National Institute for Health and Care Excellence

Final

Intrapartum care for women with existing medical conditions or obstetric complications and their babies

[D] Evidence reviews for asthma

NICE guideline NG121

Evidence reviews for women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions

March 2019

Final

Developed by the National Guideline Alliance hosted by the Royal College of Obstetricians and Gynaecologists

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Intrapartum care for women with asthma

This evidence report contains information on 2 reviews relating to intrapartum care for women with asthma.

- What are the risks and benefits of central neuraxial analgesia compared with systemic analgesia, inhaled analgesia or no analgesia for women with asthma in labour?
- What is the safety of drugs commonly used in labour in women with difficult asthma, including prostaglandins for inducing labour and prostaglandins and other uterotonics for treating postpartum haemorrhage?

Intrapartum care for women with asthma – analgesia

Review question

What are the risks and benefits of central neuraxial analgesia compared with systemic analgesia, inhaled analgesia or no analgesia for women with asthma in labour?

Introduction

The aim of this review is to compare the risks and benefits of common analgesia methods in labour in women with asthma in order to advise which type of analgesia is most suitable for, or should be avoided by, women with asthma in labour.

Summary of the protocol

See Table 1 for a summary of the population, intervention, comparison, and outcomes (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO) table

Population	Women in labour who have asthma
Intervention	• Central neuraxial analgesia (epidural or combined spinal-epidural) • Parenteral systemic analgesia, intravenous or intramuscular • Oral analgesia • Inhaled analgesia (Inhaled 50:50 mixture of oxygen and nitrous oxide, common trade name Entonox)
Comparison	• All of the above compared to each other • No pharmacological analgesia
Outcomes	For the woman: • mortality • exacerbation of asthma • women's satisfaction with labour and birth (including psychological wellbeing) • healthcare professionals' reporting of effective analgesia (reduction in pain assessed through different methods such as pain scores, block to cold, block to touch, motor block) • admission to a HDU or ITU • mode of birth For the baby: • mortality • major morbidity (respiratory depression, hypoxic ischaemic encephalopathy, or birth injuries) • admission to a neonatal unit • Apgar score at 1, 5 or 10 minutes

HDU: high dependency unit; ITU: intensive therapy unit

For further details see the full review protocol in Appendix A. The search strategies are presented in Appendix B.

Clinical evidence

Included studies

No clinical evidence was identified for this review.

See the study selection flow chart in Appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusion are listed in Appendix D.

Summary of clinical studies included in the evidence review

No clinical evidence was identified for this review (and so there are no evidence tables in Appendix E). No meta-analysis was undertaken for this review (and so there are no forest plots in Appendix F).

Quality assessment of clinical studies included in the evidence review

No clinical evidence was identified for this review (and so no quality assessment was undertaken and there are no GRADE tables in Appendix G).

Economic evidence

Included studies

No economic evidence was identified for this review.

See the study selection flow chart in Supplement 2 (Health economics).

Excluded studies

No full-text copies of articles were requested for this review and so there is no excluded studies list (see Supplement 2 (Health economics)).

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables in Supplement 2 (Health economics)).

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation (see Supplement 2 (Health economics)).

Evidence statements

No clinical evidence was identified for this review.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

Maternal and neonatal outcomes were prioritised for the review.

Mortality and exacerbation of asthma were considered as critical outcomes for the woman, because these relate to serious long-term outcomes. The committee explained that there was uncertainty over whether any form of analgesia is associated with exacerbation of asthma and maternal death. Likewise, neonatal or perinatal mortality and major neonatal morbidity, including respiratory depression, hypoxic ischaemic encephalopathy and birth injuries were regarded as critical outcomes because these are common and serious issues due to prolonged labour among women with asthma exacerbation. The committee suggested women's satisfaction with labour and birth including both psychological wellbeing and women's reporting of effective analgesia should be regarded as critical outcomes as these relate to the possibility of the woman having a birth experience similar to that of a healthy woman.

The committee considered outcomes such as maternal admission to a high-dependency unit or intensive care unit, neonatal admission to intensive care and APGAR score at 1, 5 or 10 minutes as important outcomes, as these would provide an indirect indication of seriousness of disease exacerbation. Similarly, the report of effective analgesia by healthcare professionals should be considered an important outcome.

The quality of the evidence

No clinical evidence was identified for this review.

Benefits and harms

The committee discussed the widespread belief that women with asthma should not receive the full range of analgesia used as routine care in labour because of a theoretical concern that inhaled analgesia causes tightening of the airways and that parenteral opiate analgesia causes respiratory compromise. However, no evidence of adverse outcomes from any mode of analgesia was found in the guideline review.

The committee expressed their view that there is no biological plausibility of asthma exacerbation with the use of regional or inhaled analgesia. This is because – despite any effects analgesia has on closing airways in non-pregnant women – the adrenal response to labour is so overwhelming that it is implausible that analgesia alone would be sufficient to cause an asthma attack in the intrapartum period. Thus, the committee recommended that if a woman in labour with asthma is likely to require analgesia for obstetric indications or other reasons, the same options for regional or inhaled analgesia should be offered as for women who do not have asthma.

The committee emphasised that the recommendations should not be understood to recommend giving analgesia, but rather to ensure that analgesia is not withheld if it is requested by the woman in circumstances in which it would be available a woman without asthma.

The committee noted that it would not be appropriate for respiratory compromise – for example asthma complicated with pneumonia – to be managed according to the recommendations in this guideline, although specific recommendations for this situation were beyond the scope of the guideline.

The committee explained that general anaesthesia is particularly hazardous for women with asthma and effective regional analgesia would limit the need for subsequent general anaesthesia. They also discussed that catecholamine levels could fall during labour because of regional analgesia, but not as far as the levels typical of non-pregnant women.

The main benefit of the recommendations is that women with asthma will have a full choice of analgesia options during labour. Moreover, effective analgesia for women with asthma may reduce the requirement for general anaesthesia, which carries higher risks in this population.

The committee concluded that there is no additional harm in offering a full range of analgesia options to women with asthma.

Cost effectiveness and resource use

No evidence was found for this review and the committee made a qualitative assessment of cost effectiveness.

The committee noted that there is a theoretical risk of harm of inhaled analgesia. However, they reasoned that as there was no evidence of actual harm, that it would be cost effective to offer women with asthma the same pain relief options as would be offered to women without asthma.

While practice is varied, many hospitals already offer all types of pain relief to women with asthma. The committee did not consider there would be a significant cost impact to the NHS in those units that do not already offer all types of pain relief because they will only have to adapt their practice to what they currently offer to women without asthma.

Other factors the committee took into account

Despite the lack of evidence, the committee decided to prioritise other areas addressed by the guideline for future research and therefore made no research recommendations regarding the use of analgesia for women with asthma.

Intrapartum care for women with asthma – prostaglandins

Review question

What is the safety of drugs commonly used in labour in women with difficult asthma, including prostaglandins for inducing labour and prostaglandins and other uterotonics for treating postpartum haemorrhage?

Introduction

The aim of this review is determine the safety of prostaglandins and other uterotonics used in labour for women with difficult asthma, specifically for 2 indications:

- induction of labour (group 1)
- treatment of atonic postpartum haemorrhage (group 2)

Summary of the protocol

See Table 2 for a summary of the population, intervention, comparison, and outcomes (PICO) characteristics of this review.

Table 2: Summary of the protocol (PICO) table

Population	Women in labour who have asthma (excluding intrauterine death)

Intervention	Group 1 Induction of labour using:
	• pharmacological methods
	  ○ oxytocin
	• non-pharmacological methods
	  ○ surgery:
	  - amniotomy/artificial rupture of membranes
	  ○ mechanical method
	  - various types of balloon catheters or laminaria tents
	• combination of pharmacological and non-pharmacological methods, for example, oxytocin with amniotomy
	
	Group 2 Management of atonic postpartum haemorrhage using prostaglandins (misoprostol or carboprost)

Comparison	Group 1 Induction of labour using vaginal prostaglandins Group 2 Management of atonic postpartum haemorrhage using: • oxytocin bolus • ergometrine • oxytocin combined with ergometrine • oxytocin infusion
Outcomes	Group 1 Induction of labour For the woman: • mortality • major morbidity (bronchospasm, bronchoconstriction, severe asthma, status asthmaticus, or exacerbation of acute severe asthma)

	• mode of birth • women's satisfaction with labour and birth (including psychological wellbeing) For the baby: • mortality • morbidity (hypoxic ischaemic encephalopathy, birth injuries and respiratory complications) • admission to a neonatal unit <u>Group 2</u> Management of atonic postpartum haemorrhage For the woman: • mortality • major morbidity (bronchospasm, bronchoconstriction, status asthmaticus, exacerbation of acute severe asthma, major obstetric haemorrhage, need for blood transfusion, hysterectomy) • women's satisfaction with labour and birth (including psychological wellbeing) For the baby: • mortality • major morbidity (hypoxic ischaemic encephalopathy, birth injuries and respiratory complications) • admission to a neonatal unit

For further details see the full review protocol in Appendix A. The search strategies are presented in Appendix B.

Clinical evidence

Included studies

Two retrospective case series were included in this review (see 'Summary of clinical studies included in the evidence review').

The 2 studies reported outcomes for women with asthma who received vaginal prostaglandins for induction of labour (Rooney Thompson 2015, Towers 2004). One of the studies also reported outcomes for women with asthma who received prostaglandins for treatment of atonic postpartum haemorrhage (Rooney Thompson 2015).

Evidence from the studies included in the review is summarised below (see 'Quality assessment of clinical studies included in the evidence review').

Data was reported on the critical outcome exacerbation of asthma. There was no evidence identified for the following outcomes for the woman: mortality, mode of birth (critical outcomes), or women's satisfaction with labour and birth (important outcome); and for the baby: mortality (critical outcome), morbidity (important outcome), and admission to a neonatal unit (outcome of limited importance).

There was no evidence identified that compared induction of labour using oxytocin or non-pharmacological methods, or a combination of these, to induction of labour using vaginal prostaglandins. There was also no evidence identified that compared management of atonic postpartum haemorrhage using prostaglandins to using oxytocin bolus, ergometrine, oxytocin combined with ergometrine or oxytocin infusion.

See also the study selection flow chart in Appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in Appendix D.

Summary of clinical studies included in the evidence review

Table 3 provides a summary of the included studies.

Table 3: Summary of included studies

Study	Population	Intervention/Comparison	Outcomes
Rooney Thompson 2015 Retrospective case series USA	N=234 women with asthma: • Women with active asthma who were receiving daily medication n=104 • Women with a history of asthma for which they used an inhaler on an as-needed basis n=130	• PGE1 ○ Intravaginal (n=163) ○ Rectal (n=73) ○ Sublingual (n=49) ○ 2 different routes, usually rectal and sublingual (n=51) Dose: • Range 25-4200µg • Total dose >400µg 98/234 women Indications for use: • Cervical ripening/induction of labour (n= 135) • Uterine atony/postpartum haemorrhage (n=88) • Cervical preparation prior to dilation and evacuation for intrauterine fetal demise or a fetus with lethal anomalies (n=25) • Cervical ripening/induction of labour as well as uterine/postpartum haemorrhage (n=14)	For the woman: • Asthma exacerbations
Towers 2004 Retrospective case series USA	N=189 women with asthma: • Women with active asthma that required daily medications n=27 • Women with active asthma that necessitated treatment only as needed with bronchodilators inhalers n=34	• PGE2 ○ Intravaginal gel (n=158) - number of doses per person ranged from 1 to 4 (median 2) - average exposure 1.0mg of PGE2 ○ Intravaginal suppositories (n=31) - number of 20mg suppositories per person ranged from 1 to 11 (median 3)	For the woman: • Asthma exacerbations

Study	Population	Intervention/Comparison	Outcomes
	• Women with a history of asthma and no current therapy n=128	- average exposure 69mg of PGE2 (range 20-220mg)	

PGE: prostaglandin E

See also the study evidence tables in Appendix E. No meta-analysis was undertaken for this review (and so there are no forest plots in Appendix F).

Quality assessment of clinical studies included in the evidence review

The clinical evidence profiles for this review question are presented in Table 4 and Table 5. Only evidence from case series studies were included so GRADE methodology was not used and there are no GRADE tables in Appendix G.

Table 4: Outcomes for women with asthma who received vaginal prostaglandins for induction of labour, by asthma severity

Study	Intervention	Number of women with outcome/total number of women			Quality	Importance
		Asthma severity				
		Active asthma with daily medications	History of asthma with use of inhaler on an as-needed basis	History of asthma and no current therapy		
Asthma exacerbation						
Rooney Thompson 2015 Retrospective case series	PGE1	0/63	0/72	-	Very low[1]	Critical
Towers 2004 Retrospective case series	PGE2	0/27	0/34	0/128	Very low[1]	Critical

PGE: prostaglandin E
1 Descriptive data from a case series study.

Table 5: Outcomes for the women with asthma who received prostaglandins for treatment of atonic postpartum haemorrhage, by asthma severity

Study	Intervention	Number of women with outcome/total number of women			Quality	Importance
		Asthma severity				
		Active asthma with daily medications	History of asthma with use of inhaler as needed	History of asthma and no current therapy		
Outcome: asthma exacerbation						
Rooney Thompson 2015	PGE1	0/41	0/47	-	Very low[1]	Critical

Study	Intervention	Number of women with outcome/total number of women			Quality	Importance
		Asthma severity				
		Active asthma with daily medications	History of asthma with use of inhaler as needed	History of asthma and no current therapy		
Retrospective case series						

PGE: prostaglandin E
1 Descriptive data from a case series study.

Economic evidence

Included studies

No economic evidence was identified for this review.

See the study selection flow chart in Supplement 2 (Health economics).

Excluded studies

No full-text copies of articles were requested for this review and so there is no excluded studies list (see Supplement 2 (Health economics)).

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables in Supplement 2 (Health economics)).

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation (see Supplement 2 (Health economics)).

Evidence statements

Pharmacological-based or non-pharmacological methods versus vaginal prostaglandins for induction of labour

Outcomes for the woman

Asthma exacerbation

Very low quality evidence from 1 retrospective case series of women (N=135) with active asthma who were receiving daily medications (n=63) and women with a history of asthma who used inhaler on an as-needed basis (n=72) reported that there were no asthma exacerbations following the use of vaginal PGE1 for induction of labour.

Very low quality evidence from 1 retrospective case series of women (N=189) with active asthma who were receiving daily medications (n=27), women with a history of asthma who used inhaler on an as-needed basis (n=34) and women with a history of asthma and no

current therapy (n=128) reported that there were no asthma exacerbations following the use of intravaginal PGE2 for induction of labour.

Prostaglandins versus other uterotonics for treatment of atonic postpartum haemorrhage

Outcomes for the woman

Asthma exacerbation

Very low quality evidence from 1 retrospective case series of women (N=88) with either active asthma who were receiving daily medications (n=41) or women with a history of asthma for which they used an inhaler on as-needed basis (n=47) reported that there were no asthma exacerbations following the use of PGE1 for treatment of uterine atony or postpartum haemorrhage.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

This review examined two clinical situations in which prostaglandins are commonly used, namely induction of labour and postpartum haemorrhage, and the committee prioritised a different set of outcomes for each to help inform decision-making.

For induction of labour, maternal mortality, major morbidities (bronchospasm, bronchoconstriction, severe asthma, status asthmaticus, and exacerbation of acute severe asthma), mode of birth and neonatal mortality were prioritised as critical outcomes. Women's satisfaction with labour and birth including psychological wellbeing was regarded as a critical outcome as this relates to the possibility of the woman having a birth experience similar to that of a healthy woman. Major neonatal morbidities (hypoxic ischaemic encephalopathy, birth injuries and respiratory complications) and admission to a neonatal unit were considered important outcomes because these are common and serious issues due to prolonged labour among women with asthma exacerbation.

For management of atonic postpartum haemorrhage, maternal mortality, major morbidities (bronchospasm, bronchoconstriction, severe asthma, status asthmaticus, exacerbation of acute severe asthma, major obstetric haemorrhage, need for blood transfusion, and hysterectomy) and neonatal mortality were prioritised as critical outcomes. This is because these represent long term and potentially life-altering outcomes. Women's satisfaction with labour and birth including psychological wellbeing were regarded as a critical outcome as this related to the possibility of the woman having a birth experience similar to that of a healthy woman. Major neonatal morbidity (hypoxic ischaemic encephalopathy, birth injuries and respiratory complications) and admission to a neonatal unit were considered important outcomes because these are common serious issues due to prolonged labour among women with asthma exacerbation.

The quality of the evidence

No experimental comparative studies were identified, nor were there any comparative observational studies. Case series were the only included studies. All studies were quality appraised and although some clearly reported relevant information they were assessed as being of very low quality because of the non-comparative study design. As such GRADE assessment was not performed. Considering that the outcomes of interest are quite rare, the

studies were perhaps underpowered to detect events, thus, making it difficult to draw conclusions from the available evidence.

Benefits and harms

Prostaglandin E1 (PGE1), for example, gemeprost or misoprostol, and prostaglandin E2 (PGE2), for example, dinoprostone are pharmacologically recognised as bronchodilators and they can be administered by different routes, including intravaginal, rectal and sublingual routes. In addition, the very low quality evidence included in the review reported no events of asthma exacerbation when they were administered to induce labour in women with a history of asthma. Thus, the committee considered that PGE1 and PGE2 were safe to use for cervical ripening in women with asthma, and likely to be effective based on their clinical knowledge of the drugs' effects in women without asthma. Similarly, the evidence related to use of PGE1 (misoprostol) for atonic uterine haemorrhage among postpartum women did not report any asthma exacerbation, and so the committee believed it was likely to be safe, since this accorded with their clinical judgement. The committee did not recommend any particular route of administration, as there was a lack of evidence for the superiority of one route over another and no clinical consensus.

The committee described how, in contrast, prostaglandin F2-alpha (PGF2a), commonly known as carboprost, was known to be a potent bronchoconstrictor. This indicated to the committee that, in the absence of evidence suggesting it was safe, the clinically sensible recommendation would be to not offer the drug to women with asthma. The committee discussed whether to make a strong or a weak recommendation against using the drug. They discussed how the lack of clinical trials in this area probably indicated that there is already clinical consensus, and as reliable drugs to prevent postpartum haemorrhage are already available, research into the use of PGF2a was not needed and that therefore PGF2a should not be used even in research.

The benefits of using PGE1 and PGE2 in women with asthma are significant, for example, it could be a life-saving intervention when bleeding from an atonic uterus is a complication. The harms of PGE1 and PGE2 are that women could need intensive respiratory monitoring. The committee judged that the benefits greatly outweighed the harms, as the risks could be managed with effective monitoring and the benefits were potentially lifesaving.

The committee noted that other means of induction of labour (for example, using oxytocin, amniotomy or mechanical methods) and treatment for postpartum haemorrhage (for example, using other uterotonics) are options for women with asthma just as they would be for women without asthma. There is no concern about the safety of these interventions for women with asthma, but as the focus of the review was specifically on the safety of prostaglandins in women with asthma, no recommendations were made about other means of induction of labour or treatment of postpartum haemorrhage.

Cost effectiveness and resource use

The committee made a recommendation not to offer prostaglandin F2 alpha because they were concerned about a possible risk of bronchospasm. Given the availability of safer options the committee reasoned that prostaglandin F2 alpha was unlikely to be a cost effective option.

The committee noted that the evidence did not indicate that prostaglandins E1 and E2 would worsen asthma. Therefore, they considered it would be cost effective to recommend prostaglandins E1 and E2 for inducing labour in women because these are options for women without asthma.

The committee thought that current practice with respect to the use of prostaglandins in the intrapartum period in women with asthma was well documented. However, while the committee considered that these recommendations would change practice they did not anticipate a significant resource impact to the NHS as prostaglandins are widely used for women without asthma.

Other factors the committee took into account

Despite the lack of evidence, the committee decided to prioritise other areas addressed by the guideline for future research and therefore made no research recommendations regarding the use of prostaglandins for women with asthma.

References

Rooney Thompson 2015

Rooney Thompson, M., Towers, C. V., Howard, B. C., Hennessy, M. D., Wolfe, L., Heitzman, C., The use of prostaglandin E1 in peripartum patients with asthma, American Journal of Obstetrics & Gynecology, 212, 392.e1-3, 2015

Towers 2004

Towers, C. V., Briggs, G. G., Rojas, J. A., The use of prostaglandin E2 in pregnant patients with asthma, American Journal of Obstetrics & Gynecology, 190, 1777-80; discussion 1780, 2004

Appendices

Appendix A – Review protocols

Intrapartum care for women with asthma – analgesia

Item	Details	Working notes
Area in the scope	Women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions – intrapartum care for women with asthma – analgesia	
Review question in the scope	What are the risks and benefits of not using or limiting duration of use of Entonox in women with asthma?	
Review question for the guideline	What are the risks and benefits of central neuraxial analgesia compared with systemic analgesia, inhaled analgesia or no analgesia for women with asthma in labour?	
Objective	The aim of this review is to compare the risks and benefits of common analgesia methods in labour in women with asthma in order to advise which type of analgesia is most suitable for, or should be avoided by, women with asthma in labour.	
Population and directness	Women in labour who have asthma	
Intervention	• Central neuraxial analgesia (epidural or combined spinal-epidural) • Parenteral systemic analgesia, intravenous or intramuscular • Oral analgesia • Inhaled analgesia (Inhaled 50:50 mixture of oxygen and nitrous oxide, common trade name Entonox)	
Comparison	• Any of the above interventions compared to each other • No pharmacological analgesia	
Outcomes	Critical outcomes: • for the woman: o mortality o exacerbation of asthma o women's satisfaction with labour and birth (including psychological wellbeing) • for the baby: o mortality o major morbidity (respiratory depression, hypoxic ischaemic encephalopathy, or birth injuries) Important outcomes: • for the woman: o healthcare professionals' reporting of effective analgesia (reduction in pain assessed through	

Item	Details	Working notes
	different methods such as pain scores, block to cold, block to touch, motor block) ○ admission to a high dependency unit (HDU) or intensive treatment unit (ITU) • for the baby: ○ admission to a neonatal unit ○ Apgar score at 1, 5 or 10 minutes Outcomes of limited importance: • for the woman: ○ mode of birth	
Importance of outcomes	Preliminary classification of the outcomes for decision making: • critical (up to 3 outcomes) • important but not critical (up to 3 outcomes) • of limited importance (1 outcome)	Given the small volume of evidence available for inclusion overall, the committee agreed to consider more than the nominal maximum of 7 outcomes for this question
Setting	All settings	
Stratified, subgroup and adjusted analyses	Groups that will be reviewed and analysed separately: • severity of asthma Potential confounders: • maternal age • race/ethnicity • socioeconomic status • BMI • smoking history • drugs used for management of asthma during pregnancy • other co-existing morbidities • severity of asthma	
Language	English	
Study design	• Published full-text papers only • Systematic reviews • RCTs • Only if RCTs unavailable or there is limited data to inform decision making: ○ prospective or retrospective comparative cohort studies • Prospective study designs will be prioritised over retrospective study designs • Conference abstracts will not be considered	
Search strategy	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase.	

Item	Details	Working notes
	Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques were used. See Appendix B for full strategies. Search not date-limited but studies published prior to 1997 were excluded by the reviewer(s) due to significant changes in clinical practice following publication of review article (Schatz 1997).	
Review strategy	Appraisal of methodological quality: • the methodological quality of each study will be assessed using checklists recommended in the NICE guidelines manual 2014 (for example, AMSTAR or ROBIS for systematic reviews, and Cochrane RoB tool for RCTs) and the quality of the evidence for each outcome (that is, across studies) will be assessed using GRADE • if studies report only p-values, this information will be recorded in GRADE tables without an assessment of imprecision Synthesis of data: • meta-analysis will be conducted where appropriate • default MIDs will be used; 0.8 and 1.25 for dichotomous outcomes; 0.5 times the SD of the measurement in the control arm (or median score across control arms if multiple studies are included) for continuous outcomes • for continuous data, change scores will be used in preference to final scores for data from non-RCT studies; final and change scores will not be pooled; if any study reports both, the method used in the majority of studies will be adopted	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies will be resolved through discussion between the first and second reviewers or by reference to a third person. This review question was not prioritised for health economic analysis and so no formal dual weeding, study selection (inclusion/exclusion) or data extraction into evidence tables will be undertaken. However, internal (NGA) quality assurance processes will include consideration of the outcomes of weeding, study selection and data extraction and the committee will review the results of study selection and data extraction

Item	Details	Working notes
Equalities	Equalities considerations will be considered systematically in relation to the available evidence and draft recommendations. The guideline scope includes women with cognitive or physical disability as populations for whom there may be equalities issues. Women who have received no antenatal care will be considered as a subgroup for all systematic reviews performed within the medical conditions work stream and a specific question has been included in the obstetric complications work stream for this population	
Notes/additional information	• SIGN Guideline on Management of Asthma (2014) (https://www.brit-thoracic.org.uk/document-library/clinical-information/asthma/btssign-asthma-guideline-2014/) • NICE quality standard on asthma (QS25) • NICE guideline on asthma: diagnosis, monitoring and chronic asthma management (NG80), this guideline does not exclude pregnant women or women in labour • NICE guideline on intrapartum care for healthy women and babies (CG190), this guideline provides limited guidance on women with asthma (suggested place of birth only) 1.8 Pain relief in labour: non‑regional Attitudes to pain and pain relief in childbirth 1.8.1 Healthcare professionals should think about how their own values and beliefs inform their attitude to coping with pain in labour and ensure their care supports the woman's choice. [2007] Pain‑relieving strategies 1.8.2 If a woman chooses to use breathing and relaxation techniques in labour, support her in this choice. [2007] 1.8.3 If a woman chooses to use massage techniques in labour that have been taught to birth companions, support her in this choice. [2007] 1.8.4 Offer the woman the opportunity to labour in water for pain relief. [2007] 1.8.5 For women labouring in water, monitor the temperature of the woman and the water hourly to ensure that the woman is comfortable and not becoming pyrexial. The temperature of the water should not be above 37.5°C. [2007]	

Item	Details	Working notes
	1.8.6 Keep baths and birthing pools clean using a protocol agreed with the microbiology department and, in the case of birthing pools, in accordance with the manufacturer's guidelines. [2007] 1.8.7 Do not use injected water papules. [2007] 1.8.8 Do not offer acupuncture, acupressure or hypnosis, but do not prevent women who wish to use these techniques from doing so. [2007] 1.8.9 Support the playing of music of the woman's choice in labour. [2007] Non‑pharmacological analgesia 1.8.10 Do not offer transcutaneous electrical nerve stimulation (TENS) to women in established labour. [2007] Inhalational analgesia 1.8.11 Ensure that Entonox (a 50:50 mixture of oxygen and nitrous oxide) is available in all birth settings as it may reduce pain in labour, but inform the woman that it may make her feel nauseous and light‑headed. [2007] Intravenous and intramuscular opioids 1.8.12 Ensure that pethidine, diamorphine or other opioids are available in all birth settings. Inform the woman that these will provide limited pain relief during labour and may have significant side effects for both her (drowsiness, nausea and vomiting) and her baby (short‑term respiratory depression and drowsiness which may last several days). [2007] 1.8.13 Inform the woman that pethidine, diamorphine or other opioids may interfere with breastfeeding. [2007] 1.8.14 If an intravenous or intramuscular opioid is used, also administer an antiemetic. [2007] 1.8.15 Women should not enter water (a birthing pool or bath) within 2 hours of opioid administration or if they feel drowsy. [2007] 1.9 Pain relief in labour: regional analgesia Information about regional analgesia 1.9.1 If a woman is contemplating regional analgesia, talk with her about the risks and benefits and the implications for her labour, including the arrangements and time involved for transfer of care to an obstetric unit if she is at home or in a midwifery unit (follow the general principles for transfer of care described in section 1.6). [2007, amended 2014]	

Item	Details	Working notes
	1.9.2 Provide information about epidural analgesia, including the following: ○ It is available only in obstetric units. ○ It provides more effective pain relief than opioids. ○ It is not associated with long‑term backache. ○ It is not associated with a longer first stage of labour or an increased chance of a caesarean birth. ○ It is associated with a longer second stage of labour and an increased chance of vaginal instrumental birth. ○ It will be accompanied by a more intensive level of monitoring and intravenous access, and so mobility may be reduced. [2007, amended 2014]	
Key papers	Kuczkowski KM. Labor analgesia for the parturient with respiratory disease: what does an obstetrician need to know? Arch Gynecol Obstet. 2005 Jul;272(2):160-6. Epub 2005 Jan 14.	

AMSTAR: Assessing the Methodological Quality of Systematic Reviews; BMI: Body Mass Index; CCTR: Cochrane Central Register of Controlled Trials; CDSR: Cochrane Database of Systematic Reviews; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HDU: high dependency unit; HTA: Health Technology Assessment; ITU: intensive therapy unit; MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias; ROBIS: Risk of Bias in Systematic Reviews; SD: standard deviation; SIGN: Scottish Intercollegiate Guidelines Network; TENS: transcutaneous electrical nerve stimulation

Intrapartum care for women with asthma – prostaglandins

Item	Details	Working notes
Area in the scope	Women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions – intrapartum care for women with asthma – use of prostaglandins and other uterotonics	
Review question in the scope	What is the effectiveness and safety of drugs commonly used in labour in women with difficult asthma, including prostaglandins for inducing labour and prostaglandins and other uterotonics for treating postpartum haemorrhage?	
Review question for the guideline	What is the safety of drugs commonly used in labour in women with difficult asthma, including prostaglandins for inducing labour and prostaglandins and other uterotonics for treating postpartum haemorrhage?	
Objective	The aim of this review is determine the safety of prostaglandins and other uterotonics used in labour for women with difficult asthma, specifically for 2 indications: • induction of labour (group 1) • treatment of atonic postpartum haemorrhage (group 2)	
Population and directness	Women in labour (excluding intrauterine death) who have asthma. According to the NICE quality standard for asthma (QS25): difficult asthma is defined as asthma with symptoms despite treatment with high-dose therapies or continuous or frequent use of oral steroids as identified in the BTS/SIGN guideline	

Item	Details	Working notes
	According to the NICE quality standard for asthma (QS25), objective measurement of asthma severity in adults includes: • moderate asthma: ○ SpO_2 ≥92% ○ PEF >50–75% best or predicted ○ no features of acute severe asthma • acute severe asthma: ○ PEF <50% best or predicted ○ Respiration ≥ 25/minute ○ SpO_2 ≥92% ○ pulse ≥110 beats/minute ○ cannot complete sentence in 1 breath • life-threatening asthma: ○ SpO_2 <92% ○ silent chest, cyanosis or poor respiratory effort ○ arrhythmia or hypotension ○ exhaustion or altered consciousness	
Intervention	**Group 1 – induction of labour using:** • pharmacological methods ○ oxytocin • non-pharmacological methods ○ surgery: - amniotomy/artificial rupture of membranes ○ mechanical method - various types of balloon catheters or laminaria tents • combination of pharmacological and non-pharmacological methods, for example, oxytocin with amniotomy **Group 2 – management of atonic postpartum haemorrhage using prostaglandins** (misoprostol or carboprost)	
Comparison	**Group 1 – induction of labour using vaginal prostaglandins** **Group 2 – management of atonic postpartum haemorrhage using** • oxytocin bolus • ergometrine • oxytocin combined with ergometrine • oxytocin infusion	
Outcomes	**Group 1 – induction of labour** Critical outcomes: • for the woman: ○ mortality ○ major morbidity (bronchospasm, bronchoconstriction, severe asthma, status asthmaticus, or exacerbation of acute severe asthma) ○ mode of birth • for the baby: o mortality	

Item	Details	Working notes
	Important outcomes: • for the woman: o women's satisfaction with labour and birth (including psychological wellbeing) • for the baby: o major morbidity (hypoxic ischaemic encephalopathy, birth injuries and respiratory complications) Outcomes of limited importance: • for the baby: o admission to a neonatal unit **Group 2 – management of atonic postpartum haemorrhage** Critical outcomes: • for the woman: o mortality o major morbidity (bronchospasm, bronchoconstriction, status asthmaticus, exacerbation of acute severe asthma, major obstetric haemorrhage, need for blood transfusion, hysterectomy) • for the baby: o mortality Important outcomes: • for the woman: o women's satisfaction with labour and birth (including psychological wellbeing) • for the baby: o major morbidity (hypoxic ischaemic encephalopathy, birth injuries and respiratory complications) Outcomes of limited importance: • for the baby: o admission to a neonatal unit	
Importance of outcomes	Preliminary classification of the outcomes for decision making: • critical (up to 3 outcomes) • important but not critical (up to 3 outcomes) • of limited importance (1 outcome)	
Setting	All settings	
Stratified, subgroup and adjusted analyses	Groups that will be reviewed and analysed separately: • severity of asthma In the presence of heterogeneity, the following subgroups will be considered for sensitivity analysis for group 2 – management of atonic postpartum haemorrhage: • route of prostaglandin administration: o intramuscular o intramyometrial	

Item	Details	Working notes
	Potential confounders: • maternal age • race/ethnicity • socioeconomic status • BMI • smoking history • drugs used for management of asthma during pregnancy • other co-existing morbidities • severity of asthma • seasonal asthma	
Language	English	
Study design	• Published full-text papers only • Systematic reviews • RCTs • Only if RCTs unavailable or there is limited data to inform decision making: ○ prospective or retrospective comparative cohort studies ○ case series studies • Prospective study designs will be prioritised over retrospective study designs • Conference abstracts will not be considered	
Search strategy	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques were used. See Appendix B for full strategies	
Review strategy	Appraisal of methodological quality: • the methodological quality of each study will be assessed using checklists recommended in the NICE guidelines manual 2014 (for example, AMSTAR or ROBIS for systematic reviews, and Cochrane RoB tool for RCTs) and the quality of the evidence for each outcome (that is, across studies) will be assessed using GRADE • if studies report only p-values, this information will be recorded in GRADE tables without an assessment of imprecision Synthesis of data: • meta-analysis will be conducted where appropriate • default MIDs will be used; 0.8 and 1.25 for dichotomous outcomes; 0.5 times the SD of the measurement in the control arm (or median score across control arms if multiple studies are included) for continuous outcomes • for continuous data, change scores will be used in preference to final scores for data from non-RCT studies; final and change scores will not be pooled; if any study reports both, the method used in the majority of studies will be adopted	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies will be resolved through discussion between the first and second reviewers or by

Item	Details	Working notes
		reference to a third person. This review question was not prioritised for health economic analysis and so no formal dual weeding, study selection (inclusion/exclusion) or data extraction into evidence tables will be undertaken. However, internal (NGA) quality assurance processes will include consideration of the outcomes of weeding, study selection and data extraction and the committee will review the results of study selection and data extraction
Equalities	Equalities considerations will be considered systematically in relation to the available evidence and draft recommendations. The guideline scope includes women with cognitive or physical disability as populations for whom there may be equalities issues. Women who have received no antenatal care will be considered as a subgroup for all systematic reviews performed within the medical conditions work stream and a specific question has been included in the obstetric complications work stream for this population	
Notes/additional information	NICE guideline on asthma is in development SIGN Guideline on Management of Asthma (https://www.brit-thoracic.org.uk/document-library/clinical-information/asthma/btssign-asthma-guideline-2014/) Q1: NICE guideline on induction of labour (CG70) "1.3 Recommended methods for induction of labour 1.3.2 Pharmacological methods 1.3.2.1 Vaginal PGE2 is the preferred method of induction of labour, unless there are specific clinical reasons for not using it (in particular the risk of uterine hyperstimulation). It should be administered as a gel, tablet or controlled-release pessary. Costs	

Item	Details	Working notes
	may vary over time, and trusts/units should take this into consideration when prescribing PGE2. For doses, refer to the SPCs. The recommended regimens are: • one cycle of vaginal PGE2 tablets or gel: one dose, followed by a second dose after 6 hours if labour is not established (up to a maximum of two doses) • one cycle of vaginal PGE2 controlled-release pessary: one dose over 24 hours. 1.3.2.2 When offering PGE2 for induction of labour, healthcare professionals should inform women about the associated risks of uterine hyperstimulation. 1.3.2.3 Misoprostol[5] should only be offered as a method of induction of labour to women who have intrauterine fetal death (see section 1.2.9) or in the context of a clinical trial. 1.3.2.4 Mifepristone should only be offered as a method of induction of labour to women who have intrauterine fetal death (see section 1.2.9)". "1.4 Methods that are not recommended for induction of labour 1.4.1 Pharmacological methods 1.4.1.1 The following should not be used for induction of labour: • oral PGE2 • intravenous PGE2 • extra-amniotic PGE2 • intracervical PGE2 • intravenous oxytocin alone • hyaluronidase • corticosteroids • oestrogen • vaginal nitric oxide donors. 1.4.3 Surgical methods 1.4.3.1 Amniotomy, alone or with oxytocin, should not be used as a primary method of induction of labour unless there are specific clinical reasons for not using vaginal PGE2, in particular the risk of uterine hyperstimulation. 1.4.4 Mechanical methods 1.4.4.1 Mechanical procedures (balloon catheters and laminaria tents) should not be used routinely for induction of labour." Q2: NICE guideline on Intrapartum Care for Healthy Women and Babies 2017 (http://www.nice.org.uk/guidance/cg190) "1.14.13 For active management, administer 10 IU of oxytocin by intramuscular injection with the birth of the anterior shoulder or immediately after the birth of the baby and before the cord is clamped and cut. Use oxytocin as it is associated with fewer side effects than oxytocin plus ergometrine. [2014]".	
<Insert Note here> Key papers	• Towers CV, Briggs GG, Rojas JA. Am J Obstet Gynecol. 2004 Jun;190(6):1777-80 "The use of prostaglandin E2 in pregnant patients with asthma"	

Item	Details	Working notes
	• Alfirevic Z, Kelly AJ, Dowswell T. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD003246 “Intravenous oxytocin alone for cervical ripening and induction of labour” (http://www.ncbi.nlm.nih.gov/pubmed/19821304) • WHO guidelines for the management of postpartum haemorrhage and retained placenta (http://apps.who.int/iris/bitstream/10665/44171/1/9789241598514_eng.pdf) • Bricker L, Luckas M. Cochrane Database Syst Rev. 2000;(4):CD002862 “Amniotomy alone for induction of labour” (http://www.ncbi.nlm.nih.gov/pubmed/11034776) • Luckas M, Bricker L. Cochrane Database Syst Rev. 2000;(4):CD002864 “Intravenous prostaglandin for induction of labour” (http://www.ncbi.nlm.nih.gov/pubmed/11034778) • Howarth GR, Botha DJ. Cochrane Database Syst Rev. 2001;(3):CD003250 “Amniotomy plus intravenous oxytocin for induction of labour” (http://www.ncbi.nlm.nih.gov/pubmed/11687061) • Lo L, Ho MW, Leung P. Aust N Z J Obstet Gynaecol. 1994 May;34(2):149-53 “Comparison of prostaglandin E2 vaginal tablet with amniotomy and intravenous oxytocin for induction of labour” (http://www.ncbi.nlm.nih.gov/pubmed/7980302)	

AMSTAR: Assessing the Methodological Quality of Systematic Reviews; BMI: Body Mass Index; BTS: British Thoracic Society; CCTR: Cochrane Central Register of Controlled Trials; CDSR: Cochrane Database of Systematic Reviews; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; IU: international unit; MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; PEF: peak expiratory flow; PGE: prostaglandin E; RCT: randomised controlled trial; RoB: risk of bias; ROBIS: Risk of Bias in Systematic Reviews; SD: standard deviation; SIGN: Scottish Intercollegiate Guidelines Network; SpO2: oxygen saturation; WHO: World Health Organization

Appendix B – Literature search strategies

Intrapartum care for women with asthma – analgesia

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

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	exp ASTHMA/
11	asthma$.ti,ab.
12	BRONCHIAL SPASM/
13	(Bronchospasm? or bronch$ spasm?).ti,ab.
14	BRONCHOCONSTRICTION/
15	(Bronchoconstrict$ or bronch$ constrict$).ti,ab.
16	or/10-15
17	ANALGESIA, EPIDURAL/
18	INJECTIONS, EPIDURAL/
19	((Spinal$ or spinous$) adj5 analges$).ti,ab.
20	epidural$.ti,ab.
21	CSE.ti,ab.
22	((central$ or regional$) adj5 neuraxial$ adj5 block$).ti,ab.
23	(neuraxial$ adj5 analges$).ti,ab.
24	or/17-23
25	((parenteral$ or intravenous$ or intramuscular$ or oral$) adj5 analges$).ti,ab.
26	(systemic$ adj3 analgesi$).ti,ab.
27	exp ANALGESICS, OPIOID/
28	(Opioid? or Alfentanil or Alphaprodine or Buprenorphine or Butorphanol or Codeine or Dextromoramide or Dextropropoxyphene or Dihydromorphine or Diphenoxylate or Enkephalin or Ethylketocyclazocine or Ethylmorphine or Etorphine or Fentanyl or Heroin or Hydrocodone or Hydromorphone or Levorphanol or Meperidine or Meptazinol or Methadone or Methadyl Acetate or Morphine or Nalbuphine or Opiate Alkaloid? or Opium or Oxycodone or Oxymorphone or Pentazocine or Phenazocine or Phenoperidine or Pirinitramide or Promedol or Sufentanil or Tilidine or Tramadol or pethidine or diamorphine).mp.
29	remifentanil.mp.
30	ACETAMINOPHEN/
31	(acetaminophen or paracetamol).ti,ab.
32	KETAMINE/
33	ketamine.mp.
34	or/25-33
35	(inhal$ adj3 analgesi$).ti,ab.
36	exp NITROUS OXIDE/
37	(nitrous oxide or N2O).mp.
38	laughing gas.ti,ab.
39	(gas adj2 air).ti,ab.
40	Entonox.mp.
41	Nitronox.mp.
42	sevoflurane.mp.

#	Searches
43	desflurane.mp.
44	or/35-43
45	(local$ adj3 analges$).ti,ab.
46	LIDOCAINE/
47	lignocaine.mp.
48	BUPIVACAINE/
49	bupivacaine.mp.
50	levobupivacaine.mp.
51	or/45-50
52	ANALGESIA, PATIENT-CONTROLLED/
53	(patient? adj3 control$ adj3 analges$).ti,ab.
54	or/52-53
55	((no or avoid$) adj3 analges$).ti,ab.
56	ANALGESIA, OBSTETRICAL/
57	(obstetric$ adj3 analges$).ti,ab.
58	or/56-57
59	PAIN MANAGEMENT/
60	(pain$ adj5 manag$).ti.
61	or/59-60
62	(asthma$ adj5 manag$).ti.
63	9 and 16 and (24 or 34 or 44 or 51 or 54 or 55)
64	16 and 58
65	9 and 16 and 61
66	9 and 62
67	or/63-66
68	limit 67 to english language
69	LETTER/
70	EDITORIAL/
71	NEWS/
72	exp HISTORICAL ARTICLE/
73	ANECDOTES AS TOPIC/
74	COMMENT/
75	CASE REPORT/
76	(letter or comment*).ti.
77	or/69-76
78	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
79	77 not 78
80	ANIMALS/ not HUMANS/
81	exp ANIMALS, LABORATORY/
82	exp ANIMAL EXPERIMENTATION/
83	exp MODELS, ANIMAL/
84	exp RODENTIA/
85	(rat or rats or mouse or mice).ti.
86	or/79-85
87	68 not 86

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab,kw.

#	Searches
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	exp ASTHMA/
11	asthma$.ti,ab,kw.
12	BRONCHIAL SPASM/
13	(Bronchospasm? or bronch$ spasm?).ti,ab,kw.
14	BRONCHOCONSTRICTION/
15	(Bronchoconstrict$ or bronch$ constrict$).ti,ab,kw.
16	or/10-15
17	ANALGESIA, EPIDURAL/
18	INJECTIONS, EPIDURAL/
19	((Spinal$ or spinous$) adj5 analges$).ti,ab.
20	epidural$.ti,ab,kw.
21	CSE.ti,ab.
22	((central$ or regional$) adj5 neuraxial$ adj5 block$).ti,ab.
23	(neuraxial$ adj5 analges$).ti,ab.
24	or/17-23
25	((parenteral$ or intravenous$ or intramuscular$ or oral$) adj5 analges$).ti,ab.
26	(systemic$ adj3 analgesi$).ti,ab.
27	exp ANALGESICS, OPIOID/
28	(Opioid? or Alfentanil or Alphaprodine or Buprenorphine or Butorphanol or Codeine or Dextromoramide or Dextropropoxyphene or Dihydromorphine or Diphenoxylate or Enkephalin or Ethylketocyclazocine or Ethylmorphine or Etorphine or Fentanyl or Heroin or Hydrocodone or Hydromorphone or Levorphanol or Meperidine or Meptazinol or Methadone or Methadyl Acetate or Morphine or Nalbuphine or Opiate Alkaloid? or Opium or Oxycodone or Oxymorphone or Pentazocine or Phenazocine or Phenoperidine or Pirinitramide or Promedol or Sufentanil or Tilidine or Tramadol or pethidine or diamorphine).mp.
29	remifentanil.mp.
30	ACETAMINOPHEN/
31	(acetaminophen or paracetamol).mp.
32	KETAMINE/
33	ketamine.mp.
34	or/25-33
35	(inhal$ adj3 analgesi$).ti,ab.
36	exp NITROUS OXIDE/
37	(nitrous oxide or N2O).mp.
38	laughing gas.ti,ab,kw.
39	(gas adj2 air).ti,ab.
40	Entonox.mp.
41	Nitronox.mp.
42	sevoflurane.mp.
43	desflurane.mp.
44	or/35-43
45	(local$ adj3 analges$).ti,ab.
46	LIDOCAINE/
47	lignocaine.mp.
48	BUPIVACAINE/
49	bupivacaine.mp.
50	levobupivacaine.mp.
51	or/45-50
52	ANALGESIA, PATIENT-CONTROLLED/
53	(patient? adj3 control$ adj3 analges$).ti,ab.
54	or/52-53
55	((no or avoid$) adj3 analges$).ti,ab.

#	Searches
56	ANALGESIA, OBSTETRICAL/
57	(obstetric$ adj3 analges$).ti,ab.
58	or/56-57
59	PAIN MANAGEMENT/
60	(pain$ adj5 manag$).ti.
61	or/59-60
62	(asthma$ adj5 manag$).ti.
63	9 and 16 and (24 or 34 or 44 or 51 or 54 or 55)
64	16 and 58
65	9 and 16 and 61
66	9 and 62
67	or/63-66

Database: Cochrane Database of Systematic Reviews

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	ASTHMA.kw.
11	asthma$.ti,ab.
12	BRONCHIAL SPASM.kw.
13	(Bronchospasm? or bronch$ spasm?).ti,ab.
14	BRONCHOCONSTRICTION.kw.
15	(Bronchoconstrict$ or bronch$ constrict$).ti,ab.
16	or/10-15
17	ANALGESIA, EPIDURAL.kw.
18	INJECTIONS, EPIDURAL.kw.
19	((Spinal$ or spinous$) adj5 analges$).ti,ab.
20	epidural$.ti,ab.
21	CSE.ti,ab.
22	((central$ or regional$) adj5 neuraxial$ adj5 block$).ti,ab.
23	(neuraxial$ adj5 analges$).ti,ab.
24	or/17-23
25	((parenteral$ or intravenous$ or intramuscular$ or oral$) adj5 analges$).ti,ab.
26	(systemic$ adj3 analgesi$).ti,ab.
27	ANALGESICS, OPIOID.kw.
28	(Opioid? or Alfentanil or Alphaprodine or Buprenorphine or Butorphanol or Codeine or Dextromoramide or Dextropropoxyphene or Dihydromorphine or Diphenoxylate or Enkephalin or Ethylketocyclazocine or Ethylmorphine or Etorphine or Fentanyl or Heroin or Hydrocodone or Hydromorphone or Levorphanol or Meperidine or Meptazinol or Methadone or Methadyl Acetate or Morphine or Nalbuphine or Opiate Alkaloid? or Opium or Oxycodone or Oxymorphone or Pentazocine or Phenazocine or Phenoperidine or Pirinitramide or Promedol or Sufentanil or Tilidine or Tramadol or pethidine or diamorphine).mp.
29	remifentanil.mp.
30	ACETAMINOPHEN.kw.
31	(acetaminophen or paracetamol).ti,ab.
32	KETAMINE.kw.
33	ketamine.mp.

#	Searches
34	or/25-33
35	(inhal$ adj3 analgesi$).ti,ab.
36	NITROUS OXIDE.kw.
37	(nitrous oxide or N2O).mp.
38	laughing gas.ti,ab.
39	(gas adj2 air).ti,ab.
40	Entonox.mp.
41	Nitronox.mp.
42	sevoflurane.mp.
43	desflurane.mp.
44	or/35-43
45	(local$ adj3 analges$).ti,ab.
46	LIDOCAINE.kw.
47	lignocaine.mp.
48	BUPIVACAINE.kw.
49	bupivacaine.mp.
50	levobupivacaine.mp.
51	or/45-50
52	ANALGESIA, PATIENT-CONTROLLED.kw.
53	(patient? adj3 control$ adj3 analges$).ti,ab.
54	or/52-53
55	((no or avoid$) adj3 analges$).ti,ab.
56	ANALGESIA, OBSTETRICAL.kw.
57	(obstetric$ adj3 analges$).ti,ab.
58	or/56-57
59	PAIN MANAGEMENT.kw.
60	(pain$ adj5 manag$).ti.
61	or/59-60
62	(asthma$ adj5 manag$).ti.
63	9 and 16 and (24 or 34 or 44 or 51 or 54 or 55)
64	16 and 58
65	9 and 16 and 61
66	9 and 62
67	or/63-66

Database: Database of Abstracts of Reviews of Effects

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.tw,tx.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw,tx.
8	((during or giving or give) adj3 birth?).tw,tx.
9	or/1-8
10	ASTHMA.kw.
11	asthma$.tw,tx.
12	BRONCHIAL SPASM.kw.
13	(Bronchospasm? or bronch$ spasm?).tw,tx.
14	BRONCHOCONSTRICTION.kw.
15	(Bronchoconstrict$ or bronch$ constrict$).tw,tx.
16	or/10-15
17	ANALGESIA, EPIDURAL.kw.

#	Searches
18	INJECTIONS, EPIDURAL.kw.
19	((Spinal$ or spinous$) adj5 analges$).tw,tx.
20	epidural$.tw,tx.
21	CSE.tw,tx.
22	((central$ or regional$) adj5 neuraxial$ adj5 block$).tw,tx.
23	(neuraxial$ adj5 analges$).tw,tx.
24	or/17-23
25	((parenteral$ or intravenous$ or intramuscular$ or oral$) adj5 analges$).tw,tx.
26	(systemic$ adj3 analgesi$).tw,tx.
27	ANALGESICS, OPIOID.kw.
28	(Opioid? or Alfentanil or Alphaprodine or Buprenorphine or Butorphanol or Codeine or Dextromoramide or Dextropropoxyphene or Dihydromorphine or Diphenoxylate or Enkephalin or Ethylketocyclazocine or Ethylmorphine or Etorphine or Fentanyl or Heroin or Hydrocodone or Hydromorphone or Levorphanol or Meperidine or Meptazinol or Methadone or Methadyl Acetate or Morphine or Nalbuphine or Opiate Alkaloid? or Opium or Oxycodone or Oxymorphone or Pentazocine or Phenazocine or Phenoperidine or Pirinitramide or Promedol or Sufentanil or Tilidine or Tramadol or pethidine or diamorphine).mp.
29	remifentanil.mp.
30	ACETAMINOPHEN.kw.
31	(acetaminophen or paracetamol).mp.
32	KETAMINE.kw.
33	ketamine.mp.
34	or/25-33
35	(inhal$ adj3 analgesi$).tw,tx.
36	NITROUS OXIDE.kw.
37	(nitrous oxide or N2O).mp.
38	laughing gas.tw,tx.
39	(gas adj2 air).tw,tx.
40	Entonox.mp.
41	Nitronox.mp.
42	sevoflurane.mp.
43	desflurane.mp.
44	or/35-43
45	(local$ adj3 analges$).tw,tx.
46	LIDOCAINE.kw.
47	lignocaine.mp.
48	BUPIVACAINE.kw.
49	bupivacaine.mp.
50	levobupivacaine.mp.
51	or/45-50
52	ANALGESIA, PATIENT-CONTROLLED.kw.
53	(patient? adj3 control$ adj3 analges$).tw,tx.
54	or/52-53
55	((no or avoid$) adj3 analges$).tw,tx.
56	ANALGESIA, OBSTETRICAL.kw.
57	(obstetric$ adj3 analges$).tw,tx.
58	or/56-57
59	PAIN MANAGEMENT.kw.
60	(pain$ adj5 manag$).ti.
61	or/59-60
62	(asthma$ adj5 manag$).ti.
63	9 and 16 and (24 or 34 or 44 or 51 or 54 or 55)
64	16 and 58
65	9 and 16 and 61
66	9 and 62

#	Searches
67	or/63-66

Database: Health Technology Assessment

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.tw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
8	((during or giving or give) adj3 birth?).tw.
9	or/1-8
10	exp ASTHMA/
11	asthma$.tw.
12	BRONCHIAL SPASM/
13	(Bronchospasm? or bronch$ spasm?).tw.
14	BRONCHOCONSTRICTION/
15	(Bronchoconstrict$ or bronch$ constrict$).tw.
16	or/10-15
17	ANALGESIA, EPIDURAL/
18	INJECTIONS, EPIDURAL/
19	((Spinal$ or spinous$) adj5 analges$).tw.
20	epidural$.tw.
21	CSE.tw.
22	((central$ or regional$) adj5 neuraxial$ adj5 block$).tw.
23	(neuraxial$ adj5 analges$).tw.
24	or/17-23
25	((parenteral$ or intravenous$ or intramuscular$ or oral$) adj5 analges$).tw.
26	(systemic$ adj3 analgesi$).tw.
27	exp ANALGESICS, OPIOID/
28	(Opioid? or Alfentanil or Alphaprodine or Buprenorphine or Butorphanol or Codeine or Dextromoramide or Dextropropoxyphene or Dihydromorphine or Diphenoxylate or Enkephalin or Ethylketocyclazocine or Ethylmorphine or Etorphine or Fentanyl or Heroin or Hydrocodone or Hydromorphone or Levorphanol or Meperidine or Meptazinol or Methadone or Methadyl Acetate or Morphine or Nalbuphine or Opiate Alkaloid? or Opium or Oxycodone or Oxymorphone or Pentazocine or Phenazocine or Phenoperidine or Pirinitramide or Promedol or Sufentanil or Tilidine or Tramadol or pethidine or diamorphine).mp.
29	remifentanil.mp.
30	ACETAMINOPHEN/
31	(acetaminophen or paracetamol).tw.
32	KETAMINE/
33	ketamine.mp.
34	or/25-33
35	(inhal$ adj3 analgesi$).tw.
36	exp NITROUS OXIDE/
37	(nitrous oxide or N2O).mp.
38	laughing gas.tw.
39	(gas adj2 air).tw.
40	Entonox.mp.
41	Nitronox.mp.
42	sevoflurane.mp.
43	desflurane.mp.
44	or/35-43

#	Searches
45	(local$ adj3 analges$).tw.
46	LIDOCAINE/
47	lignocaine.mp.
48	BUPIVACAINE/
49	bupivacaine.mp.
50	levobupivacaine.mp.
51	or/45-50
52	ANALGESIA, PATIENT-CONTROLLED/
53	(patient? adj3 control$ adj3 analges$).tw.
54	or/52-53
55	((no or avoid$) adj3 analges$).tw.
56	ANALGESIA, OBSTETRICAL/
57	(obstetric$ adj3 analges$).tw.
58	or/56-57
59	PAIN MANAGEMENT/
60	(pain$ adj5 manag$).tw.
61	or/59-60
62	(asthma$ adj5 manag$).tw.
63	9 and 16 and (24 or 34 or 44 or 51 or 54 or 55)
64	16 and 58
65	9 and 16 and 61
66	9 and 62
67	or/63-66

Database: Embase

#	Searches
1	*PREGNANCY/
2	*PERINATAL PERIOD/
3	exp *BIRTH/
4	exp *LABOR/
5	*PREMATURE LABOR/
6	*INTRAPARTUM CARE/
7	pregnan$.ti,ab.
8	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
9	((during or giving or give) adj3 birth?).ti,ab.
10	or/1-9
11	exp ASTHMA/
12	asthma$.ti,ab.
13	BRONCHOSPASM/
14	(Bronchospasm? or bronch$ spasm?).ti,ab.
15	BRONCHOCONSTRICTION/
16	(Bronchoconstrict$ or bronch$ constrict$).ti,ab.
17	or/11-16
18	EPIDURAL ANALGESIA/
19	EPIDURAL DRUG ADMINISTRATION/
20	((Spinal$ or spinous$) adj5 analges$).ti,ab.
21	epidural$.ti,ab.
22	CSE.ti,ab.
23	((central$ or regional$) adj5 neuraxial$ adj5 block$).ti,ab.
24	(neuraxial$ adj5 analges$).ti,ab.
25	or/18-24
26	((parenteral$ or intravenous$ or intramuscular$ or oral$) adj5 analges$).ti,ab.
27	(systemic$ adj3 analgesi$).ti,ab.
28	exp NARCOTIC ANALGESIC AGENT/

#	Searches
29	(Opioid? or Alfentanil or Alphaprodine or Buprenorphine or Butorphanol or Codeine or Dextromoramide or Dextropropoxyphene or Dihydromorphine or Diphenoxylate or Enkephalin or Ethylketocyclazocine or Ethylmorphine or Etorphine or Fentanyl or Heroin or Hydrocodone or Hydromorphone or Levorphanol or Meperidine or Meptazinol or Methadone or Methadyl Acetate or Morphine or Nalbuphine or Opiate Alkaloid? or Opium or Oxycodone or Oxymorphone or Pentazocine or Phenazocine or Phenoperidine or Pirinitramide or Promedol or Sufentanil or Tilidine or Tramadol or pethidine or diamorphine).mp.
30	remifentanil.mp.
31	PARACETAMOL/
32	(acetaminophen or paracetamol).ti,ab.
33	KETAMINE/
34	ketamine.mp.
35	or/26-34
36	(inhal$ adj3 analgesi$).ti,ab.
37	NITROUS OXIDE/
38	NITROUS OXIDE PLUS OXYGEN/
39	SEVOFLURANE/
40	DESFLURANE/
41	(nitrous oxide or N2O).mp.
42	laughing gas.ti,ab.
43	(gas adj2 air).ti,ab.
44	Entonox.mp.
45	Nitronox.mp.
46	sevoflurane.mp.
47	desflurane.mp.
48	or/36-47
49	(local$ adj3 analges$).ti,ab.
50	LIDOCAINE/
51	lignocaine.mp.
52	BUPIVACAINE/
53	bupivacaine.mp.
54	LEVOBUPIVACAINE/
55	levobupivacaine.mp.
56	or/49-55
57	PATIENT CONTROLLED ANALGESIA/
58	(patient? adj3 control$ adj3 analges$).ti,ab.
59	or/57-58
60	((no or avoid$) adj3 analges$).ti,ab.
61	OBSTETRIC ANALGESIA/
62	(obstetric$ adj3 analges$).ti,ab.
63	or/61-62
64	(pain$ adj5 manag$).ti.
65	(asthma$ adj5 manag$).ti.
66	10 and 17 and (25 or 35 or 48 or 56 or 59 or 60)
67	17 and 63
68	10 and 17 and 64
69	10 and 65
70	or/66-69
71	limit 70 to english language
72	letter.pt. or LETTER/
73	note.pt.
74	editorial.pt.
75	CASE REPORT/ or CASE STUDY/
76	(letter or comment*).ti.
77	or/72-76

#	Searches
78	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
79	77 not 78
80	ANIMAL/ not HUMAN/
81	NONHUMAN/
82	exp ANIMAL EXPERIMENT/
83	exp EXPERIMENTAL ANIMAL/
84	ANIMAL MODEL/
85	exp RODENT/
86	(rat or rats or mouse or mice).ti.
87	or/79-86
88	71 not 87

Intrapartum care for women with asthma – prostaglandins

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

#	Searches
1	exp ASTHMA/
2	asthma$.ti,ab.
3	BRONCHIAL SPASM/
4	(Bronchospasm? or bronch$ spasm?).ti,ab.
5	BRONCHOCONSTRICTION/
6	(Bronchoconstrict$ or bronch$ constrict$).ti,ab.
7	or/1-6
8	exp PROSTAGLANDINS/
9	(prostaglandin? or prostanoid? or Alprostadil or PGE1 or Dinoprostone or Dinoprost or Arbaprostil or Enprostil or Misoprostol or Rioprostil or Carboprost or Hemabate or Cloprostenol or Bimatoprost or Travoprost or PGF$ or 15 methyl PGF$ or 15?methyl?PGF$ or 15 methylprostaglandin$ or 15?methylprostaglandin$).mp.
10	exp OXYTOCICS/
11	(O#ytocic? or uterotonic? or Ergonovine or ergometrin? or Ergotamine or ergonovine or ergobasin or ergotrate or ergot or methylergometrine or Methylergonovine or syntometrine or O#ytocin? or Quipazine or Sparteine or Vasotocin or syntocinon or pitocin or carbetocin).mp.
12	or/8-11
13	LABOR, INDUCED/
14	(induc$ adj5 labo?r).ti,ab.
15	or/13-14
16	POSTPARTUM HEMORRHAGE/
17	((postpartum or post partum) adj5 (h?emorrhag$ or bleed$)).ti,ab.
18	PPH.ti,ab.
19	or/16-18
20	PREGNANCY/
21	pregnan$.ab,ti.
22	PERIPARTUM PERIOD/
23	PARTURITION/
24	exp LABOR, OBSTETRIC/

#	Searches
25	exp DELIVERY, OBSTETRIC/
26	OBSTETRIC LABOR, PREMATURE/
27	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
28	((during or giving or give) adj3 birth?).ti,ab.
29	or/20-28
30	7 and 12 and 15
31	7 and 12 and 19
32	7 and 12 and 29
33	exp *PROSTAGLANDINS/ae [Adverse Effects]
34	exp *OXYTOCICS/ae [Adverse Effects]
35	or/33-34
36	MOTHERS/
37	(mother$ or maternal$).ti.
38	(mother$ or maternal$).ab. /freq=2
39	or/36-38
40	15 and 35 and 39
41	19 and 35 and 39
42	29 and 35 and 39
43	30 or 31 or 32 or 40 or 41 or 42
44	limit 43 to english language
45	LETTER/
46	EDITORIAL/
47	NEWS/
48	exp HISTORICAL ARTICLE/
49	ANECDOTES AS TOPIC/
50	COMMENT/
51	CASE REPORT/
52	(letter or comment*).ti.
53	or/45-52
54	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
55	53 not 54
56	ANIMALS/ not HUMANS/
57	exp ANIMALS, LABORATORY/
58	exp ANIMAL EXPERIMENTATION/
59	exp MODELS, ANIMAL/
60	exp RODENTIA/
61	(rat or rats or mouse or mice).ti.
62	or/55-61
63	44 not 62

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	exp ASTHMA/
2	asthma$.ti,ab,kw.

#	Searches
3	BRONCHIAL SPASM/
4	(Bronchospasm? or bronch$ spasm?).ti,ab,kw.
5	BRONCHOCONSTRICTION/
6	(Bronchoconstrict$ or bronch$ constrict$).ti,ab,kw.
7	or/1-6
8	exp PROSTAGLANDINS/
9	(prostaglandin? or prostanoid? or Alprostadil or PGE1 or Dinoprostone or Dinoprost or Arbaprostil or Enprostil or Misoprostol or Rioprostil or Carboprost or Hemabate or Cloprostenol or Bimatoprost or Travoprost or PGF$ or 15 methyl PGF$ or 15?methyl?PGF$ or 15 methylprostaglandin$ or 15?methylprostaglandin$).mp,kw.
10	exp OXYTOCICS/
11	(O#ytocic? or uterotonic? or Ergonovine or ergometrin? or Ergotamine or ergonovine or ergobasin or ergotrate or ergot or methylergometrine or Methylergonovine or syntometrine or O#ytocin? or Quipazine or Sparteine or Vasotocin or syntocinon or pitocin or carbetocin).mp,kw.
12	or/8-11
13	LABOR, INDUCED/
14	(induc$ adj5 labo?r).ti,ab.
15	or/13-14
16	POSTPARTUM HEMORRHAGE/
17	((postpartum or post partum) adj5 (h?emorrhag$ or bleed$)).ti,ab.
18	PPH.ti,ab,kw.
19	or/16-18
20	PREGNANCY/
21	pregnan$.ab,ti,kw.
22	PERIPARTUM PERIOD/
23	PARTURITION/
24	exp LABOR, OBSTETRIC/
25	exp DELIVERY, OBSTETRIC/
26	OBSTETRIC LABOR, PREMATURE/
27	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
28	((during or giving or give) adj3 birth?).ti,ab.
29	or/20-28
30	7 and 12 and 15
31	7 and 12 and 19
32	7 and 12 and 29
33	exp *PROSTAGLANDINS/ae [Adverse Effects]
34	exp *OXYTOCICS/ae [Adverse Effects]
35	or/33-34
36	MOTHERS/
37	(mother$ or maternal$).ti.
38	(mother$ or maternal$).ab. /freq=2
39	or/36-38
40	15 and 35 and 39
41	19 and 35 and 39

#	Searches
42	29 and 35 and 39
43	30 or 31 or 32 or 40 or 41 or 42

Database: Cochrane Database of Systematic Reviews

#	Searches
1	ASTHMA.kw.
2	asthma$.ti,ab.
3	BRONCHIAL SPASM.kw.
4	(Bronchospasm? or bronch$ spasm?).ti,ab.
5	BRONCHOCONSTRICTION.kw.
6	(Bronchoconstrict$ or bronch$ constrict$).ti,ab.
7	or/1-6
8	PROSTAGLANDINS.kw.
9	(prostaglandin? or prostanoid? or Alprostadil or PGE1 or Dinoprostone or Dinoprost or Arbaprostil or Enprostil or Misoprostol or Rioprostil or Carboprost or Hemabate or Cloprostenol or Bimatoprost or Travoprost or PGF$ or 15 methyl PGF$ or 15?methyl?PGF$ or 15 methylprostaglandin$ or 15?methylprostaglandin$).mp.
10	OXYTOCICS.kw.
11	(O#ytocic? or uterotonic? or Ergonovine or ergometrin? or Ergotamine or ergonovine or ergobasin or ergotrate or ergot or methylergometrine or Methylergonovine or syntometrine or O#ytocin? or Quipazine or Sparteine or Vasotocin or syntocinon or pitocin or carbetocin).mp.
12	or/8-11
13	LABOR, INDUCED.kw.
14	(induc$ adj5 labo?r).ti,ab.
15	or/13-14
16	POSTPARTUM HEMORRHAGE.kw.
17	((postpartum or post partum) adj5 (h?emorrhag$ or bleed$)).ti,ab.
18	PPH.ti,ab.
19	or/16-18
20	PREGNANCY.kw.
21	pregnan$.ab,ti.
22	PERIPARTUM PERIOD.kw.
23	PARTURITION.kw.
24	LABOR, OBSTETRIC.kw.
25	DELIVERY, OBSTETRIC.kw.
26	OBSTETRIC LABOR, PREMATURE.kw.
27	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
28	((during or giving or give) adj3 birth?).ti,ab.
29	or/20-28
30	7 and 12 and 15
31	7 and 12 and 19
32	7 and 12 and 29
33	or/30-32

Database: Database of Abstracts of Reviews of Effects

#	Searches
1	ASTHMA.kw.
2	asthma$.tw,tx.
3	BRONCHIAL SPASM.kw.
4	(Bronchospasm? or bronch$ spasm?).tw,tx.
5	BRONCHOCONSTRICTION.kw.
6	(Bronchoconstrict$ or bronch$ constrict$).tw,tx.
7	or/1-6
8	PROSTAGLANDINS.kw.
9	(prostaglandin? or prostanoid? or Alprostadil or PGE1 or Dinoprostone or Dinoprost or Arbaprostil or Enprostil or Misoprostol or Rioprostil or Carboprost or Hemabate or Cloprostenol or Bimatoprost or Travoprost or PGF$ or 15 methyl PGF$ or 15?methyl?PGF$ or 15 methylprostaglandin$ or 15?methylprostaglandin$).mp.
10	OXYTOCICS.kw.
11	(O#ytocic? or uterotonic? or Ergonovine or ergometrin? or Ergotamine or ergonovine or ergobasin or ergotrate or ergot or methylergometrine or Methylergonovine or syntometrine or O#ytocin? or Quipazine or Sparteine or Vasotocin or syntocinon or pitocin or carbetocin).mp.
12	or/8-11
13	LABOR, INDUCED.kw.
14	(induc$ adj5 labo?r).tw,tx.
15	or/13-14
16	POSTPARTUM HEMORRHAGE.kw.
17	((postpartum or post partum) adj5 (h?emorrhag$ or bleed$)).tw,tx.
18	PPH.tw,tx.
19	or/16-18
20	PREGNANCY.kw.
21	pregnan$.tw,tx.
22	PERIPARTUM PERIOD.kw.
23	PARTURITION.kw.
24	LABOR, OBSTETRIC.kw.
25	DELIVERY, OBSTETRIC.kw.
26	OBSTETRIC LABOR, PREMATURE.kw.
27	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw,tx.
28	((during or giving or give) adj3 birth?).tw,tx.
29	or/20-28
30	7 and 12 and 15
31	7 and 12 and 19
32	7 and 12 and 29
33	or/30-32

Database: Health Technology Assessment

#	Searches
1	exp ASTHMA/
2	asthma$.tw.
3	BRONCHIAL SPASM/

#	Searches
4	(Bronchospasm? or bronch$ spasm?).tw.
5	BRONCHOCONSTRICTION/
6	(Bronchoconstrict$ or bronch$ constrict$).tw.
7	or/1-6
8	exp PROSTAGLANDINS/
9	(prostaglandin? or prostanoid? or Alprostadil or PGE1 or Dinoprostone or Dinoprost or Arbaprostil or Enprostil or Misoprostol or Rioprostil or Carboprost or Hemabate or Cloprostenol or Bimatoprost or Travoprost or PGF$ or 15 methyl PGF$ or 15?methyl?PGF$ or 15 methylprostaglandin$ or 15?methylprostaglandin$).mp.
10	exp OXYTOCICS/
11	(O#ytocic? or uterotonic? or Ergonovine or ergometrin? or Ergotamine or ergonovine or ergobasin or ergotrate or ergot or methylergometrine or Methylergonovine or syntometrine or O#ytocin? or Quipazine or Sparteine or Vasotocin or syntocinon or pitocin or carbetocin).mp.
12	or/8-11
13	LABOR, INDUCED/
14	(induc$ adj5 labo?r).tw.
15	or/13-14
16	POSTPARTUM HEMORRHAGE/
17	((postpartum or post partum) adj5 (h?emorrhag$ or bleed$)).tw.
18	PPH.tw.
19	or/16-18
20	PREGNANCY/
21	pregnan$.tw.
22	PERIPARTUM PERIOD/
23	PARTURITION/
24	exp LABOR, OBSTETRIC/
25	exp DELIVERY, OBSTETRIC/
26	OBSTETRIC LABOR, PREMATURE/
27	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
28	((during or giving or give) adj3 birth?).tw.
29	or/20-28
30	7 and 12 and 15
31	7 and 12 and 19
32	7 and 12 and 29
33	exp *PROSTAGLANDINS/ae [Adverse Effects]
34	exp *OXYTOCICS/ae [Adverse Effects]
35	or/33-34
36	MOTHERS/
37	(mother$ or maternal$).tw.
38	or/36-37
39	15 and 35 and 38
40	19 and 35 and 38
41	29 and 35 and 38
42	30 or 31 or 32 or 39 or 40 or 41

Database: Embase

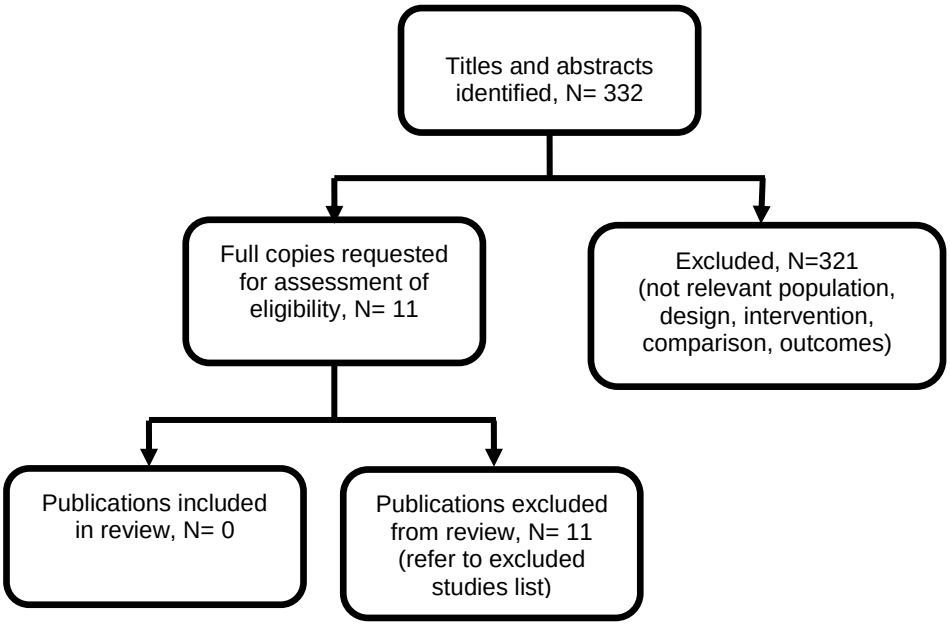
#	Searches
1	exp ASTHMA/
2	asthma$.ti,ab.
3	BRONCHOSPASM/
4	(Bronchospasm? or bronch$ spasm?).ti,ab.
5	BRONCHOCONSTRICTION/
6	(Bronchoconstrict$ or bronch$ constrict$).ti,ab.
7	or/1-6
8	exp PROSTAGLANDIN/
9	(prostaglandin? or prostanoid? or Alprostadil or PGE1 or Dinoprostone or Dinoprost or Arbaprostil or Enprostil or Misoprostol or Rioprostil or Carboprost or Hemabate or Cloprostenol or Bimatoprost or Travoprost or PGF$ or 15 methyl PGF$ or 15?methyl?PGF$ or 15 methylprostaglandin$ or 15?methylprostaglandin$).mp.
10	exp UTEROTONIC AGENT/
11	(O#ytocic? or uterotonic? or Ergonovine or ergometrin? or Ergotamine or ergonovine or ergobasin or ergotrate or ergot or methylergometrine or Methylergonovine or syntometrine or O#ytocin? or Quipazine or Sparteine or Vasotocin or syntocinon or pitocin or carbetocin).mp.
12	or/8-11
13	LABOR, INDUCTION/
14	(induc$ adj5 labo?r).ti,ab.
15	or/13-14
16	POSTPARTUM HEMORRHAGE/
17	((postpartum or post partum) adj5 (h?emorrhag$ or bleed$)).ti,ab.
18	PPH.ti,ab.
19	or/16-18
20	*PREGNANCY/
21	pregnan$.ti.
22	pregnan$.ab. /freq=3
23	INTRAPARTUM CARE/
24	*PERINATAL PERIOD/
25	*BIRTH/
26	exp *LABOR/
27	exp *DELIVERY/
28	*PREMATURE LABOR/
29	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti.
30	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ab. /freq=3
31	((during or giving or give) adj3 birth?).ti,ab.
32	or/20-31
33	7 and 12 and 15
34	7 and 12 and 19
35	7 and 12 and 32
36	exp *PROSTAGLANDINS/ae [Adverse Drug Reaction]
37	exp *UTEROTONIC AGENT/ae [Adverse Effects]
38	or/36-37
39	*MOTHER/

#	Searches
40	(mother$ or maternal$).ti.
41	(mother$ or maternal$).ab. /freq=3
42	or/39-41
43	15 and 38 and 42
44	19 and 38 and 42
45	32 and 38 and 42
46	33 or 34 or 35 or 43 or 44 or 45
47	limit 46 to english language
48	letter.pt. or LETTER/
49	note.pt.
50	editorial.pt.
51	CASE REPORT/ or CASE STUDY/
52	(letter or comment*).ti.
53	or/48-52
54	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
55	53 not 54
56	ANIMAL/ not HUMAN/
57	NONHUMAN/
58	exp ANIMAL EXPERIMENT/
59	exp EXPERIMENTAL ANIMAL/
60	ANIMAL MODEL/
61	exp RODENT/
62	(rat or rats or mouse or mice).ti.
63	or/55-62
64	47 not 63

Appendix C – Clinical evidence study selection

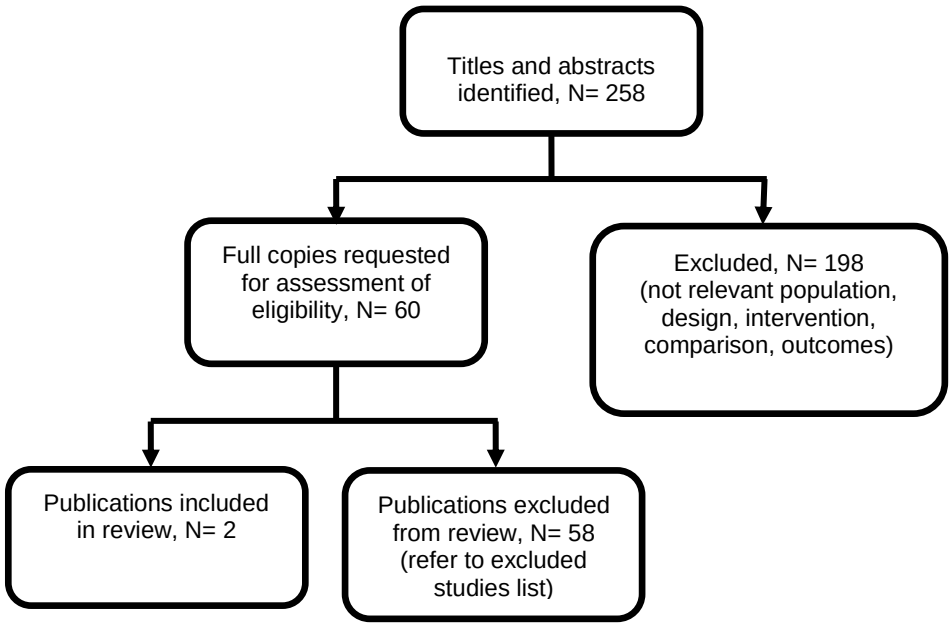
Intrapartum care for women with asthma – analgesia

Figure 1: Flow diagram of clinical evidence study selection for intrapartum care for women with asthma – analgesia



Intrapartum care for women with asthma – prostaglandins

Figure 2: Flow diagram of clinical evidence study selection for intrapartum care for women with asthma – prostaglandins



Appendix D – Excluded studies

Intrapartum care for women with asthma – analgesia

Clinical studies

Study	Reason for exclusion
British Thoracic, Society, Scottish Intercollegiate Guidelines, Network, British guideline on the management of asthma, Thorax, 69 Suppl 1, 1-192, 2014	Guideline – with no relevant references
Gibson, P. G., Powell, H., Giles, W., Clifton, V., Hensley, M., Taylor, D. R., Murphy, V., McCaffery, K. J., Asthma exacerbations during pregnancy are reduced by inflammometry (FENO) guided asthma management: A randomised controlled trial, American Journal of Respiratory and Critical Care Medicine. Conference: American Thoracic Society International Conference, ATS, 183, 2011	Intervention does not meet inclusion criteria
Grzeskowiak, L. E., Clifton, V. L., Asthma management during pregnancy: how long before we can all breathe a little easier?, Journal of Asthma, 52, 1020-2, 2015	Opinion paper on asthma management during pregnancy
Kuczkowski, K. M., Labor analgesia for the parturient with respiratory disease: what does an obstetrician need to know?, Archives of Gynecology & Obstetrics, 272, 160-6, 2005	Narrative literature review
McCallister, J. W., Asthma in pregnancy: Management strategies, Current Opinion in Pulmonary Medicine, 19, 13-17, 2013	Narrative literature review
Namazy,J.A., Schatz,M., Current guidelines for the management of asthma during pregnancy, Immunology and Allergy Clinics of North America, 26, 93-102, 2006	Guideline -with no suggestion on the best route of administration
National Heart, Lung, Blood, Institute, National Asthma, Education, Prevention Program, Asthma, Pregnancy Working, Group, NAEPP expert panel report. Managing asthma during pregnancy: recommendations for pharmacologic treatment-2004 update, Journal of Allergy & Clinical Immunology, 115, 34-46, 2005	Guideline – with no relevant references
Powell, H., Giles, W., Clifton, V., Hensley, M. J., Taylor, D. R., Murphy, V., et al.,, Asthma Exacerbations During Pregnancy Are Reduced By Inflammometry (FENO) Guided Asthma Management: A Randomised Controlled Trial [Abstract], American Journal of Respiratory and Critical Care Medicine, 183, A6414, 2011	Abstract publication of a protocol
Powell,H., Murphy,V.E., Taylor,D.R., Hensley,M.J., McCaffery,K., Giles,W., Clifton,V.L., Gibson,P.G., Management of asthma in pregnancy guided by measurement of fraction of exhaled nitric oxide: a double-blind, randomised controlled trial, Lancet, 378, 983-990, 2011	Intervention and comparator do not meet inclusion criteria
Rance, K., O'Laughlen, M. C., Managing asthma during pregnancy, Journal of the American Association of Nurse Practitioners, 25, 513-21, 2013	Narrative literature review

Richards,N.A., Yentis,S.M., Anaesthesia, analgesia and peripartum management in women with pre-existing cardiac and respiratory disease, Fetal and Maternal Medicine Review, 17, 327-347, 2006	Narrative literature review

Economic studies

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with asthma – prostaglandins

Clinical studies

Study	Reason for Exclusion
Abdulrazzaq Bastaki, S. M., Drugs update, Emirates Medical Journal, 26, 125-128, 2008	Population do not have asthma
Alfirevic,Z., Kelly,A.J., Dowswell,T., Intravenous oxytocin alone for cervical ripening and induction of labour, Cochrane Database of Systematic Reviews, -, 2009	Systematic review - with no relevant studies to include
Anonymous,, Prostaglandins, Medical Letter on Drugs & Therapeutics, 13, 80, 1971	Opinion paper
Anonymous,, Asthma in pregnancy, Obstetrics and Gynecology, 111, 457-464, 2008	Guideline – with no relevant studies to include
Anonymous,, Recently introduced products, Drug & Therapeutics Bulletin, 29, 17-9, 1991	Discussion paper
Asherkaci,H.M., Fortia,I.M., Sraiti,O.A., Abudabbous,M.A., Misoprostol usefulness on Post Partum Hemorrhage (PPH) among high risk mothers, Jamahiriya Medical Journal, 10, 213-215, 2010	A full text copy of the article could not be obtained
Beigi,A., Kabiri,M., Zarrinkoub,F., Cervical ripening with oral misoprostol at term, International Journal of Gynaecology and Obstetrics, 83, 251-255, 2003	Population do not have asthma
Booker, W. A., Huang, Y., Ananth, C. V., Wright, J. D., Cleary, K. L., D'Alton, M. E., Friedman, A. M., Administration of carboprost and intravenous labetalol to asthmatic patients during delivery hospitalizations, American Journal of Obstetrics and Gynecology, 218, S51, 2018	Conference abstract
Bricker, L., Luckas, M., Amniotomy alone for induction of labour, Cochrane Database of Systematic Reviews, CD002862, 2000	Systematic review - with no relevant studies to include
Butt,K.D., Bennett,K.A., Crane,J.M.G., Hutchens,D., Young,D.C., Randomized comparison of oral misoprostol and oxytocin for labor induction in term prelabor membrane rupture, Obstetrics and Gynecology, 94, 994-999, 1999	Population do not have asthma, and no relevant comparator
Calder,A.A., Loughney,A.D., Weir,C.J., Barber,J.W., Induction of labour in nulliparous and multiparous women: A UK, multicentre, open-label study of intravaginal misoprostol in comparison with dinoprostone, BJOG: An International Journal of Obstetrics and Gynaecology, 115, 1279-1288, 2008	Population do not have asthma, and no relevant comparator

Carlson, N. S., Current Resources for Evidence-Based Practice, March/April 2015, Journal of Midwifery and Women's Health, 60, 214-219, 2015	Discussion paper - containing case reports and a list of resources
Conway, D. I., Read, M. D., Bauer, C., Martin, R. H., Neonatal jaundice--a comparison between intravenous oxytocin and oral prostaglandin E2, Journal of International Medical Research, 4, 241-6, 1976	Population do not have asthma
Crane, J. M. G., Delaney, T., Hutchens, D., Oral misoprostol for premature rupture of membranes at term, American Journal of Obstetrics and Gynecology, 189, 720-724, 2003	Population do not have asthma
Douglas, M. J., Ward, M. E., Current pharmacology and the obstetric anesthesiologist, International Anesthesiology Clinics, 32, 1-10, 1994	Narrative literature review
Garcia-Fortea, P., Gonzalez-Mesa, E., Blasco, M., Cazorla, O., Delgado-Rios, M., Gonzalez-Valenzuela, M. J., Oxytocin administered during labor and breast-feeding: a retrospective cohort study, Journal of Maternal-Fetal & Neonatal Medicine, 27, 1598-603, 2014	Population do not have asthma, and no relevant comparator
Hankins, G. D. V., Berryman, G. K., Scott Jr, R. T., Hood, D., Maternal arterial desaturation with 15-methyl prostaglandin F<inf>2</inf> alpha for uterine atony, Obstetrics and Gynecology, 72, 367-370, 1988	Population do not have asthma
Harris, D., Technological inspiration, Innovations in Pharmaceutical Technology, 48-52, 2014	A full text copy of the article could not be obtained
Herman,A.G., Clinical use of prostaglandins in perspective, Acta Clinica Belgica, 38, 75-79, 1983	Narrative literature review
Hofmeyr,G.J., Gulmezoglu,A.M., Novikova,N., Linder,V., Ferreira,S., Piaggio,G., Misoprostol to prevent and treat postpartum haemorrhage: A systematic review and meta-analysis of maternal deaths and dose-related effects, Bulletin of the World Health Organization, 87, 666-677, 2009	Systematic review - with no relevant studies to include
Horton, E. W., Prostaglandins in clinical practice, British Journal of Hospital Medicine, 22, 260-4, 1979	Discussion paper
Howarth, G. R., Botha, D. J., Amniotomy plus intravenous oxytocin for induction of labour, Cochrane Database of Systematic Reviews, CD003250, 2001	Systematic review - with no relevant studies to include
Jozwiak, M., Rengerink, K. O., Benthem, M., Van Beek, E., Dijksterhuis, M. G. K., De Graaf, I. M., Van Huizen, M. E., Oudijk, M. A., Papatsonis, D. N. M., Perquin, D. A. M., Porath, M., Van Der Post, J. A. M., Rijnders, R. J. P., Scheepers, H. C. J., Spaanderman, M. E. A., Van Pampus, M. G., De Leeuw, J. W., Mol, B. W. J., Bloemenkamp, K. W. M., Foley catheter versus vaginal prostaglandin E2 gel for induction of labour at term (PROBAAT trial): An open-label, randomised controlled trial, The Lancet, 378, 2095-2103, 2011	Population do not have asthma
Kreisman, H., Van de Weil, W., Mitchell, C. A., Respiratory function during prostaglandin-induced labor, American Review of Respiratory Disease, 111, 564-6, 1975	Women received prostaglandins for termination of pregnancy, not for induction of labour
Lange,A.P., Secher,N.J., Westergaard,J.G., Skovgard,I., Neonatal jaundice after labour induced or stimulated by prostaglandin E2 or oxytocin, Lancet, 1, 991-994, 1982	Population do not have asthma

Lapinsky,S.E., Cardiopulmonary complications of pregnancy, Critical Care Medicine, 33, 1616-1622, 2005	Narrative literature review
Liang, C., Xu, D., He, J., Cervical ripening agent dinoprostone for delivery induction in late pregnancy mothers: Experiences of 685 cases, Clinical and Experimental Obstetrics and Gynecology, 42, 69-71, 2015	Population do not have asthma
Lo, L., Ho, M. W., Leung, P., Comparison of prostaglandin E2 vaginal tablet with amniotomy and intravenous oxytocin for induction of labour, Australian & New Zealand Journal of Obstetrics & Gynaecology, 34, 149-53, 1994	Population do not have asthma
Mabie,W.C., Asthma in pregnancy, Clinical Obstetrics and Gynecology, 39, 56-69, 1996	Narrative literature review
Maclennan, K., Croft, R., Obstetric haemorrhage, Anaesthesia and Intensive Care Medicine, 14, 337-341, 2013	Narrative literature review
Maroto Martin, M. T., Revelles Paniza, L., Ruiz Duran, S., Copado Salido, S., Barranco Armenteros, M., Puertas Prieto, A., Mechanical methods for labour induction, Journal of Perinatal Medicine. Conference: 12th World Congress of Perinatal Medicine, 43, 2015	A full text copy of the article could not be obtained
MerriKay, A. O., Mariano, J. P., Carboprost (hemabate) - A prostaglandin for postpartum haemorrhage, Drug and Therapeutics Bulletin, 29, 18, 1991	Commentary paper
Motaze, N., Mbuagbaw, L., Young, T., Prostaglandins before caesarean section for preventing neonatal respiratory distress: A cochrane systematic review, Basic & clinical pharmacology & toxicology, 115, 2014	Systematic review - with no relevant studies to include
Mousa, H. A., Alfirevic, Z., Treatment for primary postpartum haemorrhage, Cochrane Database of Systematic Reviews, CD003249, 2007	Systematic review - with no relevant studies to include
Nakano, J., The prostaglandins: their significance in clinical practice, Medical Times, 102, 47-58, 1974	Narrative literature review
Nelson-Piercy, C., De Swiet, M., Asthma in pregnancy, Fetal and Maternal Medicine Review, 6, 181-189, 1994	Narrative literature review
Oesterling, T. O., Current status of the prostaglandins, American Journal of Hospital Pharmacy, 31, 355-61, 1974	A full text copy of the article could not be obtained
O'Leary,A.M., Severe bronchospasm and hypotension after 15-methyl prostaglandin F(2alpha) in atonic post partum haemorrhage, International Journal of Obstetric Anesthesia, 3, 42-44, 1994	Case report
Olson, C. L., Chaska, B. W., Grambsch, P. M., Wiltgen, C. M., Nesse, R. E., Intrapartum intervention and delivery outcome in low-risk pregnancy, Journal of the American Board of Family Practice, 4, 83-8, 1991	Population do not have asthma, and no relevant comparator
Prysak,M., Lorenz,R.P., Kisly,A., Pregnancy outcome in nulliparous women 35 years and older, Obstetrics and Gynecology, 85, 65-70, 1995	No relevant comparison
Richards,N.A., Yentis,S.M., Anaesthesia, analgesia and peripartum management in women with pre-existing cardiac and respiratory disease, Fetal and Maternal Medicine Review, 17, 327-347, 2006	Narrative literature review
Saleem,S., Efficacy of dinoprostone, intracervical foleys and misoprostol in labor induction, Journal of the College of	A full text copy of the article could not be obtained

Physicians and Surgeons--Pakistan : JCPSP, 16, 276-279, 2006	
Saljoughian, M., Uterotonic agents: An update, U.S. Pharmacist., 36, 2011	Narrative literature review
Schatz, M., Asthma during pregnancy: Interrelationships and management, Annals of Allergy, 68, 123-138, 1992	Narrative literature review
Schmitz, T., Tararbit, K., Dupont, C., Rudigoz, R. C., Bouvier-Colle, M. H., Deneux-Tharaux, C., Prostaglandin E2 analogue sulprostone for treatment of atonic postpartum hemorrhage, Obstetrics and Gynecology, 118, 257-265, 2011	Population do not have asthma
Siddle, N., Elstein, M., Use of prostaglandins in obstetrics and gynaecology, British Journal of Family Planning, 6, 14-17, 1980	Narrative literature review
Smith, A. P., Side-effects of prostaglandins, Lancet, 2, 655, 1972	Commentary paper
Smith, P., Prostaglandins, Transactions of the Medical Society of London, 89, 31-5, 1973	Narrative literature review
Stablein,J.J., Lockey,R.F., Managing asthma during pregnancy, Comprehensive Therapy, 10, 45-52, 1984	Narrative literature review
Sundermeyer, R. L., Persons, R. K., Carrillo, M. J., FPIN's clinical inquiries. Prostaglandins to induce labor in women with asthma, American Family Physician, 90, 415, 2014	Discussion paper and narrative literature review
Venkataraman,M.T., Shanies,H.M., Pregnancy and asthma, Journal of Asthma, 34, 265-271, 1997	Narrative literature review
Vercauteren,M., Palit,S., Soetens,F., Jacquemyn,Y., Alahuhta,S., Anaesthesiological considerations on tocolytic and uterotonic therapy in obstetrics, Acta Anaesthesiologica Scandinavica, 53, 702-709, 2009	Narrative literature review
Vuilleumier, P. H., Surbek, D., Anesthesiologic management of major obstetrical hemorrhage, Trends in Anaesthesia and Critical Care, 5, 167-178, 2015	Narrative literature review
Weinberger, S. E., Weiss, S. T., Cohen, W. R., Weiss, J. W., Johnson, T. S., Pregnancy and the lung, American Review of Respiratory Disease, 121, 559-81, 1980	Narrative literature review
Winkler,M., Rath,W., Induction of labor, Contemporary Clinical Gynecology and Obstetrics, 1, 385-400, 2002	Narrative literature review
Wislicki, L., Systemic adverse reactions to prostaglandin F2 (PGF2 alpha, dinoprostone, prostin F2 alpha, prostalmon F), International Journal of Biological Research in Pregnancy, 3, 158-60, 1982	Narrative literature review
Zeteroglu,S., Sahin,G.H., Sahin,H.A., Induction of labor with misoprostol in pregnancies with advanced maternal age, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 129, 140-144, 2006	Population do not have asthma
Zurier, R. B., Prostaglandins. Their potential in clinical medicine, Postgraduate Medicine, 68, 70-81, 1980	Narrative literature review

Economic studies

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix E – Clinical evidence tables

Intrapartum care for women with asthma – analgesia

No clinical evidence was identified for this review and so there are no evidence tables.

Intrapartum care for women with asthma – prostaglandins

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Rooney Thompson, M., Towers, C. V., Howard, B. C., Hennessy, M. D., Wolfe, L., Heitzman, C., The use of prostaglandin E1 in peripartum patients with asthma, American Journal of Obstetrics & Gynecology, 212, 392.e1-3, 2015 **Ref Id** 420298 **Country/ies where the study was carried out** USA	**Sample size** N=2629 women were recorded n=234 peripartum women with asthma **Characteristics** All women received prostaglandin E1 from the pharmacy department at the University of Tennessee Medical Center, Knoxville. Peripartum women with asthma: n=104 had active asthma and were receiving daily medication n=130 had a medical history of asthma for which	**Interventions** PGE1 Indication for use for all women were • Cervical ripening/induction of labour: n=135 women • Uterine atony/postpartum haemorrhage: n=88 women • Cervical preparation prior to dilation and evacuation for intrauterine fetal demise or a fetus with lethal anomalies: n=25 women • 2 indications of cervical ripening/induction of labour as well as	**Details** Women were prospectively recorded. All medical records were retrospectively reviewed to identify peripartum women who had received PGE1 and had a diagnosis of asthma. The charts of all women were examined for any evidence of a respiratory complaint or asthma exacerbation following administration of the medication. Data on demographics and clinical characteristics were reported for all participants and disaggregated by women with active asthma and	**Results** Asthma exacerbation: 0 women (95% CI: 0-0.017) developed any clinical evidence of an asthma exacerbation. There were no reports of any deterioration in symptoms, and none of the patients required systemic corticosteroids or an increase in rescue bronchodilator use.	**Limitations** Limitations assessed using the Joanna Briggs Institute critical appraisal checklist for case series Clear inclusion criteria: Yes Condition measured in a standard, reliable way for all participants: Yes, asthma exacerbations were defined using definitions from The American Thoracic Society/European Respiratory Society official statement published in 2009. Clear definition of women with active asthma (receiving daily medication) and of women with a medical history of asthma (for which they

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type Retrospective case series **Aim of the study** To examine peripartum asthmatic women who received prostaglandin E1 and evaluate for any complications related to the drug use with a primary focus on asthma exacerbation **Study dates** Women who received PGE1 from January 2010 through December 2013 **Source of funding** Not reported	they used an inhaler on an as-needed basis Maternal age (mean): active asthma: 27.3 history of asthma: 26.2 White, n (%) active asthma: 90 (86.5%) history of asthma: 109 (84%) African American, n (%) active asthma: 11 (10.5%) history of asthma: 16 (12%) Hispanic and other, n (%) active asthma: 3 (3%) history of asthma: 5 (4%) BMI>30 kg/m^2, n (%) active asthma: 51 (49%) history of asthma: 72 (55%) BMI<30 kg/m^2, n (%) active asthma: 53 (51%) history of asthma: 58(45%) Cigarette smoker, n (%) active asthma: 44 (42%)	uterine/postpartum haemorrhage: n=14 women Indications for use for women with active asthma were • Cervical ripening/induction of labour: n= 63 women • Uterine atony/postpartum haemorrhage: n= 41 women • Cervical preparation prior to dilation and evacuation for intrauterine fetal demise or a fetus with lethal anomalies: n= 8 women Indication for use for women with a history of asthma were • Cervical ripening/induction of labour: n=72 women • Uterine atony/postpartum haemorrhage: n=47 women	those with a history of asthma. Data on indication for use, route of administration and dose of PGE1 were reported for all participants and disaggregated by women with active asthma and those with a history of asthma.		used an inhaler on an as-needed basis). Valid methods for identification of the condition in all participants: Yes, definitions as above. Consecutive inclusion of participants: Yes Complete inclusion of participants: Yes Clear reporting of the demographics of the participants: Yes (age, ethnicity, BMI, cigarette smoker, gravidity) Clear reporting of the clinical information of the participants: Yes (information on how many women had active asthma and how many had a history of asthma; information on how many women had a multiple gestation) Clear reporting of outcomes or follow-up results: Yes

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	history of asthma: 69 (53%) **Inclusion criteria** All women who were administered PGE1 in the study period from the University of Tennessee Medical Center were included. Women with a diagnosis of asthma were identified. **Exclusion criteria** Not reported	• Cervical preparation prior to dilation and evacuation for intrauterine fetal demise or a fetus with lethal anomalies: n=17 women Route of administration for all women • intravaginal: n=163 women • rectal: n=73 women • sublingual: n=49 women • PGE1 by 2 different routes, usually rectal and sublingual for treating uterine atony/postpartum haemorrhage: n=51 women Route of administration for women with active asthma were • intravaginal: n= 74 women • rectal: n= 33 women			Clear reporting of site demographic information: No, only name and location provided. Appropriate statistical analysis: Yes, only descriptive for the outcome of interest. Confidence interval for the percentage of events was provided. **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
		• sublingual: n= 28 women Route of administration for women with a history of asthma were • intravaginal: n= 89 women • rectal: n= 40 women • sublingual: n= 21 women Dose for all women • The total amount received by each person ranged from 25µg to 4200µg. • > 400µg of total dose: 98 women Dose for women with active asthma • > 400µg of total dose: n=46 women Dose for women with a history of asthma • > 400µg of total dose: n=52 women			

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Towers, C. V., Briggs, G. G., Rojas, J. A., The use of prostaglandin E2 in pregnant patients with asthma, American Journal of Obstetrics & Gynecology, 190, 1777-80; discussion 1780, 2004 **Ref Id** 441119 **Country/ies where the study was carried out** United States **Study type** Retrospective case series **Aim of the study** To examine pregnant patients with asthma who	**Sample size** N=189 women with a history of asthma or active asthma n=158 women with a history of asthma or active asthma were administered the PGE2 gel n=31 women received the 20mg vaginal suppositories **Characteristics** 27 women had active disease that required daily medications * 34 women with active disease who necessitated treatment only as needed with bronchodilators inhalers* 128 women with a history of asthma and no current therapy *	**Interventions** Intravaginal PGE2 PGE2 gel • Doses ranged from 1 to 4 (median: 2 doses) • Average exposure: 1.0 mg of PGE2) 20mg vaginal suppositories • Number of suppositories per person ranged from 1 to 11 (median:3) • Average exposure: 69mg (range 20-220mg))	**Details** The pharmacy department at Long Beach Memorial Women's Hospital prospectively recorded all pregnancies that were administered PGE2 gel or suppositories from January 1989 through December 2000. On a period basis throughout the duration of the study, every chart of PGE2 exposure was examined retrospectively for any history of asthma or active asthma. The charts of those women were then further analysed.	**Results** Clinical exacerbation in all women with history of asthma or active asthma: 0/189 (0%, 95% CI: 0 to 2%) Clinical exacerbation in women with active asthma: 0/61 (95% CI: 0-5.8%)	**Limitations** Limitations assessed using the Joanna Briggs Institute critical appraisal checklist for case series Clear inclusion criteria: Yes Condition measured in a standard, reliable way for all participants: Yes, asthma exacerbations were defined as any respiratory complaint that followed drug usage, the initiation of bronchodilator medications by women currently not in therapy, or an increase in asthma medication usage by women with active asthma. Clear distinctions were made between active asthma and history of asthma, and between women with active asthma receiving daily medications and women with active asthma that necessitated treatment only as needed.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
received prostaglandin E2. **Study dates** Women that received prostaglandin E2 from January 1989 through December 2000 **Source of funding** Not reported	In the PGE2 gel group (n=158) • 19 women had active disease that required daily medications • 29 women with active disease who necessitated treatment only as needed with bronchodilators inhalers • 110 women with a history of asthma and no current therapy In the 20mg vaginal suppositories group (n=31) • 8 women had active disease that required daily medications • 5 women with active disease who necessitated treatment only as needed with bronchodilators inhalers				Valid methods for identification of the condition in all participants: Yes, definitions as above. Consecutive inclusion of participants: Yes Complete inclusion of participants: Yes Clear reporting of the demographics of the participants: No, no details. Clear reporting of the clinical information of the participants: Yes, numbers of women with history of asthma, active asthma receiving daily medications and women with active asthma that necessitated treatment only as needed were provided. Clear reporting of outcomes or follow-up results: Yes Clear reporting of site demographic information: No,

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• 18 women with a history of asthma and no current therapy * Calculated by the NGA technical team **Inclusion criteria** All pregnancies that were administered PGE2 gel or suppositories from January 1989 through December 2000 Every chart of PGE2 exposure was examined retrospectively for any history of asthma or active asthma **Exclusion criteria** Not mentioned				only name and location provided. Appropriate statistical analysis: Yes, only descriptive for the outcome of interest. Confidence interval for the percentage of events was provided. **Other information**

CI: confidence interval; NGA: National Guideline Alliance; PGE: prostaglandin E

Appendix F – Forest plots

Intrapartum care for women with asthma – analgesia

No meta-analysis was undertaken for this review and so there are no forest plots.

Intrapartum care for women with asthma – prostaglandins

No meta-analysis was undertaken for this review and so there are no forest plots.

Appendix G – GRADE tables

Intrapartum care for women with asthma – analgesia

No clinical evidence was identified for this review and so there are no GRADE tables.

Intrapartum care for women with asthma – prostaglandins

Only case series were included in the review so there are no GRADE tables.

Appendix H – Economic evidence study selection

Intrapartum care for women with asthma – analgesia

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with asthma – prostaglandins

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix I – Economic evidence tables

Intrapartum care for women with asthma – analgesia

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with asthma – prostaglandins

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix J – Health economic evidence profiles

Intrapartum care for women with asthma – analgesia

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with asthma – prostaglandins

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix K – Health economic analysis

Intrapartum care for women with asthma – analgesia

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with asthma – prostaglandins

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix L – Research recommendations

Intrapartum care for women with asthma – analgesia

No research recommendations were made for this review question.

Intrapartum care for women with asthma – prostaglandins

No research recommendations were made for this review question.