

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## INTERVENTIONAL PROCEDURES PROGRAMME

### **Interventional procedure overview of insertion of a double balloon catheter for induction of labour in pregnant women without previous caesarean section**

In late pregnancy, if the cervix does not dilate fully, several methods can be used to encourage the cervix to open and induce labour. In this procedure, a thin plastic tube (catheter) is passed through the cervix from the vagina to the uterus. Two small balloons on the catheter are inflated either side of the cervix, one inside the uterus and one in the vagina, with the aim of causing the cervix to dilate and inducing labour.

### **Introduction**

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

### **Date prepared**

This IP overview was prepared in November 2014.

### **Procedure name**

- Insertion of a double balloon catheter for induction of labour in pregnant women without previous caesarean section

### **Specialist societies**

- Royal College of Obstetricians and Gynaecologists
- Royal College of Midwives.

## Description

### ***Indications and current treatment***

Induction of labour is the most commonly performed obstetric intervention. It occurs in up to 20% of pregnancies in the UK and is generally carried out when the risks of continuing pregnancy outweigh the benefits. It is usually more painful than spontaneous labour, and epidural analgesia and assisted delivery are more likely to be needed. Maternal and fetal indications for induction of labour include pregnancy-induced hypertensive disorders, diabetes, post-term pregnancy, estimated large-for-date fetus, thrombophilia, intra-uterine fetal growth restriction, oligohydramnios, non-reassuring fetal status and fetal death.

Various methods are used to ripen and dilate the cervix and successfully induce labour in women when the cervix is unfavourable for induction. These include pharmacological methods (prostaglandins in the form of vaginal gels or tablets, or pessaries, and oxytocin as a slow intravenous infusion), surgical methods (amniotomy, alone or with oxytocin) and mechanical methods (laminaria tents and balloon catheters introduced through the cervix into the cervical canal and the extra-amniotic space). The aim of mechanical interventions is to ripen and dilate the cervix and promote onset of labour by applying pressure on the internal cervical os by indirectly increasing local secretion of prostaglandins and oxytocin, or both. Also, mechanisms which involve neuroendocrine reflexes may promote the onset of uterine contractions. A standard Foley urinary catheter is commonly used, with the balloon inflated in the extra-amniotic space and the catheter then put under tension to pull back against the cervical os. Sometimes saline solution is also infused in the extra-amniotic space as an adjunct.

### ***What the procedure involves***

Insertion of a double balloon catheter for induction of labour at term in pregnant women aims to facilitate induction through causing dilation of the cervix when the cervix is unfavourable for induction. The double balloon is claimed to stimulate local prostaglandin release, which leads to cervical ripening, through the 2 balloons squeezing the cervix.

The procedure is usually done with the woman in a lithotomy or supine position. A sterile speculum is inserted into the vagina to gain access to the cervix. The cervix is then prepared by cleaning with an appropriate antiseptic solution before inserting the device. A double balloon catheter (with a uterine balloon and a vaginal balloon) is inserted through the cervical canal and into the uterus, so that the tip of the catheter lies in the extra-amniotic space. The uterine balloon is then inflated with a small amount of saline and the catheter is gently pulled back until the uterine balloon lies against the internal cervical os. The vaginal balloon is also inflated with saline so that it lies against the external cervical os. Both the balloons are inflated with alternative increments of small amounts of saline. Once

the balloons are fully inflated and in place on both sides of the cervix, the speculum is removed. The external end of the device is loosely taped to the woman's inner thigh.

Following the insertion of the double balloon, a fetal non-stress test is done and sometimes extra-amniotic saline is infused at the same time. The mother and fetus are monitored and the device is left in place only for up to about 12 hours. If labour begins, or spontaneous device expulsion or rupture of membranes have occurred, or if fetal distress is suspected, the balloons are deflated and the device is removed to facilitate labour management. If labour does not begin spontaneously, the membranes are ruptured artificially and oxytocin infusion is started.

### ***Outcome measures***

#### **Bishop score**

The Bishop score is a group of measurements 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.

### **Literature review**

#### ***Rapid review of literature***

The medical literature was searched to identify studies and reviews relevant to insertion of a double balloon catheter for induction of labour in pregnant women without previous caesarean section. Searches were conducted of the following databases, covering the period from their commencement to 27.11.2014: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

**Table 1 Inclusion criteria for identification of relevant studies**

<b>Characteristic</b>	<b>Criteria</b>
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Pregnant women without a previous caesarean section.
Intervention/test	Insertion of a double balloon catheter for induction of labour.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

***List of studies included in the IP overview***

This IP overview is based on 1797 patients (of which 848 patients had a double balloon catheter) from 8 randomised controlled trials.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

## Table 2 Summary of key efficacy and safety findings on insertion of a double balloon catheter for induction of labour in pregnant women without previous caesarean section

### Study 1 Salim R (2011)

#### Details

Study type	Randomised controlled trial
Country	Israel (single centre)
Recruitment period	2008–10
Study population and number	n=302 pregnant women with unfavourable cervix at term needing induction of labour 148 DBC versus 154 SBC
Age	DBC mean 29.2 years; SBC mean 28.8 years
Patient selection criteria	Women with fetal or maternal indication for induction of labour, viable singleton pregnancy, cephalic presentation, intact membranes, and Bishop score of 6 or less were included. Any contraindication for vaginal delivery, previous caesarean delivery, low-lying placenta, fetal malformations, intrauterine fetal death, clinical amnionitis, women with Hepatitis B or C, or HIV, and with a history of allergy to latex were excluded.
Technique	DBC: Cook cervical ripening balloon was inserted through the cervix and the balloons either side of the cervix were inflated with 80 ml saline. Catheter taped to the inner thigh without tension. SBC: 16F Foley catheter inserted and filled with 60 ml saline. Catheter strapped to 1 leg on slight tension. Catheter removed after 12 hours if spontaneous expulsion had not occurred. Fetal heart rate monitoring done before and for 60 minutes after catheter insertion. All patients were managed identically and membranes ruptured artificially and oxytocin infused if labour did not commence spontaneously or after catheter removal.
Follow-up	<b>24–48 hours</b>
Conflict of interest/source of funding	No conflicts of interest.

#### Analysis

**Follow-up issues:** Six women in the DBC group (1 chose to discontinue, 2 had spontaneous progression, 1 requested catheter removal because of discomfort and 2 delayed catheter removals) and 3 women in the SBC group (2 chose to discontinue during insertion and 1 delayed catheter removal) were excluded from the analysis.

**Study design issues:** Prospective study with large sample size, randomisation sequence generated in blocks of 10, concealed allocation, blinding was not performed. Management of induction of labour was standardised. Some women had prostaglandin oestradiol before catheter insertion.

Maternal and fetal indications included hypertensive disorders, diabetes, post-term pregnancy, thrombophilia, women's request, intra-uterine growth restrictions, oligohydramnios, non-reassuring fetal status, estimated large for date fetus.

**Study population issues:** Demographic and obstetric parameters were comparable between the 2 groups.

## Key efficacy and safety findings

Efficacy				Safety			
Number of patients analysed: 293				<b>Adverse events</b>			
<b>Delivery and neonatal outcomes</b>					<b>DBC % (n=148)</b>	<b>SBC % (n=145)</b>	<b>p value</b>
	<b>DBC (n=148)</b>	<b>SBC (n=145)</b>	<b>p value</b>				
<b>Time from catheter insertion to delivery (hours)*</b>	<b>19.1±6.8</b>	<b>19.4±6.0</b>	<b>0.80</b>	<b>Total adverse events</b>	<b>7.4 (11)</b>	<b>1.4 (2)</b>	<b>0.02<sup>^</sup></b>
Primiparous women	21.6±6.9 (n=78)	21.6±5.9 (n=77)	0.78	Intra-partum fever>38 <sup>o</sup> C	5.4 (8)	1.4 (2)	0.10
Multiparous women	16.4±5.6 (n=70)	16.8±5.1 (n=68)	0.63	Cord prolapse (emergency caesarean delivery done)	0.7 (1)	0	0.85
<b>Time from catheter insertion to vaginal delivery (hours)*</b>	<b>17.8±6.1</b>	<b>18.9±5.8</b>	<b>0.22</b>	Fetal malpresentation after catheter removal (1 woman delivered vaginally after external cephalic version and 1 had a caesarean section)	1.4 (2)	0	0.70
Primiparous women	20.2±6.4 (n=78)	21.1±5.7 (n=77)	0.79	Bleeding related to catheter insertion	0	0	
Multiparous women	15.6±4.9 (n=70)	16.6±5.0 (n=68)	0.22	Admission to neonatal ICU	2.7 (4)	5 (7)	0.37
<b>Vaginal delivery within 24 hours from catheter insertion % (n)</b>	<b>84.4 (103)</b>	<b>80.8 (105)</b>	<b>0.44</b>	Culture proven sepsis in newborn	1	0	
Primiparous women	64.1 (50/78)	64.9 (50/77)	0.91	Appar score <7 at 5 minutes	0	0	
Multiparous women	92.9 (65/70)	92.6 (63/68)	0.78				
<b>Mode of delivery % (n)</b>							
Spontaneous vaginal delivery	74.3 (110)	85.5 (124)	0.02 <sup>^</sup>				
Assisted vaginal delivery	8.1 (12)	4.1 (6)	0.22				
Caesarean section	17.6 (26)	10.3 (15)	0.09				
<b>Other</b>							
Epidural use % (n)	52.7 (78)	45.5 (66)	0.24				
Mean hospitalisation after delivery (days)	3.48	3.46	0.91				
Birth weight (g)*	3166±483	3215±483	0.39				
*Data are mean ± standard deviation				^Odds ratio 0.17 95% CI 0.04-0.80.			
^Odds ratio 0.49 95% CI 0.26-0.92.							
<b>Spontaneous expulsion compared with planned removal of catheter</b>							
	<b>Spontaneous expulsion (n=124)</b>	<b>Planned removal of catheter (n=169)</b>	<b>p value</b>	<b>Risk ratio (95% CI)</b>			
Time from insertion to delivery*	17.2±6.1	20.8±6.2	0.001	1.10 (1.06–1.15)			
Operative deliveries % (n) (vacuum/caesarean)	12 (15/124)	26 (44/169)	0.003	2.15 (1.26–3.69)			
*Data are mean ± standard deviation							
Abbreviations used: CI, confidence interval; DBC, double balloon catheter; SBC, single balloon catheter; ICU, intensive care unit.							

## Studies 2, 3, 4 Mei-Dan E (2012), Mei-Dan E (2014) – nested study within Mei-Dan E (2012), Walfisch A (2014) – secondary analysis

### Details

Study type	Quasi RCT
Country	Israel (single centre)
Recruitment period	2007–11
Study population and number	n=188 women at term with singleton pregnancy presented for induction of labour 100 DBC without EASI versus 88 control (SBC+EASI) <sup>2</sup> . <b>Nested study:</b> n=186 (60 DBC+EASI versus 126 SBC+EASI) <sup>3</sup> <b>Secondary analysis:</b> n=160 (60 DBC+EASI versus 100 DBC without EASI) <sup>4</sup>
Age	DBC mean 27.7 years; SBC+EASI mean 29.2 years
Patient selection criteria	Women with singleton pregnancy in a vertex presentation with intact membranes at term (37 weeks or more), various indications for induction of labour, unfavourable cervix – Bishop score $\leq 4$ were included. Women with contraindications for a vaginal delivery (placenta previa, non-vertex presentation), presence of ruptured membranes, presence of a uterine scar, and suspected fetal distress or non-reassuring fetal heart rate needing immediate intervention were excluded.
Technique	DBC group (2007–10): Cook's device was inserted through the cervix and the balloons either side of the cervix were inflated with 80 ml saline each. Catheter taped to the inner thigh without tension. Later in the course of study (2010–11), concomitant EASI at a rate of 50 ml/hour was given with DBC. SBC group (2001–11): 30ml Foley catheter (16 Fr) with concomitant EASI at a rate of 50 ml/hour was inserted. Balloon expulsion was monitored and, if not spontaneously expelled, it was removed after 12 hours. Induction of labour (either by intravenous administration of oxytocin or artificial rupture of membranes using standard protocols) commenced if Bishop score was increased by 2 or more points or cervical dilation of 3 cm. In case of failure of method of induction of labour, patient reassessed for a different method.
Follow-up	<b>48 hours</b>
Conflict of interest/source of funding	No conflicts of interest.

### Analysis

**Study design issues:** Large sample size, systematic sampling used for quasi-random allocation – women who presented for induction of labour in even months were assigned to DBC group and those on odd months to SBC group, physicians were not blinded to intervention. Standard protocols for induction of labour and oxytocin were used and management was identical in both study groups, analysis on an intention to treat basis.

Three different analyses performed to compare different combinations of 2 mechanical cervical ripening devices with or without EASI. A nested study (Mei-Dan 2014), within this RCT (Mei-Dan 2012) compared women having a DBC plus EASI (2010–11) to women having a SBC plus EASI (2007–11). A secondary analysis of the same RCT (Walfisch 2014) compared women having a DBC plus EASI to women having a DBC without EASI.

**Study population issues:** There were no significant differences in baseline demographic, obstetric characteristics and indications for induction between groups; 49% (93/188) women were nulliparous or primiparous. Indications included post-term pregnancy, hypertensive disorders, diabetes, non-reassuring fetal heart rate and oligohydramnios. Oligohydramnios was the most common indication for labour in the control group.

**Other issues:** DBC with EASI system was commercially available only during the middle of this study period.





<b>Spontaneous rupture of membranes</b>	86.3 (44)	58.4 (59)	<0.0001
<b>Oxytocin use</b>	94.7 (54)	91.1 (112)	0.55
<b>Epidural use</b>	80 (44)	75.2 (82)	0.56
<b>Delivery mode % (n)</b>			
Spontaneous vaginal delivery	80 (48)	61.6 (77)	0.01
Operative vaginal delivery	11.7 (5)	17.6 (22)	0.12
Caesarean section	8.3 (5)	20 (25)	0.05
<b>Birth weight (g)+</b>	3129±505	3113±537	0.84
<b>Apgar score (0–10) at 5 minutes+</b>	9.9±1.4	9.8±0.5	0.30
<b>Mean hospitalisation length(day)+</b>	4.29±1.8	5.69±2.9	<0.001
<b>Maternal satisfaction (Likert scale, 1–10^)+</b>	7.7±2.8	7.0±2.8	0.42

\*Active labour defined as cervical dilation of 4 cm or more in the presence of regular uterine contractions.

\*\*defined as increase in Bishop score ≥2 points and/or cervical dilation of ≥3 cm

^Higher scores indicating greater satisfaction

+Data are mean ± standard deviation

#### Obstetrical outcomes (secondary analysis of RCT, n=160)<sup>4</sup>

	<b>DBC+EASI (n=60)</b>	<b>DBC-EASI (n=100)</b>	<b>p value</b>
Spontaneous balloon expulsion % (n)	68.5 (37)	51 (51)	0.04
<b>Time from insertion to expulsion (hours, median)</b>	<b>08:30</b>	<b>11:35</b>	<b>0.01</b>
Primiparous (median)	10:20	12:32	0.002
Multiparous (median)	05:50	08:55	0.30
<b>Time from insertion to active labour* (median, hours : minutes)</b>	<b>13:40 (00:10±23:05)</b>	<b>17:30 (01:35±101.00)</b>	<b>0.001</b>
Primiparous (median)	16:11	21:0	<0.001
Multiparous (median)	11:40	14:25	0.06
<b>Time from insertion to delivery (median, hours : minutes)</b>	<b>14:19 (00:40±23:30)</b>	<b>20:45 (03:40±106:30)</b>	<b>&lt;0.001</b>
Primiparous (median)	16:35	24:30	<0.001
Multiparous (median)	13:10	16:18	0.02
<b>Time from removal to delivery (median, hours : minutes)</b>	<b>08:15 (00:29±21:34)</b>	<b>10:50 (00:53±99:30)</b>	<b>0.01</b>
Primiparous (median)	10:56	12:50	0.03
Multiparous (median)	07:20	07:44	0.21
<b>Ripening success** % (n)</b>	96.4 (54)	99 (99)	0.29
<b>Spontaneous rupture of membranes</b>	86.3 (44)	41.7 (35)	<0.001
<b>Oxytocin use</b>	94.7 (54)	89 (89)	0.26
<b>Epidural use</b>	74.6 (44)	68.7 (68)	0.47
<b>Delivery mode % (n)</b>			
Spontaneous vaginal delivery	80 (48)	67 (67)	0.1
Operative vaginal delivery	11.7 (7)	13 (13)	0.57
Caesarean section	8.3 (5)	20 (20)	0.07

<b>Birth weight (g)+</b>	3129±505	3203±565	0.41
<b>Apgar score (0–10) at 5 minutes +</b>	9.9±1.4	9.8±0.	0.53
<b>Hospitalization length (days)+</b>	4.29±1.8	6.69±5.9	<0.001
<b>Maternal satisfaction (Likert scale,1–10^)+</b>	7.7±2.8	6.5±3.2	0.2

\*Active labour defined as cervical dilation of 4 cm or more in the presence of regular uterine contractions.

\*\*Defined as increase in Bishop score  $\geq 2$  points and/or cervical dilation of  $\geq 3$  cm

^Higher scores indicating greater satisfaction

+Data are mean  $\pm$  standard deviation

Multivariate analysis found EASI to be an independent predictor of a shorter insertion to delivery time ( $p=0.03$ ).

#### Summary of 3 studies above<sup>4</sup>

	Caesarean section rate %	Insertion to delivery (median, hours)
<b>Study 2</b>		
DBC	20	20.7*
SBC+EASI	20.7	17.4
<b>Study 3</b>		
DBC+EASI	8.3	14.3*
SBC+EASI	20	15.8
<b>Study 4</b>		
DBC+EASI	8.3	14.3
DBC-EASI	20	20.7*

\*statistically significant differences between the arms ( $p \leq 0.05$ ).

Abbreviations used: DBC, double balloon catheter; EASI, extra-amniotic saline infusion; RCT, randomised controlled trial; SBC, single balloon catheter; VAS, visual analogue scale.

## Study 5 Pennell CE (2009)

### Details

Study type	Randomised controlled trial
Country	Australia (single centre)
Recruitment period	2001–03
Study population and number	n=330 nulliparous women with unfavourable cervix at term needing induction of labour 107 DBC versus 110 SBC versus 113 PGE2 gel.
Age	DBC mean 27 years, SBC mean 26 years, PGE2 mean 27 years
Patient selection criteria	Nulliparous women over 36 weeks' gestation, singleton fetus in cephalic presentation, intact membranes and Bishop's score <4 were included.  Women <16 years, with previous uterine surgery, low-lying placenta, any active or purulent infection of the lower vaginal tract, or an abnormal pre-induction fetal heart rate tracing were excluded.
Technique	DBC: Atad ripener device inserted through the cervix and the balloons either side of the cervix were inflated with 80 ml water. Catheter taped to the inner thigh without tension.  SBC: 16F Foley catheter inserted and filled with 30 ml sterile water. Catheter strapped to 1 leg on slight tension.  Catheters removed after 12 hours if spontaneous expulsion had not occurred. Fetal heart rate monitoring done before and for 60 minutes after catheter insertion.  PGE2 gel (2 mg) was placed in the vagina, repeated 6 hourly, maximum 3 doses (mean 1.8 doses). Fetal heart rate monitoring done before and for 60 minutes after each PGE dose.  Mechanical dilation patients were managed identically and membranes ruptured artificially and oxytocin infused if labour did not commence. In women with spontaneous labour, amniotomy done after cervical dilation of 3 cm, oxytocin augmentation started if there is inadequate progress 4 hours after membrane rupture.
Follow-up	<b>24–48 hours</b>
Conflict of interest/source of funding	No conflicts of interest. Study supported by a grant from the Women and Infants Research Foundation, Australia, and Adeza Biomedical Corporation supported the fetal fibronectin test kits.

### Analysis

**Follow-up issues:** Loss to follow-up described. There were 11 protocol violations (1 woman in the PGE2 group had a Foley catheter inserted after 2 doses of gel, 6 women in SBC group had PGE2 gel after insertion difficulties (n=2) or unsuccessful cervical ripening (n=4), 3 had vaginal delivery and 3 caesarean delivery. Four women in the DBC group had PGE2 gel after catheter removal for maternal side effects (n=2), or unsuccessful cervical ripening (n=2). Two of them had vaginal delivery and 2 had caesarean sections).

**Study design issues:** Large sample size, randomisation was conducted after stratification by fetal fibronectin status, generation of randomisation sequence unclear, sealed opaque envelopes used (patients chose from a selection of 12 envelopes), blinding of participants and providers was not possible but research midwives were blinded to treatment allocation. Rate of caesarean section analysed on an intention-to-treat basis using the Chi-square test.

PGE2 dosage protocol used in the study is different to that recommended by the manufacturer and British RCOG guidelines.

**Study population issues:** Homogenous group of women, no significant differences in baseline characteristics (gestation age, indications, pre-induction cervical assessment and Bishop scores) between groups. Only 5% of women were induced before 37 weeks of gestation. The majority of women had induction for prolonged pregnancy or hypertension. Indications for caesarean section were failed induction of labour, failure to progress in established labour or non-reassuring fetal status based on electronic fetal monitor (EFM) patterns.

## Key efficacy and safety findings

Efficacy					Safety					
Number of patients analysed: 330					<b>Adverse events</b>					
<b>Delivery outcomes</b>						<b>DBC % (n=107)</b>	<b>SBC % (n=110)</b>	<b>PGE2 % (n=113)</b>	<b>p value</b>	
	<b>DBC % (n=107)</b>	<b>SBC % (n=110)</b>	<b>PGE2 % (n=113)</b>	<b>p value</b>						
<b>Mode of delivery % (n)</b>										
Spontaneous vaginal delivery	36 (38)	41 (45)	38 (43)	0.715						
Assisted vaginal delivery	22 (23)	23 (25)	25 (28)	0.845						
Caesarean section	43 (46)	36 (40)	37 (42)	0.567						
<b>Indications for caesarean section</b>				<b>0.168</b>						
Non-reassuring FHR pattern	33 (15)	14 (35)	20 (47)	-						
Failure to progress	21 (46)	35 (14)	41 (17)	-						
Failed induction of labour <sup>^</sup>	22 (10)	30 (12)	12 (5)	-						
<b>Indications for assisted vaginal delivery</b>				<b>0.113</b>						
Non-reassuring fetal heart rate pattern	7 (30)	12 (48)	15 (54)	-						
Other indications	70 (16)	52 (13)	46 (12)	-						
<b>Other outcomes</b>				-						
Induction to delivery time (median, hours)*	24.5 95% CI 23.7– 30.6	23.2 95% CI 20.8– 25.8	23.8 95% CI 21.7– 26.8	0.043						
Time to active labour (median, hours)*	16.1	14.3	14.5	0.014						
Length of labour (hours)	9.8	10.3	9.0	0.152						
Vaginal delivery within 24 hours	37 (40)	48 (53)	43 (49)	0.274						
Use of analgesia (epidural)	83 (89)	81 (90)	81 (92)	0.951						
<sup>^</sup> Defined as inability to rupture the membranes after 3 doses of PGE2 or 12 hours of mechanical ripening or a cervical dilation of <4 cm after 8 hours of strong contractions										
*Estimated from Kaplan–Meier survival analysis										
<b>Neonatal outcomes</b>										
	<b>DBC % (n=107)</b>	<b>SBC % (n=110)</b>	<b>PGE2 % (n=113)</b>	<b>p value</b>						
Birth weight (g)	3540	3405	3440	0.035						
Apgar score <7 at 5 minutes	0	2 (2)	3 (3)	0.378						
<b>Arterial blood gases</b>										
pH	7.26	7.26	7.25	0.050						
					<b>Induction/intrapartum adverse event – discomfort</b> (unable to void in 2 women, decreased balloon volume in 2 women, device removed in 1 woman)	5 (5)	0	17 (15)	<0.001	
					Uterine hyperstimulation with/without FHR changes*	-	-	14 (16)		
					Abruption placenta (emergency caesarean done)	-	-	1 (1)		
					<b>Readmission to hospital</b>	<b>4 (4)</b>	<b>6 (6)</b>	<b>10 (10)</b>	<b>0.455</b>	
					Endometritis	1	2	2	-	
					Wound infection	1	2	3	-	
					UTI, increased vaginal loss and infected perineum	2	2	5	-	
					<b>Other events</b>					
					Postpartum haemorrhage >1000 ml	5 (5)	5 (5)	11 (12)	0.143	
					Maternal temperature during labour (>37.5 C)	17 (18)	17 (19)	18 (20)	0.999	
					Antibiotics during labour	24 (26)	24 (26)	17 (19)	0.316	
					*Defined as either the occurrence of 5 or more contractions in 10 minutes for 2 consecutive 10-minute periods or a contraction lasting at least 2 minutes, with or without changes in FHR patterns.					

pO <sub>2</sub>	15.4	17.5	14.7	0.003
pCO <sub>2</sub>	55.3	53.2	57.8	0.003
Neonatal admissions	21 (20)	29 (27)	33 (29)	0.245

**Patient satisfaction** (assessed using questionnaires 24–48 hours after delivery) (VAS 0–10, with maximum pain or satisfaction scoring 10)

	<b>DBC % (n=107)</b>	<b>SBC % (n=110)</b>	<b>PGE2 % (n=113)</b>	<b>p value</b>
Pain during insertion of ripening device (pain score >4)	NR	NR	NR	0.002
Pain during cervical ripening (pain score >4)	55	36	63	<0.001
Overall satisfaction with induction of labour (median score 8)	NR	NR	NR	0.179

Multivariate regression analysis showed that caesarean section (OR 4.66, 95% CI 2.84–7.65), oxytocin infusion (2.20, 1.08–4.52), gravidity >1 (0.44, 0.25–0.75) were associated with low satisfaction with induction of labour (VAS <8).

Abbreviations used: CI, confidence interval; DBC, double balloon catheter; FHR, fetal heart rate; NR, not reported; OR, odds ratio; PGE2, prostaglandin E2; SBC, single balloon catheter; UTI, urinary tract infection; VAS, visual analogue scale.

## Study 6 Kehl S (2014)

### Details

Study type	Randomised controlled trial
Country	Germany (5 centres)
Recruitment period	2011–12
Study population and number	n=326 pregnant women with an unfavourable cervix undergoing induction of labour at term 168 DBC + OM sequentially versus 158 OM alone.
Age	Mean 30 years in both groups
Patient selection criteria	Pregnant women with singleton pregnancies and a fetus in cephalic presentation at term (>259 days of gestation) with a clinical need for induction of labour were included.  Women with a favourable cervix (Bishop score >8), premature rupture of membranes, previous caesarean section, structural or chromosomal fetal malformation, intrauterine fetal death, placenta previa or any other contraindication to vaginal delivery were excluded.
Technique	DBC: on the first day, Cook's device was inserted through the cervix and the balloons either side of the cervix were inflated with 80 ml saline each. Catheter taped to the inner thigh without tension. If DBC did not fall out spontaneously, it was removed 12 hours after placement. If labour did not start after mechanical ripening, then on second day, 50 mg of OM was given 4 hourly, maximum 3 times. A dose of 100 mg was given up to 3 times after 24 hours if needed, and vaginally 4 hourly, maximum 3 times after 48 hours (on the third day).  OM alone group had the regimen described above from first day.  Artificial rupture of membranes or routine oxytocin administration were not used in this study.
Follow-up	<b>48 hours</b>
Conflict of interest/source of funding	No conflicts of interest.

### Analysis

**Follow-up issues:** In the DBC plus OM group, 6 were excluded from analysis because DBC could not be placed successfully in 4 women and 2 women deviated from the study protocol. In the OM alone group, 7 were excluded as labour started before induction in 4 women and 3 women deviated from the study protocol.

**Study design issues:** Prospective study with large sample size, study conducted in academic and non-academic hospitals, randomisation sequence generated using a computer generated randomisation scheme with 1:1 allocation for each arm of the study, sealed opaque envelopes used to conceal allocation, blinding of participants and providers was not possible. A standardised Bishop score was used in the study.

**Study population issues:** Homogenous group of women, no significant differences in baseline between groups. Majority of women had induction because the pregnancies were at or beyond 41 weeks of gestation.

## Key efficacy and safety findings

Efficacy				Safety			
Number of patients analysed: <b>313</b>							
<b>Maternal and neonatal outcomes</b>							
	<b>DBC + OM % (n=162)</b>	<b>OM % (n=151)</b>	<b>p value</b>		<b>DBC (n=162)</b>	<b>OM (n=151)</b>	<b>p value</b>
<b>Mode of delivery % (n)</b>							
Normal vaginal delivery	67.9 (110)	59.5 (90)	0.13	Chorioamnionitis	0	1	0.23
Surgical vaginal delivery	10.5 (17)	10.6 (16)	0.98	Postpartum endometritis	0	2	-
Caesarean section	21.6 (35)	29.8(45)	0.10	Infection of the new-born	4	1	-
<b>Induction to delivery interval (hours, median)</b>	<b>32.4</b>	<b>22.5</b>	<b>0.004</b>				
Nulliparous	34.1	31.6	0.19				
Parous	31.1	16.1	0.06				
<b>Other</b>							
Vaginal delivery within 48 hours	79.5 (101/127*)	84.9 (90/106*)	0.29				
Number of applications of misoprostol (median, range)	2 (0–11)	3 (1–23)	<0.001				
Total dose of misoprostol (micrograms; median, range)	100 (0–850)	200 (50–1950)	<0.001				
<b>Neonatal outcomes</b>							
Umbilical arterial pH	7.24±0.07	7.24±0.08	0.56				
<b>Apgar score &lt;7 at 5 minutes</b>	<b>4.9 (8)</b>	<b>0.7 (1)</b>	<b>0.04</b>				
Nulliparous	6	1	0.06				
Parous	2	0	0.50				
<b>Other</b>							
Epidural anaesthesia	29 (47)	25.2 (38)	0.44				
Oxytocin	44.4 (72)	44.4 (67)	1.00				
Meconium stained amniotic liquor	15.4 (25)	17.2 (26)	0.67				
*includes normal and surgical vaginal deliveries							
Abbreviations used: DBC, double balloon catheter; OM, oral misoprostol.							

## Studies 7, 8 Kehl S (2011, 2013)

### Details

Study type	Randomised controlled trial
Country	Germany (1 centre)
Recruitment period	2009–10
Study population and number	n=122 women with term pregnancies with an indication for induction of labour 59 DBC + OM sequentially versus 63 OM alone.
Age	Mean 30 years in both groups
Patient selection criteria	Women with singleton pregnancy at term >259 days of gestation; vertex presentation, indication for induction of labour, unfavourable cervix – Bishop score <8 were included. Women with previous caesarean section, structural or chromosomal fetal malformation, intrauterine fetal death, placenta previa were excluded.
Technique	DBC: on the first day, Cook's device was inserted through the cervix and the balloons either side of the cervix were inflated with 80 ml saline each. Catheter taped to the inner thigh without tension. If DBC did not fall out spontaneously, it was removed after 12 hours after placement. If labour did not start after mechanical ripening, then on the second day, 50 mg of OM was given 4 hourly, maximum of 3 times. A dose of 100 mg is given up to 3 times after 24 hours, if needed, and vaginally 4 hourly, maximum of 3 times after 48 hours (on the third day). In women with PROM, induction of labour started after 12 hours after PROM. If PROM occurred when DBC was place, then DBC was removed after 24 hours. OM alone group had the regimen described above from first day.
Follow-up	<b>48 hours</b>
Conflict of interest/source of funding	No conflicts of interest.

### Analysis

**Follow-up issues:** There were 19 incomplete questionnaires from the study group and 25 from the control group, which were excluded from the analysis.

**Study design issues:** Small sample size, random assignment by physicians with 1:1 allocation for each arm of the study. Sealed opaque envelopes were used to conceal allocation. A standardised Bishop score was used in the study.

Another publication of the same study (Kehl 2013) focused on women's acceptance and satisfaction<sup>8</sup>. After childbirth, a standardised questionnaire was given to women to complete before discharge. Level of satisfaction with regard to delivery assessed on a 5-point scale (bad to very good, or not at all to very much) or with 'yes' or 'no'; birth experience was objectively evaluated using SIL-Ger, rated on a scale from 1–7, with a total score of 70 or above indicating a positive birth experience.

**Study population issues:** There were no significant differences in baseline between groups. Most of the inductions were because of post-date pregnancies or PROM. Many women in the study were wary of mechanical labour induction as pharmacological agents are well established for this indication.



## Key efficacy and safety findings

Efficacy				Safety		
Number of patients analysed: 122				<b>Adverse events</b>		
<b>Maternal and neonatal outcomes<sup>7</sup></b>					<b>DBC (n=59)</b>	<b>OM (n=63)</b>
	<b>DBC + OM (n=59)</b>	<b>OM (n=63)</b>	<b>p value</b>			
<b>Mode of delivery % (n)</b>						
Normal vaginal delivery	62.7 (37)	66.7 (42)	0.322	Postpartum endometritis (after caesarean section)	1	0
Surgical vaginal delivery	10.2 (6)	4.8 (3)	0.436	Infection of the newborn	0	1
Caesarean section	27.1 (16)	28.6 (18)	0.10	Nausea and emesis	0	8
<b>Other</b>						
Rate of failure for IOL* (%)	9.3	21.1	0.007	Shivering	0	1
Rate of failure for IOL in women without PROM* (%)	10.8	28.2	0.002	Bladder (urination) problems	2	0
Time for IOL (median, hours)	15.3	20.8	0.158	Foreign body sensation	1	0
Time for IOL in women without PROM (median, hours)	15.8	32.6	0.024	Pain	1	2
Umbilical arterial pH <7	0	0	-			
Apgar score <7 at 5 minutes	1.7 (1)	0	-			
*Defined as no vaginal delivery within 48 hour						
<b>Satisfaction with IOL (n=78)<sup>8</sup></b>						
	<b>DBC + OM % (n=40)</b>	<b>OM % (n=38)</b>	<b>p value</b>			
<b>Labour induction</b>						
Satisfaction with labour induction (quite a lot to very much)	62.5 (25)	63.2 (24)	0.95			
Bothered by swallowing tablets (not at all to moderately)	97 (34)	97 (37)	1.00			
Bothered by placement of DBC (not at all to moderately)	70 (28)	0	0.017			
Bothered by presence of DBC (not at all to moderately)	75 (30)	0	0.002			
Would consider induced labour again and recommend it (quite a lot to very much)	75 (30)	53 (20)	0.040			
<b>Birth experience</b>						
Birth experience (SIL-Ger score)	87.7±15.8	79±17.3	0.030			
Satisfaction with childbirth (good/very good)	77.5 (31)	87 (33)	0.283			
Multivariate analysis showed that 3 independent factors were associated with a positive birth experience: satisfaction with childbirth (p<0.001), involvement in decision-making after childbirth (p=0.041) and method of induction of labour (p=0.005).						
Abbreviations used: DBC, double balloon catheter; IOL, induction of labour, OM, oral misoprostol; PROM, premature rupture of membranes; SIL-Ger, German language version of Salmon Item List.						

## Study 9 Cromi A (2012)

### Details

Study type	Randomised controlled trial
Country	Italy (single centre)
Recruitment period	2010–11
Study population and number	n=210 <b>pregnant women with unfavourable cervixes undergoing labour induction</b> 105 DBC versus 105 PGE2 vaginal insert.
Age	DBC mean 34 years, PGE2 insert mean 33 years
Patient selection criteria	Women presented with a singleton gestation, vertex presentation, Bishop score <6, intact membranes, gestational age ≥34 weeks and reassuring fetal heart tracing on admission were included. Women with antepartum bleeding, intrauterine fetal death, prior uterine scars, positive vaginal or rectal group B streptococcus screening cultures, placenta previa, or any other contraindications to vaginal delivery were excluded.
Technique	DBC: Cook's device was inserted through the cervix and the balloons either side of the cervix were inflated with 50 ml saline each. Catheter taped to the inner thigh without tension. If DBC did not fall out spontaneously, it was removed 12 hours after placement. PGE2 vaginal insert (10 mg controlled-release dinoprostone) placed high in the vaginal fornix and monitored for at least 1 hour and then allowed to ambulate. Discontinued after maximum dosing period (2 hours); onset of labour; uterine contractile abnormalities; or non-reassuring fetal heart rate patterns. Standard oxytocin dose administered to women not in labour after expulsion or removal of device or 1 hour after maximum dose of prostaglandin pessary. Standard intrapartum management according to protocols carried out.
Follow-up	<b>24–48 hours</b>
Conflict of interest/source of funding	No conflicts of interest.

### Analysis

**Follow-up issues:** Two women in PGE2 insert group deviated from protocol and were withdrawn.

**Study design issues:** Random assignment with 1:1 allocation for each arm of the study, concealed allocation, planned sample size, intention to treat analysis performed.

**Study population issues:** There were no significant differences in baseline between groups.

## Key efficacy and safety findings

Efficacy					Safety			
Number of patients analysed: <b>208</b>								
<b>Induction and intrapartum outcomes</b>								
	DBC (n=105)	PGE2 vaginal insert (n=103)	p value	Odds ratio (95% CI)		DBC (n=105)	PGE2 vaginal insert (n=103)	p value
Improvement in Bishop score (median, range)	3 (0-9)	4 (0-10)	0.09	-				
Onset of active labour % (n)	91.4 (96)	90.3 (93)	0.81	-	Device insertion failure (as a result of closed cervix, PGE2 inserted)	2	0	
Time to onset of active labour, hour (mean±SD)	15.6±4.5	16.6±8.8	0.71	-	Accidental expulsion of device (new device reinserted)	2	0	
<b>Mode of delivery (% , n)</b>					Uterine hypertonus* without fetal heart rate changes	0	3.9 (4)	0.002
Vaginal delivery	76.2 (80)	73.8 (76)	0.75	-	Tachysystole ^ with associated fetal heart rate (2 needed emergency caesarean delivery due to persistent abnormal tracing after insert withdrawal)	0	5.7 (6)	
Vacuum delivery	5.7 (6)	1.0 (1)	0.12	-	Postpartum haemorrhage (blood loss of >1000ml)	7.6 (8)	6.8 (7)	0.1
Caesarean section	23.8 (25)	26.2 (27)	0.75	0.88 (0.47–1.65)	*Single contraction lasting at least 2 minutes ^>5 contractions per 10 minutes for at least 20 minutes.			
<b>Other</b>								
Time to delivery, hour (mean±SD)	19.7±5.9	20.4±10.3	0.83	-				
Time to vaginal delivery, hour (mean±SD)	18.8±5.4	19.9±9.6	0.86	-				
Vaginal delivery within 24 hours % (n)	68.6 (72)	49.5 (51)	0.007	2.22 (1.26–3.91)				
Oxytocin administration % (n)	85.7 (90)	54.4 (56)	<0.0001	5.04 (2.58–9.84)				
Epidural rate % (n)	82.9 (87)	61.2 (63)	0.0006	3.07 (1.61–5.84)				
Length of hospitalisation (days; median, range)	3 (2–6)	3 (2–7)	0.73	-				
<b>Neonatal outcomes</b>								
Birth weight (mean±SD)	3268±582	3314±572	0.56	-				
Apgar score <7 at 5 minutes % (n)	7.6 (8)	4.8 (5)	0.57	-				
Umbilical artery blood pH<7.0 % (n)	0.9 (1)	0	1.0	-				
ICU admission % (n)	7.6 (8)	4.8 (5)	0.57	-				
Abbreviations used: CI, confidence interval; DBC, double balloon catheter; ICU, intensive care unit; OM, oral misoprostol; PGE2, prostaglandin E2; SD, standard deviation.								

## Study 10 Wang W (2014)

### Details

Study type	Randomised controlled trial
Country	China (single centre)
Recruitment period	2010–11
Study population and number	n=126 <b>primiparous women with unfavourable cervixes and oligohydramnios undergoing labour induction</b> 66 DBC versus 60 PGE2 vaginal insert (dinoprostone)
Age	DBC mean 27.9 years, PGE2 mean 27.8 years
Patient selection criteria	Women with AFI <5 cm, gestational age beyond 37 weeks, singleton pregnancy, vertex presentation, Bishop score <6, intact membranes, absence of documented uterine contraction, absence of prior caesarean section delivery history, reassuring antenatal fetal testing active and oxytocin challenge test negative were included. Women with antepartum bleeding, chorioamnionitis, placenta previa or any other contraindication to vaginal delivery were excluded from DBC insertion. Women with prostaglandin allergy, maternal asthma history, vaginitis, cervicitis at presentation or glaucoma history were excluded from pharmacological treatment.
Technique	DBC: Cook's device was inserted through the cervix and the balloons either side of the cervix were inflated with 80 ml saline each. Catheter taped to the inner thigh without tension. If DBC did not fall out spontaneously, it was removed 12 hours after placement. PGE2 vaginal tablets (10 mg controlled release dinoprostone) inserted into the posterior vagina fornix, removed after 24 hours or earlier if active labour or non-reassuring fetal heart rate monitoring. Both groups monitored, allowed to ambulate with heart rate monitoring every 2–4 hours, oxytocin used after 24 hours of unsuccessful ripening and also for augmentation in active labour.
Follow-up	<b>48 hours</b>
Conflict of interest/source of funding	No conflicts of interest. Study funded by health department in China.

### Analysis

**Follow-up issues:** Two women in the DBC group were reassigned to the PGE2 group (1 due to catheter insertion failure and 1 refused placement), 3 women from the PGE2 group were reassigned to the DBC group because of non-reassuring fetal heart rate patterns.

**Study design issues:** Random allocation to either group. No allocation concealment and blinding reported.

## Key efficacy and safety findings

Efficacy					Safety				
Number of patients analysed: 126					<b>Adverse events</b>				
<b>Induction and intrapartum outcomes</b>						<b>DBC % (n=67)</b>	<b>PGE2 vaginal insert % (n=59)</b>	<b>p value</b>	<b>OR (95% CI)</b>
Improvement in Bishop score (mean±SD)	4±1.4	3.4±1.4	0.27	-	Excessive uterine activity (tachysystole)	4.5 (3)	16.9 (10)	0.04	0.23 (0.06–0.88)
Bishop score <6 after 12 hours	19.4 (13)	32.2 (19)	0.10	0.51 (0.22–1.15)	Non-reassuring fetal heart rate	1.5 (1)	15.3 (9)	0.01	0.08 (0.01–0.69)
Onset of active labour % (n)	34.3 (23)	50.8 (30)	0.61	0.51 (0.25–1.04)	Birth canal injury	1.5 (1)	8.5 (5)	0.10	0.16 (0.02–1.44)
Oxytocin infusion % (n)	64.2 (43)	22 (13)	0.00	6.34 (2.87–14.01)	Precipitous delivery	1.5 (1)	5.1 (3)	0.34	0.28 (0.03–2.80)
Amniotomy (mean±SD)	73.1 (49)	40.7 (24)		3.97 (1.88–8.40)	Postpartum haemorrhage	1.5 (1)	3.4 (2)	0.60	0.43 (0.04–4.89)
Time to vaginal delivery, min (mean±SD)	1170±323	1122±537	0.54	-	Newborn asphyxia % (n)	4.5 (3)	5.1 (3)	1.00	0.88 (0.17–4.51)
Vaginal delivery within 24 hours	59.7 (40)	61 (36)	0.88	0.95 (0.46–1.94)	Device replacement	2	1	-	-
Caesarean section delivery	16.4 (11)	22 (13)	0.42	0.70 (0.29–1.70)	No serious side effects such as maternal placental abruption and perinatal death reported in either group.				
<b>Neonatal outcomes</b>									
Birth weight (mean±SD)	3157±317	3172±402	0.82	-					
Apgar score <7 at 5 minutes	0	3.4 (2)	0.22	1.04 (0.99–1.09)					
Umbilical cord arterial pH (mean±SD)	7.2±0.6	7.1±0.1	0.06	-					
Umbilical cord arterial pH <7.1	6 (4)	25 (15)	0.03	0.19 (0.06–0.60)					
Neonatal ICU admission % (n)	0	3.4 (2)	0.22	1.04 (0.99–1.09)					
Abbreviations used: AFI, amniotic fluid index; DBC, double balloon catheter; PGE2, prostaglandin E2; SD, standard deviation									

## Study 11 Atad J (1996)

### Details

Study type	Randomised controlled trial
Country	Israel (single centre)
Recruitment period	2010–11
Study population and number	n=95 pregnant women with unfavourable cervixes undergoing labour induction (53 primiparous, 42 multiparous) 35 DBC versus 30 PGE2 vaginal insert versus 30 oxytocin
Age	DBC mean 27.3 years, PGE2 mean 28.5 years, oxytocin mean 27.8 years
Patient selection criteria	Women with singleton pregnancy, vertex presentation, intact membranes, Bishop score 4 or less were included. Women with previous caesarean delivery, abnormal fetal monitoring, and placenta previa were excluded.
Technique	DBC: Atad ripener device was inserted through the cervix and the balloons either side of the cervix were inflated with 100 ml saline each. Catheter taped to the inner thigh without tension. If DBC did not fall out spontaneously, it was removed after 12 hours after placement. In women whose Bishop score was 5 or higher, induction of labour was resumed using artificial rupture of the membranes and/or administration of oxytocin. PGE2 vaginal tablets (3 mg) were inserted if contractions had not started 6 hours later, a second dose of 3 mg was administered in 22 women. The oxytocin group had an initial dose of 1.5 mIU/minute and a constant increase of 1.5 mIU per minute every 20 minutes until 3 contractions in 10 minutes were reached (as long as fetal monitoring was reassuring). Labour was managed according to obstetric criteria in all women.
Follow-up	<b>24–48 hours</b>
Conflict of interest/source of funding	One author had a patient licencing agreement with the manufacturer.

### Analysis

**Study design issues:** Computer generated random assignment to 1 of the 3 arms of the study, allocation concealment unclear, and lack of blinding. Women with method failure (Bishop score of <4) were crossed over to other arms in the study.

Indications for labour induction were pregnancy-induced hypertension, post-date pregnancy, diabetes, elective induction, non-reassuring non-stress test, fetal growth restriction and fetal death.

**Study population issues:** There were no significant differences in baseline between groups.

**Key efficacy and safety findings**

## Efficacy

Number of patients analysed: **95****Induction and intrapartum outcomes**

	<b>DBC (n=35)</b>	<b>PGE2 vaginal insert (n=30)</b>	<b>Oxytocin % (n=30)</b>	<b>p value</b>
Bishop score (median, range)	5 (0–7)	5 (0–9)	2.5 (0–9)	<0.1
Cervical dilation >3 cm (assessed after 12 hours of induction) % (n)	85.7 (30)	50 (15)	23.3 (7)	<0.1
Method failure* % (n)	5.7 (2)	20 (6)	53.3 (16)	<0.001
Induction to delivery, hours (mean±SD)	21.3±7.0	23.2±12.5	28.2±14.7	
Success rate for vaginal delivery % (n)	77.1 (27)	70 (21)	26.7 (8)	<0.01
Caesarean delivery % (n)	20 (7/35)	13.3 (4/30)	46.6 (14/30)	<0.05

\*Defined as a second Bishop score of no more than 4.

**Neonatal outcomes**

Neonatal outcomes were the same for all 3 methods with regard to mean weight Apgar scores at 1 and 5 minutes. Perinatal morbidity was not significantly different among the 3 groups.

Abbreviations used: DBC, double balloon catheter; PGE2, prostaglandin E2; SD, standard deviation

## **Efficacy**

### **Ripening success (Bishop score increase by 2 or more points or cervical dilation of 3 cm or more)**

A nested study (n=186) within a randomised controlled trial (RCT) of 188 pregnant women, comparing double balloon catheter (DBC) plus extra-amniotic saline infusion (EASI; n=60) against single balloon catheter (SBC) plus EASI (n=126) reported that 'ripening success' (defined as increase in Bishop score 2 or more points or cervical dilation of 3 cm or more) was comparable between the DBC and SBC groups (96.4% versus 92.7%; p=0.55)<sup>3</sup>.

A secondary analysis (n=160) of the same RCT, comparing DBC plus EASI (n=60) against DBC without EASI (n=100) reported that ripening success rate was comparable between the groups (96.4% [54/60] versus 99% [99/100]; p=0.29)<sup>4</sup>.

### **Time from catheter insertion to delivery**

An RCT of 302 pregnant women (293 in the final analysis) comparing DBC (n=148) against SBC (n=145) for induction of labour (IOL) reported that length of time from catheter insertion to delivery was 19.4±6.0 and 19.1±6.8 hours in the 2 groups respectively (p=0.8)<sup>2</sup>. Length of time was not significantly different between the groups regardless of parity (primiparous or multiparous)<sup>1</sup>.

A quasi-RCT of 188 women at term with singleton pregnancy comparing DBC (n=100) against SBC plus EASI (n=88) for IOL reported that time from insertion to delivery was significantly shorter in the SBC plus EASI group compared with the DBC group (20.5 hours versus 17.3 hours respectively; p=0.03)<sup>2</sup>. The nested study (n=186) in this RCT, comparing DBC plus EASI (n=60) against SBC plus EASI (n=126) reported balloon insertion to delivery interval was significantly shorter in the DBC plus EASI group compared with the SBC plus EASI group (14.2 hours versus 15.5 hours; p=0.04)<sup>3</sup>.

The secondary analysis (n=160) of the RCT of 188 women, comparing DBC plus EASI (n=60) against DBC without EASI (n=100) reported that catheter insertion to delivery interval was significantly shorter in the DBC plus EASI group compared with the DBC without EASI group (14.19 hours versus 20.45 hours; p<0.001)<sup>4</sup>.

An RCT of 330 nulliparous pregnant women with unfavourable cervixes compared 3 methods (DBC [n=107] versus SBC [n=110] versus prostaglandin gel [dinoprostone, n=113]) for IOL at term. The induction to delivery interval was longer in the DBC group (median 24.5 hours, 95% confidence interval [CI] 23.7 to 30.6) than the SBC group (median 23.2 hours; 95% CI 20.8 to 25.8) or the prostaglandin gel group (23.8 hours; 95% CI 21.7 to 26.8; p=0.043)<sup>5</sup>.



A multicentre RCT of 326 pregnant women with unfavourable cervixes at term comparing DBC plus oral misoprostol (OM; n=162) against OM alone (n=151) reported that median catheter insertion to delivery interval was 32.4 hours in the DBC plus OM group and 22.5 hours in the control group (OM alone; p=0.004). This difference was not seen when assessed according to parity (nulliparous p=0.19; multiparous p=0.06). The number of applications (2 versus 3; p<0.001) and dose of OM used was lower in the DBC plus OM group (100 mg versus 200 mg; p<0.001)<sup>6</sup>.

An RCT of 122 pregnant women with unfavourable cervixes at term comparing DBC plus OM (n=59) against OM alone (n=63) reported that median catheter insertion to delivery interval was 15.3 hours in the DBC plus OM group and 20.8 hours in the control group (p=0.15). Among women without premature rupture of membranes, the median times for induction were 15.8 hours versus 32.6 hours (p=0.02)<sup>7</sup>.

### Caesarean section rate

The RCT of 302 pregnant women (293 women in the final analysis) comparing DBC (n=148) against SBC (n=145) reported that caesarean delivery rate was 18% and 10% in the 2 groups respectively (p=0.9)<sup>2</sup>. The incidence of operative (vacuum or caesarean) deliveries was significantly higher in the DBC group compared with the SBC group (26% versus 14%; p=0.02; odds ratio 0.49, 95% CI 0.26 to 0.92)<sup>1</sup>.

The nested study (n=186) within the RCT of 188 women, comparing DBC plus EASI (n=60) against SBC plus EASI (n=126) reported the caesarean section delivery rate was significantly lower in the DBC group compared with the SBC group (8.3% versus 20.8%; p=0.05)<sup>3</sup>.

The secondary analysis (n=160) of the RCT of 188 women, comparing DBC plus EASI (n=60) against DBC without EASI (n=100) reported that the caesarean section delivery rate was comparable between the groups (8.3% versus 20%; p=0.07)<sup>4</sup>.

An RCT of 210 women reported no difference in caesarean delivery rates between the DBC and prostaglandin E2 (PGE2) groups (24% versus 26%; odds ratio 0.88, 95% CI, 0.47 to 1.65)<sup>9</sup>. A RCT of 126 women with oligohydramnios and a low Bishop score (less than 6) reported that there was no significant difference between the DBC group (n=67) and the dinoprostone vaginal insert group (n=59) in caesarean section rates (16% versus 22%; p=0.42)<sup>10</sup>.

The RCT of 330 nulliparous pregnant women with unfavourable cervixes comparing 3 methods (DBC [n=107] versus SBC [n=110] versus PGE2 gel [n=113]) reported no difference in caesarean delivery rates between the groups (DBC 43%, SBC 36%, PGE2 37%; p=0.567)<sup>5</sup>.

### **Vaginal delivery within 24 hours**

The RCT of 210 women with unfavourable cervixes comparing DBC (n=105) against prostaglandin gel (n=103) reported that more women in the DBC group had a vaginal delivery within 24 hours than in the prostaglandin gel group (69% versus 49% respectively; odds ratio 2.22; 95% CI 1.26 to 3.91)<sup>9</sup>.

The multicentre RCT of 326 pregnant women with unfavourable cervixes at term comparing DBC plus OM (n=162) against OM alone (n=151) reported that the rate of spontaneous vaginal delivery within 48 hours did not differ significantly between the groups (80% [101/162] versus 85% [90/106]; p=0.29)<sup>7</sup>.

### **Rate of failure to induce labour (defined as no vaginal delivery within 48 hours)**

The RCT of 122 pregnant women with an indication for IOL comparing DBC plus OM (n=59) against OM alone (n=63) reported that the rate of failure to induce labour was significantly lower in the DBC plus OM group in comparison with control group (OM alone; 9.3% versus 21.2%; p=0.007). Among women without rupture of membranes, the rates of failure for IOL were 10.8% versus 28.2% (p=0.002)<sup>7</sup>.

### **Length of hospital stay**

The secondary analysis (n=160) of the RCT of 188 women, comparing DBC plus EASI (n=60) against DBC without EASI (n=100) reported that the length of hospital stay was significantly shorter in the DBC plus EASI group compared to the DBC without EASI group (4.29±1.8 days versus 6.69±5.9 days; p<0.001)<sup>4</sup>.

### **Maternal satisfaction**

The nested study (n=186) within the RCT of 188 women, comparing DBC plus EASI (n=60) against SBC plus EASI (n=126) reported that there was no significant difference in maternal satisfaction (assessed on a scale of 1–10, with higher scores indicating greater satisfaction) in the DBC group compared with the SBC group (7.7±2.8 versus 7.0±2.8; p=0.42)<sup>3</sup>. The RCT of 122 women, comparing DBC plus OM (n=59) against OM alone (n=63) reported that women were not 'bothered' by the placement of the DBC (p=0.017) or by the presence of the catheter (p=0.002). They also reported a significant positive birth experience (on the German language version of Salmon Item List score) in the DBC group (87.7 ±15.8 versus 79.3±17.3; p=0.030)<sup>8</sup>.

### **Apgar score of less than 7 at 5 minutes**

The multicentre RCT of 326 pregnant women reported more Apgar scores of less than 7 (at 5 minutes) in the DBC plus OM group than the OM alone group (8 versus 1; p=0.04)<sup>6</sup>. In the quasi-RCT of 188 patients and the nested study (n=186), the number of Apgar scores of less than 7 (at 5 minutes) was similar between the study groups<sup>2, 3, 4</sup>.

## Safety

### Uterine hyperstimulation

Uterine hyperstimulation occurred in 14% (16/113) of women in the prostaglandin E2 (PGE2) group, with none occurring in the double balloon catheter (DBC) and single balloon catheter (SBC) groups in a randomised controlled trial (RCT) of 330 nulliparous pregnant women<sup>5</sup>. Five of these women had non-reassuring fetal heart rate patterns and tachysystole. Uterine tachysystole or hypertonus occurred more frequently in the PGE2 group compared to the DBC group (10% versus 0%;  $p=0.007$ ) in an RCT of 210 women<sup>9</sup>. The incidence of tachysystole and non-reassuring fetal heart rate status was significantly lower in the DBC group than the PGE2 group ( $p<0.05$ ) in an RCT of 126 women with oligohydramnios and unfavourable cervixes<sup>10</sup>.

### Cord pH

Cord pH was lower in the PGE2 group compared with the DBC and SBC groups (median arterial pH: DBC group 7.26, SBC 7.26, PGE2 7.25;  $p=0.05$ ) in the RCT of 330 nulliparous pregnant women<sup>5</sup>.

Newborn infants with an umbilical artery pH of less than 7.00 were more common in the PGE2 group than in the DBC group (6% versus 25%;  $p=0.03$ ) in the RCT of 126 pregnant women with oligohydramnios and unfavourable cervixes<sup>10</sup>.

### Pain

Pain (score of more than 4) was reported in 55% of women in the DBC group, 36% in the SBC group and 63% in the PGE2 group ( $p<0.001$ ) in the RCT of 330 nulliparous pregnant women<sup>5</sup>. Pain perception during the insertion procedure was similar in both groups (on a visual analogue scale 1–10, higher scores representing worse pain; mean score 3.1 versus 3.7,  $p=0.19$ ) in a nested study ( $n=186$ ) within an RCT of 188 patients comparing DBC plus extra-amniotic saline infusion (EASI;  $n=60$ ) against SBC plus EASI ( $n=126$ )<sup>3</sup>.

### Cord prolapse

Cord prolapse was reported in 1 woman in the DBC group in an RCT of 302 pregnant women (293 women in the final analysis) comparing DBC ( $n=148$ ) against SBC ( $n=145$ )<sup>1</sup>. An emergency caesarean delivery was performed.

### Abnormal fetal presentation

Fetal malpresentation (1 persistent mento-posterior presentation and 1 transverse position) after catheter removal was reported in 2 women in the DBC group in the RCT of 302 pregnant women (293 women in the final analysis) comparing DBC ( $n=148$ ) against SBC ( $n=145$ ). One had a vaginal delivery after an external cephalic version was performed and 1 had a caesarean section<sup>1</sup>.

### **Placental abruption**

Placental abruption occurred in 1 woman in the PGE2 group with none occurring in the DBC and SBC groups in the RCT of 330 nulliparous pregnant women<sup>5</sup>.

### **Intrapartum fever**

Intrapartum fever was reported in 8 and 2 women respectively in the DBC and SBC groups ( $p=0.10$ ) in the RCT of 302 pregnant women comparing DBC ( $n=148$ ) against SBC ( $n=145$ )<sup>1</sup>.

### **Postpartum endometritis**

Postpartum endometritis after caesarean section occurred in 1 woman in the DBC plus OM group ( $n=59$ ) with none in the OM alone group ( $n=63$ ) in the RCT of 122 pregnant women with unfavourable cervix at term<sup>7</sup>. Postpartum endometritis occurred in 2 women in the OM alone group ( $n=151$ ) with none occurring in the DBC group ( $n=162$ ) in an RCT of 326 pregnant women with unfavourable cervixes at term<sup>6</sup>.

### **Postpartum haemorrhage**

The incidence of postpartum haemorrhage (more than 1000 ml) was higher (but not significantly) in PGE2 group compared to DBC and SBC groups (PGE2 group=12, DBC=5, SBC=5;  $p=0.143$ ) in the RCT of 330 nulliparous pregnant women<sup>5</sup>.

### **Birth canal injury**

Birth canal injury was reported in 1 and 5 women respectively in the DBC and PGE2 groups ( $p=0.10$ ) in the RCT of 126 pregnant women with oligohydramnios and unfavourable cervixes<sup>10</sup>.

### **Maternal discomfort**

Maternal discomfort due to the ripening device was reported in 5 women in the DBC group ( $n=107$ ) in the RCT of 330 women. Two women were unable to void, 2 women had decreased balloon volume and in 1 woman the device was removed<sup>5</sup>.

### **Newborn infection**

Newborn infection occurred in the babies of 4 women in the DBC plus OM group ( $n=162$ ) and 1 in the OM alone group ( $n=151$ ) in the RCT of 326 pregnant women with unfavourable cervixes at term<sup>6</sup>.

## ***Validity and generalisability of the studies***

- Methods of mechanical induction were used alone or in combination with other interventions.

- Studies used different comparators, protocols, regimens and outcome measures of effectiveness and arrived at different conclusions.
- 2 RCTs compared the Atad double balloon catheter<sup>5, 11</sup>. All the other studies assessed the Cook's double balloon catheter.
- Comparison between DBC and SBC (Foley catheter) reported that both catheters are equally efficacious (mainly in primiparous women)<sup>1, 3, 5, 9</sup> and DBC offered no advantage over SBC or prostaglandins (in mixed parities)<sup>5</sup>. DBC is associated with more operative deliveries and adverse events<sup>9</sup>.
- Studies also compared different combinations which include SBC and DBC with or without EASI: DBC compared against SBC with EASI reported significantly higher time to delivery interval<sup>2</sup>. DBC with EASI resulted in higher vaginal delivery rates and reduced time to delivery compared to SBC with EASI. Ripening success was comparable and caesarean section rates were significantly lower in the DBC group<sup>3</sup>. Comparison of DBC with EASI against DBC without EASI reported shorter time to delivery, and comparable caesarean section and ripening success rates<sup>4</sup>. Addition of EASI to DBC or SBC resulted in a shorter induction process.
- Comparison between DBC and prostaglandins alone did not show any significant difference in the duration of induction to delivery or in caesarean delivery rates. Sequential use of DBC and PGE2 did not improve the rate of delivery within 48 hours compared with OM alone but the time to delivery and rates of failure were significantly lower in the DBC and PGE2 group, particularly in women without premature rupture of membranes<sup>6, 7</sup>. Women were also satisfied with induction of labour using DBC and it was found to have a positive impact on the birth experience<sup>8</sup>.

### ***Existing assessments of this procedure***

In 2012, a Cochrane review on mechanical methods for induction of labour (which included 71 randomised controlled trials, 9722 women) compared against placebo or no treatment, prostaglandins, or oxytocin. The mechanical methods studied were laminaria tents or synthetic equivalents, catheters (Foley catheter and Atad ripener) or extra-amniotic infusion by catheter. The review concluded no significant difference in caesarean section rates after the use of mechanical

methods, prostaglandins or misoprostol in cervical ripening. However, mechanical methods reduced the risk of hyperstimulation with fetal heart rate changes when compared with vaginal prostaglandins (Risk Ratio 0.19, 95% CI 0.08 to 0.43,  $p=0.000063$ ; 9 studies,  $n=1931$ ). The study also reported that, compared with oxytocin alone, mechanical methods of cervical ripening reduced the risk of caesarean section (RR 0.62, 95% CI 0.42 to 0.90,  $p=0.011$ ; 5 studies,  $n=398$ ). It also concluded that mechanical methods do not increase the overall number of women who had not delivered within 24 hours, however the proportion of multiparous women who did not achieve vaginal delivery within 24 hours was higher when compared with vaginal PGE<sub>2</sub>. Serious maternal and neonatal adverse events were not often reported and did not differ between the interventions. Infection reported in a few studies appeared not to be higher when using mechanical methods<sup>12</sup>.

### ***Related NICE guidance***

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

#### **Clinical guidelines**

- Induction of labour. NICE clinical guideline 70 (2008). Available from <http://www.nice.org.uk/guidance/CG70>
- Diabetes in pregnancy: management of diabetes and its complications from pre-conception to the postnatal period. NICE clinical guideline 63 (2008). Available from <http://www.nice.org.uk/guidance/CG63>
- Intrapartum care: care of healthy women and their babies during childbirth. NICE clinical guideline 190 (2014). Available from [www.nice.org.uk/CG190](http://www.nice.org.uk/CG190)
- Caesarean section. NICE clinical guideline 132 (2011). Available from [www.nice.org.uk/CG132](http://www.nice.org.uk/CG132)

### **Specialist advisers' opinions**

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to where comments are considered voluminous, or publication would be unlawful or inappropriate. Three Specialist Advisor Questionnaires for insertion of a double balloon catheter for induction of labour in pregnant women without previous caesarean section were

submitted and can be found on the [NICE website \[INSERT HYPER LINK TO MAIN IP PAGE\]](#).

## Patient commentators' opinions

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

## Issues for consideration by IPAC

- Ongoing studies:
  - NCT01091285: Induction of labor with single and double balloon catheters, a randomized controlled trial, phase 4; n=180; location: Norway; status: completed (not yet published).
  - NCT01255839: The balloon project for birth induction. A prospective multi-centre randomised comparison on induction of labour with double balloon installation device versus prostaglandin E2 Minprostin; n=825, primary outcome: success of induction of labour, duration of birth and fetal outcome; location: Denmark; status: completed (not yet published).
  - NCT01720394: Efficacy of induction of labor on term using a double balloon catheter compared to dinoprostone vaginal-insert; multicenter randomised controlled trial, phase 4; n=253; primary outcome: time interval from primary treatment to delivery; location: Austria; estimated completion date: April 2015.
  - NCT02223949: Labor induction and maternal BMI, comparison of different pre-induction cervical ripening methods, randomised controlled trial, phase 3; Cook double balloon catheter versus PGE 1 tablet in lean, overweight and obese women; n=624; primary outcome: caesarean section rate; Location: Israel; completion date: November 2016.
  - ACTRN12614000039684: Prostaglandin inpatient induction of labour compared with balloon outpatient induction of labour: a randomised controlled trial; primary outcome: composite measure of improved perinatal outcomes; n=2500; location: Australia; completion date: 2016.

## References

1. Salim R, Zafran N. et al (2011). Single-balloon compared with double-balloon catheters for induction of labor: a randomized controlled trial *Obstetrics & Gynecology* 118: 79-86
2. Mei-Dan E, Walfisch A et al (2012). Comparison of two mechanical devices for cervical ripening: a prospective quasi-randomized trial *Journal of Maternal-Fetal & Neonatal Medicine* 25: 723-727
3. Mei-Dan E, Walfisch A et al (2014). Making cervical ripening EASI: a prospective controlled comparison of single versus double balloon catheters *Journal of Maternal-Fetal & Neonatal Medicine* 27: 1765-1770
4. Walfisch A, Mei-Dan E et al (2014). Trans-cervical double balloon catheter with and without extra-amniotic saline infusion for cervical ripening: a prospective quasi-randomized trial. *J Matern.Fetal Neonatal Med.* 1-6
5. Pennell CE, Henderson JJ 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.[Erratum appears in *BJOG*. 2011 Mar;118(4):521 Note: McCleery, S [corrected to McChlery, S]] *BJOG: An International Journal of Obstetrics & Gynaecology* 116: 1443-1452
6. Kehl S, Ziegler J et al (2014). Sequential use of double-balloon catheter and oral misoprostol versus oral misoprostol alone for induction of labour at term (CRBplus trial): a multicentre, open-label randomised controlled trial. *BJOG*. 20-10-2014
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8. Kehl S, Welzel G et al (2013). Women's acceptance of a double-balloon device as an additional method for inducing labour. *European Journal of Obstetrics, Gynecology, & Reproductive Biology.* 168: 30-35
9. Cromi A, Ghezzi F et al (2012). A randomized trial of preinduction cervical ripening: dinoprostone vaginal insert versus double-balloon catheter *American Journal of Obstetrics & Gynecology.* 207: 125-127
10. Wang W, Zheng J et al (2014). Which is the safer method of labor induction for oligohydramnios women? Transcervical double balloon catheter or dinoprostone vaginal insert *Journal of Maternal-Fetal & Neonatal Medicine* 27:1805-1808
11. Atad J, Hallak M et al (1996). A randomized comparison of prostaglandin E2, oxytocin, and the double-balloon device in inducing labor. *Obstetrics & Gynecology.* 87: 223-227.



12. Jozwiak M, Bloemenkamp KWM, Kelly AJ, Mol BWJ, Irion O, Bouvain M (2012). Mechanical methods for induction of labour. Cochrane Database of Systematic Reviews, Issue 3. Art. No.: CD001233. DOI: 10.1002/14651858.CD001233.pub2.

## Appendix A: Additional papers on insertion of a double balloon catheter for induction of labour in pregnant women without previous caesarean section

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Atad J, Hallak M et al (1997). Ripening and dilatation of the unfavourable cervix for induction of labour by a double balloon device: experience with 250 cases. <i>British Journal of Obstetrics &amp; Gynaecology</i> . 104: 9-32	USA case series n=250 Women with unfavourable cervix (Bishop score <4) Double Balloon Catheter for Induction of Labour	Increase in Bishop score-mean change 4.6 (from 2.0 to 6.6, p<0.05) Mean time interval from insertion to delivery was 18.9hrs. From removal to delivery was 6.9 hrs. Caesarean section performed in 16% (39/250), others normal delivery.	Similar studies included in table 2.
Atad J, Bornstein J et al (1991). Nonpharmaceutical ripening of the unfavorable cervix and induction of labor by a novel double balloon device. <i>Obstetrics &amp; Gynecology</i> . 77: 146-152.	USA Women with unfavourable cervix (Bishop score <4) 3 phases Phase 1 n=48 PGE2 gel via cannula phase 2 (double blind RCT) n=10 PGE2gel via DBC vs 10 placebo gel via DBC Phase 3 n=50 DBC only.	In phase 1, a mean increase in 3 points in Bishop's score and mean installation to delivery time was 34.2 hours. phase 2- no sign diff in the increase of bishop score between the groups (5.8 vs 6.0) 90% women in both groups delivered vaginally with a mean of 20.8 hours after device insertion. Phase 3-a mean increase in 4.4 points in the bishop score noted.	Similar studies included in table 2.
Du C, Liu Yet al (2014). Double-balloon catheter vs. dinoprostone vaginal insert for induction of labor with an unfavorable cervix. <i>Arch.Gynecol.Obstet</i> . 19-11-2014	China RCT n=155 Women with an unfavourable cervix (DBC 76 vs dinoprostone vaginal insert 79) for IOL	Vaginal delivery rate within 24 hrs ( 50 vs 53.6%, p=0.69) Caesarean section rate (39.5 vs 31.6%, p=0.18) Oxytocin administration ( 75 vs 31.65%, p<0.001) Uterine hyper-stimulation (0 vs 10.1%, p=0.007) Neonatal outcomes similar between groups.	Similar studies included in table 2.
Gadel Rab MT, Mohammed AB et al (2014). Transcervical Foley's catheter versus Cook balloon for cervical ripening in stillbirth with	RCT n=200 100 transcervical Foley's catheter versus 100 Cook cervical ripening	Time from balloon insertion to expulsion and from balloon insertion to delivery was significantly shorter in Foley's catheter group. However, the difference between the two groups regarding time from balloon	Women with previous lower segment c-scar were included in

a scarred uterus: a randomized controlled trial. J Matern.Fetal Neonatal Med. 14: 1-5	balloon Pregnant women with stillbirth, unfavourable cervix and scarred uterus.	insertion to active labour, time from balloon expulsion to delivery, cervical ripening, caesarean section, instrumental delivery, pain score, need for analgesia, hospital stay and maternal satisfaction was not statistically significant. Foley's catheter and Cook cervical ripening balloon are comparable regarding efficacy and safety profile.	the study.
Hallak M (1997). Mechanical ripening of the unfavorable cervix for induction of labor. Contemporary Reviews in Obstetrics and Gynaecology.9 (2) (pp 99-105), 1997.Date of Publication: 1997. 1997 99-105	USA prospective randomised study n=95 women with unfavourable cervix (Bishop score <4) (35 DBC vs 30 PGE2 vs 30 oxytocin) for IOL	The change in bishop score (median 5 vs 5 vs 2.5, p<0.01) Cervical dilation of >3cm was more frequent and success rate was higher in DBC compared with PGE2 and oxytocin groups. method failure (5.7% vs 20% vs 53.3%) , induction delivery interval (mean 21.3 hrs vs 23.2 vs 28.2hrs), success rate for vaginal delivery (77.1% vs 70% vs 26.7%, p<.01).	Similar studies included in table 2.
Sciscione AC. and Rushstaller K (2013). Double-balloon catheter results in higher rate of vaginal delivery within 24 h when compared with dinoprostone vaginal insert. Evidence Based Medicine 18: 140-141	RCT 105 DBC intracervical versus 105 PGE2 vaginal insert.	The results of the trial demonstrated no difference between the two methods from time of induction to delivery, but a higher rate of vaginal delivery within a 24hr period for women receiving the intracervical catheter.	Commentary
Shechter-Maor G, Haran G et al (2014). Intra-vaginal prostaglandin E2 versus double-balloon catheter for labor induction in term oligohydramnios. J Perinatol 1-4	Israel RCT n=52 In term oligohydramnios <5cm, bishop score<6  (DBC 26 vs vaginal insert 10mg timed release PGE2 [dinoprostone] 26) for IOL	Time from induction to active labour (13 with PGE2 vs 19.5h DBC, p=0.243) No difference in caesarean rate (15.4 vs 7.7%, p=0.668). Early device removal (76.9 vs 26.9%, p=0.0001) mostly because of active labour or non-reassuring foetal heart rate. Oxytocin augmentation for IOL (53.8 VS 84.6%, P=0.034) Time to delivery (16 vs 20.5h, p=0.045).	Similar studies included in table 2.
Suffecool K, Rosenn BM et al (2014). Labor induction in nulliparous women with an unfavorable cervix: double balloon catheter versus dinoprostone. Journal of Perinatal Medicine. 42: 213-218	USA RCT n=62 Nulliparous women with an unfavourable cervix (bishop score<6) (DBC 31 vs CRA- 10mg Dinoprostone 31) for IOL	The mean induction to delivery time was shorter in the DBC group as compared to the dinoprostone group (17.9 vs 26.3 h) as time from induction to vaginal delivery (19.1 vs 24.4 h). More women in DBC group were delivered in 24 hrs compared to dinoprostone (87.1 % vs 47.4%). 50% of the women in both groups delivered by caesarean section.	Similar studies included in table 2.
Yuen PM, Pang HY et al (1996). Cervical ripening before induction of	Hong Kong Comparative	No statistical significant difference between the 3 methods. PGE2 pessary seems to be more effective-	Similar studies included in

<p>labour in patients with an unfavourable cervix: a comparative randomized study of the Atad Ripener Device, prostaglandin E2 vaginal pessary, and prostaglandin E2 intracervical gel. Australian &amp; New Zealand Journal of Obstetrics &amp; Gynaecology. 36: 291-295</p>	<p>randomised study n=119 women with unfavourable cervix (Bishop score &lt;4) (36 DBC vs 39 PGE2 gel vs 39 PGE vaginal pessary) for IOL</p>	<p>68% going to labour compared to 50% in the other 2 groups. Vaginal delivery rate - 87.2% pessary, 72% in DBC, 84.6% in gel. Duration of labour shorter in pessary 73.5% delivered in 24 hrs vs 57% DBC vs 57 % in gel. 5 developed complications during ripening period- 3 needed emergency C section, 2 had vaginal delivery.</p>	<p>table 2.</p>
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## Appendix B: Related NICE guidance for insertion of a double balloon catheter for induction of labour in pregnant women without previous caesarean section

Guidance	Recommendations
Clinical guidelines	<p><b>Induction of labour: 2008 update. NICE clinical guideline 70 ([2008]. Available from <a href="http://www.nice.org.uk/guidance/CG70">http://www.nice.org.uk/guidance/CG70</a></b></p> <p>This guidance updates and replaces NICE inherited <a href="#">clinical guideline D</a> (published in 2001).</p> <p><b>1.1 Information and decision-making</b></p> <p>This section should be read in conjunction with '<a href="#">Antenatal care: routine care for the healthy pregnant woman</a>' (NICE clinical guideline 62) and '<a href="#">Intrapartum care: care of healthy women and their babies during childbirth</a>' (NICE clinical guideline 55).</p> <p>1.1.1.1 Women should be informed that most women will go into labour spontaneously by 42 weeks. At the 38 week antenatal visit, all women should be offered information about the risks associated with pregnancies that last longer than 42 weeks, and their options. The information should cover:</p> <ul style="list-style-type: none"> <li>• membrane sweeping:</li> <li>• that membrane sweeping makes spontaneous labour more likely, and so reduces the need for formal induction of labour to prevent prolonged pregnancy</li> <li>• what a membrane sweep is</li> <li>• that discomfort and vaginal bleeding are possible from the procedure</li> <li>• induction of labour between 41<sup>+0</sup> and 42<sup>+0</sup> weeks</li> <li>• expectant management.</li> </ul> <p>1.1.1.2 Healthcare professionals should explain the following points to women being offered induction of labour:</p> <ul style="list-style-type: none"> <li>• the reasons for induction being offered</li> <li>• when, where and how induction could be carried out</li> <li>• the arrangements for support and pain relief (recognising that women are likely to find induced labour more painful than spontaneous labour) (see also <a href="#">1.6.2.1</a> and <a href="#">1.6.2.2</a>)</li> <li>• the alternative options if the woman chooses not to have induction of labour</li> <li>• the risks and benefits of induction of labour in specific circumstances and the proposed induction methods</li> <li>• that induction may not be successful and what the woman's options would be.</li> </ul> <p>1.1.1.3 Healthcare professionals offering induction of labour should:</p>

- allow the woman time to discuss the information with her partner before coming to a decision
- encourage the woman to look at a variety of sources of information
- invite the woman to ask questions, and encourage her to think about her options
- support the woman in whatever decision she makes.

## **1.2 Induction of labour in specific circumstances**

### **1.2.1 Prevention of prolonged pregnancy**

1.2.1.1 Women with uncomplicated pregnancies should be given every opportunity to go into spontaneous labour.

1.2.1.2 Women with uncomplicated pregnancies should usually be offered induction of labour between 41<sup>+0</sup> and 42<sup>+0</sup> weeks to avoid the risks of prolonged pregnancy. The exact timing should take into account the woman's preferences and local circumstances.

1.2.1.3 If a woman chooses not to have induction of labour, her decision should be respected. Healthcare professionals should discuss the woman's care with her from then on.

1.2.1.4 From 42 weeks, women who decline induction of labour should be offered increased antenatal monitoring consisting of at least twice weekly cardiotocography and ultrasound estimation of maximum amniotic pool depth<sup>[2]</sup>.

### **1.2.2 Preterm prelabour rupture of membranes**

1.2.2.1 If a woman has preterm prelabour rupture of membranes, induction of labour should not be carried out before 34 weeks unless there are additional obstetric indications (for example, infection or fetal compromise).

1.2.2.2 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 PGE<sub>2</sub><sup>[3]</sup>:

- 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.

### **1.2.3 Prelabour rupture of membranes at term**

1.2.3.1 Women with prelabour rupture of membranes at term (at or over 37 weeks) should be offered a choice of induction of labour with vaginal PGE<sub>2</sub><sup>[3]</sup> or expectant management.

1.2.3.2 Induction of labour is appropriate approximately 24 hours after prelabour rupture of the membranes at term.<sup>[4]</sup>

### **1.2.4 Previous caesarean section**

1.2.4.1 If delivery is indicated, women who have had a previous caesarean section may be offered induction of labour with vaginal PGE<sub>2</sub><sup>[3]</sup>, caesarean section or expectant management on an individual basis, taking into account the woman's circumstances and wishes. Women

	<p>should be informed of the following risks with induction of labour:</p> <ul style="list-style-type: none"> <li>• increased risk of need for emergency caesarean section during induced labour</li> <li>• increased risk of uterine rupture.</li> </ul> <p><b>1.2.5 Maternal request</b></p> <p>1.2.5.1 Induction of labour should not routinely be offered on maternal request alone. However, under exceptional circumstances (for example, if the woman's partner is soon to be posted abroad with the armed forces), induction may be considered at or after 40 weeks.</p> <p><b>1.2.6 Breech presentation</b></p> <p>1.2.6.1 Induction of labour is not generally recommended if a woman's baby is in the breech presentation. If external cephalic version is unsuccessful, declined or contraindicated, and the woman chooses not to have an elective caesarean section, induction of labour should be offered, if delivery is indicated, after discussing the associated risks with the woman.</p> <p><b>1.2.7 Fetal growth restriction</b></p> <p>1.2.7.1 If there is severe fetal growth restriction with confirmed fetal compromise, induction of labour is not recommended.</p> <p><b>1.2.8 History of precipitate labour</b></p> <p>1.2.8.1 Induction of labour to avoid a birth unattended by healthcare professionals should not be routinely offered to women with a history of precipitate labour.</p> <p><b>1.2.9 Intrauterine fetal death</b></p> <p>1.2.9.1 In the event of an intrauterine fetal death, healthcare professionals should offer support to help women and their partners and/or family cope with the emotional and physical consequences of the death. This should include offering information about specialist support.</p> <p>1.2.9.2 In the event of an intrauterine fetal death, if the woman appears to be physically well, her membranes are intact and there is no evidence of infection or bleeding, she should be offered a choice of immediate induction of labour or expectant management.</p> <p>1.2.9.3 In the event of an intrauterine fetal death, if there is evidence of ruptured membranes, infection or bleeding, immediate induction of labour is the preferred management option.</p> <p>1.2.9.4 If a woman who has had an intrauterine fetal death chooses to proceed with induction of labour, oral mifepristone, followed by vaginal PGE<sub>2</sub> or vaginal misoprostol<sup>[5]</sup>, should be offered. The choice and dose of vaginal prostaglandin should take into account the clinical circumstances, availability of preparations and local protocol.</p> <p>1.2.9.5 For women who have intrauterine fetal death and who have had a previous caesarean section, the risk of uterine rupture is increased. The dose of vaginal prostaglandin<sup>[3]</sup> should be reduced accordingly, particularly in the third trimester.</p> <p><b>1.2.10 Suspected fetal macrosomia</b></p> <p>1.2.10.1 In the absence of any other indications, induction of labour should</p>
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not be carried out simply because a healthcare professional suspects a baby is large for gestational age (macrosomic).

### **1.2.3 Prelabour rupture of membranes at term**

1.2.3.1 Women with prelabour rupture of membranes at term (at or over 37 weeks) should be offered a choice of induction of labour with vaginal PGE2 [3] or expectant management.

1.2.3.2 Induction of labour is appropriate approximately 24 hours after prelabour rupture of the membranes at term.[4]

### **1.2.4 Previous caesarean section**

1.2.4.1 If delivery is indicated, women who have had a previous caesarean section may be offered induction of labour with vaginal PGE2 [3], caesarean section or expectant management on an individual basis, taking into account the woman's circumstances and wishes. Women should be informed of the following risks with induction of labour:

- increased risk of need for emergency caesarean section during induced labour
- increased risk of uterine rupture.

### **1.2.5 Maternal request**

1.2.5.1 Induction of labour should not routinely be offered on maternal request alone. However, under exceptional circumstances (for example, if the woman's partner is soon to be posted abroad with the armed forces), induction may be considered at or after 40 weeks.

### **1.2.6 Breech presentation**

1.2.6.1 Induction of labour is not generally recommended if a woman's baby is in the breech presentation. If external cephalic version is unsuccessful, declined or contraindicated, and the woman chooses not to have an elective caesarean section, induction of labour should be offered, if delivery is indicated, after discussing the associated risks with the woman.

### **1.2.7 Fetal growth restriction**

1.2.7.1 If there is severe fetal growth restriction with confirmed fetal compromise, induction of labour is not recommended.

### **1.2.8 History of precipitate labour**

1.2.8.1 Induction of labour to avoid a birth unattended by healthcare professionals should not be routinely offered to women with a history of precipitate labour.

### **1.2.9 Intrauterine fetal death**

1.2.9.1 In the event of an intrauterine fetal death, healthcare professionals should offer support to help women and their partners and/or family cope with the emotional and physical consequences of the death. This should include offering information about specialist support.

1.2.9.2 In the event of an intrauterine fetal death, if the woman appears to be physically well, her membranes are intact and there is no evidence of infection or bleeding, she should be offered a choice of immediate induction of labour or expectant management.

1.2.9.3 In the event of an intrauterine fetal death, if there is evidence of



ruptured membranes, infection or bleeding, immediate induction of labour is the preferred management option.

1.2.9.4 If a woman who has had an intrauterine fetal death chooses to proceed with induction of labour, oral mifepristone, followed by vaginal PGE2 or vaginal misoprostol [5], should be offered. The choice and dose of vaginal prostaglandin should take into account the clinical circumstances, availability of preparations and local protocol.

1.2.9.5 For women who have intrauterine fetal death and who have had a previous caesarean section, the risk of uterine rupture is increased. The dose of vaginal prostaglandin [3] should be reduced accordingly, particularly in the third trimester.

### **1.2.10 Suspected fetal macrosomia**

1.2.10.1 In the absence of any other indications, induction of labour should not be carried out simply because a healthcare professional suspects a baby is large for gestational age (macrosomic).

## **1.3 Recommended methods for induction of labour**

Membrane sweeping involves the examining finger passing through the cervix to rotate against the wall of the uterus, to separate the chorionic membrane from the decidua. If the cervix will not admit a finger, massaging around the cervix in the vaginal fornices may achieve a similar effect. For the purpose of this guideline, membrane sweeping is regarded as an adjunct to induction of labour rather than an actual method of induction.

The Bishop score is 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 eight 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.

### **1.3.1 Membrane sweeping**

1.3.1.1 Prior to formal induction of labour, women should be offered a vaginal examination for membrane sweeping[6].

1.3.1.2 At the 40 and 41 week antenatal visits, nulliparous women should be offered a vaginal examination for membrane sweeping.

1.3.1.3 At the 41 week antenatal visit, parous women should be offered a vaginal examination for membrane sweeping.

1.3.1.4 When a vaginal examination is carried out to assess the cervix, the opportunity should be taken to offer the woman a membrane sweep.

1.3.1.5 Additional membrane sweeping may be offered if labour does not start spontaneously.

### **1.3.2 Pharmacological methods**

1.3.2.1 Vaginal PGE2 is the preferred method of induction of labour, unless there are specific clinical reasons for not using it (in particular the risk of uterine hyperstimulation). It should be administered as a gel, tablet or controlled-release pessary. Costs may vary over time, and trusts/units should take this into consideration when prescribing PGE2. For doses,

refer to the SPCs. The recommended regimens are:

- one cycle of vaginal PGE<sub>2</sub> tablets or gel: one dose, followed by a second dose after 6 hours if labour is not established (up to a maximum of two doses)
- one cycle of vaginal PGE<sub>2</sub> controlled-release pessary: one dose over 24 hours.

1.3.2.2 When offering PGE<sub>2</sub> for induction of labour, healthcare professionals should inform women about the associated risks of uterine hyperstimulation.

1.3.2.3 Misoprostol[5] should only be offered as a method of induction of labour to women who have intrauterine fetal death (see section 1.2.9) or in the context of a clinical trial.

1.3.2.4 Mifepristone should only be offered as a method of induction of labour to women who have intrauterine fetal death (see section 1.2.9).

## **1.4 Methods that are not recommended for induction of labour**

### **1.4.1 Pharmacological methods**

1.4.1.1 The following should not be used for induction of labour:

- oral PGE<sub>2</sub>
- intravenous PGE<sub>2</sub>
- extra-amniotic PGE<sub>2</sub>
- intracervical PGE<sub>2</sub>
- intravenous oxytocin alone
- hyaluronidase
- corticosteroids
- oestrogen
- vaginal nitric oxide donors.

### **1.4.2 Non-pharmacological methods**

1.4.2.1 Healthcare professionals should inform women that the available evidence does not support the following methods for induction of labour:

- herbal supplements
- acupuncture
- homeopathy
- castor oil
- hot baths
- enemas
- sexual intercourse.

### **1.4.3 Surgical methods**

1.4.3.1 Amniotomy, alone or with oxytocin, should not be used as a primary method of induction of labour unless there are specific clinical reasons for not using vaginal PGE<sub>2</sub>, in particular the risk of uterine hyperstimulation.

### **1.4.4 Mechanical methods**

1.4.4.1 Mechanical procedures (balloon catheters and laminaria tents) should not be used routinely for induction of labour.

### **1.5 Setting and timing**

1.5.1.1 In the outpatient setting, induction of labour should only be carried out if safety and support procedures are in place.

1.5.1.2 The practice of induction of labour in an outpatient setting should be audited continuously.

1.5.1.3 In the inpatient setting, induction of labour using vaginal PGE<sub>2</sub> should be carried out in the morning because of higher maternal satisfaction.

### **1.6 Monitoring and pain relief**

#### **1.6.1 Monitoring**

1.6.1.1 Wherever induction of labour is carried out, facilities should be available for continuous electronic fetal heart rate and uterine contraction monitoring.

1.6.1.2 Before induction of labour is carried out, Bishop score should be assessed and recorded, and a normal fetal heart rate pattern should be confirmed using electronic fetal monitoring.

1.6.1.3 After administration of vaginal PGE<sub>2</sub>, when contractions begin, fetal wellbeing should be assessed with continuous electronic fetal monitoring. Once the cardiotocogram is confirmed as normal, intermittent auscultation should be used unless there are clear indications for continuous electronic fetal monitoring as described in 'Intrapartum care' (NICE clinical guideline 55).

1.6.1.4 If the fetal heart rate is abnormal after administration of vaginal PGE<sub>2</sub>, recommendations on management of fetal compromise in 'Intrapartum care' (NICE clinical guideline 55) should be followed.

1.6.1.5 Bishop score should be reassessed 6 hours after vaginal PGE<sub>2</sub> tablet or gel insertion, or 24 hours after vaginal PGE<sub>2</sub> controlled-release pessary insertion, to monitor progress (see [1.3.2.1](#)).

1.6.1.6 If a woman returns home after insertion of vaginal PGE<sub>2</sub> or tablet or gel, she should be asked to contact her obstetrician/midwife:

- when contractions begin, or
- if she has had no contractions after 6 hours.

1.6.1.7 Once active labour is established, maternal and fetal monitoring should be carried out as described in 'Intrapartum care' (NICE clinical guideline 55).

#### **1.6.2 Pain relief**

1.6.2.1 Women being offered induction of labour should be informed that induced labour is likely to be more painful than spontaneous labour.

1.6.2.2 Women should be informed of the availability of pain relief options in different settings (see [1.1.1.2](#) and [1.5.1.1](#)).

1.6.2.3 During induction of labour, healthcare professionals should provide women with the pain relief appropriate for them and their pain (as

described in 'Intrapartum care' [NICE clinical guideline 55]). This can range from simple analgesics to epidural analgesia.

1.6.2.4 Birth attendants (carers and healthcare professionals) should offer women support and analgesia as required, and should encourage women to use their own coping strategies for pain relief.

1.6.2.5 The opportunity to labour in water is recommended for pain relief<sup>[7]</sup>.

## **1.7 Prevention and management of complications**

### **1.7.1 Uterine hyperstimulation**

1.7.1.1 Tocolysis should be considered if uterine hyperstimulation occurs during induction of labour.

### **1.7.2 Failed induction**

Failed induction is defined as labour not starting after one cycle of treatment as described in [1.3.2.1](#).

1.7.2.1 If induction fails, healthcare professionals should discuss this with the woman and provide support. The woman's condition and the pregnancy in general should be fully reassessed, and fetal wellbeing should be assessed using electronic fetal monitoring.

1.7.2.2 If induction fails, decisions about further management should be made in accordance with the woman's wishes, and should take into account the clinical circumstances.

1.7.2.3 If induction fails, the subsequent management options include:

- a further attempt to induce labour (the timing should depend on the clinical situation and the woman's wishes)
- caesarean section (refer to '[Caesarean section](#)' [NICE clinical guideline 13]).

1.7.2.4 For women who choose caesarean section after a failed induction, recommendations in '[Caesarean section](#)' (NICE clinical guideline 13) should be followed.

### **1.7.3 Cord prolapse**

1.7.3.1 To reduce the likelihood of cord prolapse, which may occur at the time of amniotomy, the following precautions should be taken:

- Before induction, engagement of the presenting part should be assessed.
- Obstetricians and midwives should palpate for umbilical cord presentation during the preliminary vaginal examination and avoid dislodging the baby's head.
- Amniotomy should be avoided if the baby's head is high.

1.7.3.2 Healthcare professionals should always check that there are no signs of a low-lying placental site before membrane sweeping and before induction of labour.

### **1.7.4 Uterine rupture**

1.7.4.1 If uterine rupture is suspected during induced labour, the baby should be delivered by emergency caesarean section (refer to '[Caesarean section](#)' [NICE clinical guideline 13]).

	<p><b>Induction of labour: Evidence Update 44 (July 2013) A summary of selected new evidence relevant to NICE clinical guideline 70 'Induction of labour' (2008)</b></p> <p>(Evidence Updates do not replace current accredited guidance and do not provide formal practice recommendations)</p> <p><b>Methods that are not recommended for induction of labour</b></p> <ul style="list-style-type: none"> <li>• Nitric oxide donors do not seem to be effective for induction of labour.</li> <li>• Evidence for benefits of mechanical methods of induction of labour over prostaglandins seems to be inconclusive.</li> <li>• 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.</li> </ul> <p><b>Diabetes in pregnancy: management of diabetes and its complications from pre-conception to the postnatal period. NICE clinical guideline 63 ([2008). Available from <a href="http://www.nice.org.uk/guidance/CG63">http://www.nice.org.uk/guidance/CG63</a></b></p> <p><b>This guidance is currently being updated.</b></p> <p>[There is no information relevant to mechanical induction of labour]</p> <p><b>Intrapartum care: care of healthy women and their babies during childbirth. NICE clinical guideline 190 (2014). Available from <a href="http://www.nice.org.uk/CG0190">www.nice.org.uk/CG0190</a></b></p> <p>This clinical guideline updates and replaces NICE clinical guideline 55 (published in 2007).</p> <p>[There is no information relevant to mechanical induction of labour]</p> <p><b>Caesarean section. NICE clinical guideline 132 (2011). Available from <a href="http://www.nice.org.uk/CG0132">www.nice.org.uk/CG0132</a></b></p> <p>This clinical guideline updates and replaces NICE clinical guideline 13 (published in 2004).</p> <p>[There is no information relevant to mechanical induction of labour]</p>
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## Appendix C: Literature search for insertion of a double balloon catheter for induction of labour in pregnant women without previous caesarean section

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	27/11/2014	Issue 11 of 12, November 2014
Database of Abstracts of Reviews of Effects – DARE (Cochrane Library)	27/11/2014	Issue 4 of 4, October 2014
HTA database (Cochrane Library)	27/11/2014	Issue 4 of 4, October 2014
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	27/11/2014	Issue 10 of 12, October 2014
MEDLINE (Ovid)	27/11/2014	1946 to November Week 3 2014
MEDLINE In-Process (Ovid)	27/11/2014	November 26, 2014
EMBASE (Ovid)	27/11/2014	1974 to 2014 Week 47
PubMed	27/11/2014	n/a
CINAHL (NLH Search 2.0)	27/11/2014	1981 to present
BLIC	27/11/2014	n/a

Trial sources searched on 22/10/2014

- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database
- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov

Websites searched on 22/10/2014

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)

- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference websites <<add details>>
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Pregnant Women/
2	Pregnancy/
3	(Pregnan* adj4 (woman* or women* or lady* or female*)).tw.
4	Labor, Induced/
5	(Induc* adj4 labo?r).tw.
6	Parturition/
7	Delivery, Obstetric/
8	(Parturi* or childbirth* or accouchement* or childbear* or natalit* or deliver*).tw.
9	(unfavo?r* adj4 cervi*).tw.
10	or/1-9
11	Cervical Ripening/
12	Catheterization/
13	Catheter/
14	11 and (12 or 13)
15	((Cervix* or cervic*) adj4 (ripe* or soft* or dilat* or widen* or expan*) adj4 (balloon* or catheter*)).tw.
16	(((((Double or two or duo or dual) adj4 (Inflat* or balloon* or transcervical* or transcervical*)) or double-balloon) adj4 (catheter* or tube* or device*)).tw.
17	((Extra-amniotic or extraamniotic or "extra amniotic") adj4 saline adj4 infusion*).tw.
18	EASI.tw.
19	or/14-18
20	10 and 19
21	(Cook adj4 Cervical adj4 Ripening adj4 Balloon*).tw.

22	(Atad adj4 device*).tw.
23	20 or 21 or 22
24	animals/ not humans/
25	23 not 24