National Institute for Health and Care Excellence

Final

Inducing labour

[D] Intrauterine fetal death after previous caesarean birth

NICE guideline NG207

Evidence review underpinning recommendations 1.2.30,1.2.32 and a research recommendation in the NICE guideline

November 2021

Final

This evidence review was developed by the National Guideline Alliance which is a part of the Royal College of Obstetricians and Gynaecologists

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

ISBN: 978-1-4731-4327-2

Contents

Methods to induce labour after intrauterine fetal death and previous caesarean birth.

Review question

How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth?

Introduction

Intrauterine fetal death (IUFD) is defined as death of the fetus at or after the 24+0 weeks of pregnancy. The rate of IUFD is approximately 0.5% of all pregnancies.

Options for birth after diagnosis of IUFD are expectant management, immediate induction, delayed induction or caesarean birth. Birth should be expedited where there is evidence of maternal sepsis, severe pre-eclampsia, abruption, or when it is the mother's choice.

Vaginal birth following induction may lead to quicker recovery, and avoids the risks associated with a caesarean birth. However, some women may choose to have a caesarean birth as they perceive it to be less psychologically distressing. In women who elect for vaginal birth, labour can be induced with mifepristone followed by vaginal dinoprostone or misoprostol, but consideration needs to be given to the fact that women with an IUFD who have had a previous caesarean birth may be at an increased risk of uterine rupture.

The aim of this review is to identify the most effective and safest way to induce labour in women with an IUFD who have had a previous caesarean birth.

Summary of the protocol

See Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Women with a confirmed intrauterine fetal death at or after 24 weeks' gestation, who have had a previous caesarean birth
Intervention	**<u>Pharmacological methods</u>** 1. Prostaglandins: a) Vaginal and intracervical administration • Dinoprostone (PGE_2) vaginal tablets (lactose based) • Dinoprostone (PGE_2) vaginal pessaries normal release (sometimes referred to as suppositories, manufactured using various base materials including wax and glycerine) • Dinoprostone (PGE_2) vaginal pessaries sustained release (10-12mg pessaries, single application) • Dinoprostone (PGE_2) gel, introduced via vaginal applicator • Dinoprostone (PGE_2) for intracervical administration • PGF_2 gel

	b) Extra-amniotic administration c) Intravenous administration d) Oral administration 2. Misoprostol • vaginal misoprostol (dose < 50 microgram) • vaginal misoprostol (dose ≥ 50 microgram) • oral misoprostol tablet (dose < 50 microgram) • oral misoprostol tablet (dose ≥ 50 microgram) • titrated (low-dose) oral misoprostol solution • sustained-release misoprostol insert • buccal/sublingual misoprostol 3. Oxytocin • IV oxytocin alone • IV oxytocin with amniotomy 4. Nitric oxide donors 5. Mifepristone 6. Oestrogens 7. Corticosteroids 8. Relaxin 9. Hyaluronidase **Mechanical methods** 10. Foley catheters 11. Osmotic cervical dilators (also known as laminaria or dilapan) 12. Double balloon or Cook's catheter 13. Amniotomy
Comparison	Any listed intervention compared to another
Outcomes	**Critical outcomes:** • Maternal mortality • Uterine rupture **Important outcomes:** • Vaginal birth in 24 hours • Caesarean birth • Depression/anxiety • Postpartum haemorrhage • Infection • Maternal quality of life/experience of care • Pain

IV: intravenous; PGE_2: prostaglandin E_2; PGF_2: prostaglandin F_2.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines. Please see the methods chapter for further details. Methods specific to this review question are described in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's 2014 conflicts of interest policy until 31 March 2018. From 1 April 2018, declarations of interest were recorded according to NICE's 2018 conflicts of interest policy. Those interests declared until April 2018 were reclassified according to NICE's 2018 conflicts of interest policy (see Register of Interests).

Clinical evidence

Included studies

A systematic review of the clinical literature was conducted but no studies were identified which were applicable to this review question.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review, with reasons for their exclusion, are provided in appendix K.

Summary of clinical studies included in the evidence review

No studies were identified which were applicable to this review question (and so there are no evidence tables in appendix D). No meta-analysis was undertaken for this review (and so there are no forest plots in appendix E).

Quality assessment of clinical studies included in the evidence review

No studies were identified which were applicable to this review question and so there are no evidence profiles in appendix F.

Economic evidence

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to this review question.

See the literature search strategy in appendix B.

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

Evidence statements

No clinical evidence was identified which was applicable to this review question.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The aim of this review was to assess the best method to induce labour following an intrauterine fetal death in a woman who had previously had a caesarean birth. The committee designated 2 critical outcomes: maternal mortality and uterine rupture. These outcomes were selected as the most direct indicators of safety of the different interventions considered for inducing labour in this group of women.

The committee identified 7 further outcomes as important, these were: vaginal birth in 24 hours, caesarean birth, depression/anxiety, postpartum haemorrhage, infection, maternal quality of life/experience of care, and pain. The main aim of induction of labour in intrauterine fetal death is to achieve a vaginal birth, without adverse effects for the woman, therefore the outcomes relating to mode of birth (vaginal birth in 24 hours and caesarean birth) were chosen. While the 24-hour limit may appear artificial, the committee agreed that this is a well-established outcome measure for assessing efficacy when inducing labour, and would provide a good indication of the relative efficacy of different methods.

Some of the recognised complications of induction of labour are: postpartum haemorrhage, infection, and pain, which may have lasting consequences on women's wellbeing. Finally, maternal depression/anxiety and quality of life/experience of care were considered as important outcomes. Although the committee recognised the importance of these outcomes, they were aware that data on these were likely to be sparse, and unlikely to inform decision-making in a meaningful way, therefore they considered them important rather than critical outcomes.

The quality of the evidence

Randomised controlled trials were prioritised for inclusion in the review, and it was pre-specified that non-randomised comparative studies will be considered for inclusion if insufficient evidence from randomised controlled trials was identified.

The clinical evidence search identified no studies that met the inclusion criteria for this review. Most of the excluded studies were observational, mainly excluded either because the induction of labour took place in the 1st trimester or because women had not had a previous caesarean birth.

Benefits and harms

The committee discussed that management options following intrauterine fetal death in women who have had a previous caesarean birth include expectant management, caesarean birth, or induction of labour leading to a vaginal birth. Induction of labour may be an option in women who have had a previous lower segment caesarean birth, however the committee agreed that, based on their knowledge and experience, there was an increased risk of uterine rupture in this group of women, compared to those who do not have a scarred uterus, and that women should be advised of this risk.

The committee agreed, based on their experience, that women who underwent induction of labour following intrauterine fetal death (both those with and without a previous caesarean birth) should have their uterine contractions monitored and

should receive one-to-one midwifery care to ensure any potential problems (such as hyperstimulation) were identified in a timely manner.

The committee agreed that induction of labour would only be an option in women who had had a previous caesarean birth using a lower segment incision, as they were aware from their own knowledge and experience that the risk of rupture would be too great in those with a midline incision, and that this should be specified in the recommendation. The committee emphasised that the woman's personal circumstances and preferences should be discussed and supported when discussing the different management options.

Induction of labour leading to vaginal birth may involve less postpartum discomfort, a shorter hospital stay, and a reduced period of disability compared to caesarean birth. However, no evidence was identified on the most effective and safe method to induce labour following intrauterine death in women who have had a previous caesarean birth.

The committee discussed that the previous guideline had recommended the use of vaginal prostaglandin and that the 'dose should be reduced'. The committee also discussed that in women without a previous caesarean birth, mifepristone 200mg (to sensitize the myometrium to prostaglandin-induced contractions) followed by a prostaglandin such as dinoprostone or misoprostol is used. The committee discussed the possibility of amending this regimen in women who had had a previous caesarean birth by using low doses of dinoprostone or misoprostol. However, the committee were aware that both dinoprostone and misoprostol are contraindicated in women with a previous caesarean birth and therefore they were not able to recommend a pharmacological method of induction.

The committee were aware that mifepristone (at the higher dose of 600 mg daily for 2 days) was approved for use on its own to induce labour, and was not contraindicated in women with a previous caesarean birth. However, no evidence for the safety or efficacy of mifepristone had been identified in women with a previous caesarean birth, and the committee were concerned that it may lead to a very prolonged induction process, which may be distressing for women. The committee therefore decided not to recommend mifepristone.

The committee noted that mechanical methods of induction, which did not lead to hyperstimulation, may be safe in women with a previous caesarean birth, and noted that the recommendations in the guideline for induction after caesarean birth (in women with a live baby) already stated this was an option, and so they made the same recommendation for use after an intrauterine fetal death.

The committee emphasised that this is an area that needs further research and acknowledged the emotional impact that intrauterine fetal death has on women and their relatives. They therefore made a research recommendation on this topic, with the aim of finding out the most effective and safe method to induce labour following intrauterine fetal death in women who have had a previous caesarean birth and therefore may have an increased risk of uterine rupture.

Cost effectiveness and resource use

The recommendations will raise awareness of the risks of uterine rupture in women undergoing induction of labour after a previous caesarean birth, and may increase the time required to counsel women, and lead to an increase in monitoring in women who do choose to be induced. This is not expected to lead to a substantial resource impact at national level.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.2.30 to 1.2.32 and a research recommendation in the NICE guideline.

References

There were no studies identified for inclusion in this review.

Appendices

Appendix A – Review protocol

Table 2: Review protocol for review question: How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth?

Field	Content
Actual review question	How should labour be induced in women with IUFD who have had a previous caesarean birth?
Type of review question	Intervention
Objective of the review	To determine the most effective and safest method to induce labour following IUFD in women who have had a previous caesarean birth and therefore may have an increased risk of uterine rupture.
Population	Inclusion: Women with a confirmed intrauterine fetal death at or after 24 weeks gestation, who have had a previous caesarean birth
Interventions	**Pharmacological methods** 1.Prostaglandins: a) Vaginal and intracervical administration a) Dinoprostone (PGE_2) vaginal tablets (lactose based) b) Dinoprostone (PGE_2) vaginal pessaries normal release (sometimes referred to as suppositories, manufactured using various base materials including wax and glycerine) c) Dinoprostone (PGE_2) vaginal pessaries sustained release (10-12mg pessaries, single application) d) Dinoprostone (PGE_2) gel, introduced via vaginal applicator e) Dinoprostone (PGE_2) for intracervical administration f) PGF2 gel b) Extra-amniotic administration c) Intravenous administration d) Oral administration 2. Misoprostol

Field	Content
	g) vaginal misoprostol (dose < 50 microgram) h) vaginal misoprostol (dose ≥ 50 microgram) i) oral misoprostol tablet (dose < 50 microgram) j) oral misoprostol tablet (dose ≥ 50 microgram) k) titrated (low-dose) oral misoprostol solution l) sustained-release misoprostol insert m) buccal/sublingual misoprostol 3.Oxytocin n) IV oxytocin alone o) IV oxytocin with amniotomy 4.Nitric oxide donors 5.Mifepristone 6.Oestrogens 7.Corticosteroids 8.Relaxin 9.Hyaluronidase **Mechanical methods** 10.Foley catheters 11.Osmotic cervical dilators (including luminaria and dilapan) 12.Double balloon or Cook's catheter 13.Amniotomy
Comparison	Any of the above compared to any other of listed interventions
Outcomes and prioritisation	**Critical outcomes:** • Maternal mortality • Uterine rupture **Important outcomes:** Vaginal birth in 24 hours

Field	Content
	Caesarean birth Depression/anxiety Perineal trauma Postpartum haemorrhage Infection Maternal quality of life/experience of care Pain
Study design	Randomised controlled trials (RCT) will be included, conference abstracts will not be included. Non-randomised comparative studies (NRS) will be considered for inclusion if insufficient RCT evidence is available for guideline decision making, sufficiency to be judged taking into account factors including number/quality/sample size of RCTs and outcome reporting. NRS will only be included if they have made some efforts to address confounding (for example through regression analyses or propensity score matching). If identified, systematic reviews of RCTs will be used to check for relevant primary studies for inclusion. If NRS are to be included, a similar approach to systematic reviews of NRS will be taken. If a high quality systematic review is identified that matches the full PICO criteria sufficiently, the systematic review itself will be used as the basis for this review. If it is insufficiently recent (published >1 year from date of this protocol), if more recent primary studies are published, these will be incorporated into the analysis in that review.
Other exclusion criteria	Not in English
Proposed stratified, sensitivity/sub-group analysis	When heterogeneity is encountered, evidence may be subgrouped by: b) Gestational age (<35 weeks vs >/= 35 weeks) c) IUFD due to termination vs other causes d) >1 previous Caesarean birth vs 1 previous e) Ruptured membranes vs no ruptured membranes
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI and de-duplicated.

Field	Content
	Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Duplicate screening/selection/analysis will not be undertaken for this review as this question was not prioritised for it. Included and excluded studies will be cross checked with the committee and with published systematic reviews when available. Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer. This information will be uploaded into EPPI and made available in the appendix of the evidence report. Data extraction fields will include as a minimum study location, setting, dates, source of funding, duration of follow-up, inclusion/exclusion criteria, sample size, age of participants, details of precise induction timing strategy, actual timing of birth and any outcomes matching the protocol.
Risk of bias (quality) assessment	Quality assessment of individual studies will be performed using the following checklists: Cochrane RoB tool for RCTs and quasi-RCTs ROBIS for systematic reviews if included in their entirety The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.
Strategy for data synthesis	Depending on the availability of the evidence, the findings will be summarised narratively or quantitatively. Where possible, meta-analyses will be conducted using Cochrane Review Manager software. A fixed effect meta-analysis will be conducted and data will be presented as risk ratios or odds ratios for dichotomous outcomes, and mean differences or standardised mean differences for continuous outcomes. Heterogeneity in the effect estimates of the individual studies will be assessed using the I2 statistic. I2 values of greater than 50% and 80% will be considered as significant and very significant heterogeneity, respectively. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through subgroup analysis then a random effects model will be used for meta-analysis, or the data will not be pooled. The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/ Data management:

Field	Content
	If pairwise meta-analyses are undertaken, they will be performed using Cochrane Review Manager (RevMan5). 'GRADE' will be used to assess the quality of evidence for each outcome. EPPI will be used for bibliographies/citations, study sifting, data extraction and quality assessment/critical appraisal Minimally important differences: Any statistically significant difference will be used as the minimally important difference guide for the following outcomes: Maternal death Perinatal death For all other outcomes, GRADE default values will be used of 0.8 and 1.25 for relative risk of dichotomous outcomes; 0.5 times SD of the control group for continuous outcomes, unless more appropriate values are identified by the guideline committee or in the literature.
Information sources – databases and dates	The following databases will be searched: f) Cochrane Central Register of Controlled Trials (CENTRAL) g) Cochrane Database of Systematic Reviews (CDSR) h) Embase i) MEDLINE Searches will be restricted by: j) Date: 2007 onwards k) Language: English l) Studies: Human Other searches: m) Inclusion lists of systematic reviews The full search strategies for MEDLINE database will be published in the final review.
Identify if an update	Yes – relevant evidence included in the existing guideline will be considered against the inclusion/exclusion criteria for this protocol.
Author contacts	Developer: National Guideline Alliance

Field	Content
	nga-enquiries@rcog.org.uk
Review team members	From the National Guideline Alliance: Eva Gonzalez, systematic reviewer James Gilbert, senior systematic reviewer Paul Jacklin, economist Tim Reeves, information scientist
Search strategy – for one database	For details please see appendix B.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual. Consider exploring publication bias for review questions where it may be more common, such as pharmacological questions, certain disease areas, etc. Describe any steps taken to mitigate against publication bias, such as examining trial registries.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual
Rationale/context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the NGA and chaired by Sarah Fishburn in line with section 3 of Developing NICE guidelines: the manual. Staff from the NGA undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see the methods chapter of the full guideline.
Sources of funding/support	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Roles of sponsor	NICE funds the NGA to develop guidelines for the NHS in England.
PROSPERO registration number	Not registered with PROSPERO

CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; MID: minimally important difference; NGA: National Guideline Alliance; NHS: National health service; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation

Appendix B – Literature search strategies

Search strategies for review question: How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth?

Review question search strategies

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

Date of last search: 26/03/2020

#	Searches
1	FETAL DEATH/
2	PERINATAL DEATH/
3	((intrauter$ or intra-uter$) adj3 (f?etal or f?etus$) adj3 (death? or demise or mortality)).ti,ab.
4	IUFD.ti,ab.
5	STILLBIRTH/
6	stillbirth?.ti,ab.
7	or/1-6
8	((previous$ or repeat$) adj5 (c?esar#an$ or c section$ or csection$)).ti,ab.
9	((previous$ or repeat$) adj5 (deliver$ adj3 abdom$)).ti,ab.
10	or/8-9
11	LABOR, INDUCED/
12	(labo?r adj5 induc$).ti,ab.
13	CERVICAL RIPENING/
14	(cervi$ adj3 ripen$).ti,ab.
15	((unfavo?rabl$ or un-favo?abl$ or unripe$ or un-ripe$) adj3 cervi$).ti,ab.
16	((bishop$ or cerv$) adj3 scor$).ti,ab.
17	or/11-16
18	exp PROSTAGLANDINS/
19	prostaglandin?.mp.
20	PGE?.mp.
21	MISOPROSTOL/
22	misoprostol.mp.
23	OXYTOCIN/
24	oxytocin.mp.
25	exp NITRIC OXIDE DONORS/
26	nitric oxide donor?.mp.
27	(isosorbide dinitrate or molsidomine or nitroprusside or s-nitroso-n-acetylpenicillamine or s-nitrosoglutathione or s-Nitrosothiol?).mp.
28	MIFEPRISTONE/
29	mifepristone.mp.
30	exp ESTROGENS/
31	(estrogen? or epimestrol or estradiol or alkylated estrogenic steroid? or estroneor mestranol or quinestrol or chlorotrianisene or dienestrol or diethylstilbestrol or hexestrol or zearalenone or zeranol or phytoestrogen? or coumestrol or equol or genistein).mp.
32	exp ADRENAL CORTEX HORMONES/
33	(corticosteroid? or adrenal cortex hormone? or 17-ketosteroids or androstenedione or androsterone or dehydroepiandrosterone or estrone or etiocholanolone or glucocorticoid? or beclomethasone or betamethasoneor budesonide or clobetasol or desoximetasone or dexamethasone or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or fluocortolone or fluorometholone or fluprednisolone or flurandrenolone or fluticasone-salmeterol or melengestrol acetate or methylprednisolone or paramethasoneor prednisoloneor prednisone or triamcinoloneor hydroxycorticosteroid?or 11-hydroxycorticosteroid? or aldosterone or corticosteroneor hydrocortisoneor 18-hydroxycorticosterone or tetrahydrocortisol or 17-hydroxycorticosteroid? or cortisone or cortodoxone or tetrahydrocortisone or desoxycorticosterone or 18-hydroxydesoxycorticosterone or pregnenolone or 17-alpha-hydroxypregnenolone).mp.
34	RELAXIN/
35	relaxin.mp.
36	HYALURONOGLUCOSAMINIDASE/
37	hyaluronidase.mp.
38	CATHETERS/
39	Foley catheter$.ti,ab.
40	(cervi$ adj3 dilat$).ti,ab.
41	laminaria.ti,ab.
42	dilapan.ti,ab.
43	double balloon?.ti,ab.

#	Searches
44	Cook$ catheter$.ti,ab.
45	AMNIOTOMY/
46	amniotom$.ti,ab.
47	(artifical$ adj3 ruptur$ adj3 membrane?).ti,ab.
48	AROM.ti,ab.
49	or/18-48
50	7 and 10 and 17
51	7 and 10 and 49
52	or/50-51
53	limit 52 to english language
54	limit 53 to yr="2007 -Current"
55	LETTER/
56	EDITORIAL/
57	NEWS/
58	exp HISTORICAL ARTICLE/
59	ANECDOTES AS TOPIC/
60	COMMENT/
61	CASE REPORT/
62	(letter or comment*).ti.
63	or/55-62
64	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
65	63 not 64
66	ANIMALS/ not HUMANS/
67	exp ANIMALS, LABORATORY/
68	exp ANIMAL EXPERIMENTATION/
69	exp MODELS, ANIMAL/
70	exp RODENTIA/
71	(rat or rats or mouse or mice).ti.
72	or/65-71
73	54 not 72

Databases: Embase; and Embase Classic

Date of last search: 26/03/2020

#	Searches
1	FETUS DEATH/
2	PERINATAL DEATH/
3	((intrauter$ or intra-uter$) adj3 (f?etal or f?etus$) adj3 (death? or demise or mortality)).ti,ab.
4	IUFD.ti,ab.
5	STILLBIRTH/
6	stillbirth?.ti,ab.
7	or/1-6
8	((previous$ or repeat$) adj5 (c?esar#an$ or c section$ or csection$)).ti,ab.
9	((previous$ or repeat$) adj5 (deliver$ adj3 abdom$)).ti,ab.
10	or/8-9
11	LABOR INDUCTION/
12	(labo?r adj5 induc$).ti,ab.
13	UTERINE CERVIX RIPENING/
14	(cervi$ adj3 ripen$).ti,ab.
15	((unfavo?rabl$ or un-favo?abl$ or unripe$ or un-ripe$) adj3 cervi$).ti,ab.
16	((bishop$ or cerv$) adj3 scor$).ti,ab.
17	or/11-16
18	exp PROSTAGLANDIN/
19	prostaglandin?.mp.
20	PGE?.mp.
21	MISOPROSTOL/
22	misoprostol.mp.
23	OXYTOCIN/
24	oxytocin.mp.
25	exp NITRIC OXIDE DONOR/
26	nitric oxide donor?.mp.
27	(isosorbide dinitrate or molsidomine or nitroprusside or s-nitroso-n-acetylpenicillamine or s-nitrosoglutathione or s-Nitrosothiol?).mp.
28	MIFEPRISTONE/
29	mifepristone.mp.
30	exp ESTROGEN/
31	(estrogen? or epimestrol or estradiol or alkylated estrogenic steroid? or estroneor mestranol or quinestrol or chlorotrianisene or dienestrol or diethylstilbestrol or hexestrol or zearalenone or zeranol or phytoestrogen? or coumestrol or equol or genistein).mp.

#	Searches
32	exp CORTICOSTEROID/
33	(corticosteroid? or adrenal cortex hormone? or 17-ketosteroids or androstenedione or androsterone or dehydroepiandrosterone or estrone or etiocholanolone or glucocorticoid? or beclomethasone or betamethasone or budesonide or clobetasol or desoximetasone or dexamethasone or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or fluocortolone or fluorometholone or fluprednisolone or flurandrenolone or fluticasone-salmeterol or melengestrol acetate or methylprednisolone or paramethasone or prednisolone or prednisone or triamcinolone or hydroxycorticosteroid? or 11-hydroxycorticosteroid? or aldosterone or corticosterone or hydrocortisone or 18-hydroxycorticosterone or tetrahydrocortisol or 17-hydroxycorticosteroid? or cortisone or cortodoxone or tetrahydrocortisone or desoxycorticosterone or 18-hydroxydesoxycorticosterone or pregnenolone or 17-alpha-hydroxypregnenolone).mp.
34	RELAXIN/
35	(relaxin or relaxine).mp.
36	HYALURONOGLUCOSAMINIDASE/
37	hyaluronidase.mp.
38	FOLEY BALLOON CATHETER/
39	(foley adj3 catheter$).ti,ab.
40	OSMOTIC CERVICAL DILATOR/
41	(cervi$ adj3 dilat$).ti,ab.
42	HYGROSCOPIC LAMINARIA CERVICAL DILATOR/
43	laminaria.ti,ab.
44	DILAPAN/
45	dilapan.ti,ab.
46	double balloon?.ti,ab.
47	Cook$ catheter$.ti,ab.
48	AMNIOTOMY/
49	amniotom$.ti,ab.
50	(artifical$ adj3 ruptur$ adj3 membrane?).ti,ab.
51	AROM.ti,ab.
52	or/18-51
53	7 and 10 and 17
54	7 and 10 and 52
55	or/53-54
56	limit 55 to english language
57	limit 56 to yr="2007 -Current"
58	letter.pt. or LETTER/
59	note.pt.
60	editorial.pt.
61	CASE REPORT/ or CASE STUDY/
62	(letter or comment*).ti.
63	or/58-62
64	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
65	63 not 64
66	ANIMAL/ not HUMAN/
67	NONHUMAN/
68	exp ANIMAL EXPERIMENT/
69	exp EXPERIMENTAL ANIMAL/
70	ANIMAL MODEL/
71	exp RODENT/
72	(rat or rats or mouse or mice).ti.
73	or/65-72
74	57 not 73

Databases: Cochrane Central Register of Controlled Trials; and Cochrane Database of Systematic Reviews

Date of last search: 26/03/2020

#	Searches
#1	[mh ^"FETAL DEATH"]
#2	[mh ^"PERINATAL DEATH"]
#3	((intrauter* or intra-uter*) near/3 (fetal or foetal or fetus* or foetus*) near/3 (death* or demise or mortality)):ti,ab
#4	IUFD:ti,ab
#5	[mh ^STILLBIRTH]
#6	stillbirth*:ti,ab
#7	#1 or #2 or #3 or #4 or #5 or #6
#8	((previous* or repeat*) near/5 (cesarean* or caesarean or "c section*" or csection*)):ti,ab
#9	((previous* or repeat*) near/5 (deliver* near/3 abdom*)):ti,ab
#10	#8 or #9

#	Searches
#11	[mh ^"LABOR, INDUCED"]
#12	((labor or labour) near/5 induc*):ti,ab
#13	[mh ^"CERVICAL RIPENING"]
#14	(cervi* near/3 ripen*):ti,ab
#15	((unfavorabl* or unfavourabl* or un-favorabl* or unfavourabl* or unripe* or un-ripe*) near/3 cervi*):ti,ab
#16	((bishop* or cerv*) near/3 scor*):ti,ab
#17	#11 or #12 or #13 or #14 or #15 or #16
#18	[mh PROSTAGLANDINS]
#19	prostaglandin*:ti,ab
#20	PGE*:ti,ab
#21	[mh ^MISOPROSTOL]
#22	misoprostol:ti,ab
#23	[mh ^OXYTOCIN]
#24	oxytocin:ti,ab
#25	[mh "NITRIC OXIDE DONORS"]
#26	"nitric oxide donor*":ti,ab
#27	("isosorbide dinitrate" or molsidomine or nitroprusside or "s-nitroso-n-acetylpenicillamine" or "s-nitrosoglutathione" or "s-Nitrosothiol*"):ti,ab
#28	[mh ^MIFEPRISTONE]
#29	mifepristone:ti,ab
#30	[mh ESTROGENS]
#31	(estrogen* or epimestrol or estradiol or "alkylated estrogenic steroid*" or estrone or mestranol or quinestrol or chlorotrianisene or dienestrol or diethylstilbestrol or hexestrol or zearalenone or zeranol or phytoestrogen* or coumestrol or equol or genistein):ti,ab
#32	[mh "ADRENAL CORTEX HORMONES"]
#33	(corticosteroid* or "adrenal cortex hormone*" or "17-ketosteroids" or androstenedione or androsterone or dehydroepiandrosterone or estrone or etiocholanolone or glucocorticoid* or beclomethasone or "betamethasoneor budesonide" or clobetasol or desoximetasone or dexamethasone or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or fluocortolone or fluorometholone or fluprednisolone or flurandrenolone or "fluticasone-salmeterol" or "melengestrol acetate" or methylprednisolone or "paramethasoneor prednisolone" or prednisone or triamcinolone or hydroxycorticosteroid* or "11-hydroxycorticosteroid*" or aldosterone or corticosterone or hydrocortisone or "18-hydroxycorticosterone" or tetrahydrocortisol or "17-hydroxycorticosteroid*" or cortisone or cortodoxone or tetrahydrocortisone or desoxycorticosterone or "18-hydroxydesoxycorticosterone" or pregnenolone or "17-alpha-hydroxypregnenolone"):ti,ab
#34	[mh ^RELAXIN]
#35	relaxin:ti,ab
#36	[mh ^HYALURONOGLUCOSAMINIDASE]
#37	hyaluronidase:ti,ab
#38	[mh ^CATHETERS]
#39	"Foley catheter*":ti,ab
#40	(cervi* near/3 dilat*):ti,ab
#41	laminaria:ti,ab
#42	dilapan:ti,ab
#43	"double balloon*":ti,ab
#44	"Cook* catheter*":ti,ab
#45	[mh ^AMNIOTOMY]
#46	amniotom*:ti,ab
#47	(artificial* near/3 ruptur* near/3 membrane*):ti,ab
#48	AROM:ti,ab
#49	#18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48
#50	#7 and #10 and #17
#51	#7 and #10 and #49
#52	#50 or #51
#53	#50 or #51 with Cochrane Library publication date Between Jan 2007 and Mar 2020, in Cochrane Reviews
#54	#50 or #51 with Publication Year from 2007 to 2020, in Trials

Health economics search strategies

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

Date of last search: 08/04/2020

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/

#	Searches
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	FETAL DEATH/
23	PERINATAL DEATH/
24	((intrauter$ or intra-uter$) adj3 (f?etal or f?etus$) adj3 (death? or demise or mortality)).ti,ab.
25	IUFD.ti,ab.
26	STILLBIRTH/
27	stillbirth?.ti,ab.
28	or/22-27
29	((previous$ or repeat$) adj5 (c?esar#an$ or c section$ or csection$)).ti,ab.
30	((previous$ or repeat$) adj5 (deliver$ adj3 abdom$)).ti,ab.
31	or/29-30
32	LABOR, INDUCED/
33	(labo?r adj5 induc$).ti,ab.
34	CERVICAL RIPENING/
35	(cervi$ adj3 ripen$).ti,ab.
36	((unfavo?rabl$ or un-favo?abl$ or unripe$ or un-ripe$) adj3 cervi$).ti,ab.
37	((bishop$ or cerv$) adj3 scor$).ti,ab.
38	or/32-37
39	exp PROSTAGLANDINS/
40	prostaglandin?.mp.
41	PGE?.mp.
42	MISOPROSTOL/
43	misoprostol.mp.
44	OXYTOCIN/
45	oxytocin.mp.
46	exp NITRIC OXIDE DONORS/
47	nitric oxide donor?.mp.
48	(isosorbide dinitrate or molsidomine or nitroprusside or s-nitroso-n-acetylpenicillamine or s-nitrosoglutathione or s-Nitrosothiol?).mp.
49	MIFEPRISTONE/
50	mifepristone.mp.
51	exp ESTROGENS/
52	(estrogen? or epimestrol or estradiol or alkylated estrogenic steroid? or estroneor mestranol or quinestrol or chlorotrianisene or dienestrol or diethylstilbestrol or hexestrol or zearalenone or zeranol or phytoestrogen? or coumestrol or equol or genistein).mp.
53	exp ADRENAL CORTEX HORMONES/
54	(corticosteroid? or adrenal cortex hormone? or 17-ketosteroids or androstenedione or androsterone or dehydroepiandrosterone or estrone or etiocholanolone or glucocorticoid? or beclomethasone or betamethasoneor budesonide or clobetasol or desoximetasone or dexamethasone or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or fluocortolone or fluorometholone or fluprednisolone or flurandrenolone or fluticasone-salmeterol or melengestrol acetate or methylprednisolone or paramethasoneor prednisoloneor prednisone or triamcinoloneor hydroxycorticosteroid?or 11-hydroxycorticosteroid? or aldosterone or corticosteroneor hydrocortisoneor 18-hydroxycorticosterone or tetrahydrocortisol or 17-hydroxycorticosteroid? or cortisone or cortodoxone or tetrahydrocortisone or desoxycorticosterone or 18-hydroxydesoxycorticosterone or pregnenolone or 17-alpha-hydroxypregnenolone).mp.
55	RELAXIN/
56	relaxin.mp.
57	HYALURONOGLUCOSAMINIDASE/
58	hyaluronidase.mp.
59	CATHETERS/
60	Foley catheter$.ti,ab.
61	(cervi$ adj3 dilat$).ti,ab.
62	laminaria.ti,ab.
63	dilapan.ti,ab.

#	Searches
64	double balloon?.ti,ab.
65	Cook$ catheter$.ti,ab.
66	AMNIOTOMY/
67	amniotom$.ti,ab.
68	(artifical$ adj3 ruptur$ adj3 membrane?).ti,ab.
69	AROM.ti,ab.
70	or/39-69
71	28 and 31 and 38
72	28 and 31 and 70
73	or/71-72
74	limit 73 to english language
75	limit 74 to yr="2007 -Current"
76	LETTER/
77	EDITORIAL/
78	NEWS/
79	exp HISTORICAL ARTICLE/
80	ANECDOTES AS TOPIC/
81	COMMENT/
82	CASE REPORT/
83	(letter or comment*).ti.
84	or/76-83
85	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
86	84 not 85
87	ANIMALS/ not HUMANS/
88	exp ANIMALS, LABORATORY/
89	exp ANIMAL EXPERIMENTATION/
90	exp MODELS, ANIMAL/
91	exp RODENTIA/
92	(rat or rats or mouse or mice).ti.
93	or/86-92
94	75 not 93
95	21 and 94

Databases: Embase; and Embase Classic

Date of last search: 08/04/2020

#	Searches
1	HEALTH ECONOMICS/
2	exp ECONOMIC EVALUATION/
3	exp HEALTH CARE COST/
4	exp FEE/
5	BUDGET/
6	FUNDING/
7	RESOURCE ALLOCATION/
8	budget*.ti,ab.
9	cost*.ti,ab.
10	(economic* or pharmaco?economic*).ti,ab.
11	(price* or pricing*).ti,ab.
12	(financ* or fee or fees or expenditure* or saving*).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	resourc* allocat*.ti,ab.
15	(fund or funds or funding* or funded).ti,ab.
16	(ration or rations or rationing* or rationed).ti,ab.
17	or/1-16
18	FETUS DEATH/
19	PERINATAL DEATH/
20	((intrauter$ or intra-uter$) adj3 (f?etal or f?etus$) adj3 (death? or demise or mortality)).ti,ab.
21	IUFD.ti,ab.
22	STILLBIRTH/
23	stillbirth?.ti,ab.
24	or/18-23
25	((previous$ or repeat$) adj5 (c?esar#an$ or c section$ or csection$)).ti,ab.
26	((previous$ or repeat$) adj5 (deliver$ adj3 abdom$)).ti,ab.
27	or/25-26
28	LABOR INDUCTION/
29	(labo?r adj5 induc$).ti,ab.
30	UTERINE CERVIX RIPENING/
31	(cervi$ adj3 ripen$).ti,ab.
32	((unfavo?rabl$ or un-favo?abl$ or unripe$ or un-ripe$) adj3 cervi$).ti,ab.

#	Searches
33	((bishop$ or cerv$) adj3 scor$).ti,ab.
34	or/28-33
35	exp PROSTAGLANDIN/
36	prostaglandin?.mp.
37	PGE?.mp.
38	MISOPROSTOL/
39	misoprostol.mp.
40	OXYTOCIN/
41	oxytocin.mp.
42	exp NITRIC OXIDE DONOR/
43	nitric oxide donor?.mp.
44	(isosorbide dinitrate or molsidomine or nitroprusside or s-nitroso-n-acetylpenicillamine or s-nitrosoglutathione or s-Nitrosothiol?).mp.
45	MIFEPRISTONE/
46	mifepristone.mp.
47	exp ESTROGEN/
48	(estrogen? or epimestrol or estradiol or alkylated estrogenic steroid? or estroneor mestranol or quinestrol or chlorotrianisene or dienestrol or diethylstilbestrol or hexestrol or zearalenone or zeranol or phytoestrogen? or coumestrol or equol or genistein).mp.
49	exp CORTICOSTEROID/
50	(corticosteroid? or adrenal cortex hormone? or 17-ketosteroids or androstenedione or androsterone or dehydroepiandrosterone or estrone or etiocholanolone or glucocorticoid? or beclomethasone or betamethasone or budesonide or clobetasol or desoximetasone or dexamethasone or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or fluocortolone or fluorometholone or fluprednisolone or flurandrenolone or fluticasone-salmeterol or melengestrol acetate or methylprednisolone or paramethasone or prednisolone or prednisone or triamcinolone or hydroxycorticosteroid? or 11-hydroxycorticosteroid? or aldosterone or corticosterone or hydrocortisone or 18-hydroxycorticosterone or tetrahydrocortisol or 17-hydroxycorticosteroid? or cortisone or cortodoxone or tetrahydrocortisone or desoxycorticosterone or 18-hydroxydesoxycorticosterone or pregnenolone or 17-alpha-hydroxypregnenolone).mp.
51	RELAXIN/
52	(relaxin or relaxine).mp.
53	HYALURONOGLUCOSAMINIDASE/
54	hyaluronidase.mp.
55	FOLEY BALLOON CATHETER/
56	(foley adj3 catheter$).ti,ab.
57	OSMOTIC CERVICAL DILATOR/
58	(cervi$ adj3 dilat$).ti,ab.
59	HYGROSCOPIC LAMINARIA CERVICAL DILATOR/
60	laminaria.ti,ab.
61	DILAPAN/
62	dilapan.ti,ab.
63	double balloon?.ti,ab.
64	Cook$ catheter$.ti,ab.
65	AMNIOTOMY/
66	amniotom$.ti,ab.
67	(artifical$ adj3 ruptur$ adj3 membrane?).ti,ab.
68	AROM.ti,ab.
69	or/35-68
70	24 and 27 and 34
71	24 and 27 and 69
72	or/70-71
73	limit 72 to english language
74	limit 73 to yr="2007 -Current"
75	letter.pt. or LETTER/
76	note.pt.
77	editorial.pt.
78	CASE REPORT/ or CASE STUDY/
79	(letter or comment*).ti.
80	or/75-79
81	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
82	80 not 81
83	ANIMAL/ not HUMAN/
84	NONHUMAN/
85	exp ANIMAL EXPERIMENT/
86	exp EXPERIMENTAL ANIMAL/
87	ANIMAL MODEL/
88	exp RODENT/
89	(rat or rats or mouse or mice).ti.
90	or/82-89
91	74 not 90
92	17 and 91

Database: Cochrane Central Register of Controlled Trials

Date of last search: 08/04/2020

#	Searches
#1	MeSH descriptor: [Economics] this term only
#2	MeSH descriptor: [Value of Life] this term only
#3	MeSH descriptor: [Costs and Cost Analysis] explode all trees
#4	MeSH descriptor: [Economics, Hospital] explode all trees
#5	MeSH descriptor: [Economics, Medical] explode all trees
#6	MeSH descriptor: [Resource Allocation] explode all trees
#7	MeSH descriptor: [Economics, Nursing] this term only
#8	MeSH descriptor: [Economics, Pharmaceutical] this term only
#9	MeSH descriptor: [Fees and Charges] explode all trees
#10	MeSH descriptor: [Budgets] explode all trees
#11	budget*:ti,ab
#12	cost*:ti,ab
#13	(economic* or pharmaco?economic*):ti,ab
#14	(price* or pricing*):ti,ab
#15	(financ* or fee or fees or expenditure* or saving*):ti,ab
#16	(value near/2 (money or monetary)):ti,ab
#17	resourc* allocat*:ti,ab
#18	(fund or funds or funding* or funded):ti,ab
#19	(ration or rations or rationing* or rationed) .ti,ab.
#20	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21	[mh ^"FETAL DEATH"]
#22	[mh ^"PERINATAL DEATH"]
#23	((intrauter* or intra-uter*) near/3 (fetal or foetal or fetus* or foetus*) near/3 (death* or demise or mortality)):ti,ab
#24	IUFD:ti,ab
#25	[mh ^STILLBIRTH]
#26	stillbirth*:ti,ab
#27	#21 or #22 or #23 or #24 or #25 or #26
#28	((previous* or repeat*) near/5 (cesarean* or caesarean or "c section*" or csection*)):ti,ab
#29	((previous* or repeat*) near/5 (deliver* near/3 abdom*)):ti,ab
#30	#28 or #29
#31	[mh ^"LABOR, INDUCED"]
#32	((labor or labour) near/5 induc*):ti,ab
#33	[mh ^"CERVICAL RIPENING"]
#34	(cervi* near/3 ripen*):ti,ab
#35	((unfavorabl* or unfavourabl* or un-favorabl* or unfavourabl* or unripe* or un-ripe*) near/3 cervi*):ti,ab
#36	((bishop* or cerv*) near/3 scor*):ti,ab
#37	#31 or #32 or #33 or #34 or #35 or #36
#38	[mh PROSTAGLANDINS]
#39	prostaglandin*:ti,ab
#40	PGE*:ti,ab
#41	[mh ^MISOPROSTOL]
#42	misoprostol:ti,ab
#43	[mh ^OXYTOCIN]
#44	oxytocin:ti,ab
#45	[mh "NITRIC OXIDE DONORS"]
#46	"nitric oxide donor*":ti,ab
#47	("isosorbide dinitrate" or molsidomine or nitroprusside or "s-nitroso-n-acetylpenicillamine" or "s-nitrosoglutathione" or "s-Nitrosothiol*"):ti,ab
#48	[mh ^MIFEPRISTONE]
#49	mifepristone:ti,ab
#50	[mh ESTROGENS]
#51	(estrogen* or epimestrol or estradiol or "alkylated estrogenic steroid*" or estrone or mestranol or quinestrol or chlorotrianisene or dienestrol or diethylstilbestrol or hexestrol or zearalenone or zeranol or phytoestrogen* or coumestrol or equol or genistein):ti,ab
#52	[mh "ADRENAL CORTEX HORMONES"]
#53	(corticosteroid* or "adrenal cortex hormone*" or "17-ketosteroids" or androstenedione or androsterone or dehydroepiandrosterone or estrone or etiocholanolone or glucocorticoid* or beclomethasone or "betamethasoneor budesonide" or clobetasol or desoximetasone or dexamethasone or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or fluocortolone or fluorometholone or fluprednisolone or flurandrenolone or "fluticasone-salmeterol" or "melengestrol acetate" or methylprednisolone or "paramethasoneor prednisolone" or prednisone or triamcinolone or hydroxycorticosteroid* or "11-hydroxycorticosteroid*" or aldosterone or corticosterone or hydrocortisone or "18-hydroxycorticosterone" or tetrahydrocortisol or "17-hydroxycorticosteroid*" or cortisone or cortodoxone or tetrahydrocortisone or desoxycorticosterone or "18-hydroxydesoxycorticosterone" or pregnenolone or "17-alpha-hydroxypregnenolone"):ti,ab
#54	[mh ^RELAXIN]
#55	relaxin:ti,ab
#56	[mh ^HYALURONOGLUCOSAMINIDASE]

#	Searches
#57	hyaluronidase:ti,ab
#58	[mh ^CATHETERS]
#59	"Foley catheter*":ti,ab
#60	(cervi* near/3 dilat*):ti,ab
#61	laminaria:ti,ab
#62	dilapan:ti,ab
#63	"double balloon*":ti,ab
#64	"Cook* catheter*":ti,ab
#65	[mh ^AMNIOTOMY]
#66	amniotom*:ti,ab
#67	(artificial* near/3 ruptur* near/3 membrane*):ti,ab
#68	AROM:ti,ab
#69	#38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68
#70	#27 and #30 and #37
#71	#27 and #30 and #69
#72	#70 or #71
#73	#70 or #71 with Publication Year from 2007 to 2020, in Trials
#74	#20 and #73

Database: Health Technology Assessment

Date of last search: 08/04/2020

#	Searches
1	MeSH DESCRIPTOR LABOR, INDUCED IN HTA
2	(((labor or labour) adj5 induc*)) IN HTA
3	MeSH DESCRIPTOR CERVICAL RIPENING IN HTA
4	((cervi* adj3 ripen*)) IN HTA
5	(((unfavorabl* or unfavourabl* or un-favorabl* or unfavourabl* or unripe* or un-ripe*) adj3 cervi*)) IN HTA
6	(((bishop* or cerv*) adj3 scor*)) IN HTA
7	#1 OR #2 OR #3 OR #4 OR #5 OR #6

Database: NHS Economic Evaluation Database

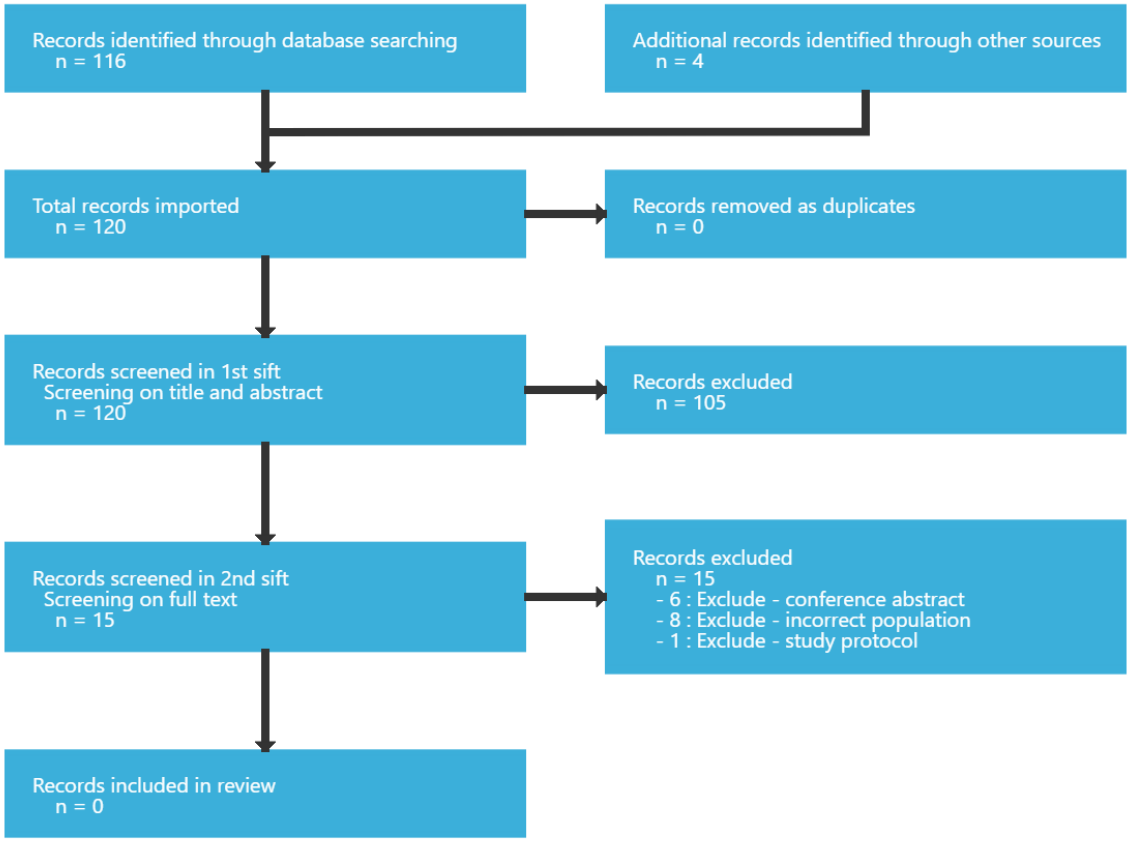
Date of last search: 08/04/2020

#	Searches
1	MeSH DESCRIPTOR LABOR, INDUCED IN NHSEED
2	(((labor or labour) adj5 induc*)) IN NHSEED
3	MeSH DESCRIPTOR CERVICAL RIPENING IN NHSEED
4	((cervi* adj3 ripen*)) IN NHSEED
5	(((unfavorabl* or unfavourabl* or un-favorabl* or unfavourabl* or unripe* or un-ripe*) adj3 cervi*)) IN NHSEED
6	(((bishop* or cerv*) adj3 scor*)) IN NHSEED
7	#1 OR #2 OR #3 OR #4 OR #5 OR #6

Appendix C – Clinical evidence study selection

Clinical evidence study selection for review question: How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth?

Figure 1: Study selection flow chart



Appendix D – Clinical evidence tables

Clinical evidence tables for review question: How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth?

No evidence was identified which was applicable to this review question.

Appendix E – Forest plots

Forest plots for review question: How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth?

No evidence was identified which was applicable to this review question.

Appendix F – GRADE tables

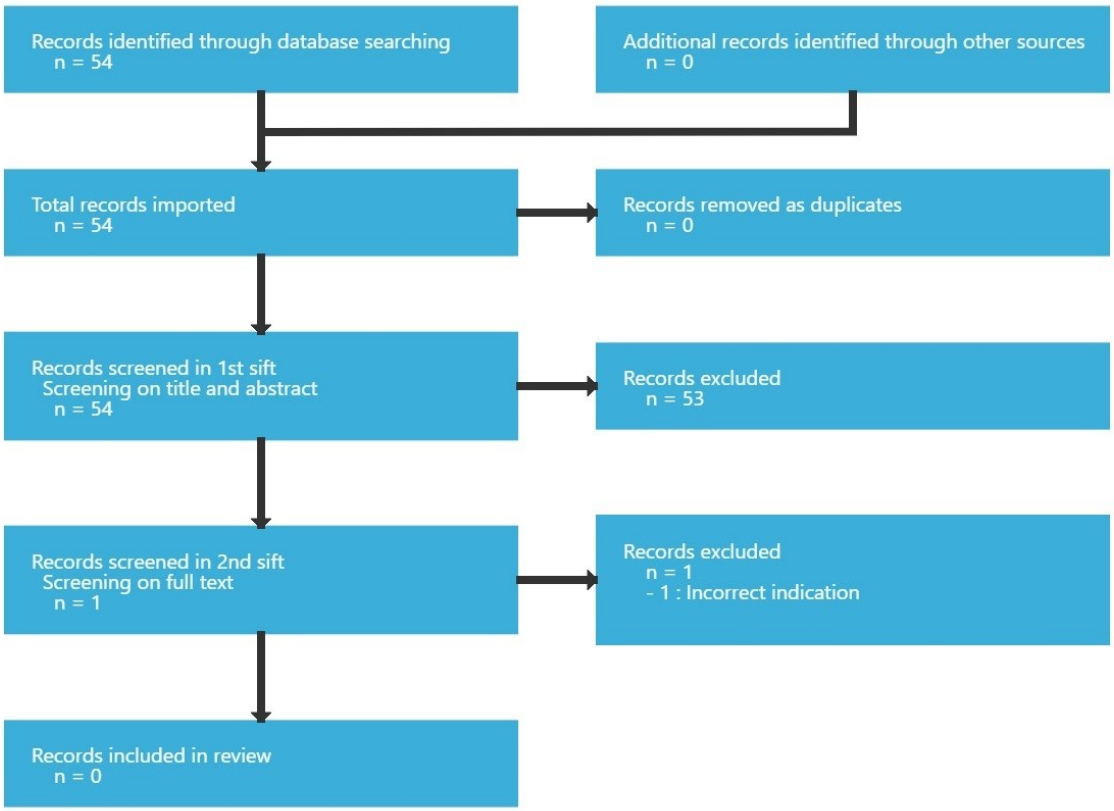
GRADE tables for review question: How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth?

No evidence was identified which was applicable to this review question.

Appendix G – Economic evidence study selection

Study selection for: How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth?

Figure 2: Study selection flowchart



Appendix H – Economic evidence tables

Economic evidence tables for review question: How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth?

No economic evidence was identified for this review.

Appendix I – Health economic evidence profiles

Health economic evidence profiles for review question: How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth?

No economic evidence was identified for this review.

Appendix J – Health economic analysis

Health economic analysis for review question: How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth?

No health economic analysis was carried out for this review question.

Appendix K – Excluded studies

Excluded studies for review question: How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth?

Clinical studies

Table 3: Excluded studies and reasons for their exclusion

Study	Reason for exclusion
Abediasl, Z., Sheikh, M., Pooransari, P., Farahani, Z., & Kalani F (2016) Vaginal misoprostol versus intravenous oxytocin for the management of second-trimester pregnancies with intrauterine fetal death: A randomized clinical trial. Journal of Obstetrics and Gynaecology Research 3: 246-251	- Exclude - incorrect population [Women were between 15 and 24 weeks gestation]
Abediasl, Z., Sheikh, M., Pooransari, P., Farahani, Z., & Kalani F (2016) Va ginal misoprostol versus intravenous oxytocin for the management of second-trimester pregnancies with intrauterine fetal death: A randomized clinical trial. Journal of Obstetrics and Gynaecology Research 42: 246-251	- Exclude - incorrect population [Women were between 15 and 24 weeks gestation]
Bhattacharjee, N.; Ganguly, R. P.; Saha, S. P. (2007) Misoprostol for termination of mid-trimester post-Caesarean pregnancy. Australian and New Zealand Journal of Obstetrics and Gynaecology 47(1): 23-25	- Exclude - incorrect population [Women were between 13 and 26 weeks gestation]
Boulot P, Hoffet M, Bachelard B, Lefort G, Hedon B, Laffargue F VJ (1993) Late vaginal induced abortion after a previous cesarean birth: potential for uterine rupture. Gynecologic and Obstetric Investigation 36(2): 87-90	- Exclude - incorrect population [No IUFD, reason for termination of pregnancy were maternal diseases and fetal anomalies]
Boyle, A., Preslar, J. P., Hogue, C. J. et al. (2016) Clinical management of stillbirth. American Journal of Obstetrics and Gynecology 214(1suppl1): 208	- Exclude - conference abstract
Chapman, S. J., Crispens, M., Owen, J., & Savage K (1996) Complications of midtrimester pregnancy termination: The effect of prior cesarean delivery. American Journal of Obstetrics and Gynecology 175(4): 889-892	- Exclude - incorrect population [Mean gestational age was 21.1 ± 3.1; not all women have had a previous caesarean birth]
Das, S. R., Parveen, T., Nahar, K. N. et al. (2013) Safety and efficacy of different doses of misoprostol in termination of intrauterine fetal death (IUFD) cases. Bangladesh journal of obstetrics and gynecology 28(1): 15-20	- Exclude - incorrect population [Women have not had a previous caesarean birth]
do Nascimento, M. I.; Cunha Ad.e, A.; Oliveira, S. R. (2014) Clinical management of the induction of labor in intrauterine fetal death: evaluation of incidence of cesarean section and related conditions. Revista brasileira de epidemiologia = Brazilian journal of epidemiology 17(1): 203-216	- Exclude - incorrect population [Women have not had a previous caesarean birth]
Glanville, E. J. and Patel, R. R. (2010) Management of women with one or more previous Caesarean sections requiring induction of labour following midtrimester termination of pregnancy or intrauterine death. Archives of	- Exclude - conference abstract

Study	Reason for exclusion
Disease in Childhood: Fetal and Neonatal Edition 95(suppl1)	
Gomez Ponce de Leon, R.; Wing, D.; Fiala, C. (2007) Misoprostol for intrauterine fetal death. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics 99suppl2: S190-3	- Exclude - conference abstract
Haque, L., Fatima, F., Mathur, M. et al. (2012) Medical management of late intrauterine death using a combination of mifepristone and misoprostol. International Journal of Gynecology and Obstetrics 119(suppl3): 810	- Exclude - conference abstract
Irct201307159568N (2013) Comparison of 2 different methods in Second trimester labor induction. http://www.who.int/trialsearch/Trial2.aspx?TrialID=IRCT201307159568N5	- Exclude - study protocol [Recruitment ended in 2014, published study is Abediasl 2016, which has been excluded from this review]
Pongsatha, S. and Tongsong, T. (2011) Outcomes of pregnancy termination by misoprostol at 14-32 weeks of gestation: A 10-year-experience. Journal of the Medical Association of Thailand 94(8): 897-901	- Exclude - incorrect population [Women were between 14 and 32 weeks gestation]
Reichman, O.; Cohen, M.; Beller, U. (2007) Prostaglandin E2 mid-trimester evacuation of the uterus for women with a previous cesarean section. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics 96(1): 32-3	- Exclude - conference abstract
Romero, V., Salari, K., Ehrenberg-Buchner, S. et al. (2012) Obstetric outcomes in women with intrauterine fetal demise and prior cesarean delivery. American Journal of Obstetrics and Gynecology 206(1suppl1): 83	- Exclude - conference abstract

Table 4: Studies excluded from the economic review

Study	Reason for exclusion
Cowett A A, Golub R M, Grobman W A. Cost-effectiveness of dilation and evacuation versus the induction of labor for second-trimester pregnancy termination. American Journal of Obstetrics and Gynecology 2006; 194(3): 768-773	Exclude – wrong indication, intervention is for 2nd trimester termination not IUFD

Appendix L – Research recommendations

Research recommendation for review question: How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth?

Research recommendation

How should labour be induced in women with intrauterine fetal death who have had a previous caesarean birth and who choose to be induced?

Why this is important

With the increase in caesarean birth rate, there are more women with IUFD and previous caesarean births. However, there are few data on the most appropriate method to induce labour in this group of women. It is important to investigate the most effective and safe method to induce labour in these women who may have an increased risk of uterine rupture.

Rationale for research recommendation

Table 5: Research recommendation rationale

Importance to 'patients' or the population	Little is known about the most appropriate method to induce labour in women with IUFD and previous caesarean births. It is important to minimise the risk of uterine rupture following induction of labour in these women.
Relevance to NICE guidance	Induction of labour in IUFD in women with previous caesarean births has been considered in this guideline and there is a lack of data on procedural safety.
Relevance to the NHS	The outcome would affect the process of induction of labour in women with IUFD and previous caesarean births provided by the NHS and may reduce procedural complication rates.
National priorities	Reducing the incidence of maternal morbidity and mortality associated with pregnancy and birth is a national priority.
Current evidence base	No evidence identified
Equality considerations	None known

IUFD: intrauterine fetal death

Modified PICO table

Table 6: Research recommendation modified PICO table

Population	Women with a confirmed intrauterine fetal death at or after 24 weeks gestation, who have had a previous caesarean birth
Intervention	**Pharmacological methods** 1. Prostaglandins: a) Vaginal and intracervical administration • Dinoprostone (PGE_2) vaginal tablets (lactose based) • Dinoprostone (PGE_2) vaginal pessaries normal release (sometimes referred to as

	suppositories, manufactured using various base materials including wax and glycerine) • Dinoprostone (PGE_2) vaginal pessaries sustained release (10-12mg pessaries, single application) • Dinoprostone (PGE_2) gel, introduced via vaginal applicator • Dinoprostone (PGE_2) for intracervical administration • PGF_2 gel b) Extra-amniotic administration c) Intravenous administration d) Oral administration 2. Misoprostol • vaginal misoprostol (dose < 50 micrograms) • vaginal misoprostol (dose ≥ 50 micrograms) • oral misoprostol tablet (dose < 50 micrograms) • oral misoprostol tablet (dose ≥ 50 micrograms) • titrated (low-dose) oral misoprostol solution • sustained-release misoprostol insert • buccal/sublingual misoprostol 3. Oxytocin • IV oxytocin alone • IV oxytocin with amniotomy 4. Nitric oxide donors 5. Mifepristone 6. Oestrogens 7. Corticosteroids 8. Relaxin 9. Hyaluronidase **Mechanical methods** 10. Foley catheters 11. Osmotic cervical dilators (also known as laminaria or dilapan) 12. Double balloon or Cook's catheter 13. Amniotomy
Comparator	Any listed intervention compared to another
Outcome	**Critical outcomes:** • Maternal mortality • Uterine rupture **Important outcomes:** • Vaginal birth in 24 hours • Caesarean birth • Depression/anxiety • Postpartum haemorrhage • Infection • Maternal quality of life/experience of care • Pain
Study design	• RCTs

	• NRS (reporting estimates adjusting for relevant confounders)
Timeframe	Short term follow-up only
Additional information	None

RCTs: randomised controlled trials; NRS: non randomised controlled trials