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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 (31 July 2015).

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

We planned that two review authors would independently assess trials for inclusion and risk of bias, extract data and check them for accuracy. However, no randomised trials were identified.

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 (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. The other alternative is 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...
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.
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.
4. Caesarean section.
5. Instrumental vaginal birth.
6. Admission to intensive care unit.
7. Infection requiring intravenous antibiotics.
8. Haemorrhage requiring blood transfusion or major haemorrhage (greater than 1000 mL).

**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).
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.
5. Woman'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**
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 pre-stated. These would have been clearly labelled as not pre-specified. 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 pre-stated outcomes.

**Search methods for identification of studies**

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

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

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 (Ovid);
3. weekly searches of Embase (Ovid);
4. monthly searches of CINAHL (EBSCO);
5. handsearches of 30 journals and the proceedings of major conferences;
6. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.
Details of the search strategies for CENTRAL, MEDLINE, Embase and CINAHL, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

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

[For the first version of the review (Dodd 2003), 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.]

**Searching other resources**

We planned to search the reference lists of any retrieved studies. We did not apply any language or date restrictions.

**Data collection and analysis**

For methods used in the previous version of this review, see Dodd 2012.

For this version of the review no reports were identified by the search, but for future updates, we plan to use the methods outlined in Appendix 2. These methods are based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

**RESULTS**

**Description of studies**

**Results of the search**

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 selective 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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This project was supported by the National Institute for Health Research, via Cochrane programme Grant funding to Cochrane.
Pregnancy and Childbirth. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health.

**References**

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Berkowitz 1988

Boulot 1993

Boulot 2000

Dodd 2004

Dodd 2010

Donner 1992

Evans 1994a

Evans 1994b

Garel 1997

Grouzet 1996

Hasson 2011

Higgins 2011

Hurst 1996

Lipitz 1994

Little 1988

Mansour 1999

Munks 2007

Porreco 1991
References to other published versions of this review

Dodd 2003
Dodd JM, Crowther CA. Reduction of the number of fetuses for women with triplet and higher order multiple pregnancies. Cochrane Database of Systematic Reviews 2003, Issue 2. [DOI: 10.1002/14651858.CD003932]

Dodd 2012
Dodd JM, Crowther CA. Reduction of the number of fetuses for women with a multiple pregnancy. Cochrane Database of Systematic Reviews 2012, Issue 10. [DOI: 10.1002/14651858.CD003932.pub2]

* 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 pregnan*c"; "multifetal reduction*"; "multi-fetal reduction*"; "fetal reduction*"; "selective fetocide"; "selective feticide"; "pregnancy reduction, multifetal" (MESH).

Appendix 2. Methods to be used in future updates

Selection of studies

Two review authors will independently assess for inclusion all the potential studies identified 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. Data will be entered into Review Manager software (RevMan 2014) and checked for accuracy.

When information regarding any of the above is unclear, we plan 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). Any disagreement will be resolved 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 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 are balanced across groups or are related to outcomes. Where sufficient information is reported, or supplied by the trial authors, we plan to 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 investigate the possibility of selective outcome reporting bias and what we find.
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.

(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 plan to 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.

**Assessment of the quality of the evidence using the GRADE approach**

We plan to use the GRADE approach as outlined in the [GRADE handbook](#) to assess the quality of the body of evidence relating to the following 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. Need for admission to the neonatal intensive care unit.
5. Neonatal death and serious infant morbidity (defined as growth restriction; seizures; birth asphyxia defined by trialists; neonatal encephalopathy; disability in childhood).
6. Maternal death and serious maternal morbidity (e.g. admission to intensive care unit, infection requiring intravenous antibiotics, haemorrhage requiring blood transfusion).
7. No surviving child.

Data permitting, we will assess the quality of the evidence for our main comparison: reduction in the number of fetuses versus expectant management.

We will use GRADEpro Guideline Development Tool to import data from Review Manager 5.3 ([RevMan 2014](#)) in order to create 'Summary of findings' tables. A summary of the intervention effect and a measure of quality for each of the above outcomes will be produced using the GRADE approach. The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome. The evidence can be downgraded from 'high quality' by one level for serious (or by two levels for very serious) limitations, depending on assessments for risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates or potential publication bias.

**Measures of treatment effect**

**Dichotomous data**

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

**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 measured the same outcome, but using 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 ICs 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 subgroup analysis to investigate the effects of the randomisation unit.
Cross-over trials
We will not include cross-over trials; this design is not feasible for this intervention.

Dealing with missing data
For included studies, we will note levels of attrition. In future updates, if eligible studies are included, the impact of including studies with high levels of missing data in the overall assessment of treatment effect will be explored 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. 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 $\tau^2$, $I^2$ and $\chi^2$ statistics. We will regard heterogeneity as substantial if an $I^2$ is greater than 30% and either a $\tau^2$ is greater than zero, or there is a low P value (less than 0.10) in the $\chi^2$ test for heterogeneity. If we identify substantial heterogeneity (above 30%), we plan to explore it by pre-specified subgroup analysis.

Assessment of reporting biases
In future updates, 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. If asymmetry 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 2014). 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 may 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 $\tau^2$ 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 so, we will 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).

We will assess subgroup differences by interaction tests available within RevMan (RevMan 2014). We will report the results of subgroup analyses quoting the $\chi^2$ statistic and P value, and the interaction test $I^2$ value.

Sensitivity analysis
We plan to carry out sensitivity analyses to explore the effect of trial quality assessed by concealment of allocation, high attrition rates, or both, with poor quality studies being excluded from the analyses in order to assess whether this makes any difference to the overall result.
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.

References

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: 31 July 2015.

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<td>5 November 2015</td>
<td>Amended</td>
<td>Internal and external sources of funding support added.</td>
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**HISTORY**

Protocol first published: Issue 4, 2002

Review first published: Issue 2, 2003

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<td>Feedback from Martin Haeusler added to review.</td>
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<tr>
<td>25 September 2009</td>
<td>New search has been performed</td>
<td>Search updated. No new trials identified.</td>
</tr>
<tr>
<td>20 September 2008</td>
<td>Amended</td>
<td>Converted to new review format.</td>
</tr>
<tr>
<td>21 October 2004</td>
<td>New search has been performed</td>
<td>Search updated. No new trials found. Dodd 2004 now published.</td>
</tr>
</tbody>
</table>
CONTRIBUTIONS OF AUTHORS

Jodie Dodd and Caroline Crowther were involved in the initial draft of the protocol and subsequent modifications. Therese Dowswell assisted with the update.

DECLARATIONS OF INTEREST

Therese Dowswell is employed by the University of Liverpool on an NIHR Cochrane Programme grant to work on a range of Cochrane Reviews. In the last three years the University of Liverpool has received a grant from the World Health Organization (WHO) for work on other Cochrane reviews that Therese has worked on. Therese has also received payment from WHO for working on other Cochrane reviews in the last three years. The Funders have no influence on the content or conclusions of the relevant Cochrane reviews.

SOURCES OF SUPPORT

Internal sources

- Department of Obstetrics and Gynaecology, The University of Adelaide, Australia.
- ARCH: Australian Research Centre for Health of Women and Babies, Robinson Research Institute, The University of Adelaide, Australia.

External sources

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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