Indications for induction of labour: a best-evidence review

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Background Rates of labour induction are increasing.

Objectives To review the evidence supporting indications for induction.

Search strategy We listed indications for labour induction and then reviewed the evidence. We searched MEDLINE and the Cochrane Library between 1980 and April 2008 using several terms and combinations, including induction of labour, premature rupture of membranes, post-term pregnancy, preterm prelabour rupture of membranes (PROM), multiple gestation, suspected macrosomia, diabetes, gestational diabetes mellitus, cardiac disease, fetal anomalies, systemic lupus erythematosis, oligohydramnios, alloimmunization, rhesus disease, intrahepatic cholestasis of pregnancy (IHCP), and intrauterine growth restriction (IUGR). We performed a review of the literature supporting each indication.

Selection criteria We identified 1387 abstracts and reviewed 418 full text articles. We preferentially included high-quality systematic reviews or large randomised trials. Where no such studies existed, we included the best evidence available from smaller randomised trials and observational studies.

Main results We included 34 full text articles. For each indication, we assigned levels of evidence and grades of recommendation based upon the GRADE system. Recommendations for induction of labour for post-term gestation, PROM at term, and premature rupture of membranes near term with pulmonary maturity are supported by the evidence. Induction for IUGR before term reduces intrauterine fetal death, but increases caesarean deliveries and neonatal deaths. Evidence is insufficient to support induction for women with insulin-requiring diabetes, twin gestation, fetal macrosomia, oligohydramnios, cholestasis of pregnancy, maternal cardiac disease and fetal gastroschisis.

Authors’ conclusions Research is needed to determine risks and benefits of induction for many commonly advocated clinical indications.

Keywords Best evidence, indications, induction.

Introduction Since the 1980s, rates of induction of labour have steadily increased. Induction currently occurs for almost 24% of infants born between 37 and 41 weeks of gestation in the USA.1 Rates of induction have also increased for preterm gestations.1 In a large United States survey involving 1573 women with singleton gestations, 41% of respondents reported undergoing attempted medical induction of labour.2

Induction may be advocated to reduce fetal or neonatal morbidity and mortality as with post-term pregnancy, oligohydramnios, suspected intrauterine growth restriction (IUGR) and fetal gastroschisis, to minimise maternal morbidity, as with maternal cardiac disease and pre-eclampsia/ eclampsia, or to benefit both mother and fetus as with pre-

Methods

We compiled a list of indications for induction. We comprehensively searched the English language literature using MEDLINE and the following databases: Cochrane Database of Systematic Reviews, ACP Journal Club, Database of Abstracts of Reviews of Effects, Cochrane Controlled Trials Register, Cochrane Methodology Register, NHS National Institute for Health Research Health Technology Assessment database, and the NHS Economic Evaluation Database. The search covered the period from January 1980 to April 2008.

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We used combinations of the following search terms: ‘induction of labor’, ‘indications’, ‘preterm premature rupture of membranes’, ‘premature rupture of membranes’, ‘post-term pregnancy’, ‘fetal macrosomia’, ‘gestational diabetes’ or ‘diabetes’, ‘oligohydramnios’, ‘ante partum testing’, ‘nonstress test’ or ‘biophysical profile’, ‘intrauterine growth restriction/retardation (IUGR)’, ‘small for gestational age’, ‘pregancy-induced hypertension’ or ‘preclampsia’, ‘multiple or twin gestation’, ‘cardiac disease’ or ‘heart disease’, ‘gastroschisis’, ‘fetal malformations’, ‘heart defects’ or ‘congenital anomalies’, ‘alloimmunization’ or ‘Rh disease’. We included studies that explored indications for induction of labour compared with expectant management or immediate delivery by caesarean section. We excluded trials comparing different methods of induction of labour or evaluating elective induction of labour. Titles and abstracts were reviewed for possible exclusion by two reviewers (E.M. and J.C.). If both reviewers excluded a citation, we eliminated that publication from further review. If at least one reviewer included the citation or if there was insufficient information to make a determination from the title and abstract, we obtained the full article for review. Most of the abstracts were excluded because they were not on topic, compared different methods of induction, or were commentaries, letters, or opinions. We also cross-checked the reference lists of all related systematic reviews for possible additional studies.

All full text articles were independently reviewed by two authors (E.M. and J.C.) for suitability for inclusion. We followed the inclusion process outlined by the British Medical Journal Clinical Evidence for performance of a ‘best evidence’ systematic review in the following manner: for each indication for induction, we included systematic reviews identified by our search, together with randomised controlled trials (RCTs) published after the date of the systematic reviews’ search dates. We also sought any additional appropriate RCTs that had not been included in the systematic reviews. For indications for which no systematic reviews existed, we included the best available evidence, including RCTs, non-randomised controlled clinical trials, cohort studies, case–control studies, and case series in a hierarchical manner. For some indications, published studies compared expectant management with expedited delivery either by induction or caesarean section. In these cases, we included studies comparing expedited delivery to expectant management.

To be included in this review, studies had to report on one or more of the following outcomes of interest: mode of delivery, maternal morbidity, and fetal or neonatal morbidity and mortality. Maternal morbidity was defined as chorioamnionitis, endometritis, transfusion, severe perineal trauma or prolonged hospitalisation. Neonatal morbidity was defined as neonatal intensive care unit (NICU) admission, 5-minute Apgar score <7, respiratory distress syndrome (RDS), shoulder dystocia, birth injury, meningitis, pneumonia, hypoxic–ischaemic encephalopathy, meconium aspiration syndrome, or sepsis.

Individual study quality ratings were assigned to each included study and systematic review by two independent reviewers (E.M. and J.C.) according to the quality rating system of the Scottish Intercollegiate Guidelines Network. Differences in quality score assignments were resolved by consensus. When our review found that induction of labour resulted in statistical improvement in one of the outcomes of interest, we calculated the number needed to treat (NNT) or harm (NNH). This is the number of women who would need to undergo induction of labour to result in one fewer or additional case of the designated outcome. For each putative indication for induction, the overall strength of scientific evidence supporting this practice was assigned. In evaluating the strength of the evidence for each indication for induction, we adhered to the GRADE system that classifies the overall quality of evidence as high, moderate, low, and very low. Recommendations resulting from this evidence base are classified as strong or weak based upon the strength of evidence and the balance of benefits and harms of a treatment.

To assign a grade of recommendation for each indication, we assigned one of four categories: ‘net benefits’, in which labour induction clearly does more good than harm, ‘trade-offs’, in which there are important trade-offs between the benefits and harms, ‘uncertain trade-offs’ in which it is not clear whether labour induction does more good or harm, and ‘net harm’ in which induction clearly does more harm than good. We classified a recommendation as ‘strong’ if the quality of evidence was high and the evidence showed net benefit for induction of labour. We classified a recommendation as ‘weak’ if the level of the evidence was high but there were important trade-offs between benefits and harms, or if the trade-offs were uncertain or the evidence showed no net benefit for induction. We also classified the recommendation as ‘weak’ if the level of evidence was moderate, low or very low. If no evidence existed regarding labour induction in a particular clinical circumstance, we made no recommendation.

Results

We reviewed 1387 abstracts from electronic database and bibliographic searches. We retrieved 418 full text articles that were reviewed by the two reviewers. Based on the review strategy and inclusion criteria outlined above, 34 studies were included in this review. Included studies are listed in Table 1. The flow of the citations, abstracts and full text articles through the review process is outlined in Figure 1. No studies evaluating induction of labour compared with expectant management for women with maternal systemic lupus erythematosus, red cell alloimmunisation, or non-reassuring or suspicious ante partum fetal testing were identified. The
evidence concerning induction of labour in all other circumstances of interest is summarised below.

### Post-term pregnancy

Our search strategy identified two systematic reviews that combined studies in which women were randomly assigned to induction of labour by a variety of methods including membrane stripping, amniotomy, prostaglandin E₂ (PGE₂) gel, misoprostol, laminaria, Foley catheter and extra-amniotic saline infusion or to expectant management. Expectant management was usually defined as antenatal testing (biochemical tests or fetal heart rate monitoring and amniotic fluid assessment) sometimes followed by induction of labour at 42, 43 or 44 weeks. Both systematic reviews support routine induction of labour after 41 or 42 completed weeks of gestation, but differ in their main findings. For the primary outcome of perinatal death, the Cochrane systematic review authored by Gulmezoglu included 12 trials with 5939 subjects, conducted between 1969 and 2005, comparing induction of labour with serial antenatal monitoring at or beyond 41 completed weeks of gestation (287 days). Of these, there were 10 trials in which women were randomised at 41 weeks of gestation and two trials in which women were randomised at 42 weeks of gestation. The combined analysis of data from these 12 trials found one fetal or neonatal death in 2986 pregnancies allocated to induction of labour versus 9 fetal or neonatal deaths among 2953 pregnancies allocated to expectant management (relative risk 0.30, 95% CI: 0.09–0.99, NNT = 369). The authors combined six studies including 1713 participants (four involving randomisation at 41 weeks and two involving randomisation at 42 weeks) that reported the incidence of meconium aspiration syndrome in the newborn. Induction of labour was associated with fewer cases of meconium aspiration syndrome than expectant...
management (12 of 860 [1.4%] versus 31 of 853 [3.6%]), although this comparison was statistically significant only in the 41-week subgroup (relative risk 0.29, 95% CI: 0.12–0.68, NNT = 41). The authors found no difference in caesarean deliveries in 10 trials randomising women at 41 completed weeks of gestation (559 of 2883 [19.4%] versus 630 of 2872 [21.9%]) and five trials randomising women at 42 completed weeks of gestation (110 of 407 [27.3%] versus 111 of 403 [27.5%]).

The Sanchez-Ramos9 review included 16 studies with 6588 subjects who were randomised to undergo either induction of labour or expectant management at or beyond 41 completed weeks’ of gestation. These studies were published between 1969 and 2002, and 12 of these studies were also included in the Cochrane review. There were fewer perinatal deaths among pregnancies allocated to induction of labour (3 of 3159 versus 10 of 3067) although this difference did not reach statistical significance (OR 0.41, 95% CI: 0.14–1.18). Sanchez-Ramos also found that a policy of routine induction of labour resulted in fewer caesarean deliveries than serial antenatal monitoring (661 of 3292 [20.1%] versus 709 of 3216 [22.0%], NNT = 51). In particular, induction of labour was associated with fewer caesarean deliveries for non-reassuring fetal heart rate tracings (143 of 2295 [6.2%] versus 183 of 2301 [8.0%], NNT = 58). Although Gulmezoglu found no difference in caesarean deliveries and Sanchez-Ramos reported a reduction, neither review found that induction of labour increased caesarean deliveries, even in the subgroup of women with unfavourable cervices.

We identified one RCT published after the systematic reviews’ search dates. This study, performed in Norway between 2002 and 2004, randomly assigned 508 women with singleton gestations at 41 weeks of gestation (289 days) to labour induction using combinations of amniotomy, oxytocin, PGE2 or misoprostol or to serial fetal surveillance until the onset of spontaneous labour, abnormal antenatal assessment or 300 days of gestation.11 This study found no differences in fetal or neonatal morbidity or in mode of delivery between groups. The authors conducted phone interviews of study participants 6 months after delivery12 and found that 74% of participants preferred induction at 41 weeks over serial antenatal monitoring. Seventy-four percent of women randomised to induction said they would prefer the same management in future pregnancies compared with 38% of women randomly assigned to serial antenatal monitoring.12

Summary
Induction of labour for gestations at or beyond 41 weeks (287 days) may reduce perinatal mortality and meconium aspiration syndrome and does not result in more caesarean deliveries than serial antenatal monitoring, even among women whose cervix is not favourable for induction. Quality of evidence: High, grade of recommendation for induction of labour beyond 41 completed weeks: strong.

PROM at term
Our search identified three systematic reviews of studies evaluating management of PROM at term.13–15 The systematic reviews by Mozurkewich and Wolf13 and by Dare et al.15 compared expedited induction of labour (via oxytocin, PGE2 or caulophyllum) with conservative management. Expedited induction was defined as commencing between 2 and 12 hours after rupture of membranes.13,15 Conservative or expectant management was usually defined as observation from 24 hours to 4 days after rupture of membranes followed by induction if spontaneous labour did not result.13,15 Mozurkewich and Wolf included 23 trials with 7493 participants, while Dare et al. included 12 trials with 6814 participants. Of these, seven studies were included in both reviews. Neither systematic review found any difference in rates of caesarean delivery or neonatal infections.

While Mozurkewich and Wolf analysed outcomes separately by method of labour induction, Dare et al. computed outcomes of induction of labour by any method compared
with expectant management. In this ‘all methods’ analysis, Dare et al.\textsuperscript{15} found that a policy of expedited labour inductions reduced admissions to the NICU from about 17.0 to 12.6\% (six studies, 5679 participants, relative risk 0.73, 95\% CI: 0.58–0.91, NNT = 23). Both systematic reviews found reduced incidence of chorioamnionitis and endometritis with expedited induction of labour compared with expectant management. For the effect of induction of labour by any method on chorioamnionitis, Dare\textsuperscript{et al.}\textsuperscript{14} combined 10 studies including 6611 women. Induction of labour reduced chorioamnionitis from 9.9 to 6.8\% (relative risk 0.74, 95\% CI: 0.56–0.97, NNT = 33). For the outcome of expedited induction of labour by any method on endometritis, Dare\textsuperscript{et al.}\textsuperscript{14} combined four studies including 445 subjects. This comparison found that induction of labour reduced postpartum endometritis from 8.3 to 2.3\% (relative risk 0.30, 95\% CI: 0.10–0.95, NNT = 17). Dare\textsuperscript{et al.} reported increased maternal satisfaction with induction of labour compared with expectant management, although this finding was based on a single large trial.\textsuperscript{43} The findings of these two reviews were heavily influenced by the results of the large multicentre TermPROM study by Hannah\textsuperscript{et al.}\textsuperscript{43}

The systematic review by Lin\textsuperscript{et al.}\textsuperscript{14} addressed a different clinical question: the role of induction of labour with misoprostol for prelabour premature rupture of membranes at term. The authors combined six small trials including a total of 451 participants comparing induction of labour with misoprostol with expectant management or placebo. In this analysis, use of misoprostol significantly increased the likelihood of vaginal delivery at less than 12 hours, but not less than 24 hours, compared with women who were allocated to placebo or expectant management. Misoprostol also significantly increased uterine tachysystole, but not hyperstimulation syndrome, compared with expectant management or placebo. No differences in mode of delivery, caesarean delivery for fetal distress, chorioamnionitis, neonatal sepsis or NICU admissions were found.

Our search identified two small RCTs comparing induction with misoprostol with expectant management that were published after the systematic reviews’ search dates.\textsuperscript{16,17} The primary outcome for the da Graca Krupa\textsuperscript{16} study, which randomised 150 participants to vaginal misoprostol or placebo, was time to delivery. The authors demonstrated a significantly shorter time from recruitment to delivery with misoprostol compared with expectant management. Vaginal misoprostol use resulted in significantly fewer caesarean deliveries than expectant management (20 versus 30.7\%), but also resulted in more uterine contractile abnormalities. No other significant differences were observed. With the exception of the finding on mode of delivery, the results were in agreement with the published meta-analysis by Lin\textsuperscript{et al.}\textsuperscript{14}

The other recent trial of misoprostol for PROM at term randomised 130 women with PROM and unfavourable cervices to oral misoprostol or placebo, followed by oxytocin if the woman was not in labour by 12 hours after rupture of membranes.\textsuperscript{17} Oral misoprostol resulted in a significantly shorter time to delivery and reduced need for oxytocin; there was no difference in other outcomes of interest.

Summary

Expedited induction of labour after PROM reduces chorioamnionitis, endometritis, and admissions to a neonatal

<table>
<thead>
<tr>
<th>Indication</th>
<th>Quality of evidence</th>
<th>Benefits/harm</th>
<th>Grade of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-term pregnancy</td>
<td>High</td>
<td>Net benefits</td>
<td>Strong</td>
</tr>
<tr>
<td>PROM</td>
<td>High</td>
<td>Net benefits</td>
<td>Strong</td>
</tr>
<tr>
<td>PPROM</td>
<td>Moderate</td>
<td>Uncertain trade-offs</td>
<td>Weak</td>
</tr>
<tr>
<td>Macrosomia</td>
<td>Moderate</td>
<td>Net harm</td>
<td>Weak (against induction)</td>
</tr>
<tr>
<td>Twin gestation</td>
<td>Low</td>
<td>Uncertain trade-offs</td>
<td>Weak</td>
</tr>
<tr>
<td>Oligohydramnios</td>
<td>Low</td>
<td>Uncertain trade-offs</td>
<td>Weak</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Moderate</td>
<td>Uncertain trade-offs</td>
<td>Weak</td>
</tr>
<tr>
<td>Cholestasis</td>
<td>Very low</td>
<td>Uncertain trade-offs</td>
<td>Weak</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>Very low</td>
<td>Uncertain trade-offs</td>
<td>Weak</td>
</tr>
<tr>
<td>Mild pre-eclampsia (preterm) induction versus expectant</td>
<td>No evidence</td>
<td>—</td>
<td>No recommendation</td>
</tr>
<tr>
<td>Severe pre-eclampsia (preterm) induction versus caesarean section</td>
<td>Moderate</td>
<td>Uncertain trade-offs</td>
<td>Weak (against induction)</td>
</tr>
<tr>
<td>Eclampsia (induction versus caesarean section)</td>
<td>Very low</td>
<td>Uncertain trade-offs</td>
<td>Weak</td>
</tr>
<tr>
<td>IUGR/SGA (preterm)</td>
<td>Low</td>
<td>Uncertain trade-offs</td>
<td>Weak</td>
</tr>
<tr>
<td>IUGR/SGA (term)</td>
<td>High</td>
<td>Trade-offs</td>
<td>Weak</td>
</tr>
<tr>
<td>Gastroschisis</td>
<td>Low</td>
<td>Uncertain trade-offs</td>
<td>Weak</td>
</tr>
</tbody>
</table>

SGA, small for gestational age.

### Preterm prelabour rupture of membranes

Our search identified one systematic review comparing intentional delivery by immediate induction of labour with expectant management in women with preterm prelabour rupture of membranes (PPROM) between 30 and 36 weeks of gestation.\(^4\) This systematic review combined four small RCTs with a total of 389 participants.\(^4\) Two of the included studies required demonstration of fetal lung maturity for entry.\(^4\) Antibiotics and steroids were not given in any of the included trials, so expectant care in these trials may not have been comparable with expectant care as it is currently practiced.

In their analysis, the authors found that immediate induction significantly reduced chorioamnionitis (9 of 190 versus 41 of 199, risk difference -0.16, 95% CI -0.23 to -0.10, NNT = 6).\(^4\) In addition, maternal length of stay was significantly shortened by immediate induction of labour (from 4.5 to 2.5 days, weighted mean difference 1.39, 95% CI: -2.03, -0.75). There was no difference in any neonatal outcome of interest including perinatal death, confirmed-onset neonatal sepsis, RDS, intraventricular haemorrhage, necrotising enterocolitis or neonatal length of stay.

In summary, no definitive study establishing the optimal timing of delivery after PPROM has been carried out. The gestational age at which induction of labour should be carried out in the absence of demonstrated pulmonary maturity has not been established. A multicentre RCT is continuing to further elucidate timing of delivery and risks and benefits of induction.\(^4\)

### Summary

In women with PPROM, induction of labour reduces the incidence of chorioamnionitis. Subjects in available trials may not be representative of current patients with PPROM, as they did not receive glucocorticoids or antibiotics. The optimal gestational age for induction of labour is not established. Quality of evidence: moderate, grade of recommendation for labour induction: weak.

### Suspected macrosomia

Our search identified two systematic reviews addressing induction for suspected macrosomia.\(^19\) The review by Irion and Boulvain\(^20\) included only two small RCTs involving 313 women. The review by Sanchez-Ramos et al.\(^19\) included these two RCTs as well as nine observational studies including 3751 subjects in total. Observational and RCTs were analysed separately. Despite these methodological differences, the Irion and Sanchez-Ramos analyses agreed in their main result, finding no difference in caesarean deliveries or shoulder dystocia. Sanchez-Ramos’ analysis of non-randomised studies suggested that the risk for caesarean delivery may be increased when induction of labour is undertaken for presumed macrosomia (149 of 898 [16.6%] versus 214 of 2540 [8.4%], NNH = 12), a finding not confirmed in the small RCTs.\(^19\) Larger randomised studies are underway to further elucidate this question.

### Summary

1. Induction of labour does not improve outcomes in the setting of suspected fetal macrosomia. Quality of evidence: moderate, grade of recommendation against induction of labour: weak.
2. Induction of labour may increase caesarean deliveries. Level of evidence: low, grade of recommendation against induction of labour: weak.

### Twin pregnancy

We identified one systematic review addressing the question of whether fetal morbidity and mortality of twin gestations are reduced by induction. This Cochrane review included a single RCT allocating 36 twin pregnancies to induction at 37 weeks of gestation or expectant management.\(^49\) The reviewers found this study severely underpowered to detect improvements in perinatal morbidity or mortality with induction. The review found no differences in birthweight, route of delivery, or maternal or neonatal outcome. The authors conclude that there is currently insufficient data to support elective delivery of otherwise uncomplicated twin pregnancies after 37 weeks of gestation.\(^21\) Definitive recommendations for timing of delivery for twin gestations should await completion of large, adequately powered RCTs now underway.\(^21\)

### Summary

The only RCT of induction of labour for twin gestations at 37 weeks is not appropriately powered to determine the benefits and harms of induction. Quality of evidence for induction of labour: low, grade of recommendation: weak.

### Oligohydramnios

We identified one randomised pilot study of induction of labour for isolated oligohydramnios.\(^22\) In this study, the investigators randomised 54 women with oligohydramnios and pregnancies at 41 weeks of gestation (288 days) to induction of labour or expectant management until 42 weeks. Women with suspected IUGR, abnormal fetal cardiotocography or abnormal umbilical artery Doppler studies were excluded. The investigators found no difference in any of their outcomes of interest including birthweight, mode of delivery, umbilical blood pH, Apgar scores or admission to neonatal intensive care. However, this study was underpowered to detect any potential benefits of induction for oligohydramnios and did not study induction for isolated...
oligohydramnios at other gestational ages. There is currently insufficient evidence to recommend routine induction of labour for oligohydramnios.

Summary
Induction of labour for oligohydramnios at term is advocated by expert opinion to reduce perinatal morbidity and mortality, but the only RCT available is not appropriately powered to test this potential benefit. Quality of evidence: low, grade of recommendation: weak.

Diabetes mellitus requiring insulin
We identified one systematic review, which included one RCT that assigned 200 women with insulin-requiring gestational diabetes mellitus or pre-existing type II diabetes to either induction at 38 weeks of gestation or expectant care. This study found no difference in the rate of caesarean delivery between these approaches but found that fetal macrosomia, defined as birthweight >4000 g was significantly reduced by induction of labour (relative risk 0.56, 95% CI: 0.32–0.98, NNT = 8). The birthweight of 23% of the babies born to expectantly managed women was at or above the 90th percentile compared with 10% of the babies born to induced women. There were more cases of shoulder dystocia in the expectantly managed group, but this difference was not statistically significant. There were no differences in other fetal or maternal morbidities. Further research is needed to confirm this finding and evaluate fetal, neonatal, and maternal morbidity.

Summary

Intrahepatic cholestasis of pregnancy
We identified one case–control study and one case series concerning induction of labour at 38 weeks of gestation in IHCP are improved by induction. In a small case–control study, Rioseco et al. compared perinatal outcomes (mortality, abnormal fetal heart rate tracings, Apgar score <7 at 1 and 5 minutes, and small for gestational age) among 320 cases who were actively managed with antenatal testing and induction of labour at 38 weeks with 320 control women who delivered at the same institution and who did not have intrahepatic cholestasis of pregnancy (IHCP). Because no difference in outcomes was demonstrated between the case and control groups, the authors concluded that induction of labour was beneficial. Roncaglia et al., followed 206 women with cholestasis of pregnancy. In this case series, 56 women had spontaneous or indicated preterm delivery. Of the remainder, 146 of 150 women underwent induction of labour at 37 weeks of gestation or at the time of diagnosis. The authors found rates of intrauterine fetal demise in this series of actively managed women to be significantly lower than historic controls in the published literature (0 of 218 versus 14 of 888, NNT = 63). Based on these data, the authors recommend induction of labour.

Summary
One cohort study of women with IHCP suggests that induction of labour may reduce intrauterine fetal death compared with expectantly managed historic controls, but this finding should be confirmed by properly conducted prospective cohort studies and RCTs. Quality of evidence: very low, grade of recommendation: weak.

Maternal cardiac disease
We identified one cohort study and two case series concerning induction of labour for severe maternal cardiac disease. The two case series studies were carried out in developing world settings and lacked control groups. Although they aimed to demonstrate safety of the induction methods employed (PGE2 or oxytocin), these studies included very small numbers of subjects (37 and 21 respectively) and no major conclusions regarding potential beneficial or harmful effects can be drawn. The third study was a prospective cohort study comparing 47 women with cardiac disease who underwent induction of labour with 74 women with cardiac disease who were managed expectantly. The induction and control groups were not well matched. The women who were induced had more severe cardiac disease than those in the expectant management group. There were significantly more caesarean deliveries performed in the expectant management group than in the labour induction group, but this difference may have been accounted for by the increased number of women with prior caesarean sections in the expectant management group. No other differences in maternal or neonatal outcome were found.

Summary
No harmful or beneficial effects have been demonstrated for induction of labour for maternal cardiac disease. Quality of evidence: very low, grade of recommendation: weak.

Hypertension/pre-eclampsia/eclampsia
Our search did not identify any studies comparing induction of labour with expectant management for mild pre-eclampsia or pregnancy-induced hypertension, although one multicentre RCT of induction of labour versus conservative management for mild pre-eclampsia or pregnancy-induced hypertension at term is continuing. We identified two RCTs comparing induction of labour (or expedited delivery) with expectant management (or delayed delivery) in the setting of severe pre-eclampsia remote from term. The Odendaal study randomly assigned 38 women with severe pre-eclampsia...
between 28 and 34 weeks to immediate induction of labour or caesarean section or to expectant management until 34 weeks of gestation. In women assigned to expectant care, delivery before 34 weeks was carried out for worsening pre-eclampsia, development of haemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome, or signs of fetal compromise.29 Pregnancies assigned to expectant care were prolonged by about 7 days on average, and significantly fewer neonates born to mothers assigned to expectant care required assisted ventilation (2 of 18 versus 7 of 20) or had one or more neonatal complications (6 of 18 versus 15 of 20).29

The Sibai study included 95 women with severe pre-eclampsia between 28 and 32 weeks of gestation who were randomly assigned to expedited delivery, whether by induction or caesarean section, or expectant care.30 This study found that expectant management prolonged pregnancy by an average of 15.4 days, increased birthweight, and reduced neonatal morbidity as measured by NICU admissions and days of NICU care required. A comparison of delivery by induction of labour versus caesarean section was not performed. Of note, pregnancies with any sign of fetal compromise, multifetal gestations, underlying medical disease, or with HELLP syndrome or low platelets (<100,000) were excluded from study.

In addition, our search identified seven case series comparing induction of labour with caesarean section for severe pre-eclampsia remote from term.31–37 These studies in aggregate address the question of failed inductions at various gestational ages and the question of whether a trial of labour is harmful to the fetus compared with elective caesarean section. Most authors found that induction of labour led to caesarean delivery in a majority of instances in which it was attempted at gestational ages less than 30–34 weeks.31,32,35–37 Most of these series found no evidence of maternal, fetal or neonatal harms when induction of labour was carried out,31–33,36 and two authors found exposure to labour to be beneficial in reducing neonatal pulmonary morbidity.33,36 By contrast, in a small series from a developing world setting, elective caesarean section appeared to be associated with reduced fetal or neonatal mortality.34

We found one small pilot study that randomised 50 nulliparous patients with eclampsia and unfavourable cervical status to caesarean section or induction of labour with misoprostol.38 This study, carried out in a developing world setting, found decreased maternal length of stay and ‘maternal complications’ with induction of labour compared with caesarean section, but was underpowered to detect differences in most neonatal outcomes.

Summary

1. Induction of labour for mild pre-eclampsia at term: No studies comparing benefits and harms exist. Quality of evidence: no evidence, grade of recommendation: no recommendation.

2. Expectant management for severe pre-eclampsia remote from term increases birthweight and reduces neonatal morbidity. Quality of evidence: moderate, grade of recommendation: weak.

3. Induction of labour versus caesarean delivery with severe pre-eclampsia remote from term: induction of labour is associated with high rates of intrapartum caesarean section but no increased harm when compared with elective caesarean section. Quality of evidence: very low, Grade of recommendation: weak.


Suspected IUGR

Our search identified two RCTs of early delivery for IUGR. The Growth Restriction Intervention Trial is a multicentre RCT that allocated 548 women with 588 fetuses between 24 and 36 weeks with suspected fetal compromise (abnormal umbilical artery Doppler studies) to immediate delivery (whether by induction of labour or caesarean section) or expectant management until the obstetrician was no longer uncertain about the need for delivery.39 Expectant management resulted in a 4-day average prolongation of pregnancy compared with immediate induction in this study. There were more stillbirths in the delayed intervention group, but these were balanced by an increase in neonatal deaths in the early intervention group. Overall, there was no difference in perinatal mortality, but immediate induction increased the number of labours resulting in caesarean delivery. Two-year follow-up studies of infant development were conducted on 98% of surviving randomised participants. There was no overall difference in severe disability between the groups. However, in the subgroup of pregnancies randomised before 31 weeks of gestation, there were more children with severe disability in the immediate delivery group compared with the delayed delivery group (14 of 107 [13%] versus 5 of 83 [5%]).40

The Disproportionate Intrauterine Growth Intervention Trial at Term study was a small pilot RCT comparing labour induction with expectant management for suspected fetal growth restriction at term.41 This study randomised 33 women with suspected IUGR (fetal abdominal circumference at <10th percentile) to immediate induction or expectant management. The study was not appropriately powered to assess differences in mode of delivery or perinatal morbidity or mortality. Expectant management resulted in pregnancy prolongation by 14.9 days on average. No advantage of labour induction was documented other than reduced need for antenatal surveillance. The investigators are currently undertaking a large multicentre RCT to determine whether induction of labour may reduce perinatal mortality.52
Summary

1 In preterm pregnancies with suspected IUGR, induction of labour does not reduce perinatal deaths or overall long-term disability. Caesarean delivery is less likely with expectant management. Quality of evidence: high, grade of recommendation: weak.

2 The currently available RCT of induction of labour for suspected IUGR at term lacked statistical power to demonstrate any benefit or harm for induction of labour. Quality of evidence: low, grade of recommendation: weak.

Gastroschisis

We identified one RCT of elective preterm delivery of the fetus with gastroschisis. This study included 42 women with prenatally diagnosed gastroschisis who were randomly assigned to induction of labour at 36 weeks of gestation or expectant management until spontaneous onset of labour.42 The primary outcomes of the study were time to full enteral feeding and length of neonatal hospital stay. Both induced and spontaneous labours were associated with high rates of caesarean delivery (39%), primarily for fetal distress. There were trends towards a shorter time to full enteral feeds (30.5 versus 37.5 days) and towards shorter neonatal hospital stay (47.5 days versus 53 days) in the induction group, although these differences were not statistically significant. This study did not have statistical power to detect differences in intrauterine or neonatal deaths. Thus, this study did not demonstrate a definitive benefit for elective induction at 36 weeks of gestation.

Summary

There is no demonstraned benefit or harm for induction of labour at 36 weeks of gestation for fetal gastroschisis, but the only available trial was underpowered to detect most outcomes. Quality of evidence: low, grade of recommendation: weak. For all indications, the quality of evidence and grades of recommendation are summarized in Table 2.

Discussion

Our best evidence review of the literature suggests that induction of labour in the clinical settings of post-term pregnancy may reduce meconium aspiration syndrome and perinatal deaths. However, the absolute risk of perinatal death with expectant management is quite small. Although induction of labour at 41 weeks of gestation has been criticised because a very large number of labour inductions are required to prevent one perinatal death,53 our number needed to treat estimate for induction (NNT = 369) compares favourably with intrapartum prophylaxis for group B streptococcus (GBS)-positive women (NNT = 1191) and universal screening for GBS (NNT = 5704), interventions routinely recommended in the USA, Canada, and Australia.54 Caesarean deliveries are not increased by a policy of induction of labour at or beyond 41 weeks of gestation.

Induction of labour for premature rupture of membranes at term reduces chorioamnionitis, endometritis, and NICU admissions without increasing caesarean deliveries. However, no difference in neonatal infectious morbidity has been demonstrated. Limited evidence suggests that induction of labour may reduce chorioamnionitis without worsening neonatal morbidity in the setting of preterm PPROM at 30–36 weeks of gestation, particularly if fetal pulmonary maturity has been established.

We also found high-quality evidence suggesting that rates of intrauterine fetal demise may be reduced by induction of labour in the setting of IUGR before term, but these intrauterine deaths may be offset by neonatal deaths such that overall perinatal mortality is not reduced.

Evidence supporting induction of labour for insulin-requiring diabetes mellitus, oligohydramnios, and twin gestations is inconclusive, because existing RCTs lack sufficient statistical power to evaluate important maternal and neonatal outcomes. There is currently not enough high-quality evidence to recommend routine induction of labour in these settings. Likewise, no beneficial effects of induction for suspected macrosomia have been found.

The literature supports expectant management (delayed induction) in carefully selected mothers with severe pre-eclampsia as this may result in improved neonatal outcomes. Induction of labour for severe pre-eclampsia remote from term may be associated with high rates of caesarean delivery.

Our review may have been limited by restricting our search to the English-language literature and by publication bias. We found that further research is necessary to identify potential risks and benefits of induction of labour in the setting of insulin-requiring diabetes mellitus, oligohydramnios, twin gestation, gastroschisis, maternal cardiac disease, and IUGR at term. Further research to determine optimal timing of delivery in the setting of PPROM is also needed.

Conclusion

Women facing a decision about induction should have the best available evidence to help them make an informed choice about the risks and benefits of the procedure. Clinicians should use the best available evidence to support decision-making and need to acknowledge when insufficient evidence is available to definitively guide care. A number of common indications for induction of labour do not have a strong evidence base from which to guide practice. Researchers and funding agencies should prioritise studies that can help to definitively guide care in these situations.

Disclosure of interests

None.
Contribution to authorship
E.M., J.C. and E.K. performed the literature searches required for this review. E.M. and J.C. reviewed all abstracts and full text articles, performed all assessments of study quality, and wrote and edited the manuscript. K.K. and V.I.K. participated in the formulation of the methods of this review and assisted in the writing and editing of the manuscript and the assignment of evidence grades.

Details of ethics approval
This is a best evidence review of previously published data and as such does not require ethics approval.

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