



# Surveillance report 2017 – Induction of labour (2008) NICE guideline CG70

Surveillance report

Published: 9 January 2017

[nice.org.uk](http://nice.org.uk)

## Contents

Surveillance decision .....	3
Reason for the decision .....	3
Commentary on selected new evidence .....	5
Methods that are recommended for the induction of labour and that are not recommended for the induction of labour .....	5
How we made the decision.....	11
New evidence .....	11
Views of topic experts .....	11
Views of stakeholders .....	11
NICE Surveillance programme project team .....	12

## Surveillance decision

We will plan an update of the following clinical areas:

- Induction of labour in specific circumstances – [suspected fetal macrosomia](#).
- [Recommended methods for induction of labour](#).
- [Methods that are not recommended for induction of labour](#).

### *Reason for the decision*

We found 182 new studies through surveillance of this guideline. New evidence that could affect recommendations was identified. Topic experts, including those who helped to develop the guideline, advised us about whether the following sections of the guideline should be updated:

#### **Induction of labour in specific circumstances – suspected fetal macrosomia**

- What are the harms and benefits of induction of labour in women with suspected fetal macrosomia?

Topic experts highlighted new evidence on induction of labour for suspected fetal macrosomia. Topic experts advised that this review question should be updated to consider the risks and benefits of induction of labour for suspected fetal macrosomia.

**Decision:** This review question should be updated.

#### **Methods for induction of labour**

- What are the harms and benefits of pharmacological-based methods in induction of labour?
- What are the harms and benefits of mechanical methods in women undergoing induction of labour?

New evidence was identified on oxytocin with amniotomy, misoprostol and PGE2 which could impact on recommendations. Topic experts advised that these questions should be updated. Topic experts advised that the question on surgical methods should be rephrased to state mechanical methods to include all the interventions considered by the review question.

**Decision:** These review questions should be updated.

## Other clinical areas

We also found new evidence that was not thought to have an effect on current recommendations. This evidence related to setting and timing and prevention and management of complications.

We did not find any new evidence related to information and decision-making or monitoring and pain relief.

## Equalities

No equalities issues were identified during the surveillance process.

## Overall decision

After considering all the new evidence and views of topic experts, we decided that a partial update is necessary for this guideline.

See [how we made the decision](#) for further information.

## Commentary on selected new evidence

With advice from topic experts we selected one study for further commentary.

### *Methods that are recommended for the induction of labour and that are not recommended for the induction of labour*

We selected a systematic review, network meta-analysis and cost-effectiveness analysis by [Alfirevic et al. 2016](#) for a full commentary because the results were found to have a potential impact on the guideline recommendations.

## What the guideline recommends

The guideline recommends vaginal prostaglandin E2 (PGE2) as the preferred method for the induction of labour. Misoprostol and mifepristone are recommended only for the induction of labour in women who have intrauterine fetal death. The guideline does not recommend amniotomy, alone or with oxytocin, as a primary method of induction of labour, unless there are specific clinical reasons not to use vaginal PGE2.

## Methods

A systematic review, network meta-analysis (NMA) and incremental cost-effectiveness analysis was undertaken.

The systematic review searched for all randomised control trials (RCTs) published before March 2014. All RCTs on mechanical, pharmacological and non-pharmacological methods, compared to placebo, no treatment or other interventions, to induce labour in women in their third trimester of pregnancy were included.

The systematic review searched for the following primary outcomes:

- vaginal delivery not achieved within 24 hours (VD24)
- uterine hyperstimulation with fetal heart rate changes
- caesarean section
- serious neonatal morbidity or death
- serious maternal morbidity or death

- instrumental delivery
- maternal satisfaction with the method used
- neonatal intensive care unit (NICU) admission
- Apgar score at 5 minutes of <7.

An NMA was conducted for each of 6 outcomes where sufficient data were available. The NMA used both direct and indirect evidence and compared consistency of these in analysis to determine model fit.

A de novo decision-tree model was used for the cost-effectiveness analysis. The costs were taken from the manufacturers, NHS reference costs and the British National Formulary. Several outcomes were accounted for in the model.

## Results

The review included 611 studies on more than 100,000 women undergoing induction of labour using 31 interventions of different dosages and routes of administration.

The interventions included in the cost-effectiveness analysis and the systematic review were:

- titrated (low dose) oral misoprostol solution
- buccal/sublingual misoprostol
- vaginal misoprostol <50 µg
- vaginal misoprostol ≥50 µg
- oral misoprostol tablet <50 µg
- oral misoprostol tablet ≥50 µg
- sustained release misoprostol vaginal pessary
- vaginal PGE2 (gel)
- vaginal PGE2 pessary (normal release)
- intracervical PGE2

- extra-amniotic PGE2
- vaginal PGE2 pessary (slow release)
- vaginal PGE2 (tablet)
- intravenous oxytocin with amniotomy
- intravenous oxytocin
- mifepristone
- double balloon or Cook's catheter
- foley catheter
- nitric oxide.

Evidence was also identified for the following interventions but these were not included in the cost-effectiveness analysis, due to limited reporting of outcomes in included studies:

- corticosteroids
- hyaluronidase
- PGF2 gel
- oral prostaglandins
- intravenous prostaglandin
- membrane sweeping
- laminaria including dilapan
- acupuncture
- sexual intercourse
- relaxin
- amniotomy
- estrogens.

The outcome VD24 includes 141 studies. The results showed that, for the interventions where VD24 was reported, the likelihood of VD24 increases in all interventions except for mifepristone and extra-amniotic PGE2. The lowest odds of not achieving VD24 were for:

- intravenous oxytocin with amniotomy (odds ratio [OR] 0.05, 95% confidence intervals [CI] 0.01–0.14)
- vaginal misoprostol  $\geq 50$  mcg (OR 0.09, 95% CI 0.06–0.24).

Caesarean section was an outcome in 307 included studies. When compared to placebo, titrated oral misoprostol had the lowest OR for caesarean section (OR 0.62, 95% CI 0.47–0.80). However, it is noted that there was uncertainty in the ranking of estimates.

Uterine hyperstimulation with fetal heart rate changes was an outcome included in 180 studies. Compared to placebo, the highest OR for this outcome were for misoprostol:

- sustained release vaginal pessary (OR 5.58, 95% CI 1.58–14.57)
- vaginal tablet  $\geq 50$  mcg (OR 4.40, 95% CI 2.22–7.94)
- buccal/sublingual (OR 4.25, 95% CI 1.71–9.02)
- oral tablet  $\geq 50$  mcg (OR 2.85, 95% CI 1.41–5.20).

NICU admissions was an outcome in 204 included studies. Compared to placebo, reduction in NICU admissions was reported for extra-amniotic PGE2 (OR 0.4, 95% CI 0.16–0.82). However, uncertainty in the effect estimates meant that no rank order was reported.

Instrumental delivery was an outcome in 299 included studies, these were interventions compared to placebo for reduction in instrumental delivery and reached statistical significance for vaginal PGE2 pessary (slow release) (OR 0.72, 95% CI 0.50–0.99) and Foley catheter (OR 0.68, 95% CI 0.50–0.91).

A significant reduction in occurrence of an Apgar score of  $\leq 7$ , when interventions were compared with placebo, occurred for nitric oxide (OR 0.49, 95% CI 0.20–0.95) and buccal/sublingual misoprostol (OR 0.41, 95% CI 0.15–0.99).

There was insufficient reporting of serious neonatal and maternal morbidity and mortality for an NMA to be conducted for this outcome. For the outcome of maternal satisfaction there was insufficient reporting to indicate a preference.



Subgroup analysis was conducted for women with:

- ruptured or unruptured membranes
- with or without previous caesarean section
- cervical assessment using Bishop score  $\leq 6$  or  $>6$
- differing gestational ages.

The results were consistent with the main results however for VD24 oxytocin with amniotomy was mostly conducted in women with a favourable Bishop score  $>6$ .

The cost-effectiveness analysis found that buccal/sublingual misoprostol and intravenous oxytocin with amniotomy have the lowest expected total cost. At a willingness-to-pay threshold of £20,000 the expected net benefit was highest for buccal/sublingual misoprostol (£14,669), then titrated (low dose) oral misoprostol solution (£14,658) and intravenous oxytocin with amniotomy (£14,652). It was the lowest for intracervical PGE2 (£10,617). Titrated low-dose oral misoprostol solution had the highest expected utility but with an ICER  $>£20,000$ . The ICER is the expected extra cost for each extra unit gain in utility compared with the prior non-dominated intervention.

Subgroup analyses were conducted for women with intact membranes and women with an unfavourable cervix. In women with intact membranes the intervention with highest net benefit was intravenous oxytocin with amniotomy. In women with an unfavourable cervix the most cost-effective interventions were buccal/sublingual misoprostol or titrated low-dose oral misoprostol solution.

## Strengths and limitations

### *Strengths*

The study included a number of strengths:

- There is a detailed protocol available.
- Two reviewers independently assessed studies and extracted data from the studies.
- Cochrane tools were used to assess risk of bias. Sensitivity analysis was conducted for high risk of bias studies.

- To account for studies at high or unclear risk of bias for allocation, for caesarean section the model only included studies at low risk of bias.
- Consistency was tested for between direct and indirect evidence.
- It is very applicable to the guideline. Efforts were made in the cost-effectiveness analysis to make it as applicable as possible to UK NHS setting. The review also includes an interpretation of the implications for the guideline.

### ***Limitations***

The authors note throughout the study that there is considerable uncertainty in the effect estimates and in the findings from the cost-effectiveness analysis. Additionally, the review is limited by the lack of reporting of outcomes of included studies. Only 20 interventions could be compared in the cost-effectiveness analysis for VD24. Half of the included studies also had a high or unclear risk of bias for allocation. Another limitation is that the search was until March 2014 and there may now be more evidence published that may affect the conclusions.

### **Impact on guideline**

The study found that intravenous oxytocin with amniotomy, and misoprostol  $\geq 50$  mcg were the most likely interventions for VD24 for women undergoing induction of labour. However, there is considerable uncertainty in the effect estimates and in the findings from the cost-effectiveness analysis. The guideline does not recommend amniotomy alone or with oxytocin for the induction of labour. It only recommends misoprostol should be offered for the induction of labour in intrauterine fetal death. There is a need to review the recommendations on methods for the induction of labour.

## How we made the decision

We check our guidelines regularly to ensure they remain up to date. We based the decision on surveillance 8 years after the publication of [induction of labour \(2008\) NICE guideline CG70](#).

For details of the process and update decisions that are available, see [ensuring that published guidelines are current and accurate](#) in 'Developing NICE guidelines: the manual'.

Previous surveillance [update decisions](#) for the guideline are on our website.

## *New evidence*

We found 54 new studies in a search for systematic reviews and RCTs published between 1 February 2013 and 11 January 2016. We also considered 3 additional studies identified by members of the Guideline Committee who originally worked on this guideline.

Evidence identified in previous surveillance 6 and 3 years after publication of the guideline was also considered. This included 125 studies identified by search.

From all sources, 182 studies were considered to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See [appendix A](#): decision matrix for summaries and references for all new evidence considered.

## *Views of topic experts*

We considered the views of topic experts, including those who helped to develop the guideline and other correspondence we have received since the publication of the guideline. This included a workshop with experts to discuss potential areas for update.

## *Views of stakeholders*

Stakeholders are consulted only if we decide not to update the guideline following checks at 4 and 8 years after publication. Because this was an 8-year surveillance review, and the decision was to update, we did not consult on the decision.

See [ensuring that published guidelines are current and accurate](#) in 'Developing NICE guidelines: the manual' for more details on our consultation processes.

### *NICE Surveillance programme project team*

**Sarah Willett**

Associate Director

**Philip Alderson**

Consultant Clinical Adviser

**Katrina Sparrow**

Technical Adviser

**Saskia Cheyne**

Technical Analyst

The NICE project team would like to thank the topic experts who participated in the surveillance process.

ISBN: 978-1-4731-2253-6