Reduction of the number of fetuses for women with a multiple pregnancy (Review)

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[Intervention Review]

Reduction of the number of fetuses for women with a multiple pregnancy

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ABSTRACT

Background

When couples are faced with the dilemma of a higher-order multiple pregnancy there are three options. Termination of the entire pregnancy has generally not been acceptable to women, especially for those with a past history of infertility. Attempting to continue with all the fetuses is associated with inherent problems of preterm birth, survival and long-term morbidity. The other alternative relates to reduction in the number of fetuses by selective termination. The acceptability of these options for the couple will depend on their social background and underlying beliefs. This review focused on reduction in the number of fetuses.

Objectives

To assess a policy of multifetal reduction with a policy of expectant management of women with a multiple pregnancy.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (13 June 2012).

Selection criteria

Randomised controlled trials with reported data that compared outcomes in mothers and babies who were managed expectantly with outcomes in women who underwent selective fetal reduction of a multiple pregnancy.

Data collection and analysis

Two review authors independently assessed trial quality and extracted data.

Main results

There were no randomised controlled trials identified.

Authors' conclusions

We found no available data from randomised trials to inform the risks and benefits of pregnancy reduction procedures for women with a multiple pregnancy. While randomised controlled trials will provide the most reliable evidence about the risks and benefits of fetal reduction procedures, reduction in the number of fetuses by selective termination may not be acceptable to women, particularly couples with a past history of infertility. The acceptability of this option, and willingness to undergo randomisation will depend on the couple's social background and beliefs, and consequently, recruitment to such a trial may prove exceptionally difficult.

PLAIN LANGUAGE SUMMARY

Reduction of the number of fetuses for women with multiple pregnancies

There was no available evidence from randomised controlled trials about the effects of reducing the number of fetuses in women pregnant with a multiple pregnancy. Evidence drawn from non-randomised studies is associated with potential bias.

When a woman carries more than one baby in pregnancy, there may be difficult decisions to face. These pregnancies are at increased risk of complications. It is possible to reduce the number of babies that the mother carries in the hope of improving the health of the remaining babies. There were no good studies to help parents make this difficult choice.

BACKGROUND

Description of the condition

There is a worldwide variation in the incidence of multiple pregnancies, ranging from 6.7 per 1000 births in Japan, to 40 per 1000 births in Nigeria (Dodd 2010). The incidence of monozygous twins is relatively constant at 3.5 per 1000 births, while the incidence of dizygous twins and higher-order multiple pregnancies varies with maternal age, parity, ethnicity and use of assisted reproductive techniques (ART) (Little 1988). The risk of multiple pregnancy from ART correlates directly with the number of embryos transferred, occurring in 17.9% of in vitro fertilisation pregnancies after transfer of two embryos, and increasing to 24.1% after transfer of four embryos (Hurst 1996). Similarly, multiple pregnancy is more common the more oocytes eggs transferred (18.7% following transfer of two oocytes and 25.8% following transfer of three oocytes) (Hurst 1996). Complications and risks for both mother and babies with twin pregnancies are well recognised and increase further for triplet or higher-order multiple pregnancies (Dodd 2010). There is concern too for long-term morbidity in survivors.

Description of the intervention

When couples are faced with the dilemma of a multiple pregnancy there are three options. Termination of the entire pregnancy has generally not been acceptable to women, especially for those with a past history of infertility. Attempting to continue with all the fetuses with the inherent problems of preterm birth, survival and long-term morbidity. Reduction in the number of fetuses by selective termination. The acceptability of these options for the couple will depend on their social background and underlying beliefs. This review focuses on reduction in the number of fetuses.

Techniques have been advocated to reduce multiple pregnancies (two or more developing babies), with the aim of reducing poor obstetric and perinatal outcomes, such as preterm birth, poor growth of the babies, and death of one or more of the babies (Evans 1994b). First trimester fetal reduction has been carried out using both transabdominal (where the needle is placed through the woman's abdominal wall) and transvaginal (where the needle is placed through the woman's vagina) approaches. These pregnancy reduction procedures involve either the aspiration or disruption of the gestational sac by gentle suction or the injection of potassium chloride (KCl) into the chest of the fetus (Evans 1994b).

How the intervention might work

There are many non-randomised cohort data available, describing the effects of fetal reduction procedures. A number of prospective, non-randomised studies have assessed pregnancy outcomes from pregnancy reduction with twins (conceived spontaneously or following assisted reproductive techniques) (Donner 1992; Groutz 1996; Mansour 1999); from pregnancy reduction with expectant

management of a triplet pregnancy (Boulot 1993; Boulot 2000; Lipitz 1994; Mansour 1999; Porreco 1991); and assessing transcervical or transvaginal procedures with transabdominal procedures (Berkowitz 1988; Boulot 1993; Evans 1994a; Shalev 1989). From a methodological perspective, the quality of the prospective cohort studies identified were generally poor, with eligibility criteria poorly stated. Women were offered reduction in the number of fetuses in the pregnancy in an inconsistent manner, based primarily on whether or not the procedure was offered by the women's treating doctor. Allocation of women to each treatment group was based on the preference of the woman and her partner. There was limited reporting of important clinical outcomes, with data available from a single trial only for many of the outcomes considered. All of these factors severely limit the reliability of any results and conclusions that can be made due to the potential for bias.

However, the findings from these studies and from a meta-analysis of prospective non-randomised studies (Dodd 2004), suggests that pregnancy reduction to twins versus expectant management for women with a triplet pregnancy appears to be associated with a reduction in pregnancy loss, antenatal complications, birth before 36 weeks, caesarean birth, low birthweight infants, and neonatal death. Outcomes from pregnancy reduction to twins appear comparable with those obtained from twin pregnancies conceived spontaneously or after assisted reproductive techniques (Dodd 2004). Although reduction of a twin pregnancy to a singleton is reported to be increasingly common (Stone 2007), the effect on risk of pregnancy complications is unclear (Hasson 2011; Stone 2007).

Why it is important to do this review

While the available non-randomised literature suggests that fetal reduction is associated with a reduction in risk of pregnancy loss, preterm birth and other pregnancy complications, the nature of the study design raises potential for risk of bias. This review aims to assess the effects of pregnancy reduction for women with a multiple pregnancy on fetal loss, preterm birth and its complications, and perinatal and neonatal mortality and morbidity from randomised trials. The preferences women have of expectant management and pregnancy reduction need to be considered as does the psychological impact of such a procedure.

OBJECTIVES

To assess a policy of expectant management of women with a multiple pregnancy with a policy of pregnancy reduction. The primary outcomes relate to the risk of preterm birth and its immediate and late complications, maternal and other neonatal morbidity and maternal, fetal and neonatal mortality.

METHODS

Criteria for considering studies for this review

Types of studies

All published, unpublished, and ongoing randomised controlled trials with reported data that compare outcomes for women and infants who were randomised to expectant management of a multiple pregnancy with outcomes for women and infants who were randomised to reduction of the pregnancy to triplets, twins or singleton.

Types of participants

Women with a multiple pregnancy (spontaneous or from assisted reproductive techniques).

Types of interventions

Pregnancy reduction, either by a transabdominal, transcervical or transvaginal approach.

Comparisons:

1. transabdominal approach versus transvaginal approach;
2. transabdominal approach versus transcervical approach;
3. transvaginal approach versus transcervical approach.

Types of outcome measures

Primary outcomes

1. Early pregnancy loss (less than 20 weeks' gestation) (loss as a direct result of the reduction technique will be a subcategory).
2. Stillbirth (death greater than 20 weeks' gestation and before birth).
3. Very preterm birth (less than 34 weeks' gestation).
4. Birthweight (less than 1500 g).
5. Need for admission to the neonatal intensive care unit.
6. Neonatal death and serious infant morbidity (defined as growth restriction; seizures; birth asphyxia defined by trialists; neonatal encephalopathy; disability in childhood).
7. Maternal death and serious maternal morbidity (e.g. admission to intensive care unit, infection requiring intravenous antibiotics, haemorrhage requiring blood transfusion).
8. No surviving child.

Perinatal and maternal morbidity are composite outcomes. This is not an ideal solution because some components are clearly less severe than others. It is possible for one intervention to cause more deaths but fewer babies with severe morbidity. All these outcomes will be rare, and a modest change in their incidence will be easier

to detect if composite outcomes are presented. The incidence of individual outcomes will be explored as secondary outcomes.

Secondary outcomes

Secondary outcomes relate to measures of effectiveness, complications, women's views, women's satisfaction and costs.

Measures of effectiveness

1. Use of maternal tocolytic therapy.
2. Maternal antenatal admission to hospital and length of stay.

Maternal outcomes

1. Antepartum haemorrhage requiring hospitalisation.
2. Preterm prelabour ruptured membranes (PPROM).
3. Chorioamnionitis requiring intravenous antibiotics.Caesarean section.
4. Instrumental vaginal birth.
5. Admission to intensive care unit.
6. Infection requiring intravenous antibiotics.
7. Haemorrhage requiring blood transfusion or major haemorrhage (greater than 1000 mL).
8. Breastfeeding and length of feeding.

Infant complications (for any infant)

1. Apgar score less than seven at five minutes.
2. Fetal metabolic acidosis at delivery less than 7.20.
3. Preterm birth (prior to 37 weeks' gestation).
4. Extremely preterm birth (prior to 28 weeks' gestation)
5. Severe growth restriction (less than the third centile for gestational age).
6. Respiratory distress syndrome.
7. Use of mechanical ventilation.
8. Admission to neonatal intensive care unit.
9. Parameters of birth asphyxia (neonatal irritability, neonatal seizures, neonatal hypotonia, abnormal level of consciousness, neonatal apnoea, tube feeding greater than 48 hours).
10. Neonatal jaundice requiring phototherapy.
11. Chronic lung disease.
12. Cerebroventricular haemorrhage;
13. Disability at childhood follow-up.

Women's and caregiver's views and measures of satisfaction

1. Woman not satisfied with their care.
2. Anxiety during pregnancy.
3. Postnatal depression.
4. Caregiver not satisfied.
5. Woman's preferences for care.
6. Caregiver's preferences for care.
7. Women's knowledge of the potential risks and benefits prior to the procedure.
8. Women's perception of participation and satisfaction with decision making.
9. Women's perception of ability to discuss care with clinician or family/friends.

Costs

1. Costs associated with expectant management versus multifetal reduction.
2. Costs associated with maternal hospitalisation and length of stay.
3. Costs associated with neonatal hospitalisation and length of stay.
4. Costs to the woman and her family.

We planned to include outcomes in the analysis if data were available according to original allocation and reasonable measures were taken to minimise observer bias. Only outcomes with available data would have been presented in the analysis tables although the lack of data in these areas would have been noted in the body of the text. We would have extracted and reported as subsidiary outcomes data that were not prestated. These would have been clearly labelled as not prespecified. The possibility has to be borne in mind that such outcomes are only reported because the difference between the groups, which is a result of chance, have reached conventional levels of statistical significance. In order to minimise the risk of bias, we planned to base the conclusions solely on the prestated outcomes.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (13 June 2012).

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

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

Details of the search strategies for CENTRAL, MEDLINE and EMBASE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current aware-

ness 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.

For the first version of the review, we also searched the Cochrane Controlled Trials Register (*The Cochrane Library* 2004, Issue 3) and PubMed (to 30 September 2002) using the search terms listed in Appendix 1.

We did not apply any language restrictions.

Data collection and analysis

We did not identify any trials for consideration. If we identify any trials or trial reports in future, we will use the methods listed in Appendix 2.

RESULTS

Description of studies

There were no randomised controlled trials identified from the search strategy.

Risk of bias in included studies

Not applicable.

Effects of interventions

Not applicable.

DISCUSSION

There were no randomised controlled trials identified that compared outcomes after pregnancy reduction with expectant management for women with a multiple pregnancy.

While randomised controlled trials will provide the most reliable evidence regarding the risks and benefits of pregnancy reduction procedures, reduction in the number of fetuses by selective termination may not be acceptable to women, especially for those with a past history of infertility. The acceptability of this option, and willingness to undergo randomisation will depend on the couple's social background and beliefs, and consequently, recruitment to such a trial may prove exceptionally difficult. However, studies have suggested that for some couples undergoing assisted reproductive techniques, fetal reduction is an option they would consider (Garel 1997; Munks 2007).

AUTHORS' CONCLUSIONS

Implications for practice

While pregnancy reduction for women with a multiple pregnancy appears to be associated with a reduction in pregnancy loss, antenatal complications, birth before 36 weeks, caesarean birth, low birthweight infants, and neonatal death, and outcomes from multifetal pregnancy reduction appear comparable with those obtained from pregnancies conceived spontaneously or after assisted reproductive techniques, the evidence is drawn from non-randomised studies, associated with potential bias.

Implications for research

While randomised controlled trials will provide the most reliable evidence about the risks and benefits of pregnancy reduction procedures, reduction in the number of fetuses by selection termination may not be acceptable to women. The acceptability of this option, and willingness to undergo randomisation will depend on the couple's social background and beliefs, and consequently, recruitment to such a trial may prove exceptionally difficult. In this context, a prospective patient preference trial, with adherence to strict eligibility criteria may provide more information about the risks and benefits of this procedure.

ACKNOWLEDGEMENTS

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* *Indicates the major publication for the study*

DATA AND ANALYSES

This review has no analyses.

APPENDICES

Appendix 1. Searching carried out for the initial version of the review

Authors searched the Cochrane Controlled Trials Register (*The Cochrane Library* 2004, Issue 3) and PubMed (to 30 September 2002)
Terms used:
"multiple pregnanc*"; "multifetal reduction*"; "multi-fetal reduction*"; "fetal reduction*"; "selective fetocide"; "selective feticide"; "pregnancy reduction, multifetal" (MESH).

Appendix 2. Methods to be used in future versions of this review

Selection of studies

Two review authors will independently assess for inclusion all the potential studies we identify as a result of the search strategy. We will resolve any disagreement through discussion or, if required, we will consult a third person.

Data extraction and management

We will design a form to extract data. For eligible studies, two review authors will extract the data using the agreed form. We will resolve discrepancies through discussion or, if required, we will consult a third person. We will enter data into Review Manager software (RevMan 2011) and check for accuracy.
When information regarding any of the above is unclear, we will attempt to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will resolve any disagreement by discussion or by involving a third assessor.

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

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

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

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

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

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

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

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

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

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

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

- low, high or unclear risk of bias.

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

We will describe for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We will state whether attrition and exclusions were reported and 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 is reported, or can be supplied by the trial authors, we will re-include missing data in the analyses which we undertake.
We will assess methods as:

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

(5) Selective reporting (checking for reporting bias)

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

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

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

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

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

(7) Overall risk of bias

We will make explicit judgements about whether studies are at high risk of bias, according to the criteria given in the *Handbook* (Higgins 2011). With reference to (1) to (6) above, we will assess the likely magnitude and direction of the bias and whether we consider it is likely to impact on the findings. We will explore the impact of the level of bias through undertaking sensitivity analyses - *see* 'Sensitivity analysis'.

Measures of treatment effect

Dichotomous data

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

Continuous data

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

Unit of analysis issues

Cluster-randomised trials

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

We will also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit.

Cross-over trials

Cross-over trials are not eligible for this review.

Dealing with missing data

For included studies, we will note levels of attrition. We will 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 will carry out analyses, as far as possible, on an intention-to-treat basis, i.e. we will attempt to include all participants randomised to each group in the analyses, and all participants will be analysed in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial will be the number randomised minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

We will assess statistical heterogeneity in each meta-analysis using the T^2, I^2 and Chi^2 statistics. We will regard heterogeneity as substantial if I^2 is greater than 30% and either T^2 is greater than zero, or there is a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases

If there are 10 or more studies in the meta-analysis, we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually, and use formal tests for funnel plot asymmetry. For continuous outcomes, we will use the test proposed by Egger 1997, and for dichotomous outcomes we will use the test proposed by Harbord 2006. If asymmetry is detected in any of these tests or is suggested by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

We will carry out statistical analysis using the Review Manager software (RevMan 2011). We will use fixed-effect meta-analysis for combining data where it is reasonable to assume that studies are estimating the same underlying treatment effect: i.e. where trials are examining the same intervention, and the trials' populations and methods are judged sufficiently similar. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity is detected, we will use random-effects meta-analysis to produce an overall summary if an average treatment effect across trials is considered clinically meaningful. The random-effects summary will be treated as the average range of possible treatment effects and we will discuss the clinical implications of treatment effects differing between trials. If the average treatment effect is not clinically meaningful we will not combine trials.

If we use random-effects analyses, the results will be presented as the average treatment effect with 95% confidence intervals, and the estimates of T^2 and I^2.

Subgroup analysis and investigation of heterogeneity

If we identify substantial heterogeneity, we will investigate it using subgroup analyses and sensitivity analyses. We will consider whether an overall summary is meaningful, and if it is, use random-effects analysis to produce it.

We plan to carry out the following subgroup analyses.

1. Gestational age at the time of fetal reduction (prior to 14 weeks' gestation versus after 14 weeks' gestation).
2. Method of approach (transabdominal versus transvaginal/transcervical).

The following outcomes will be used in subgroup analysis.

1. Early pregnancy loss (less than 20 weeks' gestation).
2. Stillbirth (death greater than 20 weeks' gestation and before birth).
3. Very preterm birth (less than 34 weeks' gestation).

For fixed-effect inverse variance meta-analyses, we will assess differences between subgroups by interaction tests. For random-effects and fixed-effect meta-analyses using methods other than inverse variance, we will assess differences between subgroups by inspection of the subgroups' confidence intervals; non-overlapping confidence intervals indicate a statistically significant difference in treatment effect between the subgroups.

Sensitivity analysis

FEEDBACK

Haeusler, October 2009

Summary

I wonder why the published studies of Evans 2001 and 1998, Boulot 2000, Macones 1993, and Berkowitz 1996 were not included in the review. Important evidence was thus lost.

This review states that "There are insufficient data available to support a policy of pregnancy reduction procedures for women with a triplet or higher order multiple pregnancy." The literature used for this review is rather outdated, excluding more recent work. Below are references to prospective trials and reviews which present evidence that reducing the number of fetuses to two is of benefit.

The Cochrane review concludes that there is almost no evidence, that RCTs are needed and that "reduction in the number of fetuses by selective termination may not be acceptable to women, especially for those with a past history of infertility". In my experience this is not true! In my practice we face the dilemma of how to deal with requests for fetal reduction from women with a triplet pregnancy. If after transfer of 3-4 embryos women have a triplet pregnancy, they ask for reduction to twins as they have been told there is evidence this has a better outcome. I searched the literature to support my opinion that today fetal reduction is no longer warranted in developed countries. Unfortunately I found evidence to support fetal reduction. Therefore I am left wondering why the Cochrane review did not identify this evidence.

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[Feedback received from Martin Haeusler, October 2009]

Reply

Thank you for your comments. Consistent with our pre-specified protocol, the aim of this review was to assess the benefits and harms associated with fetal reduction derived from randomised controlled trials. We have clarified statements relating to the available evidence to clearly indicate that there are no randomised trials on which to base clinical decisions in this area. The studies referred to are largely case control and retrospective cohort studies, and the methodology and design of these studies mean that they have a high risk of bias.

Contributors

Jodie Dodd and Caroline Crowther

WHAT'S NEW

Last assessed as up-to-date: 29 August 2012.

Date	Event	Description
23 July 2012	New citation required but conclusions have not changed	Review updated.
23 July 2012	New search has been performed	Search updated. No new trials identified.

HISTORY

Protocol first published: Issue 4, 2002

Review first published: Issue 2, 2003

Date	Event	Description
11 June 2010	Feedback has been incorporated	Feedback from Martin Haeusler added to review.
25 September 2009	New search has been performed	Search updated. No new trials identified.
20 September 2008	Amended	Converted to new review format.
21 October 2004	New search has been performed	Search updated. No new trials found. Dodd 2004 now published.

CONTRIBUTIONS OF AUTHORS

Both review authors were involved in the initial draft of the protocol and subsequent modifications.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Department of Obstetrics and Gynaecology, The University of Adelaide, Australia.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The scope of the review has been expanded to include twins.

INDEX TERMS

Medical Subject Headings (MeSH)

*Pregnancy, Multiple; Pregnancy Reduction, Multifetal [*adverse effects; *psychology]

MeSH check words

Female; Humans; Pregnancy