



WHO recommendations for Induction of labour:

Evidence base



World Health
Organization

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PART 1. STANDARD GRADE CRITERIA FOR GRADING OF EVIDENCE

Table 1. Standard GRADE criteria for grading of evidence¹

Domain	Grade	Characteristic
STUDY DESIGN	0	All randomized controlled trials
	–1	All observational studies
STUDY DESIGN LIMITATIONS	0	Most of the pooled effect provided by studies, with low risk of bias ("A")
	–1	Most of the pooled effect provided by studies with moderate ("B") or high ("C") risk of bias. Studies with high risk of bias weighs <40%
	–2	Most of the pooled effect provided by studies with moderate ("B") or high ("C") risk of bias. Studies with high risk of bias weighs ≥40%
	Note:	Low risk of bias (no limitations or minor limitations) –“A” Moderate risk of bias (serious limitations or potentially very serious limitations including unclear concealment of allocation or serious limitations, excluding limitations on randomization or concealment of allocation) –“B” High risk of bias (Limitations for randomization, concealment of allocation, including small blocked randomization (<10) or other very serious, crucial methodological limitations) –“C”
INCONSISTENCY	0	No severe heterogeneity ($I^2 < 60\%$ or $\chi^2 \geq 0.05$)
	–1	Severe, non-explained, heterogeneity ($I^2 \geq 60\%$ or $\chi^2 < 0.05$) If heterogeneity could be caused by publication bias or imprecision due to small studies, downgrade only for publication bias or imprecision (i.e. the same weakness should not be downgraded twice)
INDIRECTNESS	0	No indirectness
	–1	Presence of indirect comparison, population, intervention, comparator, or outcome.

¹ Adapted from: Schünemann H, Brozek J, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. The GRADE Working Group. Available at: <<http://ims.cochrane.org/revman/grade-pro>>. (This document is contained within the "Help" section of the GRADE profiler software version v.3.2.2.)

Domain	Grade	Characteristic
IMPRECISION		<p>The confidence interval is precise according to the figure below.</p> <p>The total cumulative study population is not very small (i.e. sample size is more than 300 participants) and the total number of events is more than 30.</p>
	-1	One of the above-mentioned conditions is not fulfilled.
	-2	The two above-mentioned are not fulfilled.
		Note: If the total number of events is less than 30 and the total cumulative sample size is appropriately large (e.g. above 3000 patients, consider not downgrading the evidence). If there are no events in both intervention and control groups, the quality of evidence in the specific outcome should be regarded as very low.
PUBLICATION BIAS	0	No evident asymmetry in the funnel plot or less than five studies to be plotted.
	-1	Evident asymmetry in funnel plot with at least five studies.

PART 2. GRADE TABLES

Note about the GRADE tables

Each GRADE table relates to one specific comparison. The evidence summarized in the tables is derived from a larger body of data extracted primarily from Cochrane reviews, which in many cases contained multiple comparisons. Additional background data can be made available upon request.

1. INDICATIONS

1.1. Induction of labour at term and beyond

Source of evidence: Gülmezoglu AM, Crowther CA, Middleton P. Induction of labour for improving birth outcomes for women at or beyond term. Cochrane Database of Systematic Reviews, 2006, Issue 4. Art. No.: CD004945; DOI: 10.1002/14651858.CD004945.pub2. (Data in this review were updated for the present guidelines. The current online published version of the review may not yet reflect the updates.)

Table 1.1.1. Induction of labour versus expectant management by gestational age

							Summary of findings					Importance
Quality assessment							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Induction of labour	Expectant management by gestational age	Relative risk (95% confidence interval)	Absolute		
Caesarean section (all gestational ages)												
20	RCT ¹	Serious ²	No serious inconsistency	No serious indirectness	No serious imprecision	None	697/3544 (19.7%)	774/3529 (21.9%)	RR 0.92 (0.8–1.06)	18 fewer per 1000 (from 44 fewer to 13 more)	⊕⊕⊕○ Moderate	Critical
								15%		12 fewer per 1000 (from 30 fewer to 9 more)		
Apgar score <7 at 5 minutes: 41 completed weeks												
6	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ³	None	24/2441 (1%)	29/2439 (1.2%)	RR 0.83 (0.49–1.41)	2 fewer per 1000 (from 6 fewer to 5 more)	⊕⊕⊕○ Moderate	Critical
								1.4%		2 fewer per 1000 (from 7 fewer to 6 more)		
Apgar score <7 at 5 minutes: 42 completed weeks												
4	RCT	Serious ²	No serious inconsistency	No serious indirectness	Very serious ^{2,4}	None	1/313 (0.3%)	7/309 (2.3%)	RR 0.24 (0.05–1.1)	17 fewer per 1000 (from 22 fewer to 2 more)	⊕○○○ Very low	Critical
								1.5%		11 fewer per 1000 (from 14 fewer to 2 more)		
Admission to neonatal intensive care unit												
10	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	302/3092 (9.8%)	336/3069 (10.9%)	RR 0.9 (0.78–1.04)	11 fewer per 1000 (from 24 fewer to 4 more)	⊕⊕⊕⊕ High	Critical
								6%		6 fewer per 1000 (from 13 fewer to 2 more)		

							Summary of findings					Importance
Quality assessment							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Induction of labour	Expectant management by gestational age	Relative risk (95% confidence interval)	Absolute		
Admission to neonatal intensive care unit: 41 completed weeks												
6	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	279/2766 (10.1%)	312/2747 (11.4%)	RR 0.89 (0.77–1.03)	12 fewer per 1000 (from 26 fewer to 3 more)	⊕⊕⊕⊕	Critical
								6%		7 fewer per 1000 (from 14 fewer to 2 more)	High	
Admission to neonatal intensive care unit: 42 completed weeks												
3	RCT	Serious ²	No serious inconsistency	No serious indirectness	Serious ³	None	23/210 (11%)	24/212 (11.3%)	RR 1.03 (0.62–1.71)	3 more per 1000 (from 43 fewer to 80 more)	⊕⊕○○	Critical
								7.8%		2 more per 1000 (from 30 fewer to 55 more)	Low	
Perinatal death: 37–40 completed weeks												
3	RCT	Serious ²	No serious inconsistency	No serious indirectness	Very serious ^{3,4}	None	0/415 (0%)	2/395 (0.5%)	RR 0.32 (0.03–3.09)	3 fewer per 1000 (from 5 fewer to 11 more)	⊕○○○	Critical
								0.6%		4 fewer per 1000 (from 6 fewer to 13 more)	Very low	
Perinatal death: 41 completed weeks												
12	RCT	Serious ²	No serious inconsistency	No serious indirectness	Serious ⁴	None	0/3164 (0%)	8/3137 (0.3%)	RR 0.27 (0.08–0.98)	2 fewer per 1000 (from 0 fewer to 2 fewer)	⊕⊕○○	Critical
								0.1%		1 fewer per 1000 (from 0 fewer to 1 fewer)	Low	
Perinatal death: 42 completed weeks												
2	RCT	Serious ²	No serious inconsistency	No serious indirectness	Very serious ^{3,4}	None	1/151 (0.7%)	3/145 (2.1%)	RR 0.41 (0.06–2.73)	12 fewer per 1000 (from 19 fewer to 36 more)	⊕○○○	Critical
								2%		12 fewer per 1000 (from 19 fewer to 35 more)	Very Low	

							Summary of findings					Importance
Quality assessment							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Induction of labour	Expectant management by gestational age	Relative risk (95% confidence interval)	Absolute		
Postpartum haemorrhage: 41 completed weeks												
2	RCT	Serious ²	No serious inconsistency	No serious indirect- ness ⁵	Serious ³	None	32/378 (8.5%)	35/379 (9.2%)	RR 0.91 (0.58–1.44)	8 fewer per 1000 (from 39 fewer to 41 more)	⊕⊕○○ Low	Critical
								7.5%		7 fewer per 1000 (from 32 fewer to 33 more)		

1 Randomized controlled trial.

2 Most of the evidence is from studies with a moderate risk of bias.

3 Imprecise confidence interval.

4 Very rare events.

5 The outcome postpartum haemorrhage is being used as proxy for severe maternal outcomes.

1.2. Induction of labour in diabetic women

Source of evidence: Boulvain M, Stan CM, Irion O. Elective delivery in diabetic pregnant women. Cochrane Database of Systematic Reviews, 2001, Issue 2. Art. No.: CD001997; DOI: 10.1002/14651858.CD001997. (Data in this review were updated for the present guidelines. The current online published version of the review may not yet reflect the updates.)

Table 1.2.1. Induction of labour versus expectant management for women with diabetes at or beyond term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Induction of labour	Expectant management	Relative risk (95% confidence interval)	Absolute		
Caesarean section												
1	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness	Very serious ²	None	25/100 (25%)	31/100 (31%)	RR 0.81 (0.52–1.26)	59 fewer per 1000 (from 149 fewer to 81 more)	⊕○○○ Very low	Critical
								31%		59 fewer per 1000 (from 149 fewer to 81 more)		
Perinatal death												
1	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness	Very serious ²	None	0/100 (0%)	0/100 (0%)	Not pooled	Not pooled	⊕○○○ Very Low	Critical
								0%		Not pooled		

1 Most of the evidence from studies with moderate/high risk of bias.

2 Confidence interval ranging from appreciable benefit to appreciable harm in a very small study population.

1.3. Induction of labour versus expectant management for suspected fetal macrosomia

Source of evidence: Irion O, Boulvain M. Induction of labour for suspected fetal macrosomia. Cochrane Database of Systematic Reviews, 1998, Issue 2. Art. No.: CD000938; DOI: 10.1002/14651858. CD000938. (Data in this review were updated for the present guidelines. The current online published version of the review may not yet reflect the updates.)

Table 1.3.1. Induction of labour versus expectant management for women with suspected macrosomia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Induction of labour	Expectant management	Relative risk (95% confidence interval)	Absolute		
Caesarean section												
4	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	157/590 (26.6%)	176/599 (29.4%)	RR 0.9 (0.75–1.09)	29 fewer per 1000 (from 73 fewer to 26 more)	⊕⊕⊕⊕ High	Critical
								29.7%		30 fewer per 1000 (from 74 fewer to 27 more)		
Apgar score <7 at 5 minutes												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	3/426 (0.7%)	2/431 (0.5%)	RR 1.51 (0.25–9.0)	2 more per 1000 (from 3 fewer to 37 more)	⊕⊕○○ Low	Critical
								0.2%		1 more per 1000 (from 2 fewer to 16 more)		
Admission to a neonatal intensive care unit												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	0/19 (0%)	0/21 (0%)	Not pooled	Not pooled	⊕○○○ Very Low	Critical
								0%		Not pooled		
Perinatal death												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	0/456 (0%)	0/460 (0%)	Not pooled	Not pooled	⊕○○○ Very Low	Critical
Shoulder dystocia												
4	RCT	No serious limitations	No serious inconsistency	Serious ³	Very serious ¹	None	14/590 (2.4%)	25/599 (4.2%)	RR 0.58 (0.31–1.09)	18 fewer per 1000 (from 29 fewer to 4 more)	⊕⊕○○ Low	Critical
								4.1%		17 fewer per 1000 (from 28 fewer to 4 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Induction of labour	Expectant management		
Fracture (any)												
4	RCT	No serious limitations	No serious inconsistency	Serious ³	Serious ²	None	2/590 (0.3%)	12/599 (2%)	RR 0.2 (0.05–0.79)	16 fewer per 1000 (from 4 fewer to 19 fewer)	⊕⊕⊕○ Moderate	Critical
								1%		8 fewer per 1000 (from 2 fewer to 9 fewer)		

1 Imprecise confidence intervals.

2 Very rare events.

3 Indirect outcome (Shoulder dystocia/fracture were used as proxies for severe perinatal morbidity).

1.4. Induction of labour for prelabour rupture of membranes at term

Source of evidence: Dare MR et al. Planned early birth versus expectant management (waiting) for prelabour rupture of membranes at term (37 weeks or more). Cochrane Database of Systematic Reviews, 2006, Issue 1. Art. No.: CD005302; DOI: 10.1002/14651858.CD005302.pub2. (Data in this review were updated for the present guidelines. The current online published version of the review may not yet reflect the updates.)

Table 1.4.1. Induction of labour versus expectant management for women with prelabour rupture of membranes at term (37 weeks or more)

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Induction of labour	Expectant management		
Maternal death												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	0/61 (0%)	0/62 (0%)	Not pooled	Not pooled	⊕⊕○○ Low	Critical
								0%		Not pooled		
Caesarean section												
12	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	333/3401 (9.8%)	360/3413 (10.5%)	RR 0.94 (0.82–1.08)	6 fewer per 1000 (from 19 fewer to 8 more)	⊕⊕⊕⊕ High	Critical
								10.9%		7 fewer per 1000 (from 20 fewer to 9 more)		
Perinatal death												
5	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ²	None	3/2946 (0.1%)	7/2924 (0.2%)	OR 0.46 (0.13–1.66)	1 fewer per 1000 (from 2 fewer to 2 more)	⊕⊕⊕○ Moderate	Critical
								0.1%		1 fewer per 1000 (from 1 fewer to 1 more)		
Apgar score <7 at 5 minutes												
6	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	335/3000 (11.2%)	366/3005 (12.2%)	RR 0.93 (0.81–1.07)	9 fewer per 1000 (from 23 fewer to 9 more)	⊕⊕⊕⊕ High	Critical
								5%		3 fewer per 1000 (from 9 fewer to 4 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Induction of labour	Expectant management		
Admission to neonatal intensive care unit or special care nursery												
5	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	356/2825 (12.6%)	484/2854 (17%)	RR 0.73 (0.58–0.91)	46 fewer per 1000 (from 15 fewer to 71 fewer)	⊕⊕⊕⊕	Critical
								17.3%		47 fewer per 1000 (from 16 fewer to 73 fewer)	High	

1 No events in only one trial. Relative effect not pooled.

2 Imprecise confidence intervals.

Table 1.4.2. Oxytocin versus expectant management/placebo for prelabour rupture of membranes at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oxytocin	Expectant management/ placebo		
Caesarean section												
7	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	183/1894 (9.7%)	196/1906 (10.3%)	RR 0.96 (0.8–1.16)	4 fewer per 1000 (from 21 fewer to 16 more)	⊕⊕⊕⊕	Critical
								12%		5 fewer per 1000 (from 24 fewer to 19 more)	High	
Perinatal death												
4	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	2/1637 (0.1%)	5/1613 (0.3%)	RR 0.46 (0.1–2.04)	2 fewer per 1000 (from 3 fewer to 3 more)	⊕⊕○○	Critical
								0.2%		1 fewer per 1000 (from 2 fewer to 2 more)	Low	
Apgar score <7 at 5 minutes												
5	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ²	None	177/1712 (10.3%)	193/1717 (11.2%)	RR 0.94 (0.78–1.14)	7 fewer per 1000 (from 25 fewer to 16 more)	⊕⊕⊕○	Critical
								5%		3 fewer per 1000 (from 11 fewer to 7 more)	Moderate	
Admission to neonatal intensive care unit or special care nursery												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	162/1427 (11.4%)	260/1456 (17.9%)	RR 0.58 (0.39–0.85)	75 fewer per 1000 (from 27 fewer to 109 fewer)	⊕⊕⊕⊕	Critical
								18.2%		76 fewer per 1000 (from 27 fewer to 111 fewer)	High	

1 Anything from a 90% reduction to more than 2-fold increase.

2 Anything from a 22% reduction to a 14% increase.

Table 1.4.3. Prostaglandins versus expectant management/placebo for prelabour rupture of membranes at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations			Prostaglandin	Expectant management/ placebo		
Caesarean section												
5	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	148/1493 (9.9%)	164/1487 (11%)	RR 0.91 (0.74–1.11)	10 fewer per 1000 (from 29 fewer to 12 more)	⊕⊕⊕⊕	Critical
								12.2%		11 fewer per 1000 (from 32 fewer to 13 more)	High	
Perinatal death												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	1/1259 (0.1%)	2/1261 (0.2%)	RR 0.5 (0.05–5.52)	1 fewer per 1000 (from 2 fewer to 7 more)	⊕⊕○○	Critical
								0.2%		1 fewer per 1000 (from 2 fewer to 9 more)	Low	
Apgar score <7 at 5 minutes												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	158/1288 (12.3%)	173/1288 (13.4%)	RR 0.91 (0.75–1.12)	12 fewer per 1000 (from 34 fewer to 16 more)	⊕⊕⊕⊕	Critical
								6.9%		6 fewer per 1000 (from 17 fewer to 8 more)	High	
Admission to neonatal intensive care unit or special care nursery												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	194/1398 (13.9%)	224/1398 (16%)	RR 0.87 (0.73–1.03)	21 fewer per 1000 (from 43 fewer to 5 more)	⊕⊕⊕⊕	Critical
								16.4%		21 fewer per 1000 (from 44 fewer to 5 more)	High	

1 Anything from a 95% reduction to a 5.5-fold increase.

Table 1.4.4. Caulophyllum versus placebo for prelabour rupture of membranes at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Caulophyllum	Placebo	Relative risk (95% confi- dence interval)	Absolute		
Caesarean section												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	2/20 (10%)	0/20 (0%)	RR 5 (0.26–98)	0 more per 1000 (from 0 fewer to 0 more)	⊕⊕○○ Low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		

1 Anything from a 74% reduction to a 98-fold increase.

1.5. Elective induction of labour at 37 weeks in women with a twin pregnancy

Source of evidence: Dodd JM, Crowther CA. Elective delivery of women with a twin pregnancy from 37 weeks' gestation. Cochrane Database of Systematic Reviews, 2003, Issue 1. Art. No.: CD003582; DOI: 10.1002/14651858.CD003582.

Table 1.5.1. Elective induction of labour at 37 weeks versus expectant management for women with a twin pregnancy

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Elective induction of labour at 37 weeks	Expectant management	Relative risk (95% confidence interval)	Absolute			
Caesarean birth													
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	3/17 (17.6%)	6/19 (31.6%)	RR 0.56 (0.16–1.9)	139 fewer per 1000 (from 265 fewer to 284 more)	⊕⊕○○ Low	Critical	
								31.6%		139 fewer per 1000 (from 265 fewer to 284 more)			
Perinatal death													
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	0/34 (0%)	0/38 (0%)	Not pooled	Not pooled	⊕⊕○○ Low	Critical	
								0%		Not pooled			
Apgar score <7 at 5 minutes													
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	0/34 (0%)	0/38 (0%)	Not pooled	Not pooled	⊕⊕○○ Low	Critical	
								0%		Not pooled			

¹ Very small study population or very rare events.

2. METHODS

2.1. Oxytocin

Source of evidence: Alfirevic Z, Kelly AJ, Dowswell T. Intravenous oxytocin alone for cervical ripening and induction of labour. Cochrane Database of Systematic Reviews, 2009, Issue 4. Art. No.: CD003246; DOI: 10.1002/14651858.CD003246.pub2.

Table 2.1.1. Oxytocin alone versus expectant management/placebo for cervical ripening and induction of labour

Quality assessment							Summary of findings				Importance	
							No. of patients		Effect			Quality
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consid- erations	Oxytocin	Expectant management/ placebo	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
3	RCT	Very serious ¹	No serious inconsistency	No serious indirectness	No serious imprecision	None	16/191 (8.4%)	112/208 (53.8%)	RR 0.16 (0.1–0.25)	452 fewer per 1000 (from 404 fewer to 485 fewer)	⊕⊕○○ Low	Critical
								54%		454 fewer per 1000 (from 405 fewer to 486 fewer)		
Caesarean section												
24	RCT	Serious ²	No serious inconsistency	No serious indirectness	No serious imprecision	None	339/3267 (10.4%)	301/3353 (9%)	RR 1.17 (1.01–1.35)	15 more per 1000 (from 1 more to 31 more)	⊕⊕⊕○ Moderate	Critical
								8.9%		15 more per 1000 (from 1 more to 31 more)		
Uterine hyperstimulation with fetal heart rate changes												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{3,4}	None	0/55 (0%)	2/45 (4.4%)	RR 0.16 (0.01–3.34)	37 fewer per 1000 (from 44 fewer to 104 more)	⊕⊕○○ Low	Critical
								4.4%		37 fewer per 1000 (from 44 fewer to 103 more)		
Apgar score <7 at 5 minutes												
11	RCT	Serious ²	No serious inconsistency	No serious indirectness	Serious ³	None	26/2394 (1.1%)	43/2464 (1.7%)	RR 0.69 (0.44–1.11)	5 fewer per 1000 (from 10 fewer to 2 more)	⊕⊕○○ Low	Critical
								1.2%		4 fewer per 1000 (from 7 fewer to 1 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consid- erations			Oxytocin	Expectant management/ placebo		
Admission to neonatal intensive care unit												
7	RCT	Serious ²	No serious inconsistency	No serious indirectness	No serious imprecision	None	264/2196 (12%)	333/2191 (15.2%)	RR 0.79 (0.68–0.92)	32 fewer per 1000 (from 12 fewer to 49 fewer)	⊕⊕⊕○ Moderate	Critical
								11.6%		24 fewer per 1000 (from 9 fewer to 37 fewer)		
Perinatal death, excluding major congenital anomalies												
8	RCT	Serious ²	No serious inconsistency	No serious indirectness	Very serious ^{3,4}	None	1/2235 (0%)	5/2271 (0.2%)	RR 0.39 (0.09–1.64)	1 fewer per 1000 (from 2 fewer to 1 more)	⊕○○○ Very low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		

1 Most of the evidence from studies with moderate/high risk of bias.

2 Most of the evidence from studies with moderate risk of bias.

3 95% confidence intervals ranging from appreciable benefit to appreciable harm.

4 Very small study population or very rare events.

Table 2.1.2. Oxytocin versus intracervical prostaglandin E2 for cervical ripening and induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consid- erations			Oxytocin	Intracervical PGE2		
Vaginal birth not achieved within 24 hours												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	63/125 (50.4%)	46/133 (34.6%)	RR 1.47 (1.1–1.96)	163 more per 1000 (from 35 more to 332 more)	⊕⊕⊕⊕ High	Critical
								33.3%		157 more per 1000 (from 33 more to 320 more)		
Caesarean section												
14	RCT	Serious ¹	No serious inconsistency	No serious indirectness	No serious imprecision	None	123/643 (19.1%)	94/688 (13.7%)	RR 1.37 (1.08–1.74)	51 more per 1000 (from 11 more to 101 more)	⊕⊕⊕○ Moderate	Critical
								11.4%		42 more per 1000 (from 9 more to 84 more)		
Uterine hyperstimulation with fetal heart rate changes												
2	RCT	Very serious ²	No serious inconsistency	No serious indirectness	Very serious ^{3,4}	None	4/132 (3%)	2/133 (1.5%)	RR 2.02 (0.38–10.75)	15 more per 1000 (from 9 fewer to 147 more)	⊕○○○ Very low	Critical
								1.2%		12 more per 1000 (from 7 fewer to 117 more)		
Apgar score <7 at 5 minutes												
6	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{3,4}	None	14/344 (4.1%)	7/357 (2%)	RR 2.05 (0.86–4.87)	21 more per 1000 (from 3 fewer to 76 more)	⊕○○○ Very low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		

1 Most of the evidence from studies with moderate risk of bias.

2 Most of the evidence from studies with moderate/high risk of bias.

3 95% confidence intervals ranging from appreciable benefit to appreciable harm.

4 Very small study population or very rare events.

Table 2.1.3. Oxytocin versus vaginal prostaglandin E2 for cervical ripening and induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consid- erations	Oxytocin alone	Vaginal PGE2	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
3	RCT	Serious ¹	No serious inconsistency	No serious indirectness	No serious imprecision	None	73/132 (55.3%)	40/128 (31.3%)	RR 1.77 (1.31–2.38)	241 more per 1000 (from 97 more to 431 more)	⊕⊕⊕○ Moderate	Critical
								34.3%		264 more per 1000 (from 106 more to 473 more)		
Caesarean section												
26	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ²	None ³	274/2259 (12.1%)	246/2255 (10.9%)	RR 1.11 (0.94–1.3)	12 more per 1000 (from 7 fewer to 33 more)	⊕⊕○○ Low	Critical
								11.2%		12 more per 1000 (from 7 fewer to 34 more)		
Uterine hyperstimulation with fetal heart rate changes												
8	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious	None	0/427 (0%)	2/416 (0.5%)	RR 0.35 (0.04–3.28)	3 fewer per 1000 (from 5 fewer to 11 more)	⊕○○○ Very low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		
Apgar score <7 at 5 minutes												
16	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ⁴	None ⁵	20/1903 (1.1%)	32/1888 (1.7%)	RR 0.62 (0.36–1.05)	6 fewer per 1000 (from 11 fewer to 1 more)	⊕⊕○○ Low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		
Admission to neonatal intensive care unit												
5	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ⁴	None	156/1428 (10.9%)	182/1417 (12.8%)	RR 0.85 (0.7–1.04)	19 fewer per 1000 (from 39 fewer to 5 more)	⊕⊕○○ Low	Critical
								5%		7 fewer per 1000 (from 15 fewer to 2 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations			Oxytocin alone	Vaginal PGE2		
Serious maternal morbidity or death												
3	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{6,7}	None	0/85 (0%)	1/90 (1.1%)	RR 0.37 (0.02–8.93)	7 fewer per 1000 (from 11 fewer to 88 more)	⊕○○○ Very low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		

1 Most of the evidence from studies with moderate risk of bias.

2 95% confidence intervals ranging from negligible benefit to appreciable harm.

3 There is some asymmetry in the funnel plot, but it is unlikely to be due to publication bias (low heterogeneity, not statistically significant results etc.).

4 95% confidence intervals ranging from appreciable benefit to negligible harm.

5 Besides the asymmetry in the funnel plot, individual studies results are not statistically significant and there is very low heterogeneity between studies.

6 Very small study population or very rare events.

7 95% confidence intervals ranging from appreciable benefit to appreciable harm.

Table 2.1.4. Oxytocin versus vaginal prostaglandin F2 α for cervical ripening and induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Oxytocin alone	Vaginal prostaglandin F2 α	Relative risk (95% confidence interval)	Absolute		
Caesarean section												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	18/136 (13.2%)	16/144 (11.1%)	RR 1.19 (0.65–2.18)	21 more per 1000 (from 39 fewer to 131 more)	⊕⊕○○ Low	Critical
								3.8%		7 more per 1000 (from 13 fewer to 45 more)		

1 95% confidence intervals ranging from appreciable benefit to appreciable harm.

2.2. Oxytocin plus amniotomy

Source of evidence: Howarth G, Botha DJ. Amniotomy plus intravenous oxytocin for induction of labour. Cochrane Database of Systematic Reviews, 2001, Issue 3. Art. No.: CD003250; DOI: 10.1002/14651858.CD003250. (Data in this review were updated for the present guidelines. The current online published version of the review may not yet reflect the updates.)

Table 2.2.1. Intravenous oxytocin and amniotomy versus placebo/no treatment for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Intravenous oxytocin plus amniotomy	Expectant management/ placebo		
Caesarean section												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	4/92 (4.3%)	1/92 (1.1%)	RR 4 (0.46–35.11)	33 more per 1000 (from 6 fewer to 371 more)	⊕⊕○○ Low	Critical
								1.1%		33 more per 1000 (from 6 fewer to 375 more)		
Serious neonatal morbidity or perinatal death												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ²	None	0/92 (0%)	1/92 (1.1%)	RR 0.33 (0.01–8.08)	7 fewer per 1000 (from 11 fewer to 77 more)	⊕⊕○○ Low	Critical
								1.1%		7 fewer per 1000 (from 11 fewer to 78 more)		

1 Anything from a 54% reduction to more than 35-fold increase.

2 Anything from a 99% reduction to more than 8-fold increase.

Table 2.2.2. Intravenous oxytocin and amniotomy versus vaginal prostaglandin for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Intravenous oxytocin and amniotomy	Vaginal prostaglandin		
Vaginal birth not achieved within 24 hours												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ²	None	9/21 (42.9%)	10/21 (47.6%)	RR 0.9 (0.46–1.75)	48 fewer per 1000 (from 257 fewer to 357 more)	⊕⊕○○ Low	Critical
								47.6%		48 fewer per 1000 (from 257 fewer to 357 more)		
Uterine hyperstimulation with fetal heart rate changes												
4	RCT	No serious limitations	Serious ³	No serious indirectness	Serious ⁴	None	18/378 (4.8%)	21/361 (5.8%)	RR 0.81 (0.45–1.45)	11 fewer per 1000 (from 32 fewer to 26 more)	⊕⊕○○ Low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		
Caesarean section												
10	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	78/574 (13.6%)	73/566 (12.9%)	RR 1.06 (0.79–1.42)	8 more per 1000 (from 27 fewer to 54 more)	⊕⊕⊕⊕ High	Critical
								14.1%		8 more per 1000 (from 30 fewer to 59 more)		
Serious maternal morbidity or death												
2	RCT	Serious ⁵	No serious inconsistency	No serious indirectness	Very serious ⁶	None	0/194 (0%)	0/184 (0%)	Not pooled	Not pooled	⊕○○○ Very low	Critical
								0%		Not pooled		
Apgar score <7 at 5 minutes												
3	RCT	Serious ⁷	Serious ⁸	No serious indirectness	Very serious ⁹	None	5/87 (5.7%)	3/89 (3.4%)	RR 1.6 (0.44 to 5.81)	20 more per 1000 (from 19 fewer to 162 more)	⊕○○○ Very low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Intravenous oxytocin and amniotomy	Vaginal prostaglandin	Relative risk (95% confidence interval)	Absolute		
Admission to neonatal intensive care unit												
2	RCT	Serious ⁵	No serious inconsistency	No serious indirectness	Very serious ¹⁰	None	9/184 (4.9%)	15/178 (8.4%)	RR 0.59 (0.27–1.29)	35 fewer per 1000 (from 62 fewer to 24 more)	⊕○○○ Very low	Critical
								4.8%		20 fewer per 1000 (from 35 fewer to 14 more)		
Perinatal death												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ¹¹	None	0/30 (0%)	0/30 (0%)	Not pooled	Not pooled	⊕○○○ Very low	Critical
								0%		Not pooled		

1 Only one small, underpowered trial.

2 Anything from a 54% reduction to a 75% increase.

3 No events in 3 trials and 39 events in one trial. Heterogeneity not applicable.

4 Anything from a 55% reduction to a 45% increase.

5 Underpowered trials.

6 No events in two underpowered trials. Relative effect not pooled.

7 Three small and underpowered trials.

8 Heterogeneity. $I^2 = 51\%$

9 Anything from a 56% reduction to a 5.81-fold increase.

10 Anything from a 73% reduction to a 29% increase.

11 No events in only one small, underpowered trial. Relative effect not pooled.

Table 2.2.3. Intravenous oxytocin and amniotomy versus intracervical prostaglandin for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Intravenous oxytocin and amniotomy	Intracervical prostaglandin		
Vaginal birth not achieved within 24 hours												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	1/30 (3.3%)	4/30 (13.3%)	RR 0.25 (0.03–2.11)	100 fewer per 1000 (from 129 fewer to 148 more)	⊕○○○ Very low	Critical
								13.3%		100 fewer per 1000 (from 129 fewer to 148 more)		
Uterine hyperstimulation with fetal heart rate changes												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ³	None	0/30 (0%)	0/30 (0%)	Not pooled	Not pooled	⊕○○○ Very low	Critical
								0%		Not pooled		
Caesarean section												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ⁴	None	1/30 (3.3%)	4/30 (13.3%)	RR 0.25 (0.03–2.11)	100 fewer per 1000 (from 129 fewer to 148 more)	⊕○○○ Very low	Critical
								13.3%		100 fewer per 1000 (from 129 fewer to 148 more)		

1 Only one small, underpowered trial.

2 Anything from a 97% reduction to a 2.11-fold increase.

3 No events in only one trial. Relative effect not pooled.

4 Anything from a 97% reduction to a 2.11-fold increase.

Table 2.2.4. Intravenous oxytocin and amniotomy versus oxytocin alone for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Intravenous oxytocin and amniotomy	Oxytocin alone	Relative risk (95% confidence interval)	Absolute		
Caesarean section												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	27/156 (17.3%)	25/153 (16.3%)	RR 1.05 (0.65–1.71)	8 more per 1000 (from 57 fewer to 116 more)	⊕⊕⊕○ Moderate	Critical
								13.2%		7 more per 1000 (from 46 fewer to 94 more)		
Apgar score <7 at 5 minutes												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ²	None	4/106 (3.8%)	1/103 (1%)	RR 3.89 (0.44–34.19)	28 more per 1000 (from 5 fewer to 322 more)	⊕⊕○○ Low	Critical
								1%		29 more per 1000 (from 6 fewer to 332 more)		

1 Anything from a 45% reduction to a 71% increase.

2 Anything from a 55% reduction to more than 34-fold increase.

Table 2.2.5. Intravenous oxytocin and amniotomy versus amniotomy alone for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Intravenous oxytocin and amniotomy	Amniotomy alone	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	3/148 (2%)	24/148 (16.2%)	RR 0.12 (0.04–0.41)	143 fewer per 1000 (from 96 fewer to 156 fewer)	⊕⊕○○ Low	Critical
								20.1%		177 fewer per 1000 (from 119 fewer to 193 fewer)		
Caesarean section												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ²	None	5/254 (2%)	11/257 (4.3%)	RR 0.46 (0.16–1.3)	23 fewer per 1000 (from 36 fewer to 13 more)	⊕⊕○○ Low	Critical
								5.7%		31 fewer per 1000 (from 48 fewer to 17 more)		
Perinatal death												
1	RCT	Serious ³	No serious inconsistency	No serious indirectness	Very serious ⁴	None	1/50 (2%)	0/50 (0%)	RR 3 (0.13–71.92)	0 more per 1000 (from 0 fewer to 0 more)	⊕○○○ Very low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		

1 Anything from a 96% to a 59% reduction.

2 Anything from a 84% reduction to a 30% increase.

3 Only one underpowered trial.

4 Anything from a 87% reduction to almost 72-fold increase.

2.3. Vaginal misoprostol

Source of evidence: Hofmeyr GJ, Gülmezoglu AM, Pileggi C. Vaginal misoprostol for cervical ripening and induction of labour. Cochrane Database of Systematic Reviews, 2003, Issue 1. Art. No.: CD000941; DOI: 10.1002/14651858.CD000941. (Data in this review were updated for the present guidelines. The current online published version of the review may not yet reflect the updates.)

Table 2.3.1. Vaginal misoprostol versus expectant management for cervical ripening and induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Vaginal misoprostol	Expectant man- agement/placebo		
Vaginal birth not achieved within 24 hours												
5	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	35/304 (11.5%)	74/465 (15.9%)	RR 0.51 (0.37–0.71)	78 fewer per 1000 (from 46 fewer to 100 fewer)	⊕⊕⊕⊕ High	Critical
								23.1%		113 fewer per 1000 (from 67 fewer to 146 fewer)		
Caesarean section												
10	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious	Reporting bias ¹	77/486 (15.8%)	137/655 (20.9%)	RR 0.81 (0.63–1.05)	40 fewer per 1000 (from 77 fewer to 10 more)	⊕⊕○○ Low	Critical
								20%		38 fewer per 1000 (from 74 fewer to 10 more)		
Uterine hyperstimulation with fetal heart rate changes												
5	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ²	None	12/288 (4.2%)	8/489 (1.6%)	RR 2.38 (0.95–5.99)	23 more per 1000 (from 1 fewer to 82 more)	⊕⊕⊕○ Moderate	Critical
								1.3%		18 more per 1000 (from 1 fewer to 65 more)		
Apgar score <7 at 5 minutes												
4	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ³	None	2/275 (0.7%)	3/442 (0.7%)	RR 2 (0.34–11.8)	7 more per 1000 (from 4 fewer to 73 more)	⊕⊕⊕○ Moderate	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Vaginal misoprostol	Expectant man- agement/placebo		
Admission to neonatal intensive care unit												
6	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ³	None	25/321 (7.8%)	39/531 (7.3%)	RR 0.94 (0.6–1.48)	4 fewer per 1000 (from 29 fewer to 35 more)	⊕⊕⊕○ Moderate	Critical
								3.8%		2 fewer per 1000 (from 15 fewer to 18 more)		
Perinatal death												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ⁴	None	0/62 (0%)	1/60 (1.7%)	RR 0.34 (0.01–8.14)	11 fewer per 1000 (from 17 fewer to 119 more)	⊕⊕○○ Low	Critical
								1.3%		9 fewer per 1000 (from 13 fewer to 93 more)		
Serious maternal complication												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ⁴	None	2/137 (1.5%)	3/135 (2.2%)	RR 0.68 (0.12–3.87)	7 fewer per 1000 (from 20 fewer to 64 more)	⊕⊕○○ Low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		
Maternal death												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ⁵	None	0/24 (0%)	0/21 (0%)	Not pooled	Not pooled	⊕○○○ Very Low	Critical
								0%		Not pooled		

1 Evident funnel plot asymmetry.

2 95% confidence interval ranging from appreciable harm to negligible benefit.

3 95% confidence interval ranging from appreciable benefit to appreciable harm.

4 95% confidence interval ranging from appreciable benefit to negligible harm in a small population size.

5 Very small sample size.

Table 2.3.2. Vaginal misoprostol versus vaginal prostaglandins for cervical ripening and induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Vaginal misoprostol	Vaginal prostag- landin		
Vaginal birth not achieved within 24 hours												
22	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	Reporting bias ¹	920/2550 (36.1%)	1179/2679 (44%)	RR 0.84 (0.78–0.89)	70 fewer per 1000 (from 48 fewer to 97 fewer)	⊕⊕⊕○ Moderate	Critical
								44.3%		71 fewer per 1000 (from 49 fewer to 97 fewer)		
Caesarean section												
33	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	621/3051 (20.4%)	743/3178 (23.4%)	RR 0.91 (0.83–1)	21 fewer per 1000 (from 40 fewer to 0 more)	⊕⊕⊕⊕ High	Critical
								20.4%		18 fewer per 1000 (from 35 fewer to 0 more)		
Uterine hyperstimulation with fetal heart rate changes												
30	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	172/2576 (6.7%)	139/2628 (5.3%)	RR 1.32 (1.07–1.63)	17 more per 1000 (from 4 more to 33 more)	⊕⊕⊕⊕ High	Critical
								2.5%		8 more per 1000 (from 2 more to 16 more)		
Apgar score <7 at 5 minutes												
17	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ²	None	59/1931 (3.1%)	60/2038 (2.9%)	RR 1.01 (0.72–1.41)	0 more per 1000 (from 8 fewer to 12 more)	⊕⊕⊕○ Moderate	Critical
								1.4%		0 more per 1000 (from 4 fewer to 6 more)		
Admission to neonatal intensive care unit												
20	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	227/2248 (10.1%)	231/2282 (10.1%)	RR 0.97 (0.82–1.15)	3 fewer per 1000 (from 18 fewer to 15 more)	⊕⊕⊕⊕ High	Critical
								5.2%		2 fewer per 1000 (from 9 fewer to 8 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Vaginal misoprostol	Vaginal prostag- landin	Relative risk (95% confidence interval)	Absolute		
Perinatal death												
6	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	4/685 (0.6%)	4/630 (0.6%)	RR 0.85 (0.24–3)	1 fewer per 1000 (from 5 fewer to 13 more)	⊕⊕⊕⊕	Critical
								0.3%		0 fewer per 1000 (from 2 fewer to 6 more)	High	
Serious maternal morbidity or death												
2	RCT	Serious	No serious inconsistency	No serious indirectness	Serious	None	0/110 (0%)	0/113 (0%)	Not pooled	Not pooled	⊕○○○	Critical
								0%		Not pooled	Very Low	
Serious maternal complications												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ³	None	1/150 (0.7%)	2/153 (1.3%)	RR 0.5 (0.05–5.39)	7 fewer per 1000 (from 12 fewer to 57 more)	⊕⊕⊕○	Critical
								1.4%		7 fewer per 1000 (from 13 fewer to 61 more)	Moderate	

1 In the funnel plot, the results of individual studies were asymmetric, and there was severe heterogeneity in the I² test, suggesting publication bias.

2 95% confidence interval ranging from appreciable benefit to appreciable harm.

3 Very rare events.

Table 2.3.3. Vaginal misoprostol versus intracervical prostaglandin for cervical ripening and induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Vaginal misoprostol	Intracervical prostaglandin	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
12	RCT	Very serious ¹	No serious inconsistency	No serious indirectness	No serious imprecision	None	248/764 (32.5%)	376/763 (49.3%)	RR 0.66 (0.58–0.74)	168 fewer per 1000 (from 128 fewer to 207 fewer)	⊕⊕○○ Low	Critical
								42.1%		143 fewer per 1000 (from 109 fewer to 177 fewer)		
Caesarean section												
27	RCT	Serious ²	No serious inconsistency	No serious indirectness	No serious imprecision	None	329/1662 (19.8%)	330/1624 (20.3%)	RR 0.97 (0.85–1.11)	6 fewer per 1000 (from 30 fewer to 22 more)	⊕⊕⊕○ Moder- ate	Critical
								19.6%		6 fewer per 1000 (from 29 fewer to 22 more)		
Uterine hyperstimulation with fetal heart rate changes												
21	RCT	Very serious ³	No serious inconsistency	No serious indirectness	No serious imprecision	None	98/1167 (8.4%)	39/1132 (3.4%)	RR 2.32 (1.64–3.28)	45 more per 1000 (from 22 more to 79 more)	⊕⊕○○ Low	Critical
								2.5%		33 more per 1000 (from 16 more to 57 more)		
Apgar score <7 at 5 minutes												
16	RCT	Serious ⁴	No serious inconsistency	No serious indirectness	Serious ⁵	None	17/1104 (1.5%)	18/1085 (1.7%)	RR 0.93 (0.51–1.7)	1 fewer per 1000 (from 8 fewer to 12 more)	⊕⊕○○ Low	Critical
								1.3%		1 fewer per 1000 (from 6 fewer to 9 more)		
Admission to neonatal intensive care unit												
12	RCT	Very serious ⁶	No serious inconsistency	No serious indirectness	Serious ⁷	None	70/839 (8.3%)	62/834 (7.4%)	RR 1.12 (0.81–1.54)	9 more per 1000 (from 14 fewer to 40 more)	⊕○○○ Very low	Critical
								6.2%		7 more per 1000 (from 12 fewer to 33 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Vaginal misoprostol	Intracervical prostaglandin	Relative risk (95% confidence interval)	Absolute		
Perinatal death												
2	RCT	Serious ⁸	No serious inconsistency	No serious indirectness	Serious ⁵	None	1/191 (0.5%)	0/187 (0%)	RR 2.85 (0.12–68.95)	0 more per 1000 (from 0 fewer to 0 more)	⊕⊕○○ Low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		

- 1 4 out of 12 studies have very serious limitations, accounting for 54.9% of the pooled effect. In addition, 4 studies have serious or potentially very serious limitations.
- 2 10 out of 27 studies have serious or potentially very serious limitations. In addition, seven studies have very serious limitations, accounting for 37.3% of the pooled results.
- 3 7 out of 21 studies have very serious limitations, accounting for 65.6% of the pooled results. In addition, four studies have potentially very serious limitations.
- 4 8 out of 16 studies have serious, potentially serious or very serious limitations. Studies with very serious limitations accounted for 21.8% of the pooled results.
- 5 95% confidence interval ranging from appreciable benefit to appreciable harm.
- 6 7 out of 12 studies have serious, potentially very serious or very serious limitations. Studies with very serious limitations, accounting for 61.8% of the pooled results.
- 7 95% confidence interval ranging from negligible benefit to appreciable harm.
- 8 1 out of 2 studies have potentially very serious limitations.

Table 2.3.4. Vaginal misoprostol versus oxytocin for cervical ripening and induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Misoprostol	Oxytocin	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
9	RCT	No serious limitations	Serious ¹	No serious indirectness	No serious imprecision	None	112/592 (18.9%)	200/608 (32.9%)	RR 0.62 (0.43–0.9)	125 fewer per 1000 (from 33 fewer to 188 fewer)	⊕⊕⊕○ Moderate	Critical
								36.2%		138 fewer per 1000 (from 36 fewer to 206 fewer)		
Caesarean section												
25	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	258/1527 (16.9%)	364/1547 (23.5%)	RR 0.76 (0.6–0.96)	56 fewer per 1000 (from 9 fewer to 94 fewer)	⊕⊕⊕⊕ High	Critical
								20%		48 fewer per 1000 (from 8 fewer to 80 fewer)		
Uterine hyperstimulation with fetal heart rate changes												
9	RCT	Serious ²	No serious inconsis- tency ³	No serious indirectness	Serious	Reporting bias ⁴	49/690 (7.1%)	28/729 (3.8%)	RR 1.43 (0.73–2.79)	17 more per 1000 (from 10 fewer to 69 more)	⊕○○○ Very low	Critical
								4.1%		18 more per 1000 (from 11 fewer to 73 more)		
Apgar score <7 at 5 minutes												
13	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	Reporting bias ⁴	22/938 (2.3%)	41/968 (4.2%)	RR 0.56 (0.34–0.92)	19 fewer per 1000 (from 3 fewer to 28 fewer)	⊕⊕⊕○ Moderate	Critical
								2%		9 fewer per 1000 (from 2 fewer to 13 fewer)		
Admission to neonatal intensive care unit												
11	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ⁵	Reporting bias ⁴	91/729 (12.5%)	107/762 (14%)	RR 0.88 (0.69–1.13)	17 fewer per 1000 (from 44 fewer to 18 more)	⊕⊕○○ Low	Critical
								8.2%		10 fewer per 1000 (from 25 fewer to 11 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Misoprostol	Oxytocin		
Perinatal death												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ⁶	None	3/181 (1.7%)	2/153 (1.3%)	RR 0.78 (0.14–4.39)	3 fewer per 1000 (from 11 fewer to 44 more)	⊕⊕⊕⊖ Moderate	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		
Serious maternal morbidity or death												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ⁷	None	2/94 (2.1%)	0/96 (0%)	RR 6.11 (0.31–119.33)	0 more per 1000 (from 0 fewer to 0 more)	⊕⊕⊖⊖ Low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		
Serious maternal complications												
1	RCT	Serious ⁸	No serious inconsistency	No serious indirectness	Very serious ⁷	None	3/50 (6%)	5/50 (10%)	RR 0.6 (0.15–2.38)	40 fewer per 1000 (from 85 fewer to 138 more)	⊕⊖⊖⊖ Very low	Critical
								10%		40 fewer per 1000 (from 85 fewer to 138 more)		

1 Unexplained heterogeneity ($I^2=70\%$).

2 5 out of 9 studies have serious or potentially very serious limitations.

3 Moderate heterogeneity that can be associated with publication bias.

4 Evident asymmetry in the funnel plot.

5 95% confidence interval ranging from appreciable benefit to negligible harm.

6 95% confidence interval ranging from appreciable benefit to appreciable harm.

7 95% confidence interval ranging from appreciable benefit to appreciable harm associated with very small sample size.

8 Only one study provided evidence in this outcome. This study has potentially very serious limitations.

Table 2.3.5. Low-dose vaginal misoprostol versus high-dose vaginal misoprostol for cervical ripening and induction of labour

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Low-dose misoprostol	High-dose misoprostol	Relative risk (95% confidence interval)	Absolute			
Vaginal birth not achieved within 24 hours													
12	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	335/943 (35.5%)	313/944 (33.2%)	RR 1.08 (0.96–1.21)	27 more per 1000 (from 13 fewer to 70 more)	⊕⊕⊕⊕	Critical	
								25.6%		20 more per 1000 (from 10 fewer to 54 more)	High		
Caesarean section													
21	RCT	Serious ¹	No serious inconsistency	No serious indirectness	No serious imprecision	None	263/1452 (18.1%)	273/1461 (18.7%)	RR 0.94 (0.76–1.16)	11 fewer per 1000 (from 45 fewer to 30 more)	⊕⊕⊕○	Critical	
								20%		12 fewer per 1000 (from 48 fewer to 32 more)	Moderate		
Uterine hyperstimulation with fetal heart rate changes													
16	RCT	Serious ²	No serious inconsistency	No serious indirectness	No serious imprecision	None	53/1262 (4.2%)	107/1278 (8.4%)	RR 0.51 (0.37–0.69)	41 fewer per 1000 (from 26 fewer to 53 fewer)	⊕⊕⊕○	Critical	
								7.4%		36 fewer per 1000 (from 23 fewer to 47 fewer)	Moderate		
Apgar score <7 at 5 minutes													
13	RCT	Serious ³	No serious inconsistency	No serious indirectness	Serious ⁴	None	19/1017 (1.9%)	25/1028 (2.4%)	RR 0.77 (0.44–1.37)	6 fewer per 1000 (from 14 fewer to 9 more)	⊕⊕○○	Critical	
								2.5%		6 fewer per 1000 (from 14 fewer to 9 more)	Low		
Admission to neonatal intensive care unit													
9	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ⁵	None	98/889 (11%)	121/906 (13.4%)	RR 0.82 (0.64–1.05)	24 fewer per 1000 (from 48 fewer to 7 more)	⊕⊕⊕○	Critical	
								7.1%		13 fewer per 1000 (from 26 fewer to 4 more)	Moderate		

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Low-dose misoprostol	High-dose misoprostol	Relative risk (95% confidence interval)	Absolute			
Perinatal death													
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ⁶	None	0/94 (0%)	5/93 (5.4%)	RR 0.17 (0.02–1.34)	45 fewer per 1000 (from 53 fewer to 18 more)	⊕⊕○○ Low	Critical	
								4.8%		40 fewer per 1000 (from 47 fewer to 16 more)			

- 1 13 out of 21 studies have serious limitations or potentially very serious limitations. In addition, one study has very serious limitations.
- 2 9 out of 16 studies have serious or potentially very serious limitations. In addition, one study has very serious limitations.
- 3 7 out of 13 studies have serious or potentially very serious limitations. In addition, one study has very serious limitations.
- 4 95% confidence interval ranging from appreciable benefit to appreciable harm.
- 5 95% confidence interval ranging from appreciable benefit to negligible harm.
- 6 95% confidence interval ranging from appreciable harm to appreciable benefit in a very small study population.

Table 2.3.6. Gel versus tablet as vaginal misoprostol formulations for cervical ripening and induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Misoprostol gel	Misoprostol tablet	Relative risk (95% confidence interval)	Absolute		
Caesarean section												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	64/233 (27.5%)	60/234 (25.6%)	RR 1.07 (0.79–1.45)	18 more per 1000 (from 54 fewer to 115 more)	⊕⊕⊕○ Moderate	Critical
								25.6%		18 more per 1000 (from 54 fewer to 115 more)		
Uterine hyperstimulation with fetal heart rate changes												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	18/233 (7.7%)	37/234 (15.8%)	RR 0.49 (0.29–0.83)	81 fewer per 1000 (from 27 fewer to 112 fewer)	⊕⊕⊕⊕ High	Critical
								15.8%		81 fewer per 1000 (from 27 fewer to 112 fewer)		
Apgar score <7 at 5 minutes												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ²	None	15/233 (6.4%)	13/234 (5.6%)	RR 1.16 (0.56–2.38)	9 more per 1000 (from 24 fewer to 77 more)	⊕⊕⊕○ Moderate	Critical
								5.6%		9 more per 1000 (from 25 fewer to 77 more)		
Admission to neonatal intensive care unit												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ³	None	22/233 (9.4%)	30/234 (12.8%)	RR 0.74 (0.44–1.24)	33 fewer per 1000 (from 72 fewer to 31 more)	⊕⊕⊕○ Moderate	Critical
								12.8%		33 fewer per 1000 (from 72 fewer to 31 more)		

1 95% confidence interval ranging from negligible benefit to appreciable harm.

2 95% confidence interval ranging from appreciable benefit to appreciable harm.

3 95% confidence interval ranging from appreciable benefit to negligible harm.

2.4. Oral misoprostol

Source of evidence: Alfirevic Z, Weeks A. Oral misoprostol for induction of labour. Cochrane Database of Systematic Reviews, 2006, Issue 2. Art. No.: CD001338; DOI: 10.1002/14651858.CD001338.pub2.

Table 2.4.1. Oral misoprostol versus placebo for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oral misoprostol	Placebo		
Vaginal birth not achieved within 24 hours												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	3/47 (6.4%)	20/49 (40.8%)	RR 0.16 (0.05–0.49)	343 fewer per 1000 (from 208 fewer to 388 fewer)	⊕⊕⊕○ Moderate	Critical
								40.8%		343 fewer per 1000 (from 208 fewer to 388 fewer)		
Caesarean section												
6	RCT	serious ²	No serious inconsistency ²	No serious indirectness	No serious imprecision	None	31/312 (9.9%)	51/317 (16.1%)	RR 0.61 (0.41–0.93)	63 fewer per 1000 (from 11 fewer to 95 fewer)	⊕⊕⊕○ Moderate	Critical
								12.9%		50 fewer per 1000 (from 9 fewer to 76 fewer)		
Uterine hyperstimulation with fetal heart rate changes												
7	RCT	serious ²	No serious inconsistency	No serious indirectness	Very serious ³	None	8/330 (2.4%)	2/339 (0.6%)	RR 2.71 (0.84–8.68)	10 more per 1000 (from 1 fewer to 45 more)	⊕○○○ Very low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		
Apgar score <7 at 5 minutes												
3	RCT	serious ²	No serious inconsistency	No serious indirectness	Very serious ³	None	5/164 (3%)	7/168 (4.2%)	RR 0.73 (0.24–2.26)	11 fewer per 1000 (from 32 fewer to 53 more)	⊕○○○ Very low	Critical
								3.9%		11 fewer per 1000 (from 30 fewer to 49 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oral misoprostol	Placebo		
Admission to neonatal intensive care unit												
4	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ³	None	12/215 (5.6%)	17/219 (7.8%)	RR 0.73 (0.37–1.44)	21 fewer per 1000 (from 49 fewer to 34 more)	⊕⊕○○ Low	Critical
								4.9%		13 fewer per 1000 (from 31 fewer to 22 more)		
Perinatal death												
1	RCT	Serious ⁴	No serious inconsistency	No serious indirectness	Very serious ⁴	None	0/39 (0%)	0/41 (0%)	Not pooled	Not pooled	⊕○○○ Very low	Critical
								0%		Not pooled		
Serious maternal morbidity or death												
1	RCT	Serious ⁴	No serious inconsistency	No serious indirectness	Very serious ⁴	None	0/39 (0%)	0/41 (0%)	Not pooled	Not pooled	⊕○○○ Very low	Critical
								0%		Not pooled		

1 Very small simple size.

2 Most of the pooled effect comes from studies with moderate risk of bias.

3 95% confidence interval ranging from negligible benefit to appreciable harm, with very rare events.

4 Effect is not estimable.

Table 2.4.2. Oral misoprostol versus oxytocin for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oral misoprostol	Oxytocin		
Vaginal birth not achieved within 24 hours												
5	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ²	None	40/277 (14.4%)	32/256 (12.5%)	RR 1.17 (0.77–1.8)	21 more per 1000 (from 29 fewer to 100 more)	⊕⊕⊕○ Moderate	Critical
								11.4%		19 more per 1000 (from 26 fewer to 91 more)		
Caesarean section												
8	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ³	None	69/531 (13%)	70/495 (14.1%)	RR 0.93 (0.69–1.26)	10 fewer per 1000 (from 44 fewer to 37 more)	⊕⊕⊕○ Moderate	Critical
								10.9%		8 fewer per 1000 (from 34 fewer to 28 more)		
Uterine hyperstimulation with fetal heart rate changes												
7	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ³	None	41/491 (8.4%)	31/456 (6.8%)	RR 1.3 (0.43–3.91)	20 more per 1000 (from 39 fewer to 198 more)	⊕⊕⊕○ Moderate	Critical
								1.5%		4 more per 1000 (from 9 fewer to 44 more)		
Apgar score <7 at 5 minutes												
4	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ⁵	None	6/376 (1.6%)	4/340 (1.2%)	RR 1.38 (0.42–4.58)	4 more per 1000 (from 7 fewer to 42 more)	⊕⊕○○ Low	Critical
								0.7%		3 more per 1000 (from 4 fewer to 25 more)		
Admission to neonatal intensive care unit												
6	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ³	None	58/452 (12.8%)	43/414 (10.4%)	RR 1.23 (0.85 to 1.77)	24 more per 1000 (from 16 fewer to 80 more)	⊕⊕⊕○ Moderate	Critical
								10.7%		25 more per 1000 (from 16 fewer to 82 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oral misoprostol	Oxytocin		
Perinatal death												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ⁵	None	1/254 (0.4%)	0/239 (0%)	RR 2.76 (0.11 to 67.13)	0 more per 1000 (from 0 fewer to 0 more)	⊕⊕○○ Low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		
Serious maternal morbidity or death												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ⁶	None	0/40 (0%)	0/40 (0%)	Not pooled	Not pooled	⊕⊕○○ Low	Critical
								0%		Not pooled		

1 Underpowered studies.

2 Anything ranging from a 23% reduction to 80% increase.

3 95% confidence interval ranging from negligible benefit to appreciable harm.

4 Severe heterogeneity.

5 95% confidence interval ranging from appreciable benefit to appreciable harm with very rare events.

6 Effect not estimable owing to a very small sample size.

Table 2.4.3. Oral misoprostol versus vaginal misoprostol for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oral misoprostol	Vaginal misoprostol		
Vaginal birth not achieved within 24 hours												
10	RCT	No serious limitations	Serious ¹	No serious indirectness	Serious ²	None	422/916 (46.1%)	395/925 (42.7%)	RR 1.05 (0.76–1.45)	21 more per 1000 (from 102 fewer to 192 more)	⊕⊕○○ Low	Critical
								44.7%		22 more per 1000 (from 107 fewer to 201 more)		
Vaginal birth not achieved within 24 hours (subgroup by quality)												
8	RCT	No serious limitations	Serious ¹	No serious indirectness	Serious ²	None	379/722 (52.5%)	298/708 (42.1%)	RR 1.27 (0.94–1.71)	114 more per 1000 (from 25 fewer to 299 more)	⊕⊕○○ Low	Critical
								43.1%		116 more per 1000 (from 26 fewer to 306 more)		
Caesarean section												
25	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	533/2573 (20.7%)	561/2523 (22.2%)	RR 0.93 (0.84–1.03)	16 fewer per 1000 (from 36 fewer to 7 more)	⊕⊕⊕⊕ High	Critical
								22.3%		16 fewer per 1000 (from 36 fewer to 7 more)		
Uterine hyperstimulation with fetal heart rate changes												
21	RCT	No serious limitations ³	No serious inconsistency	No serious indirectness	Very serious ⁴	None	187/2214 (8.4%)	186/2191 (8.5%)	RR 0.68 (0.43–1.08)	27 fewer per 1000 (from 48 fewer to 7 more)	⊕⊕○○ Low	Critical
								5.1%		16 fewer per 1000 (from 29 fewer to 4 more)		
Uterine hyperstimulation with fetal heart rate changes (subgroup by quality)												
14	RCT	No serious limitations	No serious inconsist-ency ⁵	No serious indirectness	Serious ²	None	179/1688 (10.6%)	155/1642 (9.4%)	RR 0.83 (0.51–1.35)	16 fewer per 1000 (from 46 fewer to 33 more)	⊕⊕⊕○ Moderate	Critical
								6.4%		11 fewer per 1000 (from 31 fewer to 22 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oral misoprostol	Vaginal misoprostol		
Apgar score <7 at 5 minutes												
14	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	37/1638 (2.3%)	57/1632 (3.5%)	RR 0.65 (0.44 to 0.97)	12 fewer per 1000 (from 1 fewer to 20 fewer)	⊕⊕⊕⊕	Critical
								3%		11 fewer per 1000 (from 1 fewer to 17 fewer)	High	
Admission to neonatal intensive care unit												
16	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	193/1852 (10.4%)	188/1847 (10.2%)	RR 1.02 (0.85–1.22)	2 more per 1000 (from 15 fewer to 22 more)	⊕⊕⊕⊕	Critical
								6.3%		1 more per 1000 (from 9 fewer to 14 more)	High	
Perinatal death												
8	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ⁶	None	0/677 (0%)	0/657 (0%)	Not estimable	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕⊕○	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 fewer)	Moderate	
Serious maternal morbidity or death												
6	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ⁶	None	0/496 (0%)	0/505 (0%)	Not estimable	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕○○	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 fewer)	Low	

1 Severe heterogeneity across subgroups.

2 95% confidence interval ranging from appreciable benefit to appreciable harm.

3 There is a positive correlation between misoprostol dose and the occurrence of the outcome, which can explain the overall severe heterogeneity observed.

4 The pooled estimate is imprecise (95% confidence interval ranging from appreciable benefit to negligible harm), certainly affected by the heterogeneity between groups. Nevertheless, the correlation between misoprostol dose and the occurrence of the outcome seems to be less affected by the imprecision.

5 Severe heterogeneity that could be explained by the inclusion of studies with methodological limitations. The resulting pooled effect is imprecise and the evidence is downgraded for imprecision.

6 Effect is not estimable.

Table 2.4.4. Oral misoprostol versus intracervical prostaglandin for induction of labour

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Oral misoprostol	Intracervical prostaglandin	Relative risk (95% confidence interval)	Absolute		Quality
Vaginal birth not achieved within 24 hours												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	85/227 (37.4%)	108/225 (48%)	RR 0.78 (0.63–0.97)	106 fewer per 1000 (from 14 fewer to 178 fewer)	⊕⊕⊕⊕	Critical
								50%		110 fewer per 1000 (from 15 fewer to 185 fewer)	High	
Caesarean section												
5	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	62/372 (16.7%)	73/370 (19.7%)	RR 0.84 (0.62–1.15)	32 fewer per 1000 (from 75 fewer to 30 more)	⊕⊕⊕○	Critical
								20%		32 fewer per 1000 (from 76 fewer to 30 more)	Moderate	
Uterine hyperstimulation with fetal heart rate changes												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ²	None	12/245 (4.9%)	3/245 (1.2%)	RR 3.57 (1.11–11.54)	31 more per 1000 (from 1 more to 129 more)	⊕⊕⊕○	Critical
								2%		51 more per 1000 (from 2 more to 211 more)	Moderate	
Apgar score <7 at 5 minutes												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ³	None	0/196 (0%)	2/195 (1%)	RR 0.2 (0.01–4.07)	8 fewer per 1000 (from 10 fewer to 31 more)	⊕⊕○○	Critical
								1.1%		9 fewer per 1000 (from 11 fewer to 34 more)	Low	
Admission to neonatal intensive care unit												
4	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ³	None	13/277 (4.7%)	13/275 (4.7%)	RR 1 (0.48 to 2.06)	0 fewer per 1000 (from 25 fewer to 50 more)	⊕⊕○○	Critical
								3.3%		0 fewer per 1000 (from 17 fewer to 35 more)	Low	

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Oral misoprostol	Intracervical prostaglandin	Relative risk (95% confidence interval)	Absolute			
Perinatal death													
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ⁴	None	0/196 (0%)	0/195 (0%)	Not estimable	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕○○ Low	Critical	
								0%		0 fewer per 1000 (from 0 fewer to 0 fewer)			
Serious maternal morbidity or death													
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ⁴	None	0/100 (0%)	0/100 (0%)	Not estimable	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕⊕○ Moderate	Critical	
								0%		0 fewer per 1000 (from 0 fewer to 0 fewer)			

1 95% confidence interval ranging from appreciable benefit to negligible harm.

2 Rare events.

3 95% confidence interval ranging from appreciable benefit to appreciable harm with rare events.

4 Effect not estimable.

Table 2.4.5. Oral misoprostol versus vaginal prostaglandins for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oral misoprostol	Vaginal PG		
Vaginal birth not achieved within 24 hours												
8	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	654/1676 (39%)	671/1786 (37.6%)	RR 1.05 (0.96–1.14)	19 more per 1000 (from 15 fewer to 53 more)	⊕⊕⊕⊕	Critical
								40.5%		20 more per 1000 (from 16 fewer to 57 more)	High	
Caesarean section												
12	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	403/2086 (19.3%)	541/2264 (23.9%)	RR 0.87 (0.78–0.97)	31 fewer per 1000 (from 7 fewer to 53 fewer)	⊕⊕⊕⊕	Critical
								21%		27 fewer per 1000 (from 6 fewer to 46 fewer)	High	
Uterine hyperstimulation with fetal heart rate changes												
9	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	50/1704 (2.9%)	59/1731 (3.4%)	RR 0.86 (0.59–1.23)	5 fewer per 1000 (from 14 fewer to 8 more)	⊕⊕⊕○ Moderate	Critical
								3%		4 fewer per 1000 (from 12 fewer to 7 more)		
								4.7%		16 more per 1000 (from 11 fewer to 64 more)		
Apgar score <7 at 5 minutes												
7	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	32/1498 (2.1%)	40/1522 (2.6%)	RR 0.81 (0.51 to 1.28)	5 fewer per 1000 (from 13 fewer to 7 more)	⊕⊕⊕○ Moderate	Critical
								2%		4 fewer per 1000 (from 10 fewer to 6 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oral misoprostol	Vaginal PG		
Admission to neonatal intensive care unit												
10	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	80/1921 (4.2%)	110/2100 (5.2%)	RR 0.8 (0.6–1.06)	10 fewer per 1000 (from 21 fewer to 3 more)	⊕⊕⊕○ Moderate	Critical
								7%		14 fewer per 1000 (from 28 fewer to 4 more)		
Perinatal death												
7	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ²	None	1/1608 (0.1%)	2/1623 (0.1%)	RR 0.6 (0.08–4.5)	0 fewer per 1000 (from 1 fewer to 4 more)	⊕⊕○○ Low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		
Serious maternal morbidity or death												
4	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ²	None	3/1221 (0.2%)	2/1240 (0.2%)	RR 1.53 (0.26–9.12)	1 more per 1000 (from 1 fewer to 13 more)	⊕⊕○○ Low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		

1 95% confidence interval ranging from appreciable benefit to negligible harm.

2 95% confidence interval ranging from appreciable benefit to appreciable harm with very rare event.

Table 2.4.6. 50 µg oral misoprostol versus 100 µg oral misoprostol for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			50 µg oral misoprostol	100 µg oral misoprostol		
Vaginal birth not achieved within 24 hours												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	85/126 (67.5%)	73/125 (58.4%)	RR 1.16 (0.95–1.4)	93 more per 1000 (from 29 fewer to 234 more)	⊕⊕○○ Low	Critical
								58.4%		93 more per 1000 (from 29 fewer to 234 more)		
Caesarean section												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ²	None	36/159 (22.6%)	32/158 (20.3%)	RR 1.12 (0.73–1.7)	24 more per 1000 (from 55 fewer to 142 more)	⊕⊕⊕○ Moderate	Critical
								17.3%		21 more per 1000 (from 47 fewer to 121 more)		
Uterine hyperstimulation with fetal heart rate changes												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ³	None	0/159 (0%)	2/158 (1.3%)	RR 0.2 (0.01–4.09)	10 fewer per 1000 (from 13 fewer to 39 more)	⊕⊕○○ Low	Critical
								0.8%		6 fewer per 1000 (from 8 fewer to 25 more)		
Apgar score <7 at 5 minutes												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ³	None	1/126 (0.8%)	1/125 (0.8%)	RR 0.99 (0.06–15.69)	0 fewer per 1000 (from 8 fewer to 118 more)	⊕⊕○○ Low	Critical
								0.8%		0 fewer per 1000 (from 8 fewer to 118 more)		
Admission to neonatal intensive care unit												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ⁴	None	12/126 (9.5%)	15/125 (12%)	RR 0.79 (0.39–1.63)	25 fewer per 1000 (from 73 fewer to 76 more)	⊕⊕○○ Low	Critical
								12%		25 fewer per 1000 (from 73 fewer to 76 more)		

1 Very small sample size, with 95% confidence interval ranging from negligible benefit to appreciable harm.

2 95% confidence interval ranging from negligible benefit to appreciable harm.

3 95% confidence interval ranging from appreciable benefit to appreciable harm with very rare events.

4 Very small sample size with 95% confidence interval ranging from appreciable benefit to appreciable harm.

Table 2.4.7. Up-to-four hourly versus 6-hourly oral misoprostol for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oral misoprostol Up to 4-hourly	Oral misoprostol 6-hourly		
Caesarean section												
2	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	17/111 (15.3%)	12/111 (10.8%)	RR 1.41 (0.71–2.8)	44 more per 1000 (from 31 fewer to 195 more)	⊕○○○ Very low	Critical
								10.5%		43 more per 1000 (from 30 fewer to 189 more)		
Uterine hyperstimulation with fetal heart rate changes												
2	RCT	Serious ³	No serious inconsistency	No serious indirectness	Very serious ²	None	4/111 (3.6%)	8/111 (7.2%)	RR 0.54 (0.07–4.3)	33 fewer per 1000 (from 67 fewer to 238 more)	⊕○○○ Very low	Critical
								8.1%		37 fewer per 1000 (from 75 fewer to 267 more)		

1 Very small sample size with 95% confidence interval ranging from appreciable benefit to appreciable harm.

2 Evidence from studies with moderate risk of bias.

3 Very small sample size with 95% confidence interval ranging from appreciable benefit to appreciable harm with very rare events.

Table 2.4.8. Oral misoprostol 3-hourly versus two doses of oral misoprostol followed by routine oxytocin

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Oral misoprostol 3-hourly	Oral misoprostol two doses, then routine oxytocin	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	25/100 (25%)	28/100 (28%)	RR 0.89 (0.56–1.42)	31 fewer per 1000 (from 123 fewer to 118 more)	⊕○○○ Very low	Critical
								28%		31 fewer per 1000 (from 123 fewer to 118 more)		
Caesarean section												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	13/100 (13%)	15/100 (15%)	RR 0.87 (0.44–1.73)	20 fewer per 1000 (from 84 fewer to 110 more)	⊕○○○ Very low	Critical
								15%		20 fewer per 1000 (from 84 fewer to 110 more)		
Uterine hyperstimulation with fetal heart rate changes												
1	RCT	Serious ³	No serious inconsistency	No serious indirectness	Very serious ²	None	0/100 (0%)	0/100 (0%)	RR 0 (0–0)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕○○○ Very low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 fewer)		
Apgar score <7 at 5 minutes												
1	RCT	Serious ³	No serious inconsistency	No serious indirectness	Very serious ²	None	0/100 (0%)	0/100 (0%)	RR 0 (0–0)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕○○○ Very low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 fewer)		
Admission to neonatal intensive care unit												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	1/100 (1%)	1/100 (1%)	RR 1 (0.06–15.77)	0 fewer per 1000 (from 9 fewer to 148 more)	⊕○○○ Very low	Critical
								1%		0 fewer per 1000 (from 9 fewer to 148 more)		

1 Very small sample size with 95% confidence interval ranging from appreciable benefit to appreciable harm.

2 Evidence from studies with moderate risk of bias.

3 Not estimable effect.

Table 2.4.9. Oral misoprostol 25 µg or vaginal misoprostol 25 µg for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Oral 25 µg versus	Vaginal 25 µg misoprostol	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
2	RCT	No serious limitations	Serious ¹	No serious indirectness	Serious ²	None	76/211 (36%)	85/216 (39.4%)	RR 0.51 (0.03–9.68)	193 fewer per 1000 (from 382 fewer to 3416 more)	⊕⊕○○ Low	Critical
								39.5%		194 fewer per 1000 (from 383 fewer to 3429 more)		
Caesarean section												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ³	None	4/101 (4%)	18/106 (17%)	RR 0.23 (0.08–0.67)	131 fewer per 1000 (from 56 fewer to 156 fewer)	⊕⊕⊕○ Moderate	Critical
								17%		131 fewer per 1000 (from 56 fewer to 156 fewer)		
Uterine hyperstimulation with fetal heart rate changes												
2	RCT	No serious limitations	Serious	No serious indirectness	Very serious ^{2,3}	None	5/211 (2.4%)	29/216 (13.4%)	RR 0.17 (0.03–1.08)	111 fewer per 1000 (from 130 fewer to 11 more)	⊕○○○ Very low	Critical
								13.4%		111 fewer per 1000 (from 130 fewer to 11 more)		
Apgar score <7 at 5 minutes												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	4/211 (1.9%)	11/216 (5.1%)	RR 0.4 (0.13–1.17)	31 fewer per 1000 (from 44 fewer to 9 more)	⊕⊕○○ Low	Critical
								5.1%		31 fewer per 1000 (from 44 fewer to 9 more)		
Admission to neonatal intensive care unit												
2	RCT	No serious limitations	Serious ¹	No serious indirectness	Very serious ^{2,3}	None	7/211 (3.3%)	11/216 (5.1%)	RR 0.66 (0.27–1.64)	17 fewer per 1000 (from 37 fewer to 33 more)	⊕○○○ Very low	Critical
								5.1%		17 fewer per 1000 (from 37 fewer to 33 more)		

1 Severe heterogeneity.

2 Imprecise confidence intervals.

3 Very rare events.

Table 2.4.10. Oral misoprostol 25 µg versus vaginal prostaglandin for induction of labour

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Oral misoprostol	Vaginal PG	Relative risk (95% confidence interval)	Absolute			
Vaginal birth not achieved within 24 hours													
7	RCT	No serious limitations	No serious in- consistency	No serious indirectness	No serious imprecision	None	592/1576 (37.6%)	611/1686 (36.2%)	RR 1.05 (0.96–1.15)	18 more per 1000 (from 14 fewer to 54 more)	⊕⊕⊕⊕	Critical	
								39.8%		20 more per 1000 (from 16 fewer to 60 more)	High		
Caesarean section													
8	RCT	No serious limitations	No serious in- consistency	No serious indirectness	No serious imprecision	None	296/1703 (17.4%)	397/1762 (22.5%)	RR 0.82 (0.72–0.94)	41 fewer per 1000 (from 14 fewer to 63 fewer)	⊕⊕⊕⊕	Critical	
								19.3%		35 fewer per 1000 (from 12 fewer to 54 fewer)	High		
Uterine hyperstimulation with fetal heart rate changes													
6	RCT	No serious limitations	No serious in- consistency	No serious indirectness	Serious ¹	None	40/1441 (2.8%)	45/1469 (3.1%)	RR 0.9 (0.6–1.37)	3 fewer per 1000 (from 12 fewer to 11 more)	⊕⊕⊕○	Critical	
								2.3%		2 fewer per 1000 (from 9 fewer to 9 more)	Moder- ate		
Apgar score <7 at 5 minutes													
6	RCT	No serious limitations	No serious in- consistency	No serious indirectness	Serious ¹	None	32/1470 (2.2%)	40/1492 (2.7%)	RR 0.81 (0.51–1.28)	5 fewer per 1000 (from 13 fewer to 8 more)	⊕⊕⊕○	Critical	
								2%		4 fewer per 1000 (from 10 fewer to 6 more)	Moder- ate		
Admission to neonatal intensive care unit													
8	RCT	No serious limitations	No serious in- consistency	No serious indirectness	Serious ¹	None	66/1701 (3.9%)	90/1760 (5.1%)	RR 0.79 (0.58–1.08)	11 fewer per 1000 (from 21 fewer to 4 more)	⊕⊕⊕○	Critical	
								7%		15 fewer per 1000 (from 29 fewer to 6 more)	Moder- ate		

Quality assessment							Summary of findings					
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Oral misoprostol	Vaginal PG	Relative risk (95% confidence interval)	Absolute		
Perinatal death												
6	RCT	No serious limitations	No serious in- consistency	No serious indirectness	Very serious ^{1,2}	None	1/1473 (0.1%)	2/1491 (0.1%)	RR 0.6 (0.08–4.5)	1 fewer per 1000 (from 1 fewer to 5 more)	⊕⊕○○ Low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		
Serious maternal morbidity or death												
3	RCT	Serious ³	No serious in- consistency	No serious indirectness	Very serious ²	None	3/1086 (0.3%)	2/1108 (0.2%)	RR 1.53 (0.26–9.12)	1 more per 1000 (from 1 fewer to 15 more)	⊕○○○ Very low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		

1 Imprecise confidence intervals.
2 Rare events.
3 Evidence from moderate risk of bias.

2.5. Buccal/sublingual misoprostol

Source of evidence: Amorim MMR, Muzonzini G, Hofmeyr GJ. Buccal or sublingual misoprostol for cervical ripening and induction of labour. Cochrane Database of Systematic Reviews, 2004, Issue 4. Art. No.: CD004221; DOI: 10.1002/14651858.CD004221.pub2. (Data in this review were updated for the present guidelines. The current online published version of the review may not yet reflect the updates.)

Table 2.5.1. Sublingual/buccal misoprostol versus vaginal misoprostol for cervical ripening and induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Sublingual/buccal misoprostol	Vaginal misoprostol		
Vaginal birth not achieved within 24 hours												
8	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	264/816 (32.4%)	255/826 (30.9%)	RR 1.05 (0.92–1.21)	15 more per 1000 (from 25 fewer to 65 more)	⊕⊕⊕⊕	Critical
								31.1%		16 more per 1000 (from 25 fewer to 65 more)	High	
Caesarean section												
9	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	373/1153 (32.4%)	365/1145 (31.9%)	RR 1.01 (0.9–1.14)	3 more per 1000 (from 32 fewer to 45 more)	⊕⊕⊕⊕	Critical
								28.6%		3 more per 1000 (from 29 fewer to 40 more)	High	
Uterine hyperstimulation with fetal heart rate changes												
8	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	45/816 (5.5%)	35/826 (4.2%)	RR 1.33 (0.88–2.02)	14 more per 1000 (from 5 fewer to 43 more)	⊕⊕⊕○	Critical
								2.3%		8 more per 1000 (from 3 fewer to 23 more)	Moderate	
Apgar score <7 at 5 minutes												
8	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	17/820 (2.1%)	15/827 (1.8%)	RR 1.15 (0.59–2.26)	3 more per 1000 (from 7 fewer to 23 more)	⊕⊕⊕○	Critical
								2%		3 more per 1000 (from 8 fewer to 25 more)	Moderate	

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Sublingual/buccal misoprostol	Vaginal misoprostol		
Admission to neonatal intensive care unit												
8	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	59/816 (7.2%)	49/826 (5.9%)	RR 1.23 (0.86–1.77)	14 more per 1000 (from 8 fewer to 46 more)	⊕⊕⊕○ Moderate	Critical
								4.8%		11 more per 1000 (from 7 fewer to 37 more)		
Perinatal death												
9	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{1,2}	None	1/1109 (0.1%)	0/1106 (0%)	RR 3.2 (0.13–77.1)	0 more per 1000 (from 0 fewer to 0 more)	⊕⊕○○ Low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		
Serious maternal morbidity or death												
9	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{1,2}	None	0/1194 (0%)	0/1191 (0%)	Not pooled	Not pooled	⊕○○○ Very Low	Critical
								0%		Not pooled		

1 Imprecise confidence intervals.

2 Very rare events.

Table 2.5.2. Sublingual/buccal misoprostol versus oral misoprostol for cervical ripening and induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Sublingual/buccal misoprostol	Oral misoprostol	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	70/175 (40%)	80/174 (46%)	RR 0.87 (0.68–1.11)	60 fewer per 1000 (from 147 fewer to 51 more)	⊕⊕⊕○ Moderate	Critical
								43.6%		57 fewer per 1000 (from 140 fewer to 48 more)		
Caesarean section												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	39/175 (22.3%)	47/174 (27%)	RR 0.82 (0.57–1.19)	49 fewer per 1000 (from 116 fewer to 51 more)	⊕⊕⊕○ Moderate	Critical
								27.9%		50 fewer per 1000 (from 120 fewer to 53 more)		
Uterine hyperstimulation with fetal heart rate changes												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{1,2}	None	3/175 (1.7%)	2/174 (1.1%)	RR 1.39 (0.28–6.96)	4 more per 1000 (from 8 fewer to 69 more)	⊕⊕○○ Low	Critical
								0.8%		3 more per 1000 (from 6 fewer to 48 more)		
Apgar score <7 at 5 minutes												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{1,2}	None	1/175 (0.6%)	1/174 (0.6%)	RR 0.99 (0.06–15.68)	0 fewer per 1000 (from 5 fewer to 84 more)	⊕⊕○○ Low	Critical
								0.4%		0 fewer per 1000 (from 4 fewer to 59 more)		
Admission to neonatal intensive care unit												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	17/175 (9.7%)	21/174 (12.1%)	RR 0.8 (0.44–1.47)	24 fewer per 1000 (from 68 fewer to 57 more)	⊕⊕⊕○ Moderate	Critical
								12.1%		24 fewer per 1000 (from 68 fewer to 57 more)		

1 Imprecise confidence intervals.

2 Very rare events.

2.6. Vaginal prostaglandin

Source of evidence: Kelly AJ et al. Vaginal prostaglandin (PGE2 and PGF2) for induction of labour at term. Cochrane Database of Systematic Reviews, 2009, Issue 4. Art. No.: CD003101; DOI: 10.1002/14651858.CD003101.pub2. (Data in this review were updated for the present guidelines. The current online published version of the review may not yet reflect the updates.)

Table 2.6.1. Prostaglandin E2 versus placebo/no treatment for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations			Prostaglandin E2 (all regimens)	Placebo/ no treatment		
Vaginal birth not achieved within 24 hours												
2	RCT	Serious ¹	No serious inconsistency	No serious indirectness	No serious imprecision	None	36/199 (18.1%)	183/185 (98.9%)	RR 0.19 (0.14–0.25)	801 fewer per 1000 (from 742 fewer to 851 fewer)	⊕⊕⊕○ Moderate	Critical
								95%		770 fewer per 1000 (from 712 fewer to 817 fewer)		
Caesarean section												
34	RCT	Serious ²	No serious inconsistency	No serious indirectness	No serious imprecision	None	433/3221 (13.4%)	475/3178 (14.9%)	RR 0.89 (0.79–1)	16 fewer per 1000 (from 31 fewer to 0 more)	⊕⊕⊕○ Moderate	Critical
								18%		20 fewer per 1000 (from 38 fewer to 0 more)		
Uterine hyperstimulation with fetal heart rate changes												
14	RCT	Serious ³	No serious inconsistency	No serious indirectness	No serious imprecision	None	28/642 (4.4%)	3/617 (0.5%)	RR 4.14 (1.93–8.9)	15 more per 1000 (from 5 more to 38 more)	⊕⊕⊕○ Moderate	Critical
								0%		0 more per 1000 (from 0 more to 0 more)		
Apgar score <7 at 5 minutes												
15	RCT	Serious ³	No serious inconsistency	No serious indirectness	Serious ⁴	None	48/2192 (2.2%)	36/2189 (1.6%)	RR 1.3 (0.86–1.96)	5 more per 1000 (from 2 fewer to 16 more)	⊕⊕○○ Low	Critical
								1.9%		6 more per 1000 (from 3 fewer to 18 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Prostaglandin E2 (all regimens)	Placebo/ no treatment	Relative risk (95% confidence interval)	Absolute		
Admission to neonatal intensive care unit												
11	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	174/1952 (8.9%)	186/1970 (9.4%)	RR 0.95 (0.78–1.15)	5 fewer per 1000 (from 21 fewer to 14 more)	⊕⊕⊕⊕	Critical
								7.9%		4 fewer per 1000 (from 17 fewer to 12 more)	High	
Perinatal death												
7	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ⁵	None	2/1833 (0.1%)	4/1815 (0.2%)	RR 0.56 (0.14–2.22)	1 fewer per 1000 (from 2 fewer to 3 more)	⊕⊕○○	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 more)	Low	
Serious maternal morbidity or death												
3	RCT	Very serious ⁶	No serious inconsistency	No serious indirectness	Very serious ⁷	None	3/270 (1.1%)	1/260 (0.4%)	RR 2.23 (0.34–14.76)	5 more per 1000 (from 3 fewer to 53 more)	⊕○○○	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)	Very low	

1 Evidence from studies with moderate risk of bias.

2 Most of the evidence from studies with moderate risk of bias.

3 Most of evidence comes from studies with moderate or high risk of bias.

4 95% confidence interval ranging from negligible benefit to appreciable harm.

5 95% confidence interval ranging from appreciable harm with very rare events.

6 Most of the evidence comes from studies with high risk of bias.

7 95% confidence interval ranging from appreciable benefit to appreciable harm with very rare events.

Table 2.6.2. Prostaglandin F2 α versus placebo for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Prostaglandin F2 α	Placebo	Relative risk (95% confidence interval)	Absolute		
Caesarean section												
3	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	14/241 (5.8%)	15/146 (10.3%)	RR 0.58 (0.29–1.18)	43 fewer per 1000 (from 73 fewer to 18 more)	⊕○○○ Very low	Critical
								10%		42 fewer per 1000 (from 71 fewer to 18 more)		
Uterine hyperstimulation with fetal heart rate changes												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ³	None	1/16 (6.3%)	0/16 (0%)	RR 3 (0.13–68.57)	0 more per 1000 (from 0 fewer to 0 more)	⊕○○○ Very low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		

1 Most of the evidence comes from studies with moderate risk of bias.

2 95% confidence interval ranging from appreciable benefit to negligible harm with very rare events.

3 95% confidence interval ranging from appreciable harm in a very small study population.

Table 2.6.3. Prostaglandin F2 α versus prostaglandin E2 for induction of labour at term

Quality assessment							Summary of findings					
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Prostaglandin F2	Prostaglandin E2	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	1/37 (2.7%)	2/38 (5.3%)	RR 0.51 (0.05–5.42)	26 fewer per 1000 (from 50 fewer to 233 more)	⊕⊕○○ Low	Critical
								5.3%		26 fewer per 1000 (from 50 fewer to 234 more)		
Caesarean section												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ²	None	10/53 (18.9%)	10/54 (18.5%)	RR 1.02 (0.47–2.22)	4 more per 1000 (from 98 fewer to 226 more)	⊕⊕○○ Low	Critical
								15%		3 more per 1000 (from 80 fewer to 183 more)		
Uterine hyperstimulation with fetal heart rate changes												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ²	None	1/53 (1.9%)	1/53 (1.9%)	RR 1 (0.07–14.64)	0 fewer per 1000 (from 18 fewer to 257 more)	⊕⊕○○ Low	Critical
								3.1%		0 fewer per 1000 (from 29 fewer to 423 more)		
Apgar score <7 at 5 minutes												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ²	None	0/37 (0%)	2/38 (5.3%)	RR 0.21 (0.01–4.14)	42 fewer per 1000 (from 52 fewer to 165 more)	⊕⊕○○ Low	Critical
								5.3%		42 fewer per 1000 (from 52 fewer to 166 more)		

1 95% confidence interval ranging from appreciable harm in a very small study population.

2 95% confidence interval ranging from appreciable benefit to appreciable harm in a very small study population.

Table 2.6.4. Gel versus tablet as formulation of prostaglandin E2 for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Prostaglandin E2 gel	Prostaglandin E2 tablets		
Vaginal birth not achieved within 24 hours												
2	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ²	None	67/210 (31.9%)	55/191 (28.8%)	RR 1.12 (0.85–1.49)	35 more per 1000 (from 43 fewer to 141 more)	⊕⊕○○ Low	Critical
								38%		46 more per 1000 (from 57 fewer to 186 more)		
Caesarean section												
5	RCT	Very serious ³	No serious inconsistency	No serious indirectness	Serious ⁴	None	65/443 (14.7%)	75/438 (17.1%)	RR 0.87 (0.64–1.17)	22 fewer per 1000 (from 62 fewer to 29 more)	⊕○○○ Very low	Critical
								15.1%		20 fewer per 1000 (from 54 fewer to 26 more)		
Uterine hyperstimulation with fetal heart rate changes												
1	RCT	Serious ⁵	No serious inconsistency	No serious indirectness	Very serious ⁶	None	2/100 (2%)	1/100 (1%)	RR 2 (0.18–21.71)	10 more per 1000 (from 8 fewer to 207 more)	⊕○○○ Very low	Critical
								1%		10 more per 1000 (from 8 fewer to 207 more)		
Apgar score <7 at 5 minutes												
3	RCT	Serious ⁵	No serious inconsistency	No serious indirectness	Very serious ⁶	None	3/225 (1.3%)	4/207 (1.9%)	RR 0.72 (0.18–2.87)	5 fewer per 1000 (from 16 fewer to 36 more)	⊕○○○ Very low	Critical
								1.9%		5 fewer per 1000 (from 16 fewer to 36 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Prostaglandin E2 gel	Prostaglandin E2 tablets	Relative risk (95% confidence interval)	Absolute		
Serious maternal morbidity or death												
1	RCT	Serious ⁵	No serious inconsistency	No serious indirectness	Very serious ⁶	None	0/100 (0%)	1/100 (1%)	RR 0.33 (0.01–8.09)	7 fewer per 1000 (from 10 fewer to 71 more)	⊕○○○ Very low	Critical
								1%		7 fewer per 1000 (from 10 fewer to 71 more)		

1 Most of the evidence comes from studies with moderate risk of bias.

2 95% confidence interval ranging from negligible benefit to appreciable harm in a very small study population.

3 Evidence comes from studies with moderate and high risk of bias.

4 95% confidence interval ranging from appreciable benefit to negligible harm.

5 Evidence comes from a study with moderate risk of bias.

6 95% confidence interval ranging from appreciable benefit to appreciable harm in a very small study population.

Table 2.6.5. Gel versus suppository/pessary as formulation of prostaglandin E2 for induction of labour

Quality assessment							Summary of findings						
							No. of patients		Effect		Quality		
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Prostaglandin E2 gel	Prostaglandin E2 suppository/ pessary	Relative risk (95% confidence interval)	Absolute			Importance
Caesarean section													
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	16/79 (20.3%)	25/80 (31.3%)	RR 0.65 (0.38–1.11)	109 fewer per 1000 (from 194 fewer to 34 more)	⊕⊕○○ Low	Critical	
								30.3%		106 fewer per 1000 (from 188 fewer to 33 more)			
Uterine hyperstimulation with fetal heart rate changes													
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ²	None	1/79 (1.3%)	9/80 (11.3%)	RR 0.16 (0.03–0.87)	94 fewer per 1000 (from 15 fewer to 109 fewer)	⊕⊕⊕○ Moderate	Critical	
								12.2%		102 fewer per 1000 (from 16 fewer to 118 fewer)			
Apgar score <7 at 5 minutes													
1	RCT	Serious ³	No serious inconsistency	No serious indirectness	Very serious ¹	None	0/34 (0%)	2/35 (5.7%)	RR 0.21 (0.01–4.13)	45 fewer per 1000 (from 57 fewer to 179 more)	⊕○○○ Very low	Critical	
								5.7%		45 fewer per 1000 (from 56 fewer to 178 more)			

1 95% confidence interval ranging from appreciable benefit to appreciable harm in a very small study population.

2 Very small study population.

3 The evidence comes from study with moderate risk of bias.

Table 2.6.6. Tablet versus suppository/pessary as formulation of prostaglandin E2 for induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Prostaglandin E2 tablet	Prostaglandin E2 pessary/ suppository		
Caesarean section												
3	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ²	None	23/247 (9.3%)	20/244 (8.2%)	RR 1.13 (0.64–1.99)	11 more per 1000 (from 30 fewer to 81 more)	⊕⊕○○ Low	Critical
								8.3%		11 more per 1000 (from 30 fewer to 82 more)		
Apgar score <7 at 5 minutes												
2	RCT	Serious ³	No serious inconsistency	No serious indirectness	Very serious ¹	None	12/235 (5.1%)	9/232 (3.9%)	RR 1.33 (0.58–3.05)	13 more per 1000 (from 16 fewer to 80 more)	⊕○○○ Very low	Critical
								4.4%		15 more per 1000 (from 18 fewer to 90 more)		

1 The evidence comes from studies with moderate risk of bias.

2 95% confidence interval ranging from appreciable benefit to appreciable harm.

3 95% confidence interval ranging from appreciable benefit to appreciable harm with very rare events.

Table 2.6.7. Controlled release system versus all other delivery systems for Prostaglandin E2 for induction of labour.

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Prostaglandin E2 (controlled release)	All prostaglandin E2 delivery systems	Relative risk (95% confidence interval)	Absolute			
Vaginal birth not achieved within 24 hours													
2	RCT	Very serious ¹	No serious inconsistency	No serious indirectness	Serious ²	None	87/160 (54.4%)	85/160 (53.1%)	RR 1.02 (0.84–1.25)	11 more per 1000 (from 85 fewer to 133 more)	⊕○○○ Very low	Critical	
								55.8%		11 more per 1000 (from 89 fewer to 139 more)			
Caesarean section													
8	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ³	None	83/471 (17.6%)	74/458 (16.2%)	RR 1.1 (0.83–1.46)	16 more per 1000 (from 27 fewer to 74 more)	⊕⊕○○ Low	Critical	
								16.2%		16 more per 1000 (from 28 fewer to 75 more)			
Uterine hyperstimulation with fetal heart rate changes													
4	RCT	Very serious ⁴	No serious inconsistency	No serious indirectness	Very serious ⁴	None	16/260 (6.2%)	7/253 (2.8%)	RR 2.15 (0.89–5.21)	32 more per 1000 (from 3 fewer to 116 more)	⊕○○○ Very low	Critical	
								2.4%		28 more per 1000 (from 3 fewer to 101 more)			
Apgar score <7 at 5 minutes													
2	RCT	Serious	No serious inconsistency	No serious indirectness	Very serious ⁵	None	1/120 (0.8%)	0/120 (0%)	RR 3 (0.12–72.77)	0 more per 1000 (from 0 fewer to 0 more)	⊕○○○ Very low	Critical	
								0%		0 more per 1000 (from 0 fewer to 0 more)			
Serious maternal morbidity or death													
1	RCT	Serious ⁵	No serious inconsistency	No serious indirectness	Very serious ⁶	None	0/103 (0%)	0/97 (0%)	Not pooled	Not pooled	⊕○○○ Very low	Critical	
								0%		Not pooled			

1 The evidence comes from studies with moderate and high risk of bias.

2 95% confidence interval ranging from negligible benefit to appreciable harm in a very small study population.

3 95% confidence interval ranging from appreciable benefit to appreciable harm in a very small study population.

4 95% confidence interval ranging from negligible benefit to appreciable harm with rare events.

5 The evidence comes from studies with moderate risk of bias.

6 Effect not estimable.

Table 2.6.8. Low-dose versus high-dose prostaglandin E2 for induction of labour at term

Quality assessment							Summary of findings					
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Prostaglandin E2 low dose	Prostaglandin E2 high dose	Relative risk (95% confidence interval)	Absolute		
Caesarean section												
7	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	82/732 (11.2%)	78/734 (10.6%)	RR 1.07 (0.8–1.42)	7 more per 1000 (from 21 fewer to 45 more)	⊕⊕○○ Low	Critical
								15.1%		11 more per 1000 (from 30 fewer to 63 more)		
Uterine hyperstimulation with fetal heart rate changes												
2	RCT	Serious ²	No serious inconsistency	No serious indirectness	Serious ³	None	1/69 (1.4%)	8/71 (11.3%)	RR 0.18 (0.03–0.99)	92 fewer per 1000 (from 1 fewer to 109 fewer)	⊕⊕○○ Low	Critical
								11.4%		93 fewer per 1000 (from 1 fewer to 111 fewer)		
Apgar score <7 at 5 minutes												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ⁴	None	6/537 (1.1%)	12/527 (2.3%)	RR 0.51 (0.2–1.31)	11 fewer per 1000 (from 18 fewer to 7 more)	⊕⊕○○ Low	Critical
								2.1%		10 fewer per 1000 (from 17 fewer to 7 more)		
Admission to neonatal intensive care unit												
1	RCT	No serious limitations ⁴	No serious inconsistency	No serious indirectness	Very serious ⁴	None	10/483 (2.1%)	19/472 (4%)	RR 0.51 (0.24–1.09)	20 fewer per 1000 (from 31 fewer to 4 more)	⊕⊕○○ Low	Critical
								4%		20 fewer per 1000 (from 30 fewer to 4 more)		
Perinatal death												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ⁵	None	0/483 (0%)	0/472 (0%)	RR 0 (0–0)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕○○ Low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 fewer)		

1 95% confidence interval ranging from appreciable benefit to appreciable harm.

2 Most of the evidence comes from studies with moderate risk of bias.

3 Very small study population.

4 95% confidence interval ranging from appreciable benefit to appreciable harm with very rare events.

5 Effect not estimable.

2.7. Oral prostaglandin

Source of evidence: French L. Oral prostaglandin E2 for induction of labour. Cochrane Database of Systematic Reviews, 2001, Issue 2. Art. No.: CD003098; DOI: 10.1002/14651858.CD003098. (Data in this review were updated for the present guidelines. The current online published version of the review may not yet reflect the updates.)

Table 2.7.1. Oral prostaglandins versus placebo/no treatment for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Oral prostaglandin	Placebo or no treatment	Relative risk (95% confidence interval)	Absolute		
Caesarean section												
3	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ²	None	14/105 (13.3%)	20/90 (22.2%)	RR 0.54 (0.29–0.98)	102 fewer per 1000 (from 4 fewer to 158 fewer)	⊕⊕○○ Low	Critical
								22%		101 fewer per 1000 (from 4 fewer to 156 fewer)		

1 Most of the evidence is from studies with moderate risk of bias.
2 Very small population/very rare events.

Table 2.7.2. Oral prostaglandins versus intravenous oxytocin for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oral prostaglandin	Intravenous oxytocin		
Vaginal birth not achieved within 24 hours												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	1/99 (1%)	0/102 (0%)	RR 3.09 (0.13–74.96)	0 more per 1000 (from 0 fewer to 0 more)	⊕○○○ Very low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		
Caesarean section												
8	RCT	Serious	No serious inconsistency	No serious indirectness	Serious ²	None	35/422 (8.3%)	30/402 (7.5%)	RR 1.07 (0.68–1.68)	5 more per 1000 (from 24 fewer to 51 more)	⊕⊕○○ Low	Critical
								8.3%		6 more per 1000 (from 27 fewer to 56 more)		
Uterine hyperstimulation with fetal heart rate changes												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	0/36 (0%)	0/33 (0%)	Not pooled	Not pooled	⊕○○○ Very low	Critical
								0%		Not pooled		
Apgar score <7 at 5 minutes												
4	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	3/287 (1%)	6/289 (2.1%)	RR 0.5 (0.13–1.97)	10 fewer per 1000 (from 18 fewer to 20 more)	⊕○○○ Very low	Critical
								1.9%		9 fewer per 1000 (from 17 fewer to 18 more)		
Admission to neonatal intensive care unit												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	No serious imprecision	Reporting bias ^{2,3}	4/36 (11.1%)	5/33 (15.2%)	RR 0.73 (0.21–2.5)	41 fewer per 1000 (from 120 fewer to 227 more)	⊕○○○ Very low	Critical
								15.2%		41 fewer per 1000 (from 120 fewer to 228 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oral prostaglandin	Intravenous oxytocin		
Perinatal death												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{2,3,4}	None	0/15 (0%)	0/20 (0%)	Not pooled	Not pooled	⊕○○○ Very low	Critical
								0%		Not pooled		
Serious maternal morbidity or death												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	0/15 (0%)	0/20 (0%)	Not pooled	Not pooled	⊕○○○ Very low	Critical
								0%		Not pooled		

1 Most of the evidence with moderate risk of bias.

2 Imprecise confidence interval.

3 Very small study population / very rare events.

4 Not estimable.

Table 2.7.3. Oral prostaglandins versus intracervical prostaglandins for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oral prostaglandin	Intracervical prostaglandin		
Caesarean section												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	5/25 (20%)	8/25 (32%)	RR 0.62 (0.24–1.65)	122 fewer per 1000 (from 243 fewer to 208 more)	⊕○○○ Very low	Critical
								32%		122 fewer per 1000 (from 243 fewer to 208 more)		
Apgar score <7 at 5 minutes												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	1/25 (4%)	1/25 (4%)	RR 1 (0.07–15.12)	0 fewer per 1000 (from 37 fewer to 565 more)	⊕○○○ Very low	Critical
								4%		0 fewer per 1000 (from 37 fewer to 565 more)		

1 Evidence with moderate risk of bias.

2 Imprecise confidence interval with very small study population and very rare outcomes.

Table 2.7.4. Oral prostaglandins versus vaginal prostaglandin for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Oral prostaglandin	Vaginal prostaglandin		
Caesarean section												
2	RCT	No serious limitations	Serious ¹	No serious indirectness	Very serious ²	None	8/31 (25.8%)	12/32 (37.5%)	RR 0.69 (0.33–1.47)	116 fewer per 1000 (from 251 fewer to 176 more)	⊕○○○ Very low	Critical
								36.5%		113 fewer per 1000 (from 245 fewer to 172 more)		

1 Evidence with moderate risk of bias.

2 Imprecise confidence interval with very small study population and rare events.

Table 2.7.5. High/incremental-dose versus low-dose oral prostaglandins for induction of labour at term

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Oral prostaglandin high/incremental dose	Oral prostaglandin low dose	Relative risk (95% confidence interval)	Absolute			
Z2 Caesarean section													
2	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	5/23 (21.7%)	5/23 (21.7%)	RR 1 (0.33–2.99)	0 fewer per 1000 (from 146 fewer to 433 more)	⊕○○○ Very low	Critical	
								22.5%		0 fewer per 1000 (from 151 fewer to 448 more)			

1 Evidence with moderate risk of bias.
2 Imprecise confidence interval with very small study population and very rare events.

2.8. Intracervical prostaglandin

Source of evidence: Bouvain M, Kelly AJ, Irion O. Intracervical prostaglandins for induction of labour. Cochrane Database of Systematic Reviews, 2008, Issue 1. Art. No.: CD006971. DOI: 10.1002/14651858.CD006971. (Data in this review were updated for the present guidelines. The current online published version of the review may not yet reflect the updates.)

Table 2.8.1. Intracervical prostaglandin (PGE2) versus placebo/no treatment for induction of labour at term

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Intracervical pros- taglandin (PGE2)	Placebo/no treatment	Relative risk (95% confidence interval)	Absolute		Quality
Vaginal birth not achieved within 24 hours												
4	RCT	Serious ¹	No serious in- consistency ¹	No serious indirectness	Serious ²	None	44/100 (44%)	88.3%	RR 0.61 (0.47–0.79)	344 fewer per 1000 (from 185 fewer to 468 fewer)	⊕⊕○○ Low	Critical
Caesarean section												
27	RCT	Serious ³	No serious in- consistency	No serious indirectness	No serious imprecision	None	344/1941 (17.7%)	20.8%	RR 0.88 (0.77–1)	25 fewer per 1000 (from 48 fewer to 0 more)	⊕⊕⊕○ Moderate	Critical
Uterine hyperstimulation with fetal heart rate changes												
12	RCT	Serious ⁴	No serious in- consistency	No serious indirectness	Serious ⁵	None	28/1169 (2.4%)	0.1%	RR 1.21 (0.72–2.05)	0 more per 1000 (from 0 fewer to 1 more)	⊕⊕○○ Low	Critical
Apgar score <7 at 5 minutes												
14	RCT	No serious limitations ⁶	No serious in- consistency	No serious indirectness	Serious ⁵	None ⁷	43/1333 (3.2%)	1.7%	RR 0.91 (0.62–1.34)	2 fewer per 1000 (from 6 fewer to 6 more)	⊕⊕⊕○ Moderate	Critical
Admission to neonatal intensive care unit												
4	RCT	No serious limitations	No serious in- consistency	No serious indirectness	Serious ^{2,5}	None	3/136 (2.2%)	8.8%	RR 0.32 (0.1–1.07)	60 fewer per 1000 (from 79 fewer to 6 more)	⊕⊕⊕○ Moderate	Critical
Perinatal death												
2	RCT	Serious ⁸	No serious in- consistency	No serious indirectness	Very serious ^{5,9}	None	0/587 (0%)	0.3%	RR 0.2 (0.01–4.05)	2 fewer per 1000 (from 3 fewer to 9 more)	⊕○○○ Very low	Critical
Serious maternal morbidity or death												
2	RCT	Serious ⁸	No serious in- consistency	No serious indirectness	Very serious ^{5,9}	None	0/587 (0%)	0.1%	RR 0.33 (0.01–7.96)	1 fewer per 1000 (from 1 fewer to 7 more)	⊕○○○ Very low	Critical

1 Despite the severe heterogeneity there is minimal overlapping in the confidence intervals.

2 Very small pooled study population.

3 15 out of 27 studies were considered as having moderate risk of bias.

4 6 out of 12 studies, including a study accounting for 46.6% of the pooled effect, were considered as having moderate risk of bias.

5 Confidence intervals ranging from appreciable benefit to appreciable harm.

6 9 out 14 studies were considered as having moderate risk of bias, but four studies with low risk of bias accounted for 54% of the pooled effect.

7 Despite of the apparent asymmetry in the funnel plot, there is absence of heterogeneity, full overlapping of confidence intervals and no studies with statistically significant results.

8 The two studies included in this comparison and outcome have been considered as having moderate risk of bias.

9 Very rare events.

Table 2.8.2 Intracervical prostaglandin (PGE2) versus intravaginal prostaglandins (PGE2) for induction of labour at term

Quality assessment							Summary of findings					
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Intracervical pros- taglandin (PGE2)	Intravaginal prostaglandin (PGE2)	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
11	RCT	Serious ¹	Serious ²	No serious indirectness	No serious imprecision	None	410/1122 (36.5%)	32.1%	RR 1.26 (1.12–1.41)	83 more per 1000 (from 39 more to 132 more)	⊕⊕○○ Low	Critical
Caesarean section												
28	RCT	Serious ¹	No serious inconsistency	No serious indirectness	No serious imprecision	None	363/1906 (19%)	17.1%	RR 1.07 (0.93–1.22)	12 more per 1000 (from 12 fewer to 38 more)	⊕⊕⊕○ Moderate	Critical
Uterine hyperstimulation with fetal heart rate changes												
13	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{3,4}	None	11/703 (1.6%)	1.4%	RR 0.76 (0.39–1.49)	3 fewer per 1000 (from 9 fewer to 7 more)	⊕○○○ Very low	Critical
Apgar score <7 at 5 minutes												
15	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ³	None	18/1027 (1.8%)	2.2%	RR 0.92 (0.51–1.68)	2 fewer per 1000 (from 11 fewer to 15 more)	⊕⊕○○ Low	Critical
Admission to neonatal intensive care unit												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ³	None	32/214 (15%)	16.1%	RR 0.94 (0.6–1.46)	10 fewer per 1000 (from 64 fewer to 74 more)	⊕⊕⊕○ Moderate	Critical
Perinatal death												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ³	None	0/37 (0%)	0%	Not pooled	Not pooled	⊕○○○ Very low	Critical
Serious maternal morbidity or death												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{3,4}	None	1/211 (0.5%)	0%	RR 3.07 (0.13–74.71)	0 more per 1000 (from 0 fewer to 0 more)	⊕⊕○○ Low	Critical

1 Most of the evidence from studies with moderate risk of bias.

2 Severe heterogeneity between trials (I²=69%).

3 Imprecise confidence intervals.

4 Very small study population or very rare events.

Table 2.8.3: Low-dose versus high-dose intracervical prostaglandin E2 for induction of labour at term

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Intracervical prostaglandin E2, low dose	Intracervical prostaglandin E2, high dose	Relative risk (95% confidence interval)	Absolute		Quality
Caesarean section												
2	RCT	Very serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	14/57 (24.6%)	30.9%	RR 0.79 (0.43–1.44)	65 fewer per 1000 (from 176 fewer to 136 more)	⊕○○○ Very low	Critical
Uterine hyperstimulation with fetal heart rate changes												
1	RCT	Very serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	6/42 (14.3%)	11.9%	RR 1.2 (0.4–3.63)	24 more per 1000 (from 71 fewer to 313 more)	⊕○○○ Very low	Critical

1 Most of the evidence is from a study with a high risk of bias.

2 Imprecise confidence intervals with very small study population and very rare events.

2.9. Mechanical methods of induction of labour

Source of evidence: Bouvain M et al. Mechanical methods for induction of labour. Cochrane Database of Systematic Reviews, 2001, Issue 4. Art. No.: CD001233; DOI: 10.1002/14651858.CD001233. (Data in this review were updated for the present guidelines. The current online published version of the review may not yet reflect the updates.)

Table 2.9.1. Laminaria tent versus placebo/no treatment for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Laminaria tent	Placebo/ no treatment		
Vaginal birth not achieved within 24 hours												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	18/26 (69.2%)	17/22 (77.3%)	RR 0.9 (0.64–1.26)	77 fewer per 1000 (from 278 fewer to 201 more)	⊕○○○ Very low	Critical
								77.3%		77 fewer per 1000 (from 278 fewer to 201 more)		
Caesarean section												
5	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ²	None	62/183 (33.9%)	66/189 (34.9%)	RR 0.98 (0.74–1.3)	7 fewer per 1000 (from 91 fewer to 105 more)	⊕⊕⊕○ Moderate	Critical
								33.3%		7 fewer per 1000 (from 87 fewer to 100 more)		
Apgar score <7 at 5 minutes												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	2/112 (1.8%)	6/128 (4.7%)	RR 0.38 (0.08–1.85)	29 fewer per 1000 (from 43 fewer to 40 more)	⊕⊕○○ Low	Critical
								4.7%		29 fewer per 1000 (from 43 fewer to 40 more)		

1 Evidence from studies with moderate risk of bias.

2 95% Confidence intervals ranging from appreciable benefit to appreciable harm.

3 Very small study population/very rare events.

Table 2.9.2. Laminaria tent versus prostaglandins for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Laminaria tent	Prostaglandins		
Caesarean section												
11	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ²	None	186/696 (26.7%)	170/701 (24.3%)	RR 1.11 (0.92–1.32)	27 more per 1000 (from 19 fewer to 78 more)	⊕⊕○○ Low	Critical
								24.2%		27 more per 1000 (from 19 fewer to 77 more)		
Uterine hyperstimulation with fetal heart rate changes												
5	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ³	None	0/267 (0%)	16/271 (5.9%)	RR 0.13 (0.04–0.48)	51 fewer per 1000 (from 31 fewer to 57 fewer)	⊕⊕○○ Low	Critical
								3.2%		28 fewer per 1000 (from 17 fewer to 31 fewer)		
Apgar score <7 at 5 minutes												
3	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ³	None	5/170 (2.9%)	1/175 (0.6%)	RR 5.28 (0.63–44.3)	24 more per 1000 (from 2 fewer to 247 more)	⊕⊕○○ Low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		
Admission to neonatal intensive care unit												
2	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{3,4}	None	9/126 (7.1%)	6/133 (4.5%)	RR 1.58 (0.58–4.33)	26 more per 1000 (from 19 fewer to 150 more)	⊕○○○ Very low	Critical
								5.5%		32 more per 1000 (from 23 fewer to 183 more)		
Perinatal death												
2	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{3,4}	None	1/130 (0.8%)	0/135 (0%)	RR 3.16 (0.13–76.7)	0 more per 1000 (from 0 fewer to 0 more)	⊕○○○ Very low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Laminaria tent	Prostaglandins	Relative risk (95% confidence interval)	Absolute		
Serious maternal morbidity or death												
2	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{3,4}	None	0/105 (0%)	1/108 (0.9%)	RR 0.35 (0.01–8.52)	6 fewer per 1000 (from 9 fewer to 70 more)	⊕○○○ Very low	Critical
								0.5%		3 fewer per 1000 (from 5 fewer to 38 more)		

1 Most of the evidence coming from studies with moderate risk of bias.

2 95% confidence intervals ranging from negligible benefit to appreciable harm.

3 Very small population or very rare events.

4 95% confidence intervals ranging from appreciable benefit to appreciable harm.

Table 2.9.3. Laminaria tent plus prostaglandins versus prostaglandins alone for induction of labour at term

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Laminaria tent and prostaglandins	Prostaglandins alone			
Vaginal birth not achieved within 24 hours													
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{1,2}	None	13/22 (59.1%)	12/17 (70.6%)	RR 0.84 (0.53–1.33)	113 fewer per 1000 (from 332 fewer to 233 more)	⊕⊕○○ Low	Critical	
								70.6%		113 fewer per 1000 (from 332 fewer to 233 more)			
Caesarean section													
4	RCT	serious ³	No serious inconsistency	No serious indirectness	Very serious ^{2,4}	None	35/113 (31%)	25/110 (22.7%)	RR 1.37 (0.88–2.15)	84 more per 1000 (from 27 fewer to 261 more)	⊕○○○ Very low	Critical	
								21.2%		78 more per 1000 (from 25 fewer to 244 more)			
Uterine hyperstimulation with fetal heart rate changes													
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{1,2}	None	0/19 (0%)	2/25 (8%)	RR 0.26 (0.01–5.12)	59 fewer per 1000 (from 79 fewer to 330 more)	⊕⊕○○ Low	Critical	
								8%		59 fewer per 1000 (from 79 fewer to 330 more)			
Admission to neonatal intensive care unit													
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{1,2}	None	0/19 (0%)	2/25 (8%)	RR 0.26 (0.01–5.12)	59 fewer per 1000 (from 79 fewer to 330 more)	⊕⊕○○ Low	Critical	
								8%		59 fewer per 1000 (from 79 fewer to 330 more)			

1 95% confidence intervals ranging from appreciable benefit to appreciable harm.

2 Very small study population or very rare events.

3 Most of the evidence is from studies with moderate risk of bias.

4 95% confidence intervals ranging from negligible benefit to appreciable harm.

Table 2.9.4. Laminaria tent versus oxytocin for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Laminaria tent	Oxytocin		
Caesarean section												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	8/38 (21.1%)	9/35 (25.7%)	RR 0.83 (0.36–1.89)	44 fewer per 1000 (from 165 fewer to 229 more)	⊕⊕○○ Low	Critical
								27%		46 fewer per 1000 (from 173 fewer to 240 more)		

1 95% confidence interval ranging from appreciable benefit to appreciable harm in a very small study population.

Table 2.9.5 Laminaria tent plus oxytocin versus oxytocin alone for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Laminaria tent plus oxytocin	Oxytocin alone	Relative risk (95% confidence interval)	Absolute		
Caesarean section												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	1/22 (4.5%)	4/24 (16.7%)	RR 0.27 (0.03–2.26)	122 fewer per 1000 (from 162 fewer to 210 more)	⊕⊕○○ Low	Critical
								16.7%		122 fewer per 1000 (from 162 fewer to 210 more)		

1 95% confidence interval ranging from appreciable benefit to appreciable harm in a very small study population.

Table 2.9.6. Balloon catheter versus placebo/no treatment for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Balloon catheter (Foley or Atad)	Placebo/ no treatment:		
Caesarean section												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	7/22 (31.8%)	6/22 (27.3%)	RR 1.17 (0.47–2.92)	46 more per 1000 (from 145 fewer to 524 more)	⊕○○○ Very low	Critical
								27.3%		46 more per 1000 (from 145 fewer to 524 more)		

1 Evidence from study with moderate risk of bias.
2 95% confidence interval ranging from appreciable benefit to appreciable harm in a very small study population.

Table 2.9.7. Balloon catheter versus prostaglandins for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Balloon catheter (Foley or Atad)	Prostaglandins	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
5	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	85/194 (43.8%)	87/231 (37.7%)	RR 1.23 (0.98–1.54)	87 more per 1000 (from 8 fewer–203 more)	⊕○○○ Very low	Critical
								41.8%		96 more per 1000 (from 8 fewer to 226 more)		
Caesarean section												
19	RCT	No serious limitations	Serious ¹	No serious indirectness	No serious imprecision	None	264/1019 (25.9%)	259/1031 (25.1%)	RR 1.01 (0.88–1.17)	3 more per 1000 (from 30 fewer to 43 more)	⊕⊕⊕○ Moderate	Critical
								20%		2 more per 1000 (from 24 fewer to 34 more)		
Uterine hyperstimulation with fetal heart rate changes												
7	RCT	No serious limitations	Serious ⁴	No serious indirectness	No serious imprecision	None	17/395 (4.3%)	33/428 (7.7%)	RR 0.51 (0.3–0.86)	38 fewer per 1000 (from 11 fewer to 54 fewer)	⊕⊕⊕○ Moderate	Critical
								1.7%		8 fewer per 1000 (from 2 fewer to 12 fewer)		
Apgar score <7 at 5 minutes												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{3,5}	None	0/58 (0%)	1/100 (1%)	RR 0.71 (0.03–17.06)	3 fewer per 1000 (from 10 fewer to 161 more)	⊕⊕○○ Low	Critical
								0.6%		2 fewer per 1000 (from 6 fewer to 96 more)		
Admission to neonatal intensive care unit												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ⁵	None	20/197 (10.2%)	20/189 (10.6%)	RR 0.95 (0.53–1.7)	5 fewer per 1000 (from 50 fewer to 74 more)	⊕⊕⊕○ Moderate	Critical
								10.2%		5 fewer per 1000 (from 48 fewer to 71 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Balloon catheter (Foley or Atad)	Prostaglandins		
Perinatal death												
3	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{3,5}	None	1/149 (0.7%)	1/152 (0.7%)	RR 1 (0.06–15.55)	0 fewer per 1000 (from 6 fewer to 96 more)	⊕○○○ Very low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		
Serious maternal morbidity or death												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{3,5}	None	0/149 (0%)	1/145 (0.7%)	RR 0.28 (0.01–6.8)	5 fewer per 1000 (from 7 fewer to 40 more)	⊕⊕○○ Low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		

1 Evidence from studies with moderate risk of bias.

2 95% confidence interval ranging from negligible benefit to appreciable harm.

3 Very small study population or very rare events.

4 Severe heterogeneity, which could be due to heterogeneous comparators (misoprostol and other prostaglandins used as similar comparators).

5 95% confidence intervals ranging from appreciable benefit to appreciable harm.

Table 2.9.8. Balloon catheter plus prostaglandins versus prostaglandins alone for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Balloon catheter (Foley or Atad) plus prostaglandins	Prostaglandins alone	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
3	RCT	No serious limitations	serious ¹	No serious indirectness	Serious ²	None	102/308 (33.1%)	98/303 (32.3%)	RR 1.04 (0.83–1.29)	13 more per 1000 (from 55 fewer to 94 more)	⊕⊕○○ Low	Critical
								24.2%		10 more per 1000 (from 41 fewer to 70 more)		
Caesarean section												
8	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	166/607 (27.3%)	185/601 (30.8%)	RR 0.9 (0.75–1.07)	31 fewer per 1000 (from 77 fewer to 22 more)	⊕⊕⊕⊕ High	Critical
								32.1%		32 fewer per 1000 (from 80 fewer to 22 more)		
Uterine hyperstimulation with fetal heart rate changes												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ²	None	15/243 (6.2%)	24/254 (9.4%)	RR 0.68 (0.37–1.23)	30 fewer per 1000 (from 60 fewer to 22 more)	⊕⊕⊕○ Moderate	Critical
								4.9%		16 fewer per 1000 (from 31 fewer to 11 more)		
Apgar score <7 at 5 minutes												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	8/236 (3.4%)	10/237 (4.2%)	RR 0.81 (0.32–2.02)	8 fewer per 1000 (from 29 fewer to 43 more)	⊕⊕○○ Low	Critical
								3.4%		6 fewer per 1000 (from 23 fewer to 35 more)		
Admission to neonatal intensive care unit												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{3,4}	None	14/279 (5%)	23/286 (8%)	RR 0.61 (0.33–1.12)	31 fewer per 1000 (from 54 fewer to 10 more)	⊕⊕○○ Low	Critical
								10.2%		40 fewer per 1000 (from 68 fewer to 12 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Balloon catheter (Foley or Atad) plus prostaglandins	Prostaglandins alone	Relative risk (95% confidence interval)	Absolute		
Perinatal death												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{3,4}	None	1/236 (0.4%)	3/236 (1.3%)	RR 0.42 (0.06–2.8)	7 fewer per 1000 (from 12 fewer to 23 more)	⊕⊕○○ Low	Critical
								1.9%		11 fewer per 1000 (from 18 fewer to 34 more)		

1 Severe statistical heterogeneity.

2 95% confidence intervals ranging from negligible benefit to appreciable harm.

3 Very small population or very rare events.

4 95% confidence intervals ranging from appreciable benefit to negligible harm.

Table 2.9.9. Balloon catheter versus oxytocin for induction of labour at term.

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Balloon catheter (Foley or Atad)	Oxytocin		
Caesarean section												
2	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ²	None	10/65 (15.4%)	21/60 (35%)	RR 0.43 (0.22–0.83)	199 fewer per 1000 (from 60 fewer to 273 fewer)	⊕⊕○○ Low	Critical
								35%		199 fewer per 1000 (from 60 fewer to 273 fewer)		

1 Most of the evidence from studies with moderate risk of bias.

2 Very small population or very rare events.

Table 2.9.10. Balloon catheter plus oxytocin versus misoprostol for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Foley plus oxytocin	Misoprostol	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ²	None	28/79 (35.4%)	51/79 (64.6%)	OR 0.3 (0.16–0.58)	292 fewer per 1000 (from 132 fewer to 420 fewer)	⊕⊕○○ Low	Critical
								64.6%		292 fewer per 1000 (from 132 fewer to 420 fewer)		
Caesarean section												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	24/79 (30.4%)	28/83 (33.7%)	OR 0.86 (0.44–1.66)	33 fewer per 1000 (from 154 fewer to 121 more)	⊕○○○ Very low	Critical
								33.7%		33 fewer per 1000 (from 154 fewer to 121 more)		
Uterine hyperstimulation with fetal heart rate changes												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	3/79 (3.8%)	3/83 (3.6%)	OR 1.05 (0.21–5.38)	2 more per 1000 (from 28 fewer to 132 more)	⊕○○○ Very low	Critical
								3.6%		2 more per 1000 (from 28 fewer to 131 more)		
Apgar score <7 at 5 minutes												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	3/79 (3.8%)	3/83 (3.6%)	OR 1.05 (0.21–5.38)	2 more per 1000 (from 28 fewer to 132 more)	⊕○○○ Very low	Critical
								3.6%		2 more per 1000 (from 28 fewer to 131 more)		
Admission to neonatal intensive care unit												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	16/79 (20.3%)	19/79 (24.1%)	OR 0.8 (0.38–1.7)	38 fewer per 1000 (from 133 fewer to 109 more)	⊕○○○ Very low	Critical
								24.1%		38 fewer per 1000 (from 133 fewer to 110 more)		

1 Evidence from studies with moderate risk of bias.

2 Very small study population or very rare events.

3 95% confidence intervals ranging from appreciable benefit to appreciable harm.

2.10. Induction of labour in women with fetal anomaly or after fetal death

Source of evidence: Dodd JM, Crowther CA. Misoprostol for induction of labour to terminate pregnancy in the second or third trimester for women with a fetal anomaly or after intrauterine fetal death. Cochrane Database of Systematic Reviews, 2010, Issue 4. Art. No.: CD004901. DOI: 10.1002/14651858.CD004901.pub2.

Table 2.10.1 Vaginal misoprostol versus oral misoprostol for induction of labour in women with fetal anomaly or after fetal death

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Vaginal misoprostol	Oral misoprostol	Relative risk (95% confidence interval)	Absolute		Quality
Vaginal birth not achieved within 24 hours												
6	RCT	No serious limitations	Serious ¹	No serious indirectness	No serious imprecision	None	34/246 (13.8%)	103/261 (39.5%)	RR 0.37 (0.15–0.87)	249 fewer per 1000 (from 51 fewer to 335 fewer)	⊕⊕⊕○ Moderate	Critical
								39.4%		248 fewer per 1000 (from 51 fewer to 335 fewer)		
Surgical evacuation of the uterus												
6	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ²	None	40/254 (15.7%)	48/237 (20.3%)	RR 0.79 (0.54–1.14)	43 fewer per 1000 (from 93 fewer to 28 more)	⊕⊕⊕○ Moderate	Critical
								22.9%		48 fewer per 1000 (from 105 fewer to 32 more)		

1 Most of the heterogeneity may be due to variations in the misoprostol dose. In addition, there is severe heterogeneity in the high-dose group.

2 95% confidence intervals ranging from appreciable benefit to negligible harm.

Table 2.10.2. Six-hourly vaginal misoprostol versus 12-hourly vaginal misoprostol for induction of labour in women with fetal anomaly or after fetal death

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Vaginal misoprostol 6-hourly	Vaginal misoprostol 12-hourly	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	46/187 (24.6%)	51/176 (29%)	RR 0.87 (0.62–1.22)	38 fewer per 1000 (from 110 fewer to 64 more)	⊕⊕⊕○ Moderate	Critical
								23.3%		30 fewer per 1000 (from 89 fewer to 51 more)		
Blood loss > 500 ml												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ²	None	4/140 (2.9%)	3/139 (2.2%)	RR 1.32 (0.3–5.81)	7 more per 1000 (from 15 fewer to 104 more)	⊕⊕○○ Low	Critical
								2.2%		7 more per 1000 (from 15 fewer to 106 more)		
Surgical evacuation of the uterus												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	72/214 (33.6%)	76/202 (37.6%)	RR 0.87 (0.68–1.13)	49 fewer per 1000 (from 120 fewer to 49 more)	⊕⊕⊕○ Moderate	Critical
								33.1%		43 fewer per 1000 (from 106 fewer to 43 more)		

1 95% confidence intervals ranging from appreciable benefit to negligible harm.

2 Very small study population or very rare events.

Table 2.10.3. Vaginal misoprostol versus Gemeprost (prostaglandins E1) for induction of labour in women with fetal anomaly or after fetal death

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Vaginal misoprostol	Gemeprost (PGE1)		
Vaginal birth not achieved within 24 hours												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	50/133 (37.6%)	25/102 (24.5%)	RR 1.3 (0.64–2.62)	74 more per 1000 (from 88 fewer to 397 more)	⊕⊕○○ Low	Critical
								25%		75 more per 1000 (from 90 fewer to 405 more)		
Surgical evacuation of the uterus												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	46/133 (34.6%)	46/102 (45.1%)	RR 0.75 (0.55–1.03)	113 fewer per 1000 (from 203 fewer to 14 more)	⊕⊕○○ Low	Critical
								42.6%		106 fewer per 1000 (from 192 fewer to 13 more)		

1 95% confidence intervals ranging from appreciable benefit to negligible harm in a very small study population.

Table 2.10.4. Vaginal misoprostol versus prostaglandins E2 for induction of labour in women with fetal anomaly or after fetal death

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Vaginal misoprostol	Prostaglandin E2	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
4	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	18/125 (14.4%)	28/126 (22.2%)	RR 0.62 (0.36–1.04)	84 fewer per 1000 (from 142 fewer to 9 more)	⊕○○○ Very low	Critical
								27.3%		104 fewer per 1000 (from 175 fewer to 11 more)		
Blood loss > 500 ml												
4	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ³	None	9/170 (5.3%)	2/156 (1.3%)	RR 2.73 (0.69–10.78)	22 more per 1000 (from 4 fewer to 125 more)	⊕⊕○○ Low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		
Surgical evacuation of the uterus												
5	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ⁴	None	28/199 (14.1%)	45/181 (24.9%)	RR 0.52 (0.2–1.36)	119 fewer per 1000 (from 199 fewer to 90 more)	⊕⊕○○ Low	Critical
								28%		134 fewer per 1000 (from 224 fewer to 101 more)		

1 Most of the evidence from studies with moderate risk of bias.

2 95% confidence intervals ranging from appreciable benefit to negligible harm in a very small study population.

3 95% confidence interval ranging from appreciable benefit to appreciable harm in a population with very rare events.

4 95% confidence intervals ranging from appreciable benefit to appreciable harm.

Table 2.10.5. Vaginal misoprostol versus prostaglandin F2 α for induction of labour in women with fetal anomaly or after fetal death

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Vaginal misoprostol	Prostaglandin F2 α		
Vaginal birth not achieved within 24 hours												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	26/106 (24.5%)	25/107 (23.4%)	RR 1.07 (0.28–4.06)	16 more per 1000 (from 168 fewer to 715 more)	⊕⊕○○ Low	Critical
								20%		14 more per 1000 (from 144 fewer to 612 more)		
Blood loss > 500 ml												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{1,2}	None	4/30 (13.3%)	6/31 (19.4%)	RR 0.69 (0.22–2.2)	60 fewer per 1000 (from 151 fewer to 232 more)	⊕⊕○○ Low	Critical
								19.4%		60 fewer per 1000 (from 151 fewer to 233 more)		
Surgical evacuation of the uterus												
5	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	28/220 (12.7%)	44/219 (20.1%)	RR 0.63 (0.41–0.98)	74 fewer per 1000 (from 4 fewer to 119 fewer)	⊕⊕⊕⊕ High	Critical
								19.7%		73 fewer per 1000 (from 4 fewer to 116 fewer)		

1 95% confidence interval ranging from appreciable benefit to appreciable harm in a very small study population.

2 Very small study population or very rare events.

Table 2.10.6. Vaginal misoprostol versus vaginal misoprostol and laminaria tent for induction of labour in women with fetal anomaly or after fetal death

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Vaginal misoprostol	Vaginal misoprostol and laminaria tent		
Vaginal birth not achieved within 24 hours												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	10/33 (30.3%)	11/35 (31.4%)	RR 0.96 (0.47–1.97)	13 fewer per 1000 (from 167 fewer to 305 more)	⊕○○○ Very low	Critical
								31.4%		13 fewer per 1000 (from 166 fewer to 305 more)		

1 The evidence comes from a study with moderate risk of bias.

2 95% confidence interval ranging from appreciable benefit to appreciable harm in a very small study population.

Table 2.10.7. Combined oral and vaginal misoprostol versus vaginal misoprostol alone for induction of labour in women with fetal anomaly or after fetal death

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Combined oral and vaginal misoprostol	Vaginal misoprostol alone		
Vaginal birth not achieved within 24 hours												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	7/27 (25.9%)	4/28 (14.3%)	RR 1.81 (0.6–5.5)	116 more per 1000 (from 57 fewer to 643 more)	⊕⊕○○ Low	Critical
								14.3%		116 more per 1000 (from 57 fewer to 644 more)		
Surgical evacuation of the uterus												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	12/48 (25%)	15/50 (30%)	RR 0.83 (0.44–1.57)	51 fewer per 1000 (from 168 fewer to 171 more)	⊕⊕○○ Low	Critical
								28.3%		48 fewer per 1000 (from 158 fewer to 161 more)		

1 95% confidence interval ranging from appreciable benefit to negligible harm in a very small study population.

Table 2.10.8. Combined oral and vaginal misoprostol versus oral misoprostol alone for induction of labour in women with fetal anomaly or after fetal death

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Combined oral and vaginal misoprostol	Oral misoprostol alone		
Vaginal birth not achieved within 24 hours												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	7/27 (25.9%)	16/29 (55.2%)	RR 0.47 (0.23–0.96)	292 fewer per 1000 (from 22 fewer to 425 fewer)	⊕⊕⊕○ Moderate	Critical
								55.2%		293 fewer per 1000 (from 22 fewer to 425 fewer)		
Surgical evacuation of the uterus												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{1,2}	None	8/27 (29.6%)	10/29 (34.5%)	RR 0.86 (0.4–1.85)	48 fewer per 1000 (from 207 fewer to 293 more)	⊕⊕○○ Low	Critical
								34.5%		48 fewer per 1000 (from 207 fewer to 293 more)		

1 Very small study population or very rare events.

2 95% confidence interval ranging from appreciable benefit to appreciable harm.

Table 2.10.9. Sublingual misoprostol versus vaginal misoprostol for induction of labour in women with fetal anomaly or after fetal death

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Sublingual misoprostol	Vaginal misoprostol		
Vaginal birth not achieved within 24 hours												
2	RCT	No serious limitations	Serious ¹	No serious indirectness	Serious ²	None	3/101 (3%)	14/101 (13.9%)	RR 0.24 (0.08–0.74)	105 fewer per 1000 (from 36 fewer to 128 fewer)	⊕⊕○○ Low	Critical
								13.8%		105 fewer per 1000 (from 36 fewer to 127 fewer)		
Induction-to-delivery interval (better indicated by lower values)												
2	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ²	None	101	101	-	Mean difference 4.81 lower (8.26 to 1.37 lower)	⊕⊕○○ Low	Critical

1 Evidence is from studies with moderate risk of bias.

2 Very small population or very rare events.

Table 2.10.10. Sublingual misoprostol versus oral misoprostol for induction of labour in women with fetal anomaly or after fetal death

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Sublingual misoprostol	Oral misoprostol		
Vaginal birth not achieved within 24 hours												
2	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ²	None	3/102 (2.9%)	15/102 (14.7%)	RR 0.22 (0.01–4.99)	115 fewer per 1000 (from 146 fewer to 587 more)	⊕○○○ Very low	Critical
								14.7%		115 fewer per 1000 (from 146 fewer to 587 more)		
Induction-to-delivery interval (better indicated by lower values)												
2	RCT	Serious ³	No serious inconsistency	No serious indirectness	Serious ⁴	None	101	101	-	Mean difference –7.17 (from –13.73 to –0.6)	⊕⊕○○ Low	Critical

1 Included studies present moderate risk of bias.

2 95% confidence intervals ranging from appreciable benefit to appreciable harm in a very small population with very rare events.

3 No explanation was provided.

4 Very small study population.

Table 2.10.11. Sublingual misoprostol 100 µg versus sublingual misoprostol 200 µg for induction of labour in women with fetal anomaly or after fetal death

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Sublingual misoprostol 100 µg	Sublingual misoprostol 200 µg		
Induction-to-delivery interval (better indicated by lower values)												
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ¹	None	81	81	-	Mean difference −0.47 (from −2.94 to 2.00)	⊕⊕○○ Low	Critical

1 Very small study population.

Table 2.10.12. Vaginal misoprostol low cumulative dose (<800 µg) versus vaginal misoprostol moderate cumulative dose (800 µg–2400 µg) for induction of labour in women with fetal anomaly or after fetal death

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Vaginal misoprostol low cumulative dose (<800 µg)	Vaginal misoprostol moderate cumulative dose (800 µg–2400 µg)		
Vaginal birth not achieved within 24 hours												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	21/51 (41.2%)	22/99 (22.2%)	RR 1.85 (1.13–3.03)	189 more per 1000 (from 29 more to 451 more)	⊕⊕⊕○ Moderate	Critical
								22.2%		189 more per 1000 (from 29 more to 451 more)		
Surgical evacuation of the uterus												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	12/51 (23.5%)	41/99 (41.4%)	RR 0.57 (0.33–0.98)	178 fewer per 1000 (from 8 fewer to 277 fewer)	⊕⊕⊕○ Moderate	Critical
								41.4%		178 fewer per 1000 (from 8 fewer to 277 fewer)		

1 Very small study population.

2.11. Sweeping membranes

Source of evidence: Boulvain M, Stan CM, Irion O. Membrane sweeping for induction of labour. Cochrane Database of Systematic Reviews, 2005, Issue 1. Art. No.: CD000451. DOI: 10.1002/14651858.CD000451.pub2. (Data in this review were updated for the present guidelines. The current online published version of the review may not yet reflect the updates.)

Table 2.11.1. Membranes sweeping versus no treatment for induction of labour at term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Membranes sweeping	No treatment	Relative risk (95% confidence interval)	Absolute		
Caesarean section												
21	RCT	Serious ¹	No serious inconsistency	No serious indirectness	No serious imprecision	None	190/1753 (10.8%)	199/1690 (11.8%)	RR 0.93 (0.77–1.11)	8 fewer per 1000 (from 27 fewer to 13 more)	⊕⊕⊕○ Moderate	Critical
								11.8%		8 fewer per 1000 (from 27 fewer to 13 more)		
Apgar score <7 at 5 minutes												
9	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	13/810 (1.6%)	11/787 (1.4%)	RR 1.13 (0.53–2.43)	2 more per 1000 (from 7 fewer to 20 more)	⊕⊕○○ Low	Critical
								1.5%		2 more per 1000 (from 7 fewer to 21 more)		
Serious maternal morbidity or death												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ²	None	0/132 (0%)	0/131 (0%)	Not pooled	Not pooled	⊕⊕⊕○ Moderate	Critical
								0%		Not pooled		
Admission to neonatal intensive care unit												
7	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	20/336 (6%)	21/313 (6.7%)	RR 0.92 (0.52–1.63)	5 fewer per 1000 (from 32 fewer to 42 more)	⊕⊕○○ Low	Critical
								4%		3 fewer per 1000 (from 19 fewer to 25 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Membranes sweeping	No treatment	Relative risk (95% confidence interval)	Absolute		
Perinatal death												
7	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ^{2,3}	None	4/776 (0.5%)	4/766 (0.5%)	RR 0.99 (0.29–3.39)	0 fewer per 1000 (from 4 fewer to 12 more)	⊕⊕○○ Low	Critical
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		
Not in labour or not delivered within 48 hours (not prespecified)												
5	RCT	No serious limitations	Serious ⁴	No serious indirectness	No serious imprecision	None	234/367 (63.8%)	298/359 (83%)	RR 0.77 (0.7–0.84)	191 fewer per 1000 (from 133 fewer to 249 fewer)	⊕⊕⊕○ Moderate	Critical
								79.8%		184 fewer per 1000 (from 128 fewer to 239 fewer)		
Delay to delivery (days) (not prespecified) (better indicated by lower values)												
10	RCT	No serious limitations	Serious ⁵	No serious indirectness	No serious imprecision	None ⁵	801	779	-	Mean difference 2.48 lower (3 to 1.97 lower)	⊕⊕⊕○ Moderate	Critical
Discomfort during vaginal examination (not prespecified)												
2	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	94/163 (57.7%)	32/157 (20.4%)	RR 2.83 (2.03–3.96)	373 more per 1000 (from 210 more to 603 more)	⊕⊕⊕⊕ High	Critical
								20.4%		373 more per 1000 (from 210 more to 604 more)		
Vaginal bleeding (not prespecified)												
3	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	35/200 (17.5%)	18/191 (9.4%)	RR 1.75 (1.08–2.83)	71 more per 1000 (from 8 more to 172 more)	⊕⊕⊕⊕ High	Critical
								0%		0 more per 1000 (from 0 more to 0 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations			Membranes sweeping	No treatment		
‘Formal’ induction of labour (not prespecified)												
14	RCT	No serious limitations	Serious ⁶	No serious indirectness	No serious imprecision	None ⁶	267/1243 (21.5%)	386/1203 (32.1%)	RR 0.67 (0.59–0.76)	106 fewer per 1000 (from 77 fewer to 132 fewer)	⊕⊕⊕○ Moderate	Critical
								32.1%		106 fewer per 1000 (from 77 fewer to 132 fewer)		
Maternal infection/fever (not prespecified)												
11	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ²	None	37/853 (4.3%)	34/827 (4.1%)	RR 1.05 (0.68–1.65)	2 more per 1000 (from 13 fewer to 27 more)	⊕⊕⊕○ Moderate	Critical
								3.6%		2 more per 1000 (from 12 fewer to 23 more)		

1 59.3% of evidence from studies with moderate risk of bias.

2 Imprecise confidence intervals.

3 Very rare events.

4 Severe heterogeneity ($I^2=72\%$), possible small study effect.

5 Severe heterogeneity ($I^2=87\%$) with asymmetry in funnel plot and possible small study effect.

6 Severe heterogeneity ($I^2=72\%$) with asymmetry in funnel plot.

3. TREATMENT OF UTERINE HYPERSTIMULATION

3.1. Tocolytics

Source of evidence: Kulier R, Hofmeyr GJ. Tocolytics for suspected intrapartum fetal distress. Cochrane Database of Systematic Reviews, 1998, Issue 2. Art. No.: CD000035; DOI: 10.1002/14651858.CD000035. (Data in this review were updated for the present guidelines. The current online published version of the review may not yet reflect the updates.)

Table 3.1.1. Tocolytics versus no treatment for uterine hyperstimulation

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Tocolytics	No treatment		
No improvement in fetal heart rate abnormality												
2	RCT	No serious limitations	No serious inconsistency	Serious ¹	No serious imprecision	None	6/24 (25%)	18/19 (94.7%)	RR 0.28 (0.14–0.55)	682 fewer per 1000 (from 426 fewer to 815 fewer)	⊕⊕⊕○ Moderate	Important
								95%		684 fewer per 1000 (from 427 fewer to 817 fewer)		
Apgar score <7 at 1 minute												
2	RCT	Serious ²	No serious inconsistency	Serious ¹	Very serious ³	None	4/27 (14.8%)	9/28 (32.1%)	RR 0.46 (0.16–1.3)	174 fewer per 1000 (from 270 fewer to 96 more)	⊕○○○ Very low	Important
								35.4%		191 fewer per 1000 (from 297 fewer to 106 more)		
Apgar score <7 at 5 minutes												
1	RCT	Serious ⁴	No serious inconsistency	Serious ¹	Very serious ⁵	None	0/16 (0%)	2/29 (6.9%)	RR 0.35 (0.02–6.93)	45 fewer per 1000 (from 68 fewer to 409 more)	⊕○○○ Very low	Critical
								6.9%		45 fewer per 1000 (from 68 fewer to 409 more)		
Perinatal death												
2	RCT	Serious ²	No serious inconsistency	Serious ¹	Very serious ⁶	None	0/28 (0%)	2/29 (6.9%)	RR 0.23 (0.01–4.55)	53 fewer per 1000 (from 68 fewer to 245 more)	⊕○○○ Very low	Critical
								5%		38 fewer per 1000 (from 49 fewer to 178 more)		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Tocolytics	No treatment	Relative risk (95% confidence interval)	Absolute		
Admission to neonatal intensive care unit												
1	RCT	Serious ⁴	No serious inconsistency	Serious ¹	Very serious ⁷	None	1/17 (5.9%)	0/20 (0%)	RR 3.5 (0.15–80.71)	0 more per 1000 (from 0 fewer to 0 more)	⊕○○○ Very low	Critical
								0%		0 more per 1000 (from 0 fewer to 0 more)		

1 Original trials conducted for treatment of suspected intrapartum fetal distress.

2 Small, underpowered studies.

3 Anything from a 84% reduction to a 30% increase.

4 Only one underpowered trial.

5 Anything from a 98% reduction to a 6.9-fold increase.

6 Anything from a 99% reduction to a 4.55-fold increase.

7 Anything from a 85% reduction to a 81-fold increase.

Table 3.1.2. Terbutaline versus magnesium sulfate for uterine hyperstimulation during induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Terbutaline	Magnesium sulfate		
No improvement in fetal heart rate abnormality												
1	RCT	Serious ¹	No serious inconsistency	Serious ²	Very serious ³	None	2/23 (8.7%)	7/23 (30.4%)	RR 0.29 (0.07–1.23)	216 fewer per 1000 (from 283 fewer to 70 more)	⊕○○○ Very low	Important
								30.4%		216 fewer per 1000 (from 283 fewer to 70 more)		
Failure to reduce uterine activity												
1	RCT	Serious ¹	No serious inconsistency	Serious ²	Very serious ⁴	None	0/23 (0%)	7/23 (30.4%)	RR 0.07 (0–1.1)	283 fewer per 1000 (from 304 fewer to 30 more)	⊕○○○ Very low	Important
								30.4%		283 fewer per 1000 (from 304 fewer to 30 more)		

1 Only one underpowered trial.

2 Original trials conducted to evaluate treatment of intrapartum fetal distress.

3 Anything from a 93% reduction to a 23% increase.

4 Anything from 100% reduction to a 10% increase.

Table 3.1.3. Terbutaline versus nitroglycerin for uterine hyperstimulation during induction of labour

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Terbutaline	Nitroglycerin		
No improvement in fetal heart rate abnormality												
1	RCT	No serious limitations	No serious inconsistency	Serious ¹	Serious ²	None	16/57 (28.1%)	19/53 (35.8%)	RR 0.78 (0.45–1.36)	79 fewer per 1000 (from 197 fewer to 129 more)	⊕⊕○○ Low	Important
								35.9%		79 fewer per 1000 (from 197 fewer to 129 more)		
Failure to reduce uterine activity												
1	RCT	No serious limitations	No serious inconsistency	Serious ¹	Very serious ³	None	1/56 (1.8%)	10/53 (18.9%)	RR 0.09 (0.01–0.71)	172 fewer per 1000 (from 55 fewer to 187 fewer)	⊕○○○ VERY Low	Important
								18.9%		172 fewer per 1000 (from 55 fewer to 187 fewer)		
Caesarean section												
1	RCT	No serious limitations	No serious inconsistency	Serious ¹	None	None	30/57 (52.6%)	29/53 (54.7%)	RR 0.96 (0.68–1.36)	22 fewer per 1000 (from 175 fewer to 197 more)	⊕⊕○○ Low	Critical
								54.7%		22 fewer per 1000 (from 175 fewer to 197 more)		
Maternal hypotension												
1	RCT	Serious ⁴	No serious inconsistency	Serious ¹	Very serious ⁵	None	0/57 (0%)	0/53 (0%)	Not pooled	Not pooled	⊕○○○ Very low	Critical
								0%		Not pooled		
Apgar score <7 at 5 minutes												
1	RCT	Serious ⁴	No serious inconsistency	Serious ¹	Very serious ⁵	None	0/57 (0%)	0/53 (0%)	Not pooled	Not pooled	⊕○○○ Very low	Critical
								0%		Not pooled		

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Terbutaline	Nitroglycerin	Relative risk (95% confidence interval)	Absolute		
Admission to neonatal intensive care unit												
1	RCT	No serious limitations	No serious inconsistency	Serious ¹	Very serious ⁶	None	12/57 (21.1%)	12/53 (22.6%)	RR 0.93 (0.46–1.89)	16 fewer per 1000 (from 122 fewer to 202 more)	⊕○○○ Very	Critical
								22.6%		16 fewer per 1000 (from 122 fewer to 201 more)	low	

1 Original trials conducted to evaluate treatment of intrapartum fetal distress.

2 Anything from a 55% reduction to a 36% increase.

3 Wide confidence interval, from a 99% to a 29% reduction.

4 Only one underpowered trial.

5 No events in only one trial.

6 Anything from a 54% reduction to a 89% increase.

Table 3.1.4. Atosiban versus betamimetics for uterine hyperstimulation during induction of labour

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Atosiban	Betamimetics	Relative risk (95% confidence interval)	Absolute			
No improvement in fetal heart rate abnormality													
1	RCT	Serious ¹	No serious inconsistency	Serious ²	Very serious ³	None	1/13 (7.7%)	0/13 (0%)	RR 3 (0.13–67.51)	0 more per 1000 (from 0 fewer to 0 more)	⊕○○○ Very low	Important	
								0%		0 more per 1000 (from 0 fewer to 0 more)			
Failure to reduce uterine activity													
2	RCT	No serious limitations	No serious inconsistency	Serious ²	Very serious ⁴	None	4/42 (9.5%)	3/42 (7.1%)	RR 1.29 (0.34–4.87)	21 more per 1000 (from 47 fewer to 276 more)	⊕○○○ Very low	Important	
								5.2%		15 more per 1000 (from 34 fewer to 201 more)			
Tachycardia													
1	RCT	Serious ¹	No serious inconsistency	Serious ²	Very serious ⁵	None	1/13 (7.7%)	10/13 (76.9%)	RR 0.1 (0.01–0.67)	692 fewer per 1000 (from 254 fewer to 762 fewer)	⊕○○○ Very low	Important	
								76.9%		692 fewer per 1000 (from 254 fewer to 761 fewer)			
Apgar score <7 at 1 minute													
1	RCT	Serious ¹	No serious inconsistency	Serious ²	Very serious ⁶	None	1/13 (7.7%)	2/13 (15.4%)	RR 0.5 (0.05–4.86)	77 fewer per 1000 (from 146 fewer to 594 more)	⊕○○○ Very low	Important	
								15.4%		77 fewer per 1000 (from 146 fewer to 594 more)			
Apgar score <7 at 5 minutes													
2	RCT	Serious ⁷	No serious inconsistency	Serious ²	Very serious ⁸	None	1/47 (2.1%)	2/40 (5%)	RR 0.4 (0.04–4.15)	30 fewer per 1000 (from 48 fewer to 158 more)	⊕○○○ Very low	Critical	
								3.7%		22 fewer per 1000 (from 36 fewer to 117 more)			

Quality assessment							Summary of findings					
							No. of patients		Effect			
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Atosiban	Betamimetics	Relative risk (95% confidence interval)	Absolute		Quality
Admission to neonatal intensive care unit												
1	RCT	Serious ¹	No serious inconsistency	Serious ²	Very serious ⁹	None	0/13 (0%)	1/13 (7.7%)	RR 0.33 (0.01–7.5)	52 fewer per 1000 (from 76 fewer to 500 more)	⊕○○○ Very low	Critical
								7.7%		52 fewer per 1000 (from 76 fewer to 501 more)		
Perinatal death												
1	RCT	Serious ¹	No serious inconsistency	Serious ²	Very serious ¹⁰	None	0/13 (0%)	0/13 (0%)	Not pooled	Not pooled	⊕○○○ Very low	Critical
								0%		Not pooled		

1 Only one small, underpowered trial.

2 Original trials conducted to evaluate treatments for intrapartum fetal distress.

3 Anything from a 87% reduction to a 67.5-fold increase.

4 Anything from a 66% reduction to a 4.9-fold increase.

5 Wide confidence interval, from a 99% to a 33% reduction.

6 Anything from a 95% reduction to a 4.9-fold increase.

7 Underpowered trials.

8 Anything from a 96% reduction to a 4.15-fold increase.

9 Anything from a 99% reduction to a 7.5-fold increase.

10 No events in only one underpowered trial.

Table 3.1.5. Tocolytics versus emergent delivery for uterine hyperstimulation during induction of labour

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Tocolytics	Emergent delivery	Relative risk (95% confidence interval)	Absolute		
Overall caesarean delivery												
1	RCT	No serious limitations	No serious inconsistency	Serious ¹	No serious imprecision	None	175/193 (90.7%)	159/197 (80.7%)	RR 1.12 (1.04–1.22)	97 more per 1000 (from 32 more to 178 more)	⊕⊕⊕○ Moderate	Critical
								80.7%		97 more per 1000 (from 32 more to 178 more)		
Adverse maternal effects												
1	RCT	No serious limitations	No serious inconsistency	Serious ¹	Very serious ²	None	0/193 (0%)	0/197 (0%)	Not pooled	Not pooled	⊕○○○ Very low	Important
								0%		Not pooled		
Apgar score <4 at 1 minute												
1	RCT	No serious limitations	No serious inconsistency	Serious ¹	Very serious ³	None	8/193 (4.1%)	16/197 (8.1%)	RR 0.51 (0.22–1.16)	40 fewer per 1000 (from 63 fewer to 13 more)	⊕○○○ Very low	Important
								8.1%		40 fewer per 1000 (from 63 fewer to 13 more)		
Apgar score <7 at 5 minutes												
1	RCT	No serious limitations	No serious inconsistency	Serious ¹	Very serious ⁴	None	5/193 (2.6%)	4/197 (2%)	RR 1.28 (0.35–4.68)	6 more per 1000 (from 13 fewer to 75 more)	⊕○○○ Very low	Critical
								2%		6 more per 1000 (from 13 fewer to 74 more)		
Admission to neonatal intensive care unit												
1	RCT	No serious limitations	No serious inconsistency	Serious ¹	No serious imprecision	None	16/193 (8.3%)	35/197 (17.8%)	RR 0.47 (0.27–0.81)	94 fewer per 1000 (from 34 fewer to 130 fewer)	⊕⊕⊕○ Moderate	Critical
								17.8%		94 fewer per 1000 (from 34 fewer to 130 fewer)		

1 Original trials conducted to evaluate treatment of intrapartum fetal distress.

2 No events in only one trial.

3 Anything from a 78% reduction to a 16% increase.

4 Anything from a 65% reduction to a 4.7-fold increase.

4. SETTING

4.1. Outpatient versus inpatient induction of labour

Source of evidence: Kelly AJ, Alfrevic Z, Dowswell T. Outpatient versus inpatient induction of labour for improving birth outcomes. Cochrane Database of Systematic Reviews, 2009, Issue 2. Art. No.: CD007372. DOI: 10.1002/14651858.CD007372.pub2.

Table 4.1.1. Outpatient versus inpatient induction of labour with vaginal prostaglandin E2

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations			Outpatient induction with vaginal prostaglandin E2	Inpatient induction with vaginal prostaglandin E2		
Caesarean section rate												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Very serious ¹	None	20/95 (21.1%)	18/106 (17%)	RR 1.24 (0.7–2.2)	41 more per 1000 (from 51 fewer to 204 more)	⊕⊕○○ Low	Critical
								17%		41 more per 1000 (from 51 fewer to 204 more)		
Apgar score <7 at 5 minutes												
1	RCT	Serious ²	No serious inconsistency	No serious indirectness	Very serious ³	None	2/95 (2.1%)	1/106 (0.9%)	RR 2.23 (0.21–24.22)	12 more per 1000 (from 7 fewer to 219 more)	⊕○○○ Very low	Critical
								0.9%		11 more per 1000 (from 7 fewer to 209 more)		
Admission to neonatal intensive care unit												
1	RCT	Serious ²	No serious inconsistency	No serious indirectness	Very serious ⁴	None	7/95 (7.4%)	6/106 (5.7%)	RR 1.3 (0.45–3.74)	17 more per 1000 (from 31 fewer to 155 more)	⊕○○○ Very low	Critical
								5.7%		17 more per 1000 (from 31 fewer to 156 more)		

1 Anything from a 30% reduction to a 2.2-fold increase.

2 Underpowered study.

3 Anything from a 79% reduction to a 24.2-fold increase.

4 Anything from a 55% reduction to a 3.7-fold increase.

Table 4.1.2. Outpatient versus inpatient induction of labour with controlled release systems of prostaglandin E2

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Outpatient induction with controlled release prostaglandin E2	Inpatient induction with controlled release prostaglandin E2	Relative risk (95% confidence interval)	Absolute		
Vaginal birth not achieved within 24 hours												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	34/149 (22.8%)	43/150 (28.7%)	RR 0.8 (0.54–1.17)	57 fewer per 1000 (from 132 fewer to 49 more)	⊕⊕⊕⊕	Critical
								28.7%		57 fewer per 1000 (from 132 fewer to 49 more)	High	
Uterine hyperstimulation (with or without fetal heart rate changes)												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	Serious ¹	None	15/149 (10.1%)	15/150 (10%)	RR 1.01 (0.51–1.98)	1 more per 1000 (from 49 fewer to 98 more)	⊕⊕⊕○	Critical
								10%		1 more per 1000 (from 49 fewer to 98 more)	Moder- ate	
Caesarean section rate												
1	RCT	No serious limitations	No serious inconsistency	No serious indirectness	No serious imprecision	None	35/149 (23.5%)	37/150 (24.7%)	RR 0.95 (0.64–1.42)	12 fewer per 1000 (from 89 fewer to 104 more)	⊕⊕⊕⊕	Critical
								24.7%		12 fewer per 1000 (from 89 fewer to 104 more)	High	
Admission to neonatal intensive care unit												
1	RCT	Serious ²	No serious inconsistency	No serious indirectness	Very serious ³	None	11/149 (7.4%)	8/150 (5.3%)	RR 1.38 (0.57–3.34)	20 more per 1000 (from 23 fewer to 125 more)	⊕○○○	Critical
								5.3%		20 more per 1000 (from 23 fewer to 124 more)	Very low	

1 Anything from a 49% reduction to a 98% increase.

2 Underpowered study.

3 Anything from a 43% reduction to a 3.3-fold increase.

Table 4.1.3. Outpatient versus inpatient induction of labour with Foley catheter

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other con- siderations	Outpatient induction with Foley catheter	Inpatient induction with Foley catheter	Relative risk (95% confidence interval)	Absolute			
Caesarean section rate													
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Serious ²	None	18/61 (29.5%)	22/50 (44%)	RR 0.67 (0.41–1.1)	145 fewer per 1000 (from 260 fewer to 44 more)	⊕⊕○○ Low	Critical	
								44%		145 fewer per 1000 (from 260 fewer to 44 more)			
Admission to neonatal intensive care unit													
1	RCT	Serious ¹	No serious inconsistency	No serious indirectness	Very serious ³	None	1/61 (1.6%)	4/50 (8%)	RR 0.2 (0.02–1.78)	64 fewer per 1000 (from 78 fewer to 62 more)	⊕○○○ Very low	Critical	
								8%		64 fewer per 1000 (from 78 fewer to 62 more)			

1 Underpowered study.

2 Anything from a 59% reduction to a 10% increase.

3 Anything from a 98% reduction to a 78% increase.

For more information, please contact:

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