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[Intervention Review]

Customised versus population-based growth charts as a screening tool for detecting small for gestational age infants in low-risk pregnant women

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ABSTRACT

Background

Fetal growth restriction is defined as failure to reach growth potential and considered one of the major complications of pregnancy. These infants are often, although not universally, small for gestational age (SGA). SGA is defined as a weight less than a specified percentile (usually the 10th percentile). Identification of SGA infants is important because these infants are at increased risk of perinatal morbidity and mortality. Screening for SGA is a challenge for all maternity care providers and current methods of clinical assessment fail to detect many infants who are SGA. Large observational studies suggest that customised growth charts may be better able to differentiate between constitutional and pathologic smallness. Customised charts adjust for physiological variables such as maternal weight and height, ethnicity and parity.

Objectives

To assess the benefits and harms of using population-based growth charts compared with customised growth charts as a screening tool for detection of fetal growth in pregnant women.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (12 March 2014), reviewed published guidelines and searched the reference lists of review articles.

Selection criteria

Randomised, quasi-randomised or cluster-randomised clinical trials comparing customised versus population-based growth charts used as a screening tool for detection of fetal growth in pregnant women.

Data collection and analysis

Two review authors independently assessed trials for inclusion.

Main results

No randomised trials met the inclusion criteria.

Customised versus population-based growth charts as a screening tool for detecting small for gestational age infants in low-risk pregnant women (Review)

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Authors' conclusions

There is no randomised trial evidence currently available. Further randomised trials are required to accurately assess whether the improvement in detection shown is secondary to customised charts alone or an effect of the policy change. Future research in large trials is needed to investigate the benefits and harms (including perinatal mortality) of using customised growth charts in different settings and for both fundal height and ultrasound measurements

PLAIN LANGUAGE SUMMARY

Customised versus population-based growth charts as a screening tool for detecting small for gestational age infants in low-risk pregnant women

Small for gestational age (SGA) infants are defined as having a birthweight that is less than that for 10% of the population when plotted on a growth chart based on their gestational age and sex. This definition includes both infants who are normally grown but small, and infants who do not reach their full growth potential (are growth restricted). SGA infants are at an increased risk of complications, fetal distress and even death during labour. Detecting SGA infants is a major challenge for all maternity care providers, particularly with women who have an otherwise healthy pregnancy.

Several clinical methods are commonly used for assessing an infant's growth during pregnancy including estimating the size of the uterus by examining the pregnant woman (symphysiofundal height (SFH) and single or a series of ultrasound scans).

Both of the above measurements can be plotted and followed on growth charts. Most maternity services use standard population-based growth charts in assessing fetal weight during pregnancy, and monitoring changes from the birthweight after the baby is born. Previous research suggests that customised growth charts which adjust for factors such as the mother's weight and height, ethnicity and number of babies she has had may make assessment of fetal growth more precise, reducing unnecessary consultations for investigations and parental anxiety.

Currently there are no studies available. Research is needed to assess the effect of using the charts in different settings and for both fundal height and ultrasound measurements on the health of women and their babies and should include important outcomes such as mortality.

BACKGROUND

Fetal growth restriction is defined as failure to reach growth potential and is considered one of the major complications of pregnancy. Impaired fetal growth may be due to maternal complications such as pregnancy-associated hypertension, fetal complications (including structural or chromosomal problems) or problems with placental development (which is the most common cause of impaired growth) (Grivell 2009). These infants are often, although not universally, small for gestational age (SGA). SGA is defined as a weight less than a specified percentile (usually the 10th percentile). However, it is important to note that a proportion of infants defined as SGA will actually be normally grown (constitutionally small) and another proportion truly growth restricted (pathologically small). Furthermore, some infants who have not reached their growth potential will not be less than the 10th percentile and therefore not classified as SGA (Gelbaya 2005).

Identification of SGA infants is important because these infants are at an increased risk for perinatal morbidity and mortality, associated health problems (such as neurodevelopment and intellectual consequences), persistent short stature, as well as long-term adverse consequences such as adult onset cardiovascular disease and metabolic alternations in later life (Barker 2004; Clayton 2007; Maulik 2006).

Screening for SGA is a challenge for all maternity care providers, particularly in low-risk pregnancies, and current methods of clinical assessment fail to detect many infants who are SGA (Wright 2006). Previous research has shown that, using standard methods of antenatal care, only 16% (Kean 1996) of SGA infants were detected and 26% (Hepburn 1986) of SGA infants were suspected to be small prior to birth. The majority of maternity services measure symphysiofundal height (SFH) and use a rule that normal growth should be within two weeks of gestational age. In low-risk populations, SFH as a screening tool for assessment of SGA has a low detection rate in women with a normal BMI (body mass index) (Kean 1996). Furthermore, SFH measurement has an even lower sensitivity in screening for SGA in women with an increased body mass (Jelks 2007; Stuart 1989). A Cochrane review on using SFH measurement in pregnancy for detecting abnormal fetal growth is currently being prepared (Japaraj 2009).

Thought to be more accurate than SFH as a screening tool for diagnosis of SGA are serial ultrasound measurements of estimated fetal weight over time, either alone or in combination with Doppler parameters assessing fetal well-being. Routine use of ultrasound in late pregnancy (after 24 weeks' gestation) is the subject of another Cochrane review (Bricker 2008). The accuracy of estimated fetal weight assessed by ultrasound varies with the determination of gestational age, size of the baby and maternal conditions. Previous literature has shown that the mean per cent difference of sonographically predicted birthweight ranges from 6% to 15% (Ben-Haroush 2007). The ultrasound measurements can be plotted and followed on growth charts. Most maternity services when plotting serial measurements use standard population-based growth charts in assessing the estimated fetal weight antenatally and then monitoring birthweight postnatally (Gelbaya 2005). Large observational studies suggest that customised growth charts may be better able to differentiate between constitutional and pathologic smallness (Clausson 2001; Figueras 2007; Gardosi 1992; Gardosi 1999; Mongelli 2007). Customised charts exist for both

estimated fetal weight as measured by ultrasound, birthweight and SFH (Gardosi 1999).

Customised charts adjust for physiological variables such as maternal weight and height that are known to influence birthweight and can be used to outline a curve for the expected fetal weight gain. It has been shown that, in addition to gestation and sex, maternal weight at first antenatal-clinic visit, height, ethnic group, and parity were significant determinants of birthweight. It was found that 28% of infants conventionally designated SGA (less than the 10th centile) and 22% of those designated large (higher than the 90th centile) were in fact within normal limits for the pregnancy. Conversely, 26% of infants identified as small or large, respectively, with adjusted centiles were 'missed' by conventional unadjusted centile assessment. Adjustment for physiological variables is thought to make assessment of fetal growth more precise and reduce unnecessary investigations, interventions and parental anxiety (Gardosi 1992).

Currently there are several combinations of fetal growth surveillance after a baby has been identified as growth restricted. The methods employed include serial ultrasound biometry, ultrasound estimated fetal weight and ultrasound Doppler flow velocimetry. However, the following issues need to be considered with the use of the tests: measurements require an accurate estimate of gestational age; most tests attempt to diagnose SGA infants rather than growth-restricted infants; some tests use a one-off measurement (size) to predict SGA; and in most situations no allowance is made for important prognostic factors such as maternal height, weight, ethnicity, parity and fetal gender. The assessment of these fetal surveillance regimens is the subject of another Cochrane review (Grivell 2009).

This review will include only studies where impaired fetal growth is already suspected based on a measurement of less than the 10th percentile using population-based growth charts. The scope of this review is to assess the use of customised versus population-based growth charts as a screening tool for detection of intrauterine growth restriction in a general pregnant population with regard to perinatal outcomes.

Description of the condition

Fetal growth restriction is defined as failure of a baby to reach his/her growth potential. This can be due to maternal, fetal or placental factors and implies a pathological process distinct from defining a baby as SGA. SGA is usually defined as weight less than the 10th percentile and would include both constitutionally and pathologically small infants. Conversely there will be infants who have not reached their growth potential who are not SGA.

Description of the intervention

Customised charts which adjust for variables such as maternal weight, height, ethnicity, parity and fetal gender are significant determinants of birthweight and can be used to determine fetal birthweight and outline a curve of expected fetal weight gain.

How the intervention might work

There is evidence that plotting serial fundal height measurements on individually customised growth charts can significantly improve detection of fetal growth problems while reducing unnecessary

referrals for investigations (Clausson 2001; Figueras 2007; Gardosi 1992; Gardosi 1999; Mongelli 2007).

Why it is important to do this review

The use of customised growth charts to individualise fetal weight for gestational age by adjusting for variables is increasing with countries such as the UK, Canada and New Zealand suggesting their use in standard practice. They allow for better distinction between normal and pathologically small infants. There is, however, a well-known lack of literature that directly compares the use of customised and population-based charts for antenatal growth surveillance in pregnant women and documents the perinatal outcomes. There is much variation in clinical practice. This review is important to direct future research and clinical practice in this area.

OBJECTIVES

To assess the benefits and harms of using population-based growth charts compared with customised growth charts as a screening tool for detection of fetal growth in pregnant women.

METHODS

Criteria for considering studies for this review

Types of studies

We planned to include all published and non-published randomised, quasi-randomised or cluster-randomised clinical trials comparing customised versus population-based growth charts used as a screening tool for detection of fetal growth in pregnant women.

Types of participants

Pregnant women.

Types of interventions

Customised growth charts versus population-based growth charts.

Types of outcome measures

Primary outcomes

Fetal, neonatal and infant outcomes

- Perinatal mortality (defined as both stillbirths and neonatal deaths)
- SGA at birth (defined as birthweight less than the 10th percentile for gestational age and infant sex)

Secondary outcomes

Fetal/neonatal

- Stillbirth (defined as a death of a fetus greater than 20 weeks' gestational age or 400 grams birthweight)
- Neonatal death (defined as a death of a neonate during the first 28 completed days of life)
- Gestational age at birth
- Apgar score less than seven at five minutes
- Need for resuscitation at birth
- Admission to neonatal intensive care unit
- Length of stay in neonatal intensive care unit
- Birthweight less than 2500 grams

- Hypoglycaemia (defined as low blood sugar requiring complementary feeds or intravenous fluid)
- Hypothermia (defined as low body temperature requiring heat blanket or incubator care)
- Necrotising enterocolitis
- Neonatal sepsis (defined as positive blood culture or antibiotic treatment for more than five days)

Childhood

- Neurodevelopmental problems
- Hypertension
- Child onset diabetes

Adult

- Adult onset diabetes
- Hypertension
- Cardiovascular disease
- Neurodevelopmental problems

Maternal outcomes

- Maternal mortality (defined as the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to, or aggravated by, the pregnancy or its management but not from accidental or incidental causes)
- Significant maternal morbidity (postpartum haemorrhage, admission to intensive care unit, postpartum infection)
- Mode of delivery
- Induction of labour
- Length of stay
- Successful breastfeeding

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 (12 March 2014).

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. 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 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 reviewed published guidelines and searched the reference lists of review articles.

We did not apply any language restrictions.

Data collection and analysis

This review assessed a single study, which was excluded.

See [Appendix 1](#) for methods of data collection and analysis to be used in future updates of this review, as more data become available.

Selection of studies

No new studies were identified from the updated search (2014).

RESULTS

Description of studies

See [Characteristics of excluded studies](#).

Results of the search

The search of the Pregnancy and Childbirth Group's Trials Register found one report ([Gardosi 1999](#)) which we excluded.

Included studies

There were no included studies.

Excluded studies

There was one excluded study; [Gardosi 1999](#) was a population-based cohort study evaluating the effectiveness of fundal height measurements plotted on customised growth charts as a screening method for fetal growth.

For further information, see [Characteristics of excluded studies](#).

Risk of bias in included studies

There were no included studies.

Effects of interventions

There is currently no available evidence from randomised trials to assess the role of customised fetal growths in the detection of SGA infants.

DISCUSSION

We found no evidence from randomised trials to assess the role of customised fetal growths in the detection of small for gestational age (SGA) infants.

The excluded study ([Gardosi 1999](#)), a population-based cohort study, investigated a total of 1272 women with singleton pregnancies and dating ultrasound scans before 22 weeks of gestation. The study group (667 women) and control group (605 women) were recruited from two similar catchment areas served by separate and non-overlapping groups of midwives and general practitioners. The women in the study group had their pregnancy monitored with a customised chart. The study demonstrated that serial measurement of fundal height plotted on customised charts following clinician training leads to increased antenatal detection of small babies. The detection rate for SGA babies was significantly better in the intervention group (risk ratio (RR) 0.74; 95% confidence interval (CI) 0.56 to 0.96; one trial, 143 women). This improved antenatal detection did not translate to increased numbers of infants labelled as SGA at birth with no significant difference observed between the intervention and control groups (RR 0.89; 95% CI 0.66 to 1.22; one trial; 1272 women). There were no significant differences observed between the intervention and control groups for outcomes including admission to special case nursery, stillbirth, resuscitation at birth, induction of labour, mode of delivery and preterm birth.

Antenatal detection of SGA infants is difficult and many of the assessments in use today have poor sensitivity. Customised growth charts have reportedly improved ability to detect SGA infants and are widely used with little evidence of benefit. Currently there is no randomised trial evidence that adequately addresses the question of whether the routine use of customised growth charts is an appropriate screening tool for SGA infants in low-risk pregnant women.

AUTHORS' CONCLUSIONS

Implications for practice

There is insufficient evidence at present to recommend the routine use of customised growth charts antenatally to improve outcomes for mothers and infants.

Implications for research

Further randomised trials are required to accurately assess whether the improvement in antenatal detection seen in the excluded study is secondary to customised charts alone or an effect of the policy change or training. Large trials are needed to investigate the benefits and harms (including perinatal mortality) of using customised growth charts in different settings and for both fundal height and ultrasound measurements. The potential financial costs associated with the implementation of customised growth charts include additional ultrasounds, early or late delivery and other further investigations required.

ACKNOWLEDGEMENTS

We would like to thank the editorial team at the Cochrane Pregnancy and Childbirth Group for their support with this update.

REFERENCES

References to studies excluded from this review

Gardosi 1999 {published data only}

Gardosi J, Francis A. Controlled trial of fundal height measurement plotted on customised antenatal growth charts. *British Journal of Obstetrics and Gynaecology* 1999;**106**(4):309-17.

Additional references

Barker 2004

Barker DJ. The developmental origins of adult disease. *Journal of the American College of Nutrition* 2004;**23**(6 Suppl):588S-595S.

Ben-Haroush 2007

Ben-Haroush A, Yogev Y, Hod M, Bar J. Predictive value of a single early fetal weight estimate in normal pregnancies. *European Journal of Obstetrics & Gynecology and Reproductive Biology* 2007;**130**:187-92.

Bricker 2008

Bricker L, Neilson JP, Dowswell T. Routine ultrasound in late pregnancy (after 24 weeks' gestation). *Cochrane Database of Systematic Reviews* 2008, Issue 4. [DOI: [10.1002/14651858.CD001451.pub3](https://doi.org/10.1002/14651858.CD001451.pub3)]

Clausson 2001

Clausson B, Gardosi J, Francis A, Cnattingius S. Perinatal outcome in SGA births defined by customised versus population-based birthweight standards. *BJOG: an international journal of obstetrics and gynaecology* 2001;**108**:830-4.

Clayton 2007

Clayton PE, Cianfarani S, Czernichow P, Johannsson G, Rapaport R, Rogol A. Consensus statement: management of the child born small for gestational age through to adulthood: a consensus statement of the International Societies of Pediatric Endocrinology and the Growth Hormone Research Society. *Journal of Clinical Endocrinology & Metabolism* 2007;**92**(3):804-10.

Figueras 2007

Figueras F, Figueras J, Meler E, Eixarch E, Coll O, Gratacos E, et al. Customised birthweight standards accurately predict perinatal morbidity. *Archives of Disease in Childhood. Fetal and Neonatal Edition* 2007;**92**:F277-F280.

Gardosi 1992

Gardosi J, Chang, A, Kalyan B, Sahota D, Symonds EM. Customised antenatal growth charts. *Lancet* 1992;**339**:283-7.

Gelbaya 2005

Gelbaya TA, Nardo LG. Customised fetal growth chart: a systematic review. *Journal of Obstetrics and Gynaecology* 2005;**25**(5):445-50.

Grivell 2009

Grivell RM, Wong L, Bhatia V. Regimens of fetal surveillance for impaired fetal growth. *Cochrane Database of Systematic Reviews* 2009, Issue 1. [DOI: [10.1002/14651858.CD007113.pub2](https://doi.org/10.1002/14651858.CD007113.pub2)]

Hepburn 1986

Hepburn M, Rosenberg K. An audit of the detection and management of small-for-gestational age babies. *British Journal of Obstetrics and Gynaecology* 1986;**93**:212-6.

Higgins 2011

Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Japaraj 2009

Japaraj RP, Ho JJ, Valliapan J, Sivasangari S. Symphysial fundal height measurement (SFH) in pregnancy for detecting abnormal fetal growth. *Cochrane Database of Systematic Reviews* 2009, Issue 4. [DOI: [10.1002/14651858.CD008136](https://doi.org/10.1002/14651858.CD008136)]

Jelks 2007

Jelks A, Cifuentes R, Ross M. Clinician bias in fundal height measurement. *Obstetrics & Gynecology* 2007;**110**(4):892-9.

Kean 1996

Kean LH, Liu DT. Antenatal care as a screening tool for the detection of small for gestational age babies in the low risk population. *Journal of Obstetrics and Gynaecology* 1996;**16**(2):77-82.

Maulik 2006

Maulik D. Management of fetal growth restriction: an evidence-based approach. *Clinical Obstetrics and Gynecology* 2006;**49**(2):320-34.

Mongelli 2007

Mongelli M, Figueras F, Francis A, Gardosi J. A customised birthweight centile calculator developed for an Australian population. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 2007;**47**(2):128-31.

RevMan 2012 [Computer program]

The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012.

Stuart 1989

Stuart JM, Healy TJ, Sutton M, Swingler GR. Symphysis-fundus measurements in screening for small-for-dates infants: a community based study in Gloucestershire. *Journal of the Royal College of General Practitioners* 1989;**39**:45-8.

Wright 2006

Wright J, Morse K, Kady S, Francis A. Audit of fundal height measurement plotted on customised growth charts. *MIDIRS Midwifery Digest* 2006;**16**(3):341-5.

References to other published versions of this review

Carberry 2011

Carberry AE, Gordon A, Bond DM, Hyett J, Raynes-Greenow CH, Jeffery HE. Customised versus population-

based growth charts as a screening tool for detecting small for gestational age infants in low-risk pregnant women. *Cochrane Database of Systematic Reviews* 2011, Issue 12. [DOI: [10.1002/14651858.CD008549.pub2](https://doi.org/10.1002/14651858.CD008549.pub2)]

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Gardosi 1999	This study was not a randomised nor a quasi-randomised trial. It is a population-based cohort study utilising two different geographical regions.

APPENDICES

Appendix 1. Methods of 'Data collection and analysis' to be used in future updates 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. We will enter data into Review Manager software ([RevMan 2012](#)) 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.

(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. 20% or less missing 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 standard errors 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 subgroup analysis to investigate the effects of the randomisation unit.

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 analyse all participants 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 Tau², I² and Chi² statistics. We will regard heterogeneity as substantial if an I² is greater than 30% and either the Tau² is greater than zero, or there is a low P value (less than 0.10) in the Chi² 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. 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 2012](#)). 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 we judge the trials' populations and methods to be sufficiently similar. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if we detect substantial statistical heterogeneity, we will use random-effects meta-analysis to produce an overall summary, if an average treatment effect across trials is considered clinically meaningful. We will treat the random-effects summary 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, we will present the results as the average treatment effect with 95% confidence intervals, and the estimates of Tau² and I².

We plan to exclude any analysis at risk of bias based on substantial loss to follow-up greater than 20%.

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. term versus preterm;
2. suspected intrauterine growth restriction.

We will use the following primary outcomes in subgroup analysis.

Fetal, neonatal and infant outcomes

- Mortality (stillbirth, perinatal, neonatal or infant death)
- SGA at birth

Maternal outcomes

- Maternal mortality
- Significant maternal morbidity (postpartum haemorrhage, admission to intensive care unit, postpartum infection)

We will assess subgroup differences by interaction tests available within RevMan ([RevMan 2012](#)). We will report the results of subgroup analyses quoting the Chi² statistic and P value, and the interaction test I² value.

Sensitivity analysis

We will conduct a sensitivity analysis to explore the effects of trial quality if trials of differing quality are included in the review.

We will assess the impact of excluding studies with poor methodological quality from the analysis if sufficient amounts of data are available. We will plan the analyses *a priori* in order to explore effect size differences and the robustness of conclusions. The overall point estimates of the studies with and without including the studies of poor quality based on:

1. selection bias;
2. early stopping;
3. loss to follow-up;
4. study type (if any quasi-randomised studies included).

WHAT'S NEW

Date	Event	Description
12 March 2014	New search has been performed	Search updated. No new trials identified.
26 February 2014	New citation required but conclusions have not changed	No new trials included in this 2014 update.

CONTRIBUTIONS OF AUTHORS

Angela Carberry is guarantor for the review. Angela Carberry and Dr Adrienne Gordon designed and conceived the review and drafted the protocol. Professor Heather Jeffery and Mrs Diana Bond provided a methodological and clinical perspective as well as providing general advice on the protocol. Dr Jon Hyett provided a clinical perspective and Dr Camille Raynes-Greenow provided methodological advice.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- University of Sydney, Australia.
- RPA Newborn Care, Australia.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The methods have been updated to reflect the recent *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) and RevMan (RevMan 2012).

The following fetal/neonatal secondary outcomes were assessed in the excluded study of this review.

- Preterm birth
- Referrals for investigations
- Failure to detect small for gestational age antenatally

INDEX TERMS

Medical Subject Headings (MeSH)

*Growth Charts; *Infant, Small for Gestational Age; Fetal Growth Retardation [*diagnosis]

MeSH check words

Female; Humans; Infant, Newborn; Pregnancy