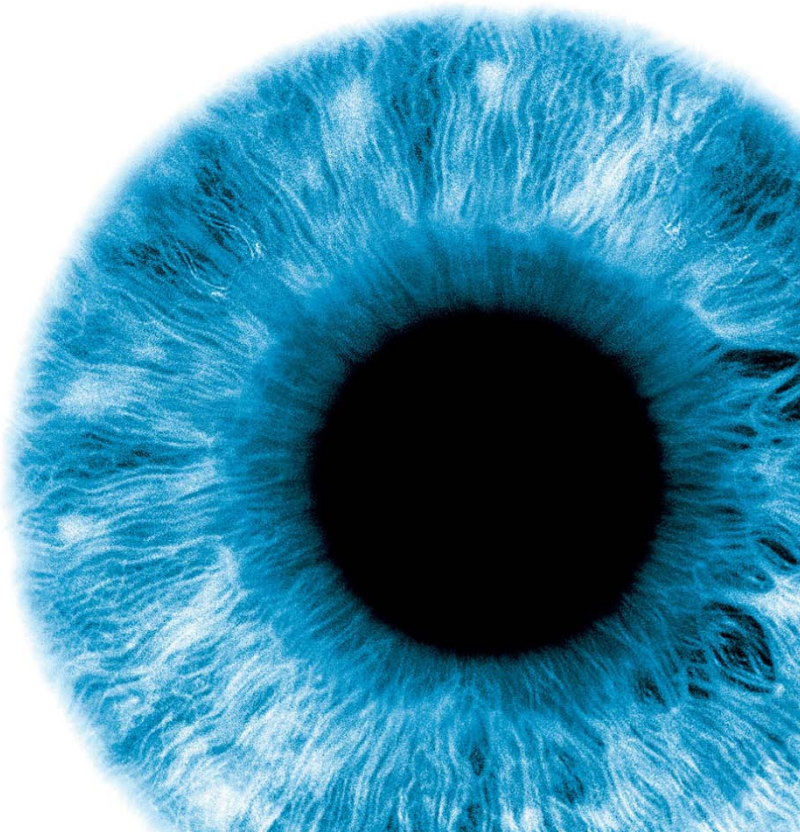
NICE National Institute for Health and Care Excellence

Induction of labour

Evidence Update July 2013

A summary of selected new evidence relevant to NICE clinical guideline 70 'Induction of labour' (2008)

Evidence Update 44



Evidence Updates provide a summary of selected new evidence published since the literature search was last conducted for the accredited guidance they relate to. They reduce the need for individuals, managers and commissioners to search for new evidence. Evidence Updates highlight key points from the new evidence and provide a commentary describing its strengths and weaknesses. They also indicate whether the new evidence may have a potential impact on current guidance. For contextual information, this Evidence Update should be read in conjunction with the relevant clinical guideline, available from the NICE Evidence Services topic page for induction of labour.

Evidence Updates do not replace current accredited guidance and do not provide formal practice recommendations.

NICE Evidence Services are a suite of services that provide online access to high quality, authoritative evidence and best practice.

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Introduction

This Evidence Update identifies new evidence that is relevant to, and may have a potential impact on, the following reference guidance:

[1] **Induction of labour. NICE clinical guideline 70 (2008).**

A search was conducted for new evidence from 17 June 2011 to 15 February 2013. A total of 741 pieces of evidence were initially identified. Following removal of duplicates and a series of automated and manual sifts, 10 items were selected for the Evidence Update (see Appendix A for details of the evidence search and selection process). An Evidence Update Advisory Group, comprising topic experts, reviewed the prioritised evidence and provided a commentary.

Although the process of updating NICE guidance is distinct from the process of an Evidence Update, the relevant NICE guidance development centres have been made aware of the new evidence, which will be considered when guidance is reviewed.

Feedback

If you have any comments you would like to make on this Evidence Update, please email contactus@evidence.nhs.uk

[1] NICE-accredited guidance is denoted by the Accreditation Mark

Key points

The following table summarises what the Evidence Update Advisory Group (EUAG) decided were the key points for this Evidence Update. It also indicates the EUAG's opinion on whether the new evidence may have a potential impact on the current guidance listed in the introduction. For further details of the evidence behind these key points, please see the full commentaries.

The section headings used in the table below are taken from the guidance.

Evidence Updates do not replace current accredited guidance and do not provide formal practice recommendations.

	Potential impact on guidance	
Key point	**Yes**	**No**
Induction of labour in specific circumstances		
• Induction of labour to avoid prolonged pregnancy may be associated with fewer perinatal deaths than expectant management.		✓
• Evidence for differences in rates of neonatal sepsis between induction of labour or expectant management in women with preterm prelabour rupture of membranes seems to be inconclusive.		✓
Recommended methods for induction of labour		
• Evidence that increasing frequency of membrane sweeping reduces the rate of induction of labour at 41 weeks' gestation seems to be inconclusive.		✓
Methods that are not recommended for induction of labour		
• Nitric oxide donors do not seem to be effective for induction of labour.		✓
• Evidence for benefits of mechanical methods of induction of labour over prostaglandins seems to be inconclusive.		✓
• Compared with prostaglandin E2, Foley (balloon) catheters do not seem to lower rates of caesarean section, and are associated with longer time to delivery and higher likelihood of needing to administer oxytocin.		✓
Setting and timing		
• Maternal and fetal safety outcomes do not seem to differ whether prostaglandins are administered in the morning or evening, but women appear to prefer morning administration.		✓
Monitoring and pain relief		
• Evidence for measurement of cervical length with transvaginal ultrasonography in predicting delivery outcomes in women scheduled for induction of labour seems to be inconclusive.		✓

1 Commentary on new evidence

These commentaries analyse the key references identified specifically for the Evidence Update. The commentaries focus on the 'key references' (those identified through the search process and prioritised by the EUAG for inclusion in the Evidence Update), which are identified in bold text. Supporting references provide context or additional information to the commentary. Section headings are taken from the guidance.

1.1 Information and decision-making

No new key evidence was found for this section.

1.2 Induction of labour in specific circumstances

Prevention of prolonged pregnancy

NICE clinical guideline 70 (NICE CG70) recommends that women with uncomplicated pregnancies should usually be offered induction of labour between 41 and 42 weeks to avoid the risks of prolonged pregnancy. The exact timing should take into account the woman's preferences and local circumstances.

In a Cochrane review including 22 randomised controlled trials (RCTs) (n=9383), **Gülmezoglu et al. (2012)** assessed induction of labour compared with waiting for spontaneous labour (expectant management) in women with pregnancies at or beyond term. Most trials induced labour at 41 weeks of gestation. When compared with expectant management, induction of labour was associated with significantly fewer:

- perinatal deaths (relative risk [RR]=0.31, 95% confidence interval [CI] 0.12 to 0.88, p=0.016; 17 trials, n=7407).
- instances of meconium aspiration syndrome (RR=0.50, 95% CI 0.34 to 0.73, p=0.00034; 8 trials, n=2371).
- caesarean sections (RR=0.89, 95% CI 0.81 to 0.97, p=0.0067; 21 trials, n=8749).

Admission to the neonatal intensive care unit was not significantly different between the induction and expectant management groups (RR 0.90, 95% CI 0.78 to 1.04, p=0.16; 10 trials, n=6161).

Risk of bias from lack of blinding was judged to be high, but blinding was not possible because of the nature of the interventions. Overall, most trials were judged to be at moderate risk of bias. However, 2 trials were published only in abstract with full publications not identified, which limited the assessment of potential bias.

This review suggests that induction of labour to avoid prolonged pregnancy may be associated with fewer perinatal deaths than expectant management. This is consistent with NICE CG70, which used a previous version of this Cochrane review from 2006 in the development of recommendations (see the full version of NICE CG70 for details). The updated results are generally similar to those of the previous review, with a narrowing of the confidence intervals for the outcomes of perinatal death. The reduction in caesarean section is now statistically significant, whereas previous results showed no significant difference.

Key reference

Gülmezoglu AM, Crowther CA, Middleton P et al. (2012) Induction of labour for improving birth outcomes for women at or beyond term. Cochrane Database of Systematic Reviews issue 6: CD004945

Preterm prelabour rupture of membranes

NICE CG70 recommends that if a woman has preterm prelabour rupture of membranes after 34 weeks, the maternity team should discuss the following factors with her before a decision is made about whether to induce labour, using vaginal prostaglandin E2 (PGE_2)[2]:

- risks to the woman (for example, sepsis, possible need for caesarean section)
- risks to the baby (for example, sepsis, problems relating to preterm birth)
- local availability of neonatal intensive care facilities.

An open-label RCT (PPROMEXIL, n=536) by **van der Ham et al. (2012a)** compared induction of labour or expectant management in women at 34–37 weeks' gestation with preterm prelabour rupture of membranes. Eligible women with singleton or twin pregnancies were enrolled within 24 hours of membrane rupture. The primary outcome was neonatal sepsis.

In the induction of labour group, women were induced, according to Dutch national guidelines, within 24 hours of randomisation (or if caesarean was planned, it was performed as soon as possible after randomisation). In the expectant management group, women were monitored according to local protocol until spontaneous delivery. Labour was induced if the woman reached 37 weeks of gestation, or if necessary because of other maternal or fetal indications. If caesarean section was planned in this group, it was performed as soon as labour started.

No significant difference in neonatal sepsis was seen between the induction of labour group (7 babies, 2.6%) and the expectant management group (11 babies, 4.1%; RR=0.64, 95% CI 0.25 to 1.6, p=0.346).

The authors then did a meta-analysis combining the results of their trial with a previously published Cochrane review comparing induction of labour with expectant management (Buchanan et al. 2010). A literature search identified no additional new studies to add to the meta-analysis. Data on neonatal sepsis were available from 8 trials (n=1230) including the present study, but no significant difference was seen between interventions (RR=1.06, 95% CI 0.64 to 1.76).

The authors noted that the main limitation of their trial was that it was underpowered. The sample size was calculated on expected rates of neonatal sepsis of 7.5% in the expectant management group and 2.5% in the induction of labour group. However, the rate in the expectant management group was lower than expected at 4.1%, so demonstrating a statistically significant difference would have needed a much larger number of participants. Additionally, the power calculation assumed that induction of labour would not increase the risk of neonatal sepsis. The results of some studies included in the meta-analysis showed a potentially increased risk of neonatal sepsis with induction of labour. Again, a larger sample size would have been needed to account for this possibility.

In a further RCT (PPROMEXIL-2, n=195), **van der Ham et al (2012b)** randomly assigned women to induction of labour or expectant management according to the trial protocol of PPROMEXIL discussed above. Again, no significant difference in neonatal sepsis was seen between the induction of labour group (3 babies, 3.0%) and the expectant management group (4 babies, 4.1%; RR=0.74, 95% CI 0.17 to 3.2). No power calculation was performed, but this trial is likely to be underpowered because the number of participants was smaller than in the

[2] Vaginal PGE_2 has been used in UK practice for many years in women with ruptured membranes. However, the summary of product characteristics (SPCs) advise that in this situation, vaginal PGE_2 is either not recommended or should be used with caution, depending on the preparation (gel, tablet or pessary). Healthcare professionals should refer to the individual SPCs before prescribing vaginal PGE_2 for women with ruptured membranes, and informed consent should be obtained and documented.

original PPROMEXIL trial, which was underpowered. These results were added to the previous meta-analysis (9 studies, n=1428). The difference between interventions remained non-significant (RR=1.02, 95% CI 0.63 to 1.65).

The results provide no conclusive evidence about differences in rates of neonatal sepsis between induction of labour or expectant management in women with preterm prelabour rupture of membranes. This is consistent with NICE CG70, which recommends discussing the risks of induction of labour with the woman before a decision is made.

Key references

van der Ham DP, Vijgen SMC, Nijhuis JG et al. (2012a) Induction of labor versus expectant management in women with preterm prelabor rupture of membranes between 34 and 37 weeks: a randomized controlled trial. PloS Medicine 9: e1001208

van der Ham DP, van der Heyden JL, Opmeer BC et al. (2012b) Management of late-preterm premature rupture of membranes: the PPROMEXIL-2 trial. American Journal of Obstetrics and Gynecology 207: e1–10

Supporting reference

Buchanan SL, Crowther CA, Levett KM et al. (2010) Planned early birth versus expectant management for women with prelabour rupture of membranes prior to 37 weeks' gestation for improving pregnancy outcome. Cochrane Database of Systematic Reviews issue 3: CD004735

1.3 Recommended methods for induction of labour

Membrane sweeping

NICE CG70 recommends that prior to formal induction of labour, women should be offered a vaginal examination for membrane sweeping. When a vaginal examination is carried out to assess the cervix, the opportunity should be taken to offer the woman a membrane sweep. Additional membrane sweeping may be offered if labour does not start spontaneously.

NICE CG70 additionally contains a research recommendation on this topic:

What are the effectiveness and acceptability of, and maternal satisfaction with, the following:

- multiple versus once-only membrane sweeping, at varying gestational ages, depending on parity
- membrane sweeping versus cervical massage?

Putnam et al. (2011) did a single-centre RCT (n=350) comparing once-weekly membrane sweeping and twice-weekly membrane sweeping with control in women with an unfavourable cervix (Bishop score ≤4) at 39 weeks' gestation. Membrane sweeping was done according to protocol until 41 weeks, when all women who had not given birth had labour induced. The primary end point was the proportion of women needing induction at 41 weeks.

Included women were older than 18 years with a singleton pregnancy who planned, and had no contraindication to, vaginal delivery. Additional inclusion criteria were reliable dating of pregnancy and ultrasound confirming the placenta was clear of the cervix.

No significant differences were seen in the proportion of women admitted for induction of labour at 41 weeks. The rates were 34% in the control group, 27% in the once-weekly membrane sweep group and 23% in the twice-weekly group (p=0.149). At baseline, the group who had twice-weekly membrane sweeping had a significantly higher proportion of women with Bishop score of 3–4 (83%) than the once weekly group (71%, p=0.04) or the control group (67%, p<0.001). The authors conducted analyses to adjust for differences in Bishop score, but the results remained non-significant.

The authors discussed the lack of balance of Bishop score between groups and noted that in hindsight the randomisation should have been stratified by Bishop score. The authors

additionally noted a potential limitation in that they did not record data for women whose cervix was so unfavourable that it would not allow a full membrane sweep, which may have provided useful additional information.

The results of this study provide no conclusive evidence that increasing frequency of membrane sweeping reduces the rate of induction of labour at 41 weeks' gestation. This evidence is unlikely to have an impact on NICE CG70 and further research is needed to answer the research recommendation on this topic.

Key reference

Putnam K, Magann EF, Doherty DA et al. (2011) Randomized clinical trial evaluating the frequency of membrane sweeping with an unfavourable cervix at 39 weeks. International Journal of Women's Health 3: 287–294

1.4 Methods that are not recommended for induction of labour

Nitric oxide donors

NICE CG70 states that vaginal nitric oxide donors should not be used for induction of labour.

In a Cochrane review, **Kelly et al. (2011)** investigated the effects of nitric oxide donors for cervical ripening or induction of labour. The analysis included 10 randomised trials (n=1889) that compared nitric oxide donors with placebo, vaginal or cervical PGE_2, and vaginal misoprostol. These comparisons were analysed separately.

Primary outcomes were vaginal delivery within 24 hours, uterine hyperstimulation with fetal heart rate changes, caesarean section, serious neonatal morbidity or perinatal death and serious maternal morbidity or death.

Nitric oxide donors did not show significant benefits in the primary outcomes compared with any other interventions assessed. Maternal side effects of headache and nausea were significantly higher in the nitric oxide group in several studies. All studies were judged to be of a generally high standard with low risk of bias.

Nitric oxide donors do not seem to be effective for induction of labour, which is consistent with recommendations in NICE CG70 not to use this intervention.

Key reference

Kelly AJ, Munson C, Minden L (2011) Nitric oxide donors for cervical ripening and induction of labour. Cochrane Database of Systematic Reviews issue 6: CD006901

Mechanical methods of induction of labour

NICE CG70 states that mechanical procedures (balloon catheters and laminaria tents) should not be used routinely for induction of labour.

General mechanical methods

Jozwiak et al. (2012) conducted a Cochrane review of 71 RCTs (n=9722) of mechanical methods for induction of labour compared with placebo or no treatment, prostaglandins, or oxytocin. The mechanical methods studied were laminaria tents or synthetic equivalents, catheters, or extra-amniotic infusion by catheter. Comparisons were of any method against any other or placebo or no treatment.

The primary outcomes of interest were vaginal delivery within 24 hours, uterine hyperstimulation with fetal heart rate changes, caesarean section, serious neonatal morbidity or perinatal death and serious maternal morbidity or death.

Many studies did not report on the outcome of vaginal delivery within 24 hours, and most of those reporting this outcome did not find any significant difference between mechanical methods and either no treatment or vaginal PGE_2. Most studies reported on caesarean

section rates. No significant differences in caesarean section rates were seen for mechanical methods compared with no treatment or prostaglandins. Mechanical methods were associated with lower rates of caesarean section than oxytocin (RR=0.62, 95% CI 0.42 to 0.90, p=0.011; 5 studies, n=398). Less uterine hyperstimulation with fetal heart rate changes occurred when balloon catheters were used, compared with any prostaglandins (RR 0.19, 95% CI 0.08 to 0.43, p=0.000063; 9 studies, n=1931). About half of included studies did not report details of allocation concealment.

These results provide no conclusive evidence that mechanical methods of induction of labour have benefits over prostaglandins, which is consistent with NICE CG70.

Key reference

Jozwiak M, Bloemenkamp KWM, Kelly AJ et al. (2012) Mechanical methods for induction of labour. Cochrane Database of Systematic Reviews issue 3: CD001233

Balloon catheters versus PGE_2

In an open-label RCT (n=824), **Jozwiak et al. (2011)** compared induction of labour using a Foley (balloon) catheter with induction of labour using vaginal PGE_2 in women at term with an unfavourable cervix (Bishop score <6). The primary outcome was caesarean section rate.

In the Foley catheter group, women had a catheter inserted past the internal os of the cervix, and the balloon was inflated with 30 ml of sterile saline or water. Women then had 1 hour of bed rest with fetal and uterine monitoring. Once the catheter was spontaneously expelled or the Bishop score was 6 or more, amniotomy was done. If uterine activity was insufficient an infusion of oxytocin was given. In the PGE_2 group, 1 mg PGE_2 gel was administered, then another 1 mg after 6 hours. When the Bishop score was 6 or more, amniotomy was done and oxytocin infusion started. In both groups, if the cervix remained unfavourable after 48 hours of treatment, the woman had 1 day of rest then induction started again.

Caesarean section rate did not differ significantly between the Foley catheter group (23%) and the PGE_2 group (20%, p=0.38). Oxytocin augmentation was significantly lower in the PGE_2 group than in the Foley catheter group (59% versus 86% respectively, p<0.0001). Time from start of induction to birth was also significantly shorter in the PGE_2 group (median=18 hours, interquartile range 12–33 hours) than in the Foley catheter group (median=29 hours, interquartile range 15–35 hours, p<0.0001). Admissions to the neonatal ward were significantly higher in the PGE_2 group (20%) compared with the Foley catheter group (12%, p=0.0019). Two serious maternal adverse events were recorded, both in the PGE_2 group: a uterine rupture and a uterine perforation.

The authors then performed a systematic review of studies comparing induction using a Foley catheter with induction using PGE_2, and found 2 studies in addition to their own. A meta-analysis of these 2 trials plus results from the present study (n=1431) suggested that there was no significant difference in the rate of caesarean section between Foley catheters and PGE_2 (OR=1.02, 95% CI 0.80 to 1.30, p=0.86).

The authors noted that the estimated 8% reduction in the rate of caesarean sections used in the power calculation was optimistic, and that in view of the results a non-inferiority design would have been more appropriate. Additionally, the authors did not assess the acceptability of the intervention to women. However, in the Foley catheter group, 2 women requested not to receive the intervention at randomisation and 5 women discontinued the intervention on request. This may indicate lower acceptability of Foley catheters than PGE_2 gel, because no women requested not to use, or to discontinue, PGE_2 gel.

Henry et al. (2013) reported an RCT (n=101) comparing a Foley catheter as outpatient treatment with inpatient PGE_2 gel for induction of labour. Women with pregnancies of gestational age of 37 weeks or more, a Bishop score of less than 7 and cervical dilation of less than 2 cm were eligible for inclusion. The primary outcomes were proportion of vaginal

births within 12 hours of admission to the birthing unit and total number of inpatient hours from randomisation to delivery.

The Foley catheter was inserted and inflated with 30 ml of sterile water. Fetal monitoring was then performed for at least 30 minutes before the woman was discharged. Women were given pain relief and a sedative with instructions to use if needed, and asked to return to the birthing unit at 7 am the next morning unless they had any concerns or if labour occurred. In the PGE_2 group, PGE_2 was administered and then fetal monitoring was performed for at least 30 minutes. Pain relief and sedation were given if needed, and the woman was transferred to the birthing unit at 7 am the next morning unless labour started or there were concerns about the mother or baby. In the birthing unit, women had amniotomy plus oxytocin infusion. If this was not possible or the cervix remained unfavourable, further clinical management was undertaken.

Vaginal delivery within 12 hours occurred significantly more often in the PGE_2 gel group (53%) compared with the Foley catheter group (28%, p=0.011). Total inpatient stay from randomisation to birth was significantly longer in the PGE_2 gel group (mean=32.4 hours, SD16.9 hours) compared with the Foley catheter group (mean=21.3 hours, SD 10.1 hours, p<0.001). However, women in the Foley catheter group had a longer stay in hospital after giving birth, so the difference in total inpatient stay (mean=96 hours, SD 38 hours) was not significantly lower than the PGE_2 group (mean=105 hours, SD 38 hours, p=0.267). Significantly more women in the Foley catheter group needed oxytocin (88%) than in the PGE_2 group (59%, p=0.01). A survey of maternal satisfaction suggested that this was higher in the Foley catheter group.

The authors noted that recruitment was lower than the sample size estimated in the power calculation (200 women) for the first primary outcome (proportion of vaginal births in 12 hours). The study met the sample size for the second primary outcome (time from randomisation to birth). Additionally, the choice of a mechanical outpatient method compared with a chemical inpatient method may have limited the assessment of inpatient versus outpatient and mechanical versus chemical means. Finally they acknowledged that using total inpatient hours would have been a better primary outcome than inpatient hours before delivery.

The results of these studies suggest that compared with PGE_2, Foley catheters do not seem to lower rates of caesarean section, and are associated with longer time to delivery and higher likelihood of needing to administer oxytocin. Therefore, this evidence is unlikely to have an impact on NICE CG70.

Key references

Henry A, Madan A, Reid R et al. (2013) Outpatient Foley catheter versus inpatient prostaglandin E2 gel for induction of labour: a randomised trial. BMC Pregnancy & Childbirth 13: 25

Jozwiak M, Rengerink KO, Benthem M et al. (2011) Foley catheter versus vaginal prostaglandin E2 gel for induction of labour at term (PROBAAT trial): an open-label, randomised controlled trial. The Lancet 378: 2095–103

1.5 Setting and timing

Timing of induction of labour

NICE CG70 recommends that in the inpatient setting, induction of labour using vaginal PGE_2 should be carried out in the morning because of higher maternal satisfaction. NICE CG70 states that intravenous oxytocin alone should not be used for induction of labour.

Bakker et al. (2013) did a Cochrane review of 3 RCTs (n=1150) comparing induction of labour in the morning with the evening. The primary outcome studied was perinatal mortality.

In 2 trials (n=746) comparing morning with evening dosing of prostaglandins for induction of labour, no perinatal mortality occurred in either trial. Both trials reported data for asphyxia at birth defined as Apgar score less than 7 at 5 minutes and admission to neonatal intensive care. No significant differences were seen for these outcomes. No significant differences were found in the risk of caesarean section or in use of epidural anaesthesia. Instrumental delivery was higher in one trial but not the other. In 1 study, significantly fewer women in the morning group reported dissatisfaction with timing of induction compared with the evening group (RR=0.21, 95% CI 0.05 to 0.89, p=0.034).

In 1 trial (n=371) of morning versus evening dosing of intravenous oxytocin, no perinatal mortality was recorded. No significant differences were seen for birth asphyxia, but significantly more babies were admitted to the maternity ward, medium care or neonatal intensive care following morning induction with oxytocin (RR=1.48, 95% CI 1.02 to 2.14, p=0.039). No significant differences were found for the maternal outcomes of mode of delivery (by caesarean section or use of instruments) or epidural anaesthesia.

The authors concluded that caregivers should preferably consider administering prostaglandins in the morning because of women's preferences, but there is no strong evidence that morning or evening dosing of oxytocin is more effective.

The finding that maternal and fetal safety outcomes do not seem to differ whether prostaglandins are administered in the morning or evening, but that women appear to prefer morning administration is consistent with the recommendation in NICE CG70 to carry out induction of labour with PGE_2 in the morning.

Key reference

Bakker JJH, van der Goes BY, Pel M et al. (2013) Morning versus evening induction of labour for improving outcomes. Cochrane Database of Systematic Reviews issue 2: CD007707

1.6 Monitoring and pain relief

Predicting outcomes of labour induction using cervical length

NICE CG70 recommends assessing and recording the Bishop score before induction of labour is carried out. NICE CG70 defines the Bishop score as a group of measurements made by doing a vaginal examination, and is based on the station, dilation, effacement (or length), position and consistency of the cervix. A score of 8 or more generally indicates that the cervix is ripe, or 'favourable' – when there is a high chance of spontaneous labour, or response to interventions made to induce labour.

Verhoeven et al. (2013) reported a systematic review (n=5029) of 30 cohort studies and 1 RCT of women scheduled for induction of labour who had ultrasonically measured cervical length as a possible alternative to the Bishop score. Most included studies used rates of caesarean section as the primary end point. Results from the studies were extracted and analysed to determine the sensitivity and specificity of measuring cervical length.

For predicting caesarean section, a cervical length of:

- 20 mm had sensitivity of 82% and specificity of 34%
- 30 mm had sensitivity of 64% and specificity of 74%
- 40 mm had sensitivity of 13% and specificity of 95%.

For prediction of no vaginal delivery within 24 hours, a cervical length of:

- 25 mm had sensitivity of 58% and specificity of 80%
- 32 mm had sensitivity of 84% and specificity of 60%.

The authors noted that most studies did not report withdrawals, and no studies reported cases in which the cervical ultrasound could not be interpreted. The authors also noted that

heterogeneity between studies in terms of indications of induction of labour or mode of induction was a potential limitation.

These results provide no evidence that measurement of cervical length with transvaginal ultrasonography is clinically useful in predicting delivery outcomes in women scheduled for induction of labour. Therefore, this evidence is unlikely to have an impact on NICE CG70.

Key reference

Verhoeven CJM, Opmeer BC, Oei SG et al. (2013) Prediction of the outcome of labor induction at term by transvaginal sonographic measurement of cervical length: a systematic review. Ultrasound in Obstetrics and Gynecology: DOI:10.1002/uog.12467

1.7 Prevention and management of complications

No new key evidence was found for this section.

2 New evidence uncertainties

During the development of the Evidence Update, the following evidence uncertainties were identified for the UK Database of Uncertainties about the Effects of Treatments (UK DUETs).

Induction of labour in specific circumstances

- Induction of labour for improving birth outcomes for women at or beyond term

Methods that are not recommended for induction of labour

- Mechanical methods for induction of labour

Setting and timing

- Morning versus evening induction of labour for improving outcomes

Further evidence uncertainties for induction of labour can be found in the UK DUETs database and in the NICE research recommendations database.

UK DUETs was established to publish uncertainties about the effects of treatments that cannot currently be answered by referring to reliable up-to-date systematic reviews of existing research evidence.

Appendix A: Methodology

Scope

The scope of this Evidence Update is taken from the scope of the reference guidance:

- Induction of labour. NICE clinical guideline 70 (2008).

Evidence from developing countries or resource-poor settings was excluded because of lack of relevance to UK practice.

Searches

The literature was searched to identify studies and reviews relevant to the scope. Searches were conducted of the following databases, covering the dates 17 June 2011 (the end of the search period for the latest review of the need to update NICE clinical guideline 70) to 15 February 2013:

- CDSR (Cochrane Database of Systematic Reviews)
- CENTRAL (Cochrane Central Register of Controlled Trials)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature)
- DARE (Database of Abstracts of Reviews of Effects)
- EMBASE (Excerpta Medica database)
- HTA (Health Technology Assessment) database
- MEDLINE (Medical Literature Analysis and Retrieval System Online)
- MEDLINE In-process
- NHS EED (Economic Evaluation Database)
- PsycINFO

Table 1 provides details of the MEDLINE search strategy used, which was adapted to search the other databases listed above. Given the breadth of the topic, it was necessary to adapt the search strategy used in the reference guidance. A specific search strategy was developed to provide a focused set of results, which was thoroughly tested to ensure that the comprehensiveness of the results was not compromised. The search strategy was used in conjunction with validated Scottish Intercollegiate Guidelines Network search filters for RCTs and systematic reviews.

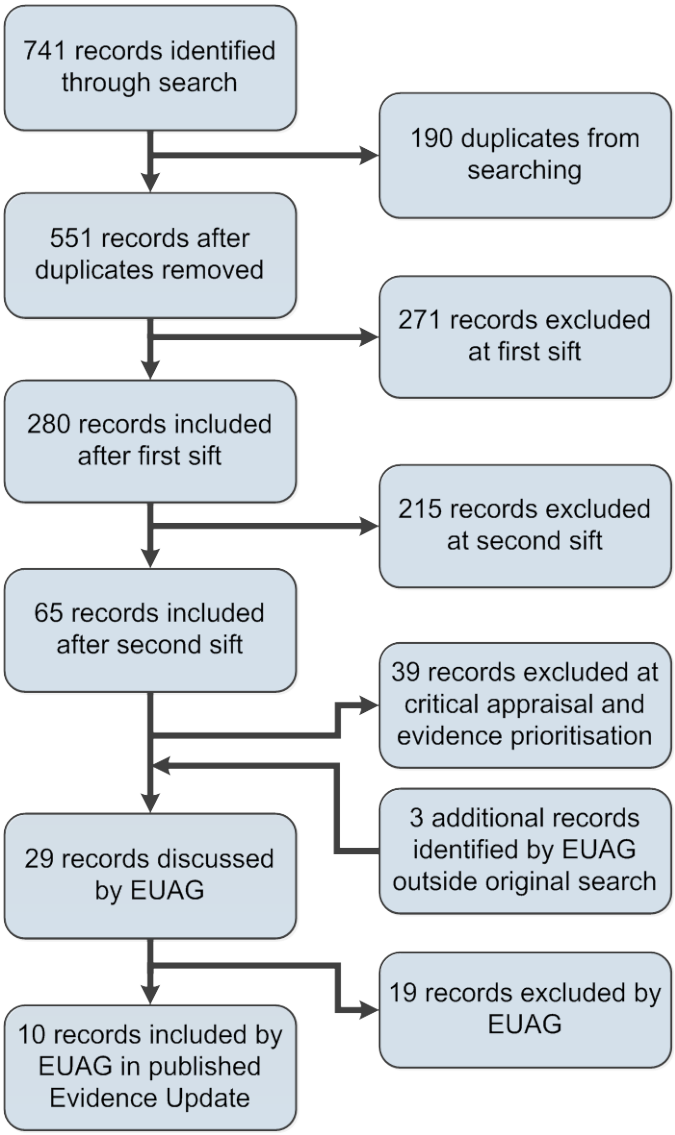
Additionally, 1 study (Bakker et al. 2013) was identified outside of the literature search. Figure 1 provides details of the evidence selection process. The long list of evidence excluded after review by the Chair of the EUAG, and the full search strategies, are available on request from contactus@evidence.nhs.uk

There is more information about how NICE Evidence Updates are developed on the NICE Evidence Services website.

Table 1 MEDLINE search strategy (adapted for individual databases)

1	Labor, Induced/
2	(induc$ adj3 labo?r$).tw.
3	amniotom$.tw.
4	artificial$ adj3 ruptur$ adj3 membrane$).tw.
5	((sweep$ or strip$) adj2 membrane$).tw.
6	Cervical Ripening/
7	(cervi$ adj2 (ripen$ or priming)).ti,ab.
8	Misoprostol/
9	misoprostol.ti,ab.
10	Dinoprostone/
11	Dinoprostone.ti,ab.
12	(prostaglandin E2 or PGE2).ti,ab.
13	Fetal Membranes, Premature Rupture/
14	(premature$ ruptur$ adj2 membrane$).ti,ab.
15	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 13 or 14

Figure 1 Flow chart of the evidence selection process



EUAG – Evidence Update Advisory Group

Appendix B: The Evidence Update Advisory Group and Evidence Update project team

Evidence Update Advisory Group

The Evidence Update Advisory Group is a group of topic experts who review the prioritised evidence obtained from the literature search and provide the commentary for the Evidence Update.

Professor Andrew Calder – Chair

Professor Emeritus of Obstetrics and Gynaecology, University of Edinburgh

Professor Zarko Alfirevic

Professor of Fetal and Maternal Medicine, Head of Department of Women's and Children's Health, Institute of Translational Medicine, University of Liverpool

Jenny Davidson

Women and Children's Division Governance Lead, Brighton and Sussex University Hospitals NHS Trust,

Dr Hassan Shehata

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