasound examinations performed by 1 of 2 experienced doctors.
Outcomes	Primary outcome: induction of labour for 'post-term' pregnancy; secondary outcomes: indices of perinatal mortality and morbidity.
Notes	The data that have been entered into this version of the review are derived from only those pregnancies that were singleton, except for perinatal mortality rates which are calculated from all pregnancies.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not described.
Allocation concealment?	Unclear	Described as the "sealed envelope method".
Blinding? Women	No	Blinding not attempted.
Blinding? Clinical staff	No	
Blinding? Outcome assessors	No	

Alesund (*Continued*)

Incomplete outcome data addressed? All outcomes	Yes	Very low levels of missing data (although denominators were not provided for all outcomes reported) . Some discrepancies between the 1984 and 2000 publications.
Free of selective reporting?	Unclear	Main outcome, and power calculation for post-term induced labour. No selective reporting bias apparent.
Free of other bias?	Unclear	Some baseline imbalance between groups. 64% of the intervention group compared to 69% of the control group were non-smokers (P = 0.02).

Helsinki

Methods	RCT (women randomised).
Participants	All women attending one of 64 health centres. Recruitment 1986-1987. 9310 women randomised (women were included even if they had had a previous scan elsewhere).
Interventions	Intervention group: (4691 randomised); ultrasound examination at 16-20 weeks. Control group: routine care (selective scanning for specific reasons).
Outcomes	Fetal outcome and clinical interventions.
Notes	77% of women in the control group underwent at least one ultrasound scan during pregnancy. Mean scans per pregnancy: 2.1 (study group), 1.8 (control group).

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not described.
Allocation concealment?	Unclear	Described as "by sealed envelope method".
Blinding? Women	No	Blinding not attempted.
Blinding? Clinical staff	No	
Blinding? Outcome assessors	No	
Incomplete outcome data addressed? All outcomes	Yes	Small loss to follow up (< 1%). Those women that did not attend for screening were included in the analysis as part of the intervention group.

Helsinki (*Continued*)

		In the intervention group of 4691 randomised 9 women were not pregnant, there were 265 miscarriages before screening and 26 women had pregnancy terminations before screening, a further 6 women were found to be not pregnant after screening. In the control group of 4619 women randomised, 2 women were not pregnant, 284 had spontaneous miscarriage before screening, and 21 had pregnancy terminations before screening.These women have not been included in the denominators in the analyses in this review.
Free of selective reporting?	Unclear	None apparent.

Johannesburg 2007

Methods	Quasi-randomised trial.
Participants	Setting: semi-urban health district serving a working class population in what was described as a "resource -constrained setting". 955 women enrolled (804 women available for analysis). Low-risk women.
Interventions	Intervention group: ultrasound screening at between 18 to 23 weeks. Control group: no routine ultrasound.
Outcomes	Inductions for post-term pregnancy, miscarriage and perinatal mortality, fetal and neonatal outcomes and clinical interventions.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	No	Allocation by day of clinic attendance.
Allocation concealment?	No	Group allocation could be anticipated in advance.
Blinding? Women	No	Not feasible.
Blinding? Clinical staff	No	
Blinding? Outcome assessors	No	
Incomplete outcome data addressed? All outcomes	No	955 women were enrolled (it was not clear how many were randomised to each group). 151 women were lost to follow up

Johannesburg 2007 (*Continued*)

		(15.7%) leaving 804 women for analysis. There were further missing data for some outcomes. Reasons for attrition were not described, and it was not clear that loss was balanced across groups.
Free of other bias?	Unclear	It was reported that there was no baseline imbalance between groups, but characteristics of women in the intervention and control groups were not described.

London 1982

Methods	Quasi-randomised trial.
Participants	1062 women attending 3 obstetric clinics in a maternity hospital in London, UK.
Interventions	All women had an ultrasound at 16 weeks. BPD measured. Intervention group: results of scan were recorded in patient notes. The BPD was used to calculate an EDD and the estimated EDD (from menstrual history) was revised if scan revealed 2 weeks or more difference in estimated gestational age. Control group: results of scan were not revealed (if a multiple pregnancy had not been identified by 26 weeks' gestation then the code was broken and this was revealed). (30% (161/531) in the comparison group had results revealed due to clinician concerns.)
Outcomes	Muliple pregnancy, EDD, perinatal mortality, and birthweight.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	No	Quasi-randomisation. Women "were divided into two groups according to the last digit of the hospital number".
Allocation concealment?	No	Group allocation could be anticipated in advance of recruitment.
Blinding? Clinical staff	No	Results of the ultrasound were not disclosed for women in the control group, but the absence of the report would be apparent to clinicians and outcome assessors.
Blinding? Outcome assessors	No	
Incomplete outcome data addressed? All outcomes	Yes	Low levels of missing data. 1095 women were randomised, 4 women were lost to follow up, there were 13 early miscarriages and 4 fetal deaths before 16 weeks, 4 women were not pregnant (it was not clear which group these women were in

London 1982 (*Continued*)

		or whether loss was balanced across groups).
Free of selective reporting?	Unclear	Main outcomes were gestational age at delivery and induction but many other outcomes were reported - it was not clear whether they had been prespecified in the study protocol.
Free of other bias?	Unclear	Women with multiple pregnancies not diagnosed by 26 weeks' gestation in the control group had the diagnosis revealed.

Missouri 1990

Methods	RCT (individual randomisation).
Participants	915 women attending for first prenatal visit at 8 general physician and 8 obstetrician clinics in Missouri, USA (study carried out 1984-1986). Exclusion criteria: women were excluded if an ultrasound was indicated at recruitment.
Interventions	Intervention group (n = 459): ultrasound scan at 10-18 weeks (most carried out between 10-12 weeks) to estimate gestational age and detect multiple pregnancy (fetal viability and uterine abnormalities noted). Control group (n = 456): usual care (scan when indicated).
Outcomes	Induction for post-dates pregnancy, detection of multiple pregnancy before 24 weeks, adverse perinatal outcome (death, admission to NICU for more than 3 days, 5 min Apgar score < 6).
Notes	Exclusion criteria were such that 58% of those approached were not eligible for inclusion. 24% of the usual care group received scans but were analysed according to randomisation group.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Described as "randomization cards" in blocks of 4 and stratified by practice site.
Allocation concealment?	Unclear	"sequentially numbered, sealed, opaque envelopes." Described as "double consent randomization", patients consented after they were aware of their randomisation group but were asked whether their records could be used in the analysis, "patients consenting to the use of their records but refusing to receive ultrasound were retained in the original assigned group for the purposes of analysis".

Missouri 1990 (*Continued*)

Blinding? Women	Unclear	9% lost to follow up after randomisation.
Blinding? Clinical staff	No	Not attempted.
Blinding? Outcome assessors	No	
Incomplete outcome data addressed? All outcomes	No	(Only 42% of women screened were eligible for inclusion in this trial). Of 415 randomised to the intervention group 11 refused consent and 46 were lost to follow up. Of the 456 randomised to the control group 5 refused and 38 were lost to follow up. A further 25 women in the intervention group refused scans but were included in the analyses according to randomisation group.
Free of selective reporting?	Yes	Main outcomes gestational age and diagnosis of multiple pregnancies.
Free of other bias?	Yes	

Norway

Methods	Long-term follow up of 2 RCTs (Alesund; Trondheim 1984) carried out 1979-81 in Norway.
Participants	*See* Alesund and Trondheim 1984. 2428 children (singletons) followed up at 8-9 years of age.
Interventions	Mothers of children in the intervention group had been offered routine ultrasound at 18 and 32 weeks' gestation. The comparison group had ultrasound selectively (by clinical indication).
Outcomes	Follow up at 8-9 years, neurological, behavioural, and developmental outcomes.
Notes	It was not clear whether long-term developmental outcomes had been specified at the outset.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	*See* Alesund and Trondheim 1984 studies. Not described.
Allocation concealment?	Unclear	Described as "sealed envelope method".

Norway (*Continued*)

Blinding? Women	No	Not attempted.
Blinding? Clinical staff	Unclear	For some outcomes child health centre staff were blind to group allocation.
Incomplete outcome data addressed? All outcomes	Unclear	Small loss to follow up for the outcomes assessed in labour or the early postnatal period. For some longer-term outcomes there were higher levels of missing data (e.g. for outcomes on handedness complete data was available for 69% of the original sample).
Free of selective reporting?	Unclear	It was not clear whether the longer term outcomes had been specified in the original study protocols.
Free of other bias?	Unclear	There were differences between the Trondheim and Alesund samples which makes interpretation of the results difficult. The Alesund sample included most pregnant women whereas the Trondheim sample was of more low-risk pregnancies.

Oxford 2006

Methods	RCT with block randomisation.
Participants	Setting: Oxford UK. 463 women attending 20 GP practices for pregnancy confirmation. Inclusion criteria: women attending in the first trimester with no obstetric indication for a first trimester scan.
Interventions	Intervention group: first trimester ultrasound scan (8-12 weeks) measuring crown-rump length by senior sonographer. EDD calculated if there were more than 5 days difference from menstrual dates. Control group: no first trimester scan. EDD from menstrual dates. Both groups had a routine anomaly scan at 18-20 weeks.
Outcomes	Induction of labour for post-term pregnancy.
Notes	Trial stopped early.

Risk of bias

Item	**Authors' judgement**	**Description**

Oxford 2006 (*Continued*)

Adequate sequence generation?	Unclear	Block randomisation (block size 6).
Allocation concealment?	Yes	Consecutively numbered, opaque, sealed envelopes.
Blinding? Women	No	
Blinding? Clinical staff	No	Results of scans in case notes.
Blinding? Outcome assessors	No	Results of scans were in case notes.
Incomplete outcome data addressed? All outcomes	Yes	463 randomised, 393 available for follow up after 24 weeks. 4 women in each group were lost to follow up. Report that the analysis was by ITT. (Loss before 24 weeks included miscarriage (24 in the intervention and 29 in the control group) these women were included in the ITT analysis.)
Free of other bias?	No	The study was not completed. Private first trimester scans were introduced while the study was being carried out and women who had had such scans were not eligible (it was not clear how many women were excluded on this basis) and this compromised recruitment. Approximately half of the desired sample was recruited and the study did not have the required power to detect differences between groups.

RADIUS

Methods	RCT after stratification by practice site.
Participants	15530 women. Inclusion criteria: women who did not have 'an indication for ultrasonography' based on medical disorder, uncertain gestational age, previous or current pregnancy complication, i.e. those who were eligible for inclusion were at low risk of adverse pregnancy outcome (and comprised 40% of the total population).
Interventions	Intervention group: (n = 7812) ultrasound screen at 18-20 and at 31-33 weeks' gestation. Control group: (n = 7718) selective ultrasonography for specific reasons only. 97% of women in the screened group had at least 2 ultrasound examinations; 55% of women in the control group had no scan at all. The mean number of scans was 2.2 (screened group) and 0.6 (controls). Ultrasound was to include a detailed study of fetal anatomy. Recruitment 1987-1991.
Outcomes	Fetal outcome and indices of care/intervention during pregnancy. The primary outcomes were fetal and neonatal mortality, and 'moderate or severe' neonatal morbidity.

RADIUS (*Continued*)

Notes		

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	According to a "computer-based randomization sequence" with stratification for practice site.
Allocation concealment?	Unclear	Not described.
Blinding? Women	No	Not attempted.
Blinding? Clinical staff	No	
Blinding? Outcome assessors	No	
Incomplete outcome data addressed? All outcomes	Yes	Analysis for primary outcomes for all women not lost to follow up (available case analysis) . 1.6% were lost to follow up and 0.8% had spontaneous miscarriages.
Free of selective reporting?	Unclear	None apparent.
Free of other bias?	Yes	Large numbers of women ineligible for inclusion (15,530 of 53,367 randomised).

Sweden

Methods	RCT.
Participants	4997 women booking for antenatal care between October 1985 and March 1987 at 19 antenatal clinics in Stockholm, Sweden. Women were approximately 11 weeks' gestation at randomisation. Inclusion criteria: all consenting women at < 19 weeks who had not already had an ultrasound scan and who did not have one of a number of pre-specified indications for ultrasound (mainly uncertainties about gestational age, medical disorder, previous complications).
Interventions	Intervention group: planned routine ultrasound at about 15 weeks (range 13-19 weeks) . Scans were carried out either in the ultrasound department or by trained midwives or obstetricians. BPD was measured and fetal viability and multiple pregnancy noted (98.7% had a scan as planned). Control groups: no routine scan unless indicated (4.1% had a scan before and 31% of

Sweden (*Continued*)

	control group women had an ultrasound scan after 19 weeks).
Outcomes	Major outcome; "neonatal morbidity" defined by admission to (and duration of stay in) neonatal ward. Follow-up data on neurodevelopmental outcome are available for around 70% of the sample at ages 8-9; these data were obtained by postal questionnaire. Data are also available on growth characteristics during childhood but not in a form that allows inclusion in the data tables; there was little difference between groups. School records of teenagers are available for 94% of singletons; data on school performance were not reported in a form that allowed us to include them in data tables.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not described.
Allocation concealment?	Yes	"opaque sealed envelope method."
Blinding? Women	No	Not feasible.
Blinding? Clinical staff	No	
Blinding? Outcome assessors	No	Not mentioned.
Incomplete outcome data addressed? All outcomes	Unclear	(32% of those otherwise eligible to participate were not included as they had indications for elective scanning.) 4997 women were randomised. There was small loss to follow up for pregnancy outcomes but greater loss to follow up and missing data for childhood developmental outcomes (> 50% attrition for some outcomes).
Free of other bias?	Unclear	No baseline imbalance apparent. We have included all women randomised in the denominators for pregnancy outcomes.

Trondheim 1984

Methods	RCT.
Participants	1009 women attending their first antenatal visit at 25 general practitioners in Trondheim, Norway. Recruitment 1979-1980.
Interventions	Intervention group: ultrasound scans at 19 and 32 weeks' gestation. At the 19 week scan the BPD was measured to assess gestational age and to predict the EDD. Placental

Trondheim 1984 (*Continued*)

	location and multiple pregnancies were noted. At the 32 week scan the mean abdominal diameter and the BPD were assessed, the placental location and presentation were noted. Control group: no routine scans.
Outcomes	Reduction in post-term labour inductions. Birthweight and NICU admission, interventions in labour.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Described as "randomly selected" "randomized to two equally large groups".
Allocation concealment?	Unclear	Described as "sealed envelope method".
Blinding? Women	No	Not attempted.
Blinding? Clinical staff	No	
Blinding? Outcome assessors	Unclear	Partial blinding of outcome assessment for some outcomes "those who assessed neonatal outcomes did not know whether mothers were cases or controls".
Incomplete outcome data addressed? All outcomes	Yes	Very low levels of missing data.1009 women were randomised; of the 510 women in the intervention group there were 13 miscarriages (3 after the screening) and 1 woman was lost to follow up; of 499 controls there were 19 miscarriages and 2 women were lost to follow up.
Free of selective reporting?	Yes	Not apparent.
Free of other bias?	Yes	None apparent.

Tygerberg 1996

Methods	RCT.
Participants	988 women attending clinics in Tygerberg, South Africa, where there was no policy for routine ultrasound and where many women did not have access to facilities for ultrasound. Recruitment between 1991-2. Randomisation at 18-24 weeks' with gestational age being estimated from menstrual history and clinical examination. Inclusion criteria: urban pregnant women attending for antenatal care before 24 weeks' gestation and planning to deliver in the Tygerberg area.

Tygerberg 1996 (*Continued*)

	Exclusion criteria: women aged over 37 and those that had already had an ultrasound. Women with increased risk of congenital abnormalities, with diabetes or rhesus sensitisation were also excluded.
Interventions	Intervention group: "routine ultrasound" by trained obstetric registrar. Results were recorded in notes. Control group: no routine ultrasound, selective ultrasound at the discretion of the managing clinician.
Outcomes	The study examined whether routine ultrasound would reduce the use of other antenatal services by improved dating and earlier diagnosis of outcomes and whether perinatal outcomes (gestational age at delivery, birthweight, perinatal mortality for babies over 28 weeks and NICU admissions) would be improved.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not described.
Allocation concealment?	Yes	"sealed, opaque envelopes."
Blinding? Women	No	Not feasible.
Blinding? Clinical staff	No	
Blinding? Outcome assessors	Unclear	Not mentioned.
Incomplete outcome data addressed? All outcomes	Unclear	988 women randomised, 8% of women excluded after randomisation. Of 496 women randomised to the intervention group 3 were not pregnant and 36 were lost to follow up. Of 492 controls 1 woman was not pregnant and 39 were lost to follow up.
Free of other bias?	Yes	No baseline imbalance apparent.

BPD: biparietal diameter
EDD: expected date of delivery
ITT: intention to treat
min: minute
NICU: neonatal intensive care unit
RCT: randomised controlled trial

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

Belanger 1996	Study design: randomised controlled trial. Intervention: scans at 16-20 weeks and 30-36 weeks versus scans only when clinically indicated in a low risk population. Participants: 286 singleton infants. Outcomes: Bayley evaluations at 6 and 18 months of age giving 2 scores, Mental Development Index and Psychomotor Development. Did not report on any measures included in the review.
Bennett 2004	Study design: randomised controlled trial. Intervention: first trimester estimation of CRL for gestational age estimation versus second trimester biometry estimation of gestational age. Participants: 218 women. Outcomes: rate of induction of labour for post-term pregnancy. This study was excluded as women were randomised to receive either a first or second trimester scan (scans in both arms of the trial were carried out before 24 weeks' gestation).
Duff 1993	In this study both groups had scans in early pregnancy. Randomised controlled trial examining an early "dating" scan versus an early "dating" scan and a further scan at 34 weeks' gestation (1528 women randomised). (Outcomes: fetal distress in labour, operative delivery, Apgar scores at delivery, birthweight, perinatal mortality and admission to NICU.
Hong Kong	In this RCT women in the intervention group received a detailed morphology scan at 12 to 14 weeks as part of scheduled nuchal scan. Women in the control group received nuchal scan at 12 to 14 weeks but no detailed morphology scan at this stage. Women in both groups received detailed morphology scans at 16-23 weeks. The study was excluded as women in both groups had an early scan.
Larsen 1992	Study design: randomised controlled study. Intervention: ultrasound estimation of fetal weight at 28 weeks and then every third week until delivery. Participants: 1000 women considered at risk of small-for-gestational-age fetus. Outcomes: number of interventions during pregnancy (elective delivery, admission to hospital), emergency intervention during labour and fetal outcome. All patients had early ultrasound estimation of gestational age.
Leung 2006	Study design: randomised controlled study. Intervention: 2-dimensional US vs 2-dimensional US followed by 3-dimensional/four dimensional US. Participants: 124 women at high risk of a fetal anomaly. Outcomes: maternal anxiety levels at first visit, 18 weeks' gestation (immediately after US examination) and 28 weeks' gestation.
Owen 1994	Study design: unclear. Intervention: monthly ultrasound estimation of fetal growth until 30 weeks and then fortnightly until delivery. Participants: 274 women with no risk factors for abnormal fetal growth. Outcomes: growth velocity. All patients had early ultrasound estimation of gestational age.

(*Continued*)

Rustico 2005	Study design: randomised controlled trial. Intervention: 2-dimensional versus 4-dimensional ultrasound in the second/third trimester of pregnancy. Participants: 100 women. Outcomes: ability of women to visualise fetal structures and movements.
Saltvedt 2006	In this study the timing of early scans was examined in groups randomised to receive scans for fetal assessment at 12 to 14 versus 15 to 18 weeks' gestation.
Schwarzler 1999	This study examined the optimal timing of scans. Women were randomised to receive scans at 18, 20, or 22 weeks' gestation.
Wald 1988	Study design: randomised controlled trial. Intervention: routine scan in early pregnancy versus no scan. Participants: unclear. Outcomes: birthweight, type of labour, mode of delivery, NICU admission, gestation at delivery. Data not available after contact with authors.

NICU: neonatal intensive care unit
US: ultrasound
vs: versus

Characteristics of studies awaiting assessment *[ordered by study ID]*

Newcastle

Methods	RCT.
Participants	15209 women randomised.
Interventions	Intervention group: early ultrasound (11-14 weeks') for fetal abnormalities including anatomic assessment and nuchal translucency screening. Controls: 19 week scan.
Outcomes	Anxiety and depression costs. Anomalies diagnosed.
Notes	The results of the trial were published in a series of brief abstracts. Denominators for results were not provided.

RCT: randomised controlled trial

DATA AND ANALYSES

Comparison 1. Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Detection of fetal abnormality before 24 weeks' gestation	2	387	Risk Ratio (M-H, Fixed, 95% CI)	3.46 [1.67, 7.14]
2 Detection of multiple pregnancy by 24 to 26 weeks' gestation (number NOT detected)	7	295	Risk Ratio (M-H, Fixed, 95% CI)	0.07 [0.03, 0.17]
3 Induction of labour for "post-term" pregnancy	8	25516	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.42, 0.83]
4 Perinatal death (all babies)	10	35735	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.70, 1.12]
5 Perinatal death (excluding lethal malformations)	8	34331	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.72, 1.27]
6 Detection of multiple pregnancy before labour (number NOT detected)	5	273	Risk Ratio (M-H, Fixed, 95% CI)	0.12 [0.03, 0.54]
7 Detection of major anomaly before birth	2	387	Risk Ratio (M-H, Fixed, 95% CI)	3.19 [1.99, 5.11]
8 Low birthweight (less than 2500 g)	8	19337	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.82, 1.33]
8.1 Singletons	4	15868	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.60, 1.15]
8.2 All babies (or not clear)	4	3469	Risk Ratio (M-H, Random, 95% CI)	1.28 [1.00, 1.64]
9 Very low birthweight (< 1500 g)	2	1584	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.27, 5.82]
9.1 Singletons	0	0	Risk Ratio (M-H, Random, 95% CI)	Not estimable
9.2 All babies or not clear	2	1584	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.27, 5.82]
10 Small for gestational age	3	17105	Risk Ratio (M-H, Random, 95% CI)	1.05 [0.81, 1.35]
11 Mean birthweight (grams)	5	23213	Mean Difference (IV, Random, 95% CI)	10.67 [-19.77, 41.11]
12 Apgar score 7 or less at 5 minutes	4	3906	Risk Ratio (M-H, Random, 95% CI)	0.76 [0.33, 1.72]
13 Admission to neonatal intensive care unit (various definitions)	8	19088	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.88, 1.02]
14 Impaired development (screened using the Denver developmental screening test) at childhood follow up	1	1657	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.70, 1.30]
15 Poor oral reading at school	1	1993	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.74, 1.41]
16 Poor reading comprehension at school	1	1984	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.56, 1.22]
17 Poor spelling at school	1	1982	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.64, 1.13]
18 Poor arithmetic at school	1	1993	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.61, 1.35]
19 Poor overall school performance	1	1993	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.62, 1.47]
20 Dyslexia	1	603	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.44, 1.34]
21 Reduced hearing in childhood	2	5418	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.68, 1.20]
22 Reduced vision in childhood	2	5417	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.68, 1.01]
23 Use of spectacles	2	5331	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.74, 1.04]

24 Non right-handedness	2	4715	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.92, 1.36]
25 Ambidexterity	1	1663	Risk Ratio (M-H, Fixed, 95% CI)	1.23 [0.92, 1.63]
26 Appropriately timed serum screening tests (number having repeat screening)	1	602	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.45, 1.76]
27 Appropriately timed anomaly scan (18 to 22 weeks)(number NOT appropriately timed)	1	602	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.55, 1.08]
28 Termination of pregnancy for fetal abnormality	5	28256	Risk Ratio (M-H, Fixed, 95% CI)	2.23 [1.10, 4.54]
29 Number of antenatal visits	2	9502	Mean Difference (IV, Random, 95% CI)	0.16 [-0.33, 0.65]
30 Antenatal hospital admission	6	17785	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.92, 1.18]
31 Induction of labour for any reason	7	24790	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.63, 0.97]
32 Caesarean section	5	22193	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.98, 1.12]
33 Mother not satisfied with care (worried about pregnancy)	1	634	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.65, 0.99]
34 Subgroup analysis by timing of scan: detection of multiple pregnancy by 24-26 weeks' gestation (number not detected)	7	295	Risk Ratio (M-H, Fixed, 95% CI)	0.07 [0.03, 0.17]
34.1 Ultrasound planned before 14 weeks	1	9	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.05, 16.36]
34.2 Ultrasound after 14 weeks	6	286	Risk Ratio (M-H, Fixed, 95% CI)	0.06 [0.02, 0.16]
35 Subgroup analysis: induction of labour for "post-term" pregnancy (early and later scans)	7	24712	Risk Ratio (M-H, Random, 95% CI)	0.61 [0.42, 0.88]
35.1 Scan before 14 weeks	2	1278	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.67, 1.46]
35.2 Scan after 14 weeks	5	23434	Risk Ratio (M-H, Random, 95% CI)	0.49 [0.31, 0.77]
36 Subgroup analysis: perinatal death (earlier and late scans)	9	34923	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.68, 1.11]
36.1 Scan before 14 weeks	2	1416	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.23, 2.30]
36.2 Scan after 14 weeks	7	33507	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.68, 1.13]
37 Subgroup analysis: detection of multiple pregnancy before 24 weeks (number not detected; concealed results	7	295	Risk Ratio (M-H, Fixed, 95% CI)	0.07 [0.03, 0.17]
37.1 Concealed results for controls	1	11	Risk Ratio (M-H, Fixed, 95% CI)	0.17 [0.01, 2.92]
37.2 Selective scan for controls	6	284	Risk Ratio (M-H, Fixed, 95% CI)	0.07 [0.02, 0.17]
38 Subgroup analysis: perinatal death. Concealed results	9	34923	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.68, 1.11]
38.1 Concealed results for controls	1	1073	Risk Ratio (M-H, Fixed, 95% CI)	1.66 [0.40, 6.93]
38.2 Selective scans for controls	8	33850	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.66, 1.09]

Analysis 1.1. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 1 Detection of fetal abnormality before 24 weeks' gestation.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 1 Detection of fetal abnormality before 24 weeks' gestation

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Alesund	2/19	0/18		5.7 %	4.75 [0.24, 92.65]
RADIUS	31/187	8/163		94.3 %	3.38 [1.60, 7.14]
Total (95% CI)	**206**	**181**		**100.0 %**	**3.46 [1.67, 7.14]**

Total events: 33 (Routine scan), 8 (Control)

Heterogeneity: Chi^2 = 0.05, df = 1 (P = 0.83); I^2 =0.0%

Test for overall effect: Z = 3.35 (P = 0.00081)

Analysis 1.2. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 2 Detection of multiple pregnancy by 24 to 26 weeks' gestation (number NOT detected).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 2 Detection of multiple pregnancy by 24 to 26 weeks' gestation (number NOT detected)

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Alesund	0/10	7/7		14.0 %	0.05 [0.00, 0.73]
Helsinki	0/36	9/38		15.0 %	0.06 [0.00, 0.92]
London 1982	0/6	2/5		4.4 %	0.17 [0.01, 2.92]
Missouri 1990	0/2	1/7		1.3 %	0.89 [0.05, 16.36]
RADIUS	1/68	23/61		39.2 %	0.04 [0.01, 0.28]
Sweden	0/25	13/20		24.2 %	0.03 [0.00, 0.47]
Trondheim 1984	1/6	1/4		1.9 %	0.67 [0.06, 7.85]
Total (95% CI)	**153**	**142**		**100.0 %**	**0.07 [0.03, 0.17]**

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Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Total events: 2 (Routine scan), 56 (Control)					
Heterogeneity: Chi^2 = 7.32, df = 6 (P = 0.29); I^2 =18%					
Test for overall effect: Z = 5.68 (P < 0.00001)					

Analysis 1.3. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 3 Induction of labour for "post-term" pregnancy.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 3 Induction of labour for "post-term" pregnancy

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Alesund	13/774	44/750		12.9 %	0.29 [0.16, 0.53]
Johannesburg 2007	6/416	14/388		8.2 %	0.40 [0.16, 1.03]
Missouri 1990	28/402	31/413		15.0 %	0.93 [0.57, 1.52]
Oxford 2006	19/233	17/230		12.6 %	1.10 [0.59, 2.07]
RADIUS	123/7617	161/7534		19.7 %	0.76 [0.60, 0.95]
Sweden	41/2389	88/2412		17.4 %	0.47 [0.33, 0.68]
Trondheim 1984	14/496	19/478		11.7 %	0.71 [0.36, 1.40]
Tygerberg 1996	1/493	14/491		2.6 %	0.07 [0.01, 0.54]
Total (95% CI)	**12820**	**12696**		**100.0 %**	**0.59 [0.42, 0.83]**
Total events: 245 (Routine scan), 388 (Control)					
Heterogeneity: Tau^2 = 0.14; Chi^2 = 22.16, df = 7 (P = 0.002); I^2 =68%					
Test for overall effect: Z = 3.01 (P = 0.0026)					

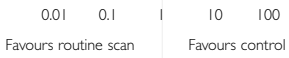
Analysis 1.4. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 4 Perinatal death (all babies).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 4 Perinatal death (all babies)

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Adelaide 1999	3/296	3/298		2.0 %	1.01 [0.20, 4.95]
Alesund	6/794	10/765		6.9 %	0.58 [0.21, 1.58]
Helsinki	20/4422	39/4350		26.7 %	0.50 [0.29, 0.86]
Johannesburg 2007	18/422	16/390		11.3 %	1.04 [0.54, 2.01]
London 1982	5/537	3/536		2.0 %	1.66 [0.40, 6.93]
Missouri 1990	2/402	4/420		2.7 %	0.52 [0.10, 2.84]
RADIUS	52/7685	41/7596		28.0 %	1.25 [0.83, 1.89]
Sweden	12/2415	12/2432		8.1 %	1.01 [0.45, 2.24]
Trondheim 1984	5/503	5/482		3.5 %	0.96 [0.28, 3.29]
Tygerberg 1996	9/496	13/494		8.8 %	0.69 [0.30, 1.60]
Total (95% CI)	**17972**	**17763**		**100.0 %**	**0.89 [0.70, 1.12]**
Total events: 132 (Routine scan), 146 (Control)					
Heterogeneity: Chi^2 = 9.52, df = 9 (P = 0.39); I^2 =5%					
Test for overall effect: Z = 1.01 (P = 0.31)					



Analysis 1.5. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 5 Perinatal death (excluding lethal malformations).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

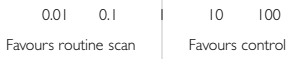
Outcome: 5 Perinatal death (excluding lethal malformations)

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Alesund	6/794	7/765		7.5 %	0.83 [0.28, 2.45]
Helsinki	17/4422	28/4350		29.5 %	0.60 [0.33, 1.09]
London 1982	4/537	3/536		3.1 %	1.33 [0.30, 5.92]
Missouri 1990	2/404	4/420		4.1 %	0.52 [0.10, 2.82]
RADIUS	42/7685	27/7596		28.4 %	1.54 [0.95, 2.49]
Sweden	10/2415	10/2432		10.4 %	1.01 [0.42, 2.42]
Trondheim 1984	5/503	5/482		5.3 %	0.96 [0.28, 3.29]
Tygerberg 1996	6/496	11/494		11.5 %	0.54 [0.20, 1.46]
Total (95% CI)	**17256**	**17075**		**100.0 %**	**0.96 [0.72, 1.27]**

Total events: 92 (Routine scan), 95 (Control)

Heterogeneity: Chi^2 = 8.11, df = 7 (P = 0.32); I^2 =14%

Test for overall effect: Z = 0.30 (P = 0.76)



Analysis 1.6. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 6 Detection of multiple pregnancy before labour (number NOT detected).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 6 Detection of multiple pregnancy before labour (number NOT detected)

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Alesund	0/10	3/7		0.10 [0.01, 1.74]
Helsinki	0/36	0/38		0.0 [0.0, 0.0]
Missouri 1990	0/2	1/7		0.89 [0.05, 16.36]
RADIUS	0/68	8/61		0.05 [0.00, 0.90]
Sweden	0/24	0/20		0.0 [0.0, 0.0]
Total (95% CI)	**140**	**133**		**0.12 [0.03, 0.54]**

Total events: 0 (Routine scan), 12 (Control)

Heterogeneity: $Chi^2 = 2.17$, df = 2 (P = 0.34); $I^2 = 8\%$

Test for overall effect: Z = 2.74 (P = 0.0061)

Analysis 1.7. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 7 Detection of major anomaly before birth.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

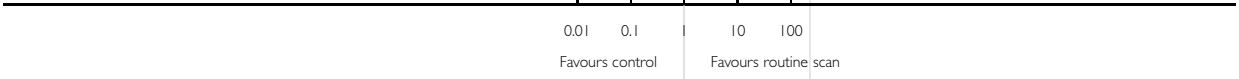
Outcome: 7 Detection of major anomaly before birth

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Alesund	2/19	0/18		2.6 %	4.75 [0.24, 92.65]
RADIUS	65/187	18/163		97.4 %	3.15 [1.95, 5.08]
Total (95% CI)	**206**	**181**		**100.0 %**	**3.19 [1.99, 5.11]**

Total events: 67 (Routine scan), 18 (Control)

Heterogeneity: $Chi^2 = 0.07$, df = 1 (P = 0.79); $I^2 = 0.0\%$

Test for overall effect: Z = 4.82 (P < 0.00001)

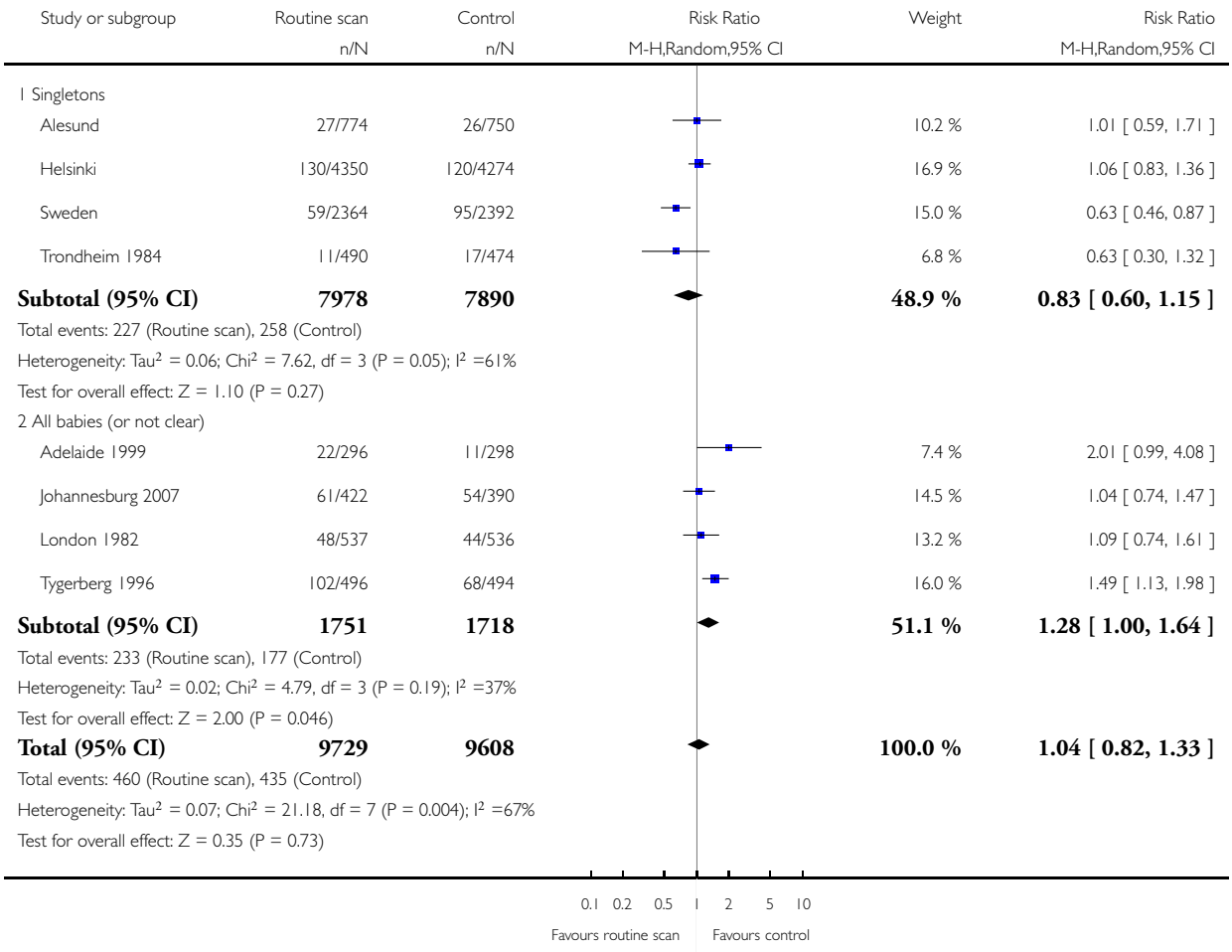


Analysis 1.8. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 8 Low birthweight (less than 2500 g).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 8 Low birthweight (less than 2500 g)



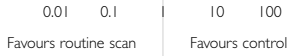
Analysis 1.9. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 9 Very low birthweight (< 1500 g).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 9 Very low birthweight (< 1500 g)

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Singletons					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (Routine scan), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
2 All babies or not clear					
Adelaide 1999	4/296	1/298		30.8 %	4.03 [0.45, 35.82]
Tygerberg 1996	12/496	16/494		69.2 %	0.75 [0.36, 1.56]
Subtotal (95% CI)	**792**	**792**		**100.0 %**	**1.26 [0.27, 5.82]**
Total events: 16 (Routine scan), 17 (Control)					
Heterogeneity: $Tau^2 = 0.74$; $Chi^2 = 2.07$, df = 1 (P = 0.15); $I^2 = 52\%$					
Test for overall effect: Z = 0.29 (P = 0.77)					
Total (95% CI)	**792**	**792**		**100.0 %**	**1.26 [0.27, 5.82]**
Total events: 16 (Routine scan), 17 (Control)					
Heterogeneity: $Tau^2 = 0.74$; $Chi^2 = 2.07$, df = 1 (P = 0.15); $I^2 = 52\%$					
Test for overall effect: Z = 0.29 (P = 0.77)					



Analysis 1.10. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 10 Small for gestational age.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 10 Small for gestational age

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
RADIUS	176/7617	170/7534		52.0 %	1.02 [0.83, 1.26]
Trondheim 1984	41/490	27/474		21.8 %	1.47 [0.92, 2.35]
Tygerberg 1996	38/496	46/494		26.2 %	0.82 [0.55, 1.24]
Total (95% CI)	**8603**	**8502**		**100.0 %**	**1.05 [0.81, 1.35]**

Total events: 255 (Routine scan), 243 (Control)

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 3.35$, df = 2 (P = 0.19); $I^2 = 40\%$

Test for overall effect: Z = 0.34 (P = 0.73)

Analysis 1.11. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 11 Mean birthweight (grams).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 11 Mean birthweight (grams)

Study or subgroup	Routine scan N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Alesund	774	3602 (562.1)	750	3563 (562.1)		16.8 %	39.00 [-17.45, 95.45]
Johannesburg 2007	422	2944 (618)	390	2962 (631)		9.5 %	-18.00 [-104.01, 68.01]
RADIUS	7617	3433 (544)	7514	3429 (535)		35.2 %	4.00 [-13.19, 21.19]
Sweden	2364	3521 (527)	2392	3479 (557)		28.2 %	42.00 [11.19, 72.81]
Tygerberg 1996	496	2890 (627.3)	494	2962 (682.2)		10.3 %	-72.00 [-153.65, 9.65]
Total (95% CI)	**11673**		**11540**			**100.0 %**	**10.67 [-19.77, 41.11]**

Heterogeneity: $Tau^2 = 608.23$; $Chi^2 = 9.87$, df = 4 (P = 0.04); $I^2 = 59\%$

Test for overall effect: Z = 0.69 (P = 0.49)

Analysis 1.12. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 12 Apgar score 7 or less at 5 minutes.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

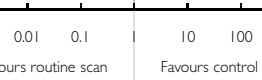
Outcome: 12 Apgar score 7 or less at 5 minutes

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Adelaide 1999	4/296	5/298		23.3 %	0.81 [0.22, 2.97]
Alesund	3/774	10/750		23.7 %	0.29 [0.08, 1.05]
Missouri 1990	2/404	4/420		16.6 %	0.52 [0.10, 2.82]
Trondheim 1984	15/490	9/474		36.4 %	1.61 [0.71, 3.65]
Total (95% CI)	**1964**	**1942**		**100.0 %**	**0.76 [0.33, 1.72]**

Total events: 24 (Routine scan), 28 (Control)

Heterogeneity: $Tau^2 = 0.30$; $Chi^2 = 5.37$, df = 3 (P = 0.15); $I^2 = 44\%$

Test for overall effect: Z = 0.67 (P = 0.51)



Analysis 1.13. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 13 Admission to neonatal intensive care unit (various definitions).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 13 Admission to neonatal intensive care unit (various definitions)

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Adelaide 1999	187/296	187/298		17.8 %	1.01 [0.89, 1.14]
Alesund	63/774	65/750		6.3 %	0.94 [0.67, 1.31]
Helsinki	366/4350	371/4274		35.8 %	0.97 [0.84, 1.11]
Johannesburg 2007	30/422	25/390		2.5 %	1.11 [0.66, 1.85]
Missouri 1990	25/404	31/420		2.9 %	0.84 [0.50, 1.39]
Sweden	231/2364	275/2392		26.2 %	0.85 [0.72, 1.00]
Trondheim 1984	17/490	22/474		2.1 %	0.75 [0.40, 1.39]
Tygerberg 1996	73/496	66/494		6.3 %	1.10 [0.81, 1.50]
Total (95% CI)	**9596**	**9492**		**100.0 %**	**0.95 [0.88, 1.02]**

Total events: 992 (Routine scan), 1042 (Control)

Heterogeneity: Chi^2 = 4.78, df = 7 (P = 0.69); I^2 =0.0%

Test for overall effect: Z = 1.39 (P = 0.17)

Analysis 1.14. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 14 Impaired development (screened using the Denver developmental screening test) at childhood follow up.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 14 Impaired development (screened using the Denver developmental screening test) at childhood follow up

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Norway	75/859	73/798		100.0 %	0.95 [0.70, 1.30]
Total (95% CI)	**859**	**798**		**100.0 %**	**0.95 [0.70, 1.30]**
Total events: 75 (Routine scan), 73 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.30 (P = 0.77)					

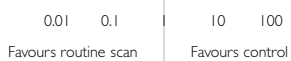
Analysis 1.15. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 15 Poor oral reading at school.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 15 Poor oral reading at school

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Norway	70/1007	67/986		100.0 %	1.02 [0.74, 1.41]
Total (95% CI)	**1007**	**986**		**100.0 %**	**1.02 [0.74, 1.41]**
Total events: 70 (Routine scan), 67 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.14 (P = 0.89)					



Analysis 1.16. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 16 Poor reading comprehension at school.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 16 Poor reading comprehension at school

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Norway	44/1005	52/979		100.0 %	0.82 [0.56, 1.22]
Total (95% CI)	**1005**	**979**		**100.0 %**	**0.82 [0.56, 1.22]**
Total events: 44 (Routine scan), 52 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.97 (P = 0.33)					

Analysis 1.17. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 17 Poor spelling at school.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 17 Poor spelling at school

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Norway	80/1001	92/981		100.0 %	0.85 [0.64, 1.13]
Total (95% CI)	**1001**	**981**		**100.0 %**	**0.85 [0.64, 1.13]**
Total events: 80 (Routine scan), 92 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.09 (P = 0.27)					

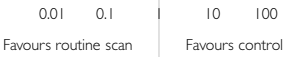
Analysis 1.18. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 18 Poor arithmetic at school.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 18 Poor arithmetic at school

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Norway	44/1004	48/989		100.0 %	0.90 [0.61, 1.35]
Total (95% CI)	**1004**	**989**		**100.0 %**	**0.90 [0.61, 1.35]**
Total events: 44 (Routine scan), 48 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.50 (P = 0.62)					



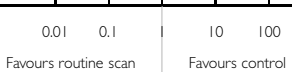
Analysis 1.19. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 19 Poor overall school performance.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 19 Poor overall school performance

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Norway	40/1006	41/987		100.0 %	0.96 [0.62, 1.47]
Total (95% CI)	**1006**	**987**		**100.0 %**	**0.96 [0.62, 1.47]**
Total events: 40 (Routine scan), 41 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.20 (P = 0.84)					



Analysis 1.20. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 20 Dyslexia.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 20 Dyslexia

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Norway	21/309	26/294		100.0 %	0.77 [0.44, 1.34]
Total (95% CI)	**309**	**294**		**100.0 %**	**0.77 [0.44, 1.34]**
Total events: 21 (Routine scan), 26 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.93 (P = 0.35)					

Analysis 1.21. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 21 Reduced hearing in childhood.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 21 Reduced hearing in childhood

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Norway	32/1112	38/1041		40.9 %	0.79 [0.50, 1.25]
Sweden	56/1651	56/1614		59.1 %	0.98 [0.68, 1.41]
Total (95% CI)	**2763**	**2655**		**100.0 %**	**0.90 [0.68, 1.20]**
Total events: 88 (Routine scan), 94 (Control)					
Heterogeneity: Chi^2 = 0.51, df = 1 (P = 0.47); I^2 =0.0%					
Test for overall effect: Z = 0.72 (P = 0.47)					

Analysis 1.22. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 22 Reduced vision in childhood.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

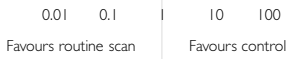
Outcome: 22 Reduced vision in childhood

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Norway	68/1113	72/1039		36.9 %	0.88 [0.64, 1.21]
Sweden	103/1651	126/1614		63.1 %	0.80 [0.62, 1.03]
Total (95% CI)	**2764**	**2653**		**100.0 %**	**0.83 [0.68, 1.01]**

Total events: 171 (Routine scan), 198 (Control)

Heterogeneity: $Chi^2 = 0.22$, df = 1 (P = 0.64); $I^2 = 0.0\%$

Test for overall effect: Z = 1.85 (P = 0.064)



Analysis 1.23. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 23 Use of spectacles.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 23 Use of spectacles

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Norway	82/1069	95/997		39.5 %	0.81 [0.61, 1.07]
Sweden	141/1651	149/1614		60.5 %	0.93 [0.74, 1.15]
Total (95% CI)	**2720**	**2611**		**100.0 %**	**0.88 [0.74, 1.04]**

Total events: 223 (Routine scan), 244 (Control)

Heterogeneity: $Chi^2 = 0.58$, df = 1 (P = 0.45); $I^2 = 0.0\%$

Test for overall effect: Z = 1.47 (P = 0.14)

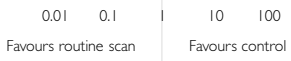
Analysis 1.24. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 24 Non right-handedness.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 24 Non right-handedness

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Norway	162/861	120/802		43.4 %	1.26 [1.01, 1.56]
Sweden	253/1544	240/1508		56.6 %	1.03 [0.88, 1.21]
Total (95% CI)	**2405**	**2310**		**100.0 %**	**1.12 [0.92, 1.36]**
Total events: 415 (Routine scan), 360 (Control)					
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 2.11$, df = 1 (P = 0.15); $I^2 = 53\%$					
Test for overall effect: Z = 1.17 (P = 0.24)					



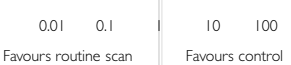
Analysis 1.25. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 25 Ambidexterity.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 25 Ambidexterity

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Norway	100/861	76/802		100.0 %	1.23 [0.92, 1.63]
Total (95% CI)	**861**	**802**		**100.0 %**	**1.23 [0.92, 1.63]**
Total events: 100 (Routine scan), 76 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.41 (P = 0.16)					



Analysis 1.26. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 26 Appropriately timed serum screening tests (number having repeat screening).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 26 Appropriately timed serum screening tests (number having repeat screening)

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Adelaide 1999	15/299	17/303		100.0 %	0.89 [0.45, 1.76]
Total (95% CI)	**299**	**303**		**100.0 %**	**0.89 [0.45, 1.76]**
Total events: 15 (Routine scan), 17 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.32 (P = 0.75)					

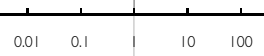
Analysis 1.27. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 27 Appropriately timed anomaly scan (18 to 22 weeks)(number NOT appropriately timed).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 27 Appropriately timed anomaly scan (18 to 22 weeks)(number NOT appropriately timed)

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Adelaide 1999	48/299	63/303		100.0 %	0.77 [0.55, 1.08]
Total (95% CI)	**299**	**303**		**100.0 %**	**0.77 [0.55, 1.08]**
Total events: 48 (Routine scan), 63 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.49 (P = 0.14)					



Analysis 1.28. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 28 Termination of pregnancy for fetal abnormality.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 28 Termination of pregnancy for fetal abnormality

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Alesund	2/825	0/803		4.6 %	4.87 [0.23, 101.22]
Helsinki	11/4691	4/4619		36.4 %	2.71 [0.86, 8.50]
Johannesburg 2007	1/416	0/388		4.7 %	2.80 [0.11, 68.49]
RADIUS	9/7812	5/7718		45.4 %	1.78 [0.60, 5.30]
Tygerberg 1996	1/493	1/491		9.0 %	1.00 [0.06, 15.88]
Total (95% CI)	**14237**	**14019**		**100.0 %**	**2.23 [1.10, 4.54]**

Total events: 24 (Routine scan), 10 (Control)

Heterogeneity: Chi^2 = 0.88, df = 4 (P = 0.93); I^2 =0.0%

Test for overall effect: Z = 2.22 (P = 0.026)

Analysis 1.29. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 29 Number of antenatal visits.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 29 Number of antenatal visits

Study or subgroup	Routine scan N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Helsinki	4386	12.9 (3.3)	4312	12.5 (3.2)		52.6 %	0.40 [0.26, 0.54]
Johannesburg 2007	416	5.8 (1.8)	388	5.9 (2)		47.4 %	-0.10 [-0.36, 0.16]
Total (95% CI)	**4802**		**4700**			**100.0 %**	**0.16 [-0.33, 0.65]**

Heterogeneity: Tau^2 = 0.11; Chi^2 = 10.89, df = 1 (P = 0.00097); I^2 =91%

Test for overall effect: Z = 0.65 (P = 0.51)

Analysis 1.30. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 30 Antenatal hospital admission.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

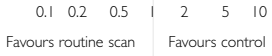
Outcome: 30 Antenatal hospital admission

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Alesund	148/774	178/750		17.4 %	0.81 [0.66, 0.98]
Helsinki	1489/4386	1469/4312		27.7 %	1.00 [0.94, 1.06]
Johannesburg 2007	68/416	51/388		9.5 %	1.24 [0.89, 1.74]
Sweden	338/2389	335/2412		21.6 %	1.02 [0.89, 1.17]
Trondheim 1984	79/496	46/478		9.3 %	1.66 [1.18, 2.33]
Tygerberg 1996	110/493	105/491		14.5 %	1.04 [0.82, 1.32]
Total (95% CI)	**8954**	**8831**		**100.0 %**	**1.04 [0.92, 1.18]**

Total events: 2232 (Routine scan), 2184 (Control)

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 15.00$, df = 5 (P = 0.01); $I^2 = 67\%$

Test for overall effect: Z = 0.61 (P = 0.54)



Analysis 1.31. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 31 Induction of labour for any reason.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

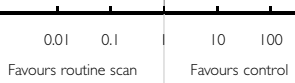
Outcome: 31 Induction of labour for any reason

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Alesund	34/774	77/750		11.8 %	0.43 [0.29, 0.63]
London 1982	104/531	107/531		15.5 %	0.97 [0.76, 1.24]
Missouri 1990	91/402	103/413		15.4 %	0.91 [0.71, 1.16]
Oxford 2006	34/233	46/230		11.5 %	0.73 [0.49, 1.09]
RADIUS	1912/7617	1858/7534		19.1 %	1.02 [0.96, 1.08]
Sweden	140/2389	218/2412		16.4 %	0.65 [0.53, 0.80]
Trondheim 1984	32/496	38/478		10.4 %	0.81 [0.52, 1.28]
Total (95% CI)	**12442**	**12348**		**100.0 %**	**0.78 [0.63, 0.97]**

Total events: 2347 (Routine scan), 2447 (Control)

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 37.57$, df = 6 ($P<0.00001$); $I^2 = 84\%$

Test for overall effect: Z = 2.24 (P = 0.025)



Analysis 1.32. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 32 Caesarean section.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

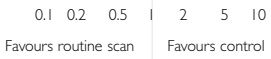
Outcome: 32 Caesarean section

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Johannesburg 2007	60/416	59/388		4.2 %	0.95 [0.68, 1.32]
Oxford 2006	33/233	27/230		1.9 %	1.21 [0.75, 1.94]
RADIUS	1205/7617	1135/7534		78.0 %	1.05 [0.97, 1.13]
Sweden	210/2389	217/2412		14.8 %	0.98 [0.82, 1.17]
Trondheim 1984	29/496	17/478		1.2 %	1.64 [0.92, 2.95]
Total (95% CI)	**11151**	**11042**		**100.0 %**	**1.05 [0.98, 1.12]**

Total events: 1537 (Routine scan), 1455 (Control)

Heterogeneity: $Chi^2 = 3.53$, df = 4 (P = 0.47); $I^2 = 0.0\%$

Test for overall effect: Z = 1.30 (P = 0.19)



Analysis 1.33. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 33 Mother not satisfied with care (worried about pregnancy).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 33 Mother not satisfied with care (worried about pregnancy)

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Adelaide 1999	98/310	128/324		100.0 %	0.80 [0.65, 0.99]
Total (95% CI)	**310**	**324**		**100.0 %**	**0.80 [0.65, 0.99]**

Total events: 98 (Routine scan), 128 (Control)

Heterogeneity: not applicable

Test for overall effect: Z = 2.06 (P = 0.039)

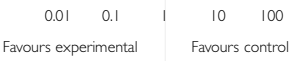
Analysis 1.34. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 34 Subgroup analysis by timing of scan: detection of multiple pregnancy by 24-26 weeks' gestation (number not detected).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 34 Subgroup analysis by timing of scan: detection of multiple pregnancy by 24-26 weeks' gestation (number not detected)

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Ultrasound planned before 14 weeks					
Missouri 1990	0/2	1/7		1.3 %	0.89 [0.05, 16.36]
Subtotal (95% CI)	**2**	**7**		**1.3 %**	**0.89 [0.05, 16.36]**
Total events: 0 (Routine scan), 1 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.08 (P = 0.94)					
2 Ultrasound after 14 weeks					
Alesund	0/10	7/7		14.0 %	0.05 [0.00, 0.73]
Helsinki	0/36	9/38		15.0 %	0.06 [0.00, 0.92]
London 1982	0/6	2/5		4.4 %	0.17 [0.01, 2.92]
RADIUS	1/68	23/61		39.2 %	0.04 [0.01, 0.28]
Sweden	0/25	13/20		24.2 %	0.03 [0.00, 0.47]
Trondheim 1984	1/6	1/4		1.9 %	0.67 [0.06, 7.85]
Subtotal (95% CI)	**151**	**135**		**98.7 %**	**0.06 [0.02, 0.16]**
Total events: 2 (Routine scan), 55 (Control)					
Heterogeneity: Chi^2 = 4.69, df = 5 (P = 0.46); I^2 =0.0%					
Test for overall effect: Z = 5.54 (P < 0.00001)					
Total (95% CI)	**153**	**142**		**100.0 %**	**0.07 [0.03, 0.17]**
Total events: 2 (Routine scan), 56 (Control)					
Heterogeneity: Chi^2 = 7.32, df = 6 (P = 0.29); I^2 =18%					
Test for overall effect: Z = 5.68 (P < 0.00001)					

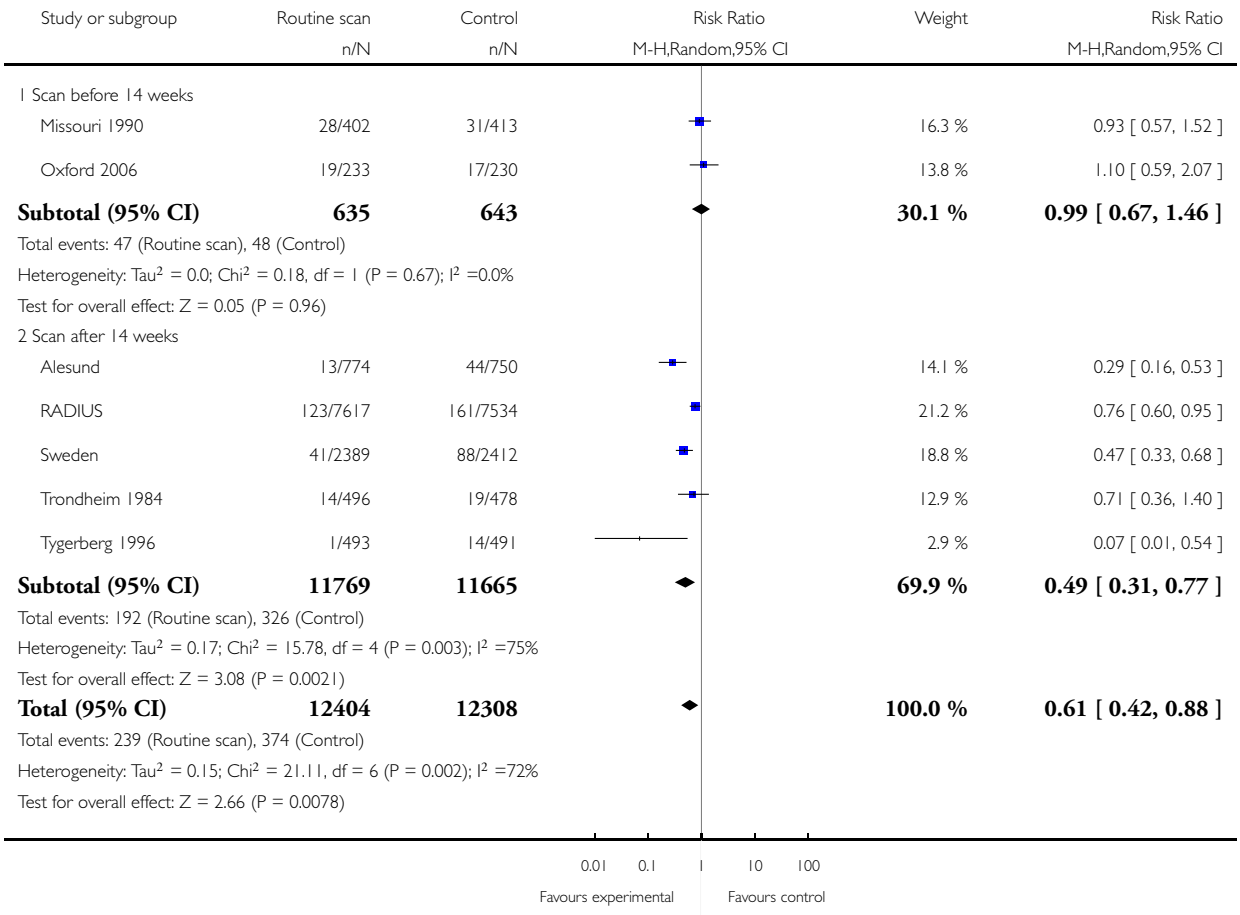


Analysis 1.35. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 35 Subgroup analysis: induction of labour for "post-term" pregnancy (early and later scans).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 35 Subgroup analysis: induction of labour for "post-term" pregnancy (early and later scans)



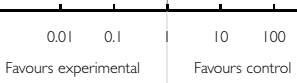
Analysis 1.36. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 36 Subgroup analysis: perinatal death (earlier and late scans).

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 36 Subgroup analysis: perinatal death (earlier and late scans)

Study or subgroup	Routine scan n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Scan before 14 weeks					
Adelaide 1999	3/296	3/298		2.3 %	1.01 [0.20, 4.95]
Missouri 1990	2/402	4/420		3.0 %	0.52 [0.10, 2.84]
Subtotal (95% CI)	**698**	**718**		**5.3 %**	**0.73 [0.23, 2.30]**
Total events: 5 (Routine scan), 7 (Control)					
Heterogeneity: Chi^2 = 0.31, df = 1 (P = 0.58); I^2 =0.0%					
Test for overall effect: Z = 0.53 (P = 0.59)					
2 Scan after 14 weeks					
Alesund	6/794	10/765		7.8 %	0.58 [0.21, 1.58]
Helsinki	20/4422	39/4350		30.1 %	0.50 [0.29, 0.86]
London 1982	5/537	3/536		2.3 %	1.66 [0.40, 6.93]
RADIUS	52/7685	41/7596		31.5 %	1.25 [0.83, 1.89]
Sweden	12/2415	12/2432		9.1 %	1.01 [0.45, 2.24]
Trondheim 1984	5/503	5/482		3.9 %	0.96 [0.28, 3.29]
Tygerberg 1996	9/496	13/494		10.0 %	0.69 [0.30, 1.60]
Subtotal (95% CI)	**16852**	**16655**		**94.7 %**	**0.87 [0.68, 1.13]**
Total events: 109 (Routine scan), 123 (Control)					
Heterogeneity: Chi^2 = 8.89, df = 6 (P = 0.18); I^2 =33%					
Test for overall effect: Z = 1.02 (P = 0.31)					
Total (95% CI)	**17550**	**17373**		**100.0 %**	**0.87 [0.68, 1.11]**
Total events: 114 (Routine scan), 130 (Control)					
Heterogeneity: Chi^2 = 9.28, df = 8 (P = 0.32); I^2 =14%					
Test for overall effect: Z = 1.11 (P = 0.27)					

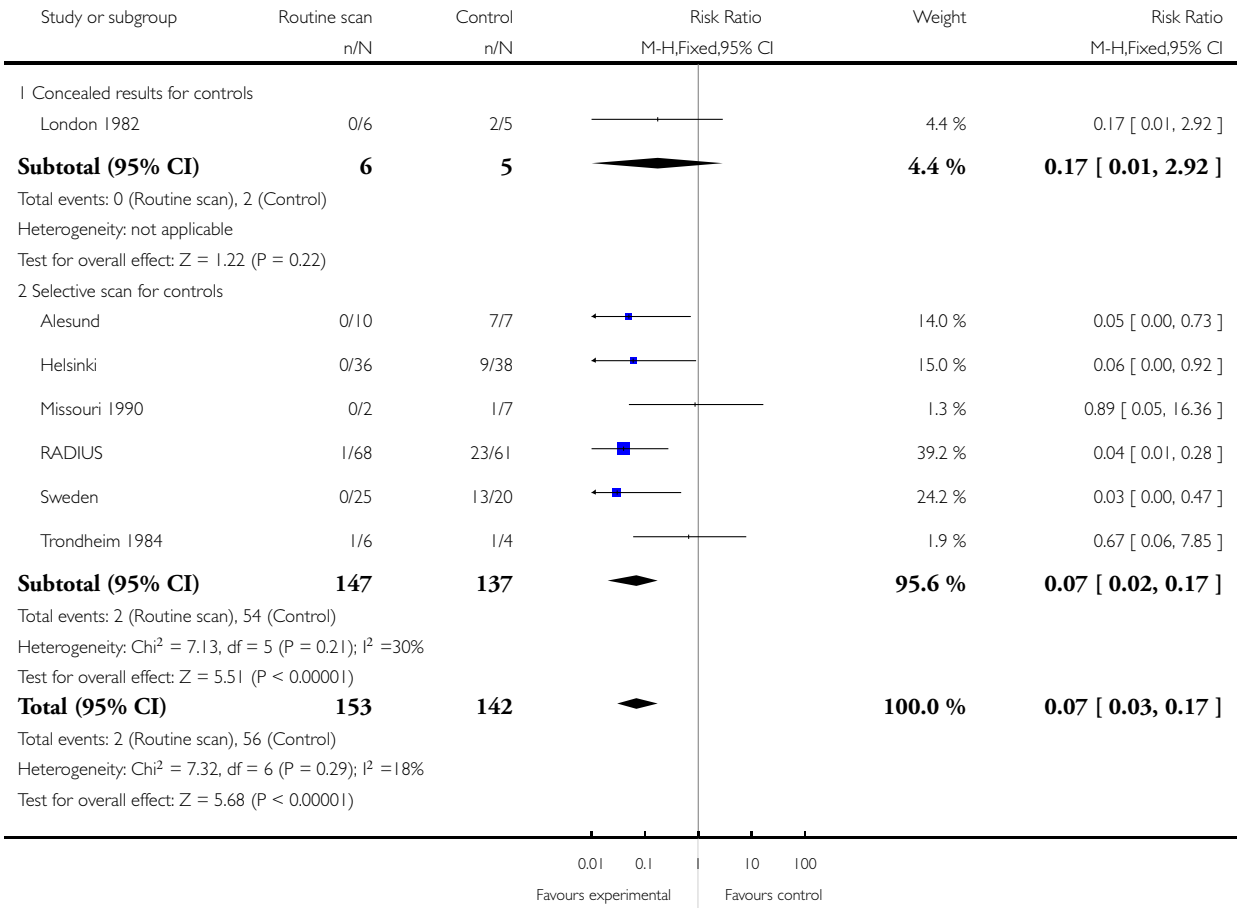


Analysis 1.37. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 37 Subgroup analysis: detection of multiple pregnancy before 24 weeks (number not detected; concealed results.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 37 Subgroup analysis: detection of multiple pregnancy before 24 weeks (number not detected; concealed results

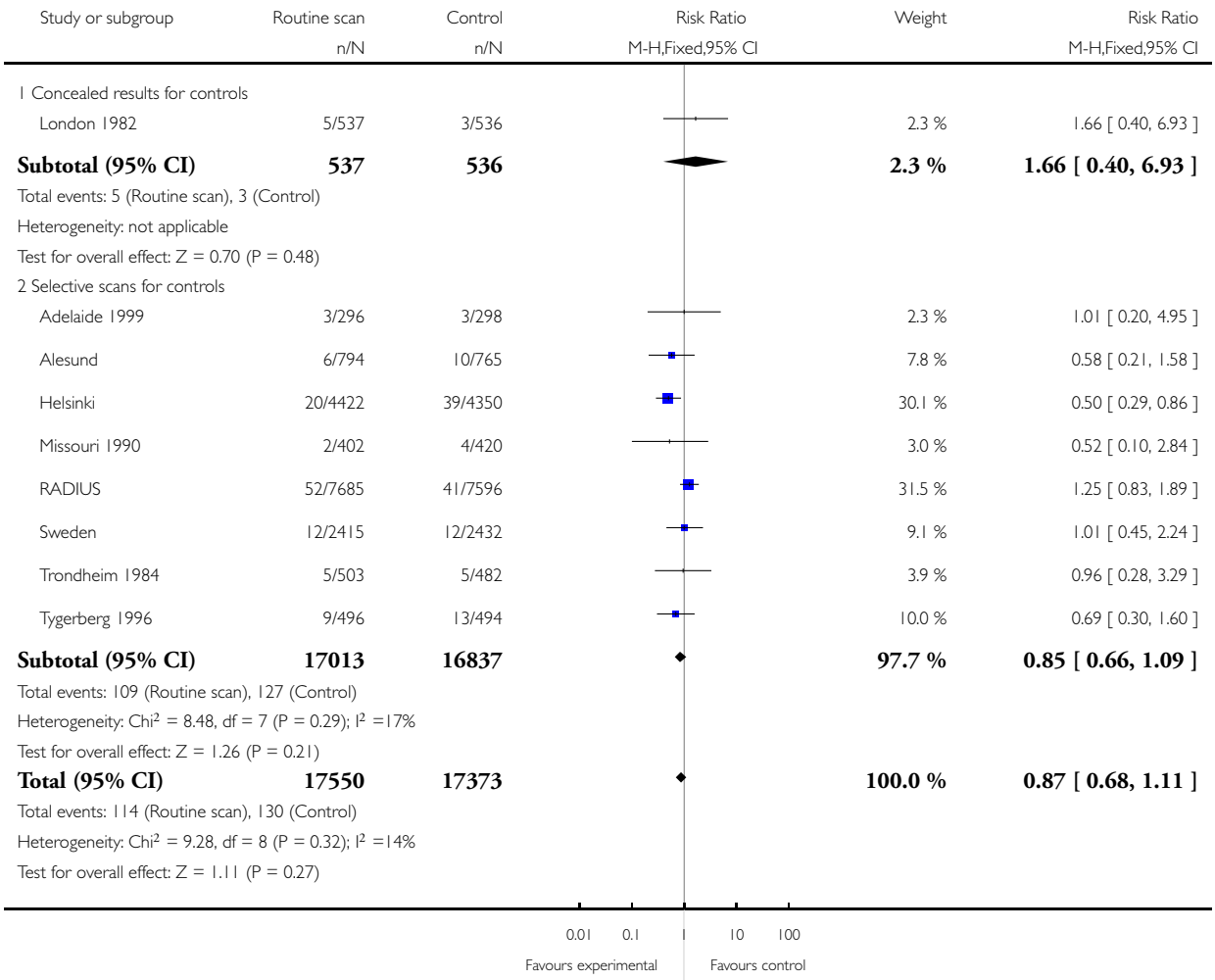


Analysis 1.38. Comparison 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy, Outcome 38 Subgroup analysis: perinatal death. Concealed results.

Review: Ultrasound for fetal assessment in early pregnancy

Comparison: 1 Routine/revealed versus selective/concealed ultrasound in early pregnancy

Outcome: 38 Subgroup analysis: perinatal death. Concealed results



HISTORY

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CONTRIBUTIONS OF AUTHORS

MK Whitworth drafted the initial protocol and review. All other authors commented on subsequent drafts of the review. Data extraction was carried out by MK Whitworth, L Bricker and T Dowswell.

DECLARATIONS OF INTEREST

None known.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The methods section has been updated.

INDEX TERMS

Medical Subject Headings (MeSH)

Congenital Abnormalities [ultrasonography]; Fetal Monitoring [*methods]; Gestational Age; Perinatal Mortality; Pregnancy Trimester, First; Pregnancy Trimester, Second; Pregnancy, Multiple; Ultrasonography, Prenatal [*methods]

MeSH check words

Female; Humans; Pregnancy