Elective preterm birth for fetal gastroschisis (Review)

Grant NH, Dorling J, Thornton JG

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Elective preterm birth for fetal gastroschisis

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ABSTRACT

Background

Gastroschisis is an uncommon congenital defect of the anterior abdominal wall that results in herniation of intestinal loops outside the abdominal cavity. Babies with gastroschisis generally do well, but there remains a mortality rate of 5% to 10% and some require prolonged parenteral nutrition and intensive care. Significant injury to the exposed bowel may occur in-utero, and earlier birth may reduce this, improve long-term outcomes and reduce complications, such as necrotising enterocolitis. However, it may also increase complications related to prematurity. There is a lack of published data in this area.

Objectives

To assess the effects of elective preterm birth for fetal gastroschisis in pregnancies complicated by this condition. The mode of birth may be either vaginal or by caesarean section, but this review is studying only timing, not the route, of birth.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group’s Trials Register (16 January 2013).

Selection criteria

Individual patient randomised controlled trials of planned preterm birth in pregnancies complicated by fetal gastroschisis, diagnosed by ultrasound scanning in time for preterm birth to be an option, and without other fetal anomalies. The intervention is planned preterm birth, prior to 37 weeks and 0 days’ gestation, versus planned later birth, at or after 37 weeks and 0 days’ gestation (mode of birth is not part of the intervention).

We did not include quasi-randomised controlled trials and cluster trials. Cross-over trials are not appropriate for this condition. Studies that were presented in abstract form only were eligible for inclusion, providing that the population included women with pregnancies affected by fetal gastroschisis, the interventions were defined and the treatment selection was randomised.

Data collection and analysis

Two review authors independently assessed for inclusion the one trial identified as a result of the search strategy and assessed trial quality. Two review authors extracted data and checked it for accuracy.
Main results

We included one study, involving 40 infants and 42 women. The trial was underpowered to detect clinically important outcome differences between the two policies. There were no significant benefits or adverse effects of elective preterm birth at 36 weeks' gestation for fetal gastroschisis. The primary outcomes were caesarean section and neonatal survival to discharge. Two babies died after birth but before discharge in the elective (intervention) group versus none in the spontaneous group (risk ratio (RR) 5.00; 95% confidence interval (CI) 0.26 to 98.00; one study, n = 40). Seven women (33%) in the elective group and nine women (43%) in the spontaneous group delivered by caesarean section (RR 0.78; 95% CI 0.36 to 1.70).

Similarly, for the secondary outcomes, there were no statistical differences in birthweight, ventilation requirements, necrotising enterocolitis and requirement for repeat surgery between the two groups. None of our prespecified maternal secondary outcomes were reported in the included study.

We also examined gestational age at birth as a non-prespecified outcome. There was a difference in gestational age at birth between the two arms of the trial (35.8 weeks (SD 0.7) in the elective group and 36.7 (SD 1.5) in the spontaneous group. Possible reasons for this small mean difference include a trend towards spontaneous preterm birth in pregnancies complicated by fetal gastroschisis.

Authors’ conclusions

This review is unable to draw any firm conclusions regarding preterm birth for infants with gastroschisis. It is not possible to say whether the intervention is beneficial or harmful for these babies or their mothers. Only one small trial is included. Further research is needed in this area.

PLAIN LANGUAGE SUMMARY

Early birth for babies with gastroschisis

Gastroschisis is where the bowel protrudes through a hole caused by a weakness in the abdominal wall and affects about one in 5000 babies. It can be detected on prenatal ultrasound scans. The defect is usually repaired surgically within a few hours of birth, and most babies eventually do well. Many, however, require prolonged intensive care support and artificial feeding, and some babies die. Some have long-term bowel problems with malabsorption. Before the baby is born, the exposed bowel can be injured, and early birth may prevent this. However, early birth may also cause complications due to prematurity for the baby and possibly longer labour for the mother. There is currently no clear guidance. This review identified one small randomised controlled trials, involving 42 women. There were no significant differences in outcomes for mother or baby when pre-term birth at 36 weeks was planned, compared with later birth. However, it was such a small trial that it does not rule out important benefits or harms from early birth. There was also small overall difference in gestational age at birth between the two groups in the trial, possibly because of the high rate of spontaneous preterm birth with this condition. Further trials are needed.

BACKGROUND

Description of the condition

Gastroschisis is a congenital defect of the anterior abdominal wall that results in herniation of intestinal loops outside of the abdominal cavity. The aetiology is unknown, although babies of younger mothers are more commonly affected (Carry 2000), suggesting environmental factors may have a part to play. The incidence is thought to be increasing, both in developed and in developing countries (Feldkamp 2007) and it currently affects approximately one in 5000 pregnancies (Loane 2007). Although usually surgically treatable with good results, many neonates require prolonged intensive care and parenteral nutrition. The costs of treatment may therefore be considerable. In addition, gastroschisis is often associated with intestinal injury such as necrosis or atresia (absence or closure of a natural passage of the body), leading to further complications, for example malabsorption, dysmotility or sepsis (Lund 2007), and a high proportion of gastroschisis pregnancies
are complicated by some degree of intrauterine growth restriction (Juhasz-Böss 2011). Overall, gastrochisis is also associated with a mortality rate of 5% to 10% (Bradnock 2011; Chabra 2005). Generally, affected infants undergo corrective surgery within hours of birth. More than one surgical procedure may be required to correct the defect. Babies with gastrochisis generally do well, but some require prolonged parenteral nutrition and intensive care (Bradnock 2011). Although most babies with gastrochisis have an excellent long-term outcome, a small proportion require repeated surgery and some have malabsorption problems from bowel atresia. The long-term effects on health outcomes remain uncertain, with little information in the literature.

The condition is usually diagnosed antenatally on routine ultrasound scanning. Unlike other congenital anomalies, gastrochisis is rarely associated with other major congenital abnormalities (Fillingham 2008). The rate of spontaneous preterm birth in pregnancies complicated by fetal gastrochisis is over 50% (Huang 2002). Anecdotally, many specialists recommend planned birth before term to minimise the risk of bowel damage, although there are no reliable data on how commonly this intervention is performed.

**Description of the intervention**

Planned preterm birth prior to 37 weeks and 0 days gestation.

**How the intervention might work**

In cases of fetal gastrochisis, it has been suggested that injury to exposed bowel loops may be sustained *in utero* due either to prolonged exposure to amniotic fluid and/or as a result of vascular compromise of the herniated loops due to a constriction effect at the umbilical ring (Langer 1989). Such injury may lead to necrosis or atresia, and may predispose to further complications, such as necrotising enterocolitis.

Planned preterm birth may pre-empt such damage and therefore improve long-term bowel function and reduce the rate of associated complications (Simmons 1996). However, it carries the risk of increasing prematurity-related complications, especially respiratory distress syndrome. This may require prolonged ventilation and oxygen therapy, with associated risks of retinopathy of prematurity, brain damage, necrotising enterocolitis and oxygen dependence.

Induction may lead to longer labours and increase the rate of caesarean section, and associated maternal complications. It may also have a direct effect on maternal puerperal complications, such as anxiety, depression and breastfeeding.

Finally, significant damage to the fetal bowel may already have occurred earlier in pregnancy.

**Why it is important to do this review**

There is currently no clear guidance in the literature, or from relevant professional bodies, on how best to manage pregnancies complicated by fetal gastrochisis. Some obstetricians (Simmons 1996) advocate planned preterm birth near term (Hadidi 2008). Studies of early birth have reported variable, often conflicting, results. A systematic review of the published evidence is urgently needed to guide management and direct future research in this area.

**OBJECTIVES**

To investigate the benefits and complications of planned preterm birth for fetal gastrochisis in pregnancies complicated by this condition, as compared with later birth. The mode of birth may be either vaginal or by caesarean section, but this is not part of the intervention.

**METHODS**

**Criteria for considering studies for this review**

**Types of studies**

We included one individual patient randomised controlled trial. We did not include quasi-randomised controlled trials and cluster trials. Cross-over trials are not appropriate for this condition. Studies that were presented in abstract form only were eligible for inclusion, providing that the population included women with pregnancies affected by fetal gastrochisis, the interventions were defined and the treatment selection was randomised.

**Types of participants**

Women with singleton pregnancies affected by fetal gastrochisis, diagnosed by ultrasound scanning in time for preterm birth to be an option, and without any other fetal anomalies.

**Types of interventions**

1. Planned preterm birth, prior to 37 weeks and 0 days’ gestation, versus
2. planned later birth, at or after 37 weeks and 0 days’ gestation (mode of birth is not part of the intervention).
Types of outcome measures

Primary outcomes

Neonatal
- Survival to hospital discharge.

Maternal
- Caesarean section.

Secondary outcomes

Neonatal
- Birthweight.
- Birthweight below 2500 g.
- Birth-related injury.
- Time to full enteral feeding, if achieved.
- Need for parenteral feeding after discharge.
- Need for oxygen after discharge.
- Length of hospital stay.
- Developmental milestones at any time period beyond six months.
- Apgar scores at five minutes.
- Apgar scores at 10 minutes.
- Cord arterial pH less than 7.10 at birth.
- Neonatal convulsions.
- Diagnosis of respiratory distress syndrome.
- Ventilation beyond 24 hours.
- Days of ventilation.
- Need for blood transfusion.
- Retinopathy of prematurity.
- Intraventricular haemorrhage.
- Necrotising enterocolitis.
- Need for repeat surgery (planned phased closure) before discharge home.
- Need for other repeat surgery (not planned phased closure) before discharge home.
- Need for ileostomy or colostomy before discharge home.
- Need for ileostomy or colostomy after discharge.
- Estimated blood loss at birth.
- Need for postnatal blood transfusion.
- Mode of infant feeding.
- Length of postnatal hospital stay.
- Endometritis.
- Need for antibiotics.
- Maternal satisfaction with birth experience.
- Maternal anxiety about the baby.
- Postnatal depression.
- Postnatal re-admission to hospital.
- Gestational age at birth (non-prespecified outcome).

Maternal
- Duration of antenatal admission to hospital.
- Need for antenatal administration of steroids.
- Need for epidural analgesia in labour.
- Operative vaginal birth.
- Perineal trauma.
- Estimated blood loss at birth.
- Need for postnatal blood transfusion.
- Mode of infant feeding.
- Length of postnatal hospital stay.
- Endometritis.
- Need for antibiotics.
- Maternal satisfaction with birth experience.
- Maternal anxiety about the baby.
- Postnatal depression.
- Postnatal re-admission to hospital.
- Gestational age at birth (non-prespecified outcome).

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 (16 January 2013). The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

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

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

We did not apply any language restrictions.

Data collection and analysis

Selection of studies

Two review authors independently assessed for inclusion the one potential study we identified as a result of the search strategy. We resolved any disagreement through discussion or, if required, we
would have consulted a third person. We planned to include studies that were presented in abstract form only, providing that the population included women with gastroschisis, the interventions were defined and the treatment selection was randomised.

**Data extraction and management**

We designed a form to extract data. For eligible studies, two review authors (Natalie Grant (NG) and Jon Dorling (JD)) extracted the data using the agreed form. We resolved any discrepancies through discussion or, if required, we would have consulted a third person. We entered data into Review Manager software (RevMan 2011) and checked them for accuracy.

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

**Assessment of risk of bias in included studies**

Two review authors (NG and Jim Thornton) independently assessed risk of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). We resolved any disagreement by discussion or by involving a third assessor.

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

   We described for the one 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 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 for the included study 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. **Blinding of participants and personnel (checking for possible performance bias)**

   We described for the included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies would be at low risk of bias if they were blinded, or if we judged that the lack of blinding would have been 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;

4. **Blinding of outcome assessment (checking for possible detection bias)**

   We described for the included study 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.

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

   We described for the included study 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 would have re-included missing data in the analyses which we undertook.

   We assessed methods as:
   - low risk of bias (e.g. studies with less than 5% incomplete data for the primary outcome; 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.

6. **Selective reporting (checking for reporting bias)**

   We described for the included study 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 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 described for the included study any important concerns we had about other possible sources of bias.
We assessed whether the one included 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 made explicit judgements about whether the included study was at high risk of bias, according to the criteria given in the Cochrane Handbook (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we considered it was likely to impact on the findings.
We planned to 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 present results as summary risk ratio with 95% confidence intervals.

Continuous data
For continuous data, we used the mean difference if outcomes were measured in the same way between trials. In future updates, 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 did not identify any cluster-randomised trials.

Cross-over trials
These are not appropriate for evaluating this intervention.

Dealing with missing data
For the one included study, we noted levels of attrition. In future updates of this review, 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 carried out analyses, as far as possible, on an intention-to-treat basis, i.e. we attempted to include all participants randomised to each group in the analyses, 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 the trial is the number randomised minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity
In future updates of this review, we will assess statistical heterogeneity in each meta-analysis using the T², I² and Chi² statistics. We would regard heterogeneity as substantial if the T² is greater than zero and either an I² is greater than 30% or there is a low P value (less than 0.10) in the Chi² test for heterogeneity.

Assessment of reporting biases
In future updates of this review, if there are 10 or more studies in the meta-analysis, we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually, and use formal tests for funnel plot asymmetry.
For continuous outcomes we will use the test proposed by Egger 1997, and for dichotomous outcomes we will use the test proposed by Harbord 2006. If we detect asymmetry in any of these tests or 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 2011).
In future updates of this review, as more data become available, we will use fixed-effect meta-analysis for combining data where it is reasonable to assume that studies are estimating the same underlying treatment effect: i.e. where trials are examining the same intervention, and the trials’ populations and methods are judged sufficiently similar. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity is detected, we will use a 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 its 95% confidence interval, and the estimates of $T^2$ and $I^2$.

Subgroup analysis and investigation of heterogeneity

If we identify substantial heterogeneity in future updates of this review, 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. Due to insufficient data we were unable to carry out the following planned subgroup analyses.

1. Normal or dilated bowel loops (as defined by the study authors) at recruitment.
2. Normal or dilated/thickened/oedematous bowel wall (as defined by the study authors) at recruitment.

We will conduct these subgroup analyses in future updates of this review.

We will use the following outcomes in subgroup analysis:

- Survival to hospital discharge.
- Maternal outcome - mode of birth (vaginal or caesarean section).

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

Sensitivity analysis

We planned to carry out sensitivity analysis limiting analyses to studies with a low risk of recruitment bias, for the primary endpoints of baby survival to hospital discharge and maternal mode of birth (vaginal or caesarean section). We will carry out these analyses in future updates as more data become available.

RESULTS

Description of studies

The search results identified one trial for consideration. One trial (involving 42 women) is included in the analysis (Logghe 2005).

Results of the search

The search of the Cochrane Pregnancy and Childbirth Group’s Trials Register retrieved four trial reports. One was of the full report for the above trial. The other three were abstracts of conference presentations of the same trial.

Included studies

This prospective, open randomised controlled trial included 42 women of up to 34 weeks’ gestation with a diagnosis of fetal gastroschisis (made by ultrasound scan) who were referred to a single fetal medicine centre in the North of England within a period of four years and five months (May 1995 to September 1999). The women were randomised to either elective birth at 36 weeks’ gestation (the ‘elective group’), or to await spontaneous labour (the ‘spontaneous group’). There were 21 women in each group.

The mode of birth was not part of the intervention in this trial. Planned or emergency caesarean section was performed for obstetric reasons only. Primary outcome measures used were time taken to tolerate full enteral feeding (150 mL/kg per day) and duration of hospital stay for the infant. Access to neonatal surgery was available at the centre.

Two women were excluded from each arm of the trial for similar reasons. The patient excluded from the elective group delivered spontaneously at 33 weeks’ gestation and the baby died very soon after birth. The patient excluded from the spontaneous group suffered an intrauterine fetal death at 31 weeks’ gestation. However, the authors of this review agreed that these women should have been included in the data analysis on an intention-to-treat basis.

In three other cases, the actual timing of birth was different from that intended through randomisation. For one woman in the elective group, induction of labour at 36 weeks’ failed and she subsequently delivered at 37 weeks’ gestation. In the elective group, another woman underwent a planned caesarean section at 34 weeks’ gestation due to intrauterine growth restriction. In the spontaneous group, one woman underwent induction of labour at 35 weeks’ gestation due to oligohydramnios and intrauterine growth restriction.

Overall, four women in the elective group and four women in the spontaneous group delivered prior to 36 weeks’ gestation. However, they were included on an intention-to-treat basis for the purposes of statistical analysis. Nonparametric data were analysed using the Mann-Whitney $U$ test, taking $P < 0.05$ as statistically significant and statistical analyses were carried out on an intention-to-treat basis.

Excluded studies

There were no excluded studies.

Risk of bias in included studies
The review authors considered the risk of bias to be generally low in the included study. Sufficient detail regarding methods was generally available in the trial report to determine this. A high risk of performance bias was thought to exist because blinding of participants and personnel involved in antenatal and intrapartum care was not possible. However, lack of blinding for these individuals is unlikely to have affected the results. Please refer to the ‘Risk of bias’ table (see Characteristics of included studies).

**Effects of interventions**

The included study (Logghe 2005) found no significant benefits or adverse effects of elective preterm birth at 36 weeks’ gestation for fetal gastroschisis. The trial provides neonatal outcome data for 20 liveborn infants in the elective group and 20 liveborn infants in the spontaneous group, and maternal outcome data for all 42 women who were initially randomised.

**Primary outcomes**

**Neonatal**

**Survival to hospital discharge**

There were two stillbirths (one in each group). Both occurred after randomisation but before the trial intervention was planned for, one at 33 weeks’ gestation in the elective group, and one at 31 weeks’ gestation in the spontaneous group (risk ratio (RR) 1.00; 95% confidence interval (CI) 0.07 to 14.95; Analysis 1.1). Two babies died after birth but before discharge in the elective group versus none in the spontaneous group (RR 5.00; 95% CI 0.26 to 98.00; Analysis 1.2).

**Caesarean section**

Seven women (33%) in the elective group and nine women (43%) in the spontaneous group delivered by caesarean section (RR 0.78; 95% CI 0.36 to 1.70; Analysis 1.3). Of the elective group, one was a planned caesarean section for severe intrauterine growth restriction and six were emergency caesarean births, five for fetal compromise and one for failure to progress in labour. All caesarean births in the spontaneous group were emergency procedures, seven for fetal compromise and two for failure to progress in labour. These differences were not statistically significant.

**Secondary outcomes**

**Neonatal**

**Birthweight**

Mean birthweight in the elective group was 2364 g (standard deviation [SD] 352) and 2338 g (SD 516) in the spontaneous group (mean difference (MD) 26.00 g; 95% CI -247.75 to 299.75; Analysis 1.4).

**Time to full enteral feeding***

The median time to full enteral feeding in surviving infants was reported as 30.5 days (range 18 to 96) in the elective group and 37.5 days (range 15 to 358) in the spontaneous group.

**Length of hospital stay***

The median length of hospital stay in surviving infants was reported as 47.5 days (range 23 to 126) in the elective group and 53 days (range 22 to 399) in the spontaneous group.

**Days of ventilation**

The mean duration of ventilation in the elective group was 2.9 days (SD 2.3) and 2.3 days (SD 1.7) in the spontaneous group (MD 0.60 days; 95% CI -0.65 to 1.85; Analysis 1.5).

**Necrotising enterocolitis**

One infant (5%) in the elective group and four infants (20%) in the spontaneous group developed necrotising enterocolitis (RR 0.25; 95% CI 0.03 to 2.05; Analysis 1.6).

**Need for repeat surgery (planned phased closure) before discharge home**

Three infants (15%) required phased closure in the elective group and four (20%) in the spontaneous group (RR 0.75, 95% CI 0.19 to 2.93; Analysis 1.7). None of these differences were statistically significant.

**Other secondary outcomes**

No data were available for the other secondary neonatal outcomes listed in the protocol. Therefore, there are many important outcomes for babies with gastroschisis, such as Apgar scores, respiratory distress syndrome, and developmental milestones, which we are not able to report on.
Maternal

No data were available for any of the secondary maternal outcomes listed in the protocol. These are also important outcomes to consider - for example, length of postnatal stay, operative vaginal delivery and maternal satisfaction.

*The necessary parametric data were not available for some outcomes (time to full enteral feeding and length of hospital stay), despite contacting the authors, and therefore we were unable to include them in the statistical analysis in this review.

Non-prespecified outcomes

Some outcomes included in the Logghe 2005 study, were not prespecified in our protocol. These are outlined in Table 1 (neonatal outcomes) and Table 2 (maternal outcomes).

Attention is drawn to the data relating to gestational age at birth for these infants. This outcome was not prespecified in the protocol, but is considered to be an important consideration. The mean gestational age at birth in the elective group was 35.8 weeks (SD 0.7) and 36.7 (SD 1.5) in the spontaneous group. The mean difference in gestation caused by the intervention was only 0.90 weeks. Possible reasons for it being so small include a trend towards spontaneous preterm birth in pregnancies complicated by fetal gastroschisis.

DISCUSSION

Only one small trial (Logghe 2005, involving 42 women) is included in this review, and therefore the conclusions must be considered carefully. In addition, this trial was underpowered to detect significant differences in any of the neonatal or maternal outcomes. This may be due to the rarity of the condition and to the difficulties of recruitment in obstetric trials.

There was no significant difference in gestational age at birth between the elective group and the spontaneous group in the trial and this implies a tendency towards spontaneous preterm birth for babies with gastroschisis. This is supported by Barseghyan 2012 who recently reported that in this small group of women, the rate of spontaneous preterm labour in pregnancies complicated by gastroschisis was approximately 50%. The cause of this is unclear but it may also explain why this trial and review has not found any benefit or harm in planning preterm birth for infants with gastroschisis.

Perhaps elective preterm birth at an even earlier gestation (at less than 36 weeks) is required to achieve significant benefits in bowel function and to improve long-term outcomes for babies with gastroschisis. However, this would increase the risk of prematurity-related complications, for example respiratory distress syndrome, and therefore, there may be no overall benefit to this approach.

Summary of main results

This review is unable to draw any firm conclusions regarding preterm birth for infants with gastroschisis. There was no significant difference in survival to hospital discharge or in any other neonatal outcomes when preterm birth is planned at 36 weeks’ gestation, compared with later birth. The trend towards a shorter time to achieve full enteral feeding and less necrotising enterocolitis for infants born after birth was planned at 36 weeks’ gestation, should be set against the two deaths before discharge in that group. There is no significant difference in the rate of caesarean section, i.e. induction of labour does not appear to increase the rate of caesarean section in this group of women.

Overall completeness and applicability of evidence

We believe we have found all randomised trials of this intervention.

Quality of the evidence

The quality of the evidence is good apart from the small sample size which means that clinically important effects have not been ruled out.

Potential biases in the review process

The single trial identified had not been registered. However, the author with a conflict of interest was not involved in assessing this trial.

Agreements and disagreements with other studies or reviews

There are no other studies relating to elective preterm birth for fetal gastroschisis.

AUTHORS’ CONCLUSIONS

Implications for practice

Gastroschisis is an uncommon, but serious, fetal anomaly which affects approximately one in 5000 pregnancies (Loane 2007). When managing this condition, it is important to consider the short-term and long-term outcomes for both mother and baby.

Due to its limited conclusions, it is unlikely that this review will impact on practice with regard to timing of birth for fetal gastroschisis. Currently, there is insufficient evidence to guide practice.
Implications for research

Further research is needed. A multi-centre randomised controlled trial is needed to measure the benefits or harm of elective preterm birth for babies with gastroschisis, and the outcomes for their mothers.

Acknowledgements

As part of the pre-publication editorial process, this review has been commented on by three peers (an editor and two referees who are external to the editorial team), a member of the Pregnancy and Childbirth Group’s international panel of consumers and the Group’s Statistical Adviser.

The National Institute for Health Research (NIHR) is the largest single funder of the Cochrane Pregnancy and Childbirth Group. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR, NHS or the Department of Health.

References

References to studies included in this review

Logghe 2005 (published data only)


Additional references

Barseghyan 2012

Bradnock 2011

Chabra 2005

Curry 2000

Egger 1997

Feldkamp 2007

Fillingham 2008

Hadidi 2008

Harbord 2006

Higgins 2011

Huang 2002

Juhasz-Böss 2011
Langer 1989

Loane 2007

Lund 2007

RevMan 2011 [Computer program]

Simmons 1996

* Indicates the major publication for the study
### Characteristics of included studies  
**Logghe 2005**

<table>
<thead>
<tr>
<th>Characteristics of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
</tr>
<tr>
<td><strong>Participants</strong></td>
</tr>
</tbody>
</table>
| **Interventions** | 1. Elective birth at 36 weeks' gestation.  
2. Await spontaneous labour, or need for elective birth for another reason  
Mode of birth was not prescribed by the trial in either group |
| **Outcomes** | Primary outcome measures were time taken to achieve full enteral feeding and duration of hospital stay |
| **Notes** | 1 baby in each arm died in utero before 36 weeks, at 33 weeks in the elective group and at 31 weeks in the spontaneous group. These 2 babies were excluded from analysis post-randomisation, and 40 babies were included in the final statistical analyses. Maternal outcome data for all 42 births were reported |

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Random numbers used and kept by a clinical trials unit.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Telephone contact for allocation.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Blinding not possible but unlikely to affect outcomes/results. Surgeons were blinded to timing and mode of birth</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Not stated whether outcome assessors were blinded to interventions</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>1 baby excluded from each group for intrauterine death post randomisation but before 36 weeks' gestation and for similar reasons (see Characteristics of included studies).</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>According to trial report, all primary outcomes were reported</td>
</tr>
</tbody>
</table>
Other bias | Low risk | No other obvious sources of bias. However, the trial was not registered
## DATA AND ANALYSES

Comparison 1. Planned preterm birth versus planned later birth

<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 Stillbirth</td>
<td>1</td>
<td>42</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.0 [0.07, 14.95]</td>
</tr>
<tr>
<td>2 Fetal death before discharge</td>
<td>1</td>
<td>40</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>5.0 [0.26, 98.00]</td>
</tr>
<tr>
<td>3 Caesarean section</td>
<td>1</td>
<td>42</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.78 [0.36, 1.70]</td>
</tr>
<tr>
<td>4 Birthweight</td>
<td>1</td>
<td>40</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>26.00 [-247.75, 299.75]</td>
</tr>
<tr>
<td>5 Days of ventilation</td>
<td>1</td>
<td>40</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>0.60 [-0.65, 1.85]</td>
</tr>
<tr>
<td>6 Necrotising enterocolitis</td>
<td>1</td>
<td>40</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.25 [0.03, 2.05]</td>
</tr>
<tr>
<td>7 Non-primary closure (need for repeat surgery)</td>
<td>1</td>
<td>40</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.75 [0.19, 2.93]</td>
</tr>
<tr>
<td>8 Gestational age at birth (non-prespecified outcome)</td>
<td>1</td>
<td>40</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-0.90 [-1.63, -0.17]</td>
</tr>
</tbody>
</table>

### Analysis 1.1. Comparison 1 Planned preterm birth versus planned later birth, Outcome 1 Stillbirth.

**Review:** Elective preterm birth for fetal gastroschisis

**Comparison:** Planned preterm birth versus planned later birth

**Outcome:** Stillbirth

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Planned preterm birth n/N</th>
<th>Planned later birth n/N</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>Logghe 2005</td>
<td>1/21</td>
<td>1/21</td>
<td>1.00 [0.07, 14.95]</td>
<td>100.0%</td>
<td>1.00 [0.07, 14.95]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>21</strong></td>
<td><strong>21</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 1 (Planned preterm birth), 1 (Planned later birth)

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P = 1.0)

Test for subgroup differences: Not applicable
**Analysis 1.2. Comparison 1 Planned preterm birth versus planned later birth, Outcome 2 Fetal death before discharge.**

Review: Elective preterm birth for fetal gastroschisis

Comparison: 1 Planned preterm birth versus planned later birth

Outcome: 2 Fetal death before discharge

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Planned preterm birth</th>
<th>Planned later birth</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>Logghe 2005</td>
<td>2/20</td>
<td>0/20</td>
<td>100.0 %</td>
<td>5.00 [0.26, 98.00 ]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 2 (Planned preterm birth), 0 (Planned later birth)

Heterogeneity: not applicable

Test for overall effect: Z = 1.06 (P = 0.29)

Test for subgroup differences: Not applicable

**Analysis 1.3. Comparison 1 Planned preterm birth versus planned later birth, Outcome 3 Caesarean section.**

Review: Elective preterm birth for fetal gastroschisis

Comparison: 1 Planned preterm birth versus planned later birth

Outcome: 3 Caesarean section

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Planned preterm birth</th>
<th>Planned later birth</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>Logghe 2005</td>
<td>7/21</td>
<td>9/21</td>
<td>100.0 %</td>
<td>0.78 [0.36, 1.70 ]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 7 (Planned preterm birth), 9 (Planned later birth)

Heterogeneity: not applicable

Test for overall effect: Z = 0.63 (P = 0.53)

Test for subgroup differences: Not applicable
Analysis 1.4. Comparison 1 Planned preterm birth versus planned later birth, Outcome 4 Birthweight.

Review: Elective preterm birth for fetal gastroschisis

Comparison: 1 Planned preterm birth versus planned later birth

Outcome: 4 Birthweight

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Planned preterm birth</th>
<th>Planned later birth</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logghe 2005</td>
<td>20 2364 (352)</td>
<td>20 2338 (516)</td>
<td>100.0 % 26.00 [ -247.75, 299.75 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>20</td>
<td>20</td>
<td>100.0 % 26.00 [ -247.75, 299.75 ]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 0.19 (P = 0.85)

Test for subgroup differences: Not applicable
Analysis 1.5. Comparison 1 Planned preterm birth versus planned later birth, Outcome 5 Days of ventilation.

Review: Elective preterm birth for fetal gastroschisis

Comparison: Planned preterm birth versus planned later birth

Outcome: 5 Days of ventilation

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Planned preterm birth</th>
<th>Planned later birth</th>
<th>Mean Difference</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
</tr>
<tr>
<td>Logghe 2005</td>
<td>20</td>
<td>2.9 (2.3)</td>
<td>20</td>
<td>2.3 (1.7)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>20</td>
<td></td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 0.94 (P = 0.35)

Test for subgroup differences: Not applicable

Analysis 1.6. Comparison 1 Planned preterm birth versus planned later birth, Outcome 6 Necrotising enterocolitis.

Review: Elective preterm birth for fetal gastroschisis

Comparison: Planned preterm birth versus planned later birth

Outcome: 6 Necrotising enterocolitis

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Planned preterm birth</th>
<th>Planned later birth</th>
<th>Risk Ratio</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Fixed,95% CI</td>
<td></td>
</tr>
<tr>
<td>Logghe 2005</td>
<td>1/20</td>
<td>4/20</td>
<td>0.25 [ 0.03, 2.05 ]</td>
<td>100.0 %</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>20</td>
<td>20</td>
<td>0.25 [ 0.03, 2.05 ]</td>
<td>100.0 %</td>
</tr>
</tbody>
</table>

Total events: 1 (Planned preterm birth), 4 (Planned later birth)

Heterogeneity: not applicable

Test for overall effect: Z = 1.29 (P = 0.20)

Test for subgroup differences: Not applicable
### Analysis 1.7. Comparison 1 Planned preterm birth versus planned later birth, Outcome 7 Non-primary closure (need for repeat surgery).

**Review:** Elective preterm birth for fetal gastroschisis  
**Comparison:** 1 Planned preterm birth versus planned later birth  
**Outcome:** 7 Non-primary closure (need for repeat surgery)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Planned preterm birth</th>
<th>Planned later birth</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>Logghe 2005</td>
<td>3/20</td>
<td>4/20</td>
<td>0.75 [0.19, 2.93]</td>
<td>100.0%</td>
<td>0.75 [0.19, 2.93]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>20</strong></td>
<td><strong>20</strong></td>
<td>100.0%</td>
<td>0.75 [0.19, 2.93]</td>
<td></td>
</tr>
</tbody>
</table>

- Total events: 3 (Planned preterm birth), 4 (Planned later birth)  
- Heterogeneity: not applicable  
- Test for overall effect: Z = 0.41 (P = 0.68)  
- Test for subgroup differences: Not applicable

### Analysis 1.8. Comparison 1 Planned preterm birth versus planned later birth, Outcome 8 Gestational age at birth (non-prespecified outcome).

**Review:** Elective preterm birth for fetal gastroschisis  
**Comparison:** 1 Planned preterm birth versus planned later birth  
**Outcome:** 8 Gestational age at birth (non-prespecified outcome)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Planned preterm birth</th>
<th>Planned later birth</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Logghe 2005</td>
<td>20 35.8 (0.7)</td>
<td>20 36.7 (1.5)</td>
<td>-0.90 [-1.63, -0.17]</td>
<td>100.0%</td>
<td>-0.90 [-1.63, -0.17]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>20</strong></td>
<td><strong>20</strong></td>
<td>100.0%</td>
<td>-0.90 [-1.63, -0.17]</td>
<td></td>
</tr>
</tbody>
</table>

- Heterogeneity: not applicable  
- Test for overall effect: Z = 2.43 (P = 0.015)  
- Test for subgroup differences: Not applicable
### ADDITIONAL TABLES

Table 1. Additional neonatal outcomes (not specified in protocol)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Elective group (n = 20)</th>
<th>Spontaneous group (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean gestational age at birth (weeks)</td>
<td>35.8 (SD 0.7)</td>
<td>36.7 (SD 1.5)</td>
</tr>
<tr>
<td>Median age at operation (hours)</td>
<td>2 (range 1-5)</td>
<td>2.5 (range 1-4)</td>
</tr>
<tr>
<td>Bowel atresia</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Ventilated</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>Median duration of parenteral nutrition in survivors (days)</td>
<td>22 (range 14-87)</td>
<td>28 (range 12-346)</td>
</tr>
<tr>
<td>Median time to full enteral feeding in survivors (days)</td>
<td>30.5 (range 18-96)</td>
<td>37.5 (range 15-358)</td>
</tr>
<tr>
<td>Median time to hospital discharge in survivors (days)</td>
<td>47.5 (range 23-126)</td>
<td>53 (range 22-399)</td>
</tr>
</tbody>
</table>

SD: standard deviation

Table 2. Additional maternal outcomes (not specified in protocol)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Elective group (n = 21)</th>
<th>Spontaneous group (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>23.3 (SD 6.2)</td>
<td>22 (SD 4.6)</td>
</tr>
<tr>
<td>Gestational age at diagnosis (weeks)</td>
<td>19 (range 14-22)</td>
<td>18 (range 15-21)</td>
</tr>
<tr>
<td>Birth before 36 weeks' gestation</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

SD: standard deviation

### CONTRIBUTIONS OF AUTHORS

Professor Jim Thornton co-ordinated, designed, and is guarantor for the review. He also provided methodological and clinical perspectives. Dr Natalie Grant wrote the protocol and full review. Jon Dorling commented on the protocol and provided a neonatology perspective. The outcomes, as specified in the protocol, were agreed by all three authors.

Dr Natalie Grant and Dr Jon Dorling assessed all potential studies for inclusion in the review and together designed a data extraction form. They independently extracted data using the agreed form. Dr Grant and Professor Thornton made a risk of bias assessment for inclusion in the review.

The final review was approved by all three authors.
DECLARATIONS OF INTEREST

Dr Natalie Grant and Dr Jon Dorling have no known conflicts of interest to declare.

Professor Jim Thornton is co-author of the included trial (Logghe 2005). He was not involved in any decisions relating to the trial, including assessment of the trial for inclusion, assessment of trial quality, data extraction or interpretation of the data.

SOURCES OF SUPPORT

Internal sources
- Nottingham University Hospitals NHS Trust, UK.
  Dr Grant is employed by Nottingham University Hospitals NHS Trust
- University of Nottingham, UK.
  Professor Thornton is employed by the University of Nottingham

External sources
- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Gestational age at birth was not a prespecified outcome in the original protocol for the review however, the review authors agreed that this was an important outcome to consider and gestational age at birth has therefore been included in the Data and analyses and in the Discussion.

INDEX TERMS

Medical Subject Headings (MeSH)
*Cesarean Section; *Fetal Diseases; *Gastrochisis; *Labor, Induced; Gestational Age; Pregnancy Outcome; Randomized Controlled Trials as Topic

MeSH check words
Female; Humans; Pregnancy