NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Centre for Clinical Practice

Review consultation document

Review of 'Induction of labour' NICE clinical guideline 70

1 Background information

Guideline issue date: 2008

3 year review: 2011

National Collaborating Centre: Women's and Children's Health

2 Consideration of the evidence

2.1 Literature search

A high-level search of randomised control trials (RCTs) identified new evidence related to the following clinical areas in the guideline:

- Induction of labour in specific circumstances
- Monitoring and pain relief for induction of labour
- Timing of induction of labour
- Complications of induction of labour.

The high-level RCT search identified 21 studies relevant to the above clinical areas. This was sufficient to allow an assessment for a proposed review decision in all but 2 areas. The assessment of these studies was based on abstract only. The studies are summarised in table 1.

From initial intelligence gathering, qualitative feedback from other NICE departments, the views expressed by the Guideline Development Group, as well as the high-level RCT search, an additional focused literature search was conducted for the following clinical areas:

- Methods of induction of labour
- Setting of induction of labour

The results of the focused searches and assessment based on abstracts only are summarised in table 2.

All references identified in the initial intelligence gathering, high-level RCT search and the focused searches are listed in appendix A.

Table 1 High-level RCT searches

Clinical area 1: Induction of labour in specific circumstances		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
What are the risks of prolonged pregnancy? What are the harms and benefits of induction of labour for the prevention of prolonged pregnancy? Relevant section of guideline 4.1 Recommendations 1.2.1.1 to 1.2.1.4 (and research recommendations)	The high-level RCT search identified two studies relevant to the clinical question. One was a Cochrane review[1] which included 19 studies comparing labour induction after 41 weeks compared with awaiting spontaneous labour indefinitely or for at least one week. The study found that labour induction is associated with fewer perinatal deaths. However, the absolute risk is very small. The study concluded that women should be counseled about the relative and absolute risks. Another meta-analysis[2] including 13 studies comparing induction of labour with expectant management for post-date pregnancy. The study found that elective labour was not associated with lower mortality. It was associated with a significantly lower rate of meconium aspiration syndrome and a significantly lower risk of delivery by caesarean section. However, the study authors stated that no individual study with adequate sample size has been published and it is difficult to make conclusions about the optimal management of pregnancies at 41 weeks. Overall, the results from these studies are consistent with the current guideline recommendations.	No new evidence identified that may change current recommendation(s).
What are the harms and benefits of induction of	The high-level RCT search identified two studies relevant to the clinical question.	No new evidence identified that may

labour in women with preterm prelabour rupture of membranes? Relevant section of guideline 4.2 Recommendations 1.2.2.1 and 1.2.2.2 (and research recommendation)	One systematic review[3] included 34 studies evaluated induction of labour for a number of indications and used GRADE to assess the level of evidence. The study concluded that there is sufficient evidence to recommend induction of labour for premature rupture of membranes near term with pulmonary maturity (no further details of included studies given in the abstract). This is consistent with the current guideline recommendations. There was another publication[4] of an economic analysis from a Dutch study of induction of labour compared with expectant management in women with preterm prelabour rupture of membranes between 34 and 37 weeks (the PPROMEXIL trial). However, abstract was not available.	change current recommendation (s) about this indication. See also focused searches in table 3 on method of induction.
What are the harms and benefits of induction of labour in women with prelabour rupture of membranes at term? Relevant section of guideline 4.3 Recommendations 1.2.3.1 and 1.2.3.2	The high-level RCT search identified four studies relevant to the clinical question. *Summary* One Cochrane review[5] included 12 studies that compared planned early birth (with oxytocin or prostaglandin) with expectant management in women at 37 weeks or later. The study found no differences in mode of birth between the groups but found that significantly fewer women had chorioamnionitis or endometritis, significantly fewer infants had neonatal intensive or special care and significantly more women viewed their care more positively in the planned birth group. (however, intravenous oxytocin is not currently recommended for induction of labour) One systematic review[3] included 34 studies evaluated induction of labour for a number of indications and used GRADE to assess the level of	No new evidence identified that may change current recommendation (s) about this indication. See also focused searches in table 3 on method of induction.

	evidence. The study concluded that there is sufficient evidence to recommend induction of labour for prelabour rupture of membranes at term (no further details of included studies given in the abstract). Another Cochrane review[6] including 61 trials which compared intravenous oxytocin with prostaglandin agents. Most studies included women with ruptured membranes. The review suggested that for women with prelabour rupture of membranes, induction with vaginal prostaglandin may increase the risk of infection for mother and baby but this should be interpreted with caution as infection was not specified in the original protocol. The authors suggested that this needs further research. (intravenous oxytocin is not currently recommended for induction of labour) One RCT[7] compared induction with misoprostol to expectant management in women with prelabour rupture of membranes at term (beyond 37 weeks). Those in the expectant group had slightly higher maternal complications (ie. chorioamnionitis, postpartum fever) but did not affect long-term maternal morbidity. Both groups had no neonatal morbidity or mortality. Overall, the results are broadly consistent with the current guideline recommendations on the use of induction in these women (however, some of the pharmacological methods used to induce labour are not currently recommended in this group – please see focused searches in table 3 for methods of induction).	
What are the harms and benefits of induction of labour in women with a	The high-level RCT search identified one study relevant to the clinical question.	No new evidence identified that may change current

previous caesarean birth? Relevant section of guideline 4.4 Recommendations 1.2.4.1 and 1.3.1.1 to 1.3.1.5(and research recommendation)	The RCT[8] compared serial membrane sweeping at term in women with planned vaginal birth after caesarean to a control group. The study found that serial membrane sweeping had no significant effect on the onset of labor, pregnancy duration, induction of labor, or repeat cesarean delivery. Since the current recommendations apply to prolonged pregnancy only, this study does not contradict the current recommendations.	recommendation (s).
What are the harms and benefits of induction of labour in women with presence of fetal growth restriction? Relevant section of guideline 4.7 Recommendations 1.2.7.1	The high-level RCT search identified one study relevant to the clinical question. The DIGITAT multi-centre equivalence trial[9] compared induction of labour with expectant monitoring. The study found no important differences in adverse neonatal outcomes (death before hospital discharge, five minute Apgar score of less than 7, umbilical artery pH of less than 7.05, or admission to the intensive care unit). This is consistent with the current guideline which does not recommend induction in this situation.	No new evidence identified that may change current recommendation (s).
What are the harms and benefits of induction of labour in women with intrauterine fetal death? What are the best	The high-level RCT search identified four studies relevant to the clinical question. All four of the studies examined misoprostol for induction of labour in	Some new evidence was identified but insufficient to invalidate current guideline recommendation(s).

methods of induction of labour in women with intrauterine fetal death? What are the best methods of induction of labour in women with intrauterine fetal death, who have had a previous caesarean birth? Relevant section of guideline 4.9 Recommendations 1.2.9.1 to 1.2.9.5	women with intrauterine fetal death. Misoprostol is currently recommended in the guideline for this indication for induction of labour (off-label use). *Summary* One Cochrane review[10] including 38 studies found that vaginal misoprostol was as effective as other prostaglandins at terminating pregnancy in the second and third trimester and that it was more effective than when misoprostol was delivered orally. However, the study also stated that there is still limited information about maternal safety. Another systematic review[11] including 14 studies found that the evidence on misoprostol for terminating pregnancy in the second and third trimester was limited and that the studies varied methodologically and in outcome measures reported. Vaginal misoprostol was found to be less effective than oral misoprostol at effecting delivering within 24 hours but not within 48 hours; it also had less side effects than oral administration. The current guideline recommends vaginal misoprostol) A small RCT (n = 44)[12] comparing vaginal with sublingual misoprostol found that both were safe and efficient but the study concluded that larger studies are needed to compare complications (sublingual misoprostol is not currently recommended in the guideline because of a lack of evidence). Another RCT[13] which compared vaginal misoprostol and intravenous sulprostone (an analogue of PGE2) found both drugs to be similarly effective with little difference in side effects except for hyperthermia which was more common with misoprostol and related to the total dose of	

	misoprostol used. Acceptability was higher in women treated with misoprostol and this was largely because of the intravenous administration of sulprostone which decreased mobility. (intravenous PGE2 is not currently recommended) Overall, some new evidence suggests that vaginal misoprostol (recommended in the current guideline) may not be the best method of administration of misoprostol. However, the evidence is not likely to be sufficient to change current guideline recommendations.	
What are the harms and benefits of induction of labour in women with suspected fetal macrosomia? Relevant section of guideline 4.10 Recommendations 1.2.10.1	The high-level RCT search identified two studies relevant to the clinical question. One systematic review[14] found little evidence that routine elective delivery (either by induction of caesarean section) for suspected macrosomia alone should be performed in the general population. One systematic review[3] included 34 studies evaluated induction of labour for a number of indications and used GRADE to assess the level of evidence. The study concluded that there is insufficient evidence to recommend induction of labour for women with fetal macrosomia (no further details of included studies given in the abstract). Overall, the evidence is consistent with the current guideline recommendation which does not recommend induction in this situation.	No new evidence identified that may change current recommendation(s).
Clinical area 2: Timing of induction of labour		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**

What are the effects (harms and benefits) when induction of labour is carried out at different days of week and at different times of day? Relevant section of guideline 6.1 Recommendations 1.5.1.3	The high-level RCT search identified one study relevant to the clinical question. This RCT[15] was based in three hospitals in Amsterdam and found that induction of labour with intravenous oxytocin in the evening (at 21:00) did not result in significantly different duration of labour, rate of instrumental delivery, rate of infection, or patient satisfaction than induction in the morning (at 07:00). The study found that neonatal outcomes were better when women were induced in the evening. The time of morning and evening induction varied from 2 to 3 hours and it is not clear which is the most appropriate to the UK setting (the current guideline included 2 RCTs which were not based in the UK and one UK-based study which compared induction at 2pm and 10 pm). Current recommendations recommend morning delivery because the evidence showed that women were more satisfied with morning delivery and this study is consistent in that patient satisfaction was not significantly different between groups induced in either the morning or evening. It is unusual that neonatal outcomes were better in the evening but no more details were provided in the abstract.	No conclusive new evidence was identified that would invalidate current recommendation(s).
Clinical area 3: Monitoring of induction of labour		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
How should labour be monitored at/during induction of labour?	The high-level RCT search identified two studies relevant to the clinical question. One RCT[16] based at six hospitals in the Netherlands compared internal	Some new evidence was identified but insufficient to change current guideline

Relevant section of guideline 7.1 Recommendations 1.6.1.1 to 1.6.1.7 (and a research recommendation)	versus external tocodynamometry for monitoring labour during induced or augmented labour. There was no significant difference in operative delivery rate, use of antibiotics during labor, time from randomization to delivery, and adverse neonatal outcomes between the groups. Another RCT[17] based in Turkey comparing intermittent fetal pulse oximetry and fetal heart rate monitoring with fetal heart rate monitoring alone after induction of labour reported that caesarean delivery rate (total rate and due to non-reassuring fetal heart rate patterns) decreased when intermittent pulse oximetry was used. There was no evidence identified for monitoring at or during induction of labour during the development of current guideline, and hence current recommendations are based on the Intrapartum care guideline (NICE clinical guideline 55). Both internal tocodynamometry and fetal pulse oximetry are methods not currently in use in the UK. As a result, these new studies are not likely to affect the recommendations.	recommendation(s).
Clinical area 4: Pain relief for induction of labour		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
What is the evidence that induced labours are more painful than spontaneous labour? What are the harms and effects of early (at induction) and late (active labour)	The high-level RCT search identified one study[18] relevant to the clinical question. This RCT was based in the UK and compared manual, electric and sham acupuncture for pain relief during induced labour in nulliparous women. The study found no analgesic benefit with acupuncture for pain relief. The current guideline does not cover acupuncture for pain relief and these	No new evidence identified that may change current recommendation(s).

administration of epidural analgesia? Relevant section of guideline 7.2 Recommendations 1.6.2.1 to 1.6.2.5	results do not suggest it should be used.	
Clinical area 5: Prevention and management of complications of induction of labour		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
How are complications of induction of labour prevented and managed? Relevant section of guideline 8 Recommendations 1.7.1.1 to 1.7.4.1 (and research recommendations about failed induction)	The high-level RCT search identified one study[19] relevant to the clinical question. This study was a secondary analysis from an RCT based in the US including nulliparous women at or beyond 36 weeks undergoing induction with a cervix of 2 cm or less dilated and less then completely effaced. The study reported that almost 40% of the women who stayed in the latent phase after 12 hours of oxytocin and membrane rupture had vaginal delivery. The study concluded that labour induction should not be considered a failure in the latent phase until oxytocin has been given for at least 12 hours after membrane rupture. Results from this study alone do not give conclusive information about the management of failed induction and are unlikely to affect the recommendations.	No conclusive new evidence was identified that would invalidate current recommendation(s).

Table 2 Focused searches

Clinical area 1: Methods of induction of labour		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
How safe is membrane sweeping for induction of labour for women with more than 1 cm of cervical dilation? Relevant section of guideline 5.2 Recommendations 1.3.1.1 to 1.3.1.5	The high level RCT search identified one study[20] which demonstrated that women with cervical dilation more than 1 cm may have an increased risk of prelabour rupture of membranes. This RCT of uncomplicated pregnancies compared 162 patients treated with membrane sweeping (> 38 weeks) and 138 with no sweeping. There were no differences in gestational age, obstetric or neonatal outcomes or in the rate of prelabour rupture of membranes. However, the patients with a cervix dilated more than 1 cm at the time of membrane sweeping (compared to no membrane sweeping) were more likely to have prelabour rupture of membranes (9.1% vs 0%, relative risk: 1.10, 95% confidence interval 1.03 to 1.18). A focused search did not reveal any additional publications reporting this outcome. However, two relevant conference abstracts were identified: • One RCT[21] of 50 women who had membrane sweeping compared with 51 in the control group reported that 2 and 4 patients, respectively, had prelabour rupture of membranes and that there were no statistically significant differences between the baseline characteristics of these patients (p = 0.68). • One study[22] which used a decision analytic model to determine the cost-effectiveness of membrane sweeping starting at 39 weeks stated that they used expectant management instead of membrane sweeping if there was a more than 2.5-fold increase in the likelihood of preterm	Some new evidence was identified but insufficient to change current guideline recommendation(s).

	rupture of membranes (the criteria to determine this risk was not reported in the abstract). Clinical advice stated that membrane sweeping is usually performed in an outpatient setting. In most cases, labour will follow without serious risk, particularly if prelabour rupture of membranes occurs during the procedure while the patient is in the hospital or clinic. However, there is a small risk that umbilical cord prolapse (with compression and fetal death) or infection (if the patient is not admitted) may occur in women who have returned home. While this new evidence demonstrates that prelabour rupture of membranes can occur after membrane sweeping, it is a known risk which the GDG was likely to be aware of during the development of current guideline. As a result, it was felt that this new evidence was not likely to change the current recommendation.	
Is vaginal PGE2 more clinically and cost-effective at inducing labour than other interventions? Relevant section of guideline 5 Recommendations 1.3.2.1 to 1.4.4.1, and research recommendations (on vaginal PGE2 (also, methods of	Through the high level RCT search 21 studies relevant to the clinical question were identified. *Compared with intravenous oxytocin* One RCT[23] based in Turkey compared vaginal PGE2 with oxytocin for labour induction in 240 women with premature rupture of membranes at term. The study found that oxytocin treatment seems to be superior to PGE2 in inducing labour in term pregnancies complicated with prelabour rupture of membranes or unfavorable cervixes. This is contradictory to current recommendations which recommend that intravenous oxytocin on its own is not used. However, it is unlikely that one RCT is sufficient to change the recommendations which are based on two systematic reviews. Two RCTs looked at dinoprostone (PGE2) with concurrent use of oxytocin	Some new evidence identified but unlikely to be sufficient to change current recommendation(s).

induction also relate to recommendations on specific circumstances for induction in section 1.2)	for cervical ripening and labour induction: - One[24] compared concurrent vaginal dinoprostone and oxytocin with intravenous oxytocin alone in term premature rupture of membranes. The study found that using both vaginal dinoprostone and intravenous oxytocin did not improve patient satisfaction of decrease time to delivery. - One[25] compared sustained-release vaginal pessary of dinoprostone with either immediate high-dose oxytocin or delayed high-dose of oxytocin (6 hours later). The study found that it was safer and more effective to give a high-dose oxytocin infusion 6 hours later for cervical ripening. The current guideline does not recommend vaginal PGE2 with concurrent use of oxytocin and it is not likely that these results would change any of the recommendations in the current guideline. *Compared with misoprostol* Though not currently licensed for use in pregnancy, off-label use of misoprostol is recommended in the current guideline induction of labour in the presence of intrauterine fetal death only. Only one new RCT was retrieved on the use of misoprostol for intrauterine death[26]. The study which compared 400 micrograms of vaginal misoprostol with 0.5 mg vaginal dinoprostone gel reported no major complications in either group and that they had comparable effectiveness but stated that the cost was the major advantage of misoprostol. This is consistent with	

	the current recommendations. The remaining studies (summarised below) report on the use of misoprostol for circumstances other than intrauterine fetal death. Three systematic reviews were retrieved: - An update of a Cochrane review[27] including 121 RCTs found that vaginal misoprostol in doses above 25 micrograms every 4 hours was more effective (required less epidural analgesia use, fewer failures to achieve vaginal delivery within 24 hours) than conventional methods including vaginal PGE2, intracervical PGE2, oxytocin or placebo) for third trimester cervical ripening and labour induction, but uterine hyperstimulation occurred more frequently. However, the study stated that the vaginal route should not be researched further as another Cochrane review has shown that the oral route of administration is preferable to the vaginal route (this other review was included as evidence in the current guideline). - One[28] included RCTs comparing intravaginal misoprostol (dosage not reported in abstract) with dinoprostone (PGE2) vaginal insert/pessary for cervical ripening and labor induction. The study found that both had similar rates of caesarean delivery, uterine hyperstimulation and fetal tachystole; neonatal outcomes were also similar between the two groups. Women treated with dinoprostone were more likely to require augmentation with oxytocin. - Another[29] looked specifically at low-dose oral misoprostol (20 micrograms every 2 hours) and compared it with dinoprostone (PGE2), vaginal misoprostol, and oxytocin for labor induction in	

	women with a viable fetus. The study found that it was at least effective as both vaginal dinoprostone and vaginal misoprostol, with lower rates of caesarean delivery and uterine hyperstimulation. The following RCTs compared vaginal PGE2 with a specific method of administration of misoprostol: **Sublingual misoprostol** One RCT[30] compared sublingual misoprostol (dosage not reported in abstract) with vaginal PGE2 gel in women greater than 24 to 48 hours after term rupture of membranes. The study reported that sublingual misoprostol leads to a shorter induction of labour time, and less need for a second dose of induction agent or oxytocin infusion. The abstract reported that those treated with the misoprostol were satisfied with the outcome, would use it again and recommend it to friends (difference in the rates of uterine hyperstimulation between groups and the patient experience with vaginal PGE2 were not reported in the abstract) **Vaginal and/or oral misoprostol** An RCT[31] based in 9 centres in the UK and one in Egypt compared titrated low-dose misoprostol (vaginal and/or oral; dosage not reported in abstract) with vaginal dinoprostone to induce labour after prelabour rupture of membranes greater than 34 weeks in women with a viable fetus. The study achieved 758 of the 1890 in the planned sample size because of an inability to obtain external funding. The study found that there were less caesarean sections in the misoprostol group but this difference was not statistically significant. A subgroup analysis showed that misoprostol may be more effective in those with an unfavourable cervix. There were also no	

	significant differences in maternal and neonatal complications, though maternal adverse effects occurred more with misoprostol. **Vaginal misoprostol** <u>No significant difference in safety (10 RCTs with varying dosage of misoprostol)</u> An RCT[32] based at 18 NHS study centres in the UK compared 25 micrograms of intravaginal misoprostol tablet with 3 mg of dinoprostone for induction of labour. The study found that the rate of vaginal deliveries within 24 hours did not significantly differ between the groups and that maternal and fetal adverse events were similar between groups. An RCT[33] found that the balloon catheter had the shortest induction to delivery interval than 25 micrograms of intravaginal misoprostol (every 4 hours) or 2 mg intravaginal PGE2/dinoprostone (every 4 hours) in prolonged pregnancy. The study reported that the both dinoprostone and misoprostol were equally safe and effective and the study also stated that misoprostol costs significantly less and is easier to store (but no safety outcomes reported in abstract). (this is contradictory to the current guideline recommendations) An RCT[34] which compared 50 micrograms of intravaginal misoprostol (every 4 hours to a maximum of 5 doses) to 10 mg of dinoprostone vaginal insert (to maximum of 12 hours) in prolonged pregnancies (≥ 37 weeks) found that misoprostol resulted in a number of significantly better efficacy outcomes (higher vaginal delivery rate within 12 hours, shorter induction to vaginal delivery time, and less oxytocin augmentation required) without a significantly different safety profile (tachysystole, uterine hyperstimulation rate of caesarean sections due to fetal distress). However, vaginal delivery	

	time within 24 hours and mode of delivery was not significantly different. An RCT[35] based at 52 sites in the USA and Canada (Misoprostol Vaginal Insert Trial) compared 50 microgram and 100 microgram misoprostol vaginal insert with 10 mg of dinoprostone vaginal insert for women requiring cervical ripening (modified Bishop score less than or equal to 4) before induction of labour. The study found that median time to vaginal delivery with the 50 microgram misoprostol vaginal insert was significantly longer than dinoprostone. Rate of caesarean delivery and safety profiles were not significantly different (but safety outcomes not reported in abstract). An RCT[36] which compared 50 micrograms of vaginal misoprostol (every 12 hours) to 2 mg of dinoprostone gel for induction of labour at term in nulliparous women with an unfavourable cervix reported that the probability of delivering within 24 hours was more than threefold higher with misoprostol but there was no difference in induction to delivery interval or a correlation between cervical parameters and induction to delivery. They study concluded that it is an effective, safe and cost-effective alternative (but safety outcomes not reported in abstract). A secondary analysis from the Misoprostol Vaginal Insert Trial[37] compared cardiotocographic abnormalities between those treated with 50 or 100 micrograms of misoprostol with 10 mg of dinoprostone in women requiring cervical ripening before induction of labor. Significantly less women treated with dinoprostone or 100 microgram misoprostol had uterine contractile abnormality (hyperstimulation, hypertonous and/or tachysystole) compared to those in the 50 microgram misoprostol group while the drug was in situ. The analysis reported no significant difference in incidence of fetal heart rate abnormalities. Cardiotocographic abnormalities were less frequent and occurred after longer exposure with MVI 50 than MVI 100 or	

	dinoprostone. Clinical outcomes were similar among the groups. An RCT[38] which assessed the safety, efficacy and cost effectiveness of vaginal misoprostol tablet with vaginal dinoprostone tablet for induction of labour reported that vaginal misoprostol was more effective, reasonably safe and less expensive. Hyperstimulation only occurred in one multiparous women treated with misoprostol. (abstract does not report dosage of misoprostol used or indication for induction) An RCT[39] comparing vaginal misoprostol with vaginal dinoprostone for induction of labour in term pregnancies reported significantly shorter induction to labour and induction to delivery with vaginal misoprostol. There was no significant difference in uterine hyperstimulation and there were no cases of uterine rupture. An RCT[40] which compared dinoprostone vaginal inserts with or without oxytocin and misoprostol with oxytocin for labour induction in nulliparous women with prolonged pregnancies reported that all three methods were equally efficient at achieving successful delivery without any maternal and fetal adverse outcomes. (dosage not reported) <u>Difference in safety not reported in the abstract</u> An RCT[41] based in Singapore compared 25 micrograms of misoprostol pessaries as a single- or double-dose compared with 3 mg of dinoprostone pessary for cervical priming in term pregnancies. The study found that a larger proportion of women had achieved a favourable Bishop score > 6 or active labour by day 2 in the misoprostol double-dose group and the dinoprostone group with no difference in time from insertion to delivery, cardiotocographic abnormalities, delivery and neonatal outcomes.	

	A secondary analysis from the Misoprostol Vaginal Insert Trial [42] considered overall factors contributing the successful labour in women requiring cervical ripening with both dinoprostone and misoprostol vaginal inserts. The analysis found that factors predicting successful induction of labour were: multiparity, BMI less than 30, height greater than 5'5", baseline modified Bishop score of 4, birth weight below 4 000 g, maternal age younger than 35 years and Hispanic race. African-American race was correlated with a higher incidence of caesarean delivery. <u>Safety outcomes significantly worse with misoprostol</u> An RCT[43] which compared vaginal misoprostol (50 micrograms every four hours up till 5 doses) with vaginal PGE2 tablet for labour induction at term. This study reported that misoprostol was more effective at successfully inducing the patient but it did not reduce the caesarean section rate and was associated with an increased chance of fetal distress. The study recommended that studies with lower doses of misoprostol are recommended. An RCT[44] based in Nepal compared 50 micrograms of intravaginal misoprostone with 0.5 mg of dinoprostone gel for induction of labour at term. The study found a slightly higher rate of caesarean section in the dinoprostone group and a significant reduction in need for oxytocin augmentation with vaginal misoprostol, but a slightly higher proportion with abnormal fetal heart rate. However, the study found no significant difference in uterine hyperstimulation, meconium passage, improvement in Bishops score, or induction to delivery time. An RCT[45] compared 50 micrograms of vaginal misoprostol at 6 hour	

	intervals (maximum of 3 doses) with 3 mg vaginal PGE2 for labour induction. Mean interval from induction to delivery was significantly longer with PGE2 and oxytocin was used more frequently but there was no statistically significant difference in feta heart rate, mode of delivery or need for neonatal intervention. However, there was a higher rate of tachysystole with misoprostol. *Economic analysis of vaginal PGE2 vs vaginal misoprostol* An RCT[38] which assessed the safety, efficacy and cost effectiveness of vaginal misoprostol tablet with vaginal dinoprostone tablet for induction of labour reported that vaginal misoprostol was more effective, reasonably safe and less expensive. (abstract does not report dosage of misoprostol used, indication for induction, or how cost-effectiveness was assessed) **Summary of vaginal PGE2 compared with misoprostol (in circumstances other than intrauterine fetal death)** In current guideline, misoprostol was not recommended for indications other than intrauterine fetal death because of the licensing issues, a risk of uterine hyperstimulation at higher doses (>25 micrograms), and the difficulty in achieving accurate lower doses with currently available preparations (100 or 200 micrograms). The new evidence that compared the safety of vaginal misoprostol with vaginal PGE2 was inconclusive. A large proportion of new evidence reported no significant differences in safety at 25, 50, 100 or 400 microgram doses while a smaller number showed worse safety outcomes with vaginal misoprostol at 50 microgram doses. While this is based on the information given in the abstracts only (where the level of details about the	

	occurrence of uterine hyperstimulation varied), there does not appear to be conclusive new evidence that doses greater than 25 micrograms are associated with higher rates of uterine hyperstimulation. As a result of the lack of evidence to suggest otherwise and the fact that misoprostol remains unlicensed for use in induction of labour, it is unlikely that the recommendations in current guideline would change. *Compared with balloon catheter* There were 3 RCTs comparing a balloon catheter with vaginal PGE2. • One Australian RCT[46] compared PGE2 gel with both single and double balloon catheters for nulliparous women with an unfavourable cervix. There was no difference in caesarean delivery rates. Uterine hyperstimulation occurred only in patients treated with PGE2, umbilical cord blood gases occurred most often in the PGE2 group, and PGE2 was associated with the most pain. The study concluded that the single balloon catheter offers the best combination of safety and patient comfort (abstract does not explicitly state that this was compared with 'vaginal' gel but this is assumed as this is the known administration of PGE2 gel). • An RCT[47] from Pakistan comparing intracervical Foley catheter balloon with PGE2 vaginal pessary for induction of labor reported that induction to delivery was significantly shorter, significantly more women needed oxytocin infusion for augmentation of labour, and there were less episodes of uterine hyperstimulation (though this was not significant) in	

	catheter group. • One RCT[33] found that the balloon catheter had the shortest induction to delivery interval than 25 micrograms of intravaginal misoprostol (every 4 hours) or 2 mg intravaginal PGE2/dinoprostone (every 4 hours) in prolonged pregnancy. The study reported that the maternal and neonatal outcomes were similar in all groups. This evidence is inconsistent with current guideline which does not recommend the use of balloon catheter, and that vaginal PGE2 is the preferred method of induction. Current recommendations are based on evidence comparing balloon catheters with intracervical prostaglandins and vaginal misoprostol only. However, it is unlikely that this limited evidence identified would be sufficient to change the current recommendations. *Compared with nitric oxide donors* One RCT[48] found that isosorbide dinitrate is associated with a lower duration of labour compared with vaginal dinoprostone (PGE2) but there was no difference in maternal or fetal outcome. The cost was higher for women treated with dinoprostone (abstract does not report if vaginal dinoprostone was given with a tablet, gel or pessary). Nitric oxide donors are not recommended in current guideline. Current guideline included an RCT showing that they are better than placebo at inducing labour but another RCT based in the UK showed that vaginal PGE2 gel was better at inducing labour. This new RCT has conflicting	

	results to the RCT included in the current guideline. However, the sample of this new study is very small compared to the RCT included in the current guideline (33 vs 33 patients compared with 199 vs 199 patients). Hence, it is unlikely to be sufficient to change the guideline recommendations.	
Is vaginal PGE2 more cost-effective as a tablet, gel, or pessary? Relevant section of guideline As above.	Through the high level RCT search six studies were identified that compared the administration of vaginal PGE2 as a gel or a pessary but only one study performed a cost-effectiveness analysis. Through the focused search one additional study was identified which compared gel with pessary administration of vaginal PGE2 but it did not perform a cost-effectiveness analysis. A cost-effectiveness analysis performed alongside a UK-based RCT[49] was found. The study compared the use of a vaginal PGE2 pessary (Propess) with vaginal PGE2 gel (Prostin) for induction of labour at term, reporting no significant differences in induction-to-delivery interval, mode of delivery, or the number of women delivering within 24 h and neonatal outcomes. However, the study found that the number of vaginal examinations was significantly lower in the group treated with the pessary. The pessary was found to be more cost effective compared with gel, largely as a result of needing only a single dose and less time required with a midwife. <u>Summary of studies of clinical effectiveness from both high-level and focused searches:</u> A number of studies reported about the clinical effectiveness of different methods of administration and are included here as the results could influence inputs into an economic model. A Cochrane review[50] found that tablet, gel and pessary appear to be equally efficacious at induction of labour, but use of a pessary was associated with a reduction in vaginal	Some new evidence identified but unlikely to be sufficient to change current recommendation(s).

	delivery rates. The review concluded that further research is needed to assess the best vehicle for delivering vaginal prostaglandins including cost-analyses. In addition, there were five new RCTs which compared a vaginal pessary with vaginal gel (four based in Italy and one in Poland). Of the four based in Italy, one[51] reported that patient satisfaction was equally good but that the application of the pessary causes more discomfort than the vaginal gel, one[52] found both were safe but there was significantly higher rate of spontaneous vaginal delivery with a pessary, one[53] concluded that both are equally efficacious but the pessary is preferred because it reduces pain, and one[54] concluded that both are efficient at cervical ripening and successful labour but the gel significantly reduced the time to vaginal delivery in multiparous women, regardless of Bishop score. The Polish study [55] reported that vaginal inserts (pessary) seemed to influence both uterine cervix and muscle while gel prepared the uterine cervix for delivery more effectively. The results from these new studies are not conclusive and, therefore, unlikely to change the current recommendations.	
Studies found in the high-level search related to methods of induction but not covered in the focused searches above	The high-level RCT search identified 58 studies about pharmacological-based methods in induction of labour, 10 studies on non-pharmacological-methods in induction of labour, and 12 studies on mechanical methods in women undergoing induction of labour. *Intracervical PGE2*	

	A Cochrane review[56] found that intracervical PGE2 appears to be effective when compared to placebo but inferior to intravaginal PGE2. However, the review found that current trials are too small to provide useful information about intracervical prostaglandins. An RCT[57] compared intravaginal misoprostol (25 microgram 4- hourly) with intracervical Cerviprime for induction of labour in women with unfavourable cervix. The study found that the rate of complications was comparable and that misoprostol had a shorter induction to delivery interval concluding that it is a safe and effective alternative to intracervical PGE2. Another RCT[58] compared oral misoprostol (50 micrograms up to a maximum of 3 doses) with intracervical PGE2 gel for premature rupture of membranes at term found that significantly more women treated with misoprostol delivered within 12 hours and that induction-to-delivery time was significantly shorter than in the PGE2 gel group. Current guideline states that intracervical PGE2 should not be used for induction of labour; this new evidence is consistent with these recommendations. *Intravenous oxytocin alone* A Cochrane review[6] including 61 trials (some RCT and some quasi experimental) found that prostaglandin agents probably increased chances of a vaginal birth within 24 hours compared with intravenous oxytocin for cervical ripening and induction of labour and that oxytocin use may increase the rate of epidurals required during labour.	

	An RCT[23] comparing oxytocin with vaginal PGE2 showed that oxytocin seems superior in inducing labour in pregnancies complicated with prelabour rupture of membranes and unfavorable cervixes. The systematic review is consistent with the current recommendation about intravenous oxytocin use (based on systematic reviews) but the more recently published RCT contradicts the recommendations. Current guideline states that intravenous oxytocin alone should not be used for induction of labour; this new evidence is consistent with these recommendations. *Misoprostol* As stated above, misoprostol is only currently recommended for intrauterine death and this is off-label use since it is not currently licensed in pregnancy. There was one new RCT on the use of misoprostol in intrauterine fetal death[13] comparing vaginal misoprostol with sulprostone (a synthetic analogue of PGE2). This study reported that both were similarly effective with little difference in side effects apart from hyperthermia, which was higher with misoprostol but was related to the dosage (but dosage used not reported in the abstract). Women reported a lack of mobility with sulprostone because of the method of administration. The results of this study are not likely to alter the current recommendation. In addition, there were 2 RCTs which included women from 24 weeks' gestation onwards. They may have included women with intrauterine fetal death but the abstract did not explicitly say so: - One[59] which compared misoprostol with oxytocin for preinduction cervical ripening reported similar vaginal delivery rates and a	

	shorter mean time from treatment to delivery in the oxytocin group, but no difference in maternal complications or neonatal outcomes between groups (method of administration and dosage of misoprostol not reported in abstract) - Another[60] which compared vaginal misoprostol with cervical Foley catheter in singleton women with 25 micrograms of vaginal misoprostol (followed by 50 microgram at 3 to 6 hour intervals) or 100 micrograms of oral misoprostol at 4 to 6 intervals, reported delivery within 24 hours was significantly more likely with the catheter and oral misoprostol. Uterine tachysystole occurred significantly less often with vaginal misoprostol. The results of these studies are not likely to alter the current recommendations. The remaining studies (summarised below) report on the use of misoprostol for circumstances other than intrauterine fetal death. <u>Compared with expectant management</u> One RCT[61] which compared oral misoprostol (100 micrograms) with expectant management in the outpatient setting for prolonged pregnancy showed no differences in the route of delivery or neonatal outcomes between groups. <u>Compared with oxytocin (not recommended in the current guideline)</u> One RCT[62] which compared postpartum blood loss after induction with misoprostol or oxytocin for prolonged pregnancy (at least 40 weeks) found misoprostol to be associated with more blood loss, especially in women	

	with a high Bishop score, suggesting it is better reserved for cases requiring cervical ripening. (dosage of misoprostol used not reported in abstract) A multi-centre RCT[63] based in Nigeria which compared misoprostol with titrated oxytocin for induction of labour in prelabour rupture of fetal membranes in women after 34 weeks found that misoprostol resulted in a significantly shorter labour and the caesarean section rate was significantly lower and that it is as safe as titrated oxytocin (dosage and method of administration of misoprostol not reported in abstract). Another RCT[64] which compared 50 micrograms of vaginal misoprostol and oxytocin with oxytocin alone in women with term pregnancies found that using misoprostol before starting oxytocin infusion is more effective at labour induction than oxytocin infusion alone in these women. <u>Compared with intracervical balloon catheter (not recommended in the current guideline)</u> A meta-analysis[65] of 9 RCTs comparing Foley catheter with intravaginal misoprostol showed that they had a similar effectiveness as induction agents. (indication for induction not clear in abstract) One RCT[66] found that the mean induction delivery interval was shortest in the vaginal misoprostol group compared with those treated with a Foley catheter or with oral misoprostol in pregnant women at term and that vaginal misoprostol appears to be safe and effective with the least complications. Another RCT[67] which compared 25 micrograms of vaginal misoprostol with Foley catheter plus oxytocin for inducing labour in women at term or post-term reported that vaginal misoprostol is more effective than and as safe	

	as the catheter and oxytocin. Another RCT[68] compared Foley catheter with vaginal misoprostol for cervical ripening but an abstract was not provided. <u>Compared with isosorbide mononitrate (not recommended in the current guideline)</u> One RCT[69] which compared oral misoprostol (every 4 hours up to 4 doses) with vaginal isosorbide mononitrate in women between 32 and 42 weeks' gestation for cervical ripening and labour induction found that the addition of vaginal isosorbide mononitrate to oral misoprostol did not reduce time to vaginal delivery and was associated with headache (dosage of misoprostol not reported in abstract). <u>Different doses or modes of administration of misoprostol:</u> There were 15 RCTs comparing different modes of administration of misoprostol: *Oral vs vaginal* Three RCTs[70,71,72] compared of oral and intravaginal misoprostol (both 50 micrograms) for prolonged pregnancy: two found that oral is as effective and safe as the intravaginal route and one found induction to delivery shorter in the oral group, abnormal contractility pattern was more common on the vaginal group but no difference in mode of delivery, neonatal outcomes or maternal side-effects.	

	One RCT[73] of women between 34 and 42 weeks' gestation found that after 20 ml of titrated misoprostol solution (1 microgram per ml) every 1 hour (4 doses) resulted in a lower incidence of uterine hyperstimulation and a lower caesarean delivery rate than 25 micrograms of vaginal misoprostol every 4 hours. Another study[74] made a similar comparison but no abstract was available. One RCT[75] found a 25 mg vaginal tablet of misoprostol as effective as 100 mg of oral misoprostol for term pregnancies. *Sublingual vs vaginal* A systematic review[76] which compared sublingual with vaginal misoprostol in term pregnancy found that the sublingual route is as effective but that the safety, optimal dosage and perinatal outcomes are not yet known. One RCT[77] reported no difference in efficacy or maternal and fetal complications in women induced at term (dosage 25 micrograms); another RCT[78] of women induced in the third trimester with a viable fetus also reported that the sublingual route was as effective and also reported that patients were more satisfied with the sublingual misoprostol (dosage 50 micrograms). *Sublingual vs oral* One RCT[79] which compared 50 micrograms sublingual with 100 micrograms oral misoprostol in women with prelabour rupture of membranes at term found both routes comparable.	

	Different dosages An RCT[80] of women with modified Bishop scores of 4 or lower found a 200 microgram dosage was associated with a significant reduction in time to vaginal delivery but did not improve the proportion with vaginal delivery by 24 hours compared with 100 or 150 micrograms. Three RCTs based in India compared intravaginal 50 microgram dosage with 25 microgram dosage. One[81] which compared a single 50 microgram dose with multiple 25 microgram doses (maximum of three) in women with obstetrical or medical indications for labour induction showed no significant differences in side effects, neonatal outcomes or clinical efficacy. Another[82] compared the same doses given every 4 hours with a maximum of five doses until the patient had three contractions in 10 minutes; the study found that more women with the smaller sized dosage required oxytocin augmentation but that there were no significant differences in type of delivery, meconium stained liquor, fetal distress, incidence of hyperstimulation, or neonatal outcomes. The third[83] which compared 25 micrograms with 50 micrograms was retrieved but no abstract was provided. *Overall Summary* As misoprostol remains unlicensed for use in pregnancy, it is unlikely that this new evidence would alter the recommendations in the current guideline to recommend misoprostol for circumstances other than intrauterine fetal death.	

	Evidence about the appropriate method of administration of misoprostol suggests that oral or buccal misoprostol may be as effective at induction in circumstances other than intrauterine fetal death. However, these results may not be applicable when terminating pregnancy when intrauterine fetal death occurs. As a result, the current recommendations for intrauterine fetal death which recommend the use of vaginal misoprostol are not likely to be changed. *Mifepristone* An update to a Cochrane review[84] reported that there is insufficient information to support the use of mifepristone to induce labour for third trimester cervical ripening or induction of labour. The review commented that some studies have suggested that its use can reduce caesarean sections for failed induction but stated that further research needs to be done. In current guideline, mifepristone is recommended only in intrauterine fetal death so these results are not likely to have an impact on the current recommendations. *Vaginal nitric oxide donors* An RCT[85] comparing nitric oxide donor isosorbide dinitrate with dinoprostone (PGE2) for cervical ripening before induction of labor at term was found but there was no abstract provided. It is not possible to see if this is consistent with the current guideline which recommends that vaginal	

	nitric oxide donors are not used. *Acupuncture* A systematic review[86]which examined the effect of acupuncture on induction of labour from 10 studies (not clear if these were RCTs) was retrieved. The study concluded that while some existing studies suggest that acupuncture may be beneficial in labour, its definitive role is still yet to be established and further randomised trials are needed. Seven RCTs were published comparing acupuncture to sham: - Three RCTs (n = 364, 89, 125)[87,88,89] found acupuncture not to be effective at reducing the need for induction methods, the duration of labour, or the caesarean section rate in women with prolonged pregnancy. - A smaller RCT (n = 16)[90] found that women treated with acupuncture had a shorter period from intervention to delivery and had shorter labours by a mean of 2 hours and 2 minutes (no significance was reported in the abstract). - Three more RCTs[91,92,93] (2 were double-blind) were found but the abstracts were not provided. The title of one study suggests that the results were negative. These findings are inconsistent and unlikely to change the current recommendations that acupuncture not be used for induction of labour.	

	Homeopathy A Cochrane review[94] reported that there is not enough evidence to show the effect of homeopathy for inducting labour. This is consistent with the current guideline recommendations. *Sexual intercourse* An RCT[95] of women requiring non-urgent labour induction compared women who were coitally active with women who were abstinent. It is not clear from the abstract if this has incorrectly been classified as a randomised study as the authors describe that the women were categorised based on what they wrote in a diary. The study found that women who reported coitus were less likely to go into spontaneous labour prior to their scheduled labour induction. This is consistent with the current guideline recommendations. *All mechanical methods* A systematic review[96] including 30 RCTs comparing mechanical methods (catheter, with or without extraamniotic saline solution infusion, Laminaria, or hygroscopic dilators) with pharmacological agents or placebo reported maternal and neonatal infectious morbidity is increased when mechanical agents are used for cervical ripening. This is consistent with the current guideline recommendations that mechanical methods should not be used.	

	Balloon catheters (not currently recommended) Balloon catheters are currently not recommended but, as stated above, there is some new evidence suggesting that it may be better than vaginal PGE. There were four additional RCTs which comparing different variations in catheter use. Two[97,98] compared a 30 ml with a 60 ml Foley balloon catheter. One reported that a 60 ml balloon was more likely to achieve delivery within 12 hours but that there was no difference in delivery within 12 hours caesarean delivery, labour complications or neonatal outcomes but there was no abstract provided for the other study. Another study[99] compared the use of a Foley catheter with a double balloon catheter in both nulliparous and multiparous women but an abstract was not provided. One RCT [100] found that the addition of oxytocin to use of a Foley catheter had no effect on the likelihood of delivery within 24 hours, vaginal delivery rate or time to delivery and that these patients had an increased use of analgesia during ripening. *Extra-amniotic saline infusion* One RCT[101] including nulliparous women with an unfavourable cervix compared women treated with a Foley intracervical catheter with women treated with extra-amniotic saline infusion with concurrent oxytocin for preinduction cervical ripening. The study showed that extra-amniotic saline infusion with oxytocin resulted in a greater change in Bishop score, shorter time to the active phase of labour and was more likely to result in a vaginal delivery without increasing the caesarean rate and maternal or neonatal	

	morbidity. Current guideline does not recommend either intracervical catheter or mechanical methods; these results are not likely to have an impact on the current recommendations.	
Clinical area 2: Setting of induction of labour		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Is outpatient induction as safe as inpatient induction? Relevant section of guideline 6 Recommendations 1.5.1.1 and 1.5.1.2 (and research recommendations)	Through the high level RCT search 7 studies relevant to the clinical question were identified. Through the focused search 2 additional studies relevant to the clinical question were identified. Studies from both searches are summarised below. There were 2 Cochrane reviews: • One[102] compared outpatient with inpatient induction of labour to improve birth outcomes. The study concluded that there is limited data and it is not possible to tell whether induction of labour is effective and safe in outpatient settings. • Another[103] reviewed different methods for induction of labour in outpatient settings. The study stated that induction of labour in outpatient settings is feasible, but that there is insufficient evidence to know which induction methods are preferred by women, or the interventions that are most effective and safe to use in outpatient settings There was a Canadian retrospective cohort study[104] comparing inpatient (n = 776) and outpatient (n = 567) inductions of labour using a dinoprostone vaginal insert. The indications for induction varied slightly between groups	Some new evidence identified but unlikely to be sufficient to change current recommendation(s).

	(outpatient more post-term gestations and inpatient more likely to have premature rupture of membranes). Outpatients had significantly higher use of epidural analgesia and oxytocin, were less likely to deliver vaginally within 24 hours and were less likely to have a Caesarean section. There were no significant differences in serious complications or fetal outcomes. A quasi-experimental study[105] of patients > 41 weeks of 392 women (half treated with endocervical PGE2 gel in the ambulatory setting and half in the control group – not described in the abstract) showed that those with PGE2 use had decrease in rate of caesarean delivery without increments of fetal and maternal morbidity (there were 2 intrauterine deaths in the control group) (intracervical PGE2 gel was not recommended in the guideline) Current guideline commented about the lack of evidence in this area, particularly from the UK. However, none of these new studies are based in the UK. <u>Studies looking at cervical ripening in the outpatient setting</u> A number of studies compared different methods of induction in an outpatient setting but did not give an overall assessment of outpatient compared with inpatient induction were retrieved and are summarised briefly below. An American RCT[61] which looked at the use of outpatient oral misoprostol compared with placebo (each for 3 days) for cervical ripening in women at 40 to 42 weeks found no differences in route of delivery or neonatal outcomes between the groups but did find that women in the intervention group had shortened time intervals from dosing to entry into active labour	

	and delivery. Three more publications looked at nitric oxide donors which are not currently recommended in the guideline. A UK based RCT (IMOP)[106] compared self-administered vaginal isosorbide mononitrate (IMN) for cervical ripening in an outpatient setting before induction of labour with placebo, reporting that IMN was more effective at inducting a change in Bishop score than placebo but it did not shorten the time to admission for delivery. An extrapolation from the same study[107] found that women preferred the opportunity to stay at home during the cervical ripening process and all but two who had problems with the IMN (not further described in the abstract) would repeat the experience. Another RCT[108] of outpatient IMN use showed that it resulted in shorter admission to delivery interval than placebo and was associated with less prostaglandin use and lower incidence of uterine tachysystole. <u>Economic evaluation</u> A UK-based cost-effectiveness analysis[109] of performing outpatient cervical ripening with IMN reported that a probability that IMN is cost-effective of 0.7 at low willingness to pay thresholds for an hour prevented from hospital admission to delivery, but stated that these results should be viewed in light of the findings from the IMOP study above. Again, nitric oxide donors are not recommended in the current guideline; this study is unlikely to change the current recommendations.	

Several ongoing clinical trials (publication dates unknown) were identified focusing on the use of vaginal PGE2 compared to other methods of induction (with balloon catheter, misoprostol, or oxytocin) or outpatient induction (an open-label, feasibility study based in the UK looking at a monitoring device for outpatient use after administration with vaginal PGE2 pessary).

No evidence was identified that was relevant to research recommendations in the original guideline.

In conclusion, some new evidence was identified during the review process but unlikely to be sufficient to change current guideline recommendations.

2.2 Guideline Development Group and National Collaborating Centre perspective

A questionnaire was distributed to GDG members and the National Collaborating Centre to find out their views about the need for a guidance update. Five responses were received, with respondents highlighting:

- the current debate in choosing between different methods of administration of vaginal PGE2 (as pessary [Propess] or gel/tablets [Prostin])
- general uncertainty among the clinical community regarding induction of labour for preterm prelabour rupture of membranes before 34 weeks
- that in the current pressure for cost savings in the NHS, outpatient induction is being considered or cost savings in the current drive for cost savings in the NHS.

Two respondents felt that there was sufficient variation in current practice related to the methods of vaginal PGE2 administration but there was some uncertainty about whether this was supported by adequate new evidence to warrant an update of the guideline. For the other topic areas highlighted the respondents generally felt that while there was sufficient variation in practice there was not likely to be sufficient new evidence to warrant an update of the guideline at this time.

Further discussions with the clinical lead at the National Collaborating Centre highlighted also the uncertainty around failed inductions. However, no new evidence about the management of failed induction was identified.

2.3 Implementation and post publication feedback

41 enquiries were received from post-publication feedback, most of which were routine. Post-publication feedback varied and there were no overall themes.

There were a number of requests for clarification of the evidence behind recommendations such as repeated inductions after failed attempts and use of membrane sweeping. Some individual queries included guidance on caring for bereaved parents who experienced intrauterine death, questions for clarification on dosing, and whether the recommendations about a vaginal examination for a membrane sweep should happen in nulliparous women at 40 and 41 weeks if the head is still free. This feedback contributed towards the development of the clinical questions as described above.

Feedback from NICE implementation team indicated that the recommendations about providing information were thought to be very important but some voiced concerns about how much time would be allocated to this locally. There were some uncertainties about the current baseline practice of membrane sweeping, and that membrane sweeps were likely to add to the workload of services. There were also some concerns about the recommendations on the use of prostaglandins (thought by some to be substantially different than current practice and based on inconclusive evidence).

No new evidence was identified through post publication enquiries or implementation feedback that would indicate a need to update the guideline.

2.4 Related NICE guidance

The following NICE guidance is related to CG70:

Guidance	**Review date**
CG54: Intrapartum care: management and	February 2011; this is

delivery of care to women in labour (2008)	currently being updated
CG13: Caesarean section (2004)	2009; this is currently being updated
Related NICE guidance not included in CG70	
CG62: Antenatal care: routine care for the healthy pregnant woman (2008)	April 2011
CG45: Antenatal and postnatal mental health (2007)	July 2011
CG63: Diabetes in pregnancy (2008)	May 2011
CG107: Hypertension in pregnancy: The management of hypertensive disorders during pregnancy (2010)	August 2013

2.5 Anti-discrimination and equalities considerations

No evidence was identified to indicate that the guideline scope does not comply with anti-discrimination and equalities legislation. The original scope includes women undergoing induction of labour for prolonged pregnancy, preterm rupture of membranes, prelabour rupture of membranes, presence of fetal growth restriction, previous caesarean section, history of precipitate labour, maternal request, breech presentation, intrauterine fetal death, or suspected macrosomia.

3 Conclusion

The process did not identify any additional areas that were not covered in the original guideline scope or that would indicate a significant change in current clinical practice. Although some new evidence was identified during the review process, the volume of evidence is unlikely to be sufficient to change current guideline recommendations. No other factors described above would invalidate or change the direction of current guideline recommendations. Therefore, the Induction of labour guideline should not be updated at this time.

4 Review recommendation

The guideline should not be updated at this time.

The guideline will be reviewed again according to current processes.

Centre for Clinical Practice

29 August 2011

Appendix A

1 Gulmezoglu AM, Crowther CA, and Middleton P. (2009) Induction of labour for improving birth outcomes for women at or beyond term. Cochrane Database of Systematic Reviews

2 Wennerholm UB, Hagberg H, Brorsson B et al. (2009) Induction of labor versus expectant management for post-date pregnancy: is there sufficient evidence for a change in clinical practice?. [Review] [43 refs]. Acta Obstetricia et Gynecologica Scandinavica 88:6-17.

3 Mozurkewich E, Chilimigras J, Koepke E et al. (2009) Indications for induction of labour: a best-evidence review. [Review] [54 refs]. BJOG: An International Journal of Obstetrics & Gynaecology 116:626-636.

4 Mol BW, Vijgen S, Opmeer B et al. (2011) Economic analysis of induction of labor versus expectant management in women with preterm prelabor rupture of membranes between 34 and 37 weeks (PPROMEXIL trial ISRCTN29313500). American Journal of Obstetrics and Gynecology 204:S336-

5 Dare MR, Middleton P, Crowther CA et al. (2006) Planned early birth versus expectant management (waiting) for prelabour rupture of membranes at term (37 weeks or more). Cochrane Database of Systematic Reviews

6 Alfirevic Z, Kelly AJ, and Dowswell T. (2009) Intravenous oxytocin alone for cervical ripening and induction of labour. [Review] [166 refs][Update of Cochrane Database Syst Rev. 2001;(3):CD003246; PMID: 11687060]. Cochrane Database of Systematic Reviews CD003246-

7 Javaid MK, Hassan S, and Tahira T. (2008) Management pre labour rupture of the membranes at term; induction of labor compared with expectant. Professional Med J 15:216-219.

8 Hamdan M, Sidhu K, Sabir N et al. (2009) Serial membrane sweeping at term in planned vaginal birth after cesarean: a randomized controlled trial. Obstetrics & Gynecology 114:745-751.

9 Boers KE, Vijgen SM, Bijlenga D et al. (2010) Induction versus expectant monitoring for intrauterine growth restriction at term: randomised equivalence trial (DIGITAT). BMJ 341:c7087-

10 Dodd JM and Crowther CA. (2010) Misoprostol for induction of labour to terminate pregnancy in the second or third trimester for women with a fetal anomaly or after intrauterine fetal death. [Review] [72 refs]. Cochrane Database of Systematic Reviews CD004901-

11 Gomez Ponce de LR and Wing DA. (2009) Misoprostol for termination of pregnancy with intrauterine fetal demise in the second and third trimester of pregnancy - a systematic review. [Review] [52 refs]. Contraception 79:259-271.

12 Geels YP, de Gouberville MC, Visser L et al. (2010) Comparing vaginal and sublingual administration of misoprostol for labour induction in women with intra-uterine fetal death. Tropical Doctor 40:77-80.

13 Van MK, Claerhout F, Debois P et al. (2009) A randomized controlled trial of misoprostol and sulprostone to end pregnancy after fetal death. Obstetrics & Gynecology International 2009:496320.

14 Henriksen T. (2008) The macrosomic fetus: a challenge in current obstetrics. [Review] [174 refs]. Acta Obstetricia et Gynecologica Scandinavica 87:134-145.

15 Bakker JJ, De VR, Pel M et al. (2009) Start of induction of labour with oxytocin in the morning or in the evening. A randomised controlled trial. BJOG: An International Journal of Obstetrics & Gynaecology 116:562-568.

16 Bakker JJ, Verhoeven CJ, Janssen PF et al. (28-1-2010) Outcomes after internal versus external tocodynamometry for monitoring labor.[Erratum appears in N Engl J Med. 2010 May 13;362(19):1849]. New England Journal of Medicine 362:306-313.

17 Caliskan E, Cakiroglu Y, Corakci A et al. (2009) Reduction in caesarean delivery with fetal heart rate monitoring and intermittent pulse oximetry after induction of labour with misoprostol. Journal of Maternal-Fetal & Neonatal Medicine 22:445-451.

18 Mackenzie IZ, Xu J, Cusick C et al. (2011) Acupuncture for pain relief during induced labour in nulliparae: a randomised controlled study. BJOG: An International Journal of Obstetrics & Gynaecology 118:440-447.

19 Rouse DJ, Weiner SJ, Bloom SL et al. (2011) Failed labor induction: Toward an objective diagnosis. Obstetrics and Gynecology 117:267-272.

20 Hill MJ, McWilliams GD, Garcia-Sur D et al. (2008) The effect of membrane sweeping on prelabor rupture of membranes: a randomized controlled trial. Obstetrics & Gynecology 111:1313-1319.

21 Kashanian M, Baradaran H, and Meshki SM. (2010) The effect of membrane sweeping at term pregnancy on the duration of pregnancy and labor induction: A randomized trial. Journal of

Maternal-Fetal and Neonatal Medicine Conference: 22nd European Congress of Perinatal Medicine, 2010 Granada Spain. Conference Start: 20100526 Conference End: 20100529. Conference Publication:226-

22 Kaimal A, Janakiraman V, and Caughey A. (2009) Weekly membrane stripping at 39 weeks is it cost-effective? American Journal of Obstetrics and Gynecology Conference: 2010 30th Annual Meeting of the Society for Maternal-Fetal Medicine, SMFM Chicago, IL United States. Conference Start: 20100201 Conference End: 20100206 Sponsor: March of Dimes. Conference Publication:S63-S64.

23 Kunt C, Kanat-Pektas M, Gungor AN et al. (2010) Randomized trial of vaginal prostaglandin E2 versus oxytocin for labor induction in term premature rupture of membranes. Taiwanese Journal of Obstetrics & Gynecology 49:57-61.

24 Tan PC, Daud SA, and Omar SZ. (2009) Concurrent dinoprostone and oxytocin for labor induction in term premature rupture of membranes: a randomized controlled trial. Obstetrics & Gynecology 113:1059-1065.

25 Gungorduk K, Yildirim G, Gungorduk O et al. (2011) Sustained-release dinoprostone vaginal pessary with concurrent high-dose oxytocin infusion compared to sustained-release dinoprostone vaginal pessary followed 6 h later by high-dose oxytocin infusion for labor induction in women at term with unfavorable cervix: a randomized controlled trial. Gynecologic & Obstetric Investigation 71:32-40.

26 Khooshideh M. (2007) The comparison of misoprostol and dinoprostone for termination of second trimester pregnancy. Journal of Medical Sciences 7:289-293.

27 Hofmeyr GJ, Gulmezoglu AM, and Pileggi C. (2010) Vaginal misoprostol for cervical ripening and induction of labour. [Review][Update of Cochrane Database Syst Rev. 2003;(1):CD000941; PMID: 12535398]. Cochrane Database of Systematic Reviews CD000941-

28 Austin SC, Sanchez-Ramos L, and Adair CD. (2010) Labor induction with intravaginal misoprostol compared with the dinoprostone vaginal insert: a systematic review and metaanalysis. [Review] [36 refs]. American Journal of Obstetrics & Gynecology 202:624-629.

29 Kundodyiwa TW, Alfirevic Z, and Weeks AD. (2009) Low-dose oral misoprostol for induction of labor: a systematic review. Obstetrics & Gynecology 113:t-83.

30 Parisaei M and Erskine KJ. (2008) Is expensive always better? Comparison of two induction agents for term rupture of membranes. Journal of Obstetrics & Gynaecology 28:290-293.

31 Bricker L, Peden H, Tomlinson AJ et al. (2008) Titrated low-dose vaginal and/or oral misoprostol to induce labour for prelabour membrane rupture: a randomised trial. BJOG: An International Journal of Obstetrics & Gynaecology 115:1503-1511.

32 Calder AA, Loughney AD, Weir CJ et al. (2008) Induction of labour in nulliparous and multiparous women: a UK, multicentre, open-label study of intravaginal misoprostol in comparison with dinoprostone. BJOG: An International Journal of Obstetrics & Gynaecology 115:1279-1288.

33 Prager M, Eneroth-Grimfors E, Edlund M et al. (2008) A randomised controlled trial of intravaginal dinoprostone, intravaginal misoprostol and transcervical balloon catheter for labour induction. BJOG: An International Journal of Obstetrics & Gynaecology 115:1443-1450.

34 Ozkan S, Caliskan E, Doger E et al. (2009) Comparative efficacy and safety of vaginal misoprostol versus dinoprostone vaginal insert in labor induction at term: a randomized trial. Archives of Gynecology & Obstetrics 280:19-24.

35 Wing DA and Misoprostol Vaginal Insert Consortium. (2008) Misoprostol vaginal insert compared with dinoprostone vaginal insert: a randomized controlled trial. Obstetrics & Gynecology 112:801-812.

36 Hosli I, Zanetti-Daellenbach R, Gairing A et al. (2008) Selection of appropriate prostaglandin for the induction of labor at term is more predictive for the achievement of delivery within 24 hours than pre-assessed cervical parameters - a prospective, randomized trial. Geburtshilfe und Frauenheilkunde 68:147-151.

37 Pevzner L, Alfirevic Z, Powers B et al. (2009) Cardiotocographic abnormalities associated with misoprostol and dinoprostone cervical ripening and labor induction. American Journal of Obstetrics and Gynecology 201:S124-

38 Begum A, Butt RM, Kouser S et al. (2009) Comparison of dinoprostone (pge2) and misoprostol (pge1) for induction of labor. J Allama Iqbal Med Coll 7:20-24.

39 Saeed GA, Fakhar S, Nisar N et al. (2011) Misoprostol for term labor induction: A randomized controlled trial. Taiwanese Journal of Obstetrics & Gynecology 50:15-19.

40 Tanir HM, Sener T, Yildiz C et al. (2008) A prospective randomized trial of labor induction with vaginal controlled-release dinoprostone

inserts with or without oxytocin and misoprostol+oxytocin. Clinical & Experimental Obstetrics & Gynecology 35:65-68.

41 Tan TC, Yan SY, Chua TM et al. (2010) A randomised controlled trial of low-dose misoprostol and dinoprostone vaginal pessaries for cervical priming. BJOG: An International Journal of Obstetrics & Gynaecology 117:1270-1277.

42 Pevzner L, Rayburn WF, Rumney P et al. (2009) Factors predicting successful labor induction with dinoprostone and misoprostol vaginal inserts. Obstetrics & Gynecology 114:t-7.

43 Wasim T and Siddiq S. (2008) Comparison of prostaglandin e2 with misoprostol for induction of labor at term. Professional Med J 15:344-349.

44 Shakya R, Shrestha J, and Thapa P. (2010) Safety and efficacy of misoprostol and dinoprostone as cervical ripening agents. Jnma, Journal of the Nepal Medical Association 49:33-37.

45 Sifakis S, Angelakis E, Avgoustinakis E et al. (2007) A randomized comparison between intravaginal misoprostol and prostaglandin E2 for labor induction. Archives of Gynecology & Obstetrics 275:263-267.

46 Pennell CE, Henderson JJ, O'Neill MJ et al. (2009) Induction of labour in nulliparous women with an unfavourable cervix: a randomised controlled trial comparing double and single balloon catheters and PGE2 gel. BJOG: An International Journal of Obstetrics & Gynaecology 116:1443-1452.

47 Naseem A, Nouman D, Iqbal J et al. (2007) Intracervical foley`s catheter balloon versus prostaglandin e2 vaginal pessary for induction of labor. J Rawal Med Coll 12:94-99.

48 Romero-Gutierrez G, Gonzalez OEB, and de Leon ALP. (2011) Isosorbide and dinoprostone for induction of labor OT - Isosorbide y dinoprostona en induccion del trabajo de parto. Ginecologia y Obstetricia de Mexico 79:285-291.

49 Kalkat RK, McMillan E, Cooper H et al. (2008) Comparison of Dinoprostone slow release pessary (Propess) with gel (Prostin) for induction of labour at term-a randomised trial. Journal of Obstetrics & Gynaecology 28:695-699.

50 Kelly AJ, Malik S, Smith L et al. (2009) Vaginal prostaglandin (PGE2 and PGF2a) for induction of labour at term. [Review] [143 refs][Update of Cochrane Database Syst Rev. 2003;(4):CD003101; PMID: 14583960]. Cochrane Database of Systematic Reviews CD003101-

51 Ferraiolo A, Dellacasa I, Bentivoglio G et al. (2010) Evaluation of patients' satisfaction of cervical ripening using dinoprostone by either intravaginal gel or pessary: an open-label, randomized, prospective study. Journal of Reproductive Medicine 55:423-429.

52 Triglia MT, Palamara F, Lojacono A et al. (2010) A randomized controlled trial of 24-hour vaginal dinoprostone pessary compared to gel for induction of labor in term pregnancies with a Bishop score < or = 4. Acta Obstetricia et Gynecologica Scandinavica 89:651-657.

53 Zanconato G, Bergamini V, Mantovani E et al. (2011) Induction of labor and pain: a randomized trial between two vaginal preparations of dinoprostone in nulliparous women with an unfavorable cervix. Journal of Maternal-Fetal & Neonatal Medicine 24:728-731.

54 Marconi AM, Bozzetti P, Morabito A et al. (2008) Comparing two dinoprostone agents for cervical ripening and induction of labor: a randomized trial. European Journal of Obstetrics, Gynecology, & Reproductive Biology 138:135-140.

55 Wielgos M, Szymusik I, Kosinska-Kaczynska K et al. (2007) The influence of dinoprostone on uterine cervix ripening and the course of labor. Neuroendocrinology Letters 28:513-517.

56 Boulvain M, Kelly A, and Irion O. (2008) Intracervical prostaglandins for induction of labour. [Review] [148 refs]. Cochrane Database of Systematic Reviews CD006971-

57 Krithika KS, Aggarwal N, and Suri V. (2008) Prospective randomised controlled trial to compare safety and efficacy of intravaginal Misoprostol with intracervical Cerviprime for induction of labour with unfavourable cervix. Journal of Obstetrics & Gynaecology 28:294-297.

58 Nagpal MB, Raghunandan C, and Saili A. (2009) Oral misoprostol versus intracervical prostaglandin E2 gel for active management of premature rupture of membranes at term. International Journal of Gynaecology & Obstetrics 106:23-26.

59 Fonseca L, Wood HC, Lucas MJ et al. (2008) Randomized trial of preinduction cervical ripening: misoprostol vs oxytocin. American Journal of Obstetrics & Gynecology 199:305-305.

60 Hill JB, Thigpen BD, Bofill JA et al. (2009) A randomized clinical trial comparing vaginal misoprostol versus cervical Foley plus oral misoprostol for cervical ripening and labor induction. American Journal of Perinatology 26:33-38.

61 Gaffaney CA, Saul LL, Rumney PJ et al. (2009) Outpatient oral misoprostol for prolonged pregnancies: a pilot investigation. American Journal of Perinatology 26:673-677.

62 ElSedeek MS, Awad EE, and ElSebaey SM. (2009) Evaluation of postpartum blood loss after misoprostol-induced labour. BJOG: An International Journal of Obstetrics & Gynaecology 116:431-435.

63 Ezechi OC, Loto OM, Ezeobi PM et al. (2008) Safety and efficacy of misoprostol in induction of labour in prelabour rupture of fetal membrane in Nigerian women: a multicenter study. Iranian Journal of Reproductive Medicine 6:83-87.

64 Balci O, Mahmoud AS, Ozdemir S et al. (2010) Induction of labor with vaginal misoprostol plus oxytocin versus oxytocin alone. International Journal of Gynaecology & Obstetrics 110:64-67.

65 Fox N, Saltzman D, Roman A et al. (2011) Intravaginal misoprostol versus Foley catheter for labour induction: a meta-analysis. BJOG: An International Journal of Obstetrics & Gynaecology 118:647-654.

66 Sheikher C, Suri N, and Kholi U. (2009) Comparative evaluation of oral misoprostol, vaginal misoprostol and intracervical Folley's catheter for induction of labour at term. JK Science 11:75-77.

67 Moraes Filho OB, Albuquerque RM, and Cecatti JG. (2010) A randomized controlled trial comparing vaginal misoprostol versus Foley catheter plus oxytocin for labor induction. Acta Obstetricia et Gynecologica Scandinavica 89:1045-1052.

68 Oliveira MVDO, von OP, Leite GKC et al. (2010) Cervical Foley catheter versus vaginal misoprostol for cervical ripening and induction of labor: a randomized clinical trial. Revista Brasileira de Ginecologia e Obstetricia 32:346-351.

69 Collingham JP, Fuh KC, Caughey AB et al. (2010) Oral misoprostol and vaginal isosorbide mononitrate for labor induction: a randomized controlled trial. Obstetrics & Gynecology 116:121-126.

70 Ayaz A, Saeed S, Farooq MU et al. (2009) Labor induction with randomized comparison of oral and intravaginal misoprostol in post date multigravida women. Malaysian Journal of Medical Sciences 16:25-30.

71 Bano K, Mahjabeen, and Bhutta SZ. (2009) Oral versus vaginal misoprostol for induction of labour at term. J Surg Pak 14:38-41.

72 Mehrotra S, Singh U, and Gupta HP. (2010) A prospective double blind study using oral versus vaginal misoprostol for labour induction. Journal of Obstetrics & Gynaecology 30:461-464.

73 Cheng SY, Ming H, and Lee JC. (2008) Titrated oral compared with vaginal misoprostol for labor induction: a randomized controlled trial. Obstetrics & Gynecology 111:119-125.

74 Nassar AH, Abdallah R, and Usta IM. (2008) Titrated oral compared with vaginal misoprostol for labor induction: A randomized controlled trial. Obstetrics and Gynecology 111:1444-1445.

75 Khazardoost S, Hakimi P, Noorzadeh M et al. (2011) Misoprostol for cervical ripening: A clinical trial in 60 pregnant women. Tehran University Medical Journal 68:595-599.

76 Souza AS, Amorim MM, and Feitosa FE. (2008) Comparison of sublingual versus vaginal misoprostol for the induction of labour: a systematic review. [Review] [24 refs]. BJOG: An International Journal of Obstetrics & Gynaecology 115:1340-1349.

77 Beigi A, Kazemipour S-M, and Tabarestani H. (2010) Induction of labor in term pregnancy: Sublingual versus vaginal misoprostol. Tehran University Medical Journal 68:175-181.

78 Zahran KM, Shahin AY, Abdellah MS et al. (2009) Sublingual versus vaginal misoprostol for induction of labor at term: a randomized prospective placebo-controlled study. Journal of Obstetrics & Gynaecology Research 35:1054-1060.

79 Malik HZ, Khawaja NP, Zahid B et al. (2010) Sublingual versus oral misoprostol for induction of labour in prelabour rupture of membranes at term. Jcpsp, Journal of the College of Physicians & Surgeons - Pakistan 20:242-245.

80 Wing DA, Miller H, Parker L et al. (2011) Misoprostol vaginal insert for successful labor induction: A randomized controlled trial. Obstetrics and Gynecology 117:533-541.

81 Girija S and Manjunath AP. (2009) Comparison of two dosing regimens of vaginal misoprostol for labour induction: A randomised controlled trial. Journal of the Turkish German Gynecology Association Artemis 10:220-225.

82 Nigam A, Madan M, Puri M et al. (2010) Labour induction with 25 micrograms versus 50 micrograms intravaginal misoprostol in full term pregnancies. Tropical Doctor 40:53-55.

83 Gupta HP, Singh U, and Mehrotra S. (2010) Comparative evaluation of 25 ug and 50ug of intravaginal misoprostol for induction of labor. Journal of Obstetrics and Gynecology of India 60:51-54.

84 Hapangama D and Neilson JP. (2009) Mifepristone for induction of labour. [Review] [52 refs][Update of Cochrane Database Syst Rev.

2000;(4):CD002865; PMID: 11034779]. Cochrane Database of Systematic Reviews CD002865-

85 Kadian ND. (2008) Comparison of nitric oxide donor isosorbide dinitrate (IDN) and dinoprostone for cervical ripening before induction of labor at term. BJOG: An International Journal of Obstetrics and Gynaecology 115:76-

86 Lim CE, Wilkinson JM, Wong WS et al. (2009) Effect of acupuncture on induction of labor. [Review] [33 refs]. Journal of Alternative & Complementary Medicine 15:1209-1214.

87 Asher GN, Coeytaux RR, Chen W et al. (2009) Acupuncture to initiate labor (Acumoms 2): a randomized, sham-controlled clinical trial. Journal of Maternal-Fetal & Neonatal Medicine 22:843-848.

88 Modlock J, Nielsen BB, and Uldbjerg N. (2010) Acupuncture for the induction of labour: a double-blind randomised controlled study. BJOG: An International Journal of Obstetrics & Gynaecology 117:1255-1261.

89 Smith CA, Crowther CA, Collins CT et al. (2008) Acupuncture to induce labor: a randomized controlled trial. Obstetrics & Gynecology 112:1067-1074.

90 Gaudet LM, Dyzak R, Aung SK et al. (2008) Effectiveness of acupuncture for the initiation of labour at term: a pilot randomized controlled trial. Journal of Obstetrics & Gynaecology Canada: JOGC 30:1118-1123.

91 Fraser R. (2011) Acupuncture for the induction of labour: A double-blind randomised controlled study. BJOG: An International Journal of Obstetrics and Gynaecology 118:376-

92 Huntley AL. (2009) Acupuncture at 38 weeks compared with sham treatment or usual care does not influence onset or type of labour. Focus on Alternative and Complementary Therapies 14:305-306.

93 Uldbjerg N, Modlock J, and Nielsen BB. (2011) Acupuncture for the induction of labour: A double-blind randomised controlled study. BJOG: An International Journal of Obstetrics and Gynaecology 118:377-

94 Smith CA. (2003) Homoeopathy for induction of labour. Cochrane Database of Systematic Reviews

95 Tan PC, Yow CM, and Omar SZ. (2009) Coitus and orgasm at term: effect on spontaneous labour and pregnancy outcome. Singapore Medical Journal 50:1062-1067.

96 Heinemann J, Gillen G, Sanchez-Ramos L et al. (187) Do mechanical methods of cervical ripening increase infectious morbidity? A systematic review. [Review] [77 refs]. American Journal of Obstetrics & Gynecology 199:177-187.

97 Delaney S, Shaffer BL, Cheng YW et al. (2010) Labor induction with a Foley balloon inflated to 30 mL compared with 60 mL: a randomized controlled trial. Obstetrics & Gynecology 115:1239-1245.

98 Kashanian M, Nazemi M, and Malakzadegan A. (2009) Comparison of 30-mL and 80-mL Foley catheter balloons and oxytocin for preinduction cervical ripening. International Journal of Gynaecology & Obstetrics 105:174-175.

99 Solt I, Ben-Harush S, Kaminskey S et al. (2009) A prospective randomized study comparing induction of labor with the foley catheter and the cervical ripening double balloon catheter in nulliparous and multiparous women. American Journal of Obstetrics and Gynecology 201:S124-

100 Pettker CM, Pocock SB, Smok DP et al. (2008) Transcervical foley catheter with and without oxytocin for cervical ripening: A randomized controlled trial. Obstetrics and Gynecology 111:1320-1326.

101 Ghanaei MM, Sharami H, and Asgari A. (2009) Labor induction in nulliparous women: A randomized controlled trial of foley catheter with extra-amniotic saline infusion. Journal of the Turkish German Gynecology Association Artemis 10:71-75.

102 Kelly AJ, Alfirevic Z, and Dowswell T. (2009) Outpatient versus inpatient induction of labour for improving birth outcomes. [Review] [16 refs]. Cochrane Database of Systematic Reviews CD007372-

103 Kelly AJ, Alfirevic Z, Norman JE et al. (2009) Different methods for the induction of labour in outpatient settings. Cochrane Database of Systematic Reviews

104 Salvador SC, Simpson ML, and Cundiff GW. (2009) Dinoprostone vaginal insert for labour induction: a comparison of outpatient and inpatient settings. Journal of Obstetrics & Gynaecology Canada: JOGC 31:1028-1034.

105 Hernandez-Castro F, Alvarez-Chavez LD, Martinez-Gaytan V et al. (2008) Ambulatory treatment of prolonged pregnancy with prostaglandin E2 gel. Revista Medica del Instituto Mexicano del Seguro Social 46:191-194.

106 Bollapragada SS, Mackenzie F, Norrie JD et al. (2009) Randomised placebo-controlled trial of outpatient (at home) cervical ripening with

isosorbide mononitrate (IMN) prior to induction of labour--clinical trial with analyses of efficacy and acceptability. The IMOP study. BJOG: An International Journal of Obstetrics & Gynaecology 116:1185-1195.

107 Reid M, Lorimer K, Norman JE et al. (2011) The home as an appropriate setting for women undertaking cervical ripening before the induction of labour. Midwifery 27:30-35.

108 Habib SM, Emam SS, and Saber AS. (2008) Outpatient cervical ripening with nitric oxide donor isosorbide mononitrate prior to induction of labor. International Journal of Gynaecology & Obstetrics 101:57-61.

109 Eddama O, Petrou S, Schroeder L et al. (2009) The cost-effectiveness of outpatient (at home) cervical ripening with isosorbide mononitrate prior to induction of labour. BJOG: An International Journal of Obstetrics & Gynaecology 116:1196-1203.