Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes (Review)

Dodd JM, Dowswell T, Crowther CA

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Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes (Review)
Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes

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ABSTRACT

Background

Regular antenatal care for women with a multiple pregnancy is accepted practice, and while most women have an increase in the number of antenatal visits, there is no consensus as to what constitutes optimal care. 'Specialised' antenatal clinics have been advocated as a way of improving outcomes for women and their infants.

Objectives

To assess, using the best available evidence, the benefits and harms of 'specialised' antenatal clinics compared with 'standard' antenatal care for women with a multiple pregnancy.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 May 2015) and reference lists of retrieved studies.

Selection criteria

All published, unpublished, and ongoing randomised controlled trials with reported data that compared outcomes in mothers and babies with a multiple pregnancy who received antenatal care specifically designed for women with a multiple pregnancy (as defined by the trial authors) with outcomes in controls who received 'standard' antenatal care (as defined by the trial authors).

Data collection and analysis

Two of the review authors independently assessed trials for inclusion and trial quality. Both review authors extracted data. Data were checked for accuracy. We graded the quality of the evidence using GRADEpro software.
Main results

Findings were based on the results of a single study with some design limitations.

Data were available from one study involving 162 women with a multiple pregnancy. For the only reported primary outcome, perinatal mortality, we are uncertain whether specialised antenatal clinics makes any difference compared to standard care (risk ratio (RR) 1.02; 95% confidence interval (CI) 0.26 to 4.03; 324 infants, very low quality evidence). Women receiving specialised antenatal care were significantly more likely to birth by caesarean section (RR 1.38; 95% CI 1.06 to 1.81; 162 women, moderate quality evidence). Data were not reported in the study on the following primary outcomes: small-for-gestational age, very preterm birth or maternal death. There were no differences identified between specialised antenatal care and standard care for other secondary outcomes examined: postnatal depression (RR 0.48; 95% CI 0.19 to 1.20; 133 women, very low quality evidence), breastfeeding (RR 0.63; 95% CI 0.24 to 1.68; 123 women, very low quality evidence), stillbirth (RR 0.68; 0.12 to 4.04) or neonatal death (RR 2.05; 95% CI 0.19 to 22.39) (324 infants).

Authors’ conclusions

There is currently limited information available from randomised controlled trials to assess the role of ‘specialised’ antenatal clinics for women with a multiple pregnancy compared with ‘standard’ antenatal care in improving maternal and infant health outcomes. The value of ‘specialised’ multiple pregnancy clinics in improving health outcomes for women and their infants requires evaluation in appropriately powered and designed randomised controlled trials.

Plain Language Summary

Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes

'Specialised' antenatal clinics versus 'standard' antenatal care for women with a multiple pregnancy.

Women carrying more than one baby are at increased risk of complications in pregnancy, which can affect the health of both mother and babies. 'Specialised' antenatal clinics have been suggested for women with a multiple pregnancy as a means of improving health outcomes for women and their infants. The review found one randomised trial involving 162 women with a multiple pregnancy. For most important outcomes the evidence was not available, or was graded very low quality due to imprecise estimates, the small sample size of the single study providing data and low numbers of events for some outcomes. There were no significant differences identified between specialised antenatal care and standard care in the chance of a baby dying in the first month of life. Women receiving specialised antenatal care were significantly more likely to give birth by caesarean section. Further information from well-designed trials reporting outcomes for women and their infants are required.
### Summary of Findings for the Main Comparison

**Specialised antenatal clinics versus standard care for women with multiple pregnancies**

**Patient or population:** Women with a multiple pregnancy for improving maternal and infant outcomes  
**Setting:** UK  
**Intervention:** ‘Specialised’ antenatal clinic  
**Comparison:** ‘Standard’ care

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Anticipated absolute effects* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>N of participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Risk with ‘standard’ care</td>
<td>Risk with ‘Specialised’ antenatal clinic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Perinatal death                       |                                      | RR 1.02 (0.26 to 4.03) | 324 (1 RCT) | ⊕⊕⊕⊕ ⊕ ⃝⃝⃝ ⃝skins VERY LOW  
|                                       | Study population                      |                          |                            |                                  |
|                                       | 24 per 1000                          | 25 per 1000 (6 to 98)   |                            |                                  |
|                                       | Moderate                              |                          |                            |                                  |
|                                       | 24 per 1000                          | 25 per 1000 (6 to 98)   |                            |                                  |
| Caesarean birth                       |                                      | RR 1.38 (1.06 to 1.81)  | 162 (1 RCT) | ⊕⊕⊕⊕ ⊕ ⃝ MODERATE  
|                                       | Study population                      |                          |                            |                                  |
|                                       | 488 per 1000                         | 673 per 1000 (517 to 883) |                        |                                  |
|                                       | Moderate                              |                          |                            |                                  |
|                                       | 488 per 1000                         | 673 per 1000 (517 to 883) |                        |                                  |
| Postnatal depression (6 months’ postpartum). EPDS score 13 or more  |                                      | RR 0.48 (0.19 to 1.20)  | 133 (1 RCT) | ⊕⊕⊕⊕ ⊕ ⃝skins VERY LOW  
| Study population                      |                                      |                          |                            |                                  |

*Note: EPDS score 13 or more indicates a likely depressive state.*

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**Explanation:**

- **Quality of the evidence** (GRADE): **VERY LOW** indicates that the evidence is of very low certainty, meaning that we are very uncertain about the estimate of effect size. **MODERATE** indicates that the evidence is of moderate certainty, meaning that we are moderately certain about the estimate of effect size. **HIGH** indicates that the evidence is of high certainty, meaning that we are very certain about the estimate of effect size. **UNWEIGHTED** indicates that the evidence does not allow for a weighted analysis.

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<table>
<thead>
<tr>
<th>Health Outcomes</th>
<th>Study Population</th>
<th>RR (95% CI)</th>
<th>Number of Studies</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breastfeeding 6 months' post-partum</td>
<td>185 per 1000 (35 to 222)</td>
<td>89 per 1000 (35 to 222)</td>
<td>RR 0.63 (0.24 to 1.68)</td>
<td>123 (1 RCT)</td>
</tr>
<tr>
<td>Small-for-gestational age</td>
<td>150 per 1000 (36 to 252)</td>
<td>95 per 1000 (36 to 252)</td>
<td>No estimable data</td>
<td></td>
</tr>
<tr>
<td>Very preterm birth (defined as birth less than 34 weeks' gestation)</td>
<td>150 per 1000 (36 to 252)</td>
<td>95 per 1000 (36 to 252)</td>
<td>No estimable data</td>
<td></td>
</tr>
</tbody>
</table>

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio
## GRADE Working Group grades of evidence

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High quality</strong></td>
<td>We are very confident that the true effect lies close to that of the estimate of the effect</td>
</tr>
<tr>
<td><strong>Moderate quality</strong></td>
<td>We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different</td>
</tr>
<tr>
<td><strong>Low quality</strong></td>
<td>Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect</td>
</tr>
<tr>
<td><strong>Very low quality</strong></td>
<td>We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect</td>
</tr>
</tbody>
</table>

1. Single study with design limitations
2. Wide 95% CI crossing the line of no effect and low event rate
3. Wide 95% CI crossing the line of no effect and estimate based on small sample size
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 (Little 1988). Monozygous twins arise from fertilisation of one egg, while dizygous twins arise from fertilisation of two eggs. Women and infants of a multiple pregnancy are at increased risk of complications when compared with women and infants of a singleton pregnancy, but there is little information obtained from randomised controlled trials to provide reliable information about the optimal care of women with a multiple pregnancy (Dodd 2005).

Description of the intervention

Specialised clinics for women with a multiple pregnancy have been advocated, with non-randomised cohort data suggesting improved perinatal outcomes with the provision of intensive antenatal education, continuity of caregiver and individualised care (Ellings 1993; Gardner 1990; Newman 1995; Ruiz 2001). Gardner and colleagues (Gardner 1990) conducted a retrospective case note review of 62 women with a multiple pregnancy, where the antenatal care was considered to be 'adequate' (37 women) or 'inappropriate' (25 women). However, it was unclear exactly what constituted 'adequate' or 'inappropriate' antenatal care. Women who received 'appropriate' antenatal care had a lower risk of perinatal mortality (68/1000 births versus 160/1000 births), and higher mean birthweight (2546 g versus 2007 g). The authors concluded that 'intensive' antenatal care for women with a multiple pregnancy was effective in promoting fetal growth and improving perinatal outcome (Gardner 1990).

Ellings and colleagues (Ellings 1993) conducted a prospective cohort study in which 89 women with a twin pregnancy were followed in a specialised twin clinic and were compared with 51 women who did not attend the specialised clinic. The allocation of women to each clinic setting was not described. Care in the specialised twin clinic involved evaluation of maternal symptoms and cervical status by a single midwife, maternal education about the risk of preterm birth, individualised modification of maternal activity levels and the opportunity for non-attendance at clinic to be monitored and the women followed up. No differences were reported in the occurrence of antenatal complications. Infants of women who attended the specialised clinic were less likely to be of very low birthweight (defined as birthweight less than 1500 g), or require admission to the neonatal intensive care unit, and had a lower risk of perinatal death. The authors concluded that the intensive perinatal care prevention education, individualisation of antenatal care and frequent assessment by a single caregiver was effective in reducing very early preterm birth and its sequelae (Ellings 1993). In a subsequent review, Newman and Ellings advocated the provision of antenatal care for women with a multiple pregnancy by "experienced and dedicated staff that can anticipate and manage the various and complex problems presented by the multi-fetal gestation" (Newman 1999).

Ruiz and colleagues (Ruiz 2001) conducted a retrospective cohort study where 30 women with a multiple pregnancy who received 'specialised' care were compared with 41 historical controls who received 'standard' care. The women in the 'specialised' care group had their care provided by a single midwife, including weekly antenatal visits, home visits and 24-hour availability for telephone support. The outcomes assessed included gestational age at birth, birthweight, length of stay in the neonatal intensive care unit and costs associated with hospitalisation. For those women who received 'specialised' care, there were no infants born before 30 weeks' gestation, the infants were of greater birthweight (mean 249 g, standard deviation (SD) 77 g), and had shorter neonatal intensive care unit stay (mean length of stay: seven days versus 17 days). The authors concluded that 'specialised' care for women with a twin pregnancy was associated with improved neonatal outcomes (Ruiz 2001).

How the intervention might work

Regular antenatal care for women with a multiple pregnancy is accepted practice, and while most women have an increase in the number of antenatal visits, there is no consensus as to what frequency schedule constitutes optimal care. Elevated blood pressure, hypertension, pre-eclampsia and eclampsia are all increased in women with a multiple pregnancy (Campbell 1999; Campbell 2004; Conde-Agudelo 2000), and increased antenatal visits should facilitate its early detection and treatment (Santerna 1995). Women with a multiple pregnancy are reported to be at increased risk of gestational diabetes (Henderson 1995; Schwartz 1999). While there are some reports that suggest women with a multiple pregnancy are at increased risk of bleeding during pregnancy from placenta praevia or placental abruption (Ananth 2001; Ananth 2003; Salihu 2005), frequent antenatal visits will not predict or prevent their occurrence. One of the greatest risks for infants of a multiple pregnancy is preterm birth. Birth before 37 weeks' gestation accounts for almost 45% of all twin births, compared with 5.6% in singleton pregnancies (Li 2011; MacDorman 2007; Patel 1983). For women with a multiple pregnancy, there is an increased risk of death of one or both of the babies, both in utero before birth (a stillbirth) and after birth when compared with women with a singleton pregnancy (Keith 1980; Patel 1983; Rydhstroem 2001; Tucker 2004).
The Royal College of Obstetricians and Gynaecologists (RCOG) guideline commissioned by the National Collaborating Centre for Women’s and Children’s Health (NICE) relating to antenatal care of women with a multiple pregnancy highlights that current evidence is based on observational studies with potential for bias. Furthermore, the information available related to maternal morbidity, and both perinatal mortality and morbidity was assessed as of low to very low quality. While the RCOG recommendations advocate provision of clinical care by a multidisciplinary team with experience and knowledge relevant to twin pregnancies, further research as to the role of specialised antenatal care is required, including evaluation of the potential benefits and harms that may arise (NICE 2011).

Why it is important to do this review

While these reports suggest a potential improvement in neonatal outcomes associated with specialised care for women with a twin pregnancy, they are limited by their non-randomised nature, with inherent potential for bias. Furthermore, there is limited reporting of clinically meaningful outcomes for both women and infants. The value of specialised antenatal care for women with a single pregnancy when compared with ‘standard’ antenatal care is the subject of a different Cochrane review (Whitworth 2011).

OBJECTIVES

To assess using the best available evidence, the value of ‘specialised’ antenatal care for women with a multiple pregnancy when compared with ‘standard’ antenatal care. The primary outcomes relate to maternal and neonatal morbidity, and maternal and perinatal mortality.

METHODS

Criteria for considering studies for this review

Types of studies

All published, unpublished and ongoing randomised controlled trials with reported data that compared outcomes in mothers and babies with a multiple pregnancy who received antenatal care specifically designed for women with a multiple pregnancy (as defined by the trial authors) with outcomes in controls who received ‘standard’ antenatal care (as defined by the trial authors). Quasi- and cluster-randomised trials were eligible for inclusion.

Types of participants

Women with a multiple pregnancy.

Types of interventions

Antenatal care specifically designed for women with a multiple pregnancy as defined by trial authors.

Types of outcome measures

Outcomes were included 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 appear in the analysis tables. In order to minimise the risk of bias the conclusions were based solely on the pre-stated outcomes.

Primary outcomes

1. Perinatal death (defined as stillbirth of one or more infants after trial entry, or death of one or more liveborn infants up to 28 days of age).
2. Small-for-gestational age (defined as birthweight less than the 10th centile for gestational age).
3. Very preterm birth (defined as birth less than 34 weeks’ gestation).

Secondary outcomes

Secondary outcomes relate to pregnancy outcomes, complications, satisfaction and costs.

Pregnancy outcomes

1. Development of antenatal complications (including pre-eclampsia, antepartum haemorrhage requiring hospitalisation, preterm labour (actual or suspected), preterm prelabour ruptured membranes, intrauterine growth restriction (estimated fetal weight less than 10th centile for gestational age)).
2. Antenatal investigations.
3. Preterm birth (defined as birth before 37 weeks’ gestation).
4. Extremely preterm birth (defined as birth before 28 weeks’ gestation).
5. Maternal admission to intensive care unit.
6. Infection requiring intravenous antibiotics.
8. Uterine rupture.
10. Postnatal depression.
Complications for infants (one or both)
1. Stillbirth* (death of one or more infants after trial entry but before birth).
2. Neonatal death* (death of one or more liveborn infants up to 28 days of age).
3. Instrumental vaginal birth.
4. Apgar score less than seven at five minutes.
5. Need for neonatal intensive care unit admission.
6. Birthweight less than 2500 g.
7. Respiratory distress syndrome.
8. Parameters of birth asphyxia (neonatal irritability, neonatal seizures, neonatal hypotonia, abnormal level of consciousness, neonatal apnoea, tube feeding greater than 48 hours).
9. Intraventricular haemorrhage or periventricular leukomalacia (as diagnosed by cranial ultrasound).
11. Disability at childhood follow-up (including deafness, blindness, neurodisability or cerebral palsy).

Measures of satisfaction include the following
1. Woman not satisfied.
2. Women’s preferences for care.

Costs include the following
2. Number of antenatal visits.
3. Number of antenatal admissions and length of admission.
4. Length of maternal postnatal stay.
5. Length of stay in neonatal intensive care unit.
6. Infant length of hospital stay.
* denotes outcomes not prespecified in the protocol

Electronic searches
We searched the Cochrane Pregnancy and Childbirth Group’s Trials Register by contacting the Trials Search Co-ordinator (31 May 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.

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.

Selection of studies
Two review authors independently assessed for inclusion the report identified as a result of the search strategy.

Data extraction and management
We designed a form to extract data. For the eligible report, two review authors extracted the data using the agreed form. We resolved discrepancies through discussion. Data were entered into Review Manager software (RevMan 2014) and checked for accuracy.

Assessment of risk of bias in included studies
Two review authors independently assessed risk of bias using the criteria outlined in the Cochrane Handbook for Systematic Reviews.
(1) Random sequence generation (checking for possible selection bias)

We described the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.
We assessed 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 described the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.
We assessed 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 described the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that the study was at low risk of bias staff and participants were blinded, or if we judged that the lack of blinding was unlikely to affect results.
We assessed 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 described the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed 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 described the completeness of data including attrition and exclusions from the analysis. We stated 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 was reported, or could be supplied by the trial authors, we planned to re-include missing data in the analyses which we undertook.
We assessed 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 described how we investigated the possibility of selective outcome reporting bias and what we found.
We assessed the methods as:
- low risk of bias (where it is clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review have been reported);
- high risk of bias (where not all the study's prespecified outcomes have been reported; one or more reported primary outcomes were not prespecified; 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 described any important concerns we had about other possible sources of bias.

(7) Overall risk of bias

We made explicit judgements about whether the study was at high risk of bias, according to the criteria given in the Handbook (Higgins 2011). With reference to (1) to (6) above, we planned to assess the likely magnitude and direction of the bias and whether we considered it is likely to impact on the findings. In future updates, 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

For this update, we assessed the quality of the evidence using the GRADE approach as outlined in the GRADE handbook in order to assess the quality of the body of evidence relating to the following outcomes.
1. Perinatal death
2. Small-for-gestational age (defined as birthweight less than the 10th centile for gestational age)
3. Very preterm birth (defined as birth less than 34 weeks' gestation)
4. Caesarean birth
5. Postnatal depression at six months
6. Breastfeeding at six months postpartum

We used GRADEpro Guideline Development Tool to import data from Review Manager 5.3 (RevMan 2014) in order to create a 'Summary of findings' table. A summary of the intervention effect and a measure of quality for each of the above outcomes was 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 presented results as summary risk ratio with 95% confidence intervals.

Continuous data
We planned to use the mean difference if results from more than one study were available and outcomes were measured in the same way between trials. We planned to use the standardised mean difference to combine trials that measured the same outcome, but used different methods. In this version of the review only one trial was included and we did not carry out meta-analysis.

Unit of analysis issues

Cluster-randomised trials
No cluster-randomised trials were identified for this version of the review. If such trials are identified in the future 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 coefficient (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. We will also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit.

Multiple pregnancies
In our main comparison for neonatal outcomes, we used the number of babies as the denominator, whereas for maternal outcomes we used the number of women as the denominator. This review focuses on multiple pregnancies and outcomes for babies from the same pregnancy (twins or higher multiples) are not independent. For some outcomes (e.g. preterm birth) outcomes for babies from the same pregnancy are likely to be the same, or very highly correlated. For other outcomes there will be a lower correlation (e.g. fetal death or infant anomaly). For breastfeeding outcomes, outcomes for twins or higher multiples are likely to be highly correlated although women may use different feeding methods for their babies depending on infant birthweight, behaviour or other considerations. To take account of the non-independence of outcomes for babies from multiple pregnancies we carried out a sensitivity analysis for infant outcomes where we treated each pregnancy as a cluster, and analysed data using methods described above for cluster-randomised trials. ICCs for individual outcomes were not reported for the trial included in the review, and we have not been able to identify published ICCs for twin pregnancy outcomes. We therefore estimated ICCs for the small number of outcomes reported for infants using a conservative ICC (assuming high correlation between outcomes for twins from the same pregnancy; e.g. if one twin was admitted to the neonatal intensive care unit, we assumed there would be an increased chance that the second twin from the same pregnancy would also be admitted compared with a baby from a different pregnancy). The effect of adjustment for correlation was to widen the 95% confidence intervals for outcomes for infants.

Cross-over trials
Cross-over trials are not an appropriate study design to be included in this review.
Dealing with missing data

For the included study, we noted levels of attrition. In future updates, if more eligible studies are included, 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, analyses were carried out, as far as possible, on an intention-to-treat basis i.e. we attempted to include all participants randomised to each group in the analyses. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

In this version of the review only one study contributed data. In future updates if data from several studies are pooled, 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 a Tau² is greater than zero, or there is a low P value (less than 0.10) in the Chi² test for heterogeneity. If we identify substantial heterogeneity (above 30%), we plan to explore it by prespecified 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 carried out statistical analysis using the Review Manager software (RevMan 2014). We did not pool data, but if we do so in future updates we will use fixed-effect meta-analysis for combining data where it was reasonable to assume that studies are estimating the same underlying treatment effect: i.e. where trials examine 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 differed 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 Tau² and I².

Subgroup analysis and investigation of heterogeneity

In future updates if more data become available and we identify substantial heterogeneity, we will investigate it using subgroup 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. assisted versus spontaneous conception;
2. parity (nulliparous versus multiparous women);
3. twins versus higher-order multiple pregnancy;
4. chorionicity of the pregnancy (dichorionic versus monochorionic);
5. type of care received (i.e. time that specialised care commenced, number of antenatal visits, use of ultrasound and Doppler assessment of umbilical artery waveform).

The subgroup analysis will be confined to the review primary outcomes (perinatal death, small-for-gestational-age infants (birth-weight less than 10th centile for gestational age and infant sex), preterm birth before 34 weeks’ gestation and maternal death). In future updates of this review, we will assess subgroup differences by interaction tests available within RevMan (RevMan 2014).

Sensitivity analysis

In future updates of this review, 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. In this version of the review we have carried out sensitivity analysis to examine the effects of adjusting the data for cluster design effect for infant outcomes.

RESULTS

Description of studies

Results of the search

The search identified an additional report for the single study already included in earlier versions of the review (Carrick-Sen 2014a).

Included studies

In this body of work (Carrick-Sen 2014b), 162 women with a multiple pregnancy were randomised to receive standard antenatal care (involving consultation with the woman’s general practitioner, consultant obstetrician, community midwife, antenatal education sessions and breastfeeding workshop), or to an intervention group...
(consisting of the above, in addition to midwifery-led antenatal and postnatal home visits, as well as an antenatal preparation for parenting programme). The primary outcome of the trial was the incidence of depression at six months’ postpartum.

**Excluded studies**
There were no excluded studies.

**Risk of bias in included studies**
See Figure 1 for summary of 'Risk of bias' assessments.

> Figure 1. 'Risk of bias' summary: review authors' judgements about each 'Risk of bias' item for each included study.
Allocation
The included randomised trial (Carrick-Sen 2014b) used a computer-generated randomisation sequence, and web-based treatment group allocation and was assessed as being at low risk of bias for methods of randomisation and allocation concealment.

Blinding
Blinding of caregivers and women was not possible, and it was not stated whether or not outcome assessors were aware of allocated treatment group although most outcomes would have been recorded in maternity case notes by staff aware of treatment allocation. This study was assessed as being at high risk of bias for these domains (Carrick-Sen 2014b).

Incomplete outcome data
For the study's primary outcome (postnatal depression at six months' postpartum), questionnaires were received from 133 (82%) of all trial participants. This is less than 20% loss to follow-up and has therefore been assessed as being at unclear risk of bias.

Selective reporting
All prespecified outcomes in a report from the UK National Health Service (NHS) R&D trial's register appear to have been reported upon in the PhD thesis reporting the trial (postnatal depression, maternal anxiety, emotional well-being, maternal satisfaction, parental stress) at all prespecified time points (six, 12, 26 and 52 weeks' postnatal). This study was assessed as being at low risk of bias for this domain (Carrick-Sen 2014b).

Other potential sources of bias
Baseline characteristics were balanced, but multiparous, single non-Caucasian women were under-represented and women with a poor command of English were excluded owing to limited resources for translation.

The outcomes for twins were not adjusted for cluster-design effect; this means that outcomes for twins from the same pregnancy were assumed to be independent. Consequently, the 95% confidence intervals (CI) for infant outcomes are narrower than would have been the case if correlation between outcomes for twins from the same pregnancy had been taken into account. This study was assessed as being at unclear risk of bias for this domain (Carrick-Sen 2014b).

Effects of interventions
See: Summary of findings for the main comparison Specialised antenatal clinics versus standard care for women with multiple pregnancies
One randomised trial involving 162 women with a twin pregnancy was included.

Primary outcomes
There were no significant differences identified between the specialised antenatal care and standard care groups for the only primary outcome reported, perinatal mortality (risk ratio (RR) 1.02; 95% confidence interval (CI) 0.26 to 4.03; one study, 324 infants, very low quality evidence) (Analysis 1.1). Other primary outcomes (small-for-gestational age (defined as birthweight less than the 10th centile for gestational age), preterm birth (defined as birth less than 34 weeks’ gestation), and maternal death were not reported).

Secondary outcomes
Women receiving specialised antenatal care were significantly more likely to require a caesarean birth (RR 1.38; 95% CI 1.06 to 1.81; one study, 162 women, moderate quality evidence) (Analysis 1.2), when compared with women receiving standard antenatal care. However, there were no significant differences between the two treatment groups for the other reported secondary outcomes postnatal depression (RR 0.48; 95% CI 0.19 to 1.20; one study, 133 women, very low quality evidence) (Analysis 1.3), breastfeeding at six months (RR 0.63; 95% CI 0.24 to 1.68; one study, 123 women, very low quality evidence) (Analysis 1.4), stillbirth (RR 0.68; 95% CI 0.12 to 4.04; one study, 324 infants, very low quality evidence) (Analysis 1.5), or neonatal death (RR 2.05; 95% CI 0.19 to 22.39; one study, 324 infants, very low quality evidence) (Analysis 1.6).

Stillbirth and neonatal death were not outcomes prespecified in the protocol. Other prespecified secondary outcomes were not reported.

Non-prespecified outcomes
We had prespecified two outcomes relating to maternal satisfaction with care: women not satisfied with care and women's preferences for care. These outcomes were not reported however, the numbers of women reporting in postal questionnaires that they were “very satisfied” with their antenatal care and with their overall care were reported. There was a trend towards women in the specialised care group being more likely to report being very satisfied with their antenatal care although the difference between groups did not reach statistical significance (RR 1.29; 95% CI 0.99 to 1.67; 133 women) (Analysis 1.7). There was no clear evidence that women receiving specialised antenatal care were more likely to be more satisfied with their overall care (including intrapartum care) (RR 1.28; 95% CI 0.91 to 1.79; 141 women) (Analysis 1.8).

The number of infants admitted to the neonatal intensive care unit was not reported although the number admitted to special care was; the criteria for admission to special care was not defined. It appeared that infants of mothers receiving specialised care were more likely to be admitted to special care although data were not adjusted for any correlation between outcomes for twins from the
same pregnancy (RR 1.43; 95% CI 1.02 to 2.00, 324 infants) (Analysis 1.9).

Sensitivity analysis
For infant outcomes (perinatal death, stillbirth, neonatal death and admission to special care), we planned to carry out sensitivity analysis adjusting the data to take account of possible correlation between outcomes for twins from the same pregnancy. Using adjusted data (assuming an intracluster correlation coefficient (ICC) of 0.5, and dividing event rates and sample sizes by 1.5 to take account of design effect), there was no evidence of a significant difference between groups for perinatal death or admission to special care (Analysis 2.1; Analysis 2.2) (due to very low event rates we were not able to adjust the data for stillbirth and neonatal death).

DISCUSSION

Summary of main results
This review identified one randomised controlled trial assessing the benefits and harms of ‘specialised’ antenatal clinics for women with a multiple pregnancy compared with ‘standard’ antenatal care, involving 162 women and 324 infants. While women in the specialised antenatal clinic were more likely to have a caesarean birth, there was limited reporting of other primary and secondary maternal and infant health outcomes specified in the review.

Overall completeness and applicability of evidence
The available literature is confined to one randomised trial, with limited reporting of primary and secondary maternal and infant health outcomes.

Quality of the evidence
The review is confined to one randomised trial, with limited reporting of primary and secondary maternal and infant health outcomes. The included randomised trial provided limited information relating to maternal and infant health outcomes. Blinding for this type of intervention is generally not feasible and this may be a source of bias and no adjustment was made for possible correlation between outcomes for twins from the same pregnancy; the study was otherwise methodologically sound.

In this 2015 update, we have assessed the quality of the evidence using the GRADE approach for the following outcomes: perinatal death, caesarean birth, postnatal depression, breastfeeding six months’ postpartum, small-for-gestational age and very preterm birth, see Summary of findings for the main comparison. The evidence was assessed as being of moderate quality for caesarean section and very low for the other outcomes (perinatal death, postnatal depression, breastfeeding six months’ postpartum). Two outcomes could not be assessed because they were not reported in the trial (small-for-gestational age and very preterm birth). For most important outcomes the evidence was not available, or was graded very low quality due to imprecise estimates, the small sample size of the single study providing data and low numbers of events for some outcomes.

Potential biases in the review process
We attempted to minimise bias during the review process by having two people assess the eligibility of studies, assess risk of bias and extract data with a third person involved to check or review each area. We attempted to be as inclusive as possible in our search.

Agreements and disagreements with other studies or reviews
While there are reports that suggest a potential improvement in neonatal outcomes associated with ‘specialised’ care for women with a twin pregnancy, they are limited by their non-randomised nature, with inherent potential for bias. Furthermore, there is limited reporting of clinically meaningful outcomes for both women and infants.

The value of ‘specialised’ multiple pregnancy clinics in improving health outcomes for women and their infants requires further evaluation by randomised controlled trials, with reporting of relevant maternal and infant health outcomes.

AUTHORS’ CONCLUSIONS

Implications for practice
There is insufficient information available from randomised controlled trials to support the role of ‘specialised’ antenatal clinics for women with a multiple pregnancy compared with ‘standard’ antenatal care in improving maternal and infant health outcomes.

Implications for research
The value of ‘specialised’ multiple pregnancy clinics in improving health outcomes for women and their infants requires further evaluation in appropriately powered and designed randomised controlled trials, with reporting of relevant health outcomes.

ACKNOWLEDGEMENTS

Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes (Review)
During the time of preparation of this review, Jodie Dodd was the recipient of the Neil Hamilton Fairley Fellowship supported by the NHMRC (ID 399224), and a NHMRC Practitioner Fellowship (ID 627005).

Therese Dowswell is supported by the NIHR Cochrane Programme Grant Project: 13/89/05 - Pregnancy and childbirth systematic reviews to support clinical guidelines.

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REFERENCES

References to studies included in this review

Carrick-Sen 2014b * [published and unpublished data]

Additional references

Ananth 2001

Ananth 2003

Campbell 1999

Campbell 2004

Carrick-Sen 2014a

Catov 2007

Conde-Agudelo 2000

Dodd 2005

Dodd 2010

Ellings 1993
Gardner 1990

Henderson 1995

Higgins 2011

Keith 1980

Li 2011

Little 1988

MacDorman 2007

Newman 1995

NICE 2011

Patel 1983

RevMan 2014

Ruiz 2001

Rydhstroem 2001

Salihu 2005

Santema 1995

Schwartz 1999

Sen 2004

Sen 2006

Tucker 2004

Whitworth 2011

Whitworth 2004

References to other published versions of this review

Dodd 2007

Dodd 2012

* Indicates the major publication for the study
## Characteristics of included studies [ordered by study ID]

### Carrick-Sen 2014b

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td>Randomised trial of 162 women with a twin pregnancy; women recruited from Newcastle-upon-Tyne, UK, between October 2000 and March 2003</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>162 women with a twin pregnancy; women booked for care prior to 20 weeks’ gestation, with no known fetal anomalies</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>Women were randomised to ‘standard’ antenatal care (involving consultation with the woman’s general practitioner, consultant obstetrician, community midwife, antenatal education sessions and breastfeeding workshop), or to a ‘specialised’ intervention group (consisting of the above, in addition to midwifery-led antenatal and postnatal home visits, as well as an antenatal preparation for parenting programme)</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>The primary outcome of the trial was the incidence of depression at 6 months’ postpartum</td>
</tr>
</tbody>
</table>

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Web-based allocation.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>Unclear risk</td>
<td>For the study’s primary outcome (postnatal depression at 6 months’ postpartum), questionnaires were received from 133 (82%) of all trial participants, so less than 20% loss. 62% of women returned all questionnaires</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All prespecified outcomes from the NHS R&amp;D trial’s register appear to have been reported upon in the report of the trial in the PhD thesis (postnatal depression, maternal anxiety, emotional well-being, maternal satisfaction, parental stress) at all prespecified time points (6, 12, 26 and 52 weeks’ postnatal)</td>
</tr>
</tbody>
</table>
Other bias | Unclear risk | “Randomisation was effective to provide two groups with the same baseline demographic and psychosocial characteristics. Acceptability and compliance with the intervention was excellent.” “Women who declined participation were more likely to be multiparous, single and non-Caucasian.” Baseline characteristics were balanced, but multiparous, single non-Caucasian women under-represented. Women with poor command of English were excluded. Data for infant outcomes were not adjusted to take account of correlation between twins from the same pregnancy. In this version of the review we carried out a sensitivity analysis assuming high correlation of outcomes for twins.

| Blinding of participants and personnel (performance bias) | High risk | Described as an “open RCT” - “Due to the visibility of the intervention the study design was based on an open RCT”

| Blinding of outcome assessment (detection bias) | High risk | Outcomes recorded in obstetric notes by staff aware of allocation and in postal questionnaires. Women in the intervention group were slightly more likely to return questionnaires.

RCT: randomised controlled trial
### Comparison 1. ’Specialised’ antenatal clinic versus ’standard’ care

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Perinatal death</td>
<td>1</td>
<td>324</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.03 [0.26, 4.03]</td>
</tr>
<tr>
<td>2 Caesarean birth</td>
<td>1</td>
<td>162</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.38 [1.06, 1.81]</td>
</tr>
<tr>
<td>3 Postnatal depression (6 months’ postpartum). EPDS score 13 or more.</td>
<td>1</td>
<td>133</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.48 [0.19, 1.20]</td>
</tr>
<tr>
<td>4 Breastfeeding 6 months’ postpartum</td>
<td>1</td>
<td>123</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.63 [0.24, 1.68]</td>
</tr>
<tr>
<td>5 Stillbirth</td>
<td>1</td>
<td>324</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.68 [0.12, 4.04]</td>
</tr>
<tr>
<td>6 Neonatal death</td>
<td>1</td>
<td>324</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>2.05 [0.19, 22.39]</td>
</tr>
<tr>
<td>7 Number of women very satisfied with antenatal care</td>
<td>1</td>
<td>133</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.29 [0.99, 1.67]</td>
</tr>
<tr>
<td>8 Number of women very satisfied with overall care</td>
<td>1</td>
<td>141</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.28 [0.91, 1.79]</td>
</tr>
<tr>
<td>9 Admission to SCBU</td>
<td>1</td>
<td>324</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.43 [1.02, 2.00]</td>
</tr>
</tbody>
</table>

### Comparison 2. Sensitivity analysis taking account of cluster design effect. ’Specialised’ antenatal clinic versus ’standard’ care

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Perinatal death</td>
<td>1</td>
<td>161</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.01 [0.15, 7.01]</td>
</tr>
<tr>
<td>2 Admission to SCBU</td>
<td>1</td>
<td>161</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.42 [0.87, 2.30]</td>
</tr>
</tbody>
</table>
### Analysis 1.1. Comparison 1 'Specialised' antenatal clinic versus 'standard' care, Outcome 1 Perinatal death.

**Review:** Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes

**Comparison:** 1 'Specialised' antenatal clinic versus 'standard' care

**Outcome:** 1 Perinatal death

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Specialised care</th>
<th>Standard care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H Fixed, 95% CI</td>
<td>M-H Fixed, 95% CI</td>
<td></td>
</tr>
<tr>
<td>Carrick-Sen 2014b</td>
<td>4/160</td>
<td>4/164</td>
<td></td>
<td>100.0 %</td>
<td>1.03 [0.26, 4.03]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>160</td>
<td>164</td>
<td>100.0 %</td>
<td>1.03 [0.26, 4.03]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 4 (Specialised care), 4 (Standard care)

Heterogeneity: not applicable

Test for overall effect: Z = 0.04 (P = 0.97)

Test for subgroup differences: Not applicable

---

### Analysis 1.2. Comparison 1 'Specialised' antenatal clinic versus 'standard' care, Outcome 2 Caesarean birth.

**Review:** Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes

**Comparison:** 1 'Specialised' antenatal clinic versus 'standard' care

**Outcome:** 2 Caesarean birth

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Specialised care</th>
<th>Standard care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H Fixed, 95% CI</td>
<td>M-H Fixed, 95% CI</td>
<td></td>
</tr>
<tr>
<td>Carrick-Sen 2014b</td>
<td>54/80</td>
<td>40/82</td>
<td></td>
<td>100.0 %</td>
<td>1.38 [1.06, 1.81]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>80</td>
<td>82</td>
<td>100.0 %</td>
<td>1.38 [1.06, 1.81]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 54 (Specialised care), 40 (Standard care)

Heterogeneity: not applicable

Test for overall effect: Z = 2.37 (P = 0.018)

Test for subgroup differences: Not applicable
Analysis 1.3. Comparison 1 'Specialised' antenatal clinic versus 'standard' care, Outcome 3 Postnatal depression (6 months' postpartum). EPDS score 13 or more.

Review: Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes

Comparison: 1 'Specialised' antenatal clinic versus 'standard' care

Outcome: 3 Postnatal depression (6 months' postpartum). EPDS score 13 or more.

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Specialised care</th>
<th>Standard care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed,95% CI</td>
<td></td>
<td>M-H,Fixed,95% CI</td>
</tr>
<tr>
<td>Carrick-Sen 2014b</td>
<td>6/68</td>
<td>12/65</td>
<td>100.0 %</td>
<td>0.48 [0.19, 1.20]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>68</strong></td>
<td><strong>65</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>0.48 [0.19, 1.20]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 6 (Specialised care), 12 (Standard care)

Heterogeneity: not applicable
Test for overall effect: Z = 1.57 (P = 0.12)
Test for subgroup differences: Not applicable

Analysis 1.4. Comparison 1 'Specialised' antenatal clinic versus 'standard' care, Outcome 4 Breastfeeding 6 months' postpartum.

Review: Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes

Comparison: 1 'Specialised' antenatal clinic versus 'standard' care

Outcome: 4 Breastfeeding 6 months' postpartum

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Specialised care</th>
<th>Standard care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed,95% CI</td>
<td></td>
<td>M-H,Fixed,95% CI</td>
</tr>
<tr>
<td>Carrick-Sen 2014b</td>
<td>6/63</td>
<td>9/60</td>
<td>100.0 %</td>
<td>0.63 [0.24, 1.68]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>63</strong></td>
<td><strong>60</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>0.63 [0.24, 1.68]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 6 (Specialised care), 9 (Standard care)

Heterogeneity: not applicable
Test for overall effect: Z = 0.92 (P = 0.36)
Test for subgroup differences: Not applicable
### Analysis 1.5. Comparison 1 'Specialised' antenatal clinic versus 'standard' care, Outcome 5 Stillbirth.

Review: Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes

Comparison: 1 'Specialised' antenatal clinic versus 'standard' care

Outcome: 5 Stillbirth

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Specialised care</th>
<th>Standard care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed,95% CI</td>
<td></td>
<td>M-H,Fixed,95% CI</td>
</tr>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed,95% CI</td>
<td></td>
<td>M-H,Fixed,95% CI</td>
</tr>
<tr>
<td>Carrick-Sen 2014b</td>
<td>2/160</td>
<td>3/164</td>
<td>100.0 %</td>
<td>0.68 [ 0.12, 4.04 ]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>160</strong></td>
<td><strong>164</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>0.68 [ 0.12, 4.04 ]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 2 (Specialised care), 3 (Standard care)
Heterogeneity: not applicable
Test for overall effect: Z = 0.42 (P = 0.67)
Test for subgroup differences: Not applicable

### Analysis 1.6. Comparison 1 'Specialised' antenatal clinic versus 'standard' care, Outcome 6 Neonatal death.

Review: Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes

Comparison: 1 'Specialised' antenatal clinic versus 'standard' care

Outcome: 6 Neonatal death

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Specialised care</th>
<th>Standard care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed,95% CI</td>
<td></td>
<td>M-H,Fixed,95% CI</td>
</tr>
<tr>
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<td>M-H,Fixed,95% CI</td>
<td></td>
<td>M-H,Fixed,95% CI</td>
</tr>
<tr>
<td>Carrick-Sen 2014b</td>
<td>2/160</td>
<td>1/164</td>
<td>100.0 %</td>
<td>2.05 [ 0.19, 22.39 ]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>160</strong></td>
<td><strong>164</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>2.05 [ 0.19, 22.39 ]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 2 (Specialised care), 1 (Standard care)
Heterogeneity: not applicable
Test for overall effect: Z = 0.59 (P = 0.56)
Test for subgroup differences: Not applicable
### Analysis 1.7. Comparison 1 'Specialised' antenatal clinic versus 'standard' care, Outcome 7 Number of women very satisfied with antenatal care.

**Review:** Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes

**Comparison:** 1 'Specialised' antenatal clinic versus 'standard' care

**Outcome:** 7 Number of women very satisfied with antenatal care

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Specialised care</th>
<th>Standard care</th>
<th>Risk Ratio M-H,Fixed, 95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H,Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carrick-Sen 2014b</td>
<td>50/69</td>
<td>36/64</td>
<td>1.29 [0.99, 1.67]</td>
<td>100.0%</td>
<td>1.29 [0.99, 1.67]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>69</strong></td>
<td><strong>64</strong></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>1.29 [0.99, 1.67]</strong></td>
</tr>
</tbody>
</table>

Total events: 50 (Specialised care), 36 (Standard care)

Heterogeneity: not applicable

Test for overall effect: Z = 1.91 (P = 0.057)

Test for subgroup differences: Not applicable

### Analysis 1.8. Comparison 1 'Specialised' antenatal clinic versus 'standard' care, Outcome 8 Number of women very satisfied with overall care.

**Review:** Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes

**Comparison:** 1 'Specialised' antenatal clinic versus 'standard' care

**Outcome:** 8 Number of women very satisfied with overall care

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Specialised care</th>
<th>Standard care</th>
<th>Risk Ratio M-H,Fixed, 95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H,Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carrick-Sen 2014b</td>
<td>40/72</td>
<td>30/69</td>
<td>1.28 [0.91, 1.79]</td>
<td>100.0%</td>
<td>1.28 [0.91, 1.79]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>72</strong></td>
<td><strong>69</strong></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>1.28 [0.91, 1.79]</strong></td>
</tr>
</tbody>
</table>

Total events: 40 (Specialised care), 30 (Standard care)

Heterogeneity: not applicable

Test for overall effect: Z = 1.42 (P = 0.16)

Test for subgroup differences: Not applicable
Analysis 1.9. Comparison 1 'Specialised' antenatal clinic versus 'standard' care, Outcome 9 Admission to SCBU.

Review: Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes

Comparison: 1 'Specialised' antenatal clinic versus 'standard' care

Outcome: 9 Admission to SCBU

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Specialised care</th>
<th>Standard care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed,95% CI</td>
<td></td>
<td>M-H,Fixed,95% CI</td>
<td></td>
</tr>
<tr>
<td>Carrick-Sen 2014b</td>
<td>57/160</td>
<td>41/164</td>
<td>1.43 [1.02, 2.00]</td>
<td>100.0 %</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>160</td>
<td>164</td>
<td>1.43 [1.02, 2.00]</td>
<td>100.0 %</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 57 (Specialised care), 41 (Standard care)
Heterogeneity: not applicable
Test for overall effect: Z = 2.06 (P = 0.039)
Test for subgroup differences: Not applicable

Analysis 2.1. Comparison 2 Sensitivity analysis taking account of cluster design effect. 'Specialised' antenatal clinic versus 'standard' care, Outcome 1 Perinatal death.

Review: Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes

Comparison: 2 Sensitivity analysis taking account of cluster design effect. 'Specialised' antenatal clinic versus 'standard' care

Outcome: 1 Perinatal death

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Specialised care</th>
<th>Standard care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed,95% CI</td>
<td></td>
<td>M-H,Fixed,95% CI</td>
<td></td>
</tr>
<tr>
<td>Carrick-Sen 2014b</td>
<td>2/80</td>
<td>2/81</td>
<td>1.01 [0.15, 7.01]</td>
<td>100.0 %</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>80</td>
<td>81</td>
<td>1.01 [0.15, 7.01]</td>
<td>100.0 %</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 2 (Specialised care), 2 (Standard care)
Heterogeneity: not applicable
Test for overall effect: Z = 0.01 (P = 0.99)
Test for subgroup differences: Not applicable
Analysis 2.2. Comparison 2 Sensitivity analysis taking account of cluster design effect. 'Specialised' antenatal clinic versus 'standard' care, Outcome 2 Admission to SCBU.

Review: Specialised antenatal clinics for women with a multiple pregnancy for improving maternal and infant outcomes

Comparison: 2 Sensitivity analysis taking account of cluster design effect. 'Specialised' antenatal clinic versus 'standard' care

Outcome: 2 Admission to SCBU

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Specialised care</th>
<th>Standard care</th>
<th>Risk Ratio</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed,95% CI</td>
<td></td>
<td>M-H,Fixed,95% CI</td>
</tr>
<tr>
<td>Carrick-Sen 2014b</td>
<td>28/80</td>
<td>20/81</td>
<td>1.42 [0.87, 2.30]</td>
<td>100.0 %</td>
<td>1.42 [0.87, 2.30]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>80</td>
<td>81</td>
<td>100.0 %</td>
<td>1.42 [0.87, 2.30]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 28 (Specialised care), 20 (Standard care)
Heterogeneity: not applicable
Test for overall effect: Z = 1.41 (P = 0.16)
Test for subgroup differences: Not applicable

A P P E N D I C E S

Appendix 1. Search methods used in previous versions of this review

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 (17 January 2011).
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. monthly searches of MEDLINE;
3. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness search of a further 37 journals.
Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Search strategies for identification of studies' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are given a code (or codes) depending on the topic. The codes are linked to review topics. The Trials Search Co-ordinator searches the register for each review using these codes rather than keywords.
In addition, we searched CENTRAL (The Cochrane Library 2005, Issue 4) and PubMed (January 1966 to January 2006). Terms used in the database searches were "multiple pregnancy", "twin pregnancy", "antenatal care", "prenatal care".
We did not apply any language restrictions.
WHAT'S NEW

Last assessed as up-to-date: 31 May 2015.

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>31 May 2015</td>
<td>New search has been performed</td>
<td>Search updated, one further report identified for the single study already included in earlier versions of the review (Carrick-Sen 2014a).</td>
</tr>
<tr>
<td>31 May 2015</td>
<td>New citation required but conclusions have not changed</td>
<td>In this version of the review the quality of the evidence from the one included study was assessed using the GRADE approach and a 'Summary of Findings' table has been added</td>
</tr>
</tbody>
</table>

HISTORY

Protocol first published: Issue 2, 2005
Review first published: Issue 2, 2007

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>11 April 2012</td>
<td>New citation required but conclusions have not changed</td>
<td>This updated review now has one included study (involving 162 women). There is still insufficient evidence to evaluate the use of specialised antenatal clinics for women with a multiple pregnancy</td>
</tr>
<tr>
<td>11 April 2012</td>
<td>New search has been performed</td>
<td>Search updated. Two new reports of one trial identified (Sen 2004; Sen 2006). The methods have been updated.</td>
</tr>
<tr>
<td>12 November 2008</td>
<td>Amended</td>
<td>Converted to new review format. Title modified.</td>
</tr>
</tbody>
</table>

CONTRIBUTIONS OF AUTHORS

Jodie Dodd drafted the initial version of the review. Jodie Dodd and Caroline Crowther contributed to data extraction, analyses and subsequent revisions of the review. Therese Dowswell contributed to this update.
DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

• Discipline 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

• National Institute for Health Research (NIHR), UK.
TD is supported by the NIHR Cochrane Programme Grant Project: 13/89/05 - Pregnancy and childbirth systematic reviews to support clinical guidelines.
• National Health and Medical Research Council, Australia Funding for the PCG Australian and New Zealand Satellite, Australia.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The following outcomes were not prespecified in the protocol.

Complications for infants (one or both)

1. Stillbirth* (death of one or more infants after trial entry but before birth).
2. Neonatal death* (death of one or more liveborn infants up to 28 days of age).

In this version of the review (2015) the quality of the evidence from the one included study was assessed using the GRADE approach and a 'Summary of Findings' table has been added.

INDEX TERMS

Medical Subject Headings (MeSH)

*Infant Welfare; *Maternal Welfare; *Pregnancy Outcome; *Pregnancy, Multiple; Cesarean Section [utilization]; Perinatal Mortality; Pregnancy, Twin; Prenatal Care [methods; *standards]; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Infant, Newborn; Pregnancy